Syntheses and Applications of Sulfilimines and Sulfoximines in Heterocycles and Photoswitches

Von der Fakultät für Mathematik, Informatik und Naturwissenschaften der RWTH Aachen University zur Erlangung des akademischen Grades einer Doktorin der Naturwissenschaften genehmigte Dissertation

vorgelegt von

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Tag der mündlichen Prüfung: 30.08.2024

Declaration of Authorship

I, Kiruthika Periasamy, declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

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1) Periasamy, K.; van Bonn, P.; Orloff, R. T.; Völcker, N.; Lu, Q.; Rissanen, K.; Bolm, C. *J. Org. Chem.* **2024**, *89*, 8286–8290.
2) Periasamy, K.; Gordeeva. S.; Bolm, C. Syntheses of Sulfilimines by Iron-Catalyzed Imidations of Sulfides with 2,2,2-Trichloroethyl Sulfamate. *J. Org. Chem.* **2024**, DOI: 10.1021/acs.joc.4c01250.

Place, Date

Signature

The research presented in this thesis was conducted from August 2020 to June 2024 at the Institute of Organic Chemistry, RWTH Aachen University, Germany, under the guidance of Prof. Dr. Carsten Bolm.

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1 Introduction

Carbon, hydrogen, oxygen, and nitrogen are traditionally recognized as the primary elements in organic chemistry. However, analyses conducted in 2014 by Njardarson and co-workers[1] have shed light on the significant role of sulfur, which ranks prominently alongside these foundational elements across various disease categories and pharmaceutical applications. In their comprehensive study covering 12 disease categories,[2] Njardarson and coworkers demonstrated that sulfur occupies either the first or second place as the most frequently utilized atom after carbon, hydrogen, oxygen, and nitrogen.[3] This finding underscores the pivotal contribution of sulfur-containing compounds in modern drug discovery and development.

Sulfur's versatility in organic chemistry arises from its capacity to form an array of functional groups and exhibit various oxidation states. Through oxidation, sulfur can generate diverse compounds such as sulfoxides, sulfones, and sulfonic acids, each possessing unique chemical properties and reactivities.[4] Furthermore, sulfur's ability to participate in substitution reactions with different nucleophiles, along with its wide range of oxidation states spanning from -2 to +6, enables the synthesis of complex sulfur-containing molecules with diverse functionalities and applications.[5]

1.1 Physicochemical properties and biological application of sulfoximines

Sulfoximines are characterized by a tetracoordinated sulfur atom. They can be viewed as aza analogs of sulfones. Since they are derived from sulfones by replacing one of the oxygen atoms attached to sulfur with a nitrogen atom (Figure 1).[7] This structural modification results in sulfoximines, which exhibit distinct properties compared to sulfones.

On the other hand, sulfilimines are tricoordinated with the sulfur atom. They can be derived from sulfoxides by replacing the oxygen atom directly bonded to sulfur with a nitrogen atom and are the aza analogs of sulfoxides (Figure 1).[6] Similar to sulfilimines, sulfoximines exhibit unique properties offering new opportunities for chemical reactivity and structural variation.

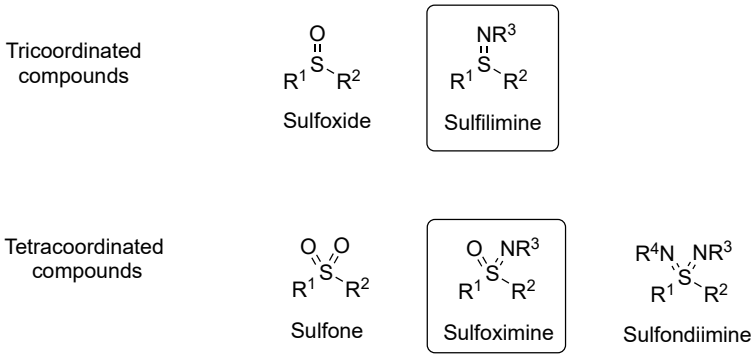


Figure 1: Various organosulfur compounds including sulfilimines and sulfoximines.

In sulfoximines the sulfur is covalently bonded to an oxygen, a nitrogen, and two carbon atoms. The S–N and S–O bonds are illustrated as pi bonds but in reality, show a strong sulfur ylid-like single bond character with two positive charges on sulfur and negative charges on nitrogen and oxygen (Figure 2).[8] Chiral sulfoximines with stereogenic centers at the sulfur atom and the presence of three modifiable sites (S–R^1,1 S–R^2, N–R^3) allows precise control over their electronic, steric, and chiral properties, tailoring them for specific applications.[9] By strategically varying substituents at these sites with electron-withdrawing or electron-donating groups, the hydrogen bond acceptor and hydrogen bond donor capabilities of sulfoximines can be finely tuned.

The nitrogen atom in *N*H-sulfoximines exhibits amphoteric characteristics due to its nucleophilic and basic nature, while the imine hydrogen atom is acidic.[7a] This unique combination of chemical properties enables diverse *N*H-functionalization strategies, offering opportunities for the development of novel synthetic methodologies centered around sulfoximine chemistry.[10] Based on the above unique properties, sulfoximines represent a promising class of compounds that can be tailored to meet specific requirements in various chemical applications.

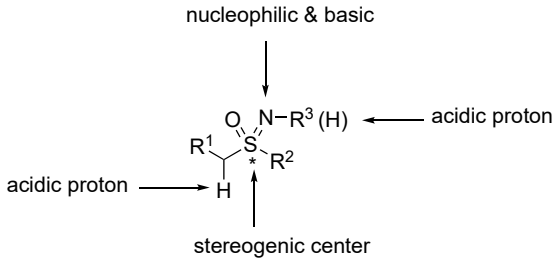
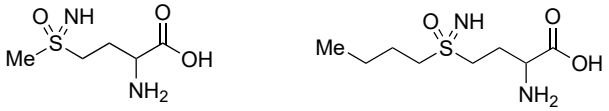


Figure 2: Properties of sulfoximines.

In 1949, Bentley and Whitehead discovered the first sulfoximine, methionine sulfoximine **1**.[11] Later, they synthesized compound **1** by reacting methionine sulfoxide with sodium azide in the presence of concentrated sulfuric acid.[12] Subsequently, its *n*-butyl analog **2** was also synthesized. Both (MSO) and (BSO) gained significant attention due to their intriguing biological activities, particularly in the context of cancer treatment.

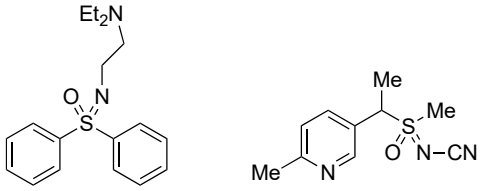


1, MSO **2**, BSO

Figure 3: Early examples of bioactive sulfoximines.[11]

In the 1970s, Satzinger and Stoss reported on suloxifen **3**, an *N*-alkyl aminosulfoximine compound with notable pharmacological properties (Figure 4).[13] Suloxifen demonstrated promising activity as a spasmolytic agent and showed potential in the treatment of asthma.[14] Suloxifen's specific chemical structure and mechanism of action likely played key roles in its observed biological activities.

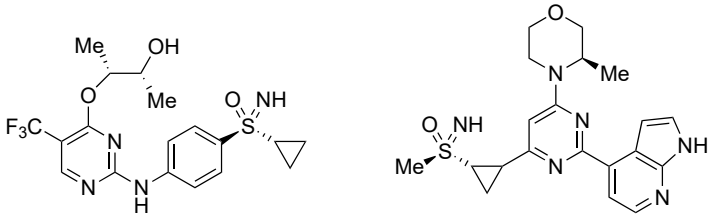
In 2005, Dow AgroSciences introduced Sulfoxaflor **4**, an *N*-cyanosulfoximine compound, as a groundbreaking insecticide from the emerging class of sulfoximines (Figure 4).[15] Sulfoxaflor was the first commercial product in this new class of insecticides, demonstrating broad-spectrum efficacy against various sap-feeding insect pests, including aphids, whiteflies, hoppers, and lygus.[16] The development and release of sulfoxaflor represented a significant milestone in agricultural chemistry. Despite the promising bioactivity of sulfoxifen, only Sulfoxaflor has successfully reached the market due to its exceptional performance and safety profile. This highlights the challenges and rigorous testing required for bringing novel insecticides to market. The commercial success of Sulfoxaflor has stimulated research and development efforts in sulfoximine-based insecticides, aiming to expand and environment friendly pest management solutions in agriculture.



3, Suloxifen **4**, Sulfoxaflor

Figure 4: Insecticide sulfoximine compounds sulfoxifen **3**[13a] and sulfoxaflor **4**.

Scientists at Bayer and AstraZeneca have reported on two notable sulfoximine compounds, BAY 1000394 **5** and AZD6738 **6**, which have recently entered clinical studies (Figure 5).[17] BAY 1000394 **5** has demonstrated significant activity in anti-tumor therapies, particularly as an inhibitor of cyclin-dependent kinases (CDK). This mechanism of action highlights its potential for disrupting cancer cell growth and positioning it as a promising candidate in cancer treatment. On the other hand, AZD6738 **6** has shown promising anti-cancer activity as an ATR (ataxia telangiectasia and RAD3-related) inhibitor.[18] By targeting the ATR protein, which plays a crucial role in DNA damage response and cell cycle regulation. The advancement of BAY 1000394 **5** and AZD6738 **6** into clinical studies leads to the growing interest in sulfoximine-based therapeutics for oncology applications.

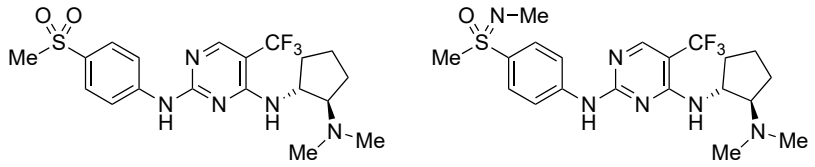


5, BAY 1000394 **6**, AZD6738

Figure 5: Sulfoximines with kinase inhibiting properties.[17,18]

Pfizer researchers have highlighted intriguing consequences associated with replacing a sulfone **7** with the corresponding sulfoximine **8**, particularly in terms of bioactivity and bioavailability (Figure 6). In their pursuit of a substitute for sulfone **7**, aiming to develop a proline-rich tyrosine kinase 2 (PYK2) inhibitor for osteoporosis treatment, they made significant findings.[19] Sulfonamide was investigated first due to its similar activity to sulfone **7**, However, it was found to be less stable in human liver microsomes, posing a limitation for further development. To address this challenge, the researchers explored various sulfoximine derivatives and discovered that *N*-methyl sulfoximine **8** demonstrated excellent activity and stability, along with favorable

oral exposure in animal models. This pivotal discovery underscores the potential of sulfoximines as viable alternatives to sulfones, offering improved pharmacological properties for therapeutic applications.



7 **8**

Figure 6: PYK2 inhibitor sulfone and sulfoximine.[19]

Lu and Vince employed the sulfoximidoyl group as a bioisostere for the secondary hydroxyl group to develop new inhibitors of HIV-1 protease (Figure 7).[20] Specifically, they investigated *N*H-sulfoximine **9**, which served as a transition-state mimic in HIV-1 protease inhibitors. This structural modification was aimed at enhancing the compounds binding affinity and pharmacological properties. *N*H-sulfoximine **9** exhibited promising results, demonstrating significant antiviral activity in cell-based assays. The ability of *N*H-sulfoximine **9** to mimic the transition state of the HIV-1 protease contributed to its efficacy as an inhibitor. By strategically replacing functional groups with bioisosteres like sulfoximidoyl, researchers aimed to optimize the molecular interactions necessary for effective enzyme inhibition.

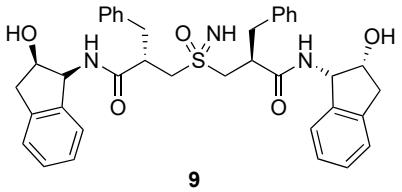


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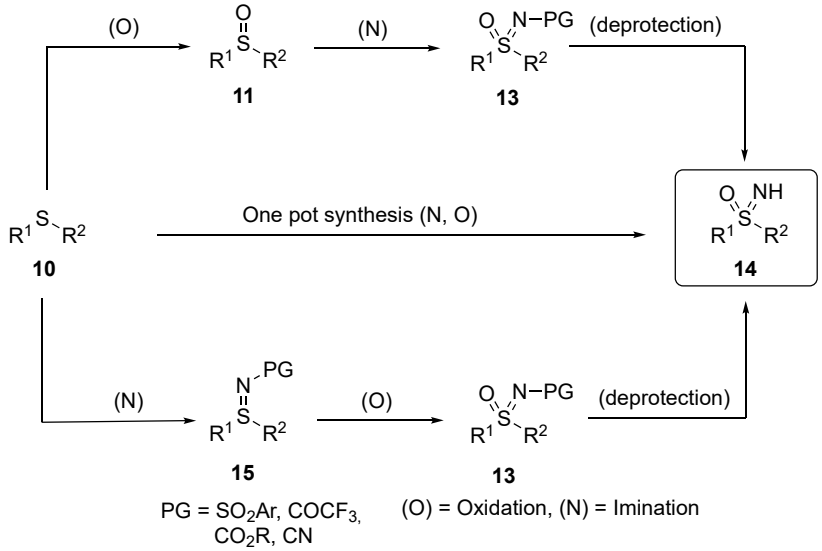
Figure 7: Sufloximine based HIV-1 protease inhibitor.[20]

1.2 Synthetic pathways to access sulfoximine

Traditional methods for synthesizing sulfoximines **14** typically start with the transformation of sulfides **10**. In these pathways, nitrogen or oxygen is initially introduced to sulfides **10**, leading to the formation of sulfilimines **15** or sulfoxides **11**, respectively. Subsequent oxidation of sulfilimines **15** or nitrogen transfer reactions involving sulfoxides **11** yield the desired

sulfoximines **14**. Generally, sulfoximines accessible through these methods are often *N*-protected derivatives **13**, which undergo a final deprotection to obtain *N*H-sulfoximines **14**.

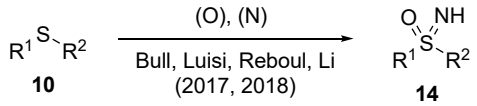


Scheme 1: Synthetic routes for the preparation of sulfoximine **14**.

The synthesis of sulfoximines typically involves the use of disubstituted sulfur as starting materials. The *N*-transfer processes crucial to these transformations have been successfully accomplished using either metal-catalyzed or metal-free procedures.[21] These methods are foundational for the synthesis of sulfoximines. In addition to conventional disubstituted sulfur-based syntheses, alternative substrates such as sulfinamides,[22] sulfinylamines,[23] sulfonimidates,[24] and sulfonimidoyl fluorides[25] have also been developed. Overall, these diverse methodologies provide multiple avenues to access these valuable compounds for various applications. Researchers have reported a straightforward one-pot formation of sulfoximines directly from sulfides, which will be discussed in detail in the upcoming section.

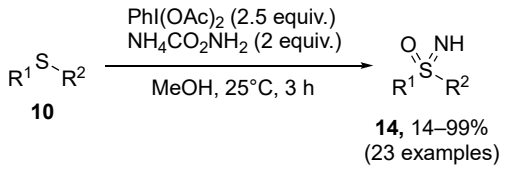
1.3 Direct synthesis of sulfoximine

A significant advancement in sulfoximine synthesis involves the direct transformation of sulfides into *N*H-sulfoximines through a chemoselective one-pot imidation/oxidation process. This breakthrough was recently reported independently by Bull,[26] Luisi,[27] Reboul,[28] and Li[29] (Scheme 2).



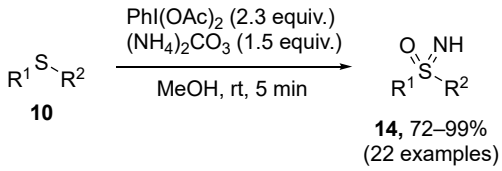
Scheme 2: One-pot synthesis of the *N*H-sulfoximines from sulfides.

In 2017, Bull and Luisi introduced a remarkably mild and well-tolerated method for directly converting sulfides **10** into *N*H-sulfoximines **14** (Scheme 3).[26] This transformation utilizes a combination of ammonium carbamate and a hypervalent iodine reagent in methanol as the solvent, achieving the conversion within just 3 hours reaction time. Their one-pot process procedure proved highly effective with a range of sulfide substrates including alkyl, aryl, benzyl, cycloalkyl, and heteroaryl sulfides. The method consistently yielded the corresponding sulfoximines in yields between 14% and 99%. This discovery offers a significant advancement in sulfoximine synthesis, providing a practical and efficient route for accessing diverse sulfoximine derivatives with broad applicability in medicinal and synthetic chemistry.



Scheme 3: One-pot synthesis of the *N*H-sulfoximines from sulfides by Bull and Luisi.[26]

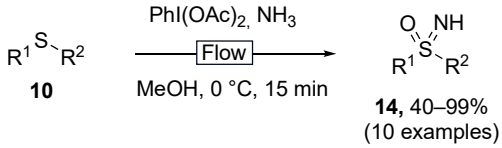
In the same year, Li and coworkers introduced a significant advancement in the synthesis of *N*H-sulfoximines **14** from sulfides **10**, offering a highly efficient and rapid method (Scheme 4).[29] Their approach also uses a hypervalent iodine reagent as the oxidizing agent with ammonium carbonate. Compared to Bull's method, which relied on ammonium carbamate, Li's method stands out for its notably increased efficiency with ammonium carbonate as nitrogen source demonstrated by a significantly shorter reaction time of 5 min. The practical synthesis of *N*H-sulfoximines **14** reported by Li and coworkers offers a straightforward route to sulfoximines from sulfides, under ambient conditions and in the presence of air. This method represents a significant advancement in sulfoximine synthesis, providing a convenient and environmentally benign protocol for accessing valuable sulfoximine derivatives.



Scheme 4: One-step synthesis of the *N*H sulfoximines from sulfides by Li.[29]

Following the above reports, the Reboul group achieved a one-pot synthesis of fluorinated *N*H-sulfoximines from sulfides, encompassing both aryl and alkyl compounds.[27,28] This method utilized a hypervalent iodine reagent as the oxidant and ammonium carbamate as the nitrogen source same as bull method. Notably, a diverse array of significant functional groups was effectively tolerated during the synthesis. An intriguing enhancement in reactivity was observed when trifluoroethanol was incorporated. Additionally, the group proposed an λ^6-acetoxysulfanenitrile intermediate based on ^{19}F NMR investigations. This proposed intermediate provides valuable insights into the mechanistic aspects underlying the synthesis of fluorinated *N*H-sulfoximines, shedding light on the intricate reaction pathways involved.

In 2017, Luisi and coworkers introduced a streamlined continuous flow method for synthesizing *N*H-sulfoximines from sulfides or sulfoxides (Scheme 5).[27] This innovative approach features a more practical stoichiometry of a hypervalent iodine reagent compared to traditional batch methods, along with the use of aqueous ammonia as the nitrogen source. The versatility of this continuous flow process was demonstrated by converting various substituted sulfides and sulfoxides, including an enantioenriched sulfoxide and a biologically relevant methionine derivative. The use of diverse substrates underscores the broad scope and applicability of this method in producing *N*H-sulfoximines with specific functionalities.



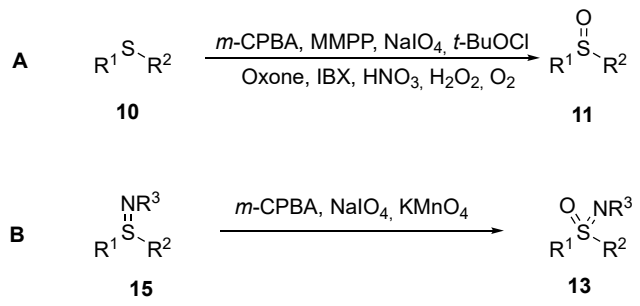
Scheme 5: One-step synthesis of the *N*H-sulfoximines from sulfides in a flow reactor.[27]

In the following section, we will discuss various oxidation protocols for sulfides and sulfilimines, which are relevant to the project. This includes different types of oxidation agents, by exploring these protocols, we aim to identify the most effective strategies for our specific project needs.

1.4 Oxidation of sulfides and sulfilimines

Since the first reported sulfoxide synthesis in 1865,[30] researchers interest in these compounds has remained strong. Sulfoxides are primarily derived from the oxidation of sulfides **10**,[31] and oxidation of sulfilimines **11** eventually leads to the formation of sulfoximines **13**. Traditional methods for the oxidation of sulfides to sulfoxides typically involve various oxidants. For example, *meta*-chloroperoxybenzoic acid (*m*-CPBA),[32] magnesium monoperoxyphthalate (MMPP),[33] Oxone,[34] sodium periodate,[35] 2-iodobenzoic acid (IBX),[36] and *tert*-butyl hypochlorite (TBHP) can be employed.[37] These methods often require stoichiometric or even excess amounts of oxidants, as well as catalysts or high temperatures. These reaction conditions can result in the formation of multiple by-products, prompting researchers to develop improved and eco-friendly procedures (Scheme 6A).

A more sustainable and popular approach is the use of hydrogen peroxide as the oxidant, since its main by-product is water.[38] Hydrogen peroxide is a clean, efficient oxidant that minimizes environmental impact. Another mild oxidant that is widely used in oxidation protocols is oxygen.[39] As an ambient and abundant gas represents, oxygen the "greenest" approach to oxidation reactions, offering a highly sustainable alternative to more traditional methods. When it comes to the oxidation of racemic sulfilimines, the most commonly used oxidants include *m*-CPBA, sodium periodate, or potassium permanganate. Each of these oxidants provides unique benefits in terms of efficiency and selectivity, making them suitable for different synthetic applications. Thus, the choice of the oxidant and the method can vary based on the specific requirements of the transformation, whether it is the need for mild conditions, high selectivity, or environmental considerations (Scheme 6B).



Scheme 6: Oxidations of sulfides and sulfilimines to sulfoxides **11** and sulfoximines **13**, respectively.

1.5 Mechanochemistry: An overview

Solvents typically constitute a major portion of the chemical waste in reactions, especially in the pharmaceutical industry. Despite efforts to recycle and reuse solvents, these processes are often inefficient and prone to contamination. Green chemistry, with its twelve principles aimed at sustainability, prioritizes reducing the use of solvents due to their environmental and safety concerns.[40] In this context, mechanochemical reaction is described by International Union of Pure and Applied Chemistry (IUPAC) as a chemical transformation occurring through the direct absorption of mechanical energy,[41] has attracted considerable interests. Mechanochemical reactions are conducted without or very small amounts of solvents, which leads to a reduction of the overall reaction waste. Over the last decade, mechanochemistry has emerged as a potent tool for green synthesis, recognized as a valuable alternative to traditional methods.[42] Mechanochemical synthesis are commonly conducted in automated ball mills in batch mode. The chemicals are added to a milling jar which contains a milling ball and is shaken or rotated depending on the machine used. The chemicals are mixed by the movement of the balls and chemical reactions are facilitated through mechanical stress. In addition to ball mills, recent results with resonant acoustic mixers and continuously operating extruders are promising for the up-scaling of mechanochemical synthesis

Beside shared parameters of reactions in solution and mechanochemical reactions such as reaction time and temperature the optimization of mechanochemical reactions includes different parameters. Small amounts of liquid can already significantly accelerate and, in some cases, enable mechanochemical reactions between solids by acting as lubricants. This improves the mixing process and enhances the homogeneity of the mixture.[43] This process is described by the concept of liquid-assisted grinding, characterized by the parameter η, which is the ratio of the liquid additive volume (µL) to the total mass of the reactants (mg).[44] Beside liquid additives also solid additives can be added to change homogeneity and concentrations. These additives are also called grinding auxiliaries and are supposed to have inert properties. Commonly used grinding auxiliaries are for example SiO_2 or NaCl. Mechanochemistry offers a promising solution by enabling solvent-free organic reactions, thus addressing the solvent issue. This method not only reduces waste but also shortens reaction times and allows for the improvement of traditional transformations, discovery of new reaction pathways, and synthesis of materials challenging to produce via solvent-based methods. Given its potential for sustainable and

efficient synthesis, mechanochemistry continues to gain attention and recognition in the field of modern synthetic chemistry.[45]

Also sulfoximines have been applied to mechanochemical reaction conditions. An early example was the palladium-catalyzed carbonylation of aryliodids with a sulfoximine as nucleophile.[46] Later other functionalizations of sulfoximines have been reported[47] as well as synthesis of sulfonimidamides and sulfonimidamide-containing heterocycles.[48]

2 Synthesis of sulfilimines by iron-catalyzed imidation of sulfides with 2,2,2-trichloroethyl sulfamate

The experimental work for this chapter was supported by Sofya Gordeeva as part of her research internships in the working group of Prof. Dr Carsten Bolm at RWTH Aachen University under the supervision of the author of this thesis. The investigations have already been published:

Periasamy, K.; Gordeeva. S.; Bolm, C. Syntheses of Sulfilimines by Iron-Catalyzed Imidations of Sulfides with 2,2,2-Trichloroethyl Sulfamate. *J. Org. Chem.* **2024**, DOI: 10.1021/acs.joc.4c01250

2.1 Introduction

2.1.1 Properties of sulfilimines

Sulfilimines, the aza-analogs of sulfoxides, consist of a sulfur atom that possesses a lone pair of electrons and is connected to two carbon substituents, denoted as R^1 and R^2. Additionally, the sulfur atom forms a bond with a nitrogen atom which is commonly illustrated as S=N double bonds but more accurately described as ylides with a negative charge on nitrogen and a positive charge on sulfur.[6c] A crucial factor influencing the stability of the S−N bond in sulfilimines is the nature of the substituent attached to the nitrogen atom, R^3 (Figure 8).[49] The characteristics of this R^3 group can significantly impact the overall stability of the molecule. Specifically, electron-withdrawing substituents at the R^3 position play an important role in stabilizing the S−N bond.[6b] These substituents achieve this by attracting electron density away from the nitrogen atom, which helps to stabilize any negative charge that may develop on the sulfur atom. This stabilization effect leads to more stable sulfilimine compounds.

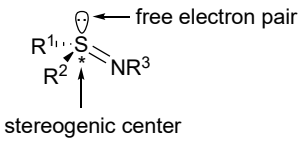


Figure 8: Properties of sulfilimines

The discovery of sulfilimines dates back to 1917 when Raper of the University of Leeds reported the synthesis of the first sulfilimine, as noted by Mann and Pope.[50] Since this pioneering work, the chemistry of sulfilimines, has undergone significant advancement. Sulfilimines have found applications as precursor for nitrenes,[51] reagents for epoxidations and aziridinations,[52] ligands in metal catalysis,[53] intermediates in organic synthesis,[54] and reactants in various bioorganic contexts.[55] Moreover, sulfilimines have gained attention due to their significant biological activities, rendering them attractive targets for medicinal and crop protection chemistry.[56] Notably, a natural sulfilimine was discovered within a collagen-IV network in 2009,[57] and other examples of sulfilimines with relevance in medicinal chemistry, crop protection and biology (Figure 9), highlighting the relevance and potential impact of sulfilimines in both chemical and biological sciences. This underscores the historical significance and versatile utility of sulfilimines, setting the stage for further exploration of their synthetic and biological properties.

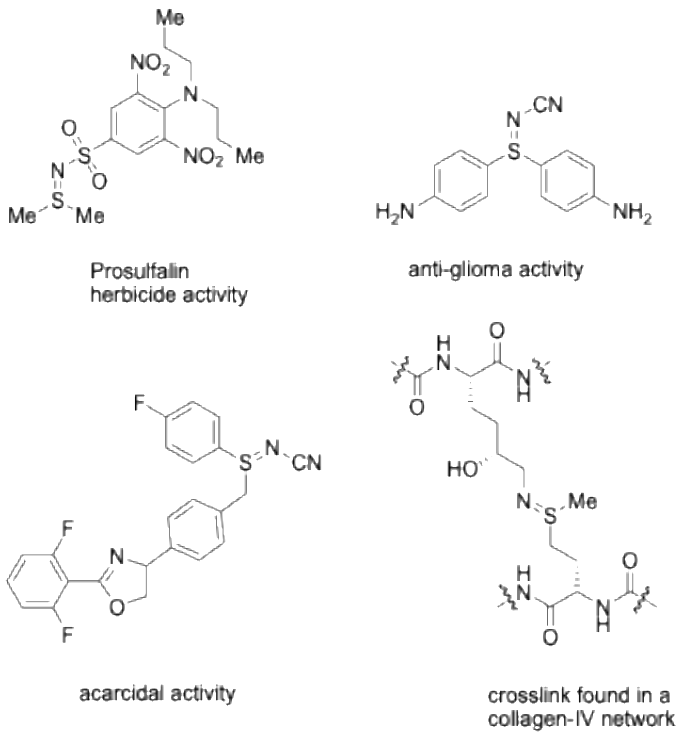


Figure 9: Selected examples of sulfilimines with relevance in medicinal chemistry, crop protection and biology.

In the following section, various imidation agents employed in iron-catalyzed syntheses of sulfilimines from sulfides are discussed. This topic is particularly relavant to this project which will discussed in section 2.2, as understanding the choice and mechanism of these imidation

agents can significantly influence the efficiency and selectivity of the synthesis process. This analysis will provide crucial insights into iron-catalyzed imidation agents and will advance this project's objectives by aiding in the development of more effective catalytic systems. Among the diverse metal-catalyzed methods in copper, manganese, rhodium, ruthenium, cobalt and silver for sulfide imidation reactions,[21a–d,58] those utilizing iron complexes[59] stand out prominently due to their exceptional substrate compatibility and the low toxicity of the catalytic metal.[60] Iron-catalyzed systems have gained significant interest owing to their ability to accommodate a wide range of substrates efficiently. Typically, these systems employ various imidating agents such as azides **(A)**, sulfonamides **(B)**, iminoiodinanes **(C)** and carbamates **(D)** (Figure 10).

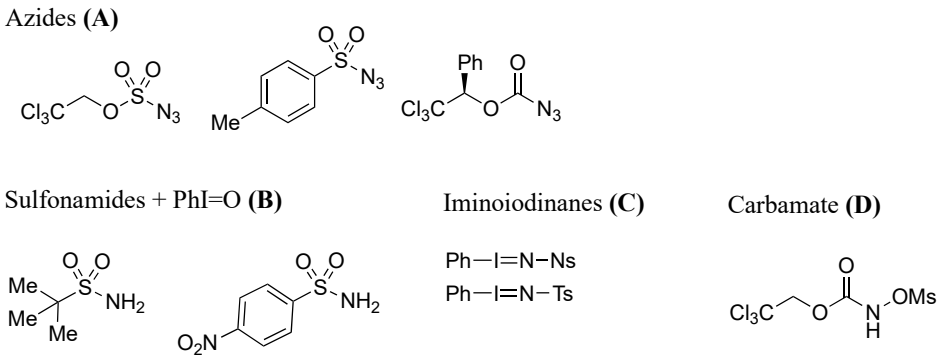


Figure 10: Imidation agents used in iron-catalyzed syntheses of sulfilimines from sulfides **(A–D).**

Azides **(A)**, in particular, have been widely utilized in iron-catalyzed sulfide imidation reactions due to their reactivity and effectiveness in promoting the desired chemical conversions. However, concerns related to the safety and handling of azides have prompted researchers to explore alternative imidating agents, such as sulfonamides and related derivatives, to achieve the desired transformations in a safer and more sustainable manner. This focus on developing iron-catalyzed systems with diverse and safer imidating agents like trichloroethyl sulfamate[61] underscores the importance of advancing synthetic methodologies that are both effective and environmental friendly in the field of chemistry.

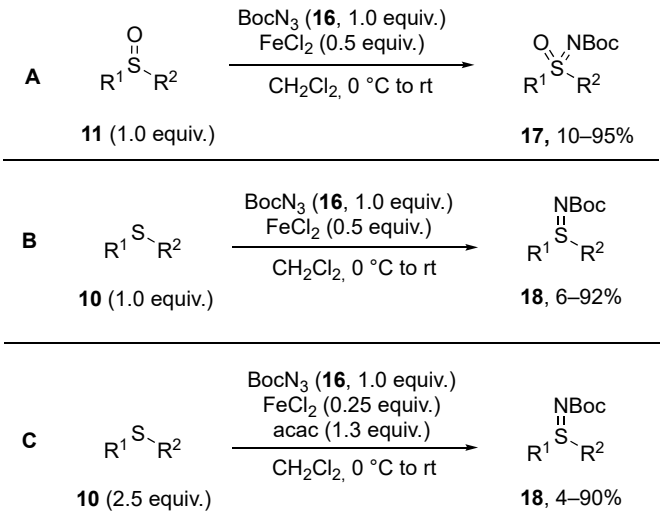
2.1.2 Iron-catalyzed sulfur imidation

Imidation with azides

The primary sources of nitrenes commonly employed in the imidation reactions of sulfides and sulfoxides are azides.[62] For example sodium azide (NaN_3), which is utilized either by reacting them with a strong acid to generate *in situ* highly reactive hydrazoic acid (HN_3), or they can be employed directly as organic azides like TsN_3 (tosyl azide) or $BocN_3$ (*tert*-butoxycarbonyl azide). The method involves the decomposition of sodium azide into hydrazoic acid, which serves as the source of the nitrene intermediate for the formation of *N*H-sulfoximine. Alternatively, organic azides like TsN_3 and $BocN_3$ can be directly incorporated into the reaction mixture to generate a nitrene upon activation, facilitating the desired substituted imidation of sulfides and sulfoxides.

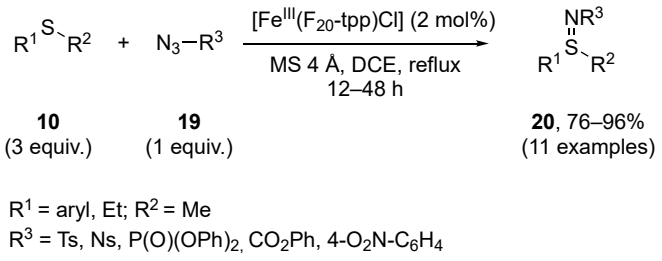
In 1999, Bach and Körber reported a method for the imidation of sulfides **10** and sulfoxides **11** to produce sulfilimines **18** and sulfoximines **17**, respectively, using *N*-*tert*-butyloxycarbonyl azide **16** in the presence of catalyst $FeCl_2$.[59b] They synthesized *N*-substituted sulfoximines **17** by employing an excess of sulfoxide **11** along with a stoichiometric amount of the iron salt and $BocN_3$, achieving moderate to excellent yields of sulfoximines **17** ranging from 10 to 95% (Scheme 7A).

A significant advantage of this process is the ability to fully recover the unused starting materials after the reaction, enhancing the economic efficiency of the synthetic route. For the imidation of sulfides **10**, using one equivalent of sulfide and 0.5 equivalents of $FeCl_2$ resulted in the formation of corresponding *N*-substituted sulfilimines **18** in yields ranging from 6% to 92% (Scheme 7B). Furthermore, the addition of acetylacetone (acac) and decreasing the amount of iron catalyst to 0.25 equivalents led to the corresponding sulfilimines **18** in yields between 4% to 90% (Scheme 7C).



Scheme 7: Iron catalyzed sulfur imidations with *N*-protected azide.[59b]

In 2010, Liu and Che developed an innovative approach for the imidation of sulfides **10** using an air-stable iron(III) porphyrin complex and *N*-protected azides **19** as nitrogen source under both, thermal and microwave-assisted conditions.[63] Under thermal condition they achieved efficient catalytic imidation of sulfides with a low catalyst loading (2 mol%) of [Fe^{III}(F_{20}-tpp)Cl] in 1,2-dichloroethane under reflux conditions. This method yielded sulfilimines 2**0** in high yields ranging from 76% to 96% (Scheme 8). Under microwave irradiation conditions, the reaction time of aziridination, allylic amination and sulfide imidation can be reduced by up to 16 fold (24–48 h versus 1.5–6 h) without significantly affecting the product yield which was between 64% and 93%.



Scheme 8: Iron(III) catalyzed imidation of sulfides using sulfonyl, phosphoryl, carboxyl and aryl azides.

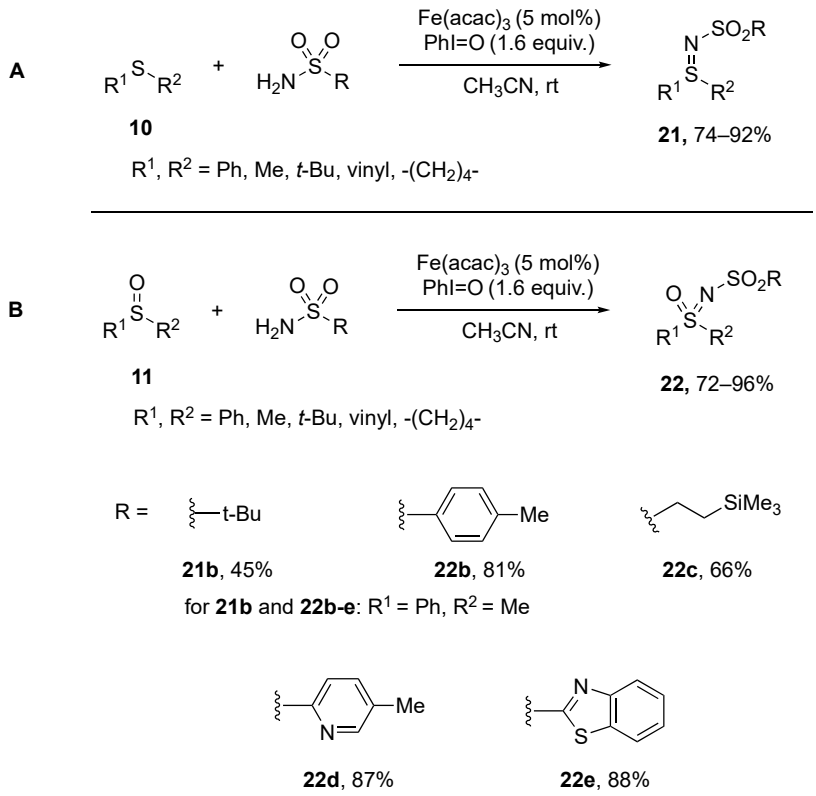
Imidation with iminoiodinanes

Imidoiodinanes are versatile reagents in organic chemistry, commonly used for nitrogen-transfer reactions.[64] These compounds, featuring a nitrogen-iodine bond, facilitate the synthesis of various nitrogen-containing molecules, such as aziridines, sulfoximines, and amides.[65]

Their high reactivity and selectivity make them valuable tools in the development of efficient and selective synthetic processes.[66]

In 2006, Bolm and coworkers introduced a groundbreaking protocol employing 5 mol% of $Fe(acac)_3$ along with various *in situ* generated sulfonimidoiodinanes (Scheme 9).[59c] This method enabled the smooth imidation of sulfoxides **11** at room temperature, yielding the corresponding sulfoximines **22** in good to excellent yields ranging from 72% to 96%. Additionally, the imidation of sulfides **10** under the same conditions produced sulfilimine **21** in moderate to high yields ranging from 74% to 92%. Competition experiments using a 1:1 mixture of sulfide **10** and sulfoxide **11** revealed that sulfide **10** was significantly more reactive than sulfoxide **11** (Scheme 9A).

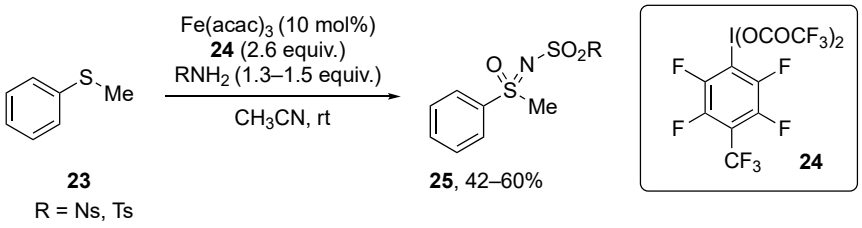
This observation was further supported by substrate scope studies, where sulfoxides **11** bearing bulky substituents like 2,4,6-trimethylphenyl failed to undergo imidation, while the corresponding sulfides **10** reacted successfully, yielding 74% of the sulfilimine product. Similarly, the sterically demanding *tert*-butylsulfonamide **21b** was only effective as an imidating agent in sulfide imidation, yielding a 45% product yield. These findings highlight the substrate selectivity and reactivity differences observed in the imidation reactions, providing valuable insights into the scope and limitations of this catalytic system for the synthesis of sulfilimines **21** and sulfoximines **22** (Scheme 9B).



Scheme 9: $Fe(acac)_3$ catalyzed imidations of sulfoxides and sulfides.[59c]

Schäger and Wirth developed a one-pot synthesis approach for sulfoximines **25** from sulfides **23**, utilizing a polyfluorinated hypervalent iodine(III) reagent **24** as the oxidant in the presence of an iron catalyst.[67] It is an iron(III)-catalyzed cascade reaction that directly converts sulfides **23** into sulfoximines **25** using hypervalent iodine(III) reagents. Previously, hypervalent iodine reagents have primarily been employed for the selective oxidation of sulfides to sulfoxides or, in the presence of amines, for converting sulfides to sulfilimines.[6b,59c]

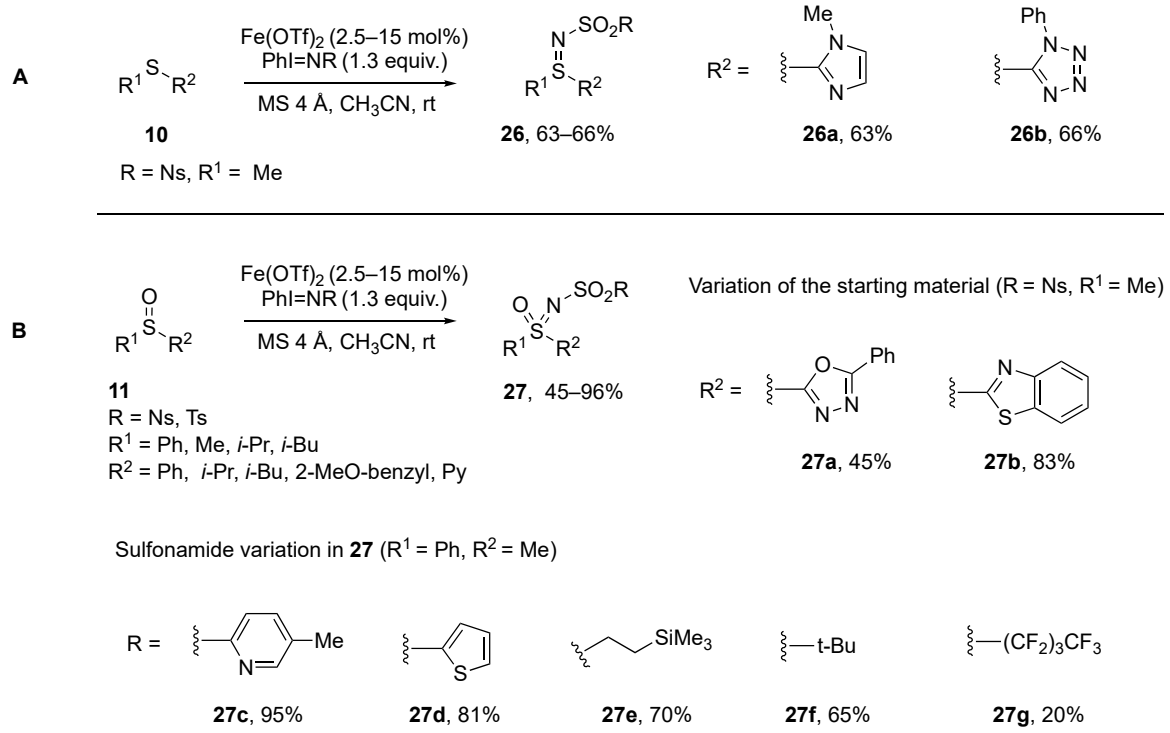
This method is notable because compound **24** demonstrated significantly higher oxidative power compared to its C_6H_5-analogues. This enhanced reactivity allowed for the *in situ* oxidation of sulfonamides to generate the active sulfonimidoiodinane species required for sulfide imidation. Subsequently, another equivalent of compound **24** was employed to oxidize the resulting sulfilimines, ultimately yielding the desired sulfoximines **25** in moderate yields (Scheme 10).



