One-Pot Syntheses of 2-(2-Sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetic Acid Derivatives *via* Reactions of 3-(2-Isothiocyanatophenyl)prop-2-enoic Acid Derivatives with Thiols or Sodium Sulfide

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Two efficient methods for the preparation of 2-(2-sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives **3** under mild conditions have been developed. The first method is based on the reaction of 3-(2-isothiocyanatophenyl)prop-2-enoates **1a**–**1c** with thiols in the presence of Et_3N in THF at room temperature, leading to the corresponding dithiocarbamate intermediates **2**, which underwent spontaneous cyclization at the same temperature by an attack of the S-atom at the prop-2-enoyl moiety in a 1,4-addition manner (*Michael* addition) to give 2-(2-sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetates in one pot. The second method involves treatment of 3-(2-isothiocyanatophenyl)prop-2-enoic acid derivatives **1b**–**1d** with Na_2S leading to the formation of 2-(2-sodiosulfanyl-4*H*-3,1-benzothiazin-4-yl)acetic acid intermediates **5** by a similar addition/cyclization sequence, which are then allowed to react with alkyl or aryl halides to afford derivatives **3**. 2-(2-Thioxo-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives **6** can be obtained by omitting the addition of halides.

Introduction. – Compounds with the 4*H*-3,1-benzothiazine skeleton have recently attracted much attention because of their biological activities [1], and a number of efficient methods for their preparation have been reported [2]. We have recently described a synthesis of 2-[2-(dialkylamino)-4*H*-3,1-benzothiazin-4-yl]acetic acids by the reaction of 3-(2-isothiocyanatophenyl)prop-2-enoic acids with secondary amines [3]. As a continuation of this work, we became interested in investigating the possibility of preparation of 4*H*-3,1-benzothiazines with a sulfanyl group at C(2) by reacting 3-(2-isothiocyanatophenyl)prop-2-enoic acid derivatives with thiols. We now report the results of our investigation, which offer a facile one-pot procedure for the synthesis of 2-(2-sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives from 3-(2-isothiocyanatophenyl)prop-2-enoates *via* cyclization of the corresponding dithiocarbamates. The 2-sulfanyl-4*H*-3,1-benzothiazine skeleton has attracted much attention because of the biological activities of some derivatives [2b][4], and some efficient methods for their preparation have been reported [5]. We also found that the use of Na_2S in place of thiols generated 2-[2-(sodiosulfanyl)-4*H*-3,1-benzothiazin-4-yl]acetic acid intermediates, which were then allowed to react with alkyl or aryl halides to afford 2-(2-sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives. Moreover, we found that 2-(2-thioxo-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives were obtained, when the reactions of 2-[2-(sodiosulfanyl)-4*H*-3,1-benzothiazin-4-yl]acetic acid intermediates were quenched with aqueous acidic solutions. The 2-thioxo-4*H*-3,1-benzothiazine skeleton is found in

some biologically active compounds [6]. However, few practical methods for the preparation of this class of 4*H*-3,1-benzothiazine derivatives have been reported so far [6b][7]. Although *Tárraga et al.* have reported the synthesis of methyl 2-(2-thioxo-4*H*-3,1-benzothiazin-4-yl)acetate by the reaction of methyl (*E*)-3-{2-[(triphenylphosphoranylidene)amino]phenyl}prop-2-enoate with CS_2, this method suffers from low yield and limited generality [7].

Results and Discussion. – First, a one-pot synthesis of 2-(2-sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetates **3** was performed by the process illustrated in *Scheme 1*. Thus, 3-(2-isothiocyanatophenyl)prop-2-enoates **1** [3] were treated with thiols in the presence of Et_3N in THF at room temperature to generate the corresponding dithiocarbamate intermediates **2**, which, at the same temperature, underwent cyclization by an attack of the S-atom at the prop-2-enoyl moiety in a 1,4-addition manner. The usual aqueous workup and subsequent purification by column chromatography on silica gel afforded the desired products **3**. The results are summarized in *Table 1*, which indicates that the yields are generally good-to-excellent. It should be noted that the use of 3-(2-isothiocyanatophenyl)-*N*,*N*-dimethylprop-2-enamide in stead of **1** resulted in the formation of complex mixtures of products, in which no trace of the desired products could be detected (data not shown).

