Carbanions Derived from 2-Alkylthiobenzothiazoles. A Novel α-Lithiomethyl Mercaptan Synthon for Mercaptomethylation.

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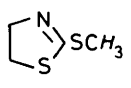
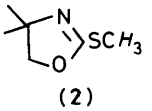
2-Methylthiobenzothiazole readily gives a methyl group lithio derivative which reacts cleanly with electrophiles. The products are conveniently converted into the corresponding thiols by BuLi at −78 °C, and this sequence thus provides a convenient two-step mercaptomethylation procedure for alkyl halides, aldehydes, and ketones.

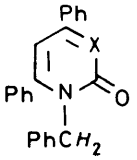
Formal dipole stabilized carbanions where part of the dipole is incorporated in a heterocyclic ring have found extensive application in synthesis.[1] Compounds (**1**)—(**5**) are representative examples[2-5] of precursors of such carbanions. However, the utilization of such carbanions derived from 2-alkylthiobenzothiazoles has not been previously reported. We envisaged the use of carbanions of this type in the α-functionalization of 2-alkylthiobenzothiazoles, stimulated by the possibility of further transformations at the active benzothiazole 2-position.[6,7]



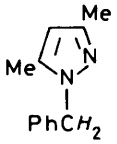
(**1**)



(**2**)



(**3**) X = CH
(**4**) X = N



(**5**)

In (**1**)—(**5**), the active H atom is italicised

Here we report the preparation and synthetic applications of carbanionic species derived from 2-alkylthiobenzothiazoles.

Results and Discussion

Reaction with 2-Methylthiobenzothiazole (**6**).—Treatment of 2-methylthiobenzothiazole (**6**) with lithium di-isopropylamide (LDA) in THF at −78 °C yielded a yellow solution of the lithio-derivative (**7**) which reacted cleanly with a variety of electrophiles to afford the corresponding substituted products (**12**) (Scheme 1) in yields ranging from 67 to 88% (Table 1). In the reaction with trimethylsilyl chloride the disubstituted product (**18**) was also isolated in 5% yield. The carbanion (**7**) failed to give a substitution product with isopropyl iodide, the starting material (**6**) being recovered unchanged.

All the products (**12**) showed in the ^{1}H n.m.r. spectrum a characteristic pseudotriplet at *ca.* 7.9 p.p.m., corresponding to the 4- and 7-H of the benzothiazole ring. Further details are given in the Experimental section. The ^{13}C n.m.r. spectra of compounds (**12**) (Table 2) displayed a characteristic pattern for the quarternary carbons in the benzothiazole ring.[8] Thus, C-2 was significantly deshielded, resonating in the region 170.4—165.1 p.p.m.; C-3a, also characteristically deshielded, appeared at 153.5—152.0 p.p.m., whereas C-7a resonated at 135.4—135.6 p.p.m. These three carbons were easily identified as singlets in the off-resonance spectrum.

Preparation of Thiols.—Previously, alkanethiols have been obtained from 2-alkylthiobenzothiazole derivatives in two steps by quaternization of the heterocyclic nitrogen followed by treatment of the resulting benzothiazolium salt (**8**) with hydrazine[9] (Scheme 1). We now find that the same transformation can be accomplished in a single step using two equivalents of butyl-lithium at −78 °C. The second equivalent is necessary because some base is consumed in the deprotonation (*vide infra*) of the 2-butylbenzothiazole (**9**) formed during the reaction (Scheme 1). Thus, 2-heptylthiobenzothiazole (**12c**) and 2-phenethylthiobenzothiazole (**12h**) gave high yields of the corresponding alkanethiols (**10**) (Table 1). Furthermore, the alcohols (**12d**) and (**12e**) underwent the same transformation in the presence of a third equivalent of butyl-lithium to yield the corresponding monothioglycols (**10d**) and (**10e**) (Table 1). In all cases the yield of the by-product 2-butylbenzothiazole (**9**) was over 80%.

The reactions involve direct and uncatalysed nucleophilic attack of the butyl carbanion at the benzothiazole 2-position. In contrast, the analogous reactions with Grignard reagents were reported to require the the presence of a nickel catalyst.[6] Similar divergent behaviour was previously observed in the reactions of 2-methylthio-4,4-dimethyl-4,5-dihydro-oxazole with organolithium compounds compared with Grignard reagents.[10] In the preparation of compounds (**10d**) and (**10h**) small amounts (*ca.* 3—4%) of the corresponding sulphides (**11d**) and (**11h**) were also found; these resulted from attack of butyl-lithium on the exocyclic sulphur with expulsion of the benzothiazyl anion.[11]

The overall sequence (**6**)→(**12**)→(**10**) thus utilizes the lithio derivative (**7**) as a reagent for the mercaptomethylation[12] of alkyl halides, aldehydes, and ketones. This new method has the advantages of a readily available starting material and mild overall conditions. The previously reported methods for mercaptomethylation have involved a four-step sequence from cyclohexanone dimethyl dithioacetal *S*-oxide,[12] a two-step sequence including $LiAlH_4$ reduction from 2,4,6-tri-isopropylthiobenzoate ester,[13a] or the alkylation of tetrahydrofuran-2-yl- and tetrahydropyran-2-yl(thiomethyl)lithium, followed by a silver nitrate–hydrogen sulphide hydrolysis.[13b]