Scheme 10: One pot $Fe(acac)_3$ catalyzed imidation with polyfluorinated hypervalent iodine(III) reagent **24**.[67]

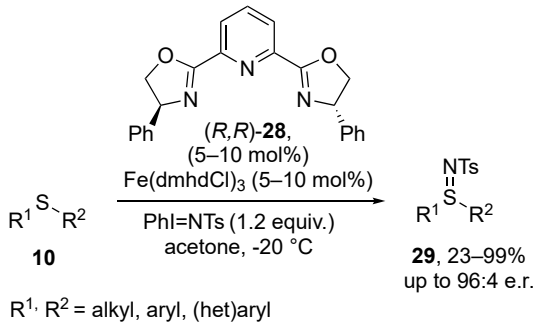
In 2009, Bolm and coworkers reported a significant advancement in the catalytic imidation of sulfides **10** and sulfoxides **11** using iron(II) triflate involving sulfonyliminoiodinanes at room temperature. The process yielded sulfilimines **26** and sulfoximines **27** within notably short reaction times (Scheme 11).[68] The researchers found that by utilizing $Fe(OTf)_2$ instead of $Fe(acac)_3$ the catalyst loading could be reduced to as low as 2.5 mol% from 10 mol%, while maintaining robust efficiency with both pre-formed and *in situ* generated sulfinimidoiodinane.[59c]

Notably, certain heterocyclic sulfides needs a slightly higher catalyst loading of 15 mol% $Fe(OTf)_2$ with PhI=NNs, giving sulfilimines **26** in yields ranging from 63% to 66% (Scheme 11A). The substrate scope of this catalytic system was broad. Even sulfoxides bearing sterically demanding substituents and various heterocyclic substrates oxadiazole **27a**, benzothiazole **27b**, imidazole **26a**, tetrazole **26b** were successfully transformed into sulfoximines **27** in yields spanning from 45% to 96%. Intriguingly, modifications to the sulfonamide component were well-tolerated, with compounds bearing pyridinyl **27c**, thiophenyl **27d**, silylethyl **27e**, *tert*-butyl **27f**, or perfluorobutyl substituents **27g** consistently delivering the desired products in yields ranging from 20% to 95% yield (Scheme 5B).



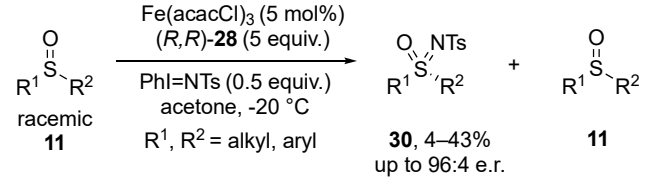
Scheme 11: Imidation of sulfides and sulfoxides catalyzed by $Fe(OTf)_2$.[68]

In 2013, Bolm and co-workers achieved a significant breakthrough by introducing the first iron-catalyzed asymmetric imidation of sulfides **10**, demonstrating a robust method with a wide range of applicable substrates yielding high enantioselectivity with poor to excellent yields 23% to 99% (Scheme 12).[59d] The research investigated the development of enantioselective sulfide imidations, identifying an optimal combination of catalytic components. The key catalytic system comprised of 5–10 mol% $Fe(dmhdCl)_3$ in conjunction with 5–10 mol% (R,R)-Ph-PyBOX **28** and PhI=NTs serving as the nitrene source. Acetone serves as an economical solvent due to its affordability and low toxicity profile. The reaction is easy to handle because air and moisture are tolerated. This combination proved to be the most effective, yielding sulfilimines **29** with exceptional efficiency and high enantiomeric ratios, reaching up to 96:4 for a board substrate scope.



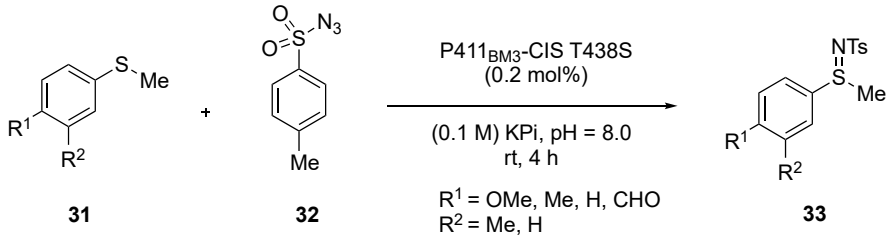
Scheme 12: Iron(III)-catalysed enantioselective sulfur imidation.[59d]

Following the above work, a kinetic resolution of chiral sulfoxides **11** has been reported (Scheme 13).[69] Utilizing a catalyst system composed of $Fe(acacCl)_3$ (5 mol%), (R,R)-**28** (5 mol%), and PhI=NTs (0.5 equiv.) as the imidating agent, racemic sulfoxides **11** were transformed into optically active sulfoximines **30**. This process yielded products with up to 43% yield and exhibited enantiomeric ratios reaching as high as 94:6, demonstrating excellent stereoselectivity.



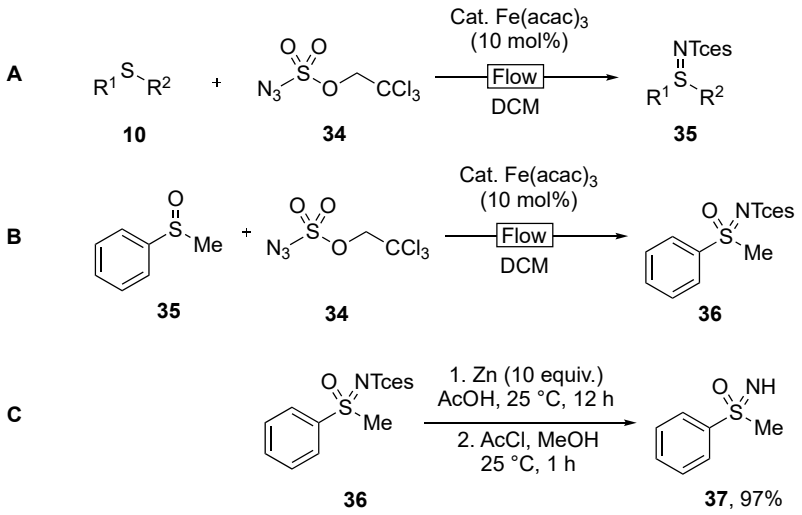
Scheme 13: Iron(III)-catalysed imidative kinetic resolution of racemic sulfoxides.[69]

In 2014, Arnold and coworkers pioneered the development of enantioselective imidation of sulfides **31** using an enzyme-catalyzed intermolecular nitrogen-atom transfer reaction (Scheme 14).[58c] In this study, enzymes from the cytochrome P450 family, containing an iron porphyrin scaffold were evaluated for their ability to catalyze sulfur imidations using various substituted azides. Notably, it was discovered, that among the tested azides only TsN_3 **32** yielded satisfactory outcomes. Among the enzymes screened, $P411_{BM3}$-CIS T438S demonstrated the highest activity, achieving a total turnover number of up to 300. Furthermore, within this enzyme series, $P411_{BM3}$-CIS T438S exhibited superior performance, achieving a total turnover number of 320. The reactions were conducted using 0.2 mol% of the enzyme in buffered water at room temperature. However, the efficiency and stereoselectivity of the reactions were found to be heavily influenced by the substrate used.



Scheme 14: Imidation of sulfides using enzyme-catalyzed intermolecular nitrogen-atom transfer.[58c]

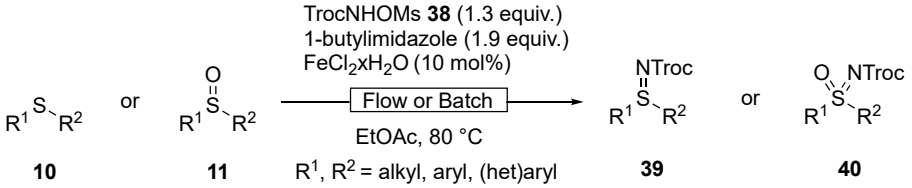
In 2016, Lebel and co-workers introduced an innovative continuous flow methodology to facilitate the imidation of sulfides **10** and sulfoxides **35** using trichloroethoxysulfonyl azide **34**, with catalytic iron(III) acetylacetonate (Scheme 15A).[59f] This process operates at ambient temperature with a residence time below 2 hours, using UVA light. The scope of this method is broad, successfully yielding aromatic and aliphatic sulfilimines **35** and sulfoximines **36** in yields ranging from 56% to 98% (Scheme 15B). Furthermore, the Tces protecting group employed in this process is efficiently removed using zinc in acetic acid, liberating the desired *N*H-sulfoximine product **37** in an excellent yield of 97% (Scheme 15C).



Scheme 15: Iron-catalyzed imidation of sulfide and sulfoxide using photochemical continuous flow synthesis.[59f]

Building on their prior work, Lebel and colleagues advanced the field by developing both batch and continuous flow methods for the iron(II)-catalyzed synthesis of sulfilimines **39** and sulfoximines **40** utilizing *N*-mesyloxycarbamates **38** (Scheme 16).[59e] The addition of 1-butylimidazole as a base played a crucial role in achieving a homogeneous reaction mixture suitable for continuous flow applications. This innovative approach demonstrates broad substrate compatibility, delivering the desired products in good to excellent yields within

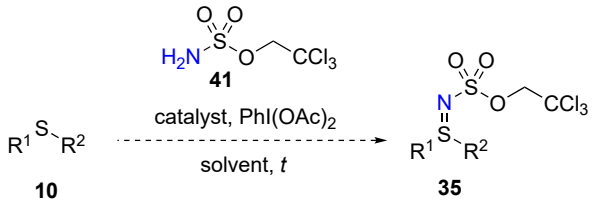
remarkably short reaction times ranging from 1 to 60 minutes. In batch reactions, the imidation of sulfides **10** with TrocNHOMs **38** produced sulfilimine products **39** in poor to excellent yields, ranging from 29% to 100%. Similarly, the imidation of sulfoxides **11** resulted in the formation of sulfoximine products **40**, with yields ranging from 41% to 96%.Transitioning to continuous flow methods, sulfide **10** imidation with TrocNHOMs **38** resulted in products **39** with yields between 69% to 96%, while sulfoxide **11** imidation resulted product **40** with yields ranging from 53% to 88%.



Scheme 16: Iron-catalyzed imidation of sulfide and sulfoxide with *N*-mesyloxycarbamates **28**.[59e]

2.2 Background and aim of the project

The increasing demand for sulfilimines in various applications has ignited extensive research into their synthesis, leading to the development of numerous efficient methods.[70] Sulfide imidation have emerged as a key strategy in this pursuit, highlighted by their effectiveness and versatility. Within the domain of metal-catalyzed reactions, iron-based complexes have gained significant attention for their remarkable substrate compatibility and the environment friendly nature as a catalyst. Notably, these systems typically employ a range of imidating agents such as azides, sulfonamides, carbamates, and iminoiodinanes, underscoring the diversity of approaches available for the synthesis of sulfilimines.



Scheme 17: Synthetic strategies for the synthesis of *N*-substituted sulfilimine **35**.

Inspired by the pioneering work of Lebel and coworkers, who showcased the effectiveness of iron-catalyzed sulfide imidations with trichloroethoxysulfonyl azides **34**, this study was driven

by the goal of establishing a comparable methodology while avoiding potentially hazardous azides. The motivation comes from the recognition of the practical challenges posed by azides, including safety concerns and handling issues. In response, this project aimed to explore alternative routes that maintain the efficiency and versatility demonstrated by Lebel's approach while reducing the risks associated with azide chemistry. As an alternative to trichloroethoxysulfonyl azides **34**, we selected 2,2-trichloroethyl sulfamate **41** was selected as our sulfide imidating agent for the synthesis of *N*-substituted sulfilimine **35**. The reaction conditions are to be optimised with different catalyst and solvent to find the corresponding sulfilimine product **35** in high yield (Scheme 17).

2.3 Result and discussion

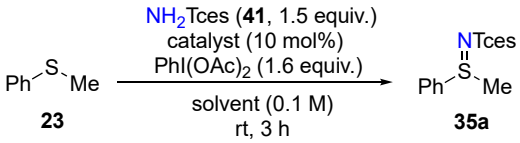
2.3.1 Optimization of the reaction conditions

In the initial phase of our project, we undertook a comprehensive optimization process with the objective of identifying the most effective catalyst for the activation of 2,2,2-trichloroethyl sulfamate **41** in sulfide imidation reactions using phenyl methyl sulfide **23** as a model substrate. Our investigation involved testing various rhodium, copper, and iron catalysts, each in 10 mol% quantities, to evaluate their ability to facilitate the desired transformations (Table 1, entries 1–11). The reactions were conducted under standardized conditions using (diacetoxyiodo)benzene (1.6 equiv.) as the oxidant and acetonitrile (0.1) as the solvent, with a reaction time of 3 hours at room temperature.

In our quest to optimize the sulfide imidation reaction using 2,2,2-trichloroethyl sulfamate **41**, we systematically evaluated a series of catalysts. Among the tested catalysts, $Rh_2(OOCCF_3)_2$ and $CuCl_2$ emerged as the top performers, yielding the desired product **35a** in 69% and 77% yield, respectively (Table 1, entries 2 and 7). Subsequent screening of iron salts as catalysts revealed that $Fe(OTf)_2$ exhibited superior catalytic activity, leading to an increased yield of 86% for product **35a** (Table 1, entry 11). Further optimization involved different solvents to enhance the reaction efficiency. Transitioning from acetonitrile to PhMe, THF, Et_2O and MeOH. Toluene proved to be particularly advantageous, yielding the optimal result of 89% for product **35a**. Thus, the best yield of the desired product **35a** was achieved by reacting sulfide **23** (0.1 mmol) with 2,2,2-trichloroethyl sulfamate **41** (1.5 equiv.) in PhMe (0.1 M) for 3 h (Table 1, entry 16)

these conditions were chosen as optimal reaction conditions and summarized in general procedure GP1.

Table 1: Optimization of the reaction conditions.[a]



entry	catalyst	solvent	yield[b] of **35a** (%)
1	$Rh_2(esp)_2$	MeCN	38
2	$Rh_2(OOCCF_3)_2$	MeCN	69
3	$Cu(acac)_2$	MeCN	34
4	$Cu(OTf)_2$	MeCN	48
5	$Cu(OAc)_2$	MeCN	68
6	$[Cu(MeCN)_4]PF_6$	MeCN	70
7	$CuCl_2$	MeCN	77
8	$FeCl_2$	MeCN	46
9	$Fe(ClO_4)_2$	MeCN	39
10	$Fe(acac)_3$	MeCN	61
11	$Fe(OTf)_2$	MeCN	86
12	$Fe(OTf)_2$	$CHCl_3$	48
13	$Fe(OTf)_2$	THF	62
14	$Fe(OTf)_2$	Et_2O	70
15	$Fe(OTf)_2$	MeOH	85
16	$Fe(OTf)_2$	toluene	89

[a]Reaction conditions: Sulfide **23** (0.10 mmol), 2,2,2-trichloroethyl sulfamate (**41**, 0.15 mmol), $PhI(OAc)_2$ (0.16 mmol), catalyst (10 mol %) in the solvent (0.1 M) at rt for 3 h.[b]Yield after column chromatography.

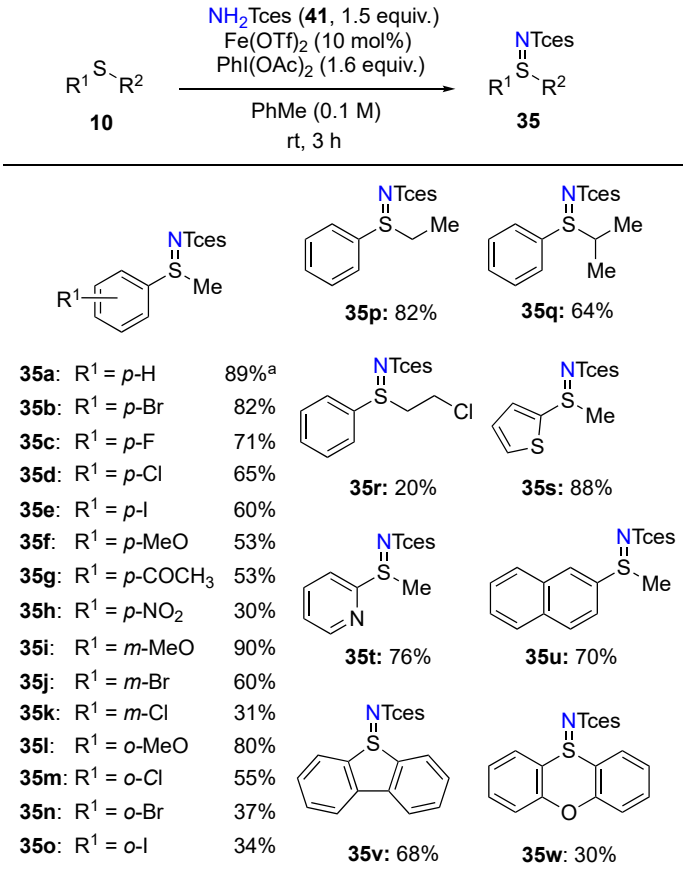
2.3.2 Substrate scope

Having the optimized reaction conditions in hand, a series of sulfides **10** were subjected to reactions with 2,2,2-trichloroethyl sulfamate **44,** yielding the corresponding sulfilimines **35** in generally good yields (Scheme 18). Initially, aryl methyl sulfides were investigated as substrates, with halo- substituted aryl groups at the *para* position providing sulfilimines (**35b–35e**) in yields ranging from 60% to 82%. Conversely, substrates bearing *p*-OMe, *p*-$COCH_3$, and *p*-NO_2 groups resulted in products (**35f**–**35h**) with yields of 53%, 53%, and 30%, respectively. *Meta*-substituted sulfides featuring OMe, Br, or Cl groups delivered products

(**35i–35k**) with yields of 90%, 60%, and 31%, respectively. *Ortho*-substituted methyl aryl sulfides containing OMe, Cl, Br, and I groups yielded products (**35l–35o**) with yields spanning from 34% to 80%.

Upon closer examination, it was observed that the presence of electron-donating groups tended to enhance product formation, while steric hindrance exerted a decreasing yield. Additionally, the influence of non-aromatic sulfur substituents on product formation was explored. Ethyl phenyl sulfide **10p** afforded **35p** in 82% yield, whereas sulfilimine **35q**, featuring a sterically demanding isopropyl substituent on sulfur, was obtained from **10q** in 64% yield. Notably, the reaction with β-chloroethyl-substituted sulfide **10r** resulted in sulfilimine **35r** with a significantly reduced yield of 20%, presumably due to potential decomposition arising from neighbour group activation.

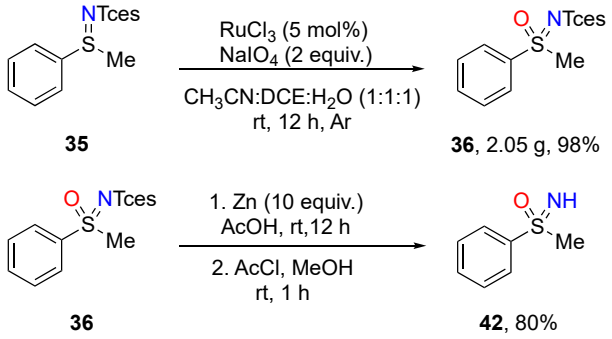
Furthermore, methyl sulfides bearing thienyl, pyridinyl, or naphthyl substituents (**10s–u**) were successfully employed, providing sulfilimines **35s**, **35t**, and **35u** in yields of 88%, 76%, and 70%, respectively. Dibenzothiophene **10v** and phenoxathiine **10w** also underwent the reaction, furnishing **35v** and **35w** in yields of 68% and 30%, respectively. These detailed investigations shed light on the substrate scope and structure-reactivity relationships within this iron-catalyzed sulfide imidation process, demonstrating its versatility and potential for accessing a diverse array of sulfilimine derivatives with varying substituent patterns and functional groups (Scheme 18).



Scheme 18: Substrate scope for sulfide imidation with trichloroethyl sulfamate. Reaction scale: 0.1 mmol. [a]In parentheses: 2 g reaction scale.

2.3.3 Functionalization of *N*-protected sulfilimine

Recognizing the significance of sulfoximines in synthetic and medicinal chemistry,[71] we embarked on a targeted strategy to demonstrate an oxidation/deprotection pathway for the synthesis of *N*H-sulfoximines **42** (Scheme 19). *N*Tces-Sulfilimine **35** was chosen as the representative starting material. Preliminary attempts using H_2O_2, *m*-CPBA, or $KMnO_4$ to oxidize the sulfilimine **35** to the desired *N*Tces-sulfoximine **36** remained unsuccessful, with no detection of the target product observed. However, a pivotal breakthrough was achieved with the adoption of a $RuCl_3$ catalyst in conjunction with sodium periodate, which resulted in the successful conversion to *N*Tces-sulfoximine **36** in an excellent yield of 98% equivalent to 2.05 g of product on the applied scale (Scheme 19).[72]

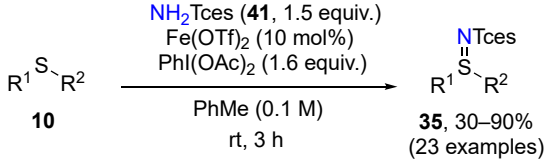


Scheme 19: Conversion of sulfilimine **35** to *N*H-sulfoximine **42**.[72]

Inspired by the protocol established by Lebel and colleagues, the *N*Tces-group of sulfoximine **36** was effectively cleaved using zinc in acetic acid.[59e,59f] This step led to the desired *NH*-sulfoximine **42** in a high yield of 80%. This strategic oxidation and deprotection approach not only highlights the efficacy of the $RuCl_3$/sodium periodate system for the transformation of sulfilimines **35** to sulfoximines **42** but also underscores the utility of zinc-mediated cleavage in accessing valuable *NH*-sulfoximine derivatives.

2.4 Conclusion

In summary, the synthesis of *N*Tces-protected sulfilimines **35** involved an iron catalyst (10 mol%), 2,2,2-trichloroethyl sulfamate **41** (1.5 equiv.) and PIDA (1.6 equiv.) to convert the corresponding sulfides **10** into *N*Tces-protected sulfilimines **35** in 30% to 90% yield (Scheme 20).[73] Notably, both acyclic and cyclic substrates exhibited excellent reactivity under mild conditions at ambient temperature, yielding the desired products in good yields after a concise 3 hour reaction period. Following the successful synthesis of *N*Tces-protected sulfilimines **35**, this product was subjected to further transformation to access sulfoximine derivatives. The oxidation of the sulfilimine **35** was accomplished using a ruthenium-catalyzed oxidation protocol with sodium periodate as the oxidant. Which leads to the corresponding *N*Tces-protected sulfoximine **36** in 98%.



Scheme 20: Synthesis of *N*Tces-protected sulfilimines **35**.[73]

To complete the desired transformation sequence, the *N*Tces protecting group was selectively cleaved using established conditions involving zinc in acetic acid. This deprotection step successfully afforded the targeted *N*H-sulfoximine **42** in 80%. The stepwise methodology employed in this synthesis not only demonstrates the utility of iron and Ru-catalyzed reactions for accessing sulfilimine **35** and sulfoximine **36** motifs but also underscores the use of selective deprotection strategies to unlock desired chemical functionalities *N*H-sulfoximine **42**.

3 Synthesis of benzo[*e*][1,4,3]oxathiazin-3-one 1-oxides from *N*H-(2-hydroxyaryl)sulfoximines

The experimental work for this chapter was supported by Runa Tschekorsky Orloff, Qiulan Lu, and Nils Völcker as part of their research internships. Additionally, Pit van Bonn, a doctoral student was involved in the execution of experiments and the analysis of the data, all in the group of Prof. Dr. Carsten Bolm at RWTH Aachen University under the supervision of the author of the thesis. The crystal structure of **97a** was determined by the working group of Prof. Dr. Kari Rissanen. The investigations have already been partially published:

Periasamy, K.; van Bonn, P.; Orloff, R. T.; Völcker, N.; Lu, Q.; Rissanen, K.; Bolm, C. Synthesis of Benzo[*e*][1,4,3]oxathiazin-3-one 1-Oxides from *N*H-S-(2-Hydroxyaryl)sulfoximines. *J. Org. Chem.* **2024**, *89*, 8286–8290.

3.1 Introduction

3.1.1 Sulfoximine-containing heterocycles

In recent decades, the accessibility of diverse sulfoximine moieties has greatly expanded with the advancement of new oxidative and transition metal catalysis techniques. Within this array, cyclic sulfoximines have emerged as a focal point of scientific interest, primarily due to their remarkable biological activities including antimicrobial, antiviral, and anti-inflammatory properties.[74] These compounds have proven to be invaluable in various scientific disciplines, particularly in asymmetric synthesis, where they function as indispensable chiral auxiliaries and ligands.[75,76] Their unique capability to induce chirality in a multitude of reactions renders them versatile tools for the synthesis of enantiomerically enriched compounds, which hold significant importance in pharmaceutical industries for the development of therapeutic agents.[77] Lovering and coworkers have shown that both a significant degree of saturation and the existence of stereogenic centers play crucial roles in facilitating the successful progression of newly discovered hits into pharmaceutical drugs during clinical trials.[78] Additionally, the potential of cyclic sulfoximines as agrochemicals has gained attention owing to their notable insecticidal and pesticidal activities, suggesting promising alternatives in agricultural applications.

Cyclic sulfoximines exhibit a diverse range of structures, properties, and applications, leading to their classification into several categories (Figure 11). Common classifications encompass exocyclic sulfoximines (**43**–**45,** Figure 11A) and endocyclic (**46**–**53,** Figure 11B), achiral and chiral cyclic sulfoximines, monocyclic and polycyclic sulfoximines, as well as substituted cyclic sulfoximines. Focusing specifically on endocyclic and exocyclic variations, a clear distinction emerges. Endocyclic sulfoximines (**46**–**53**) incorporate the sulfoximine moiety within the cyclic structure, wherein the sulfur atom or the sulfur and nitrogen atom of the sulfoximine group forms part of the ring system itself. Conversely, exocyclic sulfoximines (**43**–**45**) feature the sulfoximine moiety attached to a cyclic structure but not integrated within the ring system. Instead, it is bonded to an atom that constitutes part of the cyclic structure. A variety of potential endocyclic sulfoximine structures may exist, varying in terms of ring size, ring fusions, and the relative positioning of the sulfoximine within fused ring systems. This differentiation underscores the structural diversity within the realm of cyclic sulfoximines, which influences their reactivity and potential applications in various scientific endeavors.[71b]

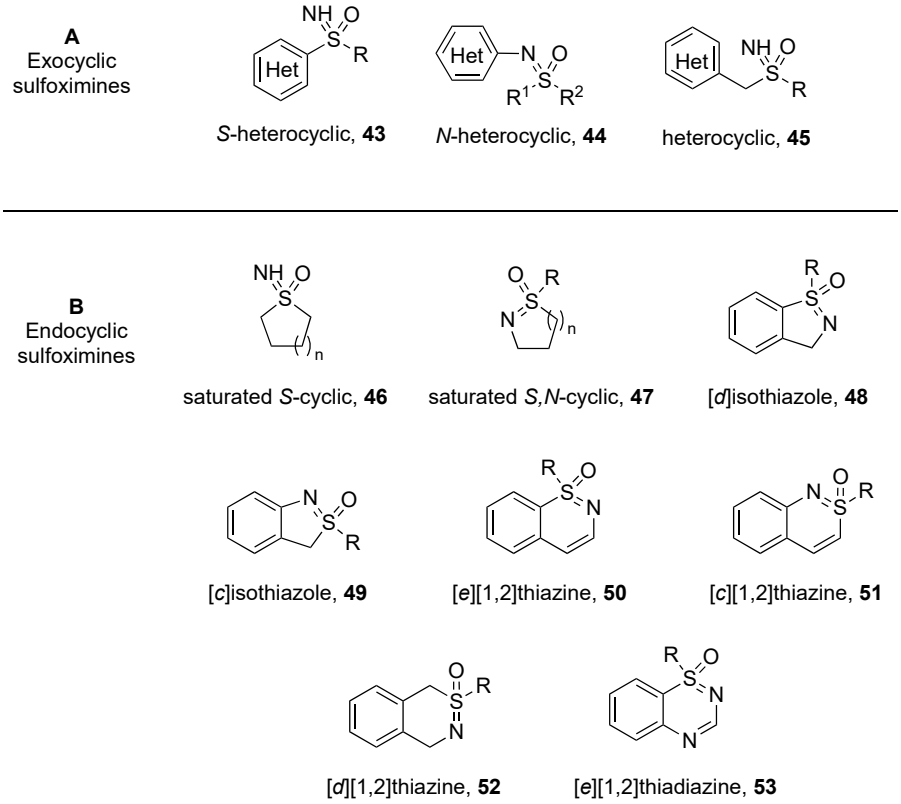
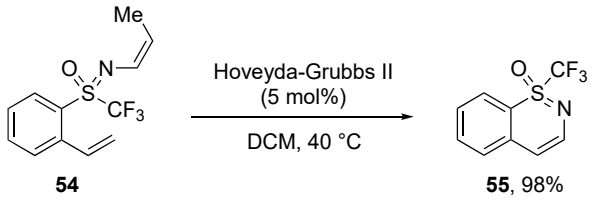


Figure 11: A representation of the various sulfoximine heterocyclic scaffolds.[71b]

Among the various cyclic sulfoximines, benzothiazine derivatives has gained significant attention due to their versatile frameworks, which offer substantial structural diversity and valuable applications in medicinal chemistry.[79]

3.1.2 Synthesis of benzothiazine derivatives

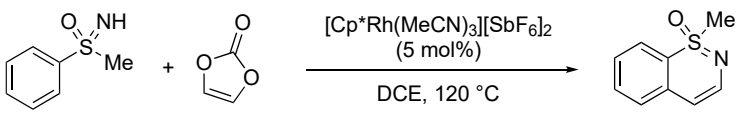
The work by Elsa, Magnier and co-workers demonstrated that benzo[*e*][1,2]thiazine 1-oxide can be prepared using a ring-closing metathesis reaction catalyzed by Hoveyda-Grubb's 2nd generation catalyst (Scheme 21).[81] This reaction occurs in dichloromethane at 40 °C. The starting material for this synthesis is vinyl sulfoximine **54**, which can be obtained in two steps from 2-iodophenyl trifluoromethyl sulfoximine with a yield of 63%. Subsequently, this compound can be cyclized to form compound **55** in an excellent yield of 98%. Attempts to access benzo[*e*][1,2]thiazine 1-oxides from *N*-alkynyl analog of **54** were unsuccessful.



54 **55**, 98%

Scheme 21: Olefin metathesis approach to benzo[*e*][1,2]thiazine 1-oxide.[81]

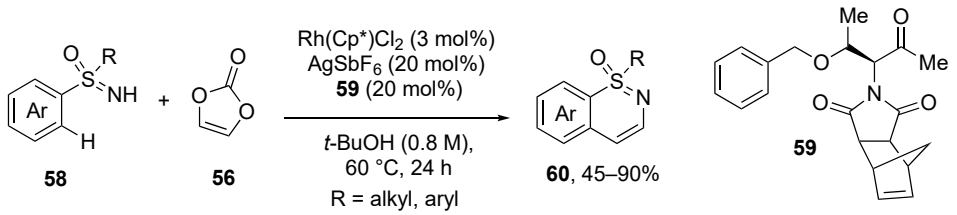
A valuable method for synthesizing benzothiazine derivative **57** involved a rhodium catalyzed annulation of sulfoximine **37** with vinylene carbonate **56**.[82] Within the range of various azaheterocycles described, one notable compound was benzo[*e*][1,2]thiazine 1-oxide **57**, as illustrated in Scheme 22. By leveraging the sulfoximine moiety of **37** as a directing group, vinylene carbonate **56** could be inserted at the *ortho* position, functioning as an acetylene equivalent, leading to further cyclization and resulting in the formation of unsubstituted benzo[*e*][1,2]thiazine 1-oxide **57**, in modest yield.



37 **56** **57**, 30%

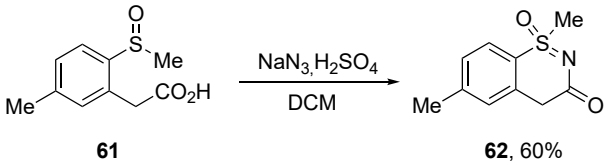
Scheme 22: Synthesis of benxo[*e*][1,2]thiazine 1-oxide by rhodium-catalyzed annulation.[82]

This study represents the synthesis of unsubstituted 1,2-benzothiazines **60** through a redox-neutral process involving rhodium(III)-catalyzed C–H activation and [4+2]-annulation of *S*–aryl sulfoximines **58** with vinylene carbonate **56** using *N*-protected amino acid ligand **59** (Scheme 23).[83] Vinylene carbonate acts both as oxidizing acetylene surrogate and efficient vinylene transfer agent resulting in the successful formation of a diverse range of 1,2-benzothiazine derivatives **60** in moderate to good yields.



Scheme 23: Synthesis of benzothiazine derivatives **60** through C–H activation and annulation via vinylene transfer.[83]

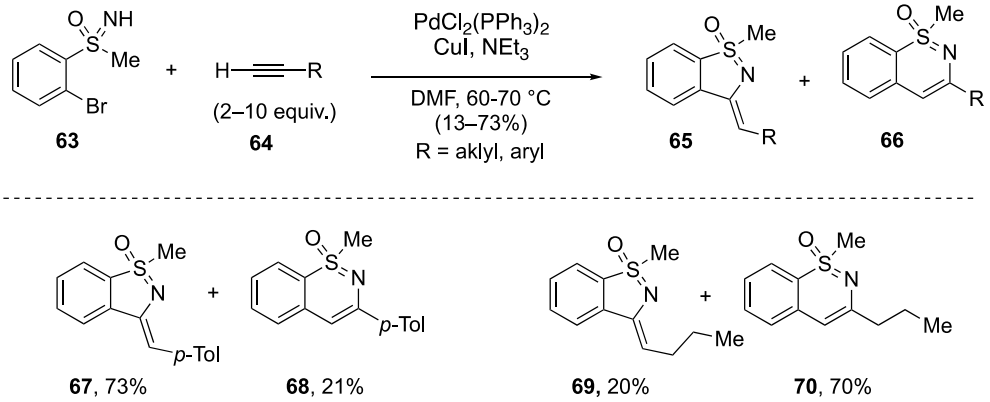
The synthesis of benzo[*e*][1,2]thiazine 1-oxide **62** dates back to 1971, credited to Cram and coworkers (Scheme 24).[84] This compound was prepared following a methodology similar to that used for its benzisothiazole 1-oxide. The synthesis involved the imidative cyclization of sulfoxide **61** with sodium azide, which yields the corresponding product in moderate yield. Sulfoxide **61** was synthesized in a two-step procedure from 2-acetylaryl thioether through Willgerodt rearrangement and subsequent oxidation of sulfur. It's noteworthy that **62** can undergo basic hydrolysis to form the open chain carboxylate salt. Upon subsequent acidification, the carboxylate salt can be re-cyclized, illustrating a reversible aspect of its chemical behaviour.



Scheme 24: Synthesis of benzo[*e*][1,2]thiazine 1-oxides **62** by Cram. [84]

In addition to stepwise syntheses,[85] Harmata documented a groundbreaking achievement in organic synthesis in 2005, reporting a transition metal-catalyzed construction of benzo[*d*]isothiazol 1-oxides. This milestone was reached by utilizing a dual Pd/Cu catalytic system to facilitate a Sonogashira-cyclization cascade of aryl bromo sulfoximines with terminal

alkynes (Scheme 25).[86] Notably, their experimentation employed 2-bromophenyl sulfoximine **63** for reaction optimization and scope evaluation, examining its reactivity with various terminal alkynes **64**. Through meticulous investigation, the optimal catalytic system was identified as $PdCl_2(PPh_3)_2$/CuI, with the base Et_3N in dimethylformamide at elevated temperatures. An intriguing observation emerged regarding the influence of the R substituent on the alkyne, which significantly impacted the product distribution. Specifically, aryl-substituted alkynes **67** and **69** favoured the formation of benzo[*d*]isothiazole 1-oxides **65**, whereas alkyl-substituted alkynes **68** and **70** predominantly yielded benzo[*e*]thiazine-1-oxides **66**.

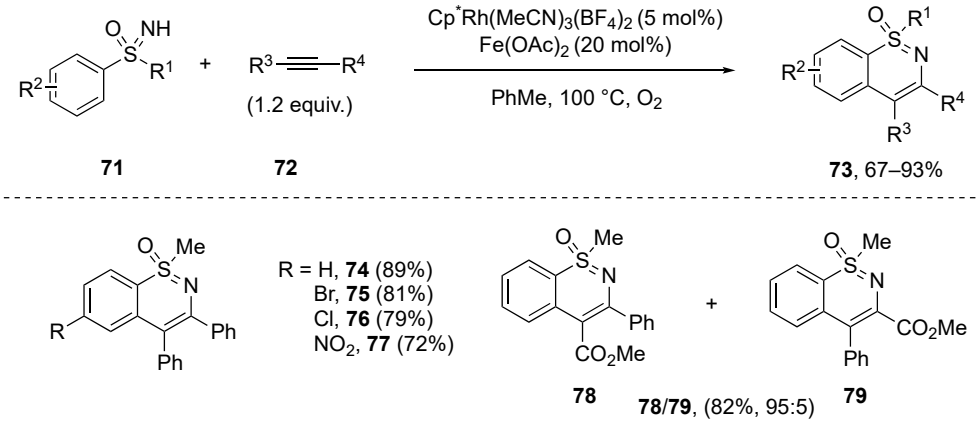


Scheme 25: Transition metal-catalyzed synthesis of benzo[*d*]isothiazole 1-oxides **65** and benzo[*e*]thiazine 1-oxides **66** from *N*H-sulfoximines and alkynes.[86]

A major breakthrough was achieved in 2013 when the Bolm group developed a more straightforward method for the synthesis of 3,4-disubstituted benzo[*e*][1,2]thiazine 1-oxides **73** using acetylenes **72** via rhodium-catalyzed annulation with aryl sulfoximines **71** marks a significant advancement in synthetic methodology (Scheme 26).[87] Mechanistically, the transformation is proposed to involve a one-pot C–H/N–H activation which is subsequently followed by an annulation of the alkyne. This approach, which eliminates the requirement for prehalogenated aryl sulfoximines, has emerged as a popular strategy for accessing substituted benzo[*e*][1,2]thiazine 1-oxides **73**. Through systematic optimization, it was determined that $Cp^*Rh(MeCN)_3(BF_4)_2$ and $Fe(OAc)_2$ constitute the optimal catalytic system in the presence of oxygen at atmospheric pressure.

Notably, other iron or copper salts, as well as the absence of O_2, proved less effective, yielding **73** in yields below 38%. Further exploration of the aryl sulfoximine scope under these

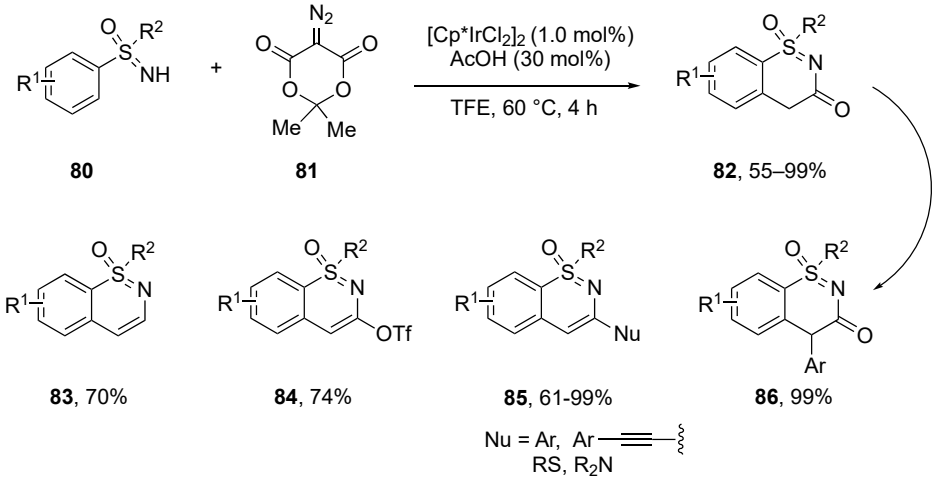
conditions revealed that diphenyl acetylene provided the desired products (**74–77**) in high yields. Regiochemical bias was observed with unsymmetrical acetylenes, favoring aryl substituents at the 3-position (**78** and **79**). In a recent development, TMS-capped acetylenes were employed for regioselective substitution at the C3-position following *in situ* desilylation, yielding products in moderate to good yields (26–63%).



Scheme 26: Synthesis of 3,4-disubstituted benzo[*e*][1,2]thiazine 1-oxides **73** by *ortho*-C–H bond activation.[87]

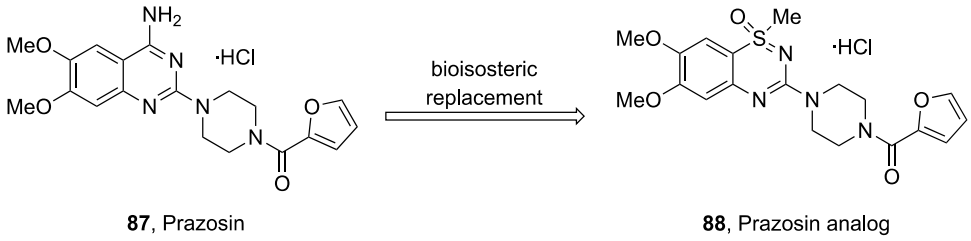
Rhodium-catalyzed *ortho*-C–H/N–H bond functionalisation with alkynes was the basis for several protocols following the same strategy for the synthesis of benzo[*e*][1,2]thiazine 1-oxides.[88] Further, enantioselective syntheses have been developed[89] and the synthesis of polycyclic derivatives.[90]

An efficient C−H cyclization of sulfoximines **80** with diazo Meldrum's acid **81**, catalyzed by iridium(III) catalyst were developed by Lee and colleagues in 2023, which resulted in the formation of cyclic sulfoximines **82** bearing a carbonyl group in good to excellent yields (Scheme 27).[88i] Subsequent treatment of sulfoximine **82** with DIBAL-H leads to the generation of a vinylene cyclization product **83** in 70% yield and also with triflic anhydride in the presence of DBU affords sulfoximine **84** having a vinyl triflate moiety in 74% yield. The sulfoximines **82**, substituted with vinyl triflate are readily employed in Pd-catalyzed cross-coupling reactions, yielding various monosubstituted sulfoximines **85** in good to excellent yields. Finally, Sulfoximine **82** was coupled with 4-bromotoluene producing the desired arylated sulfoximine **86** in a quantitative yield.



