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SYNTHESIS OF 4-(*Z*)-(HALOMETHYLIDENE)-1,4-DIHYDRO-2*H*-3,1-BENZOTHIAZINE-2-THIONES AND THEIR *S*-ALKYLATED DERIVATIVES BASED ON THE REACTION OF 2-(2,2-DIHALOETNENYL)BENZENAMINES WITH CARBON DISULFIDES

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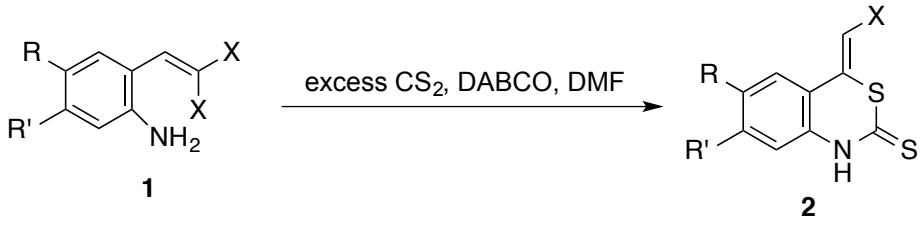
Abstract – An efficient one-pot procedure for the preparation of 4-(*Z*)-(halomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones has been developed. Thus, the reaction of 2-(2,2-dihaloethenyl)benzenamines with carbon disulfide in DMF in the presence of DABCO affords the desired products. Successive treatment of these dihydrobenzothiazinethiones with sodium hydride and alkyl halides allows the preparation of 2-(alkylsulfanyl)-4-(*Z*)-(halomethylidene)-4*H*-3,1-benzothiazines.

As part of our program to investigate the utility of 2-(2,2-dihaloethenyl)benzenamines for the preparation of benzene-fused heterocycles,[1] we designed the procedure which would provide a new route to 4-(*Z*)-(halomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones. Herein, we wish to report that these derivatives can be prepared by the reaction of 2-(2,2-dihaloethenyl)benzenamines with carbon disulfide in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO). Recently, some synthetic method for the preparation of 4-benzylidene-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones have been reported.[2] For example, Ding *et al*. reported a synthesis of 4-(*E*)- and (*Z*)-benzylidene-4*H*-3,1-benzothiazine-2-thione derivatives by the $AgNO_3$-catalyzed reaction of 2-(arylethynyl)benzenamines with carbon disulfide[2a] and a similar synthesis of (*Z*)-benzylidene-4*H*-3,1-benzothiazine-2-thione derivatives catalyzed by protonated DBU was reported by Xi *et al*.[2b] To date, however, 4-halomethylidene derivatives are unknown so far. We also describe a facile transformation of 4-(*Z*)-(halomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones into 2-(alkylsulfanyl)-4-(*Z*)-(halomethylidene)-4*H*-3,1-benzothiazines, which are

hard to prepare by the method previously reported by us.[1d] These 2-(alkylsulfanyl)-3,1-benzothiazine derivatives are also of synthetic and biological interest.[1d,3]

Our synthesis of 4-(*Z*)-(halomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones (**2**) from 2-(2,2-dihaloethenyl)benzenamines (**1**) was conducted according to the procedure shown in Scheme 1. The starting materials (**1**) were readily prepared from the respective 2-nitrobenzaldehydes according to the reported procedure.[1a,4] Compounds (**1**) were treated with excess carbon disulfide in the presence of an equivalent of 1,4-diazabicyclo[2.2.2]octane (DABCO) to afford the desired products (**2a-d**). The yields of the products and reaction conditions are summarized in Table 1. Although the products are shown to have the 4*H*-3,1-benzothiazine-2-thiol structure in the reports cited in ref. 2, the spectral data for our products (**2**) revealed that these have the 1,4-dihydro-2*H*-3,1-benzothiazine-2-thione structure. The IR spectra uniformly showed absorptions at around 3160 and 1020 cm^{-1} assignable to ν(N–H) and ν(C=S), respectively. The ^{1}H and ^{13}C NMR spectra exhibited signals at δ 11.5–13.0 due to NH and at δ 184–187 due to the thiocarbonyl, respectively. The stereochemistry of the 4-(halomethylidene) moiety was determined by NOESY analyses of the products. Thus, strong interaction between the vinyl proton and H(5) on the benzothiazine framework was observed. The use of more basic 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or triethylamine in place of DABCO for the preparation of **2a** resulted in the formation of rather complicated mixture of products; structurally undefined by-products were obtained and the yield of **2a** was lower in each case.



