# 1-(Mercaptomethyl)benzotriazole: Preparation, Reactivity and Synthetic Utility

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A convenient synthesis is reported for 1-(mercaptomethyl)benzotriazole (89%) and its reactivity is examined.

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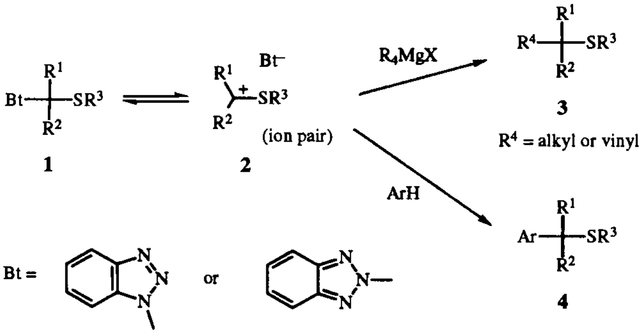
## Introduction.

α-Benzotriazolyl thioethers of type **1** (Scheme 1) were shown earlier to be effective thioalkylating reagents for Grignards [1] and electron-rich aromatic compounds [2], as well as superior precursors to vinyl sulfides [3]. This valuable reactivity is due to the good leaving-group property of benzotriazole and to the capability of sulfur to stabilize the α-carbocation **2**.

Scheme 1

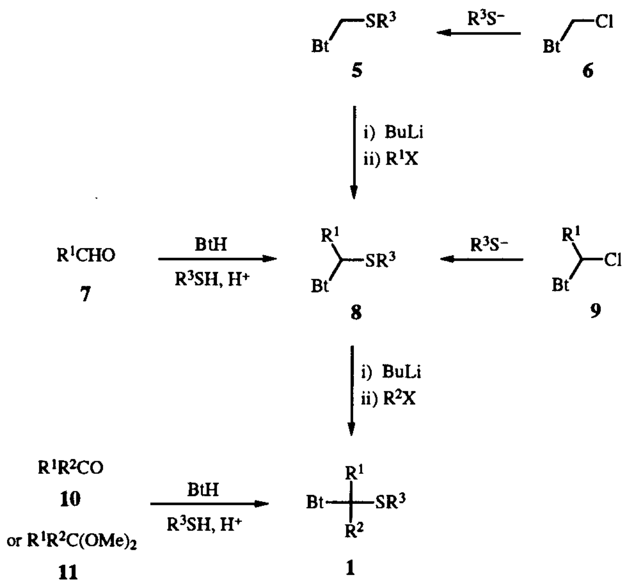


Previous synthetic routes towards α-benzotriazolyl thioethers **1**, **5** and **8** (Scheme 2) encompass the following: i) Reactions of benzotriazole with aldehydes (or acetals) and ketones (or ketals), in the presence of a thiol, which generally affords a mixture of the benzotriazol-1-yl and benzotriazol-2-yl isomers of **1** and **8** respectively [1]; ii) displacement of chlorine from 1-(chloromethyl)benzotriazole or an α-(chloro)alkylbenzotriazole by a thiolate to give **5** and **8** [1]; iii) alkylation of an α-benzotriazolyl thioether as **5** to **8** or **8** to **1** [3]. We now present a convenient synthesis of 1-(mercaptomethyl)benzotriazole (**14**) (Scheme 3) and demonstrate applications of compound **14** in new approaches to α-benzotriazolyl thioethers **1** which should be of particular value when the corresponding thiol $R^3SH$ is not readily available.

## Results and Discussion.

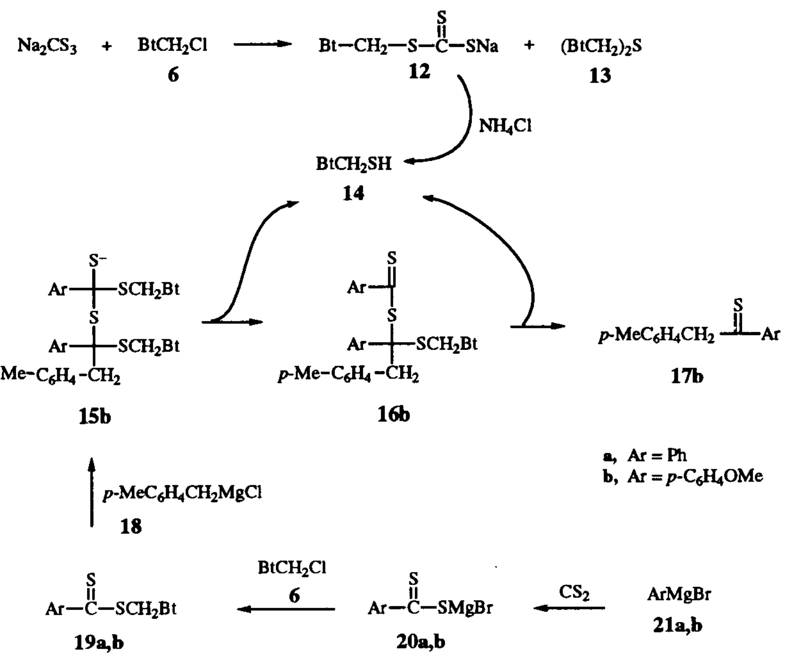
1-(Mercaptomethyl)benzotriazole (**14**) was prepared by adapting Martin and Greco's [4] synthesis of thiols from organic halides and sodium trithiocarbonate. The reaction of 1-(chloromethyl)benzotriazole (**6**) with aqueous sodium trithiocarbonate yielded the thiol **14** in 89% isolated yield (Scheme 3). 1-(Mercaptomethyl)benzotriazole is a stable solid and convenient as a shelf reagent. It was characterized by elemental analysis and $^1H$ and $^{13}C$ nmr. The chemical shift (Figure 1 and Table 1) assignments were made on the basis of standard $^1H$-$^1H$ and $^1H$-$^{13}C$ correlated spectroscopy. An interesting feature of the proton spectrum of thiol **14** is the coupling between the thiol proton and the vicinal methylene protons, indicating the absence of fast exchange of the SH.

