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BORON TRIHALIDE-METHYL SULFIDE COMPLEXES AS CONVENIENT REAGENTS FOR DEALKYLATION OF ARYL ETHERS

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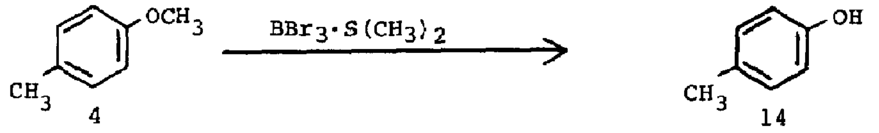
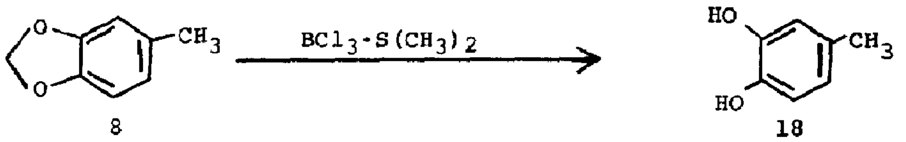
Abstract: High yield dealkylation of several aryl methyl ethers was observed upon exposure of these compounds to an excess of the boron trihalide-methyl sulfide complexes.

A choice of specific reaction conditions is now available to effect a preparatively useful nucleophilic substitution reaction on aryl methyl ethers[1] and may be termed conveniently "a demethylation reaction" as illustrated by reaction (1). However, this terminology excludes some related reactions, such as hydrolysis of the benzo-1,3-dioxole ring illustrated by reaction (2), i.e. deprotection of a phenol (catechol).[2] We report our observation of essentially quantitative demethylation of a variety of aryl methyl ethers upon exposure to a two-fold to four-fold excess of boron tribromide methyl sulfide.[3a-c] In addition we have obtained high yields of O-demethylation of some di-O-methyl ethers. We have also observed high yields for the hydrolysis of the 1,3-methylenedioxole ring of piperonal (7) to protocatechualdehyde (17) and of (8) to 3,4-dihydroxytoluene (18). We perceive this to be a quite general observation; hence, we are prompted to report our results. A number of properties of the boron trihalide-methyl sulfide addition complexes, commendable properties of which are the convenience of preparation, the long-term stability and the ease of handling, warrant their consideration as useful alternatives to existing procedures.



(1)



(2)

TABLE I

Reactant Number	Reactant	Product Number	Product	Ratio of Equivalents $BX_3 \cdot (CH_3)_2$/ether linkage	Temp. °C	Time h	vpc Yield %	Isolated Yield
1	Anisole	11	phenol	4.00^d	83.5	12	86.4	--
2	o-methylanisole	12	o-methyl phenol	3.97^d	83.5	12	97.7	67.2^a
3	m-methylanisole	13	m-methyl phenol	3.97^d	83.5	12	97.6	50.5^a
4	p-methylanisole	14	p-methyl phenol	3.79^d	83.5	12		77.7^a
5	Diethylstilbestrol-dimethyl ether	15	diethylstilbestrol	4.00^d	83.5	24	--	50.2^b
6	3,5-dimethoxytoluene	16	orcinol	3.87^d	83.5	24	--	63.7
7	piperonal	17	protocatechualdehyde	$2.00\text{-}BCl_3 \cdot S(CH_3)_2$	83.5	29.5	--	98.5
				$1.99\text{-}BBr_3 \cdot S(CH_3)_2$	83.5	4.5	--	52.9
8		18	3,4-dihydroxytoluene	$1.03\text{-}BCl_3 \cdot S(CH_3)_2$	83.5	10	--	67.9
9	vanillin	17	protocatechualdehyde	4.05^d	83.5	0.1	--	99.3
10	veratrole	19	catechol	1.23^d	95^c	12	--	82