1 **2**

Scheme 1

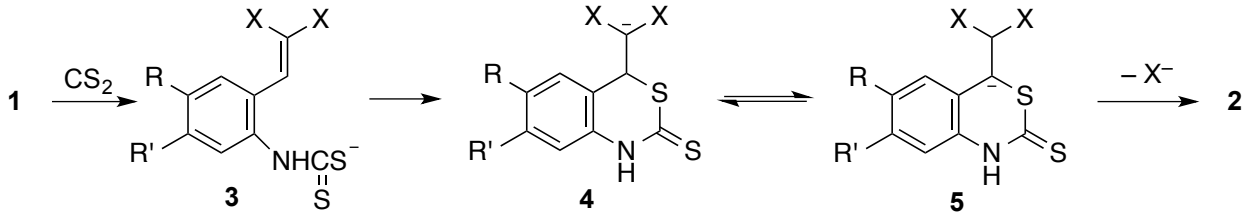
Table 1. Preparation of 4-(*Z*)-(halomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones (**2**)

Entry	**1**	Temp	Time	**2**	Yield/%[a]
1	**1a** (R = R' = H, X = Br)	0 °C	5 h	**2a**	66
2	**1b** (R = R' = H, X = Cl)	rt	overnight	**2b**	64
3	**1c** (R = Cl, R' = H, X = Br)	0 °C	14 h	**2c**	71
4	**1d** (R = H, R' = Cl, X = Br)	0 °C	48 h	**2d**	50

[a] Yields of isolated products.

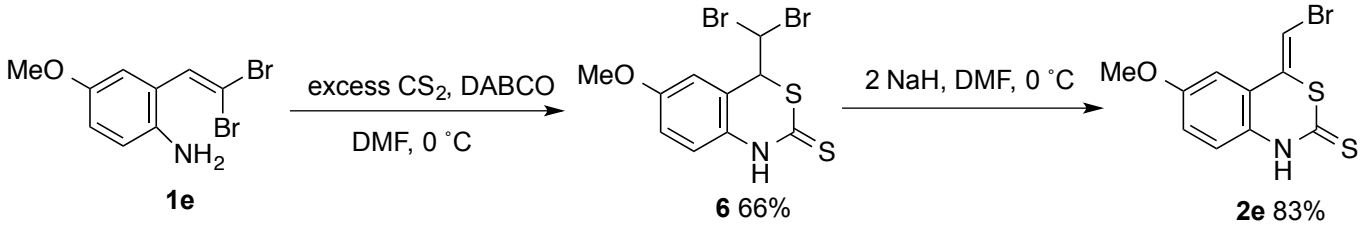
The formation of **2** from **1** is thought to proceed *via* the intermediates shown in Scheme 2. Thus, it is initiated by the addition of the amino nitrogen to carbon disulfide generating the arylcarbamodithioate intermediate (**3**). Then, this thioate anion attacks intramolecularly on the β-carbon of the dihalovinyl

moiety to produce the dihalomethyl anion intermediate (**4**). Anion transfer followed by elimination of halide anion from the resulting benzyl anion intermediate (**5**) gives rise to **2**.



Scheme 2

In practice, when 2-(2,2-dibromoethenyl)-4-methoxybenzenamine (**1e**) was subjected to the treatment with carbon disulfide in the presence of DABCO at 0 °C as described above, 4-(dibromomethyl)-6-methoxy-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (**6**) was obtained in fair yields as shown in Scheme 3. However, the reaction at room temperature resulted in the formation of an intractable mixture of products. Fortunately, compound (**6**) was treated with two equivalents of sodium hydride in DMF at 0 °C to afford 4-(*Z*)-(bromomethylidene)-6-methoxy-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (**2e**) in good yields.