Scheme 2



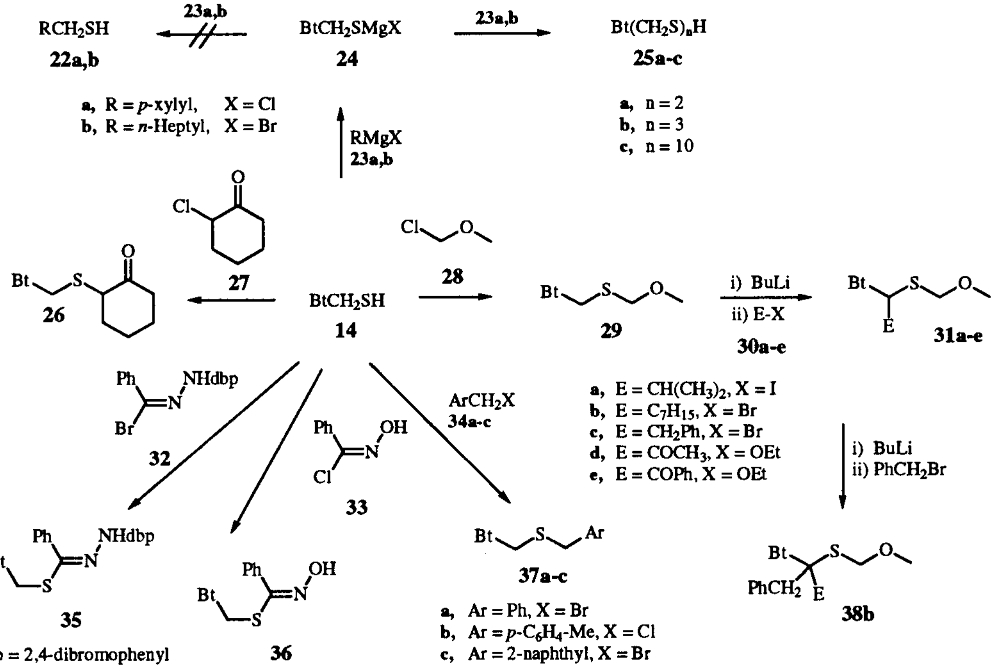
1-(Mercaptomethyl)benzotriazole was also obtained from the reaction of benzotriazolylmethyl dithiocarboxylates **19a,b** (prepared by the method of Meijer *et al.* [5]) with Grignard reagents in diethyl ether (Scheme 3). This reaction of dithioester **19b** at -78° was monitored by $^1H$ nmr. A sample taken 15 minutes after the addition of 1 equivalent of Grignard reagent for 2 equivalents of dithioester displayed, after quenching, two signals in 1:1 ratio at 5.63 ppm and 5.52 ppm in the otherwise clean region of the methylene protons of the benzotriazolylmethylthio group. This suggests that the intermediate **15b** (Scheme 3) was formed. After 2 hours, the proton spectrum of the reaction mixture indicated the presence of 1-(mer-

Scheme 3



captomethyl)benzotriazole in a 1:1 mixture with compound **16b**. The structure of compound **16b** was inferred because the reaction mixture showed the presence in the expected ratio for the following groups: i) two *para*-methoxyphenyl groups (3.69 ppm (s, 3H) + 3.72 ppm (s, 3H), 6.64 ppm (d, 2H) + 6.56 ppm (d, 2H) and 6.90 ppm (d, 2H) + 6.87 ppm (d, 2H)); ii) one *para*-xylyl group (3.37 ppm (s, 3H), 6.82 ppm (d, 2H) and 6.96 ppm (d, 2H)) and iii) one benzotriazol-1-ylmethyl group (5.63 ppm (s, 2H), 7.36 ppm (t, 1H), 7.45 ppm (t, 1H), 7.54 ppm (d, 1H) and 8.04 ppm (d, 1H)). The addition of a second equivalent of Grignard reagent **18** (for 2 equivalents of the starting dithioester **19b**) led after 1 hour to a mixture whose proton spectrum displayed the signals of thiol **14** in a 1:1 mixture with a compound containing a *para*-methoxyphenyl group, presumably **17b** (3.71 ppm (s, 3H), 6.62 ppm (d, 2H) and 6.90 ppm (d, 2H)) and a

Scheme 4



*para*-xylyl group (2.29 ppm (s, 3H), 6.98 ppm (d, 2H) and 7.02 ppm (d, 2H)). After a usual Grignard work-up, diethyl ether precipitated thiol **14** in 42% yield, identical with thiol **14** obtained from salt **12**.

The behavior of 1-(mercaptomethyl)benzotriazole (**14**) in basic conditions was investigated by heating it in an nmr tube in pyridine-$d_5$ at 80°. The $^1$H nmr spectra taken after 2 and 5 minutes indicated extensive conversion to free benzotriazole (47 mole% and 54 mole% respectively) and the formation of two products which were assigned the structures of **25a,b** (63 mole% and 16 mole% after 2 minutes and 63 mole% and 31 mole% after 5 minutes): they have the same proton chemical shifts for the benzotriazole nucleus as thiol **14**, but δ-values for the methylene protons α to the benzotriazole nucleus of 6.24 ppm and 6.10 ppm respectively, together with singlets at higher field (3.85 ppm for the major compound and 3.95 ppm and 4.09 ppm for the minor) at δ-values close to that of the protons in position 2 of 1,3-dithiane (3.70 ppm). These spectra are compatible with structures of type **25** (Scheme 4) with n = 2 in the major product **25a**

