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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c00918 • Publication Date (Web): 03 Sep 2020

Access to [2,1]benzothiazine *S,S*-dioxides from β-Substituted *o*-Nitrostyrenes and Sulfur

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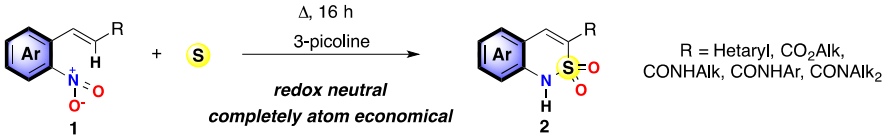


ABSTRACT: [2,1]Benzothiazine *S,S*-dioxides **2** were synthesized by simply heating *o*-nitrostyrenes with elemental sulfur in 3-picoline with complete atom economy. This reaction was found to occur without any added catalyst and consist of a cascade of reduction of the nitro group, sulfuration of a C-H of the double bond, oxidation of a sulfur atom to its highest oxidation state by the migration of two oxygen atoms from the nitro group and formation of new N-S bond. Furthermore, the method could also be applied to *o*-nitrocinnamamides and cinnamate esters.

Introduction

Cyclic sulfonamides or sultams exist widely in bioactive molecules and pharmaceuticals, which frequently serve as a key scaffold for discovery of new drugs owning to their sulfonamide pharmacophore. As a subgroup of sultam, [2,1]benzothiazine *S,S*-dioxide scaffolds have potent biological activities (Figure 1).[1] Indeed, **A** was demonstrated to be an inhibitor of nuclear factor kappaB (NF-κB), which is a pivotal transcription factor that regulates the gene expression involved in inflammation and immune responses.[2] Moreover, both **B** and **C** were found to inhibit focal adhesion kinase (FAK), which regulates cell survival and proliferation pathways. While the inhibitory activity of **C** is strong and selective,[3] the derivatives **B** can restore, in a concentration dependent manner, the antibacterial activity of CPX against SA-K2378, a norA-overexpressing strain.[4] While many RNA viruses such as Dengue, Zika, and several encephalitis viruses have been "re-discovered" over the years, non-nucleoside derivative **D** displayed inhibitory activity against dengue NS5 RNA-dependent RNA polymerase (RdRp).

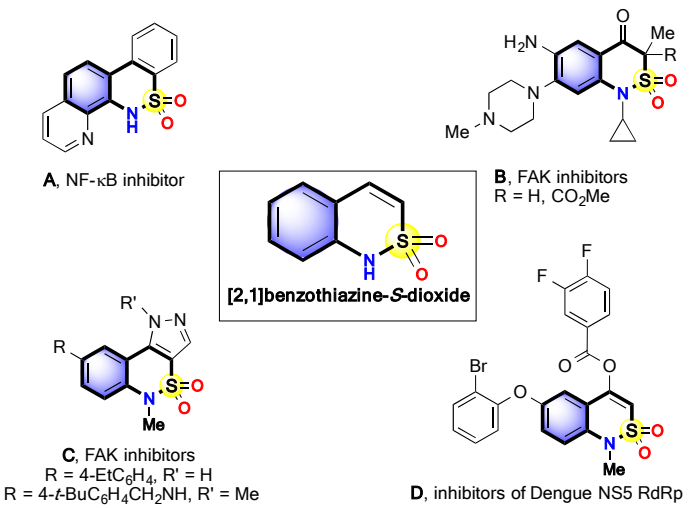


Figure 1. 2,1-Benzothiazine *S,S*-dioxide and its bioactive examples

Consequently, the construction of these heterocyclic scaffolds has drawn considerable interest (Figure 2).[5]

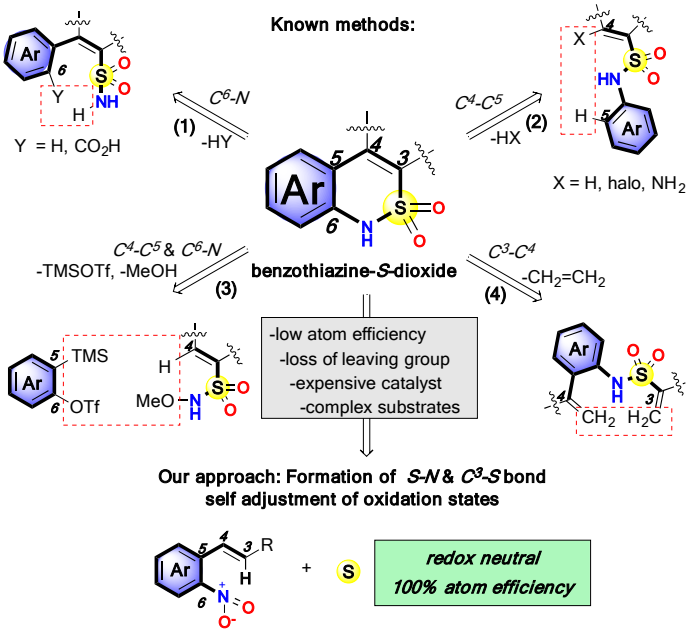


Figure 2. Synthetic approaches to 2,1-Benzothiazine *S,S*-dioxides

The first approach involves a C-N bond formation via C-H cyclizing functionalization of NH sulfonamides (Pathway 1: formation of C^6-N bond) with strong oxidizing agents, including high oxidation state iodine reagents such as $PhI(OAc)_2$/hν,[6] $PhI(OAc)_2$–I_2,[7] $PhI(OAc)_2$ or $K_2S_2O_8$ with NaBr,[8] and dibromohydantoin.[9] In some cases, further halogenation of the benzothiazine-*S,S*-dioxide products is among frequently encountered side reactions. Silver-catalyzed Minisci-type decarboxylative cyclization was also developed for this purpose.[10]

Alternatively, C^4-C^5 bond formation via C-H functionalization (Pathway 2: formation of C^4-C^5 bond) was also developed with a strong focus on using Pd catalyst.[11]

Recently, the benzyne chemistry was exploited via formation of C^4-C^5 and C^6-N (Pathway 3).[12] The ring closing metathesis reaction was also applied to the synthesis of this benzothiazine scaffold (Pathway 4).[13]

Although these strategies could provide the expected products with high degree of structural diversity, they all suffer from at least one of the following drawbacks: (i) use of expensive transition metal catalysts and reagents; (ii) involvement of starting materials that were prepared via multistep sequences of reactions with low global yields; (iii) formation of mixtures of regioisomers; and (iv) formation of only one bond (except for pathway 3).

More importantly, in term of atom efficiency, none of the above-mentioned reactions could deliver the products with conservation of the number of atoms due to the presence of leaving groups as well as activating groups in the starting materials.

