Deprotonation of benzyl isothiocyanate: a simple route to silylated benzyl isothiocyanates

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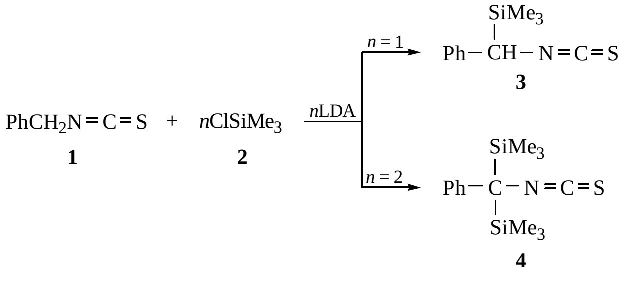
A new, convenient method for the preparation of mono- and bis(trimethylsilyl)benzyl isothiocyanates *via* lithiated benzyl isothiocyanate and chlorotrimethylsilane has been developed.

Silylated isothiocyanates, as well as isothiocyanates themselves, are important building blocks and convenient starting compounds for various organic syntheses,[1–3] including synthesis of heterocycles.[4] However, the range of known and available silylated isothiocyanates is still limited. These are mostly trimethyl-,[1] triphenyl-[5] or triethoxy-[3] silyl isothiocyanates, and mono-, bis- and tris(trimethylsilyl)methyl isothiocyanates.[3,6,7] The latter three have been obtained by addition of sulfur to mono-, bis- and tris(trimethylsilyl)methyl isocyanides[6,7] and also *via* the classic route from the corresponding amines and carbon disulfides in the presence of base.[3] Silylated benzyl isothiocyanates remain unknown, although they are even more promising synthetic intermediates owing to their phenyl group which is capable of a variety of further transformations.

Recently, as part of our systematic investigations of reactions of heterocumulenes with organometallics, we have developed a convenient synthesis of silylated methyl isocyanates, which consists of trapping the anion from methyl isothiocyanate with chlorotrimethylsilane.[8]

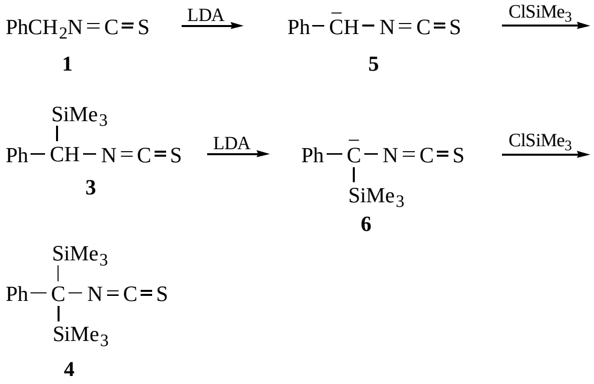
The method developed[9] for deprotonation of activated isothiocyanates, including benzyl isothiocyanate **1**, with Bu^{t}OK in THF at –70 °C was used for the synthesis of 1,3-oxazolidine-2-thione derivatives (from the reaction with aldehydes or ketones). Lithiation of **1** with lithium diisopropylamide (LDA) gave, after methylation (with methyl iodide), a thiazole derivative [5-(*N*-benzyl-*N*-methyl)amino-2-(methylthio)-4-phenyl-1,3-thiazole] in good yield (unpublished data).

In this communication we describe a simple, convenient and high-yield, one-pot synthesis of mono- (**3**) and bis- (**4**) (trimethylsilyl)benzyl isothiocyanates starting from available benzyl isothiocyanate **1**, LDA and chloromethylsilane **2**. We found that adding a solution of LDA in Et_2O–hexane at –100 to –90 °C to a mixture of **1** and **2** in THF afforded **3** and **4** depending upon the molar ratio of **1**, **2** and LDA.



These and previously obtained results (for methylisothiocyanate)[8] show that the competition between **1** and **2** for LDA is by far in favour of **1**, whereas in the same competition for **5** the winner is **2**, thus suggesting the initial selective deprotonation of **1** followed by subsequent silylation of the carbanion **5**.

The structures of isothiocyanates **3** and **4** are supported by IR, ^{1}H NMR spectroscopy and elemental analysis data.[†]



References

1 L. Drobnica, P. Kristian and J. Augustin, *The Chemistry of the N=C=S Group*, in *The Chemistry of Cyanates and their Thio Derivatives*, Part 2, ed. S. Patai, Wiley, Chichester, 1977, p. 1003.

