UNIVERSITÀ DEGLI STUDI DI PAVIA

DOTTORATO IN SCIENZE CHIMICHE E FARMACEUTICHE E INNOVAZIONE INDUSTRIALE
(XXXVI Ciclo)

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Developing new green synthetic strategies employing arylazo sulfones and dyed-auxiliary groups using visible-light

Tesi di Dottorato di
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AA 2022/2023

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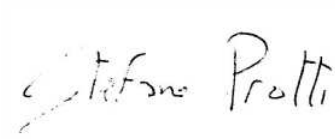


ACKNOWLEDGMENTS

In primis, ringrazio la mia famiglia che mi ha sempre sostenuto e appoggiato. “Non sei mai a casa”. Un grazie agli amici di sempre, che sono con me da quando ho iniziato questo percorso. Eddie, Corrado, Thomas, Fabio, Fefu, Chicco e Venom, grazie per esserci stati durante questi tre anni, ma anche da prima, quando ancora non avevo nemmeno la consapevolezza di cosa avrei fatto da “grande”. Ringrazio Jack, che ho avuto modo di conoscere meglio negli ultimi anni con cui ho già condiviso molto, tranne la scelta sugli anime da guardare, Black Clover fa schifo. Una menzione speciale va alle mie care amiche, Francesca detta Fatty, Bianca, Martina e Caterina detta Ranzy, siete difficili da sopportare quanto lo sono io dopo una giornata dura in laboratorio, ma grazie lo stesso, ci avete provato, tutto sommato siete ok.

Ringrazio anche tutti i miei compagni di laboratorio, avete allietato le pause pranzo sia con discorsi relativi alla chimica oppure con dibattiti di ben altro calibro e levatura. Citarvi tutti sarebbe impossibile, quindi un grazie a tutti i membri del PhotoGreen Lab che ho conosciuto durante questi tre anni. Onorevole menzione per i quattro gatti di genere maschile che mi hanno accompagnato e aiutato a sopportare la numerosa controparte femminile, in particolare Adrian, è stata dura, ma siamo sopravvissuti. Un particolare ringraziamento a Maurizio, Stefano e Davide che mi hanno insegnato tanto durante questi tre anni e mi hanno permesso di migliorare come chimico. Ringrazio anche il professor Merli per avermi permesso di svolgere molteplici analisi e aver assistito uno stolto organico nella via dell’analitica.

A special thank is dedicated to the lab mates and friends I was able to meet and know during my stay in France and thank to Luc and Geraldine, that helped me during that period. Concerning that period, I should particularly thank Camilla and Luca, I write that in English so it would be harder for her to understand it, time flew with you and was easier to cope with Ping Pong and company. I deeply thank all the collaborators that worked with me throughout the various projects, starting from Prof. Marco Bandini, Prof. Christoforos Kokotos and Prof. Xia Zhao.

Ai miei nonni

INTRODUCTION

1.1 DYEDAUXILIARY GROUPS AN EMERGING APPROACH FOR ORGANIC CHEMISTRY

The development of successful synthetic procedures able to satisfy simultaneously the needs for selectivity, efficiency, and sustainability has been considered for a longtime as *the holy grail* for every organic chemist. Photochemistry has always been considered one of the best choices to reach this goal, because the light is the only responsible for the substrate-activation. Moreover, light activates compounds generating highly reactive intermediates without the use of harsh conditions or aggressive reactants [1.1]. As a matter of fact, photons can be seen as the greenest reactant: it activates the substrate without leaving any traces at the end of the process [1.2]. Nevertheless, most organic compounds are colourless, thus imposing the need of expensive apparatus and dedicated equipment [1.3]. On the other hand, low energy-demanding visible-light sources (e.g., LEDs, compact fluorescent lamps) can be easily purchased and sunlight can be used as "infinitely available" light source [1.4]. Photochemists were attracted to find a possible way to design a chemical system able to absorb such low energy photons. Photocatalysis is a possible approach since it employs visible-light absorbing photocatalysts. These compounds absorb the radiation and, by interacting with colourless molecules, induce visible-light chemical transformations [1.5]. The ideal case, however, took place when visible photons are directly absorbed by one of the reactants present in the reaction media, inducing the photochemical event without the need for a photocatalyst. In nature many coloured compounds are present, but their direct photochemistry is not of practical and synthetical interest [1.6]. Some coloured classes of compounds have, however, an interesting photochemistry such as diarylazo compounds, which found application in supramolecular chemistry as photoswitches [1.7] and molecular machines, [1.8] or α-diketones [1.9]. Different approaches are however emerging to have/generate a visible-light absorbing species. One of the best-known routes is the formation of a coloured electron donor−acceptor (EDA) complex by mixing two (or more) colourless compounds. The irradiation of such complexes with visible-light results in valuable chemical transformations exploited in organic approaches [1.10]. A chromophore activation could be adopted as well [1.11]. This strategy involves the use of an additive (e.g., a Brønsted or a Lewis acid) to complex a colourless compound causing a bathochromic shift of the absorption spectrum to the visible region. A more intriguing situation is observed when the coloured compound can release photochemically reactive intermediates such as radicals, without the need for a photocatalyst. In the last few years, our research group developed the concept of *dyedauxiliary groups* (Figure 1.1) which are moieties able to impart both colour and photoreactivity

to an organic molecule they are tethered to [1.12]. The dyedauxiliary group should exhibit three different features:

(a) The incorporation of the dyedauxiliary group (DG, *path a*) through a functional group interconversion (FGI) in an organic compound bearing a strong R−Y bond should make the organic compound coloured, in other words, able to absorb visible-light.

(b) The so-formed R−DG bond should be photolabile to generate the reactive intermediate.

(c) The mechanism of the *dyedauxiliary* photoremoval should not depend on the nature of the group R to ensure a large versatility of this method.

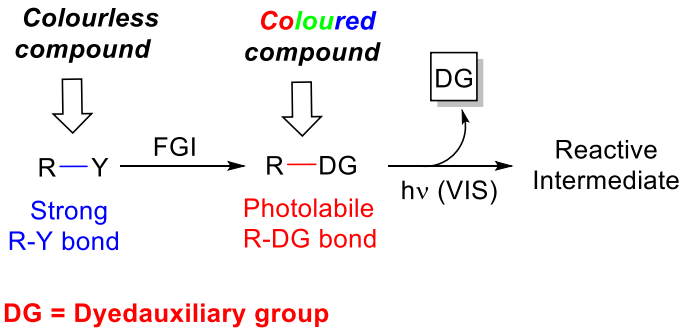
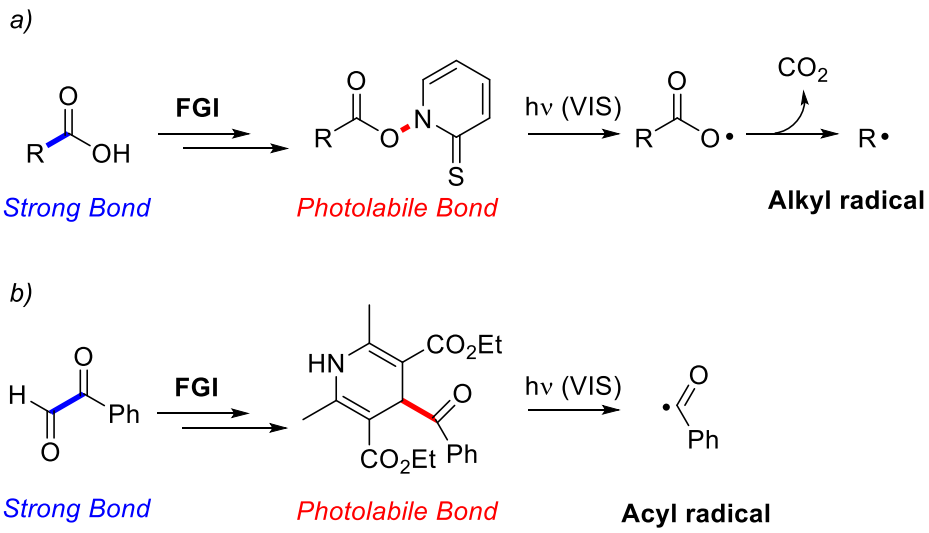


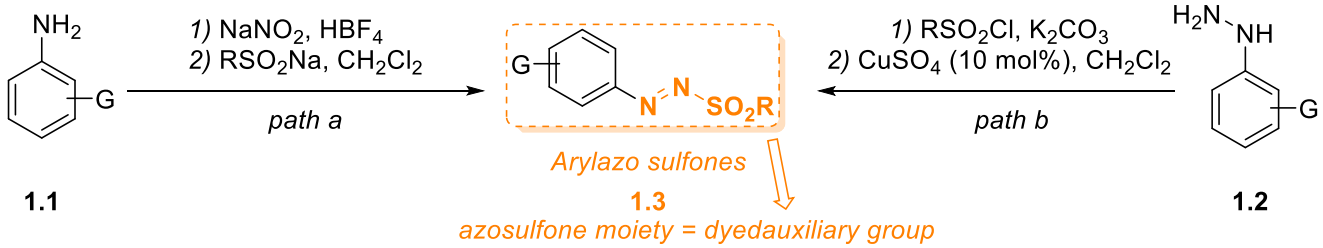
Figure 1.1 General approach of the *dyedauxiliary groups* strategy.

The use of *dyedauxiliary groups* is sparsely reported in literature and Barton esters (Scheme 1.1a) and acyl xanthates are prototypical examples of this type of approach. In the first case, the generation of a carbon-centred radical can be achieved by derivatizing a carboxylic acid. The incorporation of a thiohydroximate chromophore makes the molecules coloured. Irradiating the so-formed visible-light absorbing compound, the N−O homolysis is achieved, furnishing a carbonyloxy radical, which after carbon dioxide loss, generates a radical intermediate [1.13]. Meanwhile, acyl xanthates can be easily prepared using acid chloride and xanthate salt and exploited as a source of acyl or alkyl radical after visible-light exposure [1.14]. The generation of acyl radical can be likewise achieved by the conversion of a stable and colourless glyoxal hydrate into a coloured 4-benzoyl-1,4-dihydropyridine with a photolabile C−C bond prone to release an acyl radical after visible-light excitation (Scheme 1.1b) [1.15].



Scheme 1.1. Application of the *dyedauxiliary group* approach. a) Use of Barton esters to activate with visible-light colourless and stable carboxylic acids for the generation of alkyl radicals. b) functional group interconversion (FGI) of glyoxal hydrate to 4-benzoyl-1,4-dihydropyridine for the generation of acyl radicals.

One of the most recent developed *dyedauxiliary group* is the N_2SO_2R moiety present in (hetero)arylazo sulfones **1.3**. This class of molecules is shelf-stable, has a yellow to orange colour and can be easily synthesized from the corresponding diazonium salts **1.1** using the appropriate sulfinate salt, through a coupling reaction (Scheme 1.2, path a) [1.16]. Another approach is the oxidation of *N*-sulfonylaryl hydrazines, in turn generated from aryl hydrazine **1.2** (Scheme 1.2, path b) [1.17].



Scheme 1.2. Synthetic routes to arylazo sulfones **1.3** starting from anilines **1.1** (path a) or aryl hydrazine **1.2** (path b).

The investigation on these promising substrates showed that high temperatures [1.18] or the treatment with strong acids [1.19,1.20] and bases (e.g., CaO or pyridine) led to their decomposition with the release of aryl cations and aryl radicals. Nevertheless, the synthetic potential of arylazo sulfones under thermal conditions is scarcely studied: examples include the preparation of iodoarenes [1.21], their use

as electrophile in Grignard reagents [1.22], selenolates and tellurates anion [1.23] as well as dienophiles in [3+2] cycloadditions [1.24]. For what concerns their photochemistry, such substrates exhibit two absorption maxima, located in the UV (300−360 nm, ε=10000−20000 $M^{-1}cm^{-1}$) and in the visible region (400−450 nm, ε= 100−200 $M^{-1}cm^{-1}$, see the case of **1.3a** in Figure 1.2) assigned, respectively, to a ππ* and an nπ*transition [1.25].

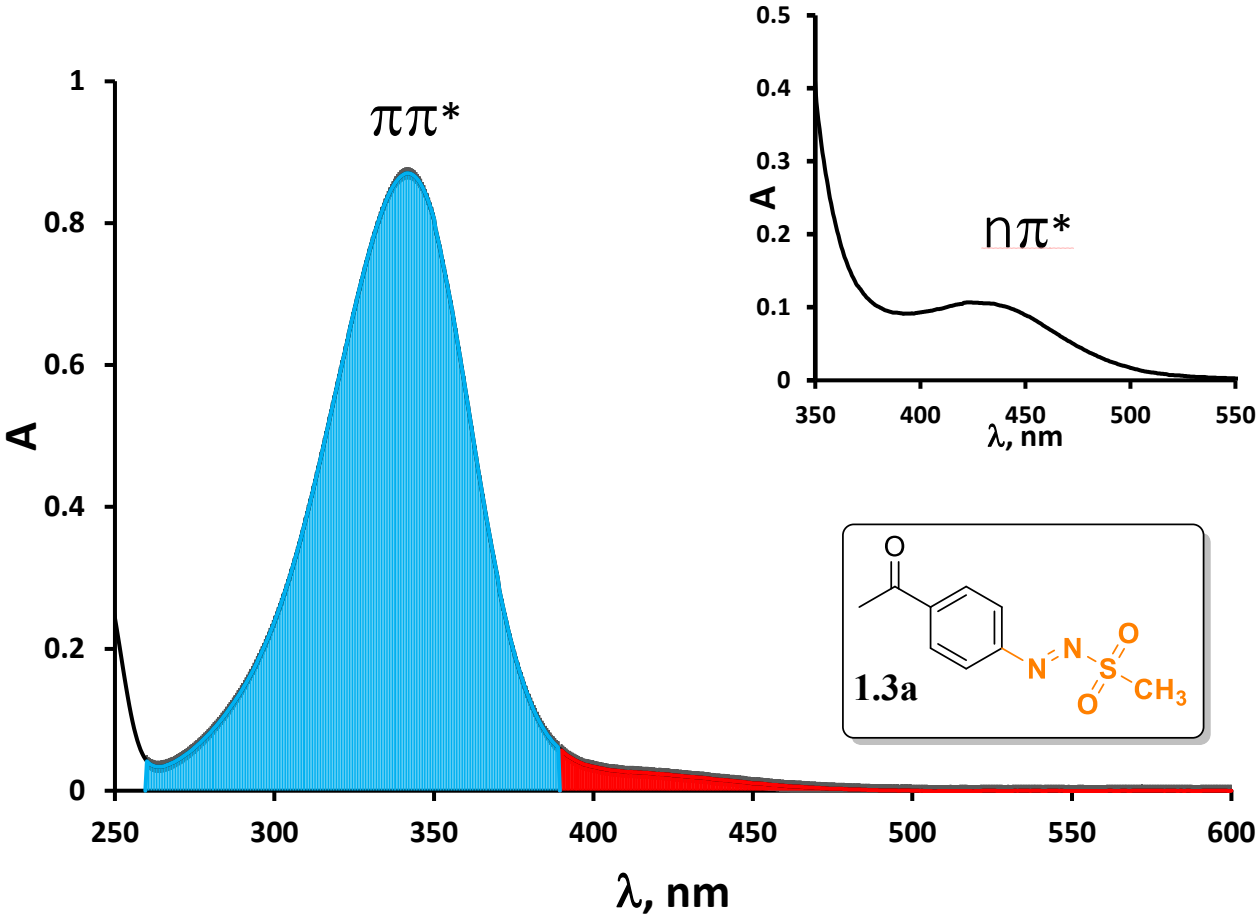
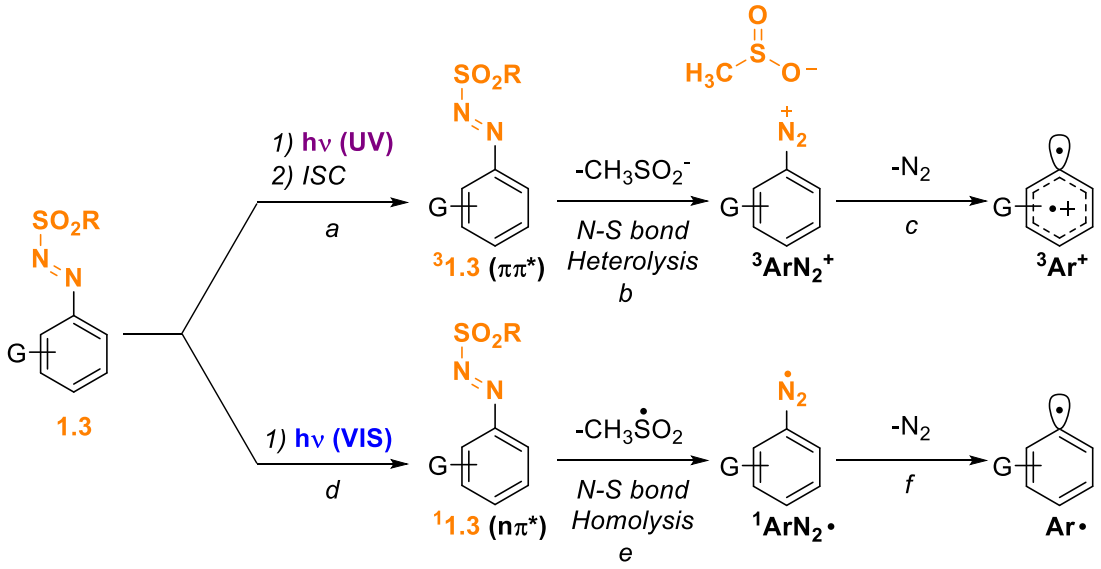


Figure 1.2. UV-visible absorption spectrum of a 5×10^{-5} M solution of **1.3a** in MeCN.

The photochemistry of these compounds was deeply investigated and reported by our research group, focusing on the different pathways that these substrates could undergo tuning the wavelength used for their excitation [1.25]. The photochemistry of arylazo sulfones is in fact dependent on the populated excited state [1.26]. For instance, upon UV irradiation, the generated ^{1}ππ* undergoes intersystem crossing (ISC) to the corresponding triplet excited state (^{3}ππ*, Scheme 3, path a) followed by heterolysis of the N−S bond yielding a diazonium salt with the same multiplicity ($^3ArN_2^+$, path b). Dediazoniation (path c) led to a triplet aryl cation ($^3Ar^+$) with methanesulfinate as counter anion. On the contrary, if the irradiation is carried out with visible-light, the populated excited state is the nπ* of **1.3** and the following photochemical step is the homolysis of the N−S bond, affording a diazenyl radical Ar−N_2• (path e), the final outcome of the irradiation is the formation of an aryl radical (Ar•)

and a methansulfonyl radical (CH_3SO_2•, path f). In the first investigations on these substrates, preliminary results showed that isomerization of the N=N bond from (*E*) to the less stable (*Z*) configuration plays a key role in the cleavage of the N–S bond [1.27].

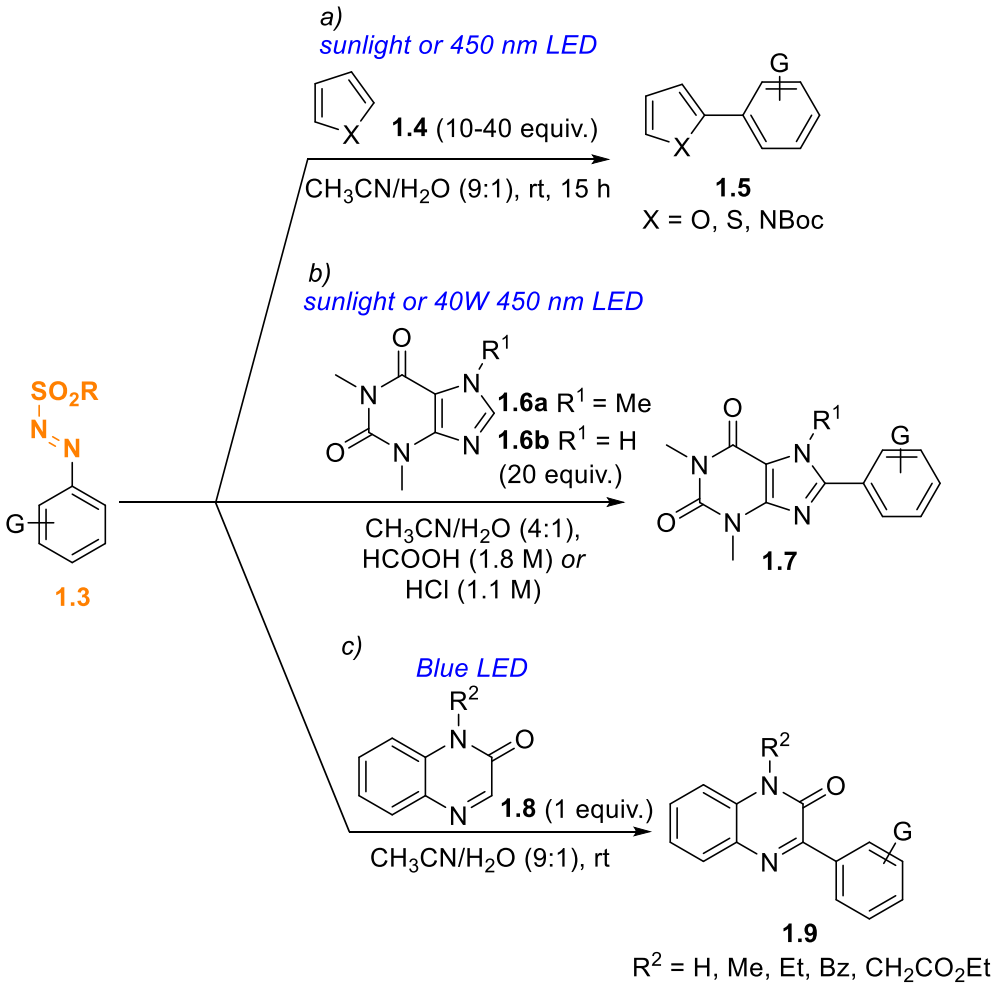


Scheme 1.3. Photochemical events occurring during the irradiation of arylazo sulfones with UV light (paths a-c) and visible light (paths d-f).

When the irradiation is carried out with a polychromatic light, namely sunlight, the aryl cation and the aryl radical are both formed. The application in synthesis of the visible-light generating radicals or cations from arylazo sulfones was recently investigated from different research groups, including ours as detailed below. The synthetical applications of arylazo sulfones can be broad, and, as stated before, it was previously reported in 1972 by Minato *et al.* [1.20] that these promising compounds could be exploited for fruitful chemical transformations.

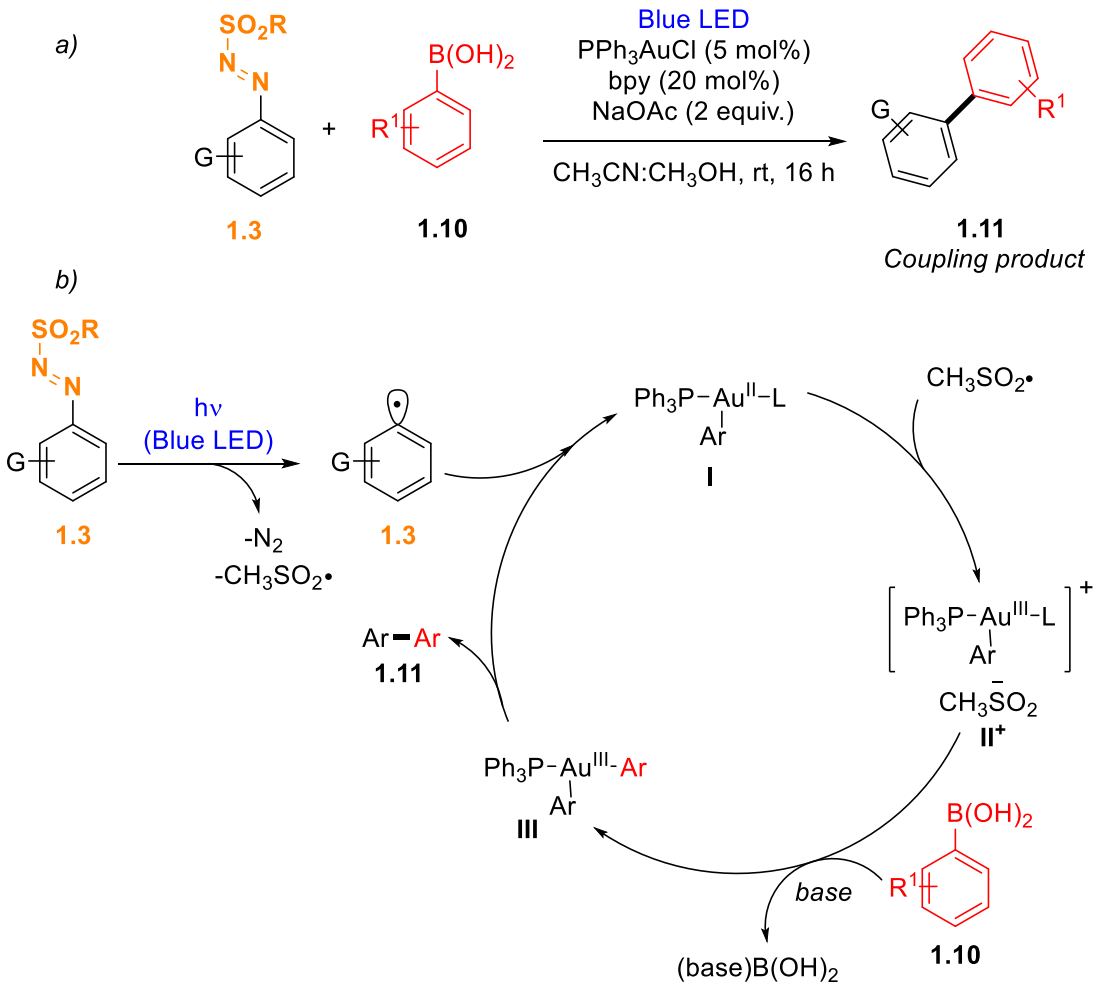
1.2 CARBON-CARBON BOND FORMATION

In 2016, our research group proposed the use of arylazo sulfones for the visible or sunlight-driven synthesis of new Ar–Ar bonds with different heteroaromatics **1.4** without the need for any (photo)catalyst (Scheme 1.4, a) [1.25]. Another C–H arylation process was adopted for the functionalization of caffeine **1.6a** and theophylline **1.6b** by using [1.28] a sunflow [1.29] apparatus (solar microcapillary reactor) able to decrease drastically the irradiation time when used. The reaction was however successfully by employing a blue KESSIL lamp (450 nm) as the light source (Scheme 1.4, b). The arylation of **1.8** was successfully performed as well yielding 3-arylquinoxalin-2(1H)-ones **1.9** (scheme 1.4, c) [1.30]. Interestingly, the latter class of compounds has a structure present in several enzyme inhibitors or anticancer drugs [1.31].



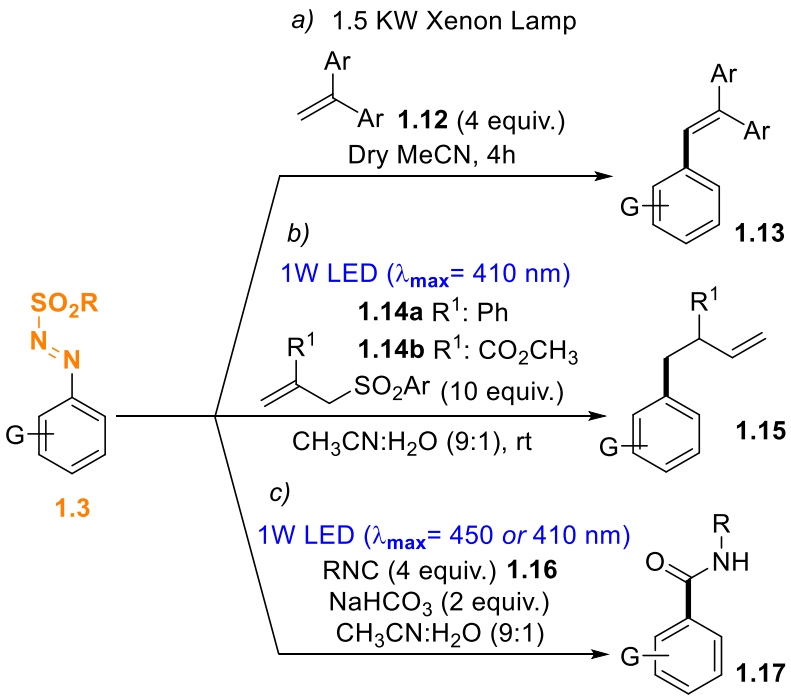
Scheme 1.4. Arylazo sulfones employed for the visible-light driven formation of new Ar−Ar bonds.

In recent literature, the use of metal catalysts to interact with carbon-centered radical grew and gained more attentions. Following this trend, our group focused on the use of a gold catalyst to achieve a Suzuki-type coupling of arylazo sulfones with arylboronic acids **1.10** (Scheme 1.5). The mechanism is promoted by the homolysis of the N−S bond in **1.3** by means of visible-light irradiation; after loss of nitrogen, the so-generated aryl radical Ar• undergoes an oxidative addition with the metal centre. The gold catalyst Au(I), now is oxidized to Au(II), which was further oxidized by the methanesulfonyl radical (CH_3SO_2•) to the Au(III) adduct **II**$^+$**.** The nucleophilic substitution at the Au(III) centre by the aryl boronic acid **1.10**, and the subsequent reductive elimination, furnished the coupling product **1.11** with the concomitant restoring of the catalyst [1.32].



Scheme 1.5. Visible-light driven Suzuki-like type coupling of arylazo sulfones with arylboronic acids.

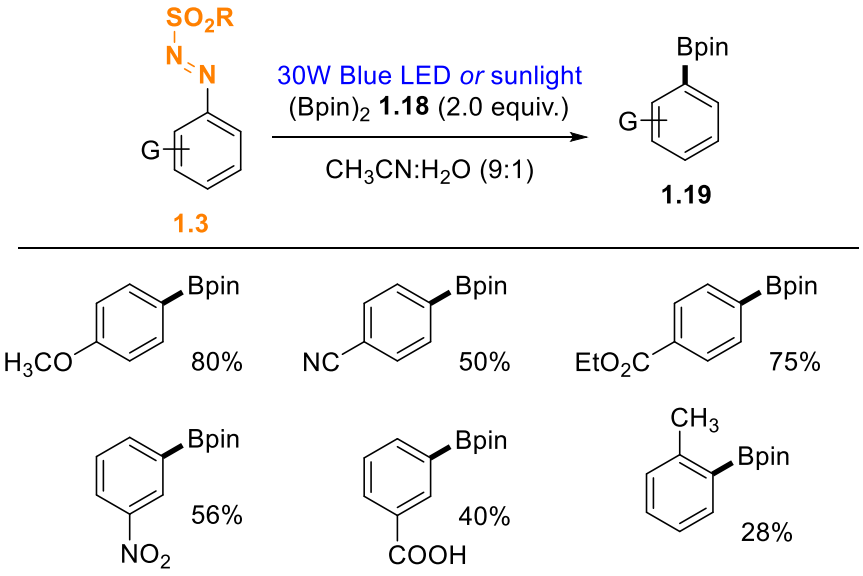
An alternative approach to forge an Ar–C(sp^2) is through the arylation of alkenes to have access to substituted triaryl-ethylenes **1.13** (Scheme 1.6, a) [1.33]. The synthesis of these compounds can be achieved with a 1500 W Xenon lamp able to simulate the solar emission spectrum. Notably, both intermediates generated from arylazo sulfones were involved in this reaction due to the lamp employed. It is noteworthy that the pathways arising from both intermediates (aryl radical and aryl cation) converged to the same targeted products. Moreover, the functionalization of arenes with an allylic group has suffered always of the use of harsh conditions or contamination of the final product by heavy metals [1.34]. A greener and milder approach was easily achieved using arylazo sulfones as starting materials with different 2-phenylallylsulfonylaryls **1.14a** and 2-((arylsulfonyl)methyl) acrylates **1.14b** (Scheme 1.6, b) [1.35]. A visible-light-driven, metal-free synthetic way to aromatic amides **1.17** was achieved via radical arylation of isonitriles **1.16** using arylazo sulfones as suitable precursors of aryl radicals in aqueous acetonitrile (Scheme 1.6, c) [1.36].



Scheme 1.6. Arylazo sulfones used for the synthesis of triarylethylenes (a) for the allylation of arenes (b) and for the formation of aryl amides starting from isonitriles (c).

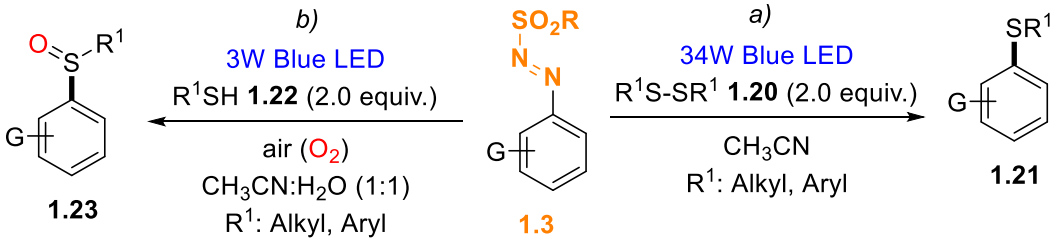
1.3 CARBON-HETEROATOM BOND FORMATION

Arylazo sulfones have not been applied only for the visible-light induced construction of new carbon-carbon bond but also for building new Aryl−X bonds. As an example, aryl boronic acids and aryl boronates, compounds widespread used for the Suzuki-Miyaura cross-coupling reaction, can be synthesized employing different type of photochemical protocols [1.37,1.38] with the need for photosensitizers and/or additives. In 2018, Fang *et al.* optimized a photocatalyst- additive-free visible-light induced borylation of arylazo sulfones **1.3** furnishing aryl boronates **1.19** starting with diboron reagent **1.18** as the borylating agent (Scheme 1.7) [1.39]. An analogous formation of Ar−B bonds was later reported, having recourse to cyclic diboranes [1.40].



Scheme 1.7. Selected examples of visible-light induced synthesis of aryl boronates starting from arylazo sulfones and diboron reagent as boron source.

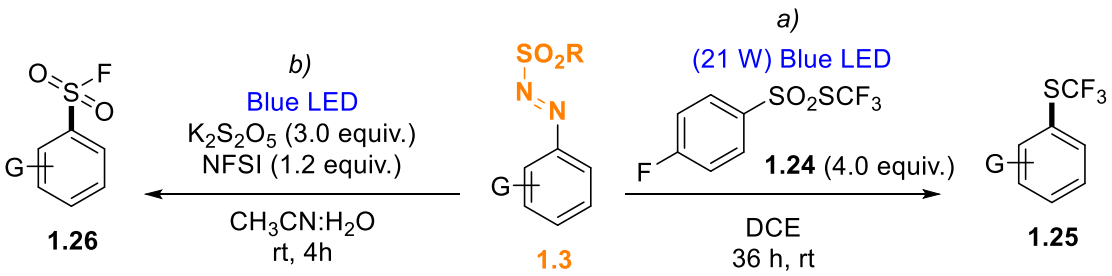
Another Ar–X bond that can be forged is the Ar–S bond. Different approaches have been outlined: the synthesis of aryl sulfides **1.21** starting from dialkyl and diaryl disulfides **1.20** (Scheme 1.8, a) was optimized and investigated by our research group in 2019 [1.40]. Meanwhile, in the same year, the formation of unsymmetrical differently functionalized aryl sulfoxides **1.23** was described by Wei *et al.* starting from commercially available thiols **1.22** and arylazo sulfones, carrying out the irradiation in an air saturated solution (Scheme 1.8, b) [1.41].



Scheme 1.8. Formation of a new Ar–S bond employing visible-light as radiation source and arylazo sulfones as starting materials. a) photochemical synthesis of aryl sulfides from disulfides. b) photochemical synthesis of aryl sulfoxide from thiols.

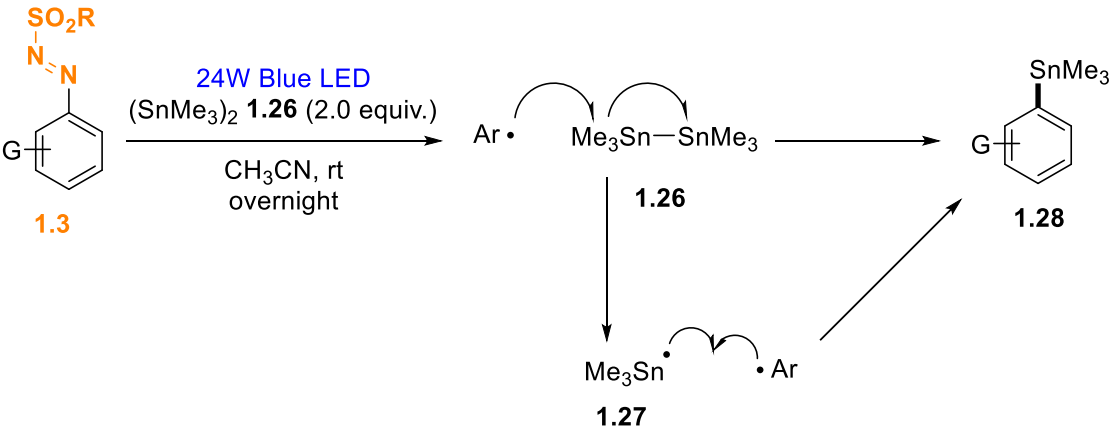
Notably, more recent examples have been provided on the formation of Ar–S bonds employing these *dyedauxiliary groups* bearing compounds: in 2021 our research group proposed an efficient method for the trifluoromethylthiolation of arenes using *S*-trifluoromethyl arylsulfonothioates **1.24** as easy-to-handle trifluoromethylthiolating agents (Scheme 1.9, a). The targeted products **1.25** were obtained

with good to quantitative yields in a metal- (photo)catalyst- and additive-free approach [1.42]. In the same year Bui *et al.* described the synthesis of sulfonyl fluorides **1.26** in modest to good yield by using $K_2S_2O_5$ and *N*-fluorobenzenesulfonimide (NFSI) as sulfonyl source and fluorinating agent, respectively (Scheme 1.9, b) [1.43].



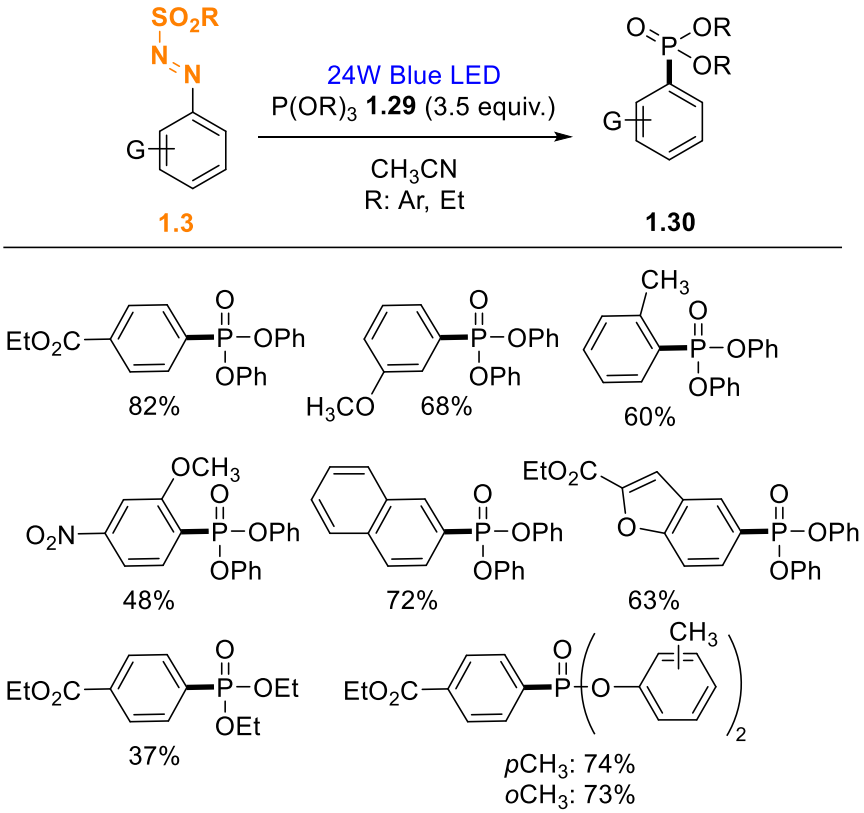
Scheme 1.9. Formation of a new Ar−S bond employing visible-light as radiation source and arylazo sulfones as starting materials. a) Photochemical synthesis of trifluoromethylthiolated arenes. b) Photochemical synthesis of sulfonyl fluorides.

Moreover, the formation of C−Sn bond (especially in the case of aryl stannanes) is particularly useful in organic synthesis [1.44]. The formation of (hetero)aryl stannanes **1.28** was achieved by our group under both photocatalyst- and metal-free conditions, in 2019 (Scheme 1.10) [1.45]. This protocol features high efficiency and extremely wide substrate scope, and the stannylation could be easily scaled to gram-scale amounts. The mechanism is presented in Scheme 1.10. The irradiation of arylazo sulfones **1.3** generates the aryl radical which is trapped by $(Me_3Sn)_2$ **1.26** to yield the final product and Me_3Sn• **1.27.** The recombination of **1.27** and the aryl radical obtained by the direct irradiation of arylazo sulfones was proposed as an alternative route to **1.28**.



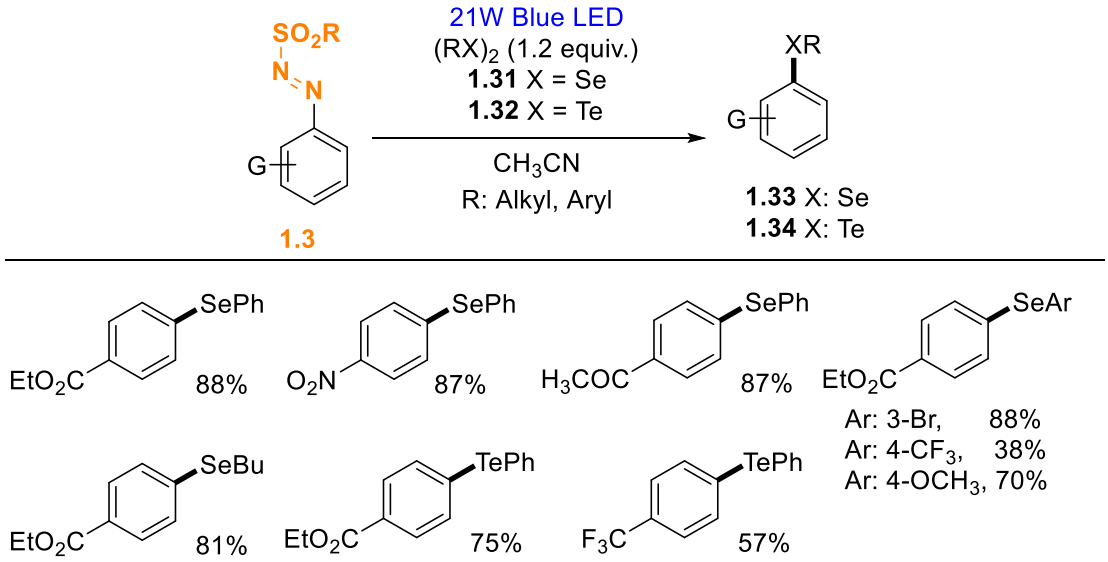
Scheme 1.10. Photochemical synthesis of aryl stannanes starting from arylazo sulfones.

Arylazo sulfones have been adopted even for the construction of C−P bonds by employing triaryl (or trialkyl) phosphites **1.29** as the phosphorus source [1.46]. The reaction gives functionalized(hetero)aryl phosphonates **1.30** in moderate to good yields (Scheme 1.11) and exhibits a wide substrates scope, especially for the excellent compatibility to electron-rich arenes and(hetero)aromatics.



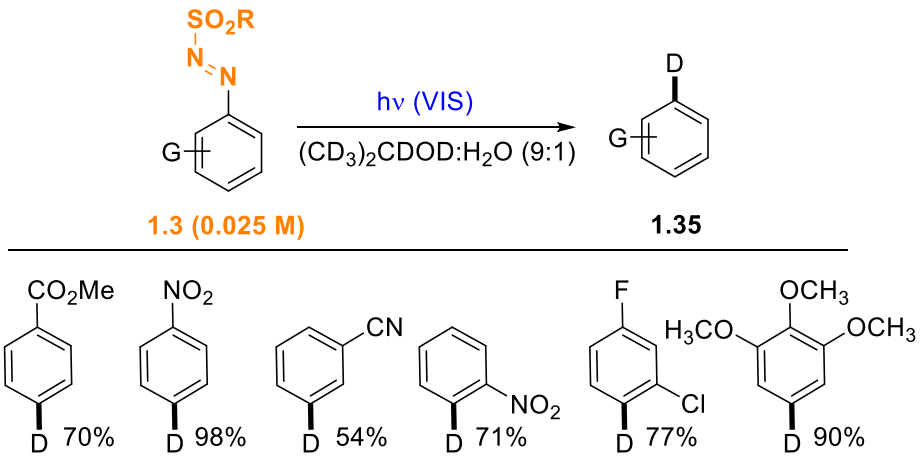
Scheme 1.11. Photochemical reaction of arylazo sulfones with triaryl (or trialkyl) phosphites.

The formation of Ar−chalcogen bond (beside sulfur) was achieved by our research group in 2020. The visible light activation of arylazo sulfones led to the formation of new Ar−Se and Ar−Te bond in a mild and metal-free way [1.47]. Aryl selenides **1.33** and aryl tellurides **1.34** were synthesised using aryl and alkyl diselenides **1.31** and ditellurides **1.32**. The lack of a photocatalyst and additives did not affect the versatility of this approach that offers more than fifty examples of compounds purified and isolated (Scheme 1.12).



Scheme 1.12. Photochemical synthesis of new Ar−chalcogen bonds employing arylazo sulfones and ditellurides and diselenides as chalcogen sources.

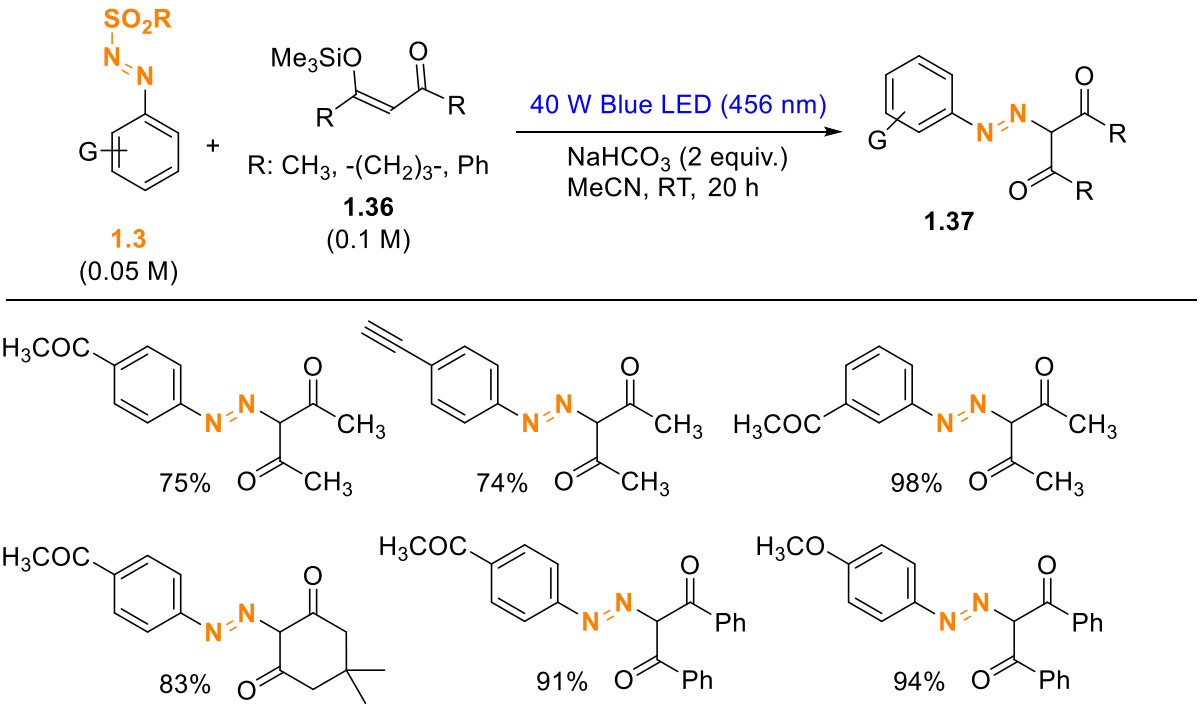
Deuterated compounds find application in the field of mass and NMR spectroscopy, and methods for the construction of aryl−D bonds were variously developed in the past decade, some of them exploiting photoredox catalysis [1.48]. Several deuterated compounds **1.35** were obtained by using arylazo sulfones through a catalyst-free visible-light-driven deutero deamination in the presence of either aqueous isopropanol-d_8 or tetrahydrofuran-d_8 as deuterium sources. Notably, the presence of a significant amount of water did not appreciably affect the deuteration yield (Scheme 1.13) [1.49].



Scheme 1.13. Aryl deuterium bond formation via arylazo sulfones.

1.4 ARYLAZO SULFONES AS HETEROATOM-CENTRED RADICAL SOURCES

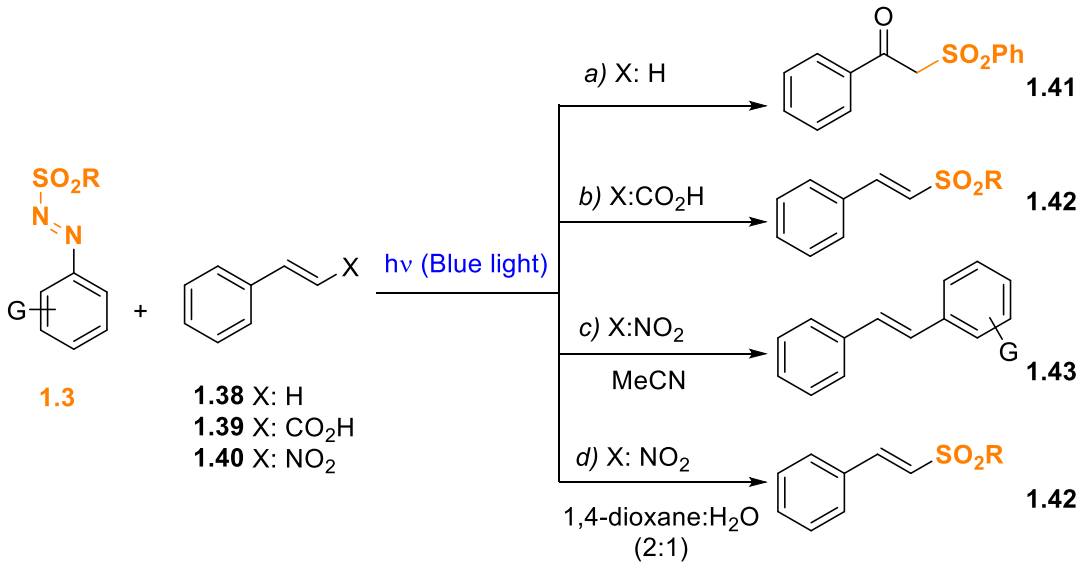
Visible light photolysis of arylazo sulfones leads to the formation of different radical intermediates. As highlighted in Scheme 1.3, the first photochemical event is the homolytic cleavage of the N−S bond furnishing an aryl diazenyl radical and a methanesulfonyl radical [1.25,1.26]. The latter species were employed in different chemical transformations, incorporating inside the final product part of the *dyedauxiliary group*. For instance, in 2020, our research group performed the aryldiazenylation of differently substituted enol silyl ethers **1.36**, giving access to a class of compound with biological activities and useful for the synthesis of *N*-containing heterocycles [1.50]. The process is straightforward and proceeds with the direct irradiation of the arylazo sulfones in the presence of a base. The loss of the methanesulfonyl radical followed by the trapping of the so-generated aryldiazenyl radical afforded compounds **1.37** in good to excellent yields (Scheme 1.14).



Scheme 1.14. Selected examples of visible-light-induced photoaddition of aryldiazenyl radicals on enol silyl ethers to form 3-aryldiazenyl-1,3-diketones.

Apart the use of diazenyl or the aryl radicals, also the photogenerated methanesulfonyl radical was employed in chemical transformations. As a matter of fact, in 2019, Wei and co-workers reported the visible-light induced sulfonylation of styrenes **1.38** with arylazo sulfones **1.3** at room temperature in an oxygenated media, to reach a series of β-oxo sulfones **1.41** [1.51]. The same group, later, proposed an analogous approach employing alkynes to obtain the same class of compounds **1.41** (Scheme 1.15,

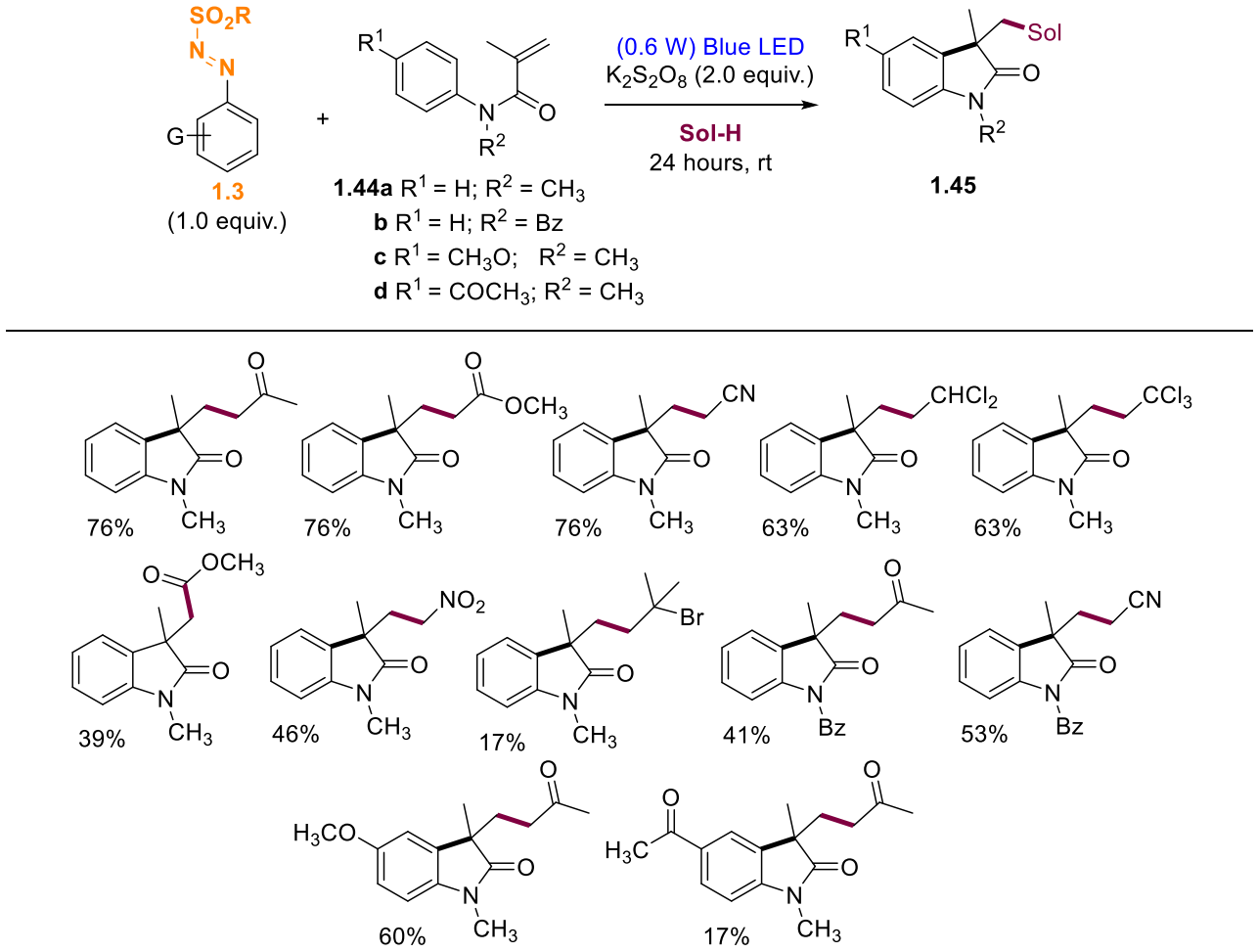
path a) [1.52]. In 2020, Yadav studied the irradiation of arylazo sulfones with cinnamic acid **1.39**. The proposed protocol afforded (*E*)-vinyl sulfones **1.42** via sulfonylation/decarboxylation (Scheme 1.15, path b) [1.53]. Finally, when arylazo sulfones are photolyzed, β-nitrostyrenes **1.40** undergo a solvent selective arylation or sulfonylation. The arylation is performed in acetonitrile and afforded stylbenes **1.43** in good to moderate yields (Scheme 1.15, c), on the other hand, the sulfonyl radical reacts with the nitroalkene forming (*E*)-vinylsufones **1.42** in a dioxane water mixture (Scheme 1.15, d) [1.54]. Both processes proceed with the loss of the nitro group after the first radical attack on the β position of β-nitrostyrenes, that could be tuned just by the solvent choice.



Scheme 1.15. Visible-light induced sulfonylation of different substrates employing arylazo sulfones. a) formation of β-oxo sulfones using styrenes. b) synthesis of (*E*)-vinyl sulfones starting from cinnamic acids via sulfonylation/decarboxylation. c) Solvent directed synthesis of stylbenes using β-nitrostyrenes. d) Solvent mediated synthesis of (*E*)-vinyl sulfones employing β-nitrostyrenes.

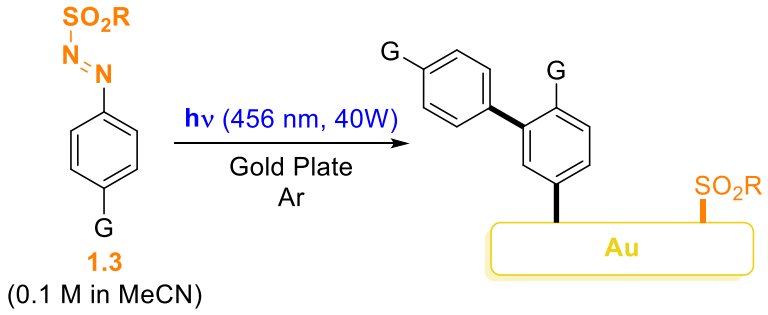
1.5 MISCELLANEOUS.

Arylazo sulfones have not been only used to promote chemical transformation in which the final products incorporate part of the photoactive molecule. For instance, in a recent methodology proposed by our research group, in 2022, arylazo sulfones have been used to promote hydrogen atom transfer (HAT) with solvents, generating a carbon-centred radical employed for the construction of new C−C bonds [1.55]. The mechanism involves a hydrogen atom abstraction from the solvents by the aryl radical formed by irradiation of arylazo sulfones. The new carbon centered radical than promotes the solventylation of differently substituted acrylamides **1.44a-d** to afford variously functionalized indolin-2-ones **1.45** (Scheme 1.16). The feasibility of this process is extended to different solvents and acrylamides or enol silyl ethers by adopting a simple set-up and benign conditions.



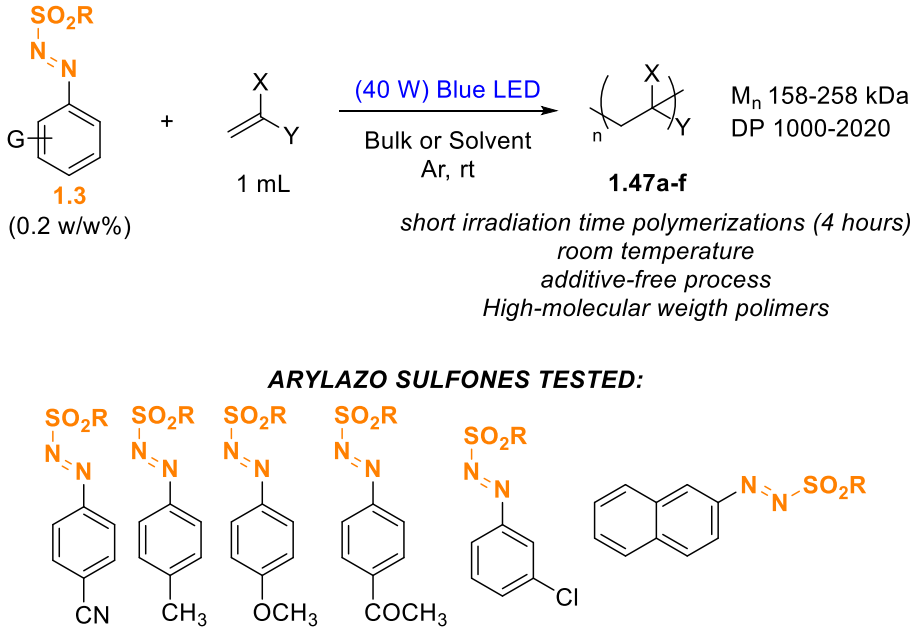
Scheme 1.16. Visible-light induced solventylation of differently substitued acrylamides.

Arylazo sulfones have been employed in the field of surface modifications. The possibility of grafting gold surfaces and carbon surfaces was achieved by means of visible-light irradiation of these compounds [1.56,1.57]. The simultaneous photografting of both differently substituted aryl and methanesulfonyl groups on a gold surface was achieved via the N−S photoinduced cleavage of arylazo sulfones and trapping of the generated aryl/methanesulfonyl radical pair (Scheme 1.17).



Scheme 1.17. Simultaneous double photografting of gold surfaces using arylazo sulfones as precursors and visible light as initiator.

The developed approach simply involves visible light as the only promoting agent and avoids the use of electro grafting or photoredox-catalyzed processes commonly employed for the surface functionalization via onium salts [1.57]. In addition, the use of arylazo sulfones as thermal [1.58, 1.59] and (rarely) photochemical [1.60] initiators in the polymerization of methacrylate esters has been sparsely reported. Given the lack of photoinitiated polymerization processes our research group focused their attention on the activation of electron-poor olefins to achieve a free-radical process employing arylazo sulfones as radical initiators and light as the only source of activation (Scheme 1.18). This approach proceeds smoothly at room temperature in bulk or in the presence of a cosolvent furnishing high molecular weight polymers in excellent yields starting from different monomers **1.46a-f** as building blocks for the polymeric structures **1.47a-f** [1.61].



Scheme 1.18. Visible-light induced polymerization of different monomers employing arylazo sulfones as initiators in bulk or in solvent with short irradiation times.

Another field in which arylazo sulfones may find application is the biological one, where they proved to be toxic toward cells. In vitro experiments were carried out investigating the effect of visible light, UV light in comparison with dark conditions. The results showed that the interactions between plasmids and the *dyedauxiliary group* bearing molecules led to the cleavage of the DNA both in dark and when exposed to light depending on their structure. The study was carried out with different non-cancer cell lines (pBluescript SK II and Highly malignant melanoma cell lines have been used for cell culture experiments) and arylazo sulfones were found to be equally toxic in both conditions analyzed (dark, light). In order to perform a control experiment with non-cancer cells, two different cell-lines were used; HFL1, a fibroblast cell line that was isolated from the lung of a white, normal

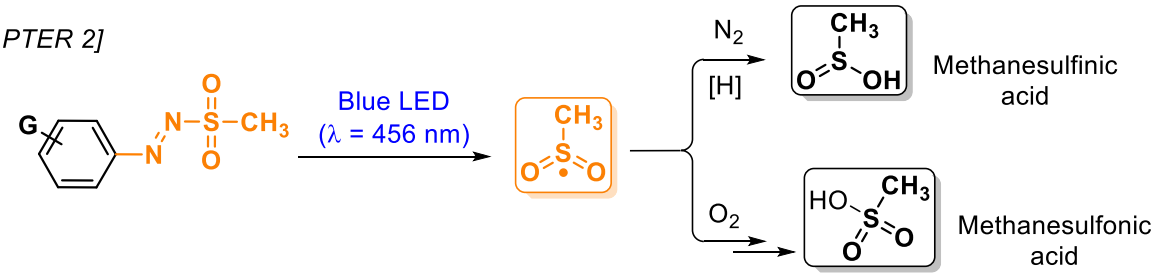
embryo, and HaCaT cell lines, human immortalized keratinocytes. The temporal and spatial control of light, therefore, might provide a chance for these novel scaffolds to be useful for the development of phototoxic pharmaceuticals, especially for azosulfones having naphthyl groups [1.62].

1.6 AIM OF THE THESIS.

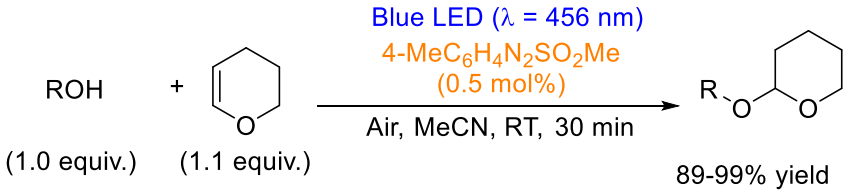
Given the great potentiality of the compounds bearing a *dyedauxiliary group*, during my PhD thesis I focus my attention on different possible applications in synthesis (see Scheme 1.19). As a first aim, we investigated the potentiality of arylazo sulfones as nonionic photoacid generators PAGs (see Chapter 2) [1.63] trying to develop a new class and new applications for such useful compounds to catalyze chemical transformations by using the acid released after their irradiation. The first reaction was the protection of alcohols as acetals catalyzed by small quantities of arylazo sulfones and triggered by visible light (see Chapter 3) [1.63]. Another application fulfilled was the conversion of the carbonyl groups present in substituted aldehydes and ketones into 1,3-dioxolanes or, in selected cases, into *N*-methyl 1,3-oxazolidines. These transformations were feasible thanks to the use of arylazo sulfones in a catalytic amount as PAGs and visible light (see Chapter 4) [1.64]. Finally, photoacid generators were used to form bis-indoyl methanes starting from aldehydes and indoles, in a simple and straightforward methodology which employed arylazo sulfones as the acidic source and again visible light (see Chapter 5) [1.65]. The second part of my thesis was focused on the study and development of new classes of *dyedauxiliary group* bearing molecules. The synthesis of new molecules such as arylazo arylsulfones, arylazo carboxylates, acylazo carboxylates and arylazo phosphine oxide are reported, together with the photophysical and photochemical investigations of the above-mentioned compounds (see Chapter 6). The last part of my PhD thesis deals with new applications of arylazo sulfones in green and smooth photochemical reactions. The synthesis of a plethora of α-aryl ketones from enol silyl ethers and arylazo sulfones and the preparation of α-aryldiazo esters (starting from silyl ketals) is presented (see Chapter 7) [1.66]. Many examples on the double functionalization of styrenes was successfully obtained furnishing α-sulfonyl hydrazones in a straightforward and undocumented fashion along with a detailed mechanistic investigation are described in Chapter 8. Moreover, the photochemistry of arylazo sulfones merged with a Gold(I) catalyst yielded several (hetero)biaryls (see Chapter 9) [1.67] in a simple methodology. To conclude, the large scope synthesis of aryl thiocyanates was achieved and the mechanism of the process was investigated in detail to highlight the first photoredox process in which arylazo sulfones are involved (see Chapter 10) [1.68].

The contents of these chapters are sketched in Scheme 1.19.

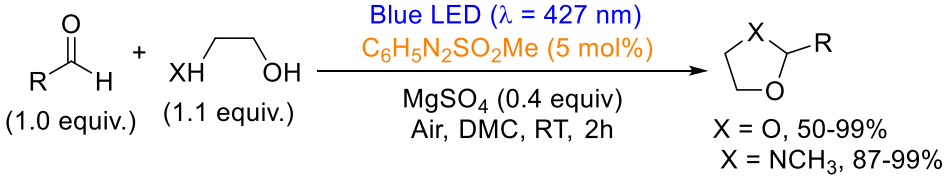
[CHAPTER 2]



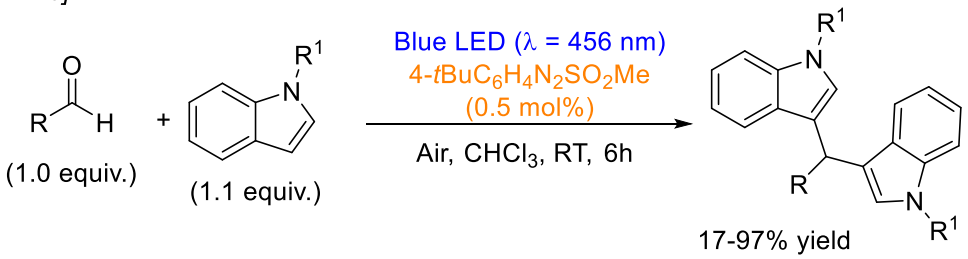
[CHAPTER 3]



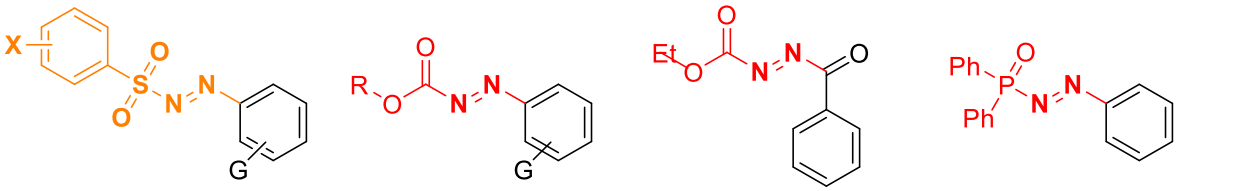
[CHAPTER 4]



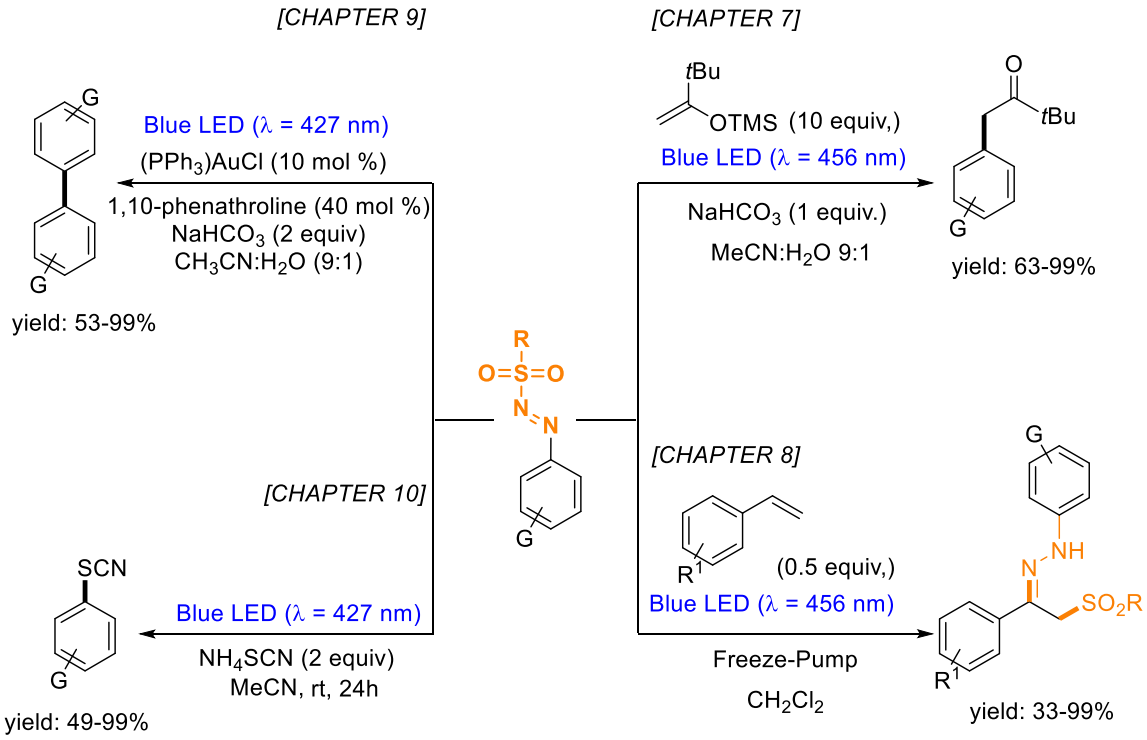
[CHAPTER 5]



[CHAPTER 6]



Arylazo arylsulfonates | Arylazo carboxylates | Acylazo carboxylates | Arylazo phospine oxide



Scheme 1.19 Topics studied and investigated in this PhD thesis.

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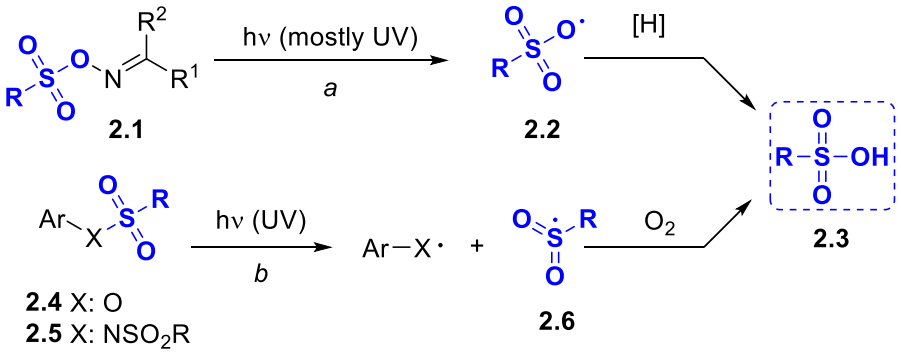
CHAPTER 2.

ARYLAZO SULFONES AS PHOTOACID GENERATORS (PAGs).

2.1 INTRODUCTION.

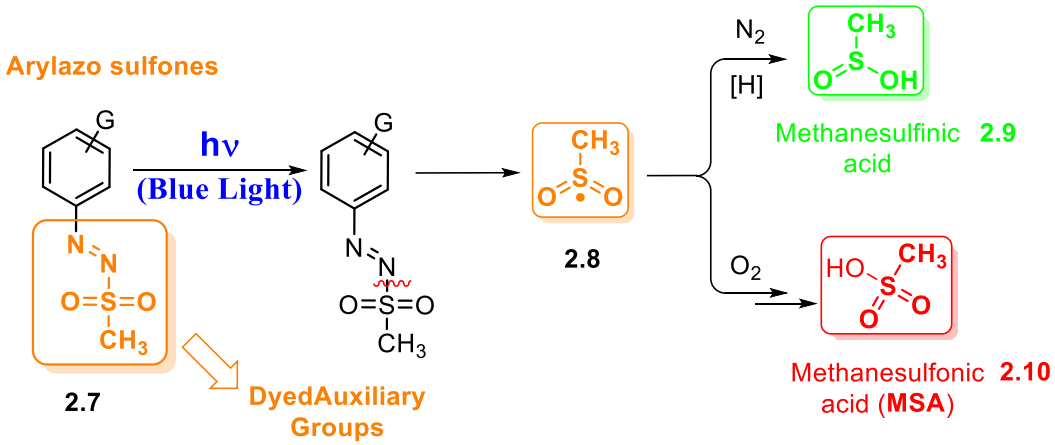
Photoacid generators, also known as PAG, are compounds able to release an acid upon irradiation. The use of this class of molecules found application in lithography and printing processes and is well-established, however, new applications (including cationic polymerizations, construction of microfluidic systems, photocurable coatings, and 3D printing) emerged in the last three decades, making the design of new class of PAGs a hot topic [2.1]. PAGs may be divided into two classes: ionic and nonionic. The former ones are salts bearing an onium cation: aryl diazonium [2.2], diaryl halonium [2.3-2.7], triaryl sulfonium [2.7-2.10] and triaryl phosphonium [2.11-2.13] generally having a halide complex anion (BF_4^-, SbF_6^-, AsF_6^-, PF_6^-, or RSO_3^-). The ionic PAG exhibit an excellent thermal stability but a limited solubility in common organic matrixes and a narrow wavelength of absorption [2.1g]. On the other hand, nonionic PAG have found several applications mainly as polymer initiators due to their good solubility in a wide range of organic solvents and polymer matrixes. Among the different nonionic PAGs tested [2.14, 2.15] compounds containing a sulfonyl moiety are appealing since they released a strong sulfonic **2.3** acid mostly via generation of the sulfonyloxy radical **2.2** (Scheme 2.1 path a) that in turn abstracts a hydrogen atom from the medium. A typical case is the photolysis of imino-sulfonate derivatives **2.1**[2.16, 2.17] that have been employed for the cationic ring-opening polymerization of ε-caprolactone [2.19]. An alternative approach involves the release of a sulfonyl radical (**2.6**) in the presence of oxygen.



Scheme 2.1. Different approach in the photorelease of sulfonic acid starting from different photoacid generators: a) from the photolysis of imino-sulfonates b) from the photolysis of *N*-arylsulfonamides.

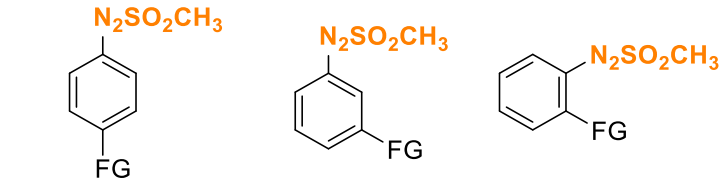
Various compounds have been successfully investigated as "caged sulfonyl radicals" [2.18] including benzylic sulfonyl compounds [2.19], aryl sulfonates (**2.4**, X = O, Scheme 2.1 path b) [2.20], and even *N*-

arylsulfonimides (**2.5**, X = NSO_2R) which were able to generate up to 2 equiv of acid per equivalent of PAG [2.21]. Most of the PAGs releasing the sulfonic acid, however, are active only in the UV region. Nevertheless, there is an interest in the development of visible-light PAGs for applications in 3D printing systems, photocurable adhesives, and incorporation in photoresists sensitive to 436 nm light (the so-called g-line [2.22]). Visible-absorbing sulfonium salts [2.23] BODIPY [2.24] and especially photochromic-based derivatives [2.25] have been devised accordingly. As part of our ongoing interest in the applications of colored dyedauxiliary-group-bearing molecules, we focused on arylazo sulfones as visible-light-active PAGs. The irradiation of arylazo sulfones **2.7** leads to the homolytic cleavage of the N−S bond forming an aryldiazenyl radical [50] and a methansulfonyl radical **2.8**. The latter species can generate sulfinic acid (**2.9**) in deoxygenated conditions (Scheme 2.2) by hydrogen abstraction or methanesulfonic acid (**2.10**) in an oxygen-saturated solution [2.20,2.21].



Scheme 2.2. Photochemical tunable generation of weak or strong acid depending on the condition in which the irradiation is carried out starting from arylazo sulfones and visible light.

Furthermore, arylazo sulfones exhibited a satisfactory thermal stability (some derivatives decompose over 145 °C) and an excellent solubility in a wide range of organic media. In view of these premises, we focused on a set of shelf-stable, easy to synthesize arylazo sulfones having a substituent in the para (**2.7a−g**), meta (**2.7h−i**), or ortho (**2.7j−k**) position (Figure 2.1).



2.7a, FG = $COCH_3$
2.7b, FG = Br
2.7c, FG = CN
2.7d, FG = Cl
2.7e, FG = CH_3
2.7f, FG = OCH_3
2.7g, FG = NO_2

2.7h, FG = $COCH_3$
2.7i, FG = CN

2.7j, FG = CN
2.7k, FG = OCH_3

Figure 2.1. Arylazo sulfones tested in this work

2.2 RESULTS AND DISCUSSION.

Arylazo sulfones **2.7a-k** were easily prepared from the corresponding anilines. The UV-visible spectra of **2.7a-k** showed an intense absorption band in the UV region (λ_{max} = 280-315 nm) and a further band in the visible-light region (λ_{max} = 412-437 nm) except for **2.7g** and **2.7k** which had a maximum centred at 395 nm (Table 2.1).

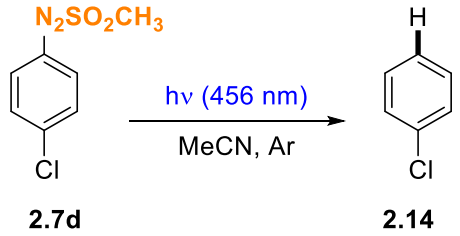
Table 2.1. Molar extinction coefficient and λ_{max} of arylazo sulfones **2.7a-k**.[a]

Arylazo sulfones	**λ_{max}** (nm), **ε** (mol L^{-1} cm^{-1})
2.7a	294, (15921) 432, (181)
2.7b	309, (16355) 425, (210)
2.7c	288, (19568) 435, (155)
2.7d	305, (14003) 424, (167)
2.7e	310, (15264) 420, (215)
2.7f	342, (17405) 425, (230)
2.7g	287, (15360) 395, (3206)
2.7h	289, (12413) 425, (157)
2.7i	289, (12680) 427, (140)
2.7j	290, (13492) 436, (123)
2.7k	294, (9238) 395, (3205)

[a] Conditions: A 10^{-4} M solution of **2.7a-k** was used to evaluate the maximum of absorption in the UV region whereas a 5×10^{-4} M solution of **2.7a-k** was used to evaluate the maximum of absorption in the visible region.

Preliminary irradiation experiments (λ = 456 nm) were carried out on a 2.5×10^{-2} M solution of compound **2.7d** in argon purged acetonitrile. The reaction has been monitored evaluating both the consumption of **2.7d** and the amounts of photoproduct(s) obtained after irradiation (Table 2.2). A total consumption of the arylazo sulfone occurred after 3 h irradiation being chlorobenzene **2.14** the only photoproduct detected.

Table 2.2. Irradiation of **2.7d** in argon purged acetonitrile at 456 nm.[a]



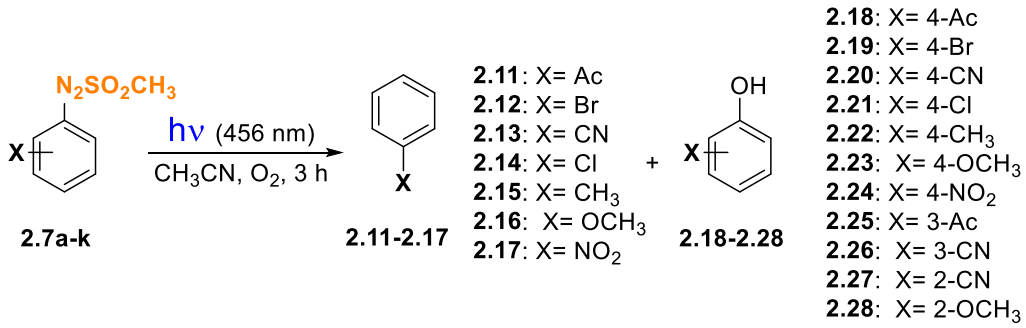
2.7d **2.14**

Time (min)	**2.7d**, consumption %[b]	**2.14**, Yield %[c]
10	5	4
30	19	13
60	45	30
80	52	35
120	76	49
180	100	63

[a] Conditions: an argon purged solution of **2.7d** (2.5×10^{-2} M) was irradiated with a 40 W Kessil Lamp with emission centred at 456 nm. [b] The consumption of the reagent was monitored through HPLC analysis. [c] Yield of **2.14** was determined through GC-FID analysis.

We then determined the disappearance quantum yields (Φ_{-1}) of **2.7a-k** upon irradiation in oxygen purged solutions along with the yields of photoproducts obtained and the amount (and the nature) of the acid release (Table 2.3). The Φ_{-1} values were quite low not exceeding 0.05 being the *p*-methyl (**2.7e**) and *p*-nitro (**2.7g**) derivatives the most photoreactive ones. Two main products were formed in the reaction viz. the dediazosulfonylated derivatives **2.11-2.17** and phenols **2.18-2.28** [2.26] the latter mainly formed with sulfones bearing electron-withdrawing groups (Table 1). The trapping of aryl radicals by molecular oxygen and the subsequent generation of phenol has been widely reported in the literature [2.26]. The low yields of compounds **2.22-2.23** and **2.27-2.28** may be due to the low stability of such compounds under the tested conditions that allow for a further oxidation to the corresponding quinones (vide infra).

Table 2.3. Photoreactivity of arylazo sulfones (**2.7a-k**) irradiated in oxygen purged solutions [a,b]



Azosulfone	Φ_{-1} [b,c]	**2.11-2.17** (%)[d]	**2.18-2.28** (%)[d]	H^+ [e] (% yield)	$MeSO_3H$ [f] (% yield)
2.7a	0.01	(**2.11**): 0	(**2.18**): 52	81	44
2.7b	0.02	(**2.12**): 5	(**2.19**): 25	74	59
2.7c	0.01	(**2.13**): 5	(**2.20**): 70	94	41
2.7d	0.02	(**2.14**): 10	(**2.21**): 71	98	95
2.7e	0.05	(**2.15**): 6	(**2.22**): 0	86	78
2.7f	0.02	(**2.16**): 20	(**2.23**): 0	78	61
2.7g	0.05	(**2.17**): 15	(**2.24**): 69	82	75
2.7h	0.02	(**2.11**): 0	(**2.25**): 71	70	58
2.7i	0.02	(**2.13**): 9	(**2.26**): 64	59	45
2.7j	0.02	(**2.13**): 14	(**2.27**): 2	86	73
2.7k	0.02	(**2.16**): 4	(**2.28**): 8	87	87

[a] Conditions: an oxygen purged acetonitrile solution of **2.7a-k** (2.5×10^{-2} M) was irradiated with a 40 W Kessil Lamp with emission centred at 456 nm for 3 h until the total consumption of the substrate. [b] The consumption of **2.7a-k** was determined through HPLC analysis. [c] Disappearance quantum yields (Φ_{-1}) were measured on a Argon-purged 10^{-2} M acetonitrile solution of the chosen arylazo sulfone (λ= 456 nm, 1×40 W Kessil lamp). [d] Yield of products were determined through GC analysis. [e] Determined by potentiometric titration with a solution of NaOH 0.1 M. [f] Determined through IC.

The acidity of the irradiated solutions was evaluated by means of potentiometric titrations with NaOH 0.1 M solution, by diluting the sample with 50 mL of deionized water (see Figures 2.2-2.12). Moreover, titration of phenols **2.18** and **2.19** was performed (Figure 2.13). The results of the present experiments exclude the contribution of phenols to the total acidity released by the irradiated arylazo sulfones.

