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AN EFFICIENT TWO-STEP SYNTHESIS OF 3-AROYL-2,3-DIHYDRO-1,4,2-BENZODITHIAZINE 1,1-DIOXIDES FROM SECONDARY BENZENESULFONAMIDES, SULFUR, AND PHENACYL BROMIDES

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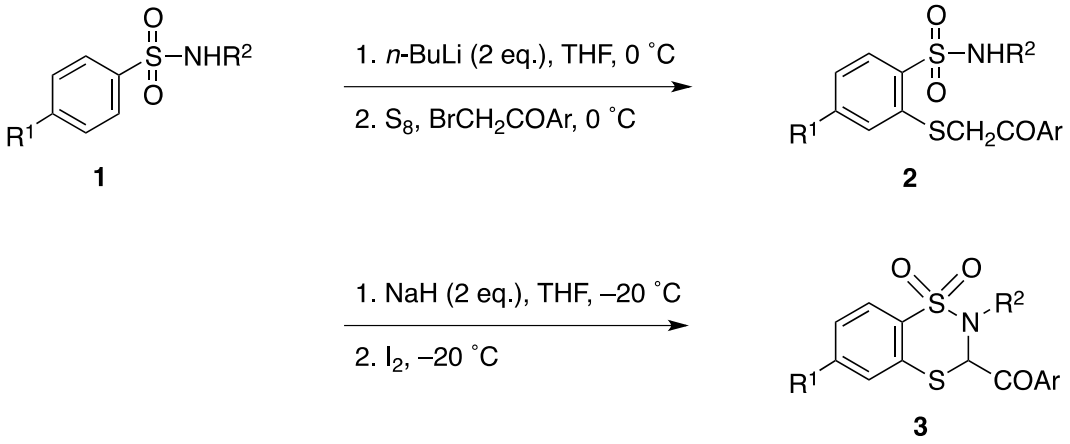
Abstract – An efficient method for the synthesis of 2-substituted 3-aroyl-2,3-dihydro-1,4,2-benzodithiazine 1,1-dioxides has been developed. Thus, 2,*N*-dilithio compounds of secondary benzenesulfonamides, generated by treating secondary benzenesulfonamides with two equivalents of butyllithium, are allowed to react with elemental sulfur and then phenacyl bromide and its derivatives to give *N*-substituted *o*-[(aroylmethyl)sulfanyl]benzenesulfonamides in moderate to good yields. Oxidative coupling of these precursors to the desired products can be achieved in moderate to good yields on successive treatment with sodium hydride and iodine under mild conditions.

Compounds with the 2,3-dihydro-1,4,2-benzodithiazine 1,1-dioxide skeleton have been known to be of potential biological interest.[1,2] Especially, some 3-aroyl derivatives have been reported to exhibit anti-HIV integrase activities.[1] The synthesis of these compounds has used the reduction of 3-aroyl-1,4,2-benzodithiazine 1,1-dioxides, obtainable by the two-step sequence starting from the reaction between primary 2-sulfanylbenzenesulfonamides and phenacyl bromides, with benzenesulfonyl hydrazide.[1] Meanwhile, we have been investigating synthetic routes to benzene-fused heterocyclic compounds by means of the reaction of 2,*N*-dilithio compounds of secondary benzenesulfonamides[3] with isothiocyanates affording the corresponding *o*-(aminosulfonyl)benzothioamides and recently demonstrated that these precursors could be transformed into (*Z*)-*N*-substituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxides,[4] (*Z*)-*N*-substituted 4*H*-1,3,2-benzodithiazin-3-imine 1,1-dioxides[5] and 1,2-benzothiazole-3(2*H*)-thione 1,1-

dioxides[6] by simple operations utilizing ordinal inexpensive reagents, such as thionyl chloride, iodine and 1,8-diazabicyclo[5.3.0]undec-7-ene (DBU), respectively, under metal-free and mild conditions. So, we were interested in developing a new approach for the preparation of 3-aroyl-2,3-dihydro-1,4,2-benzodithiazine 1,1-dioxides utilizing these dilithio compounds. We now wish to report the results of our study, which provide a facile method for the synthesis of 2-substituted 3-aroyl-2,3-dihydro-1,4,2-benzodithiazine 1,1-dioxides (**3**). It has been found that the dilithio compounds generated from secondary benzenesulfonamides (**1**) afford *N*-substituted *o*-[(aroylmethyl)sulfanyl]benzenesulfonamides (**2**) on successive treatment with elemental sulfur and phenacyl bromide and its derivatives and that intramolecular oxidative coupling of **2** can be successfully conducted with sodium hydride and iodine to give rise to this new type of 2,3-dihydro-1,4,2-benzodithiazine 1,1-dioxides (**3**).