Scheme 27: Synthesis of cyclic sulfoximine by iridium(III)-catalyzed C−H cyclization of sulfoximines with diazo Meldrum's acid.[88i]

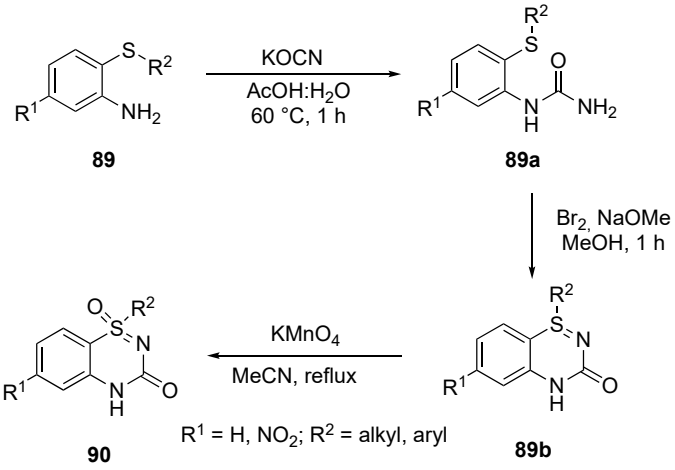
In 1979, Dillard and coworkers findings suggest that substituting the amidine moiety in antihypertensive drug Prazosin **87** with sulfoximine group yields benzo[*e*][1,2,4]thiadiazine 1-oxides **88** while maintaining their blood pressure-lowering efficacy in two distinct animal models. This implies that the sulfoximine group could potentially serve as a viable alternative to the amidine moiety in this context, offering avenues for further exploration and development in the field of antihypertensive drug design (Scheme 28).[91]



Scheme 28: Sulfoximine moiety replaced the amidine group in the quinazoline series.[91]

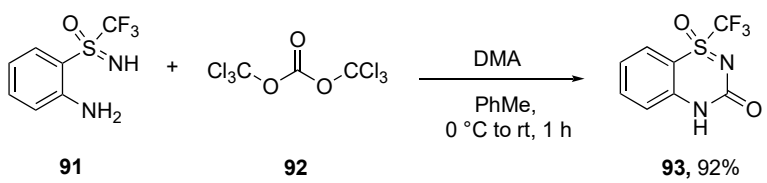
In 1964 Reinöhl and coworkers reported he synthesis of benzo[*e*][1,2,4]thiadiazine 1-oxides **90** (Scheme 29).[92] The synthetic route involved the oxidation of benzo[*e*][1,2]thiadiazine **89** using potassium permanganate in acetonitrile as the solvent. The process likely proceeds through a series of chemical reactions where potassium permanganate acts as the oxidizing agent, converting the sulfur atom in the thiadiazine ring to a sulfoxide functionality, resulting in the formation of the desired benzo[*e*][1,2,4]thiadiazine 1-oxide product **90**.

Benzo[*e*][1,2]thiadiazine **89b** was before synthesized in a two-step process from 2-aminoaryl thioether **89** though urea formation in a reaction of the amino group with cyanate followed by cyclization through intramolecular imidation of sulfur with bromine and sodium methanolate. This pioneering work has led to the development of various multiple step procedures to synthesise benzo[*e*][1,2,4]thiadiazine 1-oxides from 2-amino- or 2-nitroaryl thioethers **90**.[36b,84,85b,93] Further, metal-free[94] and metal-catalyzed synthesis from *N*H-(aryl)sulfoximines through *ortho*-C–H/N–H bond functionalizations in one[95] or in two[96] steps have been developed. In addition, enantioselective versions of this transformation using chiral ligands have been reported[97] as well as a synthesis from *N*H-2-(bromoaryl)sulfoximines.[98]



Scheme 29: First synthesis of benzo[*e*][1,2,4]thiadiazine 1-oxides by Reinöhl.[92]

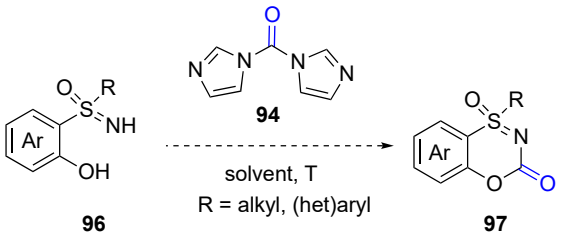
In a significant development in 2016, Vo-Thanh, Magnier, and along with their collaborators, showcased a notable cyclization reaction involving the conversion of amino sulfoximine **91** into sulfoximine urea **93** (Scheme 30).[96b] The starting material amino sulfoximine **91** can be obtained through the reduction of azido sulfoximine with an impressive yield of 98%. This reaction employed triphosgene **92** and *N,N*-dimethyl aniline (DMA) as key reagents, and it was conducted in toluene as solvent. The reaction temperature was carefully controlled within the range of 0 °C to room temperature, ultimately resulting in a good yield of the desired product



Scheme 30: Synthesis of sulfoximine urea **93** through cyclization of amino sulfoximine **91**.[96b]

3.2 Background and aim of the project

Motivated by the principles of bioisosteric replacement for enhancing lead structure optimization, we considered the synthesis of benzo[*e*][1,4,3]oxathiazine 1-oxides **97**.[99] While single-ring systems with a 3-oxathiazin-2-one 4-oxide structure have been investigated previously,[100] fused-ring system of this nature have not been reported in the literature to date. Building upon this gap in knowledge and based on an early work on benzo[*e*][1,2,4]thiadiazine 1-oxides **95**,[85b] we embarked on this study to expand the understanding of these compound **97** (Scheme 31). The reaction conditions need to be optimized by varying several parameters, including the type of carbonyl source, the choice of solvent, the temperature, and the reaction time. The goal of this optimization process is to identify the most effective conditions that will yield the corresponding sulfilimine product **97**, in high yield.

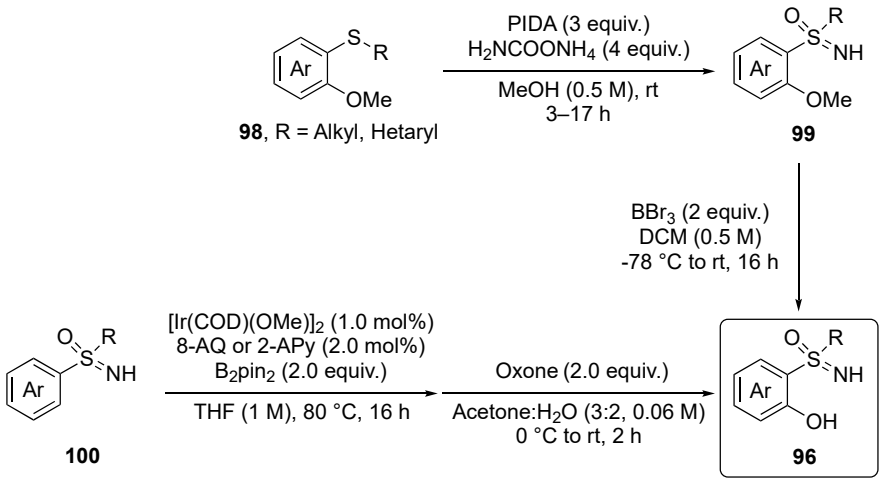


Scheme 31: Synthetic pathways towards benzo[*e*][1,4,3]oxathiazine 1-oxides **97.**

3.3 Results and discussion

3.3.1 Synthesis of starting material

*N*H-(2-hydroxyaryl)sulfoximines **96** appeared as the ideal starting materials for synthesizing target products benzo[*e*][1,4,3]oxathiazin-3-one 1-oxides **97**. The phenolic sulfoximines were accessible by oxidation/imidation of *S*-(2 methoxyaryl)thioethers **98** to yield the corresponding *N*H-(2-methoxyaryl)sulfoximine **99**,[26] which upon demethylation with BBr_3 gave **96**.[101] Alternatively, compounds **96** could be prepared by *ortho*-C–H bond borylation and subsequent oxidation starting from *N*H-(aryl)sulfoximines **100** (Scheme 32).[102] This dual approach provides versatile pathways to access the desired starting materials for further synthesis.



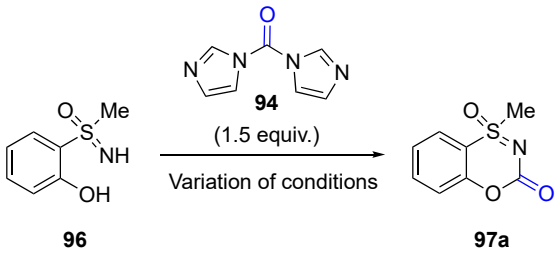
Scheme 32: Strategies for the synthesis of starting material *N*H-(2-hydroxyphenyl) sulfoximine derivative **96**.

3.3.2 Optimization of the reaction conditions

In order to optimize the reaction conditions, *N*H-(2-hydroxyphenyl)-*S*-methyl sulfoximine (**96**) was selected as the representative substrate and 1,1'-carbonyldiimidazole **94** as the carbonyl source. The expected product was **97**, and the results of the optimization process are presented in Table 2. In the initial phase of the study, various solvents were examined at room temperature including MeCN, THF, DCE, and DCM. Despite a reaction time of 16 hours, the yields of compound **97** ranged from poor to moderate yields (17–60%). The most promising result emerged from the utilization of DCE, yielding **97** in 60%. (Table 2, entry 3). Subsequent investigations involved screening solvents at temperatures ranging 40 °C to 85 °C (Table 2, entries 6–14). Notably, DCE consistently outperformed other solvents, achieving **97** in a remarkable yield of 94% at 85 °C (Table 2, entry 10). Altering the quantity of 1,1'-carbonyldiimidazole **94** from the commonly used 1.5 equiv. to 1.1 equiv. resulted in a reduced yield of **97** to 37% (Table 2, entry 11).

Surprisingly, in reactions conducted in DCM, the standard approach with 1.5 equivalents of CDI yielded 53% of **97**, while increasing CDI to three equivalents significantly lowered the yield to 15% (Table 2, entries 12 and 13). Attempts to enhance yields by introducing bases (DMAP, Cs_2CO_3, K_2CO_3, TEA, or DBU) to reactions in THF or DCM proved ineffective, with **97** yields below 13% (Table 2, entry 15–20). Thus, the best yield of the desired product **97** was achieved by reacting sulfoximine **96** (0.2 mmol) with CDI (1.5 equiv.) in DCE (0.1 M) for 16 hours in 94% as outlined in Table 2, entry 10 and summaries in the general procedure GP2.

Table 2: Optimization of the reaction condition to form benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide in solution.[a]



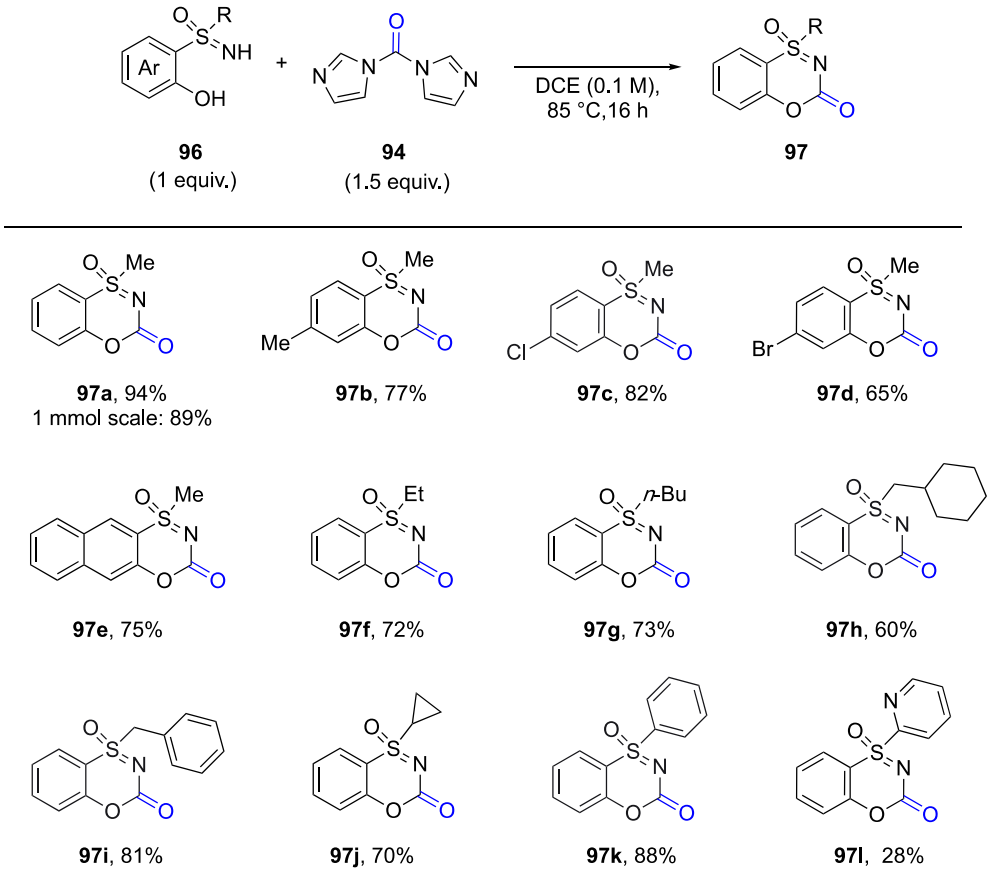
entry	base (equiv.)	solvent	temp (°C)	yield of **97a** (%)
1	–	MeCN	rt	17
2[b]	–	THF	rt	28
3	–	DCE	rt	60
4	–	DCM	rt	40
5	–	2-MeTHF	rt	trace
6	–	DMF	80	22
7	–	MeCN	80	16
8	–	THF	70	20
9	–	acetone	60	40
10	–	DCE	85	94
11[c]	–	DCE	85	37
12	–	DCM	40	53
13[d]	–	DCM	40	15
14	–	2-MeTHF	80	trace
15	DMAP (0.5)	THF	rt	10
16	DMAP (0.5)	THF	70	13
17	Cs_2CO_3 (2.0)	DCM	rt	trace
18	K_2CO_3 (2.0)	DCM	rt	trace
19	TEA (2.0)	DCM	rt	trace
20	DBU (2.0)	DCM	rt	trace

[a]Reaction conditions: sulfoximine **96** (0.2 mmol), CDI (1.5 equiv.), and solvent (0.1 M) for 16 h. [b]Reaction time was 22 h and CDI was added in two portions (1.2 equiv. at the beginning and 1.1 equiv. after 16 h). [c]CDI (1.1 equiv.). [d]CDI (3 equiv.).

3.3.3 Substrate scope

Under the optimized reaction conditions, a series of *N*H-(2-hydroxaryl)sulfoximines **96** reacted with CDI **94**, resulting in the formation of the corresponding benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97**, as depicted in (Scheme 33). Overall, the transformations proceeded smoothly,

yielding products in the range of 28% to 94%. Satisfied outcomes were observed when exploring the impact of different aryl substituents. Specifically, *N*H-(2-Hydroxyaryl) sulfoximines bearing methyl (**97b**), chloro (**97c**), or bromo (**97d**) substituents in the *para* position of the aryl group displayed high yields of 77%, 82%, and 65%, respectively. Additionally, (3-hydroxynaphthalen-2-yl)(imino)(methyl)-λ^6-sulfanone **96e** furnished **97e** in a 75% yield.



Scheme 33: Substrate scope for the synthesis of benzo[*e*][1,4,3]oxathiazin-3-one 1-oxides.

Exploring variations in the *S*-alkyl substituent revealed successful transformations, albeit with lower yields when transitioning from *S*-methyl **97a** to *S*-ethyl **97f** and *S*-butyl **97g** in 94%, 72% and 73%. Branching of the *S*-alkyl substituent in β or α positions was also feasible, providing **97h**, **97i**, and **97j** in yields of 60%, 81%, and 70%, respectively. Notably, a substrate featuring an *S*-phenyl group reacted favourably, yielding **97k** in an impressive 88%. However, **97l** with an *S*-(2-pyridinyl) substituent resulted in a reduced yield of only 28%, likely attributed to lower substrate solubility compared to similar substrates. To validate scalability, the reaction between **96a** and CDI **94** was upscaled to a one mmol scale, yielding **97a** in an impressive 89% yield.

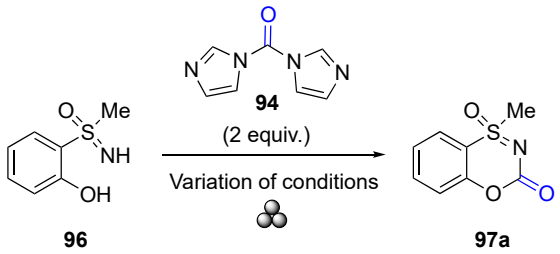
This scaling-up process underscores the practical applicability of the optimized conditions for potential large-scale synthesis. Overall, the comprehensive exploration of reaction conditions, substrate variations, and scalability provides valuable insights into the synthetic potential of the described chemical transformations.

3.3.4 Mechanochemical synthesis of benzo[*e*][1,4,3]oxathiazine-3-one 1-oxide

In recent studies, both our work and that of other investigators have highlighted the substantial benefits of solvent-free mechanochemical processes when compared to traditional solution-based systems. These advancements have not only demonstrated enhanced efficiency but also contributed significantly to sustainability improvements. In light of these progressive findings, we made a deliberate choice to explore the feasibility of a mechanochemical synthesis approach for benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97a**. The primary objective behind this exploration was to eliminate the reliance on dichloroethane as a solvent, aligning with the principles of sustainability and addressing environmental concerns.

In order to optimize the reaction conditions, *N*H-*S*-(2-hydroxyphenyl)-*S*-methyl sulfoximine (**96**) and 1,1'-carbonyldiimidazole (**94**) are selected as representative starting materials. The investigation of various conditions is summarized in Table 3. In our initial attempt, a mixture of sulfoximine **96** (0.3 mmol) and CDI **94** (0.6 mmol) was subjected to milling for 60 minutes at a frequency of 30 Hz in a yttrium partially stabilized zirconium oxide milling jar (volume: 10 mL), resulting in the observation of our product **97a** in 68% yield (Table 3, entry 1). In an endeavor to further enhance the yield, alternative approaches were explored. However, neither the use of dichloroethane as a liquid-assisted grinding agent nor the application of talcum or silica as a grinding auxiliary significantly improved the yield, with the yields ranging from 5% to 46% (Table 3, entries 2–4).

Table 3: Investigations on the mechanochemical synthesis of benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide.[a]



entry	deviation from the reaction conditions	yield of **97a** (%)
1	none	68
2	with dichloroethane (0.25 µL·mg^{-1})	46
3	with talcum (10 *wt.*%)	8
4	with silica (10 *wt.*%)	5

[a]Reaction condition: Sulfoximine **97a** (0.3 mmol), CDI (2 equiv.), and additives were milled at 30 Hz at 60 min in a ZrO_2-Y milling jar (volume: 10 mL) with two ZrO_2-Y milling balls (diameter: 10 mm) in air at room temperature.

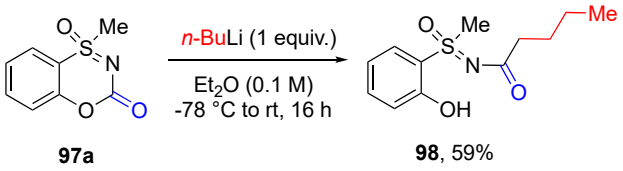
An interesting aspect of this mechanochemical process is that, unlike the conventional solution-based method, it did not necessitate additional heating. Furthermore, the product formation exhibited significantly accelerated kinetics, completing within a mere one hour timeframe as opposed to the 16 hours required in the solution-based process. Despite the slightly diminished yield of **97a** in the mechanochemical synthesis (68% compared to 94% in solution), this innovative method stands out for its avoidance of toxic dichloroethane. It is noteworthy that, while the product preparation was not entirely solvent-free due to jar extraction and final chromatographic purification with pentane/ethyl acetate, this approach represents a substantial advancement, offering new possibilities for subsequent process optimizations and emphasizing a significant step toward environmentally conscious and sustainable synthetic methodologies.

3.3.5 Functionalization of benzo[*e*][1,4,3]oxathiazine-3-one 1-oxide

To assess the reactivity of the synthesized benzo[*e*][1,4,3]oxathiazin-3-one 1-oxides **97a**, especially on the carbonyl site, a targeted investigation was conducted involving the reaction of **97a** with *n*-butyl lithium in diethyl ether, carried out within a temperature range from –78 °C to room temperature, as outlined in Scheme 34. Initially we expect the deprotonation of the methyl group. But surprisingly the outcome of this experiment revealed the formation of the

ring-opened product **98**, achieved with a moderate yield of 59%. Notably, the lithium reagent demonstrated a distinct reactivity pattern, as it did not deprotonate the relatively acidic *S*-methyl substituent. Instead, the lithium reagent acted as a nucleophile, directing its attack towards the previously installed carbonyl group.

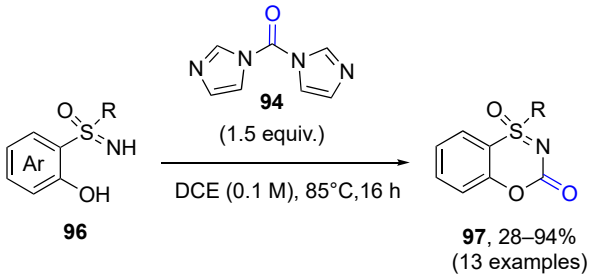
This unexpected reactivity sheds light on the intricacies of the chemical interactions at play, providing valuable insights into the behaviour of the benzo[*e*][1,4,3]oxathiazin-3-one 1-oxides **97a** in the presence of *n*-butyl lithium. The results contribute to a deeper understanding of the synthetic potential and reactivity profiles of these compounds, paving the way for further exploration and applications in organic synthesis (Scheme 34).



Scheme 34: Functionalization of benzo[*e*][1,4,3]oxathiazine-3-one 1-oxide.

3.4 Conclusion

In summary, a synthesis of benzo[*e*][1,4,3] oxathiazin-3-one 1-oxides **97a** has been developed, a novel class of three-dimensional heterocycles. This innovative molecular framework was achieved through the straightforward conversion of readily available *N*H-(2-hydroxyaryl) sulfoximines (**96**) with 1,1'-carbonyldiimidazole (**94**), resulting in products **97** with yields ranging from 28% to 94%. Importantly, the developed synthetic process demonstrates scalability and versatility, showcasing its adaptability to mechanochemical conditions, eliminating the need for additional solvents. Remarkably, this mechanochemical approach not only enhances the environmental sustainability of the synthesis but also expedites the product formation in short reaction time and without the requirement for external heating, resulting in products **97** in 68%. Which can be further optimized in future for higher yield. Further investigation of the reactivity of the heterocycles involved treatment with *n*-butyl lithium, a potent nucleophile, which resulted in carbonyl addition and subsequent ring opening.



Scheme 35: Synthesis of benzo[*e*][1,4,3] oxathiazin-3-one 1-oxides derivative.

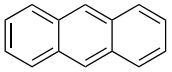
The significance of these findings extends beyond synthetic methodology, as the benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide scaffolds introduce promising opportunities in medicinal and crop protection chemistry. Given the prevalence of bioactive molecules incorporating sulfur and nitrogen as core elements, the emergence of this new heterocyclic structure opens avenues for designing compounds with diverse biological activities. The versatility, scalability, and unique reactivity patterns exhibited by these heterocycles position serve as valuable building blocks for the development of novel pharmaceuticals and agrochemicals, contributing to the advancement of drug discovery and sustainable agriculture practices.

4 Synthesis of dithienylethene sulfoximine

4.1 Introduction

4.1.1 Photochromism

The phenomenon of photochromism has a long history, with the earliest examples dating back to the latter half of the 19th century.[103] In 1867, Fritzsche made a notable discovery when he observed the bleaching of an orange-colored anthracene solution in daylight, followed by its re-coloration at night (Figure 12).[104] Interest in the phenomenon remained relatively subdued until the 1950s, when comprehensive investigations into its mechanisms and synthesis were conducted, notably by research teams led by Hirshberg and Fischer.[105]



106

Figure 12: Anthracene

Photochromism, a term rooted in the Greek words ‘phos’ (light) and ‘chroma’ (color), describes a captivating phenomenon wherein molecules undergo reversible color changes in response to light irradiation or photoisomerization.[106] This dynamic process not only alters the visible color of the molecules but also encompasses a broad spectrum of changes in their physical and chemical properties. For instance, during reversible photoisomerization, the fluorescence emission, refractive index, dielectric constant, dipole moments, electrochemical properties, conductivity, geometrical structure, and chemical reactivity of the molecules can undergo distinctive alterations under different light irradiation.[107]

Furthermore, photochromic compounds can be categorized as follows,

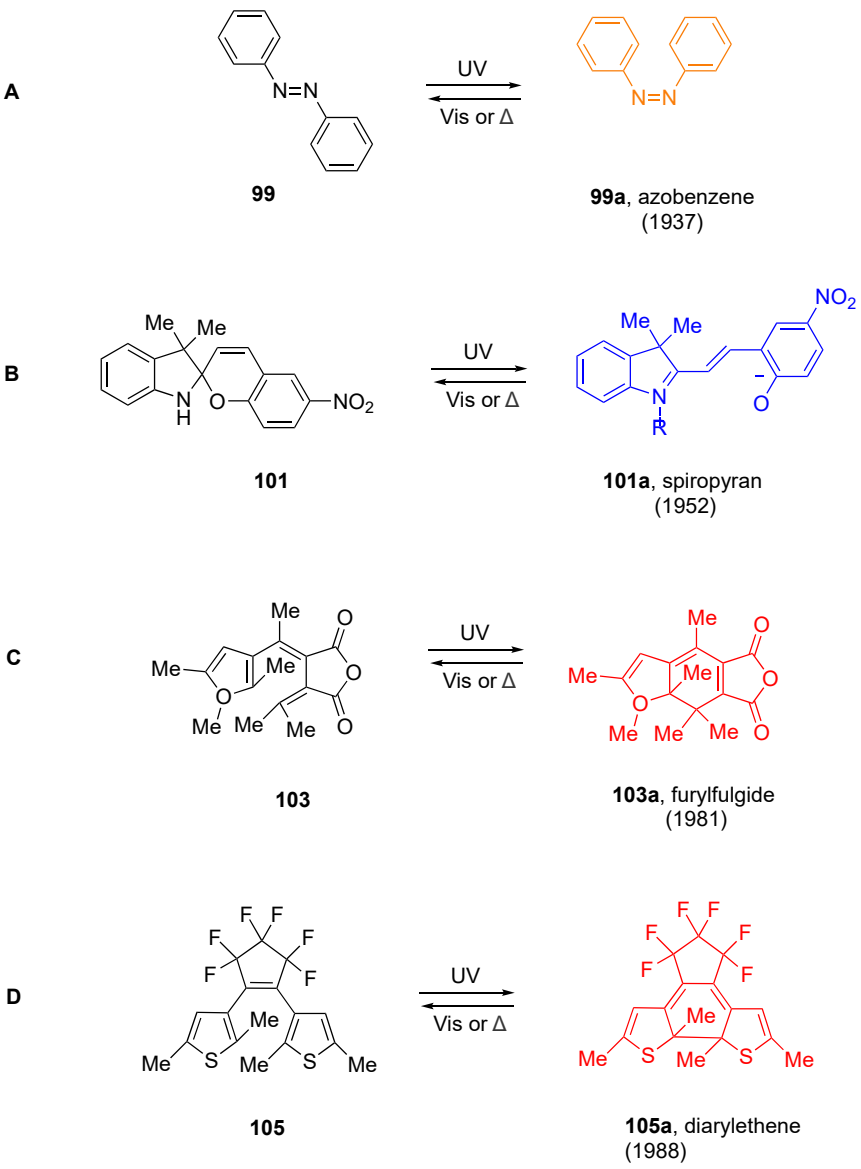
- thermally reversible T-type molecules (e.g., azobenzene and spiropyran)
- thermally irreversible P-type molecules (e.g., diarylethene and furylfulgide)

In contrast to T-type photochromic molecules, the thermally stable photogenerated isomers of P-type photochromic compounds exhibit a notable characteristic, as they do not easily revert

back to their initial isomers at room temperature without the presence of light.[108] At its core, photochromism represents a sophisticated interplay between light and molecular structure, defined by quantum mechanical principles. When molecules are exposed to light, they absorb photons and transition to higher energy states, which can lead to structural rearrangements and the formation of photoisomers. Subsequent interactions with light, such as thermal activation or additional photon absorption, can induce reversible transitions between different molecular configurations, thereby driving the observed color changes. Photochromic molecules exhibit reversible alterations in color when exposed to light. Examples of these molecules, displaying such color transformations, are illustrated in Scheme 36.

The upper two molecules, azobenzene (A)[109] and spiropyran (B),[110] represent classic examples of photochromic compounds, a class of molecules that undergo reversible changes in color upon exposure to light. When exposed to light, azobenzene shifts from a colorless state **99** to an orange color **99a**, while spiropyran transitions from colorless **101** to blue **101a** (Scheme 36). These molecules are categorized as T-type photochromic compounds due to their thermal reversibility, meaning they can revert to their original states upon the application of heat. However, there is a crucial limitation with these traditional compounds, the isomers generated on the right side of the photochemical reaction **99** and **101** are thermally unstable. Consequently, the vibrant colors they exhibit gradually fade when left in the dark, as the molecules revert to their original states over time.[111]

In contrast to azobenzene (A)[109] and spiropyran (B),[110] the lower two molecules, furylfulgide (C)[112] and diarylethene (D),[113] have been more recently developed (Scheme 36). They undergo a color change from colorless **103** and **105** to red **103a** and **105a** upon exposure to light. However, these molecules are classified as P-type photochromic compounds due to their unique properties. One distinguishing feature of P-type compounds is their thermal irreversibility, although they are photochemically reversible.[114] This means that they can revert to their original state under certain light conditions, they remain locked in their altered state under thermal conditions. In furylfulgide and diarylethene, the isomers generated on the right side of the reaction **103a** and **105a** are thermally stable. This stability means that they are less likely to revert to their colorless forms **103** and **105** in the absence of light, particularly at room temperature.[115]



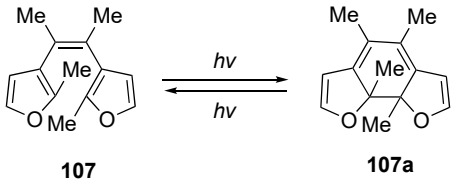
Scheme 36: Selected examples of photochromic molecules (A) azobenzene (B) spiropyran (C) furylfulgide (D) diarylethene.[116]

In the following section, we will provide an in-depth discussion on diarylethenes and examine various practical applications. By understanding these aspects, we can better appreciate how diarylethenes contribute to the innovative solutions in our research project.

4.1.2 Diarylethenes

In the year 1988, Irie and co-workers showcased an intriguing discovery, they found that by substituting the phenyl rings of a methylated *cis*-stilbene molecule with heterocyclopentene derivatives, they could synthesize a new class of compounds known as diarylethenes (Scheme

37).[103a] These diarylethene's exhibited a unique behaviour, as they were capable of switching between an open **107** and closed **107a** molecular conformation solely upon exposure to light of a specific wavelength.



107 **107a**

Scheme 37: Photochromic diarylethenes developed by Irie and coworkers.[103a]

Since the appearance of the first diarylethene in 1988, thousands of new diarylethene derivative have been synthesized in nearly thirty years.[115a] The diarylethene family consists of photochromic compounds that meet the criteria outlined below. Derived from stilbene, these compounds represent a significant advancement in the field of photochromism.[117] Departing from the traditional structure of stilbene, where phenyl rings predominate, diarylethenes incorporate five-membered heterocyclic rings characterized by low aromatic stabilization energy, such as thiophene or furan. This strategic substitution endows diarylethenes with exceptional properties, notably enhanced thermal stability in both their open- and closed-ring isomeric states.[118]

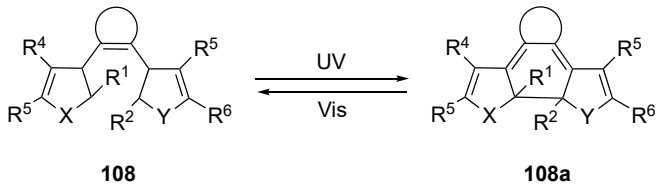
As a consequence, these compounds exhibit remarkable durability, allowing for repeated cycles of coloration and decoloration without degradation. This inherent stability is a critical feature for practical applications, ensuring prolonged functionality and reliability in molecular optical memory systems and optical switches.[119] Furthermore, the incorporation of these heterocyclic rings not only enhances thermal stability but also contributes to the versatility of diarylethenes, widening their scope for diverse applications in optoelectronic devices and beyond. The best performance of the diarylethenes is summarized as follows:[115a]

- Both isomers are thermally stable: well-designed derivatives have a half-life time at room temperature longer than 400000 years.
- Coloration/decoloration cycles can be repeated more than 10000 times.
- The quantum yield of coloration is close to 1 (100%).
- Both coloration and decoloration reactions take place in a picosecond time region.

- Many diarylethenes undergo photochromic reactions in the single crystalline phase.

As we already discussed the concept of photochromism in general at the beginning of this chapter, the following section will focus specifically on the photochromism of diarylethenes and their unique characteristics.

Diarylethenes featuring heterocyclic aryl groups have garnered recognition for their thermally irreversible nature, high sensitivity to light, and resistance to fatigue, establishing them as noteworthy photochromic compounds.[120] The photochromic mechanism underlying these compounds revolves around a reversible conversion between the open-ring isomer, characterized by a hexatriene structure, and the closed-ring isomer, which adopts a cyclohexadiene structure following the Woodward-Hoffmann rule (Scheme 38).[118] Typically, the open-ring isomer **108** appears colorless, while the closed-ring isomer **108a** exhibits colors ranging from yellow, red, to blue, contingent upon the specific molecular arrangement.



108 **108a**

Scheme 38: Schematic representation of the photochromism of diarylethenes **108**.[118]

Valuable characteristics of photochromic diarylethene

Numerous photochromic diarylethene have been synthesized, yet certain limitations hinder their viability for large-scale production of molecular optical memory systems and optical switches across various applications.[121] For a diarylethene to be truly suitable for these purposes, it must possess specific performance characteristics. Which include:[113]

- Thermal stability of both isomers
- High fatigue resistance
- High sensitivity
- Rapid response
- Reactivity in solid state

Following the breakthrough discovery of thermally irreversible photochromic diarylethenes in the mid-1980s, Irie and co–workers have endeavored to synthesize various compounds with the aim of enhancing their photochromic capabilities.[115a] The validation of theoretical predictions was substantiated through the synthesis of diverse diarylethenes featuring various aryl groups, as illustrated in Figure 13.[122] Notably, when incorporating heteroaryl groups such as thiophene **105a**, benzothiophene **109**, thiazol **112**, or oxazole **113**, characterized by their low aromatic stabilization energy, the resultant closed-ring isomers exhibit exceptional thermal stability, enduring for more than 12 hours at 80 °C.

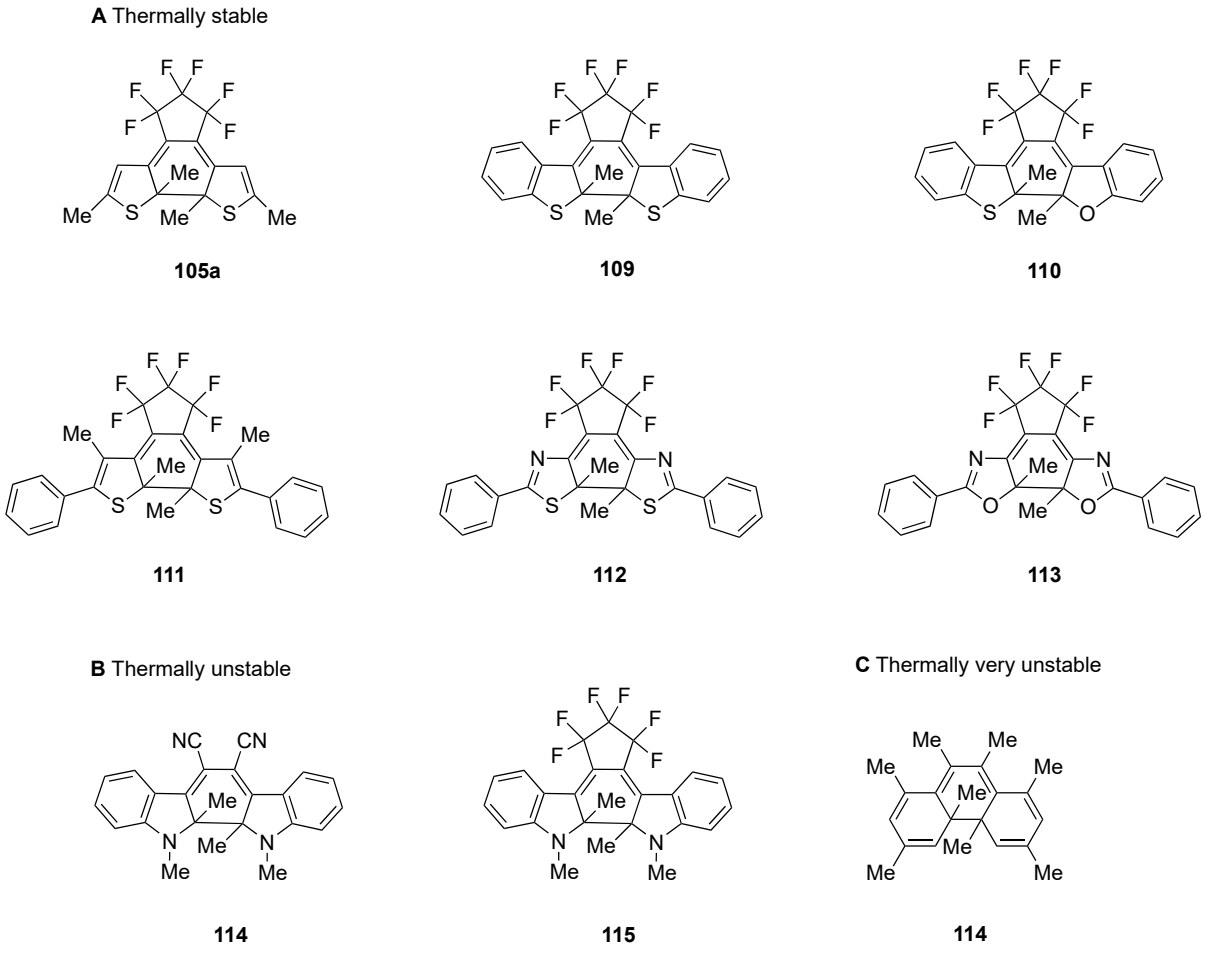


Figure 13: Thermal stability of diarylethene derivatives.[123]

Conversely, diarylethenes containing indole rings, with an intermediate level of aromatic stabilization energy, undergo thermally reversible photochromic reactions upon formation of closed-ring isomers, with half-lifetimes approximately 10 hours at 80 °C. Interestingly, the closed-ring isomer of diarylethene **114**, featuring phenyl rings, demonstrates swift reversion to

the open-ring isomer in mere minutes, even at a relatively low temperature of 20 °C, highlighting the dynamic behavior of these compounds across a range of conditions.[123]

Among the various diarylethenes, those featuring perfluorocyclopentene rings exhibit particularly unique properties. In the following section, we will explore how these compounds have significantly advanced the field of diarylethenes. Their exceptional stability and photochromic performance for potential applications.

Perfluorocyclopentene diarylethenes

Perfluorocyclopentene diarylethenes are characterized by the chemical inertness of the ethene bridge, which imparts them with an exceptional stability and a notable advantage over compounds containing alternative bridging groups.[124] This inherent stability is crucial for their widespread use in various applications.[125]

However, this advantage comes with a significant drawback because of the complexity associated with chemically modifying the perfluorocyclopentene moiety. Chemical modification of the ethene bridge is essential for understanding the correlations between the properties of these compounds and their molecular structure.[126] Few examples of perfluorocyclopentene diarylethenes are drawn in the (Figure 14).

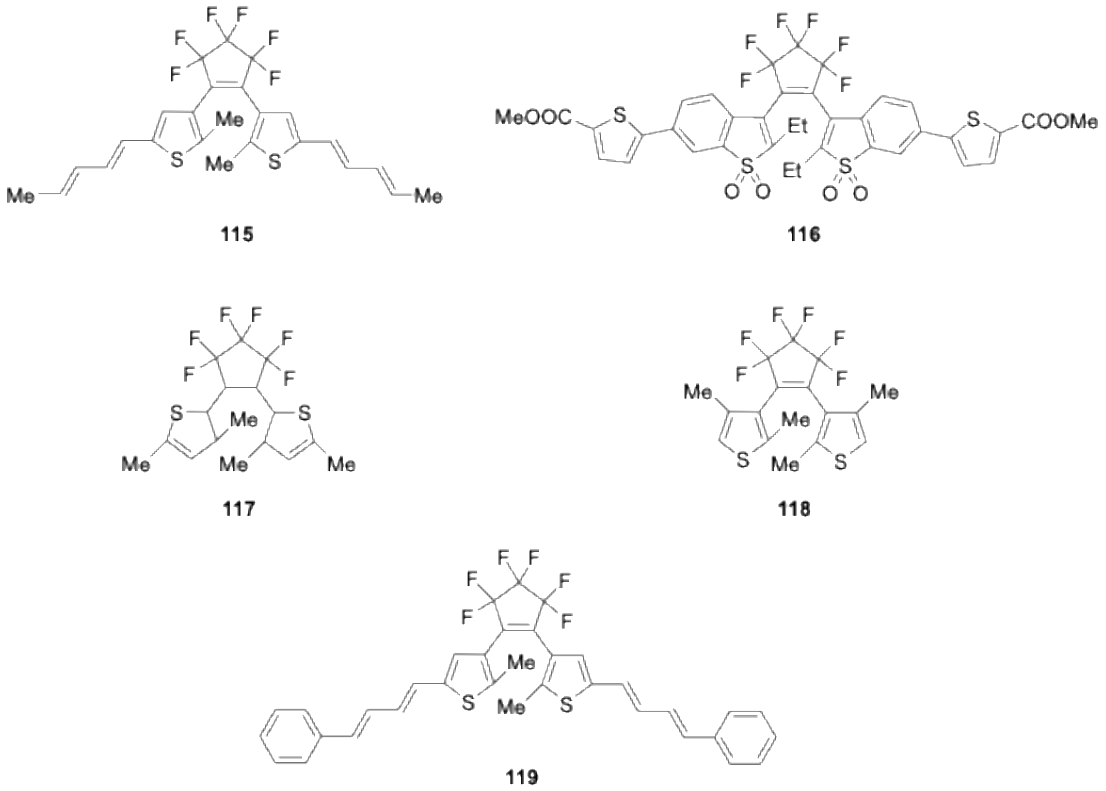
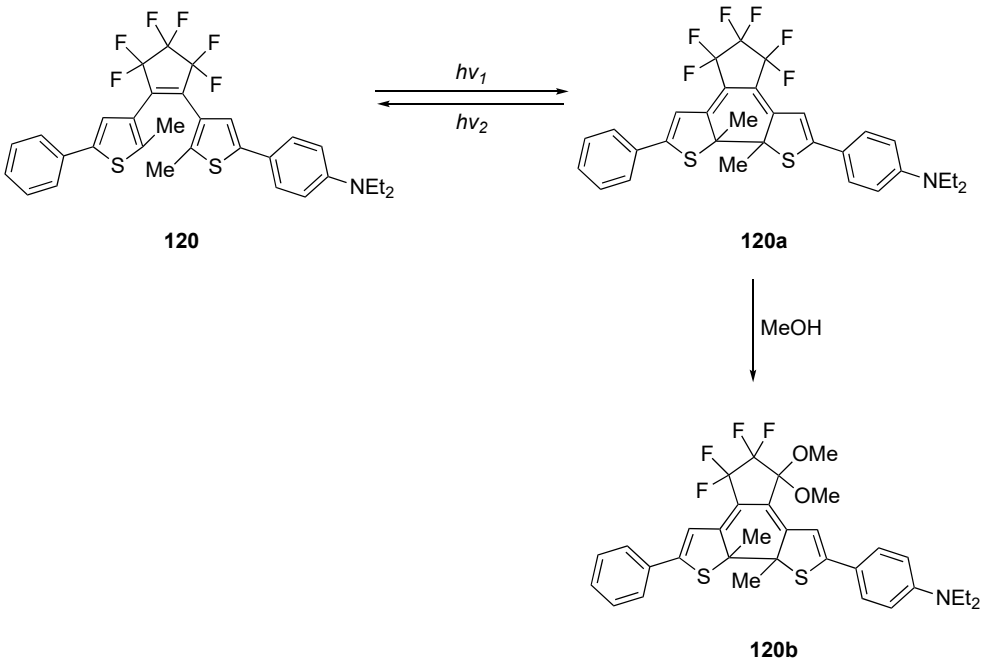


Figure 14: Examples of perfluorocyclopentene diarylethenes.

