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SELECTIVE REMOVAL OF TETRAHYDROPYRANYL ETHERS IN THE PRESENCE OF *t*-BUTYLDIMETHYLSILYL ETHERS

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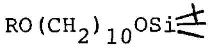
Summary: Dimethylaluminium chloride has been found to cleave THP ethers selectively without any removal of t-butyldimethylsilyl ethers

Tetrahydropyranyl (THP) and *t*-butyldimethylsilyl (TBDMS) ethers are frequently used as suitable protection for the hydroxy functionality in recent organic synthesis. TBDMS ethers can be cleaved selectively by treatment with a fluoride ion in the presence of THP ethers. Likewise, it is possible to cleave both ethers by mild acidic hydrolysis. Consequently, for a number of years we have been interested in the development of reagents for the highly selective removal of THP ethers without cleavage of TBDMS ethers under mild conditions. Judging from the reactivity of both ethers, it might be possible to cleave THP ethers selectively under the rather drastic conditions such as ozone (-50°C), peracids (50°C) and heat (>200°C).[1] However, it seems unlikely that these conditions are applicable to the synthesis of rather complex molecules such as prostaglandins and β-lactam antibiotics. In this communication we wish to report a solution to this synthetic problem.

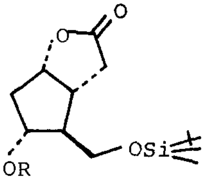
After many unsuccessful attempts we have found that dimethylaluminium chloride,[2] which is a mild Lewis acid and acts as a proton scavenger,[3] cleaves THP ethers in nearly quantitative yield without any removal of TBDMS ethers under the mild conditions. Namely, treatment of the THP ether(**1**) with 2 equiv of dimethylaluminium chloride, purchased from Toyo Stauffer Chemical Co., Ltd. in 20% hexane solution, in methylene chloride at -25°C~r.t. for 1hr followed by basic work-up (satd. $KHCO_3$ aq.) afforded the mono-ol(**2**) in 98% yield. The conditions described above could be applicable to selective deprotection of the rather complex molecules such as **3** (**4**, 96% yield), **5** (**6**, 89% yield) and **7** (**8**, ~100% yield).

Possibility of selective cleavage of other protecting groups such as MOM ethers, MEM ethers and 1-ethoxyethyl ethers in the presence of TBDMS ethers was also examined using the simple compounds (**9**, **10**, **11**). Unexpectedly, both the MOM ether(**9**) and the MEM ether(**10**) were converted to the ethyl ether(**12**) in 97% and 92% yield respectively by the action of dimethylaluminium chloride, which was probably formed *via* methyl transfer from the aluminium reagent.[4,5] On the other hand, the 1-ethoxyethyl ether(**11**) was led to the desired mono-ol(**2**) (60% yield) together with the isopropyl ether(**13**) at -25°C (31% yield).[6,7]

Selective removal of THP ethers in the presence of TBDMS ethers should be quite valuable in relation to the selection of desirable protecting groups of the hydroxy functionality in the synthesis of complex molecules. Further studies along this line are under investigation.



1: R=THP
2: R=H



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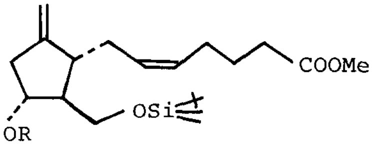
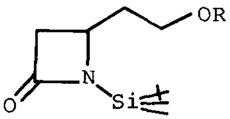
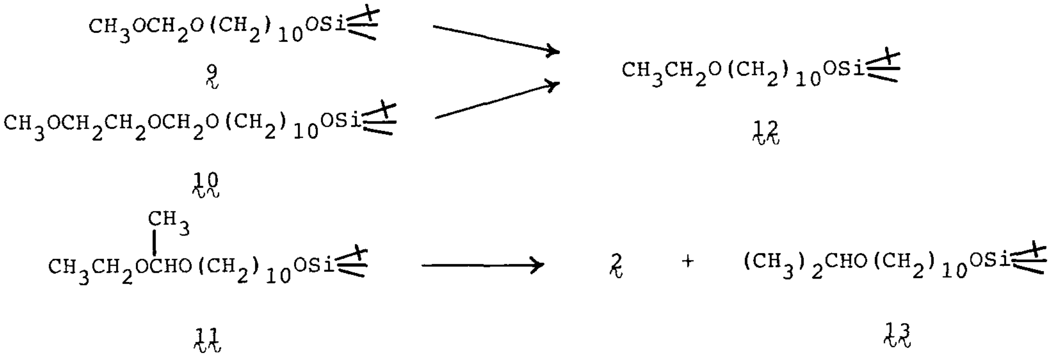
4: R=H



5: R=THP
6: R=H



7: R=THP
8: R=H



References and Notes

1) T.W. Greene, "Protective Groups in Organic Synthesis," p 298, John Wiley & Sons, New York, N.Y., 1981.

2) Methylaluminium dichloride was also found to be an excellent reagent for the present purpose. Namely, it converted 1 to 2 in 90% yield at -25°C for 0.5hr.

3) B.B. Snider, Acc. Chem. Res., 13, 426 (1980).

4) The MEM ether(10) was converted to the ethyl ether(12) even by the action of methylaluminium dichloride at -25°C∿r.t. (95% yield).

5) Treatment of the MEM ether(10) with either diethylaluminium chloride or ethylaluminium dichloride afforded the desired product(2) only in a low yield.

6) Trityl ethers are cleaved by the action of a dialkylaluminium chloride, see H. Köster and N.D. Sinha, Tetrahedron Lett., 23, 2641 (1982).

7) For the very recent reports concerning with cleavage of MEM, MOM and MTM ethers, see (a) D.R. Williams and S. Sakdarat, Tetrahedron Lett., 24, 3965 (1983); (b) Y. Guindon, H.E. Morton, and C. Yoakim, ibid., 24, 3969 (1983).

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