# Triphenylphosphine Dibromide: Effective and Selective Reagent for the Cleavage of Acetals

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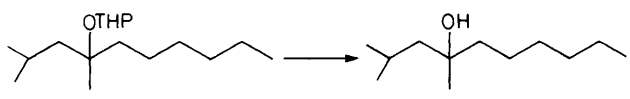
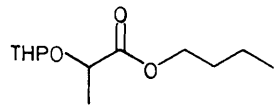
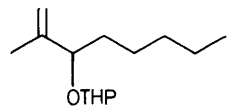
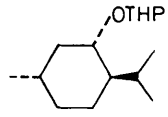
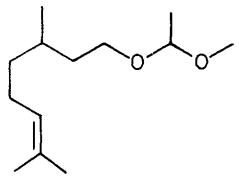
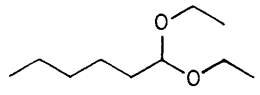
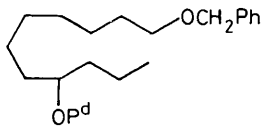
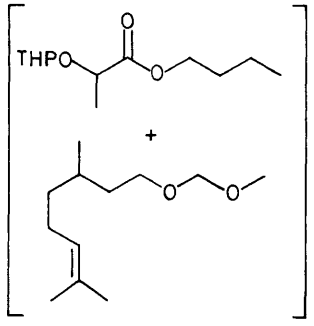
Triphenylphosphine dibromide ($PPh_3Br_2$) is a mild and highly effective reagent for hydrolysis of various acetals in dichloromethane at low temperature.

Cleavage of the acetal function is required frequently in the synthesis of polyfunctional natural products. The most common method for the deprotection of acetals, acid hydrolysis,[1] is not applicable to acid-sensitive substrates. We now find that secondary and tertiary tetrahydropyran-2-yl (THP) ethers,



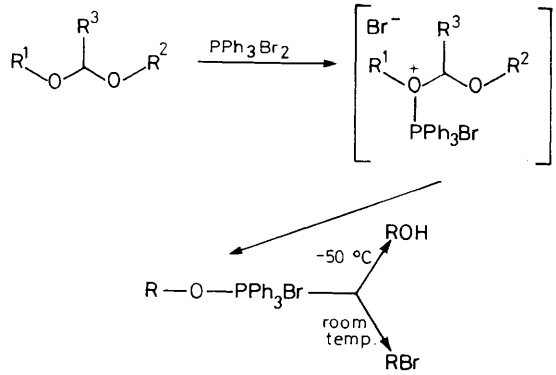

**Scheme 1.** *Reagents and conditions*: $PPh_3Br_2$, $CH_2Cl_2$, −50 °C, 92%.

**Table 1**

| Entry | Acetal | Temp[a]/°C | Time/h | Yield[b]/% |
|---|---|---|---|---|
| 1 |  | -50 | 3 | 94 |
| 2 |  | -50 | 4 | 89 |
| 3 |  | -50 | 3.5 | 85 |
| 4 |  | -50 | 2 | 97 |
| 5 |  | -50 | 1 | 74[c] |
| 6 |  | -35 | 15 | 85 |
| 7 |  | -50 | 3 | 94 |
| | | | | 0 |

[a] At temperatures above 0 °C the corresponding bromides are formed. [b] Isolated yield of pure product. [c] The volatility of the product may have resulted in a somewhat reduced yield. [d] Tri-*O*-benzyl-D-glucal.

when treated with commercially available $PPh_3Br_2$ at −50 °C, give the corresponding alcohols (Scheme 1), rather than the bromides that are produced at room temperature.[2] This is to our knowledge the first example of cleavage of this type. Therefore, the behaviour of various acetals towards this reagent was investigated.




**Scheme 2**

The procedure for deprotection is remarkably simple and mild. The following example is illustrative. $PPh_3Br_2$ (1.2 equiv.) is added under argon, at −50 °C, to a solution of acetal (1 equiv.) in anhydrous $CH_2Cl_2$ (5 ml). After completion of the reaction, ether (10 ml) is added to precipitate the triphenylphosphine oxide and hydrolyse the pentacovalent phosphorus intermediate $ROP(Ph)_3Br$. Filtration of the mixture through silica gel and evaporation of the solvent provides an essentially quantitative yield of the corresponding alcohol. The results are summarized in Table 1.

This method is efficient for the deprotection of secondary (entries 1—3) and tertiary (Scheme 1) THP ethers[3] as well as deprotection of acyclic acetal ethers (entry 4), dialkyl acetals (entry 5), and *O*-glucosides[4] (entry 6). In the latter case, longer reaction times and higher temperatures are required but, for all substrates, the reaction proceeds cleanly and the desired alcohol is formed as the only detectable product (see Table 1).

Two additional points are noteworthy. First, the acetal function can be removed with retention of stereochemistry. Thus, THP protected (−)-menthol is converted to (−)-menthol with full recovery of optical activity (entry 3). Second, a THP ether can be cleaved selectively in the presence of a methoxymethyl ether (entry 7).

The reaction probably proceeds through the pathway shown in Scheme 2. Thus, a THP ether can selectively be converted either to an alcohol or to a bromide, depending on the temperature. However, this deprotection is not applicable to primary THP ethers where the corresponding bromides are formed.

The reaction described here promises to be a useful synthetic method for the deprotection of THP ethers, especially for polyfunctional molecules, owing to the mild conditions, high yield, and speed.

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## References

1 T. W. Greene, 'Protective Groups in Organic Synthesis,' Wiley, New York, 1981.
2 P. E. Sonnet, *Synth. Commun.*, 1976, **6**, 21.
3 The THP ethers were prepared following the general procedure published by V. Bollit, C. Mioskowski, D.-S. Shin, and J. R. Falck, *Tetrahedron Lett.*, 1988, **29**, 4583.
4 The *O*-glucoside was prepared as described by V. Bollit, C. Mioskowski, P. Yadagiri, and J. R. Falck, *J. Am. Chem. Soc.*, submitted for publication.