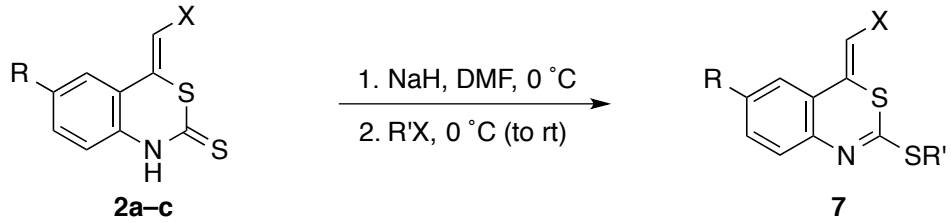


Scheme 3

We next investigated the transformation of **2a-c** into 2-(alkylsulfanyl)-4-(*Z*)-(halomethylidene)-4*H*-3,1-benzothiazines (**7**). When compounds (**2a-c**) were successively treated with an equivalent each of sodium hydride and alkyl halides in DMF at 0 °C, the corresponding desired products (**7**) were obtained in moderate to fair yields and there was no trace of the *N*-alkylated product in each case, as shown in Scheme 4 and Table 2. The results compiled in this Table indicate that the yields of **7** are generally fair-to-good, though the yield of *S*-2-bromo-4-chlorobenzyl derivative (**7b**) is somewhat lower than those of the others, probably due to steric reasons. The use of a non-activated alkyl halide, such as *n*-butyl bromide, has proven to be effective in this transformation. Although the reaction required room temperature, Entry 7 indicates that the yield is comparable to those of the others.

In further experiments, we have shown that it is possible to convert 4-(dibromomethyl)-6-methoxy-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (**6**) into 2-(alkylsulfanyl)-4-(*Z*)-(halomethylidene)-6-methoxy-

4*H*-3,1-benzothiazines (**8**) directly, as illustrated in Scheme 5. Thus, successive treatment of compound (**6**) with two equivalents of sodium hydride and an equivalent of alkyl halides gave the desired products (**8**) in moderate to fair yields.



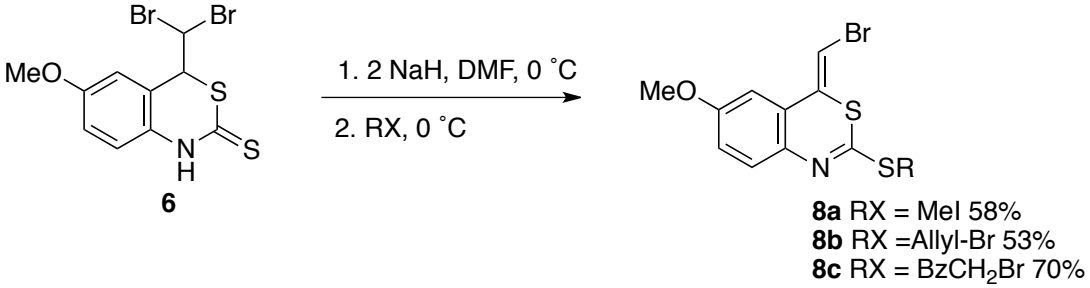
2a–c **7**

Scheme 4

Table 2. Preparation of 4-(*Z*)-(halomethylidene)-2-sulfanyl-4*H*-3,1-benzothiazines (**7**)

Entry	**2**	R'X	Temp	**7**	Yield/%[a]
1	**2a** (R = H, X = Br)	MeI	0 ˚C	**7a**	58
2	**2a**	2-Br-4-$ClC_6H_3CH_2Br$	0 ˚C	**7b**	45
3	**2a**	*tert*-$BuOCOCH_2Br$	0 ˚C	**7c**	76
4	**2b** (R = H, X = Cl)	MeI	0 ˚C	**7d**	62
5	**2b**	$NCCH_2Br$	0 ˚C	**7e**	64
6	**2c** (R = Cl, X = Br)	MeI	0 ˚C	**7f**	82
7	**2c**	*n*-BuBr	0 ˚C to rt	**7g**	56

[a] Yields of isolated products.



6

8a RX = MeI 58%
8b RX =Allyl-Br 53%
8c RX = $BzCH_2Br$ 70%

Scheme 5

In conclusion, we have developed a convenient method for the preparation of 4-(*Z*)-(halomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones from 2-(2,2-dihaloethenyl)benzenamines and these products have been transformed into 2-(alkylsulfanyl)-4-(*Z*)-(halomethylidene)-6-methoxy-4*H*-3,1-benzothiazines. The present methods may be of value in organic synthesis because of the operational simplicity as well as the ready availability of the starting materials and may 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 with a PerkinElmer Spectrum 65 FTIR spectrophotometer. ^{1}H

NMR and ^{13}C NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra were measured by a JEOL JMS-T100GCV spectrometer (EI, TOF; 70eV) or a Thermo Scientific Exactive spectrometer (ESI). 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. 2-(2,2-Dihaloethenyl)benzenamines (**1a**, **b**, **c**, and **e**) were prepared according to the reported procedure.[1a,4] All other chemicals used in this study were commercially available.

