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Ru (II)-Catalyzed Coupling-Cyclization of Sulfoximines with *alpha*-Carbonyl Sulfoxonium Ylides as an Approach to 1,2-Benzothiazines

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Abstract. A Ru(II)-catalyzed approach for the rapid assembly of 1,2-benzothiazines has been developed to enable the coupling-cyclization of aryl Csp^2-H bonds with α-carbonyl sulfoxonium ylides via Csp^2-H activation process. The present method could be further applied to the construction of the 4-substituted 1,2-benzothiazine skeletons.

Keywords: Ruthenium catalysis; Sulfoximines; Sulfur ylides; Coupling-cyclization; 1,2-Benzothiazines

Introduction

Sulfoximines are ubiquitous in many bioactive molecules.[1] Especially for the sulfoximine-containing benzothiazines (SBTs), these compounds have ever attracted attention in medicinal chemistry due to their benzo-fused sulfur-nitrogen heterocyclic skeletons decades ago (**Figure 1**).[2] However, these heterocycles have been rather neglected in recent years mainly because efficient synthetic strategies for particular benzothiazine skeletons were not well established. Since Cram reported a combined imidation-Schmidt rearrangement/cyclization of S-arylsulfoxides with sodium azides in 1973,[3] only Harmata[4] and Bolm[5] successively realized the Pd(II)- or Rh(III)-catalyzed coupling cyclization of S-aryl sulfoximines with alkynes to assemble 1,2-benzothiazines (**Scheme 1a**). In view of the fact that SBTs possess potential usefulness as scaffolds in drug chemistry, developing a novel procedure for the conversion of different coupling partners into SBTs is desirable.

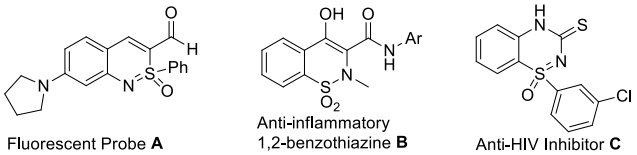

Figure 1. Selected examples of bioactive benzothiazines

Metal carbenes belong to a very important type of C1-synthons in organic chemistry,[6] and transition metal-catalyzed cascade C-H activation/C-H carbenoid insertion provides an atom- and step-economical strategy for constructing C-X bonds (X = C, N, S and O, etc).[7] Up to now, the coupling reactions of C-H bonds with diazo compounds have been well developed for furnishing structurally complex heterocycles. Among them, various ligand-functional groups including ammonium salts,[8] pyridine,[9] amide,[10] indole,[11] ketoimine,[12] omines,[13] hydroxamic acids,[14] and others[15] have been widely employed as chelation-assisted platforms to enable the C-H bond carbenoid insertion using diazo compounds as carbene precursors. In comparsion, sulfoximine-directed C-H bond carbenoid functionalization remains almost undeveloped. Up to now, only Bolm reported a Rh(III)-catalyzed coupling reaction of aryl C-H bonds with α-diazo-β-ketoesters, in which the combined directing character and nucleophilicity of sulfoximines was fully utilized to allow rapid assembly of SBTs (**Scheme 1b**).[16] Meanwhile, sulfur ylides are a more practical and safe alternative to diazo compounds, and sulfur ylide-based C-H carbenoid insertion has recently aroused increasing interest due to their distinctive chemical reactivities.[17] Given the deficiencies of synthetic methodology for diverse benzothiazine libraries, herein we plan to develop a highly regioselective approach to 1,2-benzothiazines through the Ru(II)-catalyzed coupling-cyclization of S-aryl sulfoximines with sulfur ylides.[18] More importantly, we expect the afforded SBTs could be further converted into diverse 4-substituted 1,2-benzoazines through downstream transformations (**Scheme 1c**).

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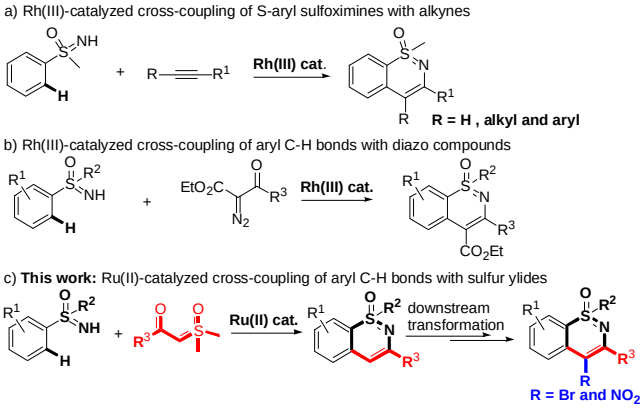
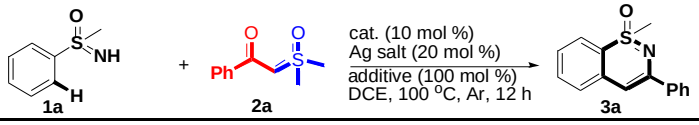


Scheme 1. Synthetic strategies toward 1,2-benzothiazines

Results and Discussion

To demonstrate the feasibility of our approach, we first screened various Ru(II), Co(III) and Cu(II) catalysts that could possibly enable the aryl C-H bond carbenoid functionalization of S-phenyl sulfoximine (**1a**) with α-benzoyl sulfoxonium ylide (**2a**) in the presence of AgOAc (20 mol %) and $PhCO_2H$ (1.0 equiv) in 1,2-dichloroethane (DCE) at 100 °C under Ar atmosphere for 12 h (**Table 1**, entries 1-6). Gratifyingly, we soon found that RuL_2 afforded 12% yield of 1-methyl-3-phenyl-1,2-benzothiazine 1-oxide (**3a**). Other catalysts such as $RuCl_3$, $Co(acac)_3$ and $Cu(OAc)_2$ could not produce **3a** at all (compare entries 1-2 and 4-6 with 3). Subsequently, a variety of silver salts including $AgClO_4$, $AgNTf_2$, $AgBF_4$ and $AgSbF_6$, were evaluated in the presence of $[RuCl_2(p\text{-cymene})]_2$ catalysts in order to increase the reaction conversion, and $AgSbF_6$ was shown to be the most efficient (compare entries 7-10 with 11), significantly improving the yield of **3a** from 12% to 51% (compare entry 3 with 11). To maximize the conversion of the reaction, the additional optimization of proton acids revealed that pivalic acid could further increase the yield to 75% (compare entries 11-13 with 14), but other acids, such as AcOH and adamantane-1-carboxylic acid ($AdCO_2H$), gave inferior results (compare entries 12-14 with 15). It should be noted that the reaction yield was decreased to 56% in the absence of protic acid (compare entry 14 with 15), and using other solvents including toluene and CF_3CH_2OH led to poorer reaction conversions (compare entries 16-17 with 14).

