Tetrahedron Letters,Vol.23,No.34,pp 3505-3506,1982 0040-4039/82/343505-02$03.00/0
Printed in Great Britain

ALKYLATION OF CARBOHYDRATES BY PHASE TRANSFER CATALYSIS

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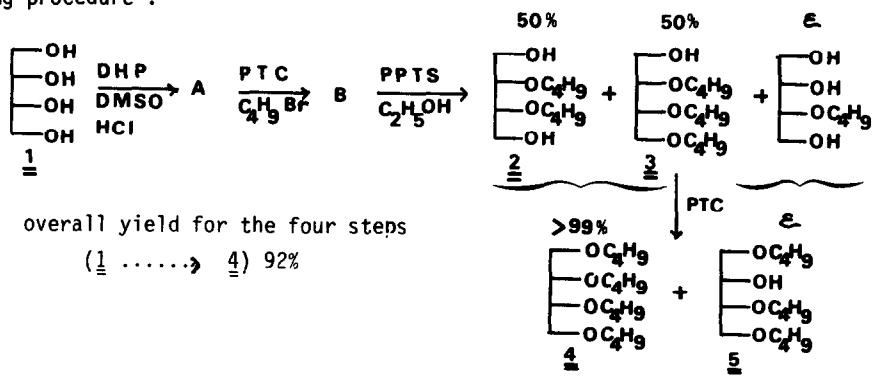
Abstract : From partially tetrahydropyranylated intermediates, carbohydrates (*meso*-erythritol and sorbitol) can be easily alkylated using phase transfer catalysis.

It is commonly admitted that under phase transfer catalysis (PTC) conditions *"Water soluble compounds (e.g., carbohydrates) cannot be reacted because their ion pairs are not present in the organic phase"*[1]. Effectively *meso*-erythritol 1 reacting with 1-bromobutane in a NaOH/Water medium in the presence of tetrabutylammonium bromide (TBAB) leads to a mixture of tri/tetra alkylated compounds (4 + 5 : 17/83%) in 15% yield. In the same way sorbitol leads to a mixture of alkylated compounds in 6% yield.

We have found that under a modification of the carbohydrate chain by a fixation of one or two tetrahydropyranyl groups (THP), the PTC reactions become possible. In this way the ion pairs are more lipophilic, the result is ether formation. The PTC preparation of alkylated carbohydrates via a lipophilic derivative[2] and O-alkylations of isopropylidene and benzylidene monosaccharide derivatives[3] have been described.

The selective tetrahydropyranylation of polyols seemed difficult because in acidic medium transposition or degradation generally occur. We have recently shown that the use of DMSO, as solvent with catalytic amount of HCl, leads to the selective protection of 1,3-butanediol[4].

Under optimized conditions, butylethers of *meso*-erythritol are easily obtained by the following procedure[5].



overall yield for the four steps
(1 ·····› 4) 92%

1 is reacted with DHP in DMSO and catalytic amount of HCl, after the DMSO has been distilled off, the crude mixture (A) is directly alkylated under PTC conditions with 1-bromobutane. The yield for these two steps is nearly quantitative. The crude mixture (B) is composed of two major products (di-THP, di-Bu 50% ; THP, tri-Bu 50% and a trace of the tri-THP, Bu ether). Several acid catalysts have been tested for the deprotection reaction but only PPTS[6] in EtOH is effective and affords, in 96,3% yield, a 50/50 mixture of 2 and 3, easily separated on silica gel column and identified by NMR, Mass spectroscopy[7] and authentic synthesis of 2.

The crude mixture of 2 and 3 is easily alkylated under PTC conditions and leads to pure tetrabutyl ether of *meso*-erythritol 4 in 96% yield. The overall yield for the four steps from starting meso erythritol to pure isolated 4 is 92%.

The same procedure applied to sorbitol gives in 90% overall yield a mixture of hexa ether 70% and two penta ethers 20% + 10%.

The advantages of the use of DMSO/HCl for selective synthesis of THP ethers of carbohydrates is clearly outlined; through these intermediates, PTC technique becomes a good method for alkylation of carbohydrates, and obtention of either partially or fully alkylated sugars.

We thank Centre National de la Recherche Scientifique for financial support (ASP N° 77).

References and notes

1 - E.V. DEHMLOV and S.S. DEHMLOV, Phase transfer catalysis, Verlag Chemie 1980 p. 87.

2 - A.F. ROSENTHAL, L.A. VARGAS and J.F. DIXON, Chemistry and Physics of Lipids 20, 205, 1977.

3 - P. di CESARE and B. GROSS, Carbohydr. Res. 48, 271, 1976.

4 - R. NOUGUIER, Tetrahedron Lett. , 1982.

5 - Meso-erythrytol (20mmol) is dissolved in DMSO (25ml), few drops of HCl are added, DHP (45mmol) dissolved in DMSO (25ml) is slowly added at room temperature, after 4 hours dry K_2CO_3 is added, and the major part of DMSO is distilled under vacuum. The residue A is stirred in a NaOH (40g) water (40ml) medium to 80°C and reacted with 1-bromobutane (60mmol), TBAB (1mmol) and toluene (40ml) for 12 hours at 80-90°C. After classical treatment the residue B (7,83g) is stirred at 50°C for 3 hours with dry ethanol (500ml) and PPTS[6] (2mmol), to yield 5,02g of 2 + 3 (96,3%).

6 - PPTS (Pyridinium p-Toluenesulfonate) is a mild acid catalyst (P.A. GRIECO, J. Org. Chem., 42, 3722, 1977), very efficient for depyranylation. With other acid catalysts more of 40% of non identified transposed products are obtained.

7 - Mass spectra were performed on a CG/MS Ribermag 1010 fitted with a W. Cot. C.P. Sil.5, and by chemical ionisation with CH_4. 2 and 3 affords the expected $(M^+ + 1)$ mass, and the THP ethers (mixture B) the $(M^+ + 1)$ mass of the corresponding deprotected alcohols.

(Received in France 10 June 1982)