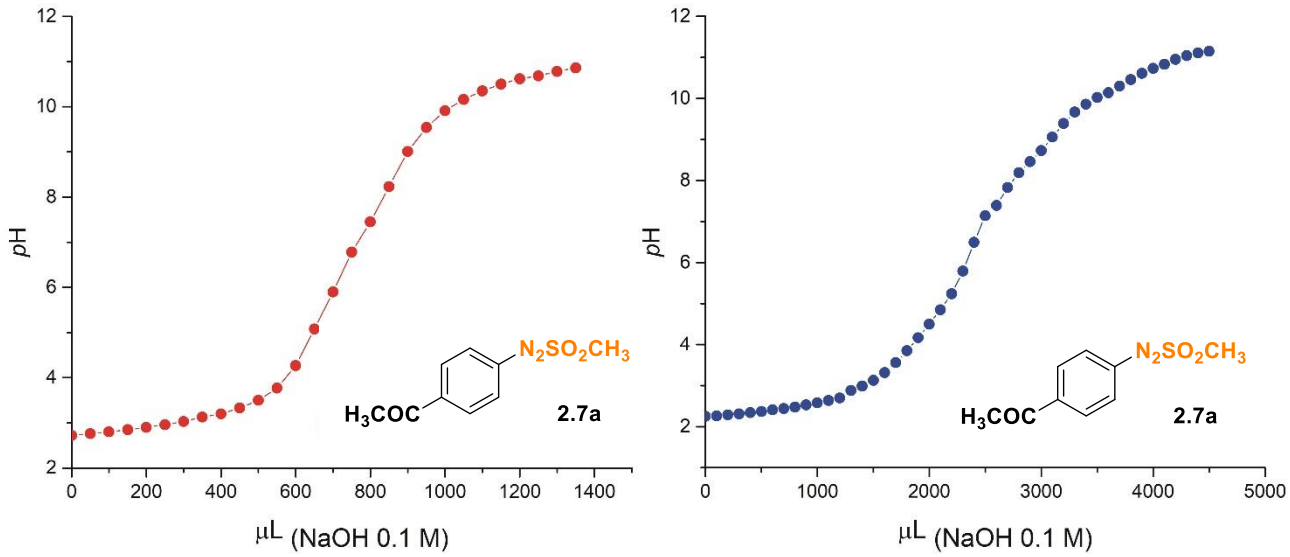


Figure 2.2. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7a** irradiated in MeCN for 3 h. (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

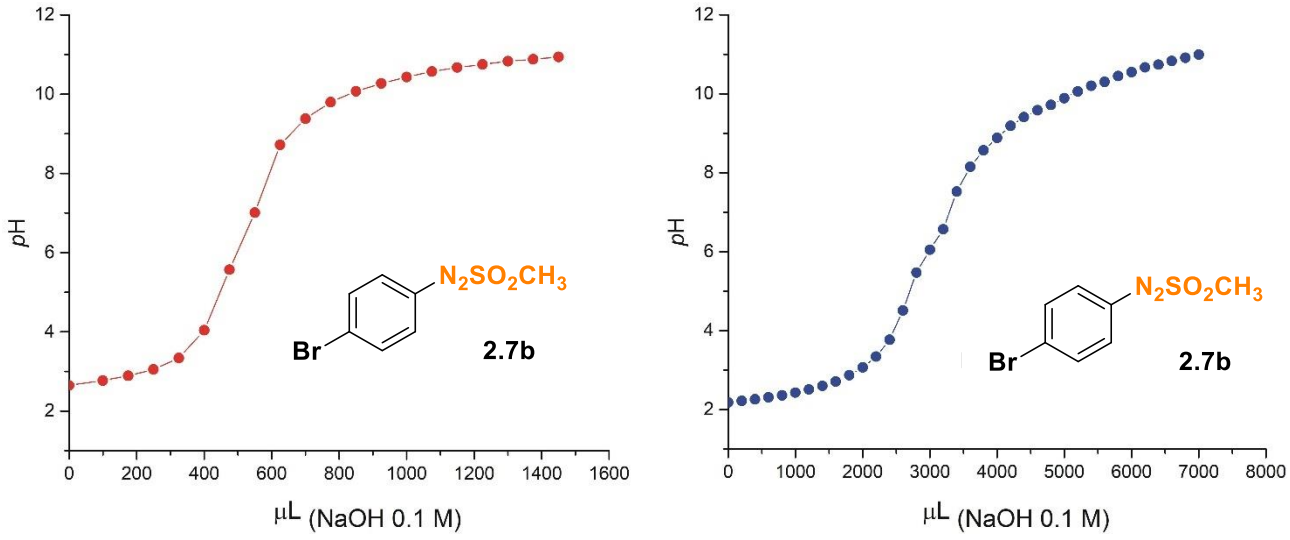


Figure 2.3. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7b** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

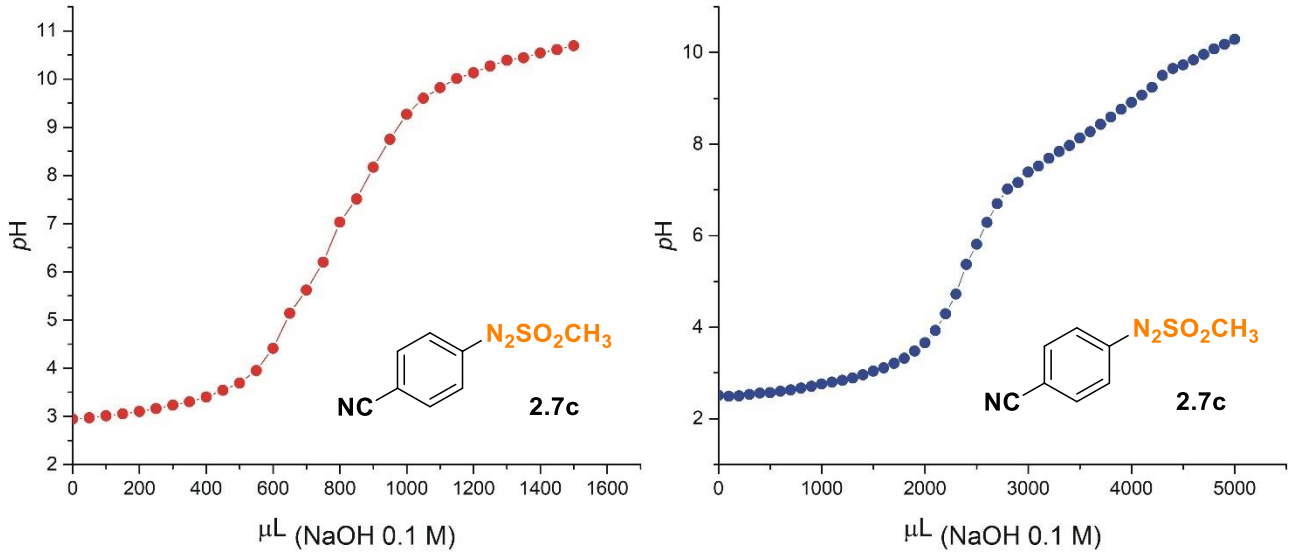


Figure 2.4. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7c** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

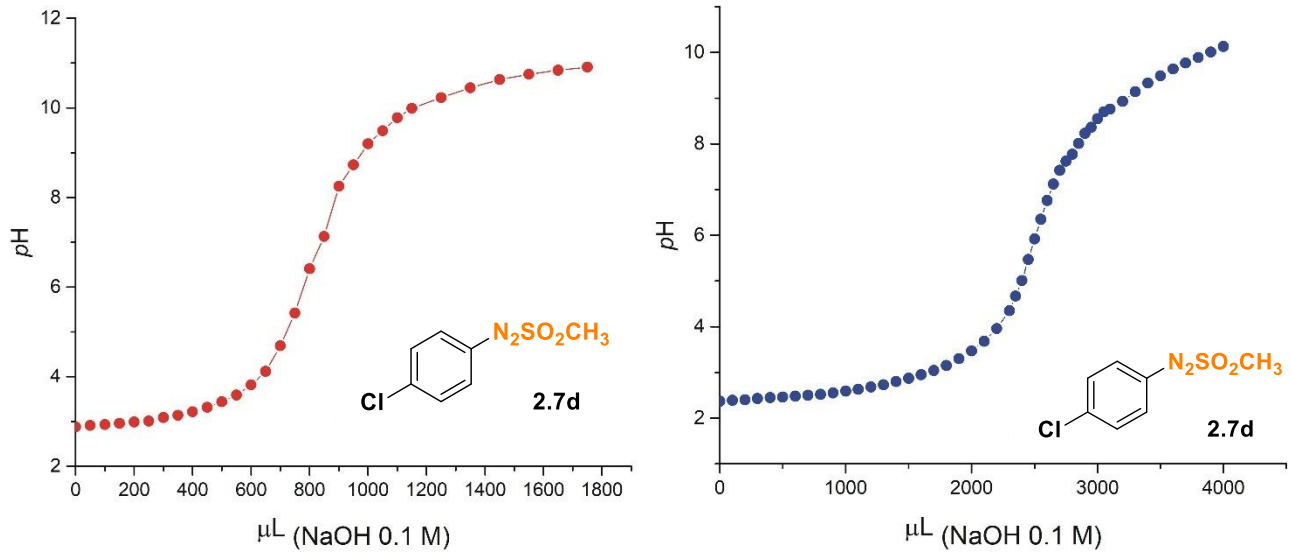


Figure 2.5. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7d** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

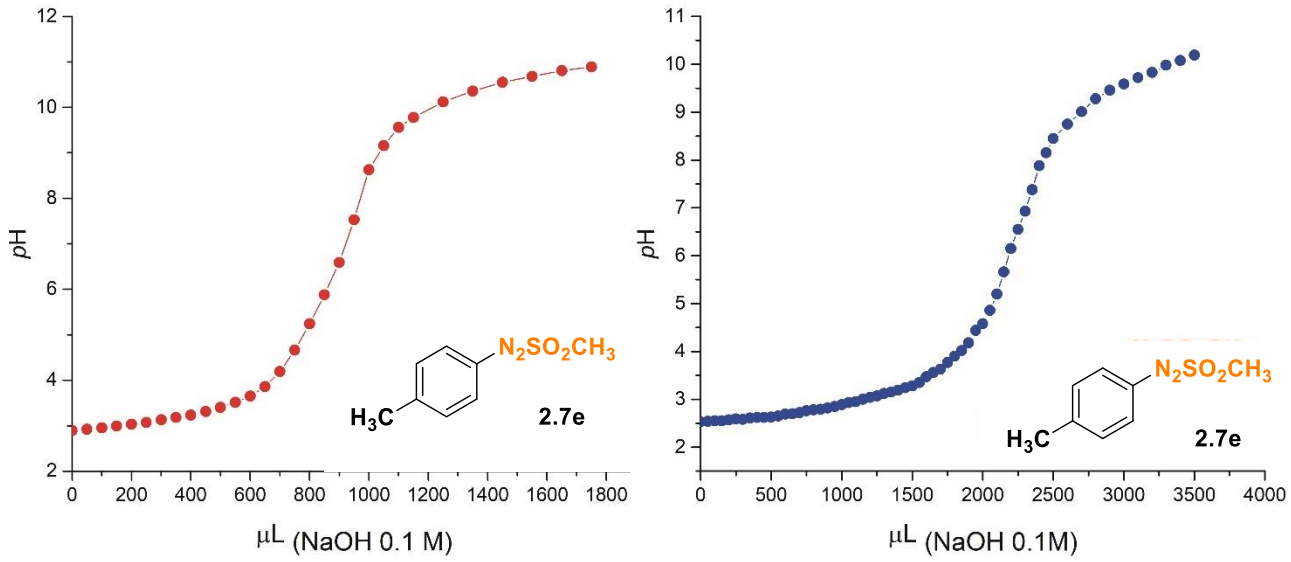


Figure 2.6. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7e** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

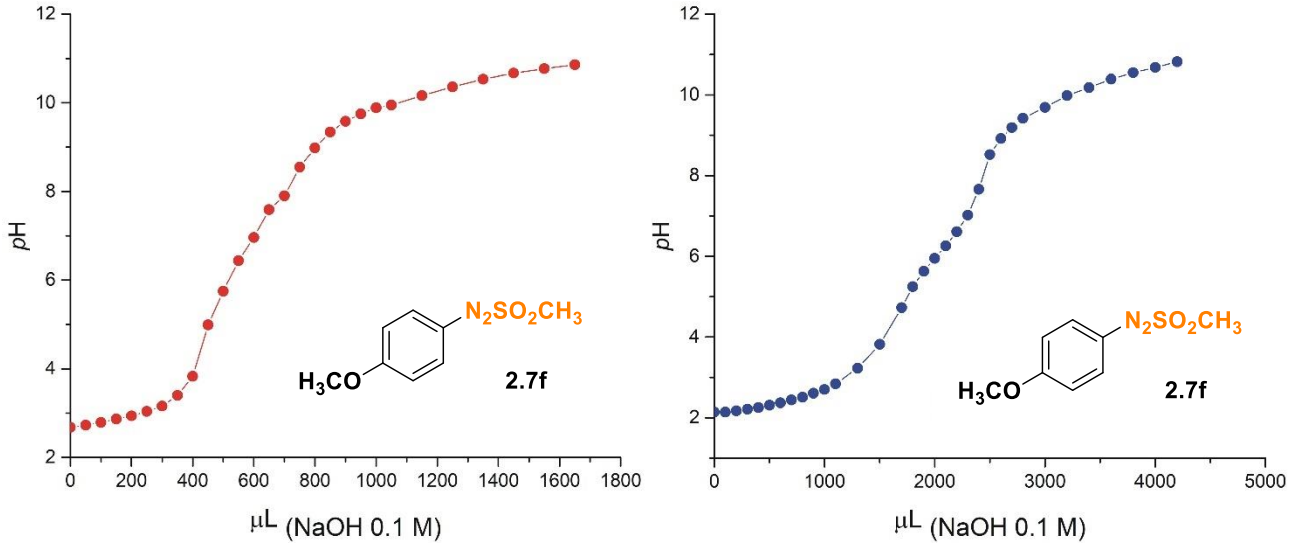


Figure 2.7. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7f** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

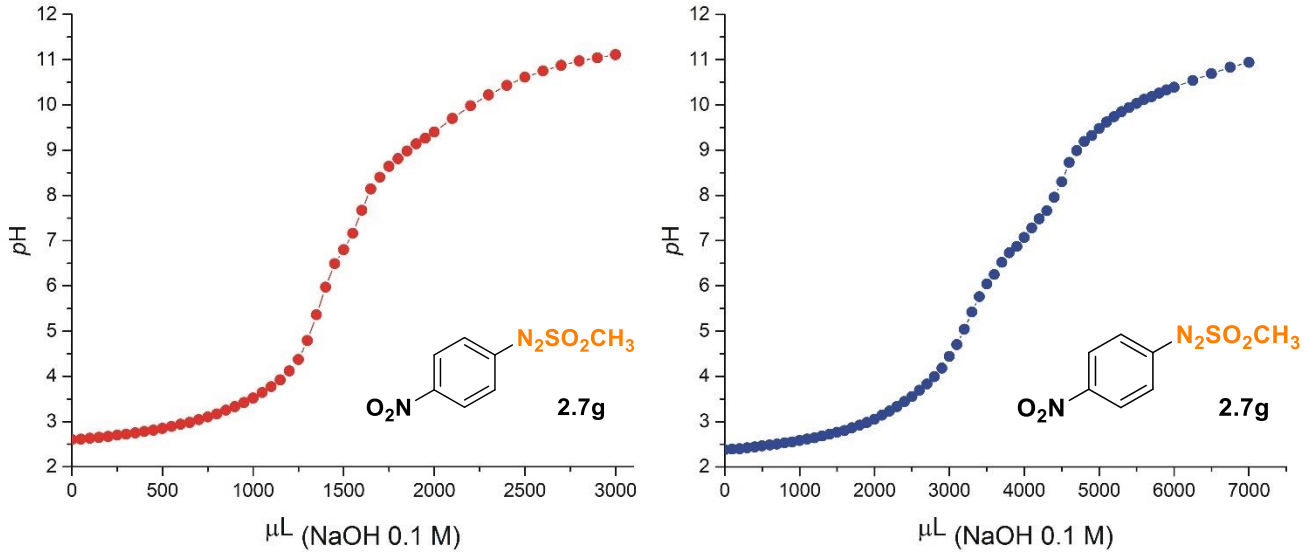


Figure 2.8. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7g** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

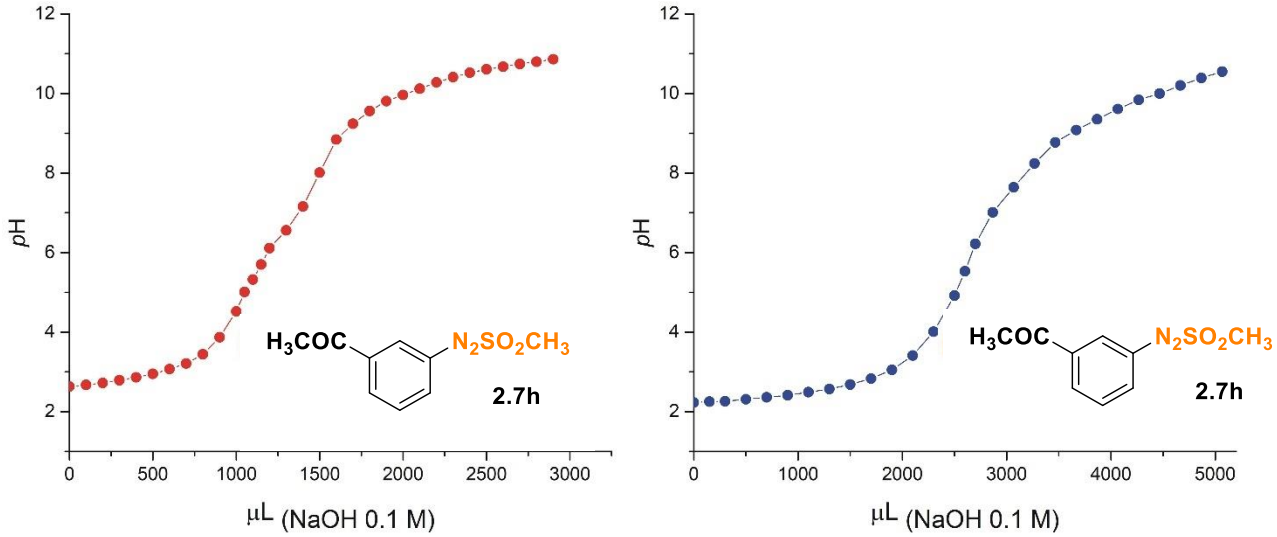


Figure 2.9. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7h** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

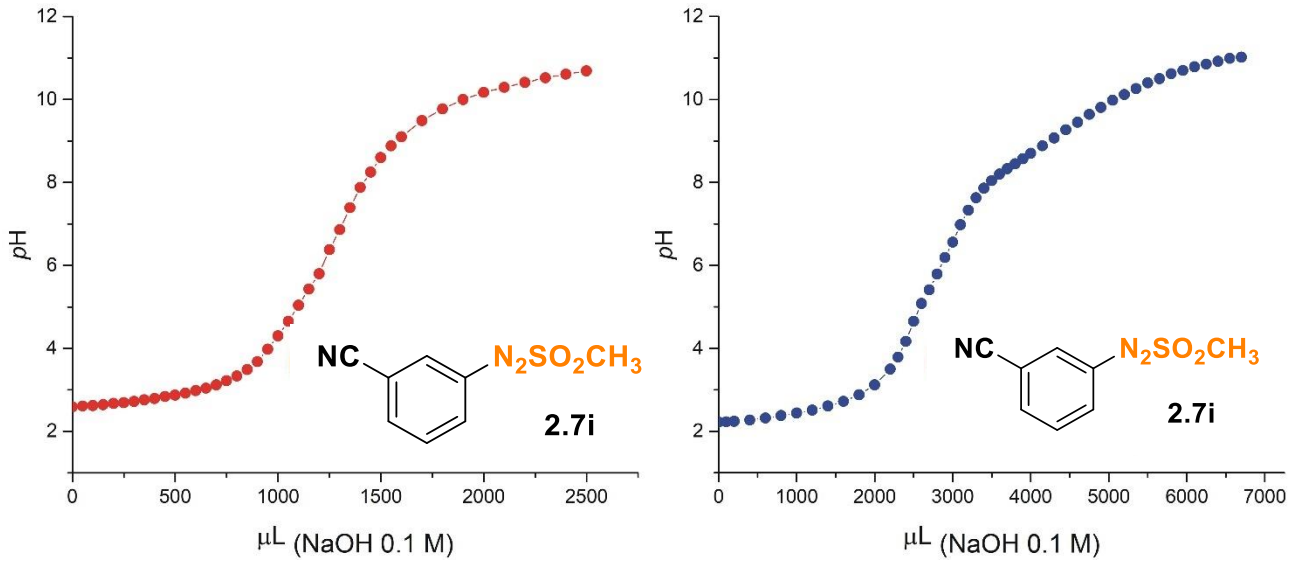


Figure 2.10. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7i** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

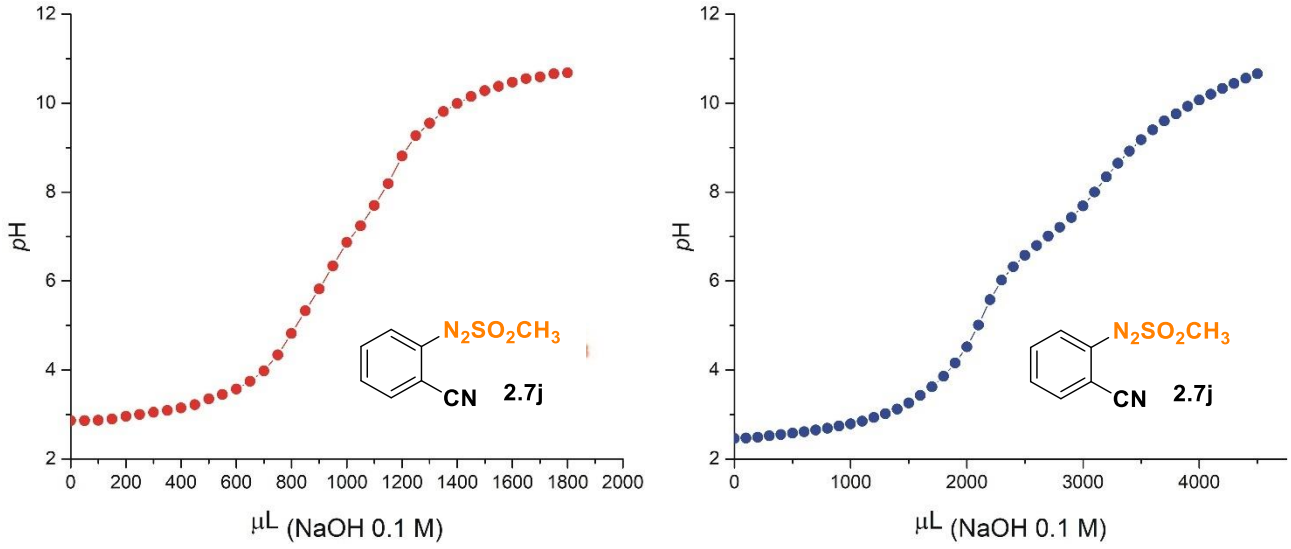


Figure 2.11. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7j** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

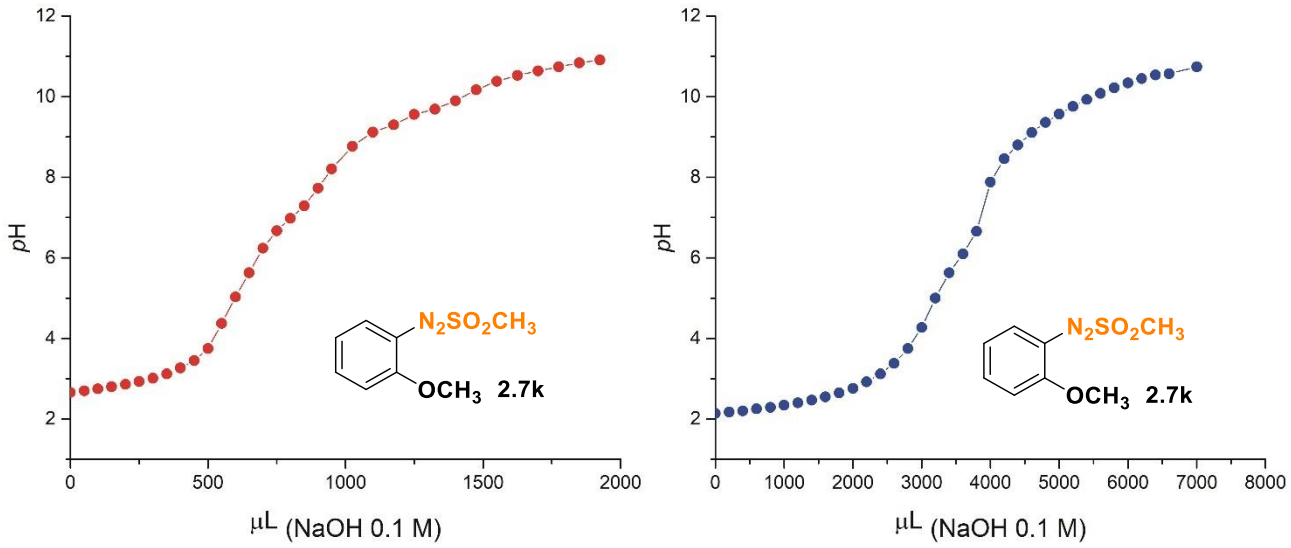


Figure 2.12. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.7k** irradiated in MeCN for 3 h (in red the titration of the Argon purged solution while in blue that of the oxygenated one).

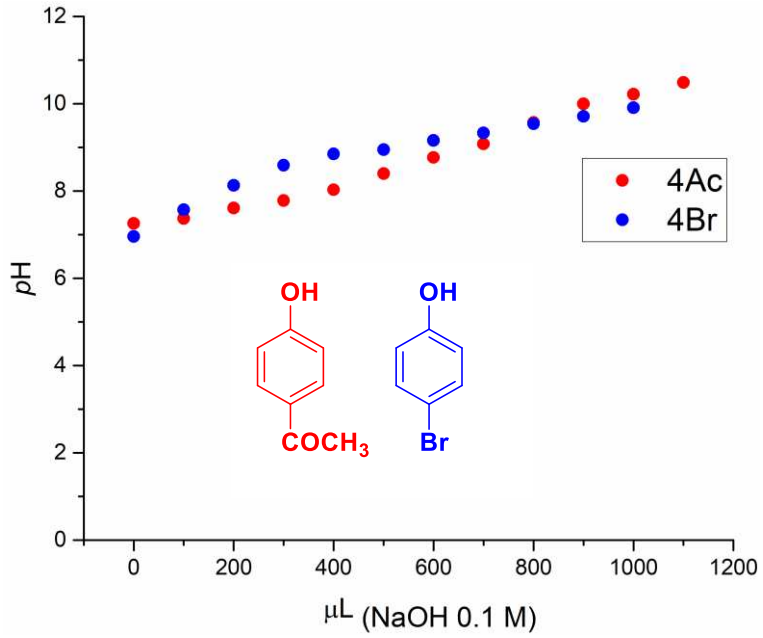


Figure 2.13. Potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.18** (in red) and **2.19** (in blue).

All the substrates studied exhibited a good to excellent acid release (up to 95%) being methane sulfonic acid the only species responsible for the acidity of the media as detected by IC analysis. As can be seen from Table 2.3, in some cases (**2.7d-f, 2.7k**) the amount of total H^+ found is in good agreement with the amount of methane sulfonic acid measured while in other cases (e.g. **2.7a, 2.7c**) the amount of H^+ found is significantly higher. We also reasoned that the phenols generated in solution could be responsible of the remaining acid contribution, but potentiometric titration of 10 mL of a 2.5×10^{-2} M solution of **2.18** or **2.19** proved that such compounds were not titrated during the measurement of the total acidity released from the irradiated arylazo sulfones. This is also confirmed by the pKa values of phenols **2.18-2.28**. GC-MS analyses of the head space of the irradiated solutions of **2.7a** and **2.7f** (Figures 2.14, 2.15) pointed out the presence of sulphur dioxide that pass undetected by IC and may account for the lack of sulphur containing acids.

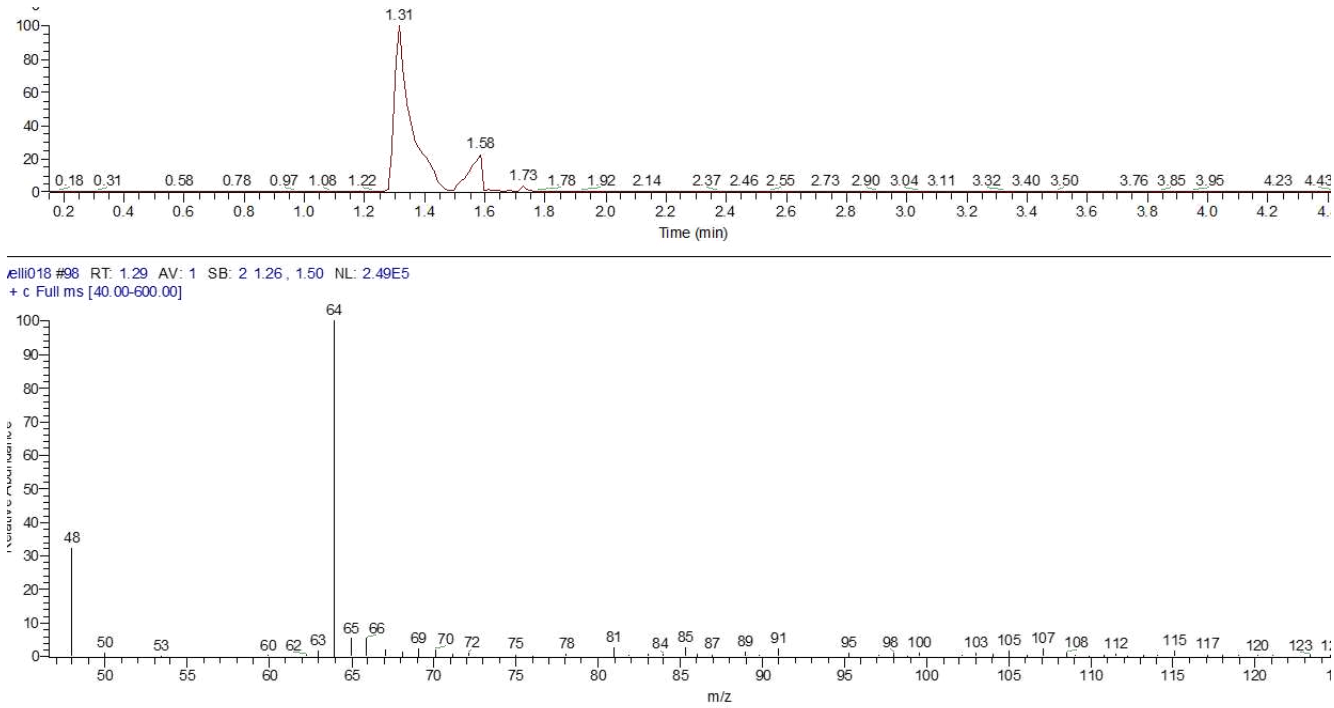


Figure 2.14. GC-MS analysis of the head space of a **2.7a** solution irradiated in oxygen-purged media.

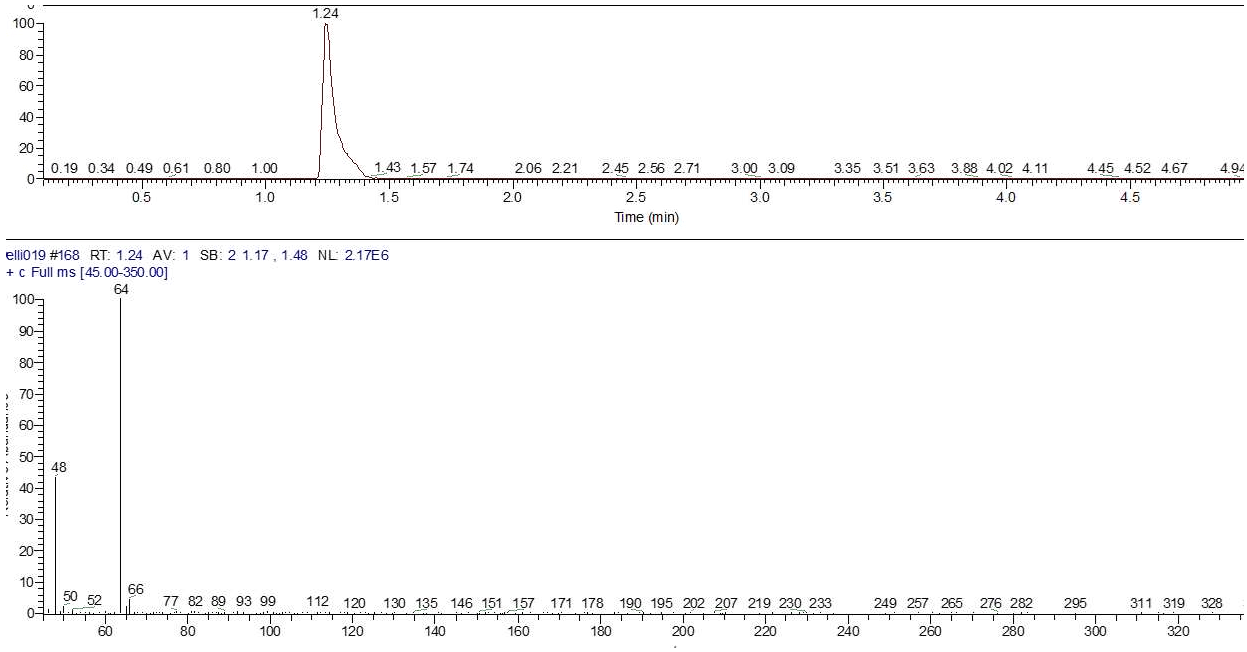
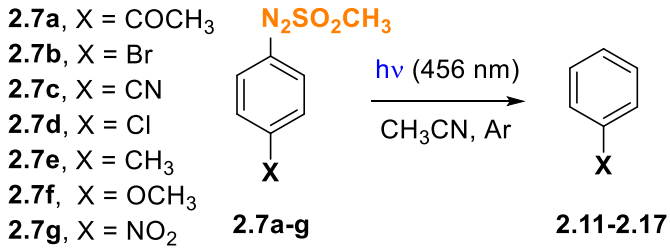


Figure 2.15. GC-MS analysis of the head space of a **2.7f** solution irradiated in argon-purged media.

Moreover, the formation of quinone-like products (by oxidation of **2.18-2.28** evidenced by the brownish colour of the solution after irradiation) known to release protons, possibly give an alternative explanation [2.27]. Irradiation experiments on selected arylazo sulfones (**2.7a-g**) were likewise carried out in argon purged conditions (Table 2.4), forming **2.11-2.17** as the exclusive products. Weak methanesulfinic acid accounted for most of the acidity liberated (in variable amounts) was detected by IC.

Table 2.4. Photoreactivity of Arylazo Sulfones (**2.7a-g**) Irradiated in Argon Purged Solutions. [a,b]



Azosulfone	**2.11-2.17** (%)[c]	H^+ [d]	$MeSO_2H$ % [e]
2.7a	(**2.11**): 44	76	52
2.7b	(**2.12**): 51	86	69
2.7c	(**2.13**): 51	69	67
2.7d	(**2.14**): 63	31	31
2.7e	(**2.15**): 76	72	71
2.7f	(**2.16**): 39	21	21
2.7g	(**2.17**): 75	42	41

[a] Conditions: an argon purged acetonitrile solution of **2.7a-g** (2.5×10^{-2} M) was irradiated with one 40 W Kessil Lamp with emission centred at 456 nm for 3 h until the total consumption of the arylazo sulfone. [b] The consumption of **2.7a-g** was determined through HPLC analysis. [c] Yields of **2.11-2.17** were determined by GC analysis. [d] Determined by potentiometric titration with a solution of NaOH 0.1 M. [e] Determined through IC.

2.3 CONCLUSIONS.

In conclusion, arylazo sulfones proved to be good nonionic photoacid generators (PAGs) under visible light irradiation conditions. This intriguing class of shelf-stable and coloured compounds were finely employed for the visible-light photochemical catalytic release of acids. The different behaviour of these sulfones in different media allowed us to tune the strength of the acid released (from weak sulfinic acid to strong sulfonic acid).

2.4 EXPERIMENTAL SECTION.

General Information. ^1H and ^{13}C NMR spectra were recorded on a 300 e 75 MHz spectrometer, respectively. The attributions were made on the basis of ^1H and ^{13}C NMR experiments; chemical shifts are reported in ppm downfield from TMS. GC analyses were performed using a HP SERIES 5890 II equipped with a fire ion detector (FID, temperature 350 °C). Analytes were separated using a Restek Rtx-5MS (30 m×0.25 mm×0.25 μm) capillary column with nitrogen as a carrier gas at 1 ml

min^{-1}. The injector temperature was 250 °C. The GC oven temperature was held at 80 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1}, and held for 10 min. The potentiometric titrations were carried out using a water solution of NaOH 0.1 M and a METLER-TOLEDO glass pHmeter. Ion chromatography analyses were performed by means of a Dionex GP40 instrument equipped with a conductimetric detector (Dionex 20 CD20) and an electrochemical suppressor (ASRS Ultra II, 4 mm) by using the following conditions: chromatographic column IONPAC AS23 (4 mm×250 mm), guard column IONPAC AG12 (4 mm×50 mm), eluent: $NaHCO_3$ 0.8 mm+Na_2CO_3 4.5 mm, flux: 1 mL min^{-1}; current imposed at detector: 50 mA. Commercially available sodium methanesulfinate and methanesulfonic acid were used as standards.

General Procedure for the Synthesis of Arylazo Sulfones. Arylazo sulfones **2.7a-j**, were previously synthesized and fully characterized by our research groups [2.28] by the following procedure: Diazonium salts [2.29] were freshly prepared prior to use from the corresponding anilines and purified by dissolving in acetonitrile and precipitation by adding cold diethyl ether. To a cooled (0 °C) suspension of the chosen diazonium salt (1 equiv, 0.3 M) in CH_2Cl_2 was added sodium methanesulfinate (1.2 equiv) in one portion. The temperature was allowed to rise to room temperature, and the solution stirred overnight. The resulting mixture was then filtered, and the obtained solution was evaporated affording the desired arylazo sulfone. The crude product was finally dissolved in CH_2Cl_2 and precipitated by adding cold *n*-hexane [2.28]. Arylazo sulfone **2.7k** was synthesized starting from the corresponding diazonium salt, prepared following a known procedure [2.28].

GC-MS Analysis. GC-MS analysis were carried out to verify the presence of sulfur containing products different from methanesulfonic or methanesulfinic acid. An oxygen purged solution of **2.7a** and an argon purged solution of **2.7f** were irradiated for 3 h in a sealed vial. After the irradiation the resulting mixtures were heated to 40 °C and the head space was injected with a sealed syringe. GC−MS analyses were carried out using a Thermo Scientific DSQII single quadrupole GC−MS system. A Restek Rtx-5MS (30 m × 0.25 mm × 0.25 μm) capillary column was used for the separation of analytes with helium as a carrier gas at 1 mL/min. The injection in the GC system was performed in splitless mode, and the injector temperature was 250 °C. The GC oven temperature was held at 35 °C for 5 min, increased to 150 °C by a temperature ramp of 3 °C min^{-1}, and held for 10 min. The transfer line temperature was 250 °C, and the ion source temperature was 250 °C. Mass spectral analyses were carried out in full scan mode. In both cases the main product was sulfur dioxide (M^+ = 64).

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CHAPTER 3

ARYLAZO SULFONES AS PAGs FOR THE PROTECTION OF ALCOHOLS AS THP-ETHERS.

3.1 INTRODUCTION.

In the previous chapter the feasibility to generate acid upon visible light exposure of arylazo sulfones was described. The aim of this part of my PhD thesis is the application of arylazo sulfones **3.1a-c** as PAGs to catalyze a chemical transformation (Figure 3.1).

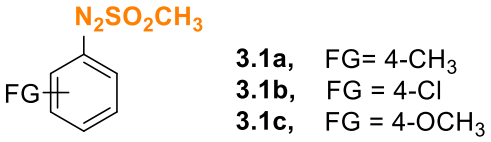


Figure 3.1. Arylazo sulfones employed as PAG in this chapter.

The efficient photorelease of acid encouraged us to test arylazo sulfones in the role of PAGs for the photochemical catalytic protection of alcohols **3.2-3.14** (Figure 3.2) by reaction with 3,4-dihydro-2H-pyran (DHP, **3.15**) and vinyl ethyl ether **3.16**.

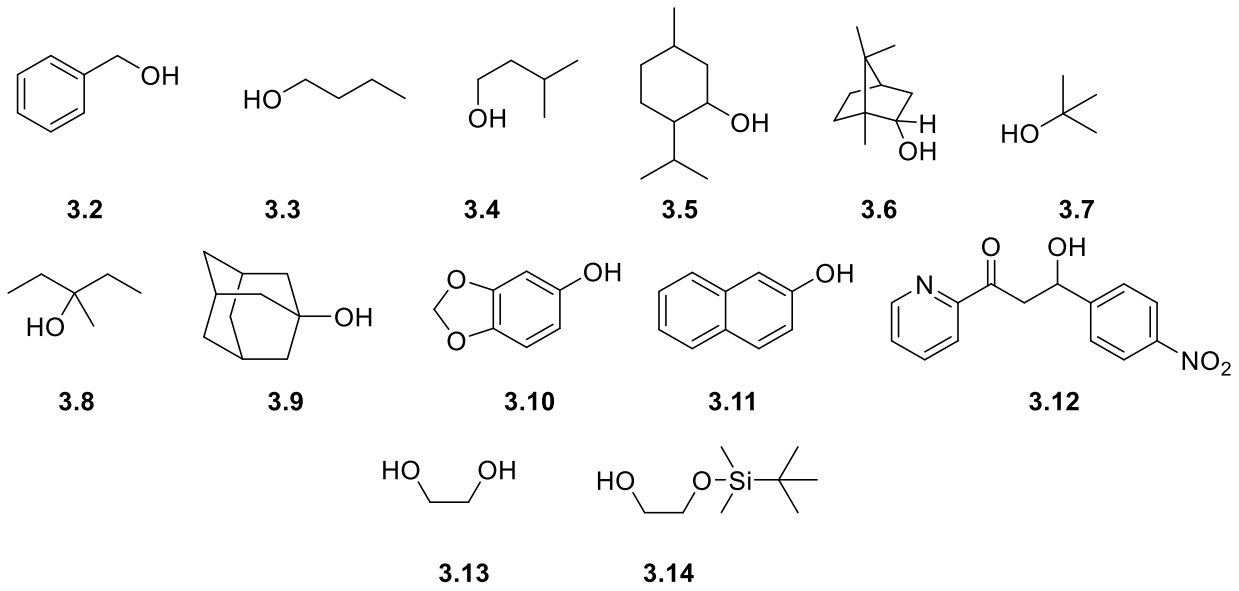
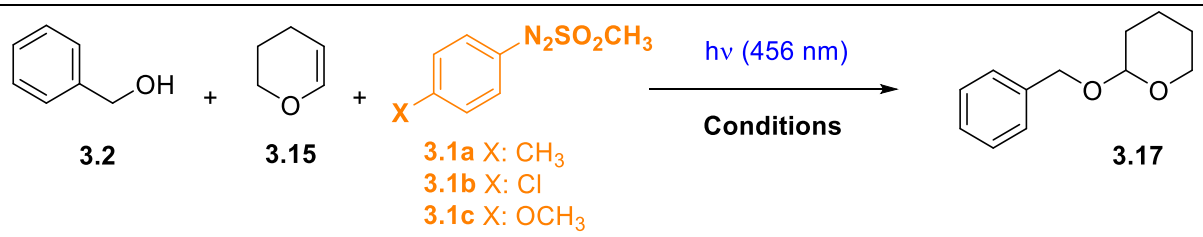


Figure 3.2. Alcohols employed for the synthesis of tetrahydropyranyl ethers or acetals using arylazo sulfones as PAG catalyst.

3.2 RESULTS AND DISCUSSION.

The protection of benzyl alcohol **3.2** as tetrahydropyranyl ether was taken as a model reaction and optimized (Table 3.1). The process was completed after 30 min irradiation in an air-equilibrated acetonitrile solution, employing only 0.5 mol% amount of an arylazo sulfone **3.1a-c**. All the sulfones tested (**3.1a-c**) were effective in promoting the synthesis of THP ether **3.17** being **3.1a** the derivative that led to an almost quantitative yield (Table 3.1). The reaction did not take place in the absence of **3.1a** and/or visible light (Table 3.1).

Table 3.1. Optimization of the Photocatalyzed Protection of **3.2**.



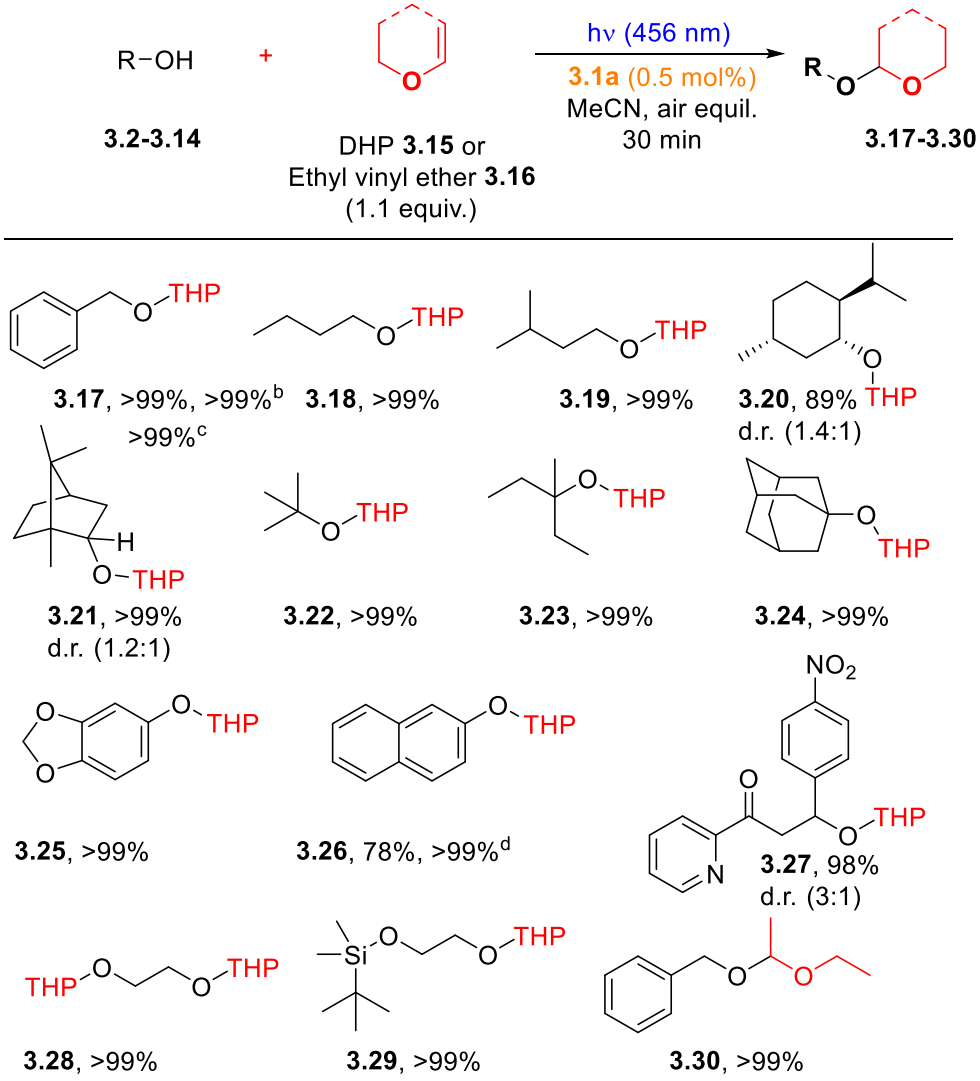
Entry	Conditions	Yield
1	**3.2** (0.5 mmol), **3.15** (1 equiv), **3.1a** (10 mol %), DCM, 24 h, O_2	7%
2	**3.2** (0.5 mmol), **3.15** (1 equiv), **3.1a** (5 mol %), DCM, 24 h, O_2	80%
3	**3.2** (0.5 mmol), **3.15** (1 equiv), **3.1a** (2.5 mol %), DCM, 24 h, O_2	82 %
4	**3.2** (0.5 mmol), **3.15** (1 equiv), **3.1a** (1.25 mol %), DCM, 24 h, O_2	85%
5	**3.2** (5 mmol), **3.15** (1 equiv), **3.1a** (0.5 mol %), DCM, 24 h, O_2	90%
6	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), DCM, 24 h, O_2	>99%
7	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 24 h, O_2	>99%
8	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 24 h, air equil.	>99%
9	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 30 min, air equil.	>99%
10	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 30 min, Ar sat.	73%
11	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1b** (0.5 mol %), MeCN, 30 min, air equil.	98%
12	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1c** (0.5 mol %), MeCN, 30 min, air equil.	94%
13	**3.2** (5 mmol), **3.15** (1.1 equiv), MeCN, 30 min, air equil.	0%
14	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 24 h, air equil., Dark	0%
15	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 24 h, air equil., 2,6-luditine (0.5 mol %)	0%
16	**3.2** (5 mmol), **3.15** (1.1 equiv), **PTSA** (0.5 mol %), MeCN, 30 min	0%
17	**3.2** (5 mmol), **3.15** (1.1 equiv), **MSA** (0.5 mol %), MeCN, 30 min	<5%

PTSA = *p*-Toluenesulfonic acid; **MSA** = Methanesulfonic acid.

Interesting, the slow release of acid was beneficial to the reaction since the addition of PTSA or methanesulfonic acid (0.5 mol%) to a mixture of **3.2** and **3.15** did not lead to the desired acetal after 30 min (Table 3.1). Compound **3.17** was isolated in >99% yield even on a 25 mmol scale (4.80 g) and by using natural sunlight (2 h) as the light source (Scheme 3.1).

With these promising results in our hands, different alcohols have been used and all of them were successfully protected as tetrahydropyranyl ethers. The protocol was efficiently extended to primary alcohols (**3.3** and **3.4**), secondary (**3.5** and **3.6**) and tertiary alcohols (compounds **3.7**-**3.9**) even when particularly congested such as adamantan-1-ol **3.9** and borneol **3.6**. In all cases an almost quantitative formation of the protected adduct occurred. Protection of phenol **3.10** and naphthol **3.11** to give ethers **3.25** and **3.26** was likewise feasible (Scheme 3.1). The presence of other functional groups (see the preparation of **3.27**) did not hamper the protection event. In the case of ethylene glycol **3.13**, the protection of both OH groups smoothly took place by employing 2.2 equiv of **3.15**. The mild conditions used allows us to efficiently protect dimethyl-*tert*-butylsilyl alcohol **3.14**, that bears a functional group sensible to acidic conditions for the desymmetrization of ethylene glycol. Finally, to prove the versatility of this protocol, **3.2** was likewise protected by using ethyl vinyl ether **3.16** to afford product **3.30** again quantitatively.

Scheme 3.1. Photochemical Catalyzed Protection of Alcohols **3.2-3.14.**[a]

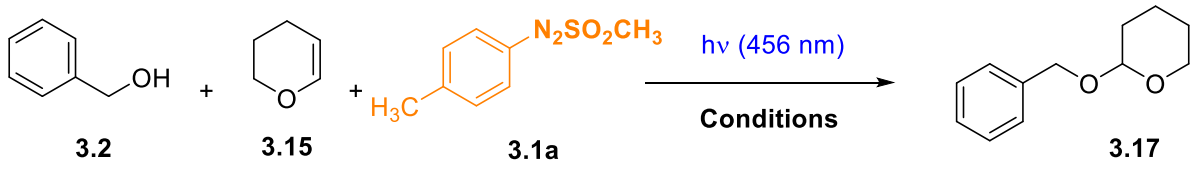


[a] Conditions: A solution containing the alcohol **3.2-3.14** (5 mmol, 1 equiv), a vinyl ether **3.15-3.16** (5.5 mmol, 1.1 equiv), **3.1a** (0.5 mol%) in 4 mL of MeCN was irradiated under air equilibrated conditions with one 40 W Kessil lamp (emission centered at 456 nm); Isolated yield shown. [b] Reaction carried out on 25 mmol scale. [c] Upon 2 h sunlight exposure. [d] Yield determined by GC analysis.

In the aim of having a better insight on the mechanism of the examined reaction, three Pyrex glass vessels were charged with arylazo sulfone **3.1a** (0.5 mol%), benzyl alcohol **3.2** (5 mmol, 1 equiv, 1.25 M) and **3.15** (5.5 mmol, 1.1 equiv, 1.375 M) in 4 mL of acetonitrile. The so-prepared mixtures were irradiated for 5, 15 and 30 minutes respectively using EvoluChem apparatus equipped with a 40W Kessil lamp (emission centred at 456 nm) placed 3 centimetres above the reaction vessel. As the irradiation stopped, Na_2CO_3 was added (5.0 mg, 0.05 mmol) and the product formation was monitored through GC analysis (Table 3.2, entries 1-3). Finally, two more glass vessels were charged with arylazo sulfone **3.1a** (0.025 mmol, 0.5 mol%), benzyl alcohol **3.2** (5 mmol, 1 equiv, 1.25 M) and **3.15**

(5.5 mmol, 1.1 equiv, 1.375 M) in 4 mL of acetonitrile and were irradiated for 5 min each, then covered with an aluminium foil for 10 min and 25 min respectively. The product formation was monitored by means of GC analysis (entries 4-5).

Table 3.2. Mechanistic investigations



3.2 **3.15** **3.1a** **3.17**

Entry	Conditions	3.17 (%Yield)
1	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 5 min, then Na_2CO_3 (0.05 mmol)	13%
2	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 15 min, then Na_2CO_3 (0.05 mmol)	48 %
3	**3.2** (5 mmol), **3.15** (1.1 equiv), **3.1a** (0.5 mol %), MeCN, 30 min, then Na_2CO_3 (0.05 mmol)	100%
4	**3.2** (5 mmol, 1 equiv), **3.15** (5.5 mmol, 1 equiv), **3.1a** (0.5 mol %), MeCN, 5 minutes, then 10 min in dark	40%
5	**3.2** (5 mmol, 1 equiv), **3.15** (5.5 mmol, 1 equiv), **3.1a** (0.5 mol %), MeCN, 5 minutes, then 25 min in dark	84%

It was apparent that the reaction proceeded even in the dark (albeit more slowly) when covering the reaction mixture with an aluminium foil after only 5 min irradiation and maintain the mixture at room temperature until 30 min (the yield of **3.17** was 84% vs >99% under continuous photolysis, compare entries 3 and 5).

3.3 CONCLUSIONS.

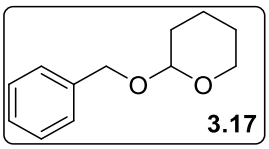
The role of arylazo sulfones as PAG has been exploited in the acid-catalysed protection of alcohols as acetals under mild conditions and upon either visible or (natural)solar light irradiation. The latter process did not require any dedicated apparatus, harsh conditions, or delicate catalysts to take place.

3.4 EXPERIMENTAL SECTION.

General Information. ^{1}H and ^{13}C NMR spectra were recorded on a 300 e 75 MHz spectrometer, respectively. The attributions were made on the basis of ^{1}H and ^{13}C NMR experiments; chemical shifts are reported in ppm downfield from TMS. GC analyses were performed using a HP SERIES 5890 II equipped with a fire ion detector (FID, temperature 350 °C). Analytes were separated using a Restek Rtx-5MS (30 m×0.25 mm×0.25 μm) capillary column with nitrogen as a carrier gas at 1 ml min^{-1}. The injector temperature was 250 °C. The GC oven temperature was held at 80 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1}, and held for 10 min.

General Procedure for the Synthesis of Starting materials. Alcohols **3.2-3.13** were commercially available except **3.12**[3.1] and **3.14**[3.2] that were prepared as previously described.

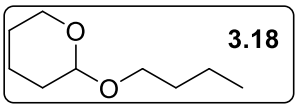
General Procedure for the photoinduced protection of alcohols. A Pyrex glass vessel was charged with the chosen alcohol (**3.2-3.14**, 5 mmol, 1 equiv, 1.25 M), the selected vinyl ether (**3.15-3.16**, 5.5 mmol, 1.1 equiv, 1.375 M), a catalytic amount of arylazo sulfone **3.1a** (0.025 mmol, 0.5 mol%) in 4 mL of acetonitrile. The so-formed mixture was irradiated for 30 min by using the EvoluChem apparatus equipped with one 40 W Kessil lamp (emission centered at 456 nm) placed 3 centimetres above the reaction vessel. The solvent was eliminated in vacuo and the residue was purified by silica gel column chromatography (cyclohexane-ethyl acetate mixture as eluant).



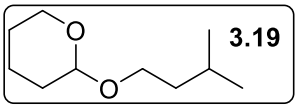
2-(Benzyloxy)tetrahydro-2H-pyran (3.17). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 μL of **3.15** (5.5 mmol, 1.1 equiv) and 520 μL of **3.2** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 960.0 mg of **3.17** (>99% yield, colourless liquid). Spectroscopic data were in accordance with literature [3.3]. ^{1}H NMR (300 MHz, acetone-d_6) δ 7.51 – 7.17 (m, 5H), 4.82–4.71 (m, 2H), 4.52 (d, J = 12.1 Hz, 1H), 3.95–3.50 (m, 2H), 1.93–1.52 (m, 6H). $^{13}C\{^{1}H\}$ NMR (75 MHz, acetone-d_6) δ 139.8, 129.0, 128.4, 128.0, 98.4, 69.2, 62.2, 31.3, 26.3, 20.0. The reaction was scaled up, starting from 25 mg (0.125 mmol, 0.5 mol%) of **3.1a** and 3.7 mL of **3.15** (27.5 mmol, 1.1 equiv) and 2.6 mL of **3.2** (25 mmol, 1 equiv) in 10 mL of acetonitrile. Purification was carried out by silica gel chromatography (eluant: neat cyclohexane) to afford 4.80 g of **3.17** (>99% yield, colourless liquid).

Sunlight promoted synthesis of 3.17. A Pyrex glass vessel was charged with **3.1a** (0.025 mmol, 0.5 mol%), benzyl alcohol **3.2** (5 mmol, 1 equiv, 1.25 M) and **3.15** (5.5 mmol, 1.1 equiv, 1.375 M) in 4 mL of acetonitrile. The mixture was placed on a window-ledge of the University of Pavia (45°11′31″

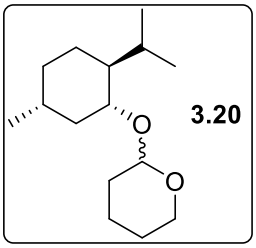
N, 9°09′33″ E, 77 above sea level, 08/04/2022, 10:00 a.m.) during a sunny day and the reaction was monitored through GC analysis. After 2 h the reaction was completed affording 960 mg of **3.17** (5 mmol, >99% yield).



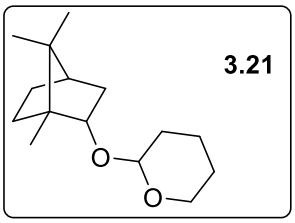
2-Butoxytetrahydro-2H-pyran (3.18). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 457 µL of **3.3** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 850.0 mg of **3.18** (>99% yield, colourless liquid). Spectroscopic data were in accordance with literature [3.4]. ^{1}H NMR (300 MHz, acetone-d_6) δ 4.56 (t, J = 3.5 Hz, 1H), 3.84–3.66 (m, 2H), 3.49–3.31 (m, 2H), 1.46 (s, 12H), 0.94 (t, J = 7.3 Hz, 3H).^{13}C{^{1}H} NMR (75 MHz, acetone-d_6) δ 99.1, 67.4, 62.1, 32.7, 31.5, 27.6, 26.5, 20.2, 14.3.



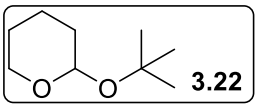
2-(Isopentyloxy)tetrahydro-2H-pyran (3.19). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 545 µL of **3.4** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 915.0 mg of **3.19** (>99% yield, colourless liquid). Spectroscopic data were in accordance with literature [3.5]. ^{1}H NMR (300 MHz, acetone-d_6) δ 4.57 (t, J = 3.4 Hz, 1H), 3.86–3.71 (m, 2H), 3.52–3.34 (m, 2H), 1.86–1.47 (m, 9H), 0.95 (d, J = 6.6 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, acetone-d_6) δ 98.8, 66.0, 61.8, 39.5, 31.5, 26.4, 25.9, 23.2, 23.0, 20.1.



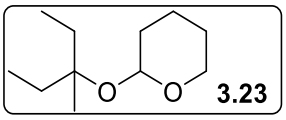
2-((2-Isopropyl-5-methylcyclohexyl)oxy)tetrahydro-2H-pyran (3.20). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 780.0 mg of **3.5** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate mixture) to afford 1.115 g of **3.20** (89% yield, colourless oil). Spectroscopic data were in accordance with literature [3.6]. The product was obtained as a diastereomeric mixture (1.4:1).^{1}H NMR (300 MHz, acetone-d_6) δ 4.84–4.57 (m, 1H), 3.88 (dtd, J = 15.0, 7.5, 4.0 Hz, 1H), 3.53–3.27 (m, 2H), 2.44–2.08 (m, 2H), 1.91–1.01 (m, 12H), 0.96–0.87 (m, 7H), 0.80 (dd, J = 6.9, 4.7 Hz, 4H). ^{13}C{^{1}H} NMR (75 MHz, acetone-d_6) δ 101.6, 95.3, 80.5, 74.6, 63.1, 62.8, 49.2, 44.5, 41.0, 35.4, 32.4, 32.3, 30.6, 26.4, 26.0, 23.9, 22.7, 21.5, 20.7, 16.7, 16.2.



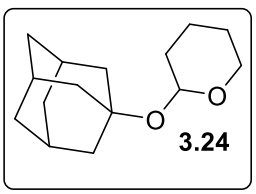
2-((1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl)oxy)tetrahydro-2H-pyran (3.21). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 770 mg of **3.6** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 1.19 g of **3.21** (>99% yield, colourless oil). Spectroscopic data were in accordance with literature [3.7]. The product was obtained as a diastereomeric mixture (1.2:1). ^{1}H NMR (300 MHz, Acetone-d_6) δ 4.68–4.52 (m, 1H), 4.10–3.52 (m, 2H), 3.44 (ddd, J = 11.5, 4.1, 1.9 Hz, 1H), 2.24–2.01 (m, 2H), 1.88–1.47 (m, 9H), 1.28–1.16 (m, 2H), 0.95–0.81 (m, 9H). ^{13}C{^{1}H} NMR (75 MHz, Acetone-d_6) δ 101.5, 96.8, 84.7, 80.0, 62.3, 50.3, 49.7, 48.6, 48.2, 46.3, 46.2, 41.0, 38.5, 36.6, 32.3, 27.7, 26.8, 20.8, 20.4, 19.5, 14.5.



2-(tert-Butoxy)tetrahydro-2H-pyran (3.22). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 478 µL of **3.7** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 850.0 mg of **3.22** (>99% yield, colourless liquid). Spectroscopic data were in accordance with literature [3.8]. ^{1}H NMR (300 MHz, Acetone-d_6) δ 4.83 (dd, J = 4.8, 2.8 Hz, 1H), 3.94–3.39 (m, 2H), 1.85–1.43 (m, 6H), 1.22 (s, 9H). ^{13}C{^{1}H} NMR (75 MHz, Acetone-d_6) δ 94.7, 74.8, 63.1, 33.8, 29.8, 27.0, 21.5.

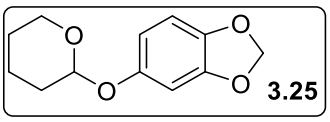


2-((3-Methylpentan-3-yl)oxy)tetrahydro-2H-pyran (3.23). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 616 µL of **3.8** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 942.0 mg of **3.23** (>99% yield, colourless liquid). Spectroscopic data were in accordance with literature [3.9]. ^{1}H NMR (300 MHz, Acetone-d_6) δ 4.82 – 4.67 (m, 1H), 4.02–3.41 (m, 2H), 2.05–1.58 (m, 4H), 1.51 (ddd, J = 9.4, 6.1, 2.3 Hz, 6H), 1.15 (d, J = 3.9 Hz, 3H), 0.87 (q, J = 7.3 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, Acetone-d_6) δ 93.6, 78.8, 63.5, 32.7, 31.5, 31.0, 25.7, 23.2, 21.0, 6.41, 6.27.

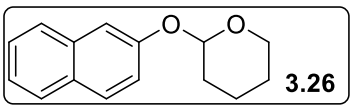


2-((Adamantan-1-yl)oxy)tetrahydro-2H-pyran (3.24). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 761 mg of **3.9** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 1.18 g of **3.24** (>99% yield, colourless oil). Spectroscopic data were in accordance with literature [3.8]. ^{1}H NMR (300

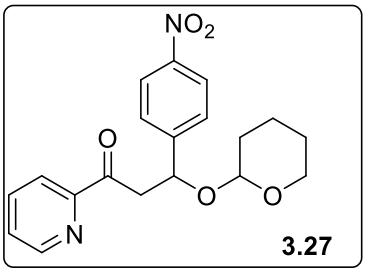
MHz, Acetone-d_6) δ 4.95 (dd, J = 4.8, 2.7 Hz, 1H), 3.93–3.38 (m, 2H), 2.13–1.42 (m, 21H). $^{13}C\{^1H\}$ NMR (75 MHz, acetone-d_6) δ 92.8,73.7, 62.8, 43.8, 37.4, 33.5, 31.8, 26.7, 21.2.



5-((Tetrahydro-2H-pyran-2-yl)oxy)benzo[d][1,3]dioxole (3.25). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 μL of **3.15** (5.5 mmol, 1.1 equiv) and 690 mg of **3.10** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: Ethyl acetate mixture) to afford 1.24 g of **3.25** (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with literature [3.10]. ^1H NMR (300 MHz, acetone-d_6) δ 6.65 (d, J = 8.3 Hz, 1H), 6.42 (d, J = 2.5 Hz, 1H), 6.29 (dd, J = 8.3, 2.5 Hz, 1H), 5.89 (s, 2H), 3.84 (d, J = 19.0 Hz, 1H), 3.60–3.22 (m, 2H), 1.69–1.47 (m, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, acetone-d_6) δ 153.5, 149.1, 141.4, 108.8, 107.2, 101.7, 98.7, 67.4, 31.4, 27.5, 26.3, 20.16.

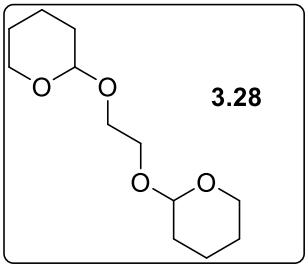


2-(Naphthalen-2-yloxy)tetrahydro-2H-pyran (3.26). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 μL of **3.15** (5.5 mmol, 1.1 equiv) and 720 mg of **3.11** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate mixture) to afford 929.0 mg of **3.26** (78% yield, >99% GC yield, yellow oil). Spectroscopic data were in accordance with literature [3.11]. ^1H NMR (300 MHz, acetone-d_6) δ 7.84 (dd, J = 8.0, 5.6 Hz, 3H), 7.61–7.28 (m, 4H), 5.62 (t, J = 3.2 Hz, 1H), 3.96–3.54 (m, 2H), 2.06–1.56 (m, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, acetone-d_6) δ 156.1, 135.8, 130.6, 130.3, 128.7, 128.1, 127.3, 124.9, 120.3, 111.6, 97.3, 62.6, 31.4, 26.2, 19.8.

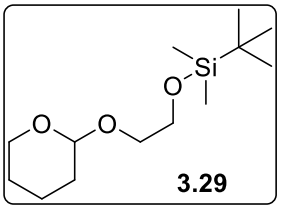


3-(4-Nitrophenyl)-1-(pyridin-2-yl)-3-((tetrahydro-2H-pyran-2-yl)oxy)propan-1-one (3.27). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 μL of **3.15** (5.5 mmol, 1.1 equiv) and 1360 mg of **3.12** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate mixture) to afford 1781.0 mg of **3.27** (98% yield, yellow oil). The product was obtained as a diastereomeric mixture (3:1). ^1H NMR (300 MHz, Acetone-d_6) δ 8.86–8.67 (m, 4H), 8.52 (d, J = 16.2 Hz, 1H), 8.39–8.25 (m, 3H), 8.30–8.20 (m, 3H), 8.25–8.13 (m, 2H), 8.19–7.90 (m, 10H), 7.84–7.66 (m, 7H), 7.71–7.59 (m, 3H), 5.58 (dd, J = 8.3, 5.2 Hz, 2H), 5.45 (dd, J = 8.4, 4.6 Hz, 1H), 4.97 (t, J = 3.5 Hz, 1H), 4.44 (t, J = 3.2 Hz, 2H), 4.01–3.74 (m, 5H), 3.58–3.33 (m, 5H), 3.30–3.17 (m, 1H), 2.87 (s, 3H), 2.06 (qui, J = 2.2 Hz, 2H), 1.81–1.34 (m, 10H), 1.29 (s, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, Acetone-d_6) δ 150.7, 150.2, 150.2, 150.1, 148.6, 141.8, 138.5, 138.3, 138.2, 130.5, 129.2, 128.6, 128.6, 128.5, 125.8, 125.0,

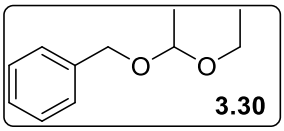
124.5, 124.2, 123.5, 122.4, 122.3, 100.4, 95.77, 75.9, 73.5, 62.9, 62.0, 46.6, 46.5, 27.6, 26.2, 26.2, 20.1, 19.5. HRMS (EI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{20}N_2O_5Na$ 379.1264; Found 379.1252.



1,2-bis((Tetrahydro-2H-pyran-2-yl)oxy)ethane (3.28). From 5 mg (0.025 mmol, 5 mol%) of **3.1a** and 1488 µL of **3.15** (11 mmol, 2.2 equiv) and 280 µL of **3.13** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate mixture) to afford 1250.0 mg of **3.28** (>99% yield, yellow oil). Spectroscopic data were in accordance with literature [3.12]. ^{1}H NMR (300 MHz, Acetone-d_6) δ 4.64 (q, J = 3.0 Hz, 2H), 3.83 (ddt, J = 11.2, 7.2, 3.7 Hz, 4H), 3.63–3.41 (m, 4H), 1.83–1.47 (m, 12H). ^{13}C{^{1}H} NMR (75 MHz, Acetone-d_6) δ 99.6, 67.7, 62.52, 32.0, 27.0, 20.6.



tert-Butyldimethyl(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)silane (3.29). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 744 µL of **3.15** (5.5 mmol, 1.1 equiv) and 865 µL of **3.14** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate mixture) to afford 1.336 g of **3.29** (>99% yield, yellow oil). Spectroscopic data were in accordance with literature [3.13]. ^{1}H NMR (300 MHz, Acetone-d_6) δ 4.64 (q, J = 3.0 Hz, 2H), 3.83 (ddt, J = 11.2, 7.2, 3.7 Hz, 4H), 3.63–3.41 (m, 4H), 1.83–1.47 (m, 12H). ^{13}C{^{1}H} NMR (75 MHz, Acetone-d_6) δ 99.6, 67.7, 62.52, 32.0, 27.0, 20.6.



((1-Ethoxyethoxy)methyl)benzene (3.30). From 5 mg (0.025 mmol, 0.5 mol%) of **3.1a** and 526 µL of ethyl vinyl ether **3.16** (5.5 mmol, 1.1 equiv) and 520 µL of **3.2** (5 mmol, 1 equiv). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 901 mg of **3.30** (>99% yield, colourless oil). Spectroscopic data were in accordance with literature [3.14]. ^{1}H NMR (300 MHz, Acetone-d_6) δ 7.43–7.34 (m, 5H), 4.93 (dd, J = 41.3, 5.3 Hz, 1H), 4.73–4.60 (m, 2H), 3.83–3.42 (m, 2H), 1.38 (d, J = 5.3 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, acetone-d_6) δ 140.4, 129.4, 128.7, 128.4, 100.4, 67.9, 61.6, 20.8, 16.3.

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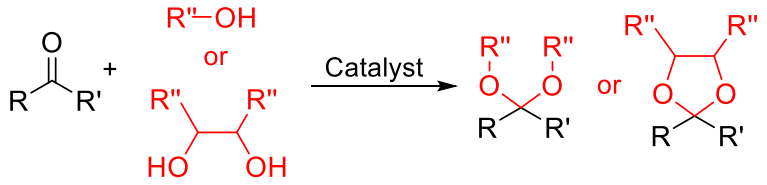
CHAPTER 4

ARYLAZO SULFONES FOR THE PHOTOCHEMICAL PROTECTION OF CARBONYLS.

4.1 INTRODUCTION.

Carbonyl is one of the most versatile functional groups to be found in organic molecules [4.1]. However, the electrophilicity of aldehydes and ketones make their protection quite common during the synthetic planning of complex molecules [4.2-4.4]. Albeit there are several strategies for the carbonyl group protection [4.5], the conversion towards nucleophilic/basic insensitive acetals is the preferred choice [4.5], also in view of the possible derivatization of these protected carbonyls [4.6]. The acetalization process usually needs the use of a (protic or Lewis) acid or, in alternative, the presence of a transition metal complex. The simplest way to convert a carbonyl into an acetal employs p-toluensulfonic acid as the acid catalyst in the presence of an excess of alcohol. The water released during the reaction should be eliminated by a drying agent or by means of a Dean–Stark apparatus that requires the heating of the mixture under reflux (T > 80 °C). It is hard to make a complete list of the plethora of the investigated alternative promoters of the reaction, that comprises both metal-based [4.7] and organo-catalysts (Scheme 4.1 a) [4.8]. Moreover, the existing methodologies mostly employ MeOH or EtOH (or even ethylene glycol) as the reaction media in the synthesis of the corresponding acetals.

a. General scheme for the carbonyl protection as acetals



Long reaction time
Excess of alcohol needed
High temperature
Harmful solvent
Metal-containing catalysts

Catalyst = Lewis acid, protic acid, transition metal complex, photocatalyst

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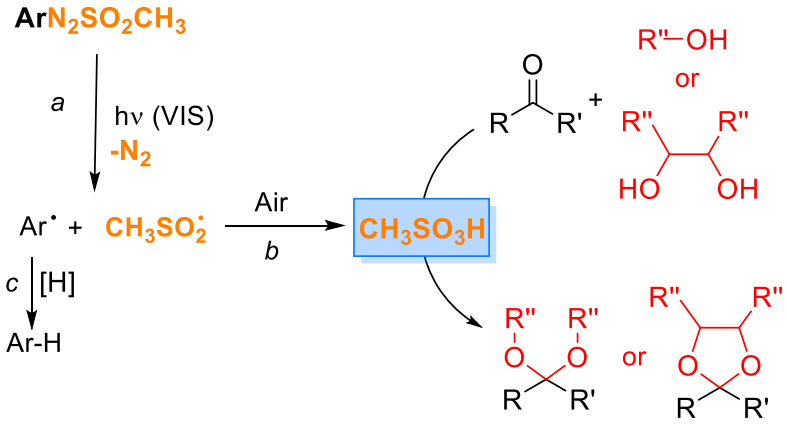
b. Reaction investigated in this chapter.



Fast reaction
Slight excess of alcohol
Room temperature
Benign solvent
Metal-free conditions

Scheme 4.1. a. Common pathways for the protection of carbonyl groups as acetals. b. reaction investigated in the present chapter.

Recently, the addition of traces of inexpensive acids (e.g. aqueous HCl) was beneficial for the acetalization process but to have short reaction times, a large excess of the alcohol is yet mandatory [4.9]. A sustainable approach may involve visible light induced acetalization processes [4.10]. The success of this route has been recently assured by the presence of a photocatalyst (PC) or, in one case, by photoacid catalysis [4.10d], but the high amount required (up to 20% mol) [4.10b,c], the drawback associated with the separation of the PC from the end compounds [4.10b] and the scope of the methods (currently applied only to aldehydes) [4.10] called for the development of a general, cost-effective, mild and chemo-selective photochemical strategy. Knowing that arylazo sulfones may behave as photoacid generators (PAGs) [4.11] we speculated that this class of compounds could be efficiently used for the general and eco-sustainable visible-light driven induced protection of carbonyls by overcoming the drawbacks of the already existing methodologies (Scheme 4.1 b).

4.2. RESULTS AND DISCUSSION.

We targeted the protection of β-ketoaldehyde **4.2** with ethylene glycol in the presence of a set of arylazo sulfones (**4.1a-d**) as the photoacid generators (Figure 4.1).

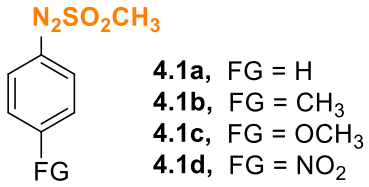
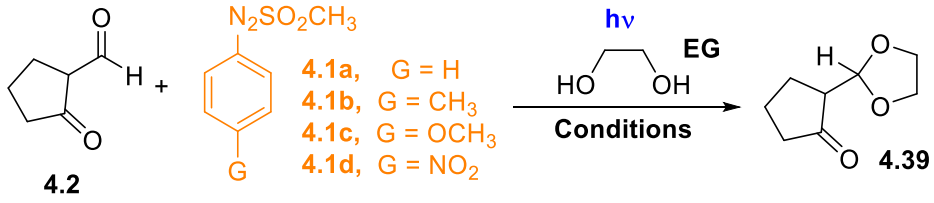


Figure 4.1. Arylazo sulfones tested in this work.

To optimize the protocol several trials were performed looking for the best performance in terms of efficiency, selectivity and sustainability (Table 4.1). Firstly, a wide range of media has been tested. The best conditions were as follows: **4.2** (0.1 M), ethylene glycol (1.1 equiv), $MgSO_4$ (0.4 equiv) as the drying agent and 1-(methylsulfonyl)-2-phenyldiazene (**4.1a**, 5 mol%) in air equilibrated dimethyl carbonate irradiated at room temperature for 2 h by means of a 40W Kessil lamp (emission centered at 427 nm). By adopting such approach, acetal **4.39** was selectively obtained in quantitative yield (without the acetalization of the ketone moiety). We also carried out a set of control experiments to verify the key role of each component of the reaction. In particular, the formation of **4.39** was not observed when a base was present (whether $NaHCO_3$ or 2,6-lutidine 5 mol%, Table 4.1, entries 13, 14) or by omitting either **4.1a** (entry 15) or light (entry 16). Interesting, no acetalization of **4.2** took place at room temperature when adding PTSA (5 mol%) in place of **4.1a** (entry 17). On-off experiments pointed out that a continuous irradiation is mandatory to achieve a complete conversion of **4.2** (Figure 4.2). Having these promising results in our hands, we decided to set out for the photochemical protection of a wide scope of aldehydes (Figure 4.3).

Table 4.1. Optimization of the acetalization reaction employing arylazo sulfones as PAGs.



Entry	Conditions	4.39 (% Yield)
1	**4.2** (0.1 mmol, 0.1 M), **EG** (0.3 mmol, 3.0 equiv), **3.1a** (5 mol%), hν (427 nm), DCM, 12 h	89 %
2	**4.2** (0.1 mmol, 0.1 M), **EG** (0.3 mmol, 3.0 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), DCM, 12 h	93%
3	**4.2** (0.1 mmol, 0.1 M), **EG** (0.3 mmol, 3.0 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), CH_3CN, 12 h	100%
4	**4.2** (0.1 mmol, 0.1 M), **EG** (0.3 mmol, 3.0 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), hν (456 nm), CH_3CN, 12 h	76%
5	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), CH_3CN, 2 h	100%
6	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (2 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), CH_3CN, 2 h	82%
7	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1b** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), CH_3CN, 2 h	99%
8	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1c** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), CH_3CN, 2 h	93%
9	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1d** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), CH_3CN, 2 h	94%
10	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), 2-Me THF, 2 h	80%
11	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), Diethyl Carbonate, 2 h	100%
12	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), Dimethyl Carbonate, 2 h	100%
13	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), $NaHCO_3$ (5 mol%), hν (427 nm), Dimethyl Carbonate, 2 h	0%
14	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (5 mol%), 2,6-lutidine (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), Dimethyl Carbonate, 2 h	0%
15	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), $MgSO_4$ (0.4 mmol), hν (427 nm), Dimethyl Carbonate, 12 h	0%
16	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **3.1a** (5 mol%), $MgSO_4$ (0.4 mmol), **no light**, Dimethyl Carbonate, 12 h	0%
17	**4.2** (0.1 mmol, 0.1 M), **EG** (0.11 mmol, 1.1 equiv), **PTSA** (5 mol%), $MgSO_4$ (0.4 mmol), hν (427 nm), Dimethyl Carbonate, 2 h	0%

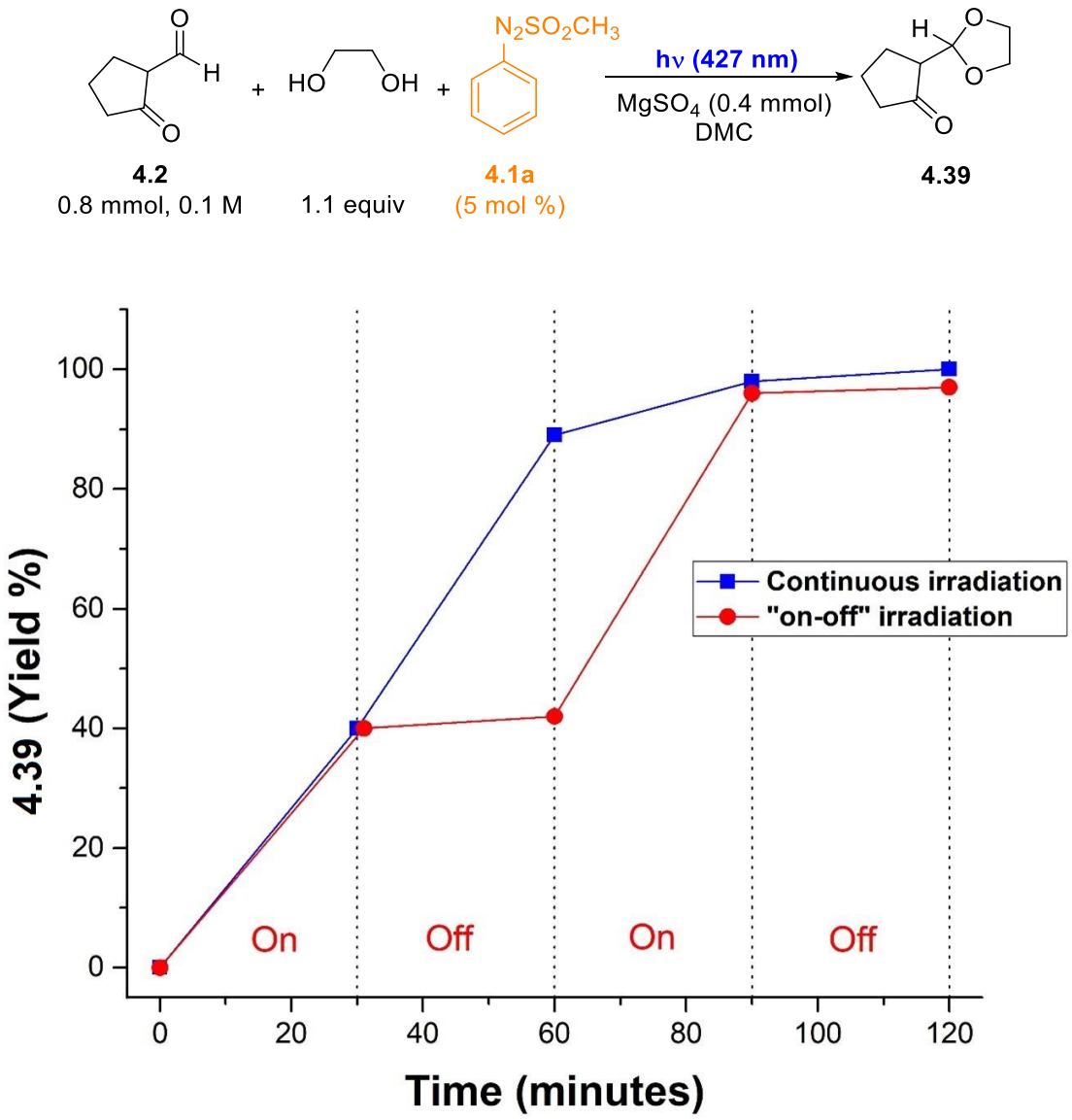


Figure 4.2. Kinetics of the synthesis of **4.39** in the presence of **4.1a**.

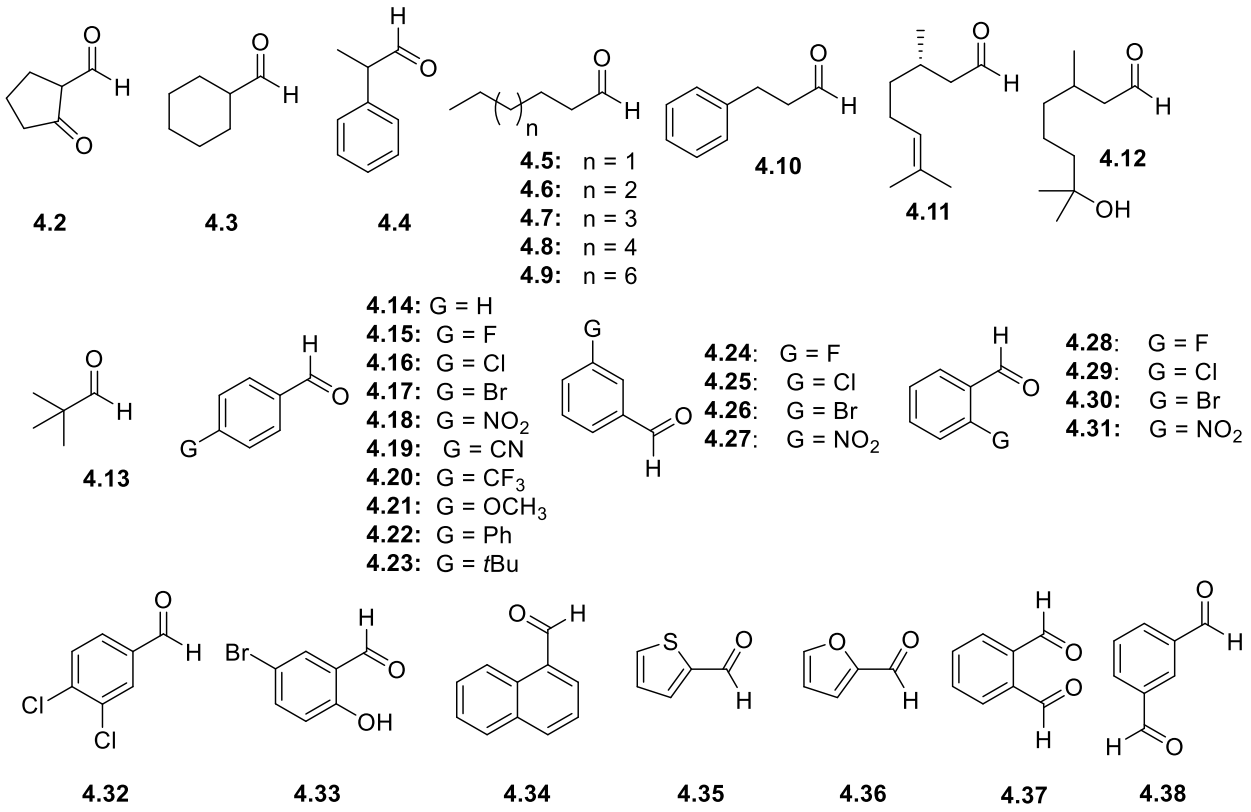
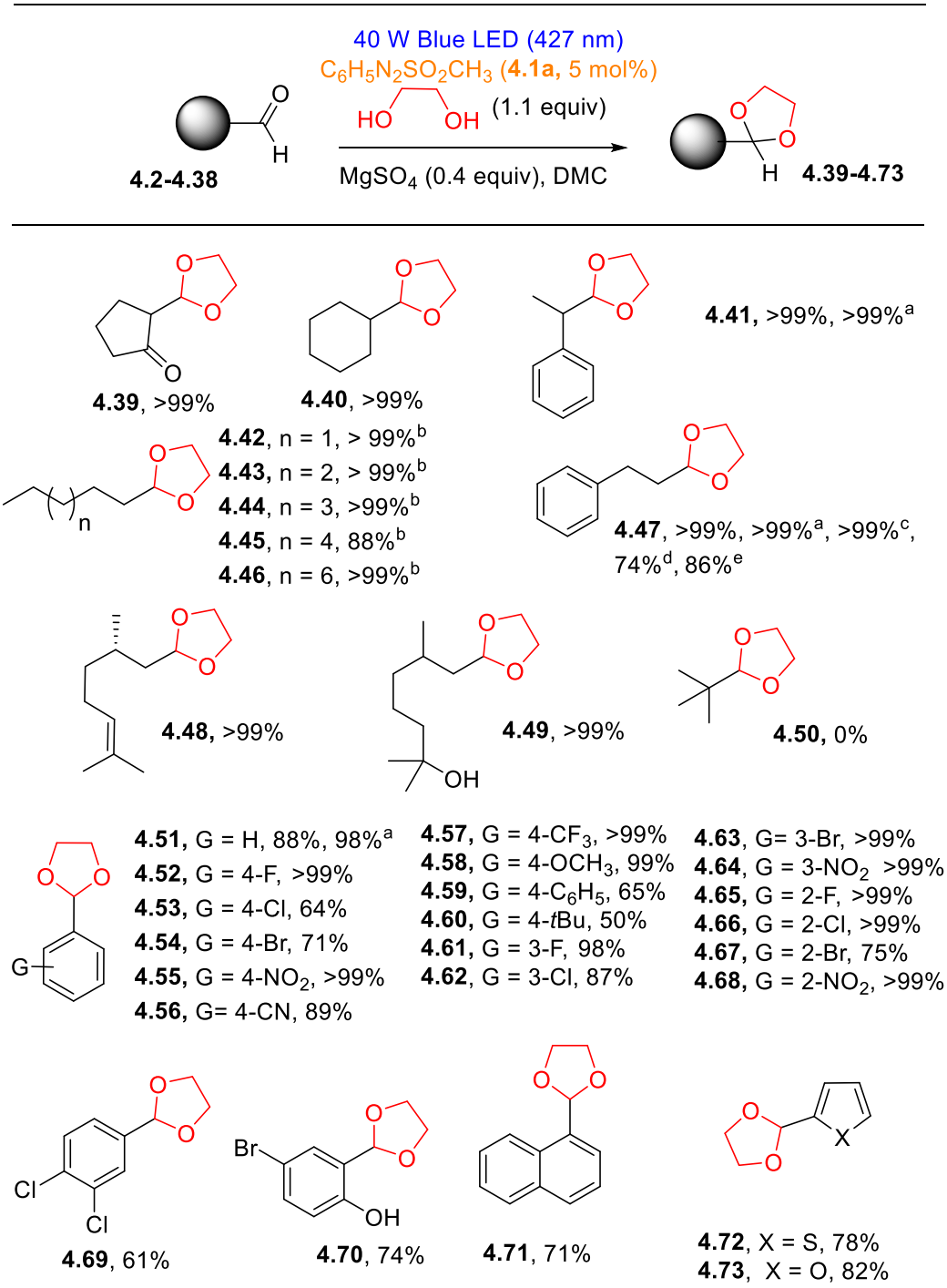


Figure 4.3**.** Aldehydes employed in the present work.

The conversion of aldehydes **4.2-4.38** into the corresponding 1,3-dioxolanes **4.39-4.73** in up to quantitative yield was performed in a smooth and benign way. The only exception was pivaldehyde **4.13** that was recovered unaltered after the irradiation (Scheme 4.1).



Scheme 4.1. Scope of the visible-light driven protection of aldehydes as 1,3-dioxolanes. Reaction conditions: **4.2-4.38** (0.8 mmol, 1 equiv), ethylene glycol (0.88 mmol, 1.1 equiv), **4.1a** (2-5 mol%), $MgSO_4$ (0.4 equiv), DMC (0.1 M), RT, 2 h. [a.] In a continuous flow reactor; [b.] 2 mol% **4.1a**; [c.] 3.6 mmol of **4.4** used; [d.] reaction performed upon sunlight exposure; [e.] under solvent free conditions, yield based on reacted **4.10**.

The scope of this work is broad and presents different examples of aldehyde that were successfully protected employing the set-up shown in Figure 4.4. Linear aldehydes **4.5-4.9** where compounds

4.42-4.46 were isolated in up to quantitative yield even when using 2 mol% **4.1a** were converted easily in the corresponding acetals. A scale up of the protocol (on 3.6 mmol **4.10**) was also performed by simply tuning the size of the reaction vessel to give **4.47** in >99% isolated yield. Acetalization may occur efficiently also by adopting sunlight as the free energy source, since compound **4.47** was obtained after exposure of the starting solution to solar light for 7 h (74% yield, Figure 4.5).

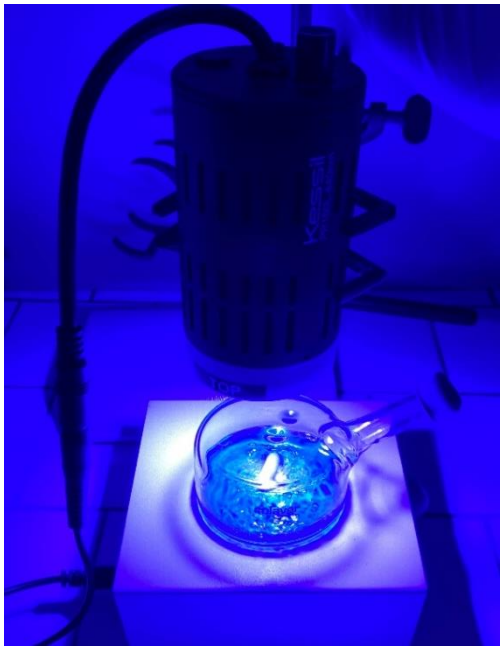


Figure 4.4. Apparatus for the visible-light mediated protection of carbonyls.

Figure 4.5. Sunlight-driven photochemical protection of aldehyde **4.10**.

Solvent-free acetalization processes have been rarely reported, [4.12] but our protocol carried out on 50 mmol scale by omitting DMC showed likewise a good performance in the synthesis of **4.47** (86% yield based on reacted **4.10**). The adoption of a flow reactor allowed us to reduce the irradiation time

to 1 h, while maintaining the same yield (> 99%, see the case of **4.4** and **4.14**, Scheme 4.1). The use of this flow apparatus did not require the addition of the heterogeneous drying agent ($MgSO_4$) to the reaction mixture (see Figures 4.6 and 4.7 for details on the reactor used).

a) b) c)

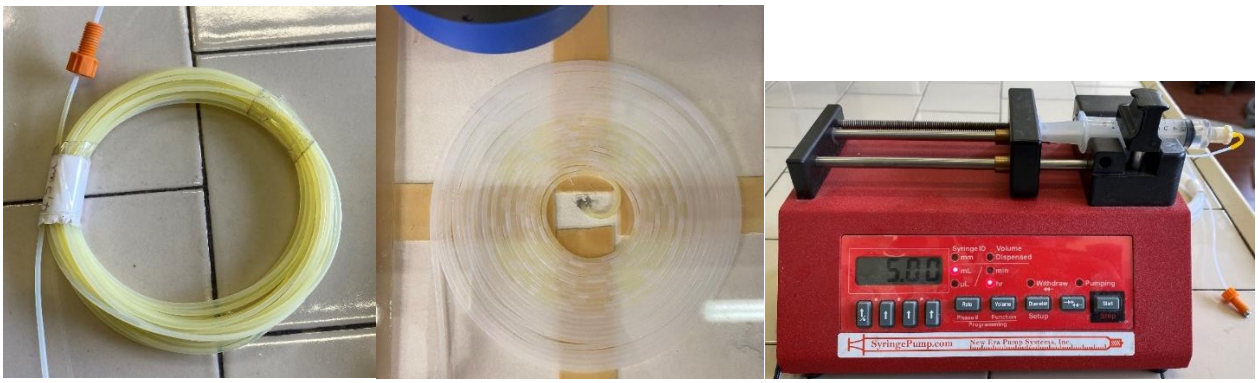
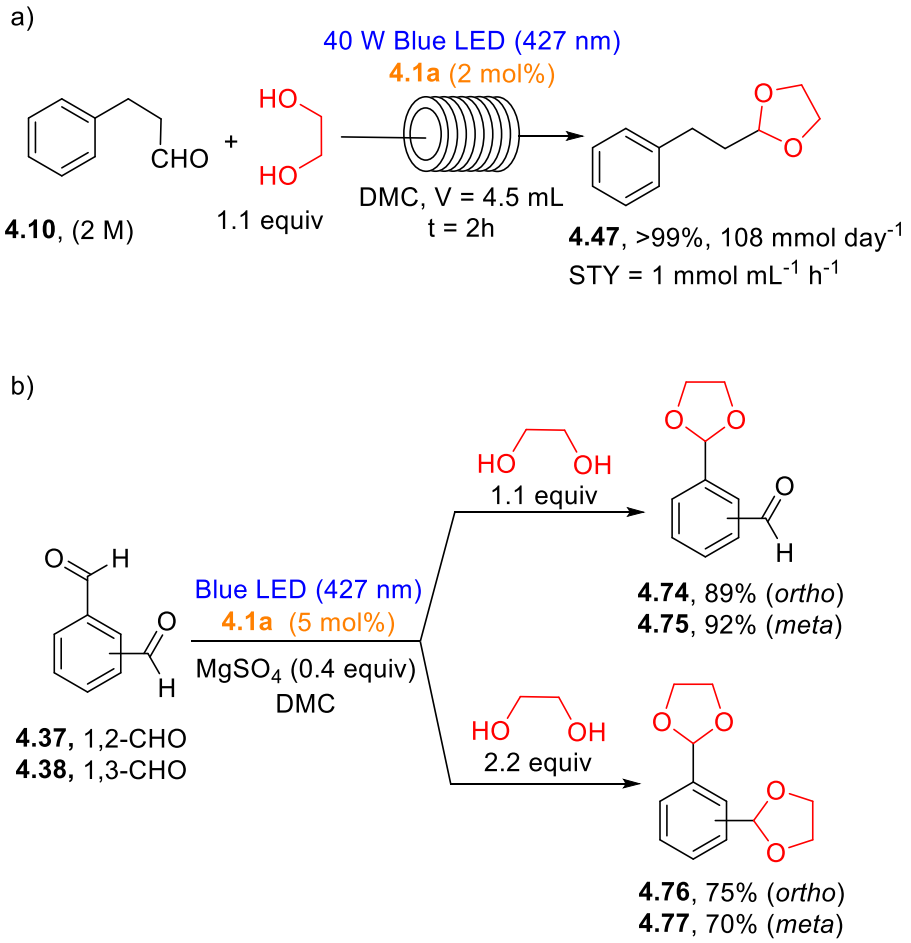


Figure 4.6. a) coiled tubing reservoir (PTFE, internal diameter: 1 mm) charged with the reaction mixture b) photochemical reactor c) syringe pump used to flow the mixture into the reactor.

a) b)

Figure 4.7. a) Experimental setup used to perform the photochemical protection of carbonyls in flow. b) View of the irradiated mixture.

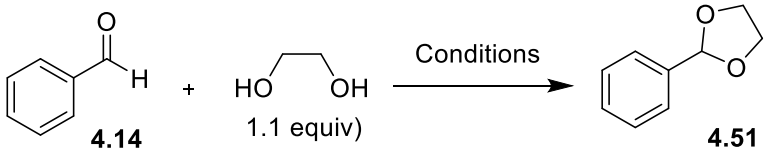
The flow protocol was then improved achieving a productivity of 108 mmol day^{-1} (Scheme 3a) in the synthesis of **4.47** (> 99% yield), starting from a 2 M solution of **4.10** and 2 mol% **4.1a**. The same yield was however obtained by using 0.5 mol% **4.1a** after 2 h irradiation and leaving the irradiated solutions in dark for further 20 h.



Scheme 4.2. a) Preparation of **4.47** under continuous flow conditions. b) Mono and di-protection of phthalaldehydes **4.37, 4.38**.

The performance of our protocol was compared with other methods reported in literature: in this scenario we investigated the synthesis of **4.51** under different thermal conditions by changing the reaction medium (e.g. DCM or toluene) even by removing the dehydrating agent. As shown in Table 4.2 the yield resulted from our approach is comparable to that obtained when performing the reaction under acid catalysis by refluxing the reaction mixture in a Dean-Stark apparatus for one night (toluene as the reaction media). On the other hand, the use of both Bronsted (PTSA, MSA) and Lewis ($ZnCl_2$) acids mostly afforded the desired product but in a lower yield.

Table 4.2. Alternative thermal conditions for the synthesis of **4.51.**

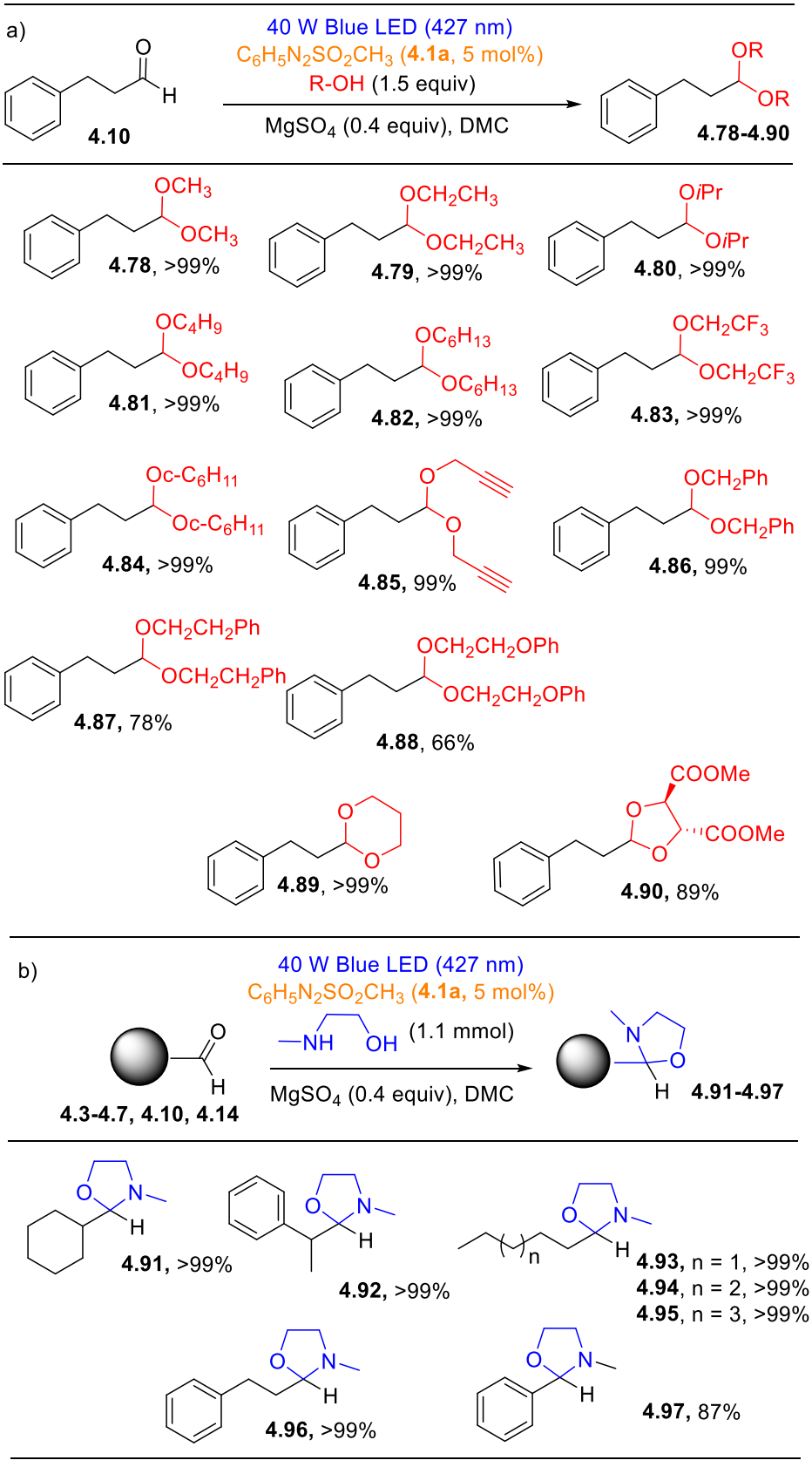


Entry	Conditions	Yield[a] (%)
1	**4.1a** (5 mol%), 40W Kessil lamp (427 nm) $MgSO_4$ (0.4 equiv), DMC, 2h (as reported in the main text)	88
2	$MeSO_3H$ (5 mol%), $MgSO_4$ (0.4 equiv), DCM, 2h	45
3	$MeSO_3H$ (10 mol%), DCM, 2h	53
4	PTSA (5 mol%), $MgSO_4$ (0.4 equiv), DCM, 2h	42
5	$ZnCl_2$ (5 mol%), $MgSO_4$ (0.4 equiv), DCM, 2h	0
6	PTSA (5 mol%), Dean Stark apparatus, Toluene, reflux overnight.	87

[a] Yield determined by GC analysis.