5-Chloro-2-(2,2-dibromoethenyl)benzenamine (1d).[5] This compound was prepared from 4-chloro-2-nitrobenzaldehyde as described for the preparation of **1a**. **1d:** yield: 64%; a beige solid; mp 54–56 ˚C (hexane); IR (KBr) 3479, 3390, 1619 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.78 (br s, 2H), 6.70 (d, *J* = 1.7 Hz, 1H), 6.75 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.25 (s, 1H).

General Procedure for the Preparation of 4-(*Z*)-(Halomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thiones (2a-d). To a stirred solution of **1** (2.0 mmol) in DMF (5 mL) containing DABCO (0.22 g, 2.0 mmol) at 0 ˚C was added CS_2 (1.5 g, 20 mmol) dropwise and stirring was continued for the time at the temperature indicated in Table 1 before H_2O (30 mL) was added. The mixture was extracted with AcOEt (3 × 15 mL), and the combined extracts were washed with H_2O (3 × 20 mL) and brine (20 mL), and dried (Na_2SO_4). Concentrated by evaporation gave a residual solid, which was triturated with Et_2O and filtered under reduced pressure to afford **2**.

4-(*Z*)-(Bromomethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (2a): a yellow solid; mp 165–167 ˚C (decomp) (hexane/THF); IR (KBr) 3150, 1608, 1014 cm^{-1}; ^1H NMR (C_4D_8O) δ 6.94 (s, 1H), 7.04–7.08 (m, 2H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 11.57 (s, 1H); ^{13}C NMR (C_4D_8O) δ 98.83, 117.86, 118.04, 124.23, 125.18, 130.58, 133.09, 136.07, 187.26. HR-MS (ESI, negative). Calcd for $C_9H_5BrNS_2$ (M–H): 269.9047. Found: *m/z* 269.9055.

4-(*Z*)-(Chloromethylidene)-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (2b): a yellow solid; mp 176–178 ˚C (decomp) (hexane/THF); IR (KBr) 3158, 1609, 1018 cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.35 (t, *J* = 7.6 Hz, 1H), 6.36 (s, 1H), 6.43 (d, *J* = 7.6 Hz, 1H), 6.56 (t, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 12.05 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 110.74, 116.25, 118.65, 124.35, 125.84, 129.17, 131.01, 135.20, 185.56. HR-MS (ESI, negative). Calcd for $C_9H_5ClNS_2$ (M–H): 225.9552. Found: *m/z* 225.9553.

4-(*Z*)-(Bromomethylidene)-6-chloro-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (2c): an orange solid; mp 175–177 ˚C (decomp) (hexane/THF); IR (KBr) 3156, 1601, 1024 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.29 (d, *J* = 8.4 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.51 (s, 1H), 7.86 (s, 1H), 13.00 (s, 1H); ^{13}C NMR

(DMSO-d_6) δ 102.59, 118.94, 120.37, 124.14, 129.88, 130.41, 130.76, 134.13, 185.98. HR-MS (ESI, negative). Calcd for $C_9H_4BrClNS_2$ (M–H): 303.8657. Found: *m/z* 303.8665.

4-(*Z*)-(Bromomethylidene)-7-chloro-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (2d): a pale-yellow solid; mp 204–206 °C (decomp) (hexane/AcOEt); IR (KBr) 3159, 1600, 1024 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.28 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.34 (d, *J* = 2.3 Hz, 1H), 7.43 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 12.96 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 101.62, 116.33, 117.94, 125.49, 126.42, 130.64, 134.99, 136.29, 186.70. HR-MS (ESI, negative). Calcd for $C_9H_4BrClNS_2$ (M–H): 303.8657. Found: *m/z* 303.8661.

4-(Dibromomethyl)-6-methoxy-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (6). 2-(2,2-Dibromoethenyl)-4-methoxybenzenamine (**1e**) (0.85 g, 2.8 mmol) was treated with CS_2 in DMF in the presence of DABCO at 0 °C and worked up as described for the preparation of **2a-d**. The residual solid was triturated with Et_2O to give **6** (0.70 g, 65%); a yellow solid; mp 175–177 °C (decomp) (hexane/THF); IR (KBr) 3169, 1012 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.81 (s, 3H), 5.18 (d, *J* = 3.1 Hz, 1H), 5.79 (d, *J* = 3.1 Hz, 1H), 6.25 (dd, *J* = 9.2, 3.1 Hz, 1H), 7.11 (d, *J* = 3.1 Hz, 1H), 7.25 (d, *J* = 9.2 Hz, 1H), 12.67 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 54.15, 54.95, 55.51, 114.92, 115.93, 118.41, 119.19, 130.58, 156.07, 186.76. HR-MS (ESI, negative). Calcd for $C_{10}H_8Br_2NOS_2$ (M–H): 379.8414. Found: *m/z* 379.8416.