Scheme 1

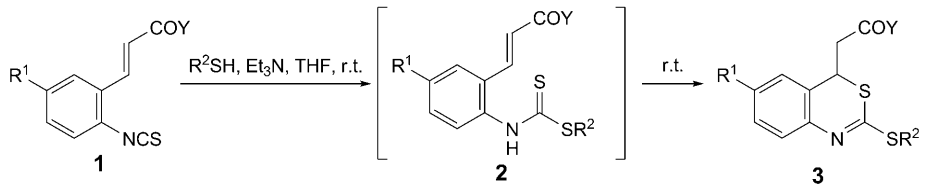


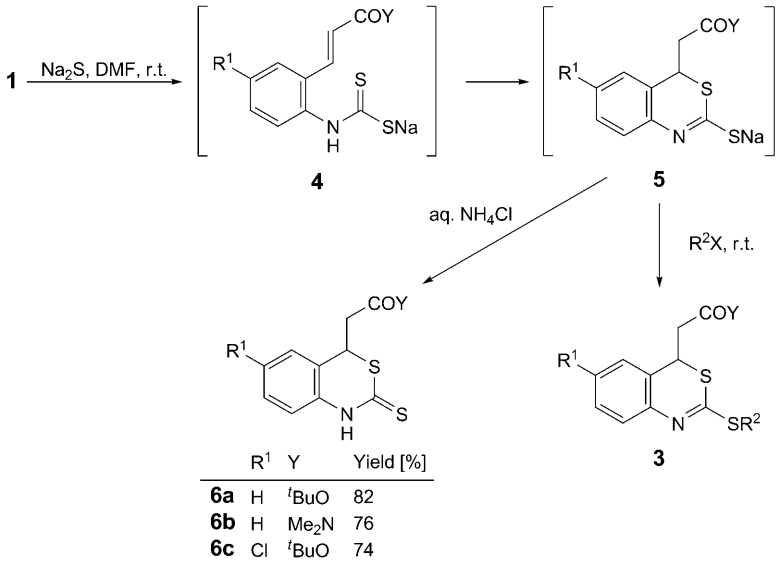
Table 1. *Preparation of 2-(2-Sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetates* **3** via **2**

Entry	Starting material	R^2	**3**	Yield[a]) [%]
1	**1a** (R^1 = H, Y = MeO)	$HOCH_2CH_2$	**3a**	75
2	**1a**	Ph	**3b**	88
3	**1a**	4-Cl–C_6H_4	**3c**	84
4	**1b** (R^1 = H, Y = *t*-BuO)	Hexyl	**3d**	76
5	**1b**	Bn	**3e**	78
6	**1b**	*t*-Bu	**3f**	74
7	**1b**	Ph	**3g**	95
8	**1c** (R^1 = Cl, Y = *t*-BuO)	4-Me–C_6H_4	**3h**	93
9	**1c**	Naphthalen-2-yl	**3i**	93

[a]) Yields of isolated products.

Next, we found that 2-(2-sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetates **3** could be prepared by using $Na_2S \cdot 9\,H_2O$ in place of thiols, as depicted in *Scheme 2*. Thus, 3-(2-isothiocyanatophenyl)prop-2-enoates **1b** and **1c** were treated with $Na_2S \cdot 9\,H_2O$ in DMF at room temperature to generate the corresponding sodium dithiocarbamate

Scheme 2



intermediates **4**, which underwent cyclization in the same manner as that mentioned above at the same temperature. These reactive intermediates **5** were allowed to react with an equimolar amount of alkyl or aryl halides at the same temperature. The usual aqueous workup and subsequent purification by column chromatography on silica gel afforded the desired products **3**. The results are compiled in *Table 2*, which indicates that the yields are generally fair-to-good. It can be seen from *Entries 8* and *9* that 3-(2-isothiocyanatophenyl)-*N,N*-dimethylpropenamide (**1d**) also provided the corresponding benzothiazine products. Moreover, we found that 2-(2-thioxo-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives **6** were obtained, when the reactions of the 2-[2-(sodiosulfanyl)-4*H*-3,1-benzothiazin-4-yl]acetic acid intermediates **5** were quenched with an aqueous acidic solution, as shown in *Scheme 2* as well. Preparation of products **3**

Table 2. *Preparation of 2-(2-Sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetic Acid Derivatives* **3** via **4** *and* **5**

Entry	**1**	R^2X	**3**	Yield[a]) [%]
1	**1b** (R^1 = H, Y = *t*-BuO)	MeI	**3j**	72
2	**1b**	BnBr	**3e**	74
3	**1b**	$BrCH_2CN$	**3k**	77
4	**1c** (R^1 = Cl, Y = *t*-BuO)	EtBr	**3l**	65
5	**1c**	4-NO_2–$C_6H_4CH_2Br$	**3m**	59
6	**1c**	4-CN–$C_6H_4CH_2Br$	**3n**	57
7	**1c**	$PhCOCH_2Br$	**3o**	52
8	**1d** (R^1 = H, Y = Me_2N)	CH_2=$CHCH_2Br$	**3p**	60
9	**1d**	2,4-$(NO_2)_2$–C_6H_3F	**3q**	64

[a]) Yields of isolated products.

or **6** carrying a COOMe function was attempted under the same conditions. However, each of the reactions resulted in the formation of an intractable mixture of products. This may be ascribed to the sensitivity of the COOMe function to saponification.

In conclusion, we have demonstrated that 2-(2-sulfanyl-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives **3** could be efficiently prepared by one-pot addition/cyclization sequences between 3-(2-isothiocyanatophenyl)prop-2-enoic acid derivatives **1**, and thiols or Na_2S. The procedure with Na_2S has been applied to the synthesis of 2-(2-thioxo-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives **6**. Notable advantages of all of the present syntheses are: *i*) simplicity of the procedure, *ii*) mild reaction conditions, and *iii*) easy availability of the starting materials.

Experimental Part

General. All of the org. solvents were dried on appropriate drying agents and distilled prior to use. All chemicals were commercially available. TLC: *Merck Kieselgel 60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E*. M.p.: *Laboratory Devices MEL-TEMP II* melting-point apparatus; uncorrected. IR Spectra: *Shimadzu FTIR-8300* spectrophotometer. ^{1}H- and ^{13}C-NMR spectra: *JEOL ECP500* FT NMR spectrometer, at 500 (^{1}H) and 125 (^{13}C) MHz; TMS as an internal reference. Low-resolution (LR) MS spectra (EI; 70 eV): *JEOL JMS AX505 HA* spectrometer.