The protection of aromatic aldehydes **4.14-4.36** was successful as well. The position and the nature of the substituents on the aromatic ring did not influence the overall acetalization yield. (Scheme 4.1). Interesting is the case of the protection of phthalaldehydes **4.37** and **4.38**. In fact, the selective mono and di-acetalization of these dialdehydes has been performed by simply tuning the amount of ethylene glycol. Thus, the desymmetrization of **4.37** and **4.38** to give **4,74** and **4.75** was achieved in a high yield with 1.1 equiv of ethylene glycol, whereas when increasing its amount up to 2,2 equiv, fully protected **4.76** and **4.77** were obtained, respectively (Scheme 4.2 b). We then moved on to change the alcohols and glycols employed for the protection of aldehyde **4.10** to tune the hydrolysis rate of the acetal formed e.g. as dimethyl, diethyl, diisopropyl and dibenzyl derivatives sparsely used in synthetic planning (Scheme 4.3 a) [4.5a]. Notably, both primary and secondary alcohols tested were viable under the optimized conditions, (see products **4.78-4.88**), as well as other diols to form a 1,3-dioxane (**4.89**) and an alkylidene derivative of D-(-) tartrate (**4.90**).

We then investigated the preparation of 2-substituted 1,3-oxazolidines (**4.91-4.97,** Scheme 4.3 b). Despite these compounds are not widely used for the carbonyl protection [4.5a], they belong to an emerging class of five membered heterocycles used as synthons in organic synthesis [4.13] and photoredox catalysis [4.14]. Thus, oxazolidines **4.91-4.97** have been prepared in satisfactory yields (mostly in >99% yield) by irradiating a mixture of an aldehyde, 2-(*N*-methylamino)ethanol (1.1 mmol) and **4.1a** (5 mol%).



Scheme 4.3. Scope of the visible-light driven protection of aldehydes as acetals or 1,3-oxazolidines. Reaction conditions: **4.10** (0.8 mmol, 1 equiv), alcohol/ diol (1.5 equiv) or 2-(*N*-methylamino)ethanol (1.1 equiv), **4.1a** (5 mol%), $MgSO_4$ (0.4 equiv), DMC (0.1 M), RT, 2 h.

We finally were able to achieve the protection of ketones **4.98-4.116** as 1,3-dioxolanes employing our protocol. However, the usual reaction conditions led to an unsatisfactory protection of the carbonyl. We then envisaged that the addition of methyl orthoformate may drive the protection to completion, since this reagent acts as dehydrating agent [4.15] or may promote the formation of the corresponding dimethyl acetal and the dioxolane from it by a transacetalization process [4.16]. Gratifyingly, the presence of only a slight excess of methyl orthoformate (1.5 equiv) was effective in the promotion of the acetalization process in only 1 h (Scheme 4.4). A plethora of ketones was selected to highlight the feasibility of this protocol and is presented in Figure 4.8.

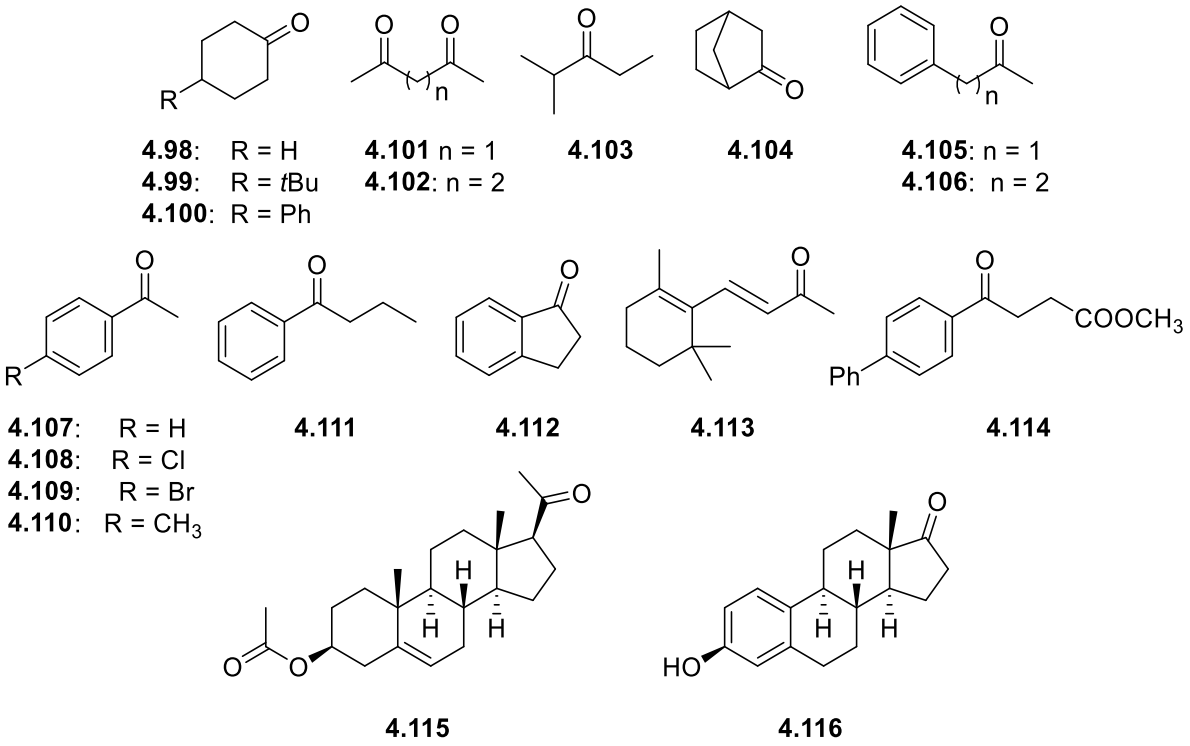
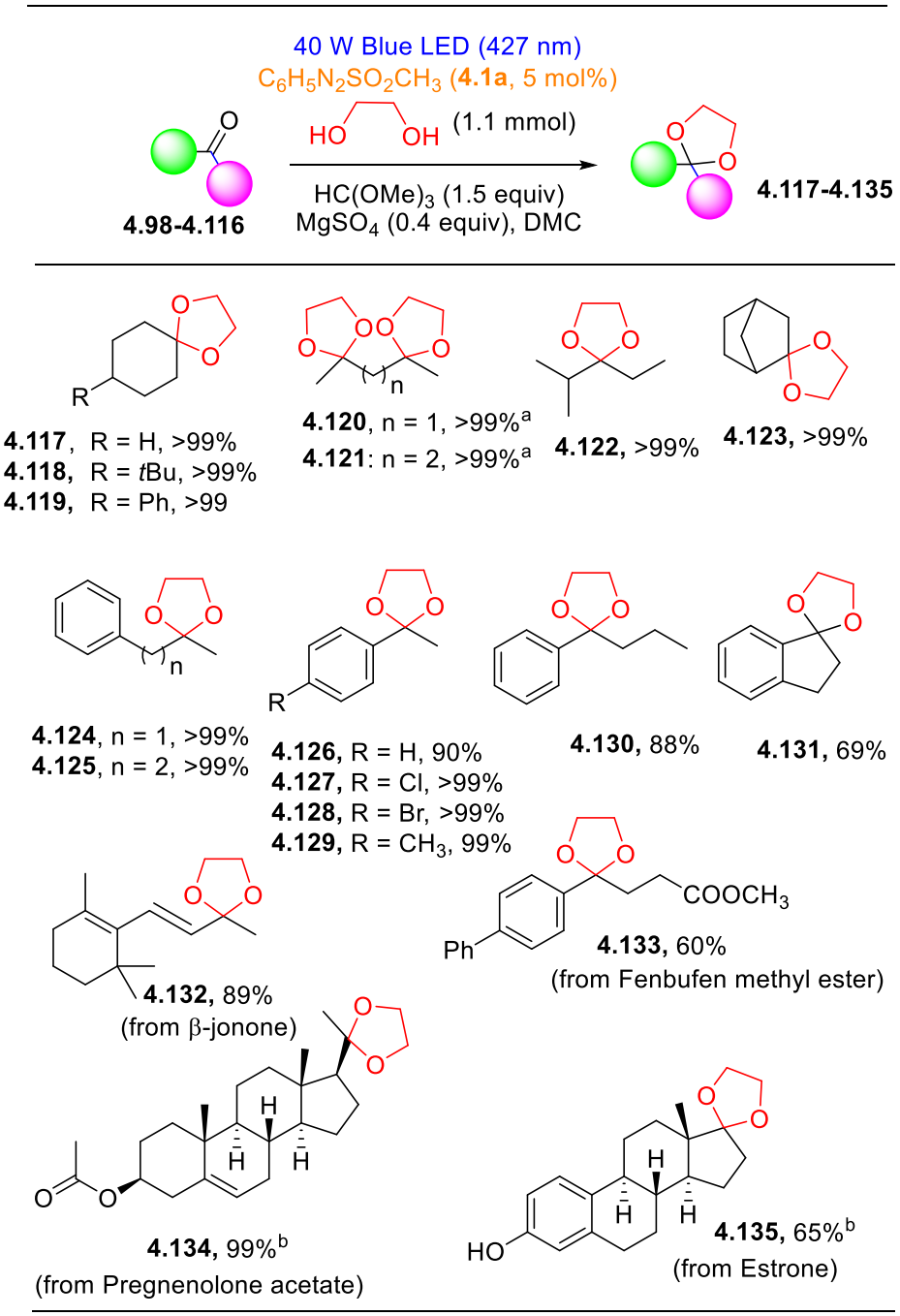


Figure 4.8**.** Ketones employed in the present chapter.

The protection of both aliphatic (**4.98-4.104**) and ketones bearing an aromatic substitutent (**4.104-4.116**) was achieved. The protection of β-ionone (**4.113**, widely used in perfumery) was carried out as a representative case of an unsaturated ketone. Even in this case, dioxolane **4.132** was formed in a good yield (89%). Interestingly, **4.132** could have a practical application, since acetalization is probably the most known approach for the preparation of pro-fragrances [4.17]. The acetalization of bioactive compounds is still feasible, as demonstrated in the synthesis of **4.133** (from Fembufen methyl ester), **4.134** (from pregnenolone acetate) and **4.135** (from estrone). In the latter two cases, however, the reaction was carried out in MeCN, due to the poor solubility of the starting ketones in

DMC (Scheme 4.4). Notably, **4.134** and **4.135** were isolated by simply filtration from the reaction mixture.



Scheme 4.4. Scope of the visible light driven protection of ketones. Reaction conditions: **4.98-4.116** (0.8 mmol, 1 equiv), ethylene glycol (1.1 equiv), **4.1a** (5 mol%), $HC(OMe)_3$ (1.5 equiv), $MgSO_4$ (0.4 equiv), DMC (0.1 M), RT, 1 h. [a.] 2.2 equiv. of ethylene glycol used; [b.] MeCN as the solvent.

4.3 CONCLUSIONS.

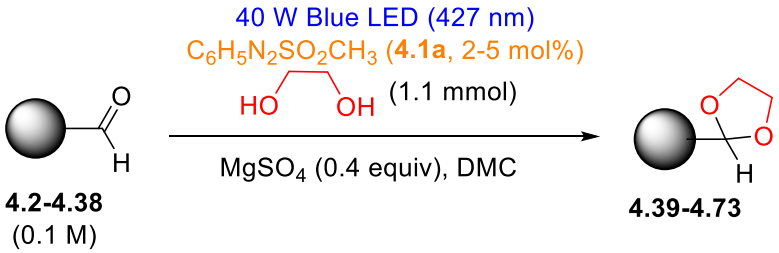
The present proposal describes a general procedure for the conversion of carbonyls into both cyclic and linear acetals and 1,3-oxazolidines, under mild conditions at room temperature. The method relie

son the slow release of a strong acid in a controllable on-off fashion by a readily prepared photoacid generator (PAG). Interestingly, this compound along with orthoformate used for the acetalization of ketones leaves no residues in the end mixture This allows for an easy work-up procedure, in most cases limited to a filtration of the reaction mixture on silica gel, assuring a high degree of purity of the desired protected carbonyl. The process takes advantage from the use of a sustainable reaction medium, dimethylcarbonate, widely considered as a green medium with low toxicity and bioaccumulation, and itis promoted by visible (or solar) light. Furthermore, the present protocol overcomes most of the limitations that characterize traditional methods, including the need for dedicated glassware, high temperature, and a large excess of the protecting agent, and maybe performed in a gram scale in batch or/and under continuous flow conditions.

4.4EXPERIMENTAL SECTION.

General Information. ^{1}H and ^{13}C NMR spectra were recorded on a 300 and 75 MHz spectrometer, respectively. The attributions were made on the basis of ^{1}H and ^{13}C NMR experiments; chemical shifts are reported in ppm downfield from TMS. GC analyses were performed using a HP SERIES 5890 II equipped with a fire ion detector (FID, temperature 350 °C). Analytes were separated using a Restek Rtx-5MS (30 m×0.25 mm×0.25 μm) capillary column with nitrogen as a carrier gas at 1 ml min^{-1}. The injector temperature was 250 °C. The GC oven temperature was held at 80 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1}, and held for 10 min. Compounds **4.2-4.38** and **4.98-4.116** were commercially available and used without further purification. Compounds **4.1a-d** (already present in the laboratory when this protocol has been developed) can be synthesized starting from the corresponding anilines [4.18].

General procedure for the visible-light mediated protection of aldehydes as 1,3-dioxolanes 4.39-4.73.



Scheme 4.5. Photochemical protection of aldehydes as 1,3-dioxolanes through arylazo sulfones as PAG.

A Pyrex glass vessel was charged with the chosen aldehyde (**4.2-4.38**, 0.8 mmol, 1 equiv, 0.1 M), ethylene glycol (0.88 mmol, 1.1 equiv, 0.11 M) a catalytic amount of arylazo sulfone **4.1a** (0.016-0.040 mmol, 2-5 mol%) and 48 mg of $MgSO_4$ (0.4 mmol) in dimethyl carbonate (DMC, 8 mL). The so-formed mixture was irradiated under stirring for 2 h by using the EvoluChem apparatus equipped with one 40 W Kessil lamp (l_{em} max = 427 nm, placed 3 cm above the glass vessel, Figure 4.4). The system was ventilated through a fan placed on the right of the lamp keeping the temperature within the reaction vessel below 30 °C. Compounds **4.42-4.46** were isolated by recovering the irradiated mixture with a few mL of DCM and by passing the resulting solution through a flash silica gel column. In the other cases, the isolation of **4.39-4.41**, **4.47-4.73** involved purification of the residue by silica gel column chromatography (cyclohexane-ethyl acetate mixture as eluant).

Procedure for the sunlight-driven synthesis of 4.47. A Pyrex glass vessel was charged with 128 mL of **4.10** (1 mmol, 1 equiv, 0.1 M), 62 mL of ethylene glycol (1.1 mmol, 1.1 equiv, 0.11 M), 9.3 mg of arylazo sulfone **4.1a** (0.05 mmol, 5 mol%) and 60 mg of $MgSO_4$ (0.5 mmol) in 10 mL of DMC (Figure 4.6). The so-formed mixture was placed outside the window of the Chemistry Department of the University of Pavia (Italy, latitude 45°11' N, 9°09' E, 77 m above sea level) in the July 2022 period with an aluminium foil underneath and let there for 7 h. The crude product was dissolved in ethyl acetate and washed with water. The organic phase was dried and acetal **4.47** was obtained in 74% yield with no further purification.

Visible-light promoted synthesis of 4.47 under solvent-free conditions. A Pyrex glass vessel was charged with 5.30 mL of **4.10** (50 mmol, 1 equiv), 3.0 mL of ethylene glycol (55 mmol, 1.1 equiv), 372 mg of **4.1a** (2 mmol, 5 mol%) and 120 mg of $MgSO_4$ (1 mmol). The so-formed mixture was irradiated for 4 h as in the General Procedure. 10 mL of EtOAc and 10 mL of distilled H_2O were added to the residue. The resulting organic phase was extracted twice with EtOAc. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated under vacuum, purified on silica gel chromatography (cyclohexane-ethyl acetate mixture as eluant). 1.32 g (9.9 mmol) of unreacted aldehyde **4.10** was recovered along with the desired acetal **4.47 (**4.79 g, 34.5 mmol, 86% yield based on consumed **4.10**).

Procedure for the visible-light mediated preparation of 4.47 under flow conditions. In an Erlenmeyer flask a 4.0 mL solution of dimethyl carbonate (DMC), 2 mmol of the chosen aldehyde (2 mmol, 0.5 M), 111 mL of ethylene glycol (2 mmol, 1 equiv) and 18.6 mg of **4.1a** (0.1 mmol, 5 mol%) was charged into a coiled tubing reservoir (PTFE, internal diameter: 1 mm; Figure 4.7, a). The

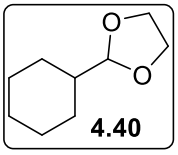
reaction mixture was then flown through the channels of the reactor (Figure 4.7 b) by means of a syringe pump (Figure 4.7, c) using a flow rate of 10 $mL \cdot h^{-1}$ upon irradiation with a LED lamp (Kessil PR-160L, 40 W, emission centered at 427 nm; see a representative picture of the experimental setup in Figure S8). A fan cooling was applied to keep temperature below 30 °C. The progress of the reaction was monitored by GC-FID and, upon completion, after 1 h the crude mixture was poured into a round-bottom flask and the solvent removed via rotary evaporation. The protected carbonyl was isolated by column chromatography (eluant: cyclohexane/ethyl acetate). By adopting this approach, compounds **4.41, 4.47** and **4.51** have been isolated in >99%, >99% and 98% yield, respectively.

Compounds **4.47** (1.42 g) was likewise formed in >99% yield by adopting a 2 M solution of **4.10** by using 2 mol% **4.1a** upon 2 h irradiation. The same yield (1.42 g) was obtained by using 0.5 mol% **4.1a** upon 2 h irradiation and leaving the irradiated solutions in dark for further 20 h.

General procedure for the visible-light mediated protection of 4.10 as acetals 4.78-4.90. A Pyrex glass vessel was charged with aldehyde **4.10** (0.8 mmol, 1 equiv, 0.1 M), the alcohol (1.5 equiv), a catalytic amount of arylazo sulfone **4.1a** (0.040 mmol, 5 mol%) and 48 mg of $MgSO_4$ (0.4 mmol) in 8 mL of dimethyl carbonate (DMC) and the mixture was irradiated for 2 h. Compounds **4.78-4.90** were purified by silica gel column chromatography (cyclohexane-ethyl acetate mixture as eluant).

2-(1,3-Dioxolan-2-yl)cyclopentan-1-one (4.39). Starting from 89.6 mg of **4.2** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (8:2 cyclohexane-ethyl acetate mixture as eluant) and 124.8 mg of **4.39** were obtained (>99% yield, colourless oil). Spectroscopic data were in accordance with the literature [4.19].

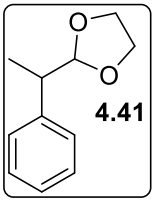
4.39. ^1H NMR (300 MHz, CD_3COCD_3) δ 5.08 (d, J = 2.5 Hz, 1H), 3.99–3.74 (m, 5H), 2.56–2.48 (m, 1H), 2.33–1.61 (m, 9H).$^{13}C\{^1H\}$ NMR (75 MHz, CD_3COCD_3) δ 216.6, 103.9, 65.9, 65.7, 51.9, 39.3, 23.4, 21.4.



2-Cyclohexyl-1,3-dioxolane (4.40). Starting from 97 mL of **4.3** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by flash silica gel filtration (neat cyclohexane as eluant) and 124.9 mg of **4.40** were obtained (>99% yield, slightly

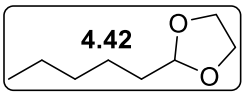
yellow oil). The same reaction was carried out by using 2 mol% **4.1a** to give **4.40** with the same yield. Spectroscopic data were in accordance with the literature [4.20].

4.40. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.59 (d, J = 5.0 Hz, 1H), 3.96 – 3.82 (m, 4H), 1.79–1.43 (m, 6H), 1.29 – 1.09 (m, 5H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 107.7, 65.0, 41.8, 27.4, 26.5, 25.9.



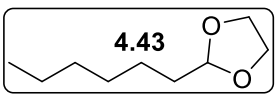
2-(1-Phenylethyl)-1,3-dioxolane (4.41). Starting from 106 mL of **4.4** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by flash silica gel filtration (neat cyclohexane as eluant) and 104.0 mg of **4.41** were obtained (>99% yield, slightly yellow oil). The same reaction performed under continuous flow conditions (1 h), starting from 268 mL of **4.4** (2 mmol, 0.5 M), 113 mL of ethylene glycol (2 mmol, 1.0 equiv) and 18.6 mg of **4.1a** (0.1 mmol, 5 mol%) in 4 mL of dimethyl carbonate gave 356 mg of product **4.41** (>99% yield). Spectroscopic data were in accordance with the literature [4.21].

4.41. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.45–7.15 (m, 5H), 4.96 (d, J = 4.5 Hz, 1H), 3.88–3.74 (m, 4H), 3.02 (qd, J = 7.1, 4.5 Hz, 1H), 1.34 (d, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 143.7, 129.4, 129.1, 127.4, 108.0, 66.0, 65.8, 44.8, 16.3.



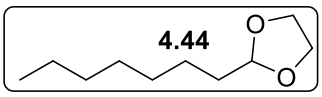
2-Pentyl-1,3-dioxolane (4.42). Starting from 98 mL of **4.5** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 3 mg of **4.1a** (0.016 mmol, 2 mol%). The compound was purified by flash silica gel filtration (neat cyclohexane as eluant) and 115.2 mg of **4.42** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.22].

4.42. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 4.78 (t, J = 4.8 Hz, 1H), 3.97–3.76 (m, 4H), 1.59 (td, J = 8.8, 7.9, 3.0 Hz, 2H), 1.43–1.29 (m, 6H), 0.92–0.84 (m, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 105.4, 65.7, 35.1, 32.9, 24.9, 23.6, 14.6.



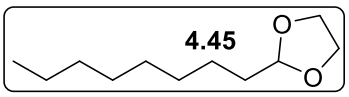
2-Hexyl-1,3-dioxolane (4.43). Starting from 112 mL of **4.6** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 3 mg of **4.1a** (0.016 mmol, 2 mol%). The compound was purified by flash silica gel filtration (neat cyclohexane as eluant) and 127.0 mg of **4.43** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.43. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.84 (t, J = 4.6 Hz, 1H), 3.97–3.82 (m, 4H), 1.63 (m, J = 8.7, 4.9 Hz, 2H), 1.28 (m, 8H), 0.87 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 104.6, 64.7, 33.8, 31.6, 29.1, 23.9, 22.4, 13.9.



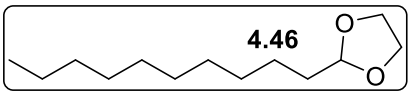
2-Heptyl-1,3-dioxolane (4.44). Starting from 125 mL of **4.7** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 3 mg of **4.1a** (0.016 mmol, 2 mol%). The compound was purified by flash silica gel filtration (neat cyclohexane as eluant) and 140.0 mg of **4.44** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.44. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82 (t, *J* = 4.8 Hz, 1H), 3.96–3.79 (m, 4H), 1.61 (dd, *J* = 8.7, 4.8 Hz, 2H), 1.38–1.24 (m, 10H), 0.88–0.83 (m, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 104.9, 64.9, 34.1, 31.9, 29.6, 29.3, 24.2, 22.7, 14.1.



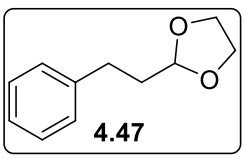
2-Octyl-1,3-dioxolane (4.45). Starting from 137 mL of **4.8** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 3 mg of **4.1a** (0.016 mmol, 2 mol%). The compound was purified by flash silica gel filtration (neat cyclohexane as eluant) and 131.0 mg of **4.45** were obtained (88% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.45. ^{1}H NMR (300 MHz, $CDCOCD_3$) δ 4.78 (t, *J* = 4.8 Hz, 1H), 3.93–3.77 (m, 4H), 1.63–1.57 (m, 2H), 1.32 (m, *J* = 5.7 Hz, 12H), 0.89 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCOCD_3$) δ 105.3, 65.6, 35.0, 30.5, 30.5, 30.2, 25.1, 23.6, 14.6.



2-Decyl-1,3-dioxolane (4.46). Starting from 165 mL of **4.9** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 3 mg of **4.1a** (0.016 mmol, 2 mol%). The compound was purified by flash silica gel filtration (neat cyclohexane as eluant) and 172.3 mg of **4.46** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.23].

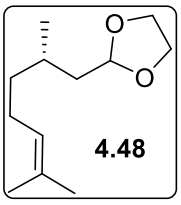
4.46. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.84 (t, *J* = 4.8 Hz, 1H), 3.98–3.82 (m, 4H), 1.65 (m, *J* = 7.7, 3.0 Hz, 2H), 1.27 (m, *J* = 5.4 Hz, 16H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 104.6, 64.7, 33.8, 31.8, 3.5, 29.4, 29.4, 29.2, 24.0, 22.5, 14.0.



2-Phenethyl-1,3-dioxolane (4.47). Starting from 104 mL of **4.10** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The products were purified by silica gel chromatography (neat cyclohexane as eluant) to afford 142.4 mg of **4.47** (>99% yield, slightly yellow oil). The same reaction performed under flow conditions with 258 mL of **4.10** (2 mmol, 0.5 M) and 113 mL of ethylene glycol (2 mmol, 1.0 equiv) and 18.6 mg of **4.1a** (0.1 mmol, 5

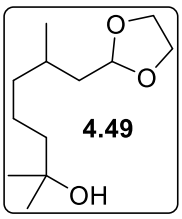
mol%) in 4 mL of dimethyl carbonate (DMC) gave 350.6 mg of product **4.47** (99% yield) in one hour. Spectroscopic data were in accordance with the literature [4.9c]. The reaction was repeated on a 3.6 mmol scale (8 mL of DMC, 0.45 M, 2 h irradiation time) to give **4.47** in >99% yield.

4.47. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.31–7.18 (m, 5H), 4.84 (t, *J* = 4.8 Hz, 1H), 3.98–3.80 (m, 4H), 2.77–2.71 (m, 2H), 1.94–1.84 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 143.1, 129.6, 129.5, 127.0, 104.7, 65.9, 37.0, 31.3.



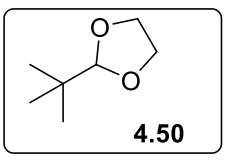
2-(2,6-Dimethylhept-5-en-1-yl)-1,3-dioxolane (4.48). Starting from 144 mL of **4.11** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The products were purified by silica gel chromatography (neat cyclohexane as eluant) to afford 158.5 mg of **4.48** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.23].

4.48. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 5.12 (m, 1H), 4.85 (t, *J* = 5.0 Hz, 1H), 3.92–3.76 (m, 4H), 2.09–1.98 (m, 2H), 1.67 (d, *J* = 1.4 Hz, 3H), 1.61 (d, *J* = 1.5 Hz, 3H), 1.49 – 1.11 (m, 5H), 0.95 (d, *J* = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 131.7, 125.7, 104.4, 65.4, 65.3, 41.9, 38.4, 26.2, 26.1, 20.4, 17.9.

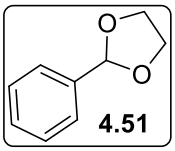


7-(1,3-Dioxolan-2-yl)-2,6-dimethylheptan-2-ol (4.49). Starting from 150 mL of **4.12** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The products were purified by silica gel chromatography (neat cyclohexane as eluant) to afford 158.5 mg of **4.49** were obtained (>99% yield, yellow oil). Spectroscopic data were in accordance with the literature [4.24].

4.49. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.86 (t, *J* = 5.0 Hz, 1H), 3.93–3.89 (m, 2H), 3.81–3.78 (m, 2H), 3.65 (s, 1H), 1.80–1.53 (m, 3H), 1.40–1.29 (m, 6H), 1.17 (s, 6H), 0.92 (d, *J* = 2.8 Hz, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 103.6, 71.0, 64.5, 43.8, 40.7, 37.6, 30.0, 28.9, 21.4, 19.7.

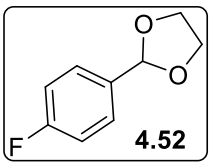


Irradiation of pivaldehyde (4.13) in the presence of ethylene glycol. Starting from 86 mL of **4.13** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). No traces of the desired product **4.50** was observed. Unreacted **4.13** was completely recovered after the irradiation.



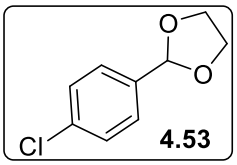
2-Phenyl-1,3-dioxolane (4.51). Starting from 81 mL of **4.14** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The products were purified by silica gel chromatography (neat cyclohexane as eluant) to afford 105.7 mg of **4.51** were obtained (88% yield, slightly yellow oil). The same reaction performed under flow conditions (1 h) starting from 203 mL of **4.14** (2 mmol, 0.5 M), 170 mL of ethylene glycol (2 mmol, 1.0 equiv) and 18.6 mg of **4.1a** (0.1 mmol, 5 mol%) in 4 mL of dimethyl carbonate (DMC) gave 238.5 mg of product **4.51** (98% yield). Spectroscopic data were in accordance with the literature [4.22].

4.51. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.41 (m, 2H), 7.35–7.29 (m, 3H), 5.67 (s, 1H), 4.03–3.90 (m, 4H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 139.7, 129.9, 129.0, 127.6, 104.4, 66.0.



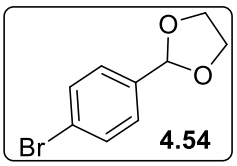
2-(4-Fluorophenyl)-1,3-dioxolane (4.52). Starting from 84 mL of **4.15** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 138.5 mg of **4.52** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.25].

4.52. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.55–7.45 (m, 2H), 7.21–7.12 (m, 2H), 5.75 (s, 1H), 4.11–3.95 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 165.7–162.4 (d, J = 247 Hz), 133.2–133.1(d, J = 7.5 Hz), 129.7–129.6 (d, J = 7.5 Hz), 115.9–115.7 (d, J = 15.0 Hz), 103.7, 66.0.



2-(4-Chlorophenyl)-1,3-dioxolane (4.53). Starting from 100 mL of **4.16** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 94.7 mg of **4.53** were obtained (64% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.22].

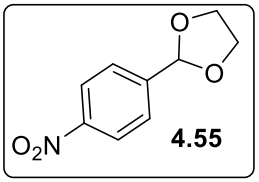
4.53. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.58–7.41 (m, 4H), 5.75 (s, 1H), 4.12–3.99 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 131.9, 130.3, 129.3, 129.2, 103.6, 66.1.



2-(4-Bromophenyl)-1,3-dioxolane (4.54). Starting from 148.0 mg of **4.17** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and

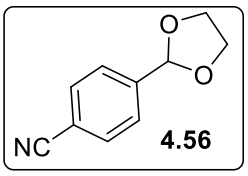
101.4 mg of **4.54** were obtained (71% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature. [4.22].

4.54. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.57 (m, 2H), 7.43 (m, 2H), 5.74 (d, *J* = 2.2 Hz, 1H), 4.12–3.97 (m, 4H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 139.4, 132.4, 129.9, 123.7, 103.9, 66.3.



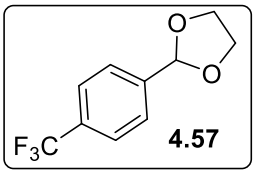
2-(4-Nitrophenyl)-1,3-dioxolane (4.55). Starting from 120.9 mg of **4.18** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 156.1 mg of **4.55** were obtained (>99% yield, yellow solid, m.p. = 89–91 °C [4.26]). Spectroscopic data were in accordance with the literature [4.22].

4.55. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 8.29–8.23 (d, *J* = 8.8 Hz, 2H), 7.78–7.72 (d, *J* = 8.8 Hz, 2H), 5.89 (s, 1H), 4.15–4.04 (m, 4H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 149.4, 146.6, 128.6, 124.3, 103.0, 66.2.



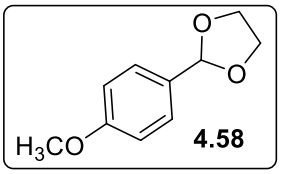
2-(4-Cyanophenyl)-1,3-dioxolane (4.56). Starting from 105.0 mg of **4.19** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 123.9 mg of **4.56** were obtained (89% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.27].

4.56. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.87–7.75 (m, 2H), 7.69–7.61 (m, 2H), 5.84 (s, 1H), 4.15–4.02 (m, 4H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 144.7, 133.0, 128.4, 119.2, 113.5, 103.2, 66.2.



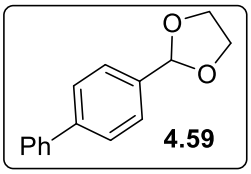
2-(4-(Trifluoromethyl)phenyl)-1,3-dioxolane (4.57). Starting from 109 mL of **4.20** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 173.9 mg of **4.57** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.25].

4.57. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61–7.52 (m, 4H), 5.80 (s, 1H), 4.06–3.97 (m, 4H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 142.1, 131.6 (q, *J* = 30.0 Hz), 125.5 (q, *J*= 4.0 Hz), 122.4 (q, *J* = 274 Hz), 102.9, 65.5.



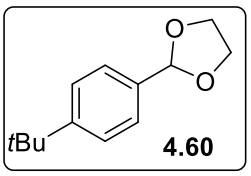
2-(4-Methoxyphenyl)-1,3-dioxolane (4.58). Starting from 97 mL of **4.21** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 142.6 mg of **4.58** were obtained (99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.25].

4.58. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.48–7.30 (d, *J* = 8.3 Hz, 2H), 7.01–6.91 (d, *J* = 8.3 Hz, 2H), 5.68 (s, 1H), 4.2 –4.05 (m, 2H), 3.98–3.94 (m, 2H), 3.80 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 161.3, 131.2, 128.9, 114.3, 104.3, 65.8, 56.1.



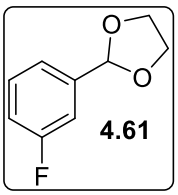
2-([1,1'-Biphenyl]-4-yl)-1,3-dioxolane (4.59). Starting from 146.0 mg of **4.22** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 117.4 mg of **4.59** were obtained (65% yield, slightly yellow solid, m.p. = 62-64 °C [4.28]). Spectroscopic data were in accordance with the literature. [4.29]

4.59. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.70–7.67 (d, 4H), 7.60–7.56 (m, 2H), 7.51–7.45 (m, 2H), 7.41–7.36 (m, 1H), 5.81 (s, 1H), 4.13–4.01 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 142.9, 141.8, 139.1, 130.1, 128.7, 128.4, 128.2, 127.9, 104.5, 66.3.



2-(4-(*tert*-Butyl)phenyl)-1,3-dioxolane (4.60). Starting from 138.0 mL of **4.23** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 82.4 mg of **4.60** were obtained (50% yield, colourless liquid). Spectroscopic data were in accordance with the literature [4.29].

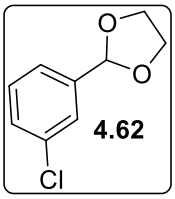
4.60. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (m, 4H), 5.83 (s, 1H), 4.21–4.03 (m, 4H), 1.35 (s, 9H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 152.1, 134.8, 126.0, 125.2, 103.6, 65.2, 34.5, 31.2.



2-(3-Fluorophenyl)-1,3-dioxolane (4.61). Starting from 83 mL of **4.24** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 131.9 mg of **4.24** were

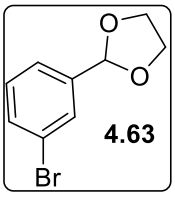
obtained (98% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.30].

4.61. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.44 (td, *J* = 7.9, 5.7 Hz, 1H), 7.35–7.28 (m, 1H), 7.24 (ddd, *J* = 9.8, 2.7, 1.5 Hz, 1H), 7.19–7.11 (m, 1H), 5.79 (s, 1H), 4.12–3.98 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 165.5–162.3 (d, *J* = 240.0 Hz), 143.0–142.9 (d, *J* = 7.5 Hz), 131.4–131.3 (d, *J* = 7.5 Hz), 123.8–123.7 (d, *J* = 7.5 Hz), 116.9–116.7 (d, *J* = 15.0 Hz), 114.5–114.2 (d, *J* = 22.5 Hz), 103.7, 66.3.



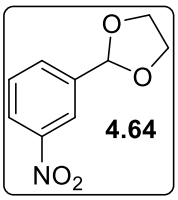
2-(3-Chlorophenyl)-1,3-dioxolane (4.62). Starting from 91 mL of **4.25** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 128.0 mg of **4.62** were obtained (87% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.62. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (t, *J* = 1.8 Hz, 1H), 7.40–7.31 (m, 3H), 5.81 (s, 1H), 4.14–4.03 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 140.2, 134.4, 129.8, 129.3, 126.7, 124.8, 102.9, 65.4.



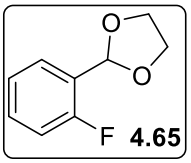
2-(3-Bromophenyl)-1,3-dioxolane (4.63). Starting from 94 mL of **4.26** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 184.0 mg of **4.63** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.63. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.65 (t, *J* = 6.0 Hz, 1H), 7.57 (m, 1H), 7.47 (m, 1H), 7.37 (d, *J* = 6.0 Hz, 1H), 5.76 (s, 1H), 4.24–3.83 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 142.5, 132.9, 131.3, 130.5, 126.6, 122.8, 103.4, 66.2.



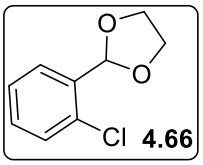
2-(3-Nitrophenyl)-1,3-dioxolane (4.64). Starting from 123.0 mg of **4.27** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 164.1 mg of **4.64** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.64. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 8.35–8.23 (m, 2H), 7.90 (m, 1H), 7.70 (t, *J* = 7.9 Hz, 1H), 5.90 (s, 1H), 4.17–4.04 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 149.3, 142.1, 133.9, 130.7, 124.7, 122.2, 102.9, 66.3.



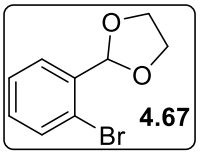
2-(2-Fluorophenyl)-1,3-dioxolane (4.65). Starting from 83 mL of **4.28** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 134.4 mg of **4.65** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.31].

4.65. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.58 (m, 1H), 7.43 (m, 1H), 7.23 (m, 1H), 7.15 (m, 1H), 6.04 (s, 1H), 4.15–4.00 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 163.7–160.4 (d, *J* = 247.5 Hz), 131.9–131.8 (d, *J* = 7.5 Hz), 129.0–128.9 (d, *J* = 7.5 Hz), 126.9–126.7 (d, *J* =15.0 Hz), 125.1–125.0 (d, *J* = 7.5 Hz), 116.4–116.2 (d, *J* =15.0 Hz), 99.4, 66.1.



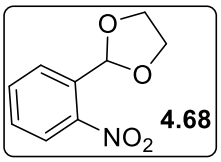
2-(2-Chlorophenyl)-1,3-dioxolane (4.66). Starting from 91 mL of **4.29** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 147.9 mg of **4.66** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.66. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.79–7.63 (m, 1H), 7.46–7.36 (m, 3H), 6.10 (s, 1H), 4.15–4.03 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 136.8, 134.2, 131.5, 130.5, 129.0, 128.0, 101.4, 66.2.



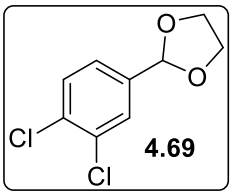
2-(2-Bromophenyl)-1,3-dioxolane (4.67). Starting from 94 mL of **4.30** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 135.1 mg of **4.67** were obtained (75% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.67. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (m, 2H), 7.36 (m, 1H), 7.28–7.21 (m, 1H), 6.13 (s, 1H), 4.18–4.08 (m, 4H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 136.6, 132.9, 130.5, 127.7, 127.3, 122.8, 102.5, 65.4.



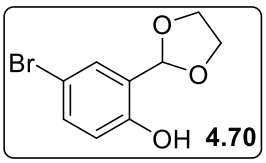
2-(2-Nitrophenyl)-1,3-dioxolane (4.68). Starting from 123.0 mg of **4.31** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 164.1 mg of **4.68** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.20].

4.68. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.58 (td, J = 7.5, 1.9 Hz, 1H), 7.43 (m, 1H), 7.23 (td, J = 7.5, 1.1 Hz, 1H), 7.15 (m, 1H), 6.04 (s, 1H), 4.15–4.00 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 133.9, 133.7, 130.8, 129.5, 128.5, 125.1, 100.2, 66.0.



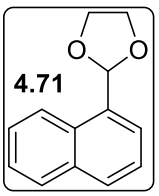
2-(3,4-Dichlorophenyl)-1,3-dioxolane (4.69). Starting from 140.0 mg of **4.32** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 107.3 mg of **4.69** were obtained (61% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.32].

4.69. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.68–7.58 (m, 2H), 7.48–7.42 (m, 1H), 5.78 (s, 1H), 4.12 – 4.00 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 140.9, 133.3, 132.8, 131.5, 129.6, 127.7, 102.9, 66.2.



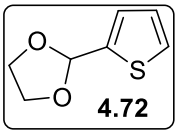
4-bromo-2-(1,3-dioxolan-2-yl)phenol (4.70). Starting from 160.0 mg of **4.33** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 146.0 mg of **4.70** were obtained (74% yield, slightly yellow oil).

4.70. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.39–7.36 (m, 1H), 6.79 (d, J = 8.6 Hz, 1H), 5.94 (s, 1H), 4.16–4.07 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 154.3, 133.3, 130.5, 123.0, 118.9, 111.7, 102.9, 64.8. HRMS (EI) m/z: $[M+H]^+$ calcd for $C_9H_9BrO_3$ 244.9808, found 244.9802.



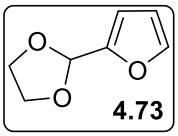
2-(naphthalen-1-yl)-1,3-dioxolane (4.71). Starting from 109 mL of **4.34** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 114.0 mg of **4.71** were obtained (71% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.30].

4.71. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 8.40–8.27 (m, 1H), 8.03–7.90 (m, 2H), 7.79 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.58–7.42 (m, 3H), 6.43 (s, 1H), 4.21–4.10 (m, 4H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 134.9, 134.7, 132.2, 130.3, 129.4, 127.0, 126.7, 126.0, 125.5, 124.7, 103.0, 66.0.



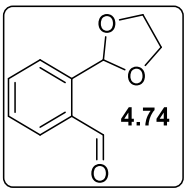
2-(thiophen-2-yl)-1,3-dioxolane (4.72). Starting from 75 mL of **4.35** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 97.3 mg of **4.72** were obtained (78% yield, yellow oil). Small traces of impurities were detected that could be attributed to the slow decomposition of compound **36**. Spectroscopic data were in accordance with the literature [4.32].

4.72. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.19 (dd, *J* = 3.5, 1.2 Hz, 1H), 7.02 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.15 (s, 1H), 4.17–4.03 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 141.8, 126.5, 126.2, 126.1, 77.3, 65.1.



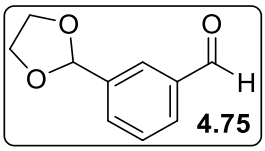
2-(Furan-2-yl)-1,3-dioxolane (4.73). Starting from 66 mL of **4.36** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 91.8 mg of **4.73** were obtained (82% yield, yellow oil). Spectroscopic data were in accordance with the literature [4.30].

4.73. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.61–6.43 (m, 1H), 6.37 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.94 (s, 1H), 4.16–4.00 (m, 4H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 151.2, 143.3, 110.3, 108.8, 97.9, 65.3.



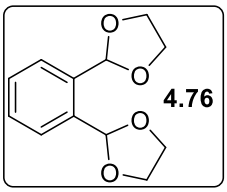
2-(1,3-Dioxolan-2-yl)benzaldehyde (4.74). Starting from 107.2 mg of **4.37** (0.8 mmol, 0.1 M) and 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%) gave 126.8 mg of product **4.74** (89% yield, colourless oil). Spectroscopic data were in accordance with the literature [4.33].

4.74.^{1}H NMR (300 MHz, $CDCl_3$) δ 10.43 (s, 1H), 7.95 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.75 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.63 (td, *J* = 7.5, 1.5 Hz, 1H), 7.54 (td, *J* = 7.5, 1.4 Hz, 1H), 6.43 (s, 1H), 4.24–4.10 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 191.7, 139.0, 134.4, 133.5, 130.0, 129.3, 126.9, 101.0, 65.3.



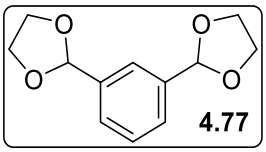
3-(1,3-Dioxolan-2-yl)benzaldehyde (4.75). Starting from 107.2 mg of **4.38** (0.8 mmol, 0.1 M) and 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 48 mg (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%) gave 131.0 mg of product **4.75** (92% yield, colourless oil). Spectroscopic data were in accordance with the literature [4.34].

4.75. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.99 (t, *J* = 1.7 Hz, 1H), 7.87 (dt, *J* = 7.6, 1.5 Hz, 1H), 7.73 (ddd, *J* = 7.7, 3.8, 2.3 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 5.86 (s, 1H), 4.14–4.01 (m, 4H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 192.0, 139.2, 136.4, 134.5, 132.5, 130.1, 129.0, 102.7, 65.3.



1,2-di(1,3-Dioxolan-2-yl)benzene (4.76). Starting from 107.2 mg of **4.37** (0.8 mmol, 0.1 M), 124 mL of ethylene glycol (1.76 mmol, 2.2 equiv), 96 mg of $MgSO_4$ (0.8 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The products were purified by silica gel chromatography (neat cyclohexane as eluant) and 106.8 mg of **4.76** were obtained (75% yield, slightly yellow oil); traces of **4.74** (< 2% yield) were detected by GC analyses. Spectroscopic data of **4.76** were in accordance with the literature [4.35].

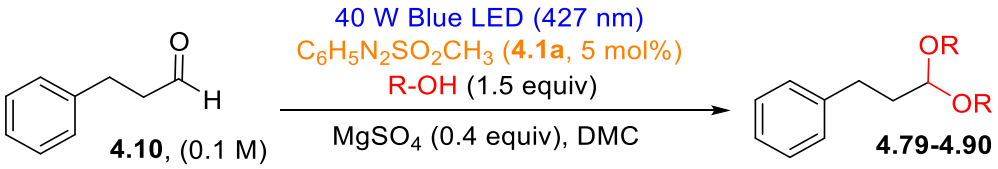
4.76. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 5.7, 3.4 Hz, 2H), 7.40 (dd, *J* = 5.8, 3.4 Hz, 2H), 6.25 (s, 2H), 4.17–4.04 (m, 8H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 136.0, 128.9, 125.9, 100.7, 100.6, 65.2.



1,2-di(1,3-Dioxolan-2-yl)benzene (4.77). Starting from 107.2 mg of **4.38** (0.8 mmol, 0.1 M) and 124 mL of ethylene glycol (1.76 mmol, 2.2 equiv), 96 mg of $MgSO_4$ (0.8 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The products were purified by silica gel chromatography (neat cyclohexane as eluant) and 99.7 mg of **4.77** were obtained (70% yield, colourless oil), traces of 1,3-di(1,3-dioxolan-2-yl)benzene (**4.75**) were detected by GC analyses. Spectroscopic data of **4.77** were in accordance with the literature [4.35].

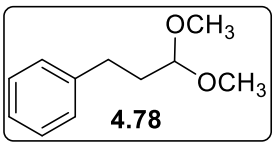
4.77.^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 1.9 Hz, 1H), 7.46–7.38 (m, 2H), 7.36–7.30 (m, 1H), 5.76 (s, 2H), 4.07–3.93 (m, 8H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 138.2, 128.3, 127.1, 124.5, 103.4, 65.1.

General procedure for the visible-light mediated protection of 4.10 as acetals 4.79-4.90.



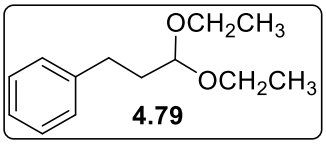
Scheme 4.6. Photochemical protection of aldehyde **4.10** as different acetals through arylazo sulfones as PAG.

A Pyrex glass vessel was charged with aldehyde **4.10** (0.8 mmol, 1 equiv, 0.1 M), the alcohol (1.5 equiv), a catalytic amount of arylazo sulfone **4.1a** (0.040 mmol, 5 mol%) and 48 mg of $MgSO_4$ (0.4 mmol) in 8 mL of dimethyl carbonate (DMC) and the mixture was irradiated for 2 h. Compounds **4.79-4.90** were purified by silica gel column chromatography (cyclohexane-ethyl acetate mixture as eluant).



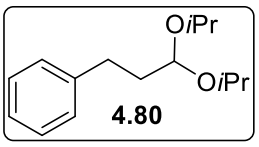
(3,3-Dimethoxypropyl)benzene (4.78). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 97 mL of methanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 149.0 mg of **4.78** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.9c].

4.78. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.27–7.18 (m, 5H), 4.36 (t, J = 5.7 Hz, 1H), 3.29 (s, 6H), 2.68–2.63 (m, 2H), 1.92–1.86 (m, 2H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 143.2, 129.6, 129.6, 127.0, 104.9, 53.2, 35.6, 31.9.



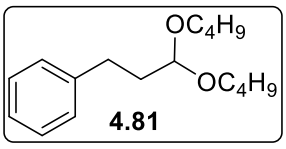
(3,3-Diethoxypropyl)benzene (4.79). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 140 mL of ethanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 167.0 mg of **4.79** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.9c].

4.79. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.27–7.10 (m, 5H), 4.50 (t, J = 5.7 Hz, 1H), 3.65 (dq, J = 9.5, 7.1 Hz, 2H), 3.49 (dq, J = 9.5, 7.0 Hz, 2H), 2.72–2.65 (m, 2H), 1.93–1.83 (m, 2H), 1.18 (t, J = 7.0 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 143.2, 129.4, 129.4, 126.8, 103.1, 61.7, 36.5, 32.0, 16.0.



(3,3-Diisopropoxypropyl)benzene (4.80). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 184 mL of isopropyl alcohol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 189.0 mg of **4.80** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.9c].

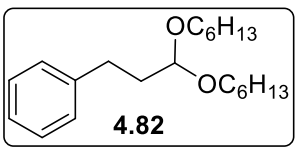
4.80. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.22 (m, 5H), 4.61 (t, *J* = 5.5 Hz, 1H), 3.91 (m, *J* = 12.3, Hz, 2H), 2.80–2.70 (m, 2H), 2.01–1.86 (m, 2H), 1.25 (d, *J* = 6.2 Hz, 6H), 1.19 (d, *J* = 6.1 Hz, 6H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.1, 128.5, 128.4, 125.4, 99.8, 67.9, 37.1, 31.2, 23.6, 22.7.



(3,3-Dibutoxypropyl)benzene (4.81). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 219 mL of 1-butanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 211.4 mg of **4.81** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.9c].

4.81. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.22 (m, 5H), 4.53 (t, *J* = 5.7 Hz, 1H), 3.64 (dt, *J* = 9.3, 6.5 Hz, 2H), 3.47 (dt, *J* = 9.3, 6.5 Hz, 2H), 2.77–2.69 (m, 2H), 2.07–1.95 (m, 2H), 1.66–1.57 (m, 4H), 1.45 (m, 4H), 0.98 (t, *J* = 7.3 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.3, 128.9, 128.8, 126.3, 102.9, 65.8, 35.5, 32.5, 31.6, 20.0, 14.4.

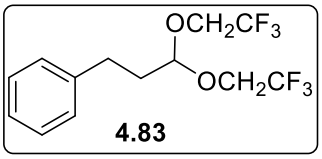
Reaction between 1i and *tert*-butanol. Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M) and 285 mL of *tert*-butanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **3.1** (0.04 mmol, 5 mol%). The reaction did not proceed and **4.10** was almost completely recovered (>99%).



(3,3-bis(Hexyloxy)propyl)benzene (4.82). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 301 mL of 1-hexanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 266.1 mg of **4.82** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.9c].

4.82. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.21–7.07 (m, 5H), 4.41 (t, *J* = 5.7 Hz, 1H), 3.52 (dt, *J* = 9.4, 6.4 Hz, 2H), 3.35 (dt, *J* = 9.3, 6.4 Hz, 2H), 2.66–2.56 (m, 2H), 1.87–1.74 (m, 2H), 1.54–1.45 (m,

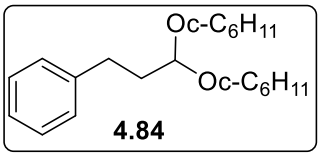
4H), 1.34–1.18 (m, 12H), 0.87–0.80 (m, 6H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 143.3, 129.6, 129.5, 127.0, 103.4, 66.5, 36.6, 32.9, 32.2, 31.2, 31.1, 27.2, 23.8, 14.9.



4.83

(3,3-bis(2,2,2-Trifluoroethoxy)propyl)benzene (4.83). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M) and 175 mL of 2,2,2-trifluoroethanol (2.4 mmol, 1.5 equiv) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 252.8 mg of **4.83** were obtained (>99% yield, colourless oil). Spectroscopic data were in accordance with the literature [4.9c].

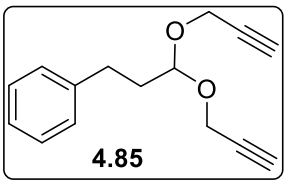
4.83. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41–7.17 (m, 5H), 4.78 (t, *J* = 5.9 Hz, 1H), 3.92 (q, *J* = 8.6 Hz, 4H), 2.78–2.71 (m, 2H), 2.07–1.99 (m, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 140.1, 128.5, 128.2, 129.2–118.1, (q, *J*=277.5 Hz,), 102.4, 62.8–61.4 (q, *J*=35.3 Hz,), 33.8, 30.3.



4.84

((3-Phenylpropane-1,1-diyl)bis(oxy))dicyclohexane (**4.84**). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 254 mL of cyclohexanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 267.3 mg of **4.84** were obtained (>99% yield, slightly yellow oil). Spectroscopic data were in accordance with the literature [4.9c].

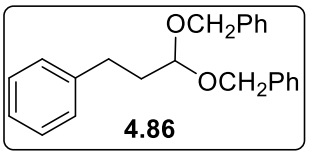
4.84. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–6.72 (m, 5H), 4.71 (m, 1H), 4.02 (t, *J* = 6.6 Hz, 1H), 3.78–3.27 (t, *J* = 6.6 Hz, 1H), 2.33–2.21 (m, 2H), 1.82–1.77 (m, 2H), 1.68–1.26 (m, 20H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 140.3, 128.2, 128.1, 128.0, 126.2, 102.3, 72.3, 34.1, 31.5, 28.2, 25.2, 23.5.



4.85

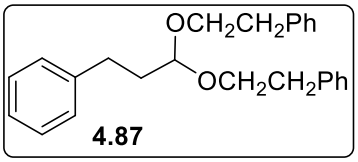
(3,3-bis(Prop-2-yn-1-yloxy)propyl)benzene (4.85). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 140 mL of propargyl alcohol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 180.5 mg of **4.85** were obtained (99% yield, colourless). Spectroscopic data were in accordance with the literature [4.9c].

4.85. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.30–7.24 (m, 5H), 4.84 (t, *J* = 5.6 Hz, 1H), 4.29 (dd, *J* = 2.5, 1.1 Hz, 4H), 2.97–2.95 (t, *J* = 3.0 Hz, 2H), 2.76–2.69 (m, 2H), 2.04–1.96 (m, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3COCD_3) δ 142.9, 130.4, 129.6, 127.1, 102.2, 81.3, 76.1, 54.2, 36.4, 31.7.



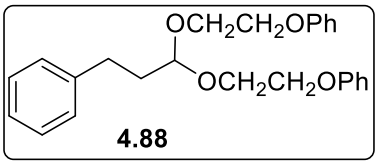
(((3-Phenylpropane-1,1-diyl)bis(oxy))bis(methylene))dibenzene (4.86). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 248 mL of benzyl alcohol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 265.8 mg of **4.86** were obtained (99% yield, colourless oil). Spectroscopic data were in accordance with the literature [4.36].

4.86. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.41–7.21 (m, 15H), 4.81 (t, *J* = 5.6 Hz, 1H), 4.74 (d, *J* = 11.9 Hz, 2H), 4.61 (d, *J* = 11.9 Hz, 2H), 2.84–2.72 (m, 2H), 2.10–1.94 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 142.9, 139.9, 129.4, 129.3, 129.2, 128.7, 128.4, 126.8, 102.3, 68.3, 36.3, 31.8.



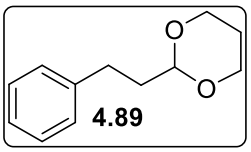
(((3-Phenylpropane-1,1-diyl)bis(oxy))bis(ethane-2,1-diyl))dibenzene (4.87). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 287nmL of 2-phenylethanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 224.8 mg of **4.87** were obtained (78% yield, slightly yellow oil).

4.87. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.29–7.18 (m, 15H), 4.48 (t, *J* = 5.7 Hz, 1H), 3.74 (dt, *J* = 9.2, 6.8 Hz, 2H), 3.65–3.55 (m, 2H), 2.96 (td, *J* = 6.9, 4.0 Hz, 2H), 2.84–2.79 (m, 4H), 2.64–2.52 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 143.2, 140.8, 130.3, 129.6, 129.5, 129.4, 129.4, 127.5, 127.3, 103.5, 67.5, 37.5, 36.3, 31.9. HRMS (EI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{28}O_2Na$ 383.1982, found 383.1979.



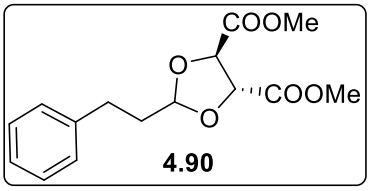
((((3-Phenylpropane-1,1-diyl)bis(oxy))bis(ethane-2,1-diyl))bis(oxy))dibenzene (4.88). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 300 mL of 2-phenoxyethanol (2.4 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 207.1 mg of **4.88** were obtained (66% yield, yellow oil).

4.88. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.35–7.18 (m, 10H), 6.98–6.88 (m, 5H), 4.73 (t, *J* = 5.8 Hz, 1H), 4.17 (t, *J* = 4.8 Hz, 4H), 4.08–3.87 (m, 4H), 2.74 (m, 2H), 2.09–1.91 (m, 2H). ^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 160.1, 142.9, 130.4, 129.3, 126.7, 126.6, 121.6, 115.5, 103.5, 68.3, 64.9, 36.0, 31.7. HRMS (EI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{28}O_4Na$ 415.1880, found 415.1872.



2-Phenethyl-1,3-dioxane (4.89). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 87 mL of 1,3-propandiol (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and153.7 mg of **4.89** were obtained (>99% yield, yellow oil). Spectroscopic data were in accordance with the literature [4.37].

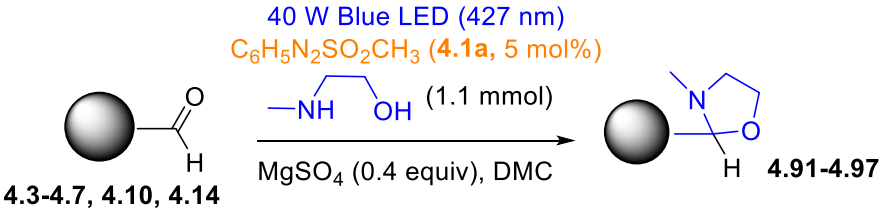
4.89. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.06 (m, 5H), 4.46 (t, J = 5.2 Hz, 1H), 4.07 (ddd, J = 11.9, 5.0, 1.4 Hz, 2H), 3.78–3.64 (m, 2H), 2.80–2.65 (m, 2H), 2.14–1.98 (m, 1H), 1.95–1.79 (m, 2H), 1.38–1.25 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 141.6, 128.4, 128.3, 125.7, 101.4, 66.8, 36.5, 30.0, 25.8.



Dimethyl (*4S,5R*)-2-benzyl-1,3-dioxolane-4,5-dicarboxylate (4.90). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 205 mL of dimethyl (*2S,3S*)-2,3-dihydroxysuccinate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The compound was purified by silica gel chromatography (neat cyclohexane as eluant) and 199.4 mg of **4.90** were obtained (89% yield, colourless liquid). Spectroscopic data were in accordance with the literature [4.38].

4.90. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.25 (m, 5H), 5.31 (t, J = 4.7 Hz, 1H), 4.84 (t, J = 3.2 Hz, 1H), 4.75 (d, J = 4.0 Hz, 1H), 3.85 (d, J = 1.7 Hz, 6H), 2.86–2.80 (m, 2H), 2.17–2.01 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.1, 169.4, 141.0, 128.3, 125.9, 106.8, 52.7, 52.6, 35.0, 29.7.

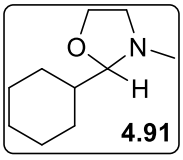
General procedure for the visible-light mediated synthesis of 1,3-oxazolidines 4.91-4.97.



Scheme 4.7. Photochemical protection of aldehydes as 1,3-oxazolidines through arylazo sulfones as PAG.

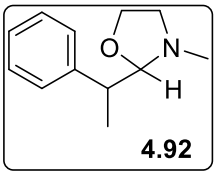
A Pyrex glass vessel was charged with the chosen aldehyde (0.8 mmol, 1 equiv, 0.1 M), *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv, 0.11 M), a catalytic amount of arylazo sulfone **4.1a** (0.040 mmol, 5 mol%) and 48 mg of $MgSO_4$ (0.4 mmol) in 8 mL of dimethyl carbonate (DMC) and the mixture was irradiated for 2 h. The photolyzed mixture was filtrated over basic aluminium oxide and,

after solvent removal, oxazolidines **4.91-4.97**were isolated as colourless oils without further purifications.



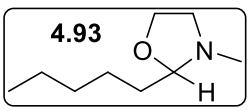
2-Cyclohexyl-3-methyloxazolidine (4.91). Starting from 97 mL of **4.3** (0.8 mmol, 0.1 M), 71 mL of *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The photolyzed mixture was filtrated over basic aluminium oxide and 135.2 mg of product **4.91** were obtained (>99% yield, colourless oil) without further purifications.

4.91. ^{1}H NMR (300 MHz, CD_3CN) δ 3.83–3.58 (m, 3H), 3.07 (ddd, *J* = 9.7, 6.3, 4.5 Hz, 1H), 2.56 (dt, *J* = 8.8, 6.9 Hz, 1H), 2.30 (s, 3H), 1.97 (m, *J* = 2.5 Hz, 1H), 1.80–1.67 (m, 4H), 1.43–1.07 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, CD_3CN) δ 102.3, 64.2, 41.7, 40.6, 30.2, 27.7, 27.5, 27.2, 26.9. HRMS (EI) m/z: $[M+H]^+$ calcd for $C_{10}H_{20}NO$ 170.1545, found 170.1536.



3-Methyl-2-(1-phenylethyl)oxazolidine (4.92). Starting from 106 mL of **4.4** (0.8 mmol, 0.1 M), 71 mL of *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The photolyzed mixture was filtrated over basic aluminium oxide and 152.8 mg of product **4.92** were obtained (>99% yield, colourless liquid) without further purifications. The product was obtained as a diastereomeric mixture (dr 0.8:1). The spectroscopic data were in accordance with the literature [4.39].

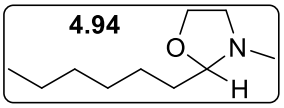
4.92. ^{1}H NMR (300 MHz, CD_3CN) δ 7.37–7.31 (m, 5H), 4.11 (d, *J* = 5.1 Hz, 0.8 H), 3.98 (d, *J* = 4.2 Hz, 1H), 3.89–3.54 (m, 5H), 3.14 (m, 2H), 3.07–2.83 (m, 4H), 2.67–2.49 (m, 2H), 2.41–2.32 (m, 3H), 2.28 (s, 3H), 1.36 (d, *J*=7.2 Hz, 2.4 H), 1.32 (d, *J*=7.0 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, CD_3CN) δ 145.5, 144.7, 129.5, 129.2, 129.1, 128.8, 127.1, 127.0, 102.6, 101.9, 65.5, 64.8, 55.5, 55.3, 43.8, 43.5, 41.1, 40.3, 18.3, 15.7.



3-Methyl-2-pentyloxazolidine (4.93). Starting from 98 mL of **4.5** (0.8 mmol, 0.1 M), 71 mL of *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a**(0.04 mmol, 5 mol%). The photolyzed mixture was filtrated over basic aluminium oxide and 126.0 mg of product **4.93** were obtained (>99% yield, colourless liquid) without further purifications.

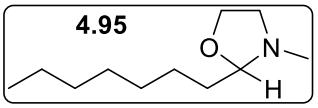
4.93. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85–3.65 (m, 3H), 3.15–3.10 (m, 1H), 3.00–2.81 (m, 1H), 2.64–2.39 (m, 2H), 2.28 (d, *J* = 2.1 Hz, 3H), 2.1–1.70 (m, 2H), 1.35–1.26 (m, 6H), 0.92–0.89 (m,

3H).$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 98.1, 64.7, 55.6, 39.3, 32.9, 25.2, 23.6, 14.5. HRMS (EI) m/z: $[M+H]^+$ calcd for $C_9H_{20}NO$ 158.1545, found 158.1542.



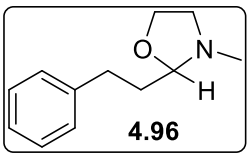
2-Hexyl-3-methyloxazolidine (4.94). Starting from 112 mL of **4.6** (0.8 mmol, 0.1 M), 71 mL of *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The photolyzed mixture was filtrated over basic aluminium oxide and 136.0 mg of product **4.94** were obtained (>99% yield, colourless liquid) without further purifications. The spectroscopic data were in accordance with the literature [4.40].

4.94. ^1H NMR (300 MHz, $CDCl_3$) δ 3.77–3.72 (m, 3H), 2.90 (t, J = 6.4 Hz, 2H), 2.28 (s, 3H), 1.35–1.31 (m, 10H), 0.89–0.87 (m, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 98.1, 63.6, 53.4, 36.0, 32.4, 29.5, 29.1, 28.8, 23.3, 14.4.



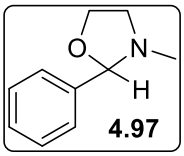
2-Heptyl-3-methyloxazolidine (4.95). Starting from 125 mL of **4.7** (0.8 mmol, 0.1 M), 71 mL of *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The photolyzed mixture was filtrated over basic aluminium oxide and 147.7.0 mg of product **4.95** were obtained (>99% yield, colourless liquid) without further purifications. The spectroscopic data were in accordance with the literature [4.41].

4.95. ^1H NMR (300 MHz, CD_3COCD_3) δ 3.88–3.62 (m, 3H), 3.30–2.97 (m, 1H), 2.51 (dt, J = 9.4, 8.0 Hz, 1H), 2.29 (s, 3H), 1.41–1.32 (m, 12H), 0.93–0.85 (m, 3H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 98.6, 65.2, 56.1, 39.8, 34.7, 33.3, 30.8, 26.2, 24.0, 15.1.



3-Methyl-2-phenethyloxazolidine (4.96). Starting from 106 mL of **4.10** (0.8 mmol, 0.1 M), 71 mL of *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The photolyzed mixture was filtrated over basic aluminium oxide and 152.8 mg of product **4.96** were obtained (>99% yield, colourless liquid) without further purifications.

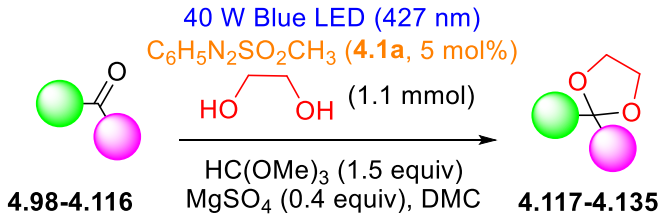
4.96. ^1H NMR (300 MHz, CD_3CN) δ 7.42–7.28 (m, 5H), 3.97–3.86 (m, 3H), 3.21 (dd, J = 9.8, 5.0 Hz, 1H), 3.01–2.71 (m, 3H), 2.64–2.57 (m, 1H), 2.38 (s, 3H), 2.03–1.93 (m, 1H), 1.90–1.80 (m, 1H).$^{13}C\{^1H\}$ NMR (75 MHz, CD_3CN) δ 143.5, 129.4, 126.7, 97.5, 64.9, 55.4, 39.5, 36.0, 31.8. HRMS (EI) m/z: $[M+H]^+$ calcd for $C_{12}H_{18}NO$ 192.1388, found 192.1378.



3-methyl-2-phenyloxazolidine (4.97) starting from 81 mL of **4.14** (0.8 mmol, 0.1 M), 71 mL of *N*-methyl aminoethanol (0.88 mmol, 1.1 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). The photolyzed mixture was filtrated over basic aluminium oxide and 113.5 mg of product **4.97** were obtained (87% yield, colourless liquid) without further purifications. The spectroscopic data were in accordance with the literature [4.41].

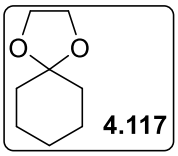
4.97. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.51–7.43 (m, 2H), 7.35 (m, 3H), 4.61 (s, 1H), 4.02–3.93 (m, 2H), 2.89 (t, *J* = 6.5 Hz, 1H), 2.70–2.59 (m, 1H), 2.23 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 135.6, 129.7, 129.2, 129.0, 99.4, 65.1, 55.7, 38.8

General procedure for the visible-light mediated protection of ketones.



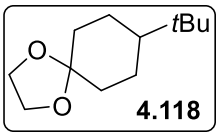
Scheme 4.8. Photochemical protection of ketones as 1,3-dioxolanes through arylazo sulfones as PAG.

A Pyrex glass vessel was charged with the chosen ketone **4.98-4.116** (0.8 mmol, 1 equiv, 0.1 M), ethylene glycol (0.88 mmol, 1.1 equiv, 0.11 M), trimethyl orthoformate (1,2 mmol, 1.5 equiv, 0.15 M), **4.1a** (0.040 mmol, 5 mol%) and 48 mg of $MgSO_4$ (0.4 mmol) in 8 mL of dimethyl carbonate (DMC). The mixture was irradiated for 1 h and the photolyzed mixture was treated with 10 mL of EtOAc and 5 mL of distilled water. The organic phase was dried, and the solvent was removed under reduced pressure affording the protected ketones **4.117-4.135** without further purifications needed.



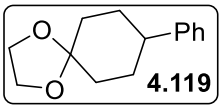
1,4-Dioxaspiro[4.5]decane (4.117). Starting from 83 mL of **4.98** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 113.6 mg of **4.117** (>99% yield, slightly red oil) have been collected. The spectroscopic data were in accordance with the literature [4.38].

4.117. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.88 (s, 4H), 1.57–1.54 (m, 8H), 1.36 (t, *J* = 4.7 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 108.9, 63.9, 35.0, 25.0, 23.8.



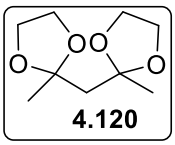
8-(*tert*-Butyl)-1,4-dioxaspiro[4.5]decane (4.118). Starting from 123.0 mg of **4.99** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 159.2 mg of **4.118** (>99% yield, colourless oil) have been collected. The spectroscopic data were in accordance with the literature [4.38].

4.118. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (s, 4H), 1.80–1.73 (m, 2H), 1.71–1.69 (m, 2H), 1.51–1.41 (m, 2H), 1.32–1.15 (m, 2H), 1.05–0.95 (m, 1H), 0.84 (s, 9H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 109.5, 64.6, 47.7, 35.7, 32.8, 28.2, 25.3.



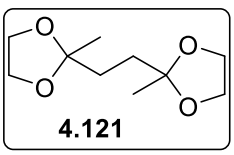
8-Phenyl-1,4-dioxaspiro[4.5]decane (4.119). Starting from 139.2 mg of **4.100** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 174.1 mg of **4.119** (>99% yield, colourless oil) have been collected. The spectroscopic data were in accordance with the literature [4.38].

4.119. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.05 (m, 5H), 4.01 (s, 4H), 2.66–2.56 (m, 1H), 2.11–1.70 (m, 8H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.5, 128.2, 126.8, 126.0, 108.4, 64.2, 43.3, 35.1, 31.5.



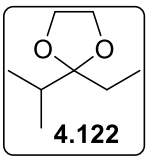
bis(2-Methyl-1,3-dioxolan-2-yl)methane (4.120). Starting from 82 mL of **4.101** (0.8 mmol, 0.1 M), 124 mL of ethylene glycol (1.76 mmol, 2.2 equiv), 262 mL of trimethyl orthoformate (2.4 mmol, 3.0 equiv), 96 mg of $MgSO_4$ (0.8 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 150.1 mg of **4.120** (>99% yield, colourless oil) have been collected. The spectroscopic data were in accordance with the literature [4.42].

4.120. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.92 (s, 8H), 1.99 (s, 2H), 1.40 (s, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 108.6, 64.3, 46.2, 24.6.



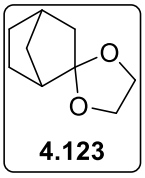
1,2-bis(2-Methyl-1,3-dioxolan-2-yl)ethane (4.121). Starting from 94 mL of **4.102** (0.8 mmol, 0.1 M), 124 mL of ethylene glycol (1.76 mmol, 2.2 equiv), 262 mL of trimethyl orthoformate (2.4 mmol, 3.0 equiv), 96 mg of $MgSO_4$ (0.8 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 162.3 mg of **4.121** (>99% yield, colourless oil) have been collected. The spectroscopic data were in accordance with the literature [4.38].

4.121. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.83–3.73 (m, 8H), 1.59 (s, 4H), 1.16 (d, J = 1.7 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 109.1, 64.0, 32.8, 23.2.



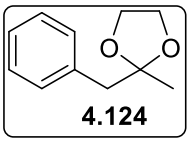
2-Ethyl-2-isopropyl-1,3-dioxolane (4.122). Starting from 100 mL of **4.103** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 115.4 mg of **4.122** (>99% yield, colourless oil) have been collected. The spectroscopic data were in accordance with the literature [4.43].

4.122. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.92 (s, 4H), 1.92 (hept, *J* = 6.9 Hz, 1H), 1.62 (d, *J* = 7.4 Hz, 2H), 0.89 (dd, *J* = 8.7, 7.2 Hz, 9H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 113.9, 65.3, 34.1, 26.8, 17.0, 7.5.



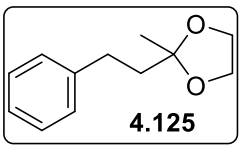
spiro[bicyclo[2.2.1]heptane-2,2'-[1,3]dioxolane] (4.123). Starting from 89 mL of **4.104** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 112.1 mg of **4.123** (>99% yield, slightly yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.43].

4.123. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.09–3.61 (m, 4H), 2.25 (d, *J* = 4.9 Hz, 1H), 2.13 (d, *J* = 4.3 Hz, 1H), 1.85–1.75 (m, 1H), 1.76–1.52 (m, 3H), 1.49–1.35 (m, 2H), 1.33–1.22 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 116.3, 64.3, 63.6, 43.5, 37.6, 35.5, 28.0, 21.9.



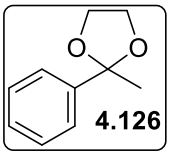
2-Benzyl-2-methyl-1,3-dioxolane (4.124). Starting from 106 mL of **4.105** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 142.4 mg of **4.124** (>99% yield, slightly yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.44].

4.124. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 5H), 4.07–3.88 (m, 2H), 3.86–3.66 (m, 2H), 2.95 (s, 2H), 1.34 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 137.1, 130.6, 128.1, 126.5, 109.9, 65.0, 63.6, 45.5, 24.5.



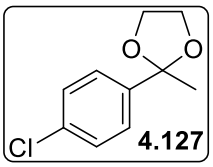
2-Methyl-2-phenethyl-1,3-dioxolane (4.125). Starting from 120 mL of **4.106** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 154.0 mg of **4.125** (>99% yield, slightly yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.23].

4.125. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.00 (m, 5H), 4.25–3.77 (m, 4H), 2.80–2.71 (m, 2H), 2.10–1.94 (m, 2H), 1.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 128.5, 128.4, 125.9, 109.8, 64.9, 41.2, 30.4, 24.1.



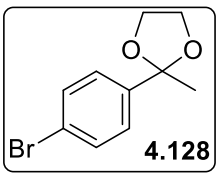
2-Methyl-2-phenyl-1,3-dioxolane (4.126). Starting from 93 mL of **4.107** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 118.5 mg of **4.126** (90% yield, yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.44].

4.126. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.42–7.25 (m, 3H), 4.07–4.03 (m, 2H), 3.82–3.77 (m, 2H), 1.68 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 128.1, 127.7, 125.1, 108.7, 64.3, 27.5.



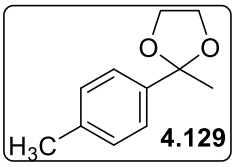
2-(4-chlorophenyl)-2-methyl-1,3-dioxolane (4.127). Starting from 104 mL of **4.108** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 158.9 mg of **4.127** (>99% yield, slightly yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.23].

4.127. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.30 (d, J = 9.0 Hz, 2H), 7.27–7.09 (m, J = 9.0 Hz, 2H), 3.97–3.89 (m, 2H), 3.70–3.63 (m, 2H), 1.54 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 133.5, 128.2, 126.7, 108.3, 64.3, 27.4.



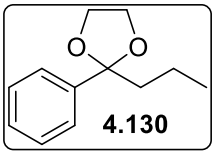
2-(4-Bromophenyl)-2-methyl-1,3-dioxolane (4.128). Starting from 159.0 mg of **4.109** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 194.5 mg of **4.128** (>99% yield, yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.45].

4.128. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52–7.44 (d, J = 9.0 Hz, 2H), 7.41–7.32 (d, J = 9.0 Hz, 2H), 4.09–4.01 (m, 2H), 3.76 (m, 2H), 1.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 131.2, 127.0, 121.8, 108.4, 64.4, 27.4.



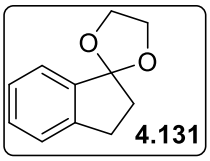
2-Methyl-2-(p-tolyl)-1,3-dioxolane (4.129). Starting from 107 mL of **4.110** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 142.6 mg of **4.129** (yield: >99%, slightly yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.46].

4.129. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.23 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 4.02–3.93 (m, 2H), 3.73–3.63 (m, 2H), 1.60 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 137.4, 128.8, 125.1, 108.8, 64.3, 27.5, 21.0.



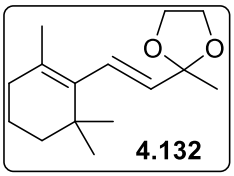
2-Phenyl-2-propyl-1,3-dioxolane (4.130). Starting from 117 mL of **4.111** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 135.3 mg of **4.130** (88% yield, colourless oil) have been collected. The spectroscopic data were in accordance with the literature [4.47].

4.130. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51–7.46 (m, 2H), 7.42–7.21 (m, 3H), 4.06–3.97 (m, 2H), 3.80–3.75 (m, 2H), 1.94–1.86 (m, 2H), 1.42–1.31 (m, 2H), 0.89 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 128.5, 128.2, 126.3, 111.0, 65.0, 43.2, 17.5, 14.7.



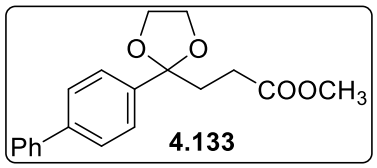
2,3-Dihydrospiro[indene-1,2'-[1,3]dioxolane] (4.131). Starting from 105.7 mg of **4.112** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 97.3 mg of **4.131** (69% yield, colourless oil) have been collected. The spectroscopic data were in accordance with the literature [4.48].

4.131. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.14 (m, 4H), 4.25–4.08 (m, 4H), 2.98 (t, *J* = 6.9 Hz, 2H), 2.35–2.04 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 141.8, 129.4, 126.8, 125.0, 122.9, 117.2, 65.1, 36.9, 28.3.



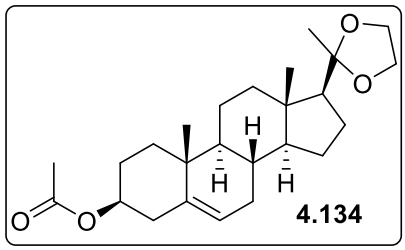
(*E*)-2-Methyl-2-(2-(2,6,6-trimethylcyclohex-1-en-1-yl)vinyl)-1,3-dioxolane (4.132). Starting from 163 mL of **4.113** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 168.3 mg of **4.132** (89% yield, yellow oil) have been collected. The spectroscopic data were in accordance with the literature [4.49].

4.132. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48–5.80 (m, 1H), 5.26 (d, *J* = 16.0 Hz, 1H), 4.06–3.63 (m, 4H), 1.97–1.76 (m, 2H), 1.61–1.27 (m, 10H), 0.93 (d, *J* = 26.5 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.3, 133.5, 128.52, 128.0, 107.5, 64.3, 39.2, 33.8, 32.5, 28.6, 25.0, 21.1, 19.1.



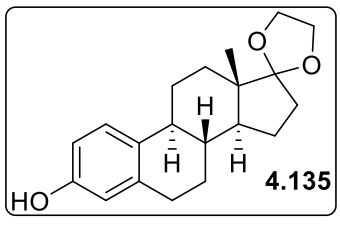
Methyl 3-(2-([1,1'-biphenyl]-4-yl)-1,3-dioxolan-2-yl)propanoate (4.133). Starting from 214.6 mg of **4.114** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%). After purification, 150.1 mg of **4.133** (60% yield, colourless oil) have been collected.

4.133. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70–7.60 (m, 4H), 7.57–7.51 (m, 2H), 7.51–7.44 (m, 2H), 7.44–7.34 (m, 1H), 4.07–3.99 (m, 2H), 3.84–3.78 (m, 2H), 3.60 (d, *J* = 2.9 Hz, 3H), 2.40 (dd, *J* = 8.4, 6.3 Hz, 2H), 2.25–2.19 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 143.0, 141.8, 130.1, 128.7, 128.1, 127.9, 127.4, 111.5, 65.9, 52.0, 36.8, 29.6. HRMS (EI) m/z: $[M+H]^+$ calcd for $C_{19}H_{21}O_4$ 313.1440, found 313.1425.



Pregnenolone acetate ethylene ketal (4.134). Starting from 286.8 mg of **4.115** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%) in acetonitrile instead of DMC due to the low solubility of **4.115** After one hour, a yellowish powder precipitated and was recovered by means of filtration, washed with cold water, finally dried affording 320.3 mg of compound **4.134** (99% yield, yellowish solid, m.p. = 164-165 °C [4.50]). Spectroscopic data were in accordance with the literature [4.50].

4.134. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (d, *J* = 5.1 Hz, 1H), 4.68–4.56 (m, 1H), 4.22–3.54 (m, 4H), 2.33 (d, *J* = 8.2 Hz, 2H), 2.04 (s, 3H), 1.88–1.41 (m, 14H), 1.31 (s, 3H), 1.22–1.10 (m, 4H), 1.03 (s, 3H), 0.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 139.6, 122.4, 111.8, 73.8, 65.0, 63.1, 58.1, 56.4, 49.9, 41.7, 39.3, 36.9, 36.5, 31.7, 31.3, 27.6, 24.4, 23.7, 21.3, 20.7, 19.2, 12.7.



Estrone ethylene ketal (4.135). Starting from 216.0 mg of **4.116** (0.8 mmol, 0.1 M), 62 mL of ethylene glycol (0.88 mmol, 1.1 equiv), 131 mL of trimethyl orthoformate (1.2 mmol, 1.5 equiv), 48 mg of $MgSO_4$ (0.4 mmol) and 7.44 mg of **4.1a** (0.04 mmol, 5 mol%) in acetonitrile instead

of DMC due to the low solubility of **4.116**. After 2 h, the solution was poured into a water saturated bicarbonate solution and a white solid precipitated. The solid was filtrated, recrystalized from methanol, and finally dried affording 163.3 mg of compound **4.135** (65% yield, white solid, m.p. = 180-184 °C [4.51]). Spectroscopic data were in accordance with the literature [4.51].

4.135. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, J = 8.4 Hz, 1H), 6.75–6.48 (m, 2H), 4.12–3.76 (m, 4H), 2.82 (d, J = 9.6 Hz, 2H), 2.51–1.30 (m, 14H), 0.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 138.0, 132.2, 126.3, 119.5, 115.2, 112.7, 65.1, 46.1, 43.5, 39.0, 30.7, 29.5, 26.8, 22.2, 14.2.

4.5. REFERENCES.

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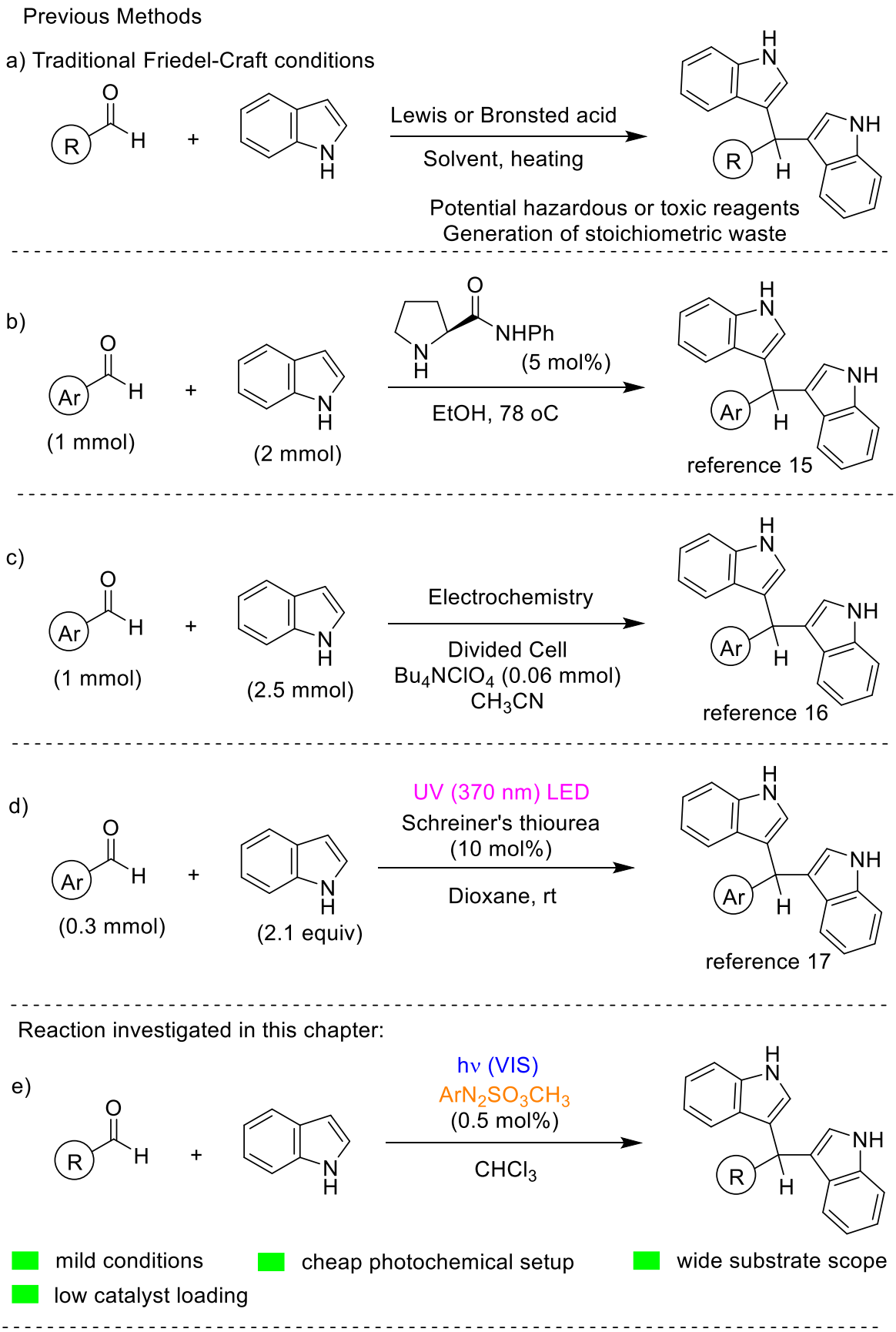
CHAPTER 5

FRIEDEL-CRAFTS ARYLATION OF ALDEHYDES WITH INDOLES UTILIZING ARYLAZO SULFONES AS THE PHOTOACID GENERATOR.

5.1. INTRODUCTION.

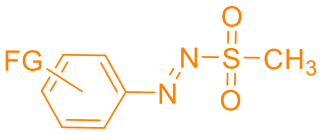
The reaction of Friedel-Crafts is a well-known process introduced in 1877 by both Friedel and Crafts [5.1]. The synthesis of bis-indolyl methanes (BIMs) and analogues is an important synthetical target, considering the biological and pharmacological properties of such compounds [5.2]. The interest shown in BIMs is evidenced by the plethora of synthetical strategies offered, being the Friedel-Crafts-type coupling between aldehydes and indoles one of the most common (Scheme 5.1). These approaches suffer of the use of toxic reactant, additives or the needs for high temperatures [5.3], however some strategies like infrared [5.4a], sonochemistry or microwave irradiations [5.4], made this protocol more appealing. Different approaches have been applied with success to this target, including, among the others, organocatalysis (Scheme 5.1, b) [5.5], electrochemistry (Scheme 5.1, c) [5.6] and even photochemistry, which potentialities in terms of sustainability have been pointed out in the last decades [5.7]. In this context, the peculiar behaviour of Schreiner's thiourea was exploited to promote a photoacidic process under blue light irradiation (Scheme 5.1, d) [5.8]. Among the different applications of arylazo sulfones in synthesis [5.9-5.12] their use as non-ionic photoacid generators (PAGs) able to generate methanesulfonic acid in oxygen-saturated or air equilibrated solution has been recently investigated [5.13-5.14]. We thus decided to propose a fast, versatile and efficient procedure for the visible-light driven synthesis of diarylmethanes via Friedel Crafts type coupling of aldehydes and (hetero)arenes (Scheme 5.1, e).



Scheme 5.1. Common synthetic pathways for the Friedel-Crafts-type reaction between indoles and aldehydes.

5.2. RESULTS AND DISCUSSION.

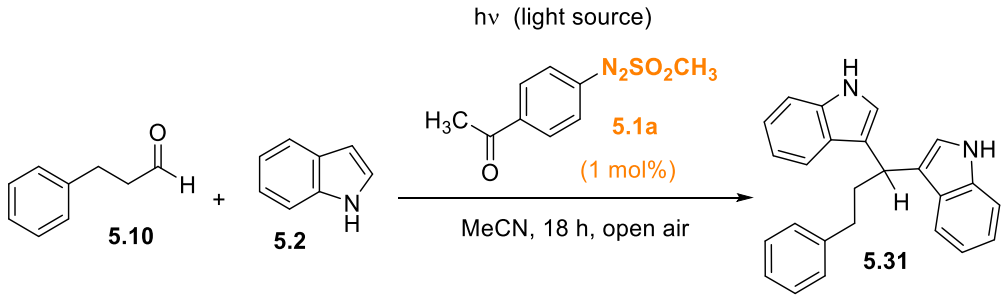
In order to investigate the feasibility of the process we decided to try with 3-phenyl propanal (**5.10**) and 1H-indole (**5.2**) to form 3,3′-(3-phenylpropane-1,1-diyl)bis(1H-indole) (**5.31**). A detailed optimization of the synthetic procedure considering the irradiation time and wavelengths, catalyst loading, substrates concentration (see Tables 5.1-5.6) has been pursued. The reaction proceeds efficiently under 456 nm and 467 nm irradiation giving similar yields (54% and 52% respectively) (Table 5.1) and chloroform was the best solvents tested (89% isolated yields, Table 5.2). Moreover, the reaction outcome was optimal in 1 mL of solvent (Table 5.3) by using 2.2. equiv of indole **5.2** (Table 5.4)**.** We thus tested differently substituted arylazo sulfones (**5.1a-h** Figure 5.1) as PAGs and *p*-tert-butylphenylazo sulfone (**5.1g**) gave the best results (96%) in a very low loading (0.5 mol%) (Table 5.5). Finally, the ideal reaction time was found to be 6 hours (Table 5.6). Control experiments highlighted that the simultaneous presence of light, oxygen and the arylazo sulfone is mandatory for the positive outcome of the reaction (see Tables 5.7).



5.1a, FG = 4-CH_3CO
5.1b, FG = 4-CH_3
5.1c, FG = 4-Cl
5.1d, FG = 3-CH_3CO
5.1e, FG = 3-Br
5.1f, FG = 2-Br
5.1g, FG = 4-tBu
5.1h, FG = 3-CN

Figure 5.1. Arylazo sulfones employed for the photochemical synthesis of bis-indolyl methanes.

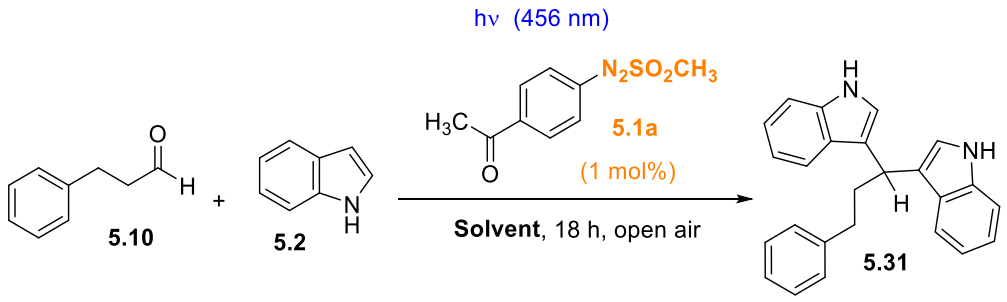
Table 5.1. Optimization of the solvent for the synthesis of **5.31**.



Entry	Irradiation Source (nm)	Yield [a] (%)
1	370	28
2	390	39
3	427	48
4	440	29
5	**456**	**60 (54)**
6	**467**	**60 (52)**
7	525	45
8	CFL	31

[a] Yield determined by ^{1}H-NMR using internal standard, yield of product after isolation by column chromatography in parenthesis. The reaction was performed with 3-phenylpropanal (**5.10**) (67 mg, 0.50 mmol), indole (**5.2**) (129 mg, 1.10 mmol), catalyst **5.1a** (1 mol%, 0.005 mmol) in MeCN (1 mL) for 18 h, under irradiation.

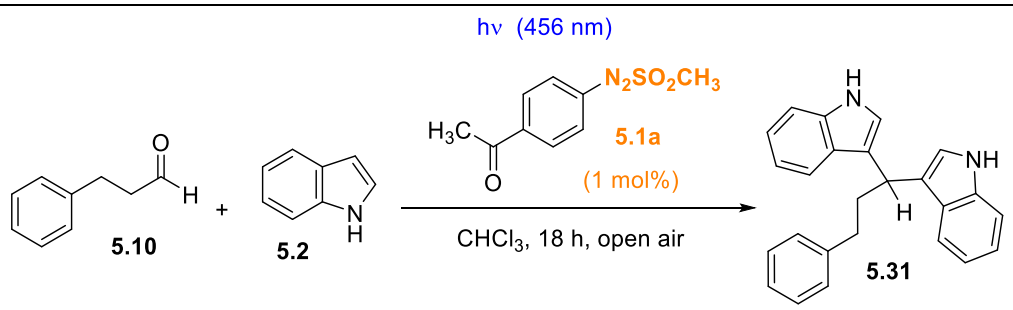
Table 5.2. Optimization of the solvent loading for the synthesis of **5.31**.