Table 1

$^1$H and $^{13}$C NMR data for Bt in Compounds Presented in Scheme 5

| Compound | | Position on benzotriazol-1-yl | | | | | |
|---|---|---|---|---|---|---|---|
| | | 3a | 4 [a] | 5 [b] | 6 [b] | 7 [a] | 7a |
| **13** | δH (ppm) | – | 8.06 | 7.44 | 7.57 | 7.77 | – |
| | δC (ppm) | 146.2 | 120.3 | 124.5 | 128.2 | 109.7 | 131.4 |
| **14** | δH (ppm) | – | 8.06 | 7.40 | 7.52 | 7.2 | – |
| | δC (ppm) | 146.3 | 120.1 | 124.2 | 127.7 | 109.6 | 131.6 |
| **19a** | δH (ppm) | – | 8.04 | 7.36 | 7.47 | 7.65 | – |
| | δC (ppm) | 145.9 | 120.0 | 124.3 | 127.9 | 110.0 | 132.3 |
| **19b** | δH (ppm) | – | 8.04 | 7.33 | 7.46 | 7.67 | – |
| | δC (ppm) | 145.9 | 119.9 | 124.2 | 127.8 | 110.2 | 132.3 |
| **26** | δH (ppm) | – | 8.07 | 7.40 | 7.54 | 7.67 | – |
| | δC (ppm) | 145.9 | 119.7 | 124.0 | 127.4 | 109.9 | 132.0 |
| **29** | δH (ppm) | – | 8.01 | 7.35 | 7.48 | 7.67 | – |
| | δC (ppm) | 145.5 | 119.2 | 123.7 | 127.1 | 109.6 | 131.8 |
| **31a** | δH (ppm) | – | 8.07 | 7.38 | 7.50 | 7.79 | – |
| | δC (ppm) | 146.3 | 119.9 | 123.9 | 127.0 | 111.1 | 131.7 |
| **31b** | δH (ppm) | – | 8.08 | 7.38 | 7.49 | 7.77 | – |
| | δC (ppm) | 146.5 | 120.1 | 124.0 | 127.1 | 110.9 | 131.9 |
| **31c** | δH (ppm) | – | 8.00 | 7.30 | 7.41 | 7.69 | – |
| | δC (ppm) | 145.9 | 119.6 | 123.7 | 126.9 | 110.3 | 131.6 |
| **31d** | δH (ppm) | – | 8.07 | 7.38 | 7.49 | 7.64 | – |
| | δC (ppm) | 146.5 | 119.9 | 124.2 | 127.6 | 111.7 | 131.9 |
| **31e** | δH (ppm) | – | 8.05 | 7.36 | 7.49 | 7.88 | – |
| | δC (ppm) | 146.8 | 119.4 | 124.2 | 127.5 | 112.7 | 132.1 |
| **35** | δH (ppm) | – | 7.94 | 7.37 | 7.54 | 7.87 | – |
| | δC (ppm) | 145.3 | 119.3 | 124.3 | 127.6 | 110.7 | 132.0 |
| **36** | δH (ppm) | – | 8.05 | 7.35–7.47 | 7.55 | 7.75 | – |
| | δC (ppm) | 145.3 | 119.3 | 124.3 | 127.5 | 110.8 | 132.0 |
| **37a** | δH (ppm) | – | 8.05 | 7.37 | 7.48 | 7.60 | – |
| | δC (ppm) | 146.2 | 119.9 | 124.1 | 127.2 | 110.1 | 131.9 |
| **37b** | δH (ppm) | | 8.07 | 7.39 | 7.50 | 7.63 | – |
| | δC (ppm) | 146.4 | 120.1 | 124.2 | 127.4 | 110.2 | 132.0 |
| **37c** | δH (ppm) | – | 8.00 | 7.28 | 7.37 | 7.48 | – |
| | δC (ppm) | 146.1 | 119.7 | 124.0 | 127.2 | 110.0 | 131.8 |
| **38b** | δH (ppm) | – | 8.08 | 7.36 | 7.44 | 8.12 | – |
| | δC (ppm) | 146.5 | 119.9 | 123.6 | 126.4 | 113.7 | 131.9 |
| **39a** | δH (ppm) | – | 8.06 | 7.38 | 7.50 | 7.68 | – |
| | δC(ppm) | 146.2 | 119.8 | 124.1 | 127.4 | 110.0 | 131.7 |
| **39b** | δH (ppm) | – | 8.08 | 7.40 | 7.50 | 7.65 | – |
| | δC (ppm) | 146.4 | 120.0 | 124.3 | 127.5 | 110.0 | 131.6 |
| **40a** | δH (ppm) | – | 8.04 | 7.39 | 7.50 | 7.68 | – |
| | δC(ppm) | 146.2 | 119.9 | 124.3 | 127.5 | 110.2 | 131.8 |
| **40b** | δH (ppm) | – | 8.06 | 7.40 | 7.52 | 7.68 | – |
| | δC (ppm) | 146.0 | 119.7 | 124.3 | 127.5 | 110.2 | 131.8 |
| **45** | δH (ppm) | – | 8.04 | 7.41 | 7.55 | 7.88 | – |
| [c] | δC (ppm) | 145.6 | 119.4 | 124.4 | 127.4 | 111.2 | 132.0 |
| **46** | δH (ppm) | – | 8.03 | 7.39 | 7.53 | 7.86 | – |
| [c] | δC (ppm) | 145.6 | 119.1 | 124.0 | 127.1 | 111.3 | 132.0 |

[a] The $^1$H signal is a doublet, 8.3 Hz. [b] The $^1$H signal is a triplet, 8.3 Hz. [c] Spectra were recorded in DMSO-$d_6$.

and n = 3 in the minor product **25b**. Furthermore, stirring thiol **14** with potassium carbonate in acetone-water for 24 hours afforded a material insoluble in alkali or acetone which did not melt but decomposed at about 160° and whose elemental analysis fitted the molecular formula of **25c** (n = 10). In agreement, 1-(mercaptomethyl)benzotriazole (**14**) with Grignard reagents **23a,b** formed free benzotriazole, but no other identifiable products.