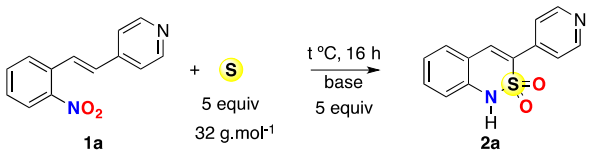
To address these issues, we suggested the incorporation of elemental sulfur to *o*-nitrostyrene **1** as a result of a cascade of oxidation of the sulfur atom, sulfuration of the C-H bond in the β-position of **2**, reduction of the nitro group. It should be noted that both aromatic nitro group and olefinic C-H bond are readily obtained. In view of huge opportunity of using nitro group as a direct nitrogen synthon for aza heterocyclic synthesis without prior reduction, we have developed a series of redox-neutral cascade reactions involving aromatic nitro group as a 6-electron oxidizing group.[14]

We have applied successfully this strategy to 2-nitrochacones to provide a wide range of sultams.[15] As a continuation of our effort in the sulfur-involved construction of complex heterocycles, herein, we described the reaction with *o*-nitrostyrenes **2** β-substituted by an aza heterocycle.

Results & Discussion

The model reaction was conducted with *o*-nitrostilbazole **1a** in sulfur (5 equiv) in the presence of 3-picoline as a basic additive (Table 1). Below 120 °C, **1a** remained unchanged (entry 1). To improve the reaction, several parameters were varied, including temperatures and base additives. Gratifyingly, at 135 °C, the desired product **2a** was isolated in 84% yield. Further screening of other bases revealed that while similar pyridine bases such as 4-picoline or pyridine could provide the expected product **2a** despite lower yields (entries 3,4), the reactions promoted by bases stronger than pyridine such as *N*-methylmorpholine, *N*-methylpiperidine or DIPEA resulted in complex mixtures even at lower temperatures (entries 5-7).

Table 1. Optimization of the reaction conditions



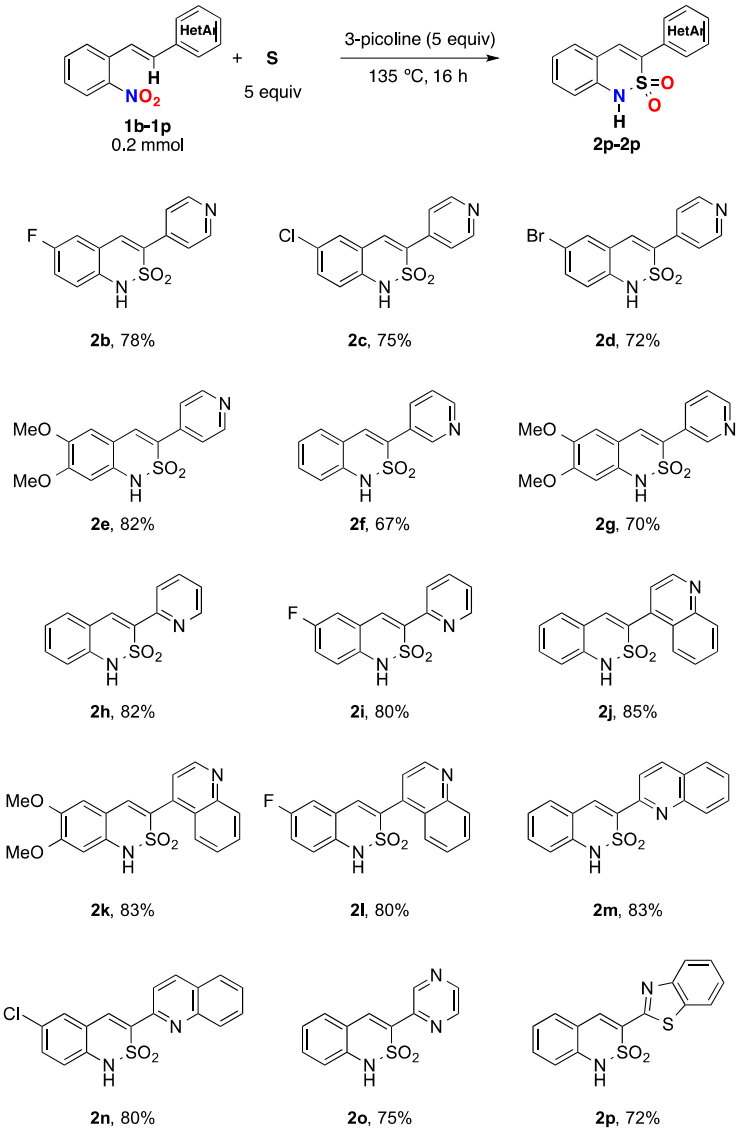
entry[a]	base	temp (°C)	yield (%)[b]
1	3-picoline	120	-
2	**3-picoline**	**135**	**84**
3	4-picoline	135	60
4	pyridine	135[c]	62
5	*N*-methylmorpholine	120[c]	25[d]
6	*N*-methylpiperidine	100	-
7	DIPEA	100	-

[a] Reaction conditions: **1a** (0.2 mmol), S (1 mmol, 32 mg), base (1 mmol, 5 equiv). [b] Isolated yield. [c] Reaction performed in a sealed tube. [c] Conversion determined by ^{1}H NMR of the crude mixture.

With the optimized reaction conditions in hand (Table 1, entry 2), the synthetic potential of this reaction was evaluated (Scheme 1). Initially, substrates with various substituents on the nitrophenyl ring were investigated. In addition to methoxy groups, the reaction tolerated various halogen substituents, which could be useful for further functionalization of the products. Generally, the desired benzothiazine **2** were obtained in acceptable to satisfactory yields (67−85%) with halogen and methoxy substituents on the phenyl moiety (**2b-2e**). To evaluate further applications of the developed protocol, other regiomeric pyridyl substrates (**1f-1i**) as well as their benzo analogs such as quinol-2-yl and quinol-4-yl (**1j-1n**) were evaluated and gave satisfactory results.

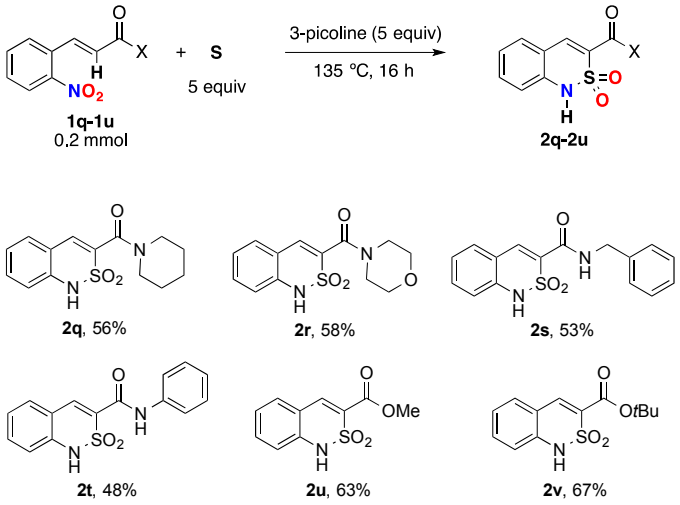
It was worth mentioning that reactions of nitro substrates bearing other heterocyclic substituent such as piperazinyl and benzothiazol-2-yl were also successful, furnishing the corresponding benzothiazines (**2o-2p**) in reasonably good yields. The common sulfonamide structure of this family of compounds was supported by X-ray diffraction analysis performed on single crystals of compounds **2b** and **2i (**CCDC 1953702 and 1953703 respectively).