Entry	Solvent	Yield [a] (%)
1	MeCN	60 (54)
2	CH_2Cl_2	68
3	**$CHCl_3$**	**92 (89)**
4	EtOAc	50
5	DMSO	51
6	Toluene	61
7	Pet. Eth.	44
8	THF	52
9	H_2O	59
10	Et_2O	39
11	MeOH	66
12	Cyrene	60
13	2-Me-THF	44

[a] Yield determined by ^{1}H-NMR using internal standard, yield of product after isolation by column chromatography in parenthesis. The reaction was performed with 3-phenylpropanal (**5.10**) (67 mg, 0.50 mmol), indole (**5.2**) (129 mg, 1.10 mmol), catalyst **5.1a** (1 mol%, 0.005 mmol) in solvent (1 mL) for 18 h, under irradiation.

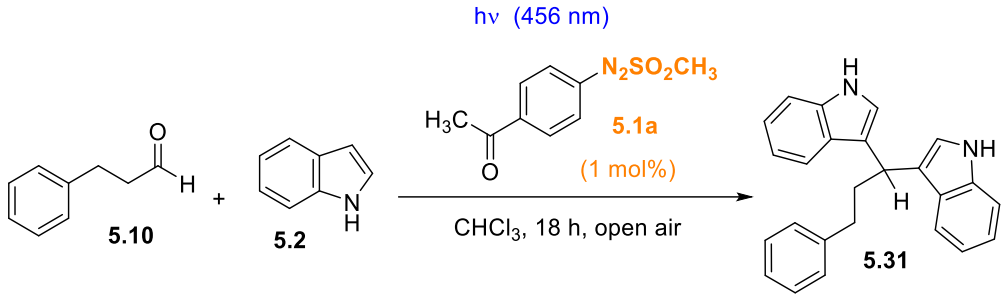
Table 5.3. Optimization of the quantity of solvent employed for the synthesis of **5.31**.



Entry	Solvent loading (mL)	Yield [a] (%)
1	0.5	82
2	**1**	**89**
3	2	91

[a] Yield determined by ^{1}H-NMR using internal standard, yield of product after isolation by column chromatography in parenthesis. The reaction was performed with 3-phenylpropanal (**5.10**) (67 mg, 0.50 mmol), indole (**5.2**) (129 mg, 1.10 mmol), catalyst **5.1a** (1 mol%, 0.005 mmol) in $CHCl_3$ (1 mL) for 18 h, under irradiation.

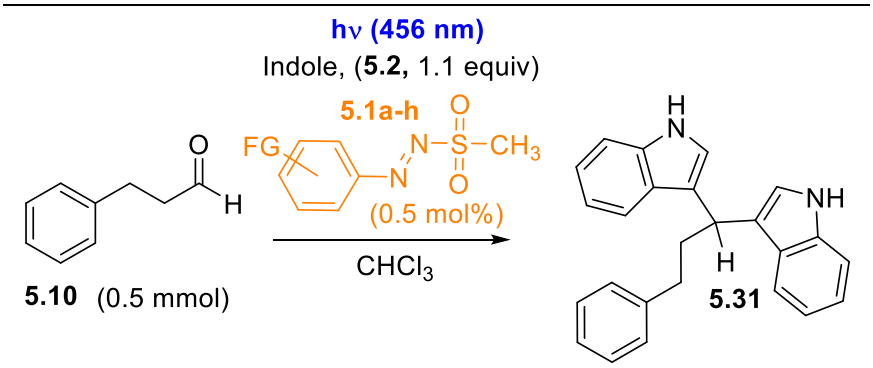
Table 5.4. Screening of the equivalents of indole **5.2** employed for the synthesis of **5.31.**



Entry	Indole equiv.	Yield [a] (%)
1	**2.2**	**89**
2	2.5	95

[a] Yield of product after isolation by column chromatography. The reaction was performed with 3-phenylpropanal (**5.10**) (67 mg, 0.50 mmol), indole (**5.2**), catalyst **5.1a** (1 mol%, 0.005 mmol) in $CHCl_3$ (1 mL) for 18 h, under blue LED irradiation.

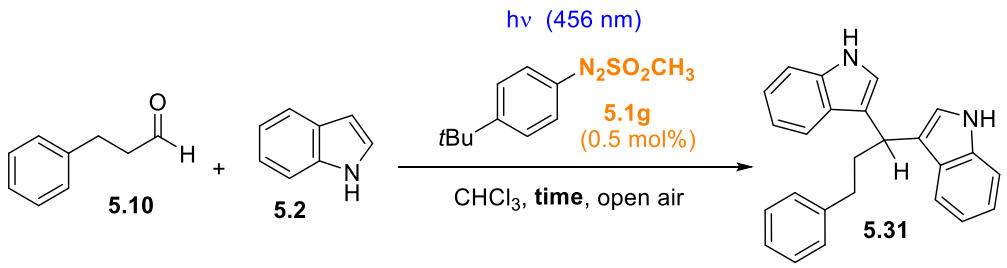
Table 5.5. Screening of the arylazo sulfones **5.1a-h** employed for the synthesis of **5.31**.



Entry	Yield [a] (%)
5.1a (FG = 4-CH_3CO)	63
5.1b (FG = 4-CH_3)	86
5.1c (FG = 4-Cl)	76
5.1d (FG = 3-CH_3CO)	89
5.1e (FG = 3-Br)	90
5.1f (FG = 2-Br)	92
5.1g (FG = 4-*t*Bu)	**96**
5.1h (FG = 3-CN)	90

[a] Yield calculated by ^{1}H-NMR using internal standard,

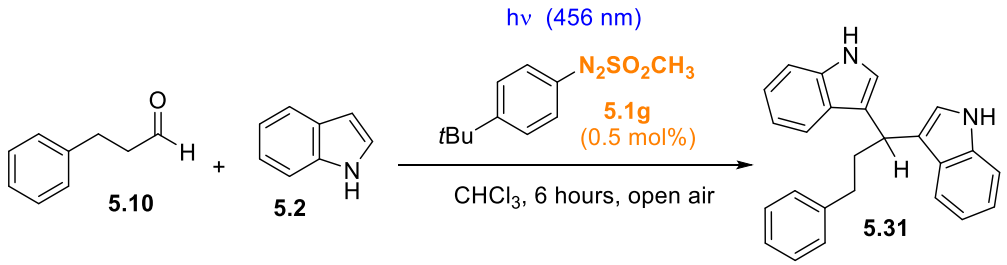
Table 5.6. Screening of the time required for the synthesis of **5.31**.



Entry	Time reaction (h)	Yield [a] (%)
1	1	80 (78)
2	3	83
3	**6**	**95 (90)**
4	18	98 (96)

[a] Yield determined by ^{1}H-NMR using internal standard, yield of product after isolation by column chromatography in parenthesis. The reaction was performed with 3-phenylpropanal (**5.10**) (67 mg, 0.50 mmol), indole (**5.2**) (129 mg, 1.10 mmol), catalyst **5.1g** (0.5 mol%, 0.0025 mmol) in $CHCl_3$ (1 mL) for 1-18 h, under blue LED irradiation.

Table 5.7. Control experiment carried out on the synthesis of **5.31**.



Entry	Variations	Notes	Yield [a] (%)
1	No catalyst	-	Traces
2	Ar atmosphere	-	63
3	No irradiation	-	29 (25)
4	No irradiation	50 °C	38
5	dark	-	17 (15)
6	TEMPO (1.0 equiv.)	-	0

[a] Yield determined by ^{1}H-NMR using internal standard, yield of product after isolation by column chromatography in parenthesis. The reaction was performed with 3-phenylpropanal (**5.10**) (67 mg, 0.50 mmol), indole (**5.2**) (129 mg, 1.10 mmol), catalyst **5.1g** (0.5 mol%, 0.0025 mmol) in $CHCl_3$ (1 mL) for 6 h, under blue LED irradiation.

We thus optimized the reaction conditions as follows: aldehyde **5.10** (0.5 mmol, 0.5 M), indole **5.2** (1.05 equiv) and arylazo sulfone **5.1g** (0.5 mol%) in chloroform (1 mL), irradiated at room temperature for 6 h at 456 nm (40 W Kessil lamp). With these promising results in our hands, we decided to test the possibility to extend the scope of this protocol on differently substituted indoles (Figure 5.2).

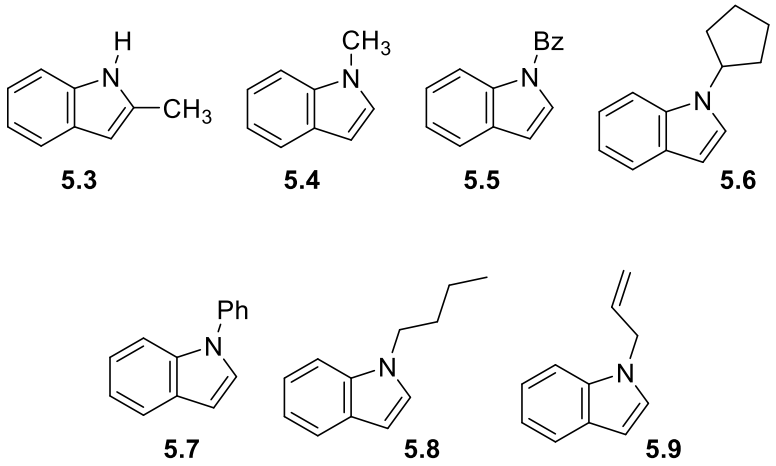
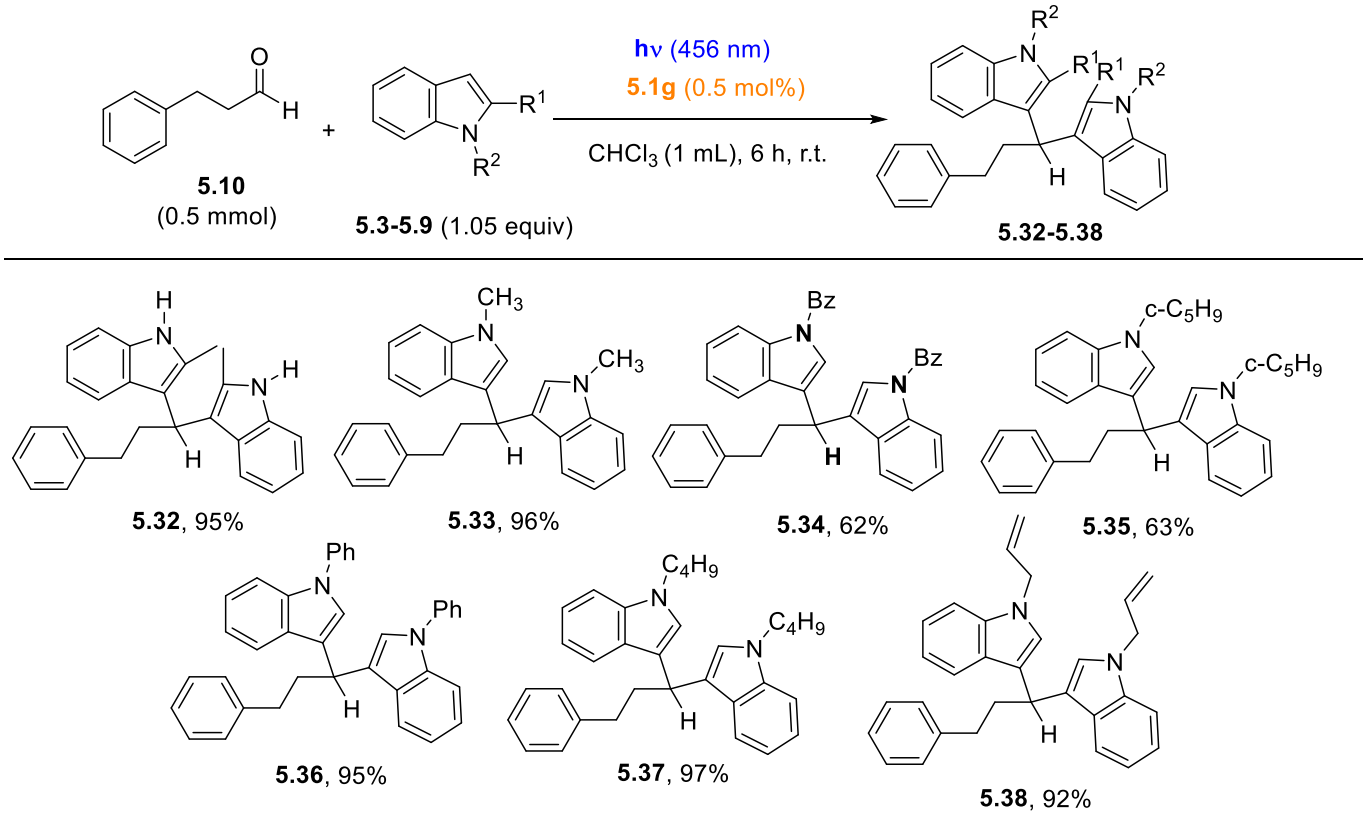


Figure 5.2. Indoles employed in the Photochemical synthesis of bis-indoyl methanes.

A variety of *N*-substituted indoles were tried with 3-phenyl propanal as counterpart (**5.10**). Sterically hindered 2-methyl indole **5.3** was proved to act as a competent nucleophile, providing access to **5.32** in 95% yield. Then, the N-substitution pattern on the indole was probed. Alkyl substituents, like methyl, butyl or benzyl, secondary alkyl substituents, like cyclopentyl, aryl substituents, like phenyl or allyl substituent were well tolerated, leading to the desired products in good to excellent yields (Scheme 5.2).



Scheme 5.2. Substrate scope. Substituted indoles.

We then moved our attention on the use of different aldehydes and few ketones (Figure 5.3).

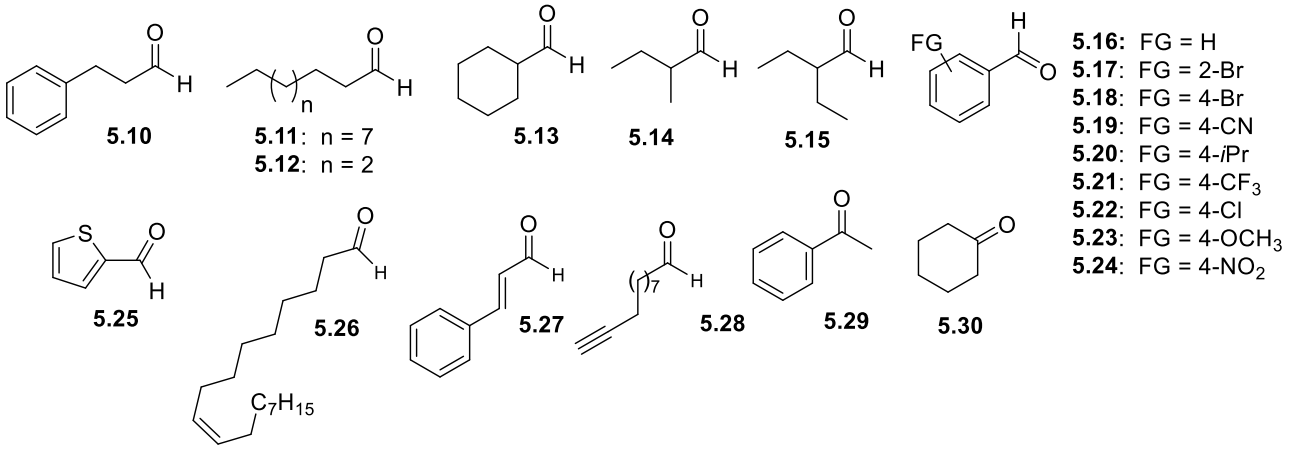
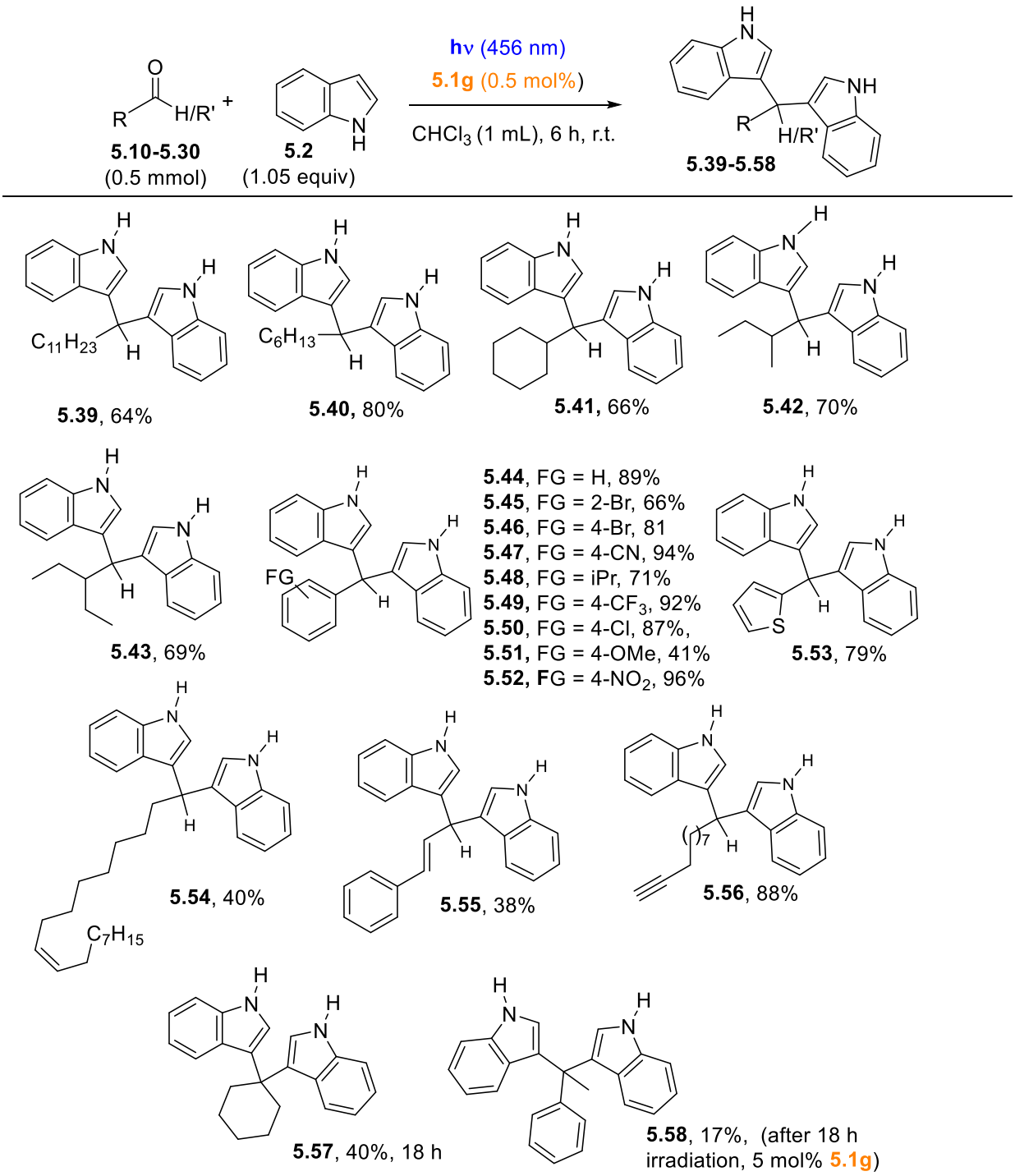


Figure 5.3. Carbonyl-bearing molecules employed in the present work used for the first time in the synthesis of bis-indolyl methanes.

We employed indole (**5.2**) as representative heteroaromatic and a variety of aliphatic aldehydes were tested. Moving to linear substrates **5.11-5.12**, bis-indoles **5.39** and **5.40**, were isolated in good amounts. Also, we explored three different cases in the class of α,α-disubstituted aldehydes substrates, and in all cases, the desired products **5.41-5.42** was obtained in good yields (66-70%) (Scheme 5.3). Aromatic aldehydes were also tried in this photochemical approach **5.16-5.25**. Benzaldehyde provided the double addition product **5.44** in a good yield. Bromine incorporation either in the para-position or the ortho-position of the aromatic ring was well tolerated, leading to products **5.45** and **5.46** in good to excellent yields. Both electron-withdrawing and electron-donating groups were well tolerated, and derivatives **5.47-5.52** were isolated in good to excellent yield, with the only exception of 4-methoxy derivative **5.51** (41%). Finally, heteroaromatic thiophene-2-carboxaldehyde (**5.25**) afforded diarylmethane **5.53** in 79% yield. Oleyl aldehyde **5.26** was employed successfully, leading to **5.54** in 40% yield. Another naturally occurring compound, cinnamaldehyde, led to **5.55** only in discrete yield, whereas aldehyde **5.28** that contains a triple bond was also efficiently converted to the corresponding arylated compound **5.56**. Unfortunately, ketones did not prove as good substrates: cyclohexanone required prolonged reaction time (18 h), affording **5.57** in 40% yield, while acetophenone only gave 17% yield of the isolated product **5.58** even after 18 h of reaction and an increase of the catalyst loading up to 5 mol% (Scheme 5.3).



Scheme 5.3. Substrates scope. Different carbonyl-bearing molecules.

5.4. CONCLUSIONS.

In conclusion, a simple, cheap and efficient photochemical protocol was developed for the activation of aldehydes in their reaction with indoles, leading to triarylmethanes. This method relies on a small organic molecule, an arylazo sulfone, belonging to an intriguing class of shelf-stable and coloured compounds for the visible-light photochemical catalytic release of acid under blue LED lamp irradiation. This slow-released acid activates efficiently both aliphatic and aromatic aldehydes to

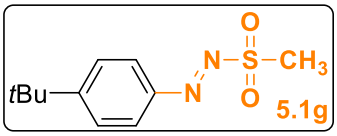
react, leading to diarylmethanes in good to high yields by adopting only a very low catalyst loading (0.5 mol%).

5.5. EXPERIMENTAL SECTION.

General information. Chromatographic purification of products was accomplished using forced-flow chromatography on Merck® Kieselgel 60 70-230 mesh. Thin-layer chromatography (TLC) was performed on aluminum backed silica plates (0.2 mm, 60 F^{254}). Visualization of the developed chromatogram was performed by fluorescence quenching using phosphomolybdic acid, anisaldehyde or potassium permanganate stains. Melting points were determined on a Buchi® 530 hot stage apparatus and are uncorrected. Mass spectra (ESI) were recorded on a Finningan® Surveyor MSQ LCMS spectrometer. HRMS spectra were recorded on a Bruker® Maxis Impact QTOF spectrometer. ^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR spectra were recorded on a Varian® Mercury (200 MHz, 188 MHz and 50 MHz, respectively) or on an Avance III HD Bruker 400 MHz (400 MHz, 376 MHz and 100 MHz, respectively), and are internally referenced to residual solvent signals. Data for ^{1}H-NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad signal), coupling constant and assignment. Data for ^{19}F-NMR are reported in terms of chemical shift (δ ppm) and are internally referenced to trifluoroacetic acid (188 MHz) or fluoroform (376 MHz). Data for ^{13}CNMR are reported in terms of chemical shift (δ ppm). Mass spectra and conversions of the reactions were recorded on a Shimadzu® GCMS-QP2010 Plus Gas Chromatograph Mass Spectrometer utilizing a MEGA® column (MEGA-5, F.T: 0.25 μm, I.D.: 0.25 mm, L: 30 m, T_{max}: 350 ºC, Column ID# 11475. Kessil lamps PR160L were used as the irradiation source. For all experiments, the intensity of the Kessil lamps was controlled in the maximum level with power consumption: 370 nm (max 43W), 390 nm (max 52W), 427 nm (max 45W), 440 nm (max 45W), 456 nm (max 50W), 467 nm (max 44W) and 525 nm (max 44W).

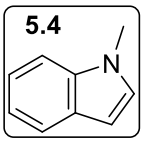
Optimization of the Reaction Conditions for the Photochemical Friedel-Crafts Arylation Between 3-Phenylpropanal (5.10) and Indole (5.2). Different explorative tests were carried out to outline the best conditions to perform this type of reaction. Irradiation sources, organic solvents, arylazo sulfones and catalyst loading were studied. The tables herein reported present the outcome of all these trials.

Synthesis of arylazo sulfones. Compounds **5.1a-h** (except **5.1g**) were already present in the laboratory when this protocol has been developed but may be readily prepared starting from the corresponding anilines [5.12].



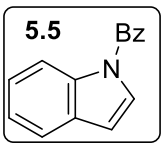
(*E*)-1-(4-(tert-butyl)phenyl)-2-(methylsulfonyl)diazene (5.1g). Compound **5.1g** was synthesized following a known procedure [5.12] Yield: 56% (1.3 g). Yellow solid. **5.1g.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 3.21 (s,3H), 1.38 (s, 9H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.9, 147.0, 126.7, 124.6, 35.6, 34.8, 31.0.

Procedures for the synthesis of the starting materials.

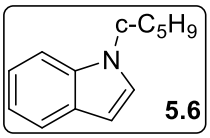


1-Methyl-indole (5.4) [5.16] To a solution of indole (352 mg, 3.00 mmol) in dry THF (6 mL) at 0 °C, NaH (180 mg, 60% dispersion in mineral oil, 4.50 mmol) was added under an argon atmosphere. The heterogenous mixture was stirred at 0 °C for 15 min and at room temperature for 1 h. The reaction mixture was then cooled at 0 °C, iodomethane (0.2 ml, 4.00 mmol) was added and allowed to warm to room temperature. After 30 min, the reaction mixture was cooled at 0 °C, quenched with NH_4Cl (5 mL) and extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine (1 x 50 ml), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The resulting oil was purified by flash chromatography (Pet. Ether/AcOEt 10:1); Green oil; 83% yield;

5.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (1H, d, *J* = 7.9 Hz, ArH), 7.38 (1H, d, *J* = 7.9 Hz, ArH), 7.28 (1H, t, *J* = 7.9 Hz, ArH), 7.16 (1H, t, *J* = 7.9 Hz, ArH), 7.10 (1H, d, *J* = 2.5 Hz, ArH), 6.54 (1H, d, *J* = 2.5 Hz, ArH), 3.84 (3H, s, NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.7, 128.7, 128.4, 121.4, 120.8, 119.2, 109.1, 100.9, 32.8; MS (ESI) m/z 154 $[M+Na]^+$.



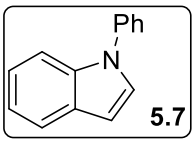
1-Benzyl-1*H*-indole (5.5) [5.17] Same procedure as above using benzyl bromide; Yellow solid, mp 39-40 °C; 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (1H, d, *J* = 7.8 Hz, ArH), 7.32-7.28 (4H, m, ArH), 7.17-7.11 (5H, m, ArH), 6.59 (1H, d, *J* = 2.3 Hz, ArH), 5.36 (2H, s, NCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.5, 136.3, 128.7, 128.6, 128.2, 127.6, 126.8, 121.7, 121.0, 119.5, 109.7, 101.7, 50.1; MS (ESI) m/z 230 $[M+Na]^+$.



1-Cyclopentyl-1*H*-indole (5.6) [5.18] Pd/C (560 mg, 20 mmol%), indole (234 mg, 2.00 mmol) and HCO_2NH_4 (420 mg, 5.00 mmol) were added into a Schlenk flask (25 mL) charged with a magnetic stir bar. After three cycles of evacuation/backfilling sequence with argon, cyclopentanone (530 µL, 6.00 mmol) and distilled water

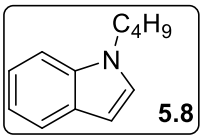
(5 mL) were added. Then, the reaction mixture was stirred in a preheated oil bath at 100 °C for 24 h. The reaction mixture was cooled to room temperature and then vacuum filtered through Celite and silica gel and washed with CH_2Cl_2. The solvent was removed *in vacuo* and the crude mixture was purified by column chromatography on silica gel (Pet. Ether/AcOEt 10:1); Green oil; 95% yield.

5.6. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (1H, d, *J* = 7.8 Hz, ArH), 7.43 (1H, d, *J* = 7.8 Hz, ArH), 7.25-7.20 (2H, m, ArH), 7.15-7.09 (1H, m, ArH), 6.52 (1H, d, *J* = 3.1 Hz, ArH), 4.87-4.79 (1H, m, NCH), 2.29-2.19 (2H, m, CH_2), 2.04-1.89 (4H, m, 2 × CH_2), 1.85-1.76 (2H, m, CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 136.1, 128.7, 124.5, 121.1, 120.9, 119.2, 109.8, 100.9, 56.9, 32.6, 24.1; MS (ESI) m/z 208 $[M+Na]^+$.



1-Phenyl-1*H*-indole (5.7) [5.17] In a Schlenk flask, iodobenzene (0.30 mL, 2.00 mmol), indole (352 mg, 3.00 mmol), Cu_2O (30 mg, 0.20 mmol) and KOH (224 mg, 4.00 mmol) were added. After addition of dry DMSO (4 mL), the reaction mixture was stirred at 120 °C for 12 h under an argon atmosphere. The reaction mixture was diluted with EtOAc (10 mL) and washed with H_2O (2 x 6 mL). The aqueous phase was extracted with EtOAc (2 x 6 mL) and the combined organic layers were washed with brine (1 x 20 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. The resulting oil was purified by flash chromatography (Pet. Ether/AcOEt 20:1); Yellow oil; 60% yield.

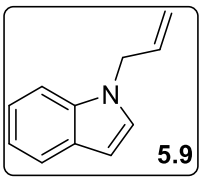
5.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (1H, d, *J* = 7.8 Hz, ArH), 7.61 (1H, d, *J* = 8.1 Hz, ArH), 7.58-7.54 (4H, m, ArH), 7.43-7.37 (2H, m, ArH), 7.30-7.18 (2H, m, ArH), 6.73 (1H, d, *J* = 3.2 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.8, 135.8, 129.6, 129.3, 127.9, 126.4, 124.4, 122.3, 121.1, 120.3, 110.5, 103.5; MS (ESI) m/z 216 $[M+Na]^+$.



1-Butyl-1*H*-indole (5.8) [5.19] NaH (90 mg, 60% dispersion in mineral oil, 3.00 mmol) was added to indole (351 mg, 3.00 mmol) in dry DMSO (5 mL) under argon at room temperature and the reaction mixture was stirred for 2 h. Then, butyl iodide (772 mg, 4.20 mmol) was added and the reaction mixture was stirred for 4.5 h. When the reaction was judged complete by TLC, water (50 mL) was added and the crude mixture was extracted with chloroform (3 x 50 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (Pet. Ether/AcOEt 20:1); Green oil; 51% yield.

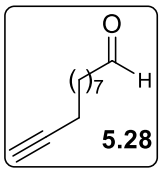
5.8. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (1H, d, *J* = 7.9 Hz, ArH), 7.38 (1H, d, *J* = 7.9 Hz, ArH), 7.23 (1H, t, *J* = 7.9 Hz, ArH), 7.15-7.09 (2H, m, ArH), 6.52 (1H, d, *J* = 2.8 Hz, ArH), 4.15 (2H, t, *J* = 7.1 Hz, NCH_2), 1.90-1.81 (2H, m, CH_2), 1.44-1.33 (2H, m, CH_2), 0.97 (3H, t, *J* = 7.4 Hz, CH_3); ^{13}C

NMR (100 MHz, $CDCl_3$) δ: 136.0, 128.5, 127.8, 121.3, 120.9, 119.1, 109.4, 100.8, 46.1, 32.3, 20.2, 13.7; MS (ESI) m/z 196 $[M+Na]^+$.



1-Allyl-1*H*-indole (5.9) [5.20] A 50 mL round-bottom flask equipped with a stir bar was charged with indole (234 mg, 2.00 mmol) and crushed potassium hydroxide (336 mg, 6.00 mmol). Then, DMSO (5 mL) was added to the flask and the solution was stirred at room temperature for 15 min. Next, allyl bromide (484 mg, 4.00 mmol) was added. The reaction mixture was further stirred at room temperature for 18 h. Then, the reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with water (15 mL). The organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The resulting oil was purified by flash chromatography; Green oil; 96% yield.

5.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (1H, d, *J* = 7.9 Hz, ArH), 7.36 (1H, d, *J* = 7.9 Hz, ArH), 7.24 (1H, t, *J* = 7.9 Hz, ArH), 7.15-7.10 (2H, m, ArH), 6.56 (1H, d, *J* = 2.5 Hz, ArH), 6.09-5.97 (1H, m, =CH), 5.26-5.19 (1H, m, =CH*H*), 5.17-5.08 (1H, m, =CH*H*), 4.77 (2H, d, *J* = 5.4 Hz, NCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.1, 133.5, 128.7, 127.8, 121.5, 120.9, 119.4, 117.2, 109.5, 101.4, 48.8; MS (ESI) m/z 180 $[M+Na]^+$.



10-Undecylnal (5.28) [5.15] A flame-dried 100 mL flask was charged with PCC (647 mg, 3.00 mmol) in dry CH_2Cl_2 (15 mL). The solution was cooled at 0 °C and 10-undecynol (537 mg, 2.00 mmol) was added dropwise. After stirring for 2 h, silica gel (100 mg) was added to the reaction mixture to quench the reaction. The reaction mixture was then vacuum filtered through Celite and silica gel and washed with diethyl ether. The solvent was removed *in vacuo* and the crude mixture was purified by column chromatography on silica gel (Pet. Ether/AcOEt 9.5:0.5), to yield the corresponding aldehyde. Colorless oil, yield 92%.

5.28. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.75 (1H, t, *J* = 1.4 Hz, CHO), 2.41 (2H, td, *J* = 7.3 and 1.4 Hz, $COCH_2$), 2.16 (2H, td, *J* = 7.0 and 2.5 Hz, CH_2), 1.93 (1H, t, *J* = 2.5 Hz, ΞCH), 1.58-1.65 (2H, m, CH_2), 1.47-1.54 (2H, m, CH_2), 1.24-1.39 (8H, m, 4 × CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.7, 84.5, 68.1, 43.8, 29.1, 29.0, 28.8, 28.5, 28.3, 21.9, 18.3; MS (ESI) m/z 189 $[M+Na]^+$.

General Procedure for the photochemical reaction between indoles and aldehydes. In a glass vial, catalyst **5.1g** (0.9 mg, 0.0025 mmol 0.5 mol%) in $CHCl_3$ (1 mL), the chosen aldehyde **5.10-5.30** (0.50 mmol, 0.5 M) and the selected indole **5.2-5.9** (1.10 mmol, 1.05 equiv) were added consecutively. The vial was left stirring under blue LED bulb irradiation (456 nm) for 6 h (except where otherwise noticed). The desired product was isolated after purification by column chromatography (Figure 5.4).

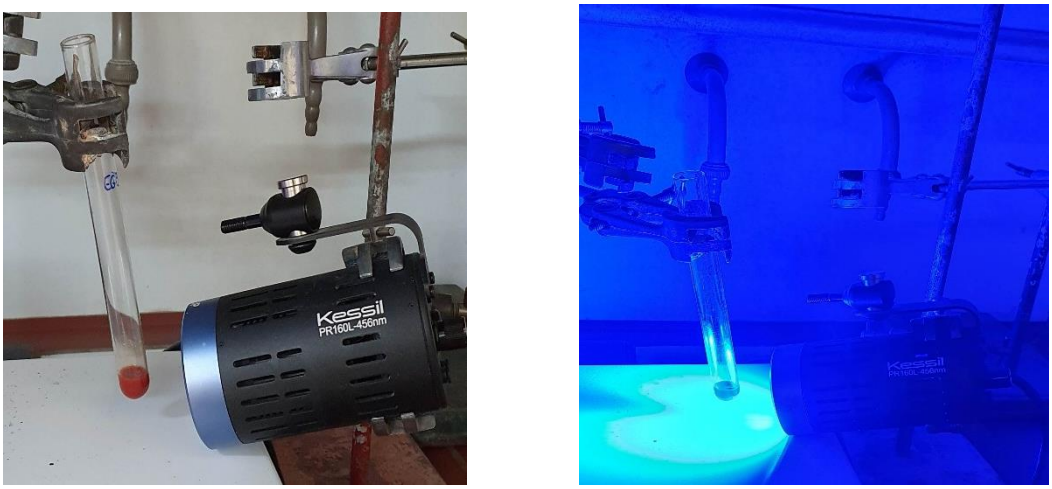
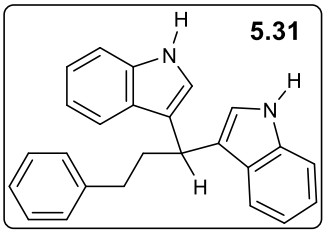
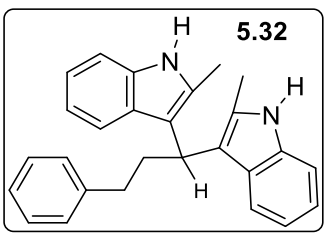


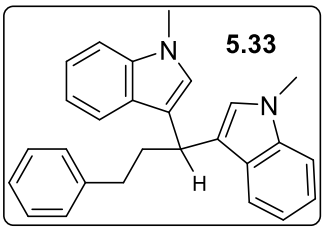
Figure 5.4**.** Photochemical set-up for the synthesis of bis-indolyl methanes.



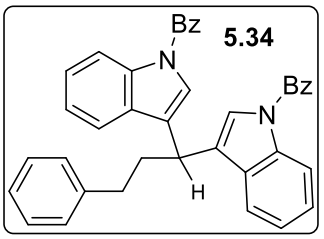
3,3′-(3-Phenylpropane-1,1-diyl)bis(1*H*-Indole) (5.31). [5.21] Brown solid; 90% yield; mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (2H, br s, 2 × NH), 7.59 (2H, d, *J* = 8.5 Hz, ArH), 7.36 (2H, d, *J* = 8.5 Hz, ArH), 7.30 (2H, d, *J* = 8.5 Hz, ArH), 7.26-7.16 (5H, m, ArH), 7.11-7.05 (2H, m, ArH), 7.03 (2H, s, ArH), 4.55 (1H, t, *J* = 8.1 Hz, CH), 2.81-2.73 (2H, m, CH_2), 2.64-2.55 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.6, 136.6, 128.5, 128.3, 127.1, 125.7, 121.8, 121.5, 120.1, 119.6, 119.1, 111.1, 37.4, 34.4, 33.5; MS (ESI) m/z 373 $[M+Na]^+$.



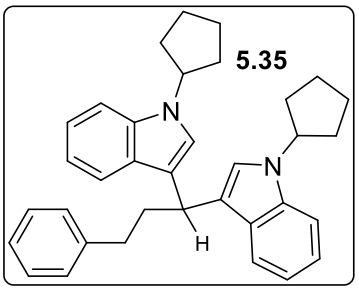
3,3'-(3-Phenylpropane-1,1-diyl)bis(2-methyl-1*H*-indole) (5.32). [5.22] Brown solid; 95% yield; mp 188-190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (2H, d, *J* = 7.5 Hz, ArH), 7.67 (2H, br s, 2 × NH), 7.29 (2H, d, *J* = 7.5 Hz, ArH), 7.26-7.16 (5H, m, ArH), 7.10 (2H, t, *J* = 7.5 Hz, ArH), 7.04 (2H, t, *J* = 7.5 Hz, ArH), 4.48 (1H, t, *J* = 7.3 Hz, CH), 2.84-2.71 (4H, m, 2 × CH_2), 2.27 (6H, s, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.5, 135.1, 130.9, 128.5, 128.4, 128.2, 125.6, 120.4, 119.3, 119.0, 114.5, 110.1, 36.2, 34.9, 34.3, 12.6; MS (ESI) m/z 401 $[M+Na]^+$.



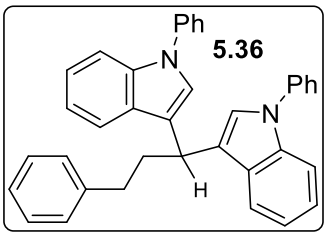
3,3'-(3-Phenylpropane-1,1-diyl)bis(1-methyl-1*H*-indole) (5.33). [5.23] Brown oil; 96% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (2H, d, *J* = 7.9 Hz, ArH), 7.34-7.27 (4H, m, ArH), 7.27-7.19 (5H, m, ArH), 7.08 (2H, t, *J* = 7.5 Hz, ArH), 6.92 (2H, s, ArH), 4.54 (1H, t, *J* = 7.4 Hz, CH), 3.76 (6H, s, 2 × NCH_3), 2.80-2.74 (2H, m, CH_2), 2.62-2.54 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.7, 137.3, 128.5, 128.2, 127.5, 126.3, 125.6, 121.3, 119.7, 118.8, 118.5, 109.1, 37.9, 34.5, 33.3, 32.6; MS (ESI) m/z 401 $[M+Na]^+$.



3,3'-(3-Phenylpropane-1,1-diyl)bis(1-benzyl-1*H*-indole) (5.34). Brown oil; 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76-7.67 (2H, m, ArH), 7.46-7.33 (10H, m, ArH), 7.31-7.23 (5H, m, ArH), 7.22-7.09 (8H, m, ArH), 5.36 (4H, s, 2 × NCH_2), 4.67 (1H, d, *J* = 6.7 Hz, CH), 2.93-2.83 (2H, m, CH_2), 2.78-2.66 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.6, 137.9, 137.0, 128.6, 128.5, 128.2, 127.4, 126.5, 125.8, 121.5, 119.9, 119.2, 118.7, 109.6, 49.7, 37.4, 34.4, 33.6; HRMS exact mass calculated for [M+Na]+ ($C_{39}H_{34}N_2Na^+$) requires *m/z* 553.2620, found *m/z* 553.2623.

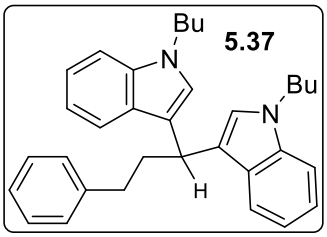


3,3'-(3-Phenylpropane-1,1-diyl)bis(1-cyclopentyl-1*H*-indole) (5.35). Brown oil; 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (2H, d, *J* = 7.9 Hz, ArH), 7.41 (2H, d, *J* = 8.2 Hz, ArH), 7.36-7.27 (3H, m, ArH), 7.25-7.19 (4H, m, ArH), 7.10 (2H, s, ArH), 7.06 (2H, t, *J* = 7.5 Hz, ArH), 4.84-4.77 (2H, m, 2 × NCH), 4.54 (1H, t, *J* = 7.3 Hz, CH), 2.78-2.71 (2H, m, CH_2), 2.65-2.58 (2H, m, CH_2), 2.25-2.15 (4H, m, 2 × CH_2), 2.02-1.86 (8H, m, 4 × CH_2), 1.84-1.76 (4H, m, 2 × CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.8, 136.8, 128.6, 128.4, 128.2, 127.7, 125.6, 122.0, 120.9, 119.8, 118.5, 118.3, 109.7, 56.8, 37.7, 34.5, 33.9, 32.5, 30.9, 24.1, 24.0; HRMS exact mass calculated for $[M+Na]^+$ ($C_{35}H_{38}N_2Na^+$) requires *m/z* 509.2932, found *m/z* 509.2923.

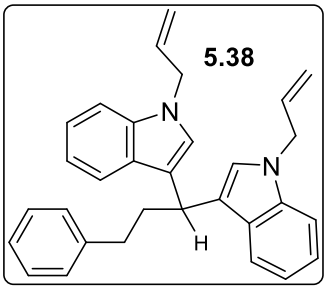


3,3'-(3-Phenylpropane-1,1-diyl)bis(1-phenyl-1*H*-indole) (5.36). Brown oil; 95% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (2H, d, *J* = 7.8 Hz, ArH), 7.85 (2H, d, *J* = 8.2 Hz, ArH), 7.22 (4H, d, *J* = 7.8 Hz, ArH), 7.67 (4H, t, *J* = 7.8 Hz, ArH), 7.57-7.54 (4H, m, ArH), 7.52-7.44 (7H, m, ArH), 7.40 (2H, t, *J* = 7.4 Hz, ArH), 4.94 (1H, t, *J* = 7.3 Hz, CH), 3.13 (2H, t, *J* = 7.7 Hz, CH_2), 2.97 (2H, q, *J* = 7.7 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.3,

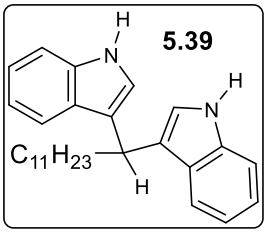
139.8, 136.4, 129.4, 128.6, 128.5, 128.3, 125.9, 125.7, 125.3, 124.1, 122.3, 120.8, 119.9, 119.8, 110.5, 37.5, 34.5, 33.3; HRMS exact mass calculated for $[M+Na]^+$ ($C_{37}H_{30}N_2Na^+$) requires *m/z* 525.2301, found *m/z* 525.2309.



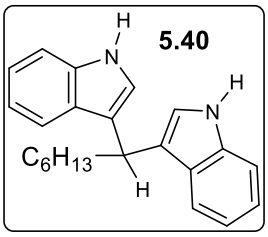
3,3'-(3-Phenylpropane-1,1-diyl)bis(1-butyl-1*H*-indole) (5.37) Red oil; 97% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (2H, d, *J* = 7.9 Hz, ArH), 7.36-7.26 (5H, m, ArH), 7.24-7.18 (4H, m, ArH), 7.04 (2H, t, *J* = 7.5 Hz, ArH), 6.97 (2H, s, ArH), 4.53 (1H, t, *J* = 7.3 Hz, CH), 4.10 (4H, t, *J* = 7.2 Hz, 2 × NCH_2), 2.79-2.71 (2H, m, CH_2), 2.64-2.54 (2H, m, CH_2), 1.89-1.76 (4H, m, 2 × CH_2), 1.42-1.27 (4H, m, 2 × CH_2), 0.96 (6H, t, *J* = 7.4 Hz, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.8, 136.6, 128.5, 128.2, 127.6, 125.6, 125.4, 121.0, 119.9, 118.5, 118.3, 109.3, 45.9, 37.7, 34.5, 33.6, 32.3, 20.2, 13.7; HRMS exact mass calculated for $[M+Na]^+$ ($C_{33}H_{38}N_2Na^+$) requires *m/z* 485.2927, found *m/z* 485.2930.



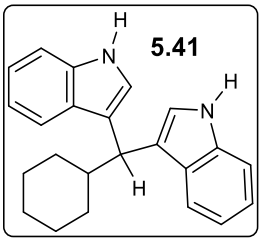
3,3'-(3-Phenylpropane-1,1-diyl)bis(1-allyl-1*H*-indole) (5.38) Brown oil; 92% yield; ^{1}H NMR (100 MHz, $CDCl_3$) δ: 7.67 (2H, d, *J* = 8.0 Hz, ArH), 7.45-7.35 (4H, m, ArH), 7.32-7.23 (5H, m, ArH), 7.13 (2H, t, *J* = 8.0 Hz, ArH), 7.05 (2H, s, ArH), 6.12-6.00 (2H, m, 2 × =CH), 5.26 (2H, dd, *J* = 10.3 and 1.5 Hz, 2 × =CH*H*), 5.14 (2H, dd, *J* = 17.3 and 1.5 Hz, 2 × =CH*H*), 4.75 (4H, d, *J* = 6.1 Hz, 2 × NCH_2), 4.62 (1H, t, *J* = 7.4 Hz, CH), 2.87-2.80 (2H, m, CH_2), 2.72-2.62 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.7, 136.7, 133.8, 128.5, 128.2, 127.7, 125.6, 125.3, 121.3, 119.8, 118.6, 116.8, 109.5, 48.6, 37.7, 34.5, 33.5; HRMS exact mass calculated for $[M+Na]^+$ ($C_{31}H_{30}N_2Na^+$) requires *m/z* 453.2301, found *m/z* 453.2302.



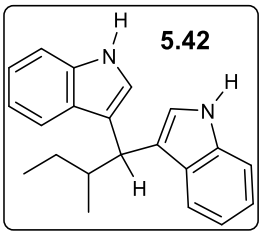
3,3'-(Dodecane-1,1-diyl)bis(1H-indole) (5.39). [5.24] Brown oil; 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (2H, br s, 2 × NH), 7.64 (2H, d, *J* = 7.4 Hz, ArH), 7.35 (2H, d, *J* = 7.4 Hz, ArH), 7.18 (2H, t, *J* = 7.4 Hz, ArH), 7.07 (2H, t, *J* = 7.4 Hz, ArH), 7.01 (2H, s, ArH), 4.51 (1H, t, *J* = 6.9 Hz, CH), 2.29-2.19 (2H, m, CH_2), 1.27 (18H, s, 9 × CH_2), 0.97-088 (3H, m, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.6, 127.2, 121.7, 121.3, 120.6, 119.7, 119.0, 111.0, 35.9, 34.0, 31.9, 29.8, 29.7, 29.7, 29.6, 29.3, 28.3, 22.7, 14.1; MS (ESI) m/z 423 $[M+Na]^+$.



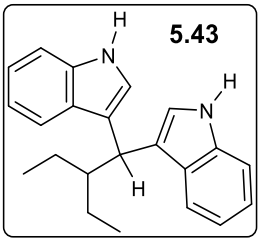
3,3´-(Heptane)bis(1*H*-Indole) (5.40). [5.25] Brown oil; 80% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (2H, br s, 2 × NH), 7.67 (2H, d, *J* = 7.5 Hz, ArH), 7.34 (2H, d, *J* = 7.5 Hz, ArH), 7.21 (2H, t, *J* = 7.5 Hz, ArH), 7.11 (2H, t, *J* = 7.5 Hz, ArH), 6.96 (2H, d, *J* = 2.1 Hz, ArH), 4.53 (1H, t, *J* = 7.4 Hz, CH), 2.33-2.21 (2H, m, CH_2), 1.50-1.41 (4H, m, 2 × CH_2), 1.37-1.29 (4H, m, 2 × CH_2), 0.93 (3H, t, *J* = 6.7 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.5, 127.2, 121.6, 121.4, 120.5, 119.6, 118.9, 111.0, 35.9, 34.0, 31.8, 29.4, 28.3, 22.7, 14.1; MS (ESI) m/z 353 $[M+Na]^+$.



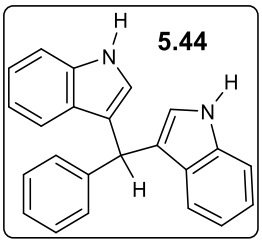
3,3´-((Cyclohexane)methylene)bis(1*H*-Indole) (5.41). [5.26] Brown solid; 66% yield; mp 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (2H, br s, 2 × NH), 7.69 (2H, d, *J* = 7.9 Hz, ArH), 7.33 (2H, d, *J* = 7.9 Hz, ArH), 7.16 (2H, t, *J* = 7.9 Hz, ArH), 7.13-7.05 (4H, m, ArH), 4.31 (1H, d, *J* = 8.8 Hz, CH), 2.34-2.23 (1H, m, CH), 1.87 (2H, d, *J* = 12.6 Hz, 2 × CH*H*), 1.75-1.62 (4H, m, 4 x CH*H*), 1.23-1.04 (4H, m, 4 × CH*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.3, 127.8, 121.6, 121.5, 119.7, 119.7, 119.0, 110.9, 42.9, 40.1, 32.4, 26.7, 26.7; MS (ESI) m/z 351 $[M+Na]^+$.



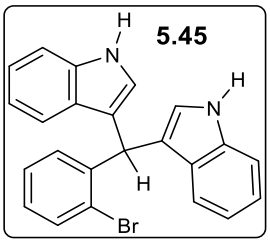
3,3´-(2-Methylbutane)bis(1*H*-Indole) (5.42). Brown oil; 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (2H, br s, 2 × NH), 7.73-7.64 (2H, m, ArH), 7.30 (2H, t, *J* = 7.9 Hz, ArH), 7.18 (2H, t, *J* = 7.9 Hz, ArH), 7.14-7.09 (2H, m, ArH), 7.06 (2H, s, ArH), 4.44 (1H, d, *J* = 7.7 Hz, CH), 2.48-2.39 (1H, m, CH), 1.74-1.63 (1H, m, CH*H*), 1.29-1.17 (1H, m, CH*H*), 1.03 (3H, d, *J* = 6.5 Hz, CH_3), 0.97 (3H, t, *J* = 7.3 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.3, 136.2, 127.9, 127.7, 121.8, 121.6, 121.6, 119.6, 119.0, 111.0, 39.4, 39.4, 28.0, 17.8, 12.0; HRMS exact mass calculated for $[M+Na]^+$ ($C_{21}H_{22}N_2Na^+$) requires *m/z* 325.1675, found *m/z* 325.1678.



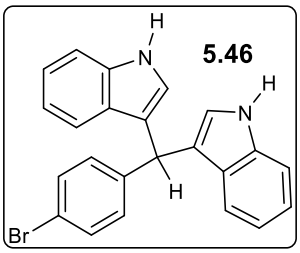
3,3´-(2-Ethylbutane)bis(1*H*-Indole) (5.43). Brown oil; 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (2H, br s, 2 × NH), 7.70 (2H, d, *J* = 7.9 Hz, ArH), 7.30 (2H, d, *J* = 7.9 Hz, ArH), 7.18 (2H, t, *J* = 7.9 Hz, ArH), 7.10 (2H, t, *J* = 7.9 Hz, ArH), 7.04 (2H, d, *J* = 2.2 Hz, ArH), 4.64 (1H, d, *J* = 7.9 Hz, CH), 2.32-2.25 (1H, m, CH), 1.64-1.55 (2H, m, 2 x C*H*H), 1.48-1.37 (2H, m, 2 × C*H*H), 0.96 (6H, t, *J* = 7.4 Hz, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.2, 127.7, 121.8, 121.6, 119.5, 119.4, 118.9, 111.0, 45.2, 36.0, 23.4, 11.5; HRMS exact mass calculated for $[M+Na]^+$ ($C_{22}H_{24}N_2Na^+$) requires *m/z* 339.1832, found *m/z* 339.1833.



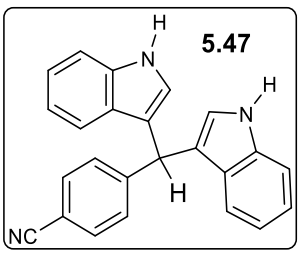
3,3´-(Phenylmethylene)bis(1*H*-Indole) (5.44). [5.21] Red foam; 89% yield; mp 140-142 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (2H, br s, 2 × NH), 7.45 (2H, d, *J* = 7.5 Hz, ArH), 7.40 (2H, d, *J* = 7.5 Hz, ArH), 7.38-7.31 (4H, m, ArH), 7.28 (1H, d, *J* = 7.5 Hz, ArH), 7.23 (2H, t, *J* = 7.5 Hz, ArH), 7.07 (2H, t, *J* = 7.5 Hz, ArH), 6.62 (2H, d, *J* = 1.6 Hz, ArH), 5.94 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.0, 136.6, 128.7, 128.2, 127.0, 126.1, 123.6, 121.9, 119.9, 119.6, 119.2, 111.0, 40.2; MS (ESI) m/z 345 $[M+Na]^+$.



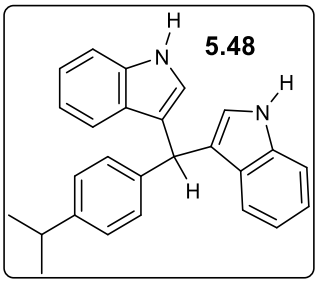
3,3´-((2-Bromophenyl)methylene)bis(1*H*-Indole) (5.45). [5.27] Pink foam; 66% yield; mp 76-78 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (2H, br s, 2 × NH), 7.66 (1H, dd, *J* = 7.6 and 1.4 Hz, ArH), 7.45 (2H, d, *J* = 7.9 Hz, ArH), 7.37 (2H, d, *J* = 7.9 Hz, ArH), 7.26 (1H, dd, *J* = 7.6 and 1.9 Hz, ArH), 7.22 (2H, t, *J* = 7.9 Hz, ArH), 7.17 (1H, td, *J* = 7.6 and 1.4 Hz, ArH), 7.12 (1H, dd, *J* = 7.6 and 1.9 Hz, ArH), 7.07 (2H, t, *J* = 7.9 Hz, ArH), 6.59 (2H, d, *J* = 2.2 Hz, ArH), 6.35 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.0, 136.7, 132.8, 130.4, 127.8, 127.3, 127.0, 124.8, 123.8, 122.0, 119.9, 119.3, 118.4, 111.1, 39.5; MS (ESI) m/z 425 $[M+Na]^+$.



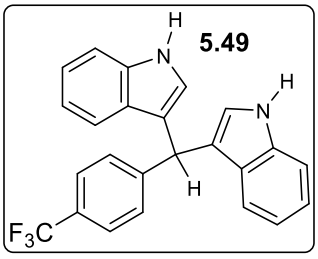
3,3´-((4-Bromophenyl)methylene)bis(1*H*-Indole) (5.46). [5.28] Red foam; 81% yield; mp 112-114 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89 (2H, br s, 2 × NH), 7.43-7.41 (4H, m, ArH), 7.36 (2H, d, *J* = 7.5 Hz, ArH), 7.29-7.19 (4H, m, ArH), 7.07 (2H, t, *J* = 7.5 Hz, ArH), 6.60 (2H, s, ArH), 5.88 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.1, 136.6, 131.2, 130.4, 126.8, 123.6, 122.0, 119.8, 119.7, 119.3, 118.9, 111.1, 39.6; MS (ESI) m/z 425 $[M+Na]^+$.



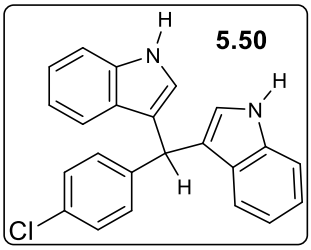
3,3´-((4-Ethynylphenyl)methylene)bis(1*H*-Indole) (5.47). [5.29] Red foam; 94% yield; mp 208-210 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (2H, br s, 2 × NH), 7.57 (2H, d, *J* = 8.2 Hz, ArH), 7.47 (2H, d, *J* = 8.2 Hz, ArH), 7.40 (2H, d, *J* = 8.2 Hz, ArH), 7.36 (2H, d, *J* = 8.2 Hz, ArH), 7.23 (2H, t, *J* = 8.2 Hz, ArH), 7.06 (2H, t, *J* = 8.2 Hz, ArH), 6.66 (2H, d, *J* = 2.2 Hz, ArH), 5.96 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 149.8, 136.7, 132.1, 129.5, 126.7, 123.6, 122.2, 119.5, 119.2, 119.1, 118.1, 111.2, 109.9, 40.3; MS (ESI) m/z 370 $[M+Na]^+$.



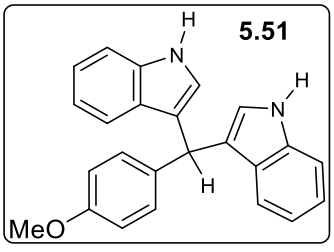
3,3′-((4-Isopropylphenyl)methylene)bis(1*H*-Indole) (5.48). [5.30] Orange oil; 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (2H, br s, 2 × NH), 7.46 (2H, d, *J* = 8.2 Hz, ArH), 7.35 (2H, td, *J* = 8.2 and 0.9 Hz, ArH), 7.31 (2H, d, *J* = 8.2 Hz, ArH), 7.24-7.16 (4H, m, ArH), 7.08-7.03 (2H, m, ArH), 6.65 (2H, dd, *J* = 2.4 and 0.9 Hz, ArH), 5.90 (1H, s, CH), 2.99-2.88 (1H, m, CH), 1.29 (6H, d, *J* = 6.9 Hz, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.4, 141.2, 136.6, 128.5, 127.1, 126.2, 123.5, 121.8, 119.9, 119.9, 119.1, 111.0, 39.7, 33.6, 24.0; MS (ESI) m/z 387 $[M+Na]^+$.



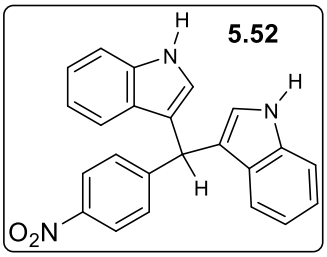
3,3′-((4-(Trifluoromethyl)phenyl)methylene)bis(1*H*-Indole) (5.49). [5.21] Pink foam; 92% yield; mp 67-69 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (2H, br s, 2 × NH), 7.60 (2H, d, *J* = 8.1 Hz, ArH), 7.51 (2H, d, *J* = 8.1 Hz, ArH), 7.46 (2H, d, *J* = 8.1 Hz, ArH), 7.38 (2H, d, *J* = 8.1 Hz, ArH), 7.32-7.24 (2H, m, ArH), 7.15-7.10 (2H, m, ArH), 6.61 (2H, d, *J* = 2.4 Hz, ArH), 6.01 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.2, 136.7, 129.1, 128.5 (q, *J* = 32.0 Hz), 126.9, 125.3, 125.3 (q, *J* = 3.7 Hz), 124.5 (q, *J* = 272 Hz), 123.8, 122.3, 119.8, 119.5, 118.8, 111.3, 40.2; ^{19}F NMR: (376 MHz, $CDCl_3$) δ: 62.1; MS (ESI) m/z 413 $[M+Na]^+$.



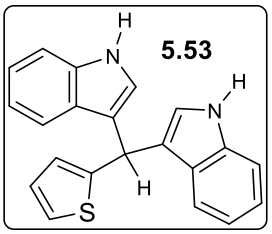
3,3′-((4-Chlorophenyl)methylene)bis(1*H*-Indole) (5.50). [5.21] Orange foam; 87% yield; mp 77-79 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (2H, br s, 2 × NH), 7.47 (2H, d, *J* = 7.9 Hz, ArH), 7.35 (2H, d, *J* = 7.9 Hz, ArH), 7.35-7.29 (4H, m, ArH), 7.28 (2H, td, *J* = 7.0 and 0.8 Hz, ArH), 7.14-7.10 (2H, m, ArH), 6.56 (2H, dd, *J* = 2.4 and 0.8 Hz, ArH), 5.93 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.5, 136.5, 131.7, 130.0, 128.3, 126.8, 123.6, 122.0, 119.7, 119.3, 118.9, 111.1, 39.5; MS (ESI) m/z 379 $[M+Na]^+$.



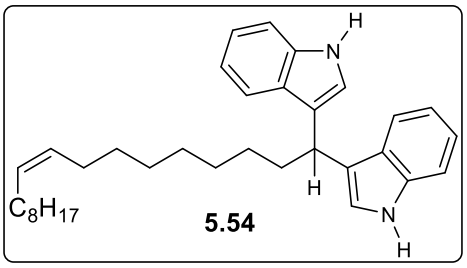
3,3′-((4-Methoxyphenyl)methylene)bis(1*H*-Indole) (5.51). [5.21] Orange solid; 41% yield; mp 188-190 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89 (2H, br s, 2 × NH), 7.43 (2H, d, *J* = 7.6 Hz, ArH), 7.37 (2H, d, *J* = 7.6 Hz, ArH), 7.31-7.26 (2H, m, ArH), 7.20 (2H, t, *J* = 7.6 Hz, ArH), 7.04 (2H, t, *J* = 7.6 Hz, ArH), 6.85 (2H, d, *J* = 8.6 Hz, ArH), 6.66 (2H, d, *J* = 1.6 Hz, ArH), 5.87 (1H, s, CH), 3.81 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.9, 136.7, 136.2, 129.6, 127.1, 123.5, 121.9, 120.0, 120.0, 119.2, 113.6, 111.0, 55.2, 39.3; MS (ESI) m/z 375 $[M+Na]^+$.



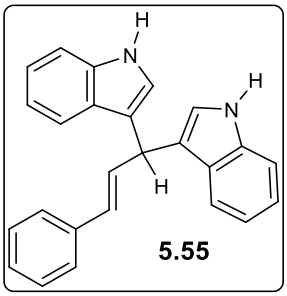
3,3´-((4-Nitrophenyl)methylene)bis(1*H*-Indole) (5.52). [5.27] Yellow solid; 96% yield; mp 217-219 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16 (2H, d, *J* = 8.7 Hz, ArH), 8.04 (2H, br s, 2 × NH), 7.53 (2H, d, *J* = 8.7 Hz, ArH), 7.41 (2H, d, *J* = 8.2 Hz, ArH), 7.36 (2H, d, *J* = 8.2 Hz, ArH), 7.23 (2H, t, *J* = 7.5 Hz, ArH), 7.05 (2H, t, *J* = 7.5 Hz, ArH), 6.71 (2H, d, *J* = 1.6 Hz, ArH), 6.02 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 151.8, 136.7, 129.5, 126.6, 123.6, 122.4, 119.6, 119.5, 118.1, 111.2, 40.2; MS (ESI) m/z 390 [M+Na]+.



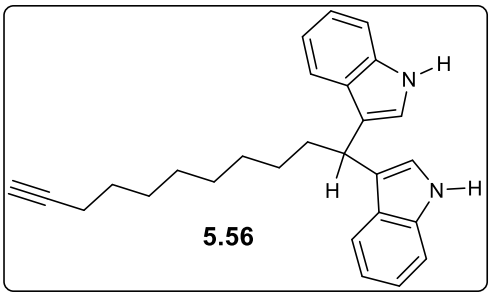
3,3´-(Thiophen-2-methylene)bis(1*H*-Indole) (5.53). [5.21]Brown solid; 79% yield; mp 181-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72 (2H, br s, 2 × NH), 7.54 (2H, d, *J* = 7.5 Hz, ArH), 7.34 (2H, d, *J* = 7.5 Hz, ArH), 7.28-7.18 (3H, m, ArH), 7.11 (2H, t, *J* = 7.5 Hz, ArH), 6.97 (2H, br s, ArH), 6.77 (2H, s, ArH), 6.22 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.6, 136.6, 126.8, 126.4, 125.1, 123.6, 123.2, 122.0, 119.8, 119.4, 111.1, 35.3; MS (ESI) m/z 351 $[M+Na]^+$.



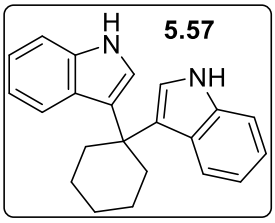
3,3´-(Oleyl-2-methylene)bis(1*H*-Indole) (5.54). Brown oil; 40% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (2H, br s, 2 × NH), 7.65 (2H, d, *J* = 7.9 Hz, ArH), 7.35 (2H, d, *J* = 7.9 Hz, ArH), 7.20 (2H, t, *J* = 7.9 Hz, ArH), 7.09 (2H, t, *J* = 7.9 Hz, ArH), 6.99 (2H, s, ArH), 5.43-5.36 (2H, m, 2 × CH=), 4.52 (1H, t, *J* = 7.4 Hz, CH), 2.32-2.22 (2H, m, CH_2), 2.13-1.97 (4H, m, 2 × CH_2), 1.45-1.24 (22H, m, 11 x CH_2), 0.99-0.90 (3H, m, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.6, 129.9, 127.2, 121.7, 121.4, 120.5, 119.6, 118.9, 111.0, 35.8, 34.0, 31.9, 29.8, 29.5, 29.3, 29.3, 28.3, 27.2, 22.7, 14.1; HRMS exact mass calculated for $[M+Na]^+$ ($C_{34}H_{46}N_2Na^+$) requires *m/z* 505.3553, found *m/z* 505.3561.



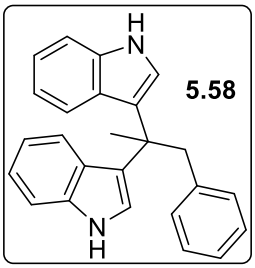
3,3´-(1-(2-Phenylethylene)methylene)bis(1*H*-Indole) (5.55). [5.31]Red oil; 38% yield (61:39 *trans:cis*); <u>*trans isomer:*</u> ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (2H, br s, 2 × NH), 7.65 (2H, d, *J* = 7.9 Hz, ArH), 7.39 (4H, t, *J* = 7.9 Hz, ArH), 7.33-7.29 (2H, m, ArH), 7.23 (3H, t, *J* = 7.9 Hz, ArH), 7.10 (2H, t, *J* = 7.9 Hz, ArH), 6.91 (2H, d, *J* = 2.2 Hz, ArH), 6.87-6.81 (1H, dd, *J* = 15.8 and 7.0 Hz, =CH), 6.58 (1H, d, *J* = 15.8 Hz, =CH), 5.44 (1H, d, *J* = 7.0 Hz, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.7, 136.7, 132.4, 129.9, 128.4, 127.0, 126.3, 122.6, 121.9, 120.0, 119.3, 118.4, 111.1, 37.4; MS (ESI) m/z 371 $[M+Na]^+$.



3,3'-(Undec-10-yne-1,1-diyl)bis(1*H*-indole) (5.56). Brown oil; 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (2H, br s, 2 × NH), 7.67 (2H, d, *J* = 8.1 Hz, ArH), 7.34 (2H, d, *J* = 8.1 Hz, ArH), 7.25-7.18 (2H, m, ArH), 7.14-7.08 (2H, m, ArH), 6.96 (2H, d, *J* = 2.2 Hz, ArH), 4.53 (1H, t, *J* = 7.4 Hz, CH), 2.30-2.19 (4H, m, 2 × CH_2), 2.01 (1H, t, *J* = 2.7 Hz, ΞCH), 1.60-1.53 (2H, m, CH_2), 1.48-1.37 (6H, m, 3 × CH_2), 1.37-1.29 (4H, m, 2 × CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.5, 127.1, 121.6, 121.4, 120.4, 119.6, 118.9, 111.0, 84.8, 68.1, 35.8, 33.9, 29.6, 29.4, 29.0, 28.7, 28.4, 28.2, 18.3; HRMS exact mass calculated for $[M+Na]^+$ ($C_{27}H_{30}N_2Na^+$) requires *m/z* 405.2302, found *m/z* 405.2313.



3,3'-(Cyclohexane-1,1-diyl)bis(1H-indole) (5.57). [5.32] White foam; 26% yield; mp 76-77 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (2H, br s, 2 × NH), 7.65 (2H, d, *J* = 8.1 Hz, ArH), 7.32 (2H, d, *J* = 8.1 Hz, ArH), 7.15 (4H, t, *J* = 7.6 Hz, ArH), 7.00 (2H, t, *J* = 7.6 Hz, ArH), 2.68-2.58 (4H, m, 4 × CH*H*), 1.79-1.62 (6H, m, 6 × CH*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.0, 126.3, 123.6, 122.0, 121.4, 121.2, 118.5, 111.0, 39.5, 36.8, 26.8, 23.0; MS (ESI) m/z 337 $[M+Na]^+$.



3,3'-(1-Phenylethane-1,1-diyl)bis(1H-indole) (5.58). [5.32] Brown foam; 17% yield, reaction time 18 h, 5 mol% catalyst; 170-172 oC; 1H NMR (400 MHz, $CDCl_3$) δ: 7.73 (2H, br s, 2 × NH), 7.45 (2H, d, *J* = 7.6 Hz, ArH), 7.40-7.34 (4H, m, ArH), 7.31-7.25 (3H, m, ArH), 7.19 (2H, t, *J* = 7.6 Hz, ArH), 7.00 (2H, t, *J* = 7.6 Hz, ArH), 6.58 (2H, s, ArH), 2.41 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.0, 137.0, 128.0, 127.7, 126.4, 125.8, 124.6, 123.4, 122.0, 121.4, 118.8, 111.1, 43.7, 28.7; MS (ESI) m/z 359 [M+Na]+

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CHAPTER 6

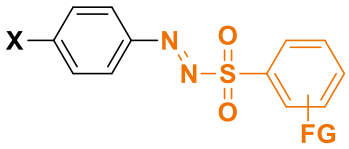
SYNTHESIS AND DEVELOPMENT OF NEW DYEDAUXILIARY GROUPS.

6.1 INTRODUCTION.

Considering the importance of *dyedauxiliary groups* in organic synthesis [6.1-6.23;6.27-6.32], in material chemistry [6.24,6.25] and in the synthesis of polymers [6.26], our group focused its attention on the development of new classes of *dyedauxiliary groups* to have new powerful radical sources useful for organic synthesis that could be activated by (visible) light. In doing so, alternative compounds have been synthesized and tested. The first class of compounds that has been prepared was that of the arylazo arylsulfones where the methyl group tethered to the sulfur atom was replaced by a substituted aryl moiety. Moreover, arylazo carboxylates along with acylazo carboxylates have been prepared as well to change the functional groups tethered to the diazo moiety. The aspect of the final products shifts from the bright yellow to orange colour characteristic of the arylazo sulfones to deeply red oils in the other cases.

6.2 RESULTS AND DISCUSSION.

The synthesis of arylazo arylsulfones was carried out, affording a plethora of bench-stable and coloured compounds **6.1a-p** (Figure 6.1).

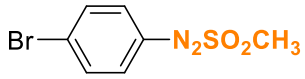
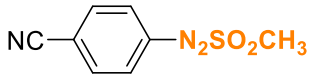
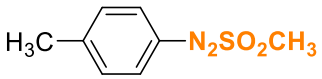


6.1a, X = Br FG = 4-NO_2	**6.1f**, X = CN FG = 4-NO_2	**6.1k**, X = CH_3 FG = 4-NO_2
6.1b, X = Br FG = H	**6.1g**, X = CN FG = H	**6.1l**, X = CH_3 FG = H
6.1c, X = Br FG = 4-CH_3	**6.1h**, X = CN FG = 4-CH_3	**6.1m**, X = CH_3 FG = 4-CH_3
6.1d, X = Br FG = 4-Br	**6.1i**, X = CN FG = 4-Br	**6.1n**, X = CH_3 FG = 4-Br
6.1e, X = Br FG = 2-OCF_3	**6.1j**, X = CN FG = 2-OCF_3	**6.1o**, X = CO_2CH_3 FG = 4-NO_2
		6.1p, X = CO_2CH_3 FG = 4-Br

Figure 6.1. Arylazo arylsulfones employed.

UV-vis spectra were recorded on these bright yellow to orange-coloured compounds showing a maximum of absorption in the UV region and one less intense band in the visible region (Table 6.1).

Table 6.1. Molar extinction coefficient ε (M^{-1} cm^{-1}) of arylazo arylsulfones studied and of some arylazo sulfones for the sake of comparison.

Compound	λ, nm (ε, $M^{-1}cm^{-1}$)	λ, nm (ε, $M^{-1}cm^{-1}$)
6.1a	314(21028)	440(355)
6.1b	313(17895)	427(241)
6.1c	313(17577)	428(336)
6.1d	315(19371)	427(423)
6.1e	421(27744)	314(232)
	309, (16355)	425, (210)
6.1f	295(22031)	367(1688)
6.1g	291(22573)	435(225)
6.1h	290(19761)	437(218)
6.1i	291(20400)	434(210)
6.1j	293(32267)	430(138)
	288, (19568)	435, (155)
6.1k	315(19372)	421(423)
6.1l	424(24955)	312(277)
6.1m	314(26854)	426(213)
6.1n	317(19942)	422(312)
	310, (15264)	420, (215)

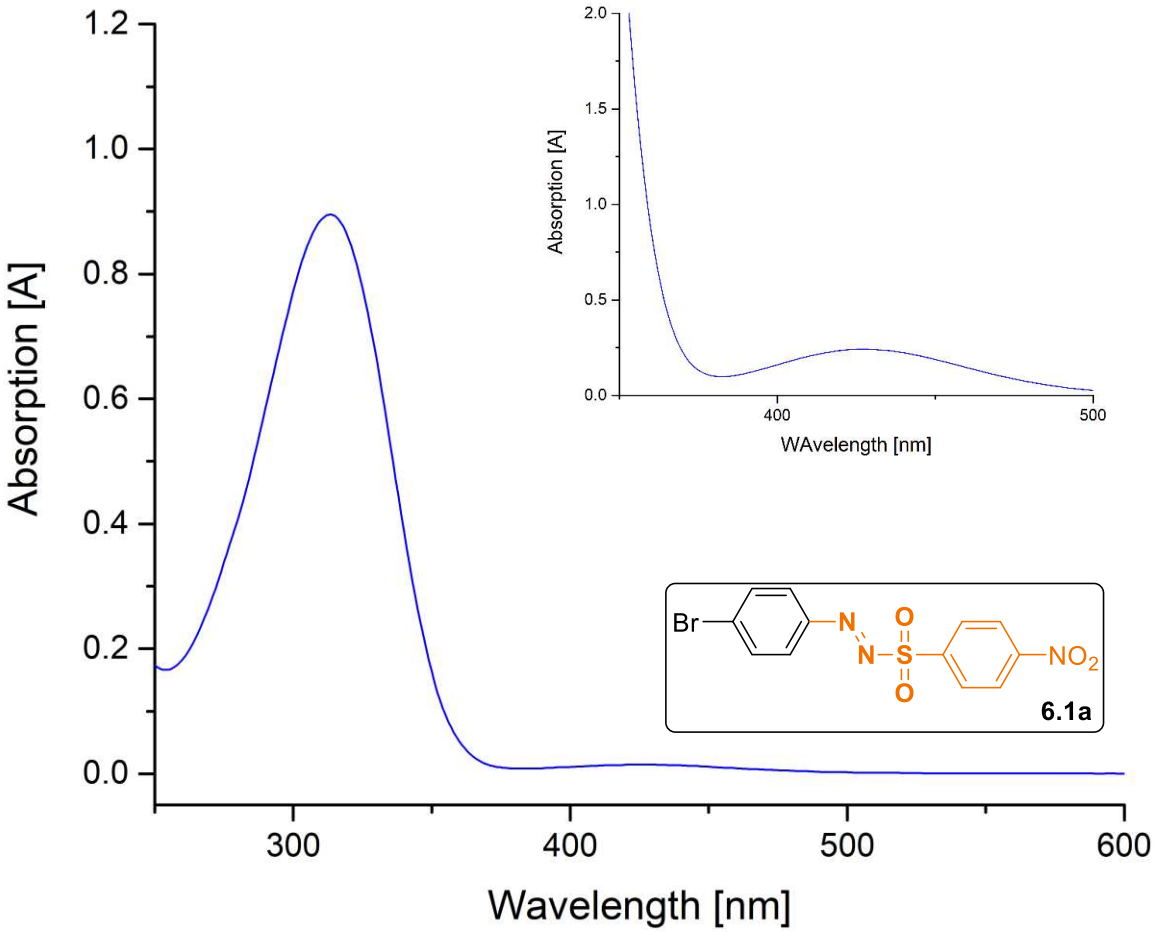
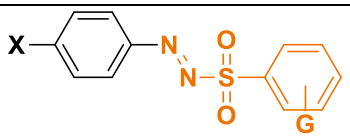


Figure 6.2. Representative UV-vis spectra of arylazo arylsulfone **6.1a** in acetonitrile 1×10^{-4}M, meanwhile the smaller portion of the spectra is **6.1a** in acetonitrile 1×10^{-3}M.

Moreover, the quantum yields of disappearance were evaluated to have a comparison with the arylazo sulfones: as a general trend, these compounds had slightly higher value of quantum yields in the visible region (427 nm). Interestingly, the values measured in the UV region (370 nm) were consistently higher (Table 6.2). With these gratifying preliminary results on the photoreactivity of compounds **6.1a-6.1p**, we tested their feasibility in the arylation of furan and mesitylene. To have a better understanding of the process, the arylating moiety (the one that actively takes part in the arylation process) was kept the same, while varying the aryl group tethered to the sulfonyl part.

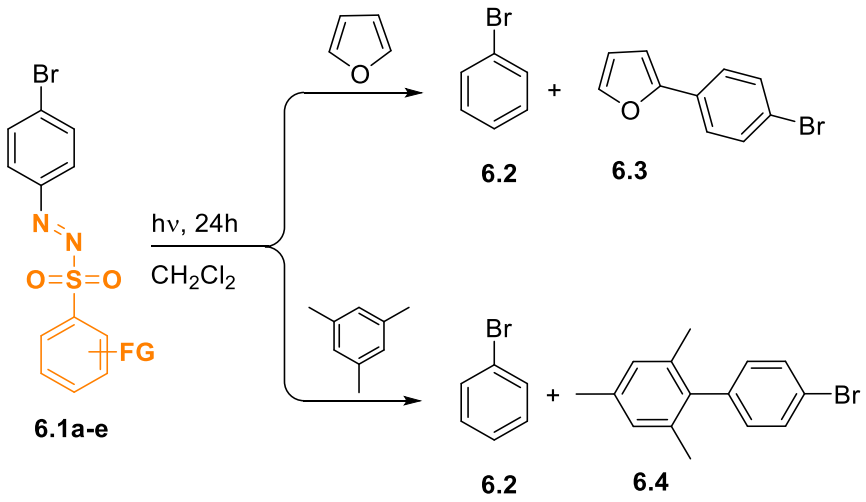
Table 6.2. Quantum yield of disappearance of arylazo arylazo sulfones **6.1a-6.1p**.



Compound	Quantum Yield (Φ_{-1}) [a]
6.1a	0.04, 0.10 [b], 0.09 [c]
6.1b	0.03
6.1c	0.03, 0.89 [d]
6.1d	0.02
6.1e	0.02
6.1f	0.03
6.1g	0.03
6.1h	0.03
6.1i	0.02
6.1j	0.01, 0.62 [d]
6.1k	0.03
6.1l	0.04
6.1m	0.03, 0.91 [d]
6.1n	0.03
6.1o	0.06
6.1p	0.03, 0.40 [d]

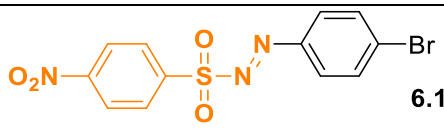
[a] Quantum yield of disappearance measured irradiating at 427 nm one quartz cuvette containing a 2.5×10^{-3} M solution of the corresponding arylazo sulfone and checking the consumption at its absorption maximum in the spectrophotometer. [b] Quantum yield measured in oxygenated solutions. [c] Quantum yield measured in argon purged solutions. [d] Quantum yield of disappearance measured at 370 nm.

Compounds **6.1a-e** (Tables 6.3-6.7 and Scheme 6.1) were tested as representative azosulfones in the arylation of furan and mesitylene. The irradiation of compound **6.1a** in DCM (for solubility reason) in the absence of traps led to the formation of bromobenzene **6.2** in 24% yield measured by GC analysis. The irradiation carried out with 10 equivalents of furan or mesitylene led to a poor arylation yield (compounds **6.3** and **6.4** were formed in less than 11% yield, Table 6.3). Irradiation in the UV region (390 or 370 nm) did not improve the arylation yield.



Scheme 6.1. General scheme for the photochemical arylation of furane or mesitylene traps.

Table 6.3. Attempted photoarylation employing arylazo arylsulfone **6.1a** as radical source.



6.1a

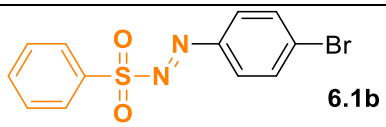
FURAN (equiv.)	MESITYLENE (equiv.)	hν (nm)	Yield **6.2** (%) [a]	Yield **6.3** (%) [a]	Yield **6.4** (%) [a]
/	/	456 nm	24	/	/
10 equiv.	/	456 nm	11	8	/
/	10 equiv.	456 nm	22	/	11
/	/	390 nm	15	/	/
10 equiv.	/	390 nm	15	12	/
/	10 equiv.	390 nm	27	/	15
/	/	370 nm	31	/	/
10 equiv.	/	370 nm	28	2	/
/	10 equiv.	370 nm	18	/	8

[a] Yields calculated by means of GC analysis. DCM as the solvent.

Arylazo arylsulfone **6.1b** was next dissolved in DCM and irradiated in the presence of 10 equivalents of furan or mesitylene at three different wavelengths (456 nm, 390 nm and 370 nm). With blue light (456 nm), the formation of arylated product **6.3** was found in a good yield (75%). Arylation of mesitylene was unsuccessful with only 6% of **6.4** detected. At 390 nm compound **6.3** was formed in

a lower yield (45%) despite the formation of **6.4** increased to 21% yield. Finally, the adoption of 370 nm gave results quite similar to that obtained under 390 nm irradiation (Table 6.4).

Table 6.4. Photoreactivity of **6.1b** in DCM.



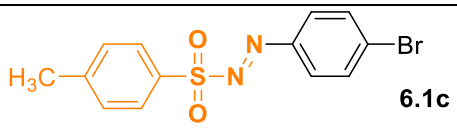
6.1b

FURAN (equiv.)	MESITYLENE (equiv.)	hν (nm)	Yield **6.2** (%) [a]	Yield **6.3** (%) [a]	Yield **6.4** (%) [a]
/	/	456 nm	17	/	/
10 equiv.	/	456 nm	8	75	/
/	10 equiv.	456 nm	27	/	6
/	/	390 nm	33	/	/
10 equiv.	/	390 nm	7	45	/
/	10 equiv.	390 nm	9	/	21
/	/	370 nm	35	/	/
10 equiv.	/	370 nm	5	42	/
/	10 equiv.	370 nm	15	/	33

[a] Yields calculated by means of GC analysis. DCM as the solvent.

Irradiation of **6.1c** in DCM at 456 nm led to the exclusive formation of **6.2** in 27% yield. In this case the formation of arylated products **6.3** and **6.4** was not so different by changing the light source and in any case modest (not higher than 44%, Table 6.5).

Table 6.5. Photoreactivity of **6.1c** in dichloromethane.



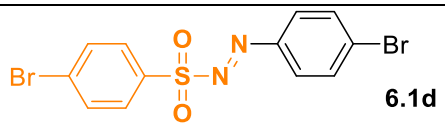
6.1c

FURAN (equiv.)	MESITYLENE (equiv.)	hν (nm)	Yield **6.2** (%) [a]	Yield **6.3** (%) [a]	Yield **6.4** (%) [a]
/	/	456 nm	27	/	/
10 equiv.	/	456 nm	3	34	/
/	10 equiv.	456 nm	7	/	21
/	/	390 nm	27	/	/
10 equiv.	/	390 nm	7	44	/
/	10 equiv.	390 nm	17	/	28
/	/	370 nm	21	/	/
10 equiv.	/	370 nm	5	27	/
/	10 equiv.	370 nm	9	/	19

[a] Yields calculated by means of GC analysis. DCM as the solvent.

Even in the case of **6.1d** the irradiation in DCM led to an exclusive photoreduction. The presence of furan and mesitylene led to unsatisfactory arylations with a low overall mass balance (Table 6.6).

Table 6.6. Photoreactivity of **6.1d** in dichloromethane.



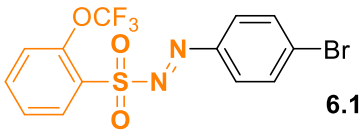
6.1d

FURAN (equiv.)	MESITYLENE (equiv.)	hν (nm)	Yield **6.2** (%) [a]	Yield **6.3** (%) [a]	Yield **6.4** (%) [a]
/	/	456 nm	33	/	/
10 equiv.	/	456 nm	12	9	/
/	10 equiv.	456 nm	29	/	21
/	/	390 nm	33	/	/
10 equiv.	/	390 nm	16	21	/
/	10 equiv.	390 nm	26	/	19
/	/	370 nm	28	/	/
10 equiv.	/	370 nm	21	22	/
/	10 equiv.	370 nm	16	/	11

[a] Yields calculated by means of GC analysis. DCM as the solvent.

Finally, the photochemistry of arylazo arylsulfone **6.1e** was investigated. Compound **6.2** was obtained in 31% yield upon blue light irradiation while the arylated product **6.3** was obtained as a minor product (30% yield) when adding furan to the reaction mixture. Biphenyl **6.4** was formed quite cleanly in 42% yield at 370 nm (Table 6.7).

Table 6.7. Photoreactivity of **6.1e** in dichloromethane.

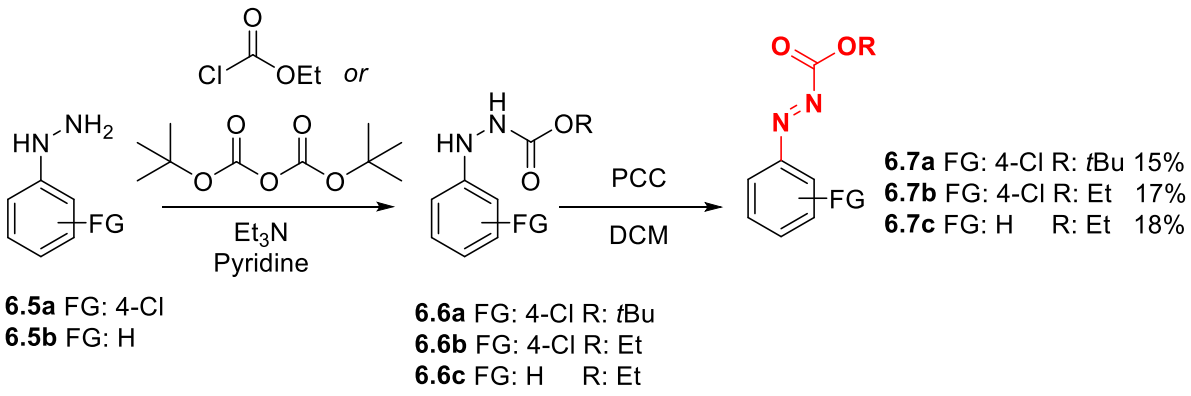


6.1e

FURAN (equiv.)	MESITYLENE (equiv.)	hν (nm)	Yield **6.2** (%) [a]	Yield **6.3** (%) [a]	Yield **6.4** (%) [a]
/	/	456 nm	31		
10 equiv.	/	456 nm	56	30	
/	10 equiv.	456 nm	24		32
/	/	390 nm	10		
10 equiv.	/	390 nm	6	17	
/	10 equiv.	390 nm	22		26
/	/	370 nm	36		
10 equiv.	/	370 nm	30	18	
/	10 equiv.	370 nm	2		41

[a] Yields calculated by means of GC analysis. DCM as the solvent.

Concerning the arylazo carboxylates, the synthesis was performed (Scheme 6.2) from differently substituted arylhydrazines **6.5a-b** by using ethyl chloroformate or Boc anhydride to form the acyl aryl hydrazines **6.6a-c**, which were then oxidized (in the presence of PCC) to the bench stable red compounds **6.7a-c**. The UV-vis absorption spectra of such compounds were recorded, showing an intense absorption band in the UV region and a less intense one above 400 nm (Figure 6.3).



Scheme 6.2. Synthesis of arylazo carboxylates.

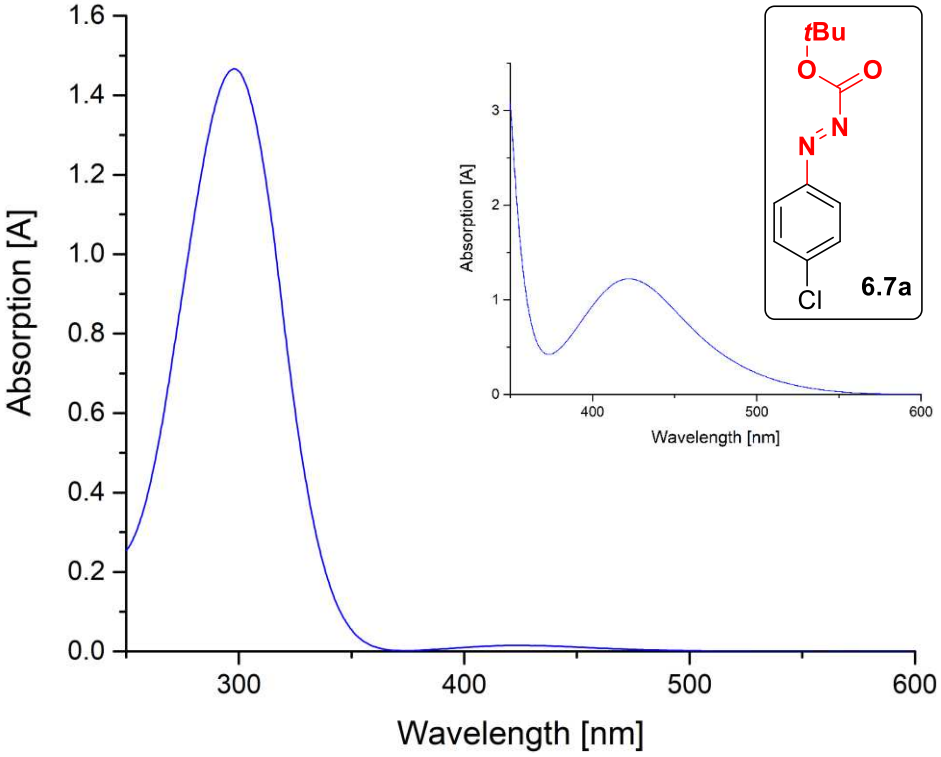
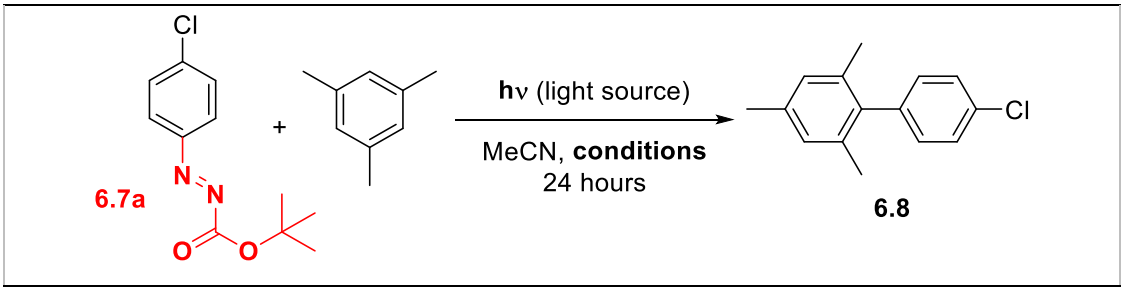


Figure 6.3. Representative UV-vis spectra of arylazo carboxylate **6.7a** in acetonitrile 1×10^{-4} M, meanwhile the smaller portion of the spectra is **6.7a** in acetonitrile 1×10^{-2} M.

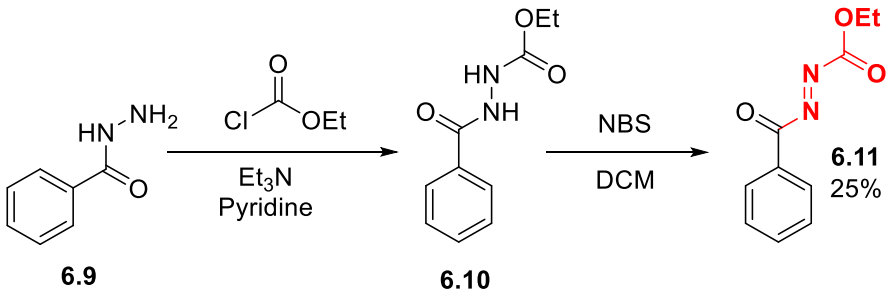
We were then intrigued to test the photochemical properties of **6.7**. The attempts performed to trap the aryl radical, possibly obtained from the photolysis of **6.7a**, by mesitylene (used in large excess 10 equiv. and 20 equiv.) were unsuccessful even by varying the irradiation wavelength. Interestingly, thermal test carried out on **6.7a-c** by refluxing the solution in the presence of mesitylene resulted in the complete recovery of the starting materials (Table 6.8).

Table 6.8. Representative photochemical trials carried out on the arylazo carboxylate **6.7a**.



CONDITIONS	MESITYLENE (equiv.)	hν (nm)	Yield **6.8** (%)
room temperature	10 equiv.	456 nm	/
room temperature	20 equiv.	456 nm	/
60°C	10 equiv.	/	/
60°C	20 equiv.	/	/
room temperature	10 equiv.	310 nm	/
room temperature	20 equiv.	310 nm	/

The synthesis of the acylazo carboxylates was next performed. To fulfil this procedure, benzohydrazide **6.9** was employed as a starting material and acylated with ethyl chloroformate. This step was quantitative and the crude product **6.10** was used for the oxidation step without further purifications. The oxidation was performed with freshly recrystalized NBS affording product **6.11** (Scheme 6.3).



Scheme 6.3**.** Synthesis of acylazo carboxylates and arylazo phosphine oxide.

Compound **6.11** is a bright red oil with a strong absorption in the UV and one in the visible (Figure 6.4).

