Chemistry of Amine–Boranes. Part 10.[1] Synthesis of Sulphides from Dithioacetals using Pyridine–Borane in Acid

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The synthesis of sulphides from dithioacetals in trifluoroacetic acid or in dichloromethane in the presence of aluminium chloride with pyridine–borane is described.

Although several amine–boranes are now commercially available, their chemistry has not been thoroughly investigated. In the course of our investigation of the chemistry of such compounds, we found that they had unique reducing abilities in acidic media.[2] In the preceding paper, we reported the reduction of aldehydes and aryl ketones with pyridine–borane in trifluoroacetic acid (TFA) to give symmetric ethers and alkylbenzenes, respectively.[3] In later work [1] we have reported a one-pot synthesis of sulphides by the reduction of the mixture of thiols and aldehydes or ketones with pyridine–borane in TFA; we describe here an investigation of the reduction of dithioacetals with pyridine–borane in TFA or in dichloromethane in the presence of aluminium chloride ($AlCl_3$).

Results and Discussion

Synthesis of Sulphides from Dithioacetals.—In the previous Part [1] the reductive thiation of carbonyl compounds with thiols and pyridine–borane in the presence of acid was described. The intermediate in this reaction was assumed to be a dithioacetal because these are easily formed when aldehydes or ketones are mixed with thiols in the presence of acid. Pyridine–borane is generally fairly stable in acid, but when it was added to TFA solution gas was immediately evolved, even with coding, and the reducing ability decreased markedly with time; the main by-product of the reaction of carbonyl compounds with thiols in the presence of this reagent was a dithioacetal which was identified by a gas chromatographic analysis of the distillation residue. Therefore, we used the dithioacetals, synthesised by the usual method,[4] as the starting material for reduction under these conditions in order to obtain better yields of the sulphides. Several dithioacetals were subjected to the pyridine–borane reduction and the results are presented in Table 1.

All the dithioacetals, except a cyclic one (**3a**), were reduced to the corresponding sulphides in good yields. The reason why the cyclic dithioacetal (**3a**) was not reduced can be explained as follows. In the case of the acyclic dithioacetals, a carbonium ion is generated by the release of one thiol moiety by acid, and is long-lived and quenched easily by hydride to give the sulphide. However, in the case of the cyclic dithioacetal, the carbonium ion is unlikely to be generated at all, and if it is generated, it immediately reacts intramolecularly with the sulphur atom because they are located close to each other. Thus, in order to reduce cyclic dithioacetals it is necessary to use a stronger acid than TFA to generate a long-lived carbonium ion which can be attacked by hydride.

The Synthesis of Sulphides using Aluminium Chloride as Acid.—Although various methods for the cleavage of acetals, by silane derivatives,[5] mixed hydrides,[6] diborane,[7] and cyanoborohydride,[8] to give ethers have been reported, there is only one example, to our knowledge, of the cleavage of dithioacetals, where calcium in liquid ammonia reduced cyclic dithioacetals to give 2-mercaptoethyl sulphides.[9]

Table 1. Synthesis of sulphides from dithioacetals

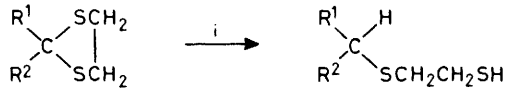
$$R^1R^2C(SR^3)_2 \xrightarrow{i} R^1R^2CHSR^3$$
(1),(3a)

Reagents: i, pyridine–BH_3–CF_3CO_2H, 5 min with cooling

Compound	R^1	R^2	R^3	Yield (%)[a] of sulphide
(1a)	Ph	H	$PhCH_2$	96
(1b)	Ph	H	$CH_3(CH_2)_6$	99
(1c)	Ph	Me	$CH_3(CH_2)_3$	76
(1d)	Et	Me	$PhCH_2$	76
(1e)	Et	H	$PhCH_2$	72[b]
(3a)	Ph	Me	$HSCH_2CH_2$	0(89)

[a] Figures in parentheses are amounts (%) of starting material recovered. [b] B.p. 95—97 °C/9 Torr (lit.,[10] b.p. 112 °C/14 Torr); b.p.s of (**1a**—**d**) are listed in ref. 1.

Table 2. Reduction of ethylene dithioacetals with pyridine–BH_3–$AlCl_3$



(2) **(3)**

Reagents: i, pyridine–BH_3–$AlCl_3$, CH_2Cl_2, 5 min with cooling

Compound	R^1	R^2	Yield[a] (%)	B.p. (°C/Torr)
(3a)	Ph	Me	79[b]	122—124/6
(3b)	$-(CH_2)_5-$		88	90—92/2[c]
(3c)	$PhCH_2$	H	0(94)	

[a] Figures in parentheses are amounts (%) of starting material recovered. [b] The small amounts of $(PhCHMeSCH_2)_2$ were detected in the distillation residue; δ($CDCl_3$) 1.47, 1.54 (6 H, d, *J* 7 Hz, CH_3 × 2), 2.38 (4 H, s, CH_2CH_2), 3.87 (2 H, q, *J* 7 Hz, CH × 2), 7.27 (10 H, s, ArH); M^+, 302.1111 ($C_{18}H_{22}S_2$ requires *M*, 302.1161). [c] Lit.,[9] b.p. 85 °C/0.6 Torr.