Scheme 1

The synthesis of the desired products (**3**) from the starting materials (**1**) was conducted using the procedure illustrated in Scheme 1. Compounds (**1**) were all obtained commercially and were treated with two equivalents of butyllithium in THF at 0 ˚C to generate the corresponding 2,*N*-dilithio compounds, which were then allowed to react with elemental sulfur at the same temperature. The resulting thiolate intermediates were subsequently alkylated with phenacyl bromide and its derivatives to give **2** in moderate to good yields as compiled in Table 1.

These precursors were then subjected to the successive treatment with two equivalent of sodium hydride and an equivalent of iodine in THF at –20 ˚C. The generation of the dianion intermediates by abstractions of the amide proton and one of the α-protons to the carbonyl with sodium hydride and subsequent their intramolecular oxidative coupling with iodine proceeded smoothly and relative cleanly at this temperature. After aqueous workup followed by recrystallization or column chromatography on silica gel, the desired products **3** were obtained. The results are summarized in Table 1 as well, which indicates the yields are moderate to fair. The precursor carrying thiophene moiety (**2h**) also worked well in the present reaction to

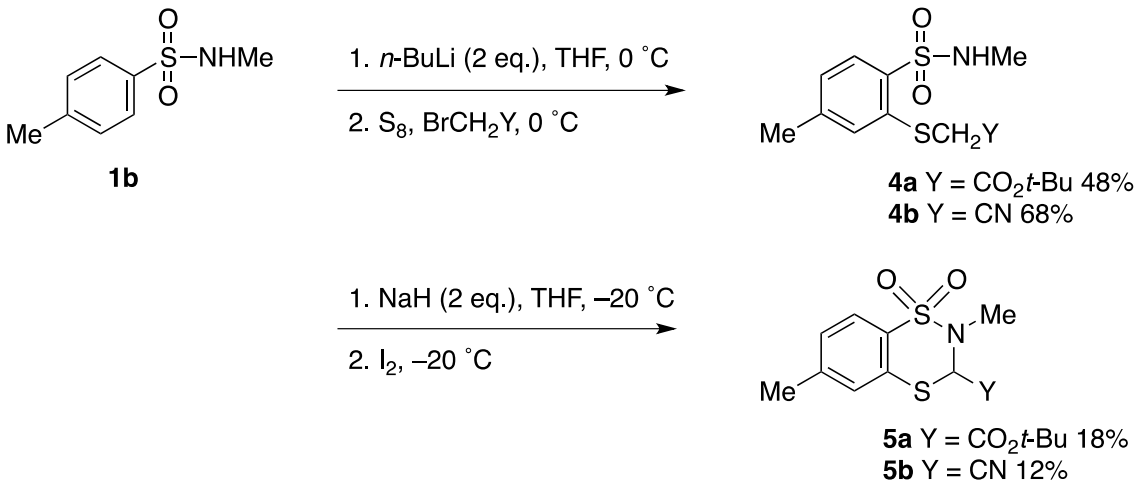
give the desired product (**3h**) in a comparable yield (Entry 8). Initially, the reactions at 0 ˚C were carried out. They, however, resulted in the formation of somewhat lower yields of the products.

Table 1. Preparation of 2-substituted 3-aroyl-2,3-dihydro-1,4,2-benzodithiazine 1,1-dioxides (**3**)

Entry	**1**	R^1	R^2	Ar in $BrCH_2COAr$	**2**	Yield/%[a]	**3**	Yield/%[a]
1	**1a**	H	Me	Ph	**2a**	56	**3a**	50
2	**1b**	Me	Me	Ph	**2b**	70	**3b**	75
3	**1c**	Me	Ph	Ph	**2c**	57	**3c**	43
4	**1d**	Cl	Me	Ph	**2d**	72	**3d**	77
5	**1d**	Cl	Me	4-MeC_6H_4	**2e**	85	**3e**	64
6	**1d**	Cl	Me	4-ClC_6H_4	**2f**	82	**3f**	72
7	**1d**	Cl	Me	naphthalen-2-yl	**2g**	80	**3g**	58
8	**1d**	Cl	Me	thiophen-2-yl	**2h**	52	**3h**	53
9	**1e**	OMe	Me	Ph	**2i**	57	**3i**	76
10	**1e**	OMe	Me	4-$MeOC_6H_4$	**2j**	67	**3j**	44

[a] Yields of isolated products.

