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DILITHIATION OF A 2,1-BENZOTHIAZINE

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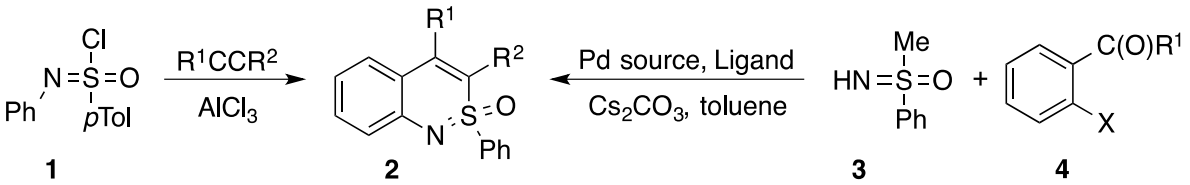
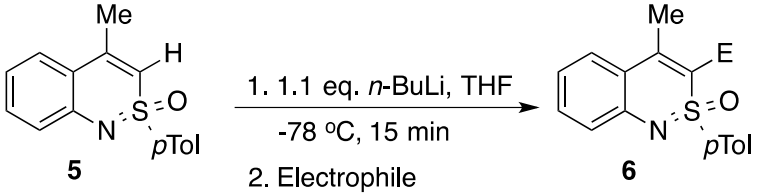
Abstract – Treatment of benzothiazine **24** with excess amounts of *n*-BuLi followed by trapping with selected electrophiles afforded products that suggested the formation of dilithio species. Interestingly, however, the scope of the electrophilic trapping was rather limited, electrophilic sources of halogens and disulfides functioning nearly uniquely and competent electrophilic trapping agents in the process.

We have been interested in the synthesis and chemistry of 2,1-benzothiazines for a number of years,[1-11] having developed two unique approaches to this compound class, one involving electrophilic aromatic substitution and the other utilizing an annulation approach based on the Buchwald-Hartwig reaction (Scheme 1).[12-16] Discovering and controlling 2,1-benzothiazine reactivity is just as impactful as creating and optimizing new syntheses to make benzothiazines. As part of that interest, we developed methods

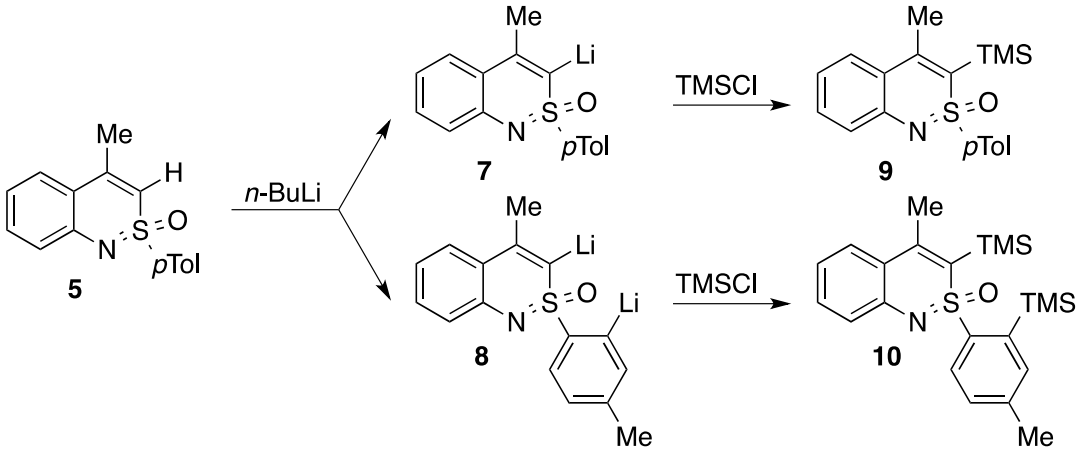


Scheme 1. Syntheses of 2,1-benzothiazines

for the further functionalization of these compounds by metalation and trapping, so that benzothiazines substituted at the α-3-position could be prepared with relative ease. For example, in 1988 we reported the first metalation chemistry of benzothiazines (cyclic sulfoximines) by functionalizing **5** at the 3-position with a variety of electrophiles (Scheme 2).[17] Yields were uniformly very good to excellent. Interestingly, when using TMSCl as an electrophile, we isolated small amounts of the adduct **10** in addition to the expected product **9**. This suggested that a double lithiation had taken place to afford **8** as an intermediate. A great deal of time passed before we had the opportunity to pursue this observation in greater depth.

