Novel Synthesis of Benzothiazole Derivatives *via* Directed Lithiation and Aryne-Mediated Cyclization Followed by Quenching with Electrophiles

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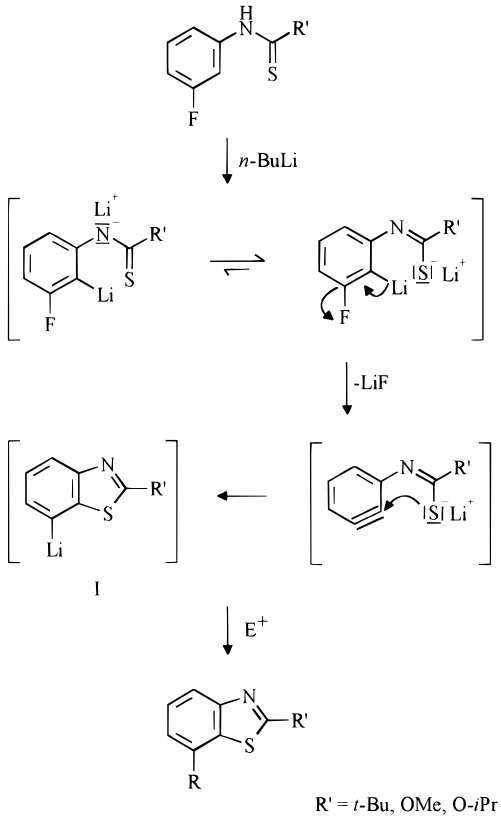
A series of benzothiazole derivatives selectively functionalized at position 7 was synthesized in the course of the following one-pot reaction sequence: directed lithiation of 2,2-dimethyl-*N*-(3-halophenyl)propanethioamides (**1**, **2**) or *N*-(3-halophenyl)-*tert*-butylthionocarbamates (**15**−**17**), cyclization of the aryne intermediate, and quenching of the resulting aryllithium with selected electrophiles.

The strategy of intramolecular trapping of benzyne intermediates with adjacent side chain nucleophiles proves to be very useful for the synthesis of various benzo-fused heterocyclic systems. In the late 1950s and early 1960s, Huisgen[1] and Bunnett[2] published first applications of this concept where the benzyne was generated with phenyllithium, sodium or potassium amide, sodium hydride, or lithium diethylamide, respectively. Although many useful applications of this reaction sequence were reviewed by Kessar,[3] only one single example[4] was mentioned where the organometallic intermediate generated in the course of the cyclization step was quenched with electrophiles other than H^+, thus allowing the regioselective introduction of an additional substituent. In 1982 Clark and Caroon[5] reported a useful extension of the scope of this methodology: *N*-Pivaloyl- and *N*-*t*-BOC-3-fluoroaniline were treated with BuLi, the benzyne intermediate was trapped in an intramolecular cyclization step, and subsequent quenching of the generated organolithium compound with various electrophiles led to a series of 7-substituted benzoxazole derivatives. Following this sequence, various 1,2,3-substituted benzenes were available *via* hydrolysis of the obtained benzoxazole precursors. Reavill and Richardson[6] published an extension of this method to the more affordable derivatives of 3-chloroaniline. A more recent example of an intramolecular cyclization *via* an aryne is the synthesis of 7-substituted indolines derived from (2-phenethyl)formamidines.[7]

The present paper reports the synthesis of benzothiazole derivatives, selectively functionalized in the 7-position, obtained simply by adaptation of the method of Clark and Caroon[5] to the corresponding thio derivatives (thioamides and thiourethanes). Although to our knowledge thiocarbonylamino functionalities have not been described so far as *ortho* directing groups, according to the general experience in this field they should be able to support *ortho* metalation.[8] The additional *ortho* activating effect of the halogen should direct the lithiation exclusively to the 2-position, initiating the expected reaction sequence shown in Scheme 1.