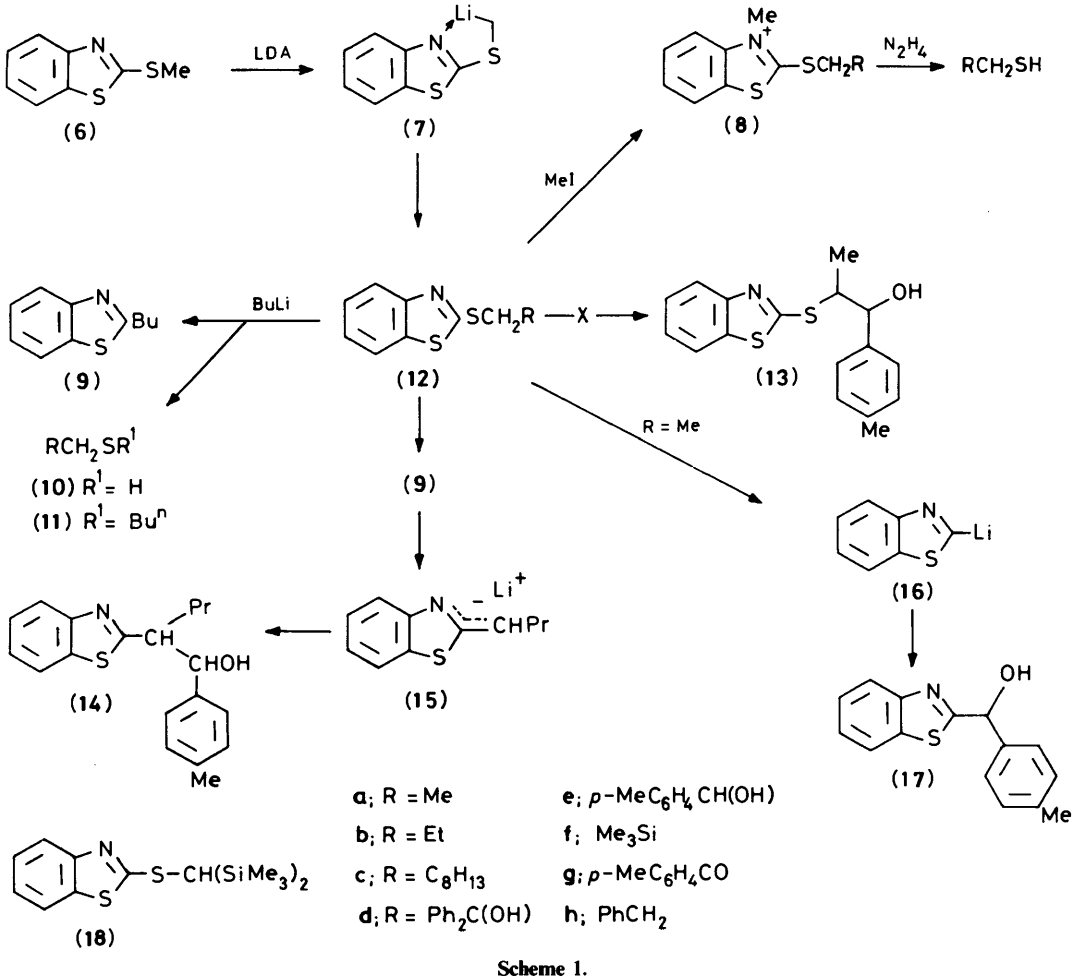
Reactions with 2-Ethylthiobenzothiazole (**12a**).—Attempts to extend this methodology to other 2-alkylthiobenzothiazoles failed. Thus, when 2-ethylthiobenzothiazole (**12a**) was successively treated with LDA and *p*-tolualdehyde in THF at −78 °C none of the expected product (**13**) was obtained (Scheme 1). Instead, the alcohol (**17**) (65%) was formed by base attack on the exocyclic sulphur to displace 2-lithiobenzothiazole (**16**), which is known to add readily to carbonyl groups.[14,15] The

mode of reaction is probably a consequence of the low kinetic acidity of the methylene protons in (**12a**), as suggested[3a] for similar failures with 2-ethylthiodihydrothiazole (**19a**)[2] and 2-ethylthiodihydro-oxazole (**19b**).[3a]

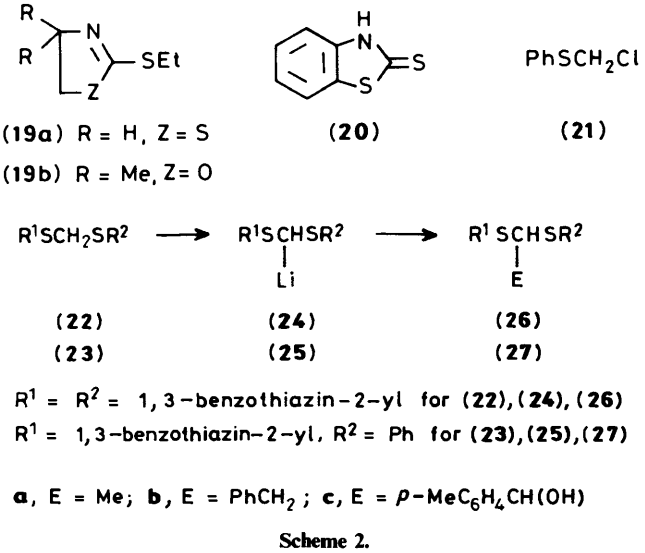
Deprotonation of (**12a**) was also attempted with butyl-lithium–tetramethylethylenediamine (TMEDA) in diethyl ether at −78 °C. However, attack at the benzothiazole 2-position again occurred to form 2-butylbenzothiazole (**9**). Addition of *p*-tolualdehyde to the reaction mixture yielded the alcohol (**14**) (Scheme 1) by addition of the resonance stabilized carbanion (**15**),[16] derived from (**9**) in the presence of butyl-lithium, to the carbonyl group (Scheme 1).