Table 1. Optimization of the reaction parameters [a]



Entry	Catalyst	Ag salts	Additives	Yield (%) [b]
1	$RuCl_3$	AgOAc	$PhCO_2H$	0
2	RuL_1 [c]	AgOAc	$PhCO_2H$	0
3	RuL_2 [d]	AgOAc	$PhCO_2H$	12
4	$Co(acac)_3$	AgOAc	$PhCO_2H$	0
5	$Cp^*Co(CO)I_2$	AgOAc	$PhCO_2H$	0
6	$Cu(OAc)_2$	AgOAc	$PhCO_2H$	0
7	RuL_2	$AgClO_4$	$PhCO_2H$	32
8	RuL_2	Ag_2CO_3	$PhCO_2H$	27
9	RuL_2	$AgNTf_2$	$PhCO_2H$	46
10	RuL_2	$AgBF_4$	$PhCO_2H$	49
11	RuL_2	$AgSbF_6$	$PhCO_2H$	51
12	RuL_2	$AgSbF_6$	AcOH	8
13	RuL_2	$AgSbF_6$	$AdCO_2H$	63
14	**RuL_2**	**$AgSbF_6$**	**PivOH**	**75**
15	RuL_2	$AgSbF_6$	–	56
16	RuL_2	$AgSbF_6$	PivOH	42[e]
17	RuL_2	$AgSbF_6$	PivOH	73[f]

[a]Unless otherwise noted, all the reactions were carried out using sulfoximine (**1a**) (0.10 mmol) and α-carbonyl ylide (**2a**) (0.20 mmol) in the presence of catalysts (5 mol %) with additive (100 mol %) in DCE (2.0 mL) at 100 °C for 12 h under Ar in a sealed reaction tube. Followed by flash chromatography on SiO_2.
[b]Isolated yield.
[c]RuL_1 refers to $RuHCl(CO)(PPh_3)$.
[d]RuL_2 refers to $[RuCl_2(p\text{-cymene})]_2$.
[e]Using toluene as solvent.
[f] Using CF_3CH_2OH as solvent.

With these optimized reaction parameters in hand, we first investigated the reactivity of various sulfoxonium ylides with S-phenyl sulfoximine (**1a**). As shown in **Table 2**, α-substituted benzoyl sulfoxonium ylides bearing halide substituents (4-F, 4-Cl and 4-Br), electron-donating groups (4-methyl

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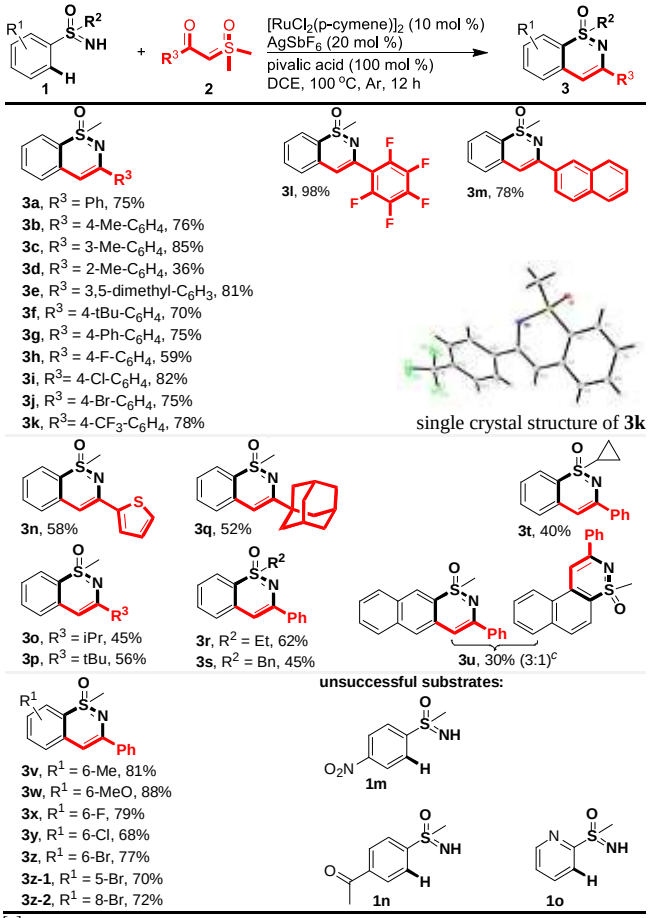
and 4-*t*Bu) and electron-withdrawing group (4-CF_3) all smoothly underwent coupling-cyclization to afford the corresponding 3-aryl 1,2-benzothiazines in good to excellent yields (**3a**, **3b** and **3f**–**3k**, 59-82%). Moreover, α-(3-methylbenzoyl)- and α-(3,5-dimethylbenzoyl)-substituted sulfur ylides also allowed for this transformation and assembled SBTs in 85% (**3c**) and 81% yields (**3e**), respectively, but α-(2-methylbenzoyl)sulfoxonium ylide led to lower yield of the product **3d** (36%) owing to the steric hindrance of *ortho*-methyl substitution. On the other hand, α-pentafluorobenzoyl sulfoxonium ylide, α-2-naphthoyl sulfoxonium ylide and α-2-thienoyl sulfoxonium ylide could also be applied to this reaction system, installing pentafluorophenyl, 2-naphthyl and 2-thienyl groups at the 3-position of 1,2-benzothiazines (**3l**–**3n**) in 58-98% yields. More importantly, besides the α-aroyl sulfoxonium ylides, we could also extend the chemistry to reactions with the α-fattyacyl sulfoxonium ylides which produced the desired 3-alkyl 1,2-benzothiazines (**3o**–**3q**) in 45-56% yields. By the way, the structure of **3k** was already unambiguously assigned by its single crystal X-ray analysis.[19]

Table 2. Substrate Scope [a, b]



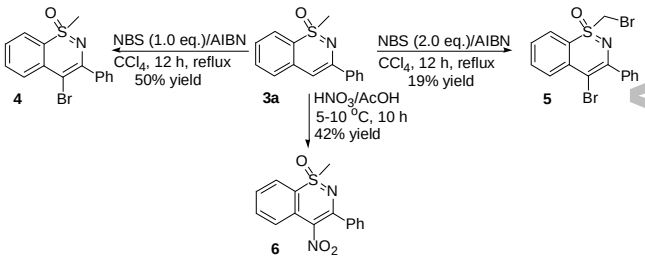
[a] Unless otherwise noted, all the reactions were carried out using sulfoximines (**1**) (0.10 mmol) and alpha-carbonyl ylide (**2a**) (0.20 mmol) in the presence of $[RuCl_2(p\text{-cymene})]_2$ (5 mol %) with PivOH (100 mol %) in DCE (2.0 mL) at 100 °C for 12 h under Ar in a sealed reaction tube. Followed by flash chromatography on SiO_2.