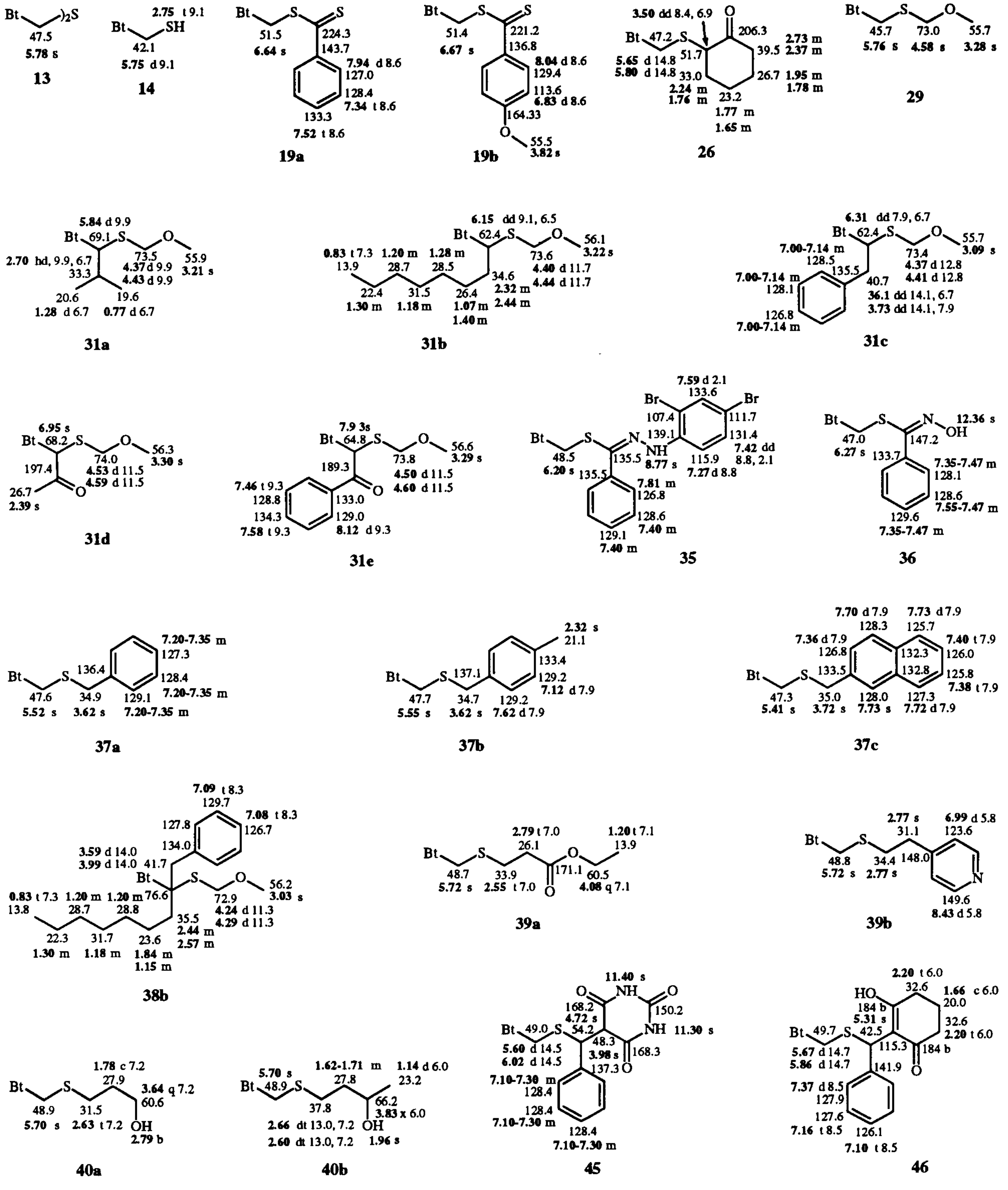


Figure 1. $^1$H and $^{13}$C chemical shifts assignments in α-benzotriazol-1yl thioethers

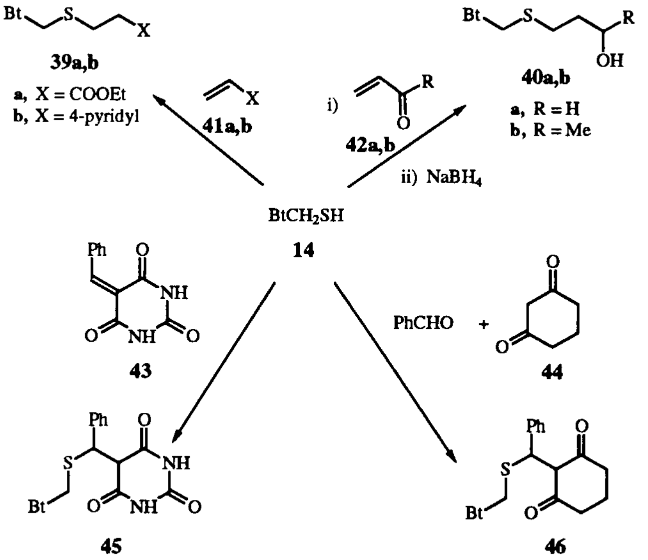
The tendency of 1-(mercaptomethyl)benzotriazole (**14**) to react with itself under basic conditions precludes most substitution reactions of type $BtCH_2SH + RX \rightarrow BtCH_2SR$, except for the substitution of reactive halogen atoms. Thus the reaction of thiol **14** with 1-bromo-2-phenylethane gave only compounds of type **25**, while arylmethyl halides **34a-c** (Scheme 4) formed the corresponding benzotriazolylmethyl arylmethyl thioethers **37a,b** in good yields.