However, the modification of perfluorocyclopentene moiety **120** through nucleophilic substitution of methoxy groups for the fluorine atoms have been reported (Scheme 39).[127] This method was successfully employed to synthesize compound **120b**, which also exhibits photochromic properties. The synthesis of compound **120b** involved subjecting diarylethene **120a** to UV irradiation in a methanol solution.[121] These advancements in chemical modification provide valuable insights into the structure-property relationships of perfluorocyclopentene diarylethenes and pave the way for further exploration and utilization of these compounds in various fields.



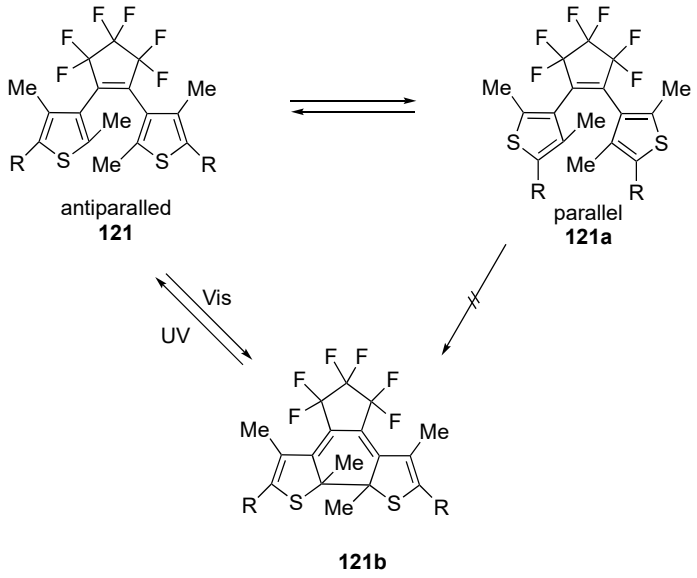
Scheme 39: Functionalization of the perfluorocyclopentene moiety. [127]

In the following section, we will discuss the different conformers of diarylethenes. Understanding the spatial arrangement of substituent groups in these compounds is crucial, as it can significantly influence their stability, reactivity, and photochromic behavior. These conformations are key to designing diarylethenes with desired properties and functionalities. This knowledge is particularly valuable in fields such as material science and molecular electronics, where precise control over molecular behavior is essential.

Conformation of diarylethene

The variation in color observed between the open-ring and closed-ring isomers stems from disparities in both their geometric and electronic configurations.[115a] In the open-ring isomer **121**, the presence of free rotation between the ethene moiety and the aryl group allows for non-planar geometry, with pi electrons primarily localized within the aryl groups. Additionally, this isomer exhibits two distinct conformations: one with the rings in mirror symmetry **121** (parallel conformation) and one with C2 symmetry **121a** (antiparallel conformation), with the photocyclization reaction occurring predominantly from the antiparallel conformation (Scheme 40). Conversely, the closed-ring isomer **121b** adopts a planar structure and exists as two enantiomers (*R*,*R* and *S*,*S*) due to asymmetric carbon atoms. Considered as an alternate polyene, this isomer features delocalized pi-electrons throughout the molecule, resulting in higher

polarizability compared to the open-ring isomer. These structural disparities contribute to variations in physical properties, such as polarizability, underscoring the influence of molecular geometry and electronic configuration on the observed differences in color and other characteristics.



Scheme 40: Conformations of diarylethenes.[115a]

Diarylethenes, renowned for their exceptional photochromic properties, have found widespread applications across various fields. Their ability to reversibly change structure and color when exposed to light makes them ideal for optical data storage. Additionally, diarylethenes are utilized in the development of advanced molecular switches and sensors, taking advantage of their rapid response times and high thermal stability. These compounds are also pivotal in designing smart materials and devices. The versatility and durability of diarylethenes continue to drive innovation in both scientific research and technological advancements. In the following section, we will discuss their applications in detail.

4.2 Application of diarylethenes

Diarylethenes have emerged as the favoured photochromic molecule for numerous applications due to their exceptional fatigue resistance and thermal stability. These properties make them ideal candidates for applications requiring prolonged use and reliability, such as optical storage and switching devices. Their ability to undergo reversible photochemical reactions, toggling

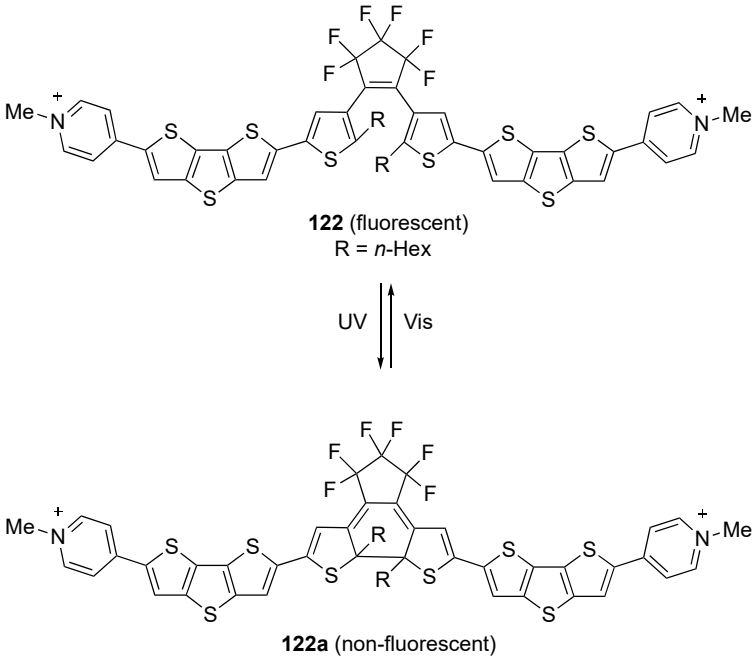
between distinct states in response to light stimuli, enables precise control and manipulation in various optical systems. Consequently, diarylethenes stand out as components in the development of robust and efficient optical devices, driving innovation in fields ranging from data storage to optoelectronics.[108a,128] In the realm of materials science, there has been a notable surge of interest in stimuli-responsive materials, owing to their remarkable versatility and potential for myriad applications across diverse fields, notably in bioengineering and information technology.[129]

Fluorescence photoswitching molecules

Conventional transmission methods often trigger photochromic reactions, leading to information loss over repeated reads. Conversely, fluorescence methods offer increased sensitivity and reduced information degradation, particularly with low readout power, ensuring minimal destruction of recorded data.[130] Several fluorescence photoswitching molecules have been successfully synthesized, and a selection of few will be discussed below.

In 1995 and 1996, Tsivgoulis and Lehn conducted a pioneering study in the synthesis of a fluorescent photoswitching molecule.[131] This molecule **122** exhibited a remarkable ability to transition between two distinct states in response to specific wavelengths of light (Scheme 41). The initial state, referred to as the open-ring isomer **122**, underwent a significant transformation when exposed to UV light with a wavelength below 400 nm while immersed in methanol. This irradiation prompted the conversion of the open-ring isomer **122** into the closed-ring isomer **122a**, achieving an impressive conversion rate of 92%. Conversely, the closed-ring isomer **122a** could be reverted back to the open-ring isomer **122** through irradiation with visible light, specifically wavelengths exceeding 600 nm. This reversible process occurred with complete efficiency, enabling the molecule to oscillate between its two distinct forms with precision and reliability.

Further characterization of the molecule's optical properties revealed intriguing insights into its fluorescence behavior. Upon excitation within the 400–500 nm spectral region, the open-ring isomer **122** exhibited pronounced fluorescence, emitting light with a peak intensity at 589 nm. In contrast, the closed-ring isomer **122a** displayed no fluorescence under similar excitation conditions, demonstrating a stark disparity in their respective photophysical responses.



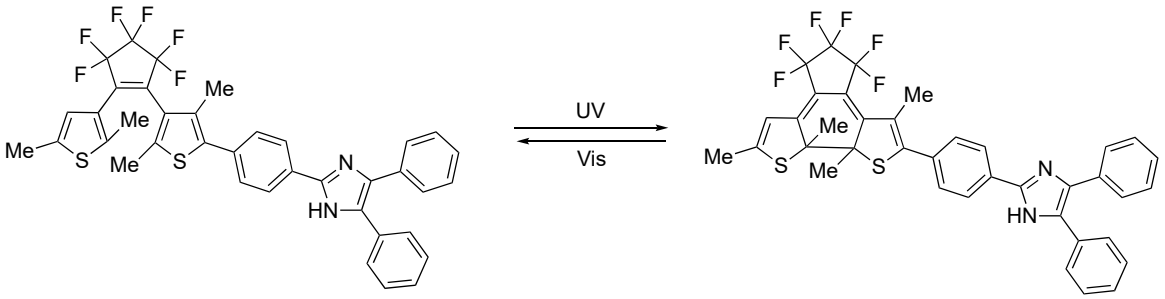
Scheme 41: Fluorescent behaviour of compound **122** upon photoswitching.[131b]

Diarylethene molecule, designated as compound **123**, was successfully synthesized by M. Irie and co-workers in 2001, incorporating a triphenylimidazole group into its structure (Scheme 42).[132] The inclusion of this group was strategically chosen due to its well-documented fluorescence quantum yield of 48%, imparting potential optical properties to the resulting compound.

The open-ring isomer **123** exhibited distinct fluorescence characteristics when subjected to excitation at 313 nm, with emission peaks observed at 390 nm and 410 nm. Despite the relatively low fluorescence quantum yield of 7.7%, the emission at these wavelengths indicated the presence of fluorescence activity in this state. However, in contrast, the closed-ring isomer **123a** displayed no detectable fluorescence under similar excitation conditions, emphasizing the significant impact of molecular conformational changes on optical properties.

Interestingly, despite the modest fluorescence quantum yield of the open-ring isomer **123**, it demonstrated a remarkably high cyclization quantum yield of 0.49. This observation suggests that the molecule efficiently undergoes cyclization upon photoexcitation, leading to the formation of the closed-ring isomer **123a** (Scheme 42). Moreover, the cycloreversion quantum yield, representing the reverse reaction from the closed-ring to the open-ring isomer, was found to be one-tenth of the cyclization reaction yield. This discrepancy underscores the

thermodynamic and kinetic preferences favoring the formation and stabilization of the closed-ring state, highlighting the complex interplay between molecular structure and photochemical reactivity.

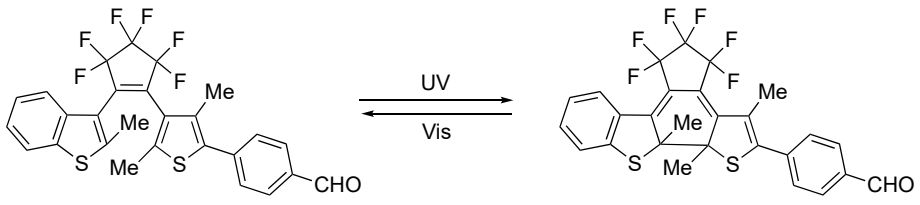


123 (fluorescent) **123a** (non-fluorescent)

Scheme 42: Fluorescent behaviour of compound **123**.[132]

In the case of diarylethene **124**, it contains a 4-formylthiophene group, which is a specific functional group attached to the diarylethene molecule (Scheme 43),[133] which exhibits a fluorescence-photoswitching property. When diarylethene is in its open-ring isomer form **124** and is irradiated with light at a wavelength of 301 nm, it exhibits fluorescence. The emission maximum, or the wavelength at which the emitted light is most intense, is measured at 420 nm. This indicates that when the molecule is in its open-ring form and absorbs light at 301 nm, it undergoes a process where it becomes electronically excited and subsequently emits light in the visible range, with a peak emission at 420 nm.

Conversely, when diarylethene is in its closed-ring isomer form **124a**, it does not exhibit fluorescence upon irradiation with 301 nm light. This suggests that the closed-ring isomer is not capable of undergoing the same electronic transitions that lead to fluorescence emission observed in the open-ring isomer.



124 (fluorescent) **124a** (non-fluorescent)

Scheme 43: Fluorescent behaviour of compound **124**.[133]

Biological applications of fluorescent diarylethene

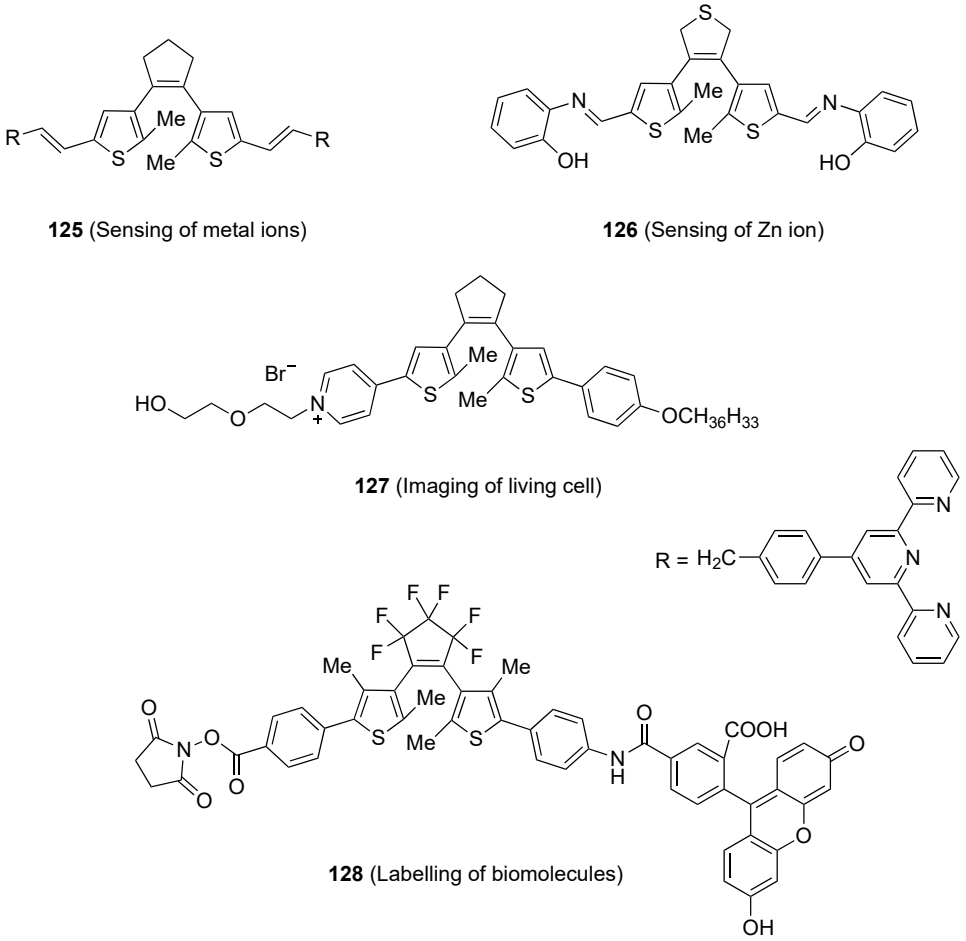
Photochromic compounds that change color reversibly upon exposure to light have captivated researchers for their promise in both technological and biological realms.[134] While there's extensive exploration of these compounds for use in devices that manipulate light, like photonic devices, their potential in biological contexts remains relatively uncharted. Few investigations have dug into how these compounds could be harnessed for creating sensors that interact with biological materials, tracking dynamic processes within living organisms, or enabling imaging of live cells.

Molecules capable of fluorescent photo switching have been employed to create fluorescent sensors designed to detect metal ions.[135] These sensors operate by undergoing reversible alterations in emission intensity and wavelength upon coordinating metal ions. For instance, one investigation by Guo and co-workers involved linking a photochromic thiophene containing compound with terpyridine units through a phenylene bridge **125**.[135] In another study by Cheng and Zeng, a diarylethene Schiff base ligand was synthesized **126**.[136] Such systems find utility in environmental and biological contexts where metal ions, like zinc, play crucial roles (Figure 15). They offer promising avenues for monitoring and understanding processes involving these essential metal ions, spanning from environmental phenomena to biological functions.

An amphiphilic diarylethene **127**, has emerged as a promising photo switchable tool for imaging live cells.[137] This amphiphilic diarylethene structure comprises hydrophilic and hydrophobic segments at either extremity of the diarylethene moiety (Figure 15). In aqueous environments, this compound self-assembles into stable vesicle nanostructures. Notably, the amphiphilic nature of this diarylethene renders it capable of permeating cellular membranes, thereby serving as an innovative biomarker for live cell imaging. Importantly, it exhibits minimal cytotoxicity, enhancing its suitability for biological applications.

In 2007 Irie and coworkers introduced an photochromic compound **128** for fluorescent tagging of proteins.[138] This compound consists of a photochromic diarylethene unit, a fluorescein-derived fluorophore, and an amine-reactive succinimidyl ester component (Figure 15). Notably, the diarylethene moiety within this derivative exhibits fluorescence photoswitching facilitated by intramolecular energy transfer from the fluorophore to

diarylethene unit. The fluorescence emitted by the diarylethene derivative undergoes efficient quenching upon photocyclization due to spectral overlap between the absorption band of the closed form acceptor and the emission band of the fluorophore functioning as the donor. Exposure to UV light results in a significant reduction in fluorescence intensity, which is fully restored upon irradiation with visible light. These findings underscore the potential of compound **128** for the precise and reversible fluorescent labelling of biomolecules, offering a means for photo controllable manipulation in biological research.



125 (Sensing of metal ions) **126** (Sensing of Zn ion)

127 (Imaging of living cell)

128 (Labelling of biomolecules)

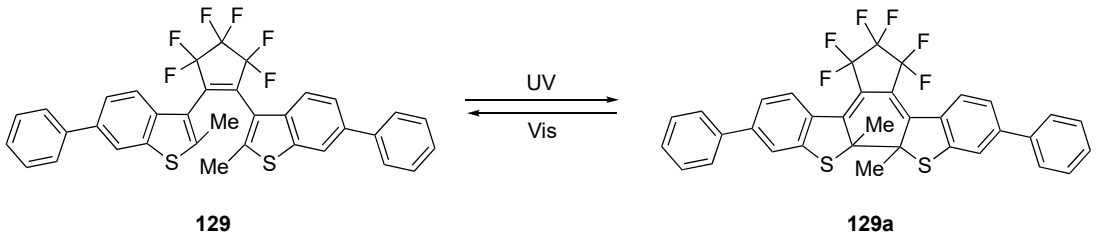
Figure 15: Diarylethene derivatives useful in biological applications.

Memory

Photochromic compounds hold promise for applications in optical memory storage.[115a] Unlike conventional optical media that rely on heat-based recording methods, photochromic optical memory utilizes a photochemical recording approach. This photon-mode recording method offers distinct advantages in terms of resolution, writing speed, and multiplex recording

capabilities, including wavelength, polarization, and phase. Among photochromic molecules, diarylethene stand out as particularly promising for photon-mode recording media due to their exceptional thermal stability, rapid response time in the picosecond range, high quantum yield of photoisomerization, and remarkable resistance to fatigue.

In their research, Uchida and coworkers made a notable finding regarding compound **129**, which contains benzothiophene rings (Scheme 44).[139] They observed substantial modifications in the infrared spectrum of this compound following photoisomerization. These observed spectral changes represent a promising avenue for the development of image recording technologies.

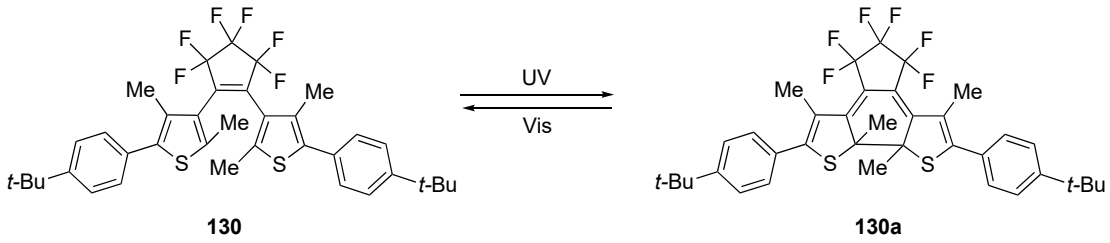


129 **129a**

Scheme 44: Compound **129** can be applied in optical memory storage.[139]

Switches

Molecular switches possess the unique ability to transition between different states, altering both their chemical composition and physical characteristics in response to external stimuli like photons, electrons, or chemicals.[140] Of these stimuli, photons offer particular convenience due to their easy and rapid switching capabilities and the ability for remote control. Among the molecules capable of photon-induced switching, diarylethene stand out. These compounds undergo interconversion between distinct open **130** and closed-ring **130a** forms upon alternating exposure to UV and visible light (Scheme 45).[141] This property positions diarylethenes as essential components in the construction of diverse light-driven molecular switches, enabling precise control and manipulation at the molecular level. Diarylethene **130** displays photochromic behavior even within a bulk amorphous system.[142] Amorphous diarylethenes are useful materials not only for switches but also for other optoelectronic applications.



Scheme 45: Diarylethene **130** displays an application in switches.[231]

Photochromic polymer containing diarylethenes

Photochromic polymers, with diarylethene derivatives integrated into their main chains[143] or side groups,[144] offer versatile solutions across diverse applications (Figure 16). These specially designed polymers exhibit reversible changes in structure and properties upon exposure to light, making them invaluable for a range of uses. Additionally, polymer films incorporating dispersed or embedded diarylethene derivatives have found widespread application in photonics.[145] These films enable precise manipulation of light-matter interactions, facilitating the development of advanced optical devices and systems. From sensors to optical switches, the utilization of photochromic polymers in photonics underscores their significance in driving innovation and addressing technological challenges.

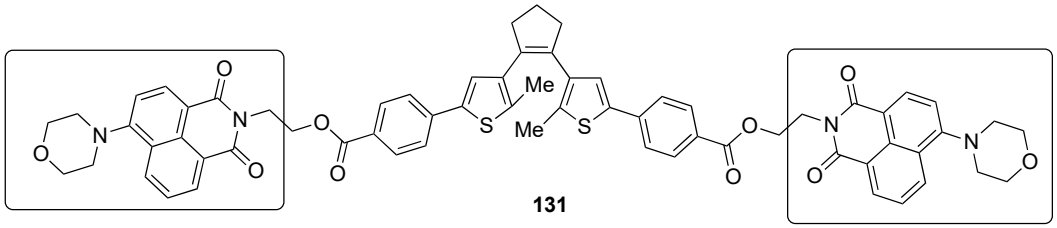
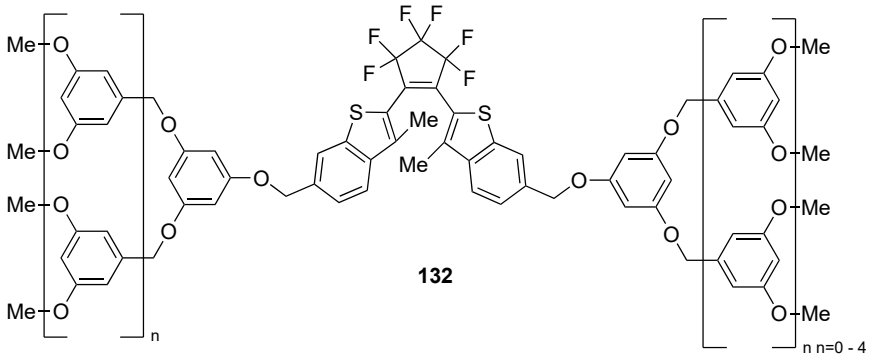


Figure 16: Bisthienylethene-bridged napthalimide dimer.

There exist two primary methods for integrating photochromic units into a polymer matrix, dispersion as dopants within the matrix or covalent grafting onto the polymer as part of the macromolecule. Dispersing photochromic units within a polymer matrix stands as a straightforward and effective approach in producing photochromic films. A plethora of studies have investigated the performance and functionality of various photochromic diarylethene derivatives embedded within polymer matrices.[145c,146]



132

Figure 17: Bisbenzothienylethene-cored dendrimers.

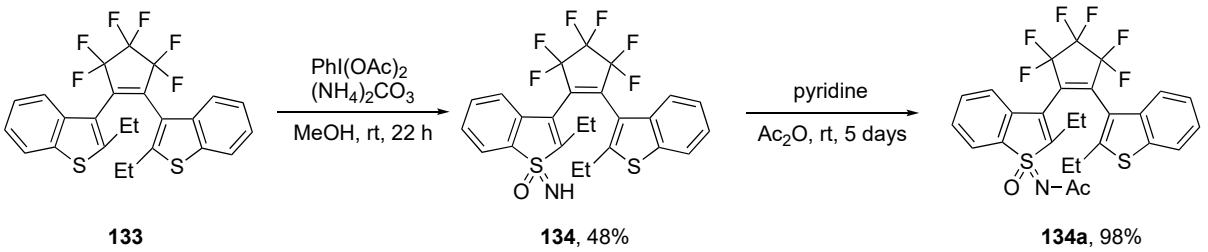
For example, bisthiophene-bridged naphthalimide dimers dispersed in polymethyl methacrylate were utilized to showcase two-dimensional recording capabilities,[147] while bisbenzo-thienylethene-cored dendrimers placed within polycarbonate of bisphenol (Figure 17). A PC films aimed to enhance photo-cyclization conversion ratios.[148] These systems have demonstrated remarkable performance within solid-state polymeric matrices. On one hand, the versatility of dispersing organic small molecules into compatible polymeric matrices facilitates the formation of solid films with desired properties.

4.3 Photochromic switching behavior of sulfoximines and sulfoxide

In 2019, our group reported one-pot *N*H-sulfoximidations of thiophene derivatives to dithienylethene-type photoswitches **134** (Scheme 46).[149] Dithienylethenes such as **133** have found numerous application as photoswitches.[134,150] Also analogous sulfones has resulted in the creation of interesting functional materials, which can be utilized in various applications. One such application is their potential use as photochromic dyes. Photochromic dyes are molecules that undergo reversible changes in color upon exposure to light of specific wavelengths. By incorporating sulfone-based compounds into these dyes, results in enhancing their performance, making them suitable for achieving super-resolution imaging.[113,115a,118] These materials have shown promise for applications in fields such as optics and materials science.

In this study, they mentioned that the steric hindrance and the electron-withdrawing hexafluorocyclopentenyl group in compound **134** posed a considerable challenge to the transformation. Consequently, a significant excess of (diacetoxyiodo)benzene (10 equiv.) and ammonium carbonate (6 equiv.) were necessary to achieve complete conversion of the

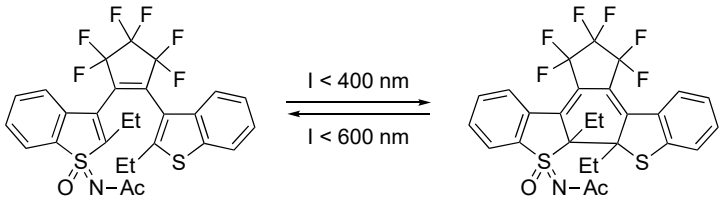
substrate. Efforts to elevate the reaction temperature resulted in decomposition. Functionalization of *N*H-moiety of **134** leads to the formation of acylated product **134a** in 98% yield. An attempt to *N*-alkylate **134a** with iodoethenes failed due to substrate degradation upon treatment with KOH.



133 **134**, 48% **134a**, 98%

Scheme 46: Syntheses of dithienylethene *N*H-sufloximine **134** and *N*-acetyl derivative **134a**.[149]

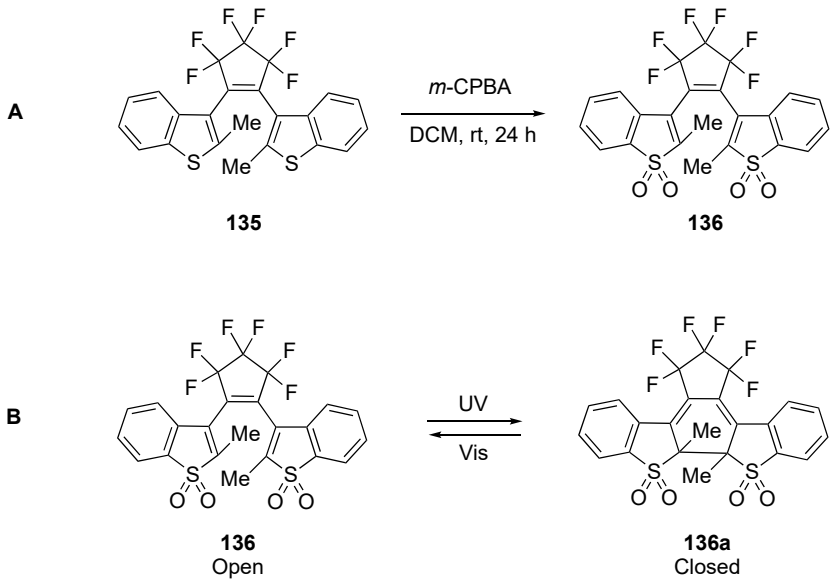
Diarylethene derivative **134** can be readily photoswitched between its open form **134** and its closed form **134a** through exposure to light (Scheme 47). This reversible process is highly dependent on specific photophysical parameters. The key determinant for the kinetics of photoswitching is the product of the absorption coefficient (ε) at the irradiation wavelength and the photoswitching quantum yield (φ).



134 **134a**

Scheme 47: Photochromic switching behavior of sulfoximines **134**.

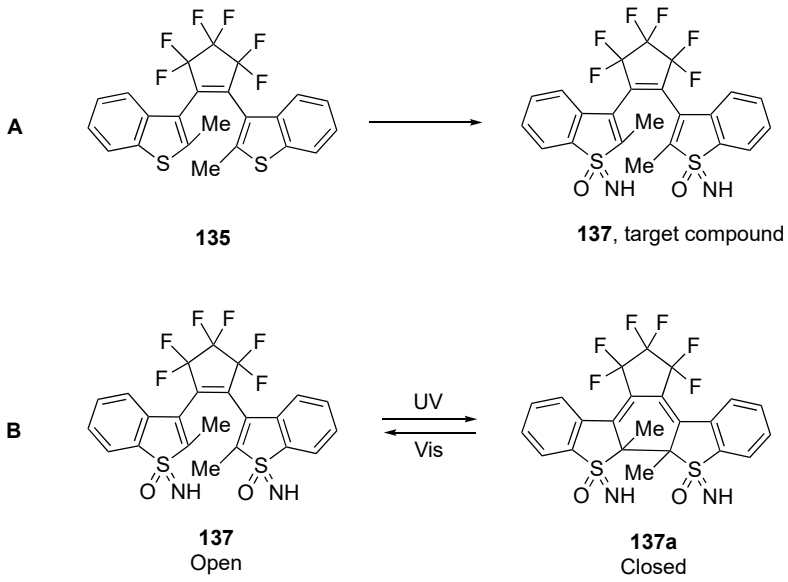
In 2005 Kim and co-workers reported highly fluorescent photochromic diarylethene in the closed form (Scheme 48B),[151] which was synthesized by the oxidation of benzothiophene derivative **135**. They observed that the fluorescence quantum yield of **136** increased after photo-cyclization, which was contrary to the findings for **135**, where the fluorescence quantum yield decreased (Scheme 48A).



Scheme 48: Fluorescent photochromic diarylethene **136a**.[151]

4.4 Background and aim of the project

In this specific area of study, research has primarily focused on a narrow range of compounds, with little exploration apart from the specific example mentioned in (Scheme 49). Our current research aims to expand this area by conducting a double imidation process targeting both sulfur moieties within compound **135**, leading to the synthesis of bissulfoximine **137**. Following synthesis, we will conduct investigations into the fluorescent behavior exhibited by compound **137**. This exploration is significant as it contributes to the understanding of how modifications to sulfoximine derivatives can impact their optical properties, potentially revealing new avenues for the design and development of functional materials with fluorescent characteristics.

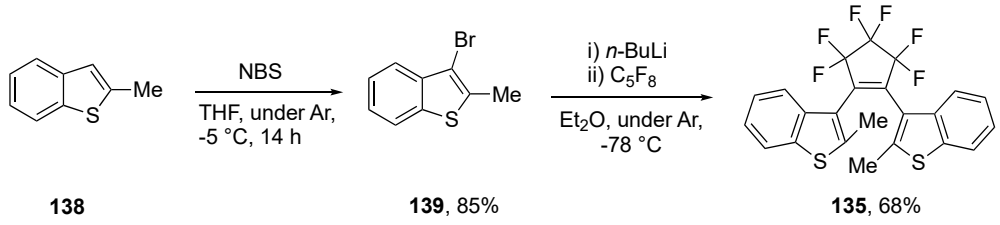


Scheme 49: (A) Planed synthesis and (B) photoswitching of sulfoximine **137**.

4.5 Results and discussion

4.5.1 Synthesis of starting material

One of the earliest and most widely used photochromic diarylethenes are compounds featuring a perfluorocyclopentene bridge.[152] Among these, dithienylethenes **135** have garnered significant attention and have been employed extensively as photoswitches in various applications. The synthesis of 3-bromo-2-methylbenzo[*b*]thiophene **136** is achieved through the bromination of 2-methylbenzo[*b*]thiophene **138**. Subsequently, the key photochromic compound, 3,3'-(perfluorocyclopent-1-ene-1,2-diyl)bis(2-methylbenzo[*b*]thiophene) **135**, is synthesized via lithiation of 3-bromo-2-methylbenzo[*b*]thiophene **136**, followed by the addition of octafluorocyclopentene (Scheme 50).[152] This sequence of reactions highlights the intricate steps involved in the preparation of functional photochromic diarylethenes.

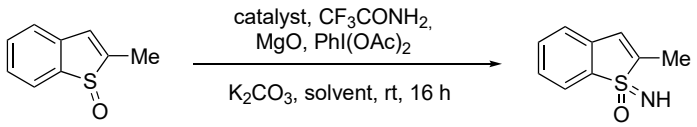


Scheme 50: Synthetic pathways towards compound **135**.[152]

4.5.2 Optimization of the reaction condition I and II

Optimization of reaction condition I for sulfoximine 141 from sulfoxide 140

Table 4: Optimization of the reaction conditions for sulfoximine **141** from sulfoxide **140**.



140 **141**

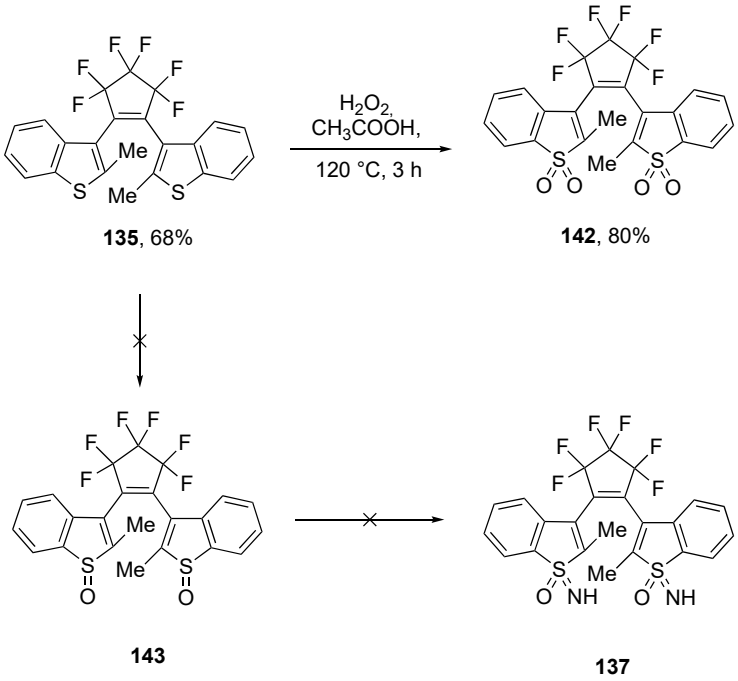
entry	catalyst	solvent	yield of **141** (%)
1	$Rh_2(OAc)_4$	MeOH	44
2	$Rh_2(esp)_2$	MeOH	53
3	$Rh_2(CF_3COO)_2$	MeOH	41
4	$[Rh_2(CF_3CF_2CF_2CO_2)_2]_2$	MeOH	56
5	$Rh_2(C_{32}H_{64}O_8)_2$	MeOH	67
6	$Rh_2(C_{32}H_{64}O_8)_2$	Et_2O	71
7	$Rh_2(C_{32}H_{64}O_8)_2$	THF	nr
8	$Rh_2(C_{32}H_{64}O_8)_2$	C	42
9	$Rh_2(C_{32}H_{64}O_8)_2$	DMSO	47
10	$Rh_2(C_{32}H_{64}O_8)_2$	$CHCl_3$	nr
11	$Rh_2(C_{32}H_{64}O_8)_2$	PhMe	82
12	$Rh_2(C_{32}H_{64}O_8)_2$	EtOAc	81
13	$Rh_2(C_{32}H_{64}O_8)_2$	DCM	56
14	$Rh_2(C_{32}H_{64}O_8)_2$	benzene	80

[a]Reaction conditions: sulfoxide (0.2 mmol), CF_3CONH_2 (0.2 mmol), $PhI(OAc)_2$ (0.5 mmol), MgO (1.0 mmol), and catalyst (2.5 mol%) in solvent (3 mL) at room temperature; then K_2CO_3 (2 equiv.) in MeOH (3 mL).

To synthesize the target sulfoximine **137**, an approach were adopted based on our prior research involving the rhodium-catalyzed imidation of sulfoxide and sulfur compounds. [153] The model substrate **140** were selected as the starting material and investigated the optimised condition (Table 4). Initially, conditions similar to those previously reported for a model substrate, 2-methylbenzo[*b*]thiophene 1-oxide, were applied, yielding a modest 44% yield (Table 4, entry 1). To enhance the reaction efficiency, a systematic evaluation of various rhodium catalysts (Table 4, entries 1-5). Notably, the $Rh_2(C_{32}H_{64}O_8)_2$ catalyst employed in methanol demonstrated a significantly improved yield of 67% (Table 4, entry 5). Subsequently, different solvents were investigated in conjunction with this catalyst. Surprisingly, tetrahydrofuran and chloroform resulted in no product formation (Table 4, entries 7 and 10), whereas acetonitrile and dimethyl sulfoxide was obtained in comparable yields 42% and 47%, respectively (Table 4,

entries 8 and 9). In contrast, solvents like toluene, ethyl acetate, and benzene gave notably higher and comparable yields of 82%, 81%, and 80%, respectively (Table 4, entries 11, 12, and 14). The final optimized reaction conditions for synthesizing the sulfoximine **137** involve using $Rh_2(C_{32}H_{64}O_8)_2$ as the catalyst and toluene as the solvent which results in a significantly improved yield of the desired product in 82% yield.

Next the developed reaction conditions for the synthesis of sulfoxide were applied. Unfortunately, despite the efforts to optimize the reaction conditions detailed in Table 1, It did not successfully obtain the intended sulfoxide product **143**. Instead, compound **135** underwent oxidation, resulting in the formation of sulfone **142** (Scheme 51). In response to this outcome, an alternative synthetic strategy outlined in Scheme 52. In this revised approach, the imidation step followed by oxidation.



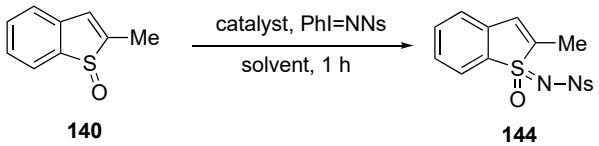
Scheme 51: Synthetic route for the synthesis of sulfoximine **137**.

Optimization of the reaction condition II for *N*-subsituted sulfoximine 144 from sulfoxide 140

The previous optimization attempt to synthesize sulfoximine **137** from sulfoxide **143** was unsuccessful. This failure was due to the inability to successfully synthesis sulfoxide **143**. Our goal was to synthesize an *N*-substituted sulfoximine **146**. Building on our previous work[68]

involving the imidation of sulfoxide by iron triflate, 2-methylbenzo[*b*]thiophene 1-oxide selected as the model substrate and used iminoiodinane (PhI=NNs) as the imidating reagent (Table 5).