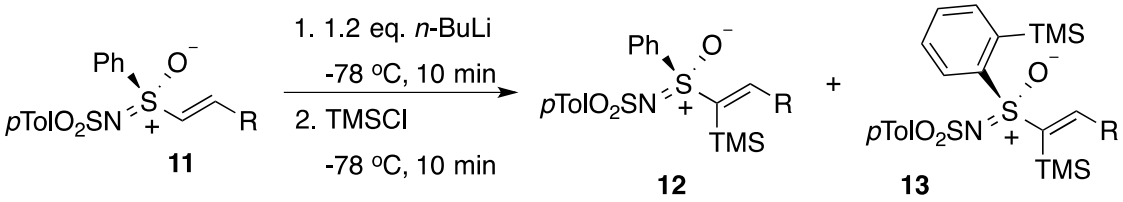


Scheme 2. α-Lithiation of benzothiazine **5**



Scheme 3. Evidence for dilithiation of benzothiazine **5**

In 1996, Jackson and coworkers reported the lithiation and trapping of sulfoximines **11** with trimethylsilyl chloride (TMSCl) during their study of Michael additions to vinyl sulfoximines (Scheme 4).[18] They also made mention of the formation of a small amount of a di-TMS product **13** presumably due to dilithiation having occurred. This "problem" was circumvented by switching from *n*-BuLi to MeLi to obtain only the *α* lithiated sulfoximine.

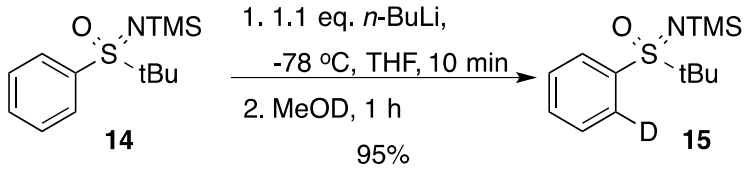


Scheme 4. Mono- and dilithiation of a vinyl sulfoximine

The following year Müller and coworkers produced a crystal structure for a tetrameric *rac*-*S*-ethyl-*N*-methyl-*S*-phenylsulfoximine cluster with *N,N,N',N'*-tetramethylethylenediamine, TMEDA.[19] This cluster was prepared by treating a racemic sulfoximine with 2 equiv. of *n*-BuLi in TMEDA and in the presence of Li_2O to create a lithio-dicarbanion.

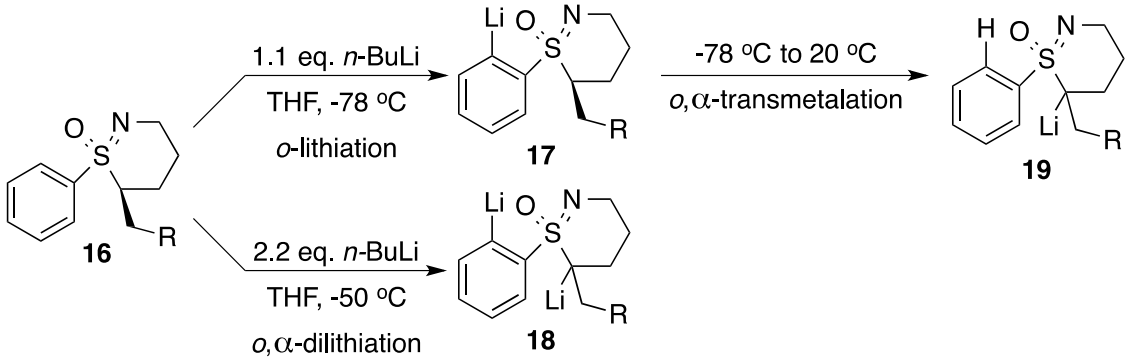
Levacher and coworkers examined the lithiation of *S*-*t*-butyl-*S*-phenylsulfoximines in 1999 and observed that the sulfoximine was an efficient *ortho*-director in aryl lithiations.[20] The reaction was optimized and

found to be general. Under the optimized conditions, deprotonation of the *ortho*-H about the *S*-phenyl ring of **14** took only 10 minutes at -78 ºC in THF. Quenching the resulting organolithium with MeOD afforded the monodeuterated product **15** with 95% deuterium incorporation (Scheme 5). Other electrophiles were also effective in trapping the metalated species.