Dithioacetal Derivatives.—Dithioacetals (**22**) (prepared as reported)[17] and (**23**) were investigated as potential acyl anion equivalents. Reaction of 2-mercaptobenzothiazole (**20**) with phenylthiomethyl chloride (**21**) in the presence of sodium ethoxide gave (**23**) (90%).

The enhanced acidity of the methylene protons in (**22**) and (**23**) was reflected in the absence of nucleophilic attack at the benzothiazole 2-position with butyl-lithium in THF at −78 °C. Instead, deprotonation gave the carbanions (**24**) and (**25**) that could be trapped only with reactive electrophiles to give the substituted products (**26**) and (**27**) (Scheme 2). The spectral (^{1}H and ^{13}C n.m.r.) properties of compounds (**26**) and (**27**) are given in Tables 3 and 4. However, aromatic esters or unactivated alkyl halides did not react with carbanions (**24**) and (**25**), nor could carbanions be cleanly generated from the monosubstituted derivatives (**26**) and (**27**).



Scheme 1.



Scheme 2.

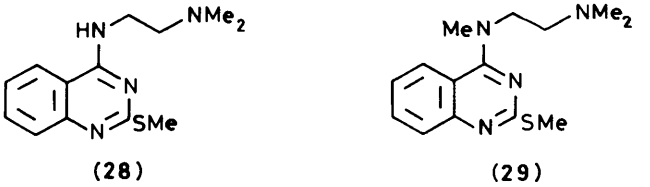


Table 1. Products and yields from lithiation of 2-methylthiobenzothiazole (**6**) and subsequent reaction with butyl-lithium

R	Products of reactions with electrophiles: Compd. no.	Yield (%)	Products of reactions with BuLi: Compd. no.	Yield (%)
Me	(**12a**)	76		
Et	(**12b**)	87[a]		
C_6H_{13}	(**12c**)	72	(**10c**)	70
$Ph_2C(OH)$	(**12d**)	84	(**10d**)	83
p-$MeC_6H_4CH(OH)$	(**12e**)	81	(**10e**)	83
			(**11e**)	3
Me_3Si	(**12f**)	86		
p-MeC_6H_4CO	(**12g**)	67		
$PhCH_2$	(**12h**)	88	(**10h**)	80
			(**11h**)	4

[a] Estimated from ^{1}H n.m.r. integration.

Table 2. Selected ^{13}C n.m.r. data[a] of the 2-alkylthiobenzothiazoles (**12**)

Compd. no.	R	C-2 (s)	C-3a (s)	C-7a (s)	C-α (t)	R
(**12c**)	C_6H_{13}	166.8	153.0	134.8	33.2	*b*
(**12d**)	$Ph_2C(OH)$	168.4	152.0	135.4	46.1	77.9[c]
(**12e**)	*p*-$MeC_6H_4CH(OH)$	167.5	152.3	135.1	42.4	72.9[d]
						20.9[e]
(**12f**)	Me_3Si	170.4	153.5	135.2	18.9	−1.7[f]
(**12g**)	*p*-MeC_6H_4CO	165.2	152.5	135.1	40.8	192.1[g]
						21.4[h]
(**12h**)	$PhCH_2$	166.1	152.7	134.8	*i*	*i*

[a] All spectra were recorded in $CDCl_3$; values are referred to $CDCl_3$; chemical shifts are given in p.p.m. [b] 31.3 (t), 28.9 (t), 28.4 (t), 22.3 (t), and 13.8 (q). [c] $Ph_2C(OH)$ (s). [d] Ar*C*H(OH) (d). [e] CH_3Ar (q). [f] Me_3Si (q). [g] *C*O (s). [h] CH_3Ar (q). [i] 35.13, 34.21.

Carbanions derived from quinazoline derivatives (**28**) and (**29**) could not be generated efficiently.[18]

Experimental

M.p.s were determined on a Kofler hot-stage microscope, and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 283B spectrophotometer. ^{1}H N.m.r. spectra were obtained on a Varian EM 360L or a Jeol JNM-PMX60 (60 MHz, continuous wave mode) spectrometer, if unspecified, or Varian XL 200 (200 MHz, FT mode) spectrometer, as specified. ^{13}C N.m.r. spectra were run on a Jeol JNM-FX100 (25 MHz) or Varian XL200 (50 MHz) spectrometer. Mass spectra and g.c.–m.s. results were obtained by Dr. R. W. King on a AEI MS 30 spectrometer.

Tetrahydrofuran (THF) and diethyl ether were dried by distillation from sodium–benzophenone ketyl. Di-isopropylamine was distilled over calcium hydride, and then stored over sodium hydroxide under an argon atmosphere. All reactions involving alkyl-lithium reagents were carried out in a dry argon atmosphere.

Flash chromatography[19] was carried out using MCB silica gel (230—400 mesh).

The following compounds were prepared using reported methods: 2-methylthiobenzothiazole (**6**) (79%), b.p. 105—110 °C/0.6 mmHg (lit.,[20] b.p. 174—175 °C/22 mmHg); 2-ethylthiobenzothiazole (**12a**) (82%), b.p. 130—131 °C/1.5 mmHg) (lit.,[20] b.p. 178 °C/18 mmHg); bisbenzothiazol-2-ylthiomethane[17] (**22**) (60%), m.p. 90—95 °C (lit.,[21] m.p. 95—96.5 °C).