Scheme 1. Synthesis of benzothiazine *S,S*-dioxides 2b-p



To further expand the scope and enrich the compound library, we attempted to synthesize benzothiazines bearing an amide or an ester group, which have been demonstrated to possess remarkable biological activity,[4] from the corresponding *o*-nitrocinnamides (**1q-1t**) or *o*-nitrocinnamates (**1u-1v**) (Scheme 2). Gratifyingly, a variety of *o*-nitrocinnamamides and esters were competent substrates to yield the corresponding benzothiazines **2q-2v** in satisfactory yields.

Scheme 2. Synthesis of benzothiazine *S,S*-dioxides 2b-p

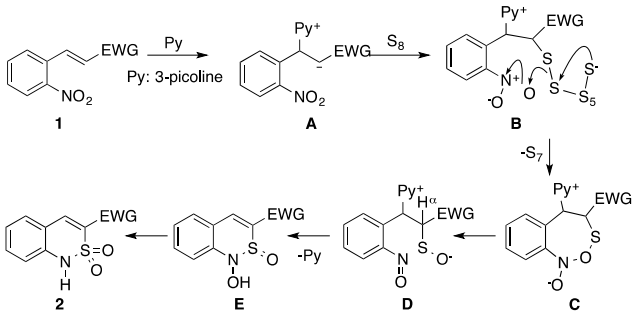


Our present method had however limitation. The reaction failed with 2-nitrostilbene as well as its derivative bearing an electron withdrawing group (EWG) on the phenyl ring without the nitro group such as 4'-cyano, 3'-nitro and 2'-carboxymethyl 2-nitrostilbenes. In these cases, the starting *o*-nitrostilbenes were recovered practically unchanged with some *trans-cis* isomerization of the olefin double bond.

It is clear that the reactivity of sulfur incorporation requires a strong EWG at the β position of *o*-nitrostyrene skeleton.

Based on these observations as well as on our previous results,[15] we propose a plausible reaction mechanism that starts with a Michael addition of the pyridine base to the olefin double bond strongly polarized by the β-EWG to form zwitterion **A** where the anionic moiety is stabilized by the β-EWG (Scheme 3). This anion species then attacks sulfur to provide polysulfide **B**. Subsequent extrusion of a smaller thiocycle **B** with simultaneous cyclization leads to 7-menbered intermediates **C**. Stepwise transfer of both oxygen atoms from nitrogen to sulfur proceeds via ring opening - ring closing process with concomitant elimination of pyridine base and furnishes the final benzothiazine *S,S*-dioxides **2**.[16]

Scheme 3. Plausible reaction pathway



In conclusion, we demonstrated that [2,1]benzothiazine *S,S*-dioxides **2** could be synthesized by simply heating *o*-nitrostyrenes **2** with elemental sulfur in 3-picoline with complete atom economy. This reaction consists in a cascade of reduction of the nitro group, sulfuration of a C-H of the double bond, oxidation of a sulfur atom to its highest oxidation state by migration of two oxygen atoms from the nitro group and formation of new N-S bond. Furthermore, the method could be applied to *o*-nitrocinnamamides and cinnamate esters. Considering the importance of organosulfur compounds, especially sulfonamide function in medicinal chemistry, we believe that this result is of great value for synthetic chemists and pharmacologists, opening new opportunities of finding of new biologically active molecules.

Experimental Section

General Information

Reagents were obtained from commercial supplier and used without further purification. Analytical thin layer chromatography (TLC) was purchased from Merck KGaA (silica gel 60 F254). Visualization of the chromatogram was performed by UV light (254 nm) or KMnO4 or vanilline stains. Flash column chromatography was carried out using kieselgel 35-70 μm particle sized silica gel (230-400 mesh). NMR Chemical shifts are reported in (δ) ppm relative to tetramethylsilane (TMS) with the residual solvent as internal reference ($CDCl_3$, δ 7.26 ppm for 1H and δ 77.0 ppm for 13C; (DMSO-d_6, δ 2.50 ppm for ^{1}H and δ 39.5 ppm for ^{13}C). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration.

General procedure for the synthesis of starting material (10 mmol scale)

Procedure A

In a round bottom flash was added 2-nitrobenzaldehyde (1 equiv), 4-picoline (1 equiv), (or 2-picoline, 2-methylquinoline, 4-methylquinoline), anhydride acetic (15 mL) and a few drops of piperidine. The mixture was then refluxed in an oil bath overnight. After completion of the reaction, the mixture was neutralized with a saturated aqueous solution of Na_2CO_3 then extracted with CH_2Cl_2 (2x50 mL). The combined organic phase was then dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum. The product was purified by recrystallization or by column chromatography (eluent hexane: ethyl acetate 2:1).

Procedure B

In a round bottom flask was added 3-bromopyridine (1 equiv), 1-nitro-2-vinylbenzene (1.2 equiv), dichlorobis(tri-*o*-tolylphosphine)palladium (5 mol %), triethylamine (3 equiv) and DMF (10 mL). The mixture was heated to 110 ˚C in and oil bath overnight and cooled to room temperature. The reaction mixture was diluted with ethyl acetate (50 mL) and the organic phase was washed with water and a solution of brine then dried over $MgSO_4$. The organic layer was then filtered and concentrated under vacuum. The crude product was purified by chromatography on silica gel (hexane/ethyl acetate: 3/1 to 1/1) to give the coupling product.

Procedure C: Synthesis of amide derivatives

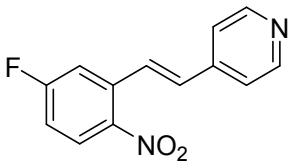
In a round bottom flash was added 2-nitrocinnamic acid (1 equiv), EDCI•HCl (1 equiv) in 10 mL of DMF. The mixture was stirred for 15 minute and HOBt (1.2 equiv), amine (1.2 equiv), and triethylamine (2 equiv) was added to this mixture respectively. After 24h, the reaction was quenched by water and extracted with ethyl acetate (2x50 mL). and the organic phase was washed with water, a solution of brine and dried over $MgSO_4$. The organic solvent was then filtered, evaporated under vacuum. The crude product was purified by chromatography on silica gel (hexane/ethyl acetate: 2/1) to give desired amide.

Procedure D: Synthesis of ester derivatives

In a round bottom flash was added 2-nitrobenzaldehyde (1 equiv) and the corresponding ylide (1.05 equiv) dissolved in dichloromethane. The mixture was stirred for 3 h at room temperature. The reaction was then quenched by water and the organic phase was washed with water, a solution of brine and dried over $MgSO_4$. The organic layer was then filtered and concentrated under vacuum. The crude product was purified by chromatography on silica gel (hexane/ethyl acetate: 9/1) to give desired ester.

Known compounds: **1a**,[17] **1f**,[17] **1h**,[17] **1j**,[18] **1u**,[19] **1y**,[19] **1q**,[20] **1s**,[20] **1t**.[21]

(*E*)-4-(5-Fluoro-2-nitrostyryl)pyridine (1b)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

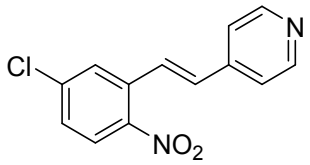
Pale yellow solid (1.09 g, 45%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, J = 5.1 Hz, 2H), 7.94 (d, J = 8.7 Hz, 1H), 7.89 (d, J = 2.1 Hz, 1H), 7.79 (d, J = 16.1 Hz, 1H), 7.62 (dd, J = 8.7, 2.1 Hz, 1H), 7.44 (d, J = 5.3 Hz, 2H), 6.99 (d, J = 16.1 Hz, 1H).