4-(*Z*)-(Bromomethylidene)-6-methoxy-1,4-dihydro-2*H*-3,1-benzothiazine-2-thione (2e). To a stirred suspension of NaH (60% in mineral oil; 0.15 g, 3.7 mmol) in DMF (4.5 mL) at 0 °C was added a solution of **6** (0.70 g, 1.8 mmol) in DMF (1.5 mL) dropwise. After 15 min, saturated aqueous NH_4Cl (20 mL) was added and the mixture was worked up as described for the preparation of **2a-d**. The residual solid was triturated with Et_2O to give **2e** (0.46 g, 83%); an orange solid; mp 148–150 °C (decomp) (hexane/THF); IR (KBr) 3165, 1649, 1021 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.78 (s, 3H), 7.06 (dd, *J* = 9.2, 2.3 Hz, 1H), 7.25–7.27 (m, 2H), 7.48 (s, 1H), 12.88 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 55.75, 101.26, 108.09, 117.99, 118.30, 120.17, 129.25, 131.62, 157.00, 183.85. HR-MS (ESI, negative). Calcd for $C_{10}H_7BrNOS_2$ (M–H): 299.9153. Found: *m/z* 299.9154.

Typical Procedure for the Preparation of 2-(Alkylsulfanyl)-4-(*Z*)-(halomethylidene)-4*H*-3,1-benzothiazines (7). 4-(*Z*)-(Bromomethylidene)-2-(methylsulfanyl)-4*H*-3,1-benzothiazine (7a). To a stirred suspension of NaH (60% in mineral oil; 20 mg, 0.50 mmol) in DMF (2 mL) at 0 °C was added a solution of **2a** (0.14 g, 0.50 mmol) in DMF (1 mL) dropwise. After evolution of H_2 gas had ceased, MeI (71 mg, 0.50 mmol) was added dropwise. After 5 min, saturated aqueous NH_4Cl (15 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL), and the combined extracts were washed with H_2O (3 × 10 mL) and brine (15 mL), dried (Na_2SO_4) and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to give **7a** (84 mg, 59%); a yellow oil; R_f 0.43 (Et_2O/hexane 1:30); IR (neat) 1603, 1571, 1547 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.63 (s, 3H), 6.74 (s, 1H), 7.21–7.25 (m, 1H),

7.36–7.41 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.06, 100.87, 119.82, 123.45, 127.44, 128.14, 130.37, 132.40, 141.83, 158.71. HR-MS (EI). Calcd for $C_{10}H_8BrNS_2$ (M): 284.9282. Found: *m/z* 284.9276. Anal. Calcd for $C_{10}H_8BrNS_2$: C, 41.97; H, 2.82; N, 4.89. Found: C, 41.74; H, 3.11; N 4.64.

2-{[(2-Bromo-4-chlorophenyl)methyl]sulfanyl}-4-(*Z*)-(bromomethylidene)-4*H*-3,1-benzothiazine (7b): a white solid; mp 103–105 °C (hexane); IR (KBr) 1602, 1571, 1553 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.58 (s, 2H), 6.76 (s, 1H), 7.21–7.27 (m, 2H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.42–7.45 (m, 2H), 7.51 (d, *J* = 8.6 Hz, 1H), 7.58 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 34.77, 101.40, 120.11, 123.63, 125.03, 127.73, 127.76, 128.04, 130.48, 132.09, 132.19, 132.48, 134.01, 135.39, 141.69, 157.28. HR-MS (EI). Calcd for $C_{16}H_{10}Br_2ClNS_2$ (M): 472.8310. Found: *m/z* 472.8296. Anal. Calcd for $C_{16}H_{10}Br_2ClNS_2$: C, 40.40; H, 2.12; N, 2.94; S, 13.48. Found: C, 40.37; H, 2.43; N, 2.85; S, 13.73.