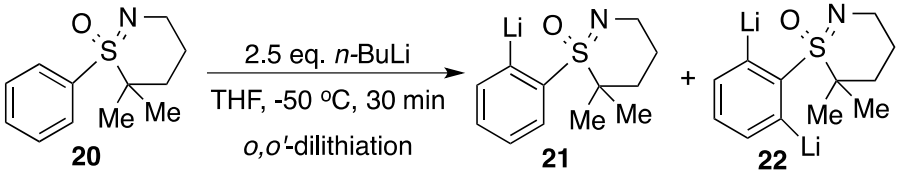


Scheme 5. Directed *ortho*-lithiation procedure of *S*-(*tert*-butyl)-*S*-phenylsulfoximine

Gais and coworkers detailed elegant lithiation chemistry of certain cyclic sulfoximines, including *ortho*-lithiation and dilithiation.[21] Interestingly, in systems represented by **16**, deprotonation in THF at -78 ºC with *n*-BuLi proceeded rapidly to produce the *ortho*-lithiation product **17**. Warming **17** to room temperature afforded the organolithium **19**, establishing **17** as the product of kinetic deprotonation and **19** as the thermodynamically more stable species. When the reaction was conducted with 2 equivalents of *n*-BuLi at -50 °C dilithiation occurred to afford **18** (Scheme 6). Double *ortho*-lithiation was possible when the alpha position of the sulfoximine was blocked by alkyl groups. Thus, treatment of **20** with 2.5 equivalents of *n*-BuLi at -50 ºC gave both the monolithiated species **21** and the dilithiated species **22** as a 1:1 mixture as determined by trapping studies (Scheme 7).



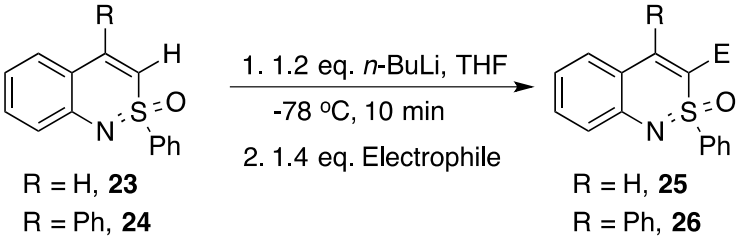
Scheme 6. Mono- and dilithiation of cyclic sulfoximines



Scheme 7. *o,o*'-Dilithiation of a cyclic phenyl sulfoximine

Finally, we recently reported further studies of the metalation of benzothiazines **23** and **24**.[22] Both could be monolithiated and trapped very efficiently with a variety of electrophiles (Scheme 8). As might be

expected based on our earliest work (vide supra), evidence for dilithiation upon the reaction of the organolithium derived from **23** with TMSCl was found: compound **27** was isolated in small amounts as a byproduct (Figure 1).

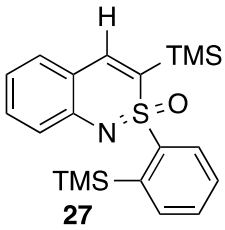


R = H, **23**
R = Ph, **24**

R = H, **25**
R = Ph, **26**

Scheme 8. Metalation chemistry of benzothiazines **23** and **24**

Given these results, we were in a good position to see if the dilithiation of benzothiazines could be developed into a synthetically useful process. We describe our initial results herein.



27

Figure 1. Further evidence for dilithiation

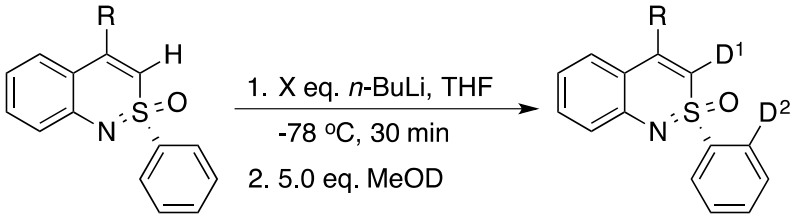
We decided to examine benzothiazines **23** and **24** for dilithiation studies. In this preliminary work, the reactions were conducted in THF at -78 °C using *n*-BuLi as the base. Trapping of the organolithium intermediates was accomplished with excess MeOD, generally after a 30 minute reaction time. The results are shown in Table 1. Deuterium incorporation was assessed by proton NMR of the crude reaction mixture.

One equivalent of base gave primarily monolithiation with an observable amount of dilithiation (Table 1, entries 1 and 2). We gradually increased the amount of base to ascertain how much would be required within the time constraints we had set. As can be seen from Table 1, it was not until 3 equivalents of base were added that complete deprotonation of the *ortho*-*S*-hydrogen was seen along with a trace amount of trilithiation (Table 1, entries 9 and 10).

Previous experience with **23** showed us that it sometimes reacted with nucleophiles, including *n*-BuLi, after position 3 had been functionalized. Though we have not rigorously examined this process, we wondered if a non-nucleophilic base might be better for both lithiation and dilithiation of **23**. To that end, we explored deprotonation with LiTMP. These results are shown in Table 1, entries 11-15. In the best case, based on deuteration, complete alpha metalation and about 80% ortho metalation was possible with 3.5 equivalents of LiTMP in THF. This bodes well for finding conditions using less base by

optimizing reaction conditions.