$^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 165.0 (d, *J* = 257.0 Hz), 150.6, 144.2, 143.4, 135.6 (d, *J* = 9.3 Hz), 132.3, 128.1 (d, *J* = 10.0 Hz), 127.9 (t, *J* = 2.0 Hz), 121.4, 116.2 (d, *J* = 23.6 Hz), 115.4 (d, *J* = 24.3 Hz).

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9FN_2NaO_2$ 267.0546. Found 267.0549.

(*E*)-4-(5-Chloro-2-nitrostyryl)pyridine (1c)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

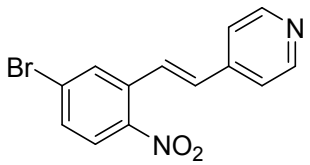
Pale yellow solid (1.23, 47%).

^1H NMR (500 MHz, $CDCl_3$) δ 8.66 – 8.49 (m, 2H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.77 (d, *J* = 16.1 Hz, 1H), 7.72 (d, *J* = 2.2 Hz, 1H), 7.44 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.43 – 7.35 (m, 2H), 6.98 (d, *J* = 16.0 Hz, 1H)

$^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 150.5, 146.1, 143.2, 139.9, 134.0, 132.2, 128.9, 128.5, 127.4, 126.6, 121.3.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9ClN_2NaO_2$ 283.0250. Found 283.0255.

(*E*)-4-(5-Bromo-2-nitrostyryl)pyridine (1d)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

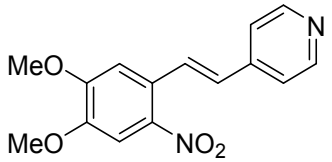
Pale yellow solid (1.65, 54%).

^1H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 5.2 Hz, 2H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.88 (d, *J* = 2.1 Hz, 1H), 7.75 (d, *J* = 16.1 Hz, 1H), 7.59 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.39 (d, *J* = 5.7 Hz, 2H), 6.97 (d, *J* = 16.1 Hz, 1H).

$^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 150.5, 146.7, 143.5, 134.1, 132.3, 132.1, 131.6, 128.5, 127.5, 126.6, 121.4.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9BrN_2NaO_2$ 326.9745. Found 326.9748

(*E*)-4-(4,5-Dimethoxy-2-nitrostyryl)pyridine (1e)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

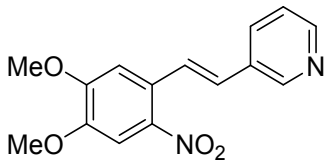
Pale yellow solid (1.60, 56%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, J = 5.1 Hz, 2H), 7.93 (dd, J = 16.1, 1.8 Hz, 1H), 7.64 (d, J = 1.5 Hz, 1H), 7.40 (d, J = 0.2 Hz, 2H), 7.06 (s, 1H), 6.86 (d, J = 16.0 Hz, 1H), 4.04 (s, 3H), 3.97 (d, J = 1.1 Hz, 3H).

^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 153.2, 149.9, 149.9, 149.0, 144.1, 140.5, 129.7, 129.6, 129.4, 127.0, 121.1, 109.5, 107.9, 56.4, 56.4.

HRMS m/z calculated for $[M+Na]^+$ $C_{15}H_{14}N_2NaO_4$ 309.0851. Found 309.0855.

(*E*)-3-(4,5-Dimethoxy-2-nitrostyryl)pyridine (1g)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

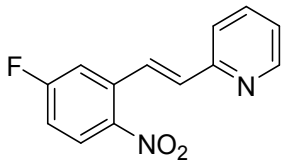
Pale yellow solid (1.52, 53%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.56 (d, J = 4.8 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 16.0 Hz, 1H), 7.66 (s, 1H), 7.42 (dt, J = 12.9, 8.1, 4.7 Hz, 1H), 7.09 (s, 1H), 6.96 (d, J = 16.1 Hz, 1H), 4.06 (s, 3H), 3.99 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 153.4, 149.4, 149.2, 148.9, 140.6, 133.1, 132.6, 128.7, 127.9, 127.3, 123.9, 109.6, 108.1, 56.7, 56.6.

HRMS m/z calculated for $[M+Na]^+$ $C_{15}H_{14}N_2NaO_4$ 309.0851. Found 309.0856.

(*E*)-2-(5-Fluoro-2-nitrostyryl)pyridine (1i)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

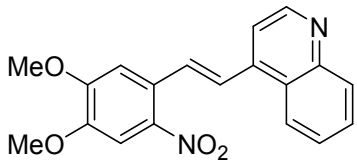
Pale yellow solid (1.56, 64%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (dt, *J* = 4.0, 2.1 Hz, 1H), 8.03 – 7.77 (m, 2H), 7.60 (tdd, *J* = 7.6, 3.6, 1.8 Hz, 1H), 7.35 (ddd, *J* = 12.6, 7.3, 3.3 Hz, 3H), 7.15 – 7.07 (m, 1H), 7.02 (ddt, *J* = 16.1, 9.5, 2.7 Hz, 2H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 164.7 (d, *J* = 256.3 Hz), 154.3, 149.9, 144.3, 136.7, 135.8 (d, *J* = 9.8 Hz), 134.2, 127.8 (d, *J* = 10.0 Hz), 126.9, 123.2, 122.5, 115.6 (d, *J* = 23.7 Hz), 115.0 (d, *J* = 24.4 Hz).

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9FN_2NaO_2$ 267.0546. Found 267.0551.

(*E*)-4-(-4,5-Dimethoxy-2-nitrostyryl)quinoline (1k)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1 to 1:1).

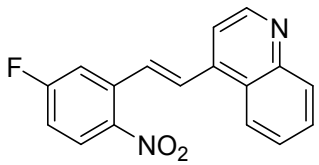
Pale yellow solid (1.58, 47%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (d, *J* = 4.3 Hz, 1H), 8.19 (t, *J* = 8.5 Hz, 2H), 7.96 (d, *J* = 15.8 Hz, 1H), 7.76 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.68 (s, 1H), 7.65 – 7.61 (m, 2H), 7.60 (d, *J* = 15.7 Hz, 1H), 7.16 (s, 1H), 4.09 (s, 3H), 4.00 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 153.4, 149.9, 149.2, 148.3, 142.6, 140.7, 131.9, 130.0, 129.7, 127.6, 126.9, 126.6, 126.3, 123.4, 117.9, 110.0, 108.1, 56.7, 56.6

HRMS m/z calculated for $[M+Na]^+$ $C_{19}H_{16}N_2NaO_4$ 359.1008. Found 359.1012.

(*E*)-4-(5-Fluoro-2-nitrostyryl)quinoline (1l)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1 to 1:1).

Pale yellow solid (1.71, 58%).