Chloromethyl methyl ether (**28**) and α-chlorocyclohexanone (**27**) reacted with thiol **14** to afford the corresponding α'-methoxy and β'-keto functionalized α-benzotriazolyl thioethers **29** and **26** in excellent yields (Scheme 4). Benzotriazolylmethyl methoxymethyl thioether **29** with butyllithium followed by electrophiles **30a-e** gave compounds **31a-e**: deprotonation of thioether **29** thus occurs selectively α, at the benzotriazolylmethyl group. The conversions **29** to **31a-e** are similar to those previously described for benzotriazolylmethyl phenyl thioether [6]. The monoheptyl derivative **31b** was further deprotonated and reacted with benzyl bromide to give the dialkylated product **38b**. A similar reaction of acyl compound **31e** failed, presumably due to the greater stability of the enolate obtained by deprotonation.

The α'-hydroxamoyl- and α'-hydrazonyl-α-benzotriazolyl thioethers **36** and **35** (Scheme 4) were prepared in good yields by the reaction of 1-(mercaptomethyl)benzotriazole (**14**) with benzhydroxamoyl chloride (**33**) and *N*-(2,4-dibromophenyl)benzhydrazonyl bromide (**32**), respectively.

1-(Mercaptomethyl)benzotriazole (**14**) adds easily to activated double bonds as in compounds **41-43** (Scheme 5) to give the α-benzotriazolyl thioethers **39**, **40** and **45**, respectively. Compound **46** was synthesized in moderate yield following the method of Fuchs and Paquette [7]. Attempts to deprotonate compounds **39a,b** led only to the elimination of thiol **14**. However, compound **14** added to α,β-unsaturated carbonyl compounds **42a,b** to give products which underwent reduction *in situ* to potentially synthetically useful benzotriazolylmethyl 3-hydroxyalkyl thioethers **40a,b**.

Scheme 5



In summary, the convenient preparation of mercaptomethylbenzotriazole allows the synthesis of compounds of type **1** with highly functionalized $R^3$ groups.

## EXPERIMENTAL

Melting points were determined on a hot-stage microscope and are uncorrected. The $^1H$ and $^{13}C$ nmr spectra were obtained at 300 and 75 MHz respectively, on a Gemini 300 instrument in deuteriochloroform (unless specified otherwise) with tetramethylsilane as an internal standard. The chemical shifts assignments are presented in Table 1 for the benzotriazol-1-yl nucleus and in Figure 1 for the other positions. J values are given in Hz. *n*-Butyllithium was purchased from Aldrich as a 2*M* solution in hexane. Tetrahydrofuran was distilled under nitrogen from sodium benzophenone ketyl prior to use.

### 1-(Mercaptomethyl)benzotriazole (**14**).

To a solution of 24 g (100 mmoles) of sodium sulfate nonahydrate in 30 ml of water, was added 9 ml (150 mmoles) of carbon disulfide and the reaction mixture was stirred at room temperature overnight. To the reddish solution obtained, 8.4 g (50 mmoles) of chloromethylbenzotriazole (**6**) was added under stirring and the mixture was allowed to react for 1.5 hours. The precipitate di-(benzotriazol-1-ylmethyl) sulfide (**13**), 0.81 g (11%) was filtered off and washed with 10 ml of water. The filtrate plus washing was poured while stirring, over 40 ml of saturated aqueous ammonium chloride. The precipitate was separated by filtration and washed with 2 x 10 ml of water then air-dried to yield 7.34 g (89%) of pure 1-(mercaptomethyl)benzotriazole, mp 92°.

*Anal.* Calcd. for $C_7H_7N_3S$: C, 50.89; H, 4.27; N, 25.43. Found: C, 50.96; H, 4.27; N, 25.70.

### Di-(benzotriazol-1-ylmethyl) Sulfide (**13**).

This compound was isolated as a by-product in the preparation of 1-(mercaptomethyl)benzotriazole, as described above, white crystals, mp 179°.

*Anal.* Calcd. for $C_{14}H_{12}N_6S$: C, 56.74; H, 4.08; N, 28.36. Found: C, 56.59; H, 4.01; N, 28.50.

### General Procedure for the Preparation of Benzotriazolylmethyl Dithiocarboxylates **19a,b**.

The Grignard reagents **21a,b** were prepared from 30 mmoles of the corresponding aryl bromide and 1.2 g (50 mmoles) of magnesium in 50 ml diethyl ether, by refluxing the reaction mixture for 4 hours. The resulting solution was decanted from the excess magnesium in a dropping funnel and added while stirring at 0° over a solution of 1.80 ml (30 mmoles) of carbon disulfide in 50 ml of diethyl ether. The reaction mixture was allowed to warm to room temperature and stirred overnight. A solution of 2.85 g (27 mmoles) of chloromethylbenzotriazole (**6**) in 50 ml of tetrahydrofuran was then added while stirring at 0° and the mixture was stirred at this temperature for 2 hours. The reaction was quenched with 50 ml of saturated aqueous ammonium chloride, the layers were separated and the aqueous one extracted with 2 x 20 ml of methylene chloride. The combined organic layers were dried over magnesium sulfate and the solvent was removed *in vacuo*. The residue was chromatographed on silica, eluting with a mixture hexane:ethyl acetate (10:1). The crude benzotriazolylmethyl dithiocarboxylates were then recrystallized from diethyl ether.

### Benzotriazol-1-ylmethyl Dithiobenzoate (**19a**).

This compound was obtained as orange crystals, mp 75°, in 75% yield.