a - after distillation

b - recrystallized from benzene

c - in toluene

d - X = Br

The results of a series of dealkylation reactions are given in Table I. The reactions were performed by mixing the reagents in 1,2-dichloroethane[4] and where it was possible the reactions were monitored by vpc and terminated when complete disappearance of the starting material had occurred. A typical experimental procedure follows: To a flame-dried 100 ml flask under an atmosphere of nitrogen was added approx. 30 ml of 1,2-dichloroethane and an amount of boron trihalide-methyl sulfide complex[2c] indicated in Table I. To this solution was added the desired number of equivalents of the aryl ether. The reaction was stirred at reflux and monitored by either tlc or vpc where convenient. When the starting material had disappeared, the reaction mixture was hydrolyzed by adding approx. 30 ml of water, stirring for 20 min and diluting with ether. The organic phase was separated and washed with 1M $NaHCO_3$ and the phenol was subsequently taken up with 1N NaOH (3x20 ml). The combined NaOH washings were acidified and the product was subsequently extracted into ether, dried ($MgSO_4$) and the solvent removed in vacuo. Further purification, when necessary, was performed as noted in the table. The products were identified by comparison with authentic materials.

All four of the boron trihalide (F, Cl, Br and I)-methyl sulfide addition compounds have been prepared and isolated in pure form.[5] The latter three exist as stable, crystalline solids. Due to the ready availability of the chloro and the bromo boron trihalides, we have focused our attention on the use of these two compounds and we have experienced no difficulty in preparing one hundred gram quantities of both the bromo and the chloro addition complexes according to the procedure outlined by Brown.[3a] Furthermore, we have stored these two addition complexes for over one year at 0°C under a dry, inert atmosphere of nitrogen. There is no loss in reactivity of either compound on brief exposure to air (i.e. weighing) or long term storage under nitrogen.

We suggest that equilibration occurs between the methyl sulfide and the aryl methyl ether vying as Lewis bases for the coordinatively unsaturated boron species.[6] This equilibration represents to us an exceedingly mild in situ release of the boron trihalide species as a powerful Lewis acid. Finally we suggest that a simplification of other experimental procedures which utilize the boron trihalides, e.g. for the transesterification reaction and for the synthesis of amides[7], might also be realized by the use of the methyl sulfide addition complexes.

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References and Notes

1. For typical procedures for removal of methyl ethers see: a) I. T. Harrison and S. Harrison, "Compendium of Organic Synthetic Methods", Vol. 3, Wiley, New York, 1977, p. 92; Vol. 2, 1974, p. 34; Vol 1, 1971, p. 92; b) C. B. Reese, in "Protective Groups in Organic Chemistry", J. F. McOmie, Ed., Plenum Press, London, 1973, pp 95-143; c) C. A. Buehler and D. E. Pearson, "Survey of Organic Synthesis", Vol. 1, Wiley, New York, 1970, p. 253; d) E. Vickery, L. F. Pahler and E. J. Eisenbraun, J. Org. Chem., 44, 4444 (1979); e) M. E. Jung, M. A. Mazurek and R. M. Lim, Synthesis, 588 (1978); f) M. E. Jung and M. A. Lyster, J. Org. Chem., 42, 3761 (1977); g) T.-L. Ho and G. A. Olah, Angew. Chem., 88, 847 (1976); h) J. F. W. McOmie, M. L. Watts and D. E West, Tetrahedron, 24, 2289 (1968); i) R. E. Ireland and D. M. Walba, Org. Synth., 56, 44 (1977); j) T. R. Kelly, H. M. Dali and W.-G. Tsang, Tetrahedr Lett., 3859 (1977); k) M. Node, K. Nishide, M. Sai and E. Fujita, Tetrahedro Lett., 5211 (1978).

2. For a discussion of the selective cleavage of an aromatic methyl ether in th presence of the methylene dioxy group see: J. Minamikawa and A. Brossi, Tetr hedron Lett., 3085 (1978) and references cited therein.

3. a) H. C. Brown and N. Ravindran, Inorg. Chem., 16, 2938 (1977); b) M. J. Bul D. E. Hamilton and J. S. Hartman, J. Chem. Soc. Dalton, 1972, 1405; c) M. Schmidt and H. D. Block, Chem. Ber., 103, 3705 (1970).

4. Although a variety of solvents including benzene, toluene, methylene chlorid and chloroform are satisfactory for effecting this reaction, we have selecte 1,2-dichloroethane as the solvent of choice for carrying out our reactions.

5. K. Kinberger and W. Siebert, Z. Naturforsch. B, 30, 55 (1975); see also foot notes # 2a and 3C.

6. M. J. Bula and J. Stephen Hartman, J. Chem. Soc. Dalton, 1973, 1047.

7. c.f. H. Yazawa, K. Tanaka and K. Kariyone, Tetrahedron Lett., 3995 (1974).

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