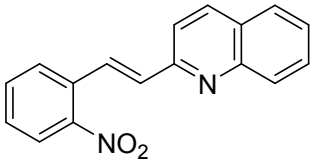
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (d, *J* = 4.6 Hz, 1H), 8.25 (d, *J* = 8.8 Hz, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.18 (dd, *J* = 9.1, 5.1 Hz, 1H), 7.89 (d, *J* = 15.7 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.74 (d, *J* = 16.0 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.54 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.22 (ddd, *J* = 9.4, 7.1, 2.7 Hz, 1H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 165.1 (d, *J* = 257.1 Hz), 150.2, 148.6, 141.8, 136.0, 135.9, 130.3, 130.0, 129.8, 129.3, 128.2 (d, *J* = 10.0 Hz), 127.2, 126.2, 123.3, 118.2, 116.2 (d, *J* = 23.6 Hz), 115.7 (d, *J* = 24.2 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -102.9.

HRMS m/z calculated for $[M+Na]^+$ $C_{17}H_{11}FN_2NaO_2$ 317.0702. Found 317.0707.

(*E*)-2-(2-Nitrostyryl)quinoline (1m)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

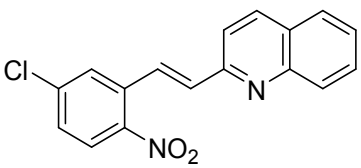
Pale yellow solid (1.71, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 16.3 Hz, 1H), 8.09 (d, *J*=8.0Hz, 1H), 8.02 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.81 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.73 – 7.70 (m, 1H), 7.68 – 7.62 (m, 1H), 7.53 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.40 (d, *J* = 16.2 Hz, 1H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 155.2, 148.2, 136.6, 134.3, 133.3, 132.3, 129.9, 129.4, 129.2, 128.8, 128.5, 127.6, 127.6, 126.7, 124.9, 118.9.

HRMS m/z calculated for $[M+Na]^+$ $C_{17}H_{12}N_2NaO_2$ 299.0796. Found 299.0798

(*E*)-2-(5-Chloro-2-nitrostyryl)quinoline (1n)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

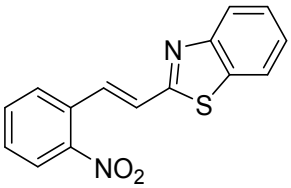
Pale yellow solid (2.02, 65%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.43 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 2.3 Hz, 1H), 8.10 (d, J = 8.8 Hz, 1H), 8.07 (d, J = 16.0 Hz, 1H), 8.03 (dd, J = 8.5, 1.1 Hz, 1H), 7.99 (dd, J = 8.2, 1.4 Hz, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.79 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H),7.69 (dd, J = 8.8, 2.3 Hz, 1H)7.67 (d, J=16.0 Hz, 1H), 7.61 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 154.8, 148.0, 147.2, 138.9, 137.4, 134.9, 133.7, 130.6, 129.6, 129.4, 128.5, 128.4, 127.9, 127.6, 127.2, 127.1, 121.4.

HRMS m/z calculated for $[M+Na]^+$ $C_{17}H_{11}ClN_2NaO_2$ 333.0407. Found 333.0413

(*E*)-2-(2-Nitrostyryl)benzo[*d*]thiazole (1p)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

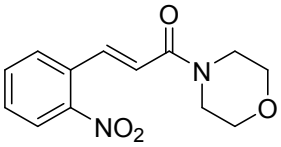
Pale yellow solid (1.64, 58%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13 (dd, J = 8.0, 1.2 Hz, 1H), 8.09 (ddd, J = 8.1, 4.9, 1.3 Hz, 2H), 8.04 (d, J = 8.8 Hz, 1H), 7.96 (d, J = 16.0 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.67 (d, J = 16.1 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.55 (tt, J = 8.3, 7.2, 2.2, 1.3 Hz, 1H), 7.47 (tt, J = 8.3, 7.2, 2.2, 1.2 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 165.5, 153.4, 148.1, 134.3, 133.8, 131.8, 130.2, 130.1, 128.8, 126.7, 125.9, 125.8, 124.8, 122.9, 122.4.

HRMS m/z calculated for $[M+Na]^+$ $C_{15}H_{10}N_2NaO_2S$ 305.0361. Found 309.0853

(*E*)-1-Morpholino-3-(2-nitrophenyl)prop-2-en-1-one (1r)



The product was purified by column chromatography (eluent hexane: ethyl acetate 2:1).

Pale yellow solid (1.13, 43%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.93 (d, *J* = 15.5 Hz, 1H), 7.63 (t, *J* = 15.8 Hz, 1H), 7.60 (d, *J* = 9.8 Hz, 1H), 7.51 (dt, *J* = 13.4, 8.5, 7.0, 1.8, 0.1 Hz, 1H), 6.68 (d, *J* = 15.4 Hz, 1H), 3.76 – 3.68 (m, 8H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 165.0, 148.4, 137.9, 133.6, 131.8, 129.9, 129.4, 125.0, 122.6, 66.9.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_{14}N_2NaO_4$ 285.0851. Found 285.0851.

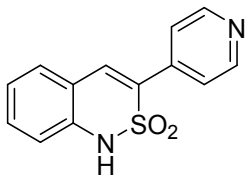
General procedure

A mixture of 2-nitrostilbazole **1** (0.2 mmol) and sulfur (32 mg, 1 mmol) in 3-picoline (93 mg) was heated and stirred in a 7-mL tube at 135 ºC under an argon atmosphere for 16 h (See Schemes 1, 2). After removal of volatiles (0.1 mmHg, 100 ºC), the residue was purified by column chromatography on silica gel (eluent hexane: ethyl acetate 2:1 to 1:1) to afford the product **2**.

1-mmol scale synthesis of **2o**

A mixture of (*E*)-2-(2-nitrostyryl)pyrazine **1o** (227 mg, 1 mmol) and sulfur (160 mg, 5 mmol) in 3-picoline (0.5 mL) was heated and stirred at 135 ºC in a 7-mL tube under an argon atmosphere for 16 h. After removal of volatiles (0.1 mmHg, 100 ºC), methanol (2 mL) was added to the residue and the resulting mixture was stirred at rt for 10 min to obtain a beige slurry (sonication could be applied). The product was filtered, washed with methanol (2 mL x 3) and dried (0.1 mmHg, 100 ºC) to afford the product **2** (199 mg, 73%).

3-(Pyridin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2a)



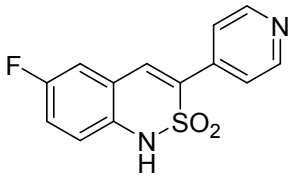
Pale yellow solid. Yield 43 mg, 84%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.83 – 8.63 (m, 2H), 8.01 (s, 1H), 7.77 – 7.70 (m, 2H), 7.69 (d, *J* = 1.5 Hz, 1H), 7.51 (td, *J* = 7.7, 1.5 Hz, 1H), 7.23 (td, *J* = 7.6, 1.1 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 150.6, 138.8, 138.6, 134.2, 133.1, 132.2, 131.0, 123.4, 121.9, 120.2, 117.9.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_{10}N_2NaO_2S$ 281.0361. Found 281.0366.

6-Fluoro-3-(pyridin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2b)



Pale yellow solid. Yield 46 mg, 78%.

