Copper-Catalyzed Dealkylations and Rhodium-Catalyzed C–H Functionalizations of NH-Sulfoximines

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I. Introduction

1. General Introduction of Sulfoximines

In 1946, methionine sulfoximine 1 (Figure 1) as a compound responsible for the toxicity of wheat flour was first reported.[1] Three years later, it was isolated and identified by the Bentley group when they investigated the action of nitrogen trichloride on proteins.[2] After that, sulfoximines and their derivatives attracted a wide spread attention not only for applications as building blocks and chiral ligands (Figure 1, Compound 2) in organic synthesis, [3] but also for their attractive biological activities.[4] Nowadays, sulfoximines are as well known for their potential in pesticide research and medicinal chemistry.[5] For example, in 2005 Dow AgroSciences reported N-cyano sulfoximine 3 (Figure 1) as a new insecticide.[6] The potent enzyme inhibitor BAY 1143572 (4) has been promoted to clinical trials (Figure 1).

Figure 1. Sulfoximine-cored compounds.

Sulfoximines are stable monoaza analogues of sulfones. The introduction of the nitrogen atom creates a distorted tetrahedral structure. Sulfoximines have two distinguishing features (Figure 2). First, sulfoximines have a mildly basic and nucleophilic nitrogen atom (Figure 2). Free sulfoximines allow for further N–H functionalizations[7] and metal-ion coordination.[8] Second, the hydrogens of the alkyl group on the α-position of the sulfur atom are acidic.[9] The substituent (R³) on the nitrogen atom can influence the acid/base properties of the compound (pKₐ is 32 when R³ = Me, while the pKₐ is 23 when R³ = Ts).[10] Additionally, the distorted tetrahedral structure leads to a configurationally stable stereogenic sulfur atom (R¹ ≠ CH₂R²), which is tolerant to various
reagents. Therefore, in the contrast to sulfones, sulfoximines offer more possibilities to construct diversely functionalized derivatives \(^{[7]}\) and are very important in asymmetric syntheses as chiral auxiliaries\(^{[10]}\) or chiral ligands\(^{[3d-g]}\).

![Figure 2. Features of sulfones and sulfoximines.](image)

### 2. Functionalizations of sulfoximines

In recent decades, great progress has been achieved in the functionalizations of sulfoximines. In general, the functionalizations of sulfoximines are classified into the following two groups: N–H and C–H functionalizations. So, in this part, some powerful strategies to functionalize sulfoximines will be introduced. Representative examples are discussed and related plausible mechanisms are presented.

#### 2.1 N-H bond functionalization

**2.1.1 N-Alkylation**

In 2014, a general method for the N-alkylation of NH-sulfoximines 5 using alkyl bromides 6 with KOH in DMSO at room temperature was developed by Bolm and co-workers\(^{[12]}\). A variety of previously inaccessible N-alkylated sulfoximines 7 were prepared in good to excellent yields (Scheme 1). This cost-effective and operationally simple protocol proved not only applicable for the preparation of N-alkylated sulfoximines, but also suitable for the synthesis of a variety of N-alkylated sulfondiimines.
abstraction of a hydrogen atom from diarylmethane salt, the cleavage of DTBP led to a coupling reactions of

A plausible mechanism was also proposed (Scheme 3).

In the same year, Bolm and co-workers reported an effective iron-catalyzed dehydrogenative coupling reactions of NH-sulfoximines 5 with diarylmethanes 9 in the presence of TBHP as an oxidant to form the corresponding N-alkylated sulfoximines 10 in moderate to good yields (Scheme 2). Various NH-sulfoximines 5 with diarylmethanes 9 were tolerated in this procedure. The authors noted that these transformations occurred by a radical process, providing a new strategy for the synthesis of N-alkylated sulfoximines with α-branched substituents.

\[
\begin{align*}
\text{S} \overset{\text{N}}{=} \text{S} \quad \text{R}^1 \text{S} \overset{\text{N}}{=} \text{S} \quad \text{R}^2 & \quad \text{KCl, DMSO, } \tau & \quad \text{R}^1 \text{S} \overset{\text{N}}{=} \text{S} \quad \text{R}^3 \\
\text{Y} & \quad \text{R}^2 \text{Br} (6) & \quad \text{Y} & \quad \text{C}, 7, 83-91\% \\
\text{Y} & \quad \text{N-Ph}, 8, 75-94\% \\
\end{align*}
\]

**Scheme 1.** The N-alkylations of sulfoximines and sulfondiimines with alkyl bromides.

A plausible mechanism was also proposed (Scheme 3). Firstly, in the presence of the Fe(II) salt, the cleavage of DTBP led to a tert-butoxide anion and the tert-butoxy radical. Then, the abstraction of a hydrogen atom from diarylmethane 9 by the tert-butoxy radical gave diarylmethane radical 9A. Single-electron transfer from 9A onto the generated iron(III) species led to benzylic cation 9B. At the same time, sulfoximine 5 reacted with the tert-butoxide anion leading to anion intermediate 5C. Subsequently, the key step took place between the benzylic cation 9B and anion intermediate 5C to provide product 10.
One year later, Cheng and co-workers described a copper-catalyzed oxidative C(sp\(^3\))–H/N–H coupling of sulfoximines 5 with simple alkanes 11 in the presence of Cu(acac)\(_2\) (10 mol %) and DTBP (di-tert-butyl peroxide, 2.0 equiv) by a radical process leading to \(N\)-alkylated sulfoximines 12 in moderate to good yields (Scheme 4).\(^{114}\) In this reaction, both symmetric and unsymmetric \(S,S\)-diaryl sulfoximines with electron-donating and electron-withdrawing groups including chloro, methoxy and phenyl enabled access to \(N\)-alkyl sulfoximines 12a-12c. Cyclic substrates, such as cyclopentane, cycloheptane and cyclooctane, all proceeded to give the desired products 12d, 12e, 12f and 12g in 44%, 81%, and 50% yields, respectively.

Scheme 4. \(N\)-Alkylation of sulfoximines with alkanes.
In 2015, the groups of Cheng and Bolm reported a silver-mediated \( N \)-trifluoromethylation of sulfoximines with TMSCF\(_3\) by a radical pathway affording the corresponding \( N \)-trifluoromethylated products 14 with satisfying functionality tolerance in moderate to good yields (Scheme 5).\(^{[15]}\) For this process, the important feature was that a catalytic amount of silver carbonate as inexpensive catalyst was used in this radical process under base-free conditions.

\[
\begin{align*}
\text{C}_8\text{H}_6\text{S}_2\text{NH} & \quad \text{TMSCF}_3 \\
R^1 & \quad \text{R}^2 \\
\text{Ag}_2\text{CO}_3 (20 \text{ mol} \%) & \quad \text{1,10-phanthrolinium (40 mol \%) 1,4-dioxane, } 60^\circ\text{C, O}_2, 12 \text{ h} \\
\text{R}^3 & \quad \text{R}^4 \\
\text{5} & \quad \text{13} \\
\text{14} & \quad \text{51-85\%}
\end{align*}
\]

\[
R^1 = \text{Ph, 4-OMeC}_6\text{H}_4, 4-\text{BrC}_6\text{H}_4, 4-\text{CNC}_6\text{H}_4, \\
4-\text{NO}_2\text{C}_6\text{H}_4, 2-\text{ClC}_6\text{H}_4, \text{Br} \\
R^2 = \text{Ve, Ph, Br, Bu, cyclohexene}
\]

**Scheme 5.** Silver-catalyzed \( N \)-trifluoromethylation of sulfoximines with TMSCF\(_3\).

### 2.1.2 \( N \)-Vinylation

In 2004, Bolm and co-workers reported palladium-catalyzed cross-coupling reactions for the preparation of \( N \)-vinylated sulfoximines employing vinyl bromides 15 with \( NH \)-sulfoximines 5, affording the desired products 16 in excellent yields (Scheme 6a).\(^{[16]}\) This method could also be applied to vinyl triflates, where cesium carbonate was required instead of \( t \)-BuONa to prevent the hydrolysis of the vinyl triflates. The yields of the \( N \)-vinylated sulfoximines were also excellent (Scheme 6b).

\[
\begin{align*}
\text{O}_8\text{S}_8\text{NH} & \quad \text{Br} \\
R^1 & \quad \text{R}^2 & \quad \text{R}^3 & \quad \text{R}^4 \\
\text{Pd(OAc)}_2 (1 \text{ mol} \%) & \quad \text{rac-BINAP (1.5 mol \%) NaO}^\text{Bu}, \text{toluene} \\
110^\circ\text{C, 24 h} & \quad \text{16, } >98\%
\end{align*}
\]

\[
R^1 = \text{Ph, 4-MeC}_6\text{H}_4, 2-\text{OMeC}_6\text{H}_4, \text{Me} \\
R^2 = \text{Me, R}^1, R^1 = -(\text{CH}_2)_n- \\
R^3 = \text{H, Me. R}^4 = \text{H, Me, Ph. R}^5 = \text{H, Me, Ph}
\]

\[
\begin{align*}
\text{O}_8\text{S}_8\text{NH} & \quad \text{TIO} \\
R^1 & \quad \text{Me} \\
\text{Pd(OAc)}_2 (1 \text{ mol} \%) & \quad \text{rac-BINAP (1.5 mol \%) Cs}_2\text{CO}_3, \text{toluene} \\
110^\circ\text{C, 24 h} & \quad \text{18, R}^1 = \text{Ph} \quad >98\% \\
\end{align*}
\]

**Scheme 6.** Palladium-catalyzed cross-coupling for the preparation of \( N \)-vinylated sulfoximines.
Later, Bolm and co-workers found that copper catalysis also worked well in this kind of reaction. Treatment of sulfoximines 5 with vinyl bromides 15 in the presence of Cul and DME DA under potassium carbonate in toluene at 110 °C for 24 h afforded N-vinyl sulfoximines 16 in good to excellent yields (Scheme 7).\textsuperscript{[17]} Compared with the reported palladium-catalyzed process, this reaction needed less reagents (metal and ligand) and had a broader substrate scope.

\[
\begin{align*}
\text{C}_6\text{H}_4\text{N} = \text{H} & \quad + \quad \text{Br} - \text{C}_2\text{H}_4 \quad \text{R}^4 \quad \text{R}^5 \\
5 & \quad 15 \quad \text{Cul (1.0 equiv)} \quad \text{DMEDA (2.0 equiv)} \\
& \quad \text{K}_2\text{CO}_3, \text{toluene} \quad 110 \, ^\circ\text{C}, 24 \, \text{h} \quad \text{R}^2, \text{R}^5 = \text{N}^+ \text{Me}, \text{Ph} \\
\end{align*}
\]

**Scheme 7.** Copper-mediated reaction for the preparation of N-vinylated sulfoximines.

On the basis of Jiang’s findings, Bolm and co-workers developed a palladium/copper co-catalyzed oxidative amidobromination for the construction of N-vinylated sulfoximines 21 using NH-sulfoximines and acrylates 20 as starting materials (Scheme 8).\textsuperscript{[18]} Then, product 21a was selected as representative starting material to demonstrate potential synthetic applications. For example, the palladium-catalyzed Suzuki-type cross-coupling of 21 with phenyl boronic acid led to aryl-substituted β-amido ester 22 in 87% yield (Scheme 9a). Utilizing Buchwald’s copper-catalyzed amidation conditions converted the ethyl carbamate into literature-unknown α,β-diamido esters 23 with low yields (34% and 28%, respectively) (Scheme 9b).

\[
\begin{align*}
\text{O}_\text{N} & \quad \text{NH} \quad + \quad \text{C} = \text{C}_2 \text{R}^3 \quad \text{C}(\text{MeCN})_2\text{Cl}_2 (5 \, \text{mol} \%) \\
5 & \quad 20 \quad \text{Cl}_2\text{Cl} (10 \, \text{mol} \%) \\
& \quad \text{LiBr, toluene, C}_2 \quad 80 \, ^\circ\text{C}, 24 \, \text{h} \quad \text{R}^1 = \text{Ph, 4-CMeC}_6\text{H}_4, 4-\text{NO}_2\text{C}_6\text{H}_4 \quad \text{Me} \\
& \quad \text{R}^2 = \text{Me, Bu, Pr, Ph} \\
& \quad \text{R}^3 = \text{Et, Bu, C}_6\text{H}_4, \text{Ph, 2,4-(Bu)}_2\text{C}_6\text{H}_4, \text{C}_6\text{F}_5, \text{PhSO}_2
\end{align*}
\]

**Scheme 8.** Palladium-catalyzed cross-coupling for preparation of N-vinylated sulfoximines.
preparation of products were very sensitive to hydrolysis. The corresponding ring were tolerated giving yne sulfoximines desired products. Aryl substituted terminal alkynes with a variety of substituents on the aromatic also sulfoximines coupling of 2.1.3

Following this work, a new method has been developed by Bolm and co-workers for the copper-catalyzed dehydrogenative C–N coupling of NH-sulfoximines 5 with terminal alkynes 24 (Scheme 10).[19] The desired yne sulfoximines 25 were obtained in good yields (48%-84%). Besides S-methyl-S-phenyl sulfoximine, also S,S-dimethyl sulfoximine and S,S-tetramethylene sulfoximine could be applied giving the desired products. Aryl substituted terminal alkynes with a variety of substituents on the aromatic ring were tolerated giving yne sulfoximines 25 in good yields. However, the author found that the products were very sensitive to hydrolysis. The corresponding N-acyl sulfoximines 26 were formed from the reaction mixtures during normal silica gel chromatography.

\[ \text{Scheme 9. Synthetic application.} \]

2.1.3 N-Alkynylation

In 2013, Bolm and co-workers first reported the copper-catalyzed dehydrogenative C–N coupling of NH-sulfoximines 5 with terminal alkynes 24 (Scheme 10).[19] The desired yne sulfoximines 25 were obtained in good yields (48%-84%). Besides S-methyl-S-phenyl sulfoximine, also S,S-dimethyl sulfoximine and S,S-tetramethylene sulfoximine could be applied giving the desired products. Aryl substituted terminal alkynes with a variety of substituents on the aromatic ring were tolerated giving yne sulfoximines 25 in good yields. However, the author found that the products were very sensitive to hydrolysis. The corresponding N-acyl sulfoximines 26 were formed from the reaction mixtures during normal silica gel chromatography.

\[ \text{Scheme 10. N-Alkynylated sulfoximines from NH-sulfoximines with terminal alkynes.} \]

Following this work, a new method has been developed by Bolm and co-workers for the preparation of N-alkynylated sulfoximines 25 involving a copper-catalyzed decarboxylative coupling of sulfoximines with aryl propiolic acids 27, which are stable and readily available (Scheme 11).[20] The reactions were performed with 10 mol % of CuBr, 20 mol % of pyridine, and
1.1 equiv of \( \text{K}_2\text{PO}_4 \) in toluene at 80 °C. A wide range of sulfoximines and aryl-substituted terminal alkynes were tolerated. The advantage of this protocol was the application of a cheap copper catalytic system and that air was the oxidant. The only byproducts from this process were water and carbon dioxide.

\[
\begin{align*}
\text{C}_2\text{H}_5\text{N}^+\text{Me}^- + \text{R}^2\equiv &\text{C}^{\equiv}\text{CH} \\
\text{Cu}^2+ (1\text{C mol %}) &\xrightarrow{\text{K}_2\text{PO}_4 (1.1 \text{equiv})} \text{Me}^- \text{C}_2\text{H}_5 \\
\text{pyridine} (20 \text{ mol %}) &\xrightarrow{\text{toluene}, 80 \degree \text{C}} \text{Me}^- \text{C}_2\text{H}_5
\end{align*}
\]

\( R^1 = \text{Me}, \text{aryl} \)
\( R^2 = 4\text{-FFh}, 4\text{-ClPh}, 3\text{-ClPh}, 2\text{-ClPh}, 2\text{-MePh}, 2\text{-BuPh}, \text{Ph} \)

**Scheme 11.** \( N \)-Alkynylated sulfoximines from \( NH \)-sulfoximines with aryl propiolic acids.

Then, the synthetic applications of \( N \)-alkynylated sulfoximines \( 25a \) and \( 25b \) were explored (Scheme 12). Firstly, reduction of the \( N \)-alkynylated sulfoximines \( 25a \) using \( \text{Pd/C} \) (10 wt %) under an atmosphere of \( \text{H}_2 \) afforded the (Z)-alkenylated sulfoximine \( 28 \) in 70% yield (ratio of \( Z/E = 21:1 \) by \( ^1\text{H NMR} \) analysis) (Scheme 12a). Then, the [2 + 2]-cycloaddition of \( 25b \) with dimethyl ketene was accomplished to afford cyclobutenone sulfoximine \( 29 \) in a yield of 81% by refluxing the \( N \)-alkynylated sulfoximine \( 25b \) with isobutyryl chloride in the presence of triethylamine (Scheme 12b).

**Scheme 12.** Derivatizations of \( N \)-alkynylated sulfoximines.
In 2014, Bolm and co-workers described another method towards yne sulfoximines 25 (Scheme 13). In this reaction, N-alkynylated sulfoximines were obtained in moderate to good yields from bromoacetylenes 30 and NH-sulfoximines 5 in the presence of Cu(OAc)$_2$ (10 mol %), 1,10-phenanthroline (20 mol %), and K$_2$CO$_3$ (2.5 equiv). Then, an efficient ruthenium-catalyzed oxidative transformation of the C–C triple bond of 25a into α-diketo moiety was demonstrated (Scheme 14).

![Scheme 13](image)

Scheme 13. N-alkynylated sulfoximines from NH-sulfoximines with bromoacetylenes.

In 2016, Bolm and co-workers developed a new, metal-free method for the preparation of N-alkynylated sulfoximines from terminal alkynes 24 with sulfoximidoyl-containing hypervalent iodine(III) reagents 33 (Scheme 15), which were obtained in excellent yields from the reaction of NH-sulfoximine 5 with methoxy(tosyloxy)iodobenzene (MTIB) in acetonitrile at room temperature (Scheme 16).

![Scheme 15](image)

Scheme 15. The preparation of N-alkynylated sulfoximines of sulfoximidoyl-containing hypervalent iodine(III) reagents with terminal alkynes.
2.1.4 N-Acylation/N-Imidoylation

In 2004, according to the approach reported by Bolm and co-workers, N-acylations of NH-sulfoximines were achieved in excellent yields by treating NH-sulfoximines 5 with acyl halides (acyl chlorides and acyl bromides) or anhydrides in the presence of a base (such as NEt₃, pyridine or t-BuOK) in CH₂Cl₂ at 0 ℃ (Scheme 17).[23] Additionally, carboxylic acids were used for the preparation of N-acylated sulfoximines 34. The desired products were obtained in satisfying yields even when bulky substituted carboxylic acids were used (Scheme 18).

![Scheme 17. The N-acylations of NH-sulfoximines with acyl halides or carboxylic acids.](image)

In 2013, Bolm and co-workers developed a copper-catalyzed oxidative reaction of sulfoximines 5 with aldehydes 35 in the presence of CuBr and TBHP in MeCN at 80 ℃ for 12 h affording a series of the corresponding N-acylated sulfoximines 34 in good to excellent yields (Scheme 18).[24] The reaction demonstrated high functional group tolerance with respect to aryl aldehydes. In addition, isopropyl aldehyde and 2-oxo-2-phenylacetaldehyde enabled this oxidative coupling to afford the corresponding products (34f and 34g), respectively.

![Scheme 16. Syntheses of hypervalent iodine reagents.](image)
one pot. This reaction exhibited a broad scope with respect to terminal alkynes. In THF at room temperature followed by oxidative reaction at 50 °C under air (Scheme 18). In 2015, Lee and co-workers reported a copper-catalyzed three-component reaction of 1-sulfonyl azides and NH-sulfoximines in THF at room temperature under air for the preparation of N-imidoyl sulfoximines in good yields. They also found that N-oxoimidoyl sulfoximines were easily obtained from the Cu-catalyzed three-component reaction in THF at room temperature followed by oxidative reaction at 50 °C under air (Scheme 19). Then, N-imidoyl sulfoximines were conveniently converted into N-oxoimidoyl sulfoximines in one pot. This reaction exhibited a broad scope with respect to terminal alkynes.

Scheme 18. N-Acylations of NH-sulfoximines with aldehydes.

In 2015, Lee and co-workers reported a copper-catalyzed three-component reaction of 1-alkynes, N-sulfonyl azides, and NH-sulfoximines 5 in THF at room temperature under air for the preparation of N-imidoyl sulfoximines 37 in good yields. They also found that N-oxoimidoyl sulfoximines were easily obtained from the Cu-catalyzed three-component reaction in THF at room temperature followed by oxidative reaction at 50 °C under air (Scheme 19). Then, N-imidoyl sulfoximines were conveniently converted into N-oxoimidoyl sulfoximines in one pot. This reaction exhibited a broad scope with respect to terminal alkynes.

Scheme 19. The preparation of N-imidoyl and N-oxoimidoyl sulfoximines from 1-alkynes, N-sulfonyl azides and sulfoximines.

2.1.5 N-Arylation

N-Aryl sulfoximines are normally synthesized by transition metal-catalyzed cross-coupling of NH-sulfoximines with aryl halides. In 1998, the first N-arylation of sulfoximines by palladium-catalyzed cross-coupling of NH-sulfoximines 5 with various aryl bromides 39 in the presence of
chelating bisphosphines (rac-BINAP or Tol-BINAP) and Cs$_2$CO$_3$ in toluene at 110 °C was reported by Bolm and co-workers.$^{[26]}$ Using this protocol, various N-arylated products 41 were obtained in good to excellent yields (Scheme 20). After that, other coupling partner such aryl sulfonates,$^{[27]}$ aryl chlorides,$^{[28]}$ and aryl iodides$^{[29]}$ were utilized in the N-arylations of sulfoximines.

**Scheme 20.** N-Arylation of NH-sulfoximines with aryl bromides.

In 2004, Bolm and co-workers reported a first copper-mediated cross-coupling reaction of sulfoximines 5 and aryl halides 39, 40 giving the N-arylated sulfoximines 41 (Scheme 21).$^{[30]}$ The reaction tolerated an extensive range of aryl iodides and aryl bromides to afford the corresponding N-arylation products 41 in yields ranging from 48% to 95%. The limitation of this method was the requirement of a stoichiometric amount of copper(I) iodide. However, one year later, the same group described a similar reactions with catalytic amounts of copper salts (10 mol %, CuI).$^{[31]}$ In addition to copper(I) iodide, other copper salts could be utilized in the N-arylation of NH-sulfoximines.$^{[32,33]}$

**Scheme 21.** N-Arylation of NH-sulfoximines with aryl iodides and aryl bromides.

In addition to aryl halides, Bolm and co-workers found that aryl boronic acids 42 could serve as coupling partners for the N-arylation of NH-sulfoximines 5 to synthesize a variety of N-arylated
sulfoximines 41 in the presence of Cu(OAc)₂ (10 mol %) in MeOH under base-free conditions at room temperature (Scheme 22).[34] Compared to palladium,[26-28] iron,[29] and copper[30-32] catalyzed N-arylations of NH-sulfoximines with aryl halides in the presence of an external base such as Cs₂CO₃ or KO'Bu at high temperature, this method was a good complement for the N-arylation of NH-sulfoximines. In addition to aryl boronic acids, diaryliodonium salts[33] arylations of NH-sulfoximines with aryl halides, aryl boronic acids and aryl siloxanes represented an efficient method for the preparation of NH-sulfoximines. In addition to aryl boronic acids, diaryliodonium salts[33] and organosilicon reagents[36] were also excellent coupling partners in the N-arylation of NH-sulfoximines.

\[
\begin{align*}
\text{O-S-NH}_R^1 \quad &\text{+} \quad R^2\text{B(OH)}^2 \quad \overset{\text{Cu(OAc)}_2 (10 \text{ mol %), MeOH, rt, 12 h}}{\text{CuBr (5 mol %), aq. FEG 400 (1:1, v/v), sonication, rt, 2-10 min.}} \quad \text{O=S-N}^1_R^1 \\
\text{R}^1 \quad &\text{R}^2 \quad \text{R}^3 \\
\text{43} \\
\end{align*}
\]

Reaction condition: CuBr (5 mol %), aq. FEG 400 (1:1, v/v), sonication, rt, 2-10 min.

\[
\begin{align*}
\text{R}^1 \quad &\text{R}^2 \quad \text{R}^3 \\
\text{44} \\
\text{Reaction condition: CuI (10 mol %), TBAF:CH}_3\text{C}(10 \text{ mol %), DCM, O, rt, 12 h}} \\
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 &= \text{Ph, 4-BrC}_6\text{H}_4, 4-\text{VeC}_6\text{H}_4, \text{Me}, \\
\text{R}^2 &= \text{Me, Et, cyclopentyl, Ph} \\
\text{R}^3 &= \text{Ph, 4-VECC}_6\text{H}_4, 4-\text{BuC}_6\text{H}_4, 4-\text{FC}_6\text{H}_4, 4-\text{ClC}_6\text{H}_4, 3-\text{MeCC}_6\text{H}_4, \\
& \text{2-VeC}_6\text{H}_4, 2\text{-thienyl} \\
\end{align*}
\]

**Scheme 22.** N-Arylation of NH-sulfoximines with aryl boronic.

The transition-metal-catalyzed N-arylation of NH-sulfoximines with aryl halides, aryl boronic acids and aryl siloxanes represented an efficient method for the preparation of N-aryl sulfoximines. In addition to these N-aryl sulfoximines, Bolm, Miura and co-workers developed an interesting and practical copper-catalyzed direct dehydrogenative C–N coupling of azoles 45 or polyfluoroarenes 46 with NH-sulfoximines 5 using 10 mol % of Cu(OAc)₂·H₂O, and 3.0 equiv of K₃PO₄ in DMF under air atmosphere to afford the corresponding N-aryl/sulfoximines in good to excellent yields (Scheme 23).[37] This reaction was successfully extended to benzoazoles, benzothiazole and polyfluoroarenes to prepare N-arylated sulfoximines.
2.1.6 N-Cyanation

In 2014, Cheng and co-workers demonstrated a copper-catalyzed oxidative N-cyanation of sec-amines, sulfoximines and 1,1,3,3-tetramethylguanidine using CuCN as the cyanation source in the presence of CuBr₂ (17 mol %), TMEDA (2.0 equiv), Na₂SO₄ (2.0 equiv) under oxygen atmosphere (Scheme 24).[38] Both S-alkyl-S-aryl sulfoximines and S,S-diarly sulfoximines were applied in this procedure, leading to N-cyano sulfoximines as potential insecticides in moderate to good yields.

Scheme 24. N-Cyanation of NH-sulfoximines with CuCN.