[b] Isolated yield.

[c] The data in parentheses is the ratio of C-H functionalization from C3-position and C1-position of naphthalene ring.

Subsequently, we evaluated the scope of S-alkyl substituted-S-phenylsulfoximines. Compared with the S-methyl-S-phenylsulfoximine (**3a**, 75% yield), S-ethyl, S-benzyl and S-cyclopropyl group-substituted sulfoximines could be transferred into the target compounds (**3r**–**3t**) in lower yields (40-62%). On the contrary, except for S-2-naphthylsulfoximine (30% of **3u**), other S-arylsulfoximines such as S-(4-methlyphenyl)sulfoximine, S-(4-methoxylphenyl) sulfoximine and S-monohalo-substituted phenylsulfoximines could more efficiently couple with α-benzoyl sulfoxonium ylide **2a** to provide the corresponding 5-, 6- or 8-substituted 1,2-benzothiazines (**3v**–**3v-2**) in good yields (68-88%), regardless of the type of substituents and substitution position on the phenyl ring. It should be noted that the electron-deficient S-phenylsulfoximines including S-(4-nitrophenyl)sulfoximine and S-(4-acetylphenyl)sulfoximine, did not afford the corresponding 1,2-benzothiazines. Moreover, S-(2-pyridyl)sulfoximine did not also tolerate the reaction system possibly due to that Ru(II) salts coordinated with pyridine "N" and imine "N" and lost their catalytic activity.

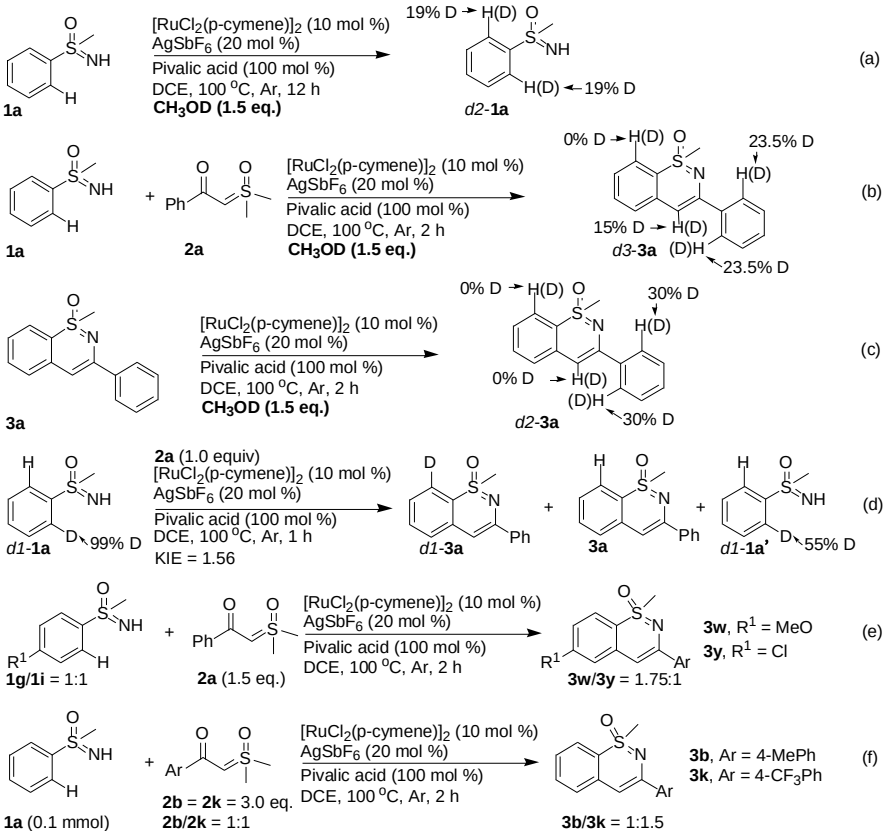
It is well known that C-Br bond can undergoes diverse chemical transformations in organic synthesis.[20] The synthetic applications of this coupling cyclization demonstrated that bromine group could be easily installed into the 4-position of 1,2-benzothiazine **3a** to form 3-bromo-1,2-benzothiazine **4** in 50% yield in the presence of 1.0 equiv of NBS. Moreover, employing 2.0 equiv of NBS could further enable the bromomethylation of **3a** to afford dibromide **5** in 19% yield. Meanwhile, nitro group could be also regioselectively induced into the 4-position of 1,2-benzothiazine **3a** to produce nitro-substituted benzothiazine (**6**) in 42% yield (see **Scheme 2**).



Scheme 2. Synthetic application of this transformation

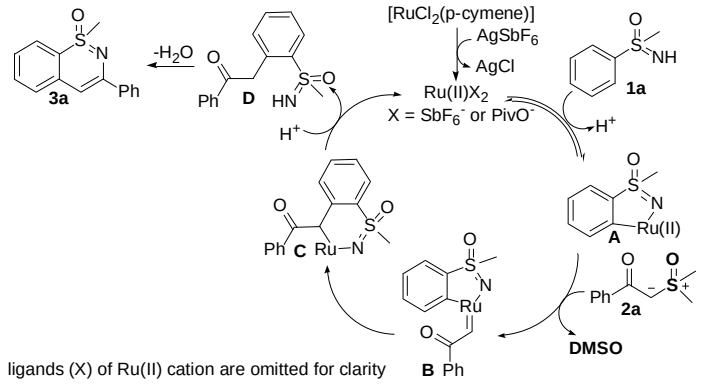
Several control experiments were conducted to elucidate the reaction mechanism. Initially, performing the H/D exchange of S-phenylsulfoximine **1a** with CH_3OD in the absence of sulfoxonium ylide (**2a**) led to the formation of the