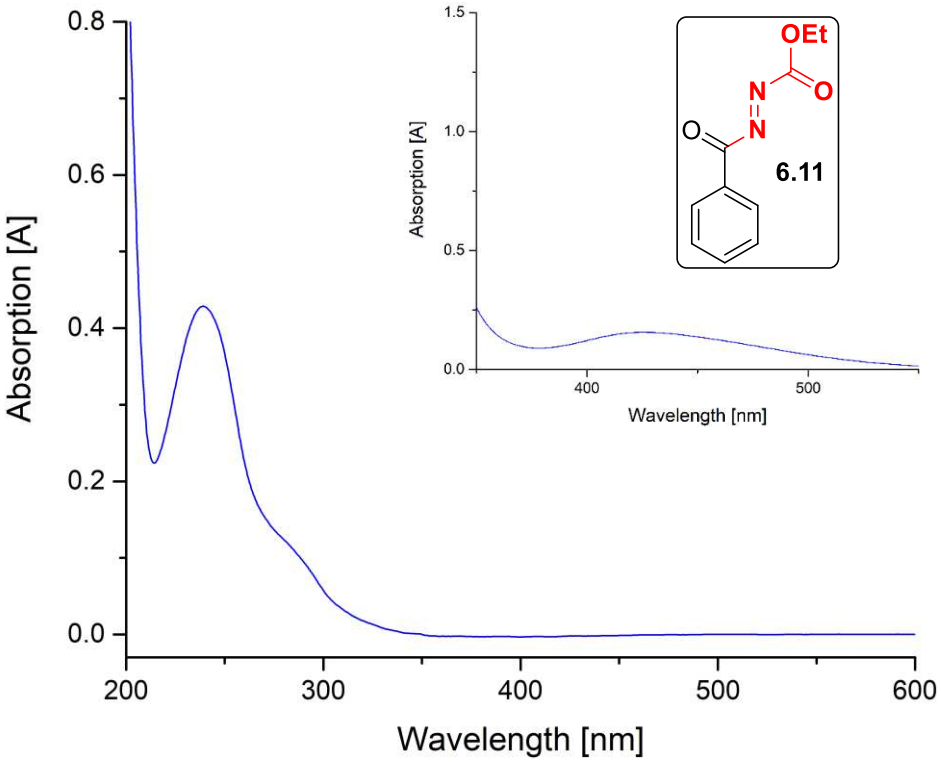
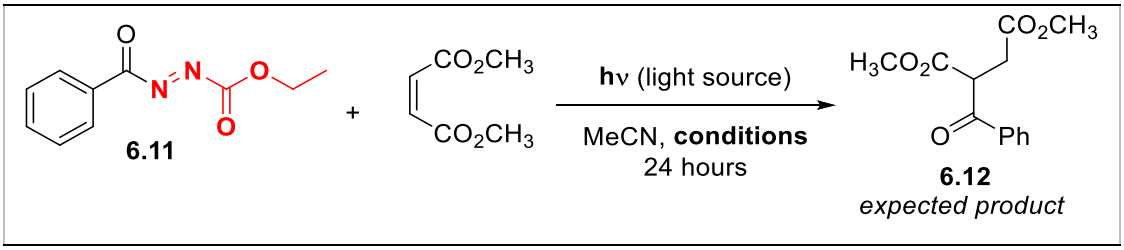


Figure 6.4. Representative UV-vis spectra of arylazo phosphine oxide **6.11** in acetonitrile 1×10^{-4}M, meanwhile the smaller portion of the spectra is **6.11** in acetonitrile 1×10^{-2}M.

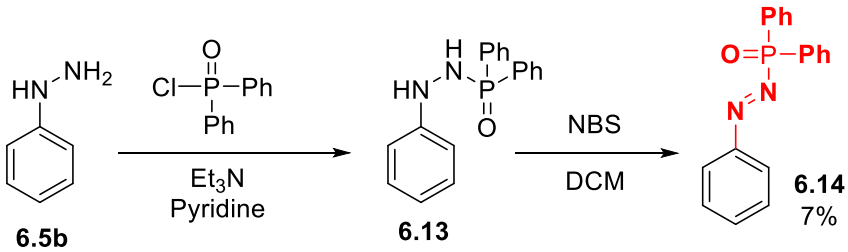
Unfortunately, compound **6.11** proved to be photochemically and thermally stable. The trials carried out were similar to the one for arylazo carboxylates, but instead of an electron-rich radical trap an electron-poor olefin was employed to trap the nucleophilic acyl radical possibly generated (Table 6.9).

Table 6.9. Photochemical trials carried out on the acylazo carboxylate **6.11**.



CONDITIONS	DIMETHYL MALEATE (equiv.)	hν (nm)	Yield **6.12** (%)
room temperature	10 equiv.	456 nm	/
room temperature	20 equiv.	456 nm	/
60°C	10 equiv.	/	/
room temperature	10 equiv.	310 nm	/
room temperature	20 equiv.	310 nm	/

Finally, arylazo phosphine oxide were prepared according to a previous procedure (Scheme 6.4). The synthesis was performed starting from arylhydrazine **6.5b** with diphenylphosphinic chloride, the second step was performed using NBS as oxidant yielding product **6.14** as a red oil in a very low yield.



Scheme 6.4**.** Synthesis of arylazo phosphine oxide.

The UV-vis spectra (Figure 6.5) were recorded and showed an intense absorption band in the UV region and a small one in the visible light region. Unluckily, even in this case, the use of this new class of compound as radical sources failed. (Table 6.10).

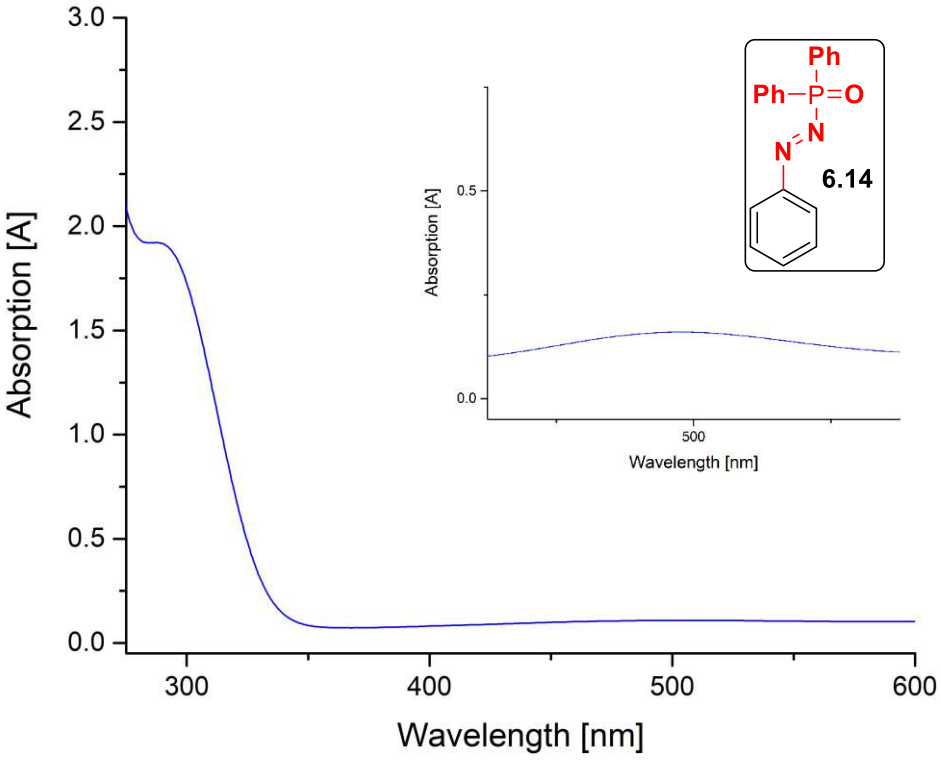
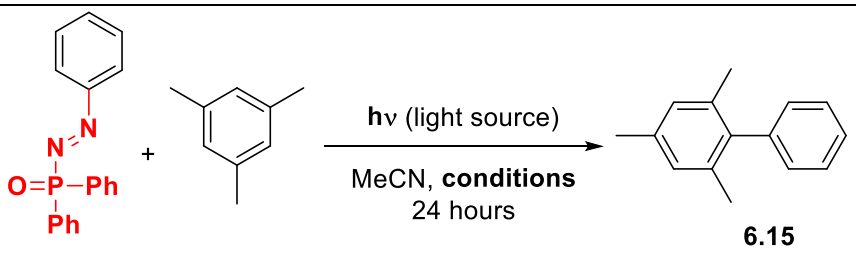


Figure 6.5. Representative UV-vis spectra of arylazo phosphine oxide **6.14** in acetonitrile 1×10^{-4}M, meanwhile the smaller portion of the spectra is **6.14** in acetonitrile 1×10^{-3}M.

Table 6.10. Photochemical trials carried out on the arylazo phosphine oxide **6.14**.



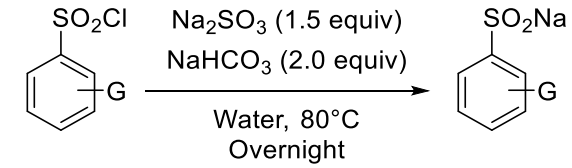
CONDITIONS	MESITYLENE (equiv.)	hν (nm)	Yield **6.15** (%)
room temperature	10 equiv.	456 nm	/
room temperature	20 equiv.	456 nm	/
60°C	20 equiv.	/	/
room temperature	10 equiv.	310 nm	/
room temperature	20 equiv.	310 nm	/

6.3 CONCLUSIONS.

In conclusion, a set of new *dyedauxiliary* groups have been tested and investigated. Arylazo arylsulfonates were a promising class of compounds and showed similar properties to the analogue arylazo sulfones. Deeper investigations must be carried out to evaluate the possibility of using both aryl radicals and sulfonyl radicals generated through the use of light from these molecules. Unfortunately, the class of arylazo carboxylates and acylazo carboxylates, prepared with a novel synthetical approach, proved to be thermally and photochemically stable. Moreover, arylazo phosphine oxide did not show any interesting photochemical behaviour under visible and UV light irradiations.

6.4 EXPERIMENTAL SECTION.

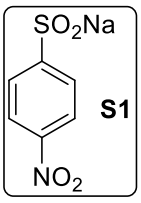
General procedure for the synthesis of sodium sulfinates. The synthesis was performed following a procedure known in literature [6.33]. The selected sulfonyl chloride is put in a round bottom flask and dissolved in 10 mL of HPLC purity water (10 mmol, 1 M) with sodium sulphite (15 mmol, 1.5 equiv) and sodium bicarbonate (20 mmol, 2 equiv). The so-formed solution was stirred and heated overnight at 80 °C. Finally, the solution is concentrated under reduced pressure and the residue was extracted with hot ethanol, which is removed under reduced pressure to afford the desired sodium sulfinate. (Scheme 6.5).



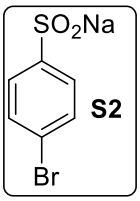
C1 G: 4-NO_2
C2 G: 4-Br
C3 G: 2-OCF_3

S1 G: 4-NO_2
S2 G: 4-Br
S3 G: 2-OCF_3

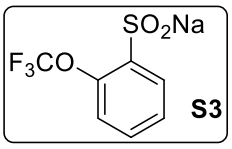
Scheme 6.5. General procedure for the synthesis of sodium sulfinates.



Synthesis of sodium 4-nitrobenzenesulfinate (S1): Starting from 2.20 g (10 mmol) of 4-nitrobenzenesulfonyl chloride **C1**, 1.87 g (15 mmol) of Na_2SO_3 and 1.66 g (20 mmol) of $NaHCO_3$ in 10 mL of water. Sodium 4-nitrobenzensulfinate **S1** was obtained as an pale orange solid 1.30 g (6.2 mmol, 62%).

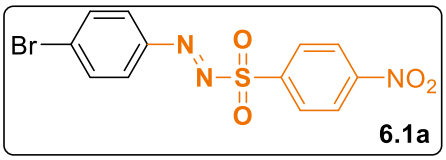


Synthesis of sodium 4-bromobenzenesulfinate (S2): Starting from 2.54 g (10 mmol) of 4-bromobenzenesulfonyl chloride **C2**, 1.87 g (15 mmol) of Na_2SO_3 and 1.66 g (20 mmol) of $NaHCO_3$ in 10 mL of water. Sodium 4-nitrobenzensulfinate **S2** was obtained as a white solid 1.16 g (4.8 mmol, 48%).

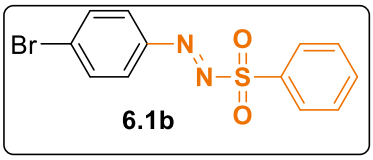


Synthesis of sodium 2-(trifluoromethoxy)benzenesulfinate (S3): Starting from 2.60 g (10 mmol) of 2-(trifluoromethoxy)benzenesulfonyl chloride **C3**, 1.87 g (15 mmol) of Na_2SO_3 and 1.66 g (20 mmol) of $NaHCO_3$ in 10 mL of water. sodium 2-(trifluoromethoxy)benzenesulfinate **S3** was obtained as a white solid 1.26 g (5.1 mmol, 51%).

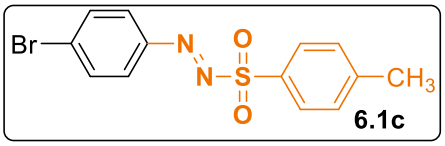
General procedure for the synthesis of arylazo arylsulfones: the synthesis of arylazo arylsulfones was performed following a procedure known in literature [6.14]. All the compounds synthesized are new, HRMS analysis was not carried out due to the instability of such compounds.



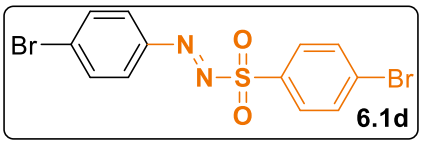
(*E*)-1-(4-bromophenyl)-2-((4-nitrophenyl)sulfonyl)diazene (6.1a). The reaction was performed employing 1.71 g (10 mmol, 1 equiv) of 4-bromoaniline, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-nitrobenzenesulfinate 2.51 g (1.2 equiv) (**S1**) affording 1.84 g of **6.1a** as an orange solid. (50% yield, m.p. (decomposition) = 120.5-120.9 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57–8.42 (m, 2H), 8.26–8.14 (m, 2H), 7.96–7.84 (m, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.4, 147.5, 138.9, 133.1, 131.85, 131.1, 125.9, 124.1.



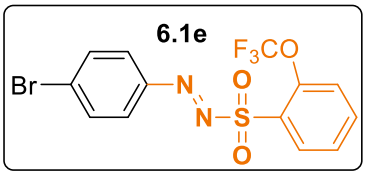
(*E*)-1-(4-bromophenyl)-2-(phenylsulfonyl)diazene (6.1b). The reaction was performed employing 1.71 g (10 mmol, 1 equiv) of 4-bromoaniline, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium benzenesulfinate 1.97 g (1.2 equiv) (**S4**) affording 2.36 g of **6.1b** as an orange solid. (73% yield, m.p. (decomposition) = 112.0-112.4 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95–7.89 (m, 2H), 7.73–7.39 (m, 8H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 148.0, 135.0, 133.1, 130.6, 130.3, 130.3, 129.4, 126.0.



(*E*)-1-(4-bromophenyl)-2-tosyldiazene (6.1c). The reaction was performed employing 1.71 g (10 mmol, 1 equiv) of 4-bromoaniline, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-methylbenzenesulfinate 2.14 g (1.2 equiv) (**S5**) affording 1.73 g of **6.1c** as a yellow solid. (51% yield, m.p. (decomposition) = 114.0-114.7 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89–7.81 (m, 2H), 7.71–7.62 (m, 4H), 7.40 (d, J = 8.1 Hz, 2H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.1, 132.8, 130.3, 129.9, 129.8, 129.7, 125.7, 21.7.

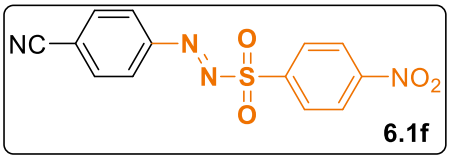


(E)-1-(4-bromophenyl)-2-((4-bromophenyl)sulfonyl)diazene (6.1d). The reaction was performed employing 1.71 g (10 mmol, 1 equiv) of 4-bromoaniline, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-bromobenzenesulfinate 2.89 g (1.2 equiv) (**S2**) affording 2.69 g of **6.1d** as a yellow solid. (67% yield, m.p. (decomposition) = 126.0-126.8 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86–7.78 (m, 2H), 7.77–7.71 (m, 2H), 7.71–7.62 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 147.6, 132.9, 132.5, 131.7, 131.6, 130.5, 130.4, 125.8.

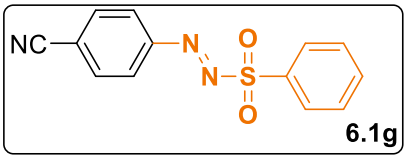


(*E*)-1-(4-bromophenyl)-2-((2-(trifluoromethoxy)phenyl)sulfonyl)diazene (6.1e). The reaction was performed employing 1.71 g (10 mmol, 1 equiv) of 4-bromoaniline 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 2-(trifluoromethoxy)benzenesulfinate 2.98 g (1.2 equiv) (**S3**) affording 1.26 g of **6.1e** as a yellow solid. (31% yield, m.p. (decomposition) = 87.3-88.5 °C). ^{1}H NMR (300

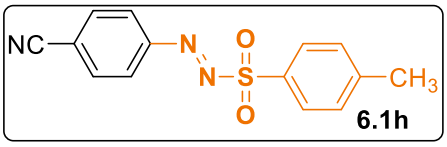
MHz, $CDCl_3$) δ 8.18 (dd, J = 7.9, 1.7 Hz, 1H), 7.80 (td, J = 8.0, 1.8 Hz, 1H), 7.75–7.63 (m, 4H), 7.54 (td, J = 7.7, 1.1 Hz, 1H), 7.46 (dt, J = 8.5, 1.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 147.5, 136.5, 132.9, 132.9, 130.4, 126.6, 125.7.



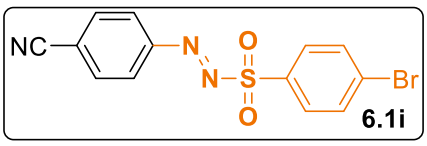
(*E*)-4-(((4-nitrophenyl)sulfonyl)diazenyl)benzonitrile (6.1f). The reaction was performed employing 1.18 g (10 mmol, 1 equiv) of 4-aminobenzonitrile, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-nitrobenzenesulfinate 2.51 g (1.2 equiv) (**S1**) affording 2.31 g of **6.1f** as an orange solid. (73% yield, m.p. (decomposition) = 88.0-88.3 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 8.58–8.42 (m, 2H), 8.27–8.14 (m, 2H), 7.96–7.84 (m, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.6, 138.2, 133.5, 131.9, 124.8, 124.2, 118.3, 117.1.



(E)-4-((phenylsulfonyl)diazenyl)benzonitrile (6.1g). The reaction was performed employing 1.18 g (10 mmol, 1 equiv) of 4-aminobenzonitrile, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium benzenesulfinate 1.97 g (1.2 equiv) (**S4**) affording 2.00 g of **6.1g** as a yellow solid. (74% yield, m.p. (decomposition) = 124.8-125.2 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 8.02–7.96 (m, 2H), 7.93–7.86 (m, 2H), 7.85–7.72 (m, 3H), 7.67–7.59 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 150.7, 135.1, 133.4, 132.2, 130.45, 129.3, 124.6, 117.6.

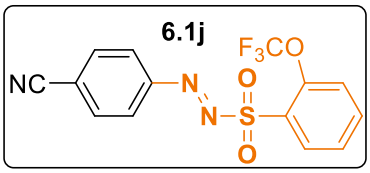


(E)-4-(tosyldiazenyl)benzonitrile (6.1h). The reaction was performed employing 1.18 g (10 mmol, 1 equiv) of 4-aminobenzonitrile, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-methylbenzenesulfinate 2.14 g (1.2 equiv) (**S5**) affording 2.39 g of **6.1h** as a yellow solid. (84% yield, m.p. (decomposition) = 130.0-130.4 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 7.93–7.81 (m, 6H), 7.45–7.2 (d, 2H, J = 8Hz), 2.51 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 150.8, 146.53, 133.4, 130.5, 130.0, 129.03, 124.6, 117.4, 117.3, 21.75.

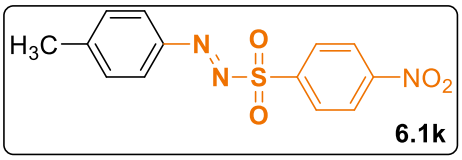


(*E*)-4-(((4-bromophenyl)sulfonyl)diazenyl)benzonitrile (6.1i). The reaction was performed employing 1.18 g (10 mmol, 1 equiv) of 4-aminobenzonitrile, 1.6 mL of isoamyl nitrite (1.2

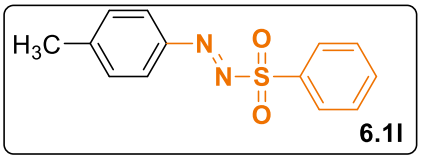
equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-bromobenzenesulfinate 2.89 g (1.2 equiv) (**S2**) affording 3.17 g of **6.1i** as a yellow solid. (91% yield, m.p. (decomposition) = 133.0-133.6 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.6 Hz, 2H), 7.86–7.72 (m, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 150.61 133.4, 132.7, 131.8, 131.1, 130.9, 124.7, 117.8, 117.2.



(*E*)-4-(((2-(trifluoromethoxy)phenyl)sulfonyl)diazenyl)benzonitrile (6.1j). The reaction was performed employing 1.18 g (10 mmol, 1 equiv) of 4-aminobenzonitrile, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 2-(trifluoromethoxy)benzenesulfinate 2.98 g (1.2 equiv) (**S3**) affording 2.17 g of **6.1j** as a yellow solid. (61% yield, m.p. (decomposition) = 61.3-61.5 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.92 (dd, *J* = 8.6, 2.1 Hz, 2H), 7.86–7.76 (m, 3H), 7.60–7.40 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 150.7, 136.8, 133.5, 132.9, 126.7, 125.4, 124.6, 121.6, 119.7, 117.8, 117.2.

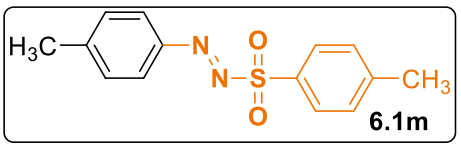


(*E*)-1-((4-nitrophenyl)sulfonyl)-2-(p-tolyl)diazene (6.1k). The reaction was performed employing 1.07 g (10 mmol, 1 equiv) of *p*-toluidine, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-nitrobenzenesulfinate 2.51 g (1.2 equiv) (**S1**) affording 1.86 g of **6.1k** as an orange solid. (61% yield, m.p. (decomposition) = 104.3-104.7 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49–8.42 (m, 2H), 8.23–8.14 (m, 2H), 7.76–7.70 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 147.6, 132.9, 132.3, 131.7, 130.3, 124.9, 123.9, 123.9, 21.9.

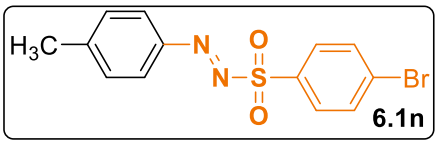


(*E*)-1-(phenylsulfonyl)-2-(p-tolyl)diazene (6.1l). The reaction was performed employing 1.07 g (10 mmol, 1 equiv) of *p*-toluidine, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium benzenesulfinate 1.97 g (1.2 equiv) (**S4**) affording 1.61 g of **6.1l** as a yellow solid. (65% yield, m.p. (decomposition) = 117.0-117.4 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ

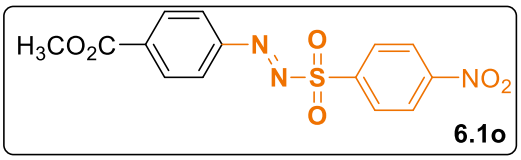
8.05–7.95 (m, 2H), 7.76–7.71 (m, 2H), 7.61 (dd, J = 8.4, 6.9 Hz, 2H), 7.35–7.25 (m, 2H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 147.2, 146.5, 134.4, 130.2, 130.1, 129.0, 124.6, 21.7.



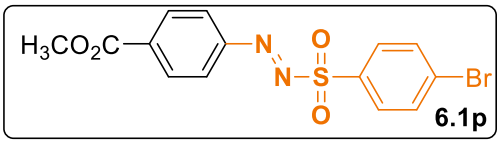
(*E*)-1-(p-tolyl)-2-tosyldiazene (6.1m). The reaction was performed employing 1.07 g (10 mmol, 1 equiv) of *p*-toluidine, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-methylbenzenesulfinate 2.14 g (1.2 equiv) (**S5**) affording 1.37 g of **6.1m** as a yellow solid. (50% yield, m.p. (decomposition) = 94.7-95.4 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 7.95–7.84 (m, 2H), 7.76–7.70 (m, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 2.7 Hz, 2H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 147.2, 146.3, 145.7, 130.3, 130.2, 130.0, 129.7, 124.5, 21.7, 21.7



(*E*)-1-((4-bromophenyl)sulfonyl)-2-(p-tolyl)diazene (6.1n). The reaction was performed employing 1.07 g (10 mmol, 1 equiv) of *p*-toluidine, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-bromobenzenesulfinate 2.89 g (1.2 equiv) (**S2**) affording 2.28 g of **6.1n** as a yellow solid. (91% yield, m.p. (decomposition) = 112.0-112.8 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 7.92–7.81 (m, 2H), 7.83–7.71 (m, 4H), 7.32 (d, J = 8.2 Hz, 2H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 146.8, 133.0, 132.4, 131.6, 130.1, 130.1, 128.3, 124.7, 21.8.

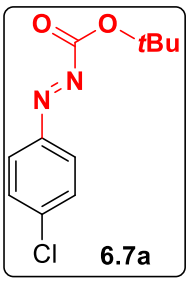


methyl (*E*)-4-(((4-nitrophenyl)sulfonyl)diazenyl)benzoate (6.1o). The reaction was performed employing 1.51 g (10 mmol, 1 equiv) of methyl 4-aminobenzoate, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-nitrobenzenesulfinate 2.51 g (1.2 equiv) (**S1**) affording 3.07 g of **6.1o** as an orange solid. (88% yield, m.p. (decomposition) = 107.2-109.8 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, J = 8.3 Hz, 2H), 8.20 (d, J = 8.4 Hz, 4H), 7.87 (d, J = 8.3 Hz, 2H), 3.97 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 165.4, 151.4, 150.9, 138.5, 135.7, 131.9, 130.8, 124.1, 52.7.

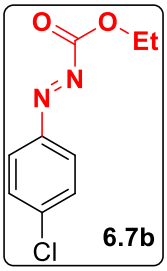


methyl (*E*)-4-(((4-bromophenyl)sulfonyl)diazenyl)benzoate (6.1p). The reaction was performed employing 1.51 g (10 mmol, 1 equiv) of methyl 4-aminobenzoate, 1.6 mL of isoamyl nitrite (1.2 equiv) forming the corresponding diazonium salt in 4 mL of HBF_4 and 2 mL of EtOH. The so formed salt was put in 50 mL of CH_2Cl_2 with sodium 4-bromobenzenesulfinate 2.89 g (1.2 equiv) (**S5**) affording 3.05 g of **6.1p** as a yellow solid. (80% yield, m.p. (decomposition) = 118.7-121.0 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22–8.15 (m, 2H), 8.01–7.67 (m, 6H), 3.98 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 165.5, 151.1, 135.3, 132.6, 131.8, 131.4, 130.8, 124.2, 52.6.

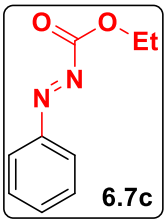
General procedure for the synthesis of arylazo carboxylates. The synthesis was performed as reported in the literature [6.34]. The selected arylhydrazine (20 mmol) was dissolved in 20 mL of pyridine and triethylamine was added (22 mmol, 1.1 equiv.). Then, the chloroformate or the anhydride were added slowly at room temperature (22 mmol, 1.1 equiv.). After two hours the reaction was completed, the solution was evaporated under reduced pressure and a solid started precipitating. The hydrazine carboxylated **6.5b** was used in the second reaction step without purification, by dissolving the compound in dichloromethane (20 mL) and PCC (21 mmol, 1.05 equiv.) was slowly added at 0°C and stirred overnight. The mixture was filtered and evaporated under reduced pressure affording the pure product after silica gel chromatography (eluent cyclohexane: ethyl acetate 99:1).



tert-butyl (*E*)-2-(4-chlorophenyl)diazene-1-carboxylate (6.7a). Starting from 2.84 g of 4-chloroarylhydrazine **6.5a** (20 mmol, 1 equiv.), 4.80 g of Boc_2O (22 mmol, 1.1 equiv.) and 4.53 g of PCC (21 mmol, 1.05 equiv.). Compound **6.7a** was obtained as a red oil (0.75 g, 15% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.32 (m, 2H), 7.18–7.13 (m, 2H), 1.42 (s, 9H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 161.2, 146.5, 135.3, 130.6, 79.3, 28.4.



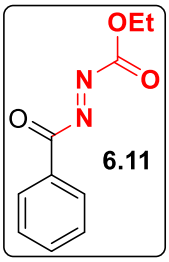
ethyl (*E*)-2-(4-chlorophenyl)diazene-1-carboxylate (6.7b). Starting from 2.84 g of 4-chloroarylhydrazine **6.5a** (20 mmol, 1 equiv.), 2.1 mL of ethyl chloroformate (22 mmol, 1.1 equiv.) and 4.53 g of PCC (21 mmol, 1.05 equiv.). Compound **6.7b** was obtained as a red oil (0.90 g, 17% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18–7.23 (m, 2H), 4.50 (q, J = 7.1 Hz, 1H), 1.43 (t, J = 7.1 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) 162.5, 147.8, 135.3, 130.9, 124.1, 67.4, 17.8.



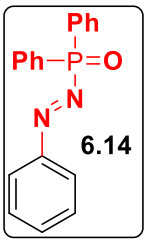
ethyl (*E*)-2-phenyldiazene-1-carboxylate (6.7c) Starting from 2.24 g of 4-chloroarylhydrazine **6.5b** (20 mmol, 1 equiv.), 2.1 mL of ethyl chloroformate (22 mmol, 1.1 equiv.) and 4.53 g of PCC (21 mmol, 1.05 equiv.). Compound **6.7c** was obtained as a red oil (0.67 g, 18% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97–7.87 (m, 3H), 7.74–7.57 (m, 2H), 4.50 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (75 MHz, CDCl3) 206.5, 135.0, 130.8, 124.3, 65.3, 14.8.

General procedure for the synthesis of acylazo carboxylates 6.11. The selected acylhydrazine **6.9** (20 mmol) was dissolved in 20 mL of pyridine and triethylamine was added (22 mmol, 1.1 equiv.). Then ethyl chloroformate was added slowly at room temperature (22 mmol, 1.1 equiv.). After two hours the reaction was completed, the solution was evaporated under reduced pressure and a solid started precipitating. The hydrazine carboxylated **6.10** was used in the second reaction step without purification, by dissolving the compound in dichloromethane (20 mL) and NBS (21 mmol, 1.05 equiv.) was slowly added at 0°C and stirred overnight. The mixture was filtered and evaporated under reduced pressure affording after silica gel chromatography (eluent cyclohexane: ethyl acetate 99:1) the pure product **6.11**.

General procedure for the synthesis of arylazo phosphine oxide 6.14. The selected arylhydrazine **6.5b** (20 mmol) was dissolved in 20 mL of pyridine and triethylamine was added (22 mmol, 1.1 equiv.). Then diphenylphosphinic chloride was added slowly at room temperature (22 mmol, 1.1 equiv.). After two hours the reaction was completed, the solution was evaporated under reduced pressure and a solid started precipitating. The crude product **6.13** was used in the second reaction step without purification, by dissolving the compound in dichloromethane (20 mL) and NBS (21 mmol, 1.05 equiv.) was slowly added at 0°C and stirred overnight. The mixture was filtered and evaporated under reduced pressure affording after silica gel chromatography (eluent cyclohexane: ethyl acetate 99:1) the pure product **6.14**.



ethyl (*E*)-2-benzoyldiazene-1-carboxylate (6.11). Starting from 2.72 g of benzohydrazide **6.9** (20 mmol, 1 equiv.), 2.1 mL of ethyl chloroformate (22 mmol, 1.1 equiv.) and 3.70 g of NBS (21 mmol, 1.05 equiv.). Compound **6.11** was obtained as a red oil (1.02 g, 25% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08–7.99 (m, 2H), 7.70–7.58 (m, 1H), 7.58–7.46 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 152.9, 135.0, 130.8, 124.3, 65.3, 14.8.



(*E*)-diphenyl(phenyldiazenyl)phosphine oxideethyl (6.14). Starting from 2.84 g of phenylhydrazine **6.5b** (20 mmol, 1 equiv.), 3.5 mL of diphenylphosphinic chloride (22 mmol, 1.1 equiv.) and 3.70 g of NBS (21 mmol, 1.05 equiv.). Compound **6.14** was obtained as a red oil (0.43 g, 7% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79–7.72 (m, 4H), 7.57–7.52 (m, 6H), 7.36–7.31 (m, 3H), 7.22–7.18 (m, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) 135.7, 134.5, 132.3, 132.1, 129.3, 128.4, 127.4, 127.1.

General approach for a photochemical experiment. The selected arylazo sulfone was dissolved in dry acetonitrile (or dichloromethane in case of insolubility) to have a 0.05 M homogenous solution. The so formed mixture was nitrogen-purged for 5 minutes, then irradiated in a pyrex glass vessel or a photoreactor (Figure 6.6) with a 40 W Kessil Lamp with a maximum of emission centred at 456 nm or 390 nm for 24 hours. The photolyzed solutions were analysed by GC.

General procedure for the coupling reaction of arylazo sulfones. The selected arylazo sulfone was dissolved in dry acetonitrile or dichloromethane in case of insolubility to have a 0.05 M homogenous solution with furane or mesitylene (1.0 M, 20 equiv). The so formed mixture was nitrogen-purged for 5 minutes, then irradiated in a photoreactor (Figure 6.6) with a 40 W Kessil Lamp with a maximum of emission centred at 456 nm for 24 hours. The photolyzed solutions were analysed by GC and the yields of the coupling products were calculated having a previously synthesized compound as standard [6.3].

Figure 6.6. Photochemical set-up employed for the coupling reaction of arylazo arylsulfones.

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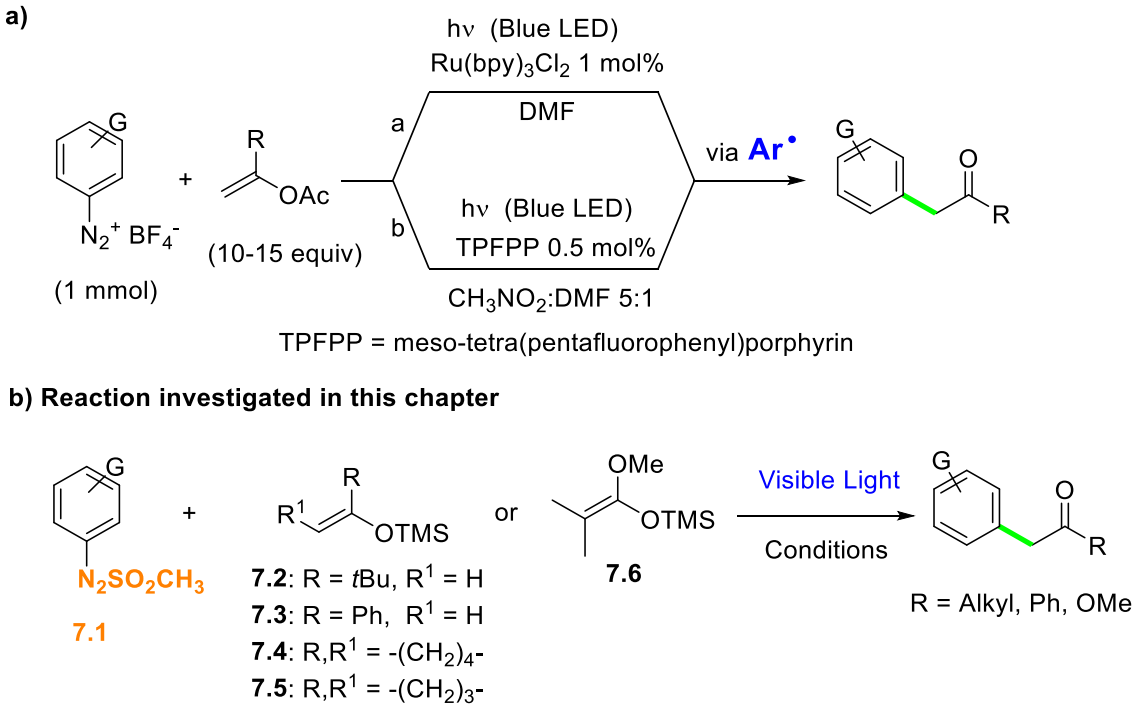
CHAPTER 7

A DYEDAUXILIARY GROUP STRATEGY FOR THE α-FUNCTIONALIZATION OF KETONES AND ESTERS.

7.1. INTRODUCTION.

Molecules bearing α-aryl carbonyls are widely spread in natural and synthetic bioactive products. One example is Prasugrel [7.1] which synthesis has always been carried out through the use of transition-metal catalyzed processes [7.2-7.3]. Visible-light photoredox catalysis offers new synthetic alternatives to organic chemists [7.4]. In such approach, a thermal stable substrate is activated by the photoexcited catalyst via monoelectronic oxidation/reduction step, generating a high energy intermediate able to react with an appropriate coupling partner [7.4]. Concerning this topic, trapping a photogenerated aryl radical by an enolate derivative (mainly enol acetates) has emerged as one of the most proposed strategies to achieve α-arylated carbonyls [7.5]. Among the suitable precursors of aryl radicals made active under photoredox catalysis conditions, the class of aryl diazonium salts is the most preferred and the reaction was carried out in the presence of Ru(II)-based complexes (Scheme 7.1, path a),[7.6] porphyrins (path b)[7.7] and organic dyes[7.8] in the role of photocatalyst. Arylazo sulfones **7.1**, molecules bearing a *dyedauxiliary group*, moieties able to impart both colour and photoreactivity to the substrate they are tethered to, proved to be a promising sustainable strategy source of reactive intermediates (aryl diazinyl, aryl and sulfonyl radicals) [7.9-7.11] upon simple exposition of the starting materials to visible (solar) light, without the need of (photo)catalysts and/or aggressive reactants. Fascinated by the versatile applications of arylazo sulfones, we speculated the opportunity to arylate electron-rich silylated alkenes **7.2-7.6** (Scheme 7.1, b).

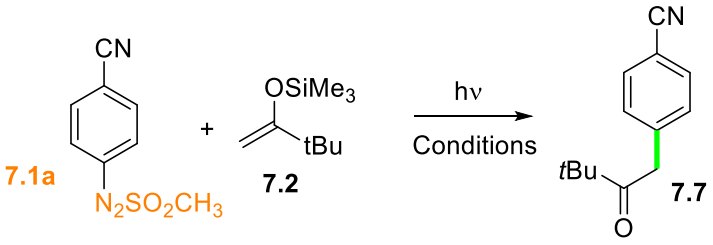


Scheme 7.1. (a) Photoredox-catalyzed synthesis of α-arylketones via arenediazonium salts. (b) Proposed arylation of enol silyl ethers and ketene silyl acetals starting from arylazo sulfones.

7.2. RESULTS AND DISCUSSION.

Preliminary experiments pointed out the feasibility of this process. (Table 7.1). Reaction optimization was carried out to find the best reaction conditions. When the reaction is performed in MeCN without $NaHCO_3$ gave no product (entry 1). The addition of a base did not significantly improve the yield (ca. 8%, entries 2 and 3). However, switching from pure acetonitrile to a mixture of acetonitrile and water (9:1) increased the arylation yield to 63% (entry 4). Moving the irradiation wavelength from 456 nm to 390 nm results in a lowering of the reaction efficiency (60% yield, entry 5). When doubling the concentration of the arylazo sulfone **7.1a** (from 0.05 M to 0.1 M) the reaction yield decreased to 39% (entry 6). Finally, in the absence light both by covering the vessel with an aluminum foil at room temperature (entry 7) and by heating the vessel at 60°C for 24 h resulted in no **7.7** formation (entries 7 and 8).

Table 7.1. Optimization process of the photochemical synthesis of **7.7**.



Entry	Conditions	7.7 (% yield)
1	**7.1a** (0.05 M), **7.2** (0.5 M), hν (456 nm), MeCN	0%
2	**7.1a** (0.05 M), **7.2** (0.5 M), hν (456 nm), $NaHCO_3$ (0.05 M) MeCN	8%
3	**7.1a** (0.05 M), **7.2** (0.5 M), hν (456 nm), $NaHCO_3$ (0.05 M) MeOH	8%
4	**7.1a** (0.05 M), **7.2** (0.5 M), hν (456 nm), $NaHCO_3$ (0.05 M), MeCN-H_2O 9:1	63%
5	**7.1a** (0.05 M), **7.2** (0.5 M), hν (390 nm), $NaHCO_3$ (0.05 M), MeCN-H_2O 9:1	60%
6	**7.1a** (0.1 M), **7.2** (0.5 M), hν (456 nm), $NaHCO_3$ (0.05 M), MeCN-H_2O 9:1	39%
7	**7.1a** (0.05 M), **7.2** (0.5 M), $NaHCO_3$ (0.05 M), MeCN-H_2O 9:1	0%
8	**7.1a** (0.05 M), **7.2** (0.5 M), T = 60°C $NaHCO_3$ (0.05 M), MeCN-H_2O 9:1	0%

With the best conditions in our hands, enol silyl ethers were found to be the preferred coupling partners, with the irradiation carried out with a 0.05 M solution of arylazo sulfones **7.1a-r** in a MeCN-H_2O 9:1 mixture, in the presence of **7.2-7.5** (0.5 M, 10 equiv.) and $NaHCO_3$ (1 equiv.) as the buffering agent. The arylazo sulfones employed for this protocol are depicted in Figure 7.1.

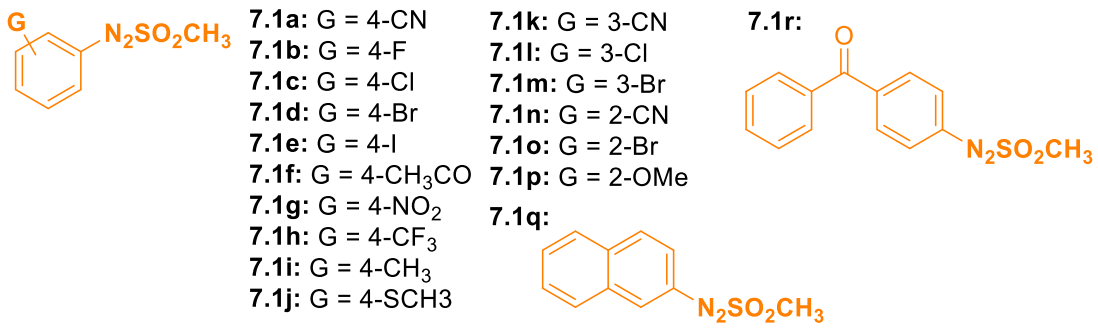
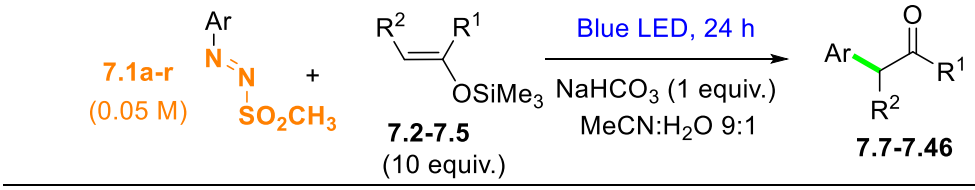
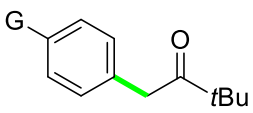


Figure 7.1. Arylazo sulfones employed in the present work.

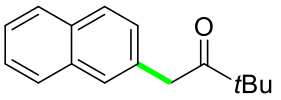
As depicted in Scheme 7.2, *t*-butyl aryl ketones **7.7-7.22** (some of them important building blocks in the preparation of bioactive molecules, including TRPV1 antagonists) [7.12] have been isolated in satisfactory to quantitative (see compounds **7.11**, **7.13** and **7.15**) yields. The presence of either electron donating or electron withdrawing substituents on the aromatic ring do not affect the efficiency of the process. α-(4-Cyanophenyl)-ketone **7.7** was isolated in 73% yield also when doubling the concentration of the starting arylazo sulfone **7.1a**, whereas the arylation resulted satisfactory under both artificial visible light and natural sunlight (see the results obtained for compound **7.17**). This visible light driven protocol was thus extended with success to 1-phenyl-1-trimethylsilyloxyethylene (**7.3**, in turn obtained from acetophenone). In this case, derivatives **7.23-7.35** were all isolated in a high amount, with the only exception of benzophenone **7.35**, that was obtained in a low yield (30%). When using cyclic enol silyl ethers **7.4-7.5**, the reaction was generally less performing, the best result obtained for 2-(2-methoxyphenyl)-cyclopentanone **7.46** (81% yield) (Scheme 7.2). With these results in our hand, we focused on the use of ketene silyl acetals, with the aim of further exploring the versatility of the arylation protocol. However, with **7.6**, α-arylazo derivatives **7.47-7.52** were isolated in discrete (see compounds **7.49, 7.51** in Scheme 7.3) to satisfactory (for **7.47, 7.48**) yields instead of the expected α-aryl-esters.



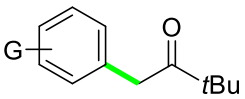


7.7, G = CN, 62%, 73%[a]
7.8, G = F, 87%
7.9, G = Cl, 92%
7.10, G = Br, 92%
7.11, G = I, 99%
7.12, G = CH_3CO, 95%

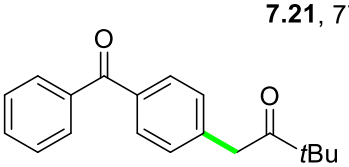
7.13, G = NO_2, 99%
7.14, G = CF_3, 92%
7.15, G = CH_3, 99%
7.16, G = SCH_3, 75%



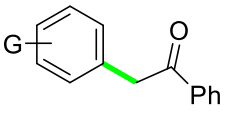
7.21, 77%



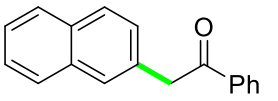
7.17, G = 3-CN, 97%, 97%[b]
7.18, G = 3-Br, 67%
7.19, G = 2-Br, 90%
7.20, G = 2-OMe, 98%



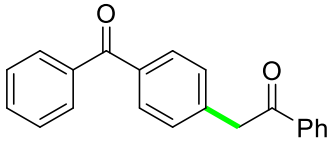
7.22, 99%



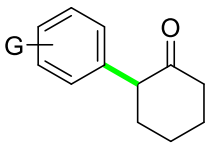
7.23, G = 4-CN, 89%
7.24, G = 4-F, 80%
7.25, G = 4-Cl, 50%
7.26, G = 4-Br, 75%
7.27, G = 4-I, 71%
7.28, G = 4-CF_3, 78%
7.29, G = 4-CH_3, 72%
7.30, G = 4-SCH_3, 80%
7.31, G = 3-Cl, 89%
7.32, G = 2-CN, 52%
7.33, G = 2-Br, 52%



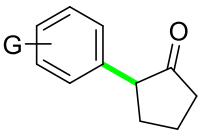
7.34, 70%



7.35, 30%

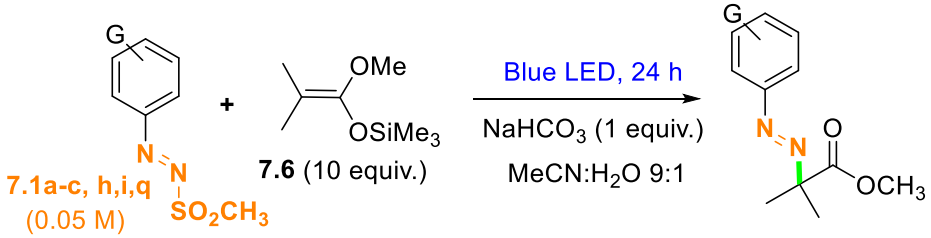


7.36, G = 4-CN, 38%
7.37, G = 4-Cl, 36%
7.38, G = 4-Br, 22%



7.39, G = 4-F, 43%
7.40, G = 4-Cl, 42%
7.41, G = 4-CH_3CO, 54%
7.42, G = 4-CF_3, 74%
7.43, G = 3-CN, 59%
7.44, G = 3-Cl, 57%
7.45, G = 2-Br, 81%
7.46, G = 2-OMe, 81%

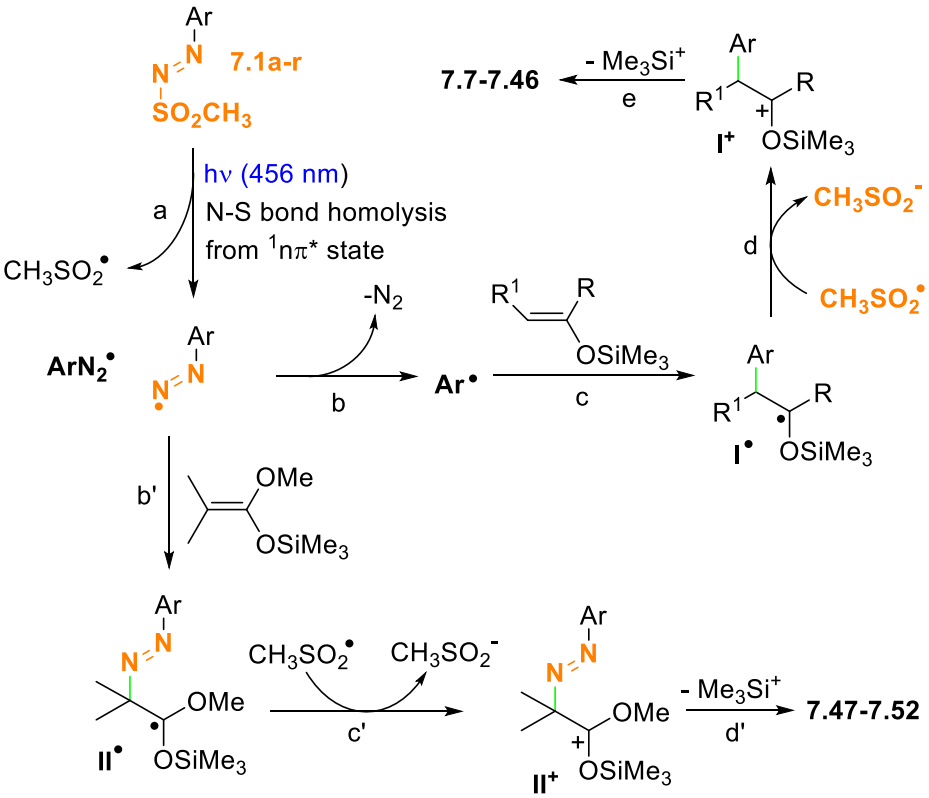
Scheme 7.2. Synthesis of α-arylketones **7.7-7.46** via arylazo sulfones. [a.] Reaction carried out on a 0.1 M solution of **7.1a** in the presence of 5 equiv. of **7.2**; [b.] reaction carried out upon natural sunlight (3 days, 9 h exposition/day).



7.47, G = 4-CN, 87%
7.48, G = 4-F, 83%
7.49, G = 4-Cl, 33%
7.50, G = 4-CF_3, 81%
7.51, G = 4-CH_3, 33%
7.52, G = 4-PhCO, 61%

Scheme 7.3. Irradiation of arylazo sulfones **7.1** in the presence of ketene silyl acetal **7.6**.

With such different outcomes a better explanation of the mechanism was mandatory. As a matter of fact, we were able to rationalize the behavior of arylazo sulfones **7.1** both on the available literature and on the nature of the products isolated. Indeed, visible light irradiation of sulfones **7.1a-7.1r** causes the homolytic cleavage of the N-S bond from the $^1(n\pi^*)$ excited state (Scheme 7.4, path a) [7.9]. Nitrogen loss from the so-generated aryldiazenyl radical (Ar-$N_2^{\bullet}$, path b) and efficient trapping of the resulting aryl radical ($Ar^{\bullet}$) by enol silyl ethers **7.2-7.5** (path c) afforded α-oxyradical **I**$^{\bullet}$. Oxidation of **I**$^{\bullet}$ (path d) and loss of the electrofugal Me_3Si^+ group (path e, that presumably undergoes hydrolysis to Me_3SiOH) resulted in the formation of α-aryl ketones **7.7-7.46**.



Scheme 7.4. Suggested mechanism for the formation of compounds **7.7-7.52.**

The fate of the reaction follows the different nucleophilicity existing between silyl ethers **7.2-7.5** and ketene silyl acetal **7.6**. The reactivity of enol ether derivatives towards electrophilic radicals was sparsely explored in the past [7.13]. Despite a comparable nucleophilicity [7.14], the ethers derived from cycloalkanones gave consistently worst results towards aryl [7.6] and trifluoromethyl [7.13c] radicals addition comparing to those derived from acetophenones. In the present work, however, arylation likewise took place efficiently even with the cyclopentanone derived **7.5**. On the other hand, in the presence of highly nucleophilic ketene silyl acetal **7.6** [7.15], trapping of Ar-$N_2^{\bullet}$ takes place before dediazoniation (path b'), and derivatives **7.47-7.52** were obtained via consecutive oxidation and Me_3Si^+ elimination of the α-oxy radical intermediate **II**$^{\bullet}$ (paths c',d'). The methanesulfonyl radical

($CH_3SO_2^{\bullet}$) arising from the N-S homolytic cleavage presumably acted as electron acceptor in both oxidation paths d, c' [7.14]. Finally, the presence of $NaHCO_3$ prevents any acid-catalyzed decomposition of the silyl derivatives employed.

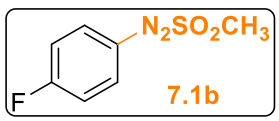
7.3 CONCLUSIONS.

The developed strategy thus further evidences the versatility of arylazo sulfones as (visible light) precursors of reactive intermediates, whose reactivity can be tuned by the employed reaction partners. Indeed, irradiation of **7.1** in the presence of enol silyl ethers results in the formation of α-aryl ketones, under metal- and photocatalyst-free conditions. The reaction occurs in satisfactory yields and high functional group tolerance. On the other hand, as already observed in the past with captodative olefins, the photochemical activation of arylazo sulfones may lead to nitrogen incorporated derivatives preventing any nitrogen loss. Thus, the reaction with ketene silyl acetals gives access (in good yield) to α-arylazo esters, important building blocks in the preparation of azo prodrugs.

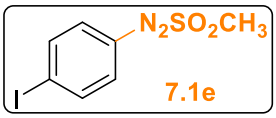
7.4 EXPERIMENTAL SECTION.

General informations. ^1H and ^{13}C NMR spectra were recorded on a 300 e 75 MHz spectrometer, respectively. The attributions were made on the basis of ^1H and ^{13}C NMR experiments; chemical shifts are reported in ppm downfield from TMS. GC analysis were performed using a HP SERIES 5890 II equipped with a fire ion detector (FID, temperature 350 °C). Analytes were separated using a Restek Rtx-5MS (30 m×0.25 mm×0.25 μm) capillary column with nitrogen as a carrier gas at 1 ml min^{-1}. The injector temperature was 250 °C. The GC oven temperature was held at 80 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1}, and held for 10 min. Silyl ethers **7.2-7.6** are commercially available and used as received.

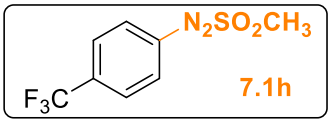
General Procedure for the Synthesis of Arylazo Sulfones. Arylazo sulfones **7.1a-r**, were previously synthesized and fully characterized [7.10] by our research group by the following procedure. Some arylazo sulfones were already present in the lab and used without any further purification. A set of new arylazo sulfones was freshly synthesized to expand the scope of the reaction.



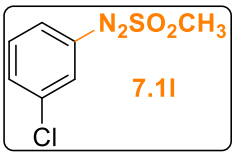
1-(4-Fluorophenyl)-2-(methylsulfonyl)diazene (7.1b). [7.10] Yield: 69% (1.4g). Yellow solid. m.p. (decomposition) = 64−66°C.^1H NMR (400 MHz, $CDCl_3$) δ 8.05−7.97 (m, 2H), 7.28 (dd, J = 11.7, 5.2 Hz, 2H), 3.23 (s, 3H).$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.9 (d, J = 259.4 Hz), 145.6 (d, J=2.9 Hz), 127.3 (d, J = 9.9 Hz), 117.1 (d, J = 23.3 Hz), 34.9.



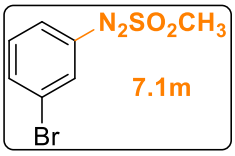
1-(4-Iodophenyl)-2-(methylsulfonyl)diazene (7.1e). [7.10] Yield: 44% (1.5 g) Yellow solid, m.p. (decomposition) = 132.0-132.4 °C. ^{1}H NMR (600·MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.6 Hz, 2 H), 7.65 (d, *J* = 8.6 Hz, 2 H), 3.22 (s, 3 H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 148.2, 139.2, 125.6, 103.6, 34.8.



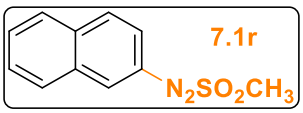
(*E*)-1-(methylsulfonyl)-2-(4-(trifluoromethyl)phenyl)diazene (7.1h). [7.10] Yield: 44% (1.2 g). Yellow solid. m.p. (decomposition) = 111−113°C.^{1}H NMR (400MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 3.27 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 150.7, 136.0 (q, *J* = 33.1 Hz), 127.0 (q, *J* = 3.7 Hz), 124.7, 123.2 (q, *J* = 273.0 Hz), 34.9.



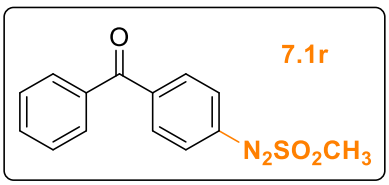
1-(3-chlorophenyl)-2-(methylsulfonyl)diazene (7.1l). [7.16] Yield: 64% (1.4 g). Yellow solid. m.p. (decomposition) = 80−82°C.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.91 (m, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.64 (dd, *J* = 8.0, 0.7Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 3.24 (s, 3H).$^{13}C\{^{1}H\}$ NMR (101MHz, $CDCl_3$) δ 149.7, 135.9, 134.9, 130.8, 123.7, 123.6, 34.9.



1-(3-bromophenyl)-2-(methylsulfonyl)diazene (7.1m). [7.10] Yield: 56% (1.6 g). Yellow solid, m.p. (decomposition) = 95-96 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 3.24 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, CDCl3) δ 149.7, 137.7, 131.0, 126.4, 124.0, 123.6, 34.8.



1-(Methylsulfonyl)-2-(naphthalen-2-yl)diazene (7.1q). [7.10] Yield: 58% (1.5 g). Yellow solid, m.p. (decomposition) = 108-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.03-8.01 (m, 1H), 7.92-7.89 (m, 3H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 3.27 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 146.6, 136.5, 133.7, 132.9, 130.1, 130.0, 129.9, 128.1, 127.6, 115.3, 34.8.



4-((Methylsulfonyl)diazenyl)phenyl)(phenyl)methanone (7.1r). [7.11] Yield: 94 % (3.4 g). Yellow solid, m.p. (decomposition) = 130 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.4 Hz, 2H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.67–7.62 (m, 1H), 7.52

(t, J = 8.0 Hz, 2H), 3.27 (s, 3H).$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 195.1, 150.6, 142.8, 136.4, 133.2,131.0, 130.0, 128.5, 124.2, 34.8.

General Procedure for the photochemical arylation of enol silyl ethers. A pyrex glass vessel was charged with the chosen arylazo sulfone (**7.1a-r**, 0.4 mmol, 1.0 equiv., 0.05 M) and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) was flushed with argon and the solid was dissolved in degassed acetonitrile:water 9:1 mixture (8.0 mL). Then, the desired enol silyl ether **7.2-7.6** was added (0.5 mmol, 10 equiv., 0.5 M). The reaction was irradiated for 24 h using an EvoluChem apparatus equipped with a 40 W Kessil lamp (λ_{em}= 456 nm, see Figure 7.2; the lamp emission spectrum is available at the link https://www.kessil.com/science/PR160L.php). The photolyzed solution was concentrated under reduced pressure and purified by silica gel column chromatography (cyclohexane-ethyl acetate mixture as eluant).

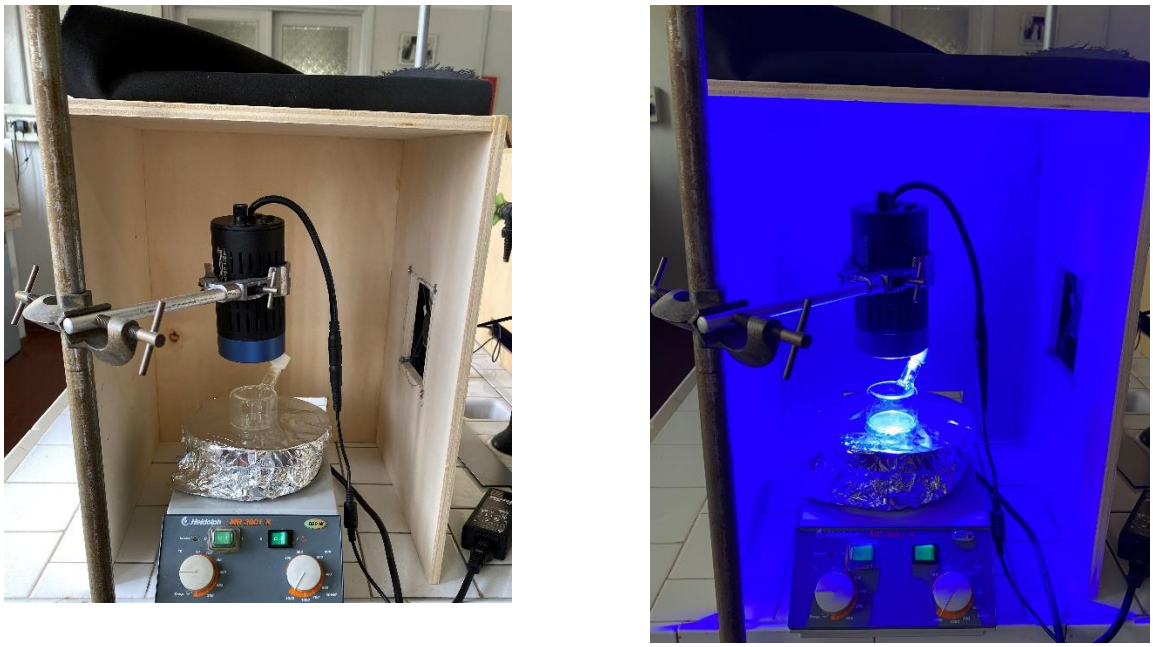
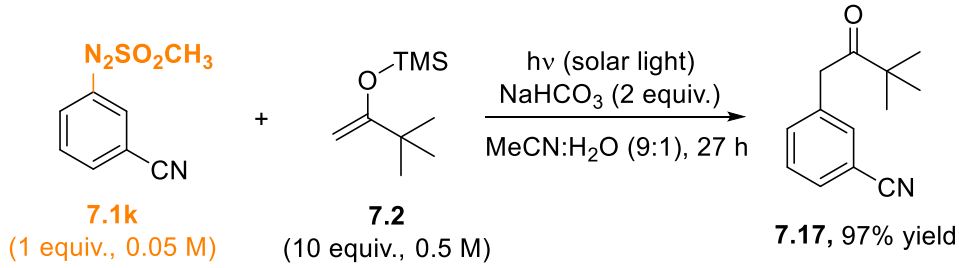


Figure 7.2. Irradiation system used to perform the reactions on this work: A 40 W Kessil lamp (with emission centered at 456 nm) is held three centimetres above the reaction vessel which was stirred gently for 24 h. A fan is placed on the right of the reaction vessel to avoid any heating of the solution.

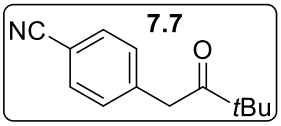
Photochemical sunlight-driven synthesis of compound 7.17.



Scheme 7.5. Photochemical synthesis of **7.17** starting from **7.2** and **7.1k** using sunlight as radiation source.

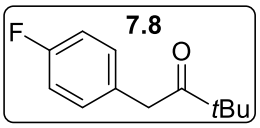
A glass vessel was charged with 91.2 mg of arylazo sulfone **7.1k** (0.436 mmol, 1.0 equiv., 0.05 M) and 64 mg of sodium bicarbonate (0.1 mmol, 2.0 equiv., 0.1 M) was flushed with argon and the solid was dissolved in degassed acetonitrile:water (9:1, 8.0 mL). Then, 800 µL of enol silyl ether **7.2** were added (4.0 mmol, 10.0 equiv.., 0.5 M). The glass vessel was put outside the laboratory window on an aluminium foil and was exposed to natural sunlight for 27 h (May 2021, Pavia, Italy, coordinates: 45° 11' 7" 44 **N** 09° 9' 45" 00 **E**, see Figure 7.3)**.** The reaction course was monitored through GC analysis. The photolyzed solution was concentrated under reduced pressure and the crude mixture obtained was purified by silica gel column chromatography (9:1 cyclohexane/ethyl acetate) affording 84.6 mg of **7.17** (97% yield, slightly yellow solid).

Figure 7.3. The reaction vessel containing the arylazo sulfone **7.1k** and the enol silyl ether **7.2** was put outside the laboratory window and exposed to solar light for three days in a row (9 h of light exposure every day). An aluminium foil was put under the reaction vessel.

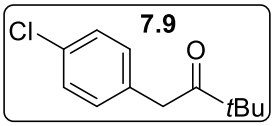


4-(3,3-Dimethyl-2-oxobutyl)benzonitrile (7.7). From 80.1 mg (0.383 mmol) of **7.1a**, 880 µL (10 equiv.) of **7.2,** 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 51.0 mg of

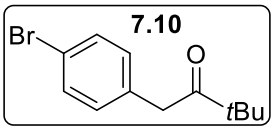
7.7 (62% yield, white solid, m.p. = 45–46°C). Compound **7.7** was likewise isolated in 73% yield when irradiating a 0.05 M solution of **7.1a** in the presence of 5 equiv. of **7.2**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 3.86 (s, 2H), 1.22 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 211.6, 140.6, 132.2, 130.6, 119.0, 110.8, 44.9, 43.3, 26.4. HRMS (EI) m/z: $[M]^+$ calcd for $C_{13}H_{15}NO$ 202.1226, found 202.1222.



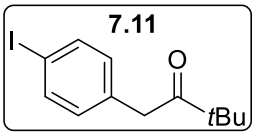
1-(4-Fluorophenyl)-3,3-dimethylbutan-2-one (7.8). From 79.0 mg (0.391 mmol) of **7.1b,** 880 µL (10 equiv.) of **7.2**, 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 66.0 mg of **7.8** (87 % yield, slightly yellow oil). Spectroscopic data were in accordance with literature data [7.17]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 3.86 (s, 2H), 1.22 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 212.8, 163.5, 160.3, 131.2, 131.1, 130.7, 115.5, 115.2, 44.7, 42.5, 26.5.



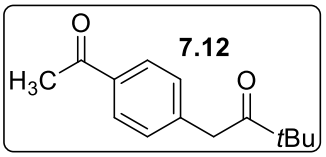
1-(4-Chlorophenyl)-3,3-dimethylbutan-2-one (7.9). From 88.0 mg (0.402 mmol) of **7.1c**, 880 µL (10 equiv.) of **7.2**, 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 77.9 mg of **7.9** (92% yield, slightly yellow solid, m.p. = 47–49 °C [7.18]). Spectroscopic data were in accordance with literature data [7.18]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 3.77 (s, 2H), 1.20 (s, 9H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 212.5, 133.5, 128.7, 44.8, 42.6, 26.5.



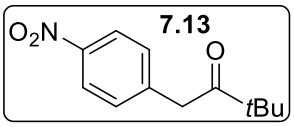
1-(4-Bromophenyl)-3,3-dimethylbutan-2-one (7.10). From 98.5 mg (0.376 mmol) **7.1d**, 880 µL (10 equiv.) of **7.2**, 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 87.9 mg of **7.10** (92% yield, slightly yellow solid, m.p. = 54–56 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 8.7, 5.4 Hz, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 3.77 (s, 2H), 1.20 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 212.8, 163.54 160.3, 131.2, 131.1, 130.7, 115.5, 115.2, 44.7, 42.4, 26.5. HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{15}OBr$ 255.0379, found 255.0374.



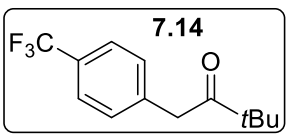
1-(4-Iodophenyl)-3,3-dimethylbutan-2-one (7.11). From 122.1 mg (0.395 mmol) of **7.1e,** 880 µL (10 equiv.) of **7.2**, and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 119.3 mg of **7.11** (99%, slightly yellow solid, m.p. = 58–60 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 3.76 (s, 2H), 1.22 (s, 9H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 212.10, 137.32, 134.46, 131.51, 44.55, 42.57, 26.25. HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{15}OI$ 303.0240, found 303.0229.



1-(4-Acetylphenyl)-3,3-dimethylbutan-2-one (7.12). from 89.0 mg (0.394 mmol) of **7.1f**, 880 µL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitruile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 81.6 mg of **7.12** (95% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 3.85 (s, 2H), 2.56 (s, 3H), 1.19 (s, 9H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 212.1, 197.9, 140.6, 129.9, 128.5, 44.8, 43.2, 26.7, 26.4. MS (m/z): 218 (5), 133 (60), 118 (10), 104 (16), 85 (30), 57 (100), 44 (52). HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{18}O_2$ 219.1380, found 219.1371.

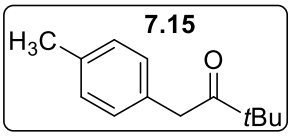


3,3-Dimethyl-1-(4-nitrophenyl)butan-2-one (7.13). From 77.8 mg (0.339 mmol) of **7.1g**, 880 µL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 87.3 mg of **7.13** (99 % yield, slightly yellow solid, m.p. = 60–61°C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 3.92 (s, 2H), 1.23 (s, 9H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 211.2, 142.4, 130.4, 123.4, 42.8, 26.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{15}NO_3$ 222.1125, found 222.1132.

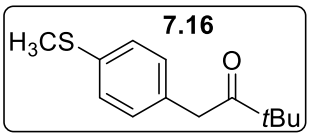


3,3-Dimethyl-1-(4-(trifluoromethyl)phenyl)butan-2-one (7.14). From 105.1 mg (0.417 mmol) of **7.1h**, 880 µL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 93.8 mg of **7.14** (92% yield, white solid, m.p. = 51–53 °C [7.19]). Spectroscopic data were in accordance with literature data [7.19]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H),

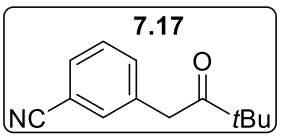
7.31 (d, J = 7.9 Hz, 2H), 3.88 (s, 2H), 1.24 (s, 9H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 211.8, 138.9, 129.9, 128.7 (q, J = 32.4 Hz), 125.2 (q, J = 3.8 Hz), 124.0 (q, J = 262.5 Hz), 44.6, 42.8, 26.2.



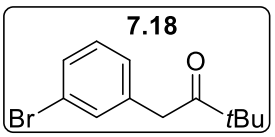
3,3-Dimethyl-1-(*p*-tolyl)butan-2-one (7.15). From 76.7 mg (0.387 mmol) of **7.1i**, 880 µL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 72.9 mg of **7.15** (99% yield, red oil). Spectroscopic data were in accordance with literature data [7.20]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 – 6.65 (m, 4H), 3.79 (s, 2H), 2.35 (s, 3H), 1.23 (s, 9H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 212.9, 136.0, 131.8, 129.3, 129.0, 44.5, 42.8, 26.3, 20.9.



3,3-Dimethyl-1-(4-(methylthio)phenyl)butan-2-one (7.16). From 88.1 mg (0.383 mmol) of **7.1j**, 880 µL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 63.8 mg of **7.16** (75% yield, red oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.23 (m, 2H), 7.20–7.00 (m, 2H), 4.02 (s, 2H), 2.44 (s, 3H), 1.29 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 212.5, 137.8, 134.4, 130.8, 127.7, 127.4, 125.5, 44.7, 41.9, 26.9, 16.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{13}H_{18}OS$ 223.1151, found 223.1142.

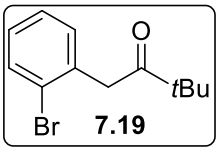


3-(3,3-Dimethyl-2-oxobutyl)benzonitrile (7.17). From 82.5 mg (0.394 mmol) of **7.1k**, 880 µL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 73.3 mg of **7.17** (97% yield, slightly yellow solid, mp = 38.5–39.7 °C [7.21]). Spectroscopic data were in accordance with literature data.[7.21] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (ddd, J = 5.5, 3.8, 1.6 Hz, 1H), 7.48–7.44 (m, 1H), 7.43 – 7.38 (m, 2H), 3.85 (s, 2H), 1.22 (s, 9H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 211.6, 136.3, 134.2, 133.1, 130.3, 129.0, 118.7, 112.3, 44.5, 42.4, 26.2.

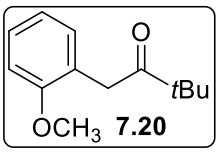


1-(3-Bromophenyl)-3,3-dimethylbutan-2-one (7.18). From 103.1 mg (0.394 mmol) of **7.1m** 880 µL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 67.2 mg of **7.18** (67% yield, yellow oil). Spectroscopic data were in accordance with literature data

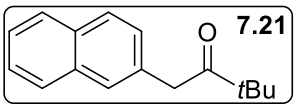
[7.22] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.32 (m, 2H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 3.79 (s, 2H), 1.23 (s, 9H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 211.9, 137.0, 132.5, 129.7, 129.7, 128.2, 122.3, 44.6, 42.6, 26.2.



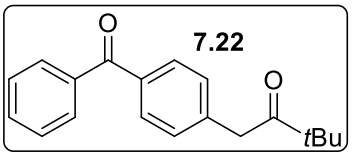
1-(2-Bromophenyl)-3,3-dimethylbutan-2-one (7.19). From 104.2 mg (0.397 mmol) of **7.1o**, 880 μL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 91.0 mg of **7.19** (90% yield, orange oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.29 (td, *J* = 7.4, 1.3 Hz, 1H), 7.15 (ddd, *J* = 14.8, 7.2, 1.8 Hz, 2H), 4.02 (s, 2H), 1.29 (s, 12H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 211.4, 135.1, 132.6, 131.8, 128.4, 127.2, 124.9, 44.5, 44.0, 26.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{15}OBr$ 255.0379, found 255.0382.



1-(2-Methoxyphenyl)-3,3-dimethylbutan-2-one (7.20). From 85.0 mg (0.397 mmol) of **7.1p**, 880 μL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 80.2 mg of **7.20** (98% yield, slightly yellow solid, m.p. = 34–35 °C [7.23]). Spectroscopic data were in accordance with literature data [7.23]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 1H), 7.11 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.01 – 6.72 (m, 2H), 3.83 (s, 3H), 3.79 (s, 3H), 1.27 (s, 9H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 213.0, 157.1, 131.2, 128.0, 124.2, 120.3, 44.4, 38.2, 26.5.

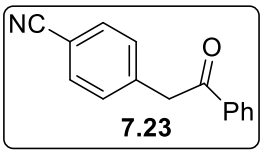


3,3-Dimethyl-1-(naphthalen-1-yl)butan-2-one (7.21). From 94.1 mg (0.402 mmol) of **7.1q**, 880 μL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 112.6 mg of **7.21** (99% yield, red solid, m.p. = 67–69 °C [7.24]). Spectroscopic data were in accordance with literature data [7.24]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 – 7.93 (m, 1H), 7.89 (ddt, *J* = 7.7, 6.6, 1.1 Hz, 2H), 7.62–7.54 (m, 2H), 7.38 (dd, *J* = 7.0, 1.2 Hz, 1H), 4.39 (s, 2H), 1.43 (s, 9H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 212.5, 133.8, 132.3, 131.5, 127.9, 127.6, 126.0, 125.5, 125.3, 123.7, 41.0, 26.7.



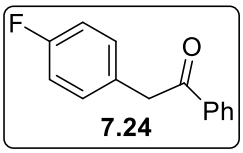
1-(3-benzoylphenyl)-3,3-dimethylbutan-2-one (7.22). From 110.6 mg (0.384 mmol) of **7.1r** 880 μL (10 equiv.) of **7.2** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water

(9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 66.8 mg of **7.22** (77%, white solid, m.p. = 78–79 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99–7.68 (m, 4H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 3.90 (s, 2H), 1.24 (s, 9H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 212.0, 139.8, 137.6, 135.8, 132.2, 130.1, 129.9, 129.5, 128.1, 44.7, 43.1, 26.2. MS (m/z): 208 (5), 196 (80), 167 (10), 118 (22),105 (26), 85 (25), 77(20), 57 (100). HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{20}O_2$ 281.1536, found 281.1524.



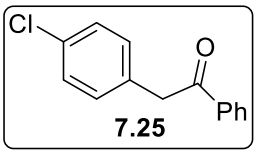
7.23

4-(2-Oxo-2-phenylethyl)benzonitrile (7.23). From 85.3 mg (0.408 mmol) of **7.1a** 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 80.2 mg of **7.23** (89% yield, slightly yellow solid, m.p. = 113–114 °C [7.25]). Spectroscopic data were in accordance with literature data [7.25]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.9 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 3H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 4.38 (s, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.1, 139.9, 136.1, 133.6, 132.2, 130.5, 128.8, 128.3, 118.7, 110.8, 45.1.



7.24

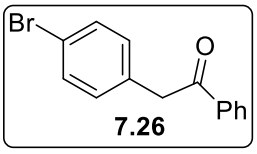
2-(4-Fluorophenyl)-1-phenylethan-1-one (7.24). From 83.8 mg (0.415 mmol) of **7.1b**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 71.1 mg of **7.24** (80% yield, yellow solid, m.p. = 109–110 °C [7.26]). Spectroscopic data were in accordance with literature data [7.27]. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 8.09 (d, *J* = 7.1 Hz, 2H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 2H), 7.36 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.09 (t, *J* = 8.9 Hz, 2H), 4.41 (s, 2H).^{13}C{^{1}H} NMR (75 MHz, CD_3COCD_3) δ 198.1, 164.6, 138.1, 134.3, 132.9, 132.7, 132.6, 132.6, 129.9, 129.6, 116.3, 116.0, 45.1.



7.25

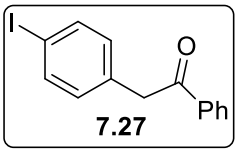
2-(4-Chlorophenyl)-1-phenylethan-1-one (7.25). From 87.2 mg (0.400 mmol) of **7.1c**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 49.0 mg of **7.25** (50% yield, yellow solid, m.p. = 137–139 °C [7.28]) Spectroscopic data were in accordance with literature data [7.27]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.2 Hz, 2H), 7.60 (t, *J* = 7.3 Hz,

1H), 7.51 (d, *J* = 7.7 Hz, 2H), 7.32 (d, *J* =8 .4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 4.28 (s, 2H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 197.0, 136.3, 133.2, 132.8, 132.8, 130.8, 128.7, 128.6, 128.4, 44.6.



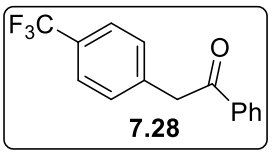
7.26

2-(4-Bromophenyl)-1-phenylethan-1-one (7.26). From 106.4 mg (0.406 mmol) of **7.1d**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 83.3 mg of **7.26** (75% yield, yellow solid, m.p. = 150–152 °C [7.29]). Spectroscopic data were in accordance with literature data [7.27]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 8.4 Hz, 4H), 7.16 (d, *J* = 8.3 Hz, 2H), 4.27 (s, 2H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 196.9, 136.3, 133.4, 133.3, 131.6, 131.2, 128.6, 128.4, 120.9, 44.6.



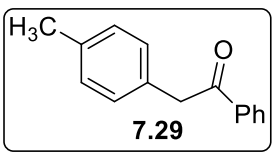
7.27

2-(4-Iodophenyl)-1-phenylethan-1-one (7.27). From 120.0 mg (0.387 mmol) of **7.1e**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification step was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 88.4 mg of **7.27** (71% yield, red solid, m.p. = 158–159 °C [7.31]). Spectroscopic data were in accordance with literature data [7.31]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06–7.96 (m, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.04 (d, *J* = 8.2 Hz, 2H), 4.25 (s, 2H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 196.9, 137.6, 136.3, 134.0, 133.3, 131.5, 128.6, 128.4, 92.4, 44.8.



7.28

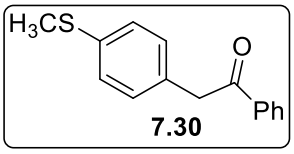
1-Phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-one (7.28). From 102.1 mg (0.405 mmol) of **7.1h**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 83.8 mg of **7.28** (78% yield, yellow solid, m.p. = 130–132 °C [7.32]). Spectroscopic data were in accordance with literature data [7.27]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 – 7.96 (m, 2H), 7.67–7.56 (m, 3H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 4.38 (s, 2H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 196.5, 138.45 136.3, 133.4, 129.9, 128.7, 128.4, 125.4 (q, *J*=3.8 Hz), 44.90.



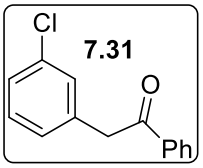
7.29

1-Phenyl-2-(*p*-tolyl)ethan-1-one (7.29). From 84.2 mg (0.425 mmol) of **7.1i**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 64.3 mg of **7.29** (72%

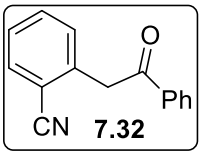
yield, yellow solid, m.p. = 95–96 °C [7.33]). Spectroscopic data were in accordance with literature data [7.27]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25–7.71 (m, 2H), 7.56 (d, *J* = 7.1 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.28 (s, 1H), 7.24 – 7.00 (m, 4H), 4.27 (s, 2H), 2.34 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.7, 136.5, 136.4, 133.0, 131.3, 130.8, 129.3, 128.5, 45.0, 21.0.



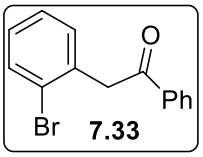
2-(4-(Methylthio)phenyl)-1-phenylethan-1-one (7.30). From 97.8 mg (0.425 mmol) of **7.1j**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 82.4 mg of **7.30** (80% yield, red brown solid, m.p. = 72–73 °C [7.34]). Spectroscopic data were in accordance with literature data [7.34]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.3 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.40 – 7.25 (m, 2H), 7.19 (d, *J* = 6.0 Hz, 2H), 4.47 (s, 2H), 2.46 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.2, 137.7, 136.7, 134.0, 133.0, 130.5, 128.5, 128.3, 127.4, 125.6, 43.4, 16.7.



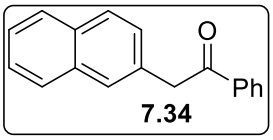
2-(3-Chlorophenyl)-1-phenylethan-1-one (7.31). From 91.9 mg (0.405 mmol) of **7.1l**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 86.2 mg of **7.31** (89% yield, yellow solid, m.p. = 40–42 °C [7.35]). Spectroscopic data were in accordance with literature data [7.27]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.33 – 7.23 (m, 3H), 7.21 – 7.12 (m, 1H), 4.28 (s, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.7, 136.3, 134.3, 133.3, 129.6, 128.7, 128.4, 127.7, 127.1, 44.8.



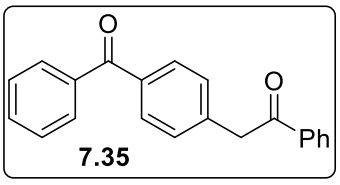
2-(2-Oxo-2-phenylethyl)benzonitrile (7.32). From 87.4 mg (0.418 mmol) of **7.1n**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane ethyl acetate mixture) to afford 48.1 mg of **7.32** (52% yield, white solid, m.p. = 110–111 °C [7.36]). Spectroscopic data were in accordance with literature data [7.37]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.4 Hz, 2H), 7.68 (t, *J* = 9.5 Hz, 1H), 7.61 (d, *J* = 6.7 Hz, 1H), 7.59–7.48 (m, 3H), 7.39 (dd, *J* = 7.5, 4.7 Hz, 2H), 4.57 (s, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 195.3, 138.5, 136.2, 133.6, 132.7, 132.7, 131.0, 128.7, 128.3, 117.8, 113.5, 43.5.



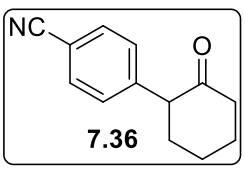
2-(2-Bromophenyl)-1-phenylethan-1-one (7.33). From 109.9 mg (0.420 mmol) of **7.1o**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 57.3 mg of **7.33** (52% yield, yellow solid, m.p. = 71–72 °C [7.38]). Spectroscopic data were in accordance with literature data [7.39]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.8 Hz, 2H), 7.77–7.58 (m, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 10.4 Hz, 2H), 7.21 (s, 1H), 4.49 (s, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.23, 136.56, 134.90, 133.20, 132.69, 131.59, 130.77, 128.60, 128.24, 127.43, 125.00, 45.67.



2-(Naphthalen-1-yl)-1-phenylethan-1-one (7.34). From 97.1 mg (0.415 mmol) of **7.1q**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 71.5 g of 29 (70% yield, red solid, m.p. = 106–107 °C [7.33].). Spectroscopic data were in accordance with literature data [7.40]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23–8.03 (m, 2H), 7.92 (d, *J* = 3.2 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.57–7.26 (m, 6H), 4.77 (s, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.5, 136.7, 133.9, 131.3, 128.6, 128.4, 127.8, 126.3, 125.7, 125.4, 123.8, 43.0.

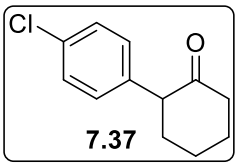


2-(3-Benzoylphenyl)-1-phenylethan-1-one (7.35). From 0.112 mg (0.389 mmol) of **7.1r**, 800 µL (10 equiv.) of **7.3** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 35.0 mg of **7.35** (30% yield, yellow solid, m.p. = 101–102 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 2H), 7.82 (d, *J* = 1.4 Hz, 4H), 7.59 (dd, *J* = 7.4, 3.0 Hz, 2H), 7.55–7.45 (m, 4H), 7.41 (d, *J* = 8.2 Hz, 2H), 4.40 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 196.2, 139.3, 137.5, 136.3, 136.1, 133.4, 132.3, 130.4, 130.0, 129.5, 128.7, 128.5, 128.2, 45.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{21}H_{16}O_2$ 301.1223, found 301.1216.



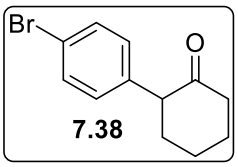
4-(2-Oxocyclohexyl)benzonitrile (7.36). From 80.9 mg (0.387 mmol) of **7.1a**, 800 µL (10 equiv.) of **7.4** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 30.0 mg of **7.36** (38% yield, slightly yellow solid, m.p. = 76-77 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 3.69 (dd, *J* = 12.2, 5.3 Hz, 1H), 2.62–2.39 (m, 2H), 2.25

(d, J = 46.9 Hz, 2H), 2.13–1.77 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.8, 144.1, 132.0, 129.4, 118.8, 110.7, 57.3, 42.1, 35.0, 27.6, 25.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{13}H_{13}NO$ 200.1070, found 200.1065.



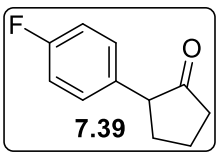
7.37

2-(4-Chlorophenyl)cyclohexan-1-one (7.37). From 91.5 mg (0.419 mmol) of **7.1c**, 800 µL (10 equiv.) of **7.4** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification step carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 30.3 mg of **7.37** (36% yield, slightly yellow solid, m.p. = 83–84°C [7.41]). Spectroscopic data were in accordance with literature data [7.42]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 3.59 (dd, J = 11.9, 5.4 Hz, 1H), 2.53–2.43 (m, 2H), 2.30 – 2.16 (m, 2H), 2.07–1.95 (m, 2H), 1.90–1.78 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 209.7, 137.1, 132.6, 129.8, 128.4, 56.7, 42.1, 35.1, 27.7, 25.2.



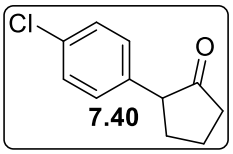
7.38

2-(4-Bromophenyl)cyclohexan-1-one (7.38). From 104.2 mg (0.397 mmol) of **7.1d**, 800 µL (10 equiv.) of **7.4** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 94.4 mg of **7.38** (22% yield, red brown solid, m.p. = 84–85 °C [7.43]). Spectroscopic data were in accordance with literature data [7.44]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 3.57 (dd, J = 11.9, 5.3 Hz, 1H), 2.54–2.42 (m, 2H), 2.25–2.05 (m, 2H), 2.03–1.93 (m, 2H), 1.85–1.78 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 210.2, 138.3, 132.0, 130.9, 121.4, 57.5, 42.8, 35.8, 28.4, 25.9.

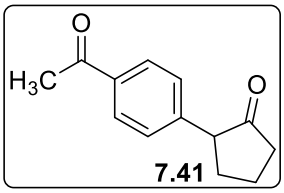


7.39

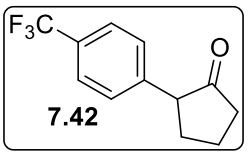
2-(4-Fluorophenyl)cyclopentan-1-one (7.39). From 80.7 mg (0.413 mmol) of 7.**1b**, 720 µL (10 equiv.) of **7.5** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 34.3 mg of **7.39** (43% yield, red oil). Spectroscopic data were in accordance with literature data [7.44]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 – 7.03 (m, 4H), 3.32 (dd, J = 10.8, 8.4 Hz, 1H), 2.54–2.46 (m, 2H), 2.30–2.13 (m, 2H), 2.13–1.98 (m, 2H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 217.7, 161.7 (q, J = 245.1 Hz), 133.8 (d, J = 3.3 Hz), 130.6, 129.4, 115.4, 115.1, 54.4, 38.1, 31.6, 20.6.



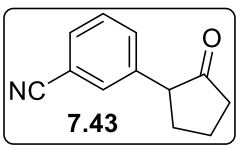
2-(4-Chlorophenyl)cyclopentan-1-one (7.40). From 107.1 mg (0.491 mmol) of **7.1c** and 720 µL of **7.5**. Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 31.6 mg of **7.40** (42% yield, red oil). Spectroscopic data were in accordance with literature data [7.45]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 3.32 (dd, *J* = 10.9, 8.4 Hz, 1H), 2.55–2.46 (m, 2H), 2.36–2.30 (m, 1H), 2.20–1.94 (m, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 217.3, 136.6, 132.7, 129.3, 128.6, 54.5, 38.1, 31.4, 20.6.



2-(4-Acetylphenyl)cyclopentan-1-one (7.41). From 94.7 mg (0.419 mmol) of **7.1f**, 720 µL (10 equiv.) of **7.5** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 45.7 mg of **7.41** (54% yield, yellow oil). Spectroscopic data were in accordance with literature data. [7.46]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 3.56–3.27 (m, 1H), 2.61 (s, 3H), 2.59–2.46 (m, 2H), 2.40–2.24 (m, 1H), 2.27–2.09 (m, 2H), 2.08–1.91 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 216.8, 197.6, 143.7, 128.5, 128.3, 55.2, 38.2, 31.3, 26.5, 20.7.

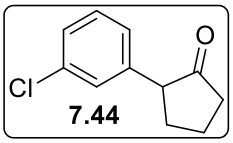


2-(4-(Trifluoromethyl)phenyl)cyclopentan-1-one (7.42). From 105.1 mg (0.417 mmol) of **7.1h**, 720 µL (10 equiv.) of **7.5** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 70.4 mg of **7.42** (74% yield, yellow oil). Spectroscopic data were in accordance with literature data [7.44]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.41 (dd, *J* = 11.3, 8.2 Hz, 1H), 2.60–2.48 (m, 2H), 2.42–2.28 (m, 1H), 2.28–2.13 (m, 2H), 2.07–1.91 (m, 1H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.5, 138.5, 136.3, 133.4, 129.9, 128.6, 128.4, 125.4 (q, *J*=3.4 Hz), 44.90, 40.5, 38.7, 28.6.

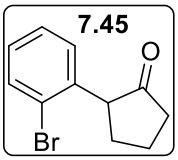


3-(2-Oxocyclopentyl)benzonitrile (7.43). From 83.2 mg (0.398 mmol) of **7.1k**, 720 µL (10 equiv.) of **7.5** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 43.4 mg of **7.43** (59% yield, slightly yellow oil). Spectroscopic data were in accordance with literature data [7.44]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63–7.40 (m, 4H), 3.49–3.27 (m, 1H), 2.59–2.49 (m, 2H), 2.39–2.20 (m, 2H),

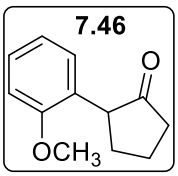
2.16–1.97 (m, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 216.2, 139.5, 132.7, 131.5, 130.5, 129.2, 118.6, 112.5, 54.4, 38.0, 31.0, 20.6.



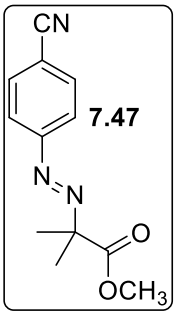
2-(3-Chlorophenyl)cyclopentan-1-one (7.44). From 83.5 mg (0.383 mmol) of **7.1l**, 720 µL (10 equiv.) of **7.5** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 42.4 mg of **7.44** (57% yield, yellow oil). Spectroscopic data were in accordance with literature data [7.44]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.22 (m, 2H), 7.21 (d, *J* = 2.0 Hz, 1H), 7.10 (dt, *J* = 6.9, 1.9 Hz, 1H), 3.31 (dd, *J* = 11.5, 7.8, Hz, 1H), 2.58–2.44 (m, 3H), 2.40–2.27 (m, 1H), 2.26–2.10 (m, 3H), 2.03–1.89 (m, 1H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 216.9, 140.2, 134.2, 129.7, 128.1, 127.0, 126.3, 54.7, 38.2, 31.4, 20.6.



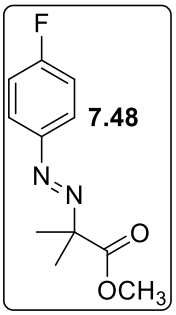
2-(2-Bromophenyl)cyclopentan-1-one (7.45). From 103.4 mg (0.395 mmol) of **7.1o**, 720 µL (10 equiv.) of **7.5** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 76.0 mg of **7.45** (81% yield, slightly yellow oil). Spectroscopic data were in accordance with literature data [7.47]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.12 (ddd, *J* = 14.6, 7.6, 1.6 Hz, 2H), 3.79 (dd, *J* = 10.9, 8.5 Hz, 1H), 2.61–2.48 (m, 2H), 2.46–2.33 (m, 1H), 2.26–2.16 (m, 1H), 2.10–1.94 (m, 2H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 217.3, 138.7, 133.0, 130.0, 128.4, 127.6, 125.0, 56.1, 38.5, 31.7, 20.8.