One year later, the same group developed a copper-catalyzed N-cyanation of sulfoximines using AIBN as a safe cyanide source, this reaction process was promoted by 10 mol % of CuI, 2.0 equiv of K₂CO₃ under an atmosphere of dioxygen leading to a variety of substituted N-cyano...
sulfoximines 50 in good yields (Scheme 25). In addition to sulfoximines, some sec-amines, as well as 1,1,3,3-tetramethylguanidine were compatible with this procedure. Noteworthy this transformation employed O2 as the clean terminal oxidant under mild conditions. Thus, it represented an important and practical progress to N-cyanation reaction.

\[ \text{Scheme 25. N-Cyanation of NH-sulfoximines with AIBN.} \]

**2.1.7 N-Thioetherification**

In 2015, Bolm and co-workers developed a method for the preparation of air and moisture-stable N-trifluoromethylthio sulfoximines 53 from NH-sulfoximines 5 via the corresponding N–Br derivatives in excellent yields (Scheme 26). This two-step process started with an easy-to-perform bromination at the sulfoximine nitrogen, followed by a reaction with silver trifluoromethanethiolate in CH3CN at room temperature for only 20 minutes. In some cases, a one-pot cascade reaction was advantageous. For example, products 53a, 53b could be obtained by a one-pot cascade reaction avoiding the isolation of the brominated sulfoximines.

\[ \text{Scheme 26. N-Thioetherification of NH-sulfoximines with AgSCF}_3 \]
In 2016, Cheng and co-workers developed a copper-catalyzed $N$-thioetherification of NH-sulfoximines 5 using the less toxic and readily available disulfides 54 as the sulfur source agents (Scheme 27).\textsuperscript{[41a]} Both $S,S$-diaryl sulfoximines and $S$-aryl-$S$-methyl sulfoximines were good coupling partners leading to the desired products (55a, 55b) in moderate to good yields. A range of diverse diaryl disulfides were also tolerated in this process to form the corresponding products (55c-55e) in good yields. Recently, a metal-free, iodine-catalyzed N–H/S–H dehydrocoupling reaction of sulfoximines with various thiols to construct various $N$-sulfenyl-sulfoximines 55 was reported by Zeng and co-workers.\textsuperscript{[41b]}

$$\begin{align*}
\text{C}_3\text{S}_2\text{NH} & \quad \text{R}_1\text{S}_2\text{S}_2\text{R}_2 \\
5 & \quad 54 \\
\xrightarrow{\text{CuI (20 mol %), NaOAc (3.0 equiv), DMF, 60 °C, 15 h}} & \quad \text{Q}_2\text{S}_2\text{N-SR}^3 \quad \text{55, 43-88%}
\end{align*}$$

Selected examples

\begin{align*}
\text{C}_3\text{S}_2\text{N-SPh} & \quad \text{C}_3\text{S}_2\text{N-SPh} & \quad \text{C}_3\text{S}_2\text{N-SPh} & \quad \text{C}_3\text{S}_2\text{N-SPh} & \quad \text{C}_3\text{S}_2\text{N-SPh} \\
55a, 76\% & \quad 55b, 76\% & \quad 55c, 71\% & \quad 55d, 73\% & \quad 55e, 74\%
\end{align*}

\textbf{Scheme 27.} $N$-Thioetherification of NH-sulfoximines with disulfides.

### 2.2 $\alpha$-C–H Bond Functionalization

#### 2.2.1 C–C Bond Construction

In 2014, Bolm and co-workers developed a rhodium-catalyzed C–H activation/oxidative couplings between $N$-acyl or $N$-aryl sulfoximines 56 with alkenes 57. The olefinations selectively occurred at the ortho-position of $S$-phenyl sulfoximines catalyzed by a combination of [Cp*RhCl$_2$]$_2$ (2 mol %), AgSbF$_6$ (10 mol %)and Cu(OAc)$_2$·H$_2$O (4.0 equiv) to afford the ortho-olefinated (Heck-type) products 58 in moderate to excellent yields (Scheme 28).\textsuperscript{[42]} The synthetic application of the ortho-olefinated products have been exemplified by conversion into the cyclic derivatives under basic condition in toluene. (Scheme 29).
in the presence of Pd(OAc)_{2}  quantitative yields (Scheme 31). Subsequent palladium-catalyzed oxidative ring-closing reactions of heterobicyclic alkenes 61 functionalizations of heterobicyclic alkenes in acceptable yields (Scheme 31). The ratio of two regioisomers depended on the substituents.

Scheme 28. Rhodium-catalyzed ortho-olefination of N-protected sulfoximines with alkenes.

Scheme 29. Synthetic applications of ortho-olefinated sulfoximines.

In the same year, Bolm and co-workers discovered rhodium-catalyzed directed C–H functionalizations of heterobicyclic alkenes 60 with NH-sulfoximines 5 (Scheme 30).

Products 61 were obtained in good to excellent yields. These products were attractive intermediates for some functionalized molecules that were difficult to be prepared by other methods. For example, by treatment of arylated 7-oxa bicycles 61a–c with methyl sulfonic acid in chloroform under reflux, a dehydration occurred providing the corresponding ortho-naphthylated products 62a–c in almost quantitative yields (Scheme 31). Subsequent palladium-catalyzed oxidative ring-closing reactions in the presence of Pd(OAc)_{2} and Phl(OAc)_{2} in toluene at 120 °C, afforded aryl-fused thiazines 63, 64 in acceptable yields (Scheme 31). The ratio of two regioisomers depended on the substituents (R^1).

Scheme 30. Rhodium-catalyzed hydroarylation of NH-sulfoximines with heterobicyclic alkenes.
were used in a similar protocol. For example, the product
sulfoximines
affording the corresponding bis ortho-arylated products 65 in low to moderate yields
(Scheme 32). Dibenzothiazine derivatives 66 were obtained by intramolecular cyclizations of ortho-arylated products 65 in the presence of Pd(OAc)2 and PhI(OAc)2 in toluene at 120 °C for 10 h (Scheme 33). Chiral dibenzothiazines were prepared when enantiopure S-phenyl sulfoximines were used in a similar protocol. For example, the product 66d was obtained with excellent ee value.

\[\text{Scheme 31. Synthetic applications.}\]

In addition to rhodium catalysis, the first ruthenium-catalyzed ortho-arylation of phenyl sulfoximines 5 with phenyl boronic acids 42 was reported by Jeganmohan and co-workers in 2015, affording the corresponding bis ortho-arylated products 65 in low to moderate yields (Scheme 32). Dibenzothiazine derivatives 66 were obtained by intramolecular cyclizations of ortho-arylated products 65 in the presence of Pd(OAc)2 and PhI(OAc)2 in toluene at 120 °C for 10 h (Scheme 33). Chiral dibenzothiazines were prepared when enantiopure S-phenyl sulfoximines were used in a similar protocol. For example, the product 66d was obtained with excellent ee value.

\[\text{Scheme 32. Ruthenium-catalyzed ortho-arylation of phenyl sulfoximines with phenyl boronic acids.}\]
2.2.2 C–N Bond Construction

In 2016, Bolm and co-workers reported rhodium(III)-catalyzed ortho-amidations of sulfoximines 5. The catalytic system of [Cp*Rh(MeCN)₃(SbF₆)₂] and NaOAc in 1,2-DCE at 100 °C for 12 h provided the desired products 68 in 44%–83% yields (Scheme 34). For further synthetic exploration, cleavage of the Boc group of sulfoximine 68a provided ortho-amino-substituted sulfoximine 69 in yield of 90%. Subsequent reactions of product 69 with carbon disulfide at 170 °C for 24 h led to cyclization forming compound 70 in 90% yield. Thiadiazine 1-oxides 71 (88%) was then obtained by treatment of 70 with methyl iodide under basic conditions at 80 °C for 20 h. Heteroaromatic thioether 71 was utilized as substrate for Liebeskind–Srogl-type cross-coupling reactions with boronic acids to allow further extension of the molecular diversity of the thiadiazine 1-oxide derivatives. For example, product 72 was obtained in 73% yield in the presence of Pd₂(dba)₃, TFP and CuTC in THF at 50 °C for 24 h (Scheme 35).
could be investigated. Firstly, Sonogashira-type cross-couplings of 2.2.3 in good yields, respectively (Scheme 36).

Scheme 34. Rhodium-catalyzed ortho-amidations of NH-sulfoximines.

Scheme 35. Synthetic applications.

2.2.3 C–Br/C–I Bond Construction

Recently, Bolm and co-workers developed a rhodium-catalyzed halogenations of N-acyl sulfoximines 56 with NBS or NIS to provide ortho-brominated 74 or ortho-iodinated sulfoximines 75 in good yields, respectively (Scheme 36). Subsequent product functionalizations were investigated. Firstly, Sonogashira-type cross-couplings of ortho-bromo and ortho-iodo sulfoximines 74a and 75a with terminal alkyynes 24a gave the corresponding alkynyalted products 76 in 58% and 92% yields (Scheme 37). Then, palladium-catalyzed Suzuki coupling reactions of 75a with boronic acids under basic conditions in MeCN/H2O afforded arylated products 77, which could be N-deacetylated and oxidatively cyclized to give benzothiazines 78 in 96% yield (Scheme 37).
Scheme 36. Rhodium-catalyzed ortho-halogenation of N-acyl sulfoximines with NBS/NIS.

Scheme 37. Synthetic applications

2.2.4 C–C and C–N Bonds Construction

In 2013, Bolm and co-workers developed a rhodium-catalyzed oxidative C–H/N–H activation of NH-sulfoximines 5 with alkynes 79 (Scheme 38). The resulting 1,2-benzothiazines were obtained in good yields (ranging from 67%-93%). Under the optimized reaction conditions, substituted sulfoximines and a series of symmetrically substituted diphenylacetylenes reacted well (80a-80d). The yields were slightly lower when aliphatic alkynes were applied. Unsymmetrically substituted alkynes led to regioisomeric products.
activation/cyclization/condensation process by reacting
methods. The desired products
synthesis of the 4-unsubstituted 1,2-benzothiazines
to provide diverse 1,2-benzothiazines in excellent yields (Scheme 40).

Two years later, Bolm and co-workers described a rhodium-catalyzed domino C–H bond
In contrast to 3,4-substituted 1,2-benzothiazines, Glorius and co-workers reported the
Rhodium-catalyzed annulations of
ketones.

selected examples

Scheme 38. Rhodium-catalyzed oxidative annihilations of NH-sulfoximines with alkynes.

In contrast to 3,4-substituted 1,2-benzothiazines, Glorius and co-workers reported the
synthesis of the 4-unsubstituted 1,2-benzothiazines 82, which were difficult to synthesize by other
methods. The desired products 82 could be obtained in good yields by treating NH-sulfoximines 5
with tosylate and mesylate 81 in the presence of [Cp*Rh(MeCN)3][SbF6]2, Cu(OAc)2, and NaOAc
in MeOH at 40 °C for 15 h (Scheme 39).[48]

Scheme 39. Rhodium-catalyzed annihilations of NH-sulfoximines with α-halo and pseudohalo
ketones.

Two years later, Bolm and co-workers described a rhodium-catalyzed domino C–H bond
activation/cyclization/condensation process by reacting NH-sulfoximines 5 with diazo compounds
83 to provide diverse 1,2-benzothiazines in excellent yields (Scheme 40).[49] This transformation
was regioselective and showed a high functional group tolerance and the only by-products from this process were N₂ and H₂O. Then, the synthetic potential of the products was investigated. Treatment of 80a with NBS/AIBN in benzene gave the methyl bromide 84, which was subsequently reacted with methyl amine in dichloromethane at room temperature, affording the tricyclic lactam 85 in 68% yield in two steps (Scheme 41a). The hydrolysis of the ethyl ester group of 80a with NaOH at 100 °C and subsequent decarboxylation provided the 1,2-benzothiazine 86 in 81% yield (Scheme 47b). The double bond in the heterocyclic core of 80a was reduced by applying a mixture of NaBH₄ and CF₃CO₂H in dichloromethane (Scheme 41b). As a result, product 87 was obtained in 90% yield (with a dr value of 85:15 as determined by NMR spectroscopy).

![Scheme 40](image)

**Scheme 40.** Rhodium-catalyzed annulation of NH-sulfoximine with diazo compounds.

![Scheme 41](image)

**Scheme 41.** Synthetic applications.

In 2017, Lee and co-workers disclosed an efficient synthetic method for the synthesis of a
wide range of 1,2-benzothiazines bearing pyridyl as well as carbonyl groups. The reaction was performed with 3 mol % of [Cp*Rh(MeCN)]3[SbF6] and 1.0 equiv of NaOAc in toluene at 100 °C. A wide range of sulfoximines and pyridotriazoles were employed to give the desired products 89 in good yields under the optimized reaction conditions (Scheme 42).[50]

Scheme 42. Rhodium-catalyzed annihilations of NH-sulfoximines with pyridotriazoles.

Soon after Lee’s work, Cheng and co-workers developed a microwave-assisted, cobalt-catalyzed direct C−H activation/double C−N bond formation reaction of NH-sulfoximines 5 with 1,4,2-dioxazol-5-ones 90 to produce diverse thia diazine-1-oxides 91 in moderate to excellent yields (Scheme 43).[51] This reaction tolerated a broad range of functional groups with respect to 1,4,2-dioxazol-5-ones and only released CO2 and H2O as the byproducts. However, this reaction was not successful when NH-sulfoximines 5 contained a nonaromatic moiety.

Scheme 43. Cobalt-catalyzed annihilations of NH-sulfoximines with 1,4,2-dioxazol-5-ones.
3. Synthesis of Sulfonimidamides

Recently, sulfonimidamides and their derivatives have become increasingly important molecules in medicinal and agricultural chemistry. However, only few synthetic approaches requiring lengthy synthetic sequence have been reported so far. All of these methods involved the nucleophilic substitution of a sulfonimidoyl chloride by an amine (Scheme 44). The key intermediates can be prepared from sulfinyl chlorides and sulfonamides. But sulfonamides are not easily accessible and have limited commercial availability, and sulfinyl chlorides are unstable and very sensitive to moisture. Many of these deficiencies have limited their use. Consequently, a one-pot methodology for the synthesis of sulfonimidamides becomes highly desirable. In this section, three examples for one-pot preparation of sulfonimidamides are discussed.

Scheme 44. Classical sulfonimidamide synthesis.

3.1 From Sulfonamides to Sulfonimidamides

In 2015, Chen and Gibson reported a multi-step, one-pot procedure to synthesize sulfonimidamides from the readily available sulfonamides. This reaction was performed under mild conditions to afford the products in moderate to excellent yields (Scheme 45). When TBS was applied as protecting group, the unprotected sulfonimidamides were obtained in good yields. Compared to typical sulfonimidamide syntheses, this method offered
a convenient, safe and efficient approach to sulfonimidamides.

![Reaction Scheme](image)

**Scheme 45.** A synthetic route to sulfonimidamides from sulfonylamides.

### 3.2 From Sulfinamides to Sulfonimidamides

In 2017, inspired by the work of Bull and Luisi for the preparation of NH-sulfoximines by NH transfer to sulfoxides using ammonium carbamate mediated by the hypervalent reagent PhI(OAc)$_2$,[55] Lücking and co-workers found that NH-sulfonimidamides 97 could be obtained from sulfinamides 94 in good to excellent yields (Scheme 46).[56] The mild reaction conditions tolerated a wide range of substituents in sulfonylamides.
organometallic reagents were found to be compatible with this transformation (performed well giving the desired products in good yields (102a-f). Also (hetero)aryl and alkyl H-sulfonimidamide was reported by Willis and co-workers (Scheme 47)[57] They developed a one-pot, three-component synthesis of sulfonimidamides from widely available organometallic reagents, amines and N-sulfinyltritylamine (TrNSO), which is a stable and readily available. The reaction tolerated a wide range of organometallic reagents and amines to furnish the corresponding NH-sulfonimidamide 102 in yields ranging from 38% to 80%. For example, the primary and secondary anilines all performed well giving the desired products in good yields (102a-f). Also (hetero)aryl and alkyl organometallic reagents were found to be compatible with this transformation (102g-j).
Select examples:

Scheme 47. A one-pot sulfinylamine-base synthesis of NH-sulfonimamide.
4. Aerobic Copper-Catalyzed C–C bond cleavage

4.1 From Ketones to Aldehydes

Compared to other transition-metal catalysts, copper catalysts is advantageous since they are inexpensive, readily available, insensitive to air, and can be handled easily. In addition, copper can access Cu$^0$, Cu$^I$, Cu$^{II}$, and Cu$^{III}$ oxidation states, which allows it to act through one-electron or two-electron processes. As a result, both radical pathways and powerful two-electron bond-forming pathways can occur. In total, these features confer copper catalysts a remarkably broad range of activities.

Oxygen is considered to be an ideal oxidant in oxidative synthetic protocols, because of its atom-economical and environmentally benign character. However, the high activation energies in reactions involving oxygen as oxidant require suitable catalysts to be employed. In combination with molecular oxygen, the chemistry of copper catalysis increases exponentially. Recently, copper-catalyzed aerobic oxidation and oxygenation reaction with molecular oxygen has been a booming topic. Among them, the copper-catalyzed C(CO)–C(α) bond cleavage reaction under oxygen atmosphere attracted our attention. In 2013, Bi and co-workers described a chemoselective oxidative cleavage of the C(CO)–C(methyl) bond of methyl ketones 103. A wide range of aromatic and aliphatic methyl ketones 103a-h could be subjected to this copper-catalyzed reaction affording the desired products 35a-d in good to excellent yields. Dihydrogen (H$_2$) and carbon dioxide (CO$_2$) were released as byproducts (Scheme 48). However, when propiophenone 104 and α-phenylacetophenone 107 were applied under standard reaction conditions, the corresponding products were not obtained (Scheme 48). The mechanistic studies disclosed an interesting reaction sequence, involving an α-oxygenation/hydration/1,2-hydride shift/C–C bond cleavage.
A plausible mechanism was proposed for this reaction (Scheme 49). Firstly, acetophenone 103 underwent oxidation to afford compound 103A, through the activation of oxygen by the cuprous salt. Compound 103A was further oxidized to intermediate 103B, which quickly converted into the compound 103C by picking up one molecule of water. Then, 1,2-hydride shift occurred, during which the methyl hydrogen atom was transferred to the carbonyl carbon, leading to the formation of intermediate 103D. Finally, C–C bond cleavage took place, giving product 35a, along with the release of formic acid. The formic acid subsequently decomposed to liberate H₂ and CO₂, while copper(II) specie was reduced to the copper(I) species, which reentered the next catalytic cycle.

Scheme 49. Proposed mechanism.
4.2 From Ketones to Amides

In 2014, Jiao and co-workers reported an aerobic oxidative C(CO)—C(α) cleavage of aryl alkyl ketones to form amides 109 by using azide 108 as the nitrogen source, new C—N bonds were formed involving CuCl₂ (10 mol %), TEMPO (20 mol %), H₂O (30.0 equiv) and 1 atm of O₂ in DMF at 120 °C, providing the corresponding products 109 in moderate to good yields (Scheme 50). A series of acetophenone derivatives 103a-f as well as more challenging aryl ketones with long-chain alkyl substituents (104b, 105a and 106b) could be efficiently cleaved and converted into the corresponding amides 109.

![Scheme 50](image)

**Scheme 50.** Cu-catalyzed oxidative C–C bond cleavage for C–N bond formation.

A plausible mechanism was proposed for this copper-catalyzed C–C bond cleavage of aryl alkyl ketones leading to amides (Scheme 51). Firstly, substrates 103-106 were attacked by the azide ion to form unstable intermediate 110A in a potentially reversible process. Then intermediate
**110A** was oxidized to intermediate **110B** in the presence of the Cu/O₂ oxidative system. Subsequently, the rearrangement of intermediate **110B** (via its resonance structure **110C**) generated intermediate **110D** through C–C bond cleavage releasing molecular nitrogen and an aldehyde as the byproducts. Finally, tautomerization of **110D** afforded the corresponding amide **109**.

![Scheme 51. Proposed mechanism.](image)

### 4.3 From Ketones to Esters

Later, a new type of copper-catalyzed C(CO)–C(α) bond cleavage of common ketones producing esters **112** was reported by the same group (Scheme 52).\(^{[62]}\) This aerobic oxidation and oxygenation process was promoted by CuBr (10 mol %), and pyridine (2.0 equiv) in PhCl. A wide range of inactive ketones including more challenging aryl long-chain alkyl ketones selectively underwent the C(O)–C(α) bond esterification. Various primary and secondary alcohols and electron-deficient phenols, especially natural alcohols worked well under standard conditions, affording the corresponding products (**112a-g**) in moderate to good yields. Interestingly, the intramolecular esterification product **112h** was obtained in 37% yield when 1-(2-(2-hydroxyethoxy)-4-methoxyphenyl)ethanone **103h** was utilized.
which were formed from Cu way, affording intermediate bond cleavage of common ketones with primary or secondary alcohols (Scheme 53). Initially, A plausible mechanism was proposed for this new type of copper-catalyzed C(CO)−C(α)

Scheme 52. Cu-catalyzed oxidative C−C bond cleavage for C−O bond formation.

A plausible mechanism was proposed for this new type of copper-catalyzed C(CO)−C(α) bond cleavage of common ketones with primary or secondary alcohols (Scheme 53). Initially, hemiketal 113A was formed by the nucleophilic addition of ketone with alcohol in a reversible way, affording intermediate 113B by dehydration. Subsequently, Cu(II) and superoxide radical, which were formed from Cu^1 and O_2 in the presence of pyridine, reacted with 113A to produce intermediate 113C. Finally, the C−C bond and O−O bond cleavage of intermediate 113C resulted in ester 112 while releasing an aldehyde as byproducts.

Scheme 53. Proposed mechanism.
5. Rhodium(III)-Catalyzed Direct C–H Functionalization

In recent years, the transition metal-catalyzed oxidative activation reactions of C–H/N–H or C–H/O–H bond combinations with subsequent alkyne or alkene annulation have become a synthetically useful protocol for the C–C and C–X (X = N, O, etc.) bond formation. Various metals such as Pd$^{II}$, Rh$^{III}$, Ru$^{II}$ have been utilized for the catalytic construction of a wide range of heterocycles. Among them, rhodium(III)-catalyzed oxidative annulation reactions represent an attractive step-economic method to construct complex molecules from readily available starting materials. In this part, representative reactions are discussed according to the different alkenes as coupling partners. A plausible mechanism for each transformation is also briefly summarized.

5.1 General Reaction Patterns and Mechanisms of the Oxidative Coupling of Arenes with Alkenes

Generally, in the rhodium(III)-catalyzed oxidative coupling reactions between arenes with alkenes, two general reaction patterns have been reported. Firstly, the reaction of arenes 114 bearing a protic E–H (E = N, O) group with alkenes 63 under oxidative conditions initially affords an ortho-olefination product 114D (Scheme 54). In this process, the anionic E atom acts as a directing group. Then, the ortho-olefination products 114D further undergo oxidative C–E coupling and cyclization giving a five- or six-membered heterocycle. Secondly, the intermediate 114A is formed from coordination of the rhodium catalyst with the anionic atom E followed by ortho C–H activation to afford a metallacycle 114B. Then, insertion of the alkene into the Rh–C bond gives an expanded rhodacycle 114C. Subsequently, the coupled product 114D is generated along with a Rh(I) species by reductive elimination of 114C. Finally, the active Rh(III) catalyst is regenerated by oxidation.
oxidative cyclization.

allylated product in regards to the allyl partner. In addition to the cyclization products tolerated a wide range of functional groups on the anilide substrates and 24 h affording the corresponding products using a slight excess of AgSbF$_6$ as oxidant and t-AmOH as solvent at 120 °C for 24 h affording the corresponding products 117 in moderate yields (Scheme 56). The reaction tolerated a wide range of functional groups on the anilide substrates and proved to be less versatile in regards to the allyl partner. In addition to the cyclization products 117, a small amount of the allylated product 118 was obtained, which could be converted into cyclization products under standard reaction conditions, indicating that reaction involved C–H bond allylation followed by oxidative cyclization.

Scheme 54. Two general reaction pathways between alkenes with arenes.

5.1.1 Rhodium(III)-Catalyzed [3+2] Cycloaddition Reactions

In 2013, Saá and co-workers developed a rhodium(III)-catalyzed direct intermolecular tandem C–H allylation and oxidative cyclization of acetanilides 115 with allyl carbonates 116a using a slight excess of AgSbF$_6$ as salt, Cu(OAc)$_2$ as oxidant and t-AmOH as solvent at 120 °C for 24 h affording the corresponding products 117 in moderate yields (Scheme 56).[68] The reaction tolerated a wide range of functional groups on the anilide substrates and proved to be less versatile in regards to the allyl partner. In addition to the cyclization products 117, a small amount of the allylated product 118 was obtained, which could be converted into cyclization products under standard reaction conditions, indicating that reaction involved C–H bond allylation followed by oxidative cyclization.
Scheme 56. Rhodium(III)-catalyzed oxidative cyclization of acetonilides with allyl carbonates.

The proposed mechanism for this rhodium(III)-catalyzed direct intermolecular tandem C–H allylation and oxidative cyclization is depicted in the Scheme 57. Firstly, the intermediate rhodacycle **115A** was formed from anilide **115** under standard reaction conditions. Then, migratory insertion of the allyl double bond into the Rh–C bond afforded a seven-membered rhodacycle **115B** with the carbonate oxygen chelating the rhodium species. Subsequently, β-oxygen elimination gave the new olefin-coordinated intermediate **115C** through an oxidative Mizoroki-Heck/β-elimination pathway. Alternatively, the same intermediate **115C** could also be formed by coordination of the allyl-bearing carbonate oxygen to the Rh(III) intermediate **115B′**, which facilitated an intramolecular S$_{2}$ process. Finally, the corresponding product **117** was released by β-hydrogen elimination and isomerization from intermediate **115C**. The active rhodium species regenerated from Cp*Rh(I) by copper(II) acetate. The appearance of small amounts of **118** was attributable to protonolysis of intermediate **115C**.

Scheme 57. Proposed catalytic cycle.
In 2015, Glorius and co-workers described a rhodium(III)-catalyzed synthesis of 1-aminooindolines 120 from arylsubstituted diazenecarboxylates 119 and alkenes 57 involving [Cp*RhCl₂]₂ (2.5 mol %) and AgOAc (10 mol %) in a mixture of DCE with HOAc at room temperature, providing the corresponding products in the moderate to good yields (Scheme 58).[69] The authors noted that 1-aminooindoles 121 could be formed in good yields when AgOAc was used as the external oxidant at 90 °C. This intermolecular annulation proceeded well under mild conditions, and tolerated a broad scope with respect to the substituents in both arylsubstituted diazenecarboxylates and alkenes.

Scheme 58. Rhodium(III)-catalyzed cyclization of arylsubstituted diazenecarboxylates and alkenes.

Two years later, Xi and co-workers disclosed a rhodium(III)-catalyzed C–H activation/[3+2] annulation of azobenzenes 122 with vinyl ketones or acrylamides 123 for the synthesis of 2-acyl (NH) indoles 124 in moderate to good yields (Scheme 59).[70] A variety of azobenzenes 122 were tolerated in this transformation. This reaction demonstrated a broad scope and high functional tolerance with respect to the vinyl ketones 123. When acrylates 57 were used under same reaction conditions, various indazoles 125 were obtained in good yields. Some examples are shown in Scheme 59.
20 authors found that compounds products respect to azomethine ylides in this transformation to form 1,2-dihydrophthalazines azomethine ylides.