deuterated *d2*-**1a** in which 19% deuterium incorporation at the *ortho*-position of benzene ring of **1a** was observed, implying that a reversible C-H bond activation process was involved in the carbene transfer reaction (**Scheme 3a**). The subsequent coupling-cyclization of S-phenylsulfoximine **1a** with α-benzoyl sulfoxonium ylide **2a** in the presence of CH_3OD could incorporate the deuterium (15% D) into the 4-position[21] of the 1,2-benzothiazine (*d3*-**3a**) (**Scheme 3b**),[22] but the treatment of 1,2-benzothiazine (**3a**) with MeOD (1.5 equiv) under the standard conditions did not result in the H/D exchange at the 4-position of *d2*-**3a** (**Scheme 3c**).[22] The combined facts (**Scheme 3b** and **3c**) indicated that metal protonation process was possibly involved in the transformation, and sulfoxide group could not lead to the C-H activation and H/D exchange at the 8-position of **3a**. Then, the kinetic isotope effect [5] between *d1*-**1a** and **2a** (K_H/K_D = 1.56) confirmed that the step of aryl Csp^2-H bond breaking possibly belongs to the rate-limiting step of this reaction, and the amount of deuterium at the *ortho*-position on the substituted phenyl ring of the recovered *d1*-**1a′** was decreased from 99% D to 55% D (**Scheme 3d**). Moreover, the competitive cross-coupling between electron-rich and electron-deficient S-phenylsulfoximines (**1g** vis **1i**) led to the formation of **3w** and **3y** with a ratio of 1.75:1 (**3w**/**3y**),[23] implying that the aryl Csp^2-H bond activation possibly proceeded through electrophilic ruthenation instead of concerted metallation-deprotonation (CMD) process (**Scheme 3e**). Finally, the competitive coupling-cyclization of α-(4-methylbenzoyl)-sulfoxonium ylide and α-(4-trifluomethylbenzoyl) sulfoxonium ylide with S-phenylsulfoximine (**1a**) (**3b**/**3k** = 1:1.5) suggested that electron-deficient sulfur ylide more easily forms a ruthenium-carbene, which cyclizes with sulfoximine **1a** to afford 1,2-benzothiazine **3k** in better conversion (**Scheme 3f**) (see SI for more details).



Scheme 3. Control experiments

On the basis of the above observations and the known Ru(II)-catalyzed Csp^2-H bond activation process,[24] we proposed a plausible mechanism in **Scheme 4**. The initial coordination of sulfoximine nitrogen of substrate **1a** to an active Ru(II) catalyst and subsequent Csp^2-H activation via electrophilic ruthenation afford a five-membered ruthenacycle **A**. Then nucleophilic attack of sulfur ylide **2a** on Ru(II) complex **A** generates Ru(II) carbene **B** with the loss of DMSO, Ru(II) carbene **B** further undergoes carbene migratory insertion to produce another six-membered ruthenacycle intermediate **C**. Finally, metal protonation followed by an intramolecular nucleophilic attack of imine to carbonyl group produces 1,2-benzothiazine **3a** with release of the Ru(II) catalysts.



Scheme 4. Possible mechanism for the transformation

Conclusion

In conclusion, we have developed a ruthenium(II)-catalyzed coupling-cyclization of S-arylsulfoximines with α-carbonyl sulfoxonium ylides. This transformation proceeds through a sequential aryl C-H carbenoid insertion/cyclization and provides an efficient access to 1,2-benzothiazine skeletons. Moreover, the afforded 1,2-benzothiazines could be converted into various 4-substituted analogues for versatile synthetic applications.

Experimental Section

General Information

Unless otherwise noted, all experiments were performed under argon atmosphere. Solvents were treated with 4 Å molecular sieves or sodium and distilled prior to use. Flash chromatography was performed on silica gel (40~63 mm) by standard technique. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C). Splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q). Splitting patterns that could not be interpreted or easily visualized are designated as multiple (m). Low resolution mass spectra were recorded using HPLC Mass Spectrometer. High resolution exact mass measurements (HR-MS) were performed on a TOF spectrometer. Infrared spectra (IR) were reported as wavelength numbers (cm^{-1}). Infrared spectra were recorded by preparing a KBr pellet containing the title compound. Crystal data were obtained by employing graphite monochromated Mo - Kα radiation (λ = 1.54178 Å) at 571 (2) K and operating in the φ-ω scan mode. The structure was solved by direct methods SHELXS-97.

The Procedure for the Preparation of sulfoxonium ylides

Ylides **2a**-**2q** were prepared according to the reported procedures.[25] To a stirred solution of potassium *tert*-butoxide (3.0 g, 27.2 mmol) in THF (30 mL) was added trimethylsulfoxonium iodide (5.0 g, 20.6 mmol) at room temperature. The resulting mixture is refluxed for 2 h. Then reaction mixture is cooled to 0 °C, followed by addition of acyl chlorides (7 mmol) in THF (5 mL). The reaction was allowed to room temperature and stirred for 3 h. Next, the solvent was evaporated, and water (15 mL) and ethyl acetate (20 mL) were added to the resulting slurry. The layers were separated and the aqueous layer was washed with ethyl acetate (2 × 30 mL) and the organic layers were combined. The organic solution was dried over anhydrous sodium sulphate (Na_2SO_4), filtered over a sintered funnel, and evaporated to dryness. The crude product was purified by flash chromatography over silica gel using EtOAc/MeOH (95:5) to afford the corresponding sulfoxonium ylides **2a**-**2q**.

Synthesis of S-arylsulfoximines [26]

S-Arylsulfoximines **1a**-**1o** were prepared according to the reported procedures.[26] To a stirred solution of sulfides (1 mmol) in MeOH (10 mL) was added the $(NH_4)_2CO_3$ (1.5 equiv.). Subsequently, $PhI(OAc)_2$ (2.3 equiv) was added and the solution was stirred at room temperature. After the disappearance of the sulfides (checked by TLC), the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (10 mmol sulfide and 100 mL of MeOH were used for the gram-scale reaction) to product S-arylsulfoximines **1a**-**1o**.

Synthesis of sulfoximines *d1*-**1a** [26, 27]

2-Bromothioanisole (2.03 g, 10 mmol) was dissolved in dry THF (20 mL), the solution was cooled to –78 °C, and *n*-BuLi (6.25 mL, 1.6 M, 10 mmol) was added drop wise. After stirring for 1 h at –78 °C. D_2O (4.0 mL) was added drop wise and stirring was continued while the Dewar flask was removed 10 min. After the addition. The mixture was allowed to stir for additional 4 h at room temperature. Then, H_2O (20 mL) was added, the phases were separated, and the aqueous layer was extracted DCM (3 × 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, concentrated and crude product was used without further purification.