Scheme 1



The conversion of *N*-(3-fluorophenyl)-2,2-dimethylpropanamide to the corresponding thioamide **1** was achieved using Lawesson reagent in 60% yield. Treating **1** with an excess of *n*-BuLi (2.8 equiv) in THF at −80 °C, gradual warming to room temperature, and quenching of the lithio species **I** with selected electrophiles led to a series of 7-substituted 2-*tert*-butylbenzothiazoles **5**, **6**, **8**−**12**. Although no efforts were undertaken to optimize the reaction conditions the expected products were obtained in good yields (47−81%) when selected electrophiles (MeI, Me_2S_2, *t*-BuNCO, CO_2, cyclohexanone, and

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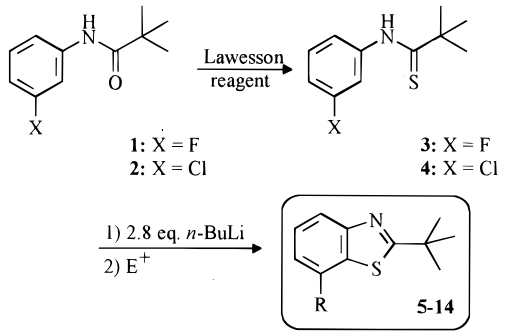
Scheme 2



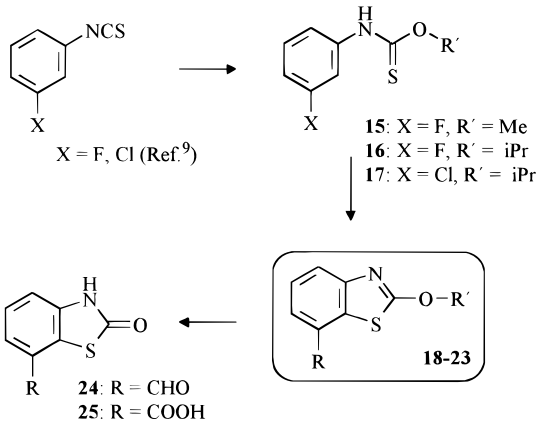
			yield (%)	
E	R		X = F	X = Cl
MeI	Me	**5**	62	
MeS_2	MeS	**6**	80	
DPPA	NH_2	**7**		33
t-BuNCO	CONH*t*-Bu	**8**	76	61
CO_2	COOH	**9**	77	81
PhCN	PhCO	**10**	66	
DMF	CHO	**11**	84	63
Cyclohexanone	$C_6H_{10}OH$	**12**	44	47
$(CH_3O)_3B$	OH	**13**		66
$[HCOH]_n$	CH_2OH	**14**		41

DMF) were applied, with only cyclohexanone giving unexpectedly poor results. The carbinol **14** was obtained in moderate yields when paraformaldehyde was used as the electrophile in the cyclization sequence or *via* reduction of the aldehyde **11**.

Reavill and Richardson[6] reported the synthesis of various benzoxazole-7-carboxylic acids starting with substituted *N*-(3-chlorophenyl)-2,2-dimethylpropanamides and *t*-BOC-anilines followed by quenching of the intermediates with CO_2 (yields: 30−53%). For comparison, the same sequence was carried out on the *N*-(3-chlorophenyl)-2,2-dimethylpropanethioamide **4**. Treatment of **4** with *n*-BuLi under the same reaction conditions as for the 3-fluoro compound **3** led to the corresponding benzothiazoles (**7**−**9**, **11**−**14**) with comparable yields; no difference in the applicability between **3** and **4** was recognized. The results are summarized in Scheme 2.