5.1.2 Rhodium(III)-Catalyzed [4+1] Cycloaddition Reactions

In 2012, Li and co-workers reported a rhodium(III)-catalyzed oxidative coupling of azomethine ylides 126 with olefins 20 (Scheme 60)\(^{[7]}\). A wide range of olefins 20 were tolerated in this transformation to form 1,2-dihydrophthalazines 127a-d in moderate to good yields. With respect to azomethine ylides 126, various functional groups on the arenes afforded the desired products 127e-i, regardless of substitution positions and electronic properties. Furthermore, the authors found that compounds 128a-g were also obtained in moderate to good yields when olefins 20 and AgOAc were used in greater excess.
Selected examples:

- $R^2 = Br$, 127a, 88%
- $R^2 = Me$, 127b, 77%
- $R^2 = Et$, 127c, 71%
- $R^2 = iBu$, 127d, 66%

- $R^2 = Br$, 128a, 88%
- $R^2 = Me$, 128b, 67%
- $R^2 = Et$, 128c, 62%
- $R^2 = iBu$, 128d, 79%

Scheme 60. Rhodium(III)-catalyzed oxidative coupling of azomethine ylides with olefins.

In 2014, Xi and co-workers described a rhodium(III)-catalyzed cascade oxidative alkenylation/cyclization of picolinamides 129 and alkenes 57 with high regio- and stereoselectivity in the presence of $[\text{Cp}^*\text{RhCl}_2]$ and Cu(OAc)$_2$ affording pyrido pyrrolone derivatives 130 in moderate to excellent yields (Scheme 61). They demonstrated a broad and high functional group tolerance with respect to picolinamides 129 and alkenes 57. Moreover, copper(II) acetate could also be used in catalytic amounts with O$_2$ serving as terminal oxidant.
of ethylene gave the corresponding alkenes 5.

5.1.3 Rhodium(III)-Catalyzed [4+2] Cycloaddition Reactions

In 2011, Glorius and co-workers developed a [4+2] annulation of the benzamides 131 and alkenes 57 in the presence of the [Cp*RhCl₂]₂ (2.5 mol %), CsOPiv (30 mol %) and PivOH (20 mol %) in ethanol at 80 °C to afford the corresponding tetrahydroisoquinolinone products 132 in moderate to good yields (Scheme 62).[73] Various substituted alkenes 57 were tolerated in this transformation (132a-e), such as styrenes and acrylates. Impressively, treatment of 131a with 5 bar of ethylene gave the corresponding product 132f in excellent yield.

Three years later, the same group reported an efficient rhodium(III)-catalyzed redox-neutral C–H activation/cyclization/isomerization of aromatic oxime esters 133 with diverse 1,3-dienes 134 for the synthesis of isoquinolines 135 resulting in complete regioselectivity in moderate to
good yields (Scheme 63). The reaction exhibited a broad scope for aromatic oxime esters 133, and 1,3-dienes 134. To expand the substrate scope, the authors used the aromatic oxime ester 133a to react with simple acrylate 57b in the presence of AgOAc as an external oxidant under the standard conditions, leading to isoquinoline 135h in 91% yield (Scheme 64).

Scheme 63. Rhodium(III)-catalyzed annulation of aromatic oxime esters with 1,3-dienes.

Scheme 64. Synthetic application.

In 2014, a facile method for the preparation of 3,4-unsubstituted isoquinolones 137 by rhodium-catalyzed C–H activation/annulation was reported by Raw and co-workers, using vinyl acetate 57 as a cheap and safe coupling partner under mild reaction conditions (Scheme 65). Under the optimal conditions, a wide range of available substituted benzamides 129 reacted well to afford the corresponding products 136 in moderate to excellent yields.
transformation to afford the corresponding products (withdrawing groups were well tolerated to generate the corresponding products at 60 ℃ for 12 h (Scheme 66).

In 2013, Glorius and co-workers developed a novel and efficient method for the synthesis of Rhodium(III)-catalyzed [4+3] Cycloaddition Reactions. Scheme 65.

In 2013, Glorius and co-workers developed a novel and efficient method for the synthesis of Rhodium(III)-catalyzed [4+3] Cycloaddition Reactions.

5.1.4 Rhodium(III)-Catalyzed [4+3] Cycloaddition Reactions

In 2013, Glorius and co-workers developed a novel and efficient method for the synthesis of azepinones 138 utilizing benzamides 131 with α,β-unsaturated aldehydes and ketones 137 in the presence of [Cp*RhCl₂][1,1] (2.5 mol %), AgSbF₆ (10 mol %) and PivOH (2.0 equiv) in 1,4-dioxane at 60 ℃ for 12 h (Scheme 66). Various benzamides 131 bearing electron-donating/electron-withdrawing groups were well tolerated to generate the corresponding products 138 in moderate to good yields (138a-e). In addition to acrolein, a few ketones were introduced in this transformation to afford the corresponding products (138f-h).
Scheme 66. Rhodium(III)-catalyzed annulation of benzamides with carbonyl compounds.

Scheme 67. Proposed mechanism.

The proposed mechanism shown in the Scheme 67. Initially, coordination of the benzamide $\text{131}$ to a $[\text{Cp}^*\text{Rh}^{\text{III}}]$ species enabled the formation of intermediate $\text{131A}$ by regioselective C–H bond cleavage. This rhodacycle could coordinate to $\text{137}$ to form $\text{131B}$, which underwent alkene insertion giving intermediate $\text{131C}$. Subsequently, the protonolysis of $\text{131C}$ delivered the carbonyl intermediate $\text{131D}$. Then, the formed Rh–N bond could add across the carbonyl group affording
the cyclorhodated intermediate 131E, which underwent protonolysis to produce seven-membered ring products 131F with release of the active [RhIII\(\text{Cp}^*\)] species. Finally, rhodium(III)-catalyzed dehydration of 131F gave to the desired enamide product 138.

In the same year, Cui and co-workers reported a rhodium(III)-catalyzed C–H activation/[4+3] cycloaddition of benzamides 131 with vinylcarbenoids 139 as three-carbon components to access corresponding azepinones 140 in moderate to excellent yields (Scheme 68).[77] This transformation occurred by a concerted metatation/deprotonation pathway to form rhodacycle 131A, which coordinated with vinylcarbenoids 139 to form intermediate 140A. Subsequent, 1,3-allylic migration afforded intermediate 140B. Then, C–N bond formation/N–O bond cleavage followed by protonation enabled the catalytic cycle. Additionally, derivation of the product was conducted with the unsaturated ester units in these azepinones. For example, compound 141 and 142 were obtained in good yields when product 140a was treated with \(m\)-CPBA and DIBAL-H, respectively (Scheme 69).

![Scheme 68. Rhodium(III)-catalyzed annulation of benzamides with vinylcarbenoides.](image-url)
Scheme 69. Synthetic applications.
II Experimental Section

6. Copper-Catalyzed Dealkylation of NH-Sulfoximines

In recent years, sulfoximines have been applied as pharmaceuticals and bioactive compounds\[^{4}\] as well as ligands\[^{3d-\,\,3l}\] and chiral auxiliaries\[^{10}\] in asymmetric syntheses. Commonly, the heteroatomic sulfoximine core is characterized by a high chemical stability making it attractive for further functionalizations, including heterocycle formation. However, a different facet of sulfoximine chemistry was illustrated in early work by Johnson\[^{78}\] and Cram\[^{79}\]. They demonstrated the preparation of sulfonamides from sulfoximines by applying reductive processes (Scheme 70).

(a) C. R. Johnson and co-workers

\[ \text{MeSO}_2\text{NH} \xrightarrow{\text{Al(Hg)}} \text{MeSO}_2\text{NMe} \]  

(b) D. J. Cram and co-workers

\[ \text{MeSO}_2\text{NH} \xrightarrow{\text{TsCl, pyridine}} \text{MeSO}_2\text{N-Ts} \]

Scheme 70. Demethylation of sulfoximines

In 2015, Bolm and co-workers reported an iron-catalyzed dealkylative acylation of N-alkylsulfoximines to afford N-acyl or N-arylsulfoximine derivatives 34 in good yields. Subsequent cleavage of the acyl or aryl group under acidic conditions generated a synthetically valuable NH-sulfoximine in excellent yields (Scheme 71).\[^{80}\]

\[ (\text{R}^3\text{CO})_2\text{O}, \text{FeCl}_3 (2.5 \text{ mol } \%) \xrightarrow{\text{HBF}_4 (2.0 \text{ equiv})} \text{MeCN, 110 °C, 72 h} \xrightarrow{\text{HCl (12 M, uq)}} \text{DCM, rt, 2 h} \xrightarrow{\text{R'}^2 \text{SO}_2\text{N}} \text{MeS} \]

Scheme 71. Iron-catalyzed acylative dealkylation of N-alkylsulfoximines.
6.1 Results and Discussion

6.1.1 Research Objective

Most of the reported approaches for the synthesis of sulfonimidamides are multistep transformations with protection/deprotection sequences (Scheme 72b). Stimulated by the significant number of reports on C–C bond cleavage reactions, and feeling challenged by observations recently made in iron-catalyzed N-demethylations of sulfoximines, we developed transition metal-catalyzed sulfoximine conversions leading to sulfonimidamides by unprecedented sequential dealkylation and amine coupling (Scheme 72a).

![Scheme 72. Methods for the preparation of sulfonimidamides](image)

6.1.2 Optimization of Reaction Conditions

In the initial screening, sulfoximine 5a and piperidine 143a were chosen as representative starting materials. The results of the optimization of the reaction condition were shown in Table 1. Treating a combination of 5a and 143a in toluene with 20 mol % of Cu(OAc)$_2$ and keeping the resulting mixture for 5 h at 110 °C under an atmosphere of dioxygen gave the desired product 144aa in 40 % yield (Table 1, entry 1). No product formation was observed when the reaction was performed under argon (Table 1, entry 2). In the absence of Cu(OAc)$_2$ no reaction occurred (Table 1, entry 3). Extending the reaction time from 5 h to 8 h resulted in a decreased yield of 144aa (32 %). However, a positive outcome was observed when the reaction was stopped after 3 h providing 144aa in 48% yield (Table 1, entries 4-6). The unique role of copper became apparent.
by the following experiments: Fe(OAc)$_2$, and Pd(OAc)$_2$ were inactive (Table 1, entries 7-9). When THF, dichloroethane, or acetonitrile were applied as solvent, the reaction led to only traces of product (Table 1, entries 10-12). Among several copper(I) salts CuCl, CuTC, CuBr and CuI, the CuTC proved optimal providing 144aa in 72% yield (Table 1, entries 13-16). As a result, the reaction conditions described in entry 14 of Table 1 were selected for the subsequent investigations.

**Table 1. Optimization of reaction conditions**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>t (h)</th>
<th>Atmosphere</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu(OAc)$_2$</td>
<td>toluene</td>
<td>5</td>
<td>O$_2$</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>Cu(OAc)$_2$</td>
<td>toluene</td>
<td>5</td>
<td>Ar</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>none</td>
<td>toluene</td>
<td>5</td>
<td>O$_2$</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Cu(OAc)$_2$</td>
<td>toluene</td>
<td>8</td>
<td>O$_2$</td>
<td>32</td>
</tr>
<tr>
<td>5</td>
<td>Cu(OAc)$_2$</td>
<td>toluene</td>
<td>3</td>
<td>O$_2$</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>Cu(OAc)$_2$</td>
<td>toluene</td>
<td>2</td>
<td>O$_2$</td>
<td>44</td>
</tr>
<tr>
<td>7</td>
<td>Fe(OAc)$_2$</td>
<td>toluene</td>
<td>3</td>
<td>O$_2$</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>Pd(OAc)$_2$</td>
<td>toluene</td>
<td>3</td>
<td>Ar</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>Pd(OAc)$_2$</td>
<td>toluene</td>
<td>3</td>
<td>O$_2$</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>Cu(OAc)$_2$</td>
<td>THF</td>
<td>3</td>
<td>O$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>11</td>
<td>Cu(OAc)$_2$</td>
<td>DCE</td>
<td>3</td>
<td>O$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>12</td>
<td>Cu(OAc)$_2$</td>
<td>MeCN</td>
<td>3</td>
<td>O$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>13</td>
<td>CuCl</td>
<td>toluene</td>
<td>3</td>
<td>O$_2$</td>
<td>46</td>
</tr>
<tr>
<td>14</td>
<td>CuTC</td>
<td>toluene</td>
<td>3</td>
<td>O$_2$</td>
<td>72</td>
</tr>
</tbody>
</table>
15  CuBr  toluene  3  O₂  36
16  Cul  toluene  3  O₂  25

Reaction conditions: 5a (0.3 mmol), 143a (8.0 equiv), catalyst (20 mol %), solvent (1.0 mL), 110 °C, O₂, 3 h.

6.1.3 Substrate Scope of Sulfoximines and Amines

With the optimized conditions in hand, we examined the scope with respect to the NH-sulfoximines (Table 2). Piperidine 143a was kept as representative reaction partner. Para-substituted sulfoximines reacted well, affording the corresponding products in yields ranging from 48% to 78% (Table 2, entries 1-8). For example, the best results in this series were obtained with the p-chloro, p-bromo, and p-nitro-substituted substrates leading to 144ea, 144fa, and 144ga, respectively, which could prove advantageous for subsequent product functionalizations. Carboxyl-containing product 144ha could also be important in that respect, albeit it was only obtained in 48% yield. 2-Naphthyl-substituted sulfoximine 5i provided the corresponding sulfonimidamide 144ia in 65% yield (Table 2, entry 9). The reactions of meta-substituted sulfoximines could easily be converted to products 144ja and 144ka in good yields (81% and 76%, respectively). Presumably due to steric compression, the ortho-substituted sulfoximine 5l yielded the product 133la in only 27% (Table 2, entry 12).

Table 2. Scope of sulfoximines.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R¹</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph (5a)</td>
<td>144aa</td>
<td>72%</td>
</tr>
</tbody>
</table>
2  4-MeC₆H₄ (5b)  

3  4-OMeC₆H₄ (5c)  

4  4-FC₆H₄ (5d)  

5  4-ClC₆H₄ (5e)  

6  4-BrC₆H₄ (5f)  

7  4-NO₂C₆H₄ (5g)  

<table>
<thead>
<tr>
<th></th>
<th>Reaction</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4-MeC₆H₄ (5b)</td>
<td>65%</td>
</tr>
<tr>
<td>3</td>
<td>4-OMeC₆H₄ (5c)</td>
<td>62%</td>
</tr>
<tr>
<td>4</td>
<td>4-FC₆H₄ (5d)</td>
<td>65%</td>
</tr>
<tr>
<td>5</td>
<td>4-ClC₆H₄ (5e)</td>
<td>78%</td>
</tr>
<tr>
<td>6</td>
<td>4-BrC₆H₄ (5f)</td>
<td>75%</td>
</tr>
<tr>
<td>7</td>
<td>4-NO₂C₆H₄ (5g)</td>
<td>75%</td>
</tr>
</tbody>
</table>
Next, we investigated the scope of the amines (Table 3). The studies were performed with NH-sulfoximine 5a as representative coupling partner, and the reaction conditions were kept as before. Various substituted piperidines and analogs could be applied leading to the corresponding products (144ab-144ag) in yields up to 73% (Table 3, entries 1-6). A problematic case was the
formation of sulfonimidamide 144ab, which was obtained in only trace amounts from the reaction of NH-sulfoximine 5a with 2-methyl piperidine 143b. However, product 144ac was obtained from NH-sulfoximine 5a and 3-methyl piperidine 143c in 71% yield as 1:1 mixture of diastereomers (using racemic starting materials). Steric effects during the coupling process could be the reason for the low yield here. To our surprise, pyrrolidine 143h and azepane 143i did not react equally well affording sulfonimidamides 144ah and 144ai in only 30% and 28% yield, respectively. Finally, when diethylamine 143j was chosen to react with NH-sulfoximine 5a, 144aj was formed in only trace amounts.

Table 3. Scope of amines.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amine (143b-j)</th>
<th>Product (144ab-aj)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>143b</td>
<td>144ab</td>
<td>trace</td>
</tr>
<tr>
<td>2</td>
<td>143c</td>
<td>144ac</td>
<td>71% (dr = 1:1)</td>
</tr>
<tr>
<td>3</td>
<td>143d</td>
<td>144ad</td>
<td>73%</td>
</tr>
</tbody>
</table>
Reaction conditions: 5a (0.3 mmol), 143 (2.4 mmol, 8.0 equiv), catalyst (20 mol %), solvent (1.0 mL), 110 °C, O2, 3 h. a)Performed with only 5.0 equiv of 143.
Until this stage of the study, only S-aryl-S-methyl sulfoximines had been applied. Then other S-aryl-S-alkyl-sulfoximines were examined under standard conditions. With S-benzyl-S-phenyl-sulfoximine 5o and 143a as substrates, 144aa was obtained in 75% yield (Scheme 73). Delightfully we noted that by using substrate 5o, 144ah and 144ai could be accessed in much better yields (79% and 68%, respectively). However, the formation of 144aj remained difficult.

**Scheme 73.** Reaction of S-benzyl-S-phenylsulfoximine with secondary amines. Standard conditions: 5o (0.3 mmol), 143 (2.4 mmol), CuTC (20 mol %), toluene (1.0 mL), 110 °C, 3 h under O₂.

**6.1.4 Control Experiment and Mechanism**

To gain insight into the reaction mechanism, a few of control experiments were conducted (Scheme 74). Firstly, product 144aa was treated with paraformaldehyde (1.2 equiv), affording N-formyl sulfonimidamide 145 (8%), which was detected as byproduct in the coupling of 5a and 144a under standard reaction conditions in 10% yield (Scheme 74a). Then, in the presence of 2,2,6,6-tetramethylpiperidine N-oxide (TEMPO) or 2,6-di-tert-butyl-4-methylphenol (BHT), the reaction between 5a and 143a was inhibited (Scheme 74b). Using (S)-S-phenyl-S-methyl sulfoximine in the coupling with 143a provided racemic 144aa (Scheme 74c). N-Functionalized sulfoximines 56a-b and analogous sulfone 146 did not react under standard conditions (Scheme 74d).
Based on the aforementioned results and earlier work,[61,62,81] a plausible mechanism for this new redox-neutral S–C to S–N bond exchange reaction was proposed (Scheme 75). The process was initiated by an interaction between the copper salt and the sulfoximine. This copper/substrate coordination was hampered when the sulfoximine nitrogen was substituted. Subsequently sulfoximine 5 was deprotonated and a single electron transfer (SET) took place to generate peroxy species 5A in the presence of the Cu/O₂ oxidative system. Peroxy species 5A lost one oxygen to give 5C, presumably via homolysis of copper peroxy species 5B. When species C expelled formaldehyde, sulfur-centered radical species 5D was formed. Finally, products 144 were obtained from the reaction of 5D with amine 143 under the copper catalysis by deprotonation and new S–N bond formation. When S-benzyl-containing sulfoximine 5o was applied as starting material in this reaction, all of the aforementioned steps are analogous, and due to the higher stabilities of the anionic and radical intermediates leading to higher reactivities.
6.1.5 Summary

In summary, we developed copper-catalyzed dealkylation/amination sequences providing sulfonimidamides from unprotected sulfoximines under an atmosphere of dioxygen in moderate to good yields. Mechanistic studies suggest the involvement of radical species, which might also prove useful as intermediates of other synthetically attractive products.

6.2 Experimental
6.2.1 General Information

Unless otherwise noted, copper salts and amines were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. The reactions were monitored by thin layer chromatography (TLC) using silica gel 60 F$_{254}$ aluminum sheets. Flash column chromatography purifications were performed using silica gel 60 (0.040-0.063 mm).

$^1$H NMR spectra were recorded at 400 MHz or 600 MHz. The solvent for NMR spectroscopy was CDCl$_3$ unless noted otherwise. Chemical shifts are reported in delta ($\delta$) units in parts per million (ppm) relative to the singlet (0 ppm) for tetramethylsilane (TMS). Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz) and integration. $^{13}$C NMR spectra were recorded at 100 MHz or 150 MHz. Chemical shifts are reported in ppm relative to 77.0 ppm for CDCl$_3$. High resolution
mass spectra (HRMS) were measured on a Thermo Scientific LTQ Orbitrap XL spectrometer with positive ion mode. Melting points were determined in open-end capillary tubes on a Büchi B-540 melting point apparatus.

6.2.2 General Procedure for the Synthesis of Sulfonimidamides 144

\[ R^1 \rightleftharpoons S \rightleftharpoons N^+ \]

A sealed tube (25 mL) equipped with a stir bar was charged with sulfoximine 5 (0.3 mmol), amine 143 (2.4 mmol), and CuTC (11.4 mg, 20 mol %), followed by addition of dry toluene (1.0 mL). The tube was flushed with dioxygen for 1 min and then sealed with a teflon lined cap. The reaction mixture was stirred at 110 °C for 3 h. After cooling to ambient temperature, the product was purified by column chromatography on silica gel with n-pentane/ethyl acetate as eluent affording 144.

6.2.3 Characterization Data of Sulfonimidamides

1-(Phenylsulfonimidoyl)piperidine (144aa)

Yellow solid, melting point: 105 – 106 °C, 72% yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.83 – 7.81 (m, 2H), 7.52 – 7.42 (m, 3H), 2.93 – 2.90 (m, 4H), 2.44 (br s, 1H), 1.57 – 1.52 (m, 4H), 1.33 – 1.28 (m, 2H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 136.0, 131.9, 128.4, 127.7, 47.7, 25.4, 23.4. MS (EI): \(m/z\) = 224 (9, \(M^+\)), 209 (1), 208 (8), 140 (11), 84 (59), 77 (26). IR (ATR): \(\nu\) = 3234, 2936, 1738, 1611, 1447, 1248, 1139, 982, 693 (cm\(^{-1}\)). HRMS \(m/z\): Calcd for \([C_{11}H_{16}N_{2}OS+H]^+\): 225.1062. Found: 225.1060.

1-(4-Methylphenylsulfonimidoyl)piperidine (144ba)

Yellow solid, melting point: 82 – 83 °C, 65% yield. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.75 (d, \(J = 7.7\) Hz, 2H), 7.29 (d, \(J = 7.2\) Hz, 2H), 2.96 – 2.95 (m, 4H), 2.41 – 2.40 (m, 4H), 1.62 – 1.58 (m, 4H), 1.38 – 1.34 (m, 2H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm) 142.7, 133.1, 129.2, 128.0, 47.9, 25.6, 23.6, 21.4. MS (EI): \(m/z\)

1-(4-Methoxyphenylsulfonimidoyl)piperidine (144ca)

Yellow solid, melting point: 65 – 66 °C, 62% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.81 – 7.77 (m, 2H), 6.97 – 6.93 (m, 2H), 3.85 (s, 3H), 2.96 – 2.93 (m, 4H), 2.38 (br s, 1H), 1.62 – 1.57 (m, 4H), 1.38 – 1.32 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 162.5, 130.0, 127.7, 113.7, 55.5, 47.9, 25.6, 23.6. MS (EI): m/z = 254 (7, M'), 170 (11), 107 (7), 84 (100). IR (ATR): ν = 3239, 2931, 1592, 1459, 1245, 1121, 1107, 700 (cm⁻¹). HRMS m/z: Calcd for [C₁₂H₁₈N₂OS⁺H]⁺: 255.1167. Found: 255.1163.

1-(4-Fluorophenylsulfonimidoyl)piperidine (144da)

Yellow solid, melting point: 63 – 64 °C, 65% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.88 – 7.84 (m, 2H), 7.17 – 7.12 (m, 2H), 2.95 – 2.93 (m, 4H), 2.46 (br s, 1H), 1.61 – 1.56 (m, 4H), 1.38 – 1.32 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 164.8 (d, J = 253.0 Hz), 132.2, 130.4 (d, J = 9.0 Hz), 115.7 (d, J = 22.0 Hz), 47.8, 25.5, 23.5. ¹⁹F NMR (282 MHz, CDCl₃) δ −106.70 – −106.88 (m). MS (EI): m/z = 242 (3, M'), 226 (2), 158 (6), 95 (7), 84 (19). IR (ATR): ν = 3239, 2932, 2834, 1595, 1467, 1249, 1132, 988, 700 (cm⁻¹). HRMS m/z: Calcd for [C₁₁H₁₃FN₂O⁻S⁺H]⁺: 243.0967. Found: 243.0961.

1-(4-Chlorophenylsulfonimidoyl)piperidine (144ea)

Yellow solid, melting point: 77 – 78 °C, 78% yield. ¹H NMR (600 MHz, CDCl₃) δ (ppm) 7.78 – 7.76 (m, 2H), 7.44 – 7.42 (m, 2H), 2.94 – 2.92 (m, 4H), 2.49 (br s, 1H), 1.59 – 1.55 (m, 4H), 1.36 – 1.32 (m, 2H). ¹³C NMR (150 MHz, CDCl₃) δ (ppm) 138.5, 134.6, 129.3, 128.8, 47.8, 25.4, 23.4. MS (EI): m/z = 258 (6, M'), 242 (5), 174 (12), 111 (21), 84 (52). IR (ATR): ν = 3251, 2932, 2834, 1595, 1467, 1249, 1132, 988, 707 (cm⁻¹). HRMS m/z: Calcd for [C₁₁H₁₃ClN₂O⁻S⁺H]⁺: 259.0672. Found: 259.0665.
1-(4-Bromophenylsulfonimidoyl)piperidine (144fa)

Yellow solid, melting point: 89 – 90 °C, 75% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.74 – 7.71 (m, 2H), 7.63 – 7.60 (m, 2H), 2.97 – 2.94 (m, 4H), 2.46 (br s, 1H), 1.63 – 1.57 (m, 4H), 1.40 – 1.34 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 135.3, 131.8, 129.5, 127.1, 47.8, 25.5, 23.5. MS (EI): m/z = 302 (4, M⁺), 286 (3), 218 (3), 155 (10), 84 (35). IR (ATR): ν = 3254, 2931, 1744, 1455, 1250, 1066, 982, 714 (cm⁻¹). HRMS m/z: Calcd for [C₁₁H₁₅BrN₂OS+H]⁺: 303.0167. Found: 303.0161.

1-(4-Nitrophenylsulfonimidoyl)piperidine (144ga)

Yellow solid, melting point: 135 – 136 °C, 75% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.35 – 8.31 (m, 2H), 8.07 – 8.03 (m, 2H), 3.03 – 3.00 (m, 4H), 2.61 (br s, 1H), 1.64 – 1.58 (m, 4H), 1.42 – 1.36 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 149.8, 142.6, 129.0, 123.9, 47.8, 25.5, 23.4. MS (EI): m/z = 269 (41, M⁺), 254 (16), 253 (100), 223 (2), 185 (61), 122 (11), 84 (36). IR (ATR): ν = 3282, 2938, 1740, 1519, 1348, 1233, 1086, 929, 698(cm⁻¹). HRMS m/z: Calcd for [C₁₁H₁₅N₃O₃S+H]⁺: 270.0912. Found: 270.0907.