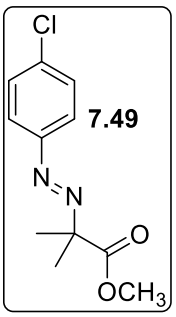
2-(2-Methoxyphenyl)cyclopentan-1-one (7.46). From 80.9 g (0.378 mmol) of **7.1p**, 720 µL (10 equiv.) of **7.5** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 95:5 Cyclohexane/ethyl acetate) to afford 58.2 mg of **7.46** (81% yield, red solid, m.p. = 107–108 °C [7.48]). Spectroscopic data were in accordance with literature data [7.47]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 7.8, 1.4 Hz, 2H), 7.09 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.96–6.85 (m, 2H), 3.79 (s, 3H), 3.39 (dd, *J* = 11.1, 8.7 Hz, 1H), 2.48–2.39 (m, 2H), 2.40–2.27 (m, 1H), 2.24–2.12 (m, 2H), 1.96–1.82 (m, 2H).$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 219.2, 156.7, 130.4, 128.2, 120.7, 111.1, 52.3, 38.1, 31.0, 21.4.



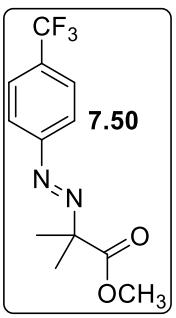
Methyl 2-((4-cyanophenyl)diazenyl)-2-methylpropanoate (7.47). From 86.7 mg (0.415 mmol) of **7.1a**, 740 µL (10 equiv.) of **7.6** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 83.4 mg of **7.47** (87% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 4H), 3.77 (s, 3H), 1.61 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 153.5, 133.0, 132.1, 126.6, 122.9, 118.1, 114.0, 76.3, 52.3, 23.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{13}N_3O_2$ 232.1081, found 232.1071.



Methyl 2-((4-fluorophenyl)diazinyl)-2-methylpropanoate (7.48). From 81.4 mg (0.403 mmol) of **7.1b**, 740 µL (10 equiv.) of **7.6** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 74.9 mg of **7.48** (83% yield, slightly yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 – 7.62 (m, 2H), 7.15 (t, J = 8.6 Hz, 2H), 3.77 (s, 3H), 1.60 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 165.82, 162.49, 124.4-124.3 (d, $J_{(C-F)}$= 8.9 Hz), 115.9-15.6 (d, $J_{(C-F)}$= 22.7 Hz), 75.3, 52.1, 23.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{13}N_2O_2F$ 225.1034, found 225.1033.

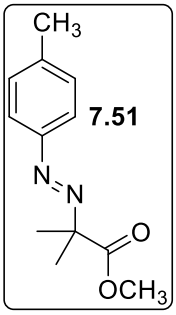


Methyl 2-(4-chlorophenyl)-2-methylpropanoate (7.49). From 91.4 mg (0.419 mmol) of **7.1c**, 740 µL (10 equiv.) of **7.6** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 30.3 g of **7.49** (33% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H), 1.60 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 149.9, 136.7, 129.1, 123.6, 75.5, 52.2, 23.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{13}N_2O_2Cl$ 241.0738, found 241.0730.

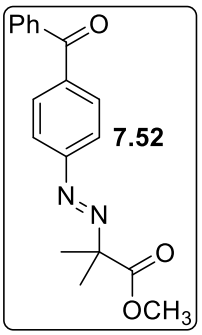


Methyl 2-methyl-2-((4-(trifluoromethyl)phenyl)diazenyl)propanoate (7.50). From 104.8 mg (0.416 mmol) of **7.1h**, 740 µL (10 equiv.) of **7.6** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate mixture) to afford 92.4 mg of **7.50** (81% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (q, J = 8.6 Hz, 4H), 3.76 (s, 3H), 1.61 (s, 6H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.4, 153.5, 129.5, 128.9 (d, $J_{(C-F)}$= 96.0 Hz), 126.1 (q, $J_{(C-F)}$= 3.7 Hz), 122.5,

120 (d, $J_{(C-F)}$ = 289.3 Hz), 118.1, 76.1, 52.2, 23.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{13}N_2O_2F_3$ 275.1002, found 275.0990.



Methyl 2-methyl-2-(p-tolyldiazenyl)propanoate (7.51). From 75.6 mg (0.391 mmol) of **7.1i**, 740 µL (10 equiv.) of **7.6** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 28.4 mg of **7.51** (33% yield, yellow oil). Spectroscopic data were in accordance with literature data. [7.49]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.2 Hz, 2H), 3.77 (s, 3H), 2.42 (s, 3H), 1.60 (s, 6H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 174.0, 149.7, 141.1, 122.2, 75.2, 52.0, 23.0, 21.2.



Methyl 2-((3-benzoylphenyl)diazenyl)-2-methylpropanoate (7.52): From 0.109.1 mg (0.389 mmol) of **7.1r**, 740 µL (10 equiv.) of **7.6** and 64 mg of $NaHCO_3$ (0.1 mmol, 0.1 M) in 8 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: 9:1 Cyclohexane/ethyl acetate) to afford 65.6 mg of **7.52** (61% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 8.5 Hz, 2H), 7.85 – 7.74 (m, 4H), 7.63 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 3.79 (s, 3H), 1.64 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.8, 173.5, 132.6, 130.8, 129.9, 128.3, 122.0, 122.0, 76.1, 52.2, 23.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{18}N_2O_3$ 311.1390, found 311.1375.

7.5. REFERENCES.

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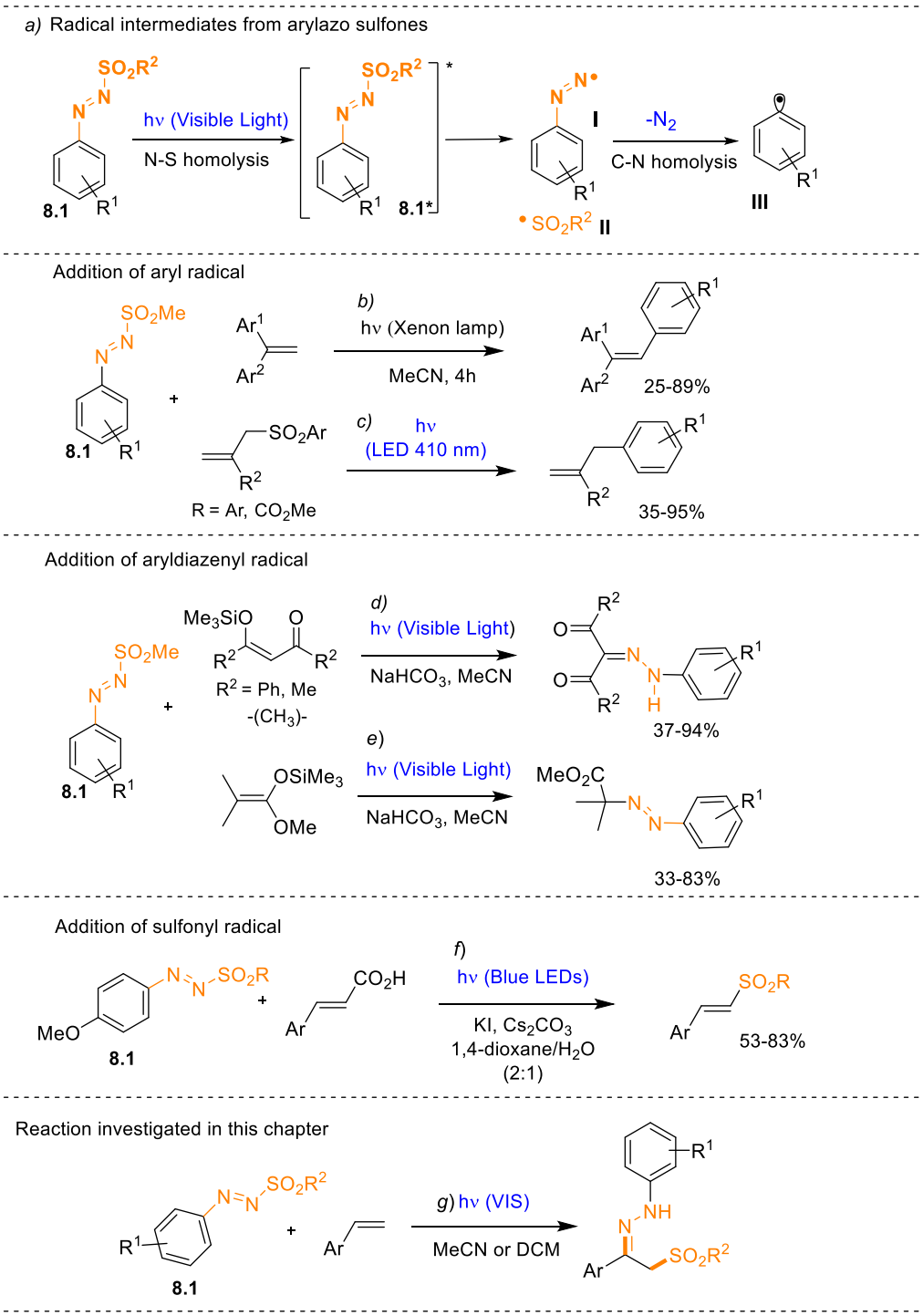
CHAPTER 8

VISIBLE-LIGHT-MEDIATED DIVERGENT AND REGIOSELECTIVE VICINAL DIFUNCTIONALIZATION OF STYRENES WITH ARYLAZO SULFONES.

8.1. INTRODUCTION.

The simultaneous functionalization of vicinal positions of alkenes in a single step is a powerful tool in organic synthesis able to generate complex molecules in a fast approach [8.1]. In this field, visible-light photocatalysis [8.1-8.2] has recently attracted much attention for developing facile intermolecular difunctionalizations of readily accessible alkenes [8.3], and two main strategies have been successfully applied. The first strategy is based on a photocatalyzed three-component approach, which involves the addition of a radical to alkenes and the subsequent capture of the resulting adduct radical by suitable reactants [8.4]. The second one relies on the use of bifunctional reagents, which, under photocatalytic conditions, results in the formation of two substituted radicals that are concomitantly incorporated into the alkenes [8.4,8.5]. In some case, difunctionalization of alkenes can also occur via the formation of an Electron Donor Acceptor (EDA) complex [8.6a-d], or via photoredox oxidation of the alkene moiety [6e]. Despite that, with these two complementary methods, various efficient alkene difunctionalizations have been reported. The use of exogenous photocatalysts, which are often relatively expensive and difficult to recycle, is a limitation in most processes [8.6]. Therefore, the development of more sustainable approaches is still highly necessary. *Dyedauxiliary groups* [8.7-8.10] are functional motifs that once tethered to a molecule make the compound coloured and photoreactive. The activation of these compounds is triggered by radiations and are considered a visible-light source of aryl radicals, aryldiazenyl radicals and sulphonyl radicals, without the employment of external (photo)catalysts (Scheme 8.1, a). This visible-light-driven process has resulted in successful alkene monofunctionalizations. For example, we developed an efficient arylation procedure of 1,1-diaryl ethylenes (Scheme 8.1, b) [8.11a] and allyl sulfones (Scheme 8.1, c) [8.11b] with arylazo sulfones yielding triaryl ethylenes and allyl arenes, respectively, in moderate to excellent yields. Furthermore, the diazenylation of enol silyl ether derivatives (Scheme 8.1, d) [8.12] and ketene silyl acetals (Scheme 8.1, d) [8.13] was also achieved through direct trapping of aryl diazenyl radicals generated from arylazo sulfones. In 2020, Chawla and co-workers used arylazo sulfones as the precursors of sulfonyl radicals and reported the sulfonylation of cinnamic acids yielding (E)-vinyl sulfones (Scheme 8.1, f) in good yields [8.14]. Arylazo sulfones proved to be a good source of radicals for the mono-functionalization of C(sp^2) bonds, however, the utilization of these substrates as radical sources for the 1,2-difunctionalization of alkenes remains scarce, and only a part of the

functionalizing agent is effectively incorporated in the final product. In view of these premises, we envisioned that the divergent reactivities of arylazo sulfones can be applied to the vicinal difunctionalization of alkenes by carefully adjusting the reaction conditions. For what concerns the part I investigated in this chapter, I focused on the regioselective synthesis of α-sulfonyl arylhydrazones products from readily available styrenes (Scheme 8.1, g).

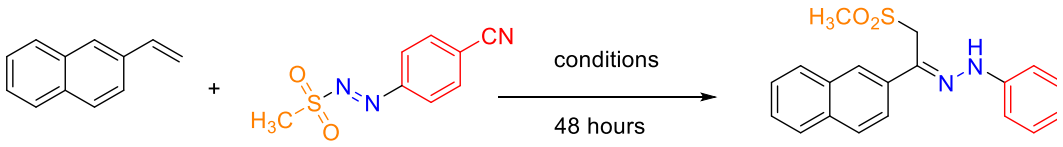


Scheme 8.1. Examples of functionalizations employing arylazo sulfones.

8.2. RESULTS AND DISCUSSION.

During my period at the ICSN (Institut de Chimie des Substances Naturelles), CNRS (Centre national de la recherche scientifique) at the University of Paris Saclay with Prof Luc Neuville and Geraldine Masson, we set out to initially study the functionalization of 4-cyanophenylazo sulfone **8.1a** and 2-vinylnaphthalene (**8.2**) upon light irradiation as a model reaction and the results are depicted in Table 8.1. As first trials, the study of different organic media was performed, highlighting the change of having better results in DMSO and DCM (entry 6 and 7). Then, compact fluorescent lamp (CFL) was used as the light source, and a product was isolated in 50% yield in degassed DCM (entry 11). The structure of the obtained compound was identified as the α-sulfonyl arylhydrazone **8.10** with (*Z*)-configuration by NMR studies. It is interesting to note that such overall addition mode has not been previously reported and provides a simple route for the synthesis of valuable α-sulfonyl arylhydrazones. When the reaction was conducted in the presence of oxygen, the conversion dramatically dropped suggesting that restrictive anaerobic conditions were required for this radical vicinal difunctionalization (entry 9). The use of other light sources such as Kessil Lamp (from 25% to 100% power, entries 12-15, 17 and 18) and EvoluChem Lamp (entries 16, 17) resulted in better yields. Upon increasing the ratio of styrenes **8.2** to **8.1a** slightly higher yields were obtained (entries 16, 17). A solvent screening pointed out that DCM and MeCN provided identical results, and then DCM was selected for further studies. Performing the reaction at a higher scale (0.2 mmol of **8.1a**), the desired product **8.10** precipitated in less than 16 h and was isolated by simple filtration (entry 18). Further analysis of the filtrate revealed the formation of another product (5% yield) corresponding to the α-sulfonyl aryl diazene product **8.10a.** When the irradiation was prolonged for 24 h, however, hydrazone **8.10** was the sole product formed in 96% yield, thereby supporting our assumption.

Table 8.1. Optimization of the reaction conditions for the photochemical synthesis of α-sulfonyl arylhydrazones.



8.2 **8.1a** **8.10**

Entry	Conditions	Yield
1	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, CH_3OH	0%
2	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, CH_3CN	<5%
3	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, Benzene	0%
4	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, DMF	15%
5	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, Acetone	0%
6	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, CH_2Cl_2	15%
7	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, DMSO	30%
8	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) CFL white bulb (25 W), CH_2Cl_2	21%
9	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, O_2, DMSO	13%
10	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Blue LED, FREEZE PUMP, DMSO	15%
11	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) CFL white bulb (25 W), FREEZE PUMP, CH_2Cl_2	73% (50%)[a]
12	**8.1a** (0.1 mmol), **8.2** (0.05 mmol) Kessil Lamp 456nm (25% power), FREEZE PUMP, CH_2Cl_2	73%[a]
13	**8.1a** (0.1 mmol), **8.2** (0.1 mmol) Kessil Lamp 456 nm (25% power), FREEZE PUMP, CH_2Cl_2	75%[a]
14	**8.1a** (0.15 mmol), **8.2** (0.1 mmol) Kessil Lamp 456 nm (25% power), FREEZE PUMP, CH_2Cl_2	83%[a]
15	**8.1a** (0.2 mmol), **8.2** (0.1 mmol) Kessil Lamp 456 nm (25% power), FREEZE PUMP, CH_2Cl_2	89%[a]
16	**8.1a** (0.4 mmol), **8.2** (0.2 mmol) Evoluchem 450 nm, FREEZE PUMP, CH_3CN	96%[a]
17	**8.1a** (0.4 mmol), **8.2** (0.2 mmol) Evoluchem 450 nm, FREEZE PUMP, CH_2Cl_2	94%[a,b]
18	**8.1a** (0.4 mmol), **8.2** (0.2 mmol) Kessil Lamp 456nm, FREEZE PUMP, CH_2Cl_2	96%[a,b]
19	**8.1a** (0.4 mmol), **8.2** (0.2 mmol) Kessil Lamp 456nm, FREEZE PUMP, CH_3CN	90%[a]
20	**8.1a** (0.4 mmol), **8.2** (0.2 mmol) **DARK**, FREEZE PUMP, CH_2Cl_2,	0%
21	**8.1a** (0.4 mmol), **8.2** (0.2 mmol) Kessil Lamp 456nm, FREEZE PUMP, CH_2Cl_2, vial covered in aluminium foil	0%

[a.] Isolated yield; [b.] reaction performed in 24 hours.

To explore the scope of this difunctionalization, various arylazo sulfones **8.1** (Figure 8.1, a). and styrene traps were studied under the optimized reaction conditions (Figure 8.1, b).

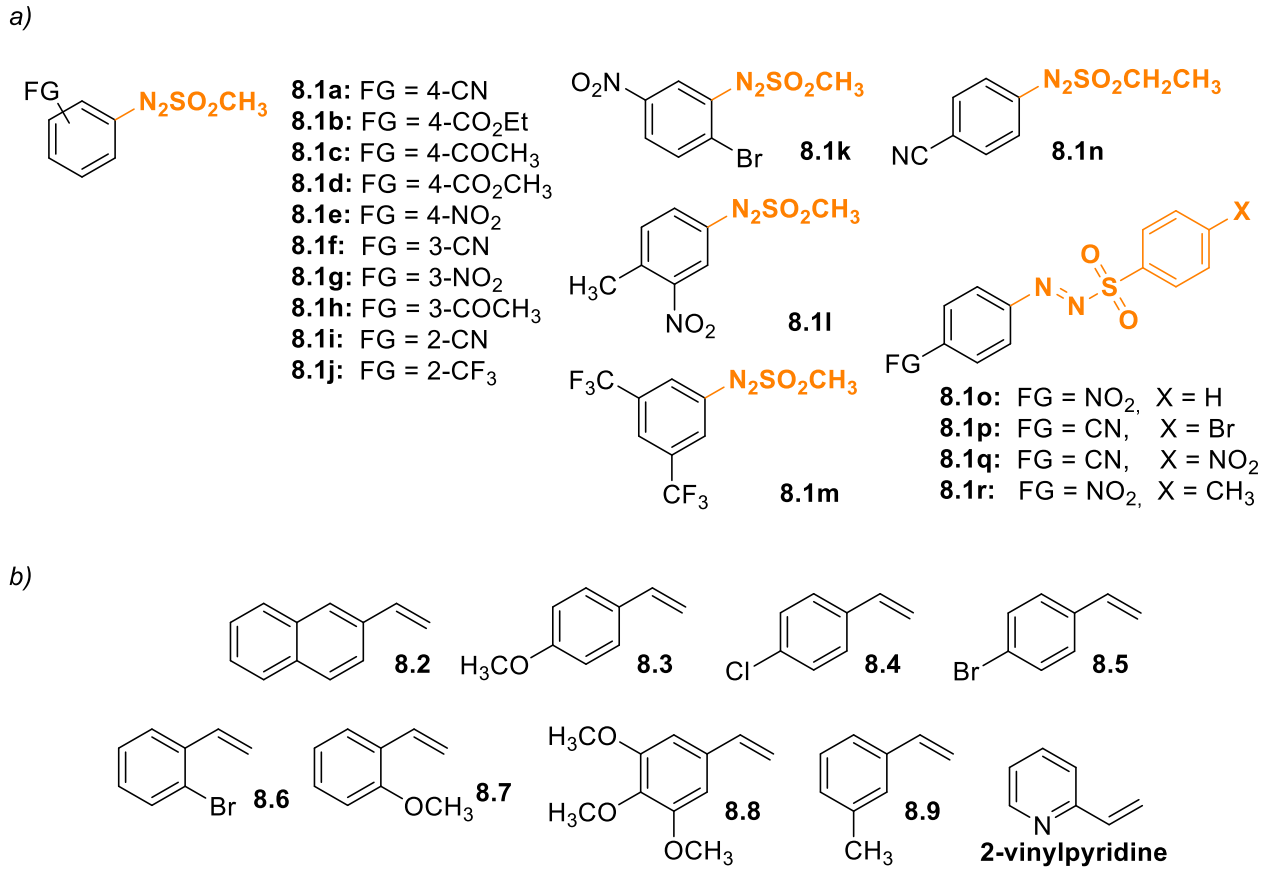
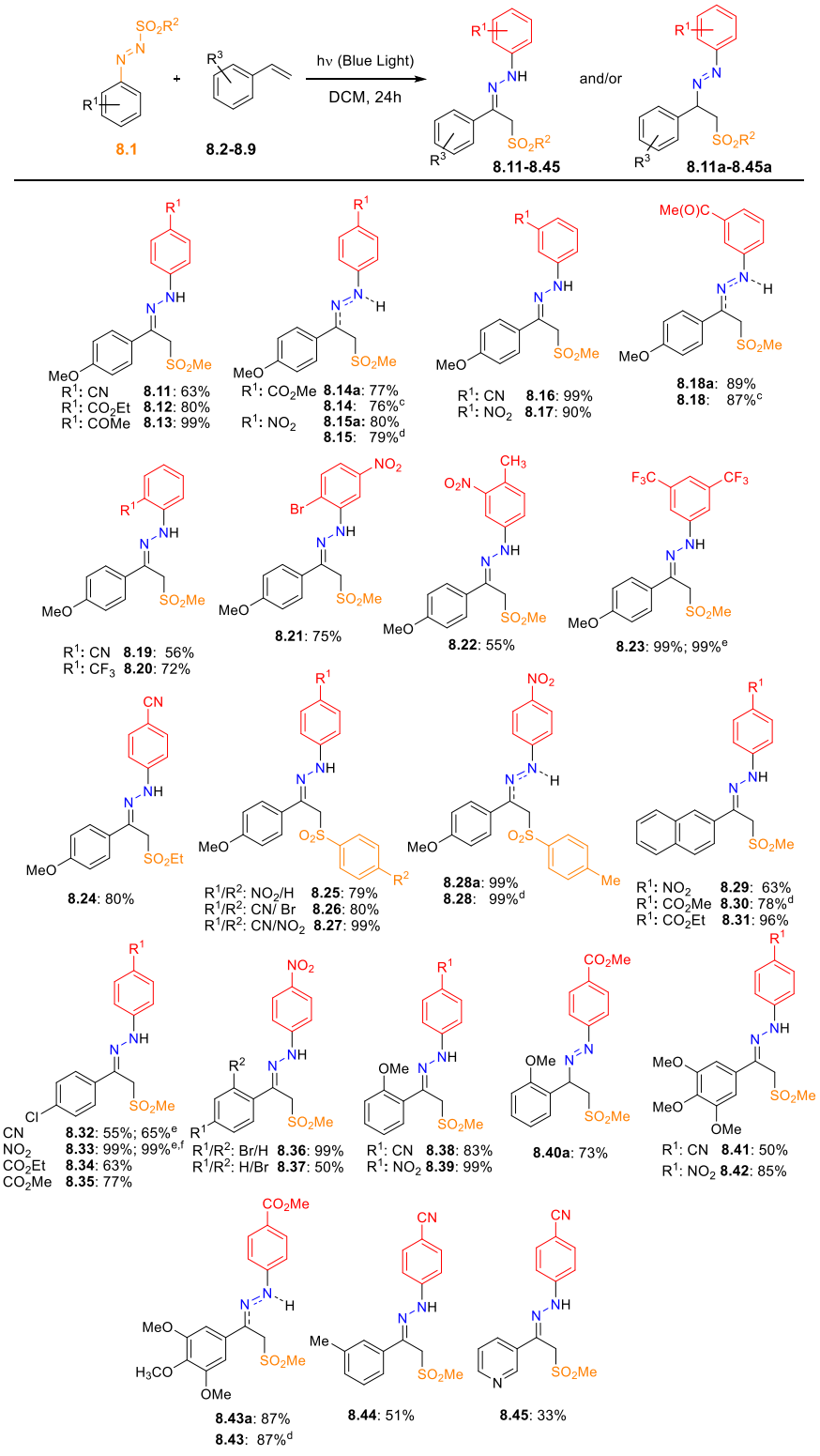


Figure 8.1. a) Arylazo sulfones used in this chapter. b) Traps employed in this chapter.

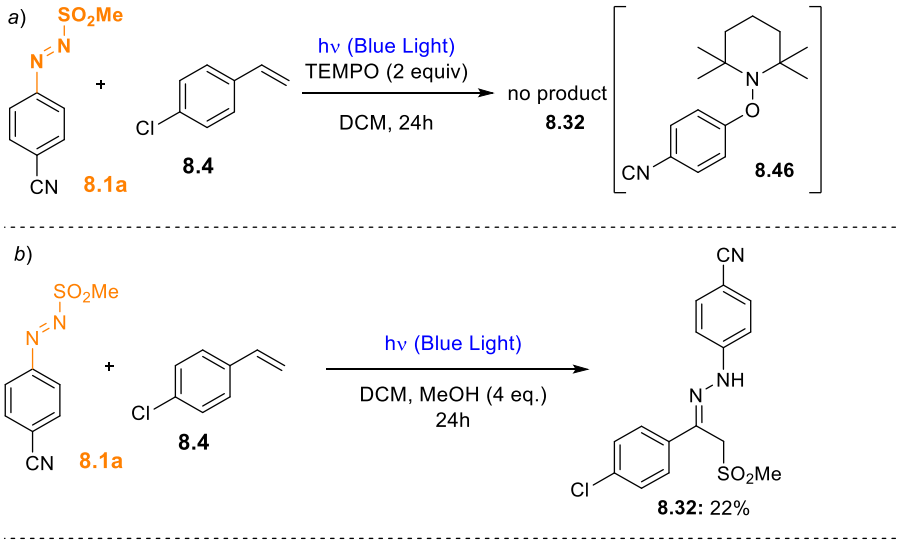
We found that the efficiency of the process was sensitive to the electronic properties of the aromatic substituents in **8.1**. Thus, with arylazo sulfones bearing electron-withdrawing substituents (such as CN, CO_2Et or $COCH_3$) reacted efficiently with 4-vinylanisole **8.3** to form the corresponding α-sulfonyl arylhydrazones **8.11-8.13** in high yields. Arylazo sulfones with substituents at the meta (**8.16**, **8.17** and **8.18**) and ortho (**8.19-8.20**) positions were well tolerated. As apparent from the results depicted in Scheme 8.2 the reaction exhibited a broad styrene scope: both electron rich and electron poor aryl rings are well tolerated, and the desired products were obtained also when using vinyl naphthalenes (**8.29-8.31**) and, although in low yield, with 3-vinyl pyridine (**8.45**). Surprisingly, with arylazo sulfones bearing aromatic electron-withdrawing substituent (e.g. p-COOMe, p-NO_2, m-CH_3CO) only the corresponding α-sulfonyl aryldiazenes were isolated under the standard reaction conditions (see for instance products **8.14a**, **8.15a** and **8.28a**), but a prolonged irradiation (36 h) resulted in the almost quantitative phototautomerization of the former compounds to the desired arylhydrazones **8.14**, **8.15** and **8.28**. Unfortunately, the electron-rich arylazo sulfones were not

suitable bifunctional reaction partners, and only a complex product mixture was observed. Gratifyingly arylazo sulfone containing both an electron-rich (CH_3) and an electron-poor (NO_2) moiety was viable and the desired product **8.22** isolated in 55% yield. The nature of the sulfone group was found to have neglecting effect on the reaction since a wide range of substituted arylsulfones was synthesized in high to almost quantitative yields (**8.25-8.27**); as previously observed when using an arylazo sulfone bearing a p-NO_2 group, the stable diazenyl product **8.28a** has been isolated and further quantitatively converted to **8.28** after prolonged irradiation. Finally, the scope of styrenes was screened, pointing out that various substituents at the ortho-, meta- and para positions were compatible to afford corresponding products **8.32-8.39** in excellent yields. 3,4,5-Trimethoxystyrene participated in the reaction decently, and the resulting hydrazones **8.41-8.42** were isolated in 50% and 85% yields, respectively, while prolonged irradiation was required for hydrazone **8.43**. 2-Vinylpyridine was also transformed into the corresponding product **8.45**, albeit in low yield. Excellent yield (99%) of **8.33** was obtained after 77 hours of exposition of the reaction mixture to natural sunlight.



Scheme 8.2. Scope of the proposed methodology. [a]. General reaction conditions: **8.1a-r** (0.20 mmol) and traps (0.40 mmol, 2 equiv), in DCM (1.0 mL) at 10 °C for 24 h irradiation carried out with a Kessil Lamp 456 nm, 40 W. [b] Yield of isolated pure product after column chromatography or precipitation. [c] 36h. [d] Yield based on the conversion of diazenyl product **8.11-8.45a**. [e] Reaction carried out on 1 mmol of **8.1**. [f] Natural sunlight was used as light source (77h).

A series of control experiments were conducted to obtain mechanistic information on these vicinal alkene difunctionalizations (Scheme 8.3). No desired product was obtained when the reaction was performed in the dark, thus demonstrating that visible-light irradiation was essential to initiate all the 1,2-difunctionalization reactions described above (Table 8.1, entry 20 and 21). The solvents do not induce significant influence on the divergence in the reactivity of **8.1a**, as the difunctionalization can be carried out in DCM as well as MeCN. The addition of MeOH (4 equiv) in the arylhydrazination reaction of **8.4** led to a loss of yield (22% vs 55 %, Scheme 8.3, b). To demonstrate the synthetic potentials of our protocol, the 1,2-sulfonyl-arylhydrazination of styrene was scaled up (1 mmol). The results are comparable (99% for **8.23**), if not better (65% and 99% for **8.32** and **8.33**, respectively, Scheme 8.3). Thereafter, a series of transformations was carried out on these difunctionalized products.



Scheme 8.3. Variations from the standard conditions.

Noteworthy, the addition of the radical scavenger 2,2,6,6-tetramethylpiperidinooxy (TEMPO) significantly inhibited both reactions. The presence of the product **8.46** resulting from the trapping of the aryl radical by TEMPO was pointed out by LC-MS analyses (Figure 8.2).

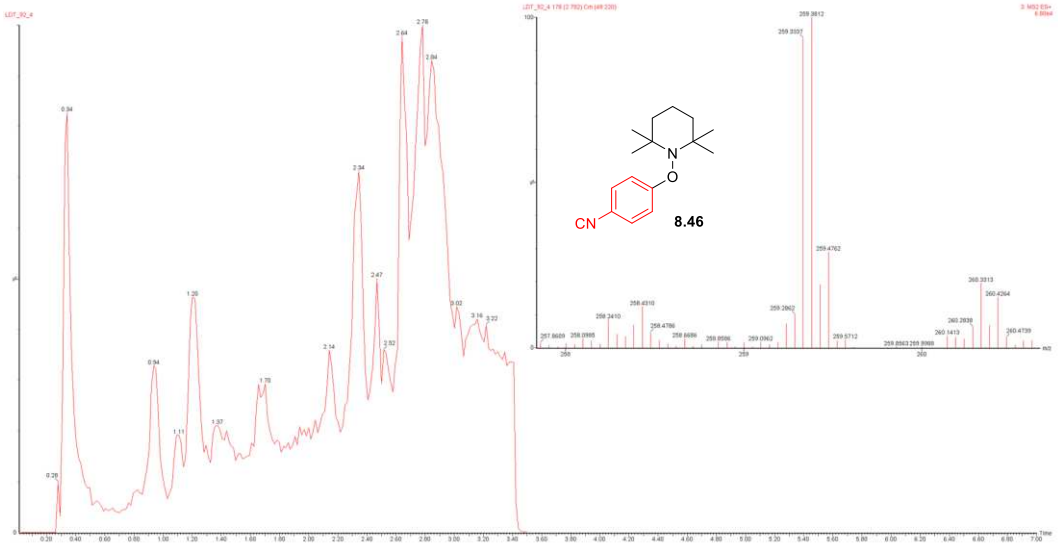


Figure 8.2. LC-MS of the photolyzed mixture of **8.1a** and **8.4** in the presence of TEMPO.

These observations support that a radical pathway is involved in the transformation. Interestingly, the light on–off gave important detail about the mechanism of the studied reaction (Figure 8.3). As a matter of fact, the irradiation of **8.1a** in the presence of **8.4** by NMR analysis showed the increament of the peak of product **8.32** even when the solution was not irradiated. Furthermore, the consumption of arylazo sulfone **8.1a** decreased and the graph could be plotted with the consumption of the starting material instead of the product formation **8.32** due to the low solubility of the latter (Figures 8.4 and 8.5).

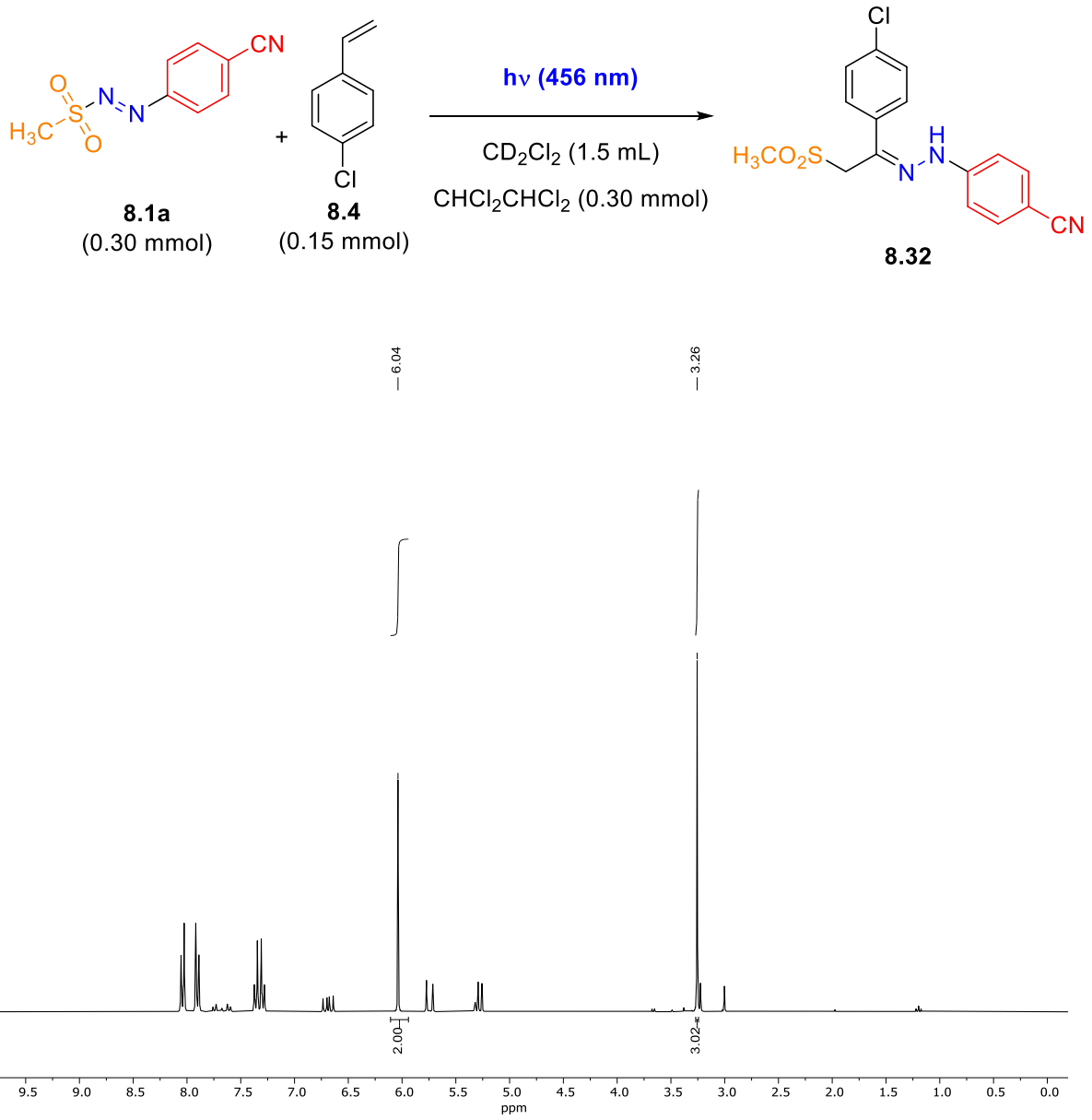


Figure 8.3. ^{1}H-NMR spectroscopy of the 4-Chlorostyrene **8.4** (0.15 mmol) and the arylazo sulfone **8.1a** (0.30 mmol) with 1,1,2,2-tetrachloroethane (0.30 mmol) as internal standard.

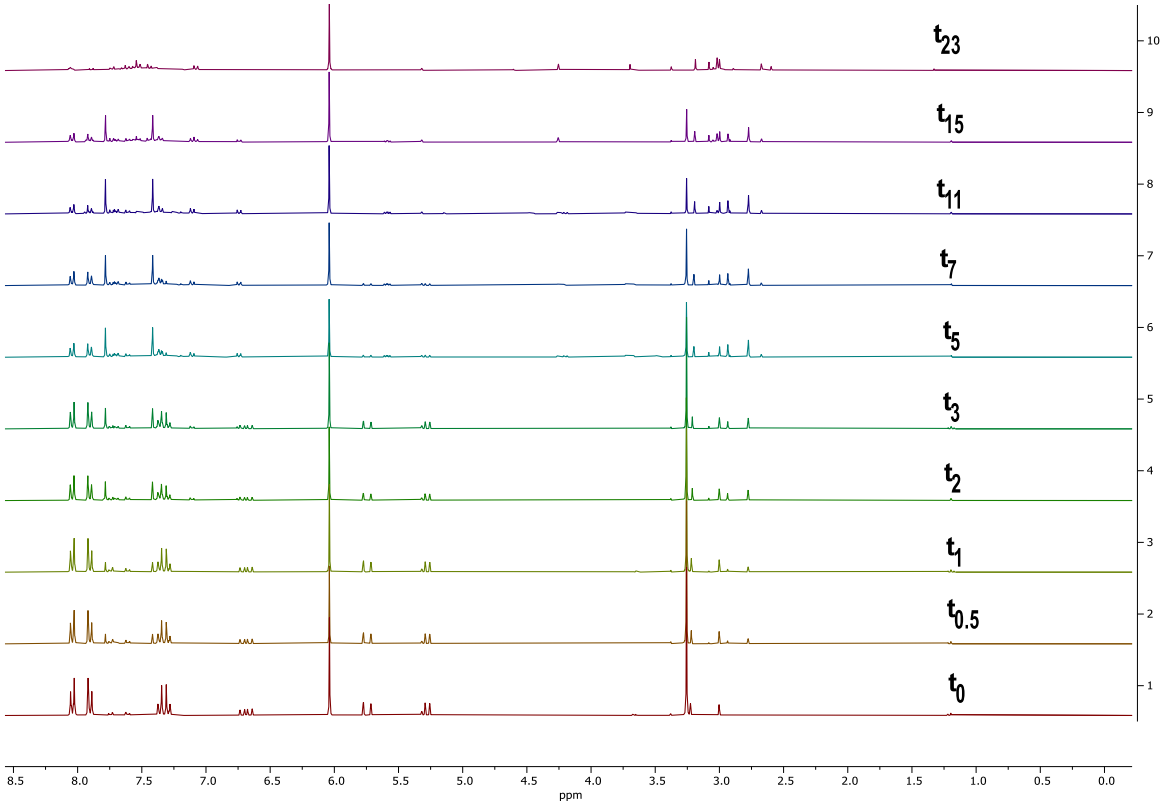


Figure 8.4. ^{1}H-NMR spectroscopy of the 4-Chlorostyrene **8.4** and the arylazo sulfone **8.1a** with 1,1,2,2-tetrachloroethane as internal standard at different times during the "on-off" experiment.

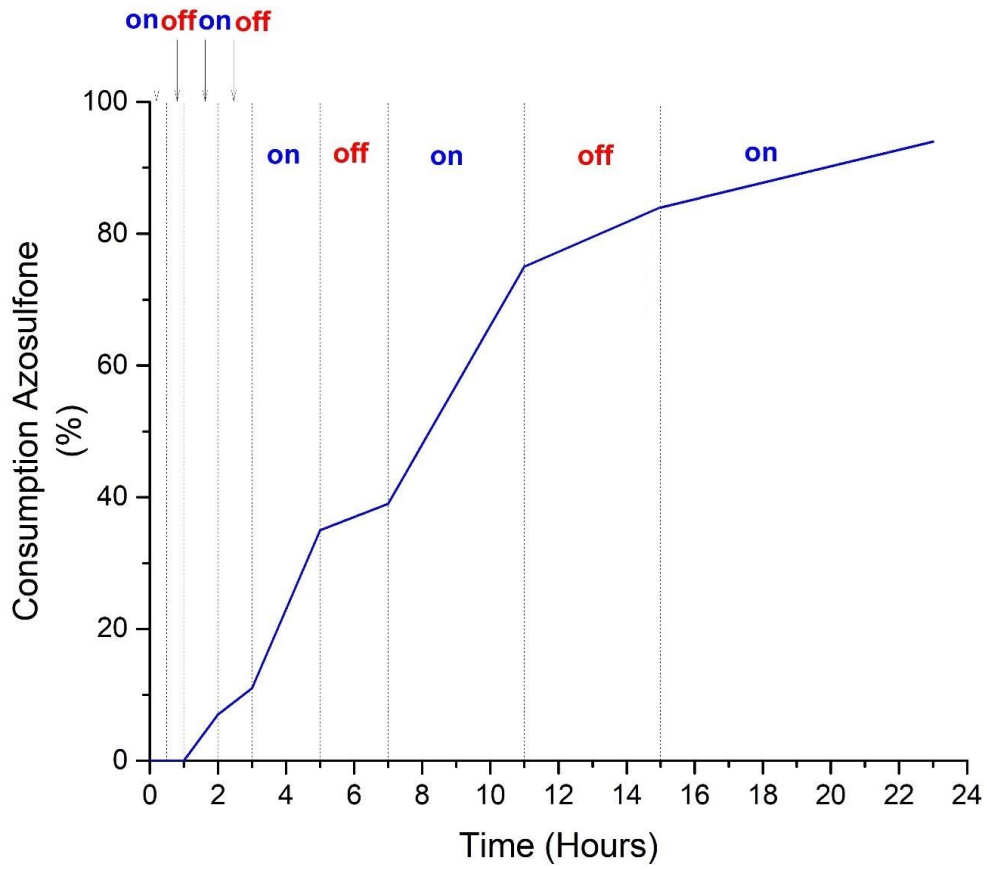


Figure 8.5. Graphic showing the consumption **8.1a** (referred to the internal standard) during the different times of the "on-off" experiment.

Indeed, the 1,2-sulfonyl-arylhydrazination reaction seems to proceed through a visible-light-initiated radical chain propagation. To have a better insight on the reaction mechanism arylazo sulfone **8.1a** and 4-chlorostyrene trap **8.4** were mixed together in an NMR tube with CD_2Cl_2 as solvent. The aforementioned solution was irradiated for 5 hours, the tube was covered in an aluminium foil, and the cup was parafilmed and put in the fridge for 12 hours and 12 more hours. The reaction was monitored with NMR spectroscopy using 1,1,2,2-tetrachloroethane as internal standard following the consumption of the arylazo sulfone **8.1a** (Figures 8.6-8.8). The consumption plot highlights the presence of a visible-light-initiated radical chain propagation as we supposed at the beginning (Figure 8.8).

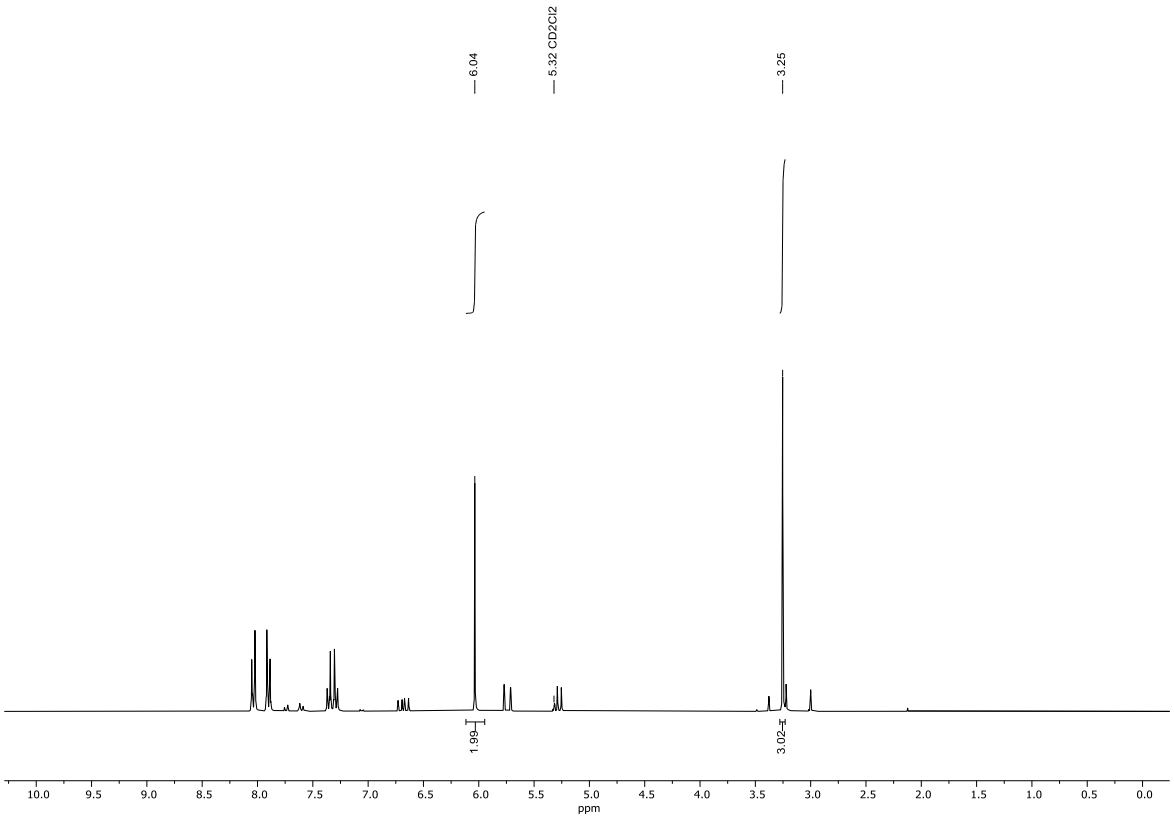


Figure 8.6. ^{1}H-NMR spectrosocpy of the 4-Chlorostyrene **8.4** (0.15 mmol) and the arylazo sulfone **8.1a** (0.30 mmol) with 1,1,2,2-tetrachloroethane (0.30 mmol) as internal standard.

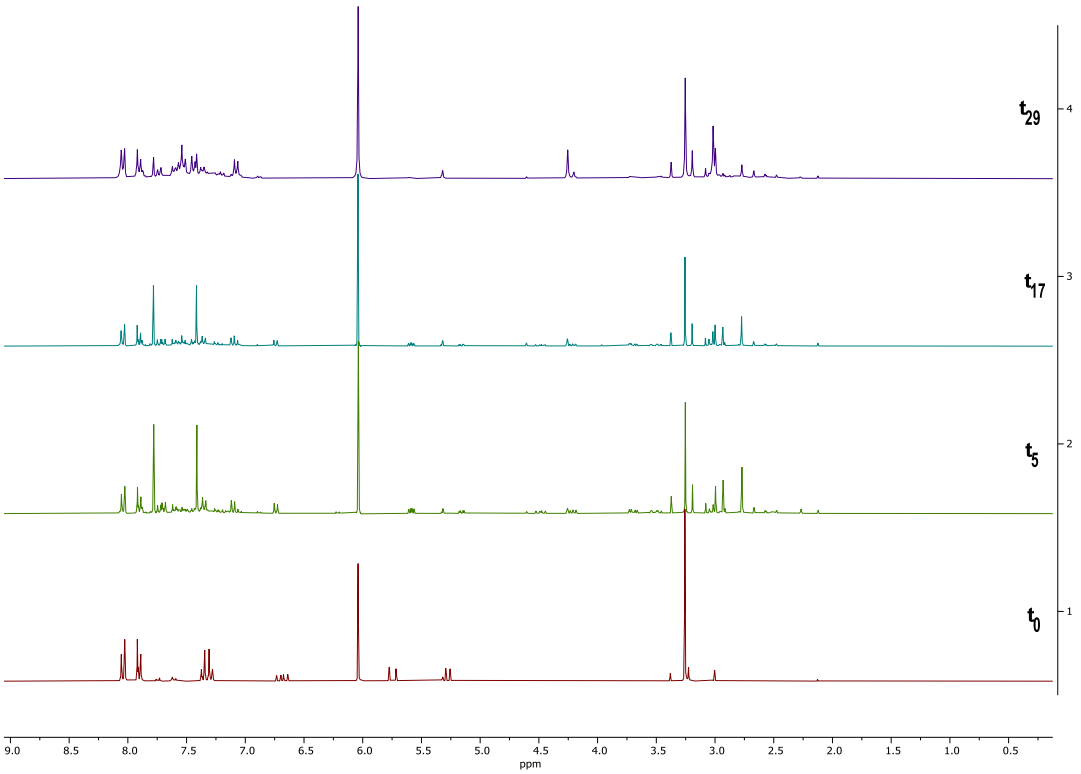


Figure 8.7. ^{1}H-NMR spectroscopy of the 4-Chlorostyrene **8.4** and the arylazo sulfone **8.1a** with 1,1,2,2-tetrachloroethane as internal standard at different times during the photo-initiated experiment.

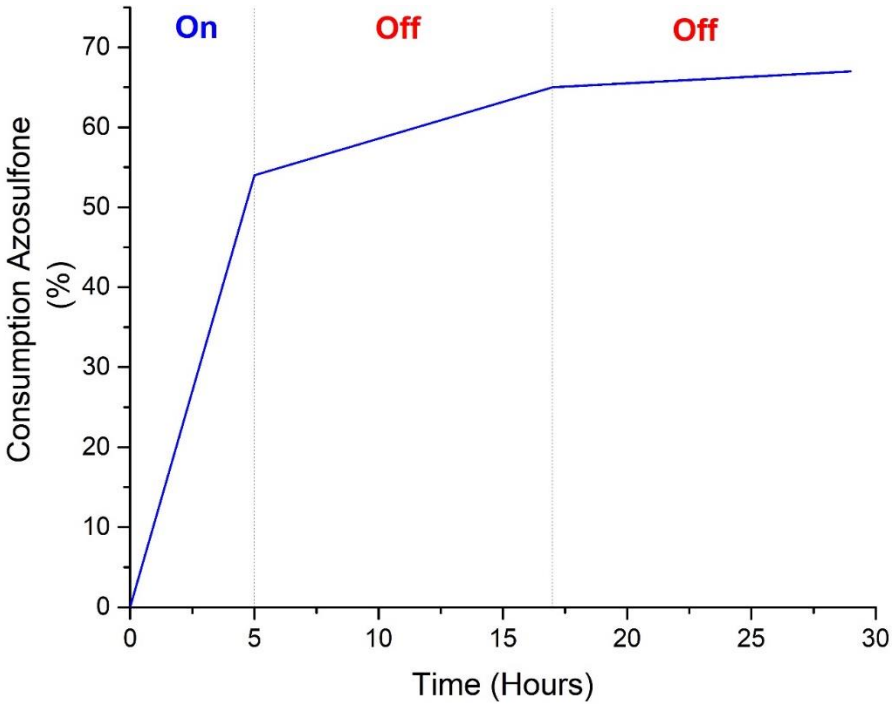
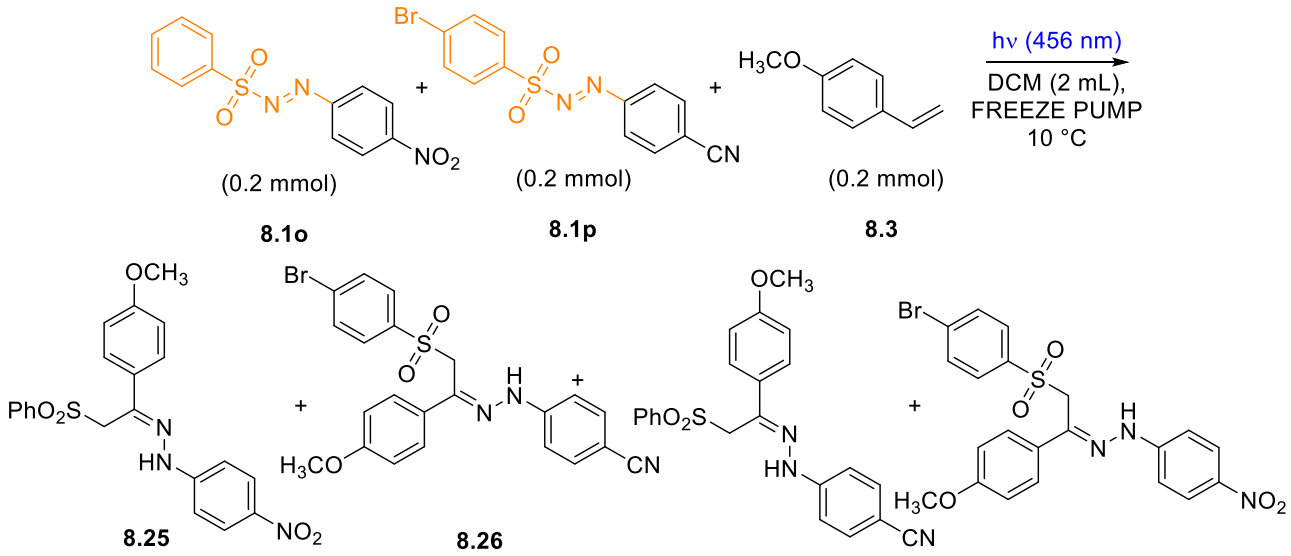


Figure 8.8. Graphic showing the azosulfone consumption (referred to the internal standard) during the different times of the "photo-initiated" experiment carried out with arylazo sulfone **8.1a** (0.3 mmol) and 4-chlorostyrene **8.4** (0.15 mmol) in presence of 1,1,2,2-tetrachloroethane as internal standard in 1.5 mL of CD_2Cl_2.

Moreover, a cross reaction experiment was carried out**.** In a flame-dried tube, arylazo sulfone **8.1o** (87.3 mg, 0.3 mmol), arylazo sulfone **8.1p** (104.4 mg, 0.3 mmol) and 4-methoxystyrene **8.3** (70 µL, 0.5 mmol) were dissolved in predistilled and anhydrous dichloromethane (2 mL). The irradiation was carried out until the consumption of the starting materials. The final NMR analysis on the inseparable hydrazones mixture confirmed the presence of four products.



Scheme 8.4. This scheme shows the chosen reaction which was performed to highlight the mechanism of the formation of the α-sulphonyl hydrazones: the experiment was carried out with arylazo sulfone **8.1o** (0.3 mmol), **8.1p** (0.3 mmol) and 4-methoxystyrene **8.3** (0.15 mmol) in 2 mL of CH_2Cl_2 irradiating with a blue Kessil Lamp (λ_{emm}= 456 nm, 40 W).

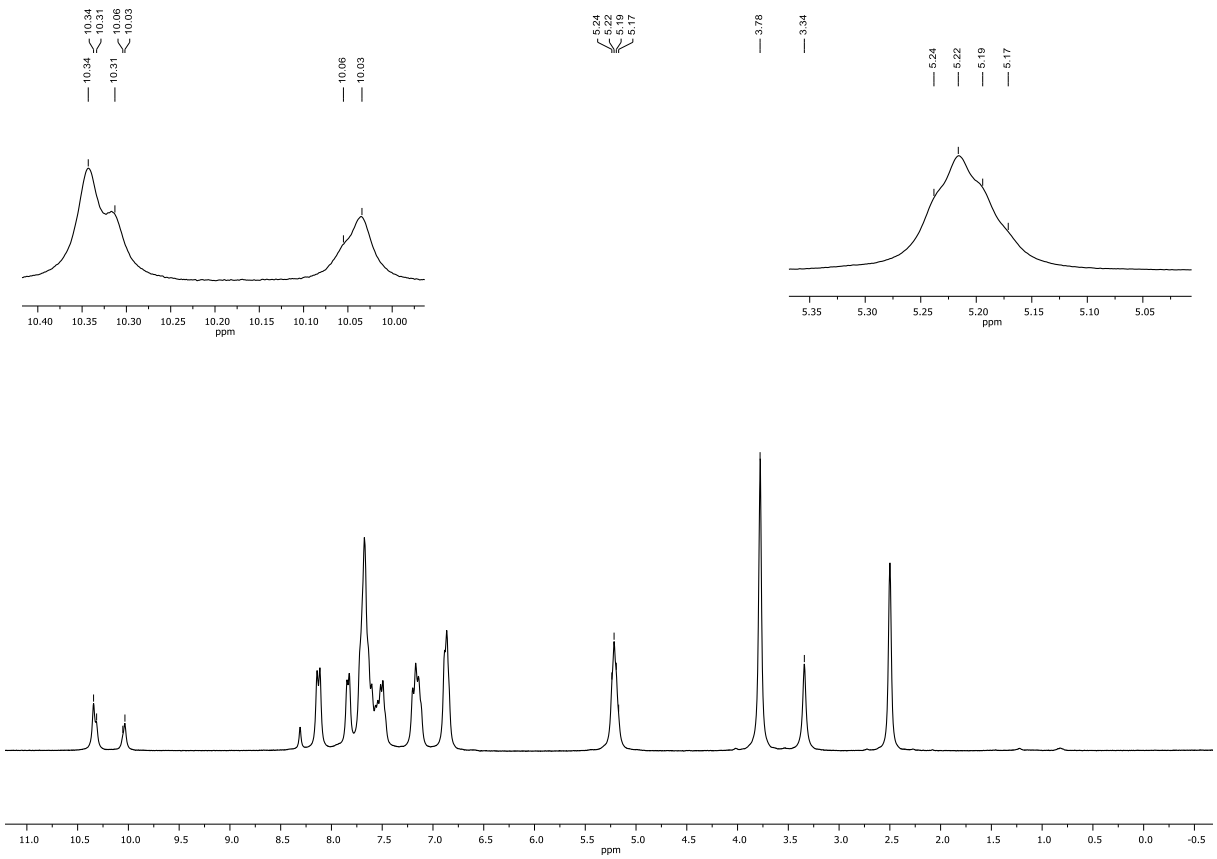
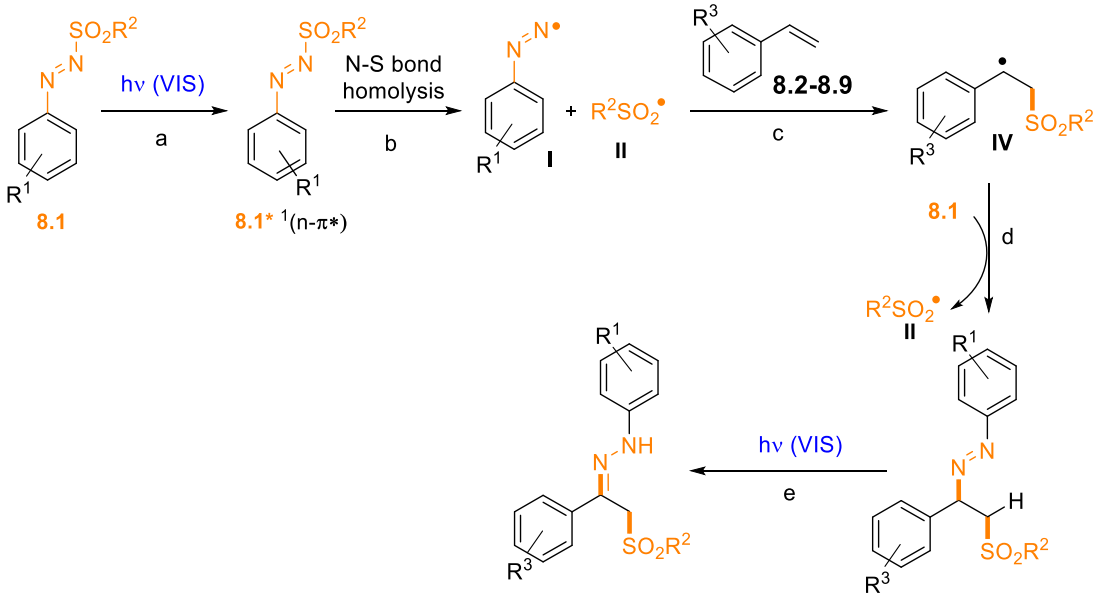


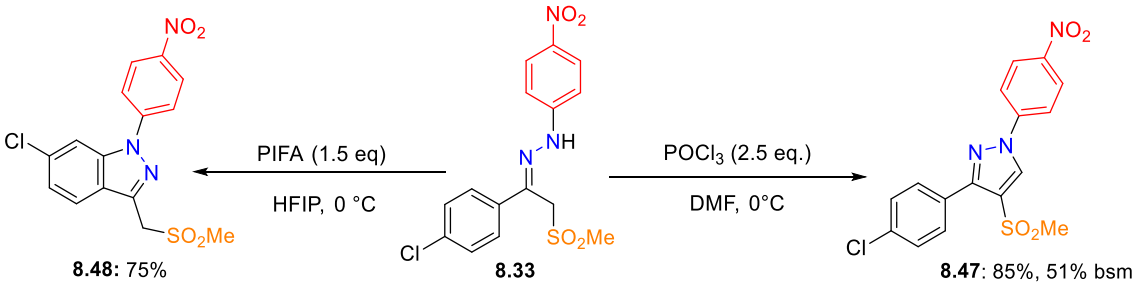
Figure 8.9. ^{1}H-NMR spectrum of the hydrazones obtained performing the cross experiment: a complex inseparable mixture of α-sulphonyl arylhydrazones is obtained.

Based on these results as well as literature precedents, [8.7,8.8,8.11-8.14] a plausible reaction mechanism is illustrated in Scheme 8.5. First, irradiation with visible light (λ = 456 nm) promotes the arylazo sulfones into ^{1}nπ*-state **8.1*** (step a) which undergoes a homolytic cleavage of the S–N bond to generate the diazenyl radical **I** and sulfonyl radical **II** (step b). In dry dichloromethane and acetonitrile, **II** is in turn trapped by non-α-substituted styrene **8.2-8.9** to form the benzylic radical species **IV** (step c) which thus react with electron-poor arylazo sulfones, to release a new sulfonyl radical **II** and α-sulfonyl aryldiazene (step d)**,** that in turn undergoes (photo)tautomerization to form the α-sulfonyl hydrazone (step e).



Scheme 8.5. Proposed mechanism for the formation of α-sulfonyl hydrazones.

Indeed, α-sulfonyl arylhydrazones **8.33** could also serve as key intermediates for the preparation of pharmaceutically important heterocycles (Scheme 8.6). For instance, the reaction of **8.33** with the Vilsmeier–Haack reagent readily afforded the valuable pyrazole **8.47** in a decent yield. [8.15] In addition, the arylhydrazone also afforded facile access to benzopyrazole **8.48** by PIFA-mediated oxidative cyclization of **8.33** in HFIP [8.16].



Scheme 8.6. Post transformations carried out starting from α-sulfonyl hydrazone **8.33**. PIFA = Phenyliodine bis(trifluoroacetate).

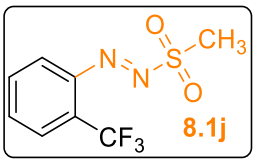
8.3. CONCLUSIONS.

In conclusion, we have developed two sets of conditions for the visible-light mediated difunctionalization of styrenes with readily available arylazo sulfones to afford α-sulfonyl arylhydrazones products, depending on the styrenes used. This protocol offers novel syntheses of α-sulfonyl arylhydrazones which are versatile building blocks for the synthesis of various heterocycles.

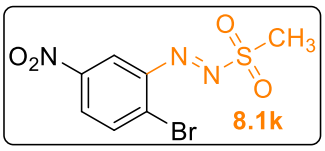
8.4. EXPERIMENTAL SECTION.

General Informations. All solvent employed in the present investigation have been distilled in the presence of the appropriate drying agent and stored over molecular sieves under argon. All reagents, including styrenes **8.2-8.9** are commercially available and used as received (unless otherwise noted). Analytical thin layer chromatography (TLC) plates (silica gel 60 F254) were visualized either with a UV lamp (254 nm), or by submersion in the chosen stain for TLC. Flash column chromatography was carried out by using 40-63 μm particle sized silica gel with air pressure. NMR experiments were carried out in the deuterated solvent of choice. Proton ^{1}H NMR spectra were recorded on a Bruker Avance 500 MHz or 300 MHz and proton-decoupled carbon $^{13}C\{^{1}H\}$ NMR spectra were recorded either at 126 MHz or 75 MHz. Proton-decoupled fluorine ^{19}F $\{^{1}H\}$ NMR spectra were recorded at 282 MHz. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent as the internal reference. The following abbreviations are used for the multiplicities: s: singlet; d: doublet; t: triplet; q: quadruplet; quint: quintuplet; m: multiplet or overlap of non-equivalent resonances; br s: broad singlet; app: apparent; rot: rotamer. Coupling constants (*J*) are reported in Hertz (Hz). High resolution mass spectra were determined on an AEI MS-9 using electrospray ionization (ESI) and a time-of-flight (TOF). Sodium *p*-bromobenzenesulfinate and sodium *p*-nitrobenzenesulfinate have been prepared according to a procedure reported in literature [8.17]. Photochemical reactions have been carried out in a EvoluChemTM PhotoRedox monobox equipped with a 456 nm Kessil lamp or an Evoluchem 450 nm blue LED lamp as the light source and a chiller running on ethanol or a fan system as the cooling system and placed on a stirrer plate (relative irradiance in the photoredox box: 28 mW cm^{-2}, see Figures 8.2,8.3).

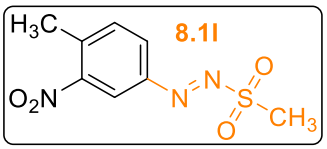
Synthesis of arylazo sulfones 8.1a-8.1r. Arylazo sulfones used for this work were already synthesized by our research group in previous works and have been brought to the host lab and used without further purifications. The synthesis of new compounds was performed following a known literature protocol [8.17].



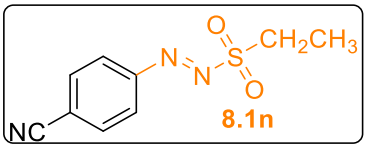
1-(Methylsulfonyl)-2-(2-(trifluoromethyl)phenyl)diazene (8.1j). From 2-(trifluoromethyl)aniline (10.0 mmol) and sodium methanesulfinate (11.0 mmol). Compound **8.1j** was isolated as a yellow crystalline solid (2.52 g, >99% yield). **(8.1j).** ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.94–7.88 (m, 2H), 7.83–7.71 (m, 2H), 3.19 (s, 3H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -57.5. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 134.9, 133.3, 127.5 (q, J = 275 Hz), 125.2, 121.5, 116.9, 34.4. m.p. (decomposition) = 101–106 °C (Hexane). Compound unstable in HRMS. IR (neat) ν (cm^{-1}): 1498, 1347, 1312, 1272, 1150, 1112, 1056, 1035, 955, 892, 771, 714.



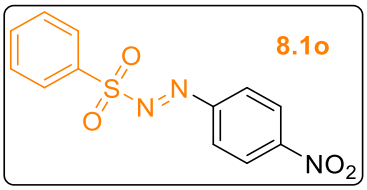
1-(2-Bromo-5-nitrophenyl)-2-(methylsulfonyl)diazene (8.1k). From 2-bromo-5-nitroaniline (10.0 mmol) and sodium methanesulfinate (11.0 mmol). Compound **8.1k** was isolated as a yellow crystalline solid (3.07 g, >99% yield). **(8.1k).**^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.67 (d, J = 2.4 Hz, 1H), 8.31 (dd, J = 8.9, 2.4 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 3.28 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 151.1, 149.6, 129.8, 127.8, 123.8, 119.4, 35.1.m.p. (decomposition) = 127–129 °C (Hexane). Compound unstable in HRMS.IR (neat) ν (cm^{-1}): 3095, 1526, 1342, 1303, 1159, 1116, 1040, 954, 903, 865, 839, 785, 745, 728, 678.



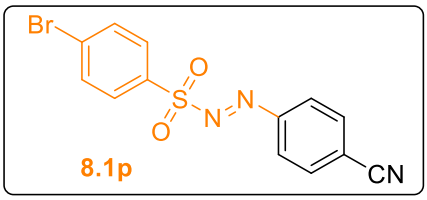
Methyl 2-(4-methyl-3-nitrophenyl)diazene-1-sulfonate (8.1l). From 4-methyl-3-nitroaniline (10.0 mmol) and sodium methanesulfinate (11.0 mmol). Compound **8.1l** was isolated as a yellow crystalline solid (2.60 g, >99% yield). **(8.1l).**^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.57 (d, J = 2.1 Hz, 1H), 8.08 (dd, J = 8.3, 2.1 Hz, 1H), 7.60 (d, J = 8.3 Hz, 1H), 3.26 (s, 3H), 2.74 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 147.6, 140.9, 134.4, 127.1, 121.7, 121.0, 35.2, 21.0. m.p. (decomposition) = 118–122 °C (Hexane). Compound unstable in HRMS. IR (neat) ν (cm^{-1}): 3082, 1612, 1529, 1495, 1339, 1164, 1071, 964, 932, 908, 836, 805, 773, 756.



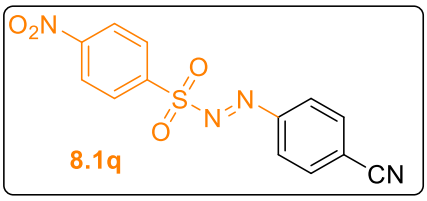
4-((Ethylsulfonyl)diazenyl)benzonitrile (8.1n). From 4-aminobenzonitrile (10.0 mmol) and sodium ethanesulfinate (11.0 mmol). Compound **8.1n** was isolated as a yellow crystalline solid (1.45 g, 65% yield). **(8.1n).** ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.13–7.98 (m, 2H), 7.95–7.81 (m, 2H), 3.52 (q, J = 7.4 Hz, 2H), 1.52 (t, J = 7.5 Hz, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 151.0, 133.7, 124.7, 117.4, 114.8, 43.2, 7.5. m.p. (decomposition) = 83–85 °C (Hexane). Compound unstable in HRMS. IR (neat) ν (cm^{-1}): 3213, 2238, 1458, 1377, 1205, 1176, 1111, 1068, 1023, 975, 954, 898, 874, 793, 770, 665.



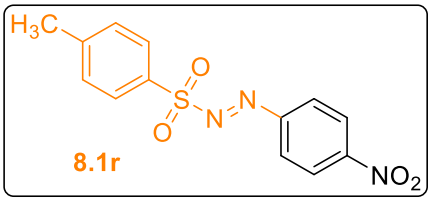
1-(4-Nitrophenyl)-2-(phenylsulfonyl)diazene (8.1o). From 4-nitroaniline (10.0 mmol) and sodium benzenesulfinate (11.0 mmol). Compound **8.1o** was isolated as a crystalline orange solid (2.91 g, >99% yield). **(8.1o).** ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.40–8.31 (m, 2H), 8.08–7.91 (m, 4H), 7.81–7.70 (m, 1H), 7.68–7.59 (m, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 135.4, 130.8, 129.6, 125.2, 125.1, 124,5, 118.0, 117,3. m.p. (decomposition) = 107–112 °C (Hexane). Compound unstable in HRMS. IR (neat) *v* (cm^{-1}): 3106, 1593, 1542, 1518, 1446, 1347, 1220, 1126, 1111, 1068, 1016, 996, 980, 865, 856, 753, 729, 691.



(1-(4-cyanophenyl)-2-(4-bromophenyl)diazene (8.1p). From 4-aminobenzonitrile (5.92 mmol) and sodium 4-Bromobenzene sulfinate (6.50 mmol). Compound **8.1p** was isolated as yellow solid (1.47 g, 91% yield). **(8.1p).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.6 Hz, 2H), 7.86 – 7.72 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.61 133.4, 132.7, 131.8, 131.1, 130.9, 124.7, 117.8, 117.2. m.p. (decomposition) = 133–133,6°C (Hexane) Compound unstable in HRMS. IR (neat) *v* (cm^{-1}): 3093, 2358, 2230, 1572, 1497,1469, 1407, 1390, 1360, 1308, 1281,1179, 1158, 1106, 1082, 1069,110, 882, 850,820, 783, 748, 701, 684.



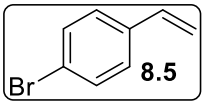
(1-(4-cyanophenyl)-2-(4-nitrophenyl)diazene (8.1q). From 4-aminobenzonitrile (5.92 mmol) and sodium 4-nitrobenzenesulfinate (6.50 mmol). Compound **8.1q** was isolated as yellow solid (1.23 g, 73% yield). **(8.1q).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58–8.42 (m, 2H), 8.27–8.14 (m, 2H), 7.96–7.84 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.6, 138.2, 133.5, 131.9, 124.8, 124.2, 118.3, 117.1.m.p.(decomposition) = 88–88,3°C (Hexane) Compound unstable in HRMS. IR (neat) *v* (cm^{-1}): 3107, 2230, 1608, 1548, 1497, 1464, 1405, 1357, 1312, 1292, 1176, 1149, 1108, 1083, 1010, 881, 854, 780, 750, 739, 689.



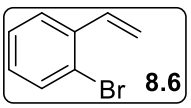
(1-(4-Nitrophenyl)-2-tosyldiazene (8.1r). From 4-nitroaniline (10.0 mmol) and sodium 4-methylbenzenesulfinate (11.0 mmol). Compound **8.1r** was isolated as a crystalline orange solid (2.29 g, 75% yield). **(8.1r).** ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 9.0 Hz, 2H), 7.96 (d, *J* = 9.0 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 2.50 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 152.2, 146.9, 130.8, 130.3, 125.2, 125.1, 124.9, 124.5, 22.0. m.p.

(decomposition) = 111–116 °C (Hexane). Compound unstable in HRMS. IR (neat) ν (cm^{-1}): 3107, 1593, 1545, 1292, 1220, 1189, 1169, 1127, 1010, 921, 854, 817, 751, 688.

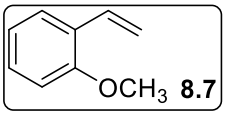
Synthesis of Styrenes 8.5-8.8. Styrenes **8.5-8.8** were synthesized by following a procedure described in literature [8.18]. To a solution of methyltriphenylphosphonium bromide (11.1 mmol, 1.1 equiv) in anhydrous THF (100 mL) was added n-Butyllithium (2.4 M in hexane, 4.8 mL, 1.1 equiv.) at 0°C under Ar. The resulting mixture was stirred for 10 min, then was allowed to warm to room temperature and maintained with stirring for 4h until the chosen aldehyde was added dropwise (1.0 M in THF, 10 mL). The solution was then stirred for 1h and quenched with NH_4Cl (10 mL). Subsequently, the mixture was poured into water and the aqueous phase was extracted with DCM (3×100 mL). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4. The dried solution was filtered, and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (eluant: cyclohexane: ethyl acetate mixture) to afford the desired product.



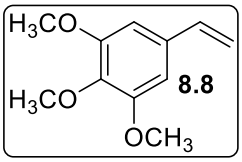
1-Bromo-4-vinylbenzene (8.5). From 4-bromobenzaldehyde (10.0 mmol), n-Butyllithium (2.4M in hexane, 4.8 mL, 1.1 equiv.) and methyltriphenylphosphonium bromide (11.1 mmol, 1.1 equiv). Purification by silica gel flash column chromatography (eluant PET/EA 99:1) afforded 1-Bromo-4-vinylbenzene **8.5** was isolated as a colourless oil (10.0 mmol, >99% yield). Spectroscopic data are in accordance with literature. [8.19] **(8.5).** ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.51 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 8.5 Hz, 2H), 6.71 (dd, J = 17.6, 10.9 Hz, 1H), 5.80 (dd, J = 17.5, 0.8 Hz, 1H), 5.35 (dd, J = 10.9, 0.9 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 136.5, 135.8, 131.7, 127.8, 121. 7, 114.6.



1-Bromo-2-vinylbenzene (8.6). From 2-bromobenzaldehyde (10.0 mmol), n-Butyllithium (2.4M in hexane, 4.8 mL, 1.1 equiv.) and methyltriphenylphosphonium bromide (11.1 mmol, 1.1 equiv). Purification by silica gel flash column chromatography (eluant PET/EA 99:1) afforded 1-Bromo-2-vinylbenzene **8.6** as a colourless oil (10 mmol, >99% yield). Spectroscopic data are in accordance with literature. [8.20] **(8.6).** ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.65 (ddd, J = 7.9, 4.2, 1.5 Hz, 2H), 7.35 (td, J = 7.6, 1.3 Hz, 1H), 7.29–7.07 (m, 2H), 5.81 (dd, J = 17.4, 1.2 Hz, 1H), 5.47 (dd, J = 11.0, 1.1 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 137.4, 135.8, 132.9, 129.1, 127.5, 126.8, 123.7, 116.7.



1-Methoxy-2-vinylbenzene (8.7). From 2-methoxybenzaldehyde (10.0 mmol), n-Butyllithium (2.4M in hexane, 4.8 mL) and methyltriphenylphosphonium bromide (11.1 mmol, 1.1 equiv). Purification by silica gel flash column chromatography (eluant PET/EA 99:1) afforded 1-Methoxy-2-vinylbenzene **8.7** as a colourless oil (10.0 mmol, >99% yield). Spectroscopic data are in accordance with literature. [8.21] **(8.7).** ^{1}H-NMR (300 MHz, $CDCl_3$**)** δ 7.48 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.26 (s, 1H), 7.06 (dd, *J* = 17.7, 11.1 Hz, 1H), 6.98–6.83 (m, 2H), 5.74 (dd, *J* = 17.7, 1.6 Hz, 1H), 5.27 (dd, *J* = 11.1, 1.6 Hz, 1H), 3.85 (s, 3H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 131.8, 129.0, 126.7, 120.8, 114.6, 111.0, 55.6.



1,2,3-Trimethoxy-5-vinylbenzene (8.8). From 3,4,5-trimethoxybenzaldehyde (10.0 mmol), n-Butyllithium (2.4M in hexane, 4.8 mL, 1.1 equiv.) and methyltriphenylphosphonium bromide (11.1 mmol, 1.1 equiv). Purification by silica gel flash column chromatography (eluant PET/EA 99:1) afforded 1,2,3-Trimethoxy-5-vinylbenzene **8.8** as a colourless oil (10.0 mmol, >99%). Spectroscopic data are in accordance with literature. [8.22] ^{1}H-NMR (300 MHz, $CDCl_3$**)** δ 6.53 – 6.41 (m, 3H), 5.52 (dd, *J* = 17.5, 0.9 Hz, 1H), 5.05 (dd, *J* = 10.8, 0.9 Hz, 1H), 3.70 (d, *J* = 5.2 Hz, 9H).^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 153.2, 138.0, 136.7, 133.2, 112.8, 103.3, 60.5, 55.8.

General procedure for the photochemical synthesis of α-sulfonyl arylhydrazones. In a flame-dried glass vessel equipped with a magnetic stirrer, the chosen arylazo sulfone **8.1a-8.1r** (0.4 mmol, 0.2 M, 2.0 equiv.) and the styrene **8.2-8.9** or 2-vinylpyridine (0.2 mmol, 0.1 M, 1.0 equiv) were dissolved in anhydrous dichloromethane or acetonitrile (2 mL). Argon was flushed into the so-formed solution and after three cycle of freeze pump, the rubber septum was parafilmed. The solution was then placed in a EvoluChem^{TM} reactor connected to a minichiller Huber based on ethanol that kept the vessel at 10 °C and finally the mixture was irradiated with a blue Kessil Lamp (λ_{em}=456 nm, 40 W) (see Figure 8.10). The irradiation was stopped after total consumption of the starting materials, monitored by TLC. Products **8.10-8.45** were isolated by precipitation with chloroform and petroleum ether or via silica gel flash column chromatography (eluant: petroleum ether: ethyl acetate mixture).

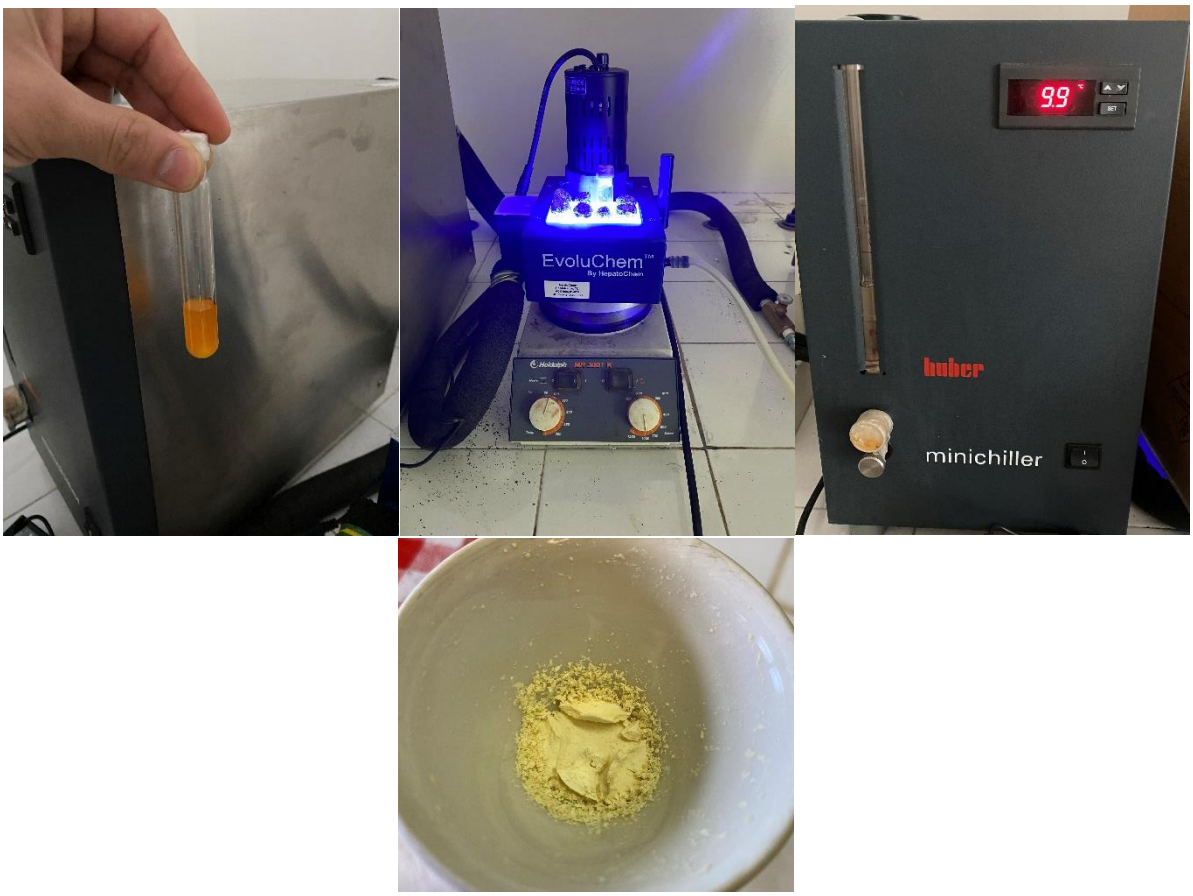


Figure 8.10. (From left to right) The solution containing the arylazo sulfone and the styrene equipped with a magnetic stirrer and with the rubber septum parafilmed. The solution irradiated in the EvoluChem^{TM} photoreactor with a blue Kessil Lamp (λ_{em}=456 nm, 40 W) connected to a minichiller Huber and the product precipitated after the total consumption of the starting materials.

General procedure for the photochemical isomerization α-sulfonylaryldiazo derivatives 8.14a, 8.15a, 8.18a and 8.28a into corresponding α-sulfonyl arylhydrazones. A solution of the selected α-sulfonylaryldiazo derivative (in a concentration between 0.06 - 0.1 M, 0.06 - 0.1 mmol) in $CDCl_3$ was placed in an NMR tube and placed in a EvoluChem^{TM} reactor equipped with a fan and cold air on the tube that kept the vessel at room temperature and was irradiated with a blue Evoluchem Lamp (λ_{em} = 450 nm, 10 W, 100% power) for prolonged time and checked at t = 0, 60, 120 and 240 minutes (see Figure 8.11). After the end of the reaction, the compound has been checked by ^{1}H-NMR and ^{13}C $\{^{1}H\}$-NMR analysis without the need of further purifications (see Figure 8.12).

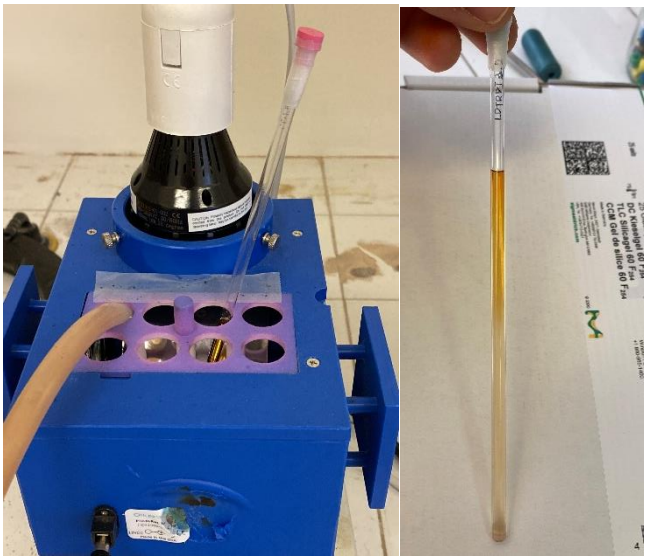
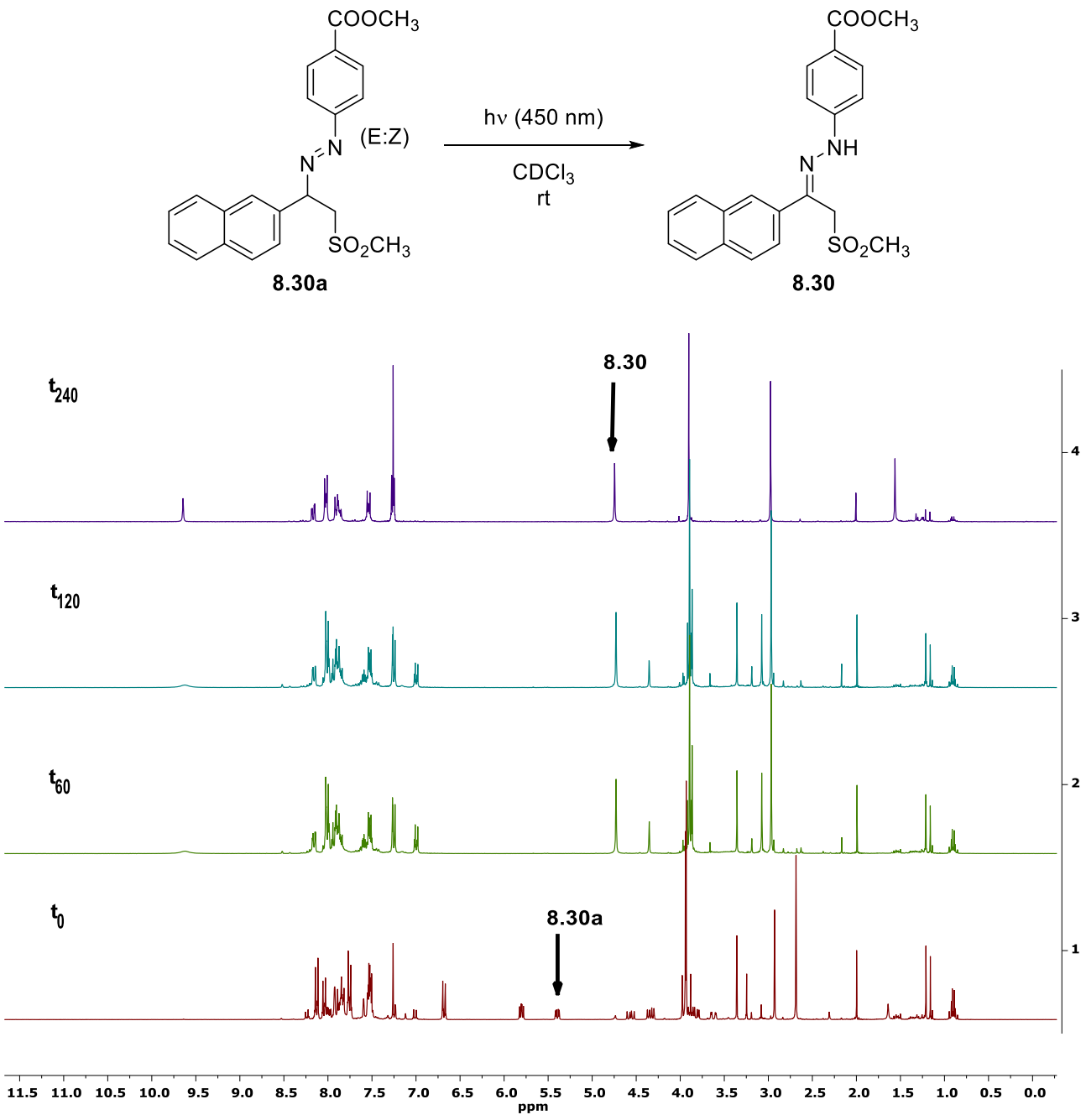


Figure 8.11. Set up employed for the photochemical isomerization of α-sulfonyl aryldiazo derivatives into α-sulfonyl arylhydrazones.


COOCH3
(E:Z)
N
N
SO2CH3
8.30a
hν (450 nm)
CDCl3
rt
COOCH3
NH
N
SO2CH3
8.30
t240
8.30
t120
t60
t0
8.30a
4
3
2
1
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

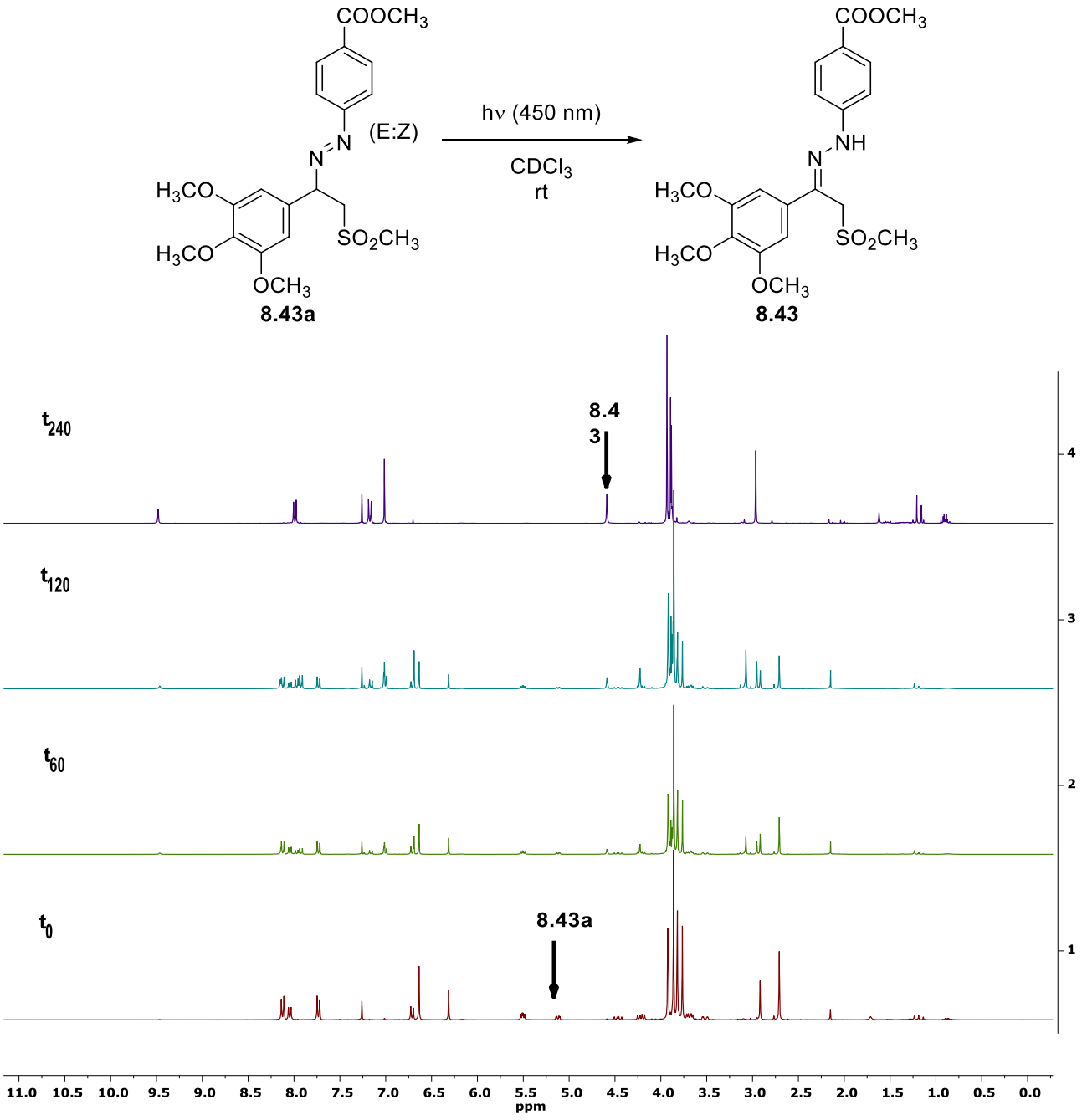


Figure 8.12. Kinetics of the photochemical isomerization α-sulfonyl aryldiazo into α-sulfonyl arylhydrazones at different time of irradiations and followed by ^{1}H-NMR analysis.

General procedure for the photochemical synthesis of α-sulfonyl arylhydrazones on 0.5 mmol scale. In a flame-dried glass vessel equipped with a magnetic stirrer the chosen arylazo sulfone **8.1a-8.1r** (1.0 mmol, 0.2 M, 2.0 equiv.) and styrenes **8.2-8.9** (0.5 mmol, 0.1 M, 1.0 equiv) were dissolved in predistilled and anhydrous dichloromethane (5 mL). Argon was flushed into the so-formed solution and after six cycles of freeze pump, the rubber septum was parafilmed. The solution was then placed

in a EvoluChem^{TM} reactor connected to a minichiller Huber based on ethanol that kept the vessel at 10 °C and finally the mixture was irradiated with a blue Kessil Lamp (λ_{em} =456 nm, 40 W) from 24 to 48 hours (see Figure 8.13). Products **8.10-8.45** were obtained by precipitation with chloroform and petroleum ether or via silica gel flash column chromatography (petroleum ether/ ethyl acetate from 7:3 to 1:1 ratio as the eluant).