2 N. A. Nedolya, B. A. Trofimov and A. Senning, *Sulfur Reports*, 1996, **17**, 183.

3 J. E. Noll, *J. Am. Chem. Soc.*, 1955, **77**, 3149.

[†] The reaction was performed under anhydrous conditions and in a nitrogen atmosphere. To a stirred solution of freshly-distilled chloromethylsilane (0.12 mol) and isothiocyanate **1** (0.10 mol) in 80 ml THF, cooled to –80 °C, was added a cold (–10 °C) solution of LDA (0.11 mol) in 70 ml hexane and 70 ml diethyl ether from a dropping funnel at –80 to –70 °C over 75 min. The cooling bath with liquid nitrogen was removed and, when the temperature reached –30 °C, the reaction mixture was heated to 25 °C and stirred at this temperature during 0.5 h. Dry work-up of the reaction mixture was carried out. The solvents were removed on a rotary evaporator. The residue was distilled *in vacuo* to give benzyl trimethylsilyl isothiocyanate **3**: yield 19 g (86%), purity 91.3% (GLC), bp 110–120 °C (0.8 mmHg), n_D^{20} 1.5646. IR, ν/cm^{-1} (film): 500, 580, 600, 620, 650, 700, 730, 740, 770, 840, 910, 1030, 1060, 1080, 1130, 1190, 1250, 1300, 1340, 1400, 1450, 1490, 1600, 2065, 2150, 2900, 2950, 3025, 3060, 3080. ^{1}H NMR (90 MHz, CCl_4, standard TMS) δ: 0.12 (s, 9H, $SiMe_3$), 4.29 (s, 1H, CH), 7.25 (m, 5H, Ph). Found (%): C 59.50, H 6.67, N 6.60, S 14.77, Si 12.46; calc. for $C_{11}H_{14}NSSi$ (%): C 59.68, H 6.83, N 6.33, S 14.48, Si 12.69.

To a stirred solution of freshly-distilled chloromethylsilane (0.15 mol) and isothiocyanate **1** (0.05 mol) in 100 ml THF, cooled to –90 °C, was added a cold (–10 °C) solution of LDA (0.15 mol) in 95 ml hexane and 70 ml diethyl ether from a dropping funnel at –95 to –90 °C over 45 min. The cooling bath with liquid nitrogen was removed and, when the temperature reached –40 °C, the reaction mixture was treated with 150 ml of *ca.* 8% aqueous solution of HBr under vigorous stirring and cooling below –5 °C. The organic layer was dried ($MgSO_4$) and the solvents removed on rotary evaporator. The crystalline residue was distilled *in vacuo* to give benzyl bis(trimethylsilyl) isothiocyanate **4**: yield 13.3 g (91%), bp 100–130 °C (0.5 mmHg), mp 63–64 °C. IR, ν/cm^{-1} (KBr): 450, 500, 600, 620, 640, 700, 740, 750, 840, 860, 915, 1035, 1040, 1090, 1170, 1250, 1400, 1450, 1490, 1600, 2045, 2145, 2900, 2955, 3040, 3060, 3090. ^{1}H NMR (90 MHz, CCl_4, standard TMS) δ: 0.15 (s, 18H, $SiMe_3$), 7.20 (m, 5H, Ph). Found (%): C 57.34, H 7.84, N 5.04, S 11.32, Si 18.46; calc. for $C_{14}H_{23}NSSi_2$ (%): C 57.28, H 7.90, N 4.77, S 10.92, Si 19.13.

4 H. Ulrich, in *Organic Chemistry, a Series of Monographs, Cycloaddition Reactions of Heterocumulenes*, ed. A. T. Blomquist, Academic Press, New York–London, 1967, vol. 9, p. 364.

5 H. Gilman, B. Hofferth and H. W. Melvin, *J. Am. Chem. Soc.*, 1950, **72**, 3045.

6 (*a*) T. Hirao, A. Yamada, Y. Ohshiro and T. Agawa, *Angew. Chem.*, 1981, **93**, 95; (*b*) T. Hirao, A. Yamada, Y. Ohshiro and T. Agawa, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 126.

7 T. Hirao, A. Yamada, K. Hayashi, Y. Ohshiro and T. Agawa, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 1163.

8 L. Brandsma, N. A. Nedolya, H. D. Verkruijsse and B. A. Trofimov, *Synthesis*, 1997, 423.

9 D. Hoppe and R. Follmann, *Chem. Ber.*, 1976, **109**, 3047.

Received: Moscow, 27th August 1997
Cambridge, 20th October 1997; Com. 7/06556F