General Procedure for the Lithiation of 2-Methylthiobenzothiazole (**6**): *Preparation of Benzothiazoles* (**12**).—A solution of 2-methylthiobenzothiazole (**6**) (2.71 g, 15 mmol) in THF (50 ml) was added dropwise to LDA [prepared from di-isopropylamine (2.5 ml) and 2.35M-butyl-lithium in hexane (7 ml, 16.5 mmol)] in THF (100 ml) at −78 °C. The temperature was kept below −70 °C throughout the addition. The resulting

Table 3. ^{1}H N.m.r. spectra[a] of the dithioacetals (**22**), (**23**), (**26**), and (**27**)

Compd. no.	R	R_1	4,7-H (m): δ	H	Other aromatic protons (m): δ	H	α-H: δ	H	M	R^1: δ	H	M
(**22**)	Benzth[b]	H	8.0	4	7.7—7.2	4	5.4	2	s			
(**23**)	Ph	H	7.9	2	7.7—7.2	7	4.8	2	s			
(**26b**)	Benzth[b]	$PhCH_2$	7.9	4	7.7—7.2	9	6.2	1	t[c]	3.7	2	d[c]
(**26c**)	Benzth[b]	*p*-$MeC_6H_4CH(OH)$	*d*		8.1—7.0	12	6.7—6.2[e]		m	5.7[f]	1	br
										2.2[g]	3	s
(**27a**)	Ph	CH_3	7.95	2	7.8—7.2	7	5.4	1	q[h]	1.8	3	d[h]
(**27b**)	Ph	$PhCH_2$	7.85	2	7.7—7.2	12	5.5	1	dd[i]	3.5	2	dd,dd[j]

[a] All spectra recorded in $CDCl_3$ with TMS as internal reference; δ = chemical shift (p.p.m), *J* = coupling constant (Hz), H = number of protons, M = multiplicity. [b] Benzothiazol-2-yl. [c] *J* 7 Hz. [d] With rest of aromatic protons. [e] Obscured by OH in the same region. [f] *CH*OH. [g] CH_3Ar. [h] *J* 7 Hz. [i] *J* 6 and 8 Hz. [j] *J* 6, 8, and 14 Hz.

Table 4. Selected ^{13}C n.m.r. data[a] of the dithioacetals (**22**), (**23**), (**26**), and (**27**)

Compd. no.	R	R^1	C-2 (s)	C-3a (s)	C-7a (s)	C-α (d)	R^1
(**22**)	Benzth[b]	H	164.6	152.6	135.4	36.3[c]	
(**23**)	Ph	H	164.8	152.7	*d*	38.9[c]	
(**26b**)	Benzth[b]	$PhCH_2$	163.8	152.9	*d*	56.0	42.1[e]
(**26c**)	Benzth[b]	*p*-$MeC_6H_4CH(OH)$	164.7	152.1	135.2	63.1	75.9[f]
			164.0				20.9[g]
(**27a**)	Ph	Me	165.0	152.9	135.2	51.4	22.9[h]
(**27b**)	Ph	$PhCH_2$	165.1	153.0	135.1	57.7	42.2[i]

[a] All spectra were recorded in $CDCl_3$; values are referred to $CDCl_3$; chemical shifts are given in p.p.m. [b] Benzothiazol-2-yl. [c] CH_2 (t). [d] It could not be unambiguously assigned. [e] $PhCH_2$ (t). [f] *C*HOH (d). [g] CH_3Ar (q). [h] CH_3 (q). [i] $PhCH_2$ (t).

yellow solution was stirred at −78 °C for 1 h. To this solution of the lithiated species (**7**), the electrophile (16.5 mmol) was added and the solution stirred at −78 °C for 4 h. The reaction mixture was poured into water (150 ml) and the aqueous layer extracted with ether (3 × 50 ml). The combined organic extracts were washed with water, dried ($MgSO_4$) and evaporated under reduced pressure (20 mmHg) to give an oil that was purified to give the products (**12**).

2-Ethylthiobenzothiazole (**12a**). The above procedure with methyl iodide gave a crude oil that was fractionally distilled to afford (**12a**) as a colourless oil (2.22 g, 76%), b.p. 126—132 °C/1.5 mmHg (lit.,[20] b.p. 178 °C/18 mmHg).

2-Propylthiobenzothiazole (**12b**). Ethyl iodide gave (**12b**) (87%, by ^1H n.m.r. integration) and (**6**) in a mixture which was analytically separated by g.c.–m.s.; data for (**12b**): $\delta_H(CDCl_3)$ [from mixture with (**6**) by difference] 8.1—7.6 (2 H, m), 7.6—7.1 (2 H, m), 3.3 (2 H, t, *J* 7 Hz), 1.8 (2 H, m), and 1.0 (3 H, t, *J* 7 Hz); *m/z* 209 (M^+, 22.5), 194 (14.07), 181 (11.72), 108 (16.43), 69 (13.41), and 41 (17.28).

2-Heptylthiobenzothiazole (**12c**). Reaction of hexyl iodide and (**6**) according to the general procedure described above afforded (**12c**). Purification of the crude product by flash chromatography on silica gel with dichloromethane–hexane (1:1) gave (**12c**) as a light yellow oil (2.88 g, 72%). Kugelrohr distillation furnished the analytical sample, b.p. 157 °C/0.8 mmHg (Found: C, 63.3; H, 7.2; N, 5.2. $C_{14}H_{19}NS_2$ requires C, 63.4; H, 7.2; N, 5.3%); $\nu_{max.}$(neat) 2 980, 2 965, 2 880, 1 560, 1 450, 1 310, 1 240, 1 075, and 990 cm^{-1}; $\delta_H(CDCl_3)$ 8.1—7.7 (2 H, m), 7.6—7.1 (2 H, m), 3.35 (2 H, t, *J* 7 Hz), 2.0—0.7 (13 H, m).