*(*E*)-3-(2-Isothiocyanatophenyl)prop-2-enoates* **1** were prepared from the corresponding *N*-(2-iodophenyl)formamides, according to the procedure reported by us in [3]. The physical, spectral, and anal. data for the new compounds are given below.

tert-*Butyl (2*E*)-3-[5-Chloro-2-(formylamino)phenyl]prop-2-enoate.* Yield: 78%. White solid. M.p. 154–155° (hexane/CH_2Cl_2). IR (KBr): 3231, 1707, 1665, 1632. ^{1}H-NMR ($CDCl_3$): 1.53 (*s*, 9 H); 6.34–6.38 (*m*, 1 H); 7.14–8.49 (*m*, 6 H). Anal. calc. for $C_{14}H_{16}ClNO_3$ (281.73): C 59.68, H 5.72, N 4.97; found: C 59.65, H 5.76, N, 5.01.

tert-*Butyl (2*E*)-3-(5-Chloro-2-isocyanatophenyl)prop-2-enoate*. Yield: 73%. White solid. M.p. 105–107° (hexane/Et_2O). IR (KBr): 2128, 1703, 1626. ^{1}H-NMR ($CDCl_3$): 1.54 (*s*, 9 H); 6.47 (*d*, *J* = 15.6, 1 H); 7.36–7.37 (*m*, 2 H); 7.63 (*d*, *J* = 0.9, 1 H); 7.80 (*d*, *J* = 15.6, 1 H). Anal. calc. for $C_{14}H_{14}ClNO_2$ (263.72): C 63.76, H 5.35, N 5.31; found: C 63.65, H 5.36, N 5.05.

tert-*Butyl (2*E*)-3-(5-Chloro-2-isothiocyanatophenyl)prop-2-enoate* (**1c**). Yield: 95%. Pale-yellow crystal. M.p. 55–56° (hexane). IR (KBr): 2074, 1709, 1638. ^{1}H-NMR ($CDCl_3$): 1.55 (*s*, 9 H); 6.40 (*d*, *J* = 16.0, 1 H); 7.24 (*d*, *J* = 8.7, 1 H); 7.31 (*dd*, *J* = 8.7, 2.3, 1 H); 7.56 (*d*, *J* = 2.3, 1 H); 7.76 (*d*, *J* = 16.0, 1 H). Anal. calc. for $C_{14}H_{14}ClNO_2S$ (295.78): C 56.85, H 4.77, N 4.74; found: C 56.63, H 4.81, N 4.52.

*Methyl {2-[(2-Hydroxyethyl)sulfanyl]-4*H*-3,1-benzothiazin-4-yl}acetate* (**3a**; *Typical Procedure*). A mixture of **1a** (0.14 g, 0.64 mmol), $HSCH_2CH_2OH$ (0.10 g, 1.28 mmol), and Et_3N (65 mg, 0.64 mmol) in THF (3 ml) was stirred at r.t. for 5 h, then sat. aq. $NaHCO_3$ (10 ml) was added. The org. materials were extracted with AcOEt (3 × 10 ml), and the combined extracts were washed with brine (10 ml), dried (anh. Na_2SO_4), and concentrated by evaporation. The residue was purified by CC (SiO_2; AcOEt/hexane, 1:2) to afford **3a** (0.14 g, 75%). White solid. M.p. 135–137° (hexane/CH_2Cl_2). IR (KBr): 3387, 1734, 1537. ^{1}H-NMR ($CDCl_3$): 2.64 (*dd*, *J* = 16.0, 6.4, 1 H); 2.74 (*dd*, *J* = 16.0, 8.7, 1 H); 3.16–3.20 (*m*, 1 H); 3.46–3.51 (*m*, 1 H); 3.68 (*s*, 3 H); 3.88–3.93 (*m*, 1 H); 4.08–4.14 (*m*, 1 H); 4.49 (*dd*, *J* = 8.7, 6.4, 1 H); 4.80 (*dd*, *J* = 6.4, 4.1, 1 H); 7.18 (*dd*, *J* = 7.8, 1.4, 1 H); 7.25 (*td*, *J* = 7.8, 1.4, 1 H); 7.32 (*dd*, *J* = 7.8, 1.4, 1 H); 7.36 (*td*, *J* = 7.8, 1.4, 1 H). ^{13}C-NMR ($CDCl_3$): 36.27; 40.14; 41.07; 51.97; 63.12; 122.86; 125.81; 126.87; 127.41; 128.97; 141.99; 161.31; 170.32. MS: 297 (80, M^+), 224 (100). Anal. calc. for $C_{13}H_{15}NO_3S_2$ (297.39): C 52.50, H 5.08, N 4.71; found: C 52.45, H 5.35, N 4.69.

*Methyl [2-(Phenylsulfanyl)-4*H*-3,1-benzothiazin-4-yl]acetate* (**3b**). Colorless oil. R_f (THF/hexane 1:5) 0.41. IR (neat): 1738, 1539. ^{1}H-NMR ($CDCl_3$): 2.64 (*dd*, *J* = 16.0, 6.4, 1 H); 2.70 (*dd*, *J* = 16.0, 8.7, 1 H); 3.65 (*s*, 3 H); 4.46 (*dd*, *J* = 8.7, 6.4, 1 H); 7.13 (*d*, *J* = 7.3, 1 H); 7.18 (*d*, *J* = 7.3, 1 H); 7.21 (*t*, *J* = 7.3, 1 H); 7.30 (*t*, *J* = 7.3, 1 H); 7.39–7.44 (*m*, 3 H); 7.62–7.63 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 40.27; 41.21; 51.90; 122.39; 126.49; 126.61; 127.25; 128.46; 129.05; 129.38; 129.51; 135.11; 142.79; 159.89; 170.35. MS: 329 (82,

M^+), 256 (100). Anal. calc. for $C_{17}H_{15}NO_2S_2$ (329.44): C 61.98, H 4.59, N 4.25; found: C 62.05, H 4.54, N 4.30.