Table 5: Optimization of the reaction conditions for *N*-subsituted sulfoximine **144** from sulfoxide **140**.[a]



140 **144**

entry	catalyst	solvent	Temp (°C)	Yield of **144** (%)
1	$Fe(acac)_3$	MeCN	rt	30
2	$Fe(OTf)_2$	MeCN	rt	58
3	$FeCl_2$	MeCN	rt	63
4	$Fe(ClO_4)_2$	MeCN	rt	27
5	$Cu(OTf)_2$	MeCN	rt	68
6	$Cu(MeCN)_4PF_6$	MeCN	rt	69
7	$CuCl_2$	MeCN	rt	20
8	$Cu(acac)_2$	MeCN	rt	25
9	$Cu(OAc)_2.H_2O$	MeCN	rt	63
10	$Cu(OAc)_2$	MeCN	rt	70
11	$Cu(OAc)_2$	Benzene	rt	20
12	$Cu(OAc)_2$	MeOH	rt	41
13	$Cu(OAc)_2$	EtOAc	rt	45
14	$Cu(OAc)_2$	DCM	rt	10
15	$Cu(OAc)_2$	THF	rt	trace
16	$Cu(OAc)_2$	$CDCl_3$	rt	trace
17	$Cu(OAc)_2$	PhMe	rt	trace
18	$Cu(OAc)_2$	Et_2O	rt	trace
19[b]	$Cu(OAc)_2$	MeCN	40	84
20[c]	$Cu(OAc)_2$	MeCN	40	78
21[d]	$Cu(OAc)_2$	MeCN	40	86

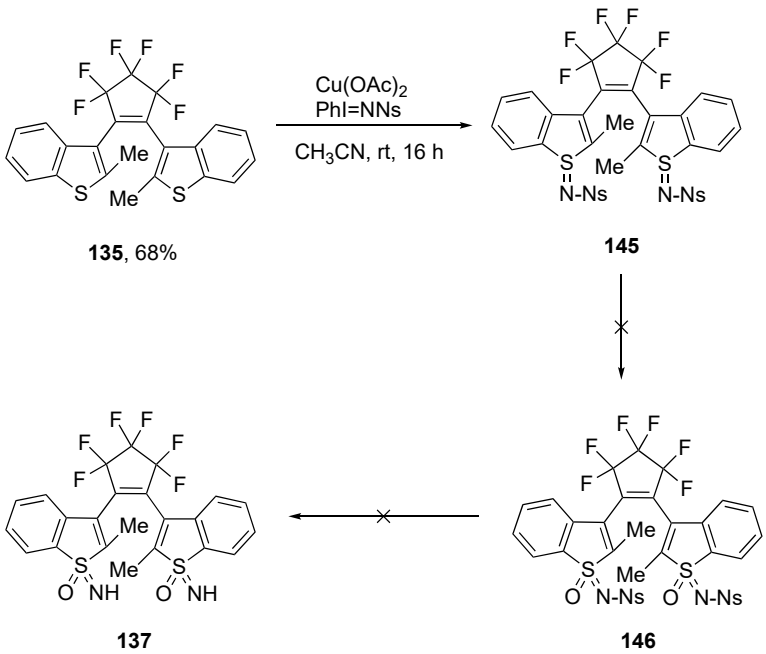
[a]Reaction conditions: sulfoxide **140** (0.2 mmol), catalyst (2.5 mol %) , PhI=Ns (1.3 equiv.), and in solvent (0.1 M) at rt. [b]MeCN (1 mL), [c]MeCN (2 mL), [d]MeCN (3 mL)

Initially, different iron catalysts were tested in acetonitrile as the solvent (Table 5, entry 1–4). Among these, iron chloride provided the product **144** in yield of 63% (Table 5, entry 3). Various copper catalysts were tested and the best result was achieved with copper acetate giving **144** in 70% yield (Table 5, entry 10). Next, different solvents were tested while using copper acetate as the catalyst. Solvents such as benzene, methanol, ethyl acetate, and dichloromethane resulted in yields ranging from 10% to 45% (Table 5, entries 11–14), which were not an improvement

over the 70% yield obtained with acetonitrile. Unfortunately, solvents like tetrahydrofuran, chloroform, toluene, and diethyl ether only produced trace amounts of the product (Table 5, entries 15–18). To further increase the yield, the temperature was raised to 40 °C, resulting in a 78% yield (Table 5, entry 20). Increasing the solvent volume by two to three milliliters further boosted the yield to 86% (Table 5, entry 21). Therefore, the optimized condition for forming **144** involves using copper acetate as the catalyst and iminoiodinane (PhI=NNs) in acetonitrile as the solvent at 40 °C, which provided the desired product in a 86% yield.

Synthesis of 137 through imidation and subsequent oxidation

Using the optimized conditions from Table 5, our objective was to synthesize the *N*-substituted sulfoximine compound **145**. Subsequent oxidation and deprotection steps were planned to yield the final desired product, **137** (Scheme 52). Following the optimized procedure, compound **145** were successfully synthesized, which was verified by high-resolution mass spectrometry. However, difficulties in calculating the yield due to the presence of four different conformers, which complicated the analysis.



Scheme 52: Synthetic route for the synthesis of sulfoximine **137**.

Despite this initial success in forming compound **145**, the subsequent oxidation step of the *N*-substituted sulfoximine was unsuccessful. As a result, the final deprotection step were unable to proceed and ultimately failed to synthesize the desired product, compound **137**.

Paralled and antiparalled conformers

In the open-ring isomer of diarylethenes, there are two distinct conformations: one with the mirror symmetry (parallel conformation) and one with C2 symmetry (antiparallel conformation).[154] The photocyclization reaction, which is essential for the photochromic behavior, can only proceed from the antiparallel conformation, making it photoactive, while the parallel conformation is photo-inactive.[155]

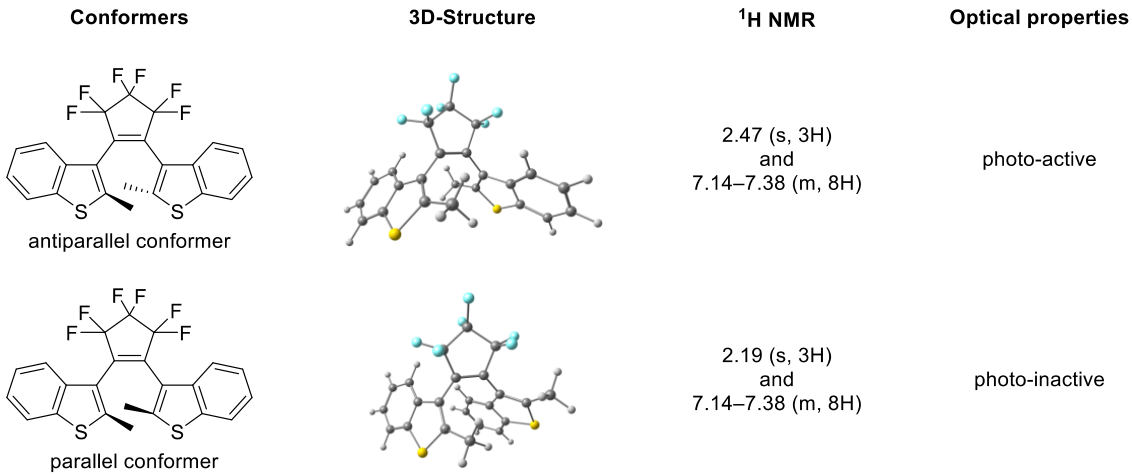


Figure 18: Parallel and antiparalled conformers of diarylethenes.

These different conformers can be identified using NMR spectroscopy. Specifically, in the antiparallel conformation, the NMR signals of the methyl protons appear at 2.47 ppm, whereas in the parallel conformation, the signals are at 2.19 ppm. This distinct difference in chemical shifts allows for precise identification and study of the conformers.[120]

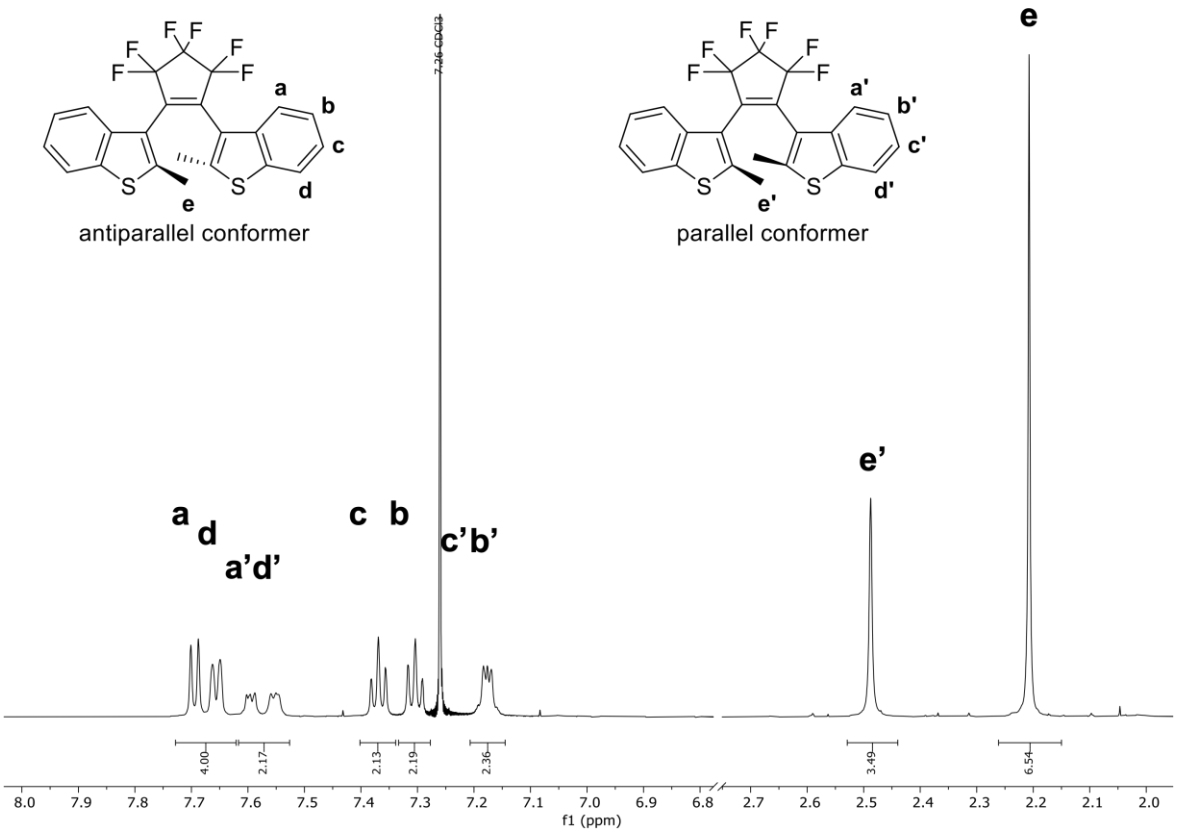


Figure 19: ^{1}H NMR spectrum of parallel and antiparalled conformers of diarylethenes.

Diastereomeric forms

All possible conformers for compound **145** were systematically examined, distinguishing between parallel and antiparallel arrangements, and denoting them using *S* and *R* configurations. In total, there are four potential conformers for both the antiparallel and parallel arrangements. The analysis revealed that the configurations in the first row (e.g., **145a** *S* and *R*, **145b** *S* and *S*) are equivalent to those in the second row (e.g., **145c** *R* and *S*, **145d** *R* and *R*) for antiparallel conformers and the analysis in the first row (e.g., **145e** *S* and *R*, **145f** *S* and *S*) are equivalent to those in the second row (e.g., **145g** *R* and *S*, **145h** *R* and *R*) for parallel conformers. This leads to only four compounds **145c** and **145d** for antiparallel, **145g** and. **145h** for paralled conformers (Figure 20).

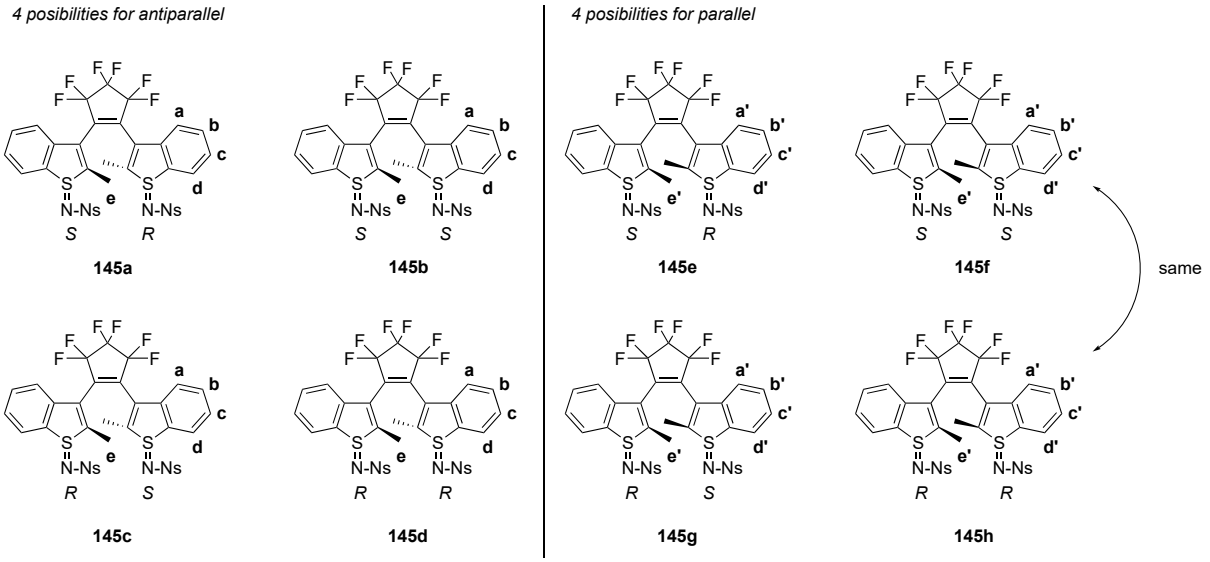


Figure 20: Diastereomeric forms of **145**.

Expected four compounds

In conclusion, four distinct conformers were anticipated for compound **145**, each expected to produce unique signals in the 1H NMR spectrum (Figure 21). Despite confirming the structure of sulfilimine **145** using high-resolution mass spectrometry (HRMS), analyzing the NMR signals proved challenging. The peaks were convoluted and closely spaced, making it difficult to differentiate between the conformers. Even with these analytical challenges, the compound was tested for its potential as a photoswitch. Unfortunately, it failed to exhibit the expected photochromic activity.

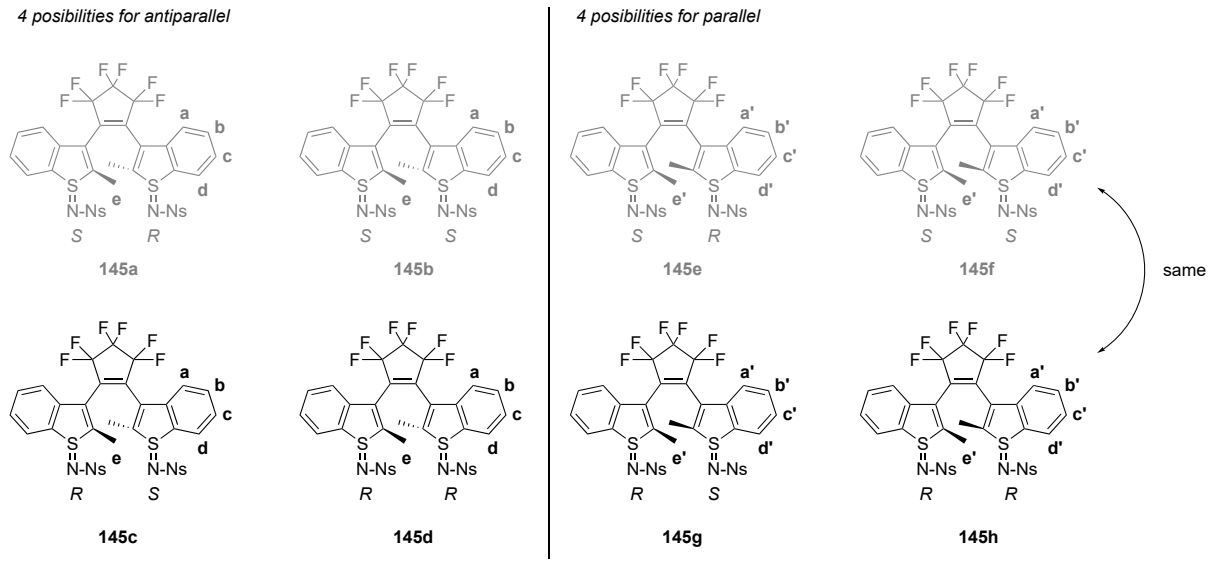
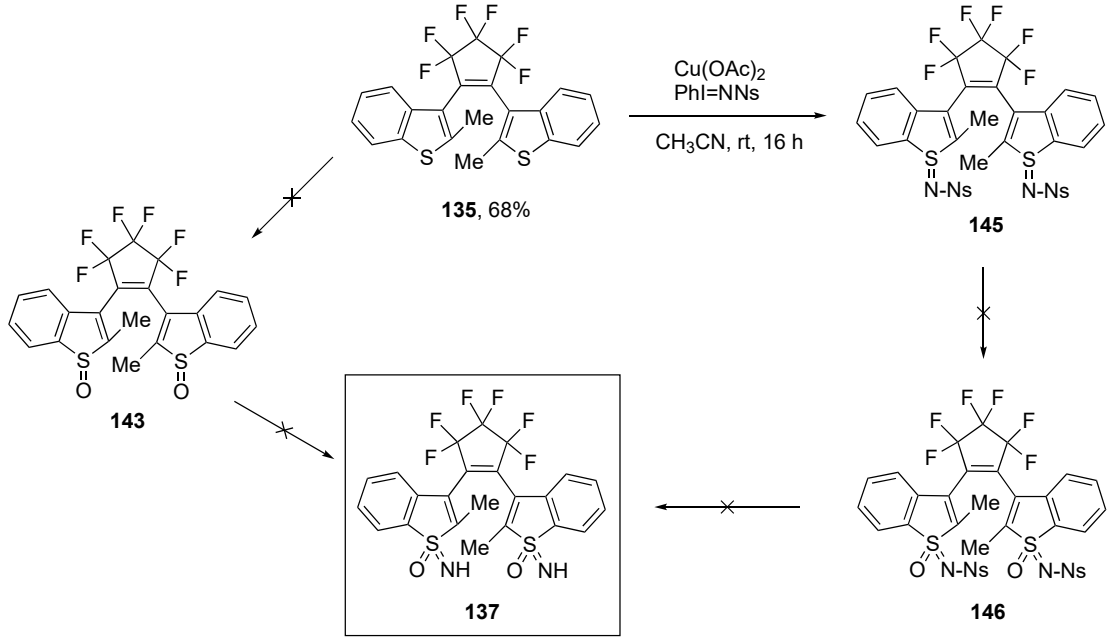


Figure 21: Four distinct compound expected in NMR.

4.6 Conclusion and outlook

To synthesize the target compound **137**, the initial attempts to form sulfoxide **143** from **135** were unsuccessful due to the failure of the imidation step necessary to create the desired sulfoximine **137**. Subsequently, attempts were made to form the *N*-substituted sulfoximine compound **145**, which proved initially successful, leading to the synthesis of compound **145**.



Scheme 53: Synthetic route for sulfoximine **137**.

However, despite this initial success, the subsequent oxidation step of the *N*-substituted sulfoximine failed. Consequently, it was not possible to proceed to the final deprotection step, and ultimately the desired compound **137**. Looking forward, the exploration of alternative imidation processes to achieve the synthesis of compound **137** (Scheme 53). If successful, its potential applications in photoswitches will be investigated, which could provide valuable insights into its utility.

5 Experimental section

5.1 General information

Methods

All reactions were conducted in air unless otherwise mentioned. Commercially available chemicals were purchased and used without addition purification unless otherwise stated. Solvents like ethyl acetate, *n*-pentane, *n*-hexane were distilled prior to use. The course of a reaction was monitored by TLC. Dry solvents were either purchased from commercial suppliers or obtained from an MBraun SPS5 (SPS) system. The mechanochemical reactions were carried out in a RETSCH Mixer Mill MM 400. Milling vessels (10 mL volumetric capacity) and milling balls (10 mm in diameter) were made of ZrO_2-Y. Sensitive reactions were performed in glove box using a MBraun Labmaster 130 glove box under an argon atmosphere. Air and moisture-sensitive procedures were conducted under argon using standard Schlenk flasks and vacuum line techniques.

Analytics

Thin layer chromatography (TLC) was performed on TLC plates with silica sheet gel 60 F_{254} aluminium sheets purchased from Merck or ALUGRAM® Xtra SIL G/UV_{254} from Macherey-Nagel. Detection of the compounds were carried out under UV light (λ = 254 nm and 366 nm) or by immersion in potassiumpermanganate ($KMnO_4$) TLC stain solutions. Flash column chromatography was performed on Silica gel (SiO_2) 60 M (0.04–0.063 mm) from Macherey-Nagel.

^{1}H and ^{13}C Nuclear magnetic resonance (NMR) spectra were recorded on a Varian VNMRS 400 (400 MHz), Varian VNMRS 600 (600 MHz), Brucker Avance Neo 400 (400 MHz), or Bruker Avance Neo 600 (600 MHz) spectrometer at ambient temperature. The Chemical shift (δ) is reported in parts per million (ppm) and referenced to the residual proton or carbon signal of the used deuterated solvent. The Coupling constants (J) are reported in Hertz (Hz). The multiplicity are reported with the following abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet.

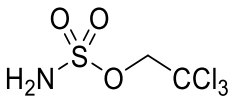
Infrared spectroscopy (IR) were recorded on a PerkinElmer Spectrum 100 FT-IR spectrometer with an attached UATR device with a KRS-5 crystal and all IR data were collected by attenuated total reflectance (ATR). Wavenumbers ν are given in cm^{-1}. The band intensity is classified into weak (w, transmission: 100–66%), medium (m, transmission: 66–33%) and strong (s, transmission: 33–0%).

Melting points (m.p) were measured with a Büchi Melting Point M-560 machine

High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific LTQ Orbitrap XL spectrometer [electrospray ionization (ESI) in positive ion mode] was used.

5.2 Experimental information for chapter 2

Synthesis of 2,2,2-trichloroethyl sulfamate (41)



The following procedure was taken from the literature: [61a] To a 100 mL three-necked flask equipped with a 25 mL dropping funnel and a drying tube filled with $CaSO_4$ were added 10 mL of MeCN and $ClSO_2NCO$ (2.7 mL, 31.3 mmol, 1.5 equiv). After cooling the solution to 0 °C, HCO_2H (1.2 mL, 31.3 mmol, 1.5 equiv) in 6 mL of MeCN was added dropwise over a 10 min period. The mixture was warmed to 23 °C and stirred for 8 h. The flask was then returned to the ice bath before a solution of 2,2,2-trichloroethanol (2.0 mL, 20.8 mmol) in 12 mL of *N*,*N*-dimethylacetamide (DMA) was added via cannula. Transfer of the alcohol was made quantitative with an additional 4 mL of DMA. The resulting mixture was warmed to 23 °C and stirred vigorously for 1.5 h. The reaction mixture was quenched by the addition of 50 mL of H_2O and poured into a separatory funnel containing 100 mL of Et_2O. The organic phase was collected and the aqueous layer was extracted with 2 × 100 mL of Et_2O. The combined organic phase was washed with 5 × 50 mL of H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the oily residue by chromatography on silica gel using *n*-hexane/ethyl acetate (2:1 (*V*:*V*)) as eluent afforded the desired product **1** as a pale white solid (4.02 g, 17.6 mmol, 84%).

R_F = 0.35 (dichloromethane:ethyl acetate = 15:1 (*V*:*V*))

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.05 – 5.02 (m, 2H), 4.70 (s, 2H) ppm.

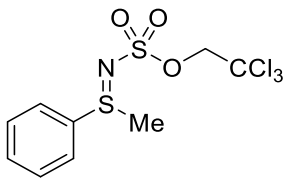
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 93.3, 78.8 ppm.

The NMR spectra are in accordance with the literature.[61a]

5.2.1 General procedure for the syntheses of *N*Tces-sulfilimines (GP1)

In air, to a screw capped reaction tube (volume: 10 mL) equipped with magnetic stir bar was added thioether (0.1 mmol, 1 equiv), 2,2,2-trichloroethoxysulfonamide (**41**, 34.3 mg, 0.15 mmol, 1.5 equiv), (diacetoxyiodo)benzene (53.1 mg, 0.16 mmol, 1.6 equiv), $Fe(OTf)_2$ (3.54 mg, 10 mol%) and toluene (2 mL, 0.1 M). The reaction tube was closed, and the reaction mixture stirred at rt for 3 h at 400 rpm. The reaction mixture was transferred to a round-bottom flask, and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel.

2,2,2-Trichloroethyl (*E*)-[methyl(phenyl)-λ^4-sulfaneylidene]sulfamate (35a)



According to the GP1, compound **35a** was obtained from methyl(phenyl)sulfane (12.4 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a pale brown solid (31.1 mg, 0.0887 mmol, 89%).

Note on scale-up: Compound **35a** was obtained from methyl(phenyl)sulfane (1.00 g, 8.05 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate) as a white solid (1.55 g, 4.42 mmol, 55%).

R_F = 0.34 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 83 – 85 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.87 – 7.84 (m, 2H), 7.67 – 7.58 (m, 3H), 4.59 – 4.49 (m, 2H), 3.00 (s, 3H) ppm.

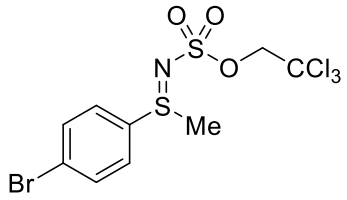
$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ =134.9, 133.5, 130.5, 126.4, 94.4, 78.0, 38.7 ppm.

IR (neat): ν = 3262 (w), 3022 (w), 1584 (w), 1386 (m), 1284 (s), 1142 (s), 1019 (m), 960 (s), 851 (m), 743 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_{10}Cl_3NO_3NaS_2$: 371.9059 $[M+Na]^+$, found 371.9056.

The NMR spectra are in accordance with the literature.[59f]

2,2,2-Trichloroethyl (*E*)-[(4-bromophenyl)(methyl)-λ^4-sulfaneylidene]sulfamate (35b)



According to the GP1, compound **35b** was obtained from (4-bromophenyl)(methyl)sulfane (20.3 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (35.1 mg, 0.0817 mmol, 82%).

R_F = 0.38 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 87 – 89 °C.

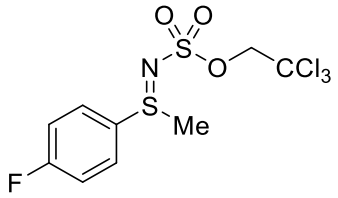
^1H NMR (600 MHz, $CDCl_3$): δ =7.76 – 7.74 (m, 2H), 7.74 – 7.71 (m, 2H), 4.60 – 4.52 (m, 2H), 3.00 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ =133.9, 133.8, 128.5, 127.8, 94.3, 78.0, 38.7 ppm.

IR (neat): ν = 3017 (w), 1731 (w), 1566 (m), 1472 (w), 1388 (m), 1334 (s), 1158 (s), 1037 (s), 961 (s), 847 (s), 769 (s), 716 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9BrCl_3NO_3NaS_2$: 449.8165 $[M+Na]^+$, found 449.8154.

2,2,2-Trichloroethyl (*E*)-[(4-fluorophenyl)(methyl)-λ^4-sulfaneylidene]sulfamate (35c)



According to the GP1, compound **35c** was obtained from (4-fluorophenyl)(methyl)sulfane (14.2 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (30.5 mg, 0.071 mmol, 71%).

R_F = 0.34 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 113 – 115 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ =7.91 – 7.86 (m, 2H), 7.30 (t, J = 8.4 Hz, 2H), 4.60 – 4.49 (m, 2H), 3.00 (s, 3H) ppm.

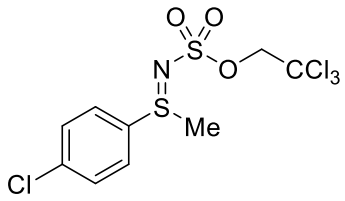
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 165.6 (d, $^1J_{C–F}$ = 256.5 Hz), 130.4 (d, $^4J_{C–F}$ = 2.8 Hz), 129.1 (d, $^3J_{C–F}$ = 9.3 Hz), 118.0 (d, $^2J_{C–F}$ = 23.1 Hz), 94.3, 77.9, 38.9 ppm.

IR (neat): ν = 2924 (w), 1738 (w), 1584 (m), 1490 (m), 1333 (s), 1236 (s), 1156 (s), 1086 (s), 1007 (s), 960 (s), 840 (s), 722 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9FCl_3NO_3NaS_2$: 389.8965 $[M+Na]^+$, found 389.8958.

The NMR spectra are in accordance with the literature.[59f]

2,2,2-Trichloroethyl (*E*)-[(4-chlorophenyl)(methyl)-λ^4-sulfaneylidene] sulfamate (35d)



According to the GP1, compound **35d** was obtained from (4-chlorophenyl)(methyl)sulfane (15.9 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless oil (24.9 mg, 0.0647 mmol, 65%).

R_F = 0.41 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

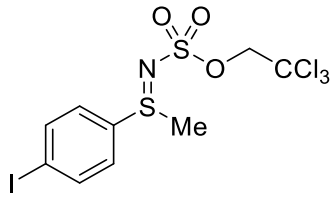
^{1}H NMR (600 MHz, $CDCl_3$): δ =7.80 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 8.7 Hz, 2H), 4.59 – 4.51 (m, 2H), 3.00 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =140.2, 133.3, 130.8, 127.8, 94.3, 77.9, 38.7 ppm.

IR (neat): ν = 2924 (w), 1740 (w), 1570 (m), 1392 (m), 1336 (s), 1160 (s), 1089 (s), 1039 (s), 1009 (s), 963 (s), 852 (s), 771 (s), 721 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9Cl_4NO_3NaS_2$: 405.8670 $[M+Na]^+$, found 405.8665.

2,2,2-Trichloroethyl (*E*)-[(4-iodophenyl)(methyl)-λ^4-sulfaneylidene]sulfamate (35e)



According to the GP1, compound **35e** was obtained from (4-iodophenyl)(methyl)sulfane (25 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (28.4 mg, 0.0596 mmol, 60%).

R_F = 0.47 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 89 – 91 °C.

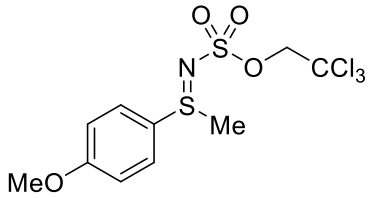
^{1}H NMR (600 MHz, $CDCl_3$): δ =7.96 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 4.56 (q, *J* = 10.9 Hz, 2H), 2.99 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =139.6, 134.6, 127.5, 100.5, 94.2, 77.8, 38.5 ppm.

IR (neat): ν = 2928 (w), 1732 (w), 1561 (m), 1426 (w), 1330 (s), 1148 (s), 1091 (m), 993 (s), 842 (s), 771 (s), 718 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9ICl_3NO_3NaS_2$: 497.8026 $[M+Na]^+$, found 497.8023.

2,2,2-Trichloroethyl (*E*)-[(4-methoxyphenyl)(methyl)-λ^4-sulfaneylidene]sulfamate (35f)



According to the GP1, compound **35f** was obtained from (4-methoxyphenyl)(methyl)sulfane (15.4 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (20.4 mg, 0.0536 mmol, 53%).

R_F = 0.28 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 119 – 121 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ =7.78 (d, *J* = 8.9 Hz, 2H), 7.07 (d, *J* = 8.9 Hz, 2H), 4.58 – 4.45 (m, 2H), 3.88 (s, 3H), 2.98 (s, 3H) ppm.

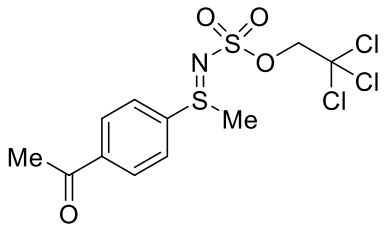
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =163.9, 128.8, 125.3, 115.9, 94.5, 78.0, 56.0, 38.6 ppm.

IR (neat): *v* = 2922 (m), 1730 (w), 1588 (s), 1495 (m), 1325 (s), 1262 (s), 1154 (s), 1085 (s), 957 (s), 832 (s), 764 (s), 713 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{10}H_{12}Cl_3NO_4NaS_2$: 401.9165 $[M+Na]^+$, found 401.9167.

The NMR spectra are in accordance with the literature.[59f]

2,2,2-Trichloroethyl (*E*)-[(4-acetylphenyl)(methyl)- λ^4-sulfaneylidene]sulfamate (35g)



According to the GP1, compound **35g** was obtained from 1-(4-(methylthio)phenyl)ethan-1-one (16.6 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (22.6 mg, 0.0526 mmol, 53%).

R_F = 0.37 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 119 – 121 °C.

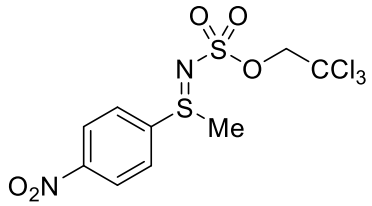
^{1}H NMR (600 MHz, $CDCl_3$): δ =8.17 – 8.14 (m, 2H), 7.98 – 7.95 (m, 2H), 4.63 – 4.55 (m, 2H), 3.03 (s, 3H), 2.66 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =196.5, 140.7, 139.4, 130.0, 126.6, 94.3, 78.0, 38.6, 27.0 ppm.

IR (neat): ν = 2932 (w), 1736 (w), 1693 (s), 1426 (m), 1335 (s), 1256 (s), 1158 (s), 1089 (m), 1007 (s), 959 (s), 847 (s), 769 (s), 720 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{11}H_{12}Cl_3NO_4NaS_2$: 413.9165 $[M+Na]^+$, found 413.9159.

2,2,2-Trichloroethyl (*E*)-[methyl(4-nitrophenyl)-λ^4-sulfaneylidene]sulfamate (35h)



According to the GP1, compound **35h** was obtained from methyl(4-nitrophenyl)sulfane (16.9 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (12 mg, 0.0303 mmol, 30%).

R_F = 0.38 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 141 – 143 °C.

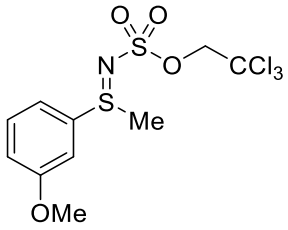
^{1}H NMR (600 MHz, $CDCl_3$): δ =8.48 – 8.45 (m, 2H), 8.10 – 8.06 (m, 2H), 4.64 – 4.58 (m, 2H), 3.07 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =150.7, 141.8, 127.5, 125.5, 94.3, 78.0, 38.7 ppm.

IR (neat): ν = 2924 (w), 1736 (w), 1605 (w), 1532 (s), 1332 (s), 1156 (s), 1088 (m), 1029 (s), 1005 (s), 961 (s), 855 (s), 778 (s), 715 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9Cl_3N_2NaO_5S_2$: 416.8910 $[M+Na]^+$, found 416.8911.

2,2,2-Trichloroethyl (*E*)-[(3-methoxyphenyl)(methyl)-λ⁴-sulfaneylidene]sulfamate (35i)



According to the GP1, compound **35i** was obtained from (3-methoxyphenyl)(methyl)sulfane (15.4 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (34.3 mg, 0.090 mmol, 90%).

R_F = 0.47 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 85 – 87 °C.

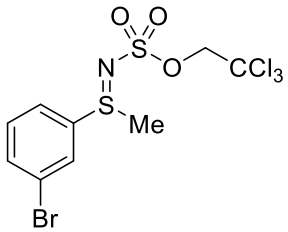
^{1}H NMR (600 MHz, $CDCl_3$): δ =7.49 – 7.45 (m, 1H), 7.40 – 7.38 (m, 1H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.12 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 4.58 – 4.48 (m, 2H), 3.87 (s, 3H), 2.99 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =161.0, 135.9, 131.4, 119.7, 118.3, 110.8, 94.3, 77.9, 56.0, 38.8 ppm.

IR (neat): *v* = 2948 (w), 1739 (w), 1594 (m), 1464 (m), 1320 (s), 1250 (s), 1155 (s), 1029 (s), 958 (s), 845 (s), 775 (s), 716 (s), 678 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{10}H_{12}Cl_3NO_4NaS_2$: 401.9165 $[M+Na]^+$, found 401.9158.

2,2,2-Trichloroethyl (*E*)-[(3-bromophenyl)(methyl)-λ⁴-sulfaneylidene]sulfamate (35j)



According to the GP1, compound **35j** was obtained from (3-bromophenyl)(methyl)sulfane (20.3 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (24.8 mg, 0.057 mmol, 60%).

R_F = 0.35 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 59 – 61 °C.

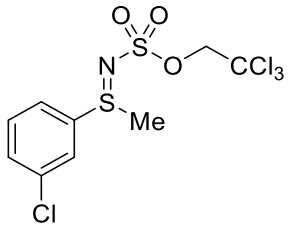
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 7.8 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.53 – 7.48 (m, 1H), 4.65 – 4.57 (m, 2H), 3.04 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 166.1, 136.6, 131.8, 129.1, 124.9, 124.5, 78.0, 64.7, 38.8 ppm.

IR (neat): ν = 2925 (w), 1731 (m), 1568 (m), 1409 m(), 1329 (s), 1158 (s), 1091 (s), 1032 (s), 957 (s), 846 z(s), 776 (s), 714 (s), 677 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9BrCl_3NO_3NaS_2$: 449.8165.$[M+Na]^+$, found 449.8157.

2,2,2-Trichloroethyl (*E*)-[(3-chlorophenyl)(methyl)-λ^4-sulfaneylidene]sulfamate (35k)



According to the GP1, compound **35k** was obtained from (3-chlorophenyl)(methyl)sulfane (15.9 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (12 mg, 0.031 mmol, 31%).

R_F = 0.43 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 60 – 62 °C.

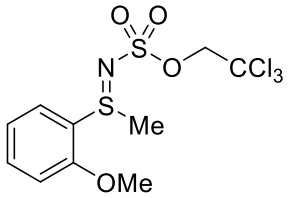
^{1}H NMR (600 MHz, $CDCl_3$): δ =7.88 (t, *J* = 1.9 Hz, 1H), 7.72 – 7.70 (m, 1H), 7.63 – 7.60 (m, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 4.62 – 4.54 (m, 2H), 3.02 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =136.9, 136.8, 133.7, 131.6, 126.3, 124.4, 94.3, 78.0, 38.8 ppm.

IR (neat): ν = 2954 (w), 1729 (w), 1573 (m), 1410 (m), 1326 (s), 1157 (s), 1031 (s), 958 (s), 847 (s), 773 (s), 714 (s), 675 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9Cl_4NO_3NaS_2$: 405.8670 $[M+Na]^+$, found 405.8694.

2,2,2-Trichloroethyl (*E*)-[(2-methoxyphenyl)(methyl)-λ⁴-sulfaneylidene]sulfamate (35l)



According to the GP1, compound **35l** was obtained from (2-methoxyphenyl)(methyl)sulfane (15.7 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a pale oil (30.3 mg, 0.079 mmol, 80%).

R_F = 0.44 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

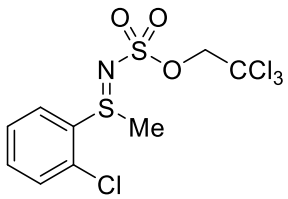
^{1}H NMR (600 MHz, $CDCl_3$): δ =8.07 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.01 (dd, *J* = 8.3, 1.0 Hz, 1H), 4.63 – 4.57 (m, 2H), 3.95 (s, 3H), 2.95 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 155.8, 134.3, 126.9, 122.5, 122.0, 111.7, 94.5, 77.9, 56.5, 37.2 ppm.

IR (neat): *v* = 2929 (m), 1734 (m), 1587 (m), 1476 (m), 1373 (w), 1337 (s), 1243 (s), 1158 (s), 1086 (s), 1002 (s), 955 (s), 843 (s), 768 (s), 721 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{10}H_{12}Cl_3NO_4NaS_2$: 401.9165 $[M+Na]^+$, found 401.9160.

2,2,2-Trichloroethyl (*E*)-[(2-chlorophenyl)(methyl)-λ⁴-sulfaneylidene]sulfamate (35m)



According to the GP1, compound **35m** was obtained from (2-chlorophenyl)(methyl)sulfane (15.9 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (20.3 mg, 0.052 mmol, 55%).

R_F = 0.43 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 88 – 90 °C.

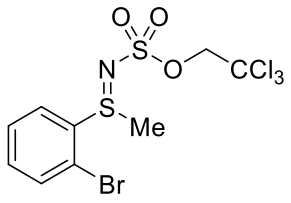
^{1}H NMR (600 MHz, $CDCl_3$): δ =8.26 (d, J = 8.0 Hz, 1H), 7.63 – 7.50 (m, 3H), 4.66 – 4.57 (m, 2H), 3.03 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =134.1, 133.5, 131.7, 131.2, 130.7, 129.1, 127.7, 78.0, 37.7 ppm.

IR (neat): v = 2927 (w), 1448 (m), 1331 (s), 1251 (m), 1155 (s), 1090 (s), 1033 (s), 998 (s), 957 (s), 848 (s), 770 (s), 721 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_9H_9Cl_4NO_3NaS_2$: 405.8670 $[M+Na]^+$, found 405.8659.

2,2,2-Trichloroethyl (*E*)-[(2-bromophenyl)(methyl)-λ^4 sulfaneylidene]sulfamate (35n)



According to the GP1, compound **35n** was obtained from (2-bromophenyl)(methyl)sulfane (20.3 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a pale oil (15.3 mg, 0.035 mmol, 37%).

R_F = 0.47 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

^{1}H NMR (600 MHz, $CDCl_3$): δ =8.02 (t, J = 8.0 Hz, 1H), 7.78 – 7.73 (m, 2H), 7.48 (t, J = 8.0 Hz, 1H), 4.57 (q, J = 10.9 Hz, 2H), 3.01 (s, 3H) ppm.

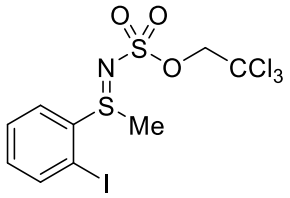
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 136.6, 134.5, 133.0, 131.8, 129.1, 124.9, 94.3, 78.0, 38.8 ppm.

IR (neat): v = 2928 (w), 1730 (w), 1564 (w), 1331 (s), 1257 (w), 1154 (s), 1089 (m), 1027 (s), 995 (s), 954 (s), 842 (s), 770 (s), 718 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_9H_9BrCl_3NO_3NaS_2$: 449.8165 $[M+Na]^+$, found 449.8157.

The NMR spectra are in accordance with the literature.[59f]

2,2,2-Trichloroethyl (*E*)-[(2-iodophenyl)(methyl)-λ^4-sulfaneylidene]sulfamate (35o)



According to the GP1, compound **35o** was obtained from (2-iodophenyl)(methyl)sulfane (26.1 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a pale oil (16.3 mg, 0.034 mmol, 34%).

R_F = 0.31 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

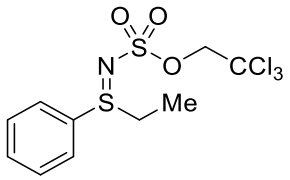
^{1}H NMR (600 MHz, $CDCl_3$): δ =8.21 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.91 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.34 (td, *J* = 7.6, 1.5 Hz, 1H), 4.64 – 4.54 (m, 2H), 3.01 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =140.4, 138.8, 134.4, 130.4, 128.2, 94.4, 94.1, 77.9, 38.3 ppm.

IR (neat): *v* = 2940 (w), 1729 (m), 1443 (m), 1334 (s), 1158 (s), 1087 (m), 1036 (s), 997 (s), 951 (s), 842 (s),767 (s), 720 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9ICl_3NO_3NaS_2$: 497.8026 $[M+Na]^+$, found 497.8014.

2,2,2-Trichloroethyl (*E*)-[ethyl(phenyl)-λ^4-sulfaneylidene]sulfamate (35p)



According to the GP1, compound **35p** was obtained from ethyl(phenyl)sulfane (13.8 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (30 mg, 0.082 mmol, 82%).

R_F = 0.45 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 83 – 85 °C.