In continuation of our study, we extended the scope of this sequence to the thiocarbamate moiety, making some 2-alkoxybenzothiazoles available. No reports were found in the literature for the conversion of the carbamate moiety to its thio analog with Lawesson reagent, and our own experiments also showed disappointing results. Therefore the 3-haloanilines were first converted to the corresponding isothiocyanates (ref 9) and subsequently treated with an alcohol to yield the thiocarbamates **15**−**17**. As is known from the literature,[10] *tert*-butyl alcohol reacts very slowly with isothiocyanates; therefore 2-propanol and methanol were used instead. Applying the same lithiation conditions as for the thioamides **3** and **4**,

Scheme 3



				yield (%)	
E	R	R′		X = F	X = Cl
DMF	CHO	Me	**18**	60	
DMF	CHO	*i*-Pr	**19**	71	70
CO_2	COOH	*i*-Pr	**20**	63	50
t-BuNCO	CONH*t*-Bu	*i*-Pr	**21**	55	
Me_2S_2	MeS	*i*-Pr	**22**	80	
$ClCONEt_2$	$CONEt_2$	*i*-Pr	**23**	25	

the methyl carbamate **15** gave no reaction while the isopropyl carbamate **16** yielded only 30% of the aldehyde expected after quenching with DMF. The yield was not improved when excess *n*-BuLi was used. When reaction conditions described for *N*-(*tert*-butoxycarbonyl)-*m*-fluoroaniline (ref 5)—*tert*-BuLi (2.8 equiv) −80 °C to −30 °C—were applied 2-alkoxybenzothiazoles, **18**−**23** were isolated in reasonable yields. Again no significant difference was observed in the reactive behavior between the corresponding fluoro and the chloro compounds (**16** *vs* **17**). In contrast to the corresponding benzoxazoles, which even under mild acidic workup conditions were hydrolyzed to yield benzoxazolones (ref 5), the corresponding 2-alkoxybenzothiazoles were rather stable compounds which could easily be isolated (Scheme 3). Under more vigorous acidic (2 M and 6 M H_2SO_4) or basic (10% NaOH or 50% KOH) conditions, **19** and **20** were converted to the benzothiazolones **24** and **25** which were extrordinary stable. Even using extremely rough hydrolytic conditions, we were not able to hydrolyze either these benzothiazolones or the 2-*tert*-butylbenzothiazoles to the corresponding 2-aminothiophenols.

Experimental Section

General. Melting points are uncorrected. The NMR spectra were recorded on a Bruker AC 200 FT-NMR-spectrometer. Microanalyses were obtained from the Institute of Physical Chemistry, University of Vienna.

2,2-Dimethyl-*N*-(3-fluorophenyl)propanamide (1) was prepared by reaction of 3-fluoroaniline and 2,2-dimethylpropanoyl chloride (1:1.1) in dry ether after addition of triethylamine at rt. The reaction mixture was washed with 2 M HCl and dried over Na_2SO_4 and the solvent evaporated: yield 98%; mp 112−114 °C (lit.[5] mp 100−101 °C).

***N*-(3-Chlorophenyl)-2,2-dimethylpropanamide (2)** was similarly prepared from 3-chloroaniline and 2,2-dimethylpropanoyl chloride: yield 98%; mp 131−134 °C (ref 11).

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2,2-Dimethyl-*N*-(3-fluorophenyl)propanethioamide (3). A solution of **1** (10.00 g, 51.21 mmol) and Lawesson reagent (11.39 g, 28.17 mmol) in 100 mL of dry toluene was refluxed for 24 h, the solvent evaporated, and the residue purified by flash chromatography (petroleum ether—ethyl acetate, 5:1) to give **3** (7.00 g, 65%) as pale yellow crystals after recrystallization from diisopropyl ether: mp 92−93 °C; ^{1}H-NMR ($CDCl_3$) δ 1.48 (s, 9H), 6.89−7.06 (m, 1H), 7.21−7.39 (m, 2H), 7.56−7.68 (m, 1H), 8.75 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ 30.1, 45.6, 111.9, 113.7, 119.9, 129.9, 140.2, 157.5, 213.7. Anal. Calcd for $C_{11}H_{14}FNS$: C, 62.53; H, 6.68; N, 6.63. Found: C, 62.48; H, 6.77; N, 6.52.