Attempts to prepare 3-*tert*-butoxylcarbonyl (**5a**) and 3-cyano derivatives (**5b**) utilizing the same sequence met with only partial success as shown in Scheme 2. Although the reactions of 2,*N*-dilithio compounds of **1b** with elemental sulfur and then *tert*-butyl 2-bromoacetate or 2-bromoacetonitrile gave the corresponding precursors (**4a**) or (**4b**) in moderate to fair yields, the conversion of these compounds to the desired products (**5a**) or (**5b**) under the above-mentioned conditions (at –20 ˚C) was very low-yielding because of the formation of rather intractable mixtures of products. We carried out the reactions at –40 ˚C in order to improve yields. However, these attempts resulted in vain. Although the reason for these results is not clear, monitoring of the reactions by TLC on silica gel suggested that they may be explained by decomposition of the products under these reaction conditions.



Scheme 2

In conclusion, we have developed an efficient synthetic route to 2-substituted 2,3-dihydro-1,4,2-benzodithiazine 1,1-dioxide derivatives, which would be difficult to prepare with conventional methods. Features of our method are readily availability of the starting materials, simple manipulations, and mild conditions using ordinary reagents. It may be of value in organic synthesis and offer interesting pharmacophores.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded as KBr disks with a PerkinElmer Spectrum 65 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz or a BRUKER Avance II 600 FT NMR spectrometer operating at 600 and 150 MHz, respectively. High-resolution MS spectra were measured by a Thermo Scientific Exactive spectrometer (DART). Elemental analyses were performed with an Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. 4-Chloro-*N*-methylbenzenesulfonamide (**1d**)[7] and 4-methoxy-*N*-methylbenzenesulfonamide (**1e**)[8] were prepared according to the procedures reported previously. *n*-BuLi was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

Typical Procedure for the Preparation of *o*-[(Aroylmethyl)sulfanyl]benzenesulfonamides (2) and Related Compounds (4). 2-{[2-(Methylaminosulfonyl)phenyl]sulfanyl}-1-phenylethanone (2a). To a stirred solution of **1a** (0.34 g, 2.0 mmol) in THF (7 mL) at 0 ˚C was added *n*-BuLi (1.6 M in hexane; 4.0 mmol) dropwise. After 40 min, a solution of sulfur (S_8) (64 mg, 0.25 mmol) in THF (10 mmol) and $PhCOCH_2Br$ (0.40 g, 2.0 mmol) were successively added, and stirring was continued for 10 min. Saturated aqueous NH_4Cl (30 mL) was added and the mixture was extracted with AcOEt (3 × 15 mL). The combined extracts were washed with brine (15 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 (Et_2O/hexane 3:1) to afford **2a** (0.36 g, 56%); a pale-yellow solid; mp 102–104 ˚C (hexane/CH_2Cl_2); IR 3261, 1697, 1321, 1170 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.48 (d, J = 4.6 Hz, 3H), 4.54 (s, 2H), 5.86 (q, J = 4.6 Hz, 1H), 7.37 (td, J = 7.4, 1.1 Hz, 1H), 7.46–7.50 (m, 3H), 7.61 (t, J = 7.4 Hz, 1H), 7.63 (dd, J = 7.4, 1.1 Hz, 1H), 7.93 (dd, J = 8.0, 1.1 Hz, 2H), 8.03 (dd, J = 8.0, 1.1 Hz, 1H); ^{13}C NMR (125 MHz) δ 29.7, 42.0, 127.3, 128.5, 128.9, 130.7, 132.79, 132.83, 133.2, 134.0, 136.1, 138.8, 193.3. Anal. Calcd for $C_{15}H_{15}NO_3S_2$: C, 56.05; H, 4.70; N, 4.36; S, 19.95. Found: C, 56.21; H, 4.77; N, 4.45; S, 19.67.

2-{[5-Methyl-2-(methylaminosulfonyl)phenyl]sulfanyl}-1-phenylethanone (2b): a pale-yellow solid; mp 141–143 ˚C (hexane/CH_2Cl_2); IR 3235, 1686 1323, 1166 cm^{-1}; ^1H NMR (500 MHz) δ 2.36 (s, 3H), 2.46 (d, *J* = 5.7 Hz, 3H), 4.53 (s, 2H), 5.82 (q, *J* = 5.7 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 7.43 (s, 1H), 7.47 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.60 (td, *J* = 7.4, 1.1 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.94 (dd, *J* = 8.0, 1.1 Hz, 2H); ^{13}C NMR (125 MHz) δ 21.2, 29.6, 42.1, 128.1, 128.5, 128.8, 130.7, 132.7, 133.7, 133.9, 136.1, 136.0, 143.7, 193.5. Anal. Calcd for $C_{16}H_{17}NO_3S_2$: C, 57.29; H, 5.11; N, 4.18. Found: C, 57.25; H, 5.18; N, 4.21.