*Methyl {2-[(4-Chlorophenyl)sulfanyl]-4*H*-3,1-benzothiazin-4-yl}acetate* (**3c**). Colorless crystals. M.p. 115–117° (hexane/Et_2O). IR (KBr): 1738, 1541. ^{1}H-NMR ($CDCl_3$): 2.62 (*dd*, *J* = 16.0, 6.4, 1 H); 2.71 (*dd*, *J* = 16.0, 8.7, 1 H); 3.66 (*s*, 3 H); 4.47 (*dd*, *J* = 8.7, 6.4, 1 H); 7.14 (*dd*, *J* = 7.8, 1.4, 1 H); 7.18 (*dd*, *J* = 7.8, 1.4, 1 H); 7.22 (*td*, *J* = 7.8, 1.4, 1 H); 7.31 (*td*, *J* = 7.8, 1.4, 1 H); 7.39 (*d*, *J* = 8.2, 2 H); 7.55 (*d*, *J* = 8.2, 2 H). ^{13}C-NMR ($CDCl_3$): 40.30; 41.21; 51.91; 122.37; 126.19; 126.64; 127.42; 127.87; 128.83; 129.25; 135.90; 136.23; 142.62; 158.89; 170.26. MS: 363 (79, M^+), 290 (100). Anal. calc. for $C_{17}H_{14}ClNO_2S_2$ (363.88): C 56.11, H 3.88, N 3.85; found: C 55.82, H 3.92, N 3.63.

tert-*Butyl [2-(Hexylsulfanyl)-4*H*-3,1-benzothiazin-4-yl]acetate* (**3d**). Pale-yellow oil. R_f (Et_2O/hexane 1:10) 0.58. IR (neat): 1730, 1537. ^{1}H-NMR ($CDCl_3$): 0.90 (distorted *t*, *J* = 7.3, 3 H); 1.31–1.33 (*m*, 5 H); 1.40–1.44 (*m*, including *s* at 1.41, 10 H); 1.68–1.75 (*m*, 2 H); 2.58 (*dd*, *J* = 16.0, 6.8, 1 H); 2.66 (*dd*, *J* = 16.0, 8.2, 1 H); 3.11 (*dt*, *J* = 13.4, 7.3, 1 H); 3.37 (*dt*, *J* = 13.4, 7.3, 1 H); 4.38 (*dd*, *J* = 8.2, 6.8, 1 H); 7.16 (*dd*, *J* = 7.3, 1.4, 1 H); 7.19 (*td*, *J* = 7.3, 1.4, 1 H); 7.28 (*dd*, *J* = 7.3, 1.4, 1 H); 7.33 (*td*, *J* = 7.3, 1.4, 1 H). ^{13}C-NMR ($CDCl_3$: 14.00; 22.49; 28.04; 28.47; 29.23; 31.29; 31.47; 40.34; 42.39; 81.37; 123.17; 123.97: 126.03; 126.53; 126.81; 128.59; 158.6; 169.25. MS: 379 (29, M^+), 323 (81), 264 (100). Anal. calc. for $C_{20}H_{29}NO_2S_2$ (379.58): C 63.28, H 7.70, N 3.69; found: C 63.04, H 7.74, N 3.58.

tert-*Butyl {2-[(Phenylmethyl)sulfanyl]-4*H*-3,1-benzothiazin-4-yl}acetate* (**3e**). White solid. M.p. 55–58° (hexane). IR (KBr): 1728, 1537. ^{1}H-NMR ($CDCl_3$): 1.41 (*s*, 9 H); 2.56 (*dd*, *J* = 15.6, 6.8, 1 H); 2.61 (*dd*, *J* = 15.6, 8.2, 1 H); 4.37–4.42 (*m*, 2 H); 4.63 (*d*, *J* = 13.3, 1 H); 7.16 (*d*, *J* = 7.3, 1 H); 7.19–7.25 (*m*, 2 H); 7.31 (*t*, *J* = 7.3, 2 H); 7.34–7.35 (*m*, 2 H); 7.41 (*d*, *J* = 7.3, 2 H). ^{13}C-NMR ($CDCl_3$): 28.04; 35.61; 40.39; 42.43; 81.44; 123.21; 126.07; 126.74; 126.86; 127.32; 128.58; 128.69; 129.14; 137.11; 142.59; 157.98; 169.19. MS: 385 (28, M^+), 329 (80), 270 (100). Anal. calc. for $C_{21}H_{23}NO_2S_2$ (385.54): C 65.42, H 6.01, N 3.63; found: C 65.27, H 6.02, N 3.79.