Methyl 4-(piperidine-1-sulfonimidoyl)benzoate (144ha)

Yellow solid, melting point: 110 – 111 °C, 48% yield. ¹H NMR (600 MHz, CDCl₃) δ (ppm) 8.14 – 8.12 (m, 2H), 7.93 – 7.91 (m, 2H), 3.93 (s, 3H), 2.97 – 2.96 (m, 4H), 2.53 (br s, 1H), 1.60 – 1.56 (m, 4H), 1.37 – 1.33 (m, 2H). ¹³C NMR (150 MHz, CDCl₃) δ (ppm) 165.8, 140.3, 133.2, 129.8, 127.8, 52.5, 47.8, 25.5, 23.5. MS (EI): m/z = 282 (12, M⁺), 267 (2), 266 (14), 198 (12), 135 (18), 84 (48). IR (ATR): ν = 3288, 3053, 2319, 1732, 1462, 1252, 1091, 944, 733(cm⁻¹). HRMS m/z: Calcd for [C₁₃H₁₈N₂O₃S+H]⁺: 283.1116. Found: 283.1108.
1-(Naphthalene-2-sulfonimidoyl)piperidine (144ia)

Yellow solid, melting point: 102 – 103 °C, 65% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 8.43 (s, 1H), 7.96 – 7.87 (m, 4H), 7.61 – 7.55 (m, 2H), 3.05 – 3.01 (m, 4H), 2.57 (br s, 1H), 1.61 – 1.58 (m, 4H), 1.34 – 1.31 (m, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 134.5, 133.4, 132.1, 129.1, 128.8, 128.6, 128.3, 127.7, 127.1, 123.6, 47.9, 25.6, 23.5. MS (EI): $m/z$ = 274 (22, M$^+$), 258 (1), 190 (5), 147 (8), 127 (85), 84 (92). IR (ATR): $\nu$ = 3262, 2925, 2090, 1613, 1455, 1254, 1132, 942, 703 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{15}$H$_{18}$N$_2$OS+H]$^+$: 275.1218. Found: 275.1213.

1-(3,5-Dichlorophenylsulfonimidoyl)piperidine (144ja)

Yellow solid, melting point: 88 – 89 °C, 65% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.75 (d, $J$ = 7.7 Hz, 2H), 7.52 (t, $J$ = 7.5 Hz, 1H), 3.01 – 3.00 (m, 4H), 2.53 (br s, 1H), 1.64 – 1.60 (m, 4H), 1.43 – 1.39 (m, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 139.5, 135.6, 132.1, 126.1, 47.9, 25.6, 23.4. MS (EI): $m/z$ = 292 (7, M$^+$), 276 (3), 208 (3), 145 (13), 84 (16). IR (ATR): $\nu$ = 3244, 2935, 2082, 1743, 1445, 1256, 1073, 973, 694 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{11}$H$_{14}$Cl$_2$N$_2$OS+Na]$^+$: 315.0102. Found: 315.0100.

1-(3-Bromophenylsulfonimidoyl)piperidine (144ka)

Yellow oil, 76% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 8.01 (s, 1H), 7.78 (d, $J$ = 7.7 Hz, 1H), 7.66 (d, $J$ = 7.7 Hz, 1H), 7.36 (d, $J$ = 7.4 Hz, 1H), 2.99 – 2.97 (m, 4H), 2.48 (br s, 1H), 1.62 – 1.58 (m, 4H), 1.40 – 1.36 (m, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 138.3, 135.1, 130.7, 130.1, 126.4, 122.7, 47.9, 25.6, 23.5. MS (EI): $m/z$ = 302 (6, M$^+$), 155 (16), 84 (59). IR (ATR): $\nu$ = 3279, 2931, 2096, 1569, 1445, 1253, 1126, 923, 684 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{11}$H$_{15}$BrN$_2$OS+H]$^+$: 303.0167. Found: 303.0661.

1-(2-Chlorophenylsulfonimidoyl)piperidine (144la)

Yellow oil, 27% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.14 (dd, $J$ = 7.9, 1.7 Hz, 1H), 7.49 (dd, $J$ = 7.8, 1.5 Hz, 1H), 7.43 (td, $J$ = 7.6, 1.8 Hz, 1H), 7.38 – 7.34 (m, 1H), 3.30 – 3.17 (m, 4H), 2.97 (br s, 1H), 1.63 – 1.50 (m, 6H). $^{13}$C NMR (100
MHz, CDCl$_3$ $\delta$ (ppm) 138.2, 132.8, 132.1, 131.6, 131.5, 126.8, 46.6, 25.8, 24.0. MS (EI): $m/z$ = 258 (7, M$^+$), 242 (2), 223 (5), 174 (5), 111 (15), 84 (78). IR (ATR): $\nu$ = 3256, 2932, 1592, 1449, 1248, 1121, 934, 708 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{11}$H$_{15}$ClN$_2$OS+H]$^+$: 259.0672. Found: 259.0667.

3-Methyl-1-(phenylsulfonimidoyl)piperidine (144ac)  

Yellow solid, melting point: 112 – 113 °C, 71% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.86 – 7.84 (m, 2H), 7.55 – 7.46 (m, 3H), 3.73 – 3.65 (m, 2H), 2.45 (br s, 1H), 2.12 (qd, $J$ = 11.6, 2.7 Hz, 1H), 1.79 (td, $J$ = 10.8, 2.8 Hz, 1H), 1.69 – 1.49 (m, 4H) 0.83 (dd, $J$ = 6.4, 2.3 Hz, 3H), 0.79 – 0.70 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 136.2, 136.1, 132.0, 128.6, 127.9, 127.8, 54.4, 53.9, 47.6, 47.1, 32.1, 32.0, 31.1, 30.9, 25.0, 24.9, 19.0, 18.9. MS (EI): $m/z$ = 238 (5, M$^+$), 222 (1), 140 (7), 98(77), 77 (22). IR (ATR): $\nu$ = 3246, 2932, 1739, 1593, 1453, 1246, 1127, 995, 703 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{12}$H$_{18}$N$_2$OS+H]$^+$: 239.1218. Found: 239.1212.

4-Methyl-1-(phenylsulfonimidoyl)piperidine (144ad)  

Yellow solid, melting point: 56 – 57 °C, 73% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.80 – 7.77 (m, 2H), 7.46 – 7.38 (m, 3H), 3.75 – 3.72m, 2H), 2.47 (br s, 1H), 2.06 – 2.04 (m, 2H), 1.55 – 1.54 (m, 2H), 0.79 – 0.77 (d, $J$ = 6.6, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 135.9, 131.8, 128.3, 127.6, 47.3, 46.8, 33.5, 33.4, 29.8, 21.1. MS (EI): $m/z$ = 238 (6, M$^+$), 222 (1), 222 (10), 140 (9), 98(97), 77 (19). IR (ATR): $\nu$ = 3249, 2939, 1739, 1449, 1232, 1112, 975, 701 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{12}$H$_{19}$N$_2$OS+H]$^+$: 239.1218. Found: 239.1216.

Methyl 1-(phenylsulfonimidoyl)piperidine-4-carboxylate (144ae)  

Yellow solid, melting point: 105 – 106 °C, 61% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.86 – 7.84 (m, 2H), 7.56 – 7.54 (m, 1H), 7.49 (dd, $J$ = 10.5, 4.7 Hz, 2H), 3.72 (dd, $J$ = 7.9, 3.9 Hz, 2H), 3.62 (s, 3H), 2.51 (br s, 1H), 2.34 (t, $J$ = 11.5 Hz, 2H), 2.19 (tt, $J$ = 10.9, 4.0 Hz, 1H), 1.93 (dd, $J$ = 9.1, 4.4 Hz, 2H), 1.75 (qqd, $J$ = 11.2, 3.9, 1.7 Hz, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 174.4,
135.9, 132.3, 128.7, 127.8, 51.8, 46.5, 46.2, 40.0, 27.9, 27.8. MS (EI): *m/z* = 282 (2, M⁺), 142(100), 140 (9), 77 (40), 59 (8). IR (ATR): ν = 3266, 2951, 1730, 1444, 1362, 1235, 1138, 986, 693 (cm⁻¹). HRMS *m/z*: Calcd for [C₁₃H₁₅N₂O₂S+Na⁺]: 305.0936. Found: 305.0934.

**4-(Phenylsulfonimidoyl)morpholine (144af)**

Yellow solid, melting point: 103 – 104 °C, 56% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 2H), 3.70 – 3.68, (m, 4H), 2.98 – 2.96 (m, 4H), 2.57 (br s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 134.9, 132.5, 128.8, 128.0, 66.4, 47.0. MS (EI): *m/z* = 226 (5, M⁺), 140 (11), 86 (45). IR (ATR): ν = 3260, 2867, 1740, 1450, 1244, 1101, 922, 697 (cm⁻¹). HRMS *m/z*: Calcd for [C₁₀H₁₄N₂O₂S+H⁺]: 227.0854. Found: 227.0852.

**4-(Phenylsulfonimidoyl)thiomorpholine (144ag)**

Yellow solid, melting point: 98 – 99 °C, 58% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 2H), 3.31 – 3.30 (m, 4H), 2.66 – 2.63 (m, 4H), 2.49 (br s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 136.5, 132.3, 128.8, 127.7, 48.7, 27.7. MS (EI): *m/z* = 242 (5, M⁺), 165 (1), 102 (48), 77 (18). IR (ATR): ν = 3279, 2924, 1740, 1445, 1245, 1114, 960, 692 (cm⁻¹). HRMS *m/z*: Calcd for [C₁₀H₁₄N₂O₂+H⁺]: 243.0626. Found: 243.0617.

**1-(Phenylsulfonimidoyl)pyrrolidine (144ah)**

Yellow solid, melting point: 86 – 87 °C, 30% yield. ¹H NMR (400 MHz, CDCl₃) δ(ppm) 7.97 – 7.94 (m, 2H), 7.57 – 7.53 (m, 1H), 7.51 – 7.47 (m, 2H), 3.24 – 3.14 (m, 4H), 2.72 (br s, 1H), 1.70 – 1.66 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 137.0, 132.1, 128.7, 127.8, 48.6, 25.2. MS (EI): *m/z* = 210 (44, M⁺), 140 (24), 77 (39), 70 (12). IR (ATR): ν = 3249, 2948, 1736, 1449, 1220, 1109, 981, 745 (cm⁻¹). HRMS *m/z*: Calcd for [C₁₀H₁₄N₂O₂+H⁺]: 211.0905. Found: 211.0898.
1-(Phenylsulfonimidoyl)azepane (144ai)

Yellow oil, 27% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.90 – 7.88 (m, 2H), 7.52 – 7.49 (m, 1H), 7.47 – 7.44 (m, 2H), 3.29 – 3.22 (m, 4H), 2.45 (br s, 1H), 1.68 – 1.62 (m, 4H), 1.56 – 1.53 (m, 4H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 139.6, 131.7, 128.7, 127.0, 49.1, 29.3, 26.7. MS (EI): $m/z$ = 238 (3, M$^+$), 140 (8), 98 (100), 77 (36). IR (ATR): $\nu$ = 3276, 2923, 1739, 1447, 1244, 1125, 979, 691 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{12}$H$_{18}$N$_2$OS+H]$^+$: 239.1218. Found: 239.1216.

N-Formyl-1-(phenylsulfonimidoyl)piperidine (145)

Yellow solid, melting point: 119 – 120 °C, 8% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 8.12 (s, 1H), 7.89 – 7.86 (m, 2H), 7.51 – 7.42 (m, 3H), 3.61 – 3.58 (m, 2H), 3.42 – 3.39 (m, 2H), 1.70 – 1.66 (m, 4H), 1.60 – 1.55 (m, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 157.3, 142.5, 131.7, 128.6, 126.4, 51.9, 44.6, 26.4, 24.8, 23.9. MS (EI): $m/z$ = 252(11, M$^+$), 84 (83), 77 (30). IR (ATR): $\nu$ = 2934, 2312, 1746, 1602, 1444, 1280, 1140, 866, 689 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{12}$H$_{16}$N$_2$O$_2$S+Na]$^+$: 275.0830. Found: 275.0825.

1,2-Benzothiazines appear rather neglected in crop protection and medicinal chemistry.\(^5\) The unique structure of 1,2-benzothiazines consists of an all-carbon aromatic fragment and an annulated nonaromatic heterocycle with a stereogenic sulfur. The preparation of the 1,2-benzothiazine core has attracted more attention in recent years. For example, in 2005, Harmata and co-workers demonstrated a synthetic approach towards 1,2-benzothiazines bearing an endo-double bond by a Sonogashira type cross-coupling of ortho-bromo sulfoximine 5u with alkyne 24 in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) and CuI under basic conditions (Scheme 76).\(^82\)

\[
\begin{align*}
\text{5u} & \quad \text{24} & \quad \text{82, up to 73\%} & \quad \text{147, up to 81\%} \\
\text{Scheme 76. Synthesis of 1,2-benzothiazines.}
\end{align*}
\]

In 2013, Bolm and co-workers reported the first rhodium-catalyzed oxidative annulation reaction of NH-sulfoximines 5 with internal alkynes 79 to furnish 1,2-benzothiazines 80 in good yields (Scheme 77a).\(^47\) Two years later, the same group developed a rhodium-catalyzed domino C–H bond activation/cyclization/condensation process starting from NH-sulfoximines 5 and diazo compounds 83, providing 1,2-benzothiazines 80 in excellent yields (Scheme 77b).\(^49\)

\[
\begin{align*}
\text{(a)} & \quad \text{5} & \quad \text{79} & \quad \text{80, 87-63\%}
\end{align*}
\]

\[
\begin{align*}
\text{(b)} & \quad \text{5} & \quad \text{83} & \quad \text{80, 32-99\%}
\end{align*}
\]

\[
\text{Scheme 77. Synthesis of 1,2-benzothiazines.}
\]
7.1 Results and Discussion

7.1.1 Research Objective

To date, many protocols for the synthesis of 1,2-benzothiazines with fully substituted heterocyclic cores exist. However, 4-unsubstituted 1,2-benzothiazines have remained difficult to prepare.\textsuperscript{[48]} Inspired by the work of Saá employing allyl carbonates as coupling partners in rhodium-catalyzed tandem C–H allylations and oxidative cyclizations of anilides leading to indoles,\textsuperscript{[68]} we wondered if a rhodium-catalyzed activation of this type might be applicable to construct 4-unsubstituted 1,2-benzothiazines. To our delight, this hypothesis was confirmed (Scheme 78).

![Scheme 78. Synthesis of 4-unsubstituted 1,2-benzothiazines.](image)

7.1.2 Optimization of Annulation Reactions

For examining this cyclization reaction, sulfoximine 5a and allyl methyl carbonate 116a were used as starting materials. The optimization results are shown in Table 4. To our delight, using [Cp*RhCl\textsubscript{2}]/AgSbF\textsubscript{6} (4 mol %/16 mol %) as the catalytic system and Cu(OAc)\textsubscript{2}·H\textsubscript{2}O (2.1 equiv) as oxidant in DCE at 100 °C, smoothly provided the desired product 82aa in 45% yield after 14 h (Table 4, entry 1). At 110 °C or 90 °C a lower yield of product 82aa was obtained (Table 4, entries 2-3). A small amount of compound 148 was observed when the reaction was run without Cu(OAc)\textsubscript{2}·H\textsubscript{2}O as oxidant, which indicated that the probable reaction course involved C–H bond allylation of sulfoximine followed by oxidative cyclization. Then, screening of a range of solvents identified DME (dimethoxyethane) as the most appropriate one providing products in yields up to 58% (Table 4, entries 4-7). A lower yield of 82aa was obtained with a longer or shorter reaction time (Table 4, entries 8-9). Replacement of [Cp*RhCl\textsubscript{2}]/AgSbF\textsubscript{6} by [Cp*Rh(CH\textsubscript{3}CN)\textsubscript{3}][SbF\textsubscript{6}]\textsubscript{2} (8 mol %) as the catalyst system (Table 4, entry 10) was less efficient. Allyl alcohol and allyl chloride showed no reactivity. However, allyl acetate 116d, allyl tert-butyl carbonate 116b, allyl diethyl
phosphate 116e and allyl benzoate 116c afforded 82a, albeit in lower yields than allyl methyl carbonate (Table 4, entries 11-14). The optimized condition was accomplished when acetic acid (HOAc, 1.0 equiv) was added to the reaction mixture to afford 82aa in 72% yield (Table 4, entry 15).

Table 4. Optimization of reaction conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Allyl source</th>
<th>Solvent</th>
<th>Temp (℃)</th>
<th>t (h)</th>
<th>Yield of 82aa (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>116a</td>
<td>DCE</td>
<td>100</td>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>116a</td>
<td>DCE</td>
<td>110</td>
<td>14</td>
<td>38</td>
</tr>
<tr>
<td>3</td>
<td>116a</td>
<td>DCE</td>
<td>90</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>116a</td>
<td>THF</td>
<td>100</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>116a</td>
<td>MeOH</td>
<td>100</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>6</td>
<td>116a</td>
<td>toluene</td>
<td>100</td>
<td>14</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td>116a</td>
<td>DME</td>
<td>100</td>
<td>14</td>
<td>58</td>
</tr>
<tr>
<td>8</td>
<td>116a</td>
<td>DME</td>
<td>100</td>
<td>14</td>
<td>51</td>
</tr>
<tr>
<td>9</td>
<td>116a</td>
<td>DME</td>
<td>100</td>
<td>8</td>
<td>50</td>
</tr>
<tr>
<td>10a</td>
<td>116a</td>
<td>DME</td>
<td>100</td>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>11</td>
<td>116b</td>
<td>DME</td>
<td>100</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>12</td>
<td>116c</td>
<td>DME</td>
<td>100</td>
<td>14</td>
<td>47</td>
</tr>
<tr>
<td>13</td>
<td>116d</td>
<td>DME</td>
<td>100</td>
<td>14</td>
<td>50</td>
</tr>
</tbody>
</table>
7.1.3 Substrate Scope of Sulfoximines and Allyl Carbonates

The scope of substituted sulfoximines is summarized in Table 5. In the series of para-substituted sulfoximines a slight influence of electronic effects was observed. Substrates with electron-donating substituents led to slightly higher product yields than sulfoximines having electron-withdrawing groups (Table 5, entries 2 and 3 versus entries 7-9). It is noteworthy that an exclusive site selectivity was observed in the reaction with meta-bromo-substituted sulfoximine 5k providing 82ka as a single regioisomeric product in 54% yield. Meta-methoxy-substituted 5o provided 36% of a 2:1 mixture of (unseparated) regioisomers 82oa and 82o′a. In addition, two S-2-naphthyl-substituted sulfoximines also showed exclusive site selectivity leading to 82ia and 82na in 63% and 58% yield, respectively (Table 5, entry 10 and 11). Varying the S-alkyl substituent of the S-phenyl sulfoximines led to the 1,2-benzothiazines (5pa-sa) in yields ranging from 60% to 71% (Table 5, entries 14-17). Presumably due to steric reasons ortho-chloro-substituted sulfoximine 5l did not react well, providing only a trace of 1,2-benzothiazine 82la (Table 5, entry 18).

Table 5. Scope of sulfoximines.

<table>
<thead>
<tr>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>R&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>116e</td>
<td>DME 100</td>
</tr>
<tr>
<td>15&lt;sup&gt;b&lt;/sup&gt;</td>
<td>116a</td>
<td>DME 100</td>
</tr>
<tr>
<td>16&lt;sup&gt;c&lt;/sup&gt;</td>
<td>116a</td>
<td>DME 100</td>
</tr>
</tbody>
</table>

Reaction conditions: sulfoximine 5a (0.3 mmol), allyl source (0.9 mmol, 3.0 equiv), [Cp*RhCl<sub>2</sub>]<sub>2</sub> (4 mol %), AgSbF<sub>6</sub> (16 mol %), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (2.1 equiv), and solvent (1.5 mL) at 100 °C for 14 h in a sealed tube under argon. <sup>a</sup>Use of [Cp*Rh(CH<sub>3</sub>CN)<sub>3</sub>][SbF<sub>6</sub>]<sub>2</sub> (8 mol %) as catalyst. <sup>b</sup>Use of HOAc (1.0 equiv) as additive. <sup>c</sup>Use of PivOH (1.0 equiv) as an additive.
<table>
<thead>
<tr>
<th>Entry</th>
<th>$R^1, R^2$</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H, Me (5a)</td>
<td>![82aa]</td>
<td>72%</td>
</tr>
<tr>
<td>2</td>
<td>4-Me, Me (5b)</td>
<td>![82ba]</td>
<td>65%</td>
</tr>
<tr>
<td>3</td>
<td>4-OMe, Me (5c)</td>
<td>![82ca]</td>
<td>63%</td>
</tr>
<tr>
<td>4</td>
<td>4-F, Me (5d)</td>
<td>![82da]</td>
<td>56%</td>
</tr>
<tr>
<td>5</td>
<td>4-Cl, Me (5e)</td>
<td>![82ea]</td>
<td>62%</td>
</tr>
<tr>
<td>6</td>
<td>4-Br, Me (5f)</td>
<td>![82fa]</td>
<td>55%</td>
</tr>
</tbody>
</table>
7  4-NO₂, Me (5g)  
   \[
   \text{C}_2\text{N} - \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} 
   \]
   \[\text{82ga}\]
   38%

8  4-C(O)Me, Me (5m)  
   \[
   \text{O} - \text{C} - \text{O} - \text{Me} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} 
   \]
   \[\text{82ma}\]
   52%

9  4-SF₅, Me (5w)  
   \[
   \text{F} - \text{S} - \text{F} - \text{Me} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} 
   \]
   \[\text{82wa}\]
   45%

10 2-Naphthyl, Me (5i)  
   \[
   \text{C} - \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} 
   \]
   \[\text{82ia}\]
   63%

11 2-Naphthyl, iPr (5n)  
   \[
   \text{C} - \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} 
   \]
   \[\text{82na}\]
   58%

12 3-Br, Me (5k)  
   \[
   \text{Br} - \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} \\
   \text{S} - \text{N} - \text{Me} 
   \]
   \[\text{82ka}\]
   54%

13 3-OMe, Me (5o)  
   \[\text{MeO} - \text{S} - \text{N} - \text{Me} + \text{MeO} - \text{S} - \text{N} - \text{Me} \]
   \[\text{82oa+82oa'} = (2:1)\]
   36%
71% 

70% 

65% 

60% 

trace

Substituted allyl carbonates were found to be inappropriate for this oxidative cyclization reaction. Sulfoximine 5a underwent no reaction with 1-methyl-2-propenyl methyl carbonate 116x and 1-propyl-2-propenyl methyl carbonate 116y. Instead, olefination products (148-150) were obtained when the reactions were performed without Cu(OAc)$_2$·H$_2$O (Scheme 79).
β-hydride elimination/isomerization sequence involving a [Rh−H] complex generated in situ. In this process a Rh(I) species was expelled and reoxidized to Rh(III) by the Cu(II) salt. If the Rh(III) species alternatively, the same species the new olefin coordinated Rh(III) species rhodacycle migratory insertion of the allyl double bond into the Rh–C bond afforded seven-membered hypothesized that after initial formation of previously proposed five-membered rhodacycle 5A′, with the carbonate oxygen chelating to the rhodium. β-oxygen elimination gave the new olefin coordinated Rh(III) species 5D′ (oxidative Mizoroki-Heck/β-elimination pathway). Alternatively, the same species 5D′ could be formed by coordination of the carbonate oxygen to Rh(III) species 5C′, which might facilitate an intramolecular nucleophilic substitution, followed by β-hydrogen elimination and isomerization, then species 5D′ released the observed product 82aa. In this process a Rh(I) species was expelled and reoxidized to Rh(III) by the Cu(II) salt. If the Cu(II) salt was absent, complex 5D′ was protonated leading to olefin 148, presumably through a β-hydride elimination/isomerization sequence involving a [Rh−H] complex generated in situ.

Scheme 79. Scope of allyl carbonates.

7.1.4 Mechanism

The two possible mechanistic scenarios for this reaction are shown in Scheme 80. We hypothesized that after initial formation of previously proposed five-membered rhodacycle 5A′, migratory insertion of the allyl double bond into the Rh–C bond afforded seven-membered rhodacycle 5B′ with the carbonate oxygen chelating to the rhodium. β-oxygen elimination gave the new olefin coordinated Rh(III) species 5D′ (oxidative Mizoroki-Heck/β-elimination pathway). Alternatively, the same species 5D′ could be formed by coordination of the carbonate oxygen to Rh(III) species 5C′, which might facilitate an intramolecular nucleophilic substitution, followed by β-hydrogen elimination and isomerization, then species 5D′ released the observed product 82aa. In this process a Rh(I) species was expelled and reoxidized to Rh(III) by the Cu(II) salt. If the Cu(II) salt was absent, complex 5D′ was protonated leading to olefin 148, presumably through a β-hydride elimination/isomerization sequence involving a [Rh−H] complex generated in situ.
7.1.5 Synthetic Transformations

To illustrate the synthetic potential of the products, 1,2-benzothiazine 82aa was selected as representative starting material (Scheme 81). Treatment of 82aa with NBS/AIBN in carbon tetrachloride gave the dibromobenzothiazine 151 in 65% yield. Reacting 151 with deprotonated pyrazole in tetrahydrofuran at room temperature afforded product 152 in 51% yield. Two other secondary amines (N-methylaniline and dibenzylamine) reacted with compound 82aa in dimethylformamide for 12 h at room temperature to provide derivatives 153 and 154 in yields of 80% and 89%, respectively. The reaction of compound 82aa with sodium azide in dimethylformamide led to a azidomethyl product, which was subsequently reacted with phenyl acetylene in toluene at room temperature under catalysis with copper(I)-thiophene-2-carboxylate providing product 155 in 71% yield (over two steps).
7.1.6 Summary

In summary, we developed a new protocol towards 4-unsubstituted 1,2-benzothiazines by rhodium (III)-catalyzed domino allylation/oxidative cyclization of \( \text{NH-sulfoximines} \) with easily accessible allyl carbonates. It allows access to a variety of synthetically valuable products in a straightforward manner. Their chemical potential has been demonstrated by further functionalization reactions.

7.2 Experimental

7.2.1 General Information

Allyl carbonates 116a-e were synthesized according to literature procedures.\(^8\) The rhodium (III) complexes \([\text{Cp}^*\text{RhCl}_2]\) and \([\text{Cp}^*\text{Rh(MeCN)}_3][\text{SbF}_5]\) were prepared according to the literature protocols.\(^8\)
7.2.2 General Procedure for the Synthesis of 1,2-Benzothiazines

A sealed tube (15 mL) was charged with sulfoximine 5 (0.3 mmol), allyl carbonate 116a (0.9 mmol), [Cp*RhCl₂]₂ (7.4 mg, 4 mol %), AgSbF₆ (16.5 mg, 16 mol %), Cu(OAc)₂·H₂O (125.0 mg, 2.1 equiv) and AcOH (18.0 mg, 0.3 mmol) Under an argon atmosphere, dry dimethoxyethane (1.5 mL) was added by syringe. After stirring the reaction mixture at 100 °C for 14 h, it was cooled to room temperature and extracted with dichloromethane (3 x 10 mL). The combined organic layers were extracted with brine (15 mL), dried over MgSO₄ and concentrated in vacuo. The product was purified by column chromatography on silica gel with n-pentane/ethyl acetate (4:1 to 2:1) as eluent to afford product 82.