To a stirred solution of sulfide (1 mmol) in MeOH (10 ml) was added the $(NH_4)_2CO_3$ (1.5 equiv.). Subsequently, $PhI(OAc)_2$ (2.3 equiv) was added and the solution was stirred at room temperature. After the disappearance of the sulfide (checked by TLC), the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography to produce *d1*-**1a** (10 mmol sulfide and 100 mL of MeOH were used for the gram-scale reaction)

Sulfoximine *d1*-1a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.5 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.58 – 7.50 (m, 2H),

4.16 (s, 1H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 133.1, 129.3, 129.2, 127.7, 127.4, 127.2, 46.0. HR-MS (ESI) calcd for $[M + 1]^+$: C_7H_8DNOS: 157.0546, found: 157.0536.

General Procedure for the Synthesis of the 1,2-Benzothioazines

A Schlenk tube (20 mL) equipped with a stir bar was loaded with the sulfoximine (0.2 mmol), sulfoxonium ylide (0.4 mmol), $[RuCl_2(p\text{-cymene})]_2$, (10 mol %, 12.2 mg) and $AgSbF_6$ (20 mol %, 14.3 mg), PivOH (1 equiv, 40.8 mg). Under an Ar atmosphere (1 atm), dry DCE (4.0 mL), was added, and the reaction mixture was allowed to stir at 100 °C for 12 h. After cooling to room temperature, the mixture was filtered through a short Celite pad. The filtrate was concentrated, and the product was purified by column chromatography using silica gel and a mixture of hexanes and ethyl acetate as eluent.

1-Methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3a): Yellow solid, 38.2 mg, 75% yield, mp 96−97 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.3 Hz, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.38 – 7.25 (m, 5H), 6.59 (s, 1H), 3.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 138.5, 136.7, 132.7, 128.9, 128.4, 127.2, 126.5, 126.4, 123.4, 118.7, 98.3, 45.5. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{15}H_{14}NOS$: 256.0777, found: 256.0791; IR (KBr): 3233, 3050, 3006, 2924, 1639, 1586, 1532, 1475, 1360, 1199, 1030, 782, 684, 475 cm^{-1}.

1-Methyl-3-(p-tolyl)benzo[e][1,2]thiazine 1-oxide (3b): Yellow solid, 40.8 mg, 76% yield, mp 123−125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.40 (dd, *J* = 14.1, 7.5 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 6.66 (s, 1H), 3.61 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 138.9, 136.8, 135.7, 132.6, 129.1, 127.1, 126.4, 126.1, 123.4, 118.6, 97.7, 45.4, 21.3. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{16}H_{16}NOS$: 270.0947, found: 270.0936; IR (KBr): 3043, 2925, 1612, 1530, 1486, 1363, 1176, 1105, 786, 545, 475 cm^{-1}.

1-Methyl-3-(m-tolyl)benzo[e][1,2]thiazine 1-oxide (3c): Yellow solid, 45.7 mg, 85% yield, mp 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.74 (m, 3H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.4 Hz, 1H), 6.68 (s, 1H), 3.62 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 138.5, 138.0, 136.7, 132.6, 129.7, 128.3, 127.3, 127.2, 126.3, 123.6, 123.4, 118.7, 98.2, 45.4, 21.5. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{16}H_{16}NOS$: 270.0947, found: 270.0936; IR (KBr): 3050, 2924, 1639, 1532, 1475, 1360, 1199, 1102, 860, 782, 684, 505, 475 cm^{-1}.

1-Methyl-3-(o-tolyl)benzo[e][1,2]thiazine 1-oxide (3d): Yellow liquid, 19.4 mg, 36% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.21 – 7.10 (m, 4H), 6.15 (s, 1H), 3.53 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 139.8, 136.5, 136.4, 132.6, 130.7, 128.9, 128.4, 127.0, 126.4, 125.7, 123.3, 118.1, 101.8, 45.1, 20.3. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{16}H_{16}NOS$: 270.0947, found: 270.0937; IR (KBr): 3046, 2925, 1628, 1531, 1488, 1397, 1174, 1072, 1003, 787, 554,480 cm^{-1}.

3-(3,5-Dimethylphenyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3e): Yellow solid, 45.9 mg, 81% yield, mp 151−153 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.62 (s, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.44 – 7.35 (m, 2H), 7.05 (s, 1H), 6.68 (s, 1H), 3.61 (s, 3H), 2.42 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 138.5, 137.9, 136.7, 132.6, 130.7, 127.2, 126.2, 124.5, 123.4, 118.7, 98.2, 45.3, 21.5. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{17}H_{18}NOS$: 284.1104, found: 284.1095; IR (KBr): 3233, 3049, 2923, 1599, 1531, 1476, 1354, 1210, 1108, 973, 849, 794, 695, 509, 481 cm^{-1}.

3-(4-(Tert-butyl)phenyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3f): Yellow solid, 43.6 mg, 70% yield, mp 206−208 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.7 Hz, 2H), 7.28 (dd, *J* = 16.8, 8.2 Hz, 2H), 6.55 (s, 1H), 3.49 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 147.3, 136.9, 135.8, 132.6, 127.1, 126.3, 126.1, 125.3, 123.4, 118.5, 97.7, 45.4, 34.7, 31.3. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{19}H_{22}NOS$: 312.1417, found: 312.1404; IR (KBr): 3033, 2924, 1615, 1532, 1487, 1363, 1175, 1105, 787, 554, 479 cm^{-1}.

3-([1,1'-Biphenyl]-4-yl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3g): Yellow solid, 49.7 mg, 75% yield, mp 148−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 1H) 7.59 – 7.51 (m, 4H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.23 (m, 3H), 6.61 (s, 1H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 141.6, 140.7, 137.5, 136.7, 132.7, 128.9, 127.5, 127.3, 127.1, 127.1, 127.0, 126.4, 123.5, 118.8, 98.3, 45.4. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{21}H_{18}NOS$: 332.1104, found: 332.1095; IR (KBr): 3031, 2928, 1631, 1530, 1482, 1398, 1199, 1002, 853, 764, 694, 490 cm^{-1}.