2-Benzothiazol-2-ylthio-1,1-diphenylethanol (**12d**). The above procedure gave an oil with benzophenone which solidified on standing. Trituration of the solid in hexane afforded the alcohol (**12d**) as white plates (4.55 g, 84%), from methanol, m.p. 132—134 °C (Found: C, 69.2; H, 4.8; N, 3.6. $C_{21}H_{17}NOS_2$ requires C, 69.4; H, 4.7; N, 3.8%); $\nu_{max.}(CHBr_3)$ 3 500—3 100 (OH), 1 560, 1 450, 1 310, 1 240, 1 080, and 1 000 cm^{-1}; $\delta_H(CDCl_3)$ 8.1—7.8 (2 H, m), 7.8—7.2 (12 H, m), 5.8 (1 H, s, OH), and 4.3 (2 H, s).

2-Benzothiazol-2-ylthio-1-(p-tolyl)ethanol. Compound (**12e**) was prepared from *p*-tolualdehyde and (**6**) as a thick oil which was purified by flash chromatography on silica gel with dichloromethane. The resulting oil (3.67 g, 81%) solidified with time. The analytically pure alcohol (**12e**) was obtained by triturating the solid in hexane, m.p. 81—84 °C (Found: C, 63.8; H, 5.0; N, 4.5. $C_{16}H_{15}NOS_2$ requires C, 63.8; H, 5.0; N, 4.6%); $\nu_{max.}(CHBr_3)$ 3 500—3 100 (OH), 1 555, 1 450, 1 310, 1 240, 1 080, and 1 000 cm^{-1}; $\delta_H(CDCl_3)$ 8.1—7.7 (2 H, m), 7.7—7.1 (6 H, m), 5.2 (1 H, dd, J_{AX} 7 Hz, J_{BX} 4 Hz), 5.0—4.3 (1 H, br, OH), 3.9—3.3 (2 H, m), and 2.3 (3 H, s).

Benzothiazol-2-ylthio(trimethylsilyl)methane (**12f**). The general procedure described above with trimethylsilyl chloride gave the silane (**12f**). Purification of the crude product by flash chromatography on silica gel with benzene–hexane (1:2) afforded (**12f**) as a colourless oil (3.26 g, 86%). The analytical sample was obtained after Kugelrohr distillation, b.p. 120 °C/1.3 mmHg (Found: C, 52.3; H, 6.0; N, 5.5. $C_{11}H_{15}NS_2Si$ requires C, 52.2; H, 5.9; N, 5.5%); $\nu_{max.}(CHBr_3)$ 1 460, 1 450, 1 425, 1 250, 1 070, and 990 cm^{-1}; $\delta_H(CDCl_3)$ 8.2—7.8 (2 H, m), 7.7—7.2 (2 H, m), 2.65 (2 H, s), and 0.2 (9 H, s). Also obtained in this reaction was *benzothiazol-2-ylthiobis(trimethylsilyl)methane* (**18**) (0.24 g, 5%) [eluted before (**12f**)] as a colourless oil (Found: M^+, 325.0811. $C_{14}H_{23}NS_2Si_2$ requires M^+, 325.0810); $\nu_{max.}$(neat) 1 550, 1 450, 1 420, 1 310, 1 240, 1 070, and 1 000; $\delta_H(CDCl_3)$ 8.1—7.8 (2 H, m), 7.7—7.2 (2 H, m), 2.7 (1 H, s), and 0.2 (18 H, s).

Benzothiazol-2-ylthiomethyl p-*Tolyl Ketone* (**12g**).—The general procedure described above was followed, using twice the amount of LDA (*ca.* 33 mmol) and methyl 4-methylbenzoate. The oil that resulted solidified on standing and the solid was triturated in hexane to afford (**12g**) (3 g, 67%), as white microcrystals from methanol, m.p. 94—95 °C (Found: C, 64.7; H, 4.3; N, 4.6. $C_{16}H_{13}NOS_2$ requires C, 64.2; H, 4.3; N, 4.7%); $\nu_{max.}(CHBr_3)$ 1 670, 1 450, 1 425, 1 310, and 990 cm^{-1}; $\delta_H(CDCl_3)$ 8.2—7.7 (4 H, m), 7.7—7.2 (4 H, m), 5.0 (2 H, s), 2.4 (3 H, s).

2-Phenethylthiobenzothiazole (**12h**). This was obtained by treating (**6**) with benzyl bromide under the standard conditions. The crude product was purified by flash chromatography on silica gel with dichloromethane–hexane (1:1) to give (**12h**) as an oil (3.58 g, 88%) (Found: C, 66.5; H, 4.9; N, 5.1. $C_{15}H_{13}NS_2$ requires C, 66.4; H, 4.8; N, 5.2%); $\nu_{max.}$(neat) 1 455, 1 450, 1 420, 1 305, 1 235, and 990 cm^{-1}; $\delta_H(CDCl_3)$ 8.1—7.0 (9 H, m), 3.75—2.85 (4 H, m).

General Procedure for the Preparation of the Thiols (**10**) *from Benzothiazoles* (**12**).—A 2- or 3-fold excess of butyl-lithium (see below for details) was added to a solution of the benzothiazole (**12**) (2 mmol) in THF (20 ml) at −78 °C. The resulting light yellow solution was stirred at −78 °C for 1 h and then poured into water (20 ml) and extracted with diethyl ether (3 × 20 ml); the organic extracts were washed with brine, dried ($MgSO_4$), and the solvents evaporated under reduced pressure (20 mmHg) to give an oil that contained the thiol (**10**) and 2-butylbenzothiazole (**9**). The thiol (**10**) was separated from (**9**) by flash chromatography (for conditions see specific examples). The benzothiazole (**9**) was further purified by Kugelrohr distillation, b.p. 105 °C/3 mmHg (lit.,[22] b.p. 132 °C/7 mmHg); $\nu_{max.}$(neat) 2 960, 2 940, 2 880, 1 510, 1 450, 1 110, and 900 cm^{-1}; $\delta_H(CDCl_3)$ 8.3—7.8 (2 H, m), 7.8—7.2 (2 H, m), 3.1 (2 H, m), and 2.1—0.7 (7 H, m); δ_C (25 MHz; $CDCl_3$) 171.6 (s), 152.9 (s), 134.7 (s), 125.3 (d), 124.1 (d), 122.0 (d), 121.0(d), 33.5 (t), 31.2 (t), 21.8 (t), and 13.3 (q).