7.2.3 Characterization Data of 1,2-Benzothiazines

1,3-Dimethylbenzo[e][1,2]thiazine 1-oxide (82aa)

Yellow solid, melting point: 93 – 95 °C, 72% yield. ¹H NMR (600 MHz, CDCl₃) δ (ppm) 7.71 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.21 (d, J = 8.1 Hz, 1H), 5.94 (s, 1H), 3.50 (s, 3H), 2.20 (s, 3H). [¹³C NMR (150 MHz, CDCl₃) δ (ppm) 148.1, 136.7, 132.5, 125.9, 125.5, 123.3, 117.2, 99.1, 45.1, 25.1. MS (EI): m/z = 193 (55, M⁺), 178 (8), 162 (5), 139 (6), 77 (27). IR (ATR): ν = 3003, 2919, 1739, 1590, 1476, 1365, 1194, 970, 748 (cm⁻¹). HRMS m/z: Calcd for [C₁₀H₁₁NOS+Na⁺]: 216.0459. Found: 216.0454.

1,3,6-Trimethylbenzo[e][1,2]thiazine 1-oxide (82ba)

Yellow solid, melting point: 128 – 130 °C, 65% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.60 (d, J = 8.2 Hz, 1H), 7.12 (d, J = 8.2, 1H), 6.99 (s, 1H), 5.86 (s, 1H), 3.46 (s, 3H), 2.38 (s, 3H), 2.18 (s, 3H). [¹³C NMR (100 MHz, CDCl₃) (ppm) 148.1, 143.2, 136.9, 126.9, 125.6, 123.3, 114.9, 98.9, 45.4, 25.1, 21.7. MS (EI): m/z = 207 (64, M⁺), 191 (2), 192 (9), 193 (1), 153 (5), 77 (29). IR (ATR): ν = 3021, 2922, 1740, 1590, 1476, 1365, 1194, 970, 748.
1473, 1353, 1190, 1049, 951, 774 (cm\(^{-1}\)). HRMS m/z: Calcd for [C\(_{11}\)H\(_{13}\)NOS+Na\(^+\)]: 230.0616

Found: 230.0611.

6-Methoxy-1,3-dimethylbenzo[e][1,2]thiazine 1-oxide (82ca)

Yellow solid, melting point: 137 – 139 °C, 63% yield. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.63 (d, \(J = 8.8\) Hz, 1H), 6.88 (dd, \(J = 8.8, 2.5\) Hz, 1H), 6.58 (d, \(J = 2.5\) Hz, 1H), 5.85 (s, 1H), 3.85 (s, 3H), 3.44 (s, 3H), 2.18 (s, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm) 165.3, 149.0, 139.4, 125.6, 114.9, 110.2, 106.7, 98.9, 55.5, 46.0, 25.1. MS (EI): \(m/z\) = 223 (98, M\(^+\)), 208 (17), 192 (7), 77 (15). IR (ATR): \(\nu\) = 2923, 2855, 1737, 1590, 1469, 1350, 1191, 1055, 902, 779 (cm\(^{-1}\)). HRMS m/z: Calcd for [C\(_{11}\)H\(_{13}\)NO\(_2\)S+H\(^+\)]: 224.0745. Found: 224.0740.

6-Fluoro-1,3-dimethylbenzo[e][1,2]thiazine 1-oxide (82da)

Yellow solid, melting point: 111 – 113 °C, 56% yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.73 (dd, \(J = 8.8, 5.3\) Hz, 1H), 7.02 (td, \(J = 8.5, 2.5\) Hz, 1H), 6.85 (dd, \(J = 9.9, 2.5\) Hz, 1H), 5.89 (s, 1H), 3.48 (s, 3H), 2.20 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 164.8 (d, \(J_{C-F} = 256\) Hz), 149.9, 139.8 (d, \(J_{C-F} = 11\) Hz), 126.5 (d, \(J_{C-F} = 10\) Hz), 114.0 (d, \(J_{C-F} = 25\) Hz), 113.4, 110.7 (d, \(J_{C-F} = 22\) Hz), 98.8 (d, \(J_{C-F} = 2\) Hz), 45.7, 25.1. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) –105.2 (m, 1F). MS (EI): \(m/z\) = 211 (62, M\(^+\)), 196 (15), 157 (5), 134 (4), 107 (20), 77 (3). IR (ATR): \(\nu\) = 3018, 2926, 2309, 1740, 1586, 1472, 1350, 1196, 1062, 952, 777 (cm\(^{-1}\)). HRMS m/z: Calcd for [C\(_{10}\)H\(_{10}\)NOSF+Na\(^+\)]: 234.0365. Found: 234.0359.

6-Chloro-1,3-dimethylbenzo[e][1,2]thiazine 1-oxide (82ea)

Yellow solid, melting point: 143 – 145 °C, 62% yield. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.57 (d, \(J = 8.5\) Hz, 1H), 7.40 (dd, \(J = 8.5, 1.8\) Hz, 1H), 7.38 (d, \(J = 1.8\) Hz, 1H), 5.87 (s, 1H), 3.48 (s, 3H), 2.20 (s, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm) 150.0, 138.8, 138.3, 125.8, 125.1, 125.0, 115.1, 98.4, 45.4, 25.1. MS (EI): \(m/z\) = 229 (29), 227 (81, M\(^+\)), 212 (19), 192 (2), 173 (38), 123 (15), 77(16). IR (ATR): \(\nu\) = 3007, 2927, 2309, 1739, 1574, 1459, 1356, 1195, 1064, 896, 781 (cm\(^{-1}\)). HRMS m/z: Calcd for [C\(_{10}\)H\(_{10}\)NOSCl+Na\(^+\)]: 250.0069. Found: 250.0064.
6-Bromo-1,3-dimethylbenzo[e][1,2]thiazine 1-oxide (82fa)

Yellow solid, melting point: 166 – 168 °C, 55% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.57 (d, $J = 8.5$ Hz, 1H), 7.40 (dd, $J = 8.5$, 1.8 Hz, 1H), 7.38 (d, $J = 1.8$ Hz, 1H), 5.87 (s, 1H), 3.48 (s, 3H), 2.20 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 150.0, 138.4, 128.5, 128.2, 127.3, 125.0, 115.5, 98.3, 45.4, 25.2. MS (EI): $m/z = 273$ (28), 271 (31, M$^+$), 256 (8), 231 (7), 194 (4), 192 (6), 77 (31). IR (ATR): $\nu = 3005$, 2924, 1737, 1571, 1459, 1339, 1188, 1065, 960, 781 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{10}$H$_{10}$NOSBr+H]$^+$: 271.9745. Found: 271.9739.

1,3-Dimethyl-6-nitrobenzo[e][1,2]thiazine 1-oxide (82ga)

Yellow solid, melting point: 132 – 134 °C, 38% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 8.11 (d, $J = 2.1$ Hz, 1H), 8.06 (dd, $J = 8.7$, 2.2 Hz, 1H), 7.87 (d, $J = 8.7$ Hz, 1H), 6.14 (s, 1H), 3.59 (s, 3H), 2.26 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 151.5, 149.8, 137.7, 125.1, 121.5, 119.8, 119.1, 99.8, 45., 25.2. MS (EI): $m/z = 238$ (94, M$^+$), 223 (12), 192 (13), 184 (5), 161 (12), 77 (15). IR (ATR): $\nu = 3095$, 2922, 1739, 1588, 1513, 1347, 1197, 1064, 826, 728 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{10}$H$_{10}$N$_2$O$_3$S+H]$^+$: 239.0490. Found: 239.0485.

1-(1,3-Dimethyl-1-oxidobenzo[e][1,2]thiazin-6-yl)ethanone (82ma)

Yellow solid, melting point: 131 – 133 °C, 52% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.83 (dd, $J = 8.4$, 1.4 Hz, 1H), 7.79 – 7.77 (m, 2H), 6.06 (s, 1H), 3.55 (s, 3H), 2.63 (s, 3H), 2.23 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 197.2, 149.5, 139.7, 136.8, 126.8, 124.1, 123.7, 119.3, 99.7, 44.9, 26.8, 25.1. MS (EI): $m/z = 235$ (100, M$^+$), 220 (4), 192 (4), 158 (2), 77 (10). IR (ATR): $\nu = 2917$, 1675, 1590, 1533, 1348, 1210, 1065, 894, 774 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{12}$H$_{13}$NO$_2$S+Na]$^+$: 258.0565. Found: 258.0560.
1-(1,3-Dimethyl-1-oxidobenzo[e][1,2]thiazin-6-yl)ethanone (82wa)

Yellow solid, melting point: 138 – 140 °C, 45% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.79 (d, $J = 8.6$ Hz, 1H), 7.66 – 7.62 (m, 2H), 6.05 (s, 1H), 3.55 (s, 3H), 2.24 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 156.6 – 156.1 (m, C-SF$_5$), 150.8, 137.2, 124.2, 124.0 (t, $J_{C-F} = 4.5$ Hz), 122.3 (t, $J_{C-F} = 4.5$ Hz), 118.2, 99.5, 45.0, 25.1. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ 83.2-81.6 (m, 1F), 60.1 (d, $J = 150$ Hz). MS (EI): $m/z$ = 319 (38, M$^+$), 265 (5), 192 (21), 127 (82), 77 (19). IR (ATR): $\nu$ = 3029, 2929, 1740, 1584, 1472, 1355, 1206, 1064, 812 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{10}$H$_{10}$NOSF$_5$+H]$^+$: 320.0202. Found: 320.0197.

7-Bromo-1,3-dimethylbenzo[e][1,2]thiazine 1-oxide (82ka)

Yellow solid, melting point: 147 – 149 °C, 54% yield. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 8.16 (d, $J = 1.5$ Hz, 1H), 7.91 (dd, $J = 8.6$, 1.9 Hz, 1H), 7.45 (d, $J = 8.6$ Hz, 1H), 6.28 (s, 1H), 3.86 (s, 3H), 2.53 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 148.9, 135.7, 135.4, 127.7, 125.7, 118.0, 117.3, 98.8, 45.2, 25.1. MS (EI): $m/z$ = 273 (45), 271 (63, M$^+$), 256 (5), 217 (86), 192 (6), 77 (14). IR (ATR): $\nu$ = 2920, 1743, 1587, 1469, 1369, 1194, 1076, 965, 772 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{10}$H$_{10}$NOSBr+Na]$^+$: 293.9564. Found: 293.9559.

7-Methoxy-1,3-dimethylbenzo[e][1,2]thiazine 1-oxide (82oa, major) and 5-Methoxy-1,3-dimethylbenzo[e][1,2]thiazine 1-oxide (82oa′a, minor) (82oa+82oa′a)

Yellow syrup, 36% yield (as isomeric mixture). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.31 (d, $J = 8.0$ Hz, 1H), 7.25 (dd, $J = 9.5$, 6.5 Hz, 1H), 7.16 – 7.11 (m, 1H), 6.94 (d, $J = 7.9$ Hz, 1H), 6.31 (s, 1H), 5.88 (s, 1H), 3.89 (s, 3H), 3.83 (s, 1H), 3.50 (s, 3H), 3.49 (s, 1H), 2.22 (s, 3H), 2.16 (s, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 157.5, 153.0, 147.8, 145.3, 130.5, 127.6, 125.4, 122.1, 117.4, 117.0, 114.7, 114.3, 104.8, 98.7, 92.8, 92.7, 55.8, 55.7, 45.1, 45.0, 25.3, 24.7. MS (EI): $m/z$ = 223 (45, M$^+$), 169 (5), 117 (7). IR (ATR): $\nu$ = 2934, 1729, 1457, 1345, 1209, 1037, 764 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{10}$H$_{10}$NOSBr+H]$^+$: 223.0667. Found: 223.0662.
1,3-Dimethylnaphtho[2,3-e][1,2]thiazine 1-oxide (82ia)

Yellow solid, melting point: 184 – 186 °C, 63% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 8.34 (s, 1H), 7.88 (d, $J = 8.4$ Hz, 1H), 7.81 (d, $J = 8.4$ Hz, 1H), 7.62 (s, 1H), 7.55 – 7.52 (m, 1H), 7.44 – 7.41 (m, 1H), 6.08 (s, 1H), 3.50 (s, 3H), 2.22 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 146.5, 135.6, 132.2, 131.2, 128.8, 128.7, 127.6, 125.5, 124.6, 122.8, 120.2, 99.3, 45.2, 25.2. MS (EI): $m/z = 243$ (72, M$^+$), 189 (5), 166 (3), 139 (9), 126 (9), 77 (4). IR (ATR): ν = 3019, 2919, 1739, 1592, 1369, 1197, 1050, 882, 744 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{14}$H$_{13}$NOS+Na]$^+$: 266.0616. Found: 266.0610.

3-Methyl-1-propynaphtho[2,3-e][1,2]thiazine 1-oxide (82na)

Yellow solid, melting point: 112 – 114 °C, 58% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 8.30 (s, 1H), 7.88 (d, $J = 8.2$ Hz, 1H), 7.81 (d, $J = 8.4$ Hz, 1H), 7.60 (s, 1H), 7.58 – 7.50 (m, 1H), 7.43 – 7.40 (m, 1H), 6.00 (s, 1H), 3.68 – 3.65 (m, 1H), 3.49 – 3.44 (m, 1H), 2.22 (s, 3H), 1.81 – 1.67 (m, 1H), 1.59 – 1.52 (m, 1H), 0.96 (t, $J = 7.5$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 147.2, 135.8, 133.3, 131.2, 128.8, 128.7, 127.6, 125.5, 124.6, 118.0, 98.4, 59.0, 25.3, 17.2, 12.6. MS (EI): $m/z = 271$ (40, M$^+$), 166 (3), 126 (15), 77 (5). IR (ATR): ν = 3051, 2959, 1738, 1587, 1371, 1182, 1034, 872, 742 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{16}$H$_{17}$NOS+H]$^+$: 272.1109. Found: 272.1104.

1-Ethyl-3-methylbenzo[e][1,2]thiazine 1-oxide (82pa)

Yellow oil, 71% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.65 (d, $J = 8.0$ Hz, 1H), 7.51 – 7.45 (m, 1H), 7.29 (t, $J = 7.6$ Hz, 1H), 7.21 (d, $J = 8.1$ Hz, 1H), 5.87 (s, 1H), 3.71 (dq, $J = 14.5$, 7.2 Hz, 1H), 3.49 (dq, $J = 14.8$, 7.4 Hz, 1H), 2.21 (s, 3H), 1.17 (t, $J = 7.3$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 149.0, 136.7, 138.1, 132.6, 125.9, 125.4, 123.7, 114.1, 98.3, 51.1, 25.1, 8.7. MS (EI): $m/z = 207$ (82, M$^+$), 178 (12), 131 (14), 116 (2), 77 (18). IR (ATR): ν = 2925, 1736, 1584, 1467, 1365, 1190, 1057, 749 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{11}$H$_{13}$NOS+H]$^+$: 208.0796. Found: 208.0791.
1-Cyclopropyl-3-methylbenzo[e][1,2]thiazine 1-oxide (82qa)

Yellow oil, 70% yield. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.79 (d, \(J = 8.1\) Hz, 1H), 7.49 – 7.46 (m, 1H), 7.32 – 7.27 (m, 1H), 7.21 (d, \(J = 8.1\) Hz, 1H), 5.95 (s, 1H), 2.82 – 2.78 (m, 1H), 2.21 (s, 3H), 1.75 – 1.71 (m, 1H), 1.41 – 1.37 (m, 1H), 1.35 – 1.28 (m, 1H), 1.22 – 1.17 (m, 1H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm) 148.3, 136.9, 132.2, 125.7, 125.3, 123.5, 117.9, 99.1, 32.4, 6.8, 4.5. MS (EI): \(m/z = 219\) (58, M\(^+\)), 178 (4), 130 (10), 116 (3), 103 (13), 89 (14), 77 (25). IR (ATR): \(\nu = 3047, 2918, 1738, 1589, 1471, 1367, 1208, 1051, 886, 740\) (cm\(^{-1}\)). HRMS \(m/z\): Calcd for \([C_{12}H_{13}NOS+H]^+\): 220.0796. Found: 220.0791.

1-Butyl-3-methylbenzo[e][1,2]thiazine 1-oxide (82ra)

Yellow oil, 65% yield. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.65 (d, \(J = 8.1\) Hz, 1H), 7.49 – 7.46 (m, 1H), 7.30 – 7.27 (m, 1H), 7.21 (d, \(J = 8.1\) Hz, 1H), 5.95 (s, 1H), 3.68 – 3.63 (m, 1H), 3.50 – 3.45 (m, 1H), 2.21 (s, 3H), 1.65 – 1.61 (m, 1H), 1.45 – 1.35 (m, 4H), 0.89 – 0.86 (m, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm) 148.8, 137.8, 132.6, 125.9, 125.4, 123.7, 114.8, 98.3, 56.4, 25.9, 25.2, 21.2, 13.5. MS (EI): \(m/z = 235\) (30, M\(^+\)), 178 (6), 159 (3), 119 (2), 116 (5), 77 (22), 76 (13), 57 (51). IR (ATR): \(\nu = 2955, 2096, 1732, 1588, 1470, 1370, 1199, 1067, 789\) (cm\(^{-1}\)). HRMS \(m/z\): Calcd for \([C_{13}H_{17}NOS+H]^+\): 236.1109. Found: 236.1104.

1-Benzyl-3-methylbenzo[e][1,2]thiazine 1-oxide (82sa)

Yellow oil, 60% yield. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.53 (d, \(J = 8.0\) Hz, 1H), 7.39 (t, \(J = 7.6\) Hz, 1H), 7.26 – 7.23 (m, 1H), 7.20 – 7.17 (m, 3H), 7.11 (d, \(J = 7.5\) Hz, 1H), 7.00 (d, \(J = 8.1\) Hz, 1H), 5.57 (s, 1H), 4.67 (d, \(J = 14.1\) Hz, 1H), 4.48 (d, \(J = 14.1\) Hz, 1H), 2.11 (s, 1H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm) 149.4, 138.9, 133.0, 131.0, 128.6, 128.3, 128.1, 125.3, 125.1, 125.0, 113.9, 98.0, 64.6, 25.0. MS (EI): \(m/z = 269\) (4, M\(^+\)), 178 (9), 153 (2), 91 (100), 89 (3), 77 (4). IR (ATR): \(\nu = 3047, 2918, 1738, 1585, 1473, 1367, 1205, 1062, 778\) (cm\(^{-1}\)). HRMS \(m/z\): Calcd for \([C_{16}H_{15}NOS+H]^+\): 270.0953. Found: 270.0947.
(Z)-1-(S-Methylsulfonimidoyl)-2-(prop-1-en-1-yl)benzene (148)

Yellow oil, 50% yield. $^1$H NMR (600 MHz, CDCl$_3$) $Z$ isomer: $\delta$ (ppm) 8.04 (dd, $J = 7.9$, 1.3 Hz, 1H), 7.55 – 7.53 (m, 1H), 7.51 – 7.48 (m, 2H), 7.36 – 7.33 (m, 1H), 6.20 (dq, $J = 15.6$, 6.7 Hz, 1H), 3.09 (s, 3H), 2.88 (bs, 1H), 1.93 (dd, $J = 6.7$, 1.8 Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $Z$ isomer: $\delta$ (ppm) 139.3, 137.9, 133.0, 131.5, 128.6, 128.3, 127.6, 127.0, 44.3, 18.8. MS (EI): $m/z$ = 195 (33, M$^+$), 180 (100), 117 (49), 78 (12), 77 (23). IR (ATR): $\nu$ = 3269, 2923, 2111, 1643, 1460, 1316, 1218, 1065, 995, 750 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{10}$H$_{13}$NOS+H]$^+$: 196.0796. Found: 196.0791.

(Z)-1-(But-1-en-1-yl)-2-(S-methylsulfonimidoyl)benzene (149)

Yellow oil, 48% yield. $^1$H NMR (600 MHz, CDCl$_3$) $Z$ isomer: $\delta$ 8.04 (d, $J = 7.9$ Hz, 1H), 7.55 (d, $J = 7.7$ Hz, 1H), 7.52 – 7.46 (m, 2H), 7.34 (t, $J = 7.6$ Hz, 1H), 6.22 (dt, $J = 15.7$, 6.6 Hz, 1H), 3.08 (s, 3H), 2.73 (bs, 1H), 2.35 – 2.21 (m, 2H), 1.09 (t, $J = 7.5$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $Z$ isomer: $\delta$ (ppm) 139.6, 138.3, 137.9, 132.9, 128.6, 128.3, 127.0, 125.6, 44.2, 13.4. MS (EI): $m/z$ = 209 (13, M$^+$), 194 (14), 180 (100), 131 (10), 78 (11), 77 (25). IR (ATR): $\nu$ = 3273, 2964, 2116, 1642, 1461, 1221, 1065, 993, 749 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{11}$H$_{15}$NOS+H]$^+$: 210.0953. Found: 210.0947.

(Z)-1-(S-Methylsulfonimidoyl)-2-(pent-1-en-1-yl)benzene (150)

Yellow oil, 45% yield. $^1$H NMR (600 MHz, CDCl$_3$) $Z$ isomer: $\delta$ 8.09 (d, $J = 7.9$ Hz, 1H), 8.05 (d, $J = 7.9$ Hz, 1H), 7.56 (d, $J = 7.7$ Hz, 1H), 7.52 – 7.49 (m, 2H), 7.35 (t, $J = 7.7$ Hz, 1H), 6.22 – 6.17 (m, 1H), 3.10 (s, 3H), 2.30 – 2.26 (m, 2H), 1.49 – 1.44 (m, 2H), 1.38 – 1.33 (m, 3H), 0.91 (t, $J = 7.3$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $Z$ isomer: $\delta$ (ppm) 139.6, 138.0, 137.1, 133.0, 128.7, 128.4, 127.0, 126.5, 44.2, 33.0, 31.3, 22.3, 13.9. MS (EI): $m/z$ = 237 (12, M$^+$), 222 (23), 180 (100), 159 (3), 78 (4), 77 (7). IR (ATR): $\nu$ = 3274, 2926, 2111, 1693, 1461, 1222, 1066, 995, 751 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{13}$H$_{19}$NOS+H]$^+$: 238.1266. Found: 238.1261.
Procedure for the synthesis of 151

A mixture of 82aa (0.4 mmol, 77.2 mg), NBS (0.8 mmol, 143.0 mg) and AIBN (20 mol %, 13.2 mg) in CCl₄ (8.0 ml) was heated to reflux for 12 h. The reaction mixture was cooled to room temperature and filtered, the filtrate was washed with saturated NaHCO₃ and brine, the organic layer was dried over MgSO₄, filtered, and concentrated. The product was purified by flash column chromatography on silica gel with n-pentane/ethyl acetate (3:1) as eluent to give the corresponding product 151 as a yellow solid.

4-Bromo-3-(bromomethyl)-1-methylbenzo[e][1,2]thiazine 1-oxide 151

Yellow solid. ¹H NMR (600 MHz, CDCl₃) δ (ppm) 7.95 (d, J = 8.5 Hz, 1H), 7.76 (dd, J = 8.1, 0.8 Hz, 1H), 7.71 – 7.68 (m, 1H), 7.54 – 7.51 (m, 1H), 4.54 (d, J = 9.6 Hz, 1H), 4.47 (d, J = 9.6 Hz, 1H), 3.56 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ (ppm) 144.2, 134.0, 133.5, 128.0, 127.7, 123.3, 121.3, 98.2, 44.5, 35.9. MS (EI): m/z = 353 (50), 351 (100, M⁺), 270 (23). IR (ATR): ν = 2925, 2329, 1744, 1454, 1321, 1200, 1050, 907, 753 (cm⁻¹). HRMS m/z: Calcd for [C₁₀H₉Br₂NOS+H]⁺: 351.8829. Found: 351.8825.

Procedure for the synthesis of 152

Solution of pyrazole (1.2 equiv, 24.9 mg) in THF (1.0 mL) was added 60% NaH (1.5 equiv, 18.0 mg) portion-wise, the suspension was stirred at room temperature for 30 min and 151 (0.3 mmol, 105.3 mg) was added. After being stirred at room temperature for 12 h, the mixture was quenched with H₂O (10.0 mL) and extracted with EtOAc (3x10 mol), the combined organic extracts were
washed with brine, dried over MgSO$_4$ and concentrated in vacuo, the residue was purified by silica gel column chromatography to afford the desired product 152.

3-((1H-pyrazol-1-yl)methyl)-4-bromo-1-methylbenzo[e][1,2]thiazine 1-oxide (152)

Yellow solid. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.96 (d, $J = 8.3$ Hz, 1H), 7.72 (d, $J = 7.9$, 1H), 7.70 – 7.67 (m, 1H), 7.60 (d, $J = 2.2$ Hz, 1H), 7.52 – 7.49 (m, 2H), 6.25 (t, $J = 2.0$ Hz, 1H), 5.45 (d, $J = 14.5$ Hz, 1H), 5.31 (d, $J = 14.5$ Hz, 1H), 3.43 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 143.0, 139.4, 134.1, 133.4, 130.1, 127.9, 127.6, 123.2, 121.1, 105.6, 97.6, 57.7, 44.4. MS (EI): $m/z =$339 (10), 337 (8, M$^+$), 258 (100). IR (ATR): $\nu =$ 2917, 2329, 1741, 1557, 1455, 1308, 1203, 1045, 753 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{13}$H$_{12}$BrN$_3$O$^+$]: 359.9782. Found: 359.9777.

Procedure for the synthesis of 153, 154

A mixture of 151 (0.3 mmol, 105.3 mg), ($^{i}$Pr)$_2$NEt (1.5 equiv, 58.0 mg) and amines (1.2 equiv) in DMF (1.0 mL) was stirred at room temperature for 12 h. Then, the reaction mixture was extracted with DCM (3 x 10 mL), the combined organic extracts were washed with brine, dried over MgSO$_4$ and concentrated in vacuo, the residue was purified by silica gel column chromatography to afford the desired product.