2-{[5-Methyl-2-(phenylaminosulfonyl)phenyl]sulfanyl}-1-phenylethanone (2c): a yellow amorphous powder; R_f 0.25 (Et_2O/hexane 1:1); IR 3271, 1680, 1344, 1161 cm^{-1}; ^1H NMR (500 MHz) δ 2.30 (s, 3H), 4.55 (s, 2H), 7.03–7.05 (m, 4H), 7.15 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.40 (s, 1H), 7.47 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.65 (br s, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz) δ 21.3, 42.6, 121.9, 125.4, 128.4, 128.6, 128.8, 129.1, 131.1, 132.4, 133.9, 134.8, 135.3, 136.4, 136.8, 144.1, 193.7. HR-MS (positive). Calcd for $C_{21}H_{20}NO_3S_2$ (M+H): 398.0884. Found: *m/z* 398.0871.

2-{[5-Chloro-2-(methylaminosulfonyl)phenyl]sulfanyl}-1-phenylethanone (2d): a pale-yellow amorphous powder; R_f 0.25 (Et_2O/hexane 1:1); IR 3313, 1685, 1326, 1167 cm^{-1}; ^1H NMR (500 MHz) δ 2.53 (d, *J* = 5.2 Hz, 3H), 4.56 (s, 2H), 5.86 (q, *J* = 5.2 Hz, 1H), 7.33 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.50 (d, *J* = 7.4 Hz, 2H), 7.58 (d, *J* = 1.7 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 2H), 7.96 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 29.7, 42.1, 127.3, 128.5, 129.0, 131.9, 132.0, 134.2, 135.0, 135.6, 137.2, 139.0, 192.9. HR-MS (positive). Calcd for $C_{15}H_{15}ClNO_3S_2$ (M+H): 356.0182. Found: *m/z* 356.0177.

2-{[2-(Methylaminosulfonyl)phenyl]sulfanyl}-1-(4-methylphenyl)ethanone (2e): a pale-yellow solid; mp 137–139 ˚C (hexane/CH_2Cl_2); IR 3268, 1687, 1326, 1169 cm^{-1}; ^1H NMR (500 MHz) δ 2.43 (s, 3H), 2.52 (d, *J* = 5.2 Hz, 3H), 4.53 (s, 2H), 5.91 (q, *J* = 5.2 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.32 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.57 (d, *J* = 1.7 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.7, 29.8, 41.9, 127.2, 128.6, 129.6, 131.8, 132.5, 135.8, 137.0, 139.0, 145.3 (2 overlapped Cs), 192.4. Anal. Calcd for $C_{16}H_{16}ClNO_3S_2$: C, 51.96; H, 4.36; N, 3.79. Found: C, 51.85; H, 4.29; N, 3.68.

2-{[5-Chloro-2-(methylaminosulfonyl)phenyl]sulfanyl}-1-(4-chlorophenyl)ethanone (2f): a pale-yellow solid; mp 108–110 ˚C (hexane/CH_2Cl_2); IR 3272, 1695, 1320, 1166 cm^{-1}; ^1H NMR (500 MHz) δ 2.57 (d, *J* = 5.7 Hz, 3H), 4.53 (s, 2H), 5.86 (q, *J* = 5.7 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* =1.7 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz,) δ 29.7, 42.3, 127.6, 129.3, 129.9, 132.0, 132.4, 133.3, 135.3, 137.4, 139.1, 140.8, 191.9. Anal. Calcd for $C_{15}H_{13}Cl_2NO_3S_2$: C, 46.16; H, 3.36; N, 3.59. Found: C, 45.73; H, 3.14; N, 3.54.

2-{[5-Chloro-2-(methylaminosulfonyl)phenyl]sulfanyl}-1-(naphthalen-2-yl)ethanone (2g): a yellow solid; mp 174–176 ˚C (hexane/CH_2Cl_2); IR 3319, 1686, 1324, 1163 cm^{-1}; ^1H NMR (500 MHz) δ 2.50 (d,

J = 5.2 Hz, 3H), 4.67 (s, 2H), 5.89 (q, *J* = 5.2 Hz, 1H), 7.32 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.62 (d, *J* = 1.7 Hz, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.95–7.98 (m, 3H), 8.48 (s, 1H); ^{13}C NMR (125 MHz) δ 29.7, 42.2, 123.6, 127.3, 127.4, 127.8, 128.9, 129.2, 129.6, 130.6, 131.9, 132.1, 132.26, 132.30, 135.6, 135.9, 137.2, 139.0, 192.8. Anal. Calcd for $C_{19}H_{16}ClNO_3S_2$: C, 56.22; H, 3.97; N, 3.45; S, 15.80. Found: C, 56.06; H, 3.95; N, 3.43; S, 15.68.