tert-*Butyl {2-[(*tert-*Butyl)sulfanyl]-4*H*-3,1-benzothiazin-4-yl}acetate* (**3f**). Colorless oil. R_f (Et_2O/hexane 1:14) 0.46. IR (neat): 1730, 1537. ^{1}H-NMR ($CDCl_3$): 1.41 (*s*, 9 H); 1.62 (*s*, 9 H); 2.55 (*dd*, *J* = 16.0, 7.3, 1 H); 2.78 (*dd*, *J* = 16.0, 7.8, 1 H); 4.57 (*dd*, *J* = 7.8, 7.3, 1 H); 7.15 (*dd*, *J* = 7.8, 1.4, 1 H); 7.20 (*td*, *J* = 7.8, 2.3, 1 H), 7.30–7.35 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 8.92; 28.05; 30.68; 40.59; 42.30; 51.15; 81.35; 126.09; 126.68; 126.93; 128.48; 157.82; 168.94; 178.85. MS: 351 (23, M^+), 295 (31), 239 (76), 180 (100). Anal. calc. for $C_{18}H_{25}NO_2S_2$ (351.53): C 61.50, H 7.17, N 3.98; found: C 61.45, H 7.30, N 3.96.

tert-*Butyl [2-(Phenylsulfanyl)-4*H*-3,1-benzothiazin-4-yl]acetate* (**3g**). White solid. M.p. 70–72° (hexane). IR (KBr): 1728, 1541. ^{1}H-NMR ($CDCl_3$): 1.39 (*s*, 9 H); 2.57 (*dd*, *J* = 15.6, 6.9, 1 H); 2.61 (*dd*, *J* = 15.6, 8.2, 1 H); 4.64 (*dd*, *J* = 8.2, 6.9, 1 H); 7.13 (*dd*, *J* = 7.3, 1.4, 1 H); 7.18 (*dd*, *J* = 7.3, 1.8, 1 H); 7.20 (*td*, *J* = 7.3, 1.4, 1 H); 7.29 (*td*, *J* = 7.3, 1.8, 1 H); 7.40–7.43 (*m*, 3 H); 7.62–7.64 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 28.03; 40.55; 42.61; 81.40; 122.53; 126.42; 126.69; 127.10; 128.62; 129.08; 129.31; 129.51; 135.16; 142.83; 160.16; 169.03. MS: 371 (29, M^+), 315 (77), 256 (100). Anal. calc. for $C_{20}H_{21}NO_2S_2$ (371.52): C 64.66, H 5.70, N 3.77; found: C 64.52, H 5.70, N 3.69.

tert-*Butyl {6-Chloro-2-[(4-methylphenyl)sulfanyl]-4*H*-3,1-benzothiazin-4-yl}acetate* (**3h**). White solid. M.p. 117–118° (hexane). IR (KBr): 1721, 1526. ^{1}H-NMR ($CDCl_3$): 1.39 (*s*, 9 H); 2.40 (*s*, 3 H); 2.54 (*dd*, *J* = 15.6, 7.3, 1 H); 2.57 (*dd*, *J* = 15.6, 8.2, 1 H); 4.34 (*dd*, *J* = 8.2, 7.3, 1 H); 7.12 (*d*, *J* = 8.7, 1 H); 7.13 (*d*, *J* = 2.3, 1 H); 7.22 (*d*, *J* = 8.2, 2 H); 7.25 (*dd*, *J* = 8.7, 2.3, 1 H); 7.49 (*d*, *J* = 8.2, 2 H). ^{13}C-NMR ($CDCl_3$) 21.36; 24.98; 40.11; 42.46; 81.64; 123.84; 125.27; 126.66; 127.68; 128.62; 129.94; 131.79; 135.37; 140.13; 141.46; 161.63; 168.67. MS: 419 (25, M^+), 363 (75), 304 (100). Anal. calc. for $C_{21}H_{22}ClNO_2S_2$ (419.99): C 60.06, H 5.28, N 3.34; found: C 60.07, H 5.38, N 3.22.

tert-*Butyl {6-Chloro-2-[(naphthalen-2-yl)sulfanyl]-4*H*-3,1-benzothiazin-4-yl}acetate* (**3i**). Colorless crystals. M.p. 131–132° (hexane/Et_2O). IR (KBr): 1722, 1537. ^{1}H-NMR ($CDCl_3$): 1.36 (*s*, 9 H); 2.56 (*dd*, *J* = 15.6, 7.3, 1 H); 2.62 (*dd*, *J* = 15.6, 7.8, 1 H); 4.36 (*dd*, *J* = 7.8, 7.3, 1 H); 7.08 (*d*, *J* = 8.7, 1 H); 7.14 (*d*, *J* = 2.3, 1 H); 7.24 (*dd*, *J* = 8.7, 2.3, 1 H); 7.53 (*td*, *J* = 6.9, 1.4, 1 H), 7.56 (*td*, *J* = 6.9, 1.4, 1 H), 7.62 (*dd*, *J* = 8.2, 1.4, 1 H), 7.85–7.88 (*m*, 3 H), 8.15 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 27.97; 40.20; 42.33; 81.70; 123.92; 126.36; 126.70 (two overlapped Cs); 127.36; 127.71; 127.77; 128.09; 128.67 (two overlapped Cs); 131.48; 131.95; 133.43; 133.47; 134.94; 141.39; 160.79; 168.63. MS: 455 (20, M^+), 399 (69), 340 (100). Anal. calc. for $C_{24}H_{22}ClNO_2S_2$ (456.02): C 63.21, H 4.86, N 3.07; found: C 63.35, H 4.86, N 3.04.