Table 1. Lithiation of 2,1-Benzothiazines **23** and **24**



R = H, **23**
R = Ph, **24**

Entry	Substrate	X (eq)	D^1 (%)	D^2 (%)
1	**23**	1.0	96	16
2	**24**	1.0	83	19
3	**23**	1.5	99	38
4	**24**	1.5	90	17
5	**23**	2.0	70	19
6	**24**	2.0	95	72
7	**23**	2.5	93	63
8	**24**	2.5	92	76
9	**23**	3.0	98	100
10	**24**	3.0	100	107
11	**23**	1.5/LiTMP[a]	77	25
12	**23**	2.0/LiTMP	92	52
14	**23**	2.5/LiTMP	94	46
14	**23**	3.0/LiTMP	95	50
15	**23**	3.5/LiTMP	95	81

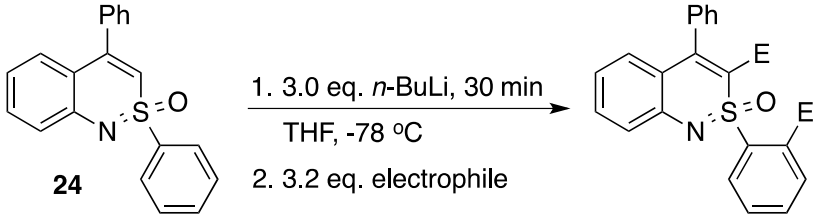
[a]TMP = 2,2,6,6-tetramethylpiperidide.

Based on the data accumulated to this point, we decided to explore the dilithiation of **24** and attempt to trap the resultant intermediate with more than a deuterium source. In some of our previous work, we noticed small amounts of dithiolated products when disulfides were used as electrophiles to trap monolithiated benzothiazine intermediates. These compounds were generally easy to separate from the corresponding sulfide products. We thus treated **24** with *n*-BuLi as per the most promising results from Table 1 and trapped the resulting diorganolithium species with a small series of disulfides. The results are summarized in Table 2. Most disulfides examined trapped extremely well (Table 2, entries 1-4). Only di-*t*-butyl disulfide provided a monosubstituted adduct in poor yield (Table 2, entry 5). Halide trapping sources worked well giving diiodo **34** and dibromo **35** (Table 2, entries 8 and 9).

Overall, this provides evidence that dilithiation occurs and the resulting dianion can be trapped by at least a few electrophilic classes. Bulkier substrates did not work well in this process, as evidenced with benzophenone as the electrophile (Table 2, entry 6). TMSCl was also a poor trap, though the hydrolytic instability of this electrophile may be partially responsible for the poor results (Table 2, entry 7). While many questions remain, this investigation is the first example of a successful dilithiation of a

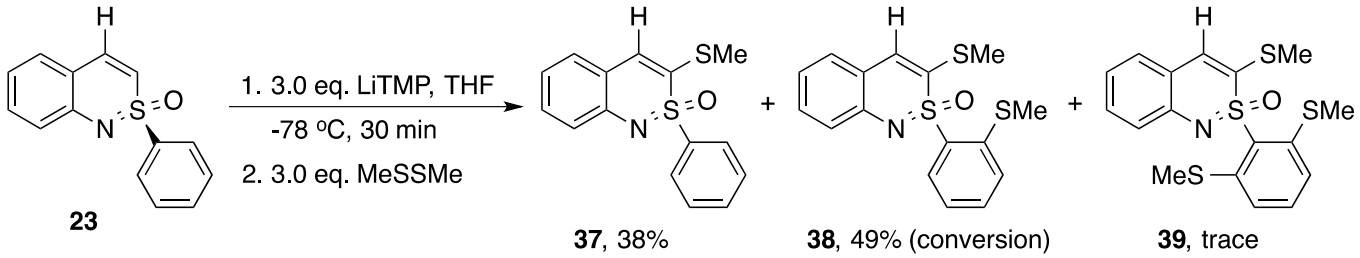
2,1-benzothiazine.

Table 2. Dilithiation Study of Benzothiazine **24**



Entry	Electrophile	E	Product	Yield (%) (Double)	Yield (%) (Single)
1	MeSSMe	SMe	**28**	95	trace
2	PhSSPh	SPh	**29**	87	9
3	EtSSEt	SEt	**30**	94	5
4	CySSCy	SCy	**31**	83	13
5	*t*BuSS*t*Bu	S*t*Bu	**32**	0	0
6	Ph_2CO	$Ph_2C(OH)$	**33**	0	0
7	TMSCl	TMS	**34**	*mixture*	*mixture*
8	I_2	I	**35**	91	0
9	$Br_2C_2Cl_4$	Br	**36**	58	0

While not studied yet in depth, we examined dilithiation of benzothiazine **23** taking into consideration the limitations of the unsubstituted 4-position when using an excess of alkyllithium base. Thus, we reacted **23** with excess LiTMP in THF at -78 °C, stirred for 30 minutes, and quenched with excess dimethyl disulfide (Scheme 9). We observed three products, only one of which (**37**) was clean enough to characterize. We obtained a very small amount of a product (**39**) that afforded a crystal that was identified by X-ray crystallography as a trisubstituted benzothiazine (Figure 2) implying the possibility of trilithiation. Further studies will be needed to optimize the dilithiation of **23** and to establish the origin of **38**.