2-{[5-Chloro-2-(methylaminosulfonyl)phenyl]sulfanyl}-1-(thiophen-2-yl)ethanone (2h): a yellow amorphous powder; R_f 0.39 (Et_2O/hexane 2:1); IR 3302, 1656, 1326, 1167 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.57 (d, *J* = 5.2 Hz, 3H), 4.46 (s, 2H), 5.93 (q, *J* = 5.2 Hz, 1H), 7.18 (dd, *J* = 4.6, 4.4 Hz, 1H), 7.33 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.60 (d, *J* = 2.3 Hz, 1H), 7.73 (dd, *J* = 4.6, 1.1 Hz, 1H), 7.79 (dd, *J* = 4.0, 1.1 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 29.8, 42.0, 127.4, 128.6, 131.9, 132.1, 133.2, 135.37, 135.41, 137.2, 139.0, 141.9, 185.9. HR-MS (positive). Calcd for $C_{13}H_{13}ClNO_3S_3$ (M+H): 361.9746. Found: *m/z* 361.9741.

2-{[5-Methoxy-2-(methylaminosulfonyl)phenyl]sulfanyl}-1-phenylethanone (2i): a yellow amorphous powder; R_f 0.28 (Et_2O/hexane 2:1); IR 3331, 1671, 1327, 1159 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.44 (d, *J* = 5.2 Hz, 3H), 3.83 (s, 3H), 4.52 (s, 2H), 5.66 (q, *J* = 5.2 Hz, 1H), 6.82 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.12 (d, *J* = 2.3 Hz, 1H), 7.47 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.60 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.94 (dd, *J* = 8.0, 1.1 Hz, 2H), 7.95 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 29.6, 41.8, 55.7, 111.7, 118.5, 128.5 (2 overlapped Cs), 128.9, 130.2, 132.8, 134.0, 135.1, 162.5, 193.3. HR-MS (positive). Calcd for $C_{16}H_{18}NO_4S_2$ (M+H): 352.0677. Found: *m/z* 352.0672.

2-{[5-Methoxy-2-(methylaminosulfonyl)phenyl]sulfanyl}-1-(methoxyphenyl)ethanone (2j): a white solid; mp 129–131 ˚C (hexane/CH_2Cl_2); IR 3247, 1686, 1319, 1166 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.46 (d, *J* = 5.2 Hz, 3H), 3.83 (s, 3H), 3.88 (s, 3H), 4.46 (s, 2H), 5.71 (q, *J* = 5.2 Hz, 1H), 6.82 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.93 (d, *J* = 9.2 Hz, 2H), 7.13 (d, *J* = 2.3 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (125 MHz) δ 29.7, 41.6, 55.6, 55.7, 111.6, 114.0, 118.4, 128.0, 130.2, 130.9, 132.7, 135.3, 162.5, 164.1, 191.8. Anal. Calcd for $C_{17}H_{19}NO_5S_2$: C, 53.53; H, 5.02; N, 3.67; S, 16.81. Found: C, 53.51; H, 5.23; N, 3.66; S, 16.70.

1,1-Dimethylethyl 2-{[5-Methyl-2-(methylaminosulfonyl)phenyl]sulfanyl}acetate (4a): a white solid; mp 90–92 ˚C (hexane/CH_2Cl_2); IR 3244, 1737, 1325, 1167 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.37 (s, 9H), 2.41 (s, 3H), 2.55 (d, *J* = 5.7 Hz, 3H), 5.91 (q, *J* = 5.7 Hz, 1H), 3.73 (s, 2H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.40 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.3, 27.8, 29.8, 38.3, 82.6, 127.7, 130.7, 132.6, 133.6, 135.6, 143.4, 168.4. Anal. Calcd for $C_{14}H_{21}NO_4S_2$: C, 50.73; H, 6.39; N, 4.23; S, 19.35. Found: C, 50.68; H, 6.65; N, 4.28; S, 19.1.