2,2-Dimethyl-*N*-(3-chlorophenyl)propanethioamide (4). A solution of **2** (50.00 g, 236.2 mmol) and Lawesson reagent (57.00 g, 141.0 mmol) in 500 mL of dry toluene was refluxed for 30 h and worked up as described for **3** to yield **4** (30.70 g, 57%) as pale yellow crystals from diisopropyl ether: mp 101−102 °C; ^{1}H-NMR ($CDCl_3$) δ 1.43 (s, 9H), 7.23 (dd, 1H), 7.33 (t, 1H), 7.48 (dd, 1H), 7.69 (ds, 1H); ^{13}C-NMR ($CDCl_3$) δ 30.1, 45.5, 123.1, 124.9, 126.9, 129.7, 134.0, 139.9, 213.9. Anal. Calcd for $C_{11}H_{14}ClNS$: C, 58.01; H, 6.20; N, 6.15. Found: C, 58.16; H, 6.02; N, 6.07.

Synthesis of Benzothiazoles *via* Lithiation of 3 and 4. General Procedure. A 5% solution of the thioamide **3** or **4**[12] (1 equiv) in dry THF was treated with *n*-BuLi (2.8 equiv 2.5 M solution in *n*-hexane) at −75 ± 5 °C. The mixture was allowed to warm to rt within 2 h, then cooled again to −65 ± 5 °C, and the electrophile (1.5 equiv) was added. At −20 °C the reaction mixture was treated with 2 M HCl or H_2O and extracted with ethyl acetate or ether, and the combined organic layers were dried over Na_2SO_4 and evaporated. The crude product was purified as described.

2-(1,1-Dimethylethyl)-7-methyl-1,3-benzothiazole (5): from **3**; electrophile, MeI; purification, flash chromatography (petroleum ether−ethyl acetate, 5:1); 62%; pale yellow liquid; bp 170−175 °C/0.4 mbar (kugelrohr distillation for analysis); ^{1}H-NMR ($CDCl_3$) δ 1.52 (s, 9H), 2.53 (s, 3H), 7.10 (d, 1H), 7.34 (t, 1H), 7.83 (d, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.3, 30.6, 38.2, 119.9, 124.5, 125.8, 131.4, 135.2, 153.0, 181.0. Anal. Calcd for $C_{12}H_{15}NS$: C, 70.20; H, 7.36; N, 6.82. Found: C, 70.45; H, 7.52; N, 6.59.

2-(1,1-Dimethylethyl)-7-(methylthio)-1,3-benzothiazole (6): from **3**; electrophile, Me_2S_2; purification, kugelrohr distillation; 80% yellow oil; bp 155−160 °C/0.53 mbar; ^{1}H-NMR ($CDCl_3$) δ 1.52 (s, 9H), 2.58 (s, 3H), 7.22 (d, 1H), 7.40 (t, 1H), 7.82 (dd, 1H); ^{13}C-NMR ($CDCl_3$) δ 16.5, 30.6, 38.3, 120.0, 122.7, 126.2, 131.0, 135.3, 152.7, 181.9. Anal. Calcd for $C_{12}H_{15}NS_2$: C, 60.72; H, 6.37; N, 5.90. Found: C, 61.18; H, 6.53; N; 5.85.

2-(1,1-Dimethylethyl)-1,3-benzothiazol-7-amine (7): from **4**; electrophile, $(PhO)_2PON_3$ (DPPA). The reaction mixture was kept at −65 ± 5 °C for 1.5 h and allowed to warm up to -20 °C during an additional 1.5 h. Red-Al (Aldrich) (10.80 g, 52.68 mmol, 3.4 M solution in toluene) was added at −80 °C. The mixture was stirred at −80 °C for 2 h and then quenched with ice water. The precipitate was filtered and washed with toluene and ether, the aqueous layer of the filtrate was extracted with ether, and the combined organic layers were dried over Na_2SO_4 and evaporated to dryness. The residue was kugelrohr distilled and recrystallized from petroleum ether to give **7**: yield 33% colorless crystals; mp 105−107 °C; ^{1}H-NMR ($CDCl_3$) δ 1.51 (s, 9H), 3.85 (bs, 2H), 6.64 (d, 1H), 7.25 (t, 1H), 7.48 (d, 1H); ^{13}C-NMR ($CDCl_3$) δ 30.7, 38.3, 109.7, 113.5, 121.7, 126.8, 140.6, 154.5, 180.7. Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.84; N, 13.58. Found: C, 64.33; H, 6.66; N, 13.40.