Scheme 9. Dilithiation of benzothiazine **23** with dimethyl disulfide

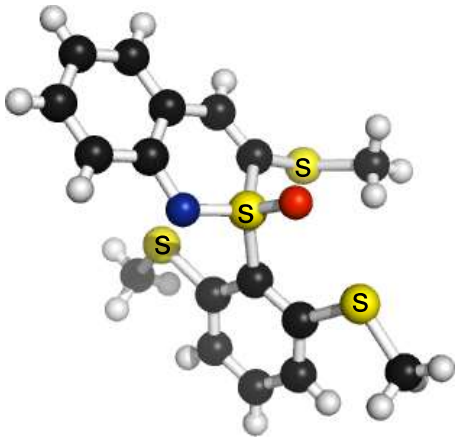
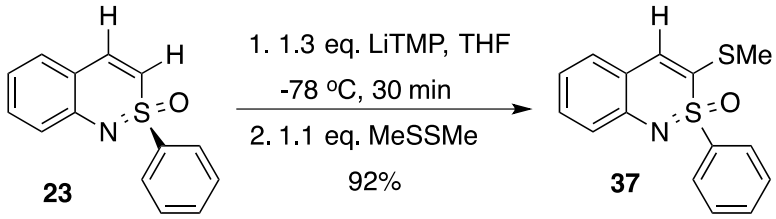


Figure 2. X-Ray crystal structure of **39**

However, the use of LiTMP in simple monometalation appeared promising. To that end, **23** was treated with a slight excess of the reagent and the resulting organolithium was trapped with dimethyl disulfide. This afforded the sulfide **37** in 92% yield (Scheme 10). Previously butylation was observed with phenyl sulfide products generated *in situ*, but, using this base circumvented that problem.



Scheme 10. Monolithiation of benzothiazine **23** with dimethyl disulfide

CONCLUSION

In summary, we have established the first dilithiations of 2,1-benzothiazines. While further work will be needed to continue optimization, this methodology offers the promise for the further development of chiral ligands from benzothiazines. Together with the results of Gais, this work provides a solid foundation for the continued development of benzothiazine and sulfoximine chemistry in the preparation of chiral ligands of use in asymmetric catalysis.

EXPERIMENTAL

All reactions performed were carried out under anhydrous conditions involving either nitrogen or argon gas. Glassware was oven dried (125 °C) and cooled by a continuous flow of dry nitrogen. Solvents were distilled under anhydrous and oxygen free conditions. Et_2O, toluene, and THF were dried over sodium metal and oxygen was removed by generation of a benzophenone ketyl. CH_2Cl_2 was dried over calcium hydride in a dry nitrogen atmosphere. In most cases, reagents were distilled prior to use if liquid; solids reagents were crystallized or used directly from a newly purchased commercial container.

Handling of pyrophoric reagents, namely organometallic reagents, was done so with glass gas tight syringes, rubber septa, and argon balloons. Air and moisture sensitive reagents were handled with a dry nitrogen filled plastic glove bag. Molecular sieves used were freshly activated by heating to 200 ^{o}C under full vacuum (<2 mm Hg) for several hours. Reaction mixtures were concentrated using rotary evaporators with both water aspiration and pneumatic vacuum pump sources depending on the boiling point of the solvent being removed. Residual solvent was removed by full vacuum when necessary. Silica gel used in chromatographic separations was purchased from Silicycle (230 – 400 mesh). Reactions were monitored by glass backed silica gel TLC plates purchased from Sigma Aldrich; all highly conjugated compounds were recognized by a UV irradiation lamp.

Melting points taken of new compounds were done so on a Fisher-Johns melting point apparatus. IR spectra were recorded via a liquid NaCl chamber on a Perkin Elmer 1600 series FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR were taken on one of three Bruker ARX-250, ARX-300, or ARX-500 Ultrashield spectrometers. Chemical shifts reported were in ppm with an internal TMS standard (TMS; δ = 0.0). Spectra were taken with $CDCl_3$ solution containing TMS. NMR data is reported as follows: chemical shift, ppm; splitting pattern (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, etc.); coupling constant, Hz; and integration. ^{13}C NMR spectra taken were ^{1}H decoupled and contained a $CDCl_3$ ($CDCl_3$; δ = 77.0) internal standard. HRMS were obtained on a Bruker 12 Tesla Apex-Qe FTICR-MS with an Apollo II ion source.