2-{[5-Methyl-2-(methylaminosulfonyl)phenyl]sulfanyl}acetonitrile (4b): a pale-yellow solid; mp 106–108 ˚C (hexane/CH_2Cl_2); IR (KBr) 3344, 3307, 2246, 1320, 1161 cm^{-1}; ^1H NMR (500 MHz) δ 2.47 (s, 3H), 2.60 (d, *J* = 5.2 Hz, 3H), 3.80 (s, 2H), 5.20 (q, *J* = 5.2 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.60 (s, 1H), 8.02 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.2, 21.8, 29.4, 116.0, 128.7, 130.5, 131.6, 137.3, 137.9, 144.7. Anal. Calcd for $C_{10}H_{12}N_2O_2S_2$: C, 46.86; H, 4.72; N, 10.93; S, 25.01. Found: C, 46.80; H, 4.74; N, 11.04; S, 24.96.

Typical Procedure for the Preparation of 2,3-Dihydro-1,4,2-benzodithiazine 1,1-Dioxides (3) and (5). (2-Methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(phenyl)methanone (3a). To a stirred suspension of NaH (60% in mineral oil; 40 mg, 1.0 mmol) in THF (3 mL) at –20 ˚C was added a solution of **2a** (0.16 g, 0.50 mmol) in THF (3 mL) dropwise. After evolution of H_2 gas had ceased, a solution of I_2 (0.13 g, 0.50 mmol) in THF (2 mL) was added dropwise and stirring was continued for 20 min. 10% aqueous $Na_2S_2O_3$ (15 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined organic layers were washed with brine (10 ml), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 (AcOEt/hexane 1:8) to afford **3a** (81 mg, 50%); a white solid; mp 195–197 ˚C (hexane/CH_2Cl_2); IR 1695, 1343, 1167 cm^{-1}; ^1H NMR (500 MHz) δ 2.71 (s, 3H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.47 (s, 1H), 7.55 (d, *J* = 7.4 Hz, 2H), 7.69 (t, *J* = 7.4 Hz, 1H), 7.95 (d, *J* = 7.4 Hz, 1H), 8.23 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (125 MHz) δ 30.7, 70.7, 126.0, 127.1, 128.1, 129.1, 129.7, 130.7, 132.5, 132.6, 133.9, 135.0, 190.9. HR-MS (positive). Calcd for $C_{15}H_{14}NO_3S_2$ (M+H): 320.0415. Found: *m/z* 320.0410. Anal. Calcd for $C_{15}H_{13}NO_3S_2$: C, 56.41; H, 4.10; N, 4.39; S, 20.08. Found: C, 56.40; H, 4.06; N, 4.46; S, 20.21.

(2,6-Dimethyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(phenyl)methanone (3b): a pale-yellow solid; mp 160–162 ˚C (hexane/CH_2Cl_2); IR 1697, 1328, 1165 cm^{-1}; ^1H NMR (500 MHz) δ 2.38 (s, 3H), 2.69 (s, 3H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 7.45 (s, 1H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (125 MHz) δ 21.4, 30.6, 70.6, 127.0, 127.1, 127.8, 128.1, 129.0, 129.7, 132.7, 133.7, 134.9, 143.5, 191.0. HR-MS (positive). Calcd for $C_{16}H_{16}NO_3S_2$ (M+H): 334.0571. Found: *m/z* 334.0568. Anal. Calcd for $C_{16}H_{15}NO_3S_2$: C, 57.64; H, 4.53; N, 4.20. Found: C, 57.62; H, 4.45; N, 4.21.

(6-Methyl-1,1-dioxo-2-phenyl-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(phenyl)methanone (3c): a white solid; mp 176–178 ˚C (hexane/CH_2Cl_2); IR 1684, 1351, 1170 cm^{-1}; ^1H NMR (500 MHz) δ 2.40 (s, 3H), 7.06–7.13 (m, 5H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.27 (s, 1H), 7.51 (t, *J* = 7.4 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.75 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (125 MHz) δ 21.5, 70.6, 126.4, 127.1, 128.4, 128.7, 128.9, 128.96, 128.98, 129.18, 129.21, 133.8, 134.49, 134.54, 135.7, 143.5, 189.9. HR-MS (DART, positive). Calcd for $C_{21}H_{18}NO_3S_2$ (M+H): 396.0728. Found: *m/z* 396.0723. Anal.

Calcd for $C_{21}H_{17}NO_3S_2$: C, 63.78; H, 4.33; N, 3.54. Found: C, 63.51; H, 4.46; N, 3.52.

