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REACTIVITY OF t-BUTYLDIMETHYLSILYL ETHERS : A FACILE CONVERSION INTO BROMIDES.

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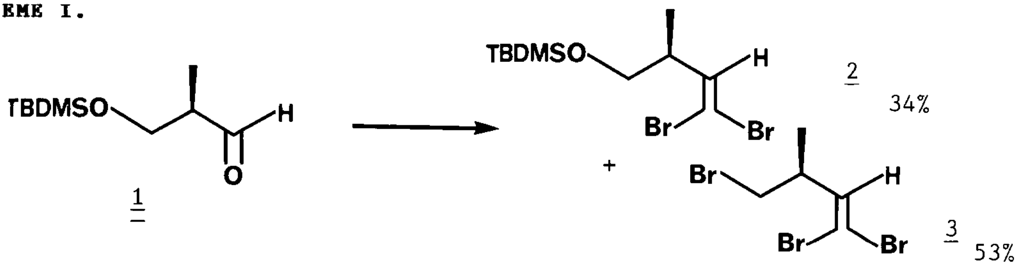
Abstract : TBDMS ether can be efficiently converted in one step into the corresponding bromides by a CBr_4, PPh_3 and acetone mixture.

The t-butyldimethylsilyl group introduced in organic synthesis by Stork et al. (1) and Corey et al. (2) is, at the moment, one of the most popular and useful protecting group for hydroxy functions. Its stability under various reaction conditions allows one to carry it unchanged through several synthetic steps (3).

In the course of a synthesis involving TBDMS protected alcohols, we found that when treated with CBr_4 and PPh_3 in dichloromethane silyl ether **1** yielded a mixture of two compounds **2** and **3**. (scheme I).

SCHEME I.



While compound **2** is clearly the result of the well known dibromovinylation of aldehydes (4) or ketones (4), in compound **3** the TBDMS ether has been replaced by a bromine atom.

Similar experiments under different reaction conditions permitted to define useful standard conditions.

In the absence of acetone, the TBDMSilyl ether remains unchanged. With acetone as a solvent the reaction gave a complex mixture of products including the desired bromide in only 30% yield. Bromination of the solvent probably leads to deactivation of the brominating entity. A much better yield was obtained with dichloromethane as a solvent using 1.5 eq. of acetone (60% yield). Finally, switching to the more polar acetonitrile proved beneficial (82% yield).

In a second set of experiments, we have submitted a variety of substrates to the conditions described below.

In a typical run, a solution of t-butyldimethylsilyloxyoctane (2.44 mmoles) in CH_3CN (10 mL) was treated with CBr_4 (1.5 eq.) and PPh_3 (1.5 eq.) at 0°C under argon. After one hour, acetone (1.5 eq.) was added at room temperature and the mixture was stirred overnight. The usual extractive workup (5) was followed by GC analysis of the crude material.

As Table I indicates, the scope of this bromination seems quite large. Primary (n-octyl, entry 6), benzylic (entry 2), allylic (entry 3) as well as secondary cyclic (entry 4) and acyclic (entry 5) silyl ethers were efficiently brominated.

$$ROSi\text{-}t\text{-}BuMe_2 \text{ ------------}\blacktriangleright RBr$$

TABLE I .

ENTRY	**R**[a]	**CBr_4** **PPh_3**	**SOLVENT**	**ACETONE**	**YIELD**[b]
1	$PhCH_2$–	1.5 eq. 1.5 eq.	CH_2Cl_2	1.5 eq.	50%
2	$PhCH_2$–	1.5 eq. 1.5 eq.	CH_3CN	1.5 eq.	80%
3	$PhCH{=}CHCH_2$-	1.5 eq. 1.5 eq.	CH_3CN	1.5 eq.	85%
4	c–C_6H_{11}-	1.5 eq. 1.5 eq.	CH_3CN	1.5 eq.	70%
5	$[Me(CH_2)_4]MeCH$–	1.5 eq. 1.5 eq.	CH_3CN	1.5 eq.	76%
6	$Me(CH_2)_7$-	1.5 eq. 1.5 eq.	CH_3CN	1.5 eq.	82%

a. The TBDMS ethers were obtained by standard procedures (ref.1, 2).
b. GC analysis of the crude mixture on CP Sil 5 25m, using commercially available bromides as standards, and NMR analysis of the crude mixture.

This transformation could prove valuable in complex natural product synthesis where it is often effected in two steps (deprotection and subsequent bromination). Some other reactions of this type (bromination of protected hydroxy groups) have been worked out including ROTHP$\blacktriangleright$RBr (PPh_3Br (6)), ROtBu--$\blacktriangleright$RBr (PPh_3Br (7)), ROMe--$\blacktriangleright$RBr (HBr ,R_4PBr (8)) but none involving a TBDMS group.

Note added in proof : In the course of preparation of this manuscript an identical transformation has been described using PPh_3Br_2 as brominating agent (9).

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5. Acetonitrile was evaporated, the resulting oil was taken up in AcOEt and filtrated over SiO_2. After several washings with AcOEt, the filtrates were combined and evaporated to yield the crude product mixture.
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