3-(4-Fluorophenyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3h): Yellow solid, 32.3 mg, 59% yield, mp 148−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.48 (t, *J* = 7.1 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 6.52 (s, 1H), 3.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.1, 146.1, 136.6, 134.7, 134.6 (d, $^2J_{C\text{-}F}$ = 12.0 Hz), 132.7, 128.4, 128.3 (d, $^2J_{C\text{-}F}$ = 32.8 Hz), 127.2, 126.4, 123.4, 118.6, 115.2 (d, $J_{C\text{-}F}$ = 85.6 Hz), 98.0, 45.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.94, -112.95, -112.96, -112.97, -112.97, -112.98, -112.99, -113.00, -113.01. HR-MS (ESI) calcd for [M + 1]+: $C_{15}H_{13}FNOS$: 274.0696, found: 274.0688; IR (KBr): 3043, 2925, 1585, 1472, 1372, 1210, 1099, 975, 856, 798, 537, 477 cm^{-1}.

3-(4-Chlorophenyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3i): Yellow solid, 47.5 mg, 82% yield, mp 168−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 2H), 7.79 (s, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.46 – 7.37 (m, 4H), 6.65 (s, 1H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 137.0, 136.4, 134.7, 132.8, 128.5, 127.8, 127.3, 126.6, 123.4, 118.8, 98.4, 45.3. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{15}H_{13}ClNOS$: 290.0401, found: 290.039155; IR (KBr): 3043, 2953, 1531, 1475, 1356, 1194, 1003, 805, 783, 530, 479 cm^{-1}.

3-(4-Bromophenyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3j): Yellow solid, 50.1 mg, 75% yield, mp 173−175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 13.9, 8.3 Hz, 2H), 7.52 – 7.43 (m, 3H), 7.34 (t, *J* = 6.6 Hz, 2H), 6.57 (s, 1H), 3.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 137.4, 136.4, 132.8, 131.5, 128.1, 127.3, 126.7, 123.4, 123.1, 118.8, 98.4, 45.4. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{15}H_{13}BrNOS$: 334.9921, found: 334.9927; IR (KBr): 3008, 2923, 1614, 1534, 1484, 1362, 1177, 1005, 786, 552, 488 cm^{-1}.

1-Methyl-3-(4-(trifluoromethyl)phenyl)benzo[e][1,2]thiazine 1-oxide (3k): Yellow solid, 50.4 mg, 78% yield, mp 189−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.2 Hz, 2H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.47 (dd, *J* = 7.5, 4.6 Hz, 2H), 6.74 (s, 1H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 141.9, 136.2, 132.9, 127.5, 127.1, 126.7, 125.3 (q, $^2J_{C\text{-}F}$ = 14.8.0 Hz), 125.2, 123.5, 119.2, 99.5, 45.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{16}H_{13}F_3NOS$: 323.0696, found: 323.0682; IR (KBr): 3042,

2927, 1614, 1532, 1484, 1362, 1176, 1005, 785, 557, 427 cm^{-1}.

1-Methyl-3-(perfluorophenyl)benzo[e][1,2]thiazine 1-oxide (3l): Yellow solid, 67.7 mg, 98% yield, mp 129−131 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 6.35 (s, 1H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.2, 133.1, 128.0, 127.2, 123.5, 119.1, 105.5, 45.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.97, -140.99, -141.03, -141.05, -154.51, -154.56, -154.62, -162.14, -162.16, -162.19, -162.21, -162.25, -162.27. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{15}H_9F_5NOS$: 346.0302, found: 346.0295; IR (KBr): 3008, 2926, 1664, 1505, 1454, 1326, 1157, 1094, 817, 665, 508, 457 cm^{-1}.

1-Methyl-3-(naphthalen-2-yl)benzo[e][1,2]thiazine 1-oxide (3m): Yellow solid, 47.6 mg, 78% yield, mp 164−166 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.93 (dd, *J* = 8.7, 1.5 Hz, 1H), 7.88 – 7.81 (m, 1H), 7.79 – 7.69 (m, 3H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.37 – 7.27 (m, 2H), 6.72 (s, 1H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 136.7, 135.7, 133.7, 133.4, 132.7, 128.8, 127.9, 127.6, 127.3, 126.5, 126.4, 126.3, 126.2, 123.9, 123.5, 118.9, 98.8, 45.4. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{19}H_{16}NOS$: 306.0947, found: 306.0941; IR (KBr): 3046, 2923, 1615, 1531, 1487, 1363, 1176, 1005, 786, 695, 560, 481 cm^{-1}.

1-Methyl-3-(thiophen-2-yl)benzo[e][1,2]thiazine 1-oxide (3n): Yellow solid, 30.3 mg, 58% yield, mp 128−129 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.60 (dd, *J* = 3.6, 0.9 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.39 – 7.32 (m, 3H), 7.09 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.61 (s, 1H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 142.1, 136.4, 132.8, 127.8, 126.9, 126.7, 126.1, 125.1, 123.5, 118.9, 97.1, 45.2. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{13}H_{12}NOS_2$: 262.0238, found: 262.0230; IR (KBr): 3234, 3094, 2990, 2927, 1628, 1486, 1397, 1174, 1003, 786, 553 cm^{-1}.

3-Isopropyl-1-methylbenzo[e][1,2]thiazine 1-oxide (3o): Yellow solid, 19.9 mg, 45% yield, mp 100−101 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 5.98 (s, 1H), 3.50 (s, 3H), 2.65 (dt, *J* = 13.6, 6.8 Hz, 1H), 1.25 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 136.9, 132.5, 126.4, 125.6, 123.4, 117.9, 96.3, 45.1, 36.4, 21.4. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{12}H_{16}NOS$: 222.0947, found: 222.0941; IR (KBr): 3008, 2927, 1616, 1585, 1487, 1363, 1176, 1005, 786, 680, 519, 494 cm^{-1}.

3-(***tert*-Butyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3p)**: Yellow liquid, 26.4 mg, 56% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.20 (dd, *J* = 17.7, 8.2 Hz, 2H), 5.97 (s, 1H), 3.37 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 137.0, 132.3, 126.8, 125.8, 123.2, 117.8, 95.2, 45.0, 37.3, 28.9. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{13}H_{18}NOS$: 236.1104, found: 236.1099; IR (KBr): 3009, 2953, 1615, 1534, 1487, 1363, 1175, 1005, 805, 787, 554, 479 cm^{-1}.