tert-*Butyl [2-(Methylsulfanyl)-4*H-*3,1-benzothiazin-4-yl]acetate* (**3j**; *Typical Procedure*). A mixture of **1b** (0.12 g, 0.45 mmol) and $Na_2S \cdot 9\ H_2O$ (0.11 g, 1.1 mmol) in DMF (3 ml) was stirred at r.t. for 30 min. The resulting mixture was then treated with MeI (64 mg, 0.45 mmol) and stirred for a further 5 min before sat. aq. NH_4Cl (10 ml) was added. The org. materials were extracted with AcOEt (3×10 ml), and the combined extracts were washed with brine (10 ml), dried (anh. Na_2SO_4), and concentrated by evaporation. The residue was purified by CC (SiO_2; Et_2O/hexane 1:10) to afford **3j** (0.10 g, 72%). White solid. M.p. 69–71° (hexane). IR (KBr): 1728, 1537. ^{1}H-NMR ($CDCl_3$): 1.41 (*s*, 9 H); 2.55 (*dd*, *J* = 15.6, 7.3, 1 H); 2.61 (*dd*, *J* = 15.6, 8.2, 1 H); 2.62 (*s*, 3 H), 4.40 (*dd*, *J* = 8.2, 7.3, 1 H); 7.16 (*dd*, *J* = 7.8, 1.4, 1 H); 7.19 (*td*, *J* = 7.8, 2.3, 1 H); 7.31 (*dd*, *J* = 7.8, 2.3, 1 H); 7.33 (*td*, *J* = 7.8, 1.4, 1 H). ^{13}C-NMR ($CDCl_3$): 14.39; 28.06; 40.34; 42.42; 81.41; 123.17; 126.10; 126.60; 126.82; 128.65; 142.65; 159.01; 169.22. MS: 309 (17, M^+), 253 (68), 194 (100). Anal. calc. for $C_{15}H_{19}NO_2S_2$ (309.45): C 58.22, H 6.19, N 4.53; found: C 58.17, H 6.34, N 4.44.

tert-*Butyl {2-[(Cyanomethyl)sulfanyl]-4*H-*3,1-benzothiazin-4-yl}acetate* (**3k**). Pale-yellow oil. R_f (Et_2O/hexane 1:3) 0.29. IR (neat): 2249, 1726, 1545. ^{1}H-NMR ($CDCl_3$): 1.42 (*s*, 9 H); 2.57 (*dd*, *J* = 16.0, 6.8, 1 H); 2.62 (*dd*, *J* = 16.0, 8.7, 1 H); 3.91 (*d*, *J* = 16.5, 1 H); 4.17 (*d*, *J* = 16.5, 1 H); 4.47 (*dd*, *J* = 8.7, 6.8, 1 H); 7.18 (*d*, *J* = 7.3, 1 H); 7.24–7.28 (*m*, 1 H); 7.37–7.38 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 16.02; 28.05; 40.58; 42.46; 81.71; 115.90; 122.79; 126.45; 126.82; 127.66; 129.03; 141.85; 168.89; 172.75. MS: 334 (20, M^+), 278 (69), 219 (100). Anal. calc. for $C_{16}H_{18}N_2O_2S_2$ (334.46): C 57.46, H 5.42, N 8.38; found: C 57.31, H 5.59, N 8.19.

tert-*Butyl [6-Chloro-2-(ethylsulfanyl)-4*H-*3,1-benzothiazin-4-yl]acetate* (**3l**). Pale-yellow oil. R_f (Et_2O/hexane 1:10) 0.38. IR (neat): 1728, 1535. ^{1}H-NMR ($CDCl_3$): 1.38 (*t*, *J* = 7.3, 3 H); 1.42 (*s*, 9 H); 2.54 (*dd*, *J* = 15.6, 7.3, 1 H); 2.60 (*dd*, *J* = 15.6, 7.8, 1 H); 3.08–3.16 (*m*, 1 H); 3.31–3.38 (*m*, 1 H); 4.34 (*dd*, *J* = 7.8, 7.3, 1 H); 7.16 (*d*, *J* = 2.3, 1 H); 7.22 (*d*, *J* = 8.2, 1 H); 7.29 (*dd*, *J* = 8.2, 2.3, 1 H). ^{13}C-NMR ($CDCl_3$): 14.43; 26.05; 28.03; 39.95; 42.24; 81.69; 124.46; 126.79; 127.35; 128.64; 131.38; 141.26; 157.54; 168.86. MS: 357 (19, M^+), 301 (72), 242 (100). Anal. calc. for $C_{16}H_{20}ClNO_2S_2$ (357.92): C 53.69, H 5.63, N 3.91; found: C 53.63, H 5.85, N 3.94.

tert-*Butyl (6-Chloro-2-{[(4-nitrophenyl)methyl]sulfanyl}-4*H-*3,1-benzothiazin-4-yl)acetate* (**3m**). Pale-yellow needle. M.p. 103–104° (hexane/Et_2O). IR (KBr): 1724, 1599, 1520, 1344. ^{1}H-NMR ($CDCl_3$): 1.42 (*s*, 9 H); 2.54 (*dd*, *J* = 15.6, 7.3, 1 H); 2.94 (*dd*, *J* = 15.6, 7.8, 1 H); 4.63 (*dd*, *J* = 7.8, 7.3, 1 H); 4.39 (*d*, *J* = 14.2, 1 H); 4.65 (*d*, *J* = 14.2, 1 H); 7.17 (*d*, *J* = 2.3, 1 H); 7.23 (*d*, *J* = 8.7, 1 H); 7.32 (*dd*, *J* = 8.7, 2.3, 1 H); 7.58 (*d*, *J* = 8.7, 2 H); 8.17 (*d*, *J* = 8.7, 2 H). ^{13}C-NMR ($CDCl_3$): 28.02; 34.66; 40.04; 42.30; 81.88; 123.79; 124.39; 126.93; 127.23; 128.88; 129.91; 132.01; 140.83; 145.11; 147.16; 157.63; 168.61. MS: 464 (20, M^+), 408 (75), 349 (100). Anal. calc. for $C_{21}H_{21}ClN_2O_4S_2$ (464.99): C 54.24, H 4.55, N 6.02; found: C 54.22, H 4.58, N 5.94.