Synthetic Procedures and Compound Characterization:

3-(Methylthio)-2-(2-(methylthio)phenyl)-4-phenylbenzo[*c*][1,2]thiazine 2-oxide (28): Lithiation Procedure A: To an oven-dried, roundbottom flask equipped with a magnetic stirbar and rubber septum, and cooled to room temperature under a flow of dry nitrogen gas, benzothiazine **24** (0.107 g, 0.338 mmol) was added. The flask was flushed with argon and freshly distilled THF (4 mL) was added via syringe. The reaction was then cooled to -78 °C in a dry ice/acetone bath. *n*-BuLi (0.467 mL, 2.17 M, 1.02 mmol) was added dropwise to the cooled solution resulting in a dark red solution. After 30 min, dimethyl disulfide (0.122 mL, 1.35 mmol) was added through the rubber septum by syringe. The reaction mixture was stirred further overnight (or until completion was observed by TLC). The mixture was quenched with saturated agueous ammonium chloride (2 mL) and extracted with CH_2Cl_2 (3 x 5 mL), concentrated under vacuum, and dried ($MgSO_4$). Purification (R_f = 0.45 in 25% EtOAc/hexanes) by flash chromatography (silica gel) with 25% EtOAc/hexanes afforded 0.131 g of **28** in 95% yield as a yellow solid. mp 193 °C. ^{1}H NMR: (250 MHz, $CDCl_3$) δ 2.05 (s, 3H), 2.36 (s, 3H),

6..84-6.97 (m, 2H), 7.23-7.19 (m, 1H), 7.31-7.69 (m, 9H), 8.40 (dd, *J* = 1.4. 7.9 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 15.9, 21.1, 119.7, 119.9, 124.0, 124.4, 125.9, 127.9, 128.2, 128.3, 128.9, 129.1, 131.1, 131.8, 133.6, 134.4, 137.0, 143.5, 145.4, 159.1; IR (NaCl, cm^{-1}) 3049, 2927, 2855, 1601, 1563, 1517, 1488, 1437, 1332, 1245, 1208, 1154, 701, 590, 556, 500, 497, 444, 402; HRMS calculated for $C_{22}H_{19}NOS_3Na$ $[M+Na]^+$ 432.0521; Found 432.0517. Deposition number CCDC-1423107 and 1423108 (polymorphs) for compound No. **28**. Free copies of the data can be obtained via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

4-Phenyl-3-(phenylthio)-2-(2-(phenylthio)phenyl)benzo[*c*][1,2]thiazine 2-oxide (29): (Lithiation Procedure A) Yellow solid in 87% yield (0.140 g). (R_f = 0.56 in 25% EtOAc/hexanes) mp 136 °C. ^{1}H NMR: (250 MHz, $CDCl_3$) δ 6.82- 6.86 (m, 1H), 6.90-6.97 (m, 2H), 7.08-7.12 (m, 7H), 7.20-7.50 (m, 12H), 8.24 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 111.1, 120.0, 120.2, 124.4, 124.8, 126.8, 127.8, 127.9, 128.1, 128.5, 128.8, 129.0, 129.2, 129.6, 129.8, 129.9, 131.0, 132.2, 133.5, 134.6, 134.8, 136.3, 143.7, 145.4, 160.6; IR (NaCl, cm^{-1}) 3023, 2927, 2855, 1601, 1581, 1561, 1514, 1490, 1441, 1332, 1213, 1153, 820, 590, 558, 499, 469, 445; HRMS calculated for $C_{32}H_{23}NOS_3Na$ $[M+Na]^+$ 556.0834; Found 556.0830.

3-(Ethylthio)-2-(2-(ethylthio)phenyl)-4-phenylbenzo[*c*][1,2]thiazine 2-oxide (30): (Lithiation Procedure A) Yellow solid in 94% yield (0.101 g). (R_f = 0.63 in 25% EtOAc/hexanes) mp 184 °C. ^{1}H NMR: (250 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.4 Hz, 3H), 1.70 (t, *J* = 7.3 Hz, 3H), 2.46-2.56 (m, 1H), 2.59-2.70 (m, 1H), 2.78-2.91 (m, 2H), 6.83 (t, *J* = 6.7 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 7.16-7.20 (m, 1H), 7.27-7.56 (m, 9H), 8.38 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 13.5, 14.3, 27.0, 32.2, 112.6, 119.6, 119.7, 124.2, 124.2, 127.6, 128.0, 128.2, 129.0, 130.9, 131.5, 133.4, 135.4, 137.1, 142.1, 145.2, 158.4; IR (NaCl, cm^{-1}) 2967, 2929, 2855, 1601, 1562, 1516, 1488, 1450, 1332, 1245, 1206, 734, 701, 590, 555, 409, 402; HRMS calculated for $C_{24}H_{23}NOS_3Na$ $[M+Na]^+$ 460.0834; Found 460.0837.