4-Bromo-3-((dibenzylamino)methyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (153)

Yellow oil. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm) 7.96 (d, $J = 8.4$ Hz, 1H), 7.71 (dd, $J = 7.9$, 0.8 Hz, 1H), 7.67 – 7.64 (m, 1H), 7.48 – 7.45 (m, 5H), 7.30 (t, $J = 7.6$ Hz, 4H), 7.22 (t, $J = 7.3$ Hz, 2H), 3.84 – 3.78 (m, 6H), 3.52 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm) 147.3, 139.5, 134.5, 133.0, 129.0, 127.9, 127.2, 126.9, 126.6, 123.0, 120.3, 98.1, 59.5, 57.8, 44.5. MS (EI): $m/z =$468 (3), 466 (4, M$^+$), 387 (19). IR (ATR): $\nu =$ 3032, 2913, 2334, 1462, 1329, 1214, 1058, 734 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{24}$H$_{23}$BrN$_2$OS$^+$]: 467.0793. Found: 467.0789.
4-Bromo-1-methyl-3-((methyl(phenyl)amino)methyl)benzo[e][1,2]thiazine 1-oxide (154)

Yellow solid. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.92 (d, $J = 8.3$ Hz, 1H), 7.70 – 7.66 (m, 2H), 7.45 (t, $J = 7.1$ Hz, 1H), 7.22 – 7.19 (m, 2H), 6.79 (d, $J = 8.1$ Hz, 1H), 6.68 (t, $J = 7.2$ Hz, 1H), 4.79 (d, $J = 16.7$ Hz, 1H), 4.36 (d, $J = 16.7$ Hz, 1H), 3.19 (s, 3H), 3.16 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 149.6, 147.5, 134.5, 133.3, 128.9, 127.0, 126.5, 123.3, 120.4, 116.2, 112.5, 96.0, 58.1, 44.5, 39.9. MS (EI): $m/z = 378$ (86), 376 (79, M$^+$), 297 (100), 120 (97). IR (ATR): $\nu = 2913$, 2338, 2106, 1475, 1327, 1199, 1019, 741 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{17}$H$_{17}$BrN$_2$O$^+$]: 377.0323. Found: 377.0319.

**Procedure for the synthesis of 155**

A mixture of 151 (0.3 mmol, 105.3 mg) and NaN$_3$ (1.5 equiv, 29.3 mg) in DMF (1.0 mL) was stirred overnight at room temperature. Then reaction mixture was extracted with DCM (3 x 10 mL), the combined organic extracts were washed with brine, dried over MgSO$_4$ and concentrated. Then a mixture of crude azidomethyl product (0.3 mmol, 93.0 mg), phenylacetylene (1.5 equiv, 46.0 mg) and CuTC (10 mol %, 5.75mg) in toluene (1 mL). The mixture was stirred overnight at room temperature. The solution was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over MgSO$_4$, filtered, and concentrated. The product was purified by flash column chromatography on silica gel with n-pentane/ethyl acetate (3:1 to 1:1) as eluent to give the corresponding product 155 as a white solid.
White solid. \(^\text{1H}\) NMR (400 MHz, DMSO) \(\delta\) (ppm) 8.55 (s, 1H), 8.22 (dd, \(J = 8.0, 0.8\) Hz, 1H), 7.93 – 7.82 (m, 4H), 7.69 – 7.65 (m, 1H), 7.43 (dd, \(J = 10.4, 4.8\) Hz, 2H), 7.34 – 7.29 (m, 1H), 5.69 (d, \(J = 15.1\) Hz, 1H), 5.61 (d, \(J = 15.1\) Hz, 1H), 3.85 (s, 3H). \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) (ppm) 146.2, 141.8, 133.7, 132.3, 130.8, 128.9, 128.3, 127.9, 126.5, 125.3, 124.2, 122.1, 121.5, 96.3, 55.2, 42.6. MS (EI): \(m/z = 416\) (4), 414 (4, \(M^+\)), 335 (54). IR (ATR): \(\nu = 2925, 2664, 2326, 1740, 1557, 1456, 1323, 1201, 1049, 753\) (cm\(^{-1}\)). HRMS \(m/z\): Calcd for \([C_{18}H_{15}BN_4OS+H]^+\): 415.0228. Found: 415.0224.

Sulfoximines, a type of molecules possessing interesting biological activities, are applied in medicinal chemistry and crop protections. Over the past two decades, Bolm and other groups have kept a high enthusiasm of studies on sulfoximine chemistry. Recently, several transition metal-catalyzed C–H functionalizations of S-aryl sulfoximines have been discovered including some leading to heterocycles. Among them, rhodium catalysis has been proven to be useful for [4+2] annulation of sulfoximines with alkynes, diazo compounds, allyl methyl carbonate, pyridotriazoles and α-halo and pseudohalo ketones for the preparation of 1,2-benzothiazine 1-oxides. However, the [4+3] annulations of sulfoximines, which leads to 1,2-benzothiazepine 1-oxides, have not been approached yet.

In previous reports, α,β-unsaturated aldehydes or ketones were used as active reaction partners underwent either Michael addition to afford alkylation products, or [3+2] cyclization to form five-membered heterocycles (Scheme 82a and 82b). Noteworthy, Glorius and co-workers reported a Cp*Rh(III)-catalyzed [4+3] cyclization of benzamides with α,β-unsaturated aldehydes and ketones. However, this cyclization was challenging and limited to a few α,β-unsaturated aldehydes and ketones (Scheme 82c).

Scheme 82. C–H activation with α,β-unsaturated carbonyl compounds

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8.1 Results and Discussion

8.1.1 Research Objective

Considering 1,2-benzothiazepines are generally regarded as privileged scaffolds found in numerous drugs and drug candidates,[88] the constructing of the 1,2-benzothiazepine skeleton appeared important. Inspired by the work of Glorius on the rhodium-catalyzed [4 + 3] annulation of benzamides with α,β-unsaturated aldehydes and ketones,[76] we hypothesized that rhodium-catalyzed C–H activation/annulation of sulfoximines with α,β-unsaturated carbonyl compounds to construct 7-membered heterocycles might be possible (Scheme 83).


8.1.2 Optimization of Annulation Reactions

For the initial screening and optimization of the reaction conditions, S-aryl-S-methyl sulfoximine 5a and α,β-unsaturated ketone 123a were subjected to the reaction conditions featuring 2.5 mol % of [Cp*RhCl₂]₂, 10 mol % of AgSbF₆, and 3.0 equiv of pivalic acid in DCE at 100 °C for 14 h. To our delight, 15% yield of annulation product 158aa was obtained, along with 50% yield of difunctionalized product 159aa (Table 6, entry 1). Considering both compounds 158aa and 158aa synthetically attractive, the subsequent reaction optimization focused on preparing them selectively. Firstly, screening of the solvents quickly revealed that toluene was optimal (Table 6, entries 2 and 3). Varying the ratio of sulfoximine 5a and ketone 123a from 1:1 to 3:1 in toluene resulted in an improved yield of 158aa (56%) (Table 6, entries 4-6). Then, a slightly better yield of 159aa was observed when the high ratio of 5a and 123a from 3:1 to 5:1 in toluene at 100 °C (Table 6, entries 7 and 8). Replacement of pivalic acid by 1-adamantanecarboxylic acid or acetic acid afforded product 158aa in 73% and 41% yields, respectively (Table 6, entries 9 and 10). Extending the reaction time from 14 h to 20 h led to 61%
yield of 158aa (Table 6, entry 11), higher catalytic loading of [Cp*RhCl\(_2\)]\(_2\) (4 mol %) had no obvious effect on the yield of 158aa (Table 6, entry 12). It is noteworthy that [RuCl\(_2\)(p-cymene)]\(_2\) also catalyzed this annulation, affording the exclusive monofunctionalized product 158aa, albeit in low yield (Table 6, entry 13). Thus, the best conditions for obtaining 158aa were the following: Use of a 3:1 ratio of 5a:123a, 2.5 mol % of [Cp*RhCl\(_2\)]\(_2\), 10 mol % of AgSbF\(_6\), 3 equiv of 1-adamantanecarboxylic acid in toluene at 100 °C for 14 h (Table 6, entry 9). Subsequently, we examined the conditions for difunctionalized sulfoximines. Surprisingly, replacement of PivOH with two equivalent copper(II) acetate monohydrate produced 159aa in 75% yield as the sole product (Table 6, entry 14). The optimized conditions were accomplished from the reaction of 5a (0.3 mmol) with 123a (0.9 mmol, 3.0 equiv) using [Cp*RhCl\(_2\)]\(_2\) (2.5 mol %), AgSbF\(_6\) (10 mol %) and Cu(OAc)\(_2\)·H\(_2\)O (2.0 equiv) in DCE (3.0 mL) at 70 °C for 6 h, affording 159aa in 89% yield after column (Table 6, entry 16). The structure of 159aa was confirmed by X-ray crystallography.\(^{[89]}\)

**Table 6.** Optimization of reaction conditions.

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<th>Entry</th>
<th>5a/123a</th>
<th>Additive</th>
<th>Solvent</th>
<th>Temp (℃)</th>
<th>t (h)</th>
<th>(158aa/159aa) (%)</th>
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</tbody>
</table>

All reactions were conducted with 0.3 mmol of 5a or 123a. a)[Cp*RhCl₂]₂ (4 mol %), AgSbF₆ (16 mol %) was used. b)[RuCl₂(p-cymene)]₂ (5 mol %) was used. c)Cu(OAc)₂·H₂O (2.0 equiv) was used.

![Figure 3](image_url)  
**Figure 3.** X-Ray crystal structure analysis of compound 158aa

### 8.1.3 Substrate Scope of Sulfoximines and α,β-Unsaturated Ketones

The scope with respected to sulfoximines is summarized in Table 6. Generally, a wide range of sulfoximines reacted with 123a, and proved to be effective in this Cp*Rh(III)-catalyzed annulation. In the presence of [Cp*RhCl₂]₂ (2.5 mol %), AgSbF₆ (10 mol %), and 1-AdCOOH (3.0 equiv) at 100 °C for 14 h, the reactions of sulfoximines 5 with 123a afforded the desired
monofunctionalized products in yields ranging from 45% to 75% (Table 7). With respect to \( S \)-aryl-\( S \)-methyl sulfoximines, various functional groups including methyl, methoxy, fluoro, chloro, ester, carbonyl, and nitro substituents on arene were tolerated in this transformation (Table 7, entries 1-8). Notably, strongly electron-deficient \( \text{para} \)-nitro sulfoximine \( 5g \) generated the product \( 158ga \) in 45% yield. Moreover, this C–H activation preferentially occurred at the less sterically hindered aryl C–H bond, as indicated by the result of benzothiazepine 1-oxide \( 158ta \) (Table 7, entry 9). To our delight, \( S \)-aryl-\( S \)-methyl sulfoximines (\( 5l \) and \( 5u \)) possessing \( \text{ortho} \)-substituents on arenes reacted well, providing the corresponding benzothiazepine 1-oxides \( 158la \) and \( 158ua \) in 75% and 68% yields (Table 7, entries 10 and 11). The reactions using \( S \)-phenyl sulfoximines with \( S \)-ethyl, \( S \)-cyclopropyl, and \( S \)-benzyl substituents proceeded smoothly providing desired products \( 158pa \), \( 158qa \) and \( 158sa \) in yields of 69%-71% (Table 7, entries 12-14). Compared to \( S \)-aryl-\( S \)-methyl sulfoximines, \( S,S \)-diphenyl sulfoximine \( 5z \) produced annulated products \( 158za \) with a slightly lower yield (Table 7, entry 15).

**Table 7.** Scope of sulfoximines.

<table>
<thead>
<tr>
<th>Entry</th>
<th>( \text{R}^1, \text{R}^2 )</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H, Me (( 5a ))</td>
<td><img src="image1.png" alt="image" /></td>
<td>73%</td>
</tr>
<tr>
<td>2</td>
<td>4-Me, Me (( 5b ))</td>
<td><img src="image2.png" alt="image" /></td>
<td>62%</td>
</tr>
</tbody>
</table>

89
3 4-OMe, Me (5e) 60%

4 4-F, Me (5d) 45%

5 4-Cl, Me (5e) 51%

6 4-NO₂, Me (5g) 45%

7 4-CO₂Me, Me (5h) 70%

8 4-C(O)Me, Me (5m) 66%
9 3-Cl, Me (5t)  
\[
\text{Cl-S-N} \quad 51\%
\]

10 2-Cl, Me (5l)  
\[
\text{Cl-S-N} \quad 75\%
\]

11 2-Br, Me (5u)  
\[
\text{Br-S-N} \quad 68\%
\]

12 H, Et (5p)  
\[
\text{S-N} \quad 71\%
\]

13 H, cyclopropyl (5q)  
\[
\quad 70\%
\]

14 H, Bn (5s)  
\[
\quad 69\%
\]
Next, substituted α,β-unsaturated ketones were examined for this annulation employing NH-sulfoximine 5a as the coupling partner. Various substituted aryl ketones reacted well irrespective of the substitution pattern of the arene (Table 8). Notably, halo and ester groups on the para position of the arene were compatible with this annulation (Table 8, entries 2-5). Meta-substituted ketones reacted well regardless of the electronic nature of the substituents, and gave products 158ag-ah in 73% and 72% yields (Table 8, entries 6 and 7). To our delight, sterically hindered 2-chlorophenyl- and 2-bromophenyl-substituted ketones were converted to the corresponding benzothiazepine 1-oxides 158ak-al in 76% and 75% yields, respectively (Table 8, entries 10 and 11). Moreover, furanyl- and thiofuranyl-substituted ketones led to a smooth annulation, providing the desired products 158am-an in 53% and 61% yields (Table 8, entries 12 and 13). Interestingly, the reaction with cyclic ketone 123o successfully led to indene-fused benzothiazepine 1-oxide 158ao in 41% yield (Table 8, entry 14). Besides aryl ketones, cyclohexyl-substituted ketone 123p was selected as representative substrate. However, only a trace amount of the desired product 158ap was observed (Table 8, entry 15).

**Table 8. Scope of α,β-unsaturated ketone.**
<table>
<thead>
<tr>
<th>Entry</th>
<th>α,β-unsaturated ketones</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td><img src="image1" alt="Image" /></td>
<td>65%</td>
</tr>
<tr>
<td></td>
<td>158ab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td><img src="image2" alt="Image" /></td>
<td>72%</td>
</tr>
<tr>
<td></td>
<td>158ac</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td><img src="image3" alt="Image" /></td>
<td>77%</td>
</tr>
<tr>
<td></td>
<td>158ad</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td><img src="image4" alt="Image" /></td>
<td>69%</td>
</tr>
<tr>
<td></td>
<td>158ae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td><img src="image5" alt="Image" /></td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td>158af</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td><img src="image6" alt="Image" /></td>
<td>73%</td>
</tr>
<tr>
<td></td>
<td>158ag</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
7  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{158ah}\]  72%

8  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{158ai}\]  65%

9  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{158aj}\]  64%

10  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{158ak}\]  76%

11  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{158al}\]  75%

12  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{CF}_3\text{O}-\text{C}==\text{C}(\text{CF}_3)\text{C}==\text{O}\]  \[\text{158am}\]  53%
| Reaction conditions: sulfoximine 5a (0.9 mmol), ketone 123 (0.3 mmol), [Cp*RhCl₂]₂ (2.5 mol %), AgSbF₆ (10 mol %), 1-AdCO:H (3.0 equiv), toluene (3.0 mL), 100 °C, 14 h. |
|---|---|---|
| 13 | ![Structure](image1) | 61% |
| 14 | ![Structure](image2) | 41% |
| 15 | ![Structure](image3) | trace |

With a slight modification of the monofunctionalization conditions, sulfoximines were reacted with 3-fold amount of ketones 123 using 2.5 mol% of [Cp*RhCl₂]₂, 10 mol % of AgSbF₆, and 2.0 equiv of copper(II) acetate monohydrate in DCE at 70 °C for 6 h, leading to a variety of alkylated benzothiazepine 1-oxides 159 (Scheme 84). Firstly, with respect to sulfoximines, the reaction using electron-neutral S-methyl-S-phenyl sulfoximine 5a with 123a gave the product 159aa in 89% yield. S-Aryl-S-methyl sulfoximines having electron-donating and -withdrawing groups on the arene led to a slightly lower product yields (159ca, 159ha and 159ga). Similar to S-phenyl S-methyl sulfoximine, S-phenyl S-ethyl and S-benzyl sulfoximines provided corresponding products (159pa and 159sa) in good yields. As for ketones as the coupling partners, 4-chlorophenyl- and furanyl-substituted ketones reacted with 5a and afforded the corresponding products 159ad and 159an in yields of 92% and 78%, respectively. The reaction with meta-bromo-substituted sulfoximine 5k and 123a produced regioisomers 159ka and 159ka’ in overall 84% yield of a 1:1 mixture.
8.1.4 Mechanism

A plausible mechanism for this transformation was shown in Scheme 85. First, sulfoximine 5 reacted with Rh(III) species forming five-membered rhodacycle 5A' by C–H bond activation. This rhodacycle could coordinate one equivalent of 123 to form 158B, which underwent alkene insertion giving intermediate 158C. Protonolysis of 158C led to the intermediate 158D and allowed the rhodium species to start a new catalytic cycle (Scheme 88). The 1,2-benzothiazepine 1-oxides formation was terminated by ring-closing elimination of water, thus converted 158D to the final product 158. In the presence of an excess of 123, 158D underwent a second ortho-functionalization providing product 159 after subsequent mono-dehydration.
8.1.5 Synthetic Transformation

To illustrate the synthetic utility of the products, benzothiazepines 158aa and 159aa were treated with m-CPBA (2.0 equiv) in the presence of NaHCO₃ aqueous solution. As a result, the double bond of the heterocycle was cleaved, and N-benzoyl sulfoximines 160 and 161 were obtained in yields of 76% and 74%, respectively (Scheme 86).
8.1.6 Summary

In summary, we have achieved a rhodium-catalyzed annulation of NH-sulfoximines with ketones providing unprecedented benzothiazepine 1-oxides in moderate to good yields. A mechanistic scheme has been proposed, and the oxidative cleavage of the double bond in the heterocycle was demonstrated.

8.2 Experimental

8.2.1 General Information

α,β-Unsaturated ketones were synthesized according to literature procedures.\(^\text{[90]}\)

8.2.2 General Procedure for the synthesis of benzothiazepine 1-oxides.

\[ \text{Procedure A: A sealed tube (15 mL) was charged with sulfoximine 5 (0.9 mmol), } \alpha,\beta-\text{unsaturated ketone 123 (0.3 mmol), } [\text{Cp*RhCl}_2]_2 (4.7 mg, 2.5 \text{ mol } \%), \text{ AgSbF}_6 (10.3 mg, 10 \text{ mol } \%), 1-\text{AdCO}_2\text{H (162.2 mg, 0.9 mmol) under an argon atmosphere, dry toluene (3.0 mL) was added by syringe. After stirring the reaction mixture at 100 °C for 14 h, it was cooled to room temperature and concentrated in vacuo. The product was purified by column chromatography on silica gel with } n\text{-pentane/ethyl acetate (4:1 to 2:1) as eluent to afford 158.} \]

\[ \text{Procedure B: A sealed tube (15 mL) was charged with sulfoximine 5 (0.3 mmol), } \alpha,\beta-\text{unsaturated ketone 123 (0.9 mmol), } [\text{Cp*RhCl}_2]_2 (4.7 mg, 2.5 \text{ mol } \%), \text{ AgSbF}_6 (10.3 mg, 10 \text{ mol } \%), \text{ Cu(OAc)}_2\cdot\text{H}_2\text{O (119.8 mg, 0.6 mmol) under an argon atmosphere, dry DCE (3.0 mL) was added by syringe. After stirring the reaction mixture at 70 °C for 6 h, it was cooled to room temperature} \]
and extracted with dichloromethane (3 x 10 mL). The combined organic layers were extracted with brine (15 mL), dried over Na₂SO₄ and concentrated in vacuo. The product was purified by column chromatography on silica gel with n-pentane/ethyl acetate (4:1 to 2:1) as eluent to afford 159.

8.2.3 Characterization Data

1-Methyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158aa)

Light yellow syrup, 59.0 mg, 73% yield. ¹H NMR (600 MHz, CDCl₃) δ (ppm) 7.97 (dd, J = 7.7, 1.4 Hz, 1H), 7.73 – 7.71 (m, 2H), 7.50 – 7.41 (m, 2H), 7.32 – 7.21 (m, 4H), 6.14 (dd, J = 7.2, 6.3 Hz, 1H), 4.16 (dd, J = 13.7, 6.1 Hz, 1H), 3.38 (s, 3H), 3.16 (dd, J = 13.7, 7.4 Hz, 1H).

13C NMR (150 MHz, CDCl₃) δ (ppm) 144.6, 142.5, 138.1, 136.4, 133.0, 130.7, 129.1, 128.0, 127.9, 127.5, 125.7, 114.4, 46.7, 32.4. MS (Cl): m/z = 270 ([M+H]+, 100), 269 (32, M⁺). IR (ATR): w = 3027, 2325, 1679, 1441, 1321, 1216, 1066, 971, 749 (cm⁻¹). HRMS m/z: Calcd. for [C₁₆H₁₅NOS+H]+: 270.0953. Found: 270.0952.

1,7-Dimethyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158ba)

Yellow syrup, 52.8 mg, 62% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.85 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 7.1 Hz, 2H), 7.29 (t, J = 7.4 Hz, 2H), 7.22 (d, J = 7.4 Hz, 2H), 7.07 (s, 1H), 6.12 (dd, J = 7.3, 6.2 Hz, 1H), 4.12 (dd, J = 13.6, 6.1 Hz, 1H), 3.35 (s, 3H), 3.08 (dd, J = 13.7, 7.4 Hz, 1H), 2.38 (s, 3H).

13C NMR (100 MHz, CDCl₃) δ (ppm) 144.6, 144.0, 142.6, 138.3, 133.3, 131.1, 129.8, 128.7, 127.9, 127.5, 125.8, 114.5, 47.0, 32.6, 21.4. MS (EI): m/z = 283 (M⁺, 78), 268 (4), 206 (4), 167 (3), 116 (9), 77 (30). IR (ATR): w = 3053, 2925, 2087, 1682, 1598, 1445, 1328, 1222, 1128, 966, 818, 757 (cm⁻¹). HRMS m/z: Calcd for [C₁₇H₁₇NOS+H]+: 284.1109. Found: 284.1106.

7-Methoxy-1-methyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158ca)

Light yellow syrup, 53.8 mg, 60% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.91 (d, J = 8.8 Hz, 1H), 7.72 (dd, J = 5.3, 3.3 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.23 (dd, J = 4.8, 3.6 Hz, 1H), 6.89 (dd, J = 8.8, 2.6 Hz, 1H), 6.74 (d, J = 2.6 Hz, 1H), 6.12 (dd, J = 7.4, 6.1 Hz, 1H), 4.13 (dd, J = 13.5, 6.1 Hz, 1H), 3.84 (s, 3H), 3.35 (s, 3H), 3.05 (dd, J = 13.6, 7.4 Hz, 1H). 13C{¹H} NMR (100 MHz, CDCl₃) δ (ppm)
162.9, 147.1, 142.8, 138.2, 127.9, 127.6, 125.8, 114.3, 114.2, 113.0, 55.5, 47.4, 33.0.

MS (EI): \( m/z = 299 \) (M⁺, 81), 268 (3), 222 (5), 77 (40). IR (ATR): \( \tilde{\nu} = 3022, 2928, 1724, 1587, 1471, 1321, 1229, 1062, 965, 752 \) (cm⁻¹). HRMS \( m/z \): Caled for [C₁₇H₁₇NO₃S+H⁺]: 300.1058. Found: 300.1056.

7-Fluoro-1-methyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158da)

Light yellow syrup, 38.7 mg, 45% yield. \(^1\)H NMR (400 MHz, CDCl₃) \( \delta \) (ppm) 7.97 (dd, \( J = 8.8, 5.6 \) Hz, 1H), 7.70 (d, \( J = 7.2 \) Hz, 2H), 7.30 (t, \( J = 7.4 \) Hz, 2H), 7.23 (t, \( J = 7.3 \) Hz, 1H), 7.09 (td, \( J = 8.4, 2.6 \) Hz, 1H), 6.97 (dd, \( J = 9.0, 2.6 \) Hz, 1H), 6.11 (dd, \( J = 7.3, 6.2 \) Hz, 1H), 4.13 (dd, \( J = 13.7, 6.1 \) Hz, 1H), 3.36 (s, 3H), 3.08 (dd, \( J = 13.7, 7.4 \) Hz, 1H). \(^{13}\)C NMR (100 MHz, CDCl₃) \( \delta \) (ppm) 164.8 (d, \( J_{C-F} = 255 \) Hz), 148.0 (d, \( J_{C-F} = 9 \) Hz), 142.9, 137.8, 133.9 (d, \( J_{C-F} = 9 \) Hz), 132.2, 128.0, 127.7, 125.8, 116.0 (d, \( J_{C-F} = 22 \) Hz), 115.1 (d, \( J_{C-F} = 22 \) Hz), 113.9, 47.0, 32.6. \(^{19}\)F NMR (376 MHz, CDCl₃) \( \delta \) -104.87 (dd, \( J = 14.2, 7.8 \) Hz). MS (EI): \( m/z = 287 \) (M⁺, 70), 268 (2), 77 (20). IR (ATR): \( \tilde{\nu} = 3042, 2929, 1731, 1686, 1599, 1498, 1318, 1129, 967, 750 \) (cm⁻¹). HRMS \( m/z \): Caled for [C₁₆H₁₄NOSF+H⁺]: 288.0858. Found: 288.0858.

7-Chloro-1-methyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158ea)

Light yellow syrup, 46.4 mg, 51% yield. \(^1\)H NMR (400 MHz, CDCl₃) \( \delta \) (ppm) 7.90 (d, \( J = 8.5 \) Hz, 1H), 7.70 (d, \( J = 7.1 \) Hz, 2H), 7.40 (dd, \( J = 8.5, 2.2 \) Hz, 1H), 7.33 – 7.27 (m, 3H), 7.26 – 7.21 (m, 1H), 6.11 (dd, \( J = 7.3, 6.2 \) Hz, 1H), 4.12 (dd, \( J = 13.7, 6.2 \) Hz, 1H), 3.37 (s, 3H), 3.09 (dd, \( J = 13.8, 7.4 \) Hz, 1H). \(^{13}\)C NMR (100 MHz, CDCl₃) \( \delta \) (ppm) 146.4, 142.9, 139.4, 137.8, 134.8, 132.5, 129.1, 128.2, 128.1, 127.8, 125.8, 113.9, 46.9, 32.4. MS (EI): \( m/z = 303 \) (M⁺, 71), 186 (3), 116 (4), 77 (50). IR (ATR): \( \tilde{\nu} = 3016, 2921, 1735, 1575, 1450, 1329, 1224, 1132, 964, 747 \) (cm⁻¹). HRMS \( m/z \): Caled for [C₁₆H₁₄NOSCl+H⁺]: 304.0563. Found: 304.0562.
1-Methyl-7-nitro-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158ga)

Orange solid, melting point: 168 – 170 °C, 42.4 mg, 45% yield. 1H NMR (600 MHz, CDCl3) δ (ppm) 8.22 (dd, J = 8.6, 2.3 Hz, 1H), 8.11 (dd, J = 7.5, 5.5 Hz, 2H), 7.70 – 7.69 (m, 2H), 7.33 – 7.31 (m, 2H), 7.27 (dt, J = 9.1, 4.4 Hz, 1H), 6.12 – 6.09 (m, 1H), 4.17 (dd, J = 14.0, 6.3 Hz, 1H), 3.43 (s, 3H), 3.34 (dd, J = 14.0, 7.2 Hz, 1H). 13C NMR (150 MHz, CDCl3) δ (ppm) 149.8, 146.2, 143.0, 142.4, 137.5, 131.9, 128.2, 128.1, 125.8, 123.9, 122.7, 112.9, 46.3, 32.4. MS (EI): m/z = 314 (M+, 78), 268 (3), 237 (3), 102 (13), 77 (38). IR (ATR): ν = 2913, 1738, 1611, 1519, 1336, 1229, 1133, 974, 895, 748 (cm–1). HRMS m/z: Calcd for [C16H14N2O3S+H] +: 315.0803. Found: 315.0803.