2-(1,1-Dimethylethyl)-*N*-(1′,1′-dimethylethyl)-1,3-benzothiazole-7-carboxamide (8): from **3**; electrophile, *t*-BuNCO; purification, recrystallization from diisopropyl ether; 76% colorless crystals; mp 177−178 °C; ^{1}H-NMR ($CDCl_3$) δ 1.51 (s, 9H), 1.53 (s, 9H), 6.25 (bs, 1H), 7.48 (t, 1H), 7.51 (dd, 1H), 8.10 (dd, 1H); ^{13}C-NMR ($CDCl_3$) δ 28.8, 30.5, 38.0, 51.9, 121.0, 125.1, 125.4, 128.4, 134.1, 154.5, 165.1, 185.9. Anal. Calcd for $C_{16}H_{22}N_2OS$: C, 66.17; H, 7.64; N, 9.65. Found: C, 66.05; H, 7.95; N, 9.59.

2-(1,1-Dimethylethyl)-1,3-benzothiazole-7-carboxylic acid (9): from **3**; electrophile, CO_2 gas; purification, recrystallization from diisopropyl ether−$CHCl_3$ (2:1); 77% yield as colorless crystals; mp 193−194 °C; ^{1}H-NMR (DMSO-d_6) δ 1.49 (s, 9H), 7.61 (t, 1H), 8.05 (d, 1H), 8.22 (d, 1H); ^{13}C-NMR (DMSO-d_6) δ 30.3, 37.8, 124.8, 126.0, 126.5, 126.9, 134.7, 153.7, 166.6, 184.0. Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 61.25; H, 5.57; N, 5.95. Found: C, 61.01; H, 5.57; N, 5.88.

7-Benzoyl-(1,1-dimethylethyl)-1,3-benzothiazole (10): from **3**; electrophile, PhCN; purification, flash chromatography (petroleum ether−ethyl acetate, 5:1) and subsequent recrystallization from petroleum ether; 66% yield as colorless crystals; mp 80−82 °C; ^{1}H-NMR ($CDCl_3$) δ 1.58 (s, 9H), 7.45−7.64 (m, 4H), 7.77−7.84 (m, 3H), 8.25 (d, 1H); ^{13}C-NMR ($CDCl_3$) δ 30.6, 38.2, 124.9, 127.3, 128.2, 129.2, 129.5, 130.1, 132.0, 135.1, 137.6, 154.6, 185.9, 195.1. Anal. Calcd for $C_{18}H_{17}NOS$: C, 73.19; H, 5.80; N, 4.75. Found: C, 72.92; H, 5.90; N, 5.00.

2-(1,1-Dimethylethyl)-1,3-benzothiazole-7-carboxaldehyde (11): From **3**; electrophile, DMF; purification, flash chromatography (petroleum ether−ethyl acetate, 5:1) and for analysis recrystallization from petroleum ether; 84% yield as colorless crystals; mp 75−76 °C; ^{1}H-NMR ($CDCl_3$) δ 1.53 (s, 9H,), 7.62 (t, 1H), 7.88 (d, 1H), 8.25 (d, 1H), 10.19 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 30.6, 38.2, 125.7, 128.5, 130.6, 130.5, 132.2, 154.6, 186.0, 190.5. Anal. Calcd for $C_{12}H_{13}NOS$: C, 65.72; H, 5.97; N, 6.39. Found: C, 65.63; H, 6.01; N, 6.29.