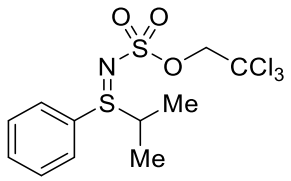
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82 – 7.79 (m, 2H), 7.65 – 7.57 (m, 3H), 4.60 – 4.47 (m, 2H), 3.27 – 3.12 (m, 2H), 1.35 (t, J = 7.3 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 133.3, 132.8, 130.3, 126.9, 94.4, 77.9, 47.9, 7.7 ppm.

IR (neat): v = 2938 (w), 1732 (w), 1449 (m), 1335 (s), 1157 (s), 1092 (m), 1032 (s), 980 (s), 846 (s), 772 (s), 724 (s), 689 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{10}H_{12}Cl_3NO_3KS_2$: 401.8955 $[M+K]^+$, found 401.8953.

2,2,2-Trichloroethyl (*E*)-[isopropyl(phenyl)-λ^4-sulfaneylidene]sulfamate (35q)



According to the GP1, compound **35q** was obtained from isopropyl(phenyl)sulfane (15.5 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a pale oil (24.3 mg, 0.0642 mmol, 64%).

R_F = 0.52 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

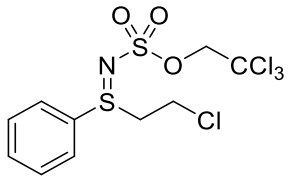
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.79 – 7.76 (m, 2H), 7.66 – 7.57 (m, 3H), 4.58 – 4.46 (m, 2H), 1.38 (d, J = 6.7 Hz, 3H), 1.32 (d, J = 6.8 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 133.3, 131.4, 130.0, 127.7, 94.4, 77.8, 55.1, 16.6, 15.8 ppm.

IR (neat): v = 2939 (w), 1731 (w), 1444 (m), 1325 (s), 1157 (s), 1086 (s), 1025 (s), 977 (s), 847 (s), 783 (s), 726 (s), 692 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{11}H_{14}Cl_3NO_3NaS_2$: 399.9372 $[M+Na]^+$, found 399.9370.

2,2,2-Trichloroethyl (*E*)-[(2-chloroethyl)(phenyl)-λ^4-sulfaneylidene]sulfamate (35r)



According to the GP1, compound **35r** was obtained from (2-chloroethyl)(phenyl)sulfane (17.3 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (08 mg, 0.02 mmol, 20%).

R_F = 0.43 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 100 – 102 °C.

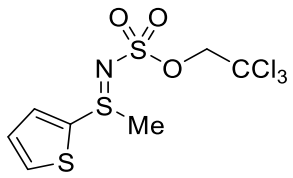
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 – 7.85 (m, 2H), 7.69 – 7.62 (m, 3H), 4.62 – 4.53 (m, 2H), 4.06 – 4.01 (m, 1H), 3.72 – 3.62 (m, 2H), 3.43 – 3.38 (m,1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 133.8, 132.5, 130.7, 126.8, 94.3, 78.0, 56.7, 36.2 ppm.

IR (neat): ν = 2938 (w), 1734 (w), 1443 (m), 1337 (s), 1282 (m), 1157 (s), 1085 (s), 1030 (s), 978 (s), 846 (s), 765 (s), 715 (s), 663 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{10}H_{12}Cl_4NO_3S_2$: 397.9007 $[M+H]^+$, found 397.9008.

2,2,2-Trichloroethyl (*E*)-[methyl(thiophen-2-yl)-λ^4-sulfaneylidene]sulfamate (35s)



According to the GP1, compound **35s** was obtained from 2-(methylthio)thiophene (13 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (31.2 mg, 0.0875 mmol, 88%).

R_F = 0.45 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 95 – 97 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.85 – 7.79 (m, 1H), 7.72 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.20 – 7.16 (m, 1H), 4.57 – 4.44 (m, 2H), 3.18 (s, 3H) ppm.

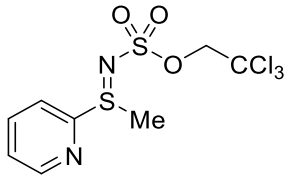
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 134.7, 134.7, 134.2, 128.2, 94.2, 78.1, 39.5 ppm.

IR (neat): ν = 3016 (w), 1735 (w), 1408 (w), 1333 (s), 1156 (s), 1093 (m), 1004 (s), 954 (s), 853 (s), 774 (s), 722 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_7H_8Cl_3NO_3NaS_3$: 377.8624 $[M+Na]^+$, found 377.8624.

The NMR spectra are in accordance with the literature.[59f]

2,2,2-Trichloroethyl (*E*)-[methyl(pyridin-2-yl)-λ^4-sulfaneylidene]sulfamate (35t)



According to the GP1, compound **35t** was obtained from 2-(methylthio)pyridine (12.5 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (26.6 mg, 0.075 mmol, 76%).

R_F = 0.36 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 82 – 84 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ =8.66 (d, J = 3.7 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.00 (td, J = 7.8, 1.7 Hz, 1H), 7.54 – 7.49 (m, 1H), 4.66 (s, 2H), 3.16 (s, 3H) ppm.

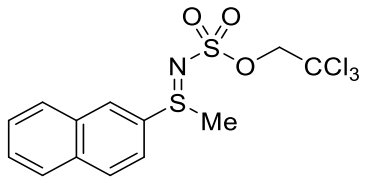
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 155.8, 150.5, 139.1, 126.3, 122.4, 94.5, 78.0, 35.2 ppm.

IR (neat): ν = 2923 (s), 1737 (w), 1576 (m), 1421 (m), 1325 (s), 1158 (s), 1038 (m), 994 (s), 951 (s), 833 (s), 774 (s), 717 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_8H_9Cl_3N_2O_3NaS_2$: 372.9012 $[M+Na]^+$, found 372.9011.

The NMR spectra are in accordance with the literature.[59f]

2,2,2-Trichloroethyl (*E*)-[methyl(naphthalen-2-yl)-λ^4-sulfaneylidene]sulfamate (35u)



According to the GP1, compound **35u** was obtained from methyl(naphthalen-2-yl)sulfane (17.8 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (28 mg, 0.069 mmol, 70%).

R_F = 0.44 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 104 – 106 °C.

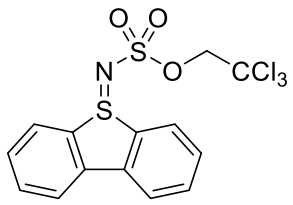
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.41 – 8.38 (m, 1H), 8.08 (d, J = 8.7 Hz, 1H), 7.95 (dd, J = 18.0, 8.0 Hz, 2H), 7.81 (dd, J = 8.7, 1.9 Hz, 1H), 7.70 – 7.65 (m, 2H), 4.63 – 4.50 (m, 2H), 3.07 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 135.3, 132.8, 131.4, 131.2, 129.5, 129.0, 128.4, 128.4, 128.3, 120.58, 94.4, 78.0, 38.6 ppm.

IR (neat): v = 2923 (m), 1731 (w), 1447 (w), 1400 (w), 1329 (s), 1156 (s), 1092 (s), 1032 (s), 999 (s), 959 (s), 846 (s), 762 (s), 721 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{13}H_{12}Cl_3NO_3NaS_2$: 421.9216 $[M+Na]^+$, found 421.9209.

2,2,2-Trichloroethyl (5λ^4-dibenzo[*b*,*d*]thiophen-5-ylidene)sulfamate (35v)



According to the GP1, compound **35v** was obtained from dibenzo[*b*,*d*]thiophene (18.6 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (28 mg, 0.068 mmol, 68%).

R_F = 0.52 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 139 – 141 °C.

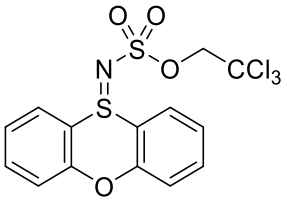
^{1}H NMR (600 MHz, $CDCl_3$): δ =8.10 – 8.07 (m, 2H), 7.94 – 7.91 (m, 2H), 7.73 (td, J = 7.6, 1.1 Hz, 2H), 7.60 (td, J = 7.7, 1.1 Hz, 2H), 4.68 (s, 2H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ =137.8, 136.7, 133.9, 130.7, 128.2, 122.9, 94.5, 78.2 ppm.

IR (neat): v = 2922 (m), 1733 (w), 1441 (m), 1332 (s), 1147 (s), 1084 (m), 1016 (s), 952 (s), 846 (s), 758 (s), 707 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{14}H_{10}Cl_3NO_3NaS_2$: 431.9059 $[M+Na]^+$, found 431.9056.

2,2,2-Trichloroethyl (10λ^4-phenoxathiin-10-ylidene)sulfamate (35w)



According to the GP1, compound **35w** was obtained from phenoxathiine (20.4 mg, 0.100 mmol, 1.00 equiv) after purification on silica gel (eluent: ethyl acetate/*n*-pentane, gradient: 1:1 → 100:0 (*V*:*V*)) as a colourless solid (12.6 mg, 0.029 mmol, 30%).

R_F = 0.47 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 143 – 145 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.96 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.75 – 7.70 (m, 2H), 7.49 – 7.42 (m, 4H), 4.46 (s, 2H) ppm.

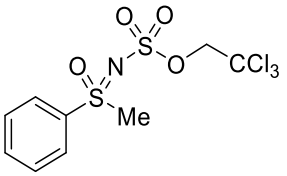
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 151.2, 135.4, 131.2, 126.0, 119.5, 113.1, 94.3, 78.0 ppm.

IR (neat): *v* = 2923 (w), 1732 (m), 1590 (m), 1460 (s), 1338 (s), 1268 (s), 1150 (s), 1099 (m), 1025 (s), 955 (s), 839 (s), 755 (s), 725 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{14}H_{10}Cl_3NO_4NaS_2$: 447.9009 $[M+Na]^+$, found 447.9002

5.2.2 Synthesis of *N*Tces-sulfoximine 36

2,2,2-Trichloroethyl [methyl(oxo)(phenyl)-λ^6-sulfaneylidene]sulfamate (36)



The following procedure was taken from the literature and slightly modified, [72] Under argon, to a solution of sulfilimine (**35a**, 2.0 g, 5.7 mmol, 1.0 equiv) in MeCN (20 mL) and DCE (20 mL) was added $RuCl_3 \cdot xH_2O$ (0.035 mmol, 5.0 mol %). The resulting mixture was stirred for 5 min, then a solution of $NaIO_4$ (2.44 g, 11.4 mmol, 2.00 equiv) in water (0.15 M) was added. The resulting solution was stirred at rt for 12 h at 400 rpm. Water was added and the two layers were

separated. The aqueous layer was extracted with DCM (3 × 20 mL). The combined organic phase was successively washed with a saturated aqueous solutions of $Na_2S_2O_3$ (2 × 20 mL) and NaCl (20 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: ethyl acetate) to afford sulfoximine **36** as a pale white colorless solid (2.05 g, 5.60 mmol, 98%).

R_F = 0.48 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 98 – 100°C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.07 – 8.03 (m, 2H), 7.80 – 7.75 (m, 1H), 7.68 (t, J = 7.8 Hz, 2H), 4.72 (s, 2H), 3.48 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 137.1, 135.2, 130.2, 127.7, 93.6, 78.7, 45.8 ppm.

IR (neat): ν = 3019 (w), 1818 (w), 1448 (w), 1353 (s), 1244 (s), 1166 (s), 1096 (s), 1072 (s), 1012 (s), 854 (s), 732 (s), 683 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_{10}Cl_3NO_4KS_2$: 403.8748 $[M+K]^+$, found 403.8753.

The NMR spectra are in accordance with the literature.[59f]

5.2.3 Synthesis of *N*H-sulfoximine 42

Imino(methyl)(phenyl)-λ^6-sulfanone (42)

The following procedure was taken from the literature:[S2] A 10 mL glass tube was loaded with zinc dust (196 mg, 3.00 mmol, 10.0 equiv) and stirred with three drops of 1,2-dibromoethane in THF (1 mL). The glass tube was sealed and the grey suspension was heated at reflux with a heat gun for 1 min. After cooling to room temperature, three drops of trimethylsilyl chloride were added and the suspension was again heated at reflux for 1 min. The resulting mixture was then stirred at room temperature for 5 min and concentrated under reduced pressure.

To the grey residue was added a magnetic stirring bar and a solution of *N*Tces-protected sulfoximine **36** (110 mg, 0.300 mmol, 1.00 equiv) in glacial acetic acid (3 mL). The resulting

mixture was then stirred at room temperature for 12 h. The reaction mixture was filtered over celite and washed with methanol (10 mL). The filtrate was concentrated under reduced pressure. Acetic acid was removed by repeated evaporation with toluene (2 × 2 mL). The residue was dissolved in dry methanol (5 mL) and acetyl chloride (308 µL, 4.30 mmol, 14.4 equiv) was added. The resulting mixture was stirred at room temperature for 1 h. After this time, the reaction was diluted with water (5 mL) and quenched by addition of a saturated aqueous K_2CO_3 solution (1.2 mL). The pH of the solution was around 8. The solution was extracted with DCE (2 × 20 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: *n*-pentane:ethyl acetate, 1:4 (*V*:*V*)) to afford *N*H-sulfoximine **42** as a colourless oil (36.4 mg, 0.235 mmol, 80%).

$\boldsymbol{R_F}$ = 0.19 (ethyl acetate)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02 – 7.99 (m, 2H), 7.63 – 7.59 (m, 1H), 7.57 – 7.53 (m, 2H), 3.10 (s, 3H), 2.34 (s, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 143.6, 133.2, 129.4, 127.8, 46.3 ppm.

The NMR spectra are in accordance with the literature.[59f]

5.3 Experimental information for chapter 3

5.3.1 General procedures (GP2, GP3, GP4 and GP5)

General procedures for the synthesis of benzo[*e*][1,4,3]oxathiazin-3-one 1-oxides (GP2)

In air, a screw capped reaction tube (volume: 10 mL) equipped with magnetic stir bar was charged with NH-S-(2-hydroxyaryl)sulfoximine (3, 0.2 mmol, 1 equiv), dichloroethane (2 mL, 0.1 M) and 1,1'-carbonyldiimidazole (48.6 mg, 0.3 mmol, 1.5 equiv). The reaction tube was closed and the resulting mixture was heated at 85 °C for 16 h at 400 rpm. After cooling to room temperature, the reaction mixture was transferred to a round-bottom flask and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel.

General Procedure for the mechanochemical synthesis of benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97a)

Under air, *N*H-*S*-(2-hydroxyphenyl)-*S*-methyl sulfoximine (**96**, 51.4 mg, 0.3 mmol, 1 equiv) and 1,1'-carbonyldiimidazole (97.3 mg, 0.6 mmol, 2 equiv) were added to a milling jar (volume: 10 mL) made out of yttrium partially stabilized zirconium oxide equipped with one ball (diameter: 10 mm) of the same material. The jar was tightly sealed and the reaction was carried out in a Retsch Mixer Mill MM 400 for 60 min at 30 Hz, then the jar was opened in air. The reaction mixture was extracted with DCM (3 × 2 mL)**,** transferred to a round-bottomed flask and the solvent was removed under reduced pressure. After purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) **97a** was obtained as a colorless solid (40 mg, 0.203 mmol, 68%).

General procedure for the conversion of benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97a)

In air, to a screw capped reaction tube (volume: 10 mL) equipped with magnetic stir bar was added 1-methyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (**97a,** 39.4 mg, 0.200 mmol, 1.00 equiv) and diethyl ether (2 mL). The resulting mixture was cooled down to –78 °C and *n*-butyl lithium (0.125 mL, 1 equiv, 1 M in hexane) was added while stirring at 400 rpm. After the addition, the reaction mixture was allowed to warm to room temperature and stirred for 16 h. Water was added and the product extracted with diethyl ether (3 ×10 mL). The organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The product was obtained after purification by column chromatography on silica gel (eluent: *n*-pentane:ethyl acetate, 2:3 (*V*:*V*)) as a colorless oil (30 mg, 0.117 mmol, 59%).

General procedure for synthesizing *S*-alkyl-*S*-(aryl)sulfanes (GP3)

The following procedure was taken from the literature and slightly modified.[157] 2-Methoxybenzenethiol (1 equiv) was dissolved in acetone (0.2 M) and potassium carbonate (1.3 equiv) was added. Alkyl halide (1.2 equiv) was added, and the reaction mixture was stirred overnight at room temperature. Water was added, and the reaction mixture was transferred to a separation funnel. The aqueous layer was extracted with diethyl ether (3 × 10 mL), the combined organic layers were washed with brine (15 mL), dried over Na_2SO_4, and filtered over

cotton. The solvent was removed under reduced pressure to afford the aryl alkyl thioether which was used for the synthesis of corresponding sulfoximine without further purification.

General procedure for synthesizing *S*,*S*-(diaryl)sulfanes (GP4)

The following procedure was taken from the literature and slightly modified.[158] The heteroaryl halide (1 equiv), 2-methoxybenzenethiol (1.1 equiv), and H_2O (25 mL) were added to a round-bottomed flask (volume: 100 mL) and stirred at 100 °C for 2 to 8 h. The course of the reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was transferred to a separation funnel and the product was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered over cotton, and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel using a mixture of *n*-hexane and ethyl acetate as the eluent.

General procedure for the synthesis of *N*H-*S*-(2-methoxyaryl)sulfoximines (GP5)

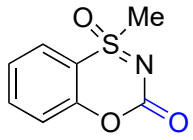
The following procedure was taken from the literature and slightly modified.[26] *S*-Alkyl-*S*-(aryl)sulfane or *S*,*S*-(diaryl)sulfane (1.0 equiv), (diacetoxyiodo)benzene (3.0 equiv), and ammonium carbamate (4.0 equiv) were added to a flask containing MeOH (0.5 M). The reaction mixture was stirred at ambient temperature for 3 h to 17 h. The course of the reaction was monitored by TLC. The solvent was removed under reduced pressure. The product was purified by flash chromatography on silica gel.

General procedure for the syntheses of *N*H-*S*-(2-hydroxyaryl)sulfoximines through CHB/oxidation

Note: Imino(methyl)(*p*-tolyl)-λ^6-sulfanone (**100b**), (4-chlorophenyl)(imino)(methyl)-λ^6-sulfanone (**100c**), benzyl(imino)(phenyl)-λ^6-sulfanone (**100i**), and iminodiphenyl-λ^6-sulfanone (**100k**) were prepared from the corresponding thioethers according to a procedure reported in the literature.[26]

5.3.2 Synthetic procedures and analytical data

1-Methyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97a)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97a** was obtained from (2-hydroxyphenyl)(imino)(methyl)-λ^6-sulfanone (**96a**, 34.2 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (37.2 mg, 0.189 mmol, 94%).

Note on scale-up: Compound **97a** was obtained from (2-hydroxyphenyl)(imino)(methyl)-λ^6-sulfanone(**96a**, 171 mg, 1.00 mmol, 1.00 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (175 mg, 0.887 mmol, 89%).

R_F = 0.35 (ethylacetate)

M.p. = 196 – 198 °C.

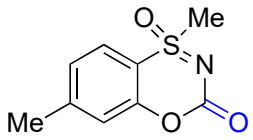
^{1}H NMR (600 MHz, $(CD_3)_2CO$): δ = 8.15 (dd, J = 8.0, 1.6 Hz, 1H), 7.87 (ddd, J = 8.8, 7.3, 1.6 Hz, 1H), 7.51 (ddd, J = 8.1, 7.4, 1.1 Hz, 1H), 7.30 (dd, J = 8.5, 1.0 Hz, 1H), 3.74 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $(CD_3)_2CO$): δ = 153.5, 145.3, 138.1, 126.1, 126.0, 119.5, 115.4, 45.5 ppm.

IR (neat): ν = 3007 (m), 2923 (m), 2190 (w), 1704 (s), 1590 (s), 1477 (s), 1451 (s), 1307 (s), 1236 (s), 1198 (s), 1135 (w), 1094 (s), 1041 (s), 959 (s), 900 (m), 764 (s), 659 (w) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_8H_7NNaO_3S$: 220.0044 $[M+Na]^+$, found 220.0040.

1,6-Dimethyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97b)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97b** was obtained from (2-hydroxy-4-methylphenyl)(imino)(methyl)-λ^6-sulfanone (**96b**, 37.1 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (32.3 mg, 0.153 mmol, 77%).

R_F = 0.57 (ethylacetate)

M.p. = 193 – 195 °C.

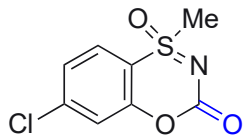
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.1 Hz, 1H), 7.21 (dd, J = 8.2, 1.5 Hz, 1H), 7.09 (s, 1H), 3.45 (s, 3H), 2.48 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 152.7, 149.8, 145.5, 126.6, 124.3, 119.3, 110.8, 46.6, 22.2 ppm.

IR (neat): ν = 2996 (m), 2913 (m), 2318 (w), 1706 (s), 1605 (s), 1445 (m), 1411 (s), 1297 (s), 1236 (s), 1166 (s), 1099 (s), 1043 (s), 873 (m), 787 (s), 676 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_9NNaO_3S$: 234.0195 $[M+Na]^+$, found 234.0192.

6-Chloro-1-methyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97c)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97c** was obtained from (4-chloro-2-hydroxyphenyl)(imino)(methyl)-λ^6-sulfanone (**96c**, 41.1 mg, 0.2 mmol,1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (38 mg, 0.164 mmol, 82%).

R_F = 0.39 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

M.p. = 182 – 184 °C.

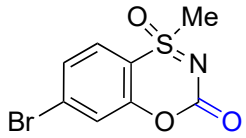
1H NMR (600 MHz, CDCl3): δ = 7.74 (d, J = 8.5 Hz, 1H), 7.40 (dd, J = 8.5, 1.9 Hz, 1H), 7.33 (d, J = 1.9 Hz, 1H), 3.48 (s, 3H) ppm.

13C{^{1}H} NMR (151 MHz, CDCl3): δ = 184.1, 164.0, 158.3, 144.0, 126.2, 125.7, 119.7, 46.5 ppm.

IR (neat): ν = 2997 (w), 2319 (w), 1725 (s), 1590 (s), 1470 (m), 1405 (s), 1227 (s), 1187 (s), 1075 (s), 1029 (s), 967 (s), 897 (m), 818 (m), 788 (s), 737 (s) cm–1.

HRMS (ESI): m/z calculated for C8H6ClNO3S: 230.9751 [M]+, found 230.9751.

6-Bromo-1-methyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97d)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97d** was obtained from (4-bromo-2-hydroxyphenyl)(imino)(methyl)-λ^6-sulfanone (**96d**, 50 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (55.2 mg, 0.2 mmol, 65%).

***R*$_F$ =** 0.41 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

M.p. = 204 – 206 °C.

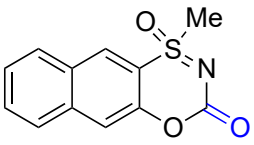
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.4 Hz, 1H), 7.55 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.50 (d, *J* = 1.8 Hz, 1H), 3.48 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 153.1, 144.3, 132.2, 129.0, 125.6, 122.7, 112.7, 46.5 ppm.

IR (neat): *ν* = 3013 (w), 2109 (w), 1713 (s), 1575 (s), 1461 (m), 1397 (s), 1322 (m), 1235 (s), 1152 (m), 1106 (m), 1037 (s), 969 (s), 914 (s), 818 (m), 783 (s), 733 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_8H_6BrNNaO_3S$: 297.9144 $[M+Na]^+$, found 297.9146.

1-Methyl-3*H*-1λ^4-naphtho[2,3-*e*][1,4,3]oxathiazin-3-one 1-oxide (97e)



According to GP2, naphtho[2,3-*e*][1,4,3]oxathiazin-3-one 1-oxide **97e** was obtained from (3-hydroxynaphthalen-2-yl)(imino)(methyl)-λ^6-sulfanone (**96e**, 44.3 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (37 mg, 0.15 mmol, 75%).

***R*$_F$** = 0.59 (ethylacetate)

M.p. = 277 – 279 °C.

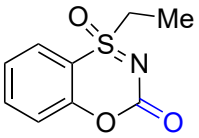
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.76 – 7.70 (m, 2H), 7.63 – 7.60 (m, 1H), 3.56 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 147.3, 137.7, 131.1,131.0, 129.8, 129.2, 128.0, 127.5, 127.0, 115.5, 114.3, 47.0 ppm.

IR (neat): ν = 3020 (w), 1710 (s), 1624 (m), 1592 (s), 1499 (m), 1449 (m), 1334 (s), 1293 (s), 1219 (s), 1167 (m), 1021 (s), 961 (m), 889 (s), 798 (s), 748 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{12}H_9NNaO_3S$: 270.0195 $[M+Na]^+$, found 270.0198.

1-Ethyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97f)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97f** was obtained from ethyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (**96f**, 37.2 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (30.5 mg, 0.144 mmol, 72%).

***R*$_F$** = 0.43 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

M.p. = 112 – 113 °C.

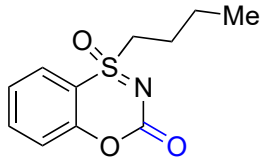
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.79 – 7.73 (m, 2H), 7.42 – 7.40 (m, 1H), 7.31 (d, J = 8.5 Hz, 1H), 3.60 – 3.49 (m, 2H), 1.33 – 1.31 (m, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 153.6, 145.7, 137.7, 125.5, 124.8, 119.5, 111.1, 52.4, 7.7 ppm.

IR (neat): v = 2976 (w), 2932 (w), 2166 (w), 1712 (s), 1590 (s), 1479 (m), 1449 (s), 1226 (s), 1094 (s), 1054 (s), 1007 (s), 901 (m), 867 (w), 802 (m), 745 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_9H_9NNaO_3S$: 234.0195 $[M+Na]^+$, found 234.0197.

1-Butyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97g)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97g** was obtained from butyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (**96g**, 42.7 mg) 0.244 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*))) as a pale yellow oil (42.4 mg, 0.177 mmol, 73%).

R_F = 0.56 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

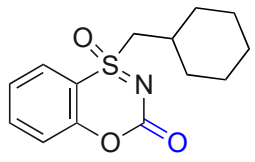
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.78 – 7.72 (m, 2H), 7.43 – 7.37 (m, 1H), 7.31 (d, J = 8.5 Hz, 1H), 3.49 (dd, J = 8.7, 7.4 Hz, 2H), 1.84 – 1.77 (m, 1H), 1.54 – 1.51 (m, 1H), 1.48 – 1.38 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 153.4, 145.6, 137.6, 125.4, 124.8, 119.5, 111.9, 57.5, 24.7, 21.3, 13.6 ppm.

IR (neat): v = 2963 (m), 2875 (m), 1706 (s), 1588 (s), 1449 (s), 1299 (s), 1249 (s), 1192 (s), 1095 (s), 1016 (s), 902 (m), 868 (w), 764 (s), 658 (w) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{11}H_{13}NNaO_3S$: 262.0508 $[M+Na]^+$, found 262.0508.

1-(Cyclohexylmethyl)-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97h)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97h** was obtained from (cyclohexylmethyl)(2-hydroxyphenyl)(imino)-λ^6-sulfanone (**96h**, 50.7 mg, 0.2 mmol,1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colourless liquid (33 mg, 0.118 mmol, 60%).

***R*$_F$** = 0.47 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

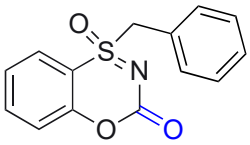
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.76 – 7.73 (m, 2H), 7.41 – 7.38 (m, 1H), 7.29 – 7.27 (m, 1H), 3.43 (dd, *J* = 14.5, 6.0 Hz, 1H), 3.34 (dd, *J* = 14.5, 6.1 Hz, 1H), 2.07 – 2.03 (m, 1H), 1.98 – 1.93 (m, 1H), 1.72 – 1.67 (m, 1H), 1.63 – 1.58 (m, 3H), 1.32 – 1.09 (m, 4H), 1.05 – 0.98 (m, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 152.8, 145.5, 137.5, 125.4, 124.8, 119.4, 113.4, 64.2, 33.1, 33.0, 32.9, 25.6 ppm.

IR (neat): ν = 2922 (s), 2855 (s), 2088 (w), 1721 (s), 1587 (s), 1476 (s), 1447 (s), 1327 (m), 1274 (s), 1214 (s), 1157 (s), 1087 (s), 1006 (s), 901 (s), 838 (m), 758 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{14}H_{17}NNaO_3S$: 302.0821 $[M+Na]^+$, found 302.0819.

1-Benzyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97i)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97i** was obtained from benzyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (**96i**, 49.5 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (44.2 mg, 0.162 mmol, 81%).

***R*$_F$** = 0.50 (ethyl acetate:*n*-pentane = 3:2 (*V*:*V*))

M.p. = 162 – 164 °C.

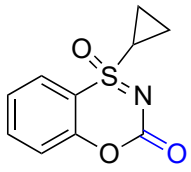
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.68 (ddd, J = 8.7, 7.4, 1.6 Hz, 1H), 7.64 (dd, J = 8.0, 1.6 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.29 – 7.25 (m, 2H), 7.10 – 7.07 (m, 2H), 7.05 (dd, J = 8.4, 1.0 Hz, 1H), 4.72 (d, J = 14.2 Hz, 1H), 4.58 (d, J = 14.2 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 153.5,145.4, 137.9, 131.2, 130.3, 129.3, 125.5, 125.5, 125.0, 118.8, 110.6, 65.0 ppm.

IR (neat): ν = 2974 (w), 2918 (w), 2325 (w), 2093 (w), 1708 (s), 1587 (s), 1448 (s), 1304 (s), 1201 (s), 1090 (s), 1019 (s), 964 (s), 871 (m), 735 (s), 698 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{14}H_{11}NNaO_3S$: 296.0350 $[M+Na]^+$, found 296.0351.

1-Cyclopropyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97j)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97j** was obtained from cyclopropyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (**96j**, 39.5 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellow oil (31.3 mg, 0.14 mmol, 70%).

R_F = 0.56 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

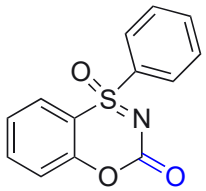
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.73 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.5 Hz, 1H), 2.78 (tt, *J* = 7.4, 4.9 Hz, 1H), 1.77 – 1.72 (m, 1H), 1.41 – 1.35 (m, 2H), 1.28 – 1.23 (m, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 152.6, 146.1, 137.1, 125.4, 124.8, 119.2, 114.5, 34.2, 7.1, 5.8 ppm.

IR (neat): ν = 3039 (w), 2166 (w), 1711 (s), 1590 (s), 1448 (s), 1234 (s), 1186 (s), 1011 (s), 881 (s), 830 (w), 761 (s), 729 (s), 656 (w) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{10}H_9NNaO_3S$: 246.0195 $[M+Na]^+$, found 246.0197.

1-Phenyl-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97k)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97k** was obtained from (2-hydroxyphenyl)(imino)(phenyl)-λ^6-sulfanone (**96k**, 46.7 mg, 0.2 mmol, 1 equiv) after

purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (45.2 mg, 0.174 mmol, 88%).

***R*$_F$** = 0.46 (ethyl acetate:*n*-pentane = 3:2 (*V*:*V*))

M.p. = 158 – 160 °C.

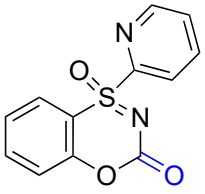
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.00 – 7.97 (m, 2H), 7.76 – 7.72 (m, 1H), 7.69 – 7.62 (m, 3H), 7.45 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.32 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.28 – 7.24 (m, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 152.6, 137.7, 136.8, 135.2, 134.5, 130.0, 128.6, 126.2, 125.6, 125.4, 119.3 ppm.

IR (neat): ν = 2922 (m), 2325 (w), 2094 (w), 1713 (s), 1586 (s), 1445 (s), 1292 (s), 1241 (s), 1189 (s), 1086 (s), 1015 (s), 900 (m), 859 (s), 733 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{13}H_9NO_3S$: 259.0299 $[M]^+$, found 259.0297.

1-(Pyridin-2-yl)-3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (97l)



According to GP2, benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide **97l** was obtained from (2-hydroxyphenyl)(imino)(pyridin-2-yl)-λ^6-sulfanone (**96l**, 46.9 mg, 0.2 mmol, 1 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colourless oil (14.4 mg, 0.0553 mmol, 28%).

***R*$_F$** = 0.65 (ethyl acetate:*n*-pentane = 3:2 (*V*:*V*))

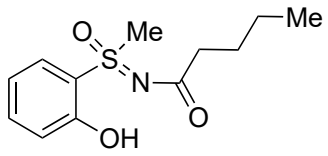
^{1}H NMR (600 MHz, $CDCl_3$): *d* = 8.17 – 8.14 (m, 1H), 7.69 (ddd, *J* = 8.1, 7.2, 2.0 Hz, 1H), 7.64 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.24 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.16 (td, *J* = 7.6, 1.3 Hz, 1H), 7.09 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.01 – 6.99 (m, 1H), 6.94 (dd, *J* = 8.4, 1.0 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): *d* = 163.3, 151.1, 147.7, 139.7, 129.8, 128.8, 128.1, 126.0, 122.3, 118.8, 111.5 ppm.

IR (neat): ν = 2920 (w), 2323 (w), 2078 (w), 1732 (w), 1570 (s), 1459 (s), 1422 (s), 1236 (s), 1203 (s), 1140 (s), 1055 (s), 989 (m), 878 (s), 808 (m), 756 (s), 675 (m) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{12}H_8N_2O_3S$: 260.0256 $[M]^+$, found 186.0372. Correct mass not found.

_N_-((2-hydroxyphenyl)(methyl)(oxo)-λ^6-sulfaneylidene)pentanamide (98)



In air, to a screw capped reaction tube (volume: 10 mL) equipped with magnetic stir bar was added 1-methyl- 3*H*-1λ^4-benzo[*e*][1,4,3]oxathiazin-3-one 1-oxide (**97a,** 39.4 mg, 0.200 mmol, 1.00 equiv) and diethyl ether (2 mL). The resulting mixture was cooled down to –78 °C and *n*-butyl lithium (0.125 mL, 1 equiv, 1 M in hexane) was added while stirring at 400 rpm. After the addition, the reaction mixture was allowed to warm to room temperature and stirred for 16 h. Water was added and the product extracted with diethyl ether (3 ×10 mL). The organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The product **98** was obtained after purification by column chromatography on silica gel (eluent: *n*- pentane:ethyl acetate, 2:3 (*V*:*V*)) as a colorless oil (30 mg, 0.117 mmol, 59%).

R_F **=** 0.51 (ethyl acetate:*n*-pentane = 2:3 (*V*:*V*))

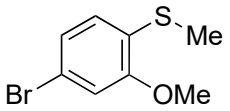
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.72 (dt, *J* = 8.3, 1.5 Hz, 1H), 7.54 (ddd, *J* = 8.7, 7.3, 1.7 Hz, 1H), 7.05 (ddd, *J* = 8.5, 5.5, 1.3 Hz, 2H), 4.13 (qt, *J* = 10.6, 6.7 Hz, 2H), 3.50 (s, 3H), 3.20 (s, 1H), 1.67 – 1.61 (m, 2H), 1.42 – 1.35 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H) ppm.

13C{1H} NMR (151 MHz, CDCl3): δ = 166.4, 158.5, 156.4, 136.9, 128.1, 120.7, 119.9, 66.6, 44.4, 30.9, 19.2, 13.8 ppm.

IR (neat): ν = 3024 (m), 2959 (m), 2872 (m), 1655 (s), 1453 (s), 1391 (m), 1223 (s), 1129 (m), 1064 (m), 969 (s), 884 (s), 837 (m), 755 (s) cm–1.

HRMS (ESI): m/z calculated for $C_{12}H_{17}NO_3NaS$: 278.0811 [M+Na]+, found 278.0811

(4-Bromo-2-methoxyphenyl)(methyl)sulfane (98d)



Following a literature known procedure,[S2] *S*-alkyl-*S*-(aryl)sulfane **98d** was obtained as a pale yellow oil (455 mg, 1.95 mmol, 20%).

R_F = 0.36 (*n*-pentane)

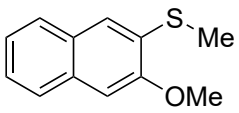
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.08 (dd, J = 8.2, 2.0 Hz, 1H), 7.00 (d, J = 8.3 Hz, 1H), 6.95 (d, J = 1.9 Hz, 1H), 3.89 (s, 3H), 2.41 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.0, 127.4, 126.5, 124.2, 119.2, 113.8, 56.2, 14.9 ppm.

IR (neat): ν = 2927 (s), 2324 (w), 2087 (w), 1731 (m), 1569 (s), 1468 (s), 1388 (s), 1241 (s), 1138 (m), 1064 (s), 1024 (s), 968 (m), 842 (s), 797 (s), 739 (w) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for C_8H_9BrOS: 231.9552 [M]+, found 231.9550.

(3-Methoxynaphthalen-2-yl)(methyl)sulfane (98e)



Following a literature known procedure,[159] *S*-alkyl-*S*-(aryl)sulfane **98e** was obtained as a white solid (432 mg, 2.11 mmol, 43%).

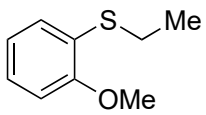
R_F = 0.52 (*n*-pentane)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.28 (s, 1H), 7.87 (d, J = 8.2 Hz, 1H), 7.76 (d, J = 8.3 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.42 – 7.37 (m, 1H), 7.14 (s, J = 2.5 Hz, 1H), 3.97 – 3.94 (m, 3H), 2.83 – 2.82 (m, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 152.6, 135.5, 135.0, 128.7, 128.4, 127.9, 126.7, 125.6, 124.8, 106.1, 55.8, 41.7 ppm.

The NMR spectra are in accordance with those reported in the literature.[159]

Ethyl(2-methoxyphenyl)sulfane (98f)



According to GP3, *S*-alkyl-*S*-(aryl)sulfane **98f** was obtained from 2-methoxybenzenethiol (701 mg, 5.00 mmol, 1.00 equiv) as a pale yellow oil and used without further purification.

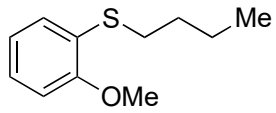
R_F = 0.60 (ethylacetate)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.26 (dd, J = 7.6, 1.7 Hz, 1H), 7.17 (td, J = 7.8, 1.6 Hz, 1H), 6.93 (td, J = 7.6, 1.2 Hz, 1H), 6.85 (dd, J = 8.2, 1.2 Hz, 1H), 3.89 (s, 3H), 2.92 (q, J = 7.4 Hz, 2H), 1.32 (t, J = 7.4 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.3, 129.1, 126.9, 125.0, 121.2, 110.5, 55.9, 26.1, 14.2 ppm.

The NMR spectra are in accordance with those reported in the literature.[160]

Butyl(2-methoxyphenyl)sulfane (98g)



According to GP3, *S*-alkyl-*S*-(aryl)sulfane **98g** was obtained from 2-methoxybenzenethiol (701 mg, 5.00 mmol, 1.00 equiv) as a pale yellow oil and used without further purification.

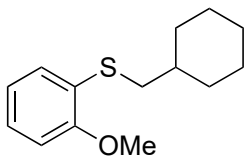
***R*$_F$** = 0.65 (ethylacetate)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.26 – 7.24 (m, 1H), 7.16 (td, J = 7.8, 1.6 Hz, 1H), 6.93 (td, J = 7.5, 1.2 Hz, 1H), 6.85 (dd, J = 8.2, 1.2 Hz, 1H), 3.89 (s, 3H), 2.92 – 2.86 (m, 2H), 1.65 (qd, J = 7.5, 5.9 Hz, 2H), 1.47 (h, J = 7.4 Hz, 2H), 0.93 (t, J = 7.4 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.2, 128.8, 126.7, 125.4, 121.2, 110.5, 55.9, 31.7, 31.1, 22.2, 13.8 ppm.

The NMR spectra are in accordance with those reported in the literature.[161]

(Cyclohexylmethyl)(2-methoxyphenyl)sulfane (98h)



According to GP3, *S*-alkyl-*S*-(aryl)sulfane **98h** was obtained from 2-methoxybenzenethiol (1033 mg, 7.000 mmol, 1.000 equiv) after purification on silica gel (eluent: *n*-hexane:ethyl acetate, 50:1 (*V*:*V*)) as a colourless oil (1.39 g, 5.88 mmol, 84%).

***R*$_F$** = 0.70 (*n*-pentane)

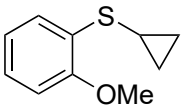
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.22 (dd, J = 7.7, 1.6 Hz, 1H), 7.15 (td, J = 7.8, 1.6 Hz, 1H), 6.92 (td, J = 7.6, 1.2 Hz, 1H), 6.84 (dd, J = 8.2, 1.2 Hz, 1H), 3.89 (s, 3H), 2.78 (d, J = 6.8 Hz, 2H), 1.90 – 195 (m, 2H), 1.75 – 1.69 (m, 2H), 1.67– 1.62 (m, 1H), 1.60 – 1.53 (m, 1H), 1.27 – 1.13 (m, 3H), 1.06 – 0.99 (m, 2H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.0, 128.3, 126.4, 126.0, 121.2, 110.4, 55.9, 39.3, 37.5, 33.1, 26.5, 26.2 ppm.

IR (neat): v = 2921 (s), 2848 (s), 2325 (w), 2100 (w), 1874 (w), 1577 (s), 1472 (s), 1240 (s), 1182 (m), 1071 (s), 1025 (s), 902 (w), 792 (w), 744 (s), 683 (m) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{14}H_{20}OS$: 236.1229 $[M]^+$, found 236.1229.

Cyclopropyl(2-methoxyphenyl)sulfane (98j)



According to GP3, *S*-alkyl-*S*-(aryl)sulfane **98j** was obtained from 2-methoxybenzenethiol (701 mg, 5.00 mmol, 1.00 equiv.) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellow oil (240 mg, 1.33 mmol, 27%).

R_F = 0.50 (ethylacetate:*n*-pentane = 1:4 (*V*:*V*))

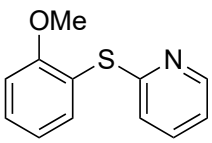
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.49 (dd, J = 7.6, 1.6 Hz, 1H), 7.14 (ddd, J = 9.0, 7.4, 1.6 Hz, 1H), 6.97 (ddd, J = 7.6, 1.2 Hz, 1H), 6.82 (dd, J = 8.1, 1.2 Hz, 1H), 3.87 (s, 3H), 2.14 – 2.08 (m, 1H), 1.11 – 1.05 (m, 2H), 0.72 – 0.66 (m, 2H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 156.7, 127.7, 126.4, 125.8, 121.3, 110.1, 55.9, 10.7, 8.6 ppm.

IR (neat): v = 3065 (w), 2936 (m), 2835 (m), 1759 (w), 1576 (s), 1471 (s), 1275 (s), 1238 (s), 1183 (m), 1071 (s), 1023 (s), 881 (m), 824 (m), 745 (s), 685 (m) cm^{-1}.

HRMS (EI): m/z calculated for $C_{10}H_{12}OS$: 180.0603 $[M]^+$, found 180.0598.