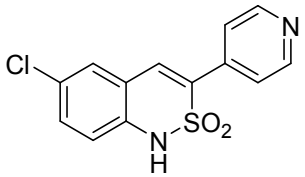
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.72 (d, J = 5.1 Hz, 2H), 7.96 (s, 1H), 7.73 – 7.64 (m, 2H), 7.56 (dd, J = 9.1, 3.0 Hz, 1H), 7.40 (td, J = 8.7, 3.0 Hz, 1H), 7.18 (dd, J = 8.9, 4.8 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 157.9 (d, J = 239.2 Hz), 150.6, 138.5, 135.3, 134.4, 133.2, 122.0,121.4 (d, J = 9.1 Hz),120.2 (d, J = 8.2 Hz), 119.5 (d, J = 23.9 Hz), 116.1 (d, J = 23.6 Hz).

^{19}F NMR (471 MHz, DMSO-d_6) δ -120.0.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9FN_2NaO_2S$ 299.0266. Found 299.0269.

6-Chloro-3-(pyridin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2c)



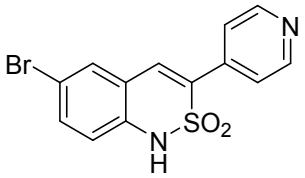
Pale yellow solid. Yield 49 mg, 75%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.64 (d, J = 5.1 Hz, 2H), 7.87 (d, J = 2.2 Hz, 1H), 7.69 (s, 1H), 7.63 (d, J = 5.5 Hz, 2H), 7.44 (dd, J = 8.7, 2.5 Hz, 1H), 7.05 (dd, J = 8.8, 1.9 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 150.4, 138.9, 138.3, 133.6, 133.0, 131.7, 129.8, 126.5, 122.1, 121.3, 120.1.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9ClN_2NaO_2S$ 314.9971. Found 314.9977.

6-Bromo-3-(pyridin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2d)



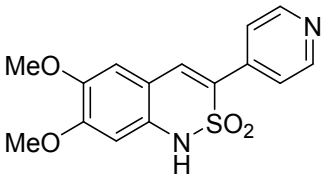
Pale yellow solid. Yield 57 mg, 72%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.79 (d, J = 5.2 Hz, 2H), 8.01 (s, 1H), 7.97 (d, J = 2.3 Hz, 1H), 7.78 (d, J = 5.2 Hz, 2H), 7.70 (dd, J = 8.7, 2.3 Hz, 1H), 7.13 (d, J = 8.6 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 149.9, 148.1, 142.5, 132.3, 131.4, 131.2, 128.1, 123.2, 122.2, 120.2, 106.3.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9BrN_2NaO_2S$ 358.9466. Found 358.9472.

6,7-Dimethoxy-3-(pyridin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2e)



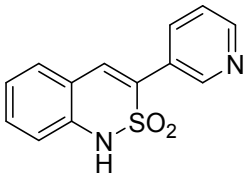
Pale yellow solid. Yield 53 mg, 82%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.67 (d, J = 6.3 Hz, 1H), 7.90 (s, 1H), 7.66 (d, J = 6.3 Hz, 1H), 7.26 (s, 1H), 6.67 (s, 1H), 3.84 (s, 3H), 3.78 (s, 3H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 152.7, 150.5, 145.5, 139.2, 134.0, 129.8, 121.5, 113.1, 112.6, 101.3, 56.3, 56.3.

HRMS m/z calculated for $[M+Na]^+$ $C_{15}H_{14}N_2NaO_4S$ 341.0572. Found 341.0572.

3-(Pyridin-3-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2f)



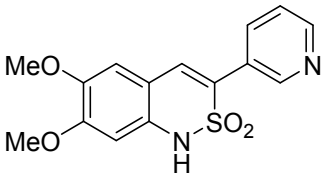
Pale yellow solid. Yield 43 mg, 67%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2.4 Hz, 1H), 8.67 (dd, J = 4.9, 1.6 Hz, 1H), 8.09 (dt, J = 8.0, 2.0 Hz, 1H), 7.84 (s, 1H), 7.66 (dd, J = 7.8, 1.5 Hz, 1H), 7.55 (dd, J = 8.0, 4.8 Hz, 1H), 7.48 (td, J = 7.8, 1.5 Hz, 1H), 7.22 (td, J = 7.6, 1.1 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 150.4, 148.6, 138.3, 135.7, 132.9, 132.9, 131.7, 130.7, 127.6, 124.2, 123.4, 120.5, 117.9.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_{10}N_2NaO_2S$ 281.0361. Found 281.0366.

6,7-Dimethoxy-3-(pyridin-3-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2g)



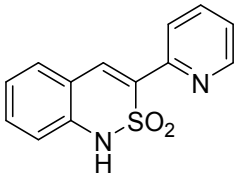
Pale yellow solid. Yield 53 mg, 70%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.84 (d, J = 2.4 Hz, 1H), 8.64 (dd, J = 4.7, 1.6 Hz, 1H), 8.05 (dt, J = 8.0, 2.0 Hz, 1H), 7.72 (s, 1H), 7.54 (dd, J = 8.0, 4.8 Hz, 1H), 7.25 (s, 1H), 6.69 (s, 1H), 3.85 (s, 3H), 3.79 (s, 3H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 152.2, 149.9, 148.3, 145.4, 135.2, 133.4, 132.7, 129.8, 127.9, 124.1, 113.4, 112.4, 101.4, 56.4, 56.2.

HRMS m/z calculated for $[M+Na]^+$ $C_{15}H_{14}N_2NaO_4S$ 341.0572. Found 341.0579

3-(Pyridin-2-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2h)



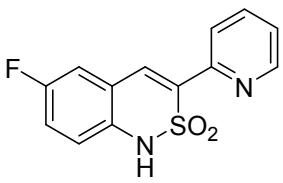
Pale yellow solid. Yield 43 mg, 82%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.70 (d, J = 4.9 Hz, 1H), 8.15 (s, 1H), 7.94 (td, J = 7.8, 1.8 Hz, 1H), 7.89 (d, J = 7.9 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.55 – 7.38 (m, 2H), 7.19 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 150.4, 149.1, 138.9, 137.9, 134.8, 133.3, 131.9, 131.0, 124.3, 123.2, 122.6, 120.2, 117.8.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_{10}N_2NaO_2S$ 281.0361. Found 281.0366.

6-Fluoro-3-(pyridin-2-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2i)



Pale yellow solid. Yield 46 mg, 80%.

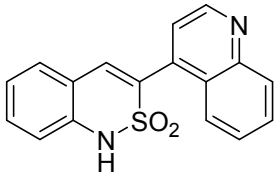
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.64 (d, J = 4.7 Hz, 1H), 8.08 (s, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.60 (dd, J = 9.1, 2.9 Hz, 1H), 7.40 (dd, J = 7.5, 4.8 Hz, 1H), 7.30 (td, J = 8.7, 2.9 Hz, 1H), 7.09 (dd, J = 9.0, 4.7 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 158.0 (d, J = 239.0 Hz), 150.5, 148.7, 137.9, 136.2, 135.1, 132.4, 124.6, 122.8, 121.6 (d, J = 9.2 Hz), 119.9 (d, J = 8.3 Hz), 119.2 (d, J = 23.9 Hz), 116.3 (d, J = 23.4 Hz).