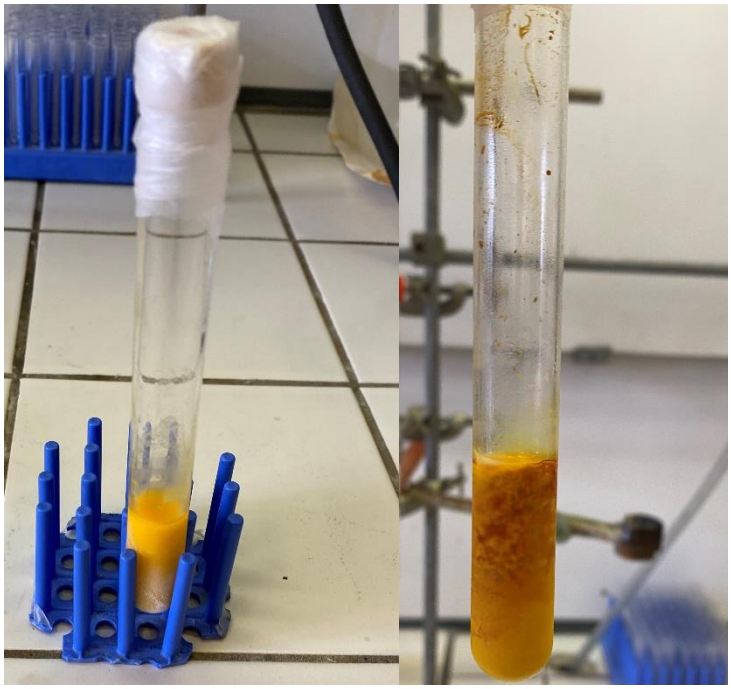
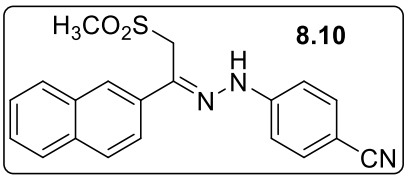


Figure 8.13. The solution containing the arylazo sulfone (1.0 mmol) and the styrene (0.5 mmol) after the six cycles of freeze pump before (left) and after the irradiation performed with a blue Kessil Lamp (λ_{em}=456 nm, 40 W) from 24 to 48 hours (right).

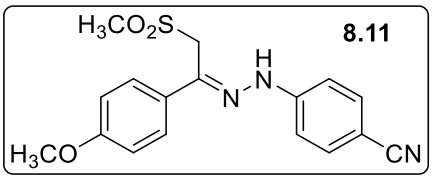
General procedure for the sunlight-driven synthesis of α-sulfonyl arylhydrazones. In a flame-dried glass vessel the chosen arylazo sulfone **8.1a-8.1r** (0.4 mmol, 0.2 M, 2.0 equiv.) and the styrene **8.2-8.9** or 2-vinylpyridine (0.2 mmol, 0.1 M, 1.0 equiv) were dissolved in predistilled and anhydrous dichloromethane (2 mL). Argon was flushed into the so-formed solution and after three cycles of freeze pump, the rubber septum was parafilmed. The solution was then placed outside under direct sunlight exposition with an aluminium foil beneath it (04/04/2023, ICSN, CNRS, Gif Sur Yvette, Paris, France, May, E: 436287.41 N: 5394673.77, 61 meters above the sea level). The temperature of the vessel was periodically checked and was always lower than 15 °C (see Figure 8.14). The irradiation was stopped after total consumption of the starting materials, monitored by TLC. Products **8.10-8.45** were obtained by precipitation with chloroform and petroleum ether or via silica gel flash column chromatography (petroleum ether/ ethyl acetate from 7:3 to 1:1 ratio as the eluant).

Figure 8.14. The vessel containing the arylazo sulfone and the styrene under direct sunlight exposition with an aluminium foil beneath it.

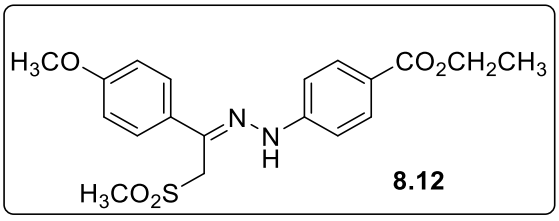
Irradiation of a mixture of 8.1a and 8.4 in the presence of TEMPO. In a flame-dried glass vessel equipped with a magnetic stirrer, arylazo sulfone **8.1a** (87.6 mg, 0.4 mmol, 2 equiv), TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv) and 4-chlorostyrene **8.4** (30 μL, 0.2 mmol) were dissolved in predistilled and anhydrous dichloromethane (2.0 mL). Argon was flushed into the so-formed solution and after six cycles of freeze pump, the rubber septum was parafilmed. The solution was then placed in a EvoluChem^{TM} reactor connected to a minichiller Huber based on ethanol that kept the vessel at 10 °C and finally the mixture was irradiated with a blue Kessil Lamp (λ_{em} =456 nm, 40 W) for 24 hours. The solvent was removed under vacuum and the resulting crude was analysed HPLC-MS.



4-(2-(2-(methylsulfonyl)-1-(naphthalen-2-yl)ethylidene)hydrazinyl)benzonitrile (8.10). Starting from 30.8 mg (0.2 mmol) of 2-vinylnaphthalene **8.2** and 87.6 mg of arylazo sulfone **8.1a** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 69.7 mg of product **8.10** (slightly pink solid, 96% yield). **(8.10).** ^{1}H-NMR (300 MHz, DMSO-*d*$_6$). δ 10.44 (s, 1H), 8.36 (d, *J* = 1.9 Hz, 1H), 8.22–8.19 (m, 1H), 7.97–7.90 (m, 3H), 7.75–7.70 (m, 2H), 7.57–7.52 (m, 2H), 7.44–7.40 (m, 2H), 5.15 (s, 2H), 3.11 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, DMSO-*d*$_6$). δ 148.3, 134.6, 133.7, 132.8, 128.4, 127.8, 127.5, 126.6, 126.5, 126.0, 123.6, 119.9, 113.4, 100.9, 50.3, 41.8. m.p. = 158–161 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: [M+H]$^{+}$ calcd for $C_{20}H_{18}N_3O_5S$ 364.1121, found 364.1122. IR (neat) *v* (cm^{-1}): 3329, 3053, 2217, 1736, 1704, 1602, 1583, 1563, 1505, 1471, 1443, 1410, 1338, 1291, 1272, 1245, 1165, 1150, 1141, 1129, 1067, 1045, 1019, 963, 927, 898, 857, 820, 783,748, 702, 666.

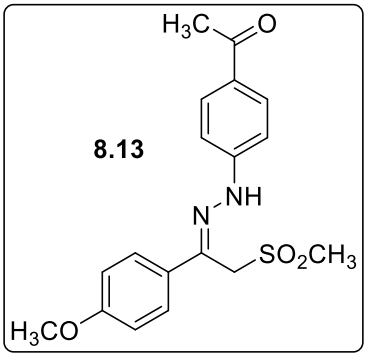


4-(2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzonitrile (8.11). Starting from 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 87.6 mg of arylazo sulfone **8.1a** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 43.1 mg of product **8.11** (white solid, 63% yield). **(8.11).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 9.48 (s, 1H), 7.78–7.71 (m, 2H), 7.61–7.53 (m, 2H), 7.21 (s, 2H), 7.01–6.95 (m, 2H), 4.59 (s, 2H), 3.86 (s, 3H), 2.94 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-*d*$_6$). δ 148.6, 133.8, 129.4, 129.0, 127.5, 119.9, 114.7, 114.1, 55.6, 53.8, 41.7. m.p. = 201–204 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: [M+H]$^{+}$ calcd for $C_{17}H_{18}N_3O_3S$ 344.1071, found 344.1068. IR (neat) *v* (cm^{-1}): 3337, 3012, 2219, 1602, 1584, 1560, 1528, 1509, 1465, 1432, 1342, 1313, 1301, 1291, 1271, 1252, 1206, 1184, 1162, 1142, 1128, 1107, 1041, 1018, 1004, 977, 967, 834, 808, 778, 755, 715, 702.

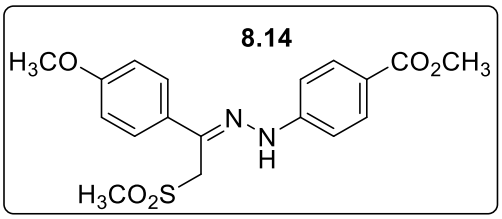


ethyl 4-(2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzoate (8.12). Starting from 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 101.6 mg of arylazo sulfone **8.1b** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 62.5 mg of product **8.12** (white solid, 80% yield). **(8.12).** ^{1}H-NMR (300 MHz, DMSO-*d*$_6$). δ 10.10 (s, 1H), 7.87 (dd, *J* = 8.9, 7.4 Hz, 4H), 7.31–7.22 (m, 2H), 6.98 (d, *J* = 8.7 Hz, 2H), 4.98 (s, 2H), 4.30–4.22 (q, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 3.07 (s, 3H), 1.29 (d, *J* = 7.0 Hz, 3H).^{13}C{^{1}H}-NMR

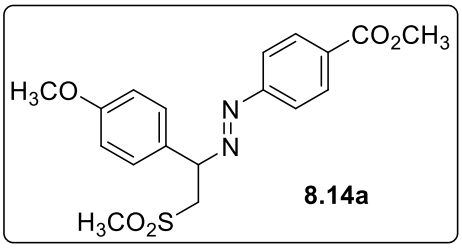
(75 MHz, DMSO-d_6). δ 165.6, 159.6,148.9, 133.1, 130.9, 129.9, 127.6, 120.4, 113.7, 112.3, 60.0, 55.2, 50.4, 41.8, 14.3. m.p. = 144–147 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{23}N_2O_5S$ 391.1329, found 391.1328. IR (neat) ν (cm^{-1}): 3317, 2981, 1705, 1605, 1511, 1303, 1261, 1165, 1125, 1109, 1102, 1060, 1016, 967, 900, 873, 844, 837, 770, 699.



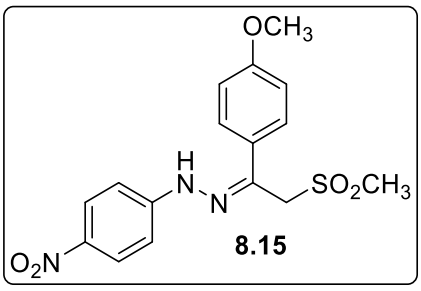
1-(4-(2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazineyl)phenyl)ethan-1-one (8.13). Starting from 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 90.4 mg of arylazo sulfone **8.1c** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 72.0 mg of product **8.13** (slightly pink solid, 99% yield). **(8.13).** ^{1}H-NMR (300 MHz, DMSO-d_6). δ 10.12 (s, 1H), 7.90–7.83 (m, 4H), 7.26 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 4.97 (s, 2H), 3.78 (s, 3H), 3.06 (s, 3H), 2.47 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 195.7, 159.6, 148.9, 133.3, 130.3, 129.9, 128.6, 127.6, 113.7, 112.1, 55.2, 50.4, 41.8, 26.2. m.p. = 75–78 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{21}N_2O_4S$ 361.1224, found 361.1225. IR (neat) ν (cm^{-1}): 3286, 3002, 1662, 1594, 1509, 1417, 1357, 1301, 1248, 1169, 1147, 1122, 1108, 1073, 1024, 1003, 956, 896, 832, 776, 743, 724, 697, 663.



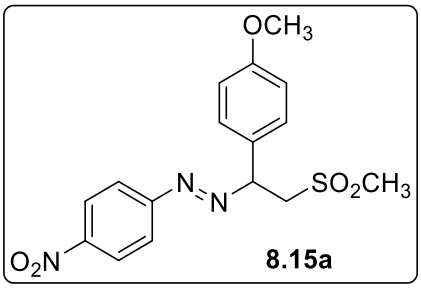
methyl 4-(2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzoate (8.14). Starting from 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 96.8 mg of arylazo sulfone **8.1d** (0.4 mmol, 2.0 equiv). The mixture was irradiated for 48 hours affording 74.2 mg of **8.14** (99% yield). **(8.14).** ^{1}H-NMR (300 MHz, DMSO-d_6). δ 10.10 (s, 1H), 7.90–7.84 (m, 4H), 7.37–7.19 (m, 2H), 7.07–6.90 (m, 2H), 4.98 (s, 2H), 3.80 (s, 6H), 3.07 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 166.1, 159.6, 149.0, 133.2, 131.0, 129.9, 127.6, 120.1, 113.7, 112.3, 55.2, 51.5, 50.5, 41.8. m.p. = 172–174 °C (Petroleum Ether) HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{19}N_2O_5S$ 377.1173, found 377.1172. IR (neat) ν (cm^{-1}): 3304, 3004, 2952, 1706, 1610, 1562, 1511, 1435, 1341, 1303, 1280, 1265, 1256, 1157, 1113, 1049, 1027, 1004, 967, 915, 838, 822, 770, 699.



methyl 4-((1-(4-methoxyphenyl)-2-(methylsulfonyl)ethyl)diazenyl)benzoate (8.14a). Starting from 30 µL (0.2 mmol) of 4-vinylanisole **8.3** and 96.8 mg of arylazo sulfone **8.1d** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 57.2 mg of product **8.14a** (yellow solid/liquid, 76% yield). Irradiation of **8.14a** (0.08 mmol) in $CDCl_3$ (1 mL) for 24 h at 450 nm and evaporation under vacuo of the photolyzed solution afforded 58.1 mg of **8.14** (yellow solid, 100% conversion yield). **(8.14a).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 8.12 (d, *J* = 8.7 Hz, 2H), 7.77–7.64 (m, 2H), 7.42–7.31 (m, 2H), 6.93 (s, 2H), 5.60 (dd, *J* = 7.4, 5.9 Hz, 1H), 4.20 (dd, *J* = 14.9, 7.3, 1H), 3.94 (s, 3H), 3.81 (s, 3H), 3.70 (dd, *J* = 14.9, 7.3, 1H), 2.65 (d, *J* = 0.8 Hz, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 165.4, 153.7, 152.9, 132.1, 130.4, 129.1, 128.4, 122.2, 114.5, 58.5, 55.1, 52.1, 42.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{21}N_2O_5S$ 377.1173, found 437.1374. IR (neat) *v* (cm^{-1}): 3245, 2922, 2952, 1715, 1705, 1605, 1435, 13030, 1262, 1100, 1045, 1028, 1008, 924, 916, 801, 771, 700.

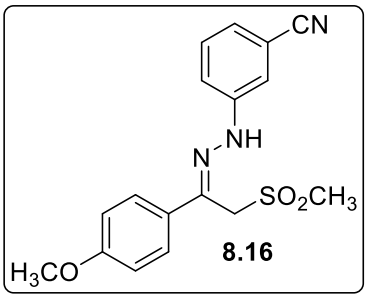


(1-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)-2-(4-nitrophenyl)hydrazine) (8.15). From 75 µL (0.5 mmol) of 4-vinylanisole **8.3** and 229.0 mg of arylazo sulfone **8.1e** (1.0 mmol, 2.0 equiv). The mixture was irradiated for 48 hours affording 181.2 mg of **8.15** (99% yield). **(8.15).** ^{1}H-NMR (300 MHz, DMSO-*d*$_6$). δ 10.48 (s, 1H), 8.18 (d, *J*=8.9 Hz, 2H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 2H), 5.02 (s, 2H), 3.81 (s, 3H), 3.07 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, DMSO-*d*$_6$). δ 160.0, 150.5, 139.2, 135.5, 129.5, 128.0, 126.0, 113.8, 112.3, 55.3, 50.5, 41.8. m.p. = 153–157 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{18}N_3O_5S$ 364.0969, found 364.0973. IR (neat) *v* (cm^{-1}): 3299, 3012, 1675, 1584, 1514, 1480, 1423, 1378, 1310, 1270, 1210, 1151, 1123, 1102, 1095, 1055, 1021, 1011, 986, 974, 899, 874, 823, 796, 767, 754, 720, 690, 673.

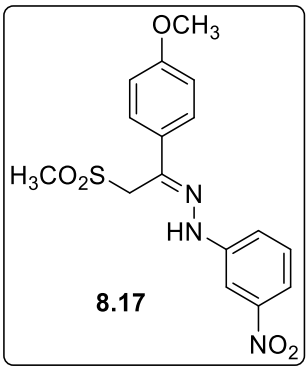


1-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethyl)-2-(4-nitrophenyl)diazene (8.15a). From 30 µL (0.2 mmol) of 4-vinylanisole **8.3** and 91.6 mg of arylazo sulfone **8.1e** (0.4 mmol, 2.0 equiv) The mixture was irradiated for 24 h. Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 58.1 mg of product **8.15a** (red solid, 80% yield).

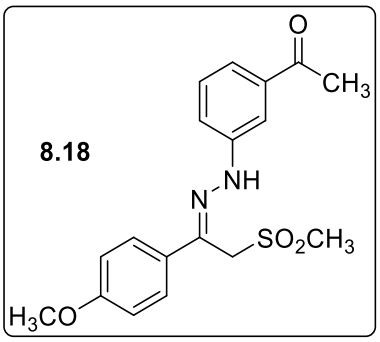
Irradiation of compound **8.15a** (0.08 mmol) in $CDCl_3$ (1 mL) and evaporation under vacuo of the photolyzed solution afforded 58.1 mg of **8.15** (yellow solid, 100% conversion yield). **(8.15a).** ^{1}H-NMR (500 MHz, $CDCl_3$). δ 8.24 (d, *J* = 8.9 Hz, 2H), 7.74 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.55 (dd, *J* = 7.5, 5.8 Hz, 1H), 4.11 (dd, *J* = 14.7, 7.5 Hz, 1H), 3.74 (s, 3H), 3.65 (dd, *J* = 14.7, 7.5 Hz, 1H), 2.62 (s, 3H).^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$). δ 160.0, 154.5, 148.9, 129.2, 127.9, 124.6, 123.2, 114.7, 75.7, 58.4, 55.2, 42.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{18}N_3O_5S$ 364.0969, found 364.0969. IR (neat) *v* (cm^{-1}): 1716, 1594, 1502, 1462, 1324, 1305, 1272, 1258, 1184, 1148, 1109, 1073, 1046, 1022, 993, 924, 845, 810, 749, 715.



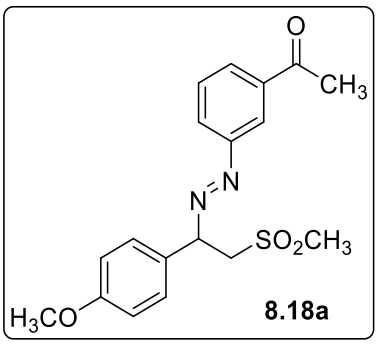
3-(2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazineyl)benzonitrile (8.16). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 87.6 mg of arylazo sulfone **8.1f** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 78.6 mg of product **8.16** (pale yellow solid, 99% yield). **(8.16).** ^{1}H-NMR (300 MHz, DMSO-*d*$_6$). δ 9.99 (s, 1H), 7.87 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 2.2 Hz, 1H), 7.48–7.45 (m, 2H), 7.25–7.21 (m, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 4.94 (s, 2H), 3.79 (s, 3H), 3.06 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-*d*$_6$). δ 159.6, 145.8, 132.8, 130.5, 129.8, 127.6, 122.9, 119.1, 117.6, 115.3, 113.7, 112.0, 55.2, 50.5, 41.8. m.p. = 197–200 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}N_3O_3S$ 344.1071, found 344.1075. IR (neat) *v* (cm^{-1}): 3313, 2930, 228, 1604, 1585, 1511, 1488, 1478, 1439, 1330, 1302, 1257, 1175, 1156, 1127, 1016, 1005, 966, 904, 871, 836, 783, 760, 737, 683.



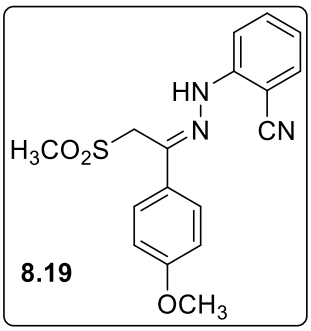
1-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)-2-(3-nitrophenyl)hydrazine (8.17). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 91.6 mg of arylazo sulfone **8.1g** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 65.3 mg of product **8.17** (white solid, 90% yield). **(8.17).** ^{1}H-NMR (300 MHz, DMSO-*d*$_6$). δ 10.18 (s, 1H), 7.98 (d, *J* = 2.3 Hz, 1H), 7.86 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.58–7.49 (m, 1H), 6.99 (d, *J* = 8.6 Hz, 2H), 4.95 (s, 2H), 3.80 (s, 3H), 3.06 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-*d*$_6$). δ 159.6, 148.7, 146.3, 133.1, 130.5, 129.8, 127.6, 118.9, 113.8, 113.7, 106.8, 55.2, 50.5, 41.8. m.p. = 200–203 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{18}N_3O_5S$ 364.0969, found 364.0965. IR (neat) *v* (cm^{-1}): 3327, 1617, 1607, 1564, 1530, 1438, 1347, 1302, 1252, 1181, 1140, 1128, 1078, 1015, 1004, 967, 942, 903, 872, 835, 812, 793, 779, 735, 672.



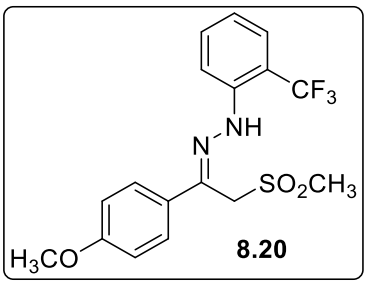
1-(3-(2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)phenyl)ethan-1-one (8.18). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 90.4 mg of arylazo sulfone **8.1h** (0.4 mmol, 2.0 equiv), irradiated for 24 hours. Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 63.7 mg of product **8.18** (yellow solid, 87% yield). **(8.18).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.91 (s, 1H), 7.95–7.77 (m, 2H), 7.76–7.64 (m, 1H), 7.55–7.38 (m, 3H), 7.06–6.88 (m, 2H), 4.94 (s, 2H), 3.80 (s, 3H), 3.07 (s, 3H), 2.58 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 197.9, 159.34 145.5, 137.7, 131.4, 130.1, 129.6, 127.3, 119.9, 117.3, 113.7, 111.9, 55.2, 50.4, 41.7, 26.8. m.p. = 194–196 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{20}N_2O_4S$ 360.1144, found 360.1148. IR (neat) ν (cm^{-1}): 3345, 2990, 1670, 1505, 1489, 1444, 1420, 1357, 1301,1245, 1210, 1190, 1154, 1126, 1100, 1098, 1046, 1007, 995, 976, 945, 900, 889, 850, 803, 790, 754, 702, 665.



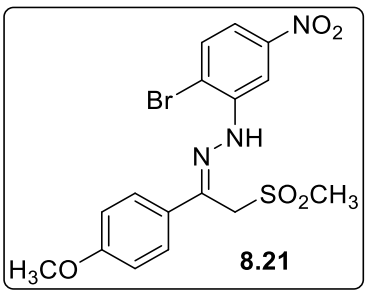
1-(3-((1-(4-methoxyphenyl)-2-(methylsulfonyl)ethyl)diazenyl)phenyl)ethan-1-one (8.18a). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 90.4 mg of arylazo sulfone **8.1h** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 64.1 mg of product **8.18a** (yellow solid/liquid, 89% yield) as a mixture of isomers that decomposed rapidly when stored in freezer and under argon. Irradiation of **8.18a**(0.09 mmol) in $CDCl_3$ (1 mL) and evaporation under vacuo of the photolyzed solution afforded 64.1 mg of **8.18** (yellow solid, 100% conversion yield) without further purifications. **(8.18a).** major isomer (E) ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.31 (s, 1H), 8.13 (t, J = 1.6 Hz, 2H), 7.93–7.84 (m, 2H), 7.71–7.62 (m, 2H), 7.44 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 5.43 (dd, J = 8.8, 4.4 Hz, 1H), 4.49–4.35 (m, 1H), 3.99 (dd, J = 14.4, 4.6 Hz, 1H), 3.74 (s, 3H), 2.93 (s, 3H), 2.62 (s, 3H). **(8.18a).** Minor isomer (Z) ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.31 (s, 1H), 8.12–8.06 (m, 1H), 7.66 (d, J = 3.2 Hz, 1H), 7.20 (d, J = 1.9 Hz, 1H), 7.13 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 5.17 (dd, J=8.8, 3.8 Hz, 1H), 4.64–4.50 (m, 1H), 3.89 (dd, J=14.5, 3.8 Hz, 1H), 3.74 (s, 3H), 2.91 (s, 3H), 2.54 (s, 3H).



2-(2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzonitrile (8.19). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 87.6 mg of arylazo sulfone **8.1i** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 38.4 mg of product **8.19** (white solid, 56% yield). **(8.19).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 9.60 (s, 1H), 7.86–7.77 (m, 2H), 7.59–7.48 (m, 3H), 7.06–6.91 (m, 3H), 4.63 (s, 2H), 3.86 (s, 3H), 3.05 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 161.0, 147.9, 136.5, 134.1, 133.0, 129.3, 127.7, 120.8, 117.1, 114.9, 114.5, 55.6, 53.6, 42.2. m.p. = 188–191 °C (Petroleum Ether) HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}N_3O_3S$ 344.1071, found 344.1073. IR (neat) ν (cm^{-1}): 3287, 2216, 1703, 1604, 1586, 1510, 1464, 1423, 1305, 1251, 1181, 1147, 1128, 1090, 1066, 1034, 1014, 1003, 967, 915, 837, 779, 756, 729.

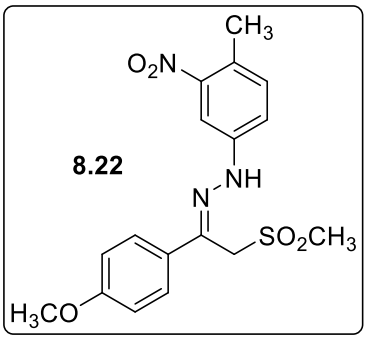


1-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)-2-(2-(trifluoromethyl)phenyl)hydrazine (8.20). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 100.8 mg of arylazo sulfone **8.1j** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 55.6 mg of product **8.20** (white solid, 72% yield). **(8.20).** ^{1}H-NMR (300 MHz, DMSO-d_6). δ 9.41 (s, 1H), 7.91 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 8.5 Hz, 1H), 7.63–7.57 (m, 2H), 7.07–6.99 (m, 3H), 4.94 (s, 2H), 3.81 (s, 3H), 3.25 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 160.1, 142.6, 138.0, 133.7, 129.5, 127.9 (q, J = 240 Hz), 126.2 (d, J = 5 Hz), 119.9, 115.5, 113.9, 55.3, 51.8, 41.7. ^{19}F NMR (282 MHz, DMSO-d_6) δ -59.6. m.p. = 127–130 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}F_3N_2O_3S$ 387.0992, found 364.0992. IR (neat) ν (cm^{-1}): 3330, 2930, 1608, 1595, 1512, 1474, 1421, 1320, 1306, 1255, 1180, 1141, 1123, 1058, 1032, 1014, 1003, 967, 836, 815, 780, 761, 727.

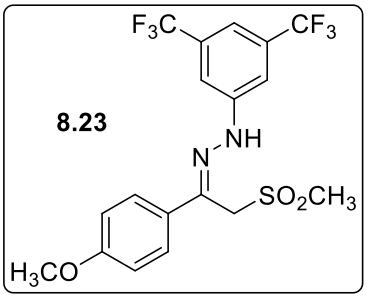


1-(2-bromo-5-nitrophenyl)-2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazine (8.21). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 122.4 mg of arylazo sulfone **8.1k** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 66.1 mg of product **8.21** (yellow solid, 75% yield). **(8.21).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.84 (s, 1H), 8.42 (s, 1H), 8.23 (d, J = 9.3 Hz, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 9.3 Hz,

1H), 7.03 (d, *J* = 8.4 Hz, 2H), 5.12 (s, 2H), 3.83 (s, 3H), 3.32 (s, 3H). $^{13}C\{^{1}H\}$-NMR (75 MHz, DMSO-d_6). δ 160.7, 147.3, 141.2, 139.8, 128.9, 128.5, 128.3, 125.0, 114.0, 113.6, 105.8, 55.3, 51.8, 41.89. m.p. = 267–270 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{17}{}^{79}BrN_3O_5S$ 442.0074, found 442.0067 HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{17}{}^{81}BrN_3O_5S$ 444.0054, found 442.0050 IR (neat) *v* (cm^{-1}): 3407, 2925, 1605, 1583, 1497, 1457, 1423, 1327, 1299, 1252, 1180, 1142, 1106, 1051, 1026, 1010, 1002, 967, 923, 890, 835, 778, 743, 705.

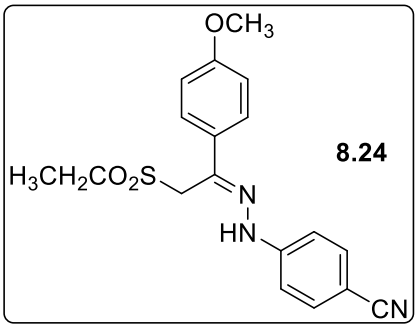


1-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)-2-(4-methyl-3-nitrophenyl)hydrazine (8.22). From 30 µL (0.2 mmol) of 4-vinylanisole **8.3** and 97.2 mg of arylazo sulfone **8.1l** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 41.5 mg of product **8.22** (yellow solid, 55% yield). **(8.22).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.03 (s, 1H), 7.87–7.80 (m, 2H), 7.77 (d, *J* = 2.3 Hz, 1H), 7.48–7.45 (m, 1H), 7.39–7.36 (m, 1H), 7.01–6.95 (m, 2H), 4.93 (s, 2H), 3.80 (s, 3H), 3.05 (s, 3H), 2.43 (s, 3H). $^{13}C\{^{1}H\}$-NMR (75 MHz, DMSO-d_6). δ 159.5, 149.3, 144.2, 133.5, 132.4, 129.9, 127.5, 122.8, 117.6, 113.7, 107.9, 55.2, 50.5, 41.8, 18.9. m.p. = 210–216 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{20}N_3O_5S$ 378.1125, found 378.1123. IR (neat) *v* (cm^{-1}): 3290, 1601, 1535, 1470, 1434, 1417, 1317, 1201, 1167, 1135, 1125, 1067, 1043, 1017, 1007, 981, 935, 909, 866, 797, 766, 717.

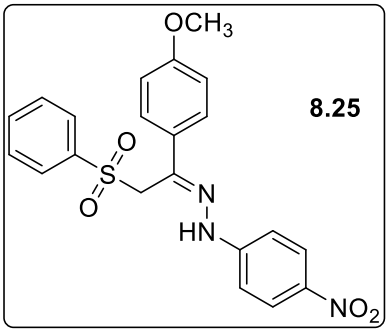


1-(3,5-bis(trifluoromethyl)phenyl)-2-(1-(4-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazine (8.23) From 30 µL (0.2 mmol) of 4-vinylanisole **8.3** and 128.0 mg of arylazo sulfone **8.1m** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 89.9 mg of product **8.23** (white solid, 99% yield). The same reaction was performed in large scale, employing 75 µL (0.5 mmol) of 4-vinylanisole **8.3** and 320.0 mg of arylazo sulfone **8.1m** (1.0 mmol, 2.0 equiv) the mixture was irradiated for 48 hours affording 224.8 mg of **8.23** (99% yield). **(8.23).** ^{1}H-NMR (300 MHz, DMSO-d_6). δ 10.36 (s, 1H), 7.92–7.81 (m, 2H), 7.73 (d, *J* = 1.5 Hz, 2H), 7.41 (s, 1H), 7.05–6.93 (m, 2H), 4.95 (s, 2H), 3.80 (s, 3H), 3.05 (s, 3H). $^{13}C\{^{1}H\}$-NMR (75 MHz, DMSO-d_6). δ 159.9, 146.6, 131.2 (q, *J* = 33 Hz), 129.4, 127.8, 123.5 (q, *J* = 273 Hz), 113.8, 112.3, 111.5 (m), 55.2, 50.6, 41.9. $^{19}F\{^{1}H\}$ NMR (282 MHz, DMSO-d_6) δ -61.81. m.p. = 134–137 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{17}F_6N_2O_3S$ 455.0866, found 455.0864. IR (neat) *v* (cm^{-1}): 3326, 2216, 1616, 1606, 1585, 1513, 1440, 1428, 1415, 1385, 1308,

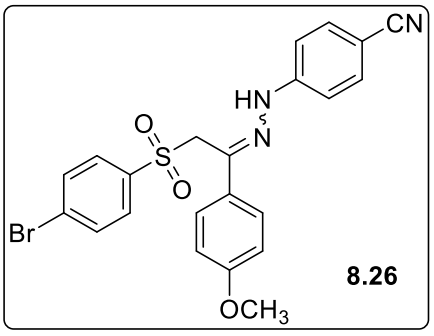
1297, 1277, 1247, 1160, 1120, 1088, 1038, 1017, 1006, 10963, 909, 870, 836, 780, 755, 722, 698, 682, 661.



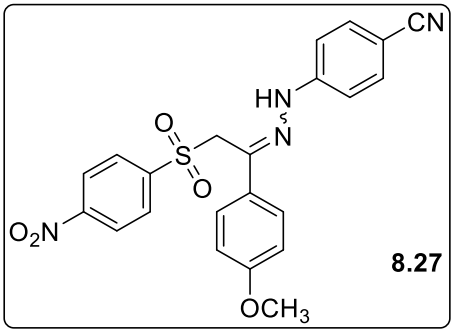
4-(2-(2-(ethylsulfonyl)-1-(4-methoxyphenyl)ethylidene)hydrazinyl)benzonitrile. (8.24). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 89.4 mg of arylazo sulfone **8.1n** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 57.2 mg of product **8.24** (white solid, 80% yield). **(8.24).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.16 (s, 1H), 7.85 (d, J = 8.9 Hz, 2H), 7.67 (d, J = 8.5 Hz, 3H), 7.41–7.26 (m, 2H), 7.07–6.94 (m, 2H), 4.95 (s, 2H), 3.80 (s, 3H), 3.18 (q, J = 7.4 Hz, 2H), 1.25 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 159.7, 148.5, 133.9, 133.6, 129.8, 127.7, 119.9, 113.7, 113.1, 100.4, 55.2, 48.8, 47.9, 5.6. m.p. = 122–125 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: [M+H]$^{+}$ calcd for $C_{18}H_{20}N_3O_3S$ 358.1227 found 358.1226. IR (neat) v (cm^{-1}): 3298, 3067, 2220, 1716, 1605, 1511, 1259, 1114, 1105, 1028, 994, 981, 814, 804, 715, 656.



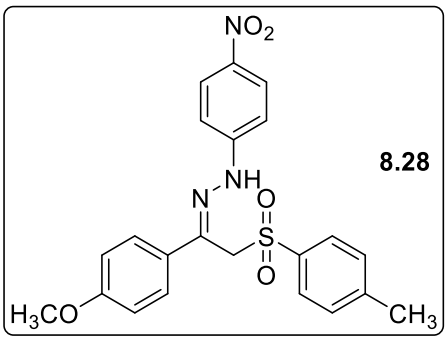
1-(1-(4-methoxyphenyl)-2-(phenylsulfonyl)ethylidene)-2-(4-nitrophenyl)hydrazine (8.25). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 116.4 mg of arylazo sulfone **8.1o** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 67.2 mg of product **8.25** (orange solid, 79% yield). **(8.25).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.34 (s, 1H), 8.12 (d, J = 9.0 Hz, 2H), 7.90–7.79 (m, 2H), 7.71 (d, J = 8.6 Hz, 2H), 7.57–7.47 (m, 3H), 7.18 (d, J = 9.0 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.22 (s, 2H), 3.78 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 159.7, 150.2, 139.0, 135.3, 134.0, 129.2, 128.9, 128.2, 127.9, 125.8, 113.6, 112.1, 55.2, 52.1. m.p. = 127–129 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: [M+H]$^{+}$ calcd for $C_{21}H_{20}N_3O_5S$ 426.1125, found 426.1129. IR (neat) v (cm^{-1}): 3332, 3063, 1592, 1498, 1480, 1312, 1295, 1272, 1249, 1220, 1187, 1150, 1104, 1012, 842, 833, 752.



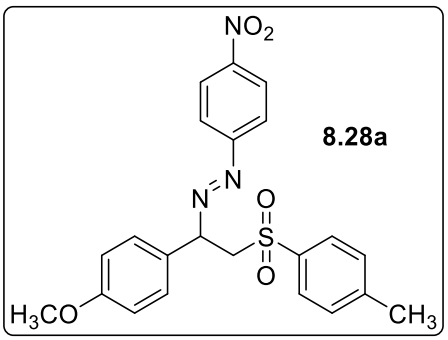
4-(2-(2-((4-bromophenyl)sulfonyl)-1-(4-methoxyphenyl)ethylidene)hydrazineyl)benzonitrile (8.26). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 139.6 mg of arylazo sulfone **8.1p** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent Toluene/EA 95:5) afforded 77.3 mg of product **8.26** (yellow solid, 80% yellow solid). Spectra of the *E* and *Z* isomers mixture **(8.26).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.86 (s, 1H), 7.76–7.69 (m, 4H), 7.49 (d, J = 8.8 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.9, 2H), 4.67 (s, 2H), 3.81 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 159.8, 159.4, 148.5, 148.1, 148.1, 138.1, 138.0, 136.9, 133.5, 133.4, 133.0, 132.2, 132.1, 131.9, 131.8, 130.2, 129.8, 129.3, 128.4, 127.8, 127.7, 124.7, 119.9, 114.3, 113.5, 113.0, 112.7, 100.3, 100.2, 100.1, 63.4, 57.9, 55.2, 55.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{19}{}^{79}BrN_3O_3S$ 484.0332, found 484.0335. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{19}{}^{81}BrN_3O_3S$ 486.0312, found 486.0310. IR (neat) ν (cm^{-1}): 3403, 3082, 2952, 2220, 1606, 1574, 1510, 1473, 1390, 1359, 1252, 1172,1068, 1010, 975, 900, 848, 834, 786, 767, 708, 658.



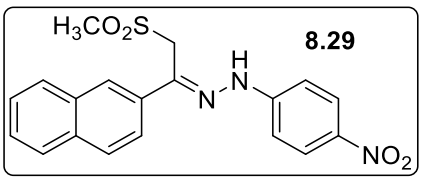
4-(2-(1-(4-methoxyphenyl)-2-((4-nitrophenyl)sulfonyl)ethylidene)hydrazineyl)benzonitrile (8.27). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 126.4 mg of arylazo sulfone **8.1q** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent Toluene/EA 95:5) afforded 88.9 mg of product **8.27** (yellow solid, 99% yield). Spectra of the *E* and *Z* isomers mixture **(8.27).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.07 (s, 1H), 9.88 (s, 1H), 8.32 (d, J = 8.9 Hz, 2H), 8.27–8.21 (m, 2H), 8.07–8.01 (m, 2H), 7.71–7.65 (m, 2H), 7.61–7.55 (m, 2H), 7.45 (d, J=8.8 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 7.12–7.06 (m, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.88–6.84 (m, 2H), 5.31 (s, 2H), 4.80 (s, 2H), 3.79 (s, 3H), 3.75 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 159.8, 159.6, 150.6, 150.2, 148.6, 148.5, 148.0, 147.4, 144.1, 136.2, 133.5, 132.9, 130.7, 130.0, 129.9, 129.2, 127.8, 124.1, 124.0, 119.8, 114.3, 113.6, 112.9, 112.7, 100.3, 97.2, 63.2, 55.2, 55.1, 52.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{19}N_4O_5S$ 451.1078, found 451.1073. IR (neat) ν (cm^{-1}): 3102, 2955, 2934, 2216, 1603, 1529, 1509, 1348, 1330, 1306, 1252, 1152, 1143, 1082, 1025, 1008, 921, 853, 837, 744, 683.



1-(1-(4-methoxyphenyl)-2-tosylethylidene)-2-(4-nitrophenyl)hydrazine (8.28). From 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 122.0 mg of arylazo sulfone **8.1r** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent Toluene/EA 95:5) afforded 88.9 mg of product **8.28** (yellow solid, 99% yield). **(8.28).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.12 (d, J = 9.3 Hz, 2H), 7.77–7.63 (m, 4H), 7.26 (d, J = 8.0 Hz, 2H), 7.18–7.07 (m, 2H), 6.92–6.83 (m, 2H), 5.16 (s, 2H), 3.78 (s, 3H), 2.17 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 159.7, 150.2, 144.6, 138.9, 136.0, 135.7, 129.3, 129.3, 128.2, 127.9, 125.7, 113.5, 112.0, 55.2, 52.3, 20.8. m.p. = 135–138 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_3O_5S$ 440.1282, found 440.1280. IR (neat) ν (cm^{-1}): 3333, 3051, 1608, 1598, 1522, 1512, 1343, 1325, 1291, 1252, 1144, 1067, 1011, 952, 858, 836, 815.

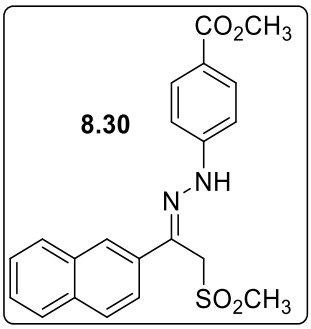


1-(1-(4-methoxyphenyl)-2-tosylethyl)-2-(4-nitrophenyl)diazene (8.28a). from 30 μL (0.2 mmol) of 4-vinylanisole **8.3** and 122.0 mg of arylazo sulfone **8.1r** (0.4 mmol, 2.0 equiv) irradiated for 24 hours. Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 87.8 mg of product **8.28a** (orange solid/liquid, 99% yield). Irradiation of **8.28a**(0.1 mmol) in $CDCl_3$ (1 mL) and evaporation *under vacuo* of the photolyzed mixture afforded 75.9 mg of **8.28** (yellow solid, 100% conversion yield) without further purifications. **(8.28a).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29–8.20 (m, 2H), 7.73–7.56 (m, 4H), 7.29–7.19 (m, 4H), 6.88–6.77 (m, 2H), 5.48 (dd, J = 9.1, 3.6 Hz, 1H), 4.48 (dd, J = 14.5, 9.1 Hz, 1H), 3.80–3.73 (m, 1H), 3.77 (s, 3H), 2.31 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 160.0, 154.7, 148.9, 144.8, 136.6, 129.9, 129.1, 128.5, 128.3, 124.5, 123.3, 114.7, 76.1, 59.7, 55.4, 21.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}N_3O_5S$ 440.1282, found 440.1279. IR (neat) ν (cm^{-1}): 2907, 1614, 1599, 1515, 1509, 1348, 1307, 1299, 1245, 1160, 1154, 1132, 1097, 1056, 1034, 1001, 985, 932, 889, 864, 840, 805, 767.

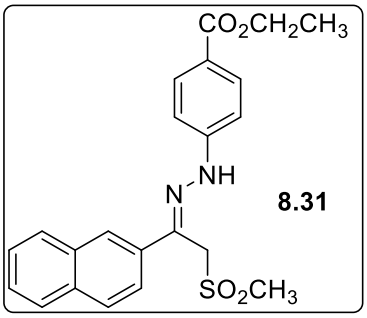


1-(2-(methylsulfonyl)-1-(naphthalen-2-yl)ethylidene)-2-(4-nitrophenyl)hydrazine (8.29). From 30.8 mg (0.2 mmol) of 2-vinylnaphthalene **8.2** and 91.6 mg of arylazo sulfone **8.1e** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 48.3 mg of product **8.29** (pale pink solid, 63% yield).

(8.29). ^{1}H-NMR (300 MHz, DMSO-d_6). δ 10.70 (s, 1H), 8.40 (s, 1H), 8.23 (d, J = 8.8 Hz, 3H), 7.95 (d, J = 8.9 Hz, 3H), 7.64–7.53 (m, 2H), 7.45 (d, J = 8.9 Hz, 2H), 5.19 (s, 2H), 3.12 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 150.1, 139.6, 135.4, 132.6, 128.2, 127.6, 127.4, 127.2, 126.5, 126.2, 126.1, 125.6, 123.5, 112.5, 50.5, 41.8. m.p. = 182–185 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{18}N_3O_4S$ 384.1020, found 384.1023. IR (neat) ν (cm^{-1}): 3334, 1670, 1594, 1559, 1501, 1326, 1297, 1272, 1156, 1126, 1109, 1079, 1073, 970, 961, 939, 855, 841, 752, 732, 656.

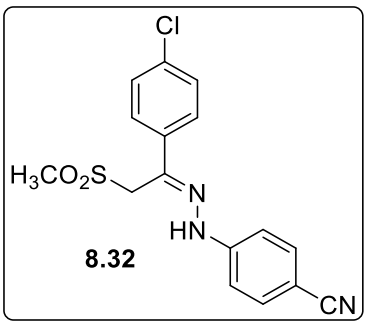


methyl 4-(2-(2-(methylsulfonyl)-1-(naphthalen-2-yl)ethylidene)hydrazinyl)benzoate (8.30). From 30.8 mg (0.2 mmol) of 2-vinylnaphthalene **8.2** and 96.8 mg of arylazo sulfone **8.1d** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 61.8 mg of product **8.30** (slightly yellow solid, 78% yield). (**8.30a).** HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{21}N_2O_4S$ 397.1224, found 397.1222. **(8.30).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 9.65 (s, 1H), 8.17 (dd, J = 8.8, 2.0 Hz, 1H), 8.07–7.99 (m, 3H), 7.92–7.85 (m, 3H), 7.57–7.51 (m, 2H), 7.27 (d, J = 1.9 Hz, 1H), 7.25 (d, J = 2.1 Hz, 1H), 4.75 (s, 2H), 3.90 (s, 3H), 2.97 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 179.8, 148.6, 139.4, 135.5, 133.7, 133.4, 131.5, 129.1, 128.6, 127.9, 127.2, 127.0, 125.0, 123.5, 113.6, 53.7, 52.0, 41.7. m.p. = 179–183 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{21}N_2O_4S$ 397.1224, found 397.1221. IR (neat) ν (cm^{-1}): 3334, 3049, 2338, 1703, 1694, 1686, 1610, 1562, 1523, 1502, 1466, 1435, 1416, 1341, 1282, 1268, 1192, 1165, 1130, 1116, 972, 852, 819, 768, 748.



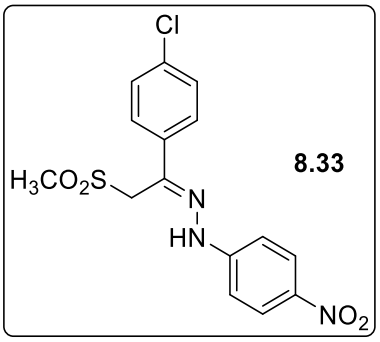
ethyl 4-(2-(2-(methylsulfonyl)-1-(naphthalen-2-yl)ethylidene)hydrazinyl)benzoate (8.31). From 30.8 (0.2 mmol) of 2-vinylnaphthalene **8.2** and 101.6 mg of arylazo sulfone **8.1b** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 78.7 mg of product **8.31** (white solid, yield 96%). **(8.31).** ^{1}H-NMR (300 MHz, DMSO-d_6). δ 10.36 (s, 1H), 8.35 (d, J = 1.9 Hz, 1H), 8.22 (dd, J = 8.9, 1.9 Hz, 1H), 7.94 (dd, J = 9.0, 6.1 Hz, 5H), 7.57–7.50 (m, 2H), 7.38 (d, J = 8.5 Hz, 2H), 5.16 (s, 2H), 4.28 (q, J = 7.1 Hz, 2H), 3.12 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H).^{13}C{^{1}H}-NMR (75MHz, DMSO-d_6). δ 148.7, 134.8, 132.9, 132.8, 132.7, 130.9, 128.3, 127.7, 127.5, 126.5, 126.5, 125.8, 123.6, 120.9, 112.6, 60.0, 50.2, 41.8, 14.3. m.p. = 184–187 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{23}N_2O_4S$ 411.1380

found 411.1380. IR (neat) ν (cm^{-1}): 3440, 2252, 2162, 1698, 1661, 1605, 1585, 1565, 1507, 1470, 1444, 1416, 1367, 1338, 1309, 1264, 1164, 1132, 1101, 1052, 1022, 1004, 865, 821, 759.



8.32

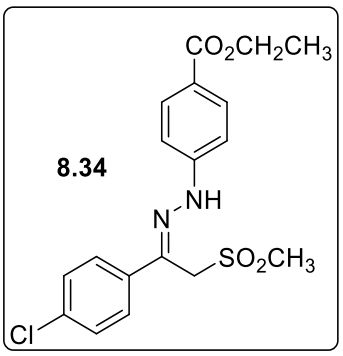
4-(2-(1-(4-chlorophenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzonitrile (8.32). From 24 µL (0.2 mmol) of 4-Chlorostyrene **8.4** and 87.6 mg of arylazo sulfone **8.1a** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 38.2 mg of product **8.32** (white solid, 55% yield). The same reaction was performed in large scale, employing 60 µL (0.5 mmol) of 4-Chlorostyrene **8.4** and 209.0 mg of arylazo sulfone **8.1a** (1.0 mmol, 2.0 equiv) the mixture was irradiated for 24 hours affording 112.8 mg of **8.32** (65% yield). **(8.32).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.39 (s, 1H), 8.01–7.87 (m, 2H), 7.70 (d, J = 8.7 Hz, 2H), 7.51–7.41 (m, 2H), 7.35 (d, J = 8.7 Hz, 2H), 5.01 (s, 2H), 3.08 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 152.7, 148.2, 136.1, 133.7, 132.6, 128.3, 127.9, 113.4, 50.3, 41.7. m.p. = 249–252 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{15}ClN_3O_2S$ 348.0575, found 348.0574. IR (neat) ν (cm^{-1}): 3333, 3016, 2220, 1705, 1608, 1576, 1551, 1517, 1491, 1453, 1398, 1387, 1344, 1291, 1266, 1206, 1165, 1130, 111, 1093, 1070, 1014, 1005, 968, 831, 760, 669.



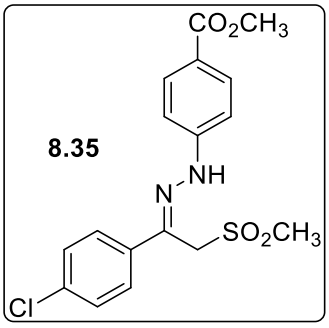
8.33

1-(1-(4-chlorophenyl)-2-(methylsulfonyl)ethylidene)-2-(4-nitrophenyl)hydrazine (8.33). From 24 µL (0.2 mmol) of 4-Chlorostyrene **8.4** and 91.6 mg of arylazo sulfone **8.1e** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 72.7 mg of product **8.33** (white solid, 99% yield). The same reaction was also performed in large scale, employing 60 µL (0.5 mmol) of 4-Chlorostyrene **8.4** and 229.0 mg of arylazo sulfone **8.1d** (1.0 mmol, 2.0 equiv) the mixture was irradiated for 24 hours affording 183.5 mg of **8.33** (99% yield). The same reaction was performed using sunlight as light source starting from 24 µL (0.2 mmol) of 4-Chlorostyrene **8.4** and 91.6 mg of arylazo sulfone **8.1d** (0.4 mmol, 2 equiv.): 11 days of irradiation (77 hours approximatively of light exposure), affording 72.7 mg of **8.33** (99% yield). **(8.33).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.64 (s, 1H), 8.20 (d, J = 9.1 Hz, 2H), 8.07–7.83 (m, 2H), 7.59–7.45 (m, 2H), 7.39 (d, J = 9.2 Hz, 2H), 5.05 (s, 2H), 3.09 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 150.2, 139.7, 135.9, 134.2, 133.5, 128.3, 128.1, 126.0, 112.7, 50.4, 41.8. m.p. = 262–265 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}ClN_3O_4S$ 368.0474,

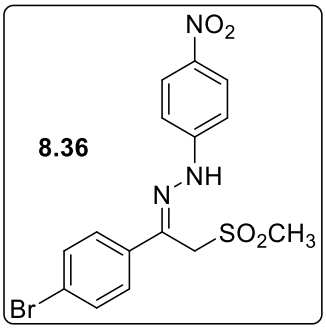
found 368.0475. IR (neat) ν (cm^{-1}): 3299, 3020, 1592, 1576, 1557, 1539, 1420, 1416, 1293, 1267, 1187, 1161, 1148, 1103, 1089, 1004, 981, 964, 924, 869, 843, 831, 794, 760, 751, 739, 701, 692.



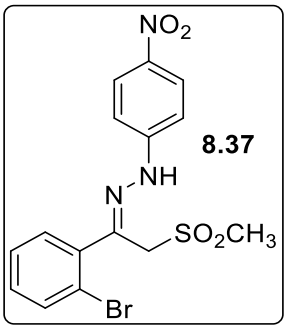
ethyl 4-(2-(1-(4-chlorophenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzoate (8.34). From 24 µL (0.2 mmol) of 4-Chlorostyrene **8.4** and 96.8 mg of arylazo sulfone **8.1b** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 58.5 mg of product **8.34** (white solid, 77% yield). **(8.34).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.30 (s, 1H), 7.92 (t, J = 8.7 Hz, 4H), 7.50–7.46 (m, 2H), 7.35–7.30 (m, 2H), 5.02 (s, 2H), 3.80 (s, 3H), 3.09 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 166.1, 148.6, 143.2, 136.2, 131.8, 131.0, 128.3, 120.7, 112.6, 51.6, 50.2, 41.7. m.p. = 232–236 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}ClN_2O_4S$ 381.0678 found 381.0681. IR (neat) ν (cm^{-1}): 3302, 2953, 1706, 1641, 1605, 1454, 1434, 1417, 1310, 1281, 1262, 1186, 1153, 1137, 1113, 1110, 1025, 1008, 956, 849, 769, 697.



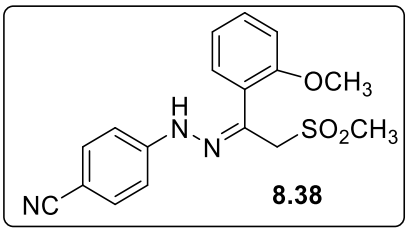
methyl 4-(2-(1-(4-chlorophenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzoate (8.35). From 24 µL (0.2 mmol) of 4-Chlorostyrene **8.4** and 101.6 mg of arylazo sulfone **8.1d** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 49.6 mg of product **8.35** (pale yellow solid, 63% yield). **(8.35).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.02–7.98 (m, 2H), 7.80–7.73 (m, 2H), 7.43–7.36 (m, 2H), 7.21–7.16 (m, 2H), 4.57 (s, 2H), 4.35 (q, J = 7.0, 2H), 2.98 (s, 3H), 1.38 (t, J = 7.0 Hz, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 166.7, 148.3, 135.3, 132.6, 131.5, 131.4, 129.3, 127.1, 123.5, 113.5, 60.8, 53.6, 41.8, 14.6. m.p. = 244–247 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{20}ClN_2O_4S$ 395.0834 found 395.0833. IR (neat) ν (cm^{-1}): 3320, 2992, 1699, 1605, 1579, 1566, 1503, 1492, 1366, 1346, 1303, 1275, 1258, 1162, 1125, 1104, 1015, 1006, 966, 852, 842, 769, 701, 654.



1-(1-(4-bromophenyl)-2-(methylsulfonyl)ethylidene)-2-(4-nitrophenyl)hydrazine (8.36). From 26 μL (0.2 mmol) of 4-bromostyrene **8.5** and 91.6 mg of arylazo sulfone **8.1e** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 82.2 mg of product **8.36** (yellow solid, 99% yield). **(8.36).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.65 (s, 1H), 8.20 (d, J = 9.2 Hz, 2H), 7.89 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 9.2 Hz, 2H), 5.05 (s, 2H), 3.10 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 150.2, 139.7, 136.2, 134.2, 131.2, 128.4, 125.9, 122.2, 112.7, 50.3, 41.8. m.p. = 299–304 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}{}^{79}BrN_3O_4S$ 411.9968 found 411.9973. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}{}^{81}BrN_3O_4S$ 413.9948 found 411.9944. IR (neat) ν (cm^{-1}): 3080, 1678, 1589, 1500, 1483, 1320, 1298, 1288, 1130, 1074, 1063, 1001, 985, 936, 930, 904, 839, 828, 750, 679.

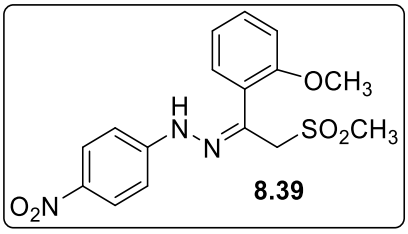


1-(1-(2-bromophenyl)-2-(methylsulfonyl)ethylidene)-2-(4-nitrophenyl)hydrazine (8.37). From 26 μL (0.2 mmol) of 2-bromostyrene **8.6** and 91.6 mg of arylazo sulfone **8.1e** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 41.1 mg of product **8.37** (yellow solid, 50% yield). **(8.37).** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.16–8.08 (m, 2H), 7.80–7.75 (m, 1H), 7.55–7.51 (m, 1H), 7.47–7.41 (m, 2H), 7.36–7.29 (m, 2H), 4.70–4.05 (m, 2H), 3.09 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6). δ 150.4, 137.7, 137.6, 133.0, 131.4, 131.0, 128.2, 125.9, 125.7, 112.57, 61.4, 40.7. m.p. = 310–315 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}{}^{79}BrN_3O_4S$ 411.9968 found 411.9968. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}{}^{81}BrN_3O_4S$ 413.9948 found 413.9946. IR (neat) ν (cm^{-1}): 3446, 2927, 1591, 1520, 1503, 1485, 1425, 1393, 1320, 1264, 1130, 1108, 1050, 1024, 1005, 896, 847, 821, 759, 753, 733, 696.



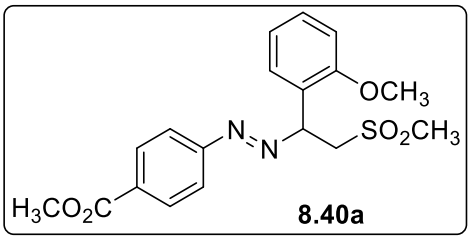
4-(2-(1-(2-methoxyphenyl)-2-(methylsulfonyl)ethylidene)hydrazinyl)benzonitrile (8.38). From 30 μL (0.2 mmol) of 2-vinylanisole **8.7** and 87.6 mg of arylazo sulfone **8.1a** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 57.0 mg of product **8.38** (pale yellow solid, 83% yield). **(8.38).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 7.91 (s, 1H), 7.53–7.47 (m, 3H), 7.35–7.29 (m, 1H), 7.15 –7.00 (m, 4H), 4.35–4.19 (m, 2H), 3.86 (s, 3H), 2.97 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 156.3, 147.2, 136.4, 133.8, 132.2, 131.3, 129.6,

121.8, 113.9, 113.1, 112.2, 102.9, 62.5, 55.9, 40.5. m.p. = 198–201 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}N_3O_3S$ 344.1071, found 344.1071. IR (neat) ν (cm^{-1}): 3309, 2218, 1609, 1579, 1518, 1489, 1464, 1417, 1305, 1260, 1170, 1133, 1071, 1043, 1021, 967, 901, 836, 759.



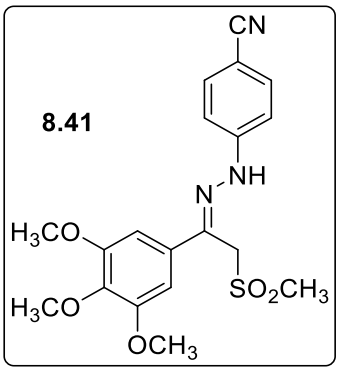
8.39

1-(1-(2-methoxyphenyl)-2-(methylsulfonyl)ethylidene)-2-(4-nitrophenyl)hydrazine (8.39). From 30 µL (0.2 mmol) of 2-vinylanisole **8.7** and 91.6 mg of arylazo sulfone **8.1e** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 72.6 mg of product **8.39** (pale yellow solid, 99% yield). **(8.39).** ^{1}H-NMR (300 MHz, CD_3COCD_3). δ 9.43 (s, 1H), 8.11 (d, J = 9.1 Hz, 2H), 7.52–7.40 (m, 2H), 7.33–7.28 (m, 2H), 7.16 (d, J = 8.3 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 4.36 (s, 2H), 3.90 (s, 3H), 2.98 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, CD_3 $COCD_3$). δ 160.0, 153.7, 144.3, 132.6, 131.4, 130.9, 126.6, 122.1, 113.3, 113.2, 113.0, 63.5, 56.3, 41.0. m.p. = 140–143 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{18}N_3O_5S$ 364.0969, found 364.0971. IR (neat) ν (cm^{-1}): 3311, 1699, 1670, 1641, 1593, 1519, 1503, 1489, 1436, 1324, 1300, 1261, 1134, 1110, 1081, 1044, 1021, 1004, 967, 846, 752, 694.

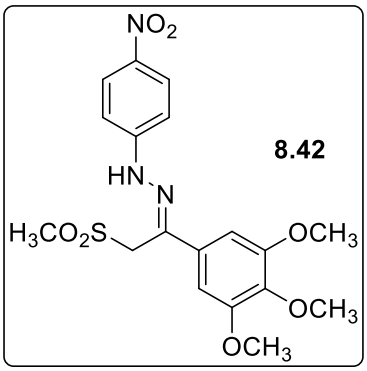


8.40a

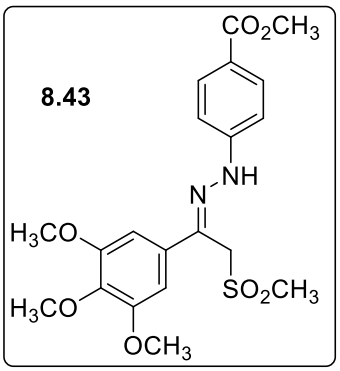
methyl 4-((1-(2-methoxyphenyl)-2-(methylsulfonyl)ethyl)diazenyl)benzoate (8.40a). From 30 µL (0.2 mmol) of 2-vinylanisole **8.7** and 96.8 mg of arylazo sulfone **8.1d** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 54.9 mg of product **8.40a** (yellow solid/liquid, 73% yield). The compound decomposed after some hours even if stored under argon in freezer. **(8.40a).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 8.16–8.11 (m, 2H), 7.75–7.71 (m, 2H), 7.37–7.29 (m, 2H), 7.01–6.94 (m, 2H), 5.92 (dd, J = 8.0, 4.5 Hz, 1H), 4.35 (dd, J = 15.0, 4.5 Hz, 1H), 3.94 (s, 3H), 3.87 (s, 3H), 3.71 (dd, J = 15.0, 4.5 Hz, 1H), 2.79 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 162.0, 154.3, 132.3, 130.8, 130.6, 130.1, 129.3, 125.9, 122.5, 121.3, 111.5, 71.0, 57.7, 55.8, 52.5, 42.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{21}N_2O_5S$ 376.1093, found 376.1092.



4-(2-(2-(methylsulfonyl)-1-(3,4,5-trimethoxyphenyl)ethylidene)hydrazinyl)benzonitrile (8.41). From 40 µL (0.2 mmol) of 3,4,5-trimethoxy styrene **8.8** and 87.6 mg of arylazo sulfone **8.1a** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 40.3 mg of product **8.41** (yellow solid, 50% yield). **(8.41).** ^{1}H-NMR (300 MHz, CD_3COCD_3). δ 9.86 (s, 1H), 7.66–7.60 (m, 2H), 7.38–7.33 (m, 2H), 7.31 (s, 2H), 4.98 (s, 2H), 3.90 (s, 6H), 3.77 (s, 3H), 3.14 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, CD_3COCD_3). δ 154.4, 149.5, 136.4, 134.4, 120.2, 114.5, 114.1, 105.3, 104.1, 103.3, 60.7, 56.6, 52.6, 42.3. m.p. = 178–182 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{22}N_3O_5S$ 404.1282 found 404.1286. IR (neat) *v* (cm^{-1}): 3013, 2218, 1606, 1592, 1507, 1464, 1426, 1415, 1371, 1338, 1304, 1241, 1172, 1125, 1103, 1054, 1023, 1003, 969, 836.

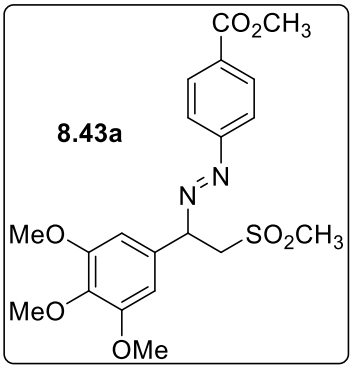


1-(2-(methylsulfonyl)-1-(3,4,5-trimethoxyphenyl)ethylidene)-2-(4-nitrophenyl)hydrazine (8.42). From 40 µL (0.2 mmol) of 3,4,5-trimethoxy styrene **8.8** and 91.6 mg of arylazo sulfone **8.1e** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 6:4) afforded 71.9 mg of product **8.42** (slightly pink solid, 85% yield). **(8.42).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 9.71 (s, 1H), 8.20 (d, *J* = 9.2 Hz, 2H), 7.19 (d, *J* = 9.1 Hz, 2H), 7.02 (s, 2H), 4.61 (s, 2H), 3.94 (s, 6H), 3.91 (s, 3H), 3.00 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 153.7, 149.9, 136.3, 131.8, 125.9, 123.4, 113.2, 105.0, 103.9, 102.5, 61.0, 56.5, 54.0, 41.8. m.p. = 200–205 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{22}N_3O_7S$ 424.1180, found 424.1180. IR (neat) *v* (cm^{-1}): 3331, 2920, 1753, 1605, 1494, 1457, 1443, 1411, 1346, 1304, 1284, 1241, 1206, 1159, 1117, 1067, 1053, 1011, 977, 960, 945, 877, 865, 777, 697.

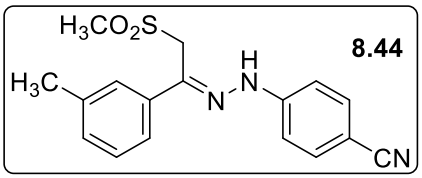


(4-(2-(2-(methylsulfonyl)-1-(3,4,5-trimethoxyphenyl)ethylidene)hydrazinyl)benzoate). (8.43). From 40 µL (0.2 mmol) of 3,4,5-trimethoxy styrene **8.8** and 96.8 mg of arylazo sulfone **8.1d** (0.4 mmol, 2.0 equiv) irradiated for 48 hours. Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 76.1 mg of product **8.43** (white solid, 88% yield). **(8.43).** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 9.48 (s, 1H), 7.99 (d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.01 (s, 2H), 4.59 (s, 2H), 3.93 (s, 6H), 3.89 (s, 3H), 3.88 (s, 3H), 2.96 (s, 3H).^{13}C{^{1}H}-

NMR (75 MHz, $CDCl_3$). δ 167.1, 153.7, 148.6, 134.2, 132.4, 131.7, 131.5, 122.9, 113.4, 112.3, 104.8, 103.7, 61.1, 56.6, 54.0, 52.0, 41.8. m.p. = 156–159 °C HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{25}N_2O_7S$ 437.1384, found 437.1366. IR (neat) *v* (cm^{-1}): 3301, 2997, 2841, 1710, 1605, 1589, 1520, 1508, 1463, 1454, 1435, 1416, 1354, 1338, 1307, 1280, 1262, 1190, 1163, 1126, 1062, 1028, 1002, 969, 922, 891, 849, 828, 771, 733, 700.

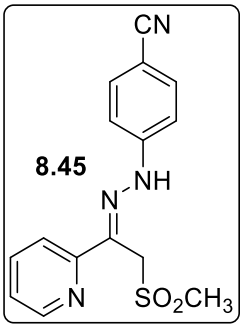


methyl 4-((2-(methylsulfonyl)-1-(3,4,5-trimethoxyphenyl)ethyl)diazenyl)benzoate (8.43a). From 40 µL (0.2 mmol) of 3,4,5-trimethoxy styrene **8.8** and 96.8 mg of arylazo sulfone **8.1d** (0.4 mmol, 2.0 equiv) irradiated for 24 hours. Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 75.9 mg of product **8.43a** (yellow liquid prone to decomposition, 87% yield, *E*-*Z* ratio 2:1). Irradiation of **8.43a** (0.09 mmol) in $CDCl_3$ (1.0 mL) and evaporation of the photolyzed solution afforded 75.9 mg of **8.43** (white solid, 100% conversion yield). **(8.43a)-Major isomer (*E*)** ^{1}H-NMR (300 MHz, $CDCl_3$). δ 8.19–8.09 (m, 2H), 7.80–7.67 (m, 2H), 6.64 (s, 2H), 5.51 (dd, *J* = 7.8, 5.1 Hz, 1H), 4.22 (dd, *J* = 14.7, 7.9 Hz, 1H), 3.92 (s, 3H), 3.86 (s, 6H), 3.82 (s, 3H), 3.68 (d, *J* = 9.5 Hz, 1H), 2.71 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 166.3, 154.0, 130.8, 130.7, 132.0, 122.6, 117.6, 105.1, 104.3, 76.4, 61.0, 58.9, 56.4, 52.5, 42.6. **(8.43a)-Minor isomer (*Z*)** δ 8.07–8.02 (m, 2H), 6.73–6.69 (m, 2H), 6.31 (s, 2H), 5.12 (dd, *J* = 9.6, 3.0 Hz, 1H), 4.51–4.43 (m, 1H), 3.92 (s, 3H), 3.82 (s, 6H), 3.77 (s, 3H), 3.55–3.49 (m, 1H), 2.92 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 166.2, 154.1, 132.6, 132.3, 132.2, 113.3, 112.3, 104.8, 103.7, 70.5, 61.0, 60.7, 58.9, 56.3, 52.4, 43.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{25}N_2O_7S$ 437.1384, found 437.1377. IR (neat) *v* (cm^{-1}): 2951, 1717, 1678, 1603, 1590, 1506, 1460, 1433, 1418, 1304, 1276, 1245, 1189, 1162, 1118, 1001, 964, 880, 849, 836, 803, 772, 717, 698.

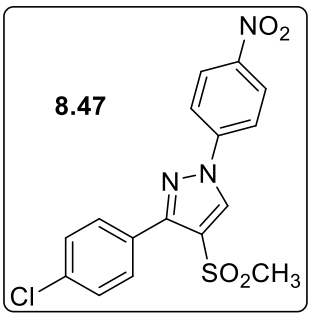


4-(2-(2-(methylsulfonyl)-1-(m-tolyl)ethylidene)hydrazinyl)benzonitrile (8.44). From 26 µL (0.2 mmol) of 3-methylstyrene **8.9** and 87.6 mg of arylazo sulfone **8.1a** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 33.4 mg of product **8.44** (slightly pink solid, 51% yield). **(8.44).** ^{1}H-NMR (300 MHz, DMSO-*d*$_6$). δ 10.29 (s, 1H), 7.79–7.59 (m, 4H), 7.35–7.28 (m, 3H), 7.18 (d, *J* = 7.6 Hz, 1H), 4.99 (s, 2H), 3.05 (s, 3H), 2.37 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, DMSO-*d*$_6$). δ 1484, 137.4, 134.0, 133.7, 129.2, 128.2, 126.7, 123.6, 119.9, 113.2, 100.7, 50.5, 41.8, 21.2. m.p. = 138–142 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}N_3O_2S$ 328.1121

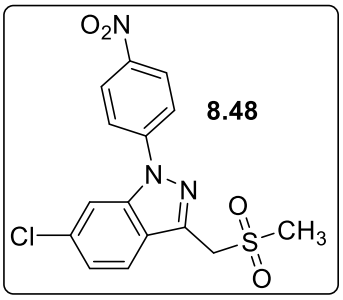
found 328.1123. IR (neat) ν (cm^{-1}): 3415, 2251, 1662, 1425, 1367, 1263, 1023, 1002, 940, 909, 861, 821, 759, 726, 679.



4-(2-(2-(methylsulfonyl)-1-(pyridin-2-yl)ethylidene)hydrazineyl)benzonitrile (8.45). From 21 μL (0.2 mmol) of 2-vinylpyridine and 83.6 mg of arylazo sulfone **8.1a** (0.4 mmol, 2.0 equiv). Purification by silica gel flash column chromatography (eluent PET/EA 7:3) afforded 20.7 mg of product **8.45** (orange solid, 33% yield). **(8.45).** ^{1}H NMR (300 MHz, CD_3CN) δ 9.66 (s, 1H), 8.62–8.52 (m, 1H), 8.25–8.22 (m, 1H), 7.82 (td, J = 7.8, 1.8 Hz, 2H), 7.66–7.63 (m, 2H), 7.41–7.34 (m, 2H), 5.03 (s, 2H), 2.96 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$). δ 148.75, 147.9, 141.8, 137.0, 135.3, 133.8, 123.8, 120.5, 114.4, 51.7, 41.4. m.p. = 121–124 °C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}N_4O_2S$ 315.0918, found 315.0916. IR (neat) ν (cm^{-1}): 3313, 3010, 2953, 2219, 1702, 1606, 1566, 1515, 1504, 1466, 1433, 1304, 1261, 1247, 1167, 1118, 1066, 1013, 968, 957, 834, 785, 780.



3-(4-chlorophenyl)-4-(methylsulfonyl)-1-(4-nitrophenyl)-1H-pyrazole (8.47). [8.15] 22 μL of $POCl_3$ (0.24 mmol, 4.0 equiv.) were added dropwise in 100 μL of distilled DMF at 0 °C and after 1 hour 22 mg of hydrazone **8.33** (0.06 mmol, 1.0 equiv.) in 200 μL in distilled DMF were added dropwise. After stirring for one hour at 0°C and for 1 hour at 80 °C the reaction was finally cooled at room temperature and poured into ice. The hydrazone was recovered partially (8 mg, 0.022 mmol) and 12.2 mg of the product **8.47** were obtained (slightly yellow solid, 51% yield, 85% conversion yield). **(8.47).** ^{1}H NMR (300 MHz, CD_3CN) δ 8.84 (s, 1H), 8.37 (d, J = 9.2 Hz, 1H), 8.08 (d, J = 9.3 Hz, 1H), 7.96 (d, J = 8.7 Hz, 1H), 7.53 (d, J = 8.6 Hz, 1H), 3.03 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, CD_3CN) δ 150.9, 136.4, 135.2, 131.7, 130.4, 129.8, 126.4, 125.7, 120.9, 45.3. m.p. = 170–172°C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{12}ClN_3O_4S$ 370.0317, found 370.0316. IR (neat) ν (cm^{-1}): 3132, 1596, 1519, 1504, 1339, 1314, 1162, 1125, 1072, 1066, 999, 980, 954, 858, 770, 751, 691.



6-chloro-3-((methylsulfonyl)methyl)-1-(4-nitrophenyl)-1H-indazole (8.48).[8.16] **Procedure for the synthesis of 1H-indazoles.** In a flame-dried glass vessel 18.4 mg of 1-(1-(4-chlorophenyl)-2-(methylsulfonyl)ethylidene)-2-(4-nitrophenyl)hydrazine **8.33** (0.05 mmol) and 32 mg of PIFA [Bis(trifluoroacetoxy)iodo]benzene (0.075 mmol, 1.5 equiv) in 2 mL of HFIP 1,1,1,3,3,3-Hexafluoro-2-propanol were dissolved at 0 °C. The reaction was stopped aftter complete consumption of the starting material checked by TLC (10 minutes). The reaction mixture was poured into 10 mL of water and extracted three times with DCM. Precipitation with chloroform and petroleum ether afforded 13.6 mg of compound **8.48** (white solid, 75% yield). **(8.48).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54–8.38 (m, 2H), 8.00–7.88 (m, 3H), 7.83 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.37 (dd, *J* = 8.6, 1.7 Hz, 1H), 4.71 (s, 2H), 2.99 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 157.7, 138.7, 136.0, 133.0, 130.9, 125.6, 124.9, 124.0, 122.9, 122.2, 110.8, 53.8, 39.9. m.p. = 143–146°C (Petroleum Ether). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}ClN_3O_4S$ 366.0317, found 366.0316. IR (neat) *ν* (cm^{-1}): 2929, 1593, 1509, 1471, 1428, 1415, 1392, 1345, 1314, 1266, 1209, 1172, 1148, 1118, 1073, 1009, 988, 963, 926, 911, 896, 849, 832, 785, 766, 750, 728, 688, 662.

Procedure for the On- Off experiment for the synthesis of 8.32. In two flame-dried NMR tubes, arylazo sulfone **8.1a** (62.7 mg, 0.3 mmol), 4-chlorostyrene **8.4** (25 µL, 0.15 mmol) and 1,1,2,2-tetrachloroethane (32 µL, 0.3 mmol) were dissolved in 1.5 mL of CD_2Cl_2. The aforementioned solution was irradiated for 30 minutes, 1 hour, 2 hours, 4 hours and finally 8 hours. Between the different irradiation times, the tube was covered in an aluminium foil, the cup was parafilmed and put in the fridge for the same amount of time that was previously irradiated. The reaction was monitored with NMR spectroscopy using 1,1,2,2-tetrachloroethane as internal standard following the consumption of the arylazo sulfone **8.1a**.

Procedure for the photo-initiated experiment for the synthesis of 8.32. The aforementioned solution was irradiated for 5 hours, the tube was covered in an aluminium foil, and the cup was parafilmed and put in the fridge for 12 hours and 12 more hours. The reaction was monitored with NMR spectroscopy using 1,1,2,2-tetrachloroethane as internal standard following the consumption of the arylazo sulfone **8.1a**.

Procedure for the cross reaction. In a flame-dried tube, arylazo sulfone **8.1o** (87.3 mg, 0.3 mmol), arylazo sulfone **8.1p** (104.4 mg, 0.3 mmol) and 4-methoxystyrene **8.3** (70 µL, 0.5 mmol) were dissolved in predistilled and anhydrous dichloromethane (2 mL). Argon was flushed into the so-

formed solution and after three cycle of freeze pump, the rubber septum was parafilmed. The solution was then placed in a EvoluChem^{TM} reactor connected to a minichiller Huber based on ethanol that kept the vessel at 10 °C and finally the mixture was irradiated with a blue Kessil Lamp (λ_{emm}=456 nm, 40 W). The irradiation was stopped after total consumption of the starting materials, monitored by TLC. The final product is an inseparable mixture of hydrazones.

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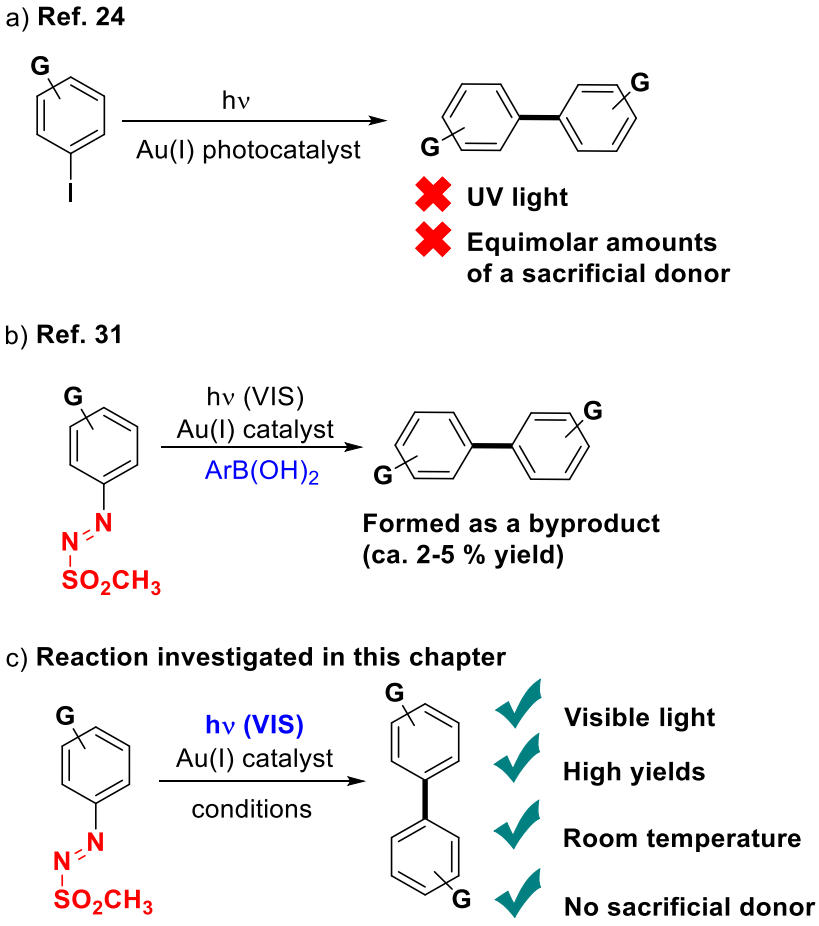
CHAPTER 9

VISIBLE LIGHT-DRIVEN, GOLD(I) CATALYZED PREPARATION OF SYMMETRICAL (HETERO)BIARYLS BY HOMOCOUPLING OF ARYLAZO SULFONES.

9.1. INTRODUCTION.

The symmetrical biaryl scaffold is widespread in natural occurring molecules [9.1] and in artificial bioactive species [9.2]. The interest in such compounds is increasing due to the applications in different fields, like as conducting and electroluminescent materials [9.3], (stereogenic) ligands [9.4] and key-constituents of molecular switches and devices [9.5]. It is noteworthy that from the early approaches, the so-called Ullmann reaction, between aryl halides under reductive conditions catalysed by copper, an impressive number of transition metal-catalysed protocol have been developed [9.7-9.12]. In this context, gold catalysed processes are widely explored and investigated. These strategies rely on the use of different substrates such as aryl boronic acids [9.13], haloarenes [9.14] and aromatics (via direct C-H bond functionalization under oxidative conditions) [9.15]. The need for a mild and benign synthetical approach for the construction of these motif is highly required. Being the photon one of the greenest reagents of them all, because it's able to activates substrates without leaving any traces (side products and/or wastes) at the end of the process [9.16], photochemistry could constitute an intriguing alternative. However, the photoinduced homocoupling processes are still largely underdeveloped [9.17]. These include the photocatalyzed Ullmann reaction of aryl halides using KNb_3O_8@AuNP [9.18], the [Au(I)]-photoredox catalyzed coupling of aryl iodides developed by Barriault and co-workers [9.19] (Scheme 9.1, a) or the dual photoredox/nickel catalyzed dimerization of aryl bromides [9.20]. The use of high energy demanding UV radiation is still required for the accomplishment of these processes [9.21], and the use of visible light could be adopted only using complex bimetallic (Ti/Pd) nanostructured composites as the photocatalyst at high temperatures [9.22]. The ongoing interest of our research group on *dyedauxiliary groups*, in this specific case on the -$N_2SO_2CH_3$ moiety, which impart colour and photoreactivity to the compound those groups are tethered to [9.23]. In particular, the *in situ* generation of aryl radicals from arylazo sulfones has been recently merged with [Au(I)] catalysis by our groups for a Suzuki-type reaction [9.24]. During this study, we were intrigued to detect in selected cases the corresponding homocoupling biaryl as a minor side-product (2-5% yield in most cases, Scheme 9.1, b) [9.24]. Stimulated by these early observations, we wondered if it was possible to design an unprecedent photocatalyst-free visible light driven protocol for the synthesis of symmetrical (hetero)biaryls (Scheme 9.1, c).



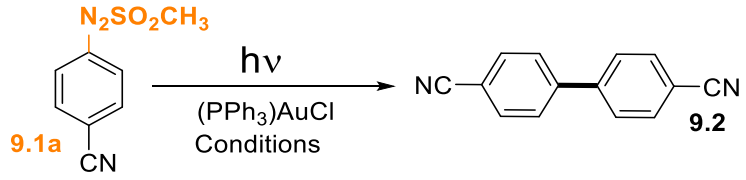
Scheme 9.1. Photoinduced homocoupling for the synthesis of biaryls a) [Au(I)] catalyzed homocoupling of aryl iodides; b) Traces amount of biaryl byproducts from the [Au(I)] gold catalyzed Suzuki-type coupling via arylazo sulfones; c) Reaction investigated in this chapter.

The present approach would represent an innovative procedure for the preparation of symmetrical biarenes via activation of an aromatic substrate upon direct visible light irradiation without the need of any sacrificial electron-donors in stoichiometric amounts.

9.2. RESULTS AND DISCUSSION.

To test our proposal, we firstly repeated the conditions applied in the Suzuki coupling but omitting the boronic acid by electing the *p*-cyanophenylazo sulfone **9.1a** as the model substrate. However, the desired biaryl **9.2** was formed only in small amounts (see Table 9.1). We then carried out an intensive study of the reaction parameters to understand how to improve the yield of the desired product. Reaction optimization was carried out to find the best reaction conditions. Irradiation of a solution of **9.1a** (0.5 M), with gold triphenylphosphine chloride (5 mol%), 2,2'-bipyridine (20 mol%) and NaOAc (2 equiv) gave biaryl **9.2** in 23% yield (entry 1). When repeating the same reaction with a lower concentration of **9.1a** (0.1 M) the desired biaryl was isolated in 58% yield (entry 2). Shifting to a acetonitrile:water 9:1 mixture did not improve significantly the product formation (ca. 42% entry 3). However, moving the irradiation wavelength from 456 nm to 427 nm led to a 51% yield of the biaryl product (entry 4). A change of the ligand (from 2,2'-bipiridine to 1,10-phenanthroline) led to a lower yield of **9.2** (43 % entry 5), but when the reaction was carried out using 1,10-phenanthroline as a ligand and $NaHCO_3$ (2 equiv.) as a base, **9.2** was obtained in 60% yield when the ligand was used in 20 mol% amount and 75% when used in 40 mol% (entries 9 and 10**,** respectively). The same conditions were employed with the irradiation wavelength centred at 390 nm resulting in the formation of **9.2** in 36% of yield (entry 11). Moreover, performing the reaction with the corresponding diazonium salt instead of the arylazo sulfone led to a limited product formation (4%, entry 12). Carrying out the reaction without sodium bicarbonate, lowered the yield to 3% (entry 13). Finally, the photochemical homocoupling of **9.1a** in the absence of the gold catalyst or light (covering the reaction vessel with an aluminium foil) led to no product formation (entries 14 and 15).

Table 9.1. Optimization of the photochemical protocol.



Entry	Conditions	9.2 (yield %)
1	**9.1a** (0.5 M), $(PPh_3)AuCl$ (5 mol%), 2,2'-bipyridine (20 mol%), NaOAc (2 equiv.), hν (456 nm), $CH_3OH:CH_3CN$ (3:1)	23%
2	**9.1a** (0.1 M), $(PPh_3)AuCl$ (5 mol%), 2,2'-bipyridine (20 mol%), NaOAc (2 equiv.), hν (456 nm), $CH_3OH:CH_3CN$ (3:1)	58%
3	**9.1a** (0.1 M), $(PPh_3)AuCl$ (5 mol%), 2,2'-bipyridine (20 mol%), NaOAc (2 equiv.), hν (456 nm), $CH_3CN:H_2O$ (9:1)	42%
4	**9.1a** (0.1 M), $(PPh_3)AuCl$ (5 mol%), 2,2'-bipyridine (20 mol%), NaOAc (2 equiv.), hν (427 nm), $CH_3CN:H_2O$ (9:1)	51%
5	**9.1a** (0.1 M), $(PPh_3)AuCl$ (5 mol%), 1,10-phenanthroline (20 mol%), NaOAc (2 equiv.), hν (427 nm), $CH_3CN:H_2O$ (9:1)	43%
6	**9.1a** (0.1 M), $(PPh_3)AuCl$ (10 mol%), 2,2'-bipyridine (20 mol%), NaOAc (2 equiv.), hν (427 nm), $CH_3CN:H_2O$ (9:1)	53%
7	**9.1a** (0.1 M), $(PPh_3)AuCl$ (10 mol%), 2,2'-bipyridine (20 mol%), $NaHCO_3$ (2 equiv.), hν (427 nm), $CH_3CN:H_2O$ (9:1)	21%
8	**9.1a** (0.1 M), $(PPh_3)AuCl$ (10 mol%), 2,2'-bipyridine (20 mol%), $PhI(OAc)_2$ (20 mol%), $NaHCO_3$ (2 equiv.), hν (427 nm), $CH_3CN:H_2O$ (9:1)	0%
9	**9.1a** (0.1 M), $(PPh_3)AuCl$ (10 mol%), 1,10-phenanthroline (20 mol%), $NaHCO_3$ (2 equiv.), hν (427 nm), $CH_3CN:H_2O$ (9:1)	60%
10	**9.1a (0.1 M), $(PPh_3)AuCl$ (10 mol%), 1,10-phenanthroline (40 mol%), $NaHCO_3$ (2 equiv.), hν (427 nm), $CH_3CN:H_2O$ (9:1)**	**75%**
11	**9.1a** (0.1 M), $(PPh_3)AuCl$ (10 mol%), 1,10-phenanthroline (40 mol%), $NaHCO_3$ (2 equiv), hν (390 nm), $CH_3CN:H_2O$ (9:1)	36%
12	4-$CNC_6H_4N_2^+$ BF_4^- (0.1 M), $(PPh_3)AuCl$ (10 mol%), 1,10-phenanthroline (40 mol%), $NaHCO_3$ (0.2 M), hν (427 nm), $CH_3CN:H_2O$ (9:1)	4%
13	**9.1a** (0.1 M), $(PPh_3)AuCl$ (10 mol%), 1,10-phenanthroline (40 mol%), hν (427 nm), $CH_3CN:H_2O$ (9:1)	3%
14	**9.1a** (0.1 M), hν (427 nm), $CH_3CN:H_2O$ (9:1)	0%
15	**9.1a 9.1a** (0.1 M), $(PPh_3)AuCl$ (10 mol%), $CH_3CN:H_2O$ (9:1)	0%

With the optimized protocol in our hand, the scope of the reaction was smoothly performed using differently substituted arylazo sulfones **9.1a-1ac** (Figure 9.1).

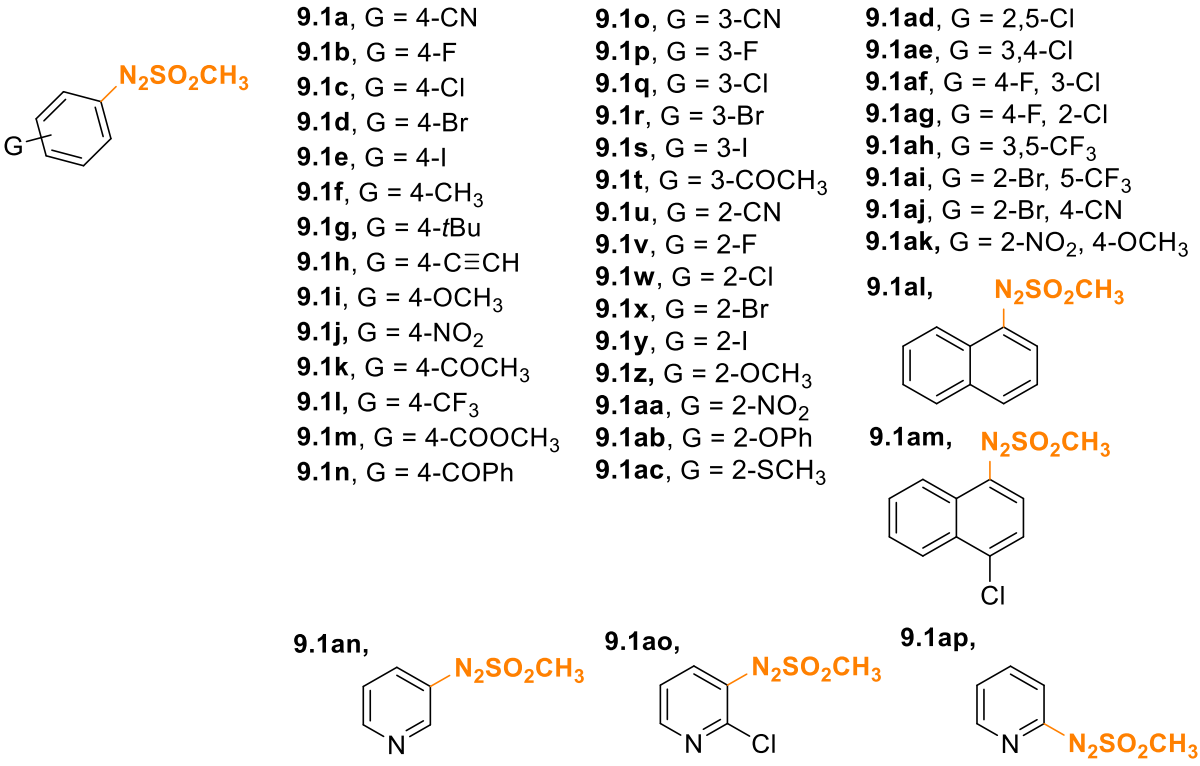
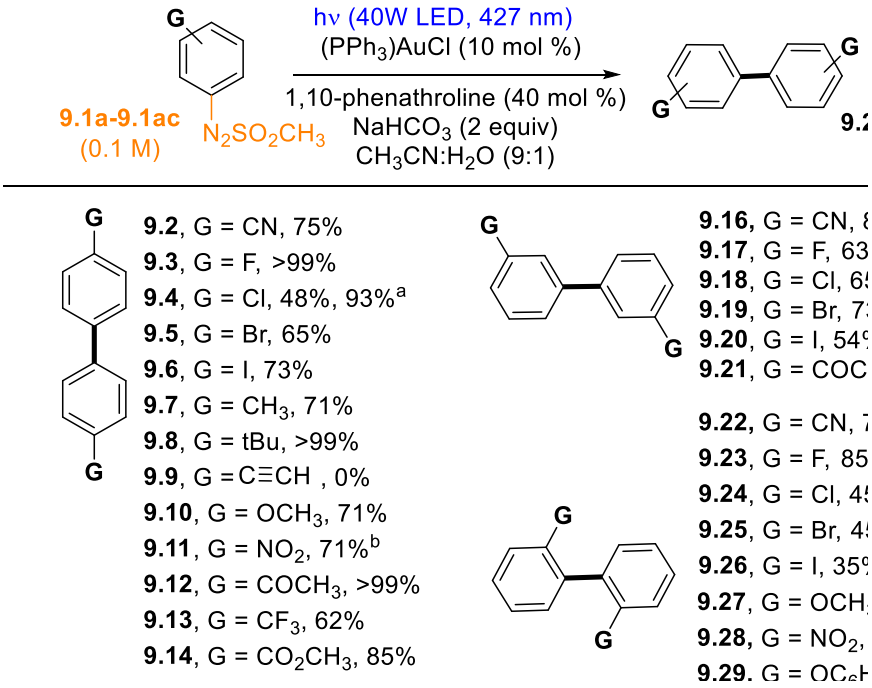


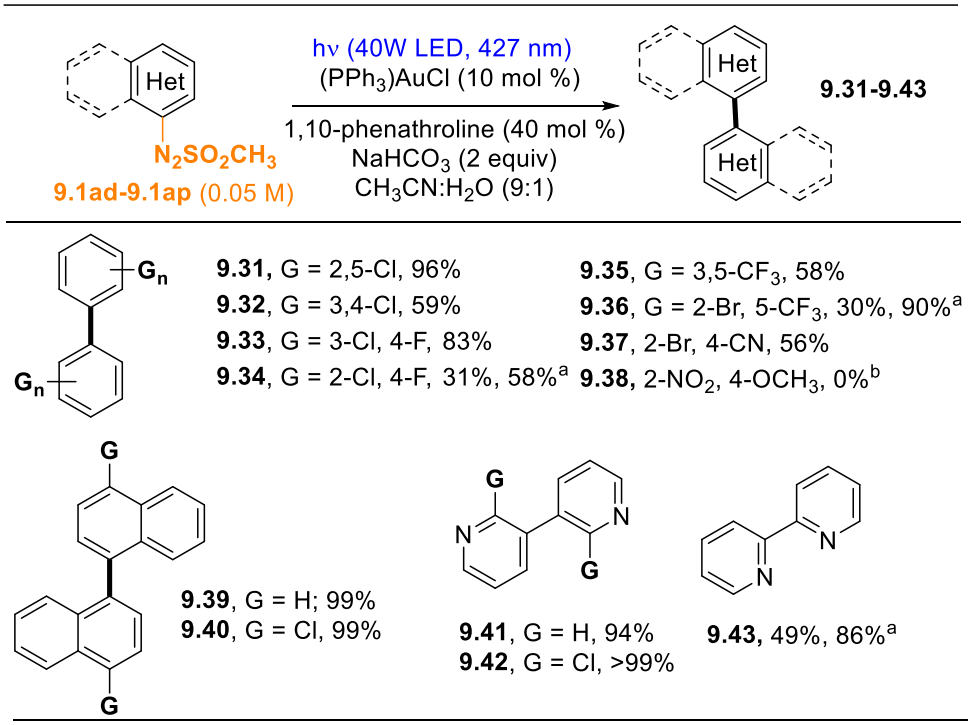
Figure 9.1. Arylazo sulfones employed in the present work.

