Tetrahedron Letters, Vol.32, No.2, pp 187-188, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

REMOVAL OF TBDMS PROTECTING GROUPS FROM CARBOHYDRATES USING CATALYTIC TRANSFER HYDROGENATION[1]

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Catalytic transfer hydrogenation provides a simple and convenient method for the cleavage of TBDMS ethers from both primary and secondary hydroxyl groups.

Since its introduction by Corey in 1972[2], the *t*-butyldimethylsilyl (TBDMS) ether has become widely used as a means of protecting hydroxyl groups. This is particularly true in nucleoside synthetic chemistry. The ease of preparation of the ether, and its stability to a wide range of reaction conditions makes it very attractive. The TBDMS ether is easily cleaved by acid or by fluoride ion (usually in the form of tetra-*n*-butylammonium fluoride (TBAF))[3]. This method of deprotection, though rapid and usually clean, often requires inconvenient methods such as ion exchange to remove residual salts, and other functions in the molecule may be affected. The use of sodium hydride in HMPA or DMPU has also been reported[4]. The present communication describes the use of catalytic transfer hydrogenation (CTH)[5] conditions to effect removal of the TBDMS group from primary and secondary hydroxyl groups. The conditions are mild (refluxing methanol:cyclohexene, 20 wt% Pd(II)O) and workup consists of simple filtration and evaporation.

TBDMS-glycerol[6] (**1**, 200 mg, 1 mmol) and Pd(II)O (40 mg) were refluxed in a 1:1 mixture of methanol:cyclohexene for 1.5 h. Silica gel TLC (ethyl acetate, ammonium molybdate stain) indicated that **1** had been completely converted to a more polar material, which comigrated with glycerol. The mixture was filtered through a layer of glass wool and the solvents were evaporated. The resulting liquid was kept *in vacuo* overnight. This product was identified as glycerol by comparison of its ^{1}H and ^{13}C NMR spectra with those of an authentic sample. 89 mg of glycerol was isolated (95% yield).

Since TBDMS ethers are important in nucleoside chemistry, a silylated ribonucleoside was subjected to these conditions. Thus, 5'-TBDMS-uridine[7] (**2**, 150 mg, 0.4 mmol) was treated as above, using 30 mg Pd(II)O. After 2 h, TLC (CH_2Cl_2:MeOH 9:1) indicated complete conversion to a product comigrating with uridine. The product was isolated as described and identified as uridine by comparison of its ^{1}H and ^{13}C NMR spectra with those of an authentic sample. The yield of uridine was quantitative.

Secondary hydroxyl groups may also be desilylated using this procedure, though more slowly than their primary counterparts. For example, 2',5'-bis(TBDMS)-uridine[7] (**3**, 250 mg, 0.5 mmol) was treated with Pd(II)O (50 mg) as above. As the reaction proceeded, compound **3** was converted to a more polar material which was itself converted to a compound chromatographically identical to uridine. After 6 h, the reaction was worked up, and the product was identified by NMR as uridine, isolated in quantitative yield. The intermediate

product can be isolated by interrupting the reaction after **3** has been consumed, working up as before, and partitioning the residue between $CHCl_3$ and water. The aqueous phase contains uridine. The organic phase contains a monosilylated material which is chromatographically and spectroscopically distinct from **2**. It was identified as 2'-TBDMS-uridine by spectroscopic comparison with authentic material prepared by detritylation of 5'-monomethoxytrityl-2'-TBDMS-uridine. The yield of this material depends on the stage at which the reaction is interrupted, but ranges between 50% and 80%. Treatment of 3',5'-bis(TBDMS) uridine follows a similar pattern, with 3'-TBDMS-uridine as the intermediate. The monosilylated uridines are each isolated as a single isomer; there is no indication of isomerisation of the silyl group between the vicinal diols[8].

To eliminate the possibility that HCl, arising from $PdCl_2$ contamination of the catalyst, was responsible for the reaction, the desilylation of **2** was attempted using cyclohexane in place of cyclohexene. No desilylation occurred, even on refluxing for several hours. The samples of **2** and of Pd(II)O for this control were taken from the same preparations as for the reaction described above.

The rate of the reaction is variable, and depends on the sample of Pd(II)O used. The results presented here are typical, but reaction times vary by a factor of up to two, even when using different samples of Pd(II)O from the same supplier[9].

In conclusion, the work described here presents a new, mild and simple procedure for the removal of TBDMS ethers from carbohydrate derivatives. Financial assistance from the University of Windsor and the use of Dr. J.M. McIntosh's facilities are gratefully acknowledged.

1. This work was presented in part at the 73rd Canadian Chemical Conference, Halifax, Nova Scotia, Canada, July 1990.
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(Received in USA 11 October 1990)