Heptane-1-thiol (**10c**). This was obtained from (**12c**) (2 mmol) and butyl-lithium (4.4 mmol) and separated from (**9**) by flash chromatography on silica gel with benzene. This gave (**10c**) (0.18 g, 69%), b.p. 170—175 °C (lit.,[23] b.p. 173—176 °C); $\delta_H(CDCl_3)$ 2.55 (2 H, q) and 1.8—0.7 (14 H, m).

2-Mercapto-1,1-diphenylethanol (**10d**). This was prepared from (**12d**) (3.4 mmol) and butyl-lithium (11 mmol). Flash chromatography on silica gel with hexane–ethyl acetate (19:1) afforded (**10d**) (0.65 g, 83%), m.p. 50—52 °C (lit.,[12] m.p. 49—52 °C); $\nu_{max.}(CHBr_3)$ 3 500 (OH) and 2 560 cm^{-1} (SH); $\delta_H(CDCl_3)$ 7.8—7.1 (10 H, m), 3.65 (1 H, s), 3.30 (2 H, d, *J* 9 Hz), and 1.2 (1 H, t, *J* 9 Hz).

2-Mercapto-1-(p-tolyl)ethanol (**10e**). From the benzothiazole (**12e**) (2.6 mmol) and butyl-lithium (8.6 mmol) after flash chromatography on silica gel with dichloromethane–hexane (4:1), gave (**10e**) as an oil (0.30 g, 70%) (Found: C, 64.2; H, 7.2; S, 19.0. $C_9H_{12}OS$ requires C, 64.2; H, 7.2; S, 19.1%); $\nu_{max.}$(neat) 3 400 (OH) and 2 560 cm^{-1} (SH); $\delta_H(CDCl_3)$ 7.3 (4 H, s), 4.7 (1 H, t), 3.1—2.5 (3 H, m), 2.35 (3 H, s), and 1.4 (1 H, t); δ_C (50 MHz; $CDCl_3$) 139.0, 137.6, 129.1, 125.7, 74.5, 33.5, and 21.0. Also obtained in this reaction was *2-butylthio-1-(p-tolyl)ethanol* (**11e**) (18 mg, 3%) as an oil (Found: M^+, 224.1255. $C_{13}H_{20}OS$ requires M^+, 224.1235); $\nu_{max.}$(neat) 3 420 (OH), 2 960, 2 920, and 2 830 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 7.2 (4 H, m), 4.7 (1 H, dd, *J* 4.1 and 10.0 Hz), 2.96 (1 H, s, br), 2.91 (1 H, dd, *J* 4.1 and 13.8 Hz), 2.70 (dd, 1 H, *J* 10.0 and 13.8 Hz), 2.55 (2 H, m), 2.35 (3 H, s), 1.70—1.30 (4 H, m), and 0.92 (t, 3 H); δ_C (50 MHz; $CDCl_3$) 139.6, 137.5, 129.1, 125.7, 71.5, 42.1, 31.8, 31.7, 21.9, 21.1, and 13.6.

2-Phenylethanethiol (**10h**). The benzothiazole (**12h**) (6.2 mmol) and butyl-lithium (14.0 mmol), after flash chromatography on silica gel with hexane–benzene (20:1), gave (**10h**) (0.68 g, 80%); this was characterized as its 2,4-dinitrophenyl derivative,[24] m.p. 89—90 °C (lit.,[24] m.p. 89.5 °C). Also obtained

in this reaction was butyl phenethyl sulphide (**11h**) as an oil (50 mg, 4%), b.p. 150 °C/9 mmHg (lit.,[25] b.p. 104 °C/1.2 mmHg); δ_H(200 MHz; $CDCl_3$) 7.40—7.10 (5 H, m), and 0.90 (3 H, t); δ_C (50 MHz; $CDCl_3$) 140.7, 128.6, 128.4, 126.3, 36.4, 33.6, 31.9, 31.7, 22.0, and 13.7.

Benzothiazol-2-yl(p-*tolyl*)*methanol* (**17**).—A solution of (**12a**) (1.95 g, 10 mmol) in THF (30 ml) was added dropwise to LDA [from di-isopropylamine (3.4 ml) and 2.35M butyl-lithium (4.7 ml, 11 mmol)] in THF (60 ml) at −78 °C. The resulting light yellow solution was stirred at −78 °C for 3 h after which tolualdehyde (1.44 g, 12 mmol) in THF (5 ml) was added dropwise. The solution was stirred at −78 °C for 3 h, poured into water (90 ml), and extracted with ether (3 × 30 ml). The organic extracts were washed with water, dried ($MgSO_4$) and evaporated to give an oil that solidified with time. The solid was triturated in cyclohexane and filtered off to afford (**17**) as needles (1.63 g, 64%) from di-isopropyl ether, m.p. 127—130 °C (Found: C, 70.5; H, 5.3; N, 5.3. $C_{15}H_{13}NOS$ requires C, 70.6; H, 5.1; N, 5.5%); $\nu_{max.}$($CHBr_3$) 3 500—2 500 (OH), 1 500, 1 430, 1 310, 1 060, 1 040, and 1 100 cm^{-1}; δ_H($CDCl_3$) 8.1—7.7 (2 H, m), 7.6—7.0 (6 H, m), 6.1 (1 H, s), 5.2—4.6 (1 H, br), and 2.3 (2 H, s); δ_C (25 MHz; $CDCl_3$) 175.6 (s), 152.6 (s), 138.4 (s), 138.1 (s), 135.1 (s), 129.4 (d), 126.6 (d), 126.0 (d), 125.0 (d), 122.9 (d), 121.7 (d), 74.1 (d), and 21.1 (q).