^{19}F NMR (471 MHz, DMSO-d_6) δ -120.0.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_9FN_2NaO_2S$ 299.0266. Found 299.0266.

3-(Quinolin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2j)



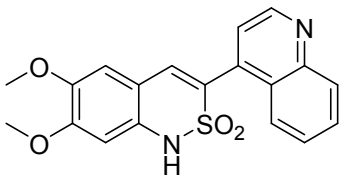
Pale yellow solid. Yield 52 mg, 85%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.02 (d, J = 4.4 Hz, 1H), 8.15 (dd, J = 8.4, 1.1 Hz, 1H), 8.10 (dd, J = 8.5, 1.3 Hz, 1H), 7.86 (ddd, J = 8.4, 6.8, 1.4 Hz, 1H), 7.74 (s, 1H), 7.72 – 7.63 (m, 3H), 7.53 (td, J = 7.8, 1.5 Hz, 1H), 7.29 – 7.14 (m, 2H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 150.4, 148.6, 138.6, 137.1, 136.9, 132.0, 131.9, 130.7, 130.5, 130.0, 128.1, 127.0, 126.0, 123.6, 123.4, 120.1, 118.1.

HRMS m/z calculated for $[M+Na]^+$ $C_{17}H_{12}N_2NaO_2S$ 331.0517. Found 331.0525

6,7-Dimethoxy-3-(quinolin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2k)



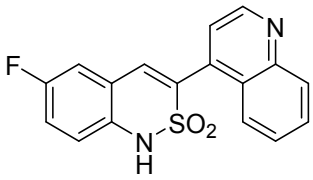
Pale yellow solid. Yield 62 mg, 83%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.00 (d, J = 4.4 Hz, 1H), 8.13 (dd, J = 8.5, 1.2 Hz, 1H), 8.11 (d, J = 7.1 Hz, 1H), 7.85 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.69 (ddd, J = 8.3, 6.8, 1.3 Hz, 1H), 7.62 (d, J = 4.3 Hz, 1H), 7.59 (s, 1H), 7.25 (s, 1H), 6.74 (s, 1H), 3.86 (s, 3H), 3.76 (s, 3H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 152.4, 150.4, 148.7, 145.5, 137.6, 135.9, 133.6, 130.4, 130.0, 128.9, 127.9, 127.1, 126.0, 123.4, 112.9, 112.5, 101.6, 56.4, 56.3.

HRMS m/z calculated for $[M+Na]^+$ $C_{19}H_{16}N_2NaO_4S$ 391.0728. Found 391.0735

6-Fluoro-3-(quinolin-4-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2l)



Pale yellow solid. Yield 55 mg, 80%.

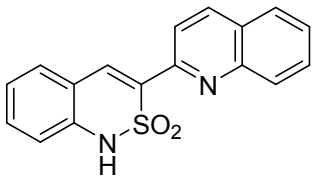
^{1}H NMR (500 MHz, DMSO-d_6) δ 9.02 (d, J = 4.3 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 4.4 Hz, 1H), 7.55 (dd, J = 9.0, 3.0 Hz, 1H), 7.47 – 7.35 (m, 1H), 7.24 (dd, J = 9.0, 4.7 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 157.9 (d, J = 239.1 Hz), 150.4, 148.6, 137.0, 135.4, 135.0, 133.3, 130.6, 130.0, 128.1, 126.8, 125.9, 123.5, 121.2 (d, J = 8.9 Hz), 120.4 (d, J = 8.3 Hz), 119.2 (d, J = 23.8 Hz), 115.9 (d, J = 23.4 Hz).

HRMS m/z calculated for $[M+Na]^+$ $C_{17}H_{11}FN_2NaO_2S$ 349.0423. Found 349.0423

^{19}F NMR (471 MHz, DMSO-d_6) δ -120.0

3-(Quinolin-2-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2m)



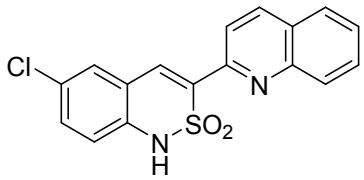
Pale yellow solid. Yield 52 mg, 83%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.44 (d, J = 8.6 Hz, 1H), 8.21 (s, 1H), 8.00 (dd, J = 8.4, 1.1 Hz, 1H), 7.97 – 7.95 (m, 1H), 7.93 (d, J = 8.6 Hz, 1H), 7.75 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.72 (dd, J = 7.8, 1.3 Hz, 1H), 7.58 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.43 (ddd, J = 8.1, 7.3, 1.5 Hz, 1H), 7.15 (td, J = 7.5, 1.1 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 149.7, 147.9, 139.0, 137.7, 135.3, 134.7, 132.2, 131.2, 130.9, 129.5, 128.4, 127.8, 127.6, 123.3, 120.4, 120.3, 117.8.

HRMS m/z calculated for $[M+Na]^+$ $C_{17}H_{12}N_2NaO_2S$ 331.0517. Found 331.0525

6-Chloro-3-(quinolin-2-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2n)



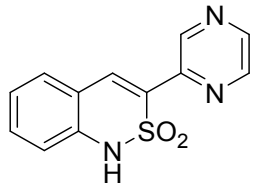
Pale yellow solid. Yield 57 mg, 80%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 (d, J = 8.6 Hz, 1H), 8.28 (s, 1H), 8.08 (d, J = 8.5 Hz, 1H), 8.04 (s, 0H), 7.99 (d, J = 8.6 Hz, 1H), 7.95 (d, J = 2.4 Hz, 1H), 7.85 (t, J = 7.7 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H), 7.56 (dd, J = 8.7, 2.5 Hz, 1H), 7.19 (d, J = 8.7 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 149.4, 147.8, 137.9, 137.7, 136.4, 133.5, 131.8, 131.0, 130.1, 129.5, 128.5, 128.0, 127.7, 127.1, 121.6, 120.4, 119.7.

HRMS m/z calculated for $[M+Na]^+$ $C_{17}H_{11}ClN_2NaO_2S$ 365.0127. Found 365.0127

3-(Pyrazin-2-yl)-1H-benzo[c][1,2]thiazine 2,2-dioxide (2o)



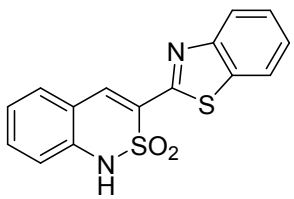
Trituration of the crude reaction mixture afford the product as a pale brown solid. Yield 44 mg, 75% in 0.2-mmol scale; 199 mg, 73% in 1-mmol scale.

^{1}H NMR (300 MHz, DMSO-d_6) δ 9.30 (d, J = 1.4 Hz, 1H), 8.95 (d, J = 5.4 Hz, 2H), 8.48 (s, 2H), 7.96 (dd, J = 5.4, 1.5 Hz, 2H), 7.82 (dd, J = 7.9, 1.5 Hz, 2H), 7.55 (ddd, J = 8.2, 7.4, 1.5 Hz, 2H), 7.23 (td, J = 7.6, 1.1 Hz, 2H), 7.17 (dd, J = 8.1, 1.0 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 159.2, 160.0, 155.9, 139.5, 136.6, 133.1, 132.3, 131.8, 123.4, 119.7, 118.9, 117.9.