The corresponding biaryls were obtained in good to quantitative yields and with excellent functional group tolerance starting from para substituted ones (**9.2-9.15**) and 3-substituted aromatic substrates (**9.16-9.21**), including the 4,4'-diacetyl derivative **9.12** (a precursor of antifungal *N,N'*-diaryl-bishydrazones)[9.25] and the benzophenone dimer **9.15** (83% yield). In the case of **9.4**, however, a higher amount of the catalyst was mandatory to achieve a 93% yield. In this series, however, the formation of **9.9** was not observed with 4-ethinylphenyl azosulfone **9.1h,** and this is probably due to the competitive reactivity of [Au(I)] complexes with alkynes [9.26]. The reaction proved slightly less efficient with *ortho*-substituted arylazo sulfones (**9.1u-9.1ac**), forcing to use, in most cases a 15 mol% amount of $(PPh_3)AuCl$ to achieve satisfactory results (see dihaloderivatives **9.24-9.27** and 2,2'-diphenoxybiphenyl **29**) (Scheme 9.2).



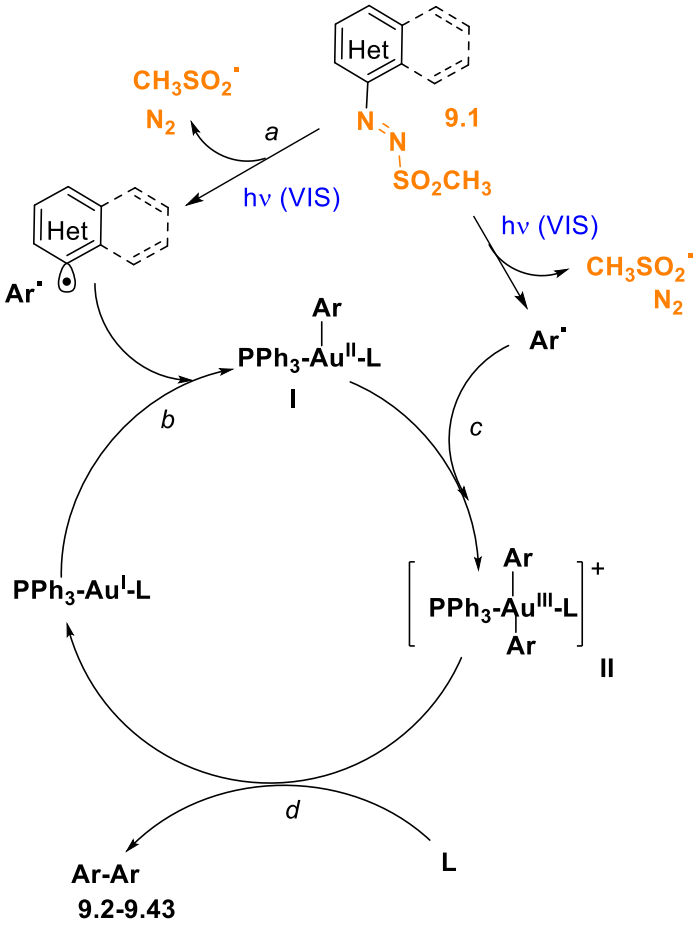
Scheme 9.2. Synthesis of symmetrical biaryls from monosubstituted arylazo sulfones. [a.] $(PPh_3)AuCl$ (15 mol%) was employed [b.] 1,2-bis(4-nitrophenyl)diazene (**9.11a**, 7% yield) was isolated as the minor product [c.] Nitrobenzene was found as the only product.

The protocol was next successfully extended to the synthesis of polysubstituted biaryls **9.31-9.38** (Scheme 9.3), such as the polychlorinated biaryls **9.31,9.32** known as alkoxyresorufin *O*-dealkylase inhibitors [9.27]. The only exception is represented by the 2,2'-dinitro derivative **9.38,** where again the hydrodeaminated *meta*-nitroanisole was formed instead**.** Interestingly, binaphthyls **9.39, 9.40** and heteroarenes **9.41-9.43** were also isolated in up to quantitative yields. Interestingly, most protocols currently available for the synthesis of bipyridines present several limitations, including the low efficiency and limited scope [9.28].



Scheme 9.3. Visible-Light Driven Preparation of (Hetero)biaryls **9.31-9.43**. [a.] $(PPh_3)AuCl$ (15 mol%) was employed; [b.] 3-Nitroanisole was found as the main product

The mechanism proposed for the homocoupling has been summarized in Scheme 9.4. Photolysis of arylazo sulfones to visible light causes the homolytic cleavage of the N-S bond, to release, after nitrogen loss from the first formed aryldiazenyl radical, an aryl ($Ar^{\bullet}$)/methanesulfonyl radical pair (Scheme 9.4, path a) [9.24]. Oxidative addition of $Ar^{\bullet}$ onto the $PPh_3Au^{I}L$ catalyst (path b) resulted in the formation of the $PPh_3Au^{II}LAr$ species **I**, which in turn intercepts a further $Ar^{\bullet}$ intermediate, to afford the Au^{III} complex **II** (path c) [9.29]. The latter undergoes reductive elimination to release Ar-Ar, while restoring the starting $PPh_3Au^{I}L$ catalyst (path d) [9.30]. The intermediacy of an aryl radical was ascertained by an experiment carried out in the presence of TEMPO (0.05 M), showing a significant lowering of the biphenyl yield (from 75% to 29% in the case of **9.2**). As for the role of the cocatalyst, bis-pyridyl and phenanthryl ligands have been frequently adopted as beneficial additive in Au-mediated photo- and electrochemical coupling reactions [9.31]. Although a conclusive answer on the real role of pyridine-based additives in Au(I)-mediated processes was not completely ascertained to date, their role as stabilizing agents of the high-oxidation state gold complexes has been postulated. In the field of light driven processes, the present Au catalyzed homocoupling results competitive in terms of efficiency and feasibility, with the other approaches already reported in literature.The use of an easily available Au complex and the absence of redox agent, characterize the present procedure.



Scheme 9.4. Proposed Mechanism.

9.3. CONCLUSIONS.

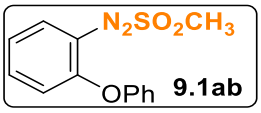
We presented herein the first visible light/Au(I)-catalysed protocol for the preparation of symmetrical (hetero)biaryls by homocoupling of arylazo sulfones at room temperature inorganic/aqueous media. The method exploits the properties of the $N_2SO_2CH_3$ moiety as a dyedauxiliary group able to be activated directly with visible light without the intermediacy of a photocatalyst and exhibits an excellent functional group tolerance. The strategy has been exploited for the preparation of a wide range of symmetrical (hetero)biaryls in good to excellent yields with an easy setup.

9.4. EXPERIMENTAL SECTION.

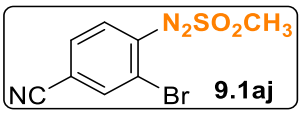
General informations. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a 300 MHz e 75 MHz spectrometer, respectively. The attributions were made on the basis of ^{1}H and ^{13}C NMR experiments; chemical shifts are reported in ppm downfield from TMS. GC analyses were performed using a HP SERIES 5890 II equipped with a fire ion detector (FID, temperature 350 °C). Analytes were separated using a Restek Rtx-5MS (30 m×0.25 mm×0.25 μm) capillary column with nitrogen as a carrier gas

at 1 ml min^{-1}. The injector temperature was 250 °C. The GC oven< temperature was held at 80 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1}, and held for 10 min.

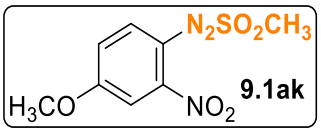
General Procedure for the Synthesis of Arylazo Sulfones 9.1a-9.1ap. Arylazo sulfones used in this work (Figure 9.1) were already synthesized from previous works and present in the laboratory. Following a known literature procedure, compounds **9.1ab**, **9.1aj**, **9.1ak**, **9.1am** were prepared [9.26]



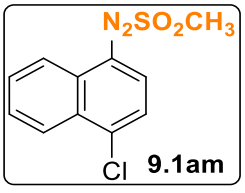
1-(Methylsulfonyl)-2-(2-phenoxyphenyl)diazene (9.1ab). (orange solid, 56% yield, m.p. (decomposition) = 87–88°C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.2, 1.7 Hz, 1H), 7.67–7.61 (m, 1H), 7.40–7.32 (m, 2H), 7.29–7.23 (m, 1H), 7.21–7.12 (m, 2H), 7.10–6.99 (m, 2H), 2.86 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 157.9, 157.0, 139.8, 137.3, 130.2, 124.3, 124.0, 121.3, 118.5, 118.1, 34.1. HRMS (ESI) *m/z*: calcd for $C_{13}H_{12}N_2O_3S^+$ ([M + H]$^+$) 299.0442; found 299.0461.



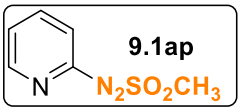
3-Bromo-4-((methylsulfonyl)diazenyl)benzonitrile (9.1aj). (Orange solid, 69% yield, m.p. (decomposition) = 132–132.5°C). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.36–7.93 (m, 1H), 7.82–7.76 (m, 2H), 3.27 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 148.6, 138.1, 132.2, 128.0, 119.2, 119.1, 116.2, 35.1. HRMS (ESI) *m/z*: calcd for $C_8H_6N_3O_2SBr^+$ ([M + H]$^+$) 287.9442; found 287.9425.



1-(4-Methoxy-2-nitrophenyl)-2-(methylsulfonyl)diazene (9.1ak) (Orange solid, 54% yield, m.p. (decomposition) = 95–97°C). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 9.1 Hz, 1H), 7.45 (d, J = 2.7 Hz, 1H), 7.34–7.13 (m, 2H), 4.03 (s, 3H), 3.16 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 165.20, 134.47, 119.71, 119.06, 109.69, 56.89. HRMS (ESI) *m/z*: calcd for $C_8H_6N_3O_2SBr^+$ ([M + H]$^+$) 286.9364; found 286.9347.



1-(4-Chloronaphthalen-1-yl)-2-(methylsulfonyl)diazene (9.1am) (Orange solid, 34% yield, m.p. (decomposition) = 125–127°C). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.76–8.49 (m, 1H), 8.42–8.18 (m, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.77–7.67 (m, 2H), 7.62 (d, J = 8.3 Hz, 1H), 3.33 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.7, 140.7, 132.4, 131.5, 129.4, 128.5, 126.1, 125.0, 123.0, 114.4, 35.4. HRMS (ESI) *m/z* calcd for $C_{11}H_9N_2O_2SCl^+$ ([M + H]$^+$) 269.0152; found 269.0158.



Procedure for the preparation of 2-((Methylsulfonyl)diazenyl)pyridine (9.1ap). *N*'-(pyridin-2-yl)methanesulfonohydrazide was initially prepared by mixing 2-hydrazinylpyridine (0.300 g, 2.7 mmol) and methanesulfonyl chloride (0.212 mL, 2.7 mmol) in 3 mL of pyridine (37.4 mmol) as previously described [9.32]. The crude mixture containing The sulfonohydrazide was oxidized by treatment with *N*-bromosuccinimide (0.475 g, 2.7 mmol) following a known procedure[41] to give **9.1ap** as a yellow solid (134.7 mg, 0.72 mmol, 26% yield, m.p. (decomposition) = 72–73°C). **(9.1ap).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91–8.64 (m, 1H), 8.01 (td, J = 7.6, 1.8 Hz, 1H), 7.94 – 7.85 (m, 1H), 7.59 (ddd, J = 7.4, 4.6, 1.3 Hz, 1H), 3.29 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 150.3, 139.8, 139.3, 118.3, 117.7, 43.0. HRMS (EsI) *m/z* calcd for $C_6H_7N_3O_2S^+$ ([M + H^+]) 186.0337; found 186.0392.

General Procedure for the photochemical synthesis of biaryls. A pyrex glass vessel was charged with the chosen arylazo sulfone (**9.1a-9.1ap**, 0.5 mmol, 1.0 equiv, 0.1 M) and 40 mg of sodium bicarbonate (1.0 mmol, 0.2 M) and the solid was dissolved in degassed acetonitrile:water (9:1, 5.0 mL), then, triphenylphosphine gold (I) chloride (0.05 mmol, 10 mol%) and 1,10-phenanthroline (40 mol%, 0.04 M) were added and the obtained mixture flushed with Argon. Irradiation was carried out for 24 h by means of a 40 W Kessil lamp (emission at 427 nm, Figure 9.2). The photolyzed solution was concentrated under reduced pressure and purified by silica gel column chromatography (cyclohexane-ethyl acetate mixture as eluant).

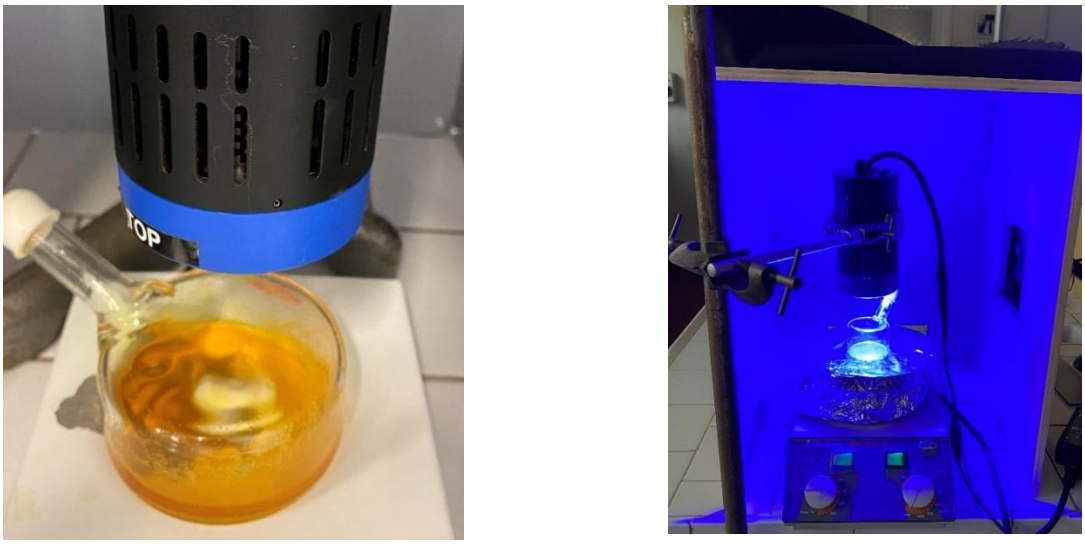
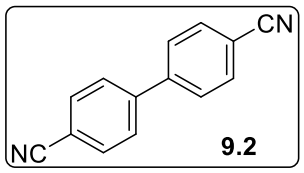
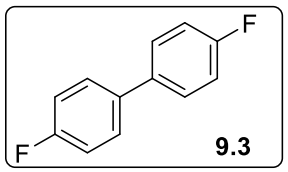


Figure 9.2. Irradiation system used in this work: A 40 W Kessil lamp (with emission centered at 427 nm) is held three centimetres above the glass reaction vessel which was stirred gently for 24 hours. A fan is placed on the right of the reaction vessel to avoid any heating of the solution.

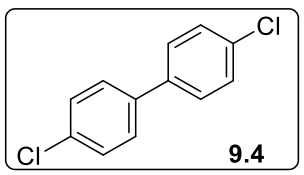
Procedure for the photochemical synthesis of biaryls 9.2 on large scale. A pyrex glass vessel was charged with the arylazo sulfone **9.1a (**2.36 mmol, 1.0 equiv, 0.1 M) and 400 mg of sodium bicarbonate (4.72 mmol, 2 equiv. 0.2 M) and the solid was dissolved in degassed acetonitrile:water (9:1, 24.0 mL), then, 118.2 mg of triphenylphosphine gold (I) chloride (0.24 mmol, 10 mol%) and 187 mg of 1,10-phenanthroline (40 mol%) were added and the obtained mixture flushed with Argon. Irradiation was carried out for 24 h by means of a 40 W Kessil lamp (emission at 427 nm). The photolyzed solution was concentrated under reduced pressure and purified by silica gel column chromatography (cyclohexane-ethyl acetate 95:5 mixture as eluant). The product **9.2** was obtained as a pale-yellow solid in 70% yield (337 mg, 1.66 mmol).



[1,1'-Biphenyl]-4,4'-dicarbonitrile (9.2). From 104.5 mg (0.500 mmol) of **9.1a**, 25.0 mg (0.05 mol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.1 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 38.3 mg of **9.2** (75% yield, white solid, m.p. = 233–234 °C). Spectroscopic data were in accordance with the literature data [9.33]. When the reaction was carried out in the presence of TEMPO (0.1 M), product **9.2** was obtained in only 29% yield. (**9.2**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 4H), 7.71 (d, J = 8.5 Hz, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 143.7, 133.07, 128.1, 118.5, 112.6.

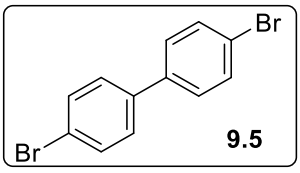


4,4'-Difluoro-1,1'-biphenyl (9.3). From 101.0 mg (0.500 mmol) of **9.1b**, 25.0 mg (0.05 mol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 47.5 mg of **9.3** (> 99% yield, white solid, m.p. = 93–95°C). Spectroscopic data were in accordance with the literature data [9.33]. (**9.3**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.40 (m, 2H), 7.39 (s, 2H), 7.32–7.25 (m, 2H), 7.14–7.05 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 164.6 (d, J = 244.5 Hz), 137.0 (d, J = 3 Hz), 129.2 (d, J = 8.3 Hz), 116.4 (d, J = 21.8 Hz).

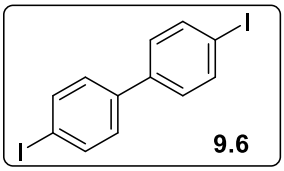


4,4'-Dichloro-1,1'-biphenyl (9.4). From 109.7 mg (0.501 mmol) of **9.1c**, 25.0 mg (0.05 mol, 10 mol%) of $(PPh_3)AuCl$, 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica

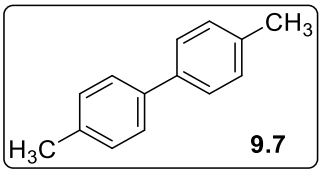
gel chromatographic column (eluant: neat cyclohexane) to afford 26.8 mg of **9.4** (48% yield, white solid, m.p. = 145–146°C). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) gave **9.4** in 93% yield. Spectroscopic data were in accordance with the literature data [9.33]. (**9.4**). ^1H NMR (300 MHz, $CDCl_3$) δ 7.52–7.46 (m, 4H), 7.46–7.40 (m, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 138.3, 133.6, 128.9, 128.1.



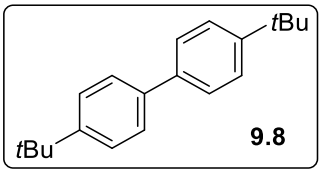
4,4'-Dibromo-1,1'-biphenyl (9.5). From 132.5 mg (0.502 mmol) of **9.1d**, 25.0 mg (0.05 mol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 50.9 mg of **9.5** (65% yield, slightly orange solid, m.p. = 165–166°C). Spectroscopic data were in accordance with the literature data [9.33]. (**9.5**). ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 8.6 Hz, 4H), 7.43 (d, J = 8.6 Hz, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 138.8, 131.9, 128.4, 121.9.



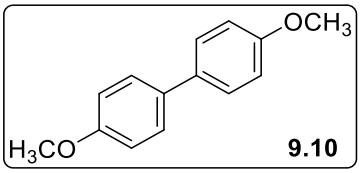
4,4'-Diiodo-1,1'-biphenyl (9.6). From 155.8 mg (0.502 mmol) of **9.1e**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 74.4 mg of **9.6** (73% yield, slightly yellow solid, m.p. = 202–203°C). Spectroscopic data were in accordance with the literature data [9.34]. (**9.6**).^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 8.6 Hz, 4H), 7.13 (d, J = 8.6 Hz, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 139.5, 138.2, 128.8, 93.6.



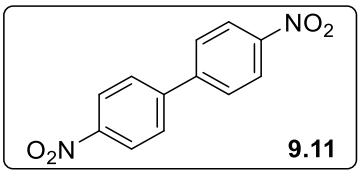
4,4'-Dimethyl-1,1'-biphenyl (9.7). From 90.0 mg (0.502 mmol) of **9.1f**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to affordm28.2 mg of **9.7** (71% yield, white solid, m.p. = 118–120°C). Spectroscopic data were in accordance with the literature data [9.35]. (**9.7**). ^1H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 8.1 Hz, 4H), 7.28 (d, J = 7.8 Hz, 4H), 2.43 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 138.2, 136.6, 129.3, 126.7, 21.0.



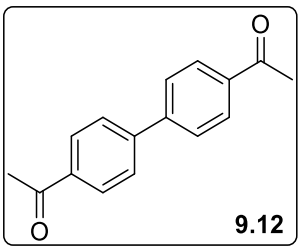
4,4'-Di-tert-butyl-1,1'-biphenyl (9.8). From 120.0 mg (0.500 mmol) of **9.1g**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 66.5 mg of **9.8** (quantitative yield, white solid, m.p. = 126–127 °C). Spectroscopic data were in accordance with the literature data [9.36]. (**9.8**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.50 (m, 4H), 7.49–7.43 (m, 4H), 1.37 (s, 18H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 150.1, 138.3, 126.8, 125.8, 34.6, 31.5.



4,4'-Dimethoxy-1,1'-biphenyl (9.10). From 119.5 mg (0.504 mmol) of **9.1i**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane:ethyl acetate 95:5) to afford 38.3 mg of **9.10** (71% yield, white solid, mp = 178–180°C). Spectroscopic data were in accordance with the literature data [9.35]. (**9.10).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 8.8 Hz, 4H), 6.97 (d, J = 8.8 Hz, 4H), 3.85 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.6, 133.4, 127.6,114.1, 55.2.

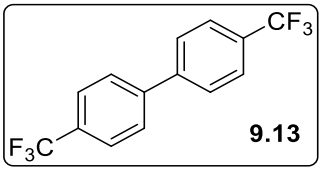


4,4'-Dinitro-1,1'-biphenyl (9.11). From 115.5 mg (0.502 mmol) of **9.1j**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 43.4 mg of **9.11** (71% yield, white solid, m.p. = 225–226°C) and 4.8 mg of 1,2-bis(4-nitrophenyl)diazene **9.11a** (7 % yield, red oil). Spectroscopic data were in accordance with the literature data [9.35]. **(9.11)**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 4H), 7.79 (d, J = 8.8 Hz, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.2, 145.1, 128.5, 124.5.

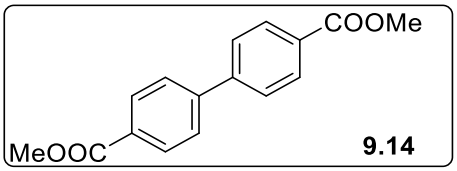


1,1'-([1,1'-Biphenyl]-4,4'-diyl)bis(ethan-1-one) (9.12). From 113.0 mg (0.500 mmol) of **9.1k**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$, 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane:

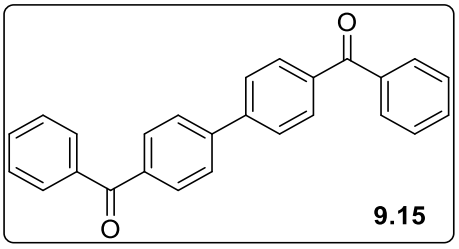
ethyl acetate 92:8) to afford 60.3 mg of **9.12** (> 99% yield, white solid, m.p. = 187–189°C). Spectroscopic data were in accordance with the literature data [9.33]. **(9.12)**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 4H), 7.71 (d, J = 8.5 Hz, 4H), 2.64 (s, 6H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 197.5, 144.2, 136.5, 128.9, 127.3, 26.6.



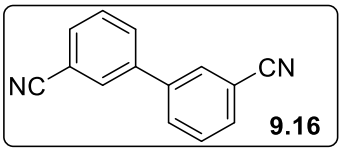
4,4'-Bis(trifluoromethyl)-1,1'-biphenyl (9.13). From 127.3 mg (0.500 mmol) of **9.1l**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane) to afford 45.0 mg of **9.13** (62% yield, white solid, m.p. = 85–87°C). Spectroscopic data were in accordance with the literature data [9.33]. **(9.13)**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83–7.58 (m, 8H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 143.4, 130.7 (q, J = 32.3 Hz), 127.8, 126.2 (q, J = 3.8 Hz), 123.5 (q, J = 270 Hz).



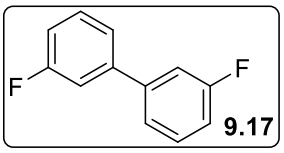
Dimethyl [1,1'-biphenyl]-4,4'-dicarboxylate (9.14). From 121.7 mg (0.500 mmol) of **9.1m**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: Cyclohexane:Ethyl acetate 9:1) to afford 57.8 mg of **9.14** (85% yield, white solid, m.p. = 215–216°C). Spectroscopic data were in accordance with the literature data [9.33]. **(9.14)**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, J = 8.3 Hz, 4H), 7.69 (d, J = 8.3 Hz, 4H), 3.95 (s, 6H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 167.4, 144.9, 130.8, 130.3, 127.8, 52.8.



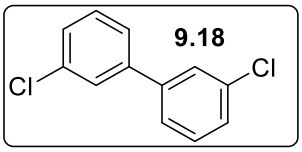
[1,1'-Biphenyl]-4,4'-diylbis(phenylmethanone) (9.15). From 144.0 mg (0.500 mmol) of **9.1n**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat Cyclohexane) to afford 75.2 mg of **9.15** (83% yield, slightly yellow solid, m.p. = 215–216 °C). Spectroscopic data were in accordance with the literature data [9.37]. **(9.15)**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 8.3 Hz, 4H), 7.87–7.82 (m, 4H), 7.77 (d, J = 8.3 Hz, 4H), 7.65 – 7.59 (m, 2H), 7.52 (dd, J = 8.2, 6.8 Hz, 4H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 196.3, 144.0, 137.7, 137.2, 132.7, 130.9, 130.2, 128.5, 127.3.



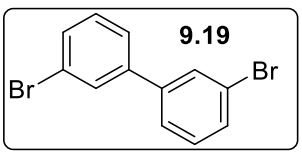
[1,1'-Biphenyl]-3,3'-dicarbonitrile (9.16). From 104.5 mg (0.500 mmol) of **9.1o**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate 95:5) to afford 40.8 mg of **9.16** (80% yield, white solid, m.p. = 190–192 °C). Spectroscopic data were in accordance with the literature data [9.33]. (**9.16**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90–7.75 (m, 4H), 7.71 (d, J = 7.7 Hz, 2H), 7.61 (t, J = 7.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 140.3, 131.9, 131.6, 130.8, 130.2, 118.5, 113.7.



3,3'-Difluoro-1,1'-biphenyl (9.17). From 101.0 mg (0.500 mmol) of **9.1p**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 29.8 mg of **9.17** (63% yield, colourless oil). Spectroscopic data were in accordance with literature data [9.38]. **(9.17)**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.34 (m, 4H), 7.29 (dt, J = 10.1, 2.1 Hz, 2H), 7.19–6.92 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 164.5 (d, J = 244.5 Hz), 142.0 (q, J = 3.8 Hz), 130.2 (d, J = 8.3 Hz), 122.5 (d, J = 3 Hz), 114.5 (d, J = 21 Hz), 113.9 (d, J = 22.5 Hz).

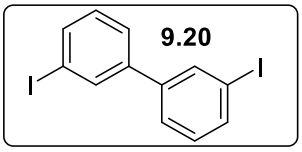


3,3'-Dichloro-1,1'-biphenyl (9.18). From 108.5 mg (0.500 mmol) of **9.1q**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 35.8 mg of **9.18** (65% yield, slightly orange oil). Spectroscopic data were in accordance with the literature data [9.33]. (**9.18**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 1.7 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.38–7.33 (m, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 141.8, 135.0, 130.3, 128.0, 127.4, 125.4.

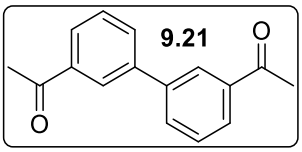


3,3'-Dibromo-1,1'-biphenyl (9.19). From 132.3 mg (0.501 mmol) of **9.1r**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 56.6 mg of **9.19** (73% yield, white solid, m.p. = 52–54°C). Spectroscopic data were in accordance with literature data [9.39]. (**9.19**). ^{1}H NMR (300 MHz,

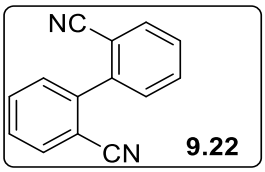
$CDCl_3$) δ 7.72 (t, *J* = 1.9 Hz, 1H), 7.51 (ddt, *J* = 9.7, 7.9, 1.1 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 141.9, 131.0, 130.5, 130.3, 125.9, 123.1.



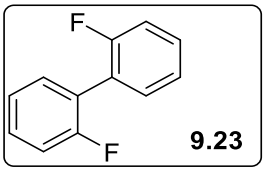
3,3'-Diiodo-1,1'-biphenyl (9.20). From 155.4 mg (0.501 mmol) of **9.1s**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 54.8 mg of **9.20** (54% yield, white solid, m.p. = 73–74°C). Spectroscopic data were in accordance with the literature data [9.40]. **(9.20)**. ^1H NMR (300 MHz, $CDCl_3$) *δ* 8.00 (d, *J* = 54.4 Hz, 1H), 7.73–7.64 (m, 1H), 7.59–7.47 (m, 1H), 7.19 (t, *J* = 7.9 Hz, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) *δ* 135.7, 131.3, 130.2, 126.1, 94.5.



1,1'-([1,1'-Biphenyl]-3,3'-diyl)bis(ethan-1-one) (9.21). From 113.0 mg (0.500 mmol) of **9.1t**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate 92:8) to afford 59.5 mg of **9.21** (> 99% yield, white solid, m.p. = 125–126°C). Spectroscopic data were in accordance with the literature data [9.39]. (**9.21**). ^1H NMR (300 MHz, $CDCl_3$) *δ* 8.19 (t, *J* = 1.8 Hz, 2H), 7.96 (m, *J* = 7.7, 1.8, 1.1 Hz, 2H), 7.81 (m, *J* = 7.7, 1.9, 1.1 Hz, 2H), 7.56 (t, *J* = 7.7 Hz, 2H), 2.66 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) *δ* 198.0, 140.8, 137.9, 131.9, 129.3, 127.9, 127.0, 26.9.

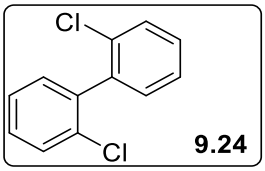


[1,1'-Biphenyl]-2,2'-dicarbonitrile (9.22). From 104.5 mg (0.500 mmol) of **9.1u**, 25.0 mg (0.05 mmol, 10 mmol%) of $(PPh_3)AuCl$, 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane: ethyl acetate 95:5) to afford 37.7 mg of **9.22** (74% yield, white solid, m.p. = 171–173°C). Spectroscopic data were in accordance with the literature data [9.41]. **(9.22)**. ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.87–7.80 (m, 2H), 7.75–7.69 (m, 2H), 7.62–7.55 (m, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) *δ* 141.3, 133.3, 132.6, 130.3, 128.9, 117.2, 112.1.

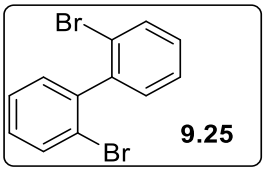


2,2'-Difluoro-1,1'-biphenyl (9.23). From 102.0 mg (0.502 mmol) of **9.1v**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of

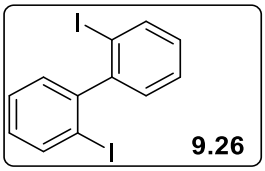
degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 40.6 mg of **9.23** (85% yield, white solid, m.p. = 116–118°C). Spectroscopic data were in accordance with the literature data [9.38]. (**9.23**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (dddd, J = 10.6, 7.9, 4.9, 2.3 Hz, 4H), 7.31–7.16 (m, 4H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 161.2, 157.9, 131.3 (t, J = 2.3 Hz), 129.5 (t, J = 4.5 Hz), 123.8 (t, J = 2.3 Hz), 115.6 (q, J = 7.5 Hz).



2,2'-Dichloro-1,1'-biphenyl (9.24). From 108.5 mg (0.500 mmol) of **9.1w**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 24.8 mg of **9.24** (45% yield, white solid, m.p. = 60–61°C). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) afforded **9.24** in 83% yield. Spectroscopic data were in accordance with the literature data [9.33]. (**9.24**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.46 (m, 2H), 7.40–7.33 (m, 4H), 7.31–7.26 (m, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 139.0, 134.1, 131.8, 130.0, 129.8, 127.1.

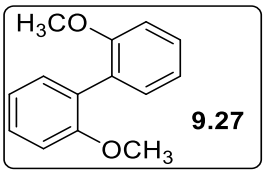


2,2'-Dibromo-1,1'-biphenyl (9.25). From 130.8 mg (0.500 mmol) of **9.1x**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 36.5 mg of **9.25** (45% yield, white solid, m.p. = 77–79 °C). The same reaction performed with 34.9 mg of $(PPh_3)AuCl$ (15 mol%) gave **9.25** in 57% yield. Spectroscopic data were in accordance with the literature data [9.42]. **(9.25)**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72–7.67 (m, 2H), 7.42–7.37 (m, 2H), 7.31–7.26 (m, 4H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 142.6, 133.1, 131.5, 129.9, 127.7, 124.1.



2,2'-Diiodo-1,1'-biphenyl (9.26). From 155.0 mg (0.501 mmol) of **9.1y**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 35.6 mg of **9.26** (35% yield, white solid, m.p. = 109–112 °C). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) afforded **9.26** in 79% yield. Spectroscopic data were in accordance with the literature data [9.42]. **(9.26)**. ^{1}H

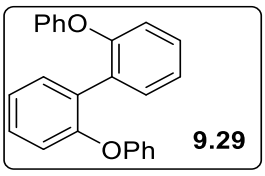
NMR (300 MHz, $CDCl_3$) δ 7.95 (dd, J = 8.0, 1.2 Hz, 2H), 7.41 (dd, J = 7.5, 1.2 Hz, 2H), 7.20 (dd, J = 7.6, 1.7 Hz, 2H), 7.09 (td, J = 7.7, 1.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 149.1, 139.0, 130.0, 129.5, 128.2, 99.8.



9.27

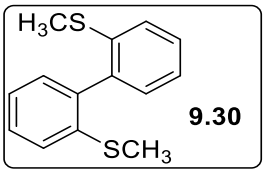
2,2'-Dimethoxy-1,1'-biphenyl (9.27). From 118.0 mg (0.500 mmol) of **9.1z**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 28.8 mg of **9.27** (54% yield, white solid, m.p. = 154–156 °C). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) gave **9.27** in 97% yield. Spectroscopic data were in accordance with the literature data [9.36]. (**9.27**). ^1H NMR (300 MHz, $CDCl_3$) δ 7.37 (ddd, J = 8.2, 7.4, 1.8 Hz, 2H), 7.29 (dd, J = 7.4, 1.9 Hz, 2H), 7.11–6.92 (m, 4H), 3.81 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 157.2, 131.6, 128.7, 128.0, 120.5, 111.2, 55.8.

Irradiation of 1-(methylsulfonyl)-2-(2-nitrophenyl)diazene (9.1aa). From 114.5 mg (0.500 mmol) of **9.1aa**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 61.5 mg of nitrobenzene (yellow solid, quantitative yield).

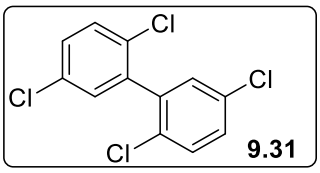


9.29

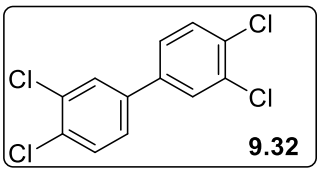
2,2'-Diphenoxy-1,1'-biphenyl (9.29). From 139.0 mg (0.500 mmol) of **9.1ab**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: Cyclohexane) to afford 19.6 mg of **9.29** (24% yield, white solid, m.p. = 100–102 °C). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) gave **9.29** in 58% yield. Spectroscopic data were in accordance with the literature data [9.43]. (**9.29**). ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (dd, J = 7.6, 1.8 Hz, 2H), 7.34–7.12 (m, 9H), 7.06–7.00 (m, 2H), 6.96–6.87 (m, 5H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 157.6, 154.8, 132.1, 129.9, 129.5, 128.9, 123.2, 122.8, 118.9, 118.8.



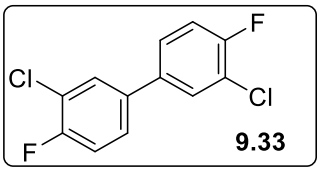
2,2'-Bis(methylthio)-1,1'-biphenyl (9.30). From 115.0 mg (0.500 mmol) of **9.1ac**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: Cyclohexane) to afford 32.6 mg of **9.30** (53% yield, white solid, m.p. = 45–46°C). Spectroscopic data were in accordance with the literature data [9.39]. (**9.30**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48–7.39 (m, 2H), 7.33 (d, J = 7.2 Hz, 2H), 7.28–7.15 (m, 4H), 2.41 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 138.5, 137.8, 129.7, 128.2, 124.7, 124.2, 15.4.



2,2',5,5'-Tetrachloro-1,1'-biphenyl (9.31). From 126.0 mg (0.500 mmol) of **9.1ad**, 25.0 mg (0.05 mol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 69.6 mg of **9.31** (96% yield, white solid, m.p. = 65–66 °C). Spectroscopic data were in accordance with the literature data [9.39]. (**9.31**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (s, 2H), 7.36 (dd, J = 8.6, 2.5 Hz, 2H), 7.28 (d, J = 2.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 138.2, 132.2, 131.5, 130.6, 130.4, 129.4.

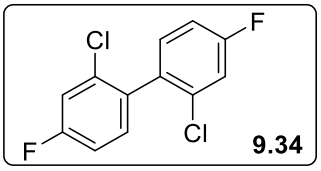


3,3',4,4'-Tetrachloro-1,1'-biphenyl (9.32). From 126.0 mg (0.500 mmol) of **9.1ae** 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 42.8 mg of **9.32** (59% yield, white solid, m.p. = 172–173 °C). Spectroscopic data were in accordance with the literature data [9.33]. (**9.32**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, J = 2.2 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.36 (dd, J = 8.4, 2.2 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 138.9, 133.4, 132.6, 131.1, 128.9, 126.3.

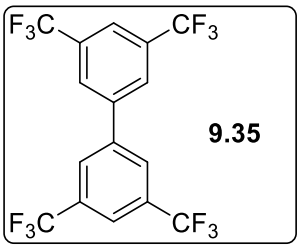


3,3'-Dichloro-4,4'-difluoro-1,1'-biphenyl (9.33). From 119.2 mg (0.500 mmol) of **9.1af**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 54.2 mg of **9.33** (83% yield, white solid, m.p. = 139–141 °C). Spectroscopic data were in accordance with literature

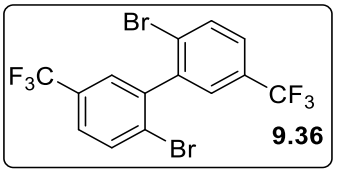
data [9.44]. (**9.33**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, J = 6.9, 2.4 Hz, 2H), 7.38 (ddd, J = 8.5, 4.5, 2.4 Hz, 2H), 7.23 (dd, J = 9.5, 7.7 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 159.7 (d, J = 249 Hz), 136.4 (d, J = 3.8 Hz), 129.3, 126.9 (d, J = 7.5 Hz), 121.8 (d, J = 18 Hz), 117.3 (d, J = 21 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.0.



2,2'-Dichloro-4,4'-difluoro-1,1'-biphenyl (9.34). From 118.9 mg (0.500 mmol) of **9.1ag**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 20.5 mg of **9.34** (31% yield, colourless liquid). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) gave **9.34** in 58% yield. Spectroscopic data were in accordance with the literature data [9.45]. (**9.34**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29–7.21 (m, 4H), 7.08 (td, J = 8.3, 2.6 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 164.0 (d, J = 249 Hz), 134.8 (d, J = 9.8 Hz), 133.7 (d, J = 3.0 Hz), 132.6 (d, J = 9.0 Hz), 114.3 (d, J = 21 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.4.

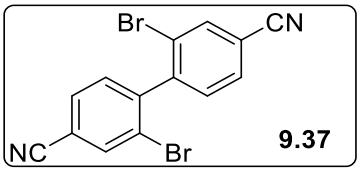


3,3',5,5'-Tetrakis(trifluoromethyl)-1,1'-biphenyl (9.35). From 171.0 mg (0.501 mmol) of **9.1ah**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mmol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 37.6 mg of **9.35** (32 % yield, white solid, m.p. = 79–81°C). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) gave **9.35** in 58% yield. Spectroscopic data were in accordance with the literature data [9.33]. (**9.35**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J = 12.4 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 140.6, 133.8 (q, J = 33.8 Hz), 128.6 (q, J = 272 Hz), 127.7 (d, J = 3.0 Hz), 122.9 (m, J = 3.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3.



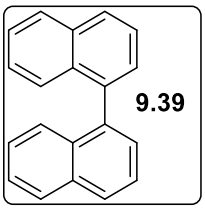
2,2'-Dibromo-5,5'-bis(trifluoromethyl)-1,1'-biphenyl (9.36). From 177.0 mg (0.504 mmol) of **9.1ai**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 36.9 mg of **9.36** (30% yield, pale yellow solid, m.p. = 98–100°C). The same reaction performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) gave **9.36** in 90% yield.

Spectroscopic data were in accordance with the literature data [9.46]. (**9.36**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 – 7.76 (m, 4H), 7.57 (dd, J = 8.3, 2.3 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 138.3, 135.9, 131.8 (q, J = 31.5 Hz), 128.3 (q, J = 272 Hz), 126.5 (q, J = 6.8 Hz), 120.3 (q, J = 1.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2.

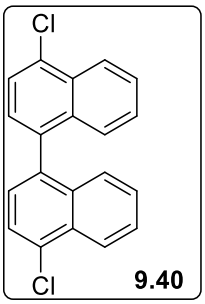


2,2'-Dibromo-[1,1'-biphenyl]-4,4'-dicarbonitrile (9.37). From 144.5 mg (0.500 mmol) of **9.1aj**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: cyclohexane:ethyl acetate 9:1) to afford 40.8 mg of **9.37** (56% yield, pale orange solid, m.p. = 180–183°C). (**9.37**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.5 Hz, 2H), 7.74–7.70 (m, 2H), 7.34 (d, J = 7.9 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 145.2, 136.3, 131.2, 123.7, 117.3, 116.9, 114.5. HRMS (ESI) *m/z* calcd for $C_{14}H_6N_2Br_2^+$ ($[M + H]^+$) 360.8970; found 360.8947.

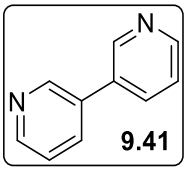
Irradiation of 1-(4-methoxy-2-nitrophenyl)-2-(methylsulfonyl)diazene (9.1ak). From 129.6 mg (0.5 mmol) of **9.1ak**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 53.6 mg of 3-nitroanisole (70% yield).



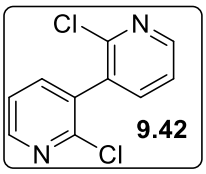
1,1'-Binaphthalene (9.39). From 117.1 mg (0.500 mmol) of **9.1al**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 62.6 mg of **9.39** (99% yield, white solid, m.p. = 159–161°C). Spectroscopic data were in accordance with the literature data [9.33]. (**9.39**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (ddd, J = 8.3, 3.1, 1.4 Hz, 2H), 7.63 (dd, J = 8.2, 7.0 Hz, 1H), 7.52 (ddt, J = 8.2, 6.8, 3.1 Hz, 2H), 7.43 (dd, J = 8.6, 1.2 Hz, 1H), 7.35 – 7.27 (m, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 138.3, 133.4, 132.7, 128.0, 127.8, 127.7, 126.4, 125.9, 125.7, 125.3.



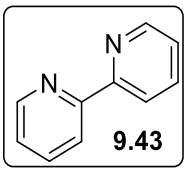
4,4'-Dichloro-1,1'-binaphthalene (9.40). From 135.6 mg (0.501 mmol) of **9.1am**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: neat cyclohexane) to afford 81.4 mg of **9.40** (99 % yield, red solid, m.p. = 217–218 °C). Spectroscopic data were in accordance with the literature data [9.47]. (**9.40**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 7.6 Hz, 2H), 7.67 – 7.52 (m, 4H), 7.38–7.35 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 137.1, 134.0, 132.2, 130.9, 127.9, 127.2, 127.0, 125.8, 124.9.



3,3'-Bipyridine (9.41). From 92.51 mg (0.500 mmol) of **9.1an**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: Cyclohexane: ethyl acetate 3:7) to afford 74.1 mg of **9.41** (94% yield, slightly yellow solid, m.p. = 64–66 °C). Spectroscopic data were in accordance with the literature data [9.48]. (**9.41**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (d, J = 2.4 Hz, 2H), 8.67 (dd, J = 4.9, 1.6 Hz, 2H), 7.91 (dt, J = 7.9, 2.0 Hz, 2H), 7.44 (dd, J = 7.9, 4.8 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 149.3, 148.1, 134.8, 133.7, 124.0.



2,2'-Dichloro-3,3'-bipyridine (9.42). From 109.5 mg (0.500 mmol) of **9.1ao**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: Cyclohexane:ethyl acetate 7:3) to afford 56.0 mg of **9.42** (>99% yield, slightly yellow solid, m.p. = 202–204 °C). Spectroscopic data were in accordance with the literature data [9.49]. (**9.42**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (dd, J = 4.8, 1.9 Hz, 2H), 7.67 (dd, J = 7.6, 1.9 Hz, 2H), 7.47–7.36 (m, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 150.4, 149.9, 140.0, 133.0, 122.5.



2,2'-Bipyridine (9.43). From 92.50 mg (0.500 mmol) of **9.1ap**, 25.0 mg (0.05 mmol, 10 mol%) of $(PPh_3)AuCl$**,** 40.0 mg of $NaHCO_3$ (1.0 mmol) and 40.0 mg of 1,10-phenanthroline (0.2 mmol, 40 mol%) in 5 mL of degassed acetonitrile:water (9:1). Purification was carried out by silica gel chromatographic column (eluant: Cyclohexane:ethyl acetate 3:7) to afford 38.6 mg of **9.43** (49% yield, slightly yellow solid, m.p. = 70–71 °C). The same reaction was performed with 37.5 mg of $(PPh_3)AuCl$ (15 mol%) and afforded

9.43 in 86% yield. Spectroscopic data were in accordance with the literature data [9.50]. (**9.43**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69–8.65 (m, 2H), 8.40 (dd, J = 8.0, 1.2 Hz, 2H), 7.81 (td, J = 7.8, 1.8 Hz, 2H), 7.29 (ddd, J = 7.5, 4.8, 1.2 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 156.0, 149.2, 137.1, 123.9, 121.3.

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CHAPTER 10

SYNTHESIS OF ARYL THIOCYANATES VIA VISIBLE LIGHT ACTIVATION OF ARYLAZO SULFONES.

10.1. INTRODUCTION.

Aryl thiocyanates are widely spread molecules bearing a functional group (aryl chalcogen atom bond bearing thiocyanides) that could be exploited to access a large variety of functional groups [10.1,10.2]. The investigations and interest in this class of molecules is due to their significant biological properties, including antifungal, antibacterial and even anticancer activity (some examples in Figure 10.1) [10.3-10.4].

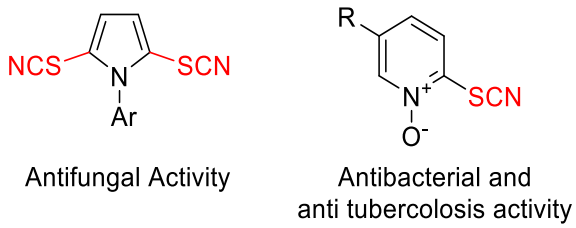
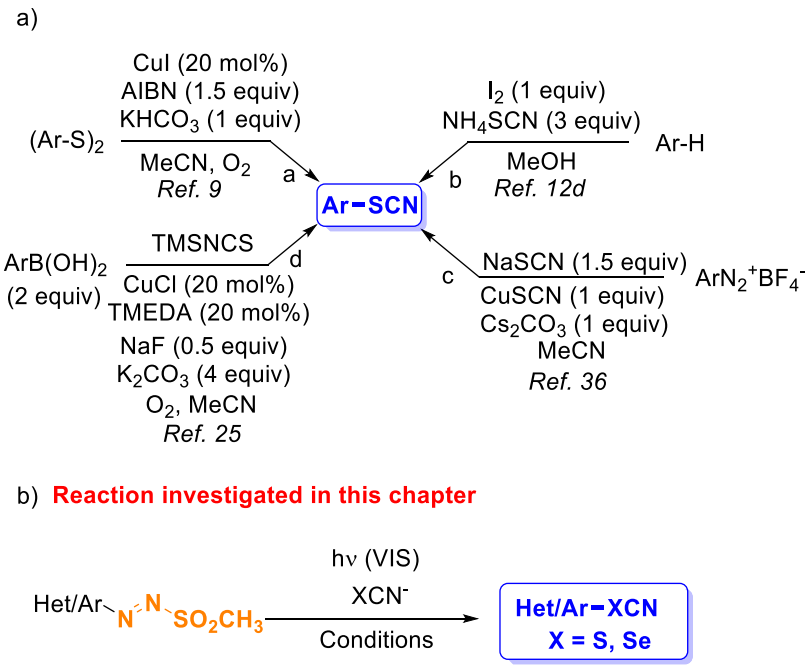


Figure 10.1. Bioactive aryl thiocyanates.

Several strategies to prepare Ar-SCN bearing molecules have been proposed, that, in accordance with literature [10.1,10.2], could be divided into three main classes, specifically a) the reaction of a sulphur containing (hetero)aromatic with a cyanating agent including azobisisobutyronitrile (AIBN, Scheme 10.1a, path a) [10.1,10.2,10.5], the activation of an Ar-H bond with a thiocyanating agent (path b) [10.6], a nucleophilic substitution occurring on an arene bearing a leaving group in the presence of a SCN^- anion (paths c,d) [10.1,10.2]. For what concerns strategy b, the SCN^- (mostly an ammonium or potassium salt) is oxidized (e.g. by halogen derivatives like selctfluor and trichloroisocyanuric acid, hypervaent iodine reagents, iodine, oxone, cerium salts, $K_2S_2O_8$ or azoderivatives) to form $^{\bullet}SCN$ radical as the key reacting species [10.7]. Regarding this topic, to achieve a milder generation of the radical $^{\bullet}SCN$, visible light photoredox catalysis [10.8]. Which exploits organic dyes (e.g. rose Bengal, eosin Y) or a semiconductor [10.9] as the photooxidant. However, in most cases such procedures exhibit a limited scope and regioselectivity; these are mainly applied to the functionalization of nitrogen-based heterocycles [10.6] and electron-rich aromatics [10.7]. As concerning strategy c, aryl boronic acids are still considered as the elective substrates, that can be converted into the desired Ar-SCN via both transition metal catalyzed [10.10] and electrochemical [10.11] activation. On the other hand, arene diazonium salts have received significant attention in the past [10.12].



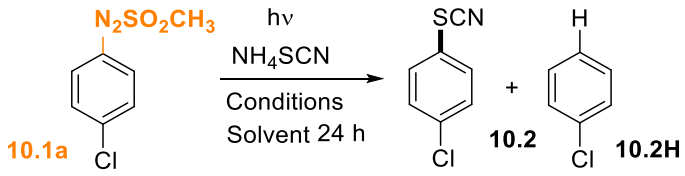
Scheme 10.1. a) Approaches proposed for the preparation of (hetero)aryl chalcogen cyanates b) Proposed strategy for the synthesis of (hetero)aryl chalcogen cyanates.

In the last decade, we have been involved in the design of an alternative arylation strategy [10.13] that makes use of compounds bearing *dyedauxiliary groups* (DGs). Such moieties impart both color and photoreactivity to the molecules to which are tethered by generating, under light irradiation, different reactive intermediates useful for synthesis [10.13]. In particular, arylazo sulfones, that are shelf stable derivatives of aryl diazonium salts bearing the $N_2SO_2CH_3$ dyedauxiliary group were found to be precursors of aryl radicals upon visible light irradiation and employed with success in a wide range of protocols for the formation of both C-C [10.14-10.15] and C-heteroatom bonds [10.16-10.17]. In view of such premises, we were intrigued to evaluate the synthetic potential of arylazo sulfones as precursors of aryl chalcogen cyanates under visible light driven conditions (Scheme 10.1, path d).

10.2. RESULTS AND DISCUSSION.

To test the feasibility of the hypotised protocol, we initially focused on the preparation of 1-chloro-4-thiocyanatobenzene **10.2** starting from arylazo sulfone **10.1a**. Ammonium thiocyanate (NH_4SCN) has been chosen as the "SCN" source, in view of its solubility in the examined media. After a screening of the reaction parameters, including solvent, concentrations of reactants, light source, and catalysts, the best reaction conditions were as follows: **10.1a** (0.25 mmol, 1 equiv), NH_4SCN (2 equiv.), $CuCl_2$ (10 mol%) in Ar-saturated MeCN (5 mL), irradiated for 24 h at 427 nm (light source: 40W Kessil Lamp). With the optimized conditions in our hand, the preparation of aryl thiocyanate **10.2** was carried out with 79% yield (Table 10.1), along with a small amount of chlorobenzene (**10.2H**, 4% yield). As pointed out in the data collected in Table 10.1, 427 nm was found as the optimal irradiation wavelength for the reaction investigated (entrtiy 1-3), whereas in the absence of $CuCl_2$ the process led to the formation of **10.2H** and **10.2** in very low yields (9% and 4%, respectively, entry 4). Increasing the quantity of NH_4SCN employed led to a less satisfactory results (entry 5) or doubling the concentration of **10.1a** (entry 6). The little amount of **10.2** observed in entries 7,8 pointed out the need for an argon atmosphere and a light source, respectively. Finally, the presence of the radical trap TEMPO (entry 9) was found to inhibit the formation of the desired product **10.2,** underlining once again the radical pathway involved in the product formation.

Table 10.1. Optimization of the photochemical synthesis of aryl thiocyanate **10.2**.



Entry	Conditions	Products (% yield)
1	**10.1a** (0.05M), NH_4SCN (2 equiv), MeCN, Ar, λ_{irr} = 456 nm	**10.2** (<5), **10.2H** (9)
2	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuCO_3$ (10 mol%), MeCN, Ar, λ_{irr} = 456 nm	**10.2** (45), **10.2H** (13)
3	**10.1a** (0.05M), NH_4SCN (2 equiv), Ar, $CuBr_2$ (10 mol%), MeCN, λ_{irr} = 456 nm	**10.2** (53), **10.2H** (9)
4	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuBr_2$ (10 mol%), MeCN-H_2O 9:1, Ar, λ_{irr} = 456 nm	[a]
5	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuBr_2$ (10 mol%), MeCN-H_2O 1:1, Ar, λ_{irr} = 456 nm	[a]
6	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuBr_2$ (10 mol%), MeOH, Ar, λ_{irr} = 456 nm	**10.2** (57), **10.2H** (29)
7	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuCl_2$ (10 mol%), MeCN, Ar, λ_{irr} = 456 nm	**10.2** (63), **10.2H** (12)
8	**10.1a** (0.05M), NH4SCN (4 equiv), $CuCl_2$ (10 mol%), MeCN, Ar, λ_{irr} = 456 nm	**10.2** (48), **10.2H** (9)
9	**10.1a** (0.1M), NH_4SCN (2 equiv), $CuCl_2$ (10 mol%), MeCN, Ar, λ_{irr} = 456 nm	**10.2** (66), **10.2H** (34)
10	**10.1a** (0.1M), NH_4SCN (2 equiv), $CuCl_2$ (5 mol%), MeCN, Ar, λ_{irr} = 456 nm	**10.2** (53), **10.2H** (28)
11	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuCl_2$ (10 mol%), MeCN, Ar, λ_{irr} = 427 nm	**10.2** (79), **10.2H** (4)
12	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuCl_2$ (10 mol%), MeCN, Ar, λ_{irr} = 390 nm	**10.2** (61), **10.2H** (13)
13	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuCl_2$ (10 mol%), MeCN, O_2	**10.2** (63), **10.2H** (11)
14	**10.1a** (0.05M), NH_4SCN (2 equiv), $CuCl_2$ (10 mol%), MeCN, Ar, no irradiation	**10.2** (22), **10.2H** (4)
15	**10.1a** (0.05M), TEMPO (1 equiv), NH_4SCN (2 equiv), $CuCl_2$ (10 mol%), MeCN, Ar, λ_{irr} = 456 nm	**10.2** (16), **10.2H** (7)

[a] A complex mixture of photoproducts was observed.

The best conditions found have been thus adopted and extended to differently substituted arylazo sulfones **10.1** and the obtained results have been resumed in Figure10.1

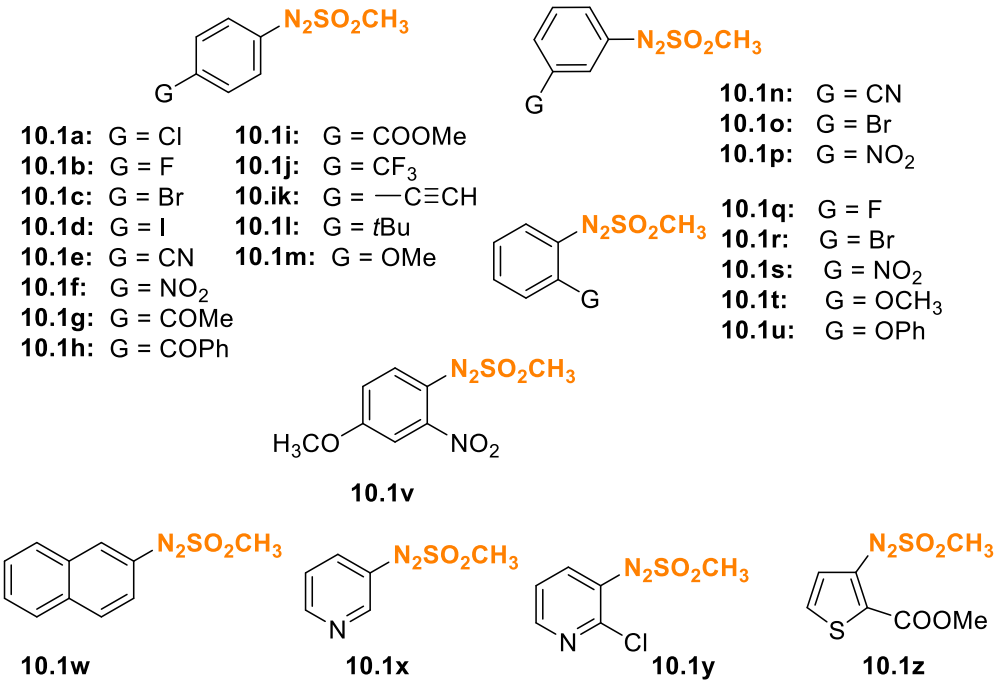
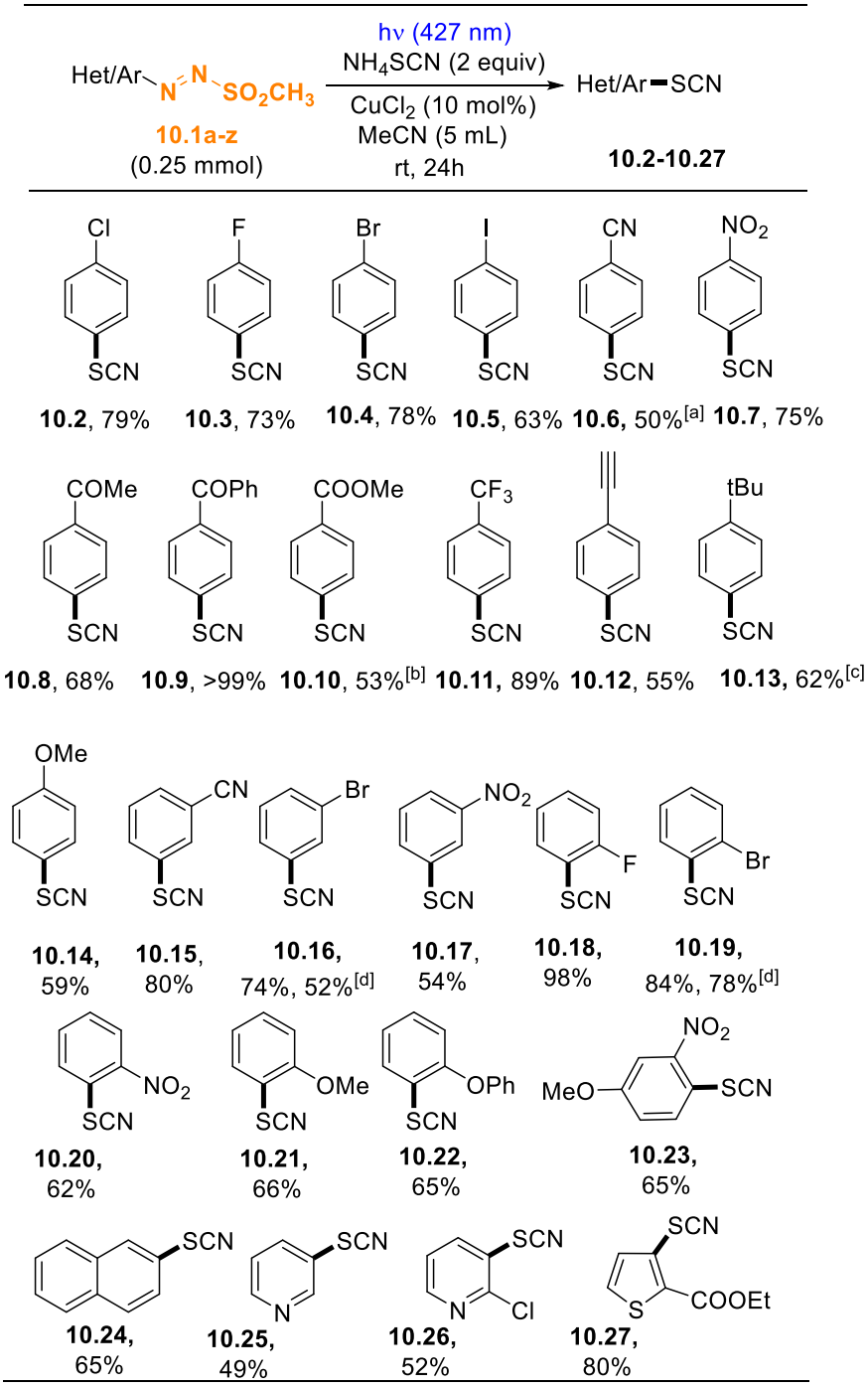


Figure 10.1. Arylazo sulfones employed in the present work.

The synthesis of aryl thiocyanates **10.2-10.27** was smoothly carried out in good to excellent fashion, the reaction was not dependant on the substitutuents tethered to the aromatic core of arylazo sulfones employed. In selected cases, the reaction was scaled up to 1 mmol (compound **10.16** and **10.19**). Furthermore, the simultaneous presence of electron-donating and electron-withdrawing groups does not affect the outcome of the reaction (see for instance compound **10.23**). This protocol was also extended to the preparation of different (hetero)aryl thiocyanates, for examples 2-thiocyanonaphthalene **10.24** and substituted pyridines **10.25**, **10.26** and thiophene **10.27** (Scheme 10.2).



Scheme 10.2. Scope of the photochemical synthesis of aryl thiocyanates starting from arylazo sulfones. [a.] Benzonitrile found as the by-product (12% GC yield); [b.] Methylbenzoate found as the by product (7% GC Yield); [c.] tButylbenzene found as the byproduct (10% GC yield); [d.] Reaction carried out on 1 mmol scale;

In view of these results, an investigation on the mechanism for the synthesis of aryl thiocyanates was performed in order to have a better overview on the pathways involved in the product formation. (Scheme 10.3). The Copper salt Cu^{II} acts as the precatalyst, with ammonium thiocyanate forms the corresponding $[Cu^{I}(SCN)_2]^-$ complex (**I**) [10.18]. The so-formed species is responsible for the visible-light absorption due to its absorption located in the the 400-600 nm region (Figure 10.2).

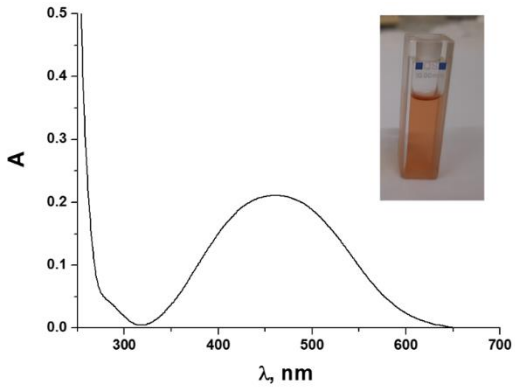


Figure 10.2. Absorption spectra of a $CuCl_2$ solution in MeCN (2×10^{-4} M) in the presence of NH_4SCN (4 equiv). Inset: Colour of the resulting $[Cu^{I}(SCN)_2]^-$ complex.

The application of Cu^{I} complexes both in photoredox catalysis [10.19] and in energy-transfer driven processes [10.20] has been discussed. In most cases, photoexcited copper(I)-based complexes are stronger reductant (E (Cu^{II}/Cu^{I*}) = -1.1 V vs SCE) than the excited states of $Ru/bpy)_3^{2+}$ (E (Ru^{III}/Ru^{II*}) = -0.81 V vs SCE) [10.21]. On the basis of the UV-absorption spectra and cyclic voltammetry analyses (see Figure 10.3-10.7) we estimated for $[CuI(SCN)_2]^-$ (**I**) a E ($\mathbf{I}^+/\mathbf{I}^*$) value of -1.58 V vs SCE. Thus, accordingly to what previously reported for other Cu^{I} based complexes [10.22], single electron transfer (SET) from the photoexcited **I*** complex to the arylazo sulfone **10.1** (E_{RED} (**10.1**/**10.1**$^{\bullet-}$) = ca. -0.9 V vs SCE, see also the redox diagram in Scheme 10.3b) [10.23] results in the formation of the corresponding radical anion **10.1**$^{\bullet-}$ that, following N_2 and $CH_3SO_2^-$ loss, releases an aryl radical (Ar$^{\bullet}$). Trapping of the latter intermediate by the Cu^{II}-based complex **II** and ensuing reductive elimination from **III** affords the desired products **10.2-10.27** while restoring the starting catalyst **I**.

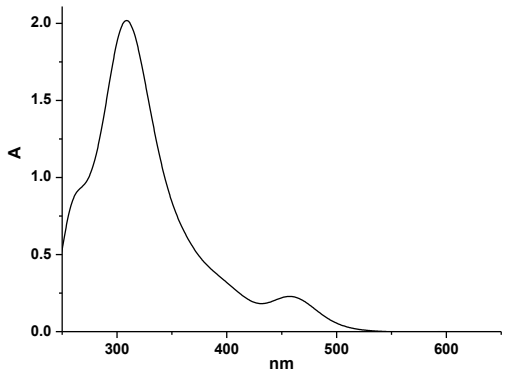


Figure 10.3. Absorption spectra of a solution of $CuCl_2$ (5×10^{-4} M) in MeCN.

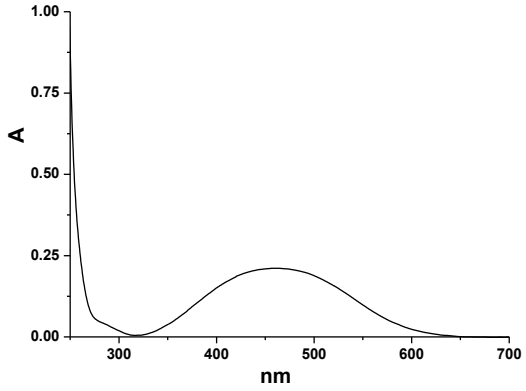


Figure 10.4. Absorption spectra of a solution of $CuCl_2$ (2×10^{-4}M) in MeCN in the presence of NH_4SCN (4 equiv).

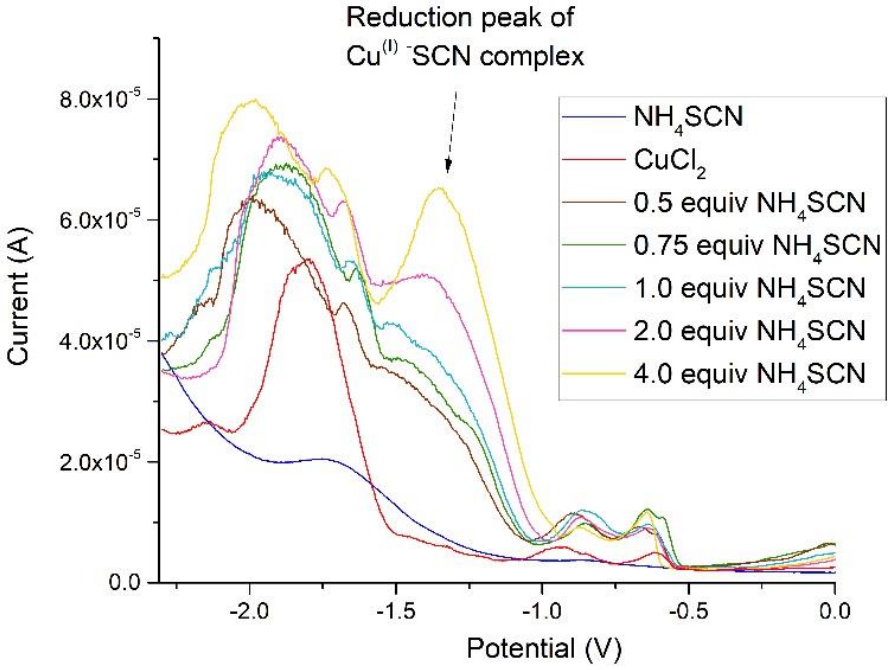


Figure 10.5. CV of a solution of $CuCl_2$ 0.002 M in acetonitrile with increasing addition of ammonium thiocyanate. E vs Ag/AgCl/NaCl (3M).

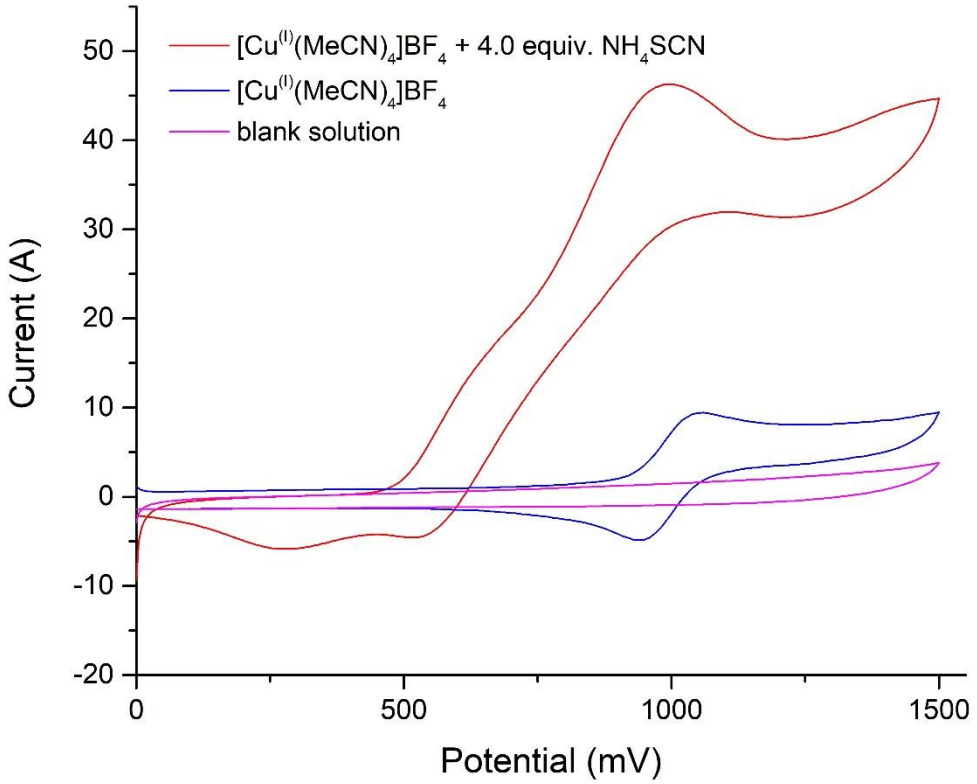
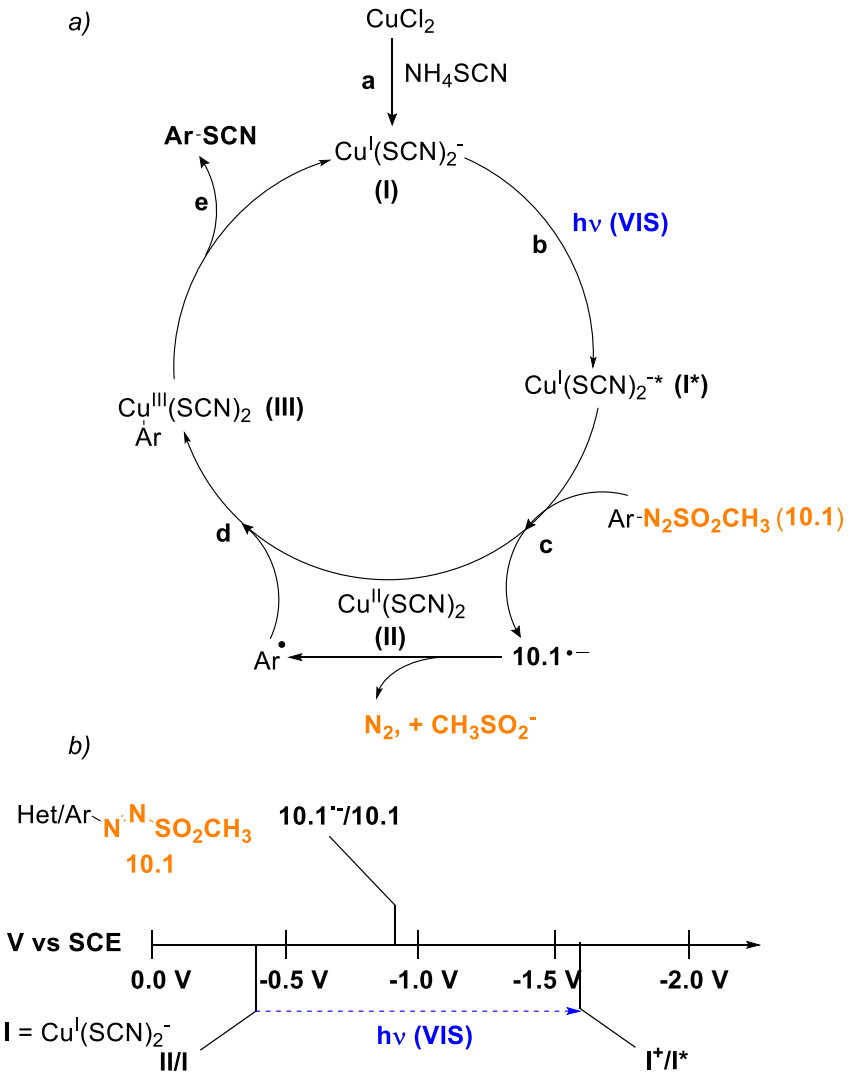


Figure 10.6. CV of a solution of $[Cu(MeCN)_4]BF_4$ 0.002 M in acetonitrile with increasing addition of ammonium thiocyanate, E vs Ag/AgCl/NaCl (3M).

On the basis of the cyclic voltammetry analyses (where a SRP(I^+/I) = -483 mV vs SCE) was observed for the in situ formed complex and the UV-Vis absorption spectrum (absorption edge, 600 nm, 2.066 eV) of the complex, we calculated a SRP* SRP(I^+/I^*) value of - 1.583 V vs SCE [10.24]. With the following investigation we were able to propose a mechanism for the reaction studied in this chapter (Scheme 10.3).



Scheme 10.3. a) Proposed mechanism for the formation of aryl thiocyanates. b) Redox diagram illustrating the feasibility of the electron transfer between **I*** and **10.1**.

10.3. CONCLUSIONS.

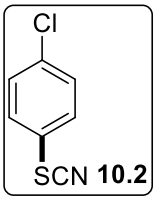
Summing up, the approach described herein allow for the easy access to aryl thiocyanates from arylazo sulfones. The activation of such substrates proceeds through a previously unobserved Cu^{I} photoredox catalysed mechanism. The yields observed are comparable to those observed by having recourse to other aromatic substrates such as aryl boronic acids (where however additives including ligands and bases are needed) and rather unstable arene diazonium salts.

10.4. EXPERIMENTAL SECTION.

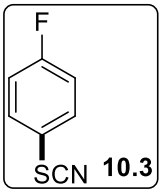
General Information. ^{1}H and ^{13}C NMR spectra were recorded on a 300(400) and 75(100) MHz spectrometer, respectively. The attributions were made based on ^{1}H and ^{13}C NMR experiments; chemical shifts are reported in ppm downfield from TMS. GC analyses were performed using a HP

SERIES 5890 II equipped with a fire ion detector (FID, temperature 350 °C). Analytes were separated using a Restek Rtx-5MS (30 m×0.25 mm×0.25 μm) capillary column with nitrogen as a carrier gas at 1 ml min^{-1}. The injector temperature was 250 °C. The GC oven temperature was held at 80 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1}, and held for 10 min. Arylazo sulfones **10.1a-10.1aa** (Figure 10.4) were already synthetised and present in the laboratory. They were used without further purifications [10.17].

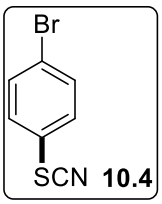
General procedure for the photochemical synthesis of compounds 10.2-10.27. An Ar-saturated solution of the chosen arylazo sulfone **10.1a-10.1z** (0.25 mmol, 0.05 M), NH_4SCN (38.2 mg, 2 equiv, 0.1 M), $CuCl_2$ (10 mol%) was irradiated for 24 h by means of a 40W Kessil lamp (emission centered at 427 nm). The photolyzed mixture was then evaporated and the crude residue isolated via silica gel column chromatography (cyclohexane:ethyl acetate mixture as eluant).



1-Chloro-4-thiocyanatobenzene (10.2). Starting from 55 mg of **10.1a** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 33.5 mg of **10.2** (79% yield, colorless oil). Spectroscopic data are in accordance with the literature [10.25]. (**10.2).** ^1H NMR (300 MHz, $CDCl_3$) δ 7.49–7.40 (m, 4H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ 136.3, 131.6, 130.6, 122.9, 110.1.

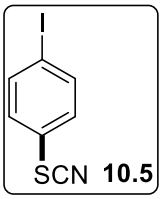


1-Fluoro-4-thiocyanatobenzene (10.3). Starting from 51 mg of **10.1b** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 27.9 mg of **10.3** (73% yield, colorless oil). Spectroscopic data are in accordance with the literature [10.26]. (**10.3).** ^1H NMR (300 MHz, $CDCl_3$) δ 7.90–7.41 (m, 2H), 7.28–7.14 (m, 2H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ 165.2–161.9 (d, J = 247.5 Hz), 133.2–133.1 (d, J = 7.5 Hz), 119.2–119.1 (d, J = 7.5 Hz), 117.7–117.4 (d, J = 22.5 Hz), 110.5.

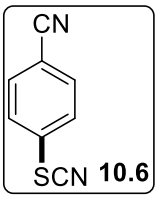


1-Bromo-4-thiocyanatobenzene (10.4). Starting from 66 mg of **10.1c** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 41.6 mg of **10.4** (78% yield, colorless solid, m.p. = 50.5–52 °C). Spectroscopic data are in accordance with the literature [10.25]. (**10.4).** ^1H NMR (300 MHz, $CDCl_3$) δ

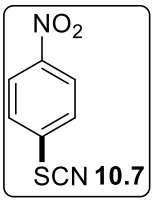
7.6 (d, *J* = 8.6 Hz, 2H), 7.4 (d, *J* = 8.6 Hz, 2H). $^{13}C\{^{1}H\}$-NMR (75 MHz, $CDCl_3$) δ 133.5, 131.6, 124.3, 123.6, 109.9.



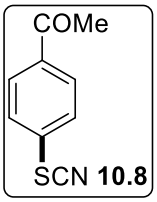
1-Iodo-4-thiocyanatobenzene (10.5). Starting from 78 mg of **10.1d** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 40.8 mg of **10.5** (63% yield, pale yellow solid, m.p. = 43–45.5 °C). Spectroscopic data are in accordance with the literature [10.27]. (**10.5**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82–7.75 (m, 2H), 7.31–7.24 (m, 2H). $^{13}C\{^{1}H\}$-NMR (75 MHz, $CDCl_3$) δ 139.3, 131.5, 124.6, 109.8, 95.5.



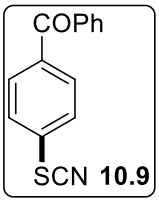
4-Thiocyanatobenzonitrile (10.6). Starting from 52 mg of **10.1e** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 20.1 mg of **10.6** (50% yield, pale yellow solid, m.p. = 43–45.5 °C). Spectroscopic data are in accordance with the literature [10.11]. (**10.6**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H).$^{13}C\{^{1}H\}$-NMR (75 MHz, $CDCl_3$) δ 133.7, 131.5, 128.9, 117.5, 113.2, 108.3.



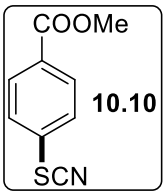
1-Nitro-4-thiocyanatobenzene (10.7). Starting from 57 mg of **10.1f** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1, 0.5% Et_3N) afforded 34.2 mg of **10.7** (75% yield, slightly yellow solid, m.p. = 127.5–129.0 °C). Spectroscopic data are in accordance with the literature [10.28]. (**10.7**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56–8.10 (m, 2H), 7.98–7.29 (m, 2H).$^{13}C\{^{1}H\}$-NMR (75 MHz, $CDCl_3$) δ 147.9, 133.3, 128.6, 125.0, 108.0.



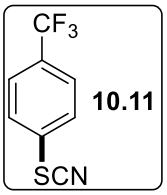
1-(4-Thiocyanatophenyl)ethan-1-one (10.8) Starting from 57 mg of **10.1g** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 30.1 mg of **10.8** (68% yield, colorless solid, m.p. = 77–79.5 °C). Spectroscopic data are in accordance with the literature [10.5]. (**10.8**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 2.61 (s, 3H).$^{13}C\{^{1}H\}$-NMR (75 MHz, $CDCl_3$) δ 196.6, 137.4, 130.7, 130.0, 128.6, 109.1, 26.7.



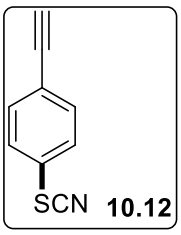
Phenyl(4-thiocyanatophenyl)methanone (10.9). Starting from 72 mg of **10.1h** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 60.2 mg of **10.9** (99% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.26]. (**10.9**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90–7.82 (m, 2H), 7.82–7.76 (m, 2H), 7.62 (d, J = 8.2 Hz, 3H), 7.51 (t, J = 7.5 Hz, 2H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 195.2, 138.2, 136.9, 133.2, 131.6, 130.1, 129.8, 128.7, 128.6, 109.3.



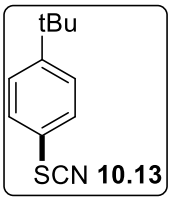
Methyl 4-thiocyanatobenzoate (10.10) Starting from 61 mg of **10.1i** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 25.6 mg of **10.10** (53% yield, colorless solid, m.p. = 61–64 °C). Spectroscopic data are in accordance with the literature [10.11]. (**10.10**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14–8.08 (m, 2H), 7.62–7.56 (m, 2H), 3.96 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 165.9, 131.3, 131.0, 128.2, 109.2, 52.6.



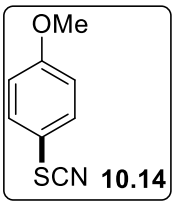
1-Thiocyanato-4-(trifluoromethyl)benzene (10.11). Starting from 63 mg of **10.1j** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 46.0 mg of **10.11** (89% yield, colorless solid, m.p. = 61–64 °C). Spectroscopic data are in accordance with the literature [10.28]. (**10.11**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 131.50 (q, J = 33.2 Hz).129.6, 129.1, 127.1 (q, J = 3.0 Hz), 124.71(q, J = 273.4 Hz), 122.00, 108.93.



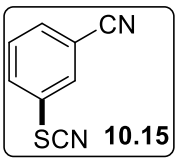
1-Ethynyl-4-thiocyanatobenzene (10.12). Starting from 52 mg of **10.1k** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of an Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1, 0.5% Et_3N) afforded 21.4 mg of **10.12** (55% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.28]. (**10.12**). ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.65 (s, 4H), 3.84 (s, 1H).^{13}C{^{1}H}-NMR (75 MHz, CD_3COCD_3) δ 134.5, 130.5, 126.6, 124.4, 110.5, 82.7, 81.5.



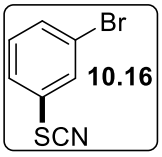
1-*tert*Butyl-4-thiocyanatobenzene (10.13). Starting from 60 mg of **10.1l** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1, 0.5% Et_3N) afforded 29.6 mg of **10.13** (62% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.28]. (**10.13).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 1.2 Hz, 4H), 1.34 (s, 9H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 153.6, 130.6, 127.5, 120.7, 111.1, 35.0, 31.3.



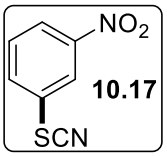
1-Methoxy-4-thiocyanatobenzene (10.14) Starting from 54 mg of **10.1m** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1) afforded 22.9 mg of **10.14** (59% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.25]. (**10.14).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 3H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 161.2, 133.7, 115.7, 113.7, 111.5, 55.4.



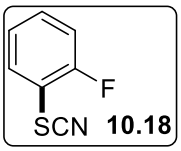
3-Thiocyanatobenzonitrile (10.15). Starting from 52 mg of **10.1n** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 32.0 mg of **10.15** (80% yield, colorless solid, m.p. = 63–65 °C). Spectroscopic data are in accordance with the literature [10.5]. (**10.15).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82–7.70 (m, 4H), 7.59 (t, *J* = 7.8 Hz, 2H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 133.4, 132.8, 132.3, 130.9, 126.9, 116.8, 114.6, 108.6.



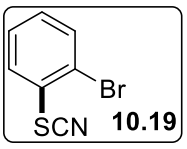
1-Bromo-3-thiocyanatobenzene (10.16). Starting from 66 mg of **10.1o** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 39.4 mg of **10.16** (74% yield, colorless oil). Spectroscopic data are in accordance with the literature [10.5]. The same reaction was performed on a 1 mmol of **10.1o** and **10.16** was isolated in 52% yield [10.5]. (**10.16).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.58–7.53 (m, 1H), 7.49–7.45 (m, 1H), 7.33 (d, *J* = 7.9 Hz, 1H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 132.8, 132.4, 131.5, 128.4, 126.5, 124.0, 109.7.



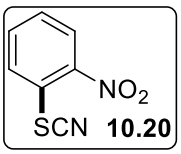
1-Nitro-3-thiocyanatobenzene (10.17). Starting from 57 mg of **10.1p** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 24.2 mg of **10.17** (54% yield, colorless solid, m.p. = 49.5–50.5 °C). Spectroscopic data are in accordance with the literature [10.30]. (**10.17**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.28 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 149.2, 135.0, 131.4, 127.5, 124.4, 108.7.



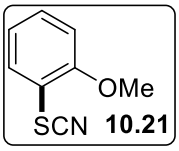
1-Fluoro-2-thiocyanatobenzene (10.18). Starting from 51 mg of **10.1q** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 37.5 mg of **10.18** (98% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.31]. (**10.18**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (td, J = 7.5, 1.7 Hz, 1H), 7.43–7.34 (m, 1H), 7.22–7.11 (m, 2H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 161.9, 158.6, 132.2, 132.0, 131.9, 125.7, 125.6, 116.8, 116.5, 111.6, 108.9.



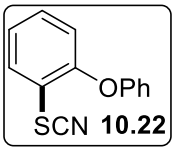
1-Bromo-2-thiocyanatobenzene (10.19). Starting from 66 mg of **10.1r** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 95:5) afforded 44.8 mg of **10.19** (84% yield, pale yellow oil). Spectroscopic data are in accordance with the literature. The same reaction was performed on a 1 mmol of **10.1r** and **10.19** was isolated in 77% yield [10.28]. (**10.19**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.0, 1.4 Hz, 1H), 7.48 (dd, J = 8.0, 1.2 Hz, 1H), 7.30 (td, J = 7.9, 1.3 Hz, 1H), 7.14 (dd, J = 7.6, 1.4 Hz, 1H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 133.7, 130.2, 129.6, 129.2, 127.3, 121.9, 109.7.



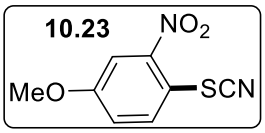
1-Nitro-2-thiocyanatobenzene (10.20). Starting from 57 mg of **10.1s** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 7:3) afforded 28.1 mg of **10.20** (62% yield, pale yellow solid, m.p. = 129–130.5 °C). Spectroscopic data are in accordance with the literature [10.26]. (**10.20**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (dd, J = 8.2, 1.5 Hz, 1H), 8.06 (dd, J = 8.2, 1.2 Hz, 1H), 7.81 (td, J = 8.3, 7.8, 1.5 Hz, 1H), 7.65 – 7.55 (m, 1H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 144.7, 135.7, 129.1, 129.0, 126.7, 126.5, 110.3.



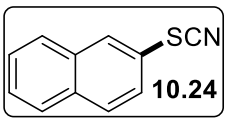
1-Methoxy-2-thiocyanatobenzene (10.21) Starting from 54 mg of **10.1t** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1) afforded 27.4 mg of **10.21** (66% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.30]. (**10.21**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (dt, *J* = 7.8, 1.6 Hz, 1H), 7.43–7.34 (m, 1H), 7.06 (dt, *J* = 7.7, 1.4 Hz, 1H), 6.94 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.92 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 156.6, 130.7, 130.1, 122.2, 113.3, 111.6, 110.6, 56.3.



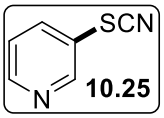
1-Phenoxy-2-thiocyanatobenzene (10.22) Starting from 69 mg of **10.1u** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1) afforded 37.1 mg of **10.22** (65% yield, pale yellow oil). (**10.22**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70–7.87 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.41–7.38 (m, 1H), 7.34–7.27 (m, 1H), 7.22–7.17 (m, 1H), 7.0.8–7.01 (m, 4H), 6.91–6.88 (dd, *J*=8.2, 1.3 Hz, 1H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 155.8, 154.9, 130.6, 130.4, 130.2, 129.9, 124.8, 123.3, 119.3, 119.0, 118.5, 116.1, 110.1. $C_{13}H_9NOS$ (227.04): calcd. C 68.70, H 3.99, N 6.16; found C 68.6, H 4.0, N 6.1.



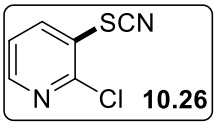
4-Methoxy-2-nitro-1-thiocyanatobenzene (10.23) Starting from 65 mg of **10.1v** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1) afforded 34.3 mg of **10.23** (65% yield, pale yellow oil). (**10.23.**) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92–7.89 (d, *J* = 9.0 Hz, 1H), 7.87–7.86 (d, *J* = 2.8 Hz, 1H), 7.37–7.33 (m, 1H), 3.9 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 160.1, 130.1, 123.1, 116.3, 110.8, 110.7, 56.4. $C_8H_6N_2O_3S$ (210.01): calcd. C 45.71, H 2.88, N 13.33; found C 45.6, H 2.9, N 13.2.



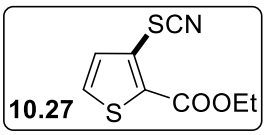
2-Thiocyanatonaphthalene (10.24). Starting from 59 mg of **10.1w** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 9:1) afforded 26.9 mg of **10.24** (58% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.28]. (**10.24**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.4 Hz, 1H), 8.03–7.94 (m, 3H), 7.73 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.69–7.63 (m, 1H), 7.54 (t, *J* = 7.8 Hz, 1H).^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ 134.5, 132.6, 132.40, 131.7, 129.2, 128.3, 127.4, 126.1, 124.4, 121.0, 110.8.



3-Thiocyanatopyridine (10.25). Starting from 47 mg of **10.1x** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 7:3, Et_3N 0.5%) afforded 16.7 mg of **10.25** (49% yield, pale yellow oil). Spectroscopic data are in accordance with the literature [10.28]. (**10.25**). ^1H NMR (300 MHz, $CDCl_3$) δ 9.08–8.46 (m, 2H), 7.94 (dt, J = 8.2, 1.9 Hz, 1H), 7.44 (dd, J = 8.2, 4.7 Hz, 1H).$^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ 150.7, 150.5, 138.1, 125.1 ,109.3.



2-Chloro-3-thiocyanatopyridine (10.26). Starting from 55 mg of **10.1y** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 7:3, Et_3N 0.5%) afforded 22.2 mg of **10.26** (52% yield, pale yellow solid, m.p. = 87.5–89.5 °C). Spectroscopic data are in accordance with the literature [10.32]. (**10.26**). ^1H NMR (300 MHz, $CDCl_3$) δ 8.50–8.41 (m, 1H), 8.07 (dd, J = 7.9, 1.4 Hz, 1H), 7.48 – 7.42 (m, 1H).$^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ 149.4, 137.5, 124.1, 123.6, 108.1.



Methyl 3-thiocyanatothiophene-2-carboxylate (10.27). Starting from 61 mg of **10.1z** (0.25 mmol, 0.05 M), NH_4SCN (2 equiv, 0.1 M), $CuCl_2$ (10 mol%) in 5 mL of Ar-saturated MeCN. Purification by column chromatography (eluant: cyclohexane:ethyl acetate 7:3) afforded 44.8 mg of **10.27** (80% yield, slightly pale yellow solid, m.p. = 112.5–114.0 °C). Spectroscopic data are in accordance with the literature [10.32]. (**10.27**). ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 5.3 Hz, 1H), 7.29 (d, J = 5.3 Hz, 1H), 3.86 (s, 3H).$^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ 162.1, 132.4, 130.1, 128.1, 110.4, 52.6.

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CONCLUSIONS

During my PhD thesis, arylazo sulfones, *dyedauxiliary group* bearing molecules, have been successfully exploited to release acid upon visible-light exposure. Their potentiality as Photoacid Generators (PAGs) have been investigated and employed for the mild and fast protection of important organic functional groups, such as alcohols and carbonyls, both protected as acetals (DHP acetals in the case of alcohols and 1,3-dioxolanes in the case of carbonyls). Not only the formation of cyclic acetals was fulfilled with arylazo sulfones as PAG, but also the formation of less stable linear ones. Moreover, PAG catalysed Friedel-Crafts arylation of aldehydes using indoles to form bis-indoyl methanes (BIM) has been presented and investigated. More applications on this field for these promising compounds are being tested and will be evaluated in the future for appealing applications. The search for new *dyedauxiliary groups* proved to be unsuccessful, even though the research on new radical sources is still ongoing. The potentiality of arylazo sulfones have been highlighted during this thesis. The application in synthesis to form α-arylketones, α-arylazo esters, α-sulphonyl hydrazones (in an undocumented and unique approach) have been performed without the need for any external (photo)catalyst in green, smooth and straightforward ways. Biaryls, an important and widespread motif in organic chemistry, have been obtained with the employment of gold(I) as catalyst in a visible-light triggered reaction, proposing a methodology able to compete with the already present and well-established techniques. Finally, aryl thiocyanates have been synthetised using photoredox catalysis and arylazo sulfones as aryl radical sources. The versatility and the potentiality of arylazo sulfones have been stressed throughout all my works and further applications will be evaluated in the near future.