Methyl-1-methyl-3-phenylbenzo[f][1,2]thiazepine-7-carboxylate 1-oxide (158ha)

Light yellow syrup, 68.7 mg, 70% yield. 1H NMR (400 MHz, CDCl3) δ (ppm) 8.04 (dt, J = 15.3, 4.9 Hz, 2H), 7.94 (d, J = 0.9 Hz, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.24 (d, J = 7.2 Hz, 1H), 6.11 (dd, J = 7.1, 6.4 Hz, 1H), 4.14 (dd, J = 13.9, 6.2 Hz, 1H), 3.95 (s, 3H), 3.39 (s, 3H), 3.27 (dd, J = 13.9, 7.3 Hz, 1H). 13C NMR (100 MHz, CDCl3) δ (ppm) 165.6, 144.6, 142.7, 140.5, 137.9, 133.9, 130.7, 130.2, 128.8, 128.0, 127.7, 125.8, 113.7, 52.6, 46.4, 32.4. MS (EI): m/z = 327 (M+, 65), 225 (4), 211 (5), 116 (8), 102 (16), 77 (58). IR (ATR): ν = 3021, 2927, 1719, 1609, 1438, 1278, 1116, 974, 907, 743 (cm–1). HRMS m/z: Calcd for [C18H17NO3S+H] +: 328.1007. Found: 328.1003.

1-(1-Methyl-1-oxido-3-phenylbenzo[f][1,2]thiazepin-7-yl)ethanone (158ma)

Yellow syrup, 61.6 mg, 66% yield. 1H NMR (400 MHz, CDCl3) δ (ppm) 8.04 (d, J = 8.2 Hz, 1H), 7.94 (dd, J = 8.2, 1.3 Hz, 1H), 7.82 (s, 1H), 7.70 (d, J = 7.1 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.24 (d, J = 7.2 Hz, 1H), 6.11 (dd, J = 7.2, 6.3 Hz, 1H), 4.15 (dd, J = 13.9, 6.3 Hz, 1H), 3.40 (s, 3H), 3.28 (dd, J = 13.9, 7.3 Hz, 1H), 2.63 (s, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 196.9, 145.0, 142.8, 140.6, 140.1, 137.9, 131.0, 128.8, 128.1, 127.8, 127.6, 125.8, 113.7, 46.5, 32.5, 26.9. MS (EI): m/z = 311 (M+, 70), 195 (3), 116 (4), 102 (10), 77 (37). IR (ATR): ν = 3018, 2929, 1739, 1687, 1569, 1408, 1224, 1130, 962, 752 (cm–1). HRMS m/z: Calcd for
[C_{18}H_{17}NO_2S+H]^+: 312.1058. Found: 312.1058.

8-Chloro-1-methyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158ta)

Light yellow syrup, 46.4 mg, 51% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.94 (d, $J = 2.2$ Hz, 1H), 7.69 (d, $J = 7.3$ Hz, 2H), 7.42 (dd, $J = 8.2$, 2.2 Hz, 1H), 7.30 (t, $J = 7.4$ Hz, 2H), 7.24 (d, $J = 7.2$ Hz, 1H), 7.19 (d, $J = 8.2$ Hz, 1H), 6.10 (dd, $J = 7.3$, 6.2 Hz, 1H), 4.08 (dd, $J = 13.8$, 6.1 Hz, 1H), 3.37 (s, 3H), 3.11 (dd, $J = 13.8$, 7.4 Hz, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 143.0, 142.5, 137.8, 137.7, 133.7, 133.1, 130.5, 128.0, 127.7, 125.7, 114.2, 46.6, 31.8. MS (EI): m/z = 303 (M$^+$, 96), 226 (2), 187 (6), 77 (9). IR (ATR): ν = 3058, 2926, 2086, 1737, 1617, 1471, 1328, 1226, 1133, 974, 856, 759 (cm$^{-1}$). HRMS m/z: Calcd for [C$_{16}$H$_{14}$NOSCl+H]$^+$: 304.0563. Found: 304.0560.

9-Chloro-1-methyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158la)

Light yellow solid, melting point: 179 – 181°C, 68.2 mg, 75% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.78 (dd, $J = 8.3$, 1.0 Hz, 2H), 7.47 (d, $J = 8.0$ Hz, 1H), 7.34 (dt, $J = 11.1$, 7.8 Hz, 3H), 7.28 – 7.24 (m, 1H), 7.21 (d, $J = 7.7$ Hz, 1H), 6.20 (dd, $J = 7.4$, 5.9 Hz, 1H), 4.30 (dd, $J = 13.7$, 5.8 Hz, 1H), 3.58 (s, 3H), 3.17 (dd, $J = 13.7$, 7.5 Hz, 1H).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 146.4, 142.3, 137.3, 136.6, 134.9, 132.7, 131.3, 129.1, 128.0, 127.8, 126.0, 115.2, 43.8, 33.8. MS (CI): m/z = 304 ([M+H]$^+$, 100), 303 (M$^+$, 2). IR (ATR): ν = 3058, 2926, 2323, 1567, 1440, 1316, 1219, 1130, 973, 755 (cm$^{-1}$). HRMS m/z: Calcd for [C$_{16}$H$_{14}$NOSCl+Na]$^+$: 326.0382. Found: 326.0377.

9-Bromo-1-methyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158ua)

Light yellow solid, melting point: 190 – 192°C, 70.8 mg, 68% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.77 (d, $J = 8.1$ Hz, 2H), 7.69 (t, $J = 4.6$ Hz, 1H), 7.32 (t, $J = 7.6$ Hz, 2H), 7.25 (dd, $J = 12.1$, 3.0 Hz, 3H), 6.20 (t, $J = 6.6$ Hz, 1H), 4.33 (dd, $J = 13.6$, 5.8 Hz, 1H), 3.59 (s, 3H), 3.15 (dd, $J = 13.5$, 7.5 Hz, 1H).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 146.8, 142.3, 138.0, 137.2, 135.2, 132.9, 129.8, 128.0, 126.0, 123.7, 115.4, 43.5, 34.2. MS (EI): m/z = 347 (M$^+$, 57), 231 (21), 116 (9), 102 (41), 77 (61). IR (ATR): ν = 3019, 2929, 2323, 1567, 1440, 1316, 1219, 1130, 973, 755 (cm$^{-1}$). HRMS m/z: Calcd for
[C\textsubscript{16}H\textsubscript{14}NOS\textsubscript{Br}+Na\textsuperscript{+}]: 369.9877. Found: 369.9874.

1-Ethyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158pa)

Light yellow syrup, 60.3 mg, 71% yield. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm) 7.92 (dd, \( J = 7.7, 1.3 \) Hz, 1H), 7.74 – 7.72 (m, 2H), 7.49 – 7.40 (m, 2H), 7.32 – 7.20 (m, 4H), 6.14 (dd, \( J = 7.4, 6.1 \) Hz, 1H), 4.20 (dd, \( J = 13.6, 6.0 \) Hz, 1H), 3.52 – 3.41 (m, 2H), 3.07 (dd, \( J = 13.7, 7.5 \) Hz, 1H), 1.43 (t, \( J = 7.4 \) Hz, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm) 145.8, 142.4, 138.3, 134.6, 133.0, 131.8, 129.2, 128.0, 127.9, 127.5, 125.9, 114.5, 133.0, 32.7. MS (EI): \textit{m/z} = 283 (M\textsuperscript{+}, 85), 206 (17), 77 (14). IR (ATR): \( \nu \) = 3056, 2938, 1735, 1617, 1444, 1325, 1219, 1131, 906, 734 (cm\textsuperscript{-1}). HRMS \textit{m/z}: Calcd for [C\textsubscript{17}H\textsubscript{17}NOS+H\textsuperscript{+}]: 284.1109. Found: 284.1104.

1-Cyclopropyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158qa)

Light yellow syrup, 62.0 mg, 70% yield. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm) 7.86 (d, \( J = 7.7 \) Hz, 1H), 7.69 (d, \( J = 7.3 \) Hz, 2H), 7.46 (td, \( J = 7.4, 1.1 \) Hz, 1H), 7.39 (t, \( J = 7.1 \) Hz, 1H), 7.28 (q, \( J = 7.3 \) Hz, 3H), 7.21 (t, \( J = 7.2 \) Hz, 1H), 6.06 (t, \( J = 6.8 \) Hz, 1H), 4.08 (dd, \( J = 13.8, 6.5 \) Hz, 1H), 3.27 (dd, \( J = 13.9, 7.1 \) Hz, 1H), 2.89 – 2.83 (m, 1H), 1.66 – 1.53 (m, 1H), 1.51 – 1.46 (m, 1H), 1.23 – 1.15 (m, 1H) 1.13 – 1.04 (m, 1H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm) 144.0, 142.3, 138.7, 136.9, 132.7, 129.9, 129.0, 127.9, 127.7, 127.4, 125.8, 112.4, 34.2, 32.4, 5.9, 5.8. MS (EI): \textit{m/z} = 295 (M\textsuperscript{+}, 100), 218 (1), 179 (2), 116 (2), 77 (15). IR (ATR): \( \nu \) = 3056, 2110, 1735, 1619, 1443, 1225, 1135, 1065, 884, 732 (cm\textsuperscript{-1}). HRMS \textit{m/z}: Calcd for [C\textsubscript{18}H\textsubscript{17}NOS+H\textsuperscript{+}]: 296.1109. Found: 296.1104.

1-Benzyl-3-phenylbenzo[f][1,2]thiazepine 1-oxide (158sa)

Light yellow syrup, 71.4 mg, 69% yield. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm) 7.76 – 7.73 (m, 3H), 7.41 (td, \( J = 7.5, 1.4 \) Hz, 1H), 7.34 – 7.30 (m, 4H), 7.25 – 7.20 (m, 3H), 7.07 (t, \( J = 7.0 \) Hz, 3H), 6.01 (dd, \( J = 7.5, 6.1 \) Hz, 1H), 4.71 (d, \( J = 13.7 \) Hz, 1H), 4.56 (d, \( J = 13.7 \) Hz, 1H), 3.37 (dd, \( J = 13.6, 6.0 \) Hz, 1H), 2.64 (dd, \( J = 13.6, 7.6 \) Hz, 1H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm) 146.8, 142.1, 138.2, 133.5, 133.2, 132.4, 131.4, 129.2, 128.7, 128.5, 128.1, 127.9, 127.6, 127.4, 125.9, 114.5, 65.1, 31.9. MS (EI): \textit{m/z} = 345 (M\textsuperscript{+}, 100), 268 (100), 218 (1), 181 (2), 106 (2), 101 (2), 77 (15). IR (ATR): \( \nu \) = 3056, 2938, 1735, 1619, 1443, 1225, 1135, 1065, 884, 732 (cm\textsuperscript{-1}). HRMS \textit{m/z}: Calcd for [C\textsubscript{18}H\textsubscript{17}NOS+H\textsuperscript{+}]: 296.1109. Found: 296.1104.

1,3-Diphenylbenzo[f][1,2]thiazepine 1-oxide (158za)

Light yellow syrup, 54.6 mg, 55% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm)
8.26 (d, J = 7.0 Hz, 2H), 7.79 (d, J = 7.7 Hz, 2H), 7.74 (d, J = 7.8 Hz, 1H), 7.63 – 7.52 (m, 3H), 7.39 (t, J = 7.4 Hz, 1H), 7.35 – 7.27 (m, 3H), 7.24 (dd, J = 11.2, 7.6 Hz, 2H), 6.15 (t, J = 6.8 Hz, 1H), 4.19 (dd, J = 14.0, 6.5 Hz, 1H), 3.35 (dd, J = 14.0, 7.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 143.8, 142.3, 141.6, 138.6, 138.0, 132.9, 132.7, 130.4, 129.1, 129.0, 128.5, 128.0, 127.8, 127.5, 125.9, 112.2, 32.3. MS (EI): m/z = 331 (M⁺, 9), 229 (2), 228 (6), 103 (9), 102 (6), 77 (44).

IR (ATR): ν = 3060, 2089, 1724, 1683, 1593, 1444, 1326, 1229, 1137, 904, 752 (cm⁻¹). HRMS m/z: Caled for [C₂₁H₁₇NOS⁺H]⁺: 332.1109. Found: 332.1104.

3-(4-Methoxyphenyl)-1-methylbenzo[f][1,2]thiazepine 1-oxide (158ab)

Yellow syrup, 58.3 mg, 65% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm)
7.96 (d, J = 8.3 Hz, 1H), 7.65 (d, J = 8.8 Hz, 2H), 7.44 (dt, J = 20.8, 7.3 Hz, 2H), 7.25 (d, J = 7.5 Hz, 1H), 6.83 (d, J = 8.8 Hz, 2H), 6.02 (t, J = 6.7 Hz, 1H), 4.13 (dd, J = 13.7, 6.1 Hz, 1H), 3.78 (s, 3H), 3.36 (s, 3H), 3.11 (dd, J = 13.8, 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 159.3, 145.0, 142.1, 136.5, 133.1, 131.0, 130.9, 129.1, 128.0, 127.1, 113.4, 112.8, 55.2, 46.8, 32.5. MS (EI): m/z = 299 (M⁺, 67), 192 (5), 153 (3), 146 (2), 103 (6). IR (ATR): ν = 3017, 2940, 2105, 1738, 1600, 1505, 1309, 1228, 969, 753 (cm⁻¹). HRMS m/z: Caled for [C₁₇H₁₇NO₂S⁺H]⁺: 300.1058. Found: 300.1055.

3-(4-Fluorophenyl)-1-methylbenzo[f][1,2]thiazepine 1-oxide (158ac)

Light yellow syrup, 62.0 mg, 72% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm)
7.98 (dd, J = 8.7, 5.6 Hz, 1H), 7.71 (d, J = 7.4 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 7.10 (td, J = 8.4, 2.5 Hz, 1H), 6.97 (dd, J = 9.0, 2.4 Hz, 1H), 6.11 (t, J = 6.7 Hz, 1H), 4.13 (dd, J = 13.7, 6.0 Hz, 1H), 3.36 (s, 3H), 3.08 (dd, J = 13.7, 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 164.8 (d, J_C-F = 255 Hz ),
148.0 (d, $J_{C-F} = 44$ Hz), 142.9, 137.8, 133.9 (d, $J_{C-F} = 10$ Hz), 132.2 (d, $J_{C-F} = 3$ Hz), 128.0, 127.7, 125.8, 116.0 (d, $J_{C-F} = 22$ Hz), 115.1 (d, $J_{C-F} = 22$ Hz), 113.9, 47.0, 32.6. $^{19}$F NMR (376 MHz, CDCl$_3$) δ -104.86 (dd, $J = 13.9, 7.8$ Hz).

MS (EI): $m/z = 287$ (M$^+$, 83), 153 (4), 134 (2), 95(3). IR (ATR): $\nu = 3062, 2111, 1739, 1599, 1470, 1330, 1223, 1132, 965, 828, 752$ (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{16}$H$_{14}$NOSF+H]$^+$: 288.0858. Found: 288.0556.

3-(4-Chlorophenyl)-1-methylbenzo[f][1,2]thiazepine 1-oxide (158ad)

Light yellow syrup, 70.0 mg, 77% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.95 (dd, $J = 7.7, 1.3$ Hz, 1H), 7.64 (d, $J = 8.7$ Hz, 2H), 7.50 – 7.39 (m, 2H), 7.27 – 7.23 (m, 3H), 6.11 (dd, $J = 7.3, 6.2$ Hz, 1H), 4.12 (dd, $J = 13.7, 6.1$ Hz, 1H), 3.36 (s, 3H), 3.14 (dd, $J = 13.7, 7.4$ Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 144.5, 141.6, 136.8, 136.4, 133.3, 133.2, 130.8, 129.3, 128.2, 128.1, 127.2, 114.9, 46.8, 32.5. MS (EI): $m/z = 303$ (M$^+$, 72), 192 (2), 153 (3), 150 (2), 111 (8). IR (ATR): $\nu = 3018, 2927, 1731, 1589, 1483, 1277, 1217, 1128, 970, 831, 752$ (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{16}$H$_{14}$NOSCl+H]$^+$: 304.0563. Found: 304.0560.

3-(4-Bromophenyl)-1-methylbenzo[f][1,2]thiazepine 1-oxide (158ae)

Light yellow syrup, 71.8 mg, 69% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.95 (d, $J = 7.7$ Hz, 1H), 7.58 (d, $J = 8.5$ Hz, 2H), 7.47 – 7.39 (m, 4H), 7.25 (d, $J = 6.7$ Hz, 1H), 6.12 (t, $J = 6.8$ Hz, 1H), 4.12 (dd, $J = 13.7, 6.1$ Hz, 1H), 3.36 (s, 3H), 3.14 (dd, $J = 13.8, 7.4$ Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 144.4, 141.6, 137.2, 136.3, 133.2, 131.0, 130.8, 129.3, 128.2, 127.5, 121.5, 115.0, 46.8, 32.5. MS (EI): $m/z = 346$ (M$^+$, 68), 268 (9), 192 (2), 155 (3). IR (ATR): $\nu = 3057, 2926, 1732, 1588, 1479, 1321, 1223, 1134, 970, 830, 751$ (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{16}$H$_{14}$NOSBr+H]$^+$: 348.0058. Found: 348.0056.
**Methyl 4-(1-methyl-1-oxidobenzof[1,2]thiazepin-3-yl)benzoate (158af)**

Light yellow syrup, 69.7 mg, 71% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.96 – 7.93 (m, 3H), 7.77 (d, J = 8.4 Hz, 2H), 7.48 – 7.39 (m, 2H), 7.25 (d, J = 6.9 Hz, 1H), 6.24 (t, J = 6.8 Hz, 1H), 4.14 (dd, J = 13.7, 6.2 Hz, 1H), 3.87 (s, 3H), 3.37 (s, 3H), 3.17 (dd, J = 13.7, 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 167.0, 144.1, 142.6, 141.8, 136.3, 133.3, 130.7, 129.4, 129.3, 128.9, 128.2, 125.6, 116.7, 51.9, 46.8, 32.5. MS (EI): m/z = 327 (M⁺, 80), 268 (72), 192 (3), 135 (14). IR (ATR): ν = 3069, 2952, 2097, 1705, 1607, 1441, 1283, 1148, 957, 746 (cm⁻¹). HRMS m/z: Calcd for [C₁₈H₁₇NOS⁺H]⁺: 328.1007. Found: 328.1000.

**3-(3-Methoxyphenyl)-1-methylbenzo[f][1,2]thiazepine 1-oxide (158ag)**

Yellow syrup, 65.5 mg, 73% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.94 (dd, J = 7.7, 1.5 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.30 – 7.28 (m, 2H), 7.24 (d, J = 7.3 Hz, 1H), 7.19 (t, J = 8.1 Hz, 1H), 6.80 – 6.75 (m, 1H), 6.11 (dd, J = 7.3, 6.3 Hz, 1H), 4.12 (dd, J = 13.7, 6.2 Hz, 1H), 3.80 (s, 3H), 3.35 (s, 3H), 3.13 (dd, J = 13.7, 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 159.4, 144.5, 142.4, 139.8, 136.8, 133.1, 130.7, 129.2, 128.9, 128.0, 118.3, 114.7, 113.5, 111.2, 55.1, 46.7, 32.5. MS (EI): m/z = 299 (M⁺, 100), 268 (31), 192 (2), 107 (5). IR (ATR): ν = 3056, 2935, 2107, 1681, 1581, 1431, 1234, 1129, 1043, 968, 736 (cm⁻¹). HRMS m/z: Calcd for [C₁₇H₁₇NO₂S⁺H]⁺: 300.1058. Found: 300.1055.

**1-Methyl-3-(3-(trifluoromethyl)phenyl)benzo[f][1,2]thiazepine 1-oxide (158ah)**

Light yellow syrup, 72.8 mg, 72% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.96 – 7.91 (m, 3H), 7.51 – 7.39 (m, 4H), 7.27 (d, J = 6.9 Hz, 1H), 6.20 (dd, J = 7.3, 6.3 Hz, 1H), 4.14 (dd, J = 13.8, 6.2 Hz, 1H), 3.39 (s, 3H), 3.20 (dd, J = 13.8, 7.3 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 144.1, 141.5, 139.2, 136.4, 133.3, 130.6, 129.3, 129.2 (d, J_C-F = 1.1 Hz), 128.5, 128.2, 124.1 (q, J_C-F = 7.4 Hz), 122.5 (q, J_C-F = 7.8 Hz), 115.7, 46.7, 32.5. ¹⁹F NMR (376 MHz, CDCl₃) δ –62.6 (s, 3F). MS (EI): m/z = 337 (M⁺, 66), 268 (11), 192 (2), 145 (8). IR (ATR): ν = 3007, 2926, 2108, 1739, 1617, 1435, 1334, 1221, 1105, 975, 752 (cm⁻¹). HRMS m/z: Calcd for [C₁₇H₁₄NOSF₃⁺H]⁺: 106
338.0826. Found: 338.0821.

1-Methyl-3-(naphthalen-2-yl)benzo[f][1,2]thiazepine 1-oxide (158ai)

Light yellow syrup, 62.2 mg, 65% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 8.32 (s, 1H), 8.03 (d, $J$ = 7.8 Hz, 1H), 7.93 (d, $J$ = 7.8 Hz, 1H), 7.81 (dd, $J$ = 8.6, 1.3 Hz, 2H), 7.77 (d, $J$ = 8.7 Hz, 1H), 7.54 – 7.44 (m, 4H), 7.32 – 7.29 (m, 1H), 6.34 – 6.32 (m, 1H), 4.25 (dd, $J$ = 13.7, 6.2 Hz, 1H), 3.46 (s, 3H), 3.24 (dd, $J$ = 13.8, 7.4 Hz, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 144.7, 142.5, 136.5, 135.5, 133.4, 133.2, 133.0, 130.9, 129.2, 128.6, 128.1, 127.4, 127.3, 125.8, 125.7, 125.3, 123.6, 115.2, 46.9, 32.7. MS (CI): $m/z$ = 320 ([M+H]$^+$, 100), 319 (M$^+$, 22), 192 (4), 153 (5), 127 (2). IR (ATR): $\tilde{\nu}$ = 3050, 2929, 2321, 1727, 1605, 1464, 1312, 1226, 1127, 966, 750 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{20}$H$_{17}$NOS+Na]$^+$: 342.0929. Found: 342.0925.

3-(Benzo[d][1,3]dioxol-5-yl)-1-methylbenzo[f][1,2]thiazepine 1-oxide (158aj)

Yellow syrup, 60.1 mg, 64% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.94 (dd, $J$ = 7.7, 1.4 Hz, 1H), 7.42 (dt, $J$ = 13.7, 7.5, 4.0 Hz, 2H), 7.25 (dt, $J$ = 9.1, 4.6 Hz, 2H), 7.18 (d, $J$ = 1.6 Hz, 1H), 6.73 (d, $J$ = 8.2 Hz), 5.97 (dd, $J$ = 7.3, 6.2 Hz, 1H), 5.89 (s, 2H), 4.10 (dd, $J$ = 13.7, 6.1 Hz, 1H), 3.34 (s, 3H), 3.09 (dd, $J$ = 13.8, 7.4 Hz, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 147.4, 147.2, 144.8, 142.1, 136.4, 133.1, 132.8, 130.8, 129.1, 128.0, 119.9, 113.3, 107.7, 106.3, 100.8, 46.7, 32.5. MS (EI): $m/z$ = 313 (M$^+$, 75), 192 (11), 167 (3), 146 (18), 121 (18). IR (ATR): $\tilde{\nu}$ = 3061, 2891, 1601, 1484, 1308, 1234, 1121, 1036, 910, 727 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{17}$H$_{15}$NO$_3$S+H]$^+$: 314.0851. Found: 314.0847.

3-(2-Chlorophenyl)-1-methylbenzo[f][1,2]thiazepine 1-oxide (158ak)

Light yellow syrup, 69.1 mg, 76% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.95 (dd, $J$ = 7.7, 1.5 Hz, 1H), 7.64 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.31 (dd, $J$ = 7.9, 1.2 Hz, 1H), 7.27 (d, $J$ = 6.6 Hz, 1H), 7.21 (td, $J$ = 7.5, 1.4 Hz, 1H), 7.15 – 7.10 (m, 1H), 5.91 (dd, $J$ = 7.2, 6.4 Hz, 1H), 4.09 (dd, $J$ = 13.9, 6.3 Hz, 1H), 3.36 (s, 3H), 3.28 (dd, $J$ = 13.9, 7.2 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 143.8, 140.0,
137.8, 136.4, 133.2, 131.9, 131.1, 129.9, 129.8, 129.2, 128.3, 128.0, 126.5, 118.8, 46.3, 32.3. MS (EI): \( m/z = 303 \) (M⁺, 88), 268 (26), 192 (2), 111 (3). IR (ATR): \( \nu = 3059, 2928, 1728, 1622, 1432, 1322, 1218, 1134, 964, 746 \) (cm⁻¹). HRMS \( m/z \): Calcd for \( [\text{C}_{16}\text{H}_{14}\text{NOSCl}+\text{H}]^+ \): 304.0563. Found: 304.0561.