(6-Chloro-2-methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(phenyl)methanone (3d): a white solid; mp 144–146 ˚C (hexane/CH_2Cl_2); IR 1701, 1348, 1168 cm^{-1}; ^1H NMR (500 MHz) δ 2.70 (s, 3H), 7.26 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.37 (d, *J* = 1.7 Hz, 1H), 7.46 (s, 1H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 8.21 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (125 MHz) δ 30.7, 71.0, 126.4, 127.5, 128.4, 129.0, 129.1, 129.7, 132.5, 135.2, 136.1, 138.9, 190.5. HR-MS (negative). Calcd for $C_{15}H_{12}ClNO_3S_2$ (M–H): 351.9863. Found: *m/z* 351.9879. Anal. Calcd for $C_{15}H_{12}ClO_3S_2$: C, 50.92; H, 3.42; N, 3.96; S, 18.12. Found: C, 50.93; H, 3.35; N, 3.94; S, 18.18.

(6-Chloro-2-methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(4-methylphenyl)methanone (3e): a pale-yellow solid; mp 183–185 ˚C (hexane/CH_2Cl_2); IR 1692, 1332, 1168 cm^{-1}; ^1H NMR (600 MHz) δ 2.46 (s, 3H), 2.69 (s, 3H), 7.26 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 2.4 Hz, 1H), 7.43 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (150 MHz) δ 22.0, 30.7, 71.1, 126.4, 127.6, 128.4, 129.0, 129.80, 129.84, 130.0, 136.3, 138.9, 146.6, 190.0. HR-MS (positive). Calcd for $C_{16}H_{15}ClNO_3S_2$ (M+H): 368.0182. Found: *m/z* 368.0177. Anal. Calcd for $C_{16}H_{14}ClNO_3S_2$: C, 52.24; H, 3.84; N, 3.81. Found: C, 51.91; H, 3.73; N, 3.77.

(6-Chloro-2-methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(4-chlorophenyl)methanone (3f): a white solid; mp 187–189 ˚C (hexane/CH_2Cl_2); IR (KBr) 1697, 1350, 1168 cm^{-1}; ^1H NMR (500 MHz) δ 2.69 (s, 3H), 7.27 (d, *J* = 8.6 Hz, 1H), 7.36 (s, 1H), 7.41 (s, 1H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.88 (d, *J* = 8.6 Hz, 1H), 8.16 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz) δ 30.7, 70.9, 126.5, 127.6, 128.4, 128.9, 129.5, 130.7, 131.0, 135.8, 139.0, 141.9, 189.5. HR-MS (negative). Calcd for $C_{15}H_{10}Cl_2NO_3S_2$ (M–H): 385.9479. Found: *m/z* 385.9488. Anal. Calcd for $C_{15}H_{11}Cl_2NO_3S_2$: C, 46.40; H, 2.86; N, 3.61; S, 16.51. Found: C, 46.46; H, 2.60; N, 3.59; S, 16.28.

(6-Chloro-2-methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(naphthalen-2-yl)methanone (3g): a white solid; mp 153–155 ˚C (hexane/CH_2Cl_2); IR 1672, 1353, 1184 cm^{-1}; ^1H NMR (500 MHz) δ 2.71 (s, 3H), 7.25 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.37 (d, *J* = 2.3 Hz, 1H), 7.59 (s, 1H), 7.60 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.67 (ddd, *J* = 8.0, 7.4, 1.1 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.6 Hz, 1H), 8.13 (dd, *J* = 8.6, 2.3 Hz, 1H), 8.83 (s, 1H); ^{13}C NMR (125 MHz) δ 30.7, 71.1, 124.1, 126.4, 127.2, 127.5, 127.8, 128.3, 128.9, 129.0, 129.6, 129.7, 130.3, 132.2, 132.5, 136.1, 138.8, 171.1, 190.3. HR-MS (negative). Calcd for $C_{19}H_{13}ClNO_3S_2$ (M–H): 402.0026. Found: *m/z* 402.0037. Anal. Calcd for $C_{19}H_{14}ClNO_3S_2$: C, 56.50; H, 3.49; N, 3.47; S, 15.88. Found: C, 66.64; H, 3.36; N, 3.46; S, 15.87.