*Anal.* Calcd. for $C_{14}H_{11}N_3S_2$: C, 58.92; H, 3.89; N, 14.72. Found: C, 59.21; H, 3.87; N, 14.81.

### Benzotriazol-1-ylmethyl Dithio-*para*-methoxybenzoate (**19b**).

This compound was obtained as red crystals, mp 91°, in 22% yield.

*Anal.* Calcd. for $C_{15}H_{13}N_3OS_2$: C, 57.12; H., 4.15; N, 13.32. Found: C, 57.32; H, 4.16; N, 13.30.

### The Reaction of Benzotriazol-1-ylmethyl Dithiocarboxylates **19a,b** with *para*-Xylylmagnesium Bromide (**18**).

The Grignard reagent **18** was prepared from 30 mmoles of *para*-xylyl chloride and 1.2 g (50 mmoles) of magnesium in 50 ml of diethyl ether, by refluxing the reaction mixture for 4 hours. The resulting solution was decanted from the excess magnesium in a dropping funnel and added at -78° in portions, with stirring, over a solution of 5 mmoles of benzotriazol-1-ylmethyl dithiocarboxylate **19a** or **19b** in 20 ml of diethyl ether. For the reaction of compound **19b**, after each addition a sample of 2 ml of the reaction mixture was withdrawn into syringe and immediately poured over 1 ml of saturated aqueous ammonium chloride. The organic layer was then separated and the solvent removed *in vacuo* and replaced with chloroform-$d_3$ to prepare a sample for nmr control. One hour after the completion of the addition, the reaction mixture was quenched with 10 ml of a saturated aqueous solution of ammonium chloride. The organic layer was separated, dried (sodium sulfate) and then the solvent removed *in vacuo*. The residue was triturated in 10 ml of diethyl ether to yield 1-(methylmercapto)benzotriazole identical to that prepared from salt **12**. The yield was 26% in the reaction of **19a** and 42% in the reaction of **19b**.

### Reaction of 1-(Mercaptomethyl)benzotriazole (**14**) with Potassium Carbonate.

To a solution of 0.83 g (5 mmoles) of 1-(mercaptomethyl)benzotriazole in 5 ml of acetone was added 2 ml of a saturated aqueous solution of potassium carbonate. The mixture was stirred at room temperature for 24 hours, the solution decanted and the precipitate stirred with 10 ml of a 5% aqueous sodium hydroxide solution. The precipitate was separated by filtration and washed on the filter with 20 ml of water and 20 ml of acetone and then dried. The material did not melt, but decomposed at about 165°. Its elemental analysis fitted formula **25c**, yield 65%.

*Anal.* Calcd. for $C_{16}H_{25}N_3S_{10}$: C, 33.13; H, 4.34; N, 7.27. Found: C, 32.78; H, 4.08; N, 7.34.

### Benzotriazol-1-ylmethyl Cyclohexanon-2-yl Thioether (**26**).

To a solution of 3.30 g (20 mmoles) of 1-(mercaptomethyl)benzotriazole (**14**) and 3.1 ml (22 mmoles) of triethylamine 40 ml of ethyl acetate, 2.65 g (20 mmoles) of α-chlorocyclohexanone (**27**) was added in portions at 0°, under nitrogen and stirring. The reaction mixture was stirred at 0° for 1 hour, the triethylamine hydrochloride filtered off and the filtrate washed with 3 x 25 ml of water, then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* to yield 5.19 g (99%) of the title compound as colorless crystals, mp 78°.

*Anal.* Calcd. for $C_{13}H_{15}N_3OS$: C, 59.75; H, 5.79; N, 16.08. Found: C, 59.76; H, 5.75; N, 16.00.

### Benzotriazol-1-ylmethyl Methoxymethyl Thioether (**29**).

To a solution of 8.25 g (50 mmoles) of 1-(mercaptomethyl)benzotriazole (**14**) and 7 ml (50 mmoles) of triethylamine in 150 ml of ethyl acetate, 4.2 ml (55 mmoles) of chloromethyl methyl ether (**28**) was added at 0° under nitrogen and stirring. The reaction mixture was stirred at 0° for 1 hour and the triethylamine hydrochloride filtered off. The filtrate was washed with 3 x 25 ml of water then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue recrystallized from 20 ml of diethyl ether to yield 9.72 g (83%) of the title compound as colorless crystals, mp 52°.

*Anal.* Calcd. for $C_9H_{11}N_3OS$: C, 51.66; H, 5.30; N, 20.08. Found: C, 51.57; H, 5.29; N, 20.17.

### General Procedure for the Reaction of Benzotriazol-1-ylmethyl Methoxymethyl Thioether (**29**) with Electrophiles.

To a solution of 2.09 g (10 mmoles) of benzotriazol-1-ylmethyl methoxymethyl thioether (**29**) in 80 ml of tetrahydrofuran was added 5 ml of a 2*M* solution of *n*-butyllithium in hexane at -78°, under nitrogen and with stirring. After 15 minutes, 10 mmoles of the electrophile was added. The reaction mixture was stirred at -78° for 2 hours and at room temperature for 12 hours and quenched with 20 ml of saturated aqueous ammonium chloride solution. The layers were separated and the aqueous one was extracted with 2 x 10 ml of methylene chloride. The joint organic layers were dried over anhydrous sodium sulfate and the solvent removed *in vacuo* to yield the crude product. This was purified by recrystallization or by column chromatography on silica, eluting with hexane:ethyl acetate 10:1.

### 1-(Benzotriazol-1-yl)-2-methylpropyl Methoxymethyl Thioether (**31a**).

This compound was obtained in the reaction of benzotriazol-1-ylmethyl methoxymethyl thioether (**29**) with isopropyl iodide. Column chromatography of the crude product afforded the pure compound in 62% yield, white crystals mp 57°.