We have already noted that pyridine–borane–TFA failed to reduce the cyclic dithioacetal (**3a**), and this time pyridine–borane–$AlCl_3$ in dichloromethane was used for the reduction. The results are presented in Table 2. Ethylene dithioacetals, produced from ketones, were reduced to the 2-mercaptoethyl sulphides, but phenylacetaldehyde ethylene dithioacetal (**3c**) was recovered quantitatively. This remarkable difference between dithioacetals from aldehydes, and those from ketones can be explained by the difference in stability of the carbonium ion generated by $AlCl_3$ and/or the steric effects on the cyclisation caused by the difference in bulkiness between a hydrogen atom and an alkyl group.

It is obvious that the reducing power of pyridine–borane–

$AlCl_3$ toward dithioacetals is stronger than that of pyridine–borane–TFA. Other Lewis acids such as boron trifluoride–diethyl ether and zinc chloride were subjected to the same reaction, but the starting ethylene dithioacetal was recovered. The pyridine–borane–$AlCl_3$ system was applied to the one-pot synthesis of sulphides from thiols and carbonyl compounds in the same way as the pyridine–borane–TFA system. From benzaldehyde and heptane-1-thiol, benzyl heptyl sulphide was obtained in 72.6% yield and also benzyl alcohol, which was not detected in the case of the reduction with pyridine–borane–TFA, in 12.8% yield.

Pyridine–borane–$AlCl_3$ in dichloromethane also reduced benzaldehyde dibenzyl dithioacetal to dibenzyl sulphide quantitatively. This system afforded equally good results as those from the pyridine–borane–TFA system for the synthesis of sulphides.

Experimental

All m.p.s are uncorrected. N.m.r. spectra (tetramethylsilane as internal standard) were obtained with a JNM-C-60HL spectrometer, mass spectra with Shimadzu LKB-9000 instrument, and accurate mass spectra with a JEOL JMS-O1SG spectrometer.

Reagents.—The aldehydes and ketones used were commercially available. The dithioacetals were prepared from the corresponding carbonyl compounds and thiols in the presence of Lewis acids by the usual method and purified by distillation or chromatography over silica gel, using benzene–hexane (1:1 v/v) as eluant.

General Procedure for the Synthesis of the Sulphides from the Dithioacetals with Pyridine–Borane in TFA.—Pyridine–borane (0.3 ml) was added to a mixture of propionaldehyde dibenzyl dithioacetal (290 mg, 1 mmol), CH_2Cl_2 (1.5 ml), and TFA (4 ml) with cooling. After being stirred for 5 min, the solvent was removed under reduced pressure, 10% NaOH (15 ml) was added to the residue, and after several minutes the solution was extracted with benzene (20 ml × 2) and the combined extracts were washed with saturated aqueous NaCl (20 ml), dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel using benzene–hexane (2:3, v/v) for elution to give benzyl propyl sulphide (**1e**) (119 mg, 72%), b.p. 95—97 °C/9 Torr (lit.,[10] b.p. 112 °C/14 Torr).

General Procedure for the Reduction of Ethylene Dithioacetals with Pyridine–Borane–$AlCl_3$ in CH_2Cl_2.—Pyridine–borane (0.44 ml) was added to a mixture of cyclohexanone ethylene dithioacetal (256 mg, 1.47 mmol), $AlCl_3$ (589 mg, 4.41 mmol), and CH_2Cl_2 (4 ml) with cooling. After being stirred for 5 min, the CH_2Cl_2 was evaporated under reduced pressure. 10% Na_2CO_3 (15 ml) was carefully added to the residue with cooling and the insoluble material which appeared was filtered off. The aqueous layer was extracted with benzene (20 ml × 2), and the combined extracts were washed with saturated aqueous NaCl (20 ml), dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel using benzene–hexane (1:1 v/v) as eluant to give cyclohexyl 2-mercaptoethyl sulphide (**3b**) (225 mg, 88%), b.p. 90—92 °C/2 Torr (lit.,[9] b.p. 85 °C/0.6 Torr).

N.M.R. Data of the Products.—All the products showed reasonable n.m.r. data. The n.m.r. data of the new compounds are as follows: δ($CDCl_3$) (**1b**) 0.6—1.8 [13 H, m, $(CH_2)_5CH_3$], 2.2—2.6 (2 H, br t, SCH_2C), 3.65 (2 H, s, $ArCH_2S$), and 7.25 (5 H, s, ArH); (**3a**) 1.53 (3 H, d, *J* 7 Hz, Me), 1.54 (1 H, SH, overlapped with Me), 2.50, 2.57 (4 H, d, CH_2CH_2), 3.95 (1 H, q, *J* 7 Hz, CHS), and 7.25 (5 H, s, ArH).

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