1,1-Dimethylethyl 2-{[4-(*Z*)-(Bromomethylidene)-4*H*-3,1-benzothiazin-2-yl]sulfanyl}acetate (7c): a white solid; mp 77–79 °C (hexane); IR (KBr) 1730, 1603, 1572, 1557 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 9H), 3.91 (s, 2H), 6.77 (s, 1H), 7.24 (ddd, *J* = 8.0, 7.4, 1,1 Hz, 1H), 7.33 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.39–7.41 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 27.98, 34.51, 82.27, 101.31, 119.95, 123.51, 127.72, 128.16, 130.40, 132.18, 141.62, 156.89, 167.29. HR-MS (ESI, positive). Calcd for $C_{15}H_{17}BrNO_2S_2$ (M+H): 385.9884. Found: *m/z* 385.9868. Anal. Calcd for $C_{15}H_{16}BrNO_2S_2$: C, 46.64; H, 4.17; N, 3.63. Found: C, 46.48; H, 4.03; N, 3.54.

4-(*Z*)-(Chloromethylidene)-2-(methylsulfanyl)-4*H*-3,1-benzothiazine (7d): a yellow oil; R_f 0.48 (Et_2O/hexane 1:50); IR (KBr) 1603, 1574, 1551 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.64 (s, 3H), 6.58 (s, 1H), 7.23 (ddd, *J* = 8.6, 6.3, 2.3 Hz, 1H), 7.36–7.38 (m, 2H), 7.40 (dd, *J* = 8.0, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.08, 111.48, 118.63, 123.37, 127.41, 128.18, 129.59, 130.33, 141.73, 158.40. HR-MS (EI). Calcd for $C_{10}H_8ClNS_2$ (M): 240.9787. Found: *m/z* 240.9790. Anal. Calcd for $C_{10}H_8ClNS_2$: C, 49.68; H, 3.34; N, 5.79. Found: C, 49.69; H, 3.45; N, 5.78.

2-{[4-(*Z*)-(Chloromethylidene)-4*H*-3,1-benzothiazin-2-yl]sulfanyl}acetonitrile (7e): a yellow solid; mp 121–123 °C (hexane/$CHCl_3$); IR (KBr) 2245, 1602, 1557 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.03 (s, 2H), 6.64 (s, 1H), 7.29 (ddd, *J* = 8.6, 8.0, 4.0 Hz, 1H), 7.39–7.44 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 15.92, 112.75, 115.66, 118.72, 123.47, 128.41, 128.44, 128.47, 130.65, 140.87, 153.90. HR-MS (EI). Calcd for $C_{11}H_7ClN_2S_2$ (M): 265.9739. Found: *m/z* 265.9728. Anal. Calcd for $C_{11}H_7ClN_2S_2$: C, 49.53; H, 2.65; N, 10.50. Found: C, 49.53; H, 2.71; N, 10.27.

4-(*Z*)-(Bromomethylidene)-6-chloro-2-(methylsulfanyl)-4*H*-3,1-benzothiazine (7f): a yellow solid; mp 90–92 °C (hexane/CH_2Cl_2); IR (KBr) 1621, 1598, 1550 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.63 (s, 3H), 6.77 (s, 1H), 7.31 (d, *J* = 8.6 Hz, 1H), 7.35 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.38 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.11, 102.19, 121.07, 123.38, 129.44, 130.33, 131.37, 132.63, 140.48, 159.45. HR-MS (EI). Calcd for

$C_{10}H_7BrClNS_2$ (M): 318.8892. Found: *m/z* 318.8888. Anal. Calcd for $C_{10}H_7BrClNS_2$: C, 37.46; H, 2.20; N, 4.37; S, 20.00. Found: C, 37.80; H, 2.49; N, 4.34; S, 20.21.

4-(*Z*)-(Bromomethylidene)-2-(butylsulfanyl)-6-chloro-4*H*-3,1-benzothiazine (7g): a yellow oil; R_f 0.48 (CH_2Cl_2/hexane 1:5); IR (neat) 1596, 1551 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (t, *J* = 7.4 Hz, 3H), 1.42–1.48 (m, 2H), 1.68–1.74 (m, 2H), 3.25 (t, *J* = 7.4 Hz, 2H), 6.76 (s, 1H), 7.28 (d, *J* = 8.6 Hz, 1H), 7.34 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.37 (d, *J* = 1.7Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.63, 21.90, 31.06, 31.30, 102.10, 121.13, 123.38, 129.40, 130.28, 131.57, 132.55, 140.53, 159.13. HR-MS (EI). Calcd for $C_{13}H_{13}BrClNS_2$ (M): 360.9361. Found: *m/z* 360.9363. Anal. Calcd for $C_{13}H_{13}BrClNS_2$: C, 43.05; H, 3.61; N, 3.86. Found: C, 43.04; H, 3.73; N 3.81.