1-[2-(1,1-Dimethylethyl)-7-(1,3-benzothiazolyl)]cyclohexanol (12): from **3**; electrophile, cyclohexanone; purification, flash chromatography (petroleum ether− ethyl acetate, 5:1) and subsequent recrystallization from MeO-*tert*-Bu; 44% yield as colorless crystals; mp 119−119.5 °C; ^{1}H-NMR ($CDCl_3$) δ 1.50 (s, 9H), 1.61−2.05 (m, 11H), 7.30 (dd, 1H), 7.41 (t, 1H), 7.89 (dd, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.8, 25.4, 30.6, 37.1, 37.8, 73.9, 119.9, 121.4, 125.5, 130.7, 143.4, 154.5, 183.0. Anal. Calcd for $C_{17}H_{24}NOS$: C, 70.30; H, 8.33; N, 4.82. Found: C, 70.41; H, 8.13; N, 5.04.

2-(1,1-Dimethylethyl)-1,3-benzothiazol-7-ol (13): from **4**; $B(OMe)_3$ (0.5 mL) was added at −80 °C, the reaction mixture was stirred at 0 °C for 1 h. Glacial AcOH (1.19 mL) and H_2O_2 (2.98 mL, 30%) were added, and the solution was stirred overnight, quenched with H_2O, and acidified with 2 M HCl, followed by the usual workup: purification, flash chromatography (petroleum ether−ethyl acetate, 5:1); 66% yields as orange crystals; mp 154−156 °C; ^{1}H-NMR ($CDCl_3$) δ 1.53 (s, 9H), 6.79 (d, 1H), 7.24 (t, 1H), 7.54 (d, 1H), 8.83 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ 30.7, 38.7, 109.6, 113.8, 122.8, 127.2, 151.6, 154.4, 183.7. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.50; H, 7.52; N, 6.47.

2-(1,1-Dimethylethyl)-1,3-benzothiazole-7-methanol (14): from **4**; electrophile, paraformaldehyde; purification, flash chromatography (petroleum ether−ethyl acetate, 5:1) and subsequent kugelrohr distillation (150 °C/0.01 mbar) for analysis; 41% yield as colorless crystals; mp 139−140 °C; ^{1}H-NMR ($CDCl_3$) δ 1.56 (s, 9H), 2.30 (bs, 1H), 4.91 (s, 2H), 7.30 (d, 1H), 7.41 (t, 1H), 7.92 (d, 1H); ^{13}C-NMR ($CDCl_3$) δ 30.3, 37.8, 62.6, 120.5, 121.7, 125.5, 131.6, 136.3, 152.9, 181.5. Anal. Calcd for $C_{12}H_{15}NOS$: C, 65.12; H, 6.83; N, 6.33. Found: C, 65.26; H, 6.76; N, 6.56.

Synthesis of Thiocarbamates 15−17. General Procedure. A solution of the corresponding isothiocyanate and methanol (10 equiv) or 2-propanol (10 equiv) respectively—in the case of 2-propanol, 1 equiv of triethylamine was added—was refluxed for 12 h under N_2. The reaction mixture was concentrated, and the residual crude product was filtered and recrystallized.

***N*-(3-Fluorophenyl)thiocarbamic acid *O*-methyl ester (15):** 79% yield as colorless crystals; mp 60−61 °C (petroleum ether); ^{1}H-NMR ($CDCl_3$) δ 4.15 (s, 3H), 6.73−6.94 (m, 1H), 7.07 (bs, 1H), 7.15−7.35 (m, 2H), 8.90 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ 59.7, 109.1, 112.1, 116.8, 130.1, 138.4, 162.7, 189.1. Anal. Calcd for C_8H_8FNOS: C, 51.88; H, 4.35; N, 7.56. Found: C, 51.85; H, 4.16; N, 7.49.

(12) If the reaction was run with both educts yields are shown in Scheme 2.

***N*-(3-Fluorophenyl)carbamic acid *O*-(1-methylethyl) ester (16):** 71% yield as colorless crystals; mp 76−77 °C (petroleum ether); ^{1}H-NMR ($CDCl_3$) δ 1.42 (d, 6H), 5.78 (h, 1H), 6.87 (dt, 1H), 7.01 (bs, 1H), 7.21−7.35 (m, 2H), 8.25 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.5, 77.2, 108.9, 112.2, 116.6, 129.9, 138.6, 162.6, 187.4. Anal. Calcd for $C_{10}H_{12}FNOS$: C, 56.32; H, 5.67; N, 6.57. Found: C, 56.46; H, 5.53; N, 6.72.