HRMS m/z calculated for $[M+Na]^+$ $C_{12}H_9N_3NaO_2S$ 282.0313. Found 282.0327.

3-(Benzothiazol-2-yl)-1*H*-benzo[*c*][1,2]thiazine 2,2-dioxide (2p)



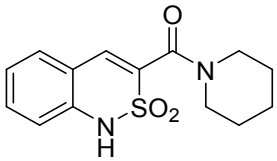
Pale yellow solid. Yield 53 mg, 72%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.36 (s, 1H), 8.13 (d, J = 7.9 Hz, 1H), 8.03 (d, J = 8.1 Hz, 1H), 7.80 (dd, J = 7.9, 1.4 Hz, 1H), 7.60 – 7.41 (m, 3H), 7.18 (t, J = 7.6 Hz, 1H), 7.11 (d, J = 8.1 Hz, 1H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 157.7, 153.0, 139.0, 135.6, 135.3, 133.1, 131.7, 129.5, 127.5, 126.6, 123.7, 123.4, 122.9, 120.0, 118.1.

HRMS m/z calculated for $[M+Na]^+$ $C_{15}H_{10}N_2NaO_2S_2$ 337.0081. Found 337.0088

(2,2-Dioxido-1*H*-benzo[*c*][1,2]thiazin-3-yl)(piperidin-1-yl)methanone (2q)



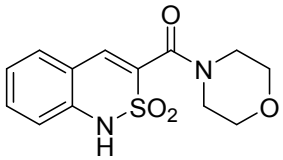
Pale yellow solid. Yield 49 mg, 56%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.52 (dd, J = 7.8, 1.4 Hz, 1H), 7.48 (s, 1H), 7.38 (td, J = 7.8, 1.5 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 8.1 Hz, 1H), 3.46 (br, 4H), 1.55-1.53 (m, 2H), 1.49 – 1.35 (m, 4H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 133.4, 131.9, 131.8, 130.6, 123.1, 119.6, 118.3, 24.3, 20.6.

HRMS m/z calculated for $[M+Na]^+$ $C_{14}H_{16}N_2NaO_3S$ 315.0779. Found 315.0784

(2,2-Dioxido-1H-benzo[c][1,2]thiazin-3-yl)(morpholino)methanone (2r)



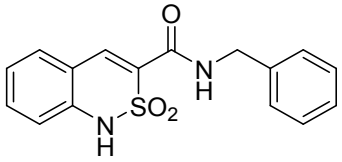
Pale yellow solid. Yield 49 mg, 58%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.56 (s, 1H), 7.53 (dd, J = 7.8, 1.4 Hz, 1H), 7.41 (td, J = 7.8, 1.5 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 3.52 (br, 8H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 160.1, 138.7, 134.5, 132.2, 131.0, 130.8, 123.4, 119.6, 118.2, 66.7.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_{14}N_2NaO_4S$ 317.0572. Found 317.0578

***N*-Benzyl-1*H*-benzo[*c*][1,2]thiazine-3-carboxamide 2,2-dioxide (2s)**



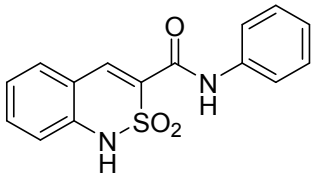
Pale yellow solid. Yield 53 mg, 53%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.72 (t, J = 6.0 Hz, 1H), 8.04 (s, 1H), 7.74 (dd, J = 7.9, 1.5 Hz, 1H), 7.53 (td, J = 7.8, 1.5 Hz, 1H), 7.42 – 7.32 (m, 4H), 7.27 (td, J = 6.0, 2.7 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.14 (d, J = 8.1 Hz, 1H), 4.47 (d, J = 6.0 Hz, 2H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 159.9, 139.5, 139.3, 137.7, 133.0, 131.5, 130.2, 128.9, 127.8, 127.5, 123.3, 119.2, 117.9, 43.2.

HRMS m/z calculated for $[M+Na]^+$ $C_{16}H_{14}N_2NaO_3S$ 337.0623. Found 337.0627

_N_-Phenyl-1_H_-benzo[_c_][1,2]thiazine-3-carboxamide 2,2-dioxide (2t)



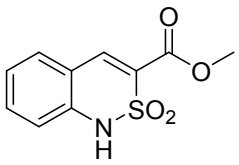
Pale yellow solid. Yield 50 mg, 48%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.39 (s, 1H), 8.08 (s, 1H), 7.72 (dd, J = 7.8, 1.4 Hz, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.57 – 7.47 (m, 1H), 7.37 (t, J = 7.9 Hz, 2H), 7.20 (t, J = 7.5 Hz, 1H), 7.13 (dd, J = 8.1, 5.4 Hz, 2H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 159.1, 140.3, 138.8, 137.4, 133.0, 131.4, 130.7, 129.3, 124.7, 123.0, 120.4, 119.1, 118.2.

HRMS m/z calculated for $[M+Na]^+$ $C_{15}H_{12}N_2NaO_3S$ 323.0466. Found 323.0468

Methyl 1_H_-benzo[_c_][1,2]thiazine-3-carboxylate 2,2-dioxide (2u)



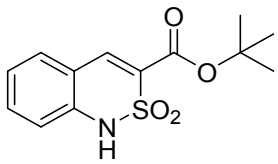
Pale yellow solid. Yield 40 mg, 63%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.86 (s, 1H), 7.31 (d, J = 7.8 Hz, 1H), 7.22 – 7.02 (m, 1H), 6.69 (d, J = 8.4 Hz, 1H), 6.58 (t, J = 7.4 Hz, 1H), 3.75 (s, 3H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 164.5, 141.3, 132.1, 131.1, 121.0, 116.7, 52.1.

HRMS m/z calculated for $[M+Na]^+$ $C_{10}H_9NNaO_4S$ 262.0150. Found 262.0153.

***tert*-Butyl 1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-dioxide (2v)**



Pale yellow solid. Yield 47 mg, 67%.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.65 (s, 1H), 7.19 (dd, J = 8.0, 1.6 Hz, 1H), 7.09 (ddd, J = 8.4, 6.8, 1.7 Hz, 1H), 6.61 (d, J = 8.4 Hz, 1H), 6.51 – 6.36 (m, 1H), 1.48 (s, 9H).

^{13}C{1H} NMR (125 MHz, DMSO-d_6) δ 163.6, 151.7, 140.6, 131.8, 131.1, 121.9, 120.5, 116.9, 115.3, 80.7, 40.8, 28.89.

HRMS m/z calculated for $[M+Na]^+$ $C_{13}H_{15}NNaO_4S$ 304.0619. Found 304.0622.

ASSOCIATED CONTENT

Supporting information

The Supporting Information is available free of charge on the
ACS Publications website at DOI: 10.1021/acs.joc.xxxxxxx.
Copies of ^{1}H and ^{13}C NMR spectra data for all new compounds. X-ray crystallographic data for **2b** and **2i** (CCDC 1953702 and 1953703 respectively).
This material is available free of charge via the Internet at http://pubs.acs.org.

ACKNOWLEDGMENTS

We thank Arch Nguyen Xuan Thang for his valuable assistance in the preparation of the cover.

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