(6-Chloro-2-methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(thiophen-2-yl)methanone (3h): a white solid; mp 154–156 ˚C (hexane/CH_2Cl_2); IR 1668, 1348, 1168 cm^{-1}; ^1H NMR (500 MHz) δ 2.79 (s,

3H), 7.24–7.28 (m, 2H), 7.29 (s, 1H), 7.37 (d, *J* = 2.3 Hz, 1H), 7.84 (d, *J* = 5.2 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 8.30 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (125 MHz) δ 31.0, 71.2, 126.5, 127.5, 128.4, 128.8, 129.0, 135.9, 136.0, 136.8, 138.3, 138.9, 182.7. HR-MS (positive). Calcd for $C_{13}H_{11}ClNO_3S_3$ (M+H): 359.9589. Found: *m/z* 358.9584. Anal. Calcd for $C_{13}H_{10}ClNO_3S_3$: C, 43.39; H, 2.80; N, 3.89; S, 26.73. Found: C, 43.40; H, 2.83; N, 3.90; S, 26.95.

(6-Methoxy-2-methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(phenyl)methanone (3i): a white solid; mp 176–178 ˚C (hexane/CH_2Cl_2); IR 1686, 1340, 1166 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.69 (s, 3H), 3.85 (s, 3H), 6.81 (dd, *J* = 8.0, 2.3 Hz, 1H), 6.83 (s, 1H), 7.46 (s, 1H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.69 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 8.23 (dd, *J* = 7.4, 1.1 Hz, 2H); ^{13}C NMR (125 MHz) δ 30.7, 55.7, 70.8, 111.7, 113.1, 122.6, 128.8, 129.0, 129.7, 132.7, 135.0, 135.9, 162.1, 191.0. HR-MS (positive). Calcd for $C_{16}H_{16}NO_4S_2$ (M+H): 350.0520. Found: *m/z* 350.0515. Anal. Calcd for $C_{16}H_{15}NO_4S_2$: C, 55.00; H, 4.33; N, 4.01; S, 18.35. Found: C, 54.80; H, 4.36; N, 3.99; S, 18.32.

(6-Methoxy-2-methyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazin-3-yl)(4-methoxyphenyl)methanone (3j): a white solid; mp 164–166 ˚C (hexane/CH_2Cl_2); IR 1673, 1345, 1178 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.69 (s, 3H), 3.85 (s, 3H), 3.91 (s, 3H), 6.81 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.82 (s, 1H), 7.00 (d, *J* = 9.2 Hz, 2H), 7.41 (s, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 8.23 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz) δ 30.5, 55.6, 55.7, 70.9, 111.7, 113.0, 114.2, 122.7, 125.6, 128.7, 132.2, 136.2, 162.1, 164.9, 189.0. HR-MS (positive). Calcd for $C_{17}H_{18}NO_5S_2$ (M+H): 380.0626. Found: *m/z* 380.0625. Anal. Calcd for $C_{17}H_{17}NO_5S_2$: C, 53.81; H, 4.52; N, 3.69; S, 16.90. Found: C, 53.69; H, 4.69; N, 3.69; S, 16.81.

1,1-Dimethylethyl 2,6-Dimethy-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazine-3-carboxylate (5a): a white solid; mp 111–113 ˚C (hexane/CH_2Cl_2); IR 1725, 1341, 1174 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.55 (s, 9H), 2.35 (s, 3H), 2.83 (s, 3H), 6.54 (s, 1H), 7.07 (d, *J* = 7.4 Hz, 1H), 7.08 (s, 1H), 7.80 (dd, *J* = 7.4, 1.7 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.4, 27.9, 30.9, 65.0, 85.2, 127.0, 127.1, 127.3, 127.4, 134.2, 143.3, 163.8. HR-MS (positive). Calcd for $C_{14}H_{20}NO_4S_2$ (M+H): 330.0833. Found: *m/z* 330.0829. Anal. Calcd for $C_{14}H_{19}NO_4S_2$: C, 51.04; H, 5.81; N, 4.25; S, 19.46. Found: C, 50.99; H, 6.06; N, 4.28; S, 19.33.

2,6-Dimethyl-1,1-dioxo-2,3-dihydro-1,4,2-benzodithiazine-3-carbonitrile (5b): a white solid; mp 137–139 ˚C (hexane/CH_2Cl_2); IR 2244, 1357, 1172 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.38 (s, 3H), 3.00 (s, 3H), 6.78 (s, 1H), 7.06 (s, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.5, 32.1, 52.4, 112.1, 125.9, 126.9, 127.4, 128.0, 132.0, 144.4. HR-MS (positive). Calcd for $C_{10}H_{11}N_2O_2S_2$ (M+H): 255.0262. Found: *m/z* 255.0254. Anal. Calcd for $C_{10}H_{10}N_2O_2S_2$: C, 47.23; H, 3.96; N, 11.02; S, 25.21. Found: C, 47.03; H, 3.88; N, 11.03; S, 25.12.

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