***N*-(3-Chlorophenyl)thiocarbamic acid *O*-(1-methylethyl) ester (17):** 76% yield as colorless crystals; mp 83−85 °C (diisopropyl ether); ^{1}H-NMR ($CDCl_3$) δ 1.39 (d, 6H), 5.67 (h, 1H), 7.06−7.20 (m, 3H), 7.31 (s, 1H), 8.94 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.6, 77.6, 119.5, 121.7, 125.1, 129.9, 134.4, 138.2, 187.6. Anal. Calcd for $C_{10}H_{12}ClNOS$: C, 52.28; H, 5.26; N, 6.10. Found: C, 52.15; H, 5.15; N, 6.02.

Lithiation of 15, 16, and 17. General Procedure. A 5% solution of thiocarbamic acid esters **15, 16**, and **17**[13] was treated with 2.6−3 equiv of *t*-BuLi (1.6 M solution in pentane) at −80 ± 5 °C, and then the reaction mixture was slowly warmed to −30 °C. The electrophile was added at −70 °C, and the mixture was quenched with water or 2 M HCl at −30 °C and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, the solvent was evaporated, and the crude product was further purified as described.

2-(1-Methoxy)-1,3-benzothiazole-7-carboxaldehyde (18): From **15**; electrophile, DMF; purification, recrystallization from diisopropyl ether; 60% yield as yellow crystals; mp 130−132 °C; ^{1}H-NMR ($CDCl_3$) δ 4.22 (s, 3H), 7.59 (t, 1H), 7.79 (dd, 1H), 7.98 (dd, 1H), 10.14 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 58.8, 126.0, 126.5, 127.0, 129.6, 130.2, 151.7, 177.1, 190.6. Anal. Calcd for $C_9H_7NO_2S$: C, 55.95; H, 3.65; N, 7.25. Found: C, 56.24; H, 3.69; N, 7.01.

2-(1-Methylethoxy)-1,3-benzothiazole-7-carboxaldehyde (19): from **16**; electrophile, DMF; purification, flash chromatography (petroleum ether−ethyl acetate, 5:1); 71% yield as pale yellow crystals; mp 51−52 °C; ^{1}H-NMR ($CDCl_3$) δ 1.48 (d, 6H), 5.45 (h, 1H,), 7.56 (t, 1H), 7.74 (dd, 1H), 7.92 (dd, 1H), 10.13 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.7, 76.1, 125.6, 126.0, 128.5, 129.4, 130.0, 151.0, 176.1, 190.3. Anal. Calcd for $C_{11}H_{11}NO_2S$: C, 59.71; H, 5.01; N, 6.33. Found: C, 59.55; H, 4.84; N, 6.24.

2-(1-Methylethoxy)-1,3-benzothiazole-7-carboxylic acid (20): from **16**; electrophile, CO_2 gas; purification, digestion with diisopropyl ether; 63% yield as pale yellow crystals; mp 186−188 °C; ^{1}H-NMR (DMSO-d_6) δ 1.44 (d, 6H), 5.38 (h, 1H), 7.55 (t, 1H), 7.83 (dd, 1H), 7.94 (dd, 2H), 13.60 (bs, 1H); ^{13}C-NMR (DMSO-d_6) δ 21.5, 76.0, 124.3, 124.6, 124.8, 126.0, 131.9, 150.1, 166.7, 174.4. Anal. Calcd for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90. Found: C, 55.89; H, 4.58; N, 5.62.

(13) If both educts (**16, 17**) were used, see Scheme 3 for yields.