3-((3r,5r,7r)-Adamantan-1-yl)-1-methylbenzo[e][1,2]thiazine 1-oxide (3q): Yellow solid, 32.6 mg, 52% yield, mp 145−147 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.31 (dd, *J* = 15.0, 7.8 Hz, 2H), 6.00 (s, 1H), 3.46 (s, 3H), 2.09 (s, 3H), 1.95 (q, *J* = 12.2 Hz, 6H), 1.83 – 1.71 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 137.1, 132.3, 126.8, 125.7, 123.2, 118.0, 95.1, 45.0, 40.7, 38.7, 37.0, 28.7. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{19}H_{24}NOS$: 314.1573, found: 314.1565; IR (KBr): 3046, 2927, 1615, 1531, 1486, 1363, 1176, 1005, 787, 508, 481 cm^{-1}.

1-Ethyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3r): Yellow solid, 33.4 mg, 62% yield, mp 120−121 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.4 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.49 – 7.33 (m, 5H), 6.63 (s, 1H), 3.87 – 3.75 (m, 1H), 3.71 – 3.58 (m, 1H), 1.28 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 138.7, 138.0, 132.8, 128.8, 128.4, 127.2, 126.5, 126.2, 123.9, 115.7, 97.5, 51.3, 8.7. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{16}H_{16}NOS$: 270.0947, found: 270.0933; IR (KBr): 3046, 2927, 1615, 1533, 1486, 1364, 1176, 1005, 785, 552, 494 cm^{-1}.

1-Benzyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3s): Yellow liquid, 29.8 mg, 45% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.2 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.36 (m, 4H), 7.33 – 7.25 (m, 3H), 7.22 – 7.17 (m, 3H), 6.37 (s, 1H), 4.78 (d, *J* = 13.9 Hz, 1H), 4.65 (d, *J* = 13.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 138.8, 138.5, 133.1, 131.2, 128.8, 128.8, 128.4, 128.3, 128.0, 126.7, 126.3, 125.9, 125.1, 115.4, 97.4, 64.7. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{21}H_{18}NOS$: 332.1104, found: 332.1097; IR (KBr): 3030, 3027, 1603, 1532, 1486, 1356, 1174, 1103, 787, 690, 556 cm^{-1}.

1-Cyclopropyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3t): Yellow liquid, 22.5 mg, 40% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.48 – 7.36 (m, 5H), 6.70 (s, 1H), 3.01 – 2.92 (m, 1H), 1.92 – 1.82 (m, 1H), 1.43 – 1.31 (m, 2H), 1.27 – 1.16 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 138.8, 136.9, 132.4, 128.8, 128.3, 127.0, 126.5, 126.2, 123.7, 119.4, 98.2, 32.9, 6.6, 5.0. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{17}H_{16}NOS$: 282.0947, found: 282.0931; IR (KBr): 3029, 2924, 1630, 1530, 1486, 1355, 1175, 1003, 786, 690, 551 cm^{-1}.

1-Methyl-3-phenylnaphtho[2,3-e][1,2]thiazine 1-oxide (3u): Yellow solid, 18.3 mg, 30% yield, mp 149−151 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.06 (d, J = 7.4 Hz, 1H), 8.00 (d, J = 7.4 Hz, 2H), 7.92 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.83 (s, 1H), 7.74 (d, J = 5.0 Hz, 1H), 7.68 (dd, J = 6.2, 3.2 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.47 – 7.41 (m, 4H), 7.40 – 7.34 (m, 1H), 3.69 (s, 1H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 145.6, 139.1, 138.7, 135.7, 134.8, 132.2, 131.7, 129.2, 129.0, 128.9, 128.8, 128.8, 128.5, 128.4, 127.8, 127.4, 126.9, 126.5, 126.4, 126.0, 124.7, 124.5, 123.9, 121.3, 119.2, 98.8, 93.7, 45.8, 45.4. HR-MS (ESI) calcd for [M + 1]+: $C_{19}H_{16}NOS$: 306.0947, found: 306.0938; IR (KBr): 3030, 2923, 1615, 1532, 1488, 1363, 1175, 1105, 787, 613, 575, 468 cm^{-1}.

1,6-Dimethyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3v): Yellow liquid, 43.6 mg, 81% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.8 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.30 – 7.24 (m, 1H), 7.12 (d, *J* = 6.8 Hz, 2H), 6.51 (s, 1H), 3.48 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 143.4, 138.6, 136.9, 128.8, 128.4, 127.8, 126.9, 126.5, 123.4, 116.4, 98.1, 45.6, 21.8. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{16}H_{16}NOS$: 270.0947, found: 270.0937; IR (KBr): 3036, 2987, 1615, 1532, 1487, 1363, 1175, 1105, 787, 558, 489 cm^{-1}.

6-Methoxy-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3w): Yellow solid, 50.2 mg, 88% yield, mp 123−125 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.48 – 7.36 (m, 3H), 6.96 (d, *J* = 8.7 Hz, 1H), 6.79 (s, 1H), 6.59 (s, 1H), 3.90 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 147.8, 139.3, 138.6, 128.9, 128.4, 126.6, 125.6, 115.7, 111.7, 108.0, 98.7, 55.6, 46.1. HR-MS (ESI) calcd for $[M + 1]^+$: $C_{16}H_{16}NO_2S$: 286.0896, found: 286.0887; IR (KBr): 3030, 3004, 2927, 1594, 1532, 1467, 1203, 1099, 855, 762, 690, 519, 427 cm^{-1}.

6-Fluoro-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3x): Yellow solid, 43.2 mg, 79% yield, mp 139−141 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.4 Hz, 2H), 7.71 (dd, *J* = 8.6, 5.3 Hz, 1H), 7.38 – 7.26 (m, 3H), 6.99 (dd, *J* = 20.9, 10.1 Hz, 2H), 6.52 (s, 1H), 3.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 163.6, 148.6,

139.8, 139.7, 138.1, 129.3, 128.4, 126.6, 126.6, 115.0, 114.9, 114.8 (d, $^2J_{C-F}$ = 8.4 Hz), 114.7, 112.1, 111.9, 97.8, 97.7 (d, $^2J_{C-F}$ = 10.4 Hz), 45.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.03, -105.05, -105.06, -105.07, -105.08, -105.09. HR-MS (ESI) calcd for [M + 1]+: $C_{15}H_{13}FNOS$: 274.0696, found: 274.0690; IR (KBr): 3008, 2927, 1588, 1532, 1479, 1360, 1202, 1106, 835, 799, 512, 476 cm^{-1}.