2-[(2-Methoxyphenyl)thio]pyridine (98l)



According to GP4, *S*,*S*-(diaryl)sulfane **98l** was obtained from 2-bromopyridine (798 mg, 5 mmol, 1.00 equiv) after 8 h reaction time and purification on silica gel (eluent: *n*-hexane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colourless liquid (462 mg, 2.13 mmol, 43%).[S6]

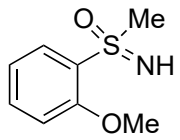
R_F = 0.35 (ethylacetate:*n*-hexane = 4:1 (*V*:*V*))

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.41 – 8.40 (m, 1H), 7.58 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.44 – 7.41 (m, 2H), 7.02 – 6.95 (m, 3H), 6.83 (dt, *J* = 8.1, 1.0 Hz, 1H), 3.81 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 161.0, 159.9, 149.6, 137.1, 136.5, 131.4, 121.5, 121.0, 119.7, 119.0, 111.8, 56.1 ppm.

The NMR spectra are in accordance with those reported in the literature.[158]

Imino(2-methoxyphenyl)(methyl)-λ^6-sulfanone (99a)



Following a literature known procedure,[26] *N*H-*S*-(2-methoxyaryl)sulfoximine **99a** was obtained as a colorless solid (4.11 g, 22.2 mmol, 70%).

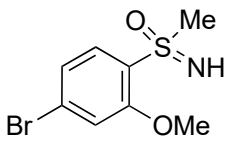
R_F = 0.24 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.60 (ddd, *J* = 8.3, 7.3, 1.8 Hz, 1H), 7.23 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.11 (td, *J* = 7.5, 1.0 Hz, 1H), 4.19 (s, 1H), 3.92 (s, 3H), 3.14 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 156.3, 134.3, 132.1, 128.4, 120.1, 113.0, 56.2, 43.9 ppm.

The NMR spectra are in accordance with those reported in the literature.[26]

(4-Bromo-2-methoxyphenyl)(imino)(methyl)-λ^6-sulfanone (99d)



According to GP5, *N*H-*S*-(2-methoxyaryl)sulfoximine **99d** was obtained from (4-bromo-2-methoxyphenyl)(methyl)sulfane (**98d**, 583 mg, 2.50 mmol, 1.00 equiv) after

purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellow oil (428 mg, 1.62 mmol, 65%).

R_F = 0.36 (ethylacetate)

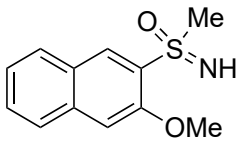
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.4 Hz, 1H), 7.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.12 (d, *J* = 1.8 Hz, 1H), 3.93 (s, 3H), 3.18 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.2, 130.8, 130.7, 129.1, 124.0, 116.1, 56.7, 44.0 ppm.

IR (neat): ν = 3270 (m), 2939 (w), 2098 (w), 1575 (s), 1468 (s), 1388 (s), 1316 (w), 1248 (s), 1217 (s), 1061 (s), 1002 (s), 952 (s), 848 (s), 751 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_8H_{10}BrNO_2S$: 262.9610 $[M]^+$, found 262.9610.

Imino(3-methoxynaphthalen-2-yl)(methyl)-λ^6-sulfanone (99e)



According to GP5, *N*H-*S*-(2-methoxyaryl)sulfoximine **99e** was obtained from (3-methoxynaphthalen-2-yl)(methyl)sulfane (**98e**, 409 mg, 2.00 mmol, 1.00 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*) as a colourless oil (262 mg, 1.11 mmol, 56%).

R_F = 0.26 (ethylacetate)

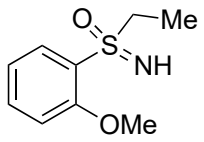
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.54 (s, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.59 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.45 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.28 (s, 1H), 4.09 (s, 3H), 3.37 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 153.5, 136.8, 132.6, 131.2, 129.4, 127.5, 126.6, 125.3, 107.8, 56.4, 44.3 ppm.

IR (neat): ν = 3270 (w), 2937 (w), 2080 (w), 1719 (m), 1625 (s), 1591 (s), 1464 (s), 1326 (s), 1215 (s), 1051 (s), 1011 (s), 955 (s), 835 (m), 752 (s), 714 (m) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{12}H_{13}NNaO_2S$: 258.0559 $[M+Na]^+$, found 258.0561

Ethyl(imino)(2-methoxyphenyl)-λ⁶-sulfanone (99f)



According to GP5, *N*H-*S*-(2-methoxyaryl)sulfoximine **99f** was obtained from ethyl(2-methoxyphenyl)sulfane (**98f**, 507 mg, 3.00 mmol, 1.00 equiv.) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellow oil (400 mg, 2.01 mmol, 67%).

R_F = 0.48 (ethylacetate)

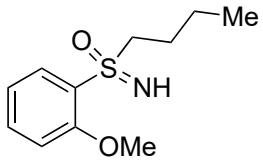
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 7.95 (dd, J = 7.8, 1.8 Hz, 1H), 7.59 – 7.50 (m, 1H), 7.14 – 7.00 (m, 2H), 3.97 (s, 3H), 3.55 – 3.34 (m, 2H), 1.25 (td, J = 7.4, 1.1 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $(CD_3)_2SO$): δ = 157.1, 134.9, 130.7, 129.2, 120.8, 112.4, 56.3, 49.7, 7.6 ppm.

IR (neat): v = 3228 (s), 2973 (w), 2086 (w), 1713 (w), 1587 (s), 1459 (s), 1195 (s), 1104 (s), 1071 (s), 1048 (s), 977 (s), 871 (s) (m), 760 (s), 733 (s), cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_{13}NNaO_2S$: 222.0559 $[M+Na]^+$, found 222.0554

Butyl(imino)(2-methoxyphenyl)-λ⁶-sulfanone (99g)



According to GP5, *N*H-*S*-(2-methoxyaryl)sulfoximine **99g** was obtained from butyl(2-methoxyphenyl)sulfane (**98g**, 704 mg, 3.58 mmol, 1.00 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellow oil (470 mg, 2.07 mmol, 58%).

R_F = 0.42 (ethylacetate)

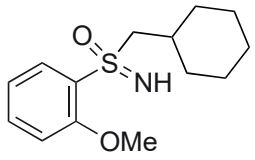
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82 (dd, J = 7.7, 1.8 Hz, 1H), 7.63 – 7.57 (m, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 4.14 (s, 1H), 3.90 (d, J = 1.6 Hz, 3H), 3.31 – 3.25 (m, 2H), 1.50 – 1.40 (m, 2H), 1.24 – 1.33(m, 2H), 0.84 – 0.77 (m, 3H) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ = 156.5, 134.4, 130.3, 129.4, 120.2, 112.9, 56.2, 54.2, 24.9, 20.8, 13.5 ppm.

IR (neat): ν = 3537 (w), 3272 (m), 2958 (s), 2872 (m), 2326 (w), 1716 (w), 1586 (s), 1473 (s), 1246 (s), 1134 (m), 1088 (m), 1056 (m), 978 (s), 801 (s), 759 cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{11}H_{17}NNaO_2S$ 250.0872 $[M+Na]^+$, found 250.0869.

(Cyclohexylmethyl)(imino)(2-methoxyphenyl)-λ⁶-sulfanone (99h)



According to GP5, *N*H-*S*-(2-methoxyaryl)sulfoximine **99h** was obtained from (cyclohexylmethyl)(2-methoxyphenyl)sulfane (**98h**, 1.18 g, 5.00 mmol, 1.00 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellowish oil (1.07 g, 4.00 mmol, 80%).

$\boldsymbol{R_F}$ = 0.43 (ethylacetate)

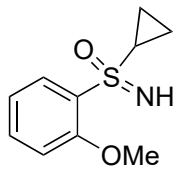
^1H NMR (600 MHz, $CDCl_3$): δ = 7.96 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.58 – 7.50 (m, 1H), 7.09 (td, *J* = 7.6, 1.0 Hz, 1H), 7.02 (dd, *J* = 8.3, 1.0 Hz, 1H), 3.98 (s, 3H), 3.37 (dd, *J* = 14.1, 6.5 Hz, 1H), 3.28 (dd, *J* = 14.1, 5.8 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.88 – 1.83 (m, 1H), 1.80 – 1.76 (m, 1H), 1.67 – 1.56 (m, 3H), 1.30 – 1.18 (m, 2H), 1.16 – 0.98 (m, 3H) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ = 156.9, 134.7, 131.3, 130.0, 120.9, 112.4, 61.9, 56.3, 33.4, 33.2, 26.0, 25.9, 25.8 ppm.

IR (neat): ν = 3273 (w), 2923 (s), 2850 (s), 2082 (w), 1719 (m), 1586 (s), 1474 (s), 1246 (s), 1164 (s), 1133 (s), 1062 (s), 975 (s), 830 (w), 757 (s), 681 (w) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{14}H_{21}NNaO_2S$: 290.1185 $[M+Na]^+$, found 290.1182.

Cyclopropyl(imino)(2-methoxyphenyl)-λ⁶-sulfanone (99j)



According to GP5, *N*H-*S*-(2-methoxyaryl)sulfoximine **99j** was obtained from cyclopropyl(2-methoxyphenyl)sulfane (**98j**, 236 mg, 1.31 mmol, 1.00 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colourless oil (198 mg, 0.936 mmol, 72%).

R_F = 0.33 (ethylacetate)

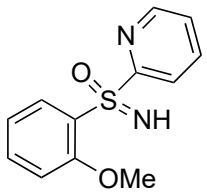
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.57 – 7.50 (m, 1H), 7.10 – 7.02 (m, 2H), 4.00 (s, 3H), 3.07 (tt, *J* = 8.0, 4.8 Hz, 1H), 1.44 – 1.40 (m, 1H), 1.16 – 1.11 (m, 1H), 1.07 – 1.02 (m, 1H), 0.92 – 0.88 (m, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.0, 134.4, 131.2, 129.4, 120.6, 112.5, 56.3, 32.5, 5.3, 5.3 ppm.

IR (neat): *v* = 3229 (s), 2973 (m), 2031 (w), 1714 (w), 1586 (s), 1459 (s), 1208 (s), 1138 (s), 1104 (s), 977 (s), 870 (s), 797 (s), 759 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{10}H_{14}NO_2S$: 212.0739 $[M+H]^+$, found 212.0739.

Imino(2-methoxyphenyl)(pyridin-2-yl)-λ^6-sulfanone (99l)



According to GP5, *N*H-*S*-(2-methoxyaryl)sulfoximine **99l** was obtained from 2-[(2-methoxyphenyl)thio]pyridine (**98l**, 435 mg, 2.00 mmol, 1.00 equiv) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (386 mg, 1.55 mmol, 78%).

R_F = 0.27 (ethylacetate)

M.p. = 146 – 147 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.64 – 8.59 (m, 1H), 8.31 – 8.28 (m, 2H), 7.96 – 7.88 (m, 1H), 7.57 – 7.51 (m, 1H), 7.44 (ddd, *J* = 7.6, 4.7, 1.1 Hz, 1H), 7.19 – 7.11 (m, 1H), 6.90 (dd, *J* = 8.4, 1.0 Hz, 1H), 3.64 (s, 3H) ppm.

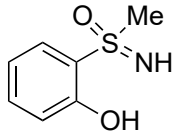
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 160.7, 156.9, 149.7, 137.6, 135.2, 130.7, 129.1, 126.3, 122.7, 120.9, 112.5, 56.0 ppm.

IR (neat): ν = 3263 (s), 3052 (w), 2110 (w), 1728 (w), 1575 (s), 1475 (s), 1427 (s), 1276 (s), 1227 (s), 1107 (m), 978 (s), 860 (w), 771 (s), 734 (s), 683 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{12}H_{12}N_2NaO_2S$: 271.0511 $[M+Na]^+$, found 271.0517.

2.4.4 Syntheses of *N*H-*S*-(2-hydroxyaryl)sulfoximines through demethylation

(2-Hydroxyphenyl)(imino)(methyl)-λ⁶-sulfanone (96a)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96a** was obtained from imino(2-methoxyphenyl)(methyl)-λ⁶-sulfanone (**99a**, 4.03 g, 21.7 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a white solid (2.4 g, 64.6 mmol, 65%).

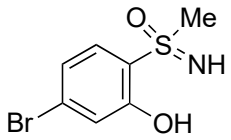
R_F = 0.50 (ethyl acetate:*n*-pentane = 2:3 (*V*:*V*))

1H NMR (600 MHz, $CDCl_3$): δ = 7.74 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.03 – 6.98 (m, 2H), 3.19 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ = 156.6, 136.1, 128.4, 122.1, 120.1, 119.1, 48.4 ppm.

The NMR spectra are in accordance with those reported in the literature.[26]

(4-Bromo-2-hydroxyphenyl)(imino)(methyl)-λ⁶-sulfanone (96d)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96d** was obtained from (4-bromo-2-methoxyphenyl)(imino)(methyl)-λ⁶-sulfanone (**99d**, 158 mg, 0.632 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellow solid (84.2 mg, 0.337 mmol, 56%).

***R*$_F$ =** 0.51 (ethyl acetate:*n*-pentane = 3:2 (*V*:*V*))

M.p. = 121 – 123 °C.

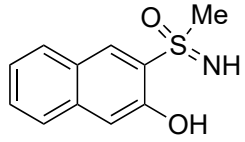
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 8.5 Hz, 1H), 7.20 (d, *J* = 1.9 Hz, 1H), 7.13 (dd, *J* = 8.5, 1.9 Hz, 1H), 3.18 (s, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.3, 130.3, 129.6, 123.5, 122.3, 121.1, 48.7 ppm.

IR (neat): *v* = 3212 (s), 2649 (m), 2089 (w), 1786 (m), 1572 (s), 1476 (w), 1402 (s), 1319 (m), 1251 (m), 1200 (s), 1014 (s), 882 (s), 801 (s), 754 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_7H_9BrNO_2S$: 249.9531 $[M+H]^+$, found 249.9529.

(3-Hydroxynaphthalen-2-yl)(imino)(methyl)-λ^6-sulfanone (96e)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96e** was obtained from imino(3-methoxynaphthalen-2-yl)(methyl)-λ^6-sulfanone (**99e**, 235 mg, 1.06 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale brown solid (99 mg, 0.447 mmol, 45%).

***R*$_F$ =** 0.70 (ethylacetate)

M.p. = 156 – 158 °C.

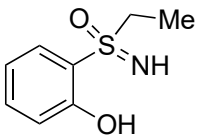
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.41 (s, 1H), 7.85 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.55 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.42 – 7.37 (m, 2H), 3.25 (s, 3H) ppm

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 151.5, 138.1, 130.9, 129.6, 129.2, 127.4, 126.6, 125.5, 124.9, 113.7, 48.2 ppm.

IR (neat): *v* = 3260 (w), 2922 (m), 1715 (w), 1587 (m), 1398 (w), 1360 (m), 1259 (s), 1201 (m), 1010 (s), 887 (m), 791 (s), 753 (s), 692 (m) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{11}H_{12}NO_2S$: 222.0583 $[M+H]^+$, found 222.0583.

Ethyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (96f)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96f** was obtained from ethyl(imino)(2-methoxyphenyl)-λ^6-sulfanone (**99f**, 374 mg, 1.88 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale orange solid (279 mg, 1.51 mmol, 80%).

R_F = 0.67 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

M.p. = 60 – 62 °C.

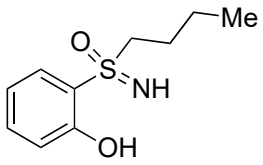
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.68 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.51 – 7.47 (m, 1H), 6.99 (dd, *J* = 11.2, 8.0 Hz, 2H), 3.29 – 3.16 (m, 2H), 1.29 (t, *J* = 7.4 Hz, 3H). ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.5, 136.2, 129.2, 119.9, 119.6, 119.1, 54.5, 7.9 ppm.

IR (neat): ν = 3276 (s), 3245 (s), 2925 (w), 1664 (w), 1584 (s), 1460 (s), 1401 (s), 1314 (m), 1259 (s), 1182 (s), 1124 (s), 999 (s), 971 (s), 824 (s), 754 (s), 659 (m) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_8H_{11}NNaO_2S$: 208.0402 $[M+Na]^+$, found 208.0405.

Butyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (96g)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96g** was obtained from butyl(imino)(2-methoxyphenyl)-λ^6-sulfanone (**99g**, 313 mg, 1.38 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a brown oil (239 mg, 1.12 mmol, 81%).

R_F = 0.65 (ethylacetate:*n*-pentane = 4:1 (*V*:*V*))

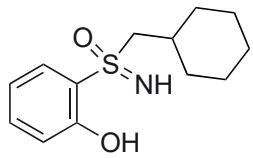
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.69 (d, J = 7.9 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 6.99 (t, J = 9.4 Hz, 2H), 3.18 (d, J = 8.8 Hz, 2H), 1.75 – 1.63 (m, 2H), 1.43 – 1.34 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.3, 136.2, 129.1, 120.4, 119.9, 119.1, 59.9, 25.0, 21.5, 13.7 ppm.

IR (neat): v = 3281 (m), 2935 (m), 1732 (w), 1585 (s), 1462 (s), 1403 (s), 1313 (s), 1197 (s), 1124 (m), 1063 (m), 990 (s), 836 (s), 756 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{10}H_{15}NNaO_2S$: 236.0715 $[M+Na]^+$, found 236.0716.

(Cyclohexylmethyl)(2-hydroxyphenyl)(imino)-λ^6-sulfanone (96h)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96h** was obtained from (cyclohexylmethyl)(imino)(2-methoxyphenyl)-λ^6-sulfanone (**99h**, 802 mg, 3.17 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellowish oil (587 mg, 2.32 mmol, 78%).

***R*$_F$** = 0.75 (ethyl acetate:*n*-pentane = 1:1 (*V*:*V*))

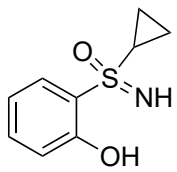
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.71 – 7.67 (m, 1H), 7.50 – 7.46 (m, 1H), 7.02 – 6.96 (m, 2H), 3.13 – 3.06 (m, 2H), 1.97 – 1.91 (m, 1H), 1.87 – 1.81 (m, 1H), 1.77 – 1.73 (m, 1H), 1.69 – 1.59 (m, 3H), 1.30 – 1.23 (m, 2H), 1.17 – 1.01 (m, 3H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.0, 136.1, 128.9, 121.6, 119.9, 119.1, 66.5, 33.3, 25.9, 25.8, 25.8 ppm.

IR (neat): v = 3281 (m), 2924 (s), 2852 (s), 2331 (m), 1894 (w), 1586 (s), 1462 (s), 1401 (s), 1313 (s), 1204 (s), 1126 (m), 1062 (m), 988 (s), 836 (s), 755 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{13}H_{19}NNaO_2S$: 276.1028 $[M+Na]^+$, found 276.1026.

Cyclopropyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (96j)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96j** was obtained from cyclopropyl(imino)(2-methoxyphenyl)-λ^6-sulfanone (**99j**, 189 mg, 0.895 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale yellow oil (123 mg, 0.624 mmol, 70%).

R_F = 0.70 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

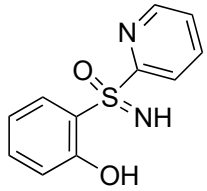
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.67 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.48 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H), 7.01 – 6.95 (m, 2H), 2.65 (tt, *J* = 7.9, 4.8 Hz, 1H), 1.34 – 1.23 (m, 2H), 1.08 – 0.99 (m, 2H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 156.9, 135.9, 128.8, 121.4, 119.8, 119.2, 36.8, 6.9, 5.2 ppm

IR (neat): ν = 3275 (m), 3046 (w), 1725 (w), 1585 (s), 1463 (s), 1408 (s), 1312 (s), 1207 (s), 1125 (m), 1043 (s), 984 (s), 833 (s), 694 (s), 661 (m) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_9H_{11}NO_2S$: 197.0505 $[M]^+$, found 197.0503.

(2-Hydroxyphenyl)(imino)(pyridin-2-yl)-λ^6-sulfanone (96l)



Applying the reaction conditions based on a report in the literature,[101] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96l** was obtained from imino(2-methoxyphenyl)(pyridin-2-yl)-λ^6-sulfanone (**99l**, 346 mg, 1.48 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a pale purple solid (118 mg, 0.504 mmol, 37%).

R_F = 0.76 (ethylacetate)

M.p. = 108 – 110 °C.

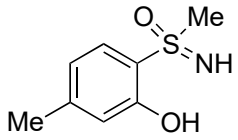
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.68 (ddd, J = 4.7, 1.8, 0.9 Hz, 1H), 8.07 (dt, J = 7.9, 1.0 Hz, 1H), 7.90 (td, J = 7.8, 1.8 Hz, 1H), 7.73 (dd, J = 8.1, 1.7 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.00 (dd, J = 8.4, 1.2 Hz, 1H), 6.91 (ddd, J = 8.2, 7.2, 1.2 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 161.2, 158.0, 150.5, 138.5, 136.6, 129.7, 127.0, 121.5, 119.7, 119.5, 119.3 ppm.

IR (neat): ν = 3261 (s), 2089 (w), 1734 (w), 1578 (s), 1456 (s), 1423 (s), 1314 (m), 1256 (s), 1202 (s), 1122 (m), 1081 (w), 979 (s), 760 (s), 679 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_{11}H_{10}N_2NaO_2S$: 257.0355 $[M+Na]^+$, found 257.0352.

(2-Hydroxy-4-methylphenyl)(imino)(methyl)-λ^6-sulfanone (96b)



Applying the reaction conditions based on a report in the literature,[102] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96b** was synthesized from imino(methyl)(*p*-tolyl)-λ^6-sulfanone (**100b**, 1016 mg, 6.000 mmol) in a one-pot synthesis through iridium-catalysed *ortho*-C–H borylation (CHB) with 2-aminopyridine (11.4 mg, 0.121 mmol, 2 mol %) as the ligand followed by oxidation with oxone. After purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) **96b** was obtained as a pale pink solid (250 mg, 1.35 mmol, 25%).

R_F = 0.70 (ethylacetate)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.61 (d, J = 8.1 Hz, 1H), 6.81 (d, J = 13.9 Hz, 2H), 3.17 (s, 3H), 2.36 (s, 3H) ppm.

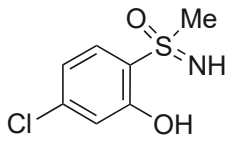
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 156.6, 147.6, 128.4, 126.6, 121.3, 119.3, 48.6, 21.8 ppm.

IR (neat): ν = 3218 (s), 2496 (m), 1799 (m), 1590 (s), 1407 (s), 1374 (s), 1306 (s), 1276 (m), 1198 (s), 1018 (s), 885 (m), 804 (s), 756 (s), 733 (s) cm^{-1}.

HRMS (ESI): m/z calculated for $C_8H_{12}NO_2S$: 186.0583 $[M+H]^+$, found 186.0583.

The NMR spectra are in accordance with those reported in the literature.[102]

(4-Chloro-2-hydroxyphenyl)(imino)(methyl)-λ^6-sulfanone (96c)



Applying the reaction conditions based on a report in the literature,[102] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96c** was synthesized from (4-chlorophenyl)(imino)(methyl)-λ^6-sulfanone (**100c**, 284 mg, 1.50 mmol) in a one-pot synthesis through iridium-catalysed *ortho*-C–H borylation (CHB) followed by oxidation with oxone. After purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) **96c** was obtained as a light brown solid (238 mg, 1.16 mmol, 77%).

$\boldsymbol{R_F}$ = 0.73 (ethyl acetate:*n*-pentane = 4:1 (*V*:*V*))

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.6 Hz, 1H), 7.04 (s, 1H), 6.98 (d, *J* = 8.7 Hz, 1H), 3.19 (s, 3H) ppm.

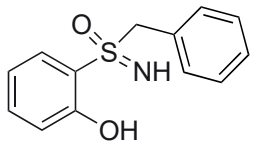
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.5, 142.0, 129.6, 129.1, 120.7, 119.3, 48.8 ppm.

IR (neat): *v* = 3339 (m), 2486 (w), 1791 (m), 1580 (s), 1416 (s), 1300 (m), 1257 (m), 1202 (s), 1144 (s), 1057 (s), 1000 (s), 901 (s), 873 (s), 809 (s), 755 (s), 673 (w) cm^{-1}.

HRMS (EI): *m*/*z* calculated for $C_7H_8ClNO_2S$: 204.9958 $[M]^+$, found 204.9957.

The NMR spectra are in accordance with those reported in the literature.[102]

Benzyl(2-hydroxyphenyl)(imino)-λ^6-sulfanone (96i)



Applying the reaction conditions based on a report in the literature,[102] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96i** was synthesized from benzyl(imino)(phenyl)-λ^6-sulfanone (**100i**, 347 mg, 1.50 mmol) in a one-pot synthesis through iridium-catalysed *ortho*-C–H borylation (CHB) followed by oxidation with oxone. After purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) **96i** was obtained as a light brown oil (222 mg, 0.898 mmol, 60%).

R_F = 0.75 (ethyl acetate:*n*-pentane = 3:2 (*V*:*V*))

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.62 – 7.58 (m, 1H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.20 (d, *J* = 7.1 Hz, 2H), 6.97 – 6.91 (m, 2H), 4.45 (d, *J* = 13.0 Hz, 1H), 4.28 (d, *J* = 13.0 Hz, 1H) ppm.

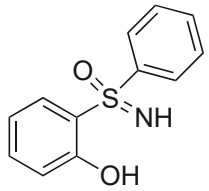
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 157.3, 136.3, 131.2, 129.4, 129.3, 129.0, 127.6, 119.7, 119.2, 118.9, 66.9 ppm.

IR (neat): ν = 3227 (m), 2914 (m), 2100 (w), 1800 (w), 1583 (s), 1402 (m), 1402 (s), 1315 (m), 1258 (s), 1187 (s), 1065 (m), 991 (s), 839 (m), 780 (s), 747 (s), 695 (s) cm^{-1}.

HRMS (ESI): *m*/*z* calculated for $C_{13}H_{13}NNaO_2S$: 270.0565 $[M+Na]^+$, found 270.0553.

The NMR spectra are in accordance with those reported in the literature.[102]

(2-Hydroxyphenyl)(imino)(phenyl)-λ^6-sulfanone (96k)



Applying the reaction conditions based on a report in the literature,[102] *N*H-*S*-(2-hydroxyaryl)sulfoximine **96k** was synthesized from iminodiphenyl-λ^6-sulfanone (**100k**, 326 mg, 1.50 mmol) in a one-pot synthesis through iridium-catalysed *ortho*-C–H borylation (CHB) followed by oxidation with oxone. After purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) the product **96k** was obtained as a light brown solid (222 mg, 0.909 mmol, 61%).

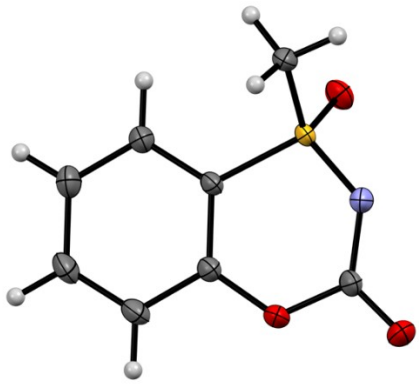
R_F = 0.72 (ethyl acetate:*n*-pentane = 3:2 (*V*:*V*))

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.91 – 7.88 (m, 2H), 7.53 – 7.50 (m, 1H), 7.48 – 7.44 (m, 1H), 7.42 – 7.38 (m, 2H), 7.33 – 7.27 (m, 1H). 6.87 – 6.86 (m, 1H), 6.80 – 6.75 (m, 1H) ppm.

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 156.9, 145.3, 136.2, 135.7, 133.3, 129.5, 129.1, 128.7, 127.2, 120.5, 119.9, 119.4 ppm.

The NMR spectra are in accordance with those reported in the literature.[162]

X-ray crystallographic studies (97a)



$C_8H_7NO_3S$,

$M = 197.21$ gmol^{-1},

colourless block,

$0.24 \times 0.19 \times 0.15$ mm^3,

monoclinic,

space group *P21/c* (no. 14),

$a = 7.7382(2)$ Å, $b = 14.6023(3)$ Å, $c = 7.4028(1)$ Å, $\beta = 93.072(2)°$,

$V = 835.28(3)$ Å^3,

$Z = 4$,

$D_{calc} = 1.5689$ g/cm^3,

F(000) = 408,

$\mu = 3.246$ mm^{-1},

T = 120.0(1) K,

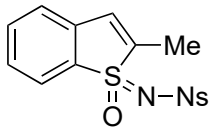
$\theta_{max} = 79.25°$,

7597 total reflections, 1681 with $I_o > 2\sigma(I_o)$, $R_{int} = 0.0668$, 1785 data, 119 parameters, 0 restraints, GooF = 1.094, $R_1 = 0.0503$ and $wR_2 = 0.1384$ [$I_o > 2\sigma(I_o)$], $R_1 = 0.0516$ and $wR_2 = 0.1398$ (all reflections), $0.582 < d\Delta\rho < -0.591$ eÅ^{-3}.

5.4 Experimental information for chapter 4

5.4.1 Synthetic procedures and analytical data

_N_-(2-methyl-1-oxido-1λ^4-benzo[_b_]thiophen-1-ylidene)-4-nitrobenzenesulfonamide (144)

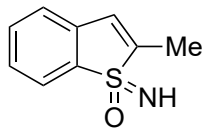


N-(2-methyl-1-oxido-1λ^4-benzo[*b*]thiophen-1-ylidene)-4-nitrobenzenesulfonamide **144** was obtained from sulfoxide (**140**, 32.8 mg, 0.2 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colorless solid (30.5 mg, 0.185 mmol, 86%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.67 – 8.59 (m, 2H), 8.56 – 8.47 (m, 3H), 7.87 (dt, 2H), 7.64 (d, 1H), 7.54 (s, 1H), 2.53 (d, 3H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ = 149.1, 149.4, 140.5, 135.9, 134.9, 132.5, 130.5, 129.8, 128.2, 125.5, 124.8, 124.2, 9.8 ppm.

1-imino-2-methyl-1*H*-1λ^4-benzo[*b*]thiophene 1-oxide (141)



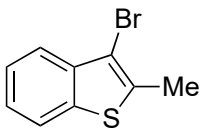
1-imino-2-methyl-1H-1λ^4-benzo[*b*]thiophene 1-oxide **141** was synthesized from sulfoxide (**140**, 32.8 mg, 0.2 mmol) after purification on silica gel (eluent: *n*-pentane:ethyl acetate, gradient: 1:4 → 0:100 (*V*:*V*)) as a colourless solid (29.5 mg, 0.165 mmol, 72%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.73 (d, J = 7.4 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 6.72 (s, 1H), 3.13 (s, 1H), 2.24 (s, 3H) ppm

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ = 143.6, 139.4, 133.0, 132.6, 129.2, 124.5, 124.2, 121.1, 9.1 ppm.

The NMR spectra are in accordance with those reported in the literature.[149]

3-bromo-2-methylbenzo[*b*]thiopheneoxides (139)



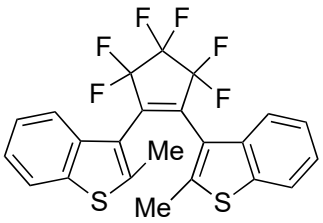
The following procedure was taken from the literature,[152] Under argon atmosphere, *N*-bromosuccinimide (6.55 g, 36.8 mmol) was added to a −5 °C solution of 1 (5.53 g, 34.1 mmol) in THF (62 mL), and the solution was stirred for 14 hours. The reaction was quenched by addition of Na_2CO_3 solution (saturated, 20 mL) and $Na_2S_2O_3$ solution (saturated, 20 mL), and stirred for 30 minutes. The aqueous phase was separated and extracted with Et_2O (3 × 40 mL). After evaporation of the solvent, the crude product was dissolved in hexane and filtered over SiO_2 to give **139** as off-white oil (7.62 g, 31.6 mmol, 85%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.73–7.68 (m, 2H), 7.53–7.38 (m, 2H), 2.57 (s, 3H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ = 138.6, 137.3, 135.3, 125.0, 124.9, 122.7, 122.3, 106.7, 15.6 ppm.

The NMR spectra are in accordance with those reported in the literature.[163]

3,3'-(perfluorocyclopent-1-ene-1,2-diyl)bis(2-methylbenzo[*b*]thiophene) (135)



The following procedure was taken from the literature,[152] Under argon atmosphere, n-BuLi (1.6 M in hexane, 13 mL, 20.8 mmol) was added dropwise to a cooled (−78 °C) solution of **139** (4.39 g, 18.2 mmol) in dry Et_2O (160 mL). After stirring for 4 h, perfluorocyclopentene (1.22 mL, 9.10 mmol) was added slowly (in the course of one hour). The solution was slowly warmed to room temperature, and after stirring for 3 h, hydrochloric acid (1 m, 100 mL) was added. The aqueous phase was extracted with Et_2O (3 × 50 mL), the combined organic solutions dried over Na_2SO_4, the solvent evaporated under reduced pressure, and the crude product

purified by column chromatography (ca. 200 g SiO_2, hexane). **135** (2.90 g, 4.63 mmol, 68%) was obtained as colorless crystals.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.19 (s, 3H), 2.47 (s, 3H), 7.14-7.38 (m, 8H) ppm

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ = 142.6, 141.1, 138.3, 138.2, 138.0, 124.6,124.4, 124.3, 122.1, 121.8, 119.4, 119.1, 15.2, 15.1 ppm.

The NMR spectra are in accordance with those reported in the literature.[164]

6 Abbreviations

Ac	acetyl
acac	acetylacetonate
AcOH	acetic acid
aq.	aqueous
Ar	aryl, argon
2-APy	2-Aminopyridine
8-AQ	8-aminoquinoline
Bn	benzyl
Bu	butyl
Boc	*tert*-butyloxycarbonyl
BSO	buthionine sulfoximine
cat.	catalyst
Cbz	carboxybenzyl
CDK	cyclin-dependent kinase
CDI	1,1'-carbonyldiimidazole
d	doublet
d.r.	diastereomeric ratio
DCE	1,2-dichloroethane
DCM	dichloromethane
dmhd	4-chloro-2,6-dimethyl-3,5-heptanedionate)
DMAP	4-dimethylaminopyridine
DMA	*N,N*-dimethyl aniline
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
equiv.	equivalent
EI	electron ionization
EtOAc	ethyl acetate
EtOH	ethanol
GC	gas chromatography
GP	general procedure
h	hour
het	heterocycle
Hz	Hertz
HRMS	high resolution mass spectrometry

i	*iso*
IR	infrared spectroscopy
J	coupling constant (in Hz)
M.p	melting point
m-	*meta*-
m	mutiplet
m-CPBA	*meta*-chloroperbenzoic acid
M	metal or molar
Me	methyl
MeCN	acetonitrile
MeOH	methanol
min	minute(s)
mL	milliliter
MS	mass spectrometry or molecular sieve
Ms	mesyl
MSO	methionine sulfoximine
MSH	*O*-mesitylsulfonylhydroxylamine
MMPP	magnesium monoperoxyphthalate
n.r	no reaction
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
Nu	nucleophile
Ns	nosyl
o-	*ortho*-
OAc	acetate
p-	*para*-
ppm	parts per million
PG	protecting group
Pr	propyl
Ph	phenyl
PIDA	phenyliodine diacetate, $PhI(OAc)_2$
Py	pyridyl
R_f	retardation factor
R	*R*-configuration
rpm	revolutions per minute
rt	room temperature

sat.	saturated
s	singlet
S	*S*-configuration
t	time, triplet, tertiary
T	temperature
Tces	trichloroethoxysulfonyl
Troc	trichloroethoxycarbonyl
Tf	triflate
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TM	transition metal
TMS-	trimethylsilyl-
Tol	tolyl
Ts	tosyl
UV	ultraviolet
Vis	visible
V	volume
vs	versus
wt%	percentage by mass
δ	chemical shift (in ppm)

7 References

(1) Ilardi, E. A.; Vitaku, E.; Njardarson, J. T. *J. Med. Chem.* **2014**, *57*, 2832–2842.

(2) Ilardi, E. A.; Vitaku, E.; Njardarson, J. T. *J. Chem. Educ.* **2013**, *90*, 1403–1405.

(3) Smith, B. R.; Eastman, C. M.; Njardarson, J. T. *J. Med. Chem.* **2014**, *57*, 9764–9773.

(4) Jeanguenat, A.; Lamberth, C. *Pest Manag. Sci.* **2023**, *79*, 2647–2663.

(5) Clayden, J.; Greeves, N.; Warren, S. *Organic chemistry*; Oxford University Press, Oxford, **2012**.

(6) (a) Furukawa, N.; Oae, S. *Ind. Eng. Chem. Prod. Res. Dev.* **1981**, *20*, 260–270. (b) Taylor, P. C, *Sulfur Reports* **1999**, *21*, 241–280. (c) Gilchrist, T. L.; Moody, C. J. *Chem. Rev.* **1977**, *77*, 409–435.

(7) (a) Reggelin, M.; Zur, C. *Synthesis* **2000**, 1–64. (b) Johnson, C. R. *Acc. Chem. Res.* **1973**, *6*, 341–347.

(8) (a) Glendening, E. D.; Shrout, A. L. *J. Phys. Chem. A* **2005**, *109*, 4966–4972. (b) Kumar, P. S.; Bharatam, P. *Tetrahedron* **2005**, *61*, 5633–5639.

(9) Bentley, R. *Chem. Soc. Rev.* **2005**, *34*, 609–624.

(10) (a) Cho, G. Y.; Rémy, P.; Jansson, J.; Moessner, C.; Bolm, C. *Org. Lett.* **2004**, *6*, 3293–3296. (b) Correa, A.; Bolm, C. *Adv. Synth. Catal.* **2008**, *350*, 391–394. (c) Teng, F.; Cheng, J.; Bolm, C. *Org. Lett.* **2015**, *17*, 3166–3169.

(11) Bentley, H.; McDermott, E.; Pace, J.; Whitehead, J.; Moran, T. *Nature* **1949**, *163*, 675–676.

(12) Bentley, H.; McDermott, E.; Whitehead, J. *Proc. R. Soc. Lond. B.* **1951**, *138*, 265–272.

(13) (a) Satzinger, G.; Stoss, P. *Arzneimittelforschung* **1970**, *20*, 1214–1217. (b) Longhurst, C.; Babcock, J. M.; Denholm, I.; Gorman, K.; Thomas, J. D.; Sparks, T. C. *Pest Manag. Sci.* **2013**, *69*, 809–813.

(14) Bartoszyk, G.; Dooley, D.; Barth, H.; Hartenstein, J.; Satzinger, G. *J. Pharm. Pharmacol.* **1987**, *39*, 407–408.

(15) Zhu, Y.; Loso, M. R.; Watson, G. B.; Sparks, T. C.; Rogers, R. B.; Huang, J. X.; Gerwick, B. C.; Babcock, J. M.; Kelley, D.; Hegde, V. B. *J. Agric. Food Chem.* **2011**, *59*, 2950–2957.

(16) Babcock, J. M.; Gerwick, C. B.; Huang, J. X.; Loso, M. R.; Nakamura, G.; Nolting, S. P.; Rogers, R. B.; Sparks, T. C.; Thomas, J.; Watson, G. B. *Pest Manag. Sci.* **2011**, *67*, 328–334.

(17) Siemeister, G.; Lücking, U.; Wengner, A. M.; Lienau, P.; Steinke, W.; Schatz, C.; Mumberg, D.; Ziegelbauer, K. *Mol. Cancer Ther.* **2012**, *11*, 2265–2273.

(18) (a) Foote, K.; Nissink, J.; Turner, P. (AstraZeneca), WO 2011154737 A1 20111215, **2011**. (b) Gutmann, B. Elsner, P. O'Keaney-McMullan, A. Goundry, W. Roberge, D. M. Kappe. C.O. *Org. Process Res. Dev* **2015**, *19*, 1062–1067.

(19) Walker, D. P.; Zawistoski, M. P.; McGlynn, M. A.; Li, J.-C.; Kung, D. W.; Bonnette, P. C.; Baumann, A.; Buckbinder, L.; Houser, J. A.; Boer, J. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3253–3258.

(20) (a) Lu, D.; Vince, R. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5614–5619. (b) Lu, D.; Sham, Y. Y.; Vince, R. *Bioorg. Med. Chem.* **2010**, *18*, 2037–2048.

(21) (a) Tsujihara, K.; Furukawa, N.; Oae, K.; Oae, S. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2631–2635. (b) Armstrong, A.; Cooke, R. S. *Chem. Commun.* **2002**, 904–905. (c) Gracia Mancheño, O.; Bistri, O.; Bolm, C. *Org. Lett.* **2007**, *9*, 3809-3811. (d) Klein, M.; Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2021**, *60*, 23197–23201; *Angew. Chem.* **2021**, *133*, 23382–23387

(22) Davies, T. Q.; Tilby, M. J.; Ren, J.; Parker, N. A.; Skolc, D.; Hall, A.; Duarte, F.; Willis, M. C. *J. Am. Chem. Soc.* **2020**, *142*, 15445–15453.

(23) Matos, P. M.; Lewis, W.; Moore, J. C.; Stockman, R. A. *Org. Lett.* **2018**, *20*, 3674–3677.

(24) Teng, S.; Shultz, Z. P.; Shan, C.; Wojtas, L.; Lopchuk, J. M. *Nat. Chem.* **2024**, *16*, 183–192.

(25) Zhao, S.; Zeng, D.; Wang, M.; Jiang, X. *Nat. Commun.* **2024**, *15*, 727.

(26) Tota, A.; Zenzola, M.; Chawner, S. J.; St John-Campbell, S.; Carlucci, C.; Romanazzi, G.; Degennaro, L.; Bull, J. A.; Luisi, R. *Chem. Commun.* **2017**, *53*, 348–351.

(27) Degennaro, L.; Tota, A.; De Angelis, S.; Andresini, M.; Cardellicchio, C.; Capozzi, M. A.; Romanazzi, G.; Luisi, R. A. *Eur. J. Org. Chem.* **2017**, 6486–6490.

(28) Chaabouni, S.; Lohier, J. F.; Barthelemy, A. L.; Glachet, T.; Anselmi, E.; Dagousset, G.; Diter, P.; Pégot, B.; Magnier, E.; Reboul, V. *Chem. Eur. J.* **2018**, *24*, 17006–17010.

(29) Xie, Y.; Zhou, B.; Zhou, S.; Zhou, S.; Wei, W.; Liu, J.; Zhan, Y.; Cheng, D.; Chen, M.; Li, Y. *ChemistrySelect* **2017**, *2*, 1620–1624.

(30) Märcker, C. *Liebigs Ann.* **1865**, *136*, 75–95.

(31) Skolia, E.; Gkizis, P. L.; Kokotos, C. G. *ChemPlusChem* **2022**, *87*, e202200008.

(32) (a) Modena, G.; Todesco, P. E. *J. Chem. Soc.* **1962**, 4920–4926. (b) Kaiser, G.; Cooper, R. D.; Koehler, R.; Murphy, C.; Webber, J.; Wright, I. G.; Van Heyningen, E. *J. Org. Chem.* **1970**, *35*, 2430–2433.

(33) Chen, M.-Y.; Patkar, L. N.; Lin, C. *J. Org. Chem.* **2004**, *69*, 2884–2887.

(34) (a) Bagherzadeh, M.; Amini, M.; Boghaei, D. M.; Najafpour, M. M.; McKee, V. *Appl. Organomet. Chem.* **2011**, *25*, 559–563. (b) Kupwade, R.; Khot, S.; Lad, U.; Desai, U.; Wadgaonkar, P. *Rev. Chem. Intermed.* **2017**, *43*, 6875–6888.