***N*-(1,1-Dimethylethyl)-2-(1-methylethoxy)-1,3-benzothiazole-7-carboxamide (21):** from **16**; electrophile, *t*-BuN-CO; purification, flash chromatography (petroleum ether−ethyl acetate, 9:1); 55% yield as yellow crystals; mp 124−125 °C; ^{1}H-NMR ($CDCl_3$) δ 1.45 (s, 9H), 1.50 (d, 6H), 5.41 (h, 1H), 6.17 (bs, 1H), 7.32−7.42 (m, 2H), 7.76 (q, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.8, 28.8, 51.8, 75.0, 119.2, 123.0, 125.0, 127.8, 131.5, 151.0, 165.0, 176.0. Anal. Calcd for $C_{15}H_{20}N_2O_2S$: C, 61.62; H, 6.89; N, 9.58. Found: C, 61.90; H, 7.12; N, 9.86.

2-(1-Methylethoxy)-7-(methylthio)-1,3-benzothiazole (22): from **16**; electrophile, Me_2S_2; purification, kugelrohr distillation; 80% yield as yellow liquid; bp 170−172 °C/14 mbar; ^{1}H-NMR ($CDCl_3$) δ 1.49 (d, 6H), 2.56 (s, 1H), 5.43 (h, 1H), 7.16 (d, 1H), 7.30 (t, 1H), 7.71 (d, 1H); ^{13}C-NMR ($CDCl_3$) δ 16.8, 21.8, 76.0, 118.3, 122.4, 126.3, 130.3, 149.3, 172.4. Anal. Calcd for $C_{11}H_{13}NOS_2$: C, 55.20; H, 5.47; N, 5.85. Found: C, 55.46; H, 5.70; N, 6.01.

***N*,*N*-Diethyl-2-(1-methylethoxy)-1,3-benzothiazole-7-carboxamide (23):** from **16**; electrophile, $ClCONMe_2$; purification, flash chromatography (petroleum ether−ethyl acetate, 5:1); 25% yield as yellow oil; ^{1}H-NMR ($CDCl_3$) δ 1.20 (t, 6H), 1.40 (d, 6H), 3.46 (q, 4H), 5.40 (h, 1H), 7.21 (dd, 1H), 7.32 (t, 1H), 7.65 (dd, 1H); ^{13}C-NMR ($CDCl_3$) 21.9, 28.9, 51.9, 75.7, 119.4, 123.2, 125.2, 128.0, 131.5, 151.5, 165.1, 176.2. Anal. Calcd for $C_{15}H_{20}N_2O_2S$: C, 61.62; H, 6.89; N, 9.58. Found: C, 61.88; H, 6.86; N, 9.60.

2-Oxo-2,3-dihydro-1,3-benzothiazole-7-carboxaldehyde (24). A solution of **19** (0.20 g, 1.04 mmol) in 10 mL of 2 M H_2SO_4 was refluxed for 2 days. The mixture was extracted with ethyl acetate, and the dried combined organic layers were evaporated to dryness. The crude aldehyde was digested with diisopropyl ether to yield 83% as orange crystals of **24**: mp 253−255 °C; ^{1}H-NMR (DMSO-d_6) δ 7.41 (d, 1H), 7.54 (t, 1H), 7.81 (d, 1H), 10.09 (s, 1H); ^{13}C-NMR (DMSO-d_6) δ 116.8, 121.7, 126.7, 128.2, 129.7, 137.7, 171.6, 192.3. Anal. Calcd for $C_8H_5NO_2S$: C, 53.62; H, 2.81; N, 7.82. Found: C, 53.42; N, 2.62; N, 7.64.

2-Oxo-2,3-dihydro-1,3-benzothiazole-7-carboxylic Acid (25). **20** (0.50 g, 2.1 mmol) was treated as described for **24**, and the crude product was filtered by suction and digested with distilled H_2O to yield 98% as colorless crystals of **25**; mp >320 °C; ^{1}H-NMR (DMSO-d_6) δ 7.29−7.50 (m, 2H), 7.72 (d, 1H), 11.96 (bs, 1H); ^{13}C-NMR (DMSO-d_6) δ 115.3, 123.6, 124.3, 125.3, 126.1, 137.6, 166.5, 171.4. Anal. Calcd for $C_8H_5NO_3S$: C, 49.23; H, 2.58; N, 7.18. Found: C, 49.01; H, 2.49; N, 6.63.

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