6-Chloro-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3y): Yellow solid, 39.4 mg, 68% yield, mp 140−142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.48 – 7.39 (m, 4H), 7.35 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.61 (s, 1H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 138.9, 138.3, 138.1, 129.3, 128.4, 126.6, 126.6, 126.3, 125.1, 116.6, 97.4, 45.6. HR-MS (ESI) calcd for [M + 1]$^+$: $C_{15}H_{13}ClNOS$: 290.0402, found: 290.0388; IR (KBr): 3009, 2927, 1615, 1564, 1454, 1390, 1198, 1027, 785, 692, 484 cm^{-1}.

6-Bromo-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (3z): Yellow solid, 51.5 mg, 77% yield, mp 167−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.4 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.50 (s, 1H), 7.43 – 7.29 (m, 4H), 6.50 (s, 1H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 138.4, 138.1, 129.4, 129.3, 128.5, 127.4, 126.6, 125.0, 117.0, 97.3, 45.6. HR-MS (ESI) calcd for [M + 1]$^+$: $C_{15}H_{13}BrNOS$: 333.9896, found: 333.9883; IR (KBr): 3008, 2925, 1614, 1531, 1487, 1363, 1176, 1005, 787, 563, 479 cm^{-1}.

5-Bromo-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide(3z-1): Yellow solid, 48.1 mg, 72% yield, mp 185−187 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.0 Hz, 2H), 7.62 – 7.56 (m, 1H), 7.45 (dd, *J* = 13.8, 6.3 Hz, 3H), 7.39 (dd, *J* = 6.7, 2.6 Hz, 2H), 6.67 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 139.9, 137.8, 132.9, 131.7, 129.2, 128.4, 127.4, 126.5, 118.8, 118.6, 98.0, 49.9. HR-MS (ESI) calcd for [M + 1]$^+$: $C_{15}H_{13}BrNOS$: 333.9896, found: 333.9892; IR (KBr): 3006, 2925, 1617, 1512, 1488, 1366, 1264, 1098, 1002, 811, 689, 519, 479 cm^{-1}.

8-Bromo-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide(3z-2): Yellow solid, 50.1 mg, 75% yield, mp 127−129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.0 Hz, 2H), 7.62 – 7.56 (m, 1H), 7.45 (dd, *J* = 13.8, 6.3 Hz, 3H), 7.39 (dd, *J* = 6.7, 2.6 Hz, 2H), 6.67 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 139.9, 137.8, 132.9, 131.7, 129.2, 128.4, 127.4, 126.5, 118.8, 118.6, 98.0, 49.9. HR-MS (ESI) calcd for [M + 1]$^+$: $C_{15}H_{13}BrNOS$: 333.9896, found: 333.9863; IR (KBr): 3008, 2925, 1604, 1531, 1487, 1356, 1218, 1174, 1103, 773, 558, 463 cm^{-1}.

Synthetic Applications of This Transformation

Preparation of 4-bromo-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide[28]

A mixture of **3a** (0.4 mmol, 77.2 mg), NBS (0.4 mmol, 71 mg) and AIBN (0.08 mmol, 13.2 mg) in CCl_4 (8 mL) was heated to reflux for 12 h. The reaction mixture was cooled to room temperature and filtered. The filtrate was washed with saturated $NaHCO_3$ and brine, and the organic layer was dried over Na_2SO_4, 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 product **4**.

4-Bromo-1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (4): Yellow solid, 33.4 mg, 50% yield, mp 120−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.75 (t, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.39 (m, 3H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 140.5, 134.8, 133.3, 129.5, 128.6, 128.0, 127.8, 127.3, 123.1, 120.9, 96.1, 44.4. HR-MS (ESI) calcd for [M + 1]$^+$: $C_{15}H_{13}BrNOS$: 333.9896, found: 333.9892; IR (KBr): 3009, 2923, 1613, 1533, 1485, 1363, 1177, 1006, 786, 547, 425 cm^{-1}.

Preparation of 4-bromo-1-(bromomethyl)-3-phenylbenzo[e][1,2]thiazine 1-oxide[28]

A mixture of **3a** (0.4 mmol, 77.2 mg), NBS (0.8 mmol, 142 mg) and AIBN (0.08 mmol, 13.2 mg) in CCl_4 (8 mL) was heated to reflux for 12 h. The reaction mixture was cooled to room temperature and filtered. The filtrate was washed with saturated $NaHCO_3$ and brine, and the organic layer was dried over Na_2SO_4, filtered, and concentrated. The product was purified by flash column chromatography on silica gel with n-pentane/ethyl acetate (15:1) as eluent to give product **5**.

4-Bromo-1-(bromomethyl)-3-phenylbenzo[e][1,2] thiazine 1-oxide: (5): yellow liquid, 15.7 mg, 19% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.80 (t, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.50 – 7.40 (m, 3H), 5.03 (d, *J* = 12.1 Hz, 1H), 4.85 (d, *J* = 12.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 140.3, 137.7, 134.7, 129.2, 128.8, 128.0, 127.9, 127.7, 125.1, 116.0, 96.1, 47.3. HR-MS (ESI) calcd for [M + 1]$^+$: $C_{15}H_{12}Br_2NOS$: 411.9001, found: 411.9000; IR (KBr): 3009, 2927, 1614, 1531, 1487, 1363, 1176, 1005, 786, 553, 494 cm^{-1}.

Synthesis of 1-methyl-4-nitro-3 phenylbenzo[e][1,2]thiazine 1-oxide [29]

It was introduced by nitration of **3a** (0.2 mmol, 51 mg) with concentrated nitric acid (0.4 mmol, 50.4 mg)in acetic acid at temperature below 15°C. The mixture was allowed to stir for 10 h at room temperature. Then, H_2O (10 mL) was added, the phases were separated, and the aqueous layer was extracted DCM (3 × 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, concentrated and the oily crude product was purified by flash column chromatography on silica gel to give product **6** in 42% yield.

1-Methyl-4-nitro-3-phenylbenzo[e][1,2]thiazine 1-oxide: (6): yellow liquid, 25.2 mg, 42% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 2.1 Hz, 2H), 7.64 – 7.56 (m, 3H), 7.47 – 7.38 (m, 3H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 134.3, 130.1, 129.2, 128.7, 128.0, 127.8, 124.0, 122.2, 117.5, 29.7. HR MS (ESI) calcd for [M + 1]$^+$: $C_{15}H_{13}N_2O_3S$: 301.0641, found: 301.0642; IR (KBr): 3219, 3007, 2925, 1615, 1528, 1486, 1363, 1176, 1005, 786, 520, 435 cm^{-1}.

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FULL PAPER

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