tert-*Butyl (6-Chloro-2-{[(4-cyanophenyl)methyl]sulfanyl}-4*H-*3,1-benzothiazin-4-yl)acetate* (**3n**). Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.29. IR (neat): 2230, 1728, 1537. ^{1}H-NMR ($CDCl_3$): 1.42 (*s*, 9 H); 2.54 (*dd*, *J* = 15.6, 7.3, 1 H); 2.58 (*dd*, *J* = 15.6, 7.8, 1 H); 4.35 (*d*, *J* = 14.2, 1 H); 4.36 (*dd*, *J* = 7.8, 7.3, 1 H); 4.62 (*d*, *J* = 14.2, 1 H); 7.17 (*d*, *J* = 2.3, 1 H); 7.22 (*d*, *J* = 8.7, 1 H); 7.32 (*dd*, *J* = 8.7, 2.3, 1 H); 7.51 (*d*, *J* = 8.2, 2 H); 7.60 (*d*, *J* = 8.2, 2 H). ^{13}C-NMR ($CDCl_3$): 28.03; 34.98; 40.04; 42.30; 81.87; 111.24; 118.63; 124.41; 126.92; 127.24; 128.86; 129.80; 131.97; 132.35; 140.86; 143.00; 157.76; 168.63. MS: 444 (24, M^+), 388 (75), 329 (100). Anal. calc. for $C_{22}H_{21}ClN_2O_2S_2$ (445.00): C 59.38, H 4.76, N 6.30; found: C 59.45, H 4.95, N 6.05.

tert-*Butyl {6-Chloro-2-[(2-oxo-2-phenylethyl)sulfanyl]-4*H-*3,1-benzothiazin-4-yl}acetate* (**3o**) Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.44. IR (neat): 1728, 1694, 1537. ^{1}H-NMR ($CDCl_3$): 1.42 (*s*, 9 H); 2.52 (*dd*, *J* = 16.0, 7.3, 1 H); 2.58 (*dd*, *J* = 16.0, 7.8, 1 H); 4.36 (*dd*, *J* = 7.8, 7.3, 1 H); 4.63 (*d*, *J* = 16.0, 1 H); 4.68 (*d*, *J* = 16.0, 1 H); 6.97 (*d*, *J* = 8.2, 1 H); 7.15 (*d*, *J* = 2.3, 1 H); 7.22 (*dd*, *J* = 8.2, 2.3, 1 H); 7.51 (*t*, *J* = 7.8, 2 H); 7.62 (*t*, *J* = 7.8, 1 H); 8.05 (*d*, *J* = 7.8, 2 H). ^{13}C-NMR ($CDCl_3$): 28.02; 38.11; 39.97; 42.30; 81.81; 124.34; 126.81; 127.18; 128.52; 128.71; 128.75; 131.75; 133.63; 135.95; 140.82; 157.85; 168.72; 193.43. MS: 447 (22, M^+), 391 (74), 332 (100). Anal. calc. for $C_{22}H_{22}ClNO_3S_2$ (448.00): C 58.98, H 4.95, N 3.13; found: C 58.88, H 5.04, N 3.12.

N,N-*Dimethyl-2-{2-[(prop-2-en-1-yl)sulfanyl]-4*H-*3,1-benzothiazin-4-yl}acetamide* (**3p**). Pale-yellow oil. R_f (AcOEt/hexane 1:3) 0.31. IR (neat): 1647, 1537. ^{1}H-NMR ($CDCl_3$): 2.57 (*dd*, *J* = 15.6, 6.0, 1 H); 2.76 (*dd*, *J* = 15.6, 8.6, 1 H); 2.80 (*s*, 3 H); 2.92 (*s*, 3 H), 3.74–3.78 (*m*, 1 H); 4.07 (*dd*, *J* = 13.8, 8.2,

1 H); 4.63 (*dd*, *J* = 8.6, 6.0, 1 H); 5.14 (*dd*, *J* = 10.0, 1.4, 1 H); 5.29 – 5.33 (*m*, 1 H); 5.91 – 5.99 (*m*, 1 H); 7.19 (*dd*, *J* = 7.8, 2.3, 1 H); 7.22 (*td*, *J* = 7.8, 1.4, 1 H); 7.30 (*dd*, *J* = 7.8, 1.4, 1 H); 7.34 (*td*, *J* = 7.8, 2.3, 1 H). ^{13}C-NMR ($CDCl_3$): 31.32; 35.51; 37.17; 39.77; 40.73; 118.39; 123.58; 125.97; 126.94; 127.08; 128.59; 133.03; 142.68; 158.56; 169.17. MS: 306 (100, M^+). Anal. calc. for $C_{15}H_{18}N_2OS_2$ (306.45): C 58.79, H 5.92, N 9.14; found: C 58.77, H 6.01, N 9.02.