*Anal.* Calcd. for $C_{12}H_{17}N_3OS$: C, 57.34; H, 6.82; N, 16.72. Found: C, 57.65; H, 7.02; N, 16.60.

### 1-(Benzotriazol-1-yl)octyl Methoxymethyl Thioether (**31b**).

This compound was obtained in the reaction of benzotriazol-1-ylmethyl methoxymethyl thioether (**29**) with heptyl bromide. The reaction afforded the pure compound in 90% yield as a colorless oil.

*Anal.* Calcd. for $C_{16}H_{25}N_3OS$: C, 62.51; H, 8.20; N, 13.68. Found: C, 62.15; H, 8.48; N, 13.74.

### (Benzotriazol-1-yl)(benzyl)methyl Methoxymethyl Thioether (**31c**).

This compound was obtained in the reaction of benzotriazol-1-ylmethyl methoxymethyl thioether (**29**) with benzyl bromide. The reaction afforded the pure compound in 92% yield as a colorless oil; hrms: (POS FAB NBA). Calcd. for $C_{16}H_{18}N_3OS$: 300.1171 (M+1). Found: 300.1170. Satisfactory elemental analysis could not be obtained for this compound.

### (Benzotriazol-1-yl)(acetyl)methyl Methoxymethyl Thioether (**31d**).

This compound was obtained in the reaction of benzotriazol-1-ylmethyl methoxymethyl thioether (**29**) with ethyl acetate. Column chromatography of the crude product afforded the pure compound in 62% yield as a colorless oil; hrms: (POS FAB NBA). Calcd. for $C_{11}H_{14}N_3O_2S$: 252.0807 (M+1). Found: 252.0798. Satisfactory elemental analysis could not be obtained for this compound.

### (Benzotriazol-1-yl)(benzoyl)methyl Methoxymethyl Thioether (**31e**).

This compound was obtained in the reaction of benzotriazol-1-ylmethyl methoxymethyl thioether (**29**) with ethyl benzoate. Column chromatography of the crude product afforded the pure compound in 58% yield as white crystals, mp 58°.

*Anal.* Calcd. for $C_{16}H_{15}N_3O_2S$: C, 61.32; H, 4.82; N, 13.41. Found: C, 61.54; H, 4.84; N, 13.38.

### *N*-(2,4-Dibromophenyl)benzhydrazonyl Benzotriazol-1-ylmethyl Thioether (**35**).

To a solution of 2.8 ml (20 mmoles) of triethylamine and 2.17 g (5 mmoles) of *N*-(2,4-dibromophenyl)benzhydrazonyl bromide (**32**) in 40 ml of tetrahydrofuran, 0.82 g (5 mmoles) of 1-(mercaptomethyl)benzotriazole (**14**) was added at room temperature, in portions, with stirring. The reaction mixture was stirred at reflux overnight. The triethylamine hydrochloride was filtered off and the filtrate washed with 20 ml of saturated aqueous ammonium chloride solution, then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue triturated in 10 ml of diethyl ether to give 2.09 g (78%) of the title compound as white crystals, mp 141°.

*Anal.* Calcd. for $C_{20}H_{15}N_5SBr_2$: C, 46.44; H, 2.92; N, 13.54. Found: C, 46.46; H, 2.89; N, 13.79.

### Benzohydroxamoyl Benzotriazol-1-ylmethyl Thioether (**36**).

To a stirred solution of 0.70 ml (5 mmoles) of triethylamine in 40 ml of tetrahydrofuran, 0.82 g (5 mmoles) of benzohydroxamoyl chloride (**33**) was added at 0°, then, in portions, 0.82 g (5 mmoles) of 1-(mercaptomethyl)benzotriazole (**14**). The reaction mixture was then stirred at room temperature overnight. The triethylamine hydrochloride was filtered off and the reaction mixture washed with 20 ml of saturated aqueous ammonium chloride solution and dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue triturated with chloroform to give 0.88 g (62%) of the title compound as white crystals, mp 194°.

*Anal.* Calcd. for $C_{14}H_{12}N_4OS$: C, 59.14; H, 4.25; N, 19.70. Found: C, 59.44; H, 4.27; N, 19.79.

### General Procedure for the Reaction of 1-(Mercaptomethyl)benzotriazole (**14**) with Halomethylaromatics.

To a solution of 3.30 g (20 mmoles) of 1-(mercaptomethyl)benzotriazole and 2.8 ml (20 mmoles) of triethylamine in 50 ml of methylene chloride, 20 mmoles of halomethylaromatic was added at room temperature under nitrogen and stirring. The reaction mixture was stirred for 12 hours, washed with 3 x 25 ml of water and dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue recrystallized from 10 ml of ethyl acetate.

### Benzatriazolylmethyl Phenylmethyl Thioether (**37a**).

This compound was obtained in the reaction of 1-(mercaptomethyl)benzotriazole (**14**) with benzyl bromide in 88% yield, as white crystals, mp 110°.

*Anal.* Calcd. for $C_{14}H_{13}N_3S$: C, 65.86; H, 5.13; N, 16.46. Found: C, 65.73; H, 5.08; N, 16.59.

### Benzotriazolylmethyl (4-Methylphenyl)methyl Thioether (**37b**).

This compound was obtained in the reaction of 1-(mercaptomethyl)benzotriazole (**14**) with *p*-xylyl chloride in 84% yield, as white crystals, mp 144°.

*Anal.* Calcd. for $C_{15}H_{15}N_3S$: C, 66.89; H, 5.57; N, 15.70. Found: C, 66.81; H, 5.57; N, 15.70.