2-*Benzothiazol-2-yl*-1-(p-*tolyl*)*pentan*-1-*ol* (**14**).—A solution of butyl-lithium (6 mmol) and TMEDA (0.9 ml, 6 mmol) in diethyl ether (10 ml) was added to (**12a**) (0.97 g, 5 mmol) in diethyl ether (50 ml) at −78 °C. The resulting yellow solution was stirred at −78 °C for 10 min after which *p*-tolualdehyde (0.7 ml, 6 mmol) in ether (2 ml) was added. The mixture was stirred at −78 °C for 1.5 h after which it was poured into water (50 ml), and the aqueous layer extracted with ether (3 × 30 ml), the combined organic extracts were washed with water, dried ($MgSO_4$), and evaporated under reduced pressure (20 mmHg) to leave an oil which solidified with time. The solid was stirred in cyclohexane and filtered off to give the alcohol (**14**) (0.25 g, 32%), m.p. 130—133 °C (Found: C, 73.0; H, 7.0; N, 4.3. $C_{19}H_{21}NOS$ requires C, 73.3; H, 6.7; N, 4.5%); $\nu_{max.}$($CHBr_3$) 3 580 (OH), 3 500—3 100 (OH), 1 510, and 1 050 cm^{-1}; δ_H($CDCl_3$) 8.0—7.6 (2 H, m), 7.6—7.0 (6 H, m), 4.95 (1 H, d), 4.2—3.6 (1 H, br), 3.4 (1 H, q), 2.3 (3, H, s), and 2.0—0.7 (7 H, m); δ_C (25 MHz; $CDCl_3$) 173.6 (s), 152.7 (s), 139.6 (s), 137.1 (s), 134.3 (s), 128.9 (d), 126.1 (d), 125.8 (d), 124.7 (d), 122.6 (d), 121.3 (d), 76.6 (d), 51.8 (d), 35.2 (t), 21.0 (q), 20.4 (t), and 13.8 (q).

Phenylthiomethyl Chloride (**21**).—Paraformaldehyde (7.5 g, 250 mmol) was stirred in benzene (50 ml) and concentrated hydrochloric acid (100 ml) was added dropwise (over 5 min) with stirring. The stirred mixture was warmed to 30 °C (inner temperature) and thiophenol (22 g, 200 mmol) was added dropwise (over 25 min). After the addition was half-complete, the mixture was heated to 40 °C (inner temperature) while the addition proceeded. After the addition was complete, the mixture was stirred and heated at 60 °C (inner temperature) in a water-bath for 2.5 h. After being cooled, the two layers were separated, and the organic layer was washed with water, dried ($MgSO_4$), and evaporated under reduced pressure (20 mmHg). The residual oil was distilled to give product (**21**) (22.6 g, 71%), b.p. 90—95 °C/3.5 mmHg (lit.,[26] b.p. 66 °C/0.2 mmHg). The chloride (**21**) was stored at −10 °C and protected against moisture to avoid decomposition.

2-(*Phenylthiomethylthio*)*benzothiazole* (**23**).—The chloride (**21**) (10.4 g, 66 mmol) was added to a solution of 2-mercaptobenzothiazole (**20**) (11 g, 66 mmol) in ethanol (20 ml) containing sodium ethoxide (66 mmol), and the mixture was stirred at room temperature for 1.75 h. The solvent was removed under reduced pressure (20 mmHg) and the residue extracted between dichloromethane (50 ml) and water (20 ml). The organic extracts were dried ($MgSO_4$) and evaporated to give (**23**) as an oil (17.2 g, 90%) (pure by t.l.c., ^1H and ^{13}C n.m.r.) that could not be distilled without decomposition (Found: M^+ 289.0052 $C_{14}H_{11}NS_3$ requires M^+, 289.0054); $\nu_{max.}$($CHBr_3$) 1 475, 1 450, 1 420, 1 070, and 990 cm^{-1}; ^1H and ^{13}C n.m.r. data are given in Tables 3 and 4, respectively.

General Procedure for the Lithiation of Dithioacetals (**22**) *and* (**23**).—Butyl-lithium (2.2 mmol) was added dropwise to a solution of (**22**) or (**23**) (2 mmol) in THF (20 ml) at −78 °C and the resulting solution was stirred for 1 h at this temperature.

1,1-*Bisbenzothiazol-2-ylthio-2-phenylethane* (**26b**). To the carbanion derived from (**22**), prepared as described above, benzyl bromide (2.2 mmol) in THF (2 ml) was added. The reaction mixture was stirred at −78 °C for 1 h and then at −40 °C for 4 h. It was then quenched with water (15 ml) and extracted with dichloromethane (3 × 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure (20 mmHg) to give (**26b**) as an oil that crystallized when stirred with light petroleum (0.58 g, 66%); it recrystallized as needles from absolute ethanol, m.p. 131—132 °C (Found: C, 60.6; H, 3.6; N, 6.3. $C_{22}H_{16}N_2S_4$ requires C, 60.5; H, 3.7; N, 6.4%); $\nu_{max.}$($CHBr_3$) 1 450, 1 420, 1 310, 1 240, and 990 cm^{-1}; ^1H and ^{13}C n.m.r. data are given in Tables 3 and 4, respectively.