Typical Procedure for the Preparation of 2-(Alkylsulfanyl)-4-(*Z*)-(bromomethylidene)-6-methoxy-4*H*-3,1-benzothiazines (8). 4-(*Z*)-(Bromomethylidene)-6-methoxy-2-(methylsulfanyl)-4*H*-3,1-benzothiazine (8a). Compound (**6**) (0.22 g, 0.58 mmol) was treated with NaH (60% in mineral oil; 46 mg, 1.2 mmol) in DMF (3 mL) as described for the preparation of **7a**. After 15 min, MeI (82 mg, 0.58 mmol) was added. The resulting mixture was worked up and the crude product was purified as described for the preparation of **7a** to give **8a** (0.11 g, 58%); a yellow solid; mp 52–54 ˚C (hexane/CH_2Cl_2); IR (KBr) 1610, 1540 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.62 (s, 3H), 3.84 (s, 3H), 6.76 (s, 1H), 6.89 (d, *J* = 2.3 Hz, 1H), 6.97 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.04, 55.60, 100.68, 107.72, 116.38, 120.44, 129.57, 132.68, 136.08, 155.40, 158.64. HR-MS (ESI, positive). Calcd for $C_{11}H_{11}BrNOS_2$ (M+H): 315.9465. Found: *m/z* 315.9455. Anal. Calcd for $C_{11}H_{10}BrNOS_2$: C, 41.78; H, 3.19; N 4.43. Found: C, 41.60; H, 3.16; N, 4.20.

4-(*Z*)-(Bromomethylidene)-6-methoxy-2-[(prop-2-enyl)sulfanyl]-4*H*-3,1-benzothiazine (8b): a yellow oil; R_f 0.52 (Et_2O/hexane 1:25); IR (neat) 1636, 1609, 1550 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.84 (s, 3H), 3.89 (d, *J* = 7.1 Hz, 2H), 5.15 (dd, *J* = 9.9, 0.8 Hz, 1H), 5.31 (dt, *J* = 16.9, 1.2 Hz, 1H), 5.95 (ddt, *J* = 16.9, 9.9, 7.1 Hz, 1H), 6.75 (s, 1H), 6.88 (d, *J* = 2.8 Hz, 1H), 6.97 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.32 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 34.12, 55.64, 100.80, 107.81, 116.42, 118.62, 120.62, 129.65, 132.80, 132.90, 136.11, 154.08, 158.82. HR-MS (EI). Calcd for $C_{13}H_{12}BrNOS_2$ (M): 340.9544. Found: *m/z* 340.9534. Anal. Calcd for $C_{13}H_{12}BrNOS_2$: C, 45.62; H, 3.53; N, 4.09. Found: C, 45.82; H, 3.93; N, 4.13.

2-{[4-(*Z*)-(Bromomethylidene)-6-methoxy-4*H*-3,1-benzothiazin-2-yl]sulfanyl}-1-phenylethanone (8c): a yellow solid; mp 138–140 ˚C (hexane/CH_2Cl_2); IR (KBr) 1674, 1610, 1541 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.81 (s, 3H), 4.67 (s, 2H), 6.75 (s, 1H), 6.86 (d, *J* = 2.9 Hz, 1H), 6.87 (dd, *J* = 8.0, 2.9 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.51 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.62 (td, *J* = 7.4, 1.1 Hz, 1H), 8.06 (dd, *J* = 8.0, 1.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 37.80, 55.58, 101.16, 107.73, 116.32, 120.55, 128.51, 128.73, 129.33, 132.28, 133.58, 135.68, 145.97, 153.44, 158.79, 193.35. HR-MS (ESI, positive). Calcd for

$C_{18}H_{15}BrNO_2S_2$ (M+H): 419.9727. Found: *m/z* 419.9720. Anal. Calcd for $C_{18}H_{14}BrNO_2S_2$: C, 51.43; H, 3.36; N, 3.33; S, 15.25. Found: C, 51.21; H, 3.40; N, 3.14; S, 14.95.

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