3-(Cyclohexylthio)-2-(2-(cyclohexylthio)phenyl)-4-phenylbenzo[*c*][1,2]thiazine 2-oxide (31): (Lithiation Procedure A) Yellow solid in 83% yield (0.110 mg). (R_f = 0.53 in 25% EtOAc/hexanes) mp 117 °C. ^{1}H NMR: (250 MHz, $CDCl_3$) δ 0.85-1.26 (m, 10H), 1.34-1.89 (m, 10H), 2.96-2.97 (m, 1H), 2.21-2.23 (m, 1H), 6.80 (t, *J* = 8.2 Hz, 1H), 6.92 (d, *J* = 8.1 Hz, 1H), 7.23-7.59 (m, 9H), 8.38 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 25.4, 25.5, 25.6, 25.6, 25.7, 25.9, 32.4, 32.6, 33.0, 33.6, 45.5, 50.4, 113.1, 119.3, 119.8, 124.0, 124.9, 127.8, 128.0, 128.4, 129.0, 129.3, 130.1, 130.7, 130.9, 131.3, 133.0, 137.1, 137.7, 140.5, 145.3, 157.9; IR (NaCl, cm^{-1}) 3032, 2934, 2855, 1600, 1562, 1514, 1489, 1449, 1332, 1244, 1211, 1154, 1050, 997, 971, 820, 590, 556, 456, 452**;** HRMS calculated for $C_{32}H_{35}NOS_3Na$ $[M+Na]^+$ 568.1773; Found 568.1771.

3-Iodo-2-(2-iodophenyl)-4-phenylbenzo[*c*][1,2]thiazine 2-oxide (35): (Lithiation Procedure A) Brown solid in 91% yield (0.110 g). (R_f = 0.64 in 25% EtOAc/hexanes) mp 174 °C. ^{1}H NMR: (250 MHz, $CDCl_3$) δ 6.86 (t, *J* = 8.2 Hz, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 7.23–7.36 (m, 4H), 7.41–7.55 (m, 4H), 7.63 (t, *J* = 7.9 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 98.0, 120.0, 120.4, 124.1, 127.6, 128.4, 128.7, 128.7, 128.8, 129.0, 131.9, 132.2, 134.4, 139.7, 141.0, 142.9, 145.4, 159.1; IR (NaCl, cm^{-1}) 3065, 3044, 2928, 1599, 1566, 1515, 1491, 1342, 1328, 1248, 1218, 1154, 998, 959, 599, 587, 548, 489, 424; HRMS calculated for $C_{20}H_{13}I_2NOSNa$ $[M+Na]^+$ 591.8699; Found 591.8696.

3-Bromo-2-(2-iodophenyl)-4-phenylbenzo[*c*][1,2]thiazine 2-oxide (36): (Lithiation Procedure A) Brown solid in 58% yield (0.058 g). (R_f = 0.73 in 25% EtOAc/hexanes) mp 172 °C. ^{1}H NMR:(250 MHz, $CDCl_3$) δ 6.86–6.98 (m, 2H), 7.20–7.24 (m, 2H), 7.28 (t, *J* = 8.2 Hz, 2H), 7.36–7.63 (m, 5H), 7.79 (d, *J* = 7.8 Hz, 1H), 8.51 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 100.9, 119.8, 120.5, 124.0, 124.8, 127.7, 128.1, 128.2, 128.7, 128.7, 131.9, 132.2, 134.9, 135.8, 136.5, 137.0, 144.3, 153.9; IR (NaCl, cm^{-1}) 3068, 3033, 2931, 1600,1567, 1523, 1443, 1343, 1333, 1250, 1224, 1155, 1043, 971, 605, 587, 551, 483, 464, 412; HRMS calculated for $C_{20}H_{13}Br_2NOSNa$ $[M+Na]^+$ 495.8977; Found 495.8975.