(35) Leonard, N. J.; Johnson, C. R. *J. Org. Chem.* **1962**, *27*, 282–284.

(36) (a) Moorthy, J. N.; Singhal, N.; Senapati, K. *Tetrahedron Lett.* **2008**, *49*, 80–84. (b) Dillard, R. D.; Pavey, D. E. (Eli Lily and Company), US4171361A, **1977**.

(37) (a) Russo, A.; Lattanzi, A. *Adv. Synth. Catal.* **2009**, *351*, 521–524. (b) Kumar, S.; Verma, S.; Jain, S. L.; Sain, B. *Tetrahedron Lett.* **2011**, *52*, 3393–3396.

(38) (a) Kowalski, P.; Mitka, K.; Ossowska, K.; Kolarska, Z. *Tetrahedron* **2005**, *61*, 1933–1953. (b) Kaczorowska, K.; Kolarska, Z.; Mitka, K.; Kowalski, P. *Tetrahedron* **2005**, *61*, 8315–8327.

(39) (a) Imada, Y.; Kitagawa, T.; Wang, H.-K.; Komiya, N.; Naota, T. *Tetrahedron Lett.* **2013**, *54*, 621–624. (b) Murahashi, S.-I.; Zhang, D.; Iida, H.; Miyawaki, T.; Uenaka, M.; Murano, K.; Meguro, K. *Chem. Commun.* **2014**, *50*, 10295–10298.

(40) Kar, S.; Sanderson, H.; Roy, K.; Benfenati, E.; Leszczynski, J. *Chem. Rev.* **2021**, *122*, 3637–3710.

(41) Horie, K.; Barón, M.; Fox, R.; He, J.; Hess, M.; Kahovec, J., etal; Kitayama, T.; Kubisa, P.; Maréchal, E.; Mormann, W. *Pure Appl. Chem.* **2004**, *76*, 889–906.

(42) (a) Colacino, E.; Delogu, F.; Hanusa, T. *ACS Sustainable Chem. Eng.* **2021**, *9*, 10662–10663; (b) Bento, O.; Luttringer, F.; Mohy El Dine, T.; Pétry, N.; Bantreil, X.; Lamaty, F. *Eur. J. Org. Chem.* **2022**, e202101516.

(43) Tan, D.; Loots, L.; Friščić, T. *Chem. Commun.* **2016**, *52*, 7760–7781.

(44) (a) Ramesh, R.; Sonawane, S.; Reddy, D. S.; Bandichhor, R. *Protecting-Group-Free Organic Synthesis: Improving Economy and Efficiency*, John Wiley & Sons, Hoboken, New Jersey, **2018**. (b) Ying, P.; Yu, J.; Su, W. *Adv. Synth. Catal.* **2021**, *363*, 1246–1271.

(45) (a) Virieux, D.; Delogu, F.; Porcheddu, A.; García, F.; Colacino, E. *J. Org. Chem.* **2021**, *86*, 13885–13894. (b) Cortés-Lobo, A.; Hernández, J. G. *ChemPlusChem* **2024**, e202400257. (c) Egorov, I. N.; Santra, S.; Kopchuk, D. S.; Kovalev, I. S.; Zyryanov, G. V.; Majee, A.; Ranu, B. C.; Rusinov, V. L.; Chupakhin, O. N. *Green Chem.* **2020**, *22*, 302–315. (d) Zholdassov, Y. S.; Kwok, R. W.; Shlain, M. A.; Patel, M.; Marianski, M.; Braunschweig, A. B. *RSC Mechanochem.* **2024**, *1*, 11–32.

(46) van Bonn, P.; Bolm, C.; Hernández, J. G. *Chem. Eur. J.* **2020**, *26*, 2576-2580.

(47) (a) Kong, D.; Ma, D.; Wu, P.; Bolm, C. *ACS Sustain. Chem. Eng.* **2022**, *10*, 2863–2867. (b) Schumacher, C.; Fergen, H.; Puttreddy, R.; Truong, K.-N.; Rinesch, T.; Rissanen, K.; Bolm, C. *Org. Chem. Front.* **2020**, *7*, 3896–3906.

(48) (a) Schöbel, J.-H.; Elbers, P.; Truong, K.-N.; Rissanen, K.; Bolm, C. *Adv. Synth. Catal.* **2021**, *363*, 1322–1329. (b) Terhorst, S.; Jansen, T.; Langletz, T.; Bolm, C. *Org. Lett.* **2022**, *24*, 4109–4113. (c) Pan, S.; Mulks, F. F.; Wu, P.; Rissanen, K.; Bolm, C. *Angew. Chem.* **2024**, *63*, e202316702; *Angew. Chem.* **2024**, *136*, e202316702.

(49) Tsuchiya, S.; Seno, M. *J. Chem. Soc., Chem. Commun.* **1983**, 413–414.

(50) (a) Mann, F. G.; Pope, W. J. *J. Chem. Soc., Trans.* **1922**, *121*, 1052–1055.

(51) (a) Desikan, V.; Liu, Y.; Toscano, J. P.; Jenks, W. S. *J. Org. Chem.* **2007**, *72*, 6848–6859. (b) Tian, X.; Song, L.; Hashmi, A. S. K. *Chem. Eur. J.* **2020**, *26*, 3197–3204. (c) Antoni, P. W.; Mackenroth, A. V.; Mulks, F. F.; Rudolph, M.; Helmchen, G.; Hashmi, A. S. K. *Chem. Eur. J.* **2020**, *26*, 8235–8238. (d) Heilmann, T.; Lopez-Soria, J. M.; Ulbrich, J.; Kircher, J.; Li, Z.; Worbs, B.; Golz, C.; Mata, R. A.; Alcarazo, M. *Angew. Chem. Int. Ed.* **2024**, *63*, e202403826; *Angew. Chem.* **2024***, 136,* e202403826.

(52) (a) Johnson, C. R.; Mori, K.; Nakanishi, A. *J. Org. Chem.* **1979**, *44*, 2065–2067. (b) Fujita, T.; Maeda, T.; Ju Kim, B.; Tatami, A.; Miyamoto, D.; Kawaguchi, H.; Tsuchiya, N.; Yoshida, M.; Kawashima, W.; Morita, H. *J. Sulphur Chem.* **2008**, *29*, 459–465.

(53) (a) Takada, H.; Oda, M.; Oyamada, A.; Ohe, K.; Uemura, S. *Chirality* **2000**, *12*, 299–312. (b) Thakur, V. V.; Ramesh Kumar, N. S. C.; Sudalai, A. *Tetrahedron Lett.* **2004**, *45*, 2915–2918. (c) Huang, Z.; Sam, Q. P.; Dong, G. *Chem. Sci.* **2015**, *6*, 5491–5498.

(54) (a) Padwa, A.; Nara, S.; Wang, Q. *Tetrahedron Lett.* **2006**, *47*, 595–597. (b) Raghavan, S.; Kumar, C. N. A *Tetrahedron Lett.* **2006**, *47*, 1585–1588. (c) Silveira, G. P.; Marino, J. P. *J. Org. Chem.* **2013**, *78*, 3379–3383.

(55) (a) Lin, S.; Yang, X.; Jia, S.; Weeks, A. M.; Hornsby, M.; Lee, P. S.; Nichiporuk, R. V.; Iavarone, A. T.; Wells, J. A.; Toste, F. D. *Science* **2017**, *355*, 597–602. (b) Meng, T.; Wells, L. A.; Wang, T.; Wang, J.; Zhang, S.; Wang, J.; Kozlowski, M. C.; Jia, T. *J. Am. Chem. Soc.* **2022**, *144*, 12476–12487.

(56) (a) Chen, X. Y.; Buschmann, H.; Bolm, C. *Synlett* **2012**, *23*, 2808–2810. (b) Karpel-Massler, G.; Kast, R. E.; Siegelin, M. D.; Dwucet, A.; Schneider, E.; Westhoff, M.-A.; Wirtz, C. R.; Chen, X. Y.; Halatsch, M.-E.; Bolm, C. *Neurochem. Res.* **2017**, *42*, 3382–3389. (c) Steinkamp, A.-D.; Seling, N.; Lee, S.; Boedtkjer, E.; Bolm, C. *MedChemComm* **2015**, *6*, 2163–2169. (d) Yu, X.; Zhang, Y.; Liu, Y.; Li, Y.; Wang, Q. *J. Agric. Food Chem.* **2019**, *67*, 4224–4231.

(57) Vanacore, R.; Ham, A.-J. L.; Voehler, M.; Sanders, C. R.; Conrads, T. P.; Veenstra, T. D.; Sharpless, K. B.; Dawson, P. E.; Hudson, B. G. *Science* **2009**, *325*, 1230–1234.

(58) (a) Marzinzik, A. L.; Sharpless, K. B. *J. Org. Chem.* **2001**, *66*, 594–596. (b) García Mancheño, O.; Bistri, O.; Bolm, C. *Org. Lett.* **2007**, *9*, 3809–3811. (c) Farwell, C. C.; McIntosh, J. A.; Hyster, T. K.; Wang, Z. J.; Arnold, F. H. *J. Am. Chem. Soc.* **2014**, *136*, 8766–8771. (d) Han, M.; Tang, Z.; Li, G.-x.; Wang, Q. *Tetrahedron Lett.* **2022**, *102*, 153925.

(59) (a) Bach, T.; Korber, C. *Tetrahedron Lett.* **1998**, *39*, 5015–5016. (b) Bach, T.; Körber, C. *Eur. J. Org. Chem.* **1999**, 1033–1039. (c) Gracia Mancheño, O.; Bolm, C. *Org. Lett.* **2006**, *8*, 2349–2352. (d) Wang, J.; Frings, M.; Bolm, C. *Angew. Chem. Int. Ed.* **2013**, *52*, 8661–8665; *Angew. Chem.* **2013**, *125*, 8823–8827. (e) Lai, C.; Mathieu, G.; Tabarez, L. P. G.; Lebel, H. *Chem. Eur. J.* **2019**, *25*, 9423–9426. (f) Lebel, H.; Piras, H.; Borduy, M. *ACS Catal.* **2016**, *6*, 1109–1112.

(60) Bauer, E. B. in *Iron Catalysis II*, Springer International Publishing, Basel, **2015**; pp. 1–18.

(61) (a) Fiori, K. W.; Du Bois, J. *J. Am. Chem. Soc.* **2007**, *129*, 562–568. (b) Guthikonda, K.; Du Bois, J. *J. Am. Chem. Soc.* **2002**, *124*, 13672–13673.

(62) Bauer, V. J.; Fanshawe, W. J.; Safir, S. *J. Org. Chem.* **1966**, *31*, 3440–3441.

(63) Liu, Y.; Che, C. M. *Chem. Eur. J.* **2010**, *16*, 10494–10501.

(64) Bizet, V.; Hendriks, C. M. M.; Bolm, C. *Chem. Soc. Rev.* **2015**, *44*, 3378–3390.

(65) Wang, Y. C.; Lai, X.-J.; Huang, K.; Yadav, S.; Qiu, G.; Zhang, L.; Zhou, H. *Org. Chem. Front.* **2021**, *8*, 1677–1693.

(66) Luisi, R.; Bull, J. A. *Molecules* **2023**, *28*, 1120.

(67) Schäfer, S.; Wirth, T. *Angew. Chem. Int. Ed.* **2010**, *15*, 2786–2789; *Angew. Chem.* **2010**, *122*, 2846–2850.

(68) Gracia Mancheño, O.; Dallimore, J.; Plant, A.; Bolm, C. *Org. Lett.* **2009**, *11*, 2429–2432.

(69) Wang, J.; Frings, M.; Bolm, C. *Chem. Eur. J.* **2014**, *20*, 966–969.

(70) (a) van Leest, N. P.; van der Vlugt, J. I.; de Bruin, B. *Chem. Eur. J.* **2021**, *27*, 371–378. (b) Hendriks, C. M.; Lamers, P.; Engel, J.; Bolm, C. *Adv. Synth. Catal.* **2013**, *355*, 3363–3368. (c) Zhang, Z. X.; Davies, T. Q.; Willis, M. C. *J. Am. Chem. Soc.* **2019**, *141*, 13022–13027. (d) Andresini, M.; Tota, A.; Degennaro, L.; Bull, J. A.; Luisi, R. *Chem. Eur. J.* **2021**, *27*, 17293–17321. (e) Chen, Y.; Fang, D. M.; Huang, H. S.; Nie, X. K.; Zhang, S. Q.; Cui, X.; Tang, Z.; Li, G. X. *Org Lett* **2023**, *25*, 2134–2138.

(71) (a) Zheng, W.; Chen, X.; Chen, F.; He, Z.; Zeng, Q. *Chem. Rec.* **2021**, *21*, 396–416. (b) Shultz, Z. P.; Lopchuk, J. M. in *Advances in Heterocyclic Chemistry*, Vol. 138; Elsevier, Amsterdam, **2022**; pp. 61–158. (c) Lücking, U. *Angew. Chem. Int. Ed.* **2013**, *52*, 9399–9408; *Angew. Chem.* **2013**, *125*, 9570–9580. (d) Frings, M.; Bolm, C.; Blum, A.; Gnamm, C. *Eur. J. Med. Chem.* **2017**, *126*, 225–245. (e) Han, Y.; Xing, K.; Zhang, J.; Tong, T.; Shi, Y.; Cao, H.; Yu, H.; Zhang, Y.; Liu, D.; Zhao, L. *Eur. J. Med. Chem.* **2021**, *209*, 112885. (f) Lücking, U. *Chem. Eur. J.* **2022**, *28*, e202201993 (g) Tilby, M. J.; Willis, M. C. *Expert Opin. Drug Discov.* **2021**, *16*, 1227–1231. (h) Bacci, L.; Convertini, S.; Rossaro, B. *J. Entomol. Acarol. Res*. **2018**, *50*, 7836. (72) Lebel, H.; Piras, H. *J. Org. Chem.* **2015**, *80*, 3572–3585.

(73) Periasamy, K.; Gordeeva, S.; Bolm, C. *J. Org. Chem.* **2024**, DOI: 10.1021/acs.joc.4c01250.

(74) Zhao, C.; Rakesh, K. P.; Ravidar, L.; Fang, W.-Y.; Qin, H.-L. *Eur. J. Med. Chem.* **2019**, *162*, 679–734.

(75) (a) Frings, M.; Atodiresei, I.; Wang, Y.; Runsink, J.; Raabe, G.; Bolm, C. *Chem. Eur. J.* **2010**, *16*, 4577–4587. (b) Frings, M.; Goedert, D.; Bolm, C. *Chem. Commun.* **2010**, *46*, 5497–5499.

(76) Benetskiy, E. B.; Bolm, C. *Tetrahedron: Asymmetry* **2011**, *22*, 373–378.

(77) Goldberg, F. W.; Kettle, J. G.; Kogej, T.; Perry, M. W. D.; Tomkinson, N. P. *Drug Discov. Today* **2015**, *20*, 11–17.

(78) (a) Lovering, F.; Bikker, J.; Humblet, C. *J. Med. Chem.* **2009**, *52*, 6752–6756. (b) Walters, W. P.; Green, J.; Weiss, J. R.; Murcko, M. A. *J. Med. Chem.* **2011**, *54*, 6405–6416. (c) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451–3479.

(79) Varga, M.; Kapui, Z.; Bátori, S.; Nagy, L. T.; Vasvári-Debreczy, L.; Mikus, E.; Urbán-Szabó, K.; Arányi, P. *Eur. J. Med. Chem.* **2003**, *38*, 421–425.

(80) Sparks, T. C.; Watson, G. B.; Loso, M. R.; Geng, C.; Babcock, J. M.; Thomas, J. D. *Pestic. Biochem. Physiol.* **2013**, *107*, 1–7.

(81) Barthelemy, A. L.; Prieto, A.; Diter, P.; Hannedouche, J.; Toffano, M.; Anselmi, E.; Magnier, E. *Eur. J. Org. Chem.* **2018**, 3764–3770.

(82) Ghosh, K.; Nishii, Y.; Miura, M. *ACS Catal.* **2019**, *9*, 11455–11460.

(83) Kondalarao, K.; Sau, S.; Sahoo, A. K. *Molecules* **2023**, *28*, 5014.

(84) Williams, T. R.; Cram, D. J. *J. Am. Chem. Soc.* **1971**, *93*, 7333–7335.

(85) (a) Stoss, P.; Satzinger, G. *Chem. Ber.* **1972**, *105*, 2575–2583. (b) Williams, T. R.; Cram, D. J. *J. Org. Chem.* **1973**, *38*, 20–26. (c) Lombardino, J. G.; Kuhla, D. E. in *Adv. Heterocycl. Chem.* (Eds.: Katritzky, A. R., Boulton, A. J.); Vol. 28; Academic Press, New York, **1981**; pp. 73–126.

(86) Harmata, M.; Rayanil, K.O.; Gomes, M. G.; Zheng, P.; Calkins, N. L.; Kim, S.-Y.; Fan, Y.; Bumbu, V.; Lee, D. R.; Wacharasindhu, S.; Hong, X. *Org. Lett.* **2005**, *7*, 143–145.

(87) Dong, W.; Wang, L.; Parthasarathy, K.; Pan, F.; Bolm, C. *Angew. Chem. Int. Ed.* **2013**, *52*, 11573–11576; *Angew. Chem.* **2013**, *125*, 11787–11790.

(88) (a) Yu, D.-G.; de Azambuja, F.; Glorius, F. *Angew. Chem. Int. Ed.* **2014**, *53*, 2754–2758; *Angew. Chem.* **2014**, *126*, 2792–2796. (b) Cheng, Y.; Bolm, C. *Angew. Chem. Int. Ed.* **2015**, *54*, 12349–12352; *Angew. Chem.* **2015**, *127*, 12526–12529. (c) Jeon, W. H.; Son, J.-Y.; Kim, J. E.; Lee, P. H. *Org. Lett.* **2016**, *18*, 3498–3501. (d) Wen, J.; Tiwari, D. P.; Bolm, C. *Org. Lett.* **2017**, *19*, 1706–1709. (e) Aher, Y. N.; Lade, D. M.; Pawar, A. B. *Chem. Commun.* **2018**, *54*, 6288–6291. (f) Zheng, G.; Tian, M.; Xu, Y.; Chen, X.; Li, X. *Org. Chem. Front.* **2018**, *5*, 998–1002. (g) Hanchate, V.; Muniraj, N.; Prabhu, K. R. *J. Org. Chem.* **2019**, *84*, 8248–8255. (h) Liu, Y.-z.; Hu, Y.; Lv, G.-h.; Nie, R.-f.; Peng, Y.; Zhang, C.; Lv, S.-y.; Hai, L.; Wang, H.-j.; Wu, Y. *ACS Sustainable Chem. Eng.* **2019**, *7*, 13425–13429. (i) Han, G. U.; Kim, S.; Han, S. H.; Maeng, C.; Ko, G. H.; Lee, K.; Noh, H. C.; Lee, P. H. *J. Org. Chem.* **2023**, *88*, 11702–11711.

(89) (a) Shen, B.; Wan, B.; Li, X. *Angew. Chem. Int. Ed.* **2018**, *57*, 15534–15538; *Angew. Chem.* **2018**, *130*, 15760–15764. (b) Sun, Y.; Cramer, N. *Angew. Chem. Int. Ed.* **2018**, *57*, 15539–15543; *Angew. Chem.* **2018**, *130*, 15765–15769.

(90) (a) Ko, G. H.; Son, J.-Y.; Kim, H.; Maeng, C.; Baek, Y.; Seo, B.; Um, K.; Lee, P. H. *Adv. Synth. Catal.* **2017**, *359*, 3362–3370. (b) Li, Y.; Liu, X.-Y.; Xu, Y.-J.; Dong, L. *Org. Chem. Front.* **2019**, *6*, 2457–2461. (c) Li, S.; Liu, L.; Wang, R.; Yang, Y.; Li, J.; Wei, J. *Org. Lett.* **2020**, *22*, 7470–7474. (d) Wang, B.; Han, X.; Li, J.; Li, C.; Liu, H. *Molecules* **2020**, *25*, 2515. (e) Huang, G.; Shan, Y.; Yu, J.-T.; Pan, C *Org. Biomol. Chem.* **2021**, *19*, 10085–10089. (f) Li, J.;

Li, H.; Fang, D.; Liu, L.; Han, X.; Sun, J.; Li, C.; Zhou, Y.; Ye, D.; Liu, H. *J. Org. Chem.* **2021**, *86*, 15217–15227.

(91) Dillard, R. D.; Yen, T. T.; Stark, P.; Pavey, D. E. *J. Med. Chem.* **1980**, *23*, 717–722.

(92) Wagner, A. W.; Reinöhl, G. *Liebigs Ann.* **1964**, *675*, 189–199.

(93) (a) Cohnen, E.; Mahnke, J. *Chem. Ber.* **1972**, *105*, 757–769. (b) Stoss, P.; Satzinger, G. (Goedecke AG), DE2530792, **1975**. (c) Sowinski, F. A.; Vogt, B. R.; E. R. (Squibb and Sons, Inc.), DE2455232, **1975**. (d) Stoss, P.; Satzinger, G; *Chem. Ber.*, **1976**, 109, 2097. (e) Dillard, R. D.; Yen, T. T.; Stark, P.; Pavey, D. E. *J. Med. Chem.* **1980**, *23*, 717–722. (f) Barth, H.; Hartenstein, J.; Satzinger, G.; Fritschi, E.; Osswald, H.; Bartoszyk, G. (Goedecke AG), DE3433037, **1986**. (g) Ager, I. R.; Barnes, A. C.; Danswan, G. W.; Hairsine, P. W.; Kay, D. P.; Kennewell, P. D.; Matharu, S. S.; Miller, P.; Robson, P. *J. Med. Chem.* **1988**, *31*, 1098–1115. (h) Oh, I. S.; Seo, Y. J.; Hyun, J. Y.; Lim, H. J.; Lee, D.-H.; Park, S. J. *ACS Omega* **2022**, *7*, 2160–2169. (i) Hommelsheim, R.; Bausch, S.; Selvakumar, A.; Amer, M. M.; Truong, K.-N.; Rissanen, K.; Bolm, C. C*hem. Eur. J.* **2023***, 29,* e202203729. (j) Hommelsheim, R.; Bausch, S.; Van Nahl, R.; Ward, J. S.; Rissanen, K.; Bolm, C. *Green Chem.,* **2023***, 25,* 3021–3026. (94) Ma, Y.-N.; Guo, C.-Y.; Zhao, Q.; Zhang, J.; Chen, X. *Green Chem.* **2018**, *20*, 2953–2958.

(95) (a) Huang, J.; Huang, Y.; Wang, T.; Huang, Q.; Wang, Z.; Chen, Z. *Org. Lett.* **2017**, *19*, 1128–1131. (b) Li, Y.; Liu, C.-F.; Liu, X.-Y.; Xu, Y.-J.; Dong, L. *Org. Chem. Front.* **2019**, *6*, 1458–1462. (c) Shi, P.; Tu, Y.; Wang, C.; Kong, D.; Ma, D.; Bolm, C. *Org. Lett.* **2020**, *22*, 8842–8845. (d) Xu, H.-B.; Yang, J.-H.; Chai, X.-Y.; Zhu, Y.-Y.; Dong, L. *Org. Lett.* **2020**, *22*, 2060–2063.

(96) (a) Cheng, Y.; Dong, W.; Wang, H.; Bolm, C. *Chem. Eur. J.* **2016**, *22*, 10821–10824. (b) Le, T.-N.; Diter, P.; Pégot, B.; Bournaud, C.; Toffano, M.; Guillot, R.; Vo-Thanh, G.; Magnier, E. *Org. Lett.* **2016**, *18*, 5102–5105.

(97) (a) Hirata, Y.; Sekine, D.; Kato, Y.; Lin, L.; Kojima, M.; Yoshino, T.; Matsunaga, S. Cobalt(III)/Chiral Carboxylic Acid-Catalyzed Enantioselective Synthesis of Benzothiadiazine-1-oxides via C−H Activation. *Angew. Chem. Int. Ed.* **2022**, *61*, e202205341; *Angew. Chem.* **2022**, *134*, e202205341. (b) Zhou, Y.-B.; Zhou, T.; Qian, P.-F.; Li, J.-Y.; Shi, B.-F. *ACS Catal.* **2022**, *12*, 9806–9811.

(98) Wu, C.; Huang, R.; Zhang, M.; Chen, Z. *J. Org. Chem.* **2020**, *85*, 841–850.

(99) (a) Lima, L. M.; Barreiro, E. J. *Curr. Med. Chem.* **2005**, *12*, 23–49. (b) Kumari, S.; Carmona, A. V.; Tiwari, A. K.; Trippier, P. C. *J. Med. Chem.* **2020**, *63*, 12290–12358.

(100) (a) Hwang, K. J.; Logusch, E. W.; Brannigan, L. H.; Thompson, M. R. *J. Org. Chem.* **1987**, *52*, 3435–3441. (b) Zhiming Zhao, Z.; Wu, S.; Liu, Y.; Hua, M.; Hao, S. WO 2022/078309 A1, **2023**.

(101) Bolm, C.; Mueller, P.; Harms, K. *Acta Chem. Scand.* **1996**, *50*, 305–315.

(102) van Bonn, P.; Soerensen, S.; Schmitz, N.; Bolm, C. *Adv. Synth. Catal.* **2024**, *366*, 725–732.

(103) (a) Irie, M.; Mohri, M. *J. Org. Chem.* **1988**, *53*, 803–808. (b) Hanazawa, M.; Sumiya, R.; Horikawa, Y.; Irie, M. *J. Chem. Soc., Chem. Commun.* **1992**, 206–207. (c) Heiligman-Rim, R.; Hirshberg, Y.; Fischer, E. *J. Chem. Soc.* **1961**, 156–163.

(104) Fritzsche, J. *J. prakt. Chem.* **1867**, *101*, 333–343.

(105) Heiligman-Rim, R.; Hirshberg, Y.; Fischer, E. *J. Phys. Chem* **1962**, *66*, 2470–2477.

(106) Dürr, H.; Bouas-Laurent, H. *Photochromism: Molecules and Systems*. Elsevier, Amsterdam, **2003**.

(107) (a) Tian, H.; Zhang, J. *Photochromic materials: preparation, properties and applications*; John Wiley & Sons, Hoboken, New Jersey, **2016**. (b) El'tsov, A. V. *Organic Photochromes*. Springer, New York, **2012**.

(108) (a) Kawata, S.; Kawata, Y. *Chem. Rev.* **2000**, *100*, 1777–1788. (b) Nakatani, K.; Piard, J.; Yu, P.; Métivier, R. in *Photochromic Materials: Preparation, Properties and Applications* (Eds.: Tian, H.; Zhang, J.). John Wiley & Sons, Hoboken, New Jersey, **2016**, pp. 1–45.

(109) Hartley, G. S. *Nature* **1937**, *140*, 281–281.

(110) Hirshberg, Y.; Fischer, E. *J. Chem. Soc.* **1954**, 3129–3137.

(111) (a) Bandara, H. D.; Burdette, S. C. *Chem. Soc. Rev.* **2012**, *41*, 1809–1825. (b) Rad, J. K.; Balzade, Z.; Mahdavian, A. *J. Photochem. Photobiol. C: Photochem. Rev.* **2022**, *51*, 100487.

(112) Heller, H. G.; Oliver, S. *J. Chem. Soc., Perkin Trans.* **1981**, 197–201.

(113) Irie, M. *Chem. Rev.* **2000**, *100*, 1685–1716.

(114) Kobatake, S. in *Progress in the Science of Functional Dyes* (Eds.: Ooyama, Y.; Yagi, S.). Springer, Singapure, **2021**, pp. 263–281.

(115) (a) Irie, M.; Fukaminato, T.; Matsuda, K.; Kobatake, S. *Chem. Rev.* **2014**, *114*, 12174–12277. (b) Kochman, M. A.; Gryber, T.; Durbeej, B.; Kubas, A. *Phys. Chem. Chem. Phys.* **2022**, *24*, 18103–18118.

(116) Irie, M. *Proc. Jpn. Acad. B* **2010**, *86*, 472–483.

(117) Jago, D.; Gaschk, E. E.; Koutsantonis, G. A. *Aust. J. Chem.* **2023**, *76*, 635–654.

(118) Matsuda, K.; Irie, M. *J. Photochem. Photobiol. C: Photochem. Rev.* **2004**, *5*, 169–182.

(119) Pu, S. Z.; Sun, Q.; Fan, C. B.; Wang, R. J.; Liu, G. *J. Mater. Chem. C* **2016**, *4*, 3075–3093.

(120) Irie, M.; Uchida, K. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 985–996.

(121) Shirinian, V. Z.; Lonshakov, D.; Lvov, A.; Krayushkin, M. M. *Russ. Chem. Rev.* **2013**, *82*, 511.

(122) Kobatake, S.; Irie, M. *Annu. Rep. Prog. Chem., Sect. C* **2003**, *99*, 277–313.

(123) Irie, M. *Pure Appl. Chem.* **2015**, *87*, 617–626.

(124) Irie, M.; Sakemura, K.; Okinaka, M.; Uchida, K. *J. Org. Chem.* **1995**, *60*, 8305–8309.

(125) Hatano, E.; Morimoto, M.; Hyodo, K.; Yasuda, N.; Yokojima, S.; Nakamura, S.; Uchida, K. *Chem. Eur. J.* **2016**, *22*, 12680–12683.

(126) Maurel, F.; Perrier, A.; Perpète, E. A.; Jacquemin, D. *J. Photochem. Photobiol. A: Chem.* **2008**, *199*, 211–223.

(127) Kobatake, S.; Imao, S.; Yamashiro, Y.; Terakawa, Y. *Tetrahedron Lett.* **2011**, *52*, 1905–1908.

(128) Raymo, F. M.; Tomasulo, M. *Chem. Soc. Rev.* **2005**, *34*, 327–336.

(129) (a) Zhao, H.; Al-Atar, U.; Pace, T. C.; Bohne, C.; Branda, N. R. *J. Photochem. Photobiol. A: Chem.* **2008**, *200*, 74–82. (b) Belser, P.; De Cola, L.; Hartl, F.; Adamo, V.; Bozic, B.; Chriqui, Y.; Iyer, V. M.; Jukes, R. T.; Kühni, J.; Querol, M. *Adv. Funct. Mater.* **2006**, *16*, 195–208. (c) Gust, D.; Moore, T. A.; Moore, A. L. *Chem. Commun.* **2006**, 1169–1178. (d) Tian, H.; Feng, Y. *J. Mater. Chem.* **2008**, *18*, 1617–1622.

(130) (a) Irie, M.; Ishida, H.; Tsujioka, T. *Jpn. J. Appl. Phys.* **1999**, *38*, 6114. (b) Tsujioka, T.; Irie, M. *Jpn. J. Appl. Phys.* **1999**, *38*, 4100.

(131) (a) Tsivgoulis, G. M.; Lehn, J. M. *Angew. Chem. Int. Ed.* **1995**, *34*, 1119–1122. (b) Tsivgoulis, G. M.; Lehn, J. M. *Chem. Eur. J.* **1996**, *2*, 1399–1406.

(132) Yagi, K.; Soong, C. F.; Irie, M. *J. Org. Chem.* **2001**, *66*, 5419–5423.

(133) Takeshita, M.; Irie, M. *Chem. Lett.* **1998**, *27*, 1123–1124.

(134) Li, Z.; Zeng, X.; Gao, C.; Song, J.; He, F.; He, T.; Guo, H.; Yin, J. *Coord. Chem. Rev.* **2023**, *497*, 215451.

(135) Hu, H.; Zhu, M.; Meng, X.; Zhang, Z.; Wei, K.; Guo, Q. *J. Photochem. Photobiol. A: Chem.* **2007**, *189*, 307–313.

(136) Chen, Y.; Zeng, D. X. *ChemPhysChem* **2004**, *5*, 564–566.

(137) Zou, Y.; Yi, T.; Xiao, S.; Li, F.; Li, C.; Gao, X.; Wu, J.; Yu, M.; Huang, C. *J. Am. Chem. Soc.* **2008**, *130*, 15750–15751.

(138) Soh, N.; Yoshida, K.; Nakajima, H.; Nakano, K.; Imato, T.; Fukaminato, T.; Irie, M. *Chem. Commun.* **2007**, 5206–5208.

(139) (a) Uchida, K.; Saito, M.; Murakami, A.; Nakamura, S.; Irie, M. *Adv. Mater.* **2003**, *15*, 121–125. (b) Takata, A.; Yokojima, S.; Nakagawa, H.; Matsuzawa, Y.; Murakami, A.; Nakamura, S.; Irie, M.; Uchida, K. *J. Phys. Org. Chem.* **2007**, *20*, 998–1006.

(140) Browne, W. R.; Feringa, B. L in *Molecular Switches.* Wiley-VCH, Weinheim, **2011**, pp. 121–179.

(141) (a) Kaneuchi, Y.; Kawai, T. K. T.; Hamaguchi, M. H. M.; Yoshino, K. Y. K.; Irie, M. I. M. *Jpn. J. Appl. Phys.* **1997**, *36*, 3736. (b) Kawai, T.; Koshido, T.; Yoshino, K *Appl. Phys. Lett.* **1995**, *67*, 795–797.

(142) Kawai, T.; Fukuda, N.; Gröschl, D.; Kobatake, S.; Irie, M. *Jpn. J. Appl. Phys.* **1999**, *38*, L1194.

(143) (a) Bertarelli, C.; Gallazzi, M. C.; Stellacci, F.; Zerbi, G.; Stagira, S.; Nisoli, M.; De Silvestri, S. *Chem. Phys. Lett.* **2002**, *359*, 278–282. (b) Lee, J.; Kwon, T.; Kim, E. *Tetrahedron Lett.* **2007**, *48*, 249–254. (c) Kawai, T.; Nakashima, Y.; Kunitake, T.; Irie, M. *Curr. Appl. Phys.* **2005**, *5*, 139–142.

(144) (a) Hayasaka, H.; Tamura, K.; Akagi, K. *Macromol.* **2008**, *41*, 2341–2346. (b) Kobatake, S.; Yamashita, I. *Tetrahedron* **2008**, *64*, 7611–7618.

(145) (a) Fukaminato, T.; Umemoto, T.; Iwata, Y.; Yokojima, S.; Yoneyama, M.; Nakamura, S.; Irie, M. *J. Am. Chem. Soc.* **2007**, *129*, 5932–5938. (b) Murase, S.; Teramoto, M.; Furukawa, H.; Miyashita, Y.; Horie, K. *Macromol.* **2003**, *36*, 964–966. (c) Medvedeva, D.; Bobrovsky, A.; Boiko, N.; Shibaev, V.; Shirinyan, V.; Krayushkin, M. *Macromol. Chem. Phys.* **2006**, *207*, 770–778.

(146) (a) Kitagawa, D.; Yamashita, I.; Kobatake, S. *Chem. Commun.* **2010**, *46*, 3723–3725. (b) Bagley, M. C.; Dale, J. W.; Merritt, E. A.; Xiong, X. *Chem. Rev.* **2005**, *105*, 685–714. (c) Uchida, K.; Saito, M.; Murakami, A.; Kobayashi, T.; Nakamura, S.; Irie, M. *Chem. Eur. J.* **2005**, *11*, 534–542.

(147) Jiang, G.; Wang, S.; Yuan, W.; Jiang, L.; Song, Y.; Tian, H.; Zhu, D. *Chem. Mater.* **2006**, *18*, 235–237.

(148) Fujimoto, Y.; Ubukata, T.; Yokoyama, Y. *Chem. Commun.* **2008**, 5755–5757.

(149) Verbelen, B.; Siemes, E.; Ehnbom, A.; Räuber, C.; Rissanen, K.; Wöll, D.; Bolm, C. *Org. Lett.* **2019**, *21*, 4293–4297.

(150) (a) Tian, H.; Yang, S. *Chem. Soc. Rev.* **2004**, *33*, 85–97. (b) Lvov, A. G.; Klimenko, L. S.; Bykov, V. N.; Hecht, S. *Chem. Eur. J.* **2024**, *30*, e202303654.

(151) Jeong, Y. C.; Yang, S. I.; Ahn, K. H.; Kim, E. *Chem. Commun.* **2005**, 2503–2505.

(152) Schleper, A. L.; Bossi, M. L.; Belov, V. N.; Hell, S. W. *Beilstein J. Org. Chem.* **2019**, *15*, 2344–2354.

(153) Okamura, H.; Bolm, C. *Org. Lett.* **2004**, *6*, 1305–1307.

(154) Irie, M.; Miyatake, O.; Uchida, K.; Eriguchi, T. *J. Am. Chem. Soc.* **1994**, *116*, 9894–9900.

(155) Irie, M.; Miyatake, O.; Uchida, K. *J. Am. Chem. Soc.* **1992**, *114*, 8715–8716.

(156) Barrez, E.; Laurent, G.; Pavageau, C.; Sliwa, M.; Métivier, R. *Phys. Chem. Chem. Phys.* **2018**, *20*, 2470–2479.

(157) Morgan, K. F.; Hollingsworth, I. A.; Bull, J. A. *Org. Biomol. Chem.* **2015**, *13*, 5265–5272.

(158) Sreedhar, B.; Reddy, P. S.; Reddy, M. A. *Synthesis* **2009**, *2009*, 1732–1738.

(159) Niimi, K.; Kang, M. J.; Miyazaki, E.; Osaka, I.; Takimiya, K. *Org. Lett.* **2011**, *13*, 3430–3433.

(160) Pérez-Encabo, A.; Perrio, S.; Slawin, A. M. Z.; Thomas, S. E.; Wierzchleyski, A. T.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 629–642.

(161) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803–2806.

(162) Song, S.-Y.; Zhou, X.; Ke, Z.; Xu, S. *Angew. Chem. Int. Ed.* **2023**, *62*, e202217130; *Angew. Chem.* **2023**, *135*, e202217130.

(163) Fredrich, S.; Bonasera, A.; Valderrey, V.; Hecht, S. *J. Am. Chem. Soc.* **2018**, *140*, 6432–6440.

(164) Vazquez, A. J.; Nudelman, N. S. *J. Phys. Org. Chem.* **2012**, *25*, 925–932.

8 Acknowledgement

This past four years of my doctoral studies has been filled with many wonderful memories, each of which holds a special place in my heart. I would like to take this opportunity to thank everyone who made my time in Aachen memorable. I am deeply grateful to Prof. Dr. Carsten Bolm for providing me with the opportunity to join his research group, where I benefited from stimulating research topics and excellent working conditions. His support throughout this journey have been invaluable.

I also wish to express my sincere thanks to my second examiner, Prof. Dr. Markus Albrecht.

I am very thankful to Dr. Ingo Schiffers for his assistance and suggestions with administrative tasks, which have saved a considerable amount of time. I also want to extend my gratitude to Daniela Heeren, Ina Groß, Lea Flecken, and Stefanie Zimmer for their support and help in meeting our needs. Additionally, I acknowledge Dr. Christoph Räuber for his help with NMR analyses. I appreciate the contributions of the departments responsible for mass and IR analytics, as well as the chem-store and Werkstatt teams. Thank you, Susi Pohlmann and Pierre Winandy, for making our work easier by assisting with experimental tasks and orders.

Additionally, I am also thankful to all the researchers and bachelor student I had the privilege of supervising over the years in Lab 5.06. In particular, I want to thank Runa Tschekorsky Orloff, Nils Völcker, Qiulan Lu, and Sofya Gordeeva for your assistance; you all definitely brought me closer to completing my journey. A special thanks goes to Arndt Collong, Shulei Pan, Marco Passia, and Pit van Bonn for proofreading my thesis.

I wish to thank my coworkers in the group, Dr. Francesco Puccetti, Dr. Christian Schumacher, Dr. Marc Calin, Dr. Britta Kübbers, Dr. Deshen Kong, Dr. Hannah Fergen, Dr. Ding Ma, Dr. Peng Shi, Dr. Chenyang Wang, Dr. Matthew Williams, Dr. Laura Adarve Cardona, Dr. Mostafa Amer, Dr. Sourav Biswas, Dr. Joachim Demaerel, Dr. Marina Cardoso Dilelio, Dr. Diego Gamba Sanchez, Dr. Martina Gerace, Dr. Xianliang Wang, Dr. Florian Mulks, Dr. Victoria S. Pfennig (I'll always remember all those conversations we had when we ran into each other), Marcus Frings, Sandra Bausch, Renè Hommelsheim, Marco Passia, Peng Wu, Shulei Pan, Lena

Hanek, Yijie Hu, Tim Jansen, Heliana Núnez Ponce, Calogero Quaranta, Chandan Chittapriya Sahu, Benjamin James Statham, Tianhao Zhang und Stefanie Zimmer.

I am especially grateful to my lab-mates in Lab 5.06: Dr. Jan-Hendrik Schöbel, Dr. Felix Krauskopf, and Pola Hild. A special thanks goes to Dr. Steven Terhorst for assisting me in the beginning of my doctoral studies. I spent most of my time with Arndt Collong and Marcus Becker; as much as I loved coming to the lab for the chemistry, I equally enjoyed seeing you both. I couldn't have wished for better labmates. The joy, fun, and unforgettable music made my stay truly memorable. Thank you very much for everything.

I feel incredibly fortunate to have made so many wonderful friends from around the world during my years in Aachen. I would like to thank my amazing friends Shulei, Shraddha, Marina, Swetha, Elanor, Luda, and Ilona for the beautiful times we've shared together.

I would like to thank my friend, Dr. Ruth-Christine Ganardi, for all the timeless evenings with endless conversations. We shared so many beautiful memories together, and your support helped me overcome numerous challenges.

Additionally, I would like to acknowledge people in India who have supported me throughout this journey: my friends Lavanya and Manoj Kumar; my teachers Sathiaseelan and Sharmila Lydia; my relatives Suresh, Parasakthi and Kalaivani; my parents Eswari and Periasamy; my brother Deepak; and my grandmothers Uthami and Kuppai. Despite the distance, their love and our endless phone conversations have brought me joy and provided me comfort during tough times.

I want to extend my heartfelt thanks to Karin, Bonnie, Mia, Daniel, and Levi for the wonderful memories and unwavering support. I feel incredibly lucky and grateful to be surrounded by such a loving family. Lastly, I express my deepest gratitude to my partner, Pit van Bonn. Thank you for standing by my side during the highs and lows, and for your constant encouragement. Your love, unwavering support and understanding have been my rock throughout this journey.

9 Curriculum Vitae

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Publications List

1. Hagui, W.; Periasamy, K.; Soulé, J.-F. Synthesis of 2,2'-Bipyridines through Catalytic C−C Bond Formations from C−H Bonds. *Eur. J. Org. Chem.* **2021**, 5388-5402.
2. Periasamy K.; van Bonn, P.; Orloff, R. T.; Völcker, N.; Lu, Q.; Rissanen, K.; Bolm, C. Synthesis of Benzo[e][1,4,3]oxathiazin-3-one 1-Oxides from *N*H-S-(2-Hydroxyaryl)sulfoximines. *J. Org. Chem.* **2024**, *89*, 8286–8290.
3. Periasamy, K.; Gordeeva.S.; Bolm, C. Syntheses of Sulfilimines by Iron-Catalyzed Imidations of Sulfides with 2,2,2-Trichloroethyl Sulfamate. *J. Org. Chem.* **2024**, DOI: 10.1021/acs.joc.4c01250.