2,2-*Bisbenzothiazol-2-ylthio*-1-(p-*tolyl*)*ethanol* (**26c**). To the solution obtained from compound (**22**), following the general procedure, *p*-tolualdehyde (2 2 mmol) in THF (2 ml) was added and the mixture stirred at −78 °C for 1.75 h. The reaction mixture was quenched with methanol, extracted between water and chloroform, and the combined organic extracts were washed with water and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to yield (**26c**) as a thick oil (0.79 g, 83%); ^1H and ^{13}C n.m.r. data are given in Tables 3 and 4, respectively.

1-*Benzothiazol-2-ylthio*-1-*phenylthioethane* (**27a**). The general procedure was used with compound (**23**). To the resulting solution, methyl iodide (2.2 mmol) in THF (2 ml) was added, and the solution stirred at −78 °C for 5 h. The same work-up as for (**26b**) afforded (**27a**) as an oil (0.48 g, 80%) (pure by ^1H and ^{13}C n.m.r.) (Found: M^+, 303.0227. $C_{15}H_{13}NS_3$ requires M^+, 303.0210); ^1H and ^{13}C n.m.r. data are given in Tables 3 and 4, respectively.

1-*Benzothiazol-2-ylthio-2-phenyl*-1-*phenylthioethane* (**27b**). This was obtained in 83% yield from (**23**) and benzyl bromide using the procedure previously described for (**26b**). The residue obtained after evaporation was stirred in 95% ethanol: the product formed microcrystals from absolute ethanol, m.p. 87—90 °C (Found: C, 66.2; H, 4.5; N, 3.6. $C_{21}H_{17}NS_3$ requires C, 66.5; H, 4.5; N, 3.7%); $\nu_{max.}$($CHBr_3$) 1 580, 1 450, and 990 cm^{-1}; ^1H and ^{13}C n.m.r. data are given in Tables 3 and 4, respectively.

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References

1 For reviews see: (*a*) P. Beak and D. B. Reitz, *Chem. Rev.*, 1978, **78**, 275; (*b*) H. W. Gschwend and H. R. Rodriguez, *Org. React.*, N.Y., 1979, **26**, 1.
2 K. Hirai and Y. Kishida, *Heterocycles*, 1974, **2**, 185.
3 (*a*) A. I. Meyers and M. E. Ford, *J. Org. Chem.*, 1976, **41**, 1735; (*b*) C. R. Johnson and K. Tanaka, *Synthesis*, 1976, 413

4 A. R. Katritzky, J. Arrowsmith, Z. Bahari, C. Jayaram, T. Siddiqui, and S. Vassilatos, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2851.
5 A. R. Katritzky, H. J. Salgado, A. Chermprapai, and N. K. Ponkshe, *J. Chem. Soc., Perkin Trans. 1*, 1982, 153.
6 H. Takei, M. Miura, H. Sugimura, and H. Okamura, *Chem. Lett.*, 1979, 1447.
7 F. Babudri, G. Bartoli, F. Ciminale, S. Florio, and G. Ingrosso, *Tetrahedron Lett.*, 1984, **25**, 2047.
8 S. N. Sawhney and D. W. Boykin, *J. Org. Chem.*, 1979, **44**, 1136.
9 Y. Ueno, C. Tanaka, and M. Okawara, *Tetrahedron Lett.*, 1984, **25**, 2675.
10 B. L. Chenard, *J. Org. Chem.*, 1983, **48**, 2610.
11 See: A. Krief, *Tetrahedron*, 1980, **36**, 2531.
12 K. Ogura, S. Furukawa, and G. Tsuchihashi, *Synthesis*, 1976, 202.
13 (*a*) P. Beak, B. G. McKinnie, and D. B. Reitz, *Tetrahedron Lett.*, 1977, 1839; (*b*) E. Block and M. Aslam, *J. Am. Chem. Soc.*, 1985, **107**, 6729.
14 E. J. Corey and D. L. Boger, *Tetrahedron Lett.*, 1978, 5.
15 H. Chikashita and K. Itoh, *Heterocycles*, 1985, **23**, 295.
16 For related resonance stabilized carbanions see: (*a*) ref. 14; (*b*) A. I. Meyers, G. Knaus, K. Kamata, and M. E. Ford, *J. Am. Chem. Soc.*, 1976, **98**, 567; (*c*) M. W. Anderson M. J. Begley, R. C. F. Jones, and J. Saunders, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2599.
17 E. B. Knott, *J. Chem. Soc.*, 1955, 933.
18 For details on the preparation and reactions of these compounds see: J. M. Aurrecoechea, *Ph.D. Dissertation*, University of Florida, 1985.
19 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
20 J. D. Kendall and H. G. Suggate, *J. Chem. Soc.*, 1949, 1503.
21 R. F. Brookes, J. E. Cranham, W. A. Cummings, D. Greenwood, B. S. Jackson, and H. A. Stevenson, *J. Sci. Food Agric.*, 1957, **8**, 31 (*Chem. Abstr.*, 1957, **51**, 9629f).
22 J. Metzger and H. Plank, *Bull. Soc. Chim. Fr.*, 1956, 1692.
23 'Dictionary of Organic Compounds,' Chapman and Hall, London, 1982, vol. 3, p. 2866.
24 R. W. Bost, J. O. Turner, and R. D. Norton, *J. Am. Chem. Soc.*, 1932, **54**, 1985.
25 E. S. Huyser and L. Kim, *J. Org. Chem.*, 1968, **33**, 94.
26 B. M. Trost and R. A. Kuntz, *J. Org. Chem.*, 1974, **39**, 2648.

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