3-(Methylthio)-2-phenylbenzo[*c*][1,2]thiazine 2-oxide (37): Lithiation Procedure B: To an oven-dried, roundbottom flask equipped with a magnetic stirbar and rubber septum, and cooled to room temperature under a flow of dry nitrogen gas, benzothiazine **23** (0.515 g, 2.13 mmol) was added. The flask was flushed with argon, and freshly distilled THF (21 mL) was added via syringe. The reaction was then cooled to -78 °C via a dry ice/acetone bath. Then LiTMP (4.55 mL, 0.68 M in THF, 2.87 mmol) was added dropwise to the cooled solution resulting in a dark red solution. After 30 min, dimethyl disulfide (0.211 mL, 2.34 mmol) was added through the rubber septum by syringe. The reaction mixture was stirred further overnight (or until completion was observed by TLC). The mixture was quenched with saturated agueous ammonium chloride (5 mL) and extracted with CH_2Cl_2 (3 x 10 mL), concentrated under vacuum, and dried ($MgSO_4$). Purification (R_f= 0.49 in 25% EtOAc/hexanes) by flash chromatography (silica gel) with 25% EtOAc/hexanes afforded 0.565 g **37** (92%) as a very viscous orange oil. ^{1}H NMR: (250 MHz, $CDCl_3$) δ 2.21 (s, 3H), 6.94 (t, *J* = 6.9 Hz, 1H), 7.26-7.30 (m, 2H), 7.36 (t, *J* = 7.1 Hz, 1H), 7.43-7.57 (m, 3H), 7.76 (s, 1H), 7.86 (d, *J* = 7.0 Hz, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 20.7, 117.7, 118.5, 119.9, 123.0, 128.3, 128.9, 129.2, 131.7, 133.1, 138.7, 143.8, 144.1; IR (NaCl, cm^{-1}) 3071, 2927, 1604, 1579, 1534, 1286, 1210, 1127, 993, 909, 583, 495, 454, 439; HRMS calculated for $C_{15}H_{13}NOS_2Na$ $[M+Na]^+$ 310.0331; Found 310.0328.

2-(2,6-Bis(methylthio)phenyl)-3-(methylthio)benzo[*c*][1,2]thiazine 2-oxide (39). Deposition number CCDC-1423106 for compound No. **39**. Free copies of the data can be obtained via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic

Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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REFERENCES

1. M. Harmata and X. Hong, *Org. Lett.*, 2005, **7**, 3581.
2. M. Harmata, Y. Chen, and C. L. Barnes, *Org. Lett.*, 2007, **9**, 4701.
3. M. Harmata and X. Hong, *Org. Lett.*, 2007, **9**, 2701.
4. M. Harmata and P. Zheng, *Org. Lett.*, 2007, **9**, 5251.
5. X. Hong and M. Harmata, *Prog. Heterocycl. Chem.*, 2008, 1.
6. M. Harmata, Z. Cai, and Y. Chen, *J. Org. Chem.*, 2009, **74**, 5559.
7. M. Harmata, K. Rayanil, V. R. Espejo, and C. L. Barnes, *J. Org. Chem.*, 2009, **74**, 3214.
8. M. Harmata, W. Ying, and C. L. Barnes, *Tetrahedron Lett.*, 2009, **50**, 2326.
9. Y. Chen and M. Harmata, *Tetrahedron Lett.*, 2011, **52**, 4069.
10. N. Yongpruksa, S. Pandey, G. A. Baker, and M. Harmata, *Org. Biomol. Chem.*, 2011, **9**, 7979.
11. Z. Cai and M. Harmata, *Tetrahedron Lett.*, 2013, **54**, 814.
12. M. Harmata and E. O. Schlemper, *Tetrahedron Lett.*, 1987, **28**, 5997.
13. M. Harmata, R. J. Claassen II, and C. L. Barnes, *J. Org. Chem.*, 1991, **56**, 5059.
14. M. Harmata and N. Pavri, *Angew. Chem. Int. Ed.*, 1999, **38**, 2419.
15. M. Harmata, X. Hong, and S. K. Ghosh, *Tetrahedron Lett.*, 2004, **45**, 5233.
16. N. Yongpruksa, N. L. Calkins, and M. Harmata, *Chem. Commun.*, 2011, **47**, 7665.
17. M. Harmata, *Tetrahedron Lett.*, 1988, **29**, 5229.
18. R. F. W. Jackson, A. D. Briggs, P. A. Brown, W. Clegg, M. R. J. Elsegood, and C. Frampton, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1673.
19. J. F. K. Müller, M. Neuburger, and M. Zehnder, *Helv. Chim. Acta*, 1997, **80**, 2182.
20. V. Levacher, B. L. Eriksen, M. Begtrup, G. Dupas, G. Quéguiner, J. Duflos, and J. Bourguignon, *Tetrahedron Lett.*, 1999, **40**, 1665.
21. M. Wessels, V. Mahajan, S. Boßhammer, G. Raabe, and H.- J. Gais, *Eur. J. Org. Chem.*, 2011, 2431.
22. N. L. Calkins and M. Harmata, *Synthesis*, 2013, **45**, 1785.