### Benzotriazolylmethyl 2-Naphthylmethyl Thioether (**37c**).

This compound was obtained in the reaction of 1-(mercaptomethyl)benzotriazole (**14**) with 2-(bromomethyl)naphthalene in 74% yield, as white crystals, mp 113°.

*Anal.* Calcd. for $C_{18}H_{15}N_3S$: C, 70.79; H, 4.95; N, 13.76. Found: C, 71.05; H, 4.99; N, 14.03.

### 2-(Benzotriazol-1-yl)-1-phenylnonyl Methoxymethyl Thioether (**38b**).

This compound was obtained following the general procedure for the reaction of benzotriazol-1-ylmethyl methoxymethyl thioether (**29**) with electrophiles, as in the reaction of benzotriazol-1-yl-heptylmethyl methoxymethyl thioether (**31b**) with benzyl bromide. Column chromatography of the crude product afforded the pure compound in 80% yield as a colorless oil; hrms: (POS FAB NBA). Calcd. for $C_{23}H_{32}N_3OS$: 398.2266 (M+1). Found: 398.2242. Satisfactory elemental analysis could not be obtained for this compound.

### Benzotriazol-1-ylmethyl 2-(Ethoxycarbonyl)ethyl Thioether (**39a**).

A solution of 3.30 g (20 mmoles) of 1-(mercaptomethyl)benzotriazole and 2.4 ml (20 mmoles) of ethyl acrylate in 50 ml of methanol was stirred for 12 hours at room temperature under nitrogen. The solvent was removed *in vacuo,* to give 5.00 g (yield 94%) of the tide compound, as a colorless oil.

*Anal.* Calcd. for $C_{12}H_{15}N_3O_2S$: C, 54.32; H, 5.69. Found: C, 54.15; H, 5.69.

### Benzotriazol-1-ylmethyl 2-(Pyridin-4-yl)ethyl Thioether (**39b**).

A solution of 3.30 g (20 mmoles) of 1-(mercaptomethyl)benzotriazole and 2.2 ml (20 mmoles) of 4-vinylpyridine in 50 ml of methanol was stirred for 12 hours at room temperature under nitrogen. The solvent was removed *in vacuo,* and the residue recrystallized from 20 ml of ethyl acetate to give 3.47 g (yield 64%) of the title compound as white crystals, mp 99°.

*Anal.* Calcd. for $C_{14}H_{14}N_4S$: C, 62.20; H, 5.22; N, 20.72. Found: C, 62.29; H, 5.16; N, 20.86.

### General Method for the Preparation of the Benzotriazol-1-ylmethyl 3-Hydroxyalkyl Thioethers.

A solution of 1.67 g (10 mmoles) of 1-(mercaptomethyl)benzotriazole and 10 mmoles of the α,β-unsaturated carbonyl compound in 50 ml of methanol was stirred for 12 hours at room temperature under nitrogen, 0.8 g (20 mmoles) of sodium borohydrate was then added in portions and the mixture was stirred at room temperature for 2 hours. The solvent was removed *in vacuo* and the residue was stirred with 50 ml of water for 2 hours and extracted with 3 x 20 ml of methylene chloride. The extract was dried over anhydrous sodium sulfate and the solvent removed *in vacuo,* to give an oil which was chromatographed on silica, eluting with hexane-ethyl acetate 5:1 to yield the pure title compound.

### Benzotriazol-1-ylmethyl 3-Hydroxypropyl Thioether (**40a**).

This compound was obtained in 80% yield upon departing from acrolein as a colorless oil.

*Anal.* Calcd. for $C_{10}H_{13}N_3OS$: C, 53.79; H, 5.74; N, 18.82. Found: C, 52.06; H, 5.74; N, 19.09.

### Benzotriazol-1-ylmethyl 3-Hydroxybutyl Thioether (**40b**).

This compound was obtained in 84% yield when departing from methyl vinyl ketone as a colorless oil.

*Anal.* Calcd. for $C_{11}H_{15}N_3OS$: C, 55.67; H, 6.37. Found: C, 55.29; H, 6.38.

### Benzotriazol-1-ylmethyl (Phenyl)[2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrion-5-yl]methyl Thioether (**45**).

A solution of 3.30 g (20 mmoles) of 1-(mercaptomethyl)benzotriazole (**14**) and 4.20 g (20 mmoles) of benzalbarbituric acid [8] (43) in 250 ml of methanol was stirred for 12 hours at room temperature under nitrogen. The solvent was partially removed *in vacuo,* to a volume of *ca. 50* ml. The product was filtered and washed with 20 ml of methanol and then triturated in acetone to yield 6.30 g (97%) of the title compound as colorless solid, mp 189°.

*Anal.* Calcd. for $C_{18}H_{15}N_5O_2S$: H, 3.96; N, 18.36. Found: H, 3.83; N, 18.17.

### Benzotriazol-1-ylmethyl (Phenyl)(1,3-cyclohexandion-2-yl)methyl Thioether (**46**).

To a suspension of 2 g of silica in 20 ml of methylene chloride were added 0.82 g (5 mmoles) of 1-(mercaptomethyl)benzotriazole (**14**), 0.56 g (5 mmoles) of 1,3-cyclohexandione (**44**) and 1 ml (10 mmoles) of benzaldehyde. The reaction mixture was stirred for 24 hours at room temperature under nitrogen. The solvent was removed *in vacuo* and the residue was fed into a chromatographic column (OD *ca.* 20 mm) in top of *ca.* 50 ml silica The column was eluted with 500 ml of ethyl acetate-hexane 1:1 and the product was collected while eluting with 250 ml of ethyl acetate with 20% methanol. Removal of the solvent *in vacuo* yielded 0.89 g (48%) of the title compound, mp 161°.

*Anal.* Calcd. for $C_{20}H_{19}N_3O_2S$: H, 5.12; N, 11.37. Found: H, 5.12; N, 11.73.

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