*2-[2-[(2,4-Dinitrophenyl)sulfanyl]-4*H-*3,1-benzothiazin-4-yl]*-N,N-*dimethylacetamide* (**3q**). Yellow solid. M.p. 194 – 196° (hexane/AcOEt). IR (KBr): 1643, 1593, 1524, 1333. ^{1}H-NMR ((D_6)DMSO): 2.64 (*dd*, *J* = 16.4, 5.0, 1 H); 2.80 – 2.85 (*m* including *s* at 2.80 and *s* at 2.83, 7 H); 2.84 (*dd*, *J* = 9.1, 5.0, 1 H); 7.12 (*d*, *J* = 7.3, 1 H); 7.32 – 7.39 (*m*, 3 H); 8.22 (*d*, *J* = 8.7, 1 H); 8.51 (*dd*, *J* = 8.7, 2.7, 1 H); 8.88 (*d*, *J* = 2.7, 1 H). ^{13}C-NMR: ((D_6)DMSO): 34.94; 36.46; 39.61; 40.42; 120.84; 123.20; 126.09; 127.41; 127.73; 128.57; 128.75; 134.30; 135.62; 146.92; 148.54; 155.47; 165.83; 168.12. MS: 432 (100, M^+). Anal. calc. for $C_{18}H_{16}N_4O_5S_2$ (432.47): C 49.99, H 3.73, N 12.95; found: C 49.91, H 4.03, N 13.04.

Omission of the addition of halides before aqueous workup in the procedure for the preparation of **3** afforded 2-(2-thioxo-4*H*-3,1-benzothiazin-4-yl)acetic acid derivatives **6**.

tert-*Butyl (1,4-Dihydro-2-thioxo-2*H-*3,1-benzothiazin-4-yl)acetate* (**6a**). Yellow solid. M.p. 136 – 138° (hexane/Et_2O). IR (KBr): 3130, 1721, 1150. ^{1}H-NMR ($CDCl_3$): 1.42 (*s*, 9 H); 2.70 (*dd*, *J* = 16.0, 7.3, 1 H); 2.85 (*dd*, *J* = 16.0, 7.8, 1 H); 4.42 (*dd*, *J* = 7.8, 7.3, 1 H); 7.02 (*d*, *J* = 7.8, 1 H); 7.18 (*t*, *J* = 7.8, 1 H); 7.26 (*d*, *J* = 7.8, 1 H); 7.32 (*t*, *J* = 7.8, 1 H); 10.18 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 28.01; 42.30; 43.54; 81.92; 117.23; 121.92; 125.77; 127.71; 129.07; 135.97; 168.77; 193.02. MS: 295 (20, M^+), 239 (72), 180 (100). Anal. calc. for $C_{14}H_{17}NO_2S_2$ (295.42): C 56.92, H 5.80, N 4.74; found: C 56.81, H 5.82, N 4.74.

*2-(1,4-Dihydro-2-thioxo-2*H-*3,1-benzothiazin-4-yl)*-N,N-*dimethylacetamide* (**6b**). Pale-yellow solid. M.p. 173 – 174° (hexane/CH_3Cl). IR (KBr): 3153, 1628, 1148. ^{1}H-NMR ($CDCl_3$): 2.71 (*dd*, *J* = 16.0, 6.0, 1 H); 2.86 (*s*, 3 H); 2.95 (*s*, 3 H); 2.99 (*dd*, *J* = 16.0, 8.7, 1 H); 4.67 (*dd*, *J* = 8.7, 6.0, 1 H); 6.99 (*d*, *J* = 7.3, 1 H); 7.18 (*t*, *J* = 7.3, 1 H); 7.32 (*t*, *J* = 7.3, 1 H); 7.33 (*d*, *J* = 7.3, 1 H); 9.87 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 35.64; 37.12; 41.40; 42.66; 117.23; 122.33; 125.90; 128.00; 128.93; 136.15; 168.80; 193.47. MS: 266 (100, M^+). Anal. calc. for $C_{12}H_{14}N_2OS_2$ (266.38): C 54.11, H 5.30, N 10.52; found: C 53.97, H 5.57, N 10.32.

tert-*Butyl (6-Chloro-1,4-dihydro-2-thioxo-2*H-*3,1-benzothiazin-4-yl)acetate* (**6c**). Pale-yellow solid. M.p. 126 – 128° (hexane/Et_2O). IR (KBr): 3154, 1726, 1150. ^{1}H-NMR ($CDCl_3$): 1.43 (*s*, 9 H); 2.70 (*dd*, *J* = 16.0, 7.8, 1 H); 2.84 (*dd*, *J* = 16.0, 7.8, 1 H); 4.38 (*t*, *J* = 7.8, 1 H); 6.98 (*d*, *J* = 8.2, 1 H); 7.27 (*d*, *J* = 2.3, 1 H); 7.29 (*dd*, *J* = 8.2, 2.3 Hz, 1 H); 10.17 (*s*, 1 H); ^{13}C-NMR ($CDCl_3$): 28.00; 42.01; 43.33; 82.26; 118.40; 123.53; 127.74; 129.09; 130.67; 134.59; 168.43; 192.70. MS: 329 (20, M^+), 273 (72), 214 (100). Anal. calc. for $C_{14}H_{16}ClNO_2S_2$ (329.87): C 50.98, H 4.89, N 4.25; found: C 50.94, H 5.03, N 4.13.

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