3-(2-Bromophenyl)-1-methylbenzo[\( f \)][1,2]thiazepine 1-oxide (158al)

Light yellow syrup, 78.1 mg, 75% yield. \(^1\)H NMR (400 MHz, CDCl₃) δ (ppm) 7.92 (dd, \( J = 7.8, 1.3 \) Hz, 1H), 7.56 (dd, \( J = 7.7, 1.7 \) Hz, 1H), 7.52 – 7.47 (m, 2H), 7.45 (td, \( J = 7.6, 1.3 \) Hz, 1H), 7.28 – 7.23 (m, 2H), 7.06 (td, \( J = 7.7, 1.7 \) Hz, 1H), 5.74 (t, \( J = 6.8 \) Hz, 1H), 4.01 (dd, \( J = 14.0, 6.5 \) Hz, 1H), 3.41 – 3.32 (m, 4H). \(^{13}\)C NMR (100 MHz, CDCl₃) δ (ppm) 143.3, 142.0, 140.3, 136.5, 133.2, 133.0, 129.3, 129.2, 128.6, 127.9, 127.1, 122.0, 117.2, 46.0, 32.0. MS (EI): \( m/z = 346 \) (M⁺, 63), 268 (81), 192 (5), 153 (9). IR (ATR): \( \nu = 3025, 2928, 1736, 1617, 1444, 1333, 1202, 1127, 960, 750 \) (cm⁻¹). HRMS \( m/z \): Calcd for \( [\text{C}_{16}\text{H}_{14}\text{NOSBr}+\text{Na}]^+ \): 369.9877. Found: 369.9872

1-Methyl-3-(thiophen-2-yl)benzo[\( f \)][1,2]thiazepine 1-oxide (158am)

Yellow syrup, 43.7 mg, 53% yield. \(^1\)H NMR (400 MHz, CDCl₃) δ (ppm) 7.93 (dd, \( J = 7.8, 1.2 \) Hz, 1H), 7.46 – 7.39 (m, 2H), 7.29 (d, \( J = 3.6 \) Hz, 1H), 7.24 (d, \( J = 7.7 \) Hz, 1H), 7.11 (d, \( J = 5.0 \) Hz, 1H), 6.93 (dd, \( J = 5.0, 3.7 \) Hz, 1H), 6.02 (t, \( J = 6.8 \) Hz, 1H), 4.08 (dd, \( J = 14.0, 6.3 \) Hz, 1H), 3.34 (s, 3H), 3.14 (dd, \( J = 14.0, 7.3 \) Hz, 1H). \(^{13}\)C NMR (100 MHz, CDCl₃) δ (ppm) 144.2, 143.9, 137.5, 136.8, 133.1, 130.4, 129.3, 128.0, 127.2, 124.4, 124.3, 113.0, 46.4, 32.2. MS (EI): \( m/z = 275 \) (M⁺, 100), 260 (12), 83 (31). IR (ATR): \( \nu = 3274, 3066, 2931, 2072, 1923, 1741, 1630, 1522, 1319, 1229, 1124, 964, 706 \) (cm⁻¹). HRMS \( m/z \): Calcd for \( [\text{C}_{14}\text{H}_{13}\text{NOS}_2+\text{H}]^+ \): 276.0517. Found: 276.0512.

3-(Furan-2-yl)-1-methylbenzo[\( f \)][1,2]thiazepine 1-oxide (158an)

Yellow syrup, 47.4 mg, 61% yield. \(^1\)H NMR (400 MHz, CDCl₃) δ (ppm) 7.93 (d, \( J = 7.7 \) Hz, 1H), 7.44 (dd, \( J = 21.5, 10.8, 6.4 \) Hz, 2H), 7.28 – 7.24 (m, 2H), 6.60 (d, \( J = 3.2 \) Hz, 1H), 6.35 (dd, \( J = 3.0, 1.7 \) Hz, 1H), 6.11 (t, \( J = 6.9 \) Hz, 1H), 4.10 (dd, \( J = 13.7, 6.2 \) Hz, 1H), 3.34 (s, 3H), 3.17 (dd, \( J = 13.9, 7.4 \) Hz, 1H). \(^{13}\)C NMR (100 MHz,
CDCl₃ δ (ppm) 153.4, 144.5, 141.9, 136.9, 133.9, 133.1, 130.6, 129.4, 128.0, 113.2, 111.3, 107.8, 46.5, 31.9. MS (EI): m/z = 259 (M⁺, 100), 167 (10), 153 (2). IR (ATR): ν = 2933, 1716, 1674, 1480, 1324, 1226, 1136, 971, 743 (cm⁻¹). HRMS m/z: Calcd for [C₁₄H₁₁NO₂S⁺H⁺]: 260.0745. Found: 260.0741.

5-Methyl-11,12-dihydrobenzo[f]inden[1,2-c][1,2]thiazepine 5-oxide (158ao)

White solid, melting point: 60 – 62 °C, 34.6 mg, 41% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.58 (dd, J = 7.9, 0.8 Hz, 1H), 7.51 – 7.43 (m, 2H), 7.35 – 7.29 (m, 2H), 7.26 (t, J = 8.7 Hz, 2H), 7.13 (td, J = 7.4, 1.1 Hz, 1H), 4.43 (d, J = 15.8 Hz, 1H), 3.66 (d, J = 15.8 Hz, 1H), 3.59 (s, 3H), 3.40 (q, J = 22.4 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 144.6, 141.0, 140.3, 138.0, 132.9, 129.5, 126.9, 126.1, 124.3, 123.0, 122.7, 117.9, 116.2, 42.2, 39.8, 33.4. MS (CI): m/z = 282 ([M+H⁺], 65), 281 (M⁺, 13), 153 (30). IR (ATR): ν = 3025, 2925, 2313, 1739, 1677, 1579, 1447, 1323, 1215, 1133, 1045, 971, 750 (cm⁻¹). HRMS m/z: Calcd for [C₁₇H₁₅NOS⁺Na⁺]: 304.0772. Found: 304.0767.

3-(1-Methyl-1-oxido-3-phenylbenzo[f][1,2]thiazepin-9-yl)-1-phenylpropan-1-one (159aa)

Yellow solid, melting point: 182 – 184 °C, 107.1 mg, 89% yield. ¹H NMR (600 MHz, CDCl₃) δ (ppm) 7.92 (d, J = 7.5 Hz, 1H), 7.79 (d, J = 7.4 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.9 Hz, 1H), 7.36 (d, J = 7.5 Hz, 1H), 7.32 (dd, J = 12.8, 5.3 Hz, 1H), 7.23 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 7.3 Hz, 1H), 6.27 (dd, J = 7.2, 6.1 Hz, 1H), 4.30 (dd, J = 13.5, 5.9 Hz, 1H), 3.69 – 3.63 (m, 1H), 3.58 – 3.53 (m, 1H), 3.48 (s, 3H), 3.25 – 3.20 (m, 1H), 3.14 – 3.08 (m, 2H). ¹³C NMR (150 MHz, CDCl₃) δ (ppm) 199.0, 145.5, 144.6, 142.1, 137.5, 136.9, 136.6, 132.9, 132.5, 131.7, 128.7, 128.4, 128.0, 127.6, 125.8, 115.8, 45.8, 41.3, 34.1, 29.8. MS (EI): m/z = 401 (M⁺, 39), 296 (72), 105 (100), 77 (93). IR (ATR): ν = 3030, 2935, 2313, 1739, 1677, 1579, 1447, 1323, 1215, 1133, 1045, 971, 750 (cm⁻¹). HRMS m/z: Calcd for [C₂₅H₂₃NO₂S⁺H⁺]: 402.1528. Found: 402.1525.
3-(7-Methoxy-1-methyl-1-oxido-3-phenylbenzo[f][1,2]thiazepin-9-yl)-1-phenylpropan-1-one (159ca)

Yellow solid, melting point: 82 – 84 °C, 103.4 mg, 80% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.91 (d, $J = 7.8$ Hz, 2H), 7.77 (d, $J = 7.9$ Hz, 2H), 7.48 (t, $J = 7.3$ Hz, 1H), 7.37 (t, $J = 7.5$ Hz, 2H), 7.29 (t, $J = 7.4$ Hz, 2H), 7.22 (dd, $J = 13.2$, 6.2 Hz, 1H), 6.81 (s, 1H), 6.63 (s, 1H), 6.22 (t, $J = 6.5$ Hz, 1H), 4.25 (dd, $J = 13.3$, 5.7 Hz, 1H), 3.80 (s, 3H), 3.68 – 3.61 (m, 1H), 3.55 – 3.43 (m, 1H), 3.43 (s, 3H), 3.19 – 3.08 (m, 2H), 3.03 (dd, $J = 13.5$, 7.5 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 199.1, 161.7, 147.8, 147.1, 142.3, 137.6, 132.9, 128.4, 128.0, 127.9, 127.5, 116.5, 115.2, 113.6, 55.3, 46.2, 41.3, 34.6, 30.1. MS (EI): m/z = 431 (M$^+$, 5), 326 (15), 105 (100), 77 (60). IR (ATR): ν = 3052, 2935, 2321, 1679, 1583, 1445, 1282, 1129, 1075, 966, 746 (cm$^{-1}$). HRMS m/z: Calcd for [C$_{26}$H$_{25}$NO$_3$S$+$Na]$^+$: 432.1633. Found: 432.1628.

Methyl-1-methyl-9-(3-oxo-3-phenylpropyl)-3-phenylbenzo[f][1,2]thiazepine-7-Carboxylate -1-oxide (159ha)

Yellow solid, melting point: 84 – 86 °C, 108.8 mg, 79% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.97 (s, 1H), 7.91 (d, $J = 7.5$ Hz, 2H), 7.80 (s, 1H), 7.76 (d, $J = 7.4$ Hz, 2H), 7.49 (t, $J = 7.3$ Hz, 1H), 7.38 (t, $J = 7.7$ Hz, 2H), 7.30 (t, $J = 7.3$ Hz, 2H), 7.22 (t, $J = 7.2$ Hz, 1H), 6.25 (t, $J = 6.6$ Hz, 1H), 4.31 (dd, $J = 13.5$, 5.8 Hz, 1H), 3.92 (s, 3H), 3.70 – 3.62 (m, 1H), 3.59 – 3.52 (m, 1H), 3.49 (s, 3H), 3.31 – 3.10 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 198.6, 165.4, 145.7, 145.0, 132.9, 132.8, 132.1, 129.3, 128.4, 128.0, 127.9, 127.7, 125.7, 115.4, 52.5, 45.5, 41.0, 34.0, 29.8. MS (EI): m/z = 459 (M$^+$, 3), 354 (11), 105 (100), 77 (73). IR (ATR): ν = 3018, 2946, 2316, 1725, 1681, 1572, 1441, 1293, 1128, 975, 749 (cm$^{-1}$). HRMS m/z: Calcd for [C$_{22}$H$_{25}$NO$_4$S$+$H]$^+$: 460.1583. Found: 460.1582.
3-(1-Methyl-7-nitro-1-oxido-3-phenylbenzo[f][1,2]thiazepin-9-yl)-1-phenylpropan-1-one (159ga)

Orange solid, melting point: 87 – 89 °C, 97.7 mg, 73% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 8.16 (d, $J = 2.4$ Hz, 1H), 7.98 (d, $J = 2.4$ Hz, 1H), 7.92 (d, $J = 7.3$ Hz, 2H), 7.75 (d, $J = 7.4$ Hz, 2H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.41 (t, $J = 7.8$ Hz, 2H), 7.33 (t, $J = 7.6$ Hz, 2H), 7.26 (t, $J = 7.9$ Hz, 1H), 6.26 (dd, $J = 7.2$, 6.0 Hz, 1H), 4.37 (dd, $J = 13.7$, 5.8 Hz, 1H), 3.67 – 3.63 (m, 1H), 3.55 (s, 3H), 3.38 – 3.34 (m, 1H), 3.25 (dd, $J = 13.7$, 7.3 Hz, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 198.2, 148.7, 147.6, 147.2, 142.8, 142.5, 136.7, 136.3, 133.3, 128.8, 128.6, 128.1, 128.0, 125.8, 125.5, 122.8, 114.8, 48.6, 40.5, 34.2, 29.9. MS (CI): $m/z = 447 ([M+H]^+$, 5), 133 (100). IR (ATR): $\nu = 3021, 2936, 2326, 1740, 1680, 1524, 1347, 1220, 969, 746$ (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{25}$H$_{22}$N$_2$O$_4$S$^+$$+H]^+$: 447.1379. Found: 447.1379.

3-(1-Ethyl-1-oxido-3-phenylbenzo[f][1,2]thiazepin-9-yl)-1-phenylpropan-1-one (159pa)

Yellow solid, melting point: 104 – 106 °C, 99.6 mg, 80% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.92 (d, $J = 7.5$ Hz, 2H), 7.79 (d, $J = 7.5$ Hz, 2H), 7.50 (t, $J = 7.4$ Hz, 1H), 7.41 – 7.34 (m, 3H), 7.34 – 7.29 (m, 3H), 7.23 (t, $J = 7.3$ Hz, 1H), 7.15 (d, $J = 7.2$ Hz, 1H), 6.24 (dd, $J = 7.0$, 6.3 Hz, 1H), 4.32 (dd, $J = 13.5$, 5.8 Hz, 1H), 3.70 – 3.65 (m, 1H), 3.63 – 3.50 (m, 3H), 3.21 – 3.16 (m, 1H), 3.12 – 3.04 (m, 2H), 1.50 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 199.1, 146.6, 144.8, 141.8, 137.6, 136.6, 134.9, 132.9, 132.5, 131.9, 128.6, 128.4, 128.1, 128.0, 127.6, 125.8, 115.1, 52.3, 41.6, 34.2, 30.1, 8.8. MS (EI): $m/z = 415 (11, M^+)$, 338 (4), 310 (80), 105 (100), 77 (70). IR (ATR): $\nu = 2941, 2112, 1739, 1680, 1580, 1449, 1369, 1210, 978, 743$ (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{26}$H$_{28}$NO$_2$S$^+$$+Na]^+$: 438.1504. Found: 438.1549.
3-(1-Benzyl-1-oxido-3-phenylbenzo[f][1,2]thiazepin-9-yl)-1-phenylpropan-1-one (159sa)

Light yellow solid, melting point: 71 – 73 °C, 113.1 mg, 79% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.94 (d, $J = 7.6$ Hz, 2H), 7.77 (d, $J = 7.6$ Hz, 2H), 7.51 (t, $J = 7.3$ Hz, 1H), 7.40 (t, $J = 7.7$ Hz, 2H), 7.34 – 7.28 (m, 5H), 7.24 – 7.17 (m, 5H), 6.92 (d, $J = 6.9$ Hz, 1H), 6.07 (t, $J = 6.7$ Hz, 1H), 4.73 (q, $J = 13.5$ Hz, 2H), 3.72 – 3.62 (m, 2H), 3.42 (dd, $J = 13.4$, 5.9 Hz, 1H), 3.11 (ddd, $J = 16.3$, 9.1, 5.1 Hz, 1H), 2.63 (dd, $J = 13.5$, 7.4 Hz, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 199.2, 147.5, 145.3, 141.6, 136.8, 133.7, 132.9, 132.7, 131.7, 131.4, 129.3, 128.7, 128.4, 128.2, 128.1, 128.0, 127.5, 125.9, 114.7, 63.7, 41.6, 33.5, 30.3. MS (EI): $m/z$ = 477 (M$^+$, 3), 358 (2), 105 (100), 91 (78), 77 (81). IR (ATR): $\nu$ = 3059, 2931, 2327, 1679, 1580, 1449, 1278, 1217, 1122, 975, 745 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{31}$H$_{27}$NO$_2$S+H]$^+$: 478.1841. Found: 478.1837.

1-(4-Chlorophenyl)-3-(3-(4-chlorophenyl)-1-methyl-1-oxidobenzo[f][1,2]thiazepin-9-yl)propan-1-one (159ad)

Yellow solid, melting point: 186 – 188 °C, 129.5 mg, 92% yield. $^1$H NMR (600 MHz, CDCl$_3$) δ (ppm) 7.85 (d, $J = 8.6$ Hz, 2H), 7.70 (d, $J = 8.6$ Hz, 2H), 7.39 – 7.32 (m, 3H), 7.32 (d, $J = 7.4$ Hz, 1H), 7.26 (d, $J = 8.6$ Hz, 2H), 7.15 (d, $J = 7.4$ Hz, 1H), 6.24 (dd, $J = 7.2$, 6.1 Hz, 1H), 4.27 (dd, $J = 13.5$, 5.9 Hz, 1H), 3.63 – 3.57 (m, 1H), 3.55 – 3.50 (m, 1H), 3.46 (s, 3H), 3.18 (ddd, $J = 13.1$, 10.3, 5.1 Hz, 1H), 3.10 (dd, $J = 13.6$, 7.4 Hz, 1H), 3.05 (ddd, $J = 17.6$, 9.9, 5.2 Hz, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ (ppm) 197.8, 145.4, 144.4, 141.1, 139.4, 136.7, 136.1, 134.8, 133.4, 132.6, 131.9, 129.5, 128.9, 128.8, 128.2, 127.1, 116.3, 45.8, 41.4, 34.1, 29.9. MS (EI): $m/z$ = 469 (M$^+$, 3), 139 (100), 111 (63). IR (ATR): $\nu$ = 3016, 2936, 2048, 1739, 1582, 1478, 1368, 1216, 1093, 974, 774 (cm$^{-1}$). HRMS $m/z$: Calcd for [C$_{26}$H$_{21}$NO$_2$Cl$_2$Na]$^+$: 492.0568. Found: 492.0563.
1-(Furan-2-yl)-3-(3-(furan-2-yl)-1-methyl-1-oxidobenzo[f][1,2]thiazepin-9-yl)propan-1-one (159an)

Yellow solid, melting point: 90 – 92 °C, 89.2 mg, 78% yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.51 (d, \(J = 0.9\) Hz, 1H), 7.36 – 7.29 (m, 3H), 7.16 (d, \(J = 3.6\) Hz, 1H), 7.12 (dd, \(J = 7.0, 1.5\) Hz, 1H), 6.62 (d, \(J = 3.2\) Hz, 1H), 6.46 (dd, \(J = 3.5, 1.7\) Hz, 1H), 6.36 (dd, \(J = 3.3, 1.8\) Hz, 1H), 6.20 – 6.14 (m, 1H), 4.24 (dd, \(J = 13.7, 6.1\) Hz, 1H), 3.49 – 3.42 (m, 2H), 3.42 (s, 3H), 3.23 – 3.16 (m, 1H), 3.09 (dd, \(J = 13.7, 7.5\) Hz, 1H), 3.01 – 2.92 (m, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 188.0, 153.1, 152.2, 146.3, 145.5, 144.1, 142.0, 137.2, 133.6, 132.5, 131.6, 128.9, 117.5, 114.9, 112.1, 111.3, 108.2, 45.6, 40.8, 33.5, 29.5. MS (EI): \(m/z = 381\) (M\(^+\), 7), 286 (53), 95 (100). IR (ATR): \(\nu = 3133, 2934, 2053, 1739, 1668, 1567, 1463, 1318, 1224, 1151, 976, 735\) (cm\(^{-1}\)). HRMS \(m/z\): Calcd for [C\(_{21}\)H\(_{19}\)NO\(_4\)S+Na\]^+: 404.0932. Found: 404.0927.

3-(8-Bromo-1-methyl-1-oxido-3-phenylbenzo[f][1,2]thiazepin-9-yl)-1-phenylpropan-1-one (159ka)

3-(6-Bromo-1-methyl-1-oxido-3-phenylbenzo[f][1,2]thiazepin-9-yl)-1-phenylpropan-1-one (159ka')

Yellow solid, melting point: 80 – 82 °C, 121.0 mg, 84% yield. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.96 – 7.89 (m, 4H), 7.76 (t, \(J = 7.6\) Hz, 4H), 7.68 (dd, \(J = 8.3, 3.9\) Hz, 2H), 7.51 (dd, \(J = 12.5, 7.3\) Hz, 2H), 7.40 (t, \(J = 7.2\) Hz, 4H), 7.31 (q, \(J = 7.8\) Hz, 4H), 7.24 (d, \(J = 7.3\) Hz, 2H), 7.18 (d, \(J = 8.3\) Hz, 1H), 7.05 (d, \(J = 8.3\) Hz, 1H), 6.29 – 6.19 (m, 2H), 4.26 (dd, \(J = 13.6, 5.8\) Hz, 1H), 4.17 – 4.09 (m, 1H), 3.93 (dd, \(J = 13.7, 7.4\) Hz, 1H), 3.67 – 3.59 (m, 3H), 3.53 – 3.42 (m, 8H), 3.29 – 3.23 (m, 1H), 3.22 – 3.14 (m, 1H), 3.14 – 3.04 (m, 2H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm) 198.8, 198.7, 144.9, 144.3, 143.7, 142.7, 142.5, 137.2, 137.1, 136.7, 136.4, 133.1, 132.9, 132.3, 130.0, 128.5, 1284.4, 128.1, 128.0, 127.8, 127.7, 125.8, 125.7, 122.6, 115.3, 114.2, 45.8, 45.7, 41.1, 38.2, 33.9, 32.1, 30.2, 29.9. MS (EI): \(m/z = 479\) (M\(^+\), 4), 374 (21), 105 (100), 77 (83). IR (ATR): \(\nu = 3015,\)
0.2 mmol of 158aa (or 159aa) and 10 mL of DCM were added to a round-bottom flask. The solution was stirred for 5 min. Aqueous NaHCO₃ solution (0.5 M, 10 mL) was added afterward. m-CPBA (69.0 mg, 0.4 mmol) was added to the biphasic solution and the solution was stirred at rt for 24 h. Then the mixture was poured into a separatory funnel. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layer was washed with NaHCO₃ solution (0.5 M, brine), and dried over MgSO₄. The solvent was removed by the rotary evaporation. The residue was subjected to flash chromatography on silica gel using ethyl acetate/pentane (v/v, 1:2) as eluent to give desired product 160 or 161.

*N*-Bezoyl-*S*-methyl-*S*-[2-oxoethyl]phenyl sulfoximine (160)

Light yellow syrup, 68.6 mg, 76% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.82 (s, 1H), 8.12 (dd, J = 8.2, 1.0 Hz, 2H), 8.01 (d, J = 8.0 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.49 (q, J = 7.2 Hz, 3H), 7.40 (t, J = 7.7 Hz, 3H), 7.29 (d, J = 7.6 Hz, 1H), 4.69 (d, J = 18.0 Hz, 1H), 4.08 (d, J = 18.0 Hz, 1H), 3.41 (s, 4H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 198.2, 173.9, 137.6, 135.3, 134.0, 133.7, 133.1, 132.2, 129.3, 128.9, 128.8, 128.0, 48.4, 44.2. MS (EI): m/z = 302 ([M+H]+, 8), 224 (6), 196 (4), 105 (100), 77 (36). IR (ATR): ν = 3021, 2930, 1977, 1730, 1616, 1446, 1281, 1126, 967, 831, 713
(cm⁻¹). HRMS m/z: Calcd for [C₁₆H₁₅NO₃S+Na⁺]: 324.0670. Found: 324.0668.

**N-Bezoyl-S-methyl-S-((2-oxoethyl)-6-[(3-oxo-3-phenylpropyl)phenyl] sulfoximine (161)**

White solid, melting point: 177 – 179 °C, 96.1 mg, 74% yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.88 (s, 1H), 7.99 (d, J = 6.8 Hz, 2H), 7.50 – 7.44 (m, 3H), 7.41 (t, J = 7.4 Hz, 1H), 7.36 (d, J = 6.7 Hz, 1H), 7.22 (t, J = 7.8 Hz, 2H), 7.18 – 7.08 (m, 4H), 5.12 (d, J = 18.3 Hz, 1H), 3.83 (d, J = 18.3 Hz, 1H), 3.65 – 3.57 (m, 1H), 3.45 (s, 3H), 3.39 – 3.31 (m, 1H), 3.09 – 2.98 (m, 2H).

¹³C NMR (100 MHz, CDCl₃) δ (ppm) 199.0, 197.8, 174.0, 141.4, 136.3, 135.9, 135.8, 134.7, 133.4, 133.1, 132.8, 132.0, 129.0, 128.2, 127.9, 127.6, 50.5, 44.4, 40.7, 28.6. MS (EI): m/z = 105 (100), 77 (46). IR (ATR): ν = 3059, 2838, 2323, 1722, 1682, 1607, 1450, 1278, 1204, 1126, 974, 713 (cm⁻¹). HRMS m/z: Calcd for [C₂₅H₂₅NO₄S+Na⁺]: 456.1245. Found: 456.1240.
### III. List of Abbreviations

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<td>Boc</td>
<td>tert-butyloxycarbonyl</td>
</tr>
<tr>
<td>BHT</td>
<td>2,6-di-tert-butyl-4-methylphenol</td>
</tr>
<tr>
<td>Bn</td>
<td>benzyl</td>
</tr>
<tr>
<td>°C</td>
<td>centigrade</td>
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<tr>
<td>Bu</td>
<td>butyl</td>
</tr>
<tr>
<td>nBu</td>
<td>$n$-butyl</td>
</tr>
<tr>
<td>tBu</td>
<td>$t$-butyl</td>
</tr>
<tr>
<td>Cp*</td>
<td>1,2,3,4,5-pentamethylcyclopentadiene</td>
</tr>
<tr>
<td>Cbz</td>
<td>carboxybenzyl</td>
</tr>
<tr>
<td>CPME</td>
<td>cyclopentyl methyl ether</td>
</tr>
<tr>
<td>δ</td>
<td>chemical shift</td>
</tr>
<tr>
<td>d</td>
<td>doublet (NMR signal)</td>
</tr>
<tr>
<td>dba</td>
<td>4-phenyl-3-buten-2-one</td>
</tr>
<tr>
<td>DCC</td>
<td>dicyclohexylcarbodiimide</td>
</tr>
<tr>
<td>DCE</td>
<td>1,2-dichloroethane</td>
</tr>
<tr>
<td>DCM</td>
<td>dichloromethane</td>
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<tr>
<td>DG</td>
<td>directing group</td>
</tr>
<tr>
<td>DMEDA</td>
<td>$N,N'$-dimethylformamide</td>
</tr>
<tr>
<td>DME</td>
<td>dimethoxyethane</td>
</tr>
<tr>
<td>DMAP</td>
<td>4-dimethylaminopyridine</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>PivOH</td>
<td>2,2-dimethylpropanoic acid</td>
</tr>
<tr>
<td>Pr</td>
<td>propyl</td>
</tr>
<tr>
<td>'Pr</td>
<td>isopropyl</td>
</tr>
<tr>
<td>rt</td>
<td>room temperature</td>
</tr>
<tr>
<td>s</td>
<td>singlet (NMR signal)</td>
</tr>
<tr>
<td>SET</td>
<td>single electron transfer</td>
</tr>
<tr>
<td>TBAF</td>
<td>tetra-(n)-butylammonium fluoride</td>
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<tr>
<td>TBAI</td>
<td>tetra-(n)-butylammonium iodide</td>
</tr>
<tr>
<td>TBHP</td>
<td>tert-butyl hydroperoxide</td>
</tr>
<tr>
<td>TC</td>
<td>thiophene-2-carboxylate</td>
</tr>
<tr>
<td>TEMPO</td>
<td>(2,2,6,6-tetramethylpiperidin-1-yl)oxyl</td>
</tr>
<tr>
<td>tert</td>
<td>tertiary</td>
</tr>
<tr>
<td>'AmOH</td>
<td>tert-Amyl alcohol</td>
</tr>
<tr>
<td>Tf</td>
<td>trifluoromethylsulfonyl</td>
</tr>
<tr>
<td>TFA</td>
<td>trifluoroacetic acid</td>
</tr>
<tr>
<td>TFP</td>
<td>trifluoperazine</td>
</tr>
<tr>
<td>TfOH</td>
<td>trifluoromethanesulfonic acid</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMEDA</td>
<td>tetramethylethylenediamine</td>
</tr>
<tr>
<td>TMS</td>
<td>trimethylsilyl</td>
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IV. References


[89] The crystal structure of 145aa was determined by X-ray diffraction analysis. CCDC-1564782 contains the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre

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Journal publications:


(2) “1, 2-Benzothiazines from Sulfoximines and Allyl Methyl Carbonate by Rhodium-Catalyzed Cross-Coupling and Oxidative Cyclization” J. Wen, D. P. Tiwari, C. Bolm, Org. Lett. 2017, 19, 1706.


(4) “Synthesis of N-Propargylsulfoximines by Copper-Catalyzed A3-Couplings” H. Cheng, J.


