Tetrahedron Letters,Vol.23,No.29,pp 2951-2952,1982 0040-4039/82/292951-02$03.00/0
Printed in Great Britain

ACID CATALYSED REACTIONS BETWEEN DIOLS AND VINYL-ETHERS IN BASIC SOLVENTS TOWARDS A SELECTIVE PROTECTION OF POLYOLS BY 2,3-DIHYDRO-4H-PYRAN

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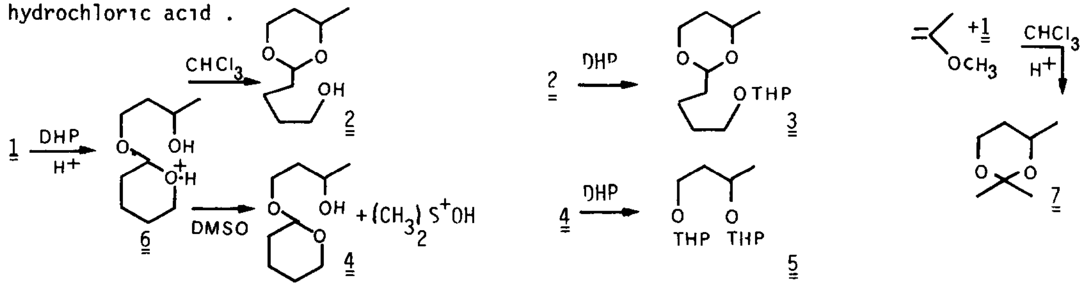
Abstract - Acid catalysed synthesis of THP ethers of 1,3-butanediol takes place much more selectively and in high yields if DMSO is used as solvent, instead in $CHCl_3$, even with mild acid catalysts, rearranged 1,3-dioxans are obtained

In an attempt to prepare alkylated sugar derivatives from partially tetrahydropyranylated intermediates[1], we have found that the nature of the solvent plays a prominent part in the protection of alcohol functions. In order to rationalize these results on a simple model we have studied the acid catalysed reaction between 1,3-butanediol 1 and 2,3-dihydro-4H-pyran (DHP)[2] or 2-methoxy propene[3], with chloroform and DMSO as solvent

The expected tetrahydropyranyl ethers (THP ethers) 4 and 5 are minor products of the reaction between DHP and 1 with acid catalysts such as HCl, CH_3SO_3H or $pCH_3C_6H_4SO_3H$ in chloroform. Instead 1,3-dioxans 2 and 3 are obtained in high yields[4]

In the same way in $CHCl_3$ as solvent and HCl as catalyst, 1 treated with 2-methoxypropene gave no 2-methoxypropyl ethers but only the 1,3 dioxan 7[5]

We have found however, that with a large excess of basic solvents such as DMSO or DMF, it becomes possible to introduce one or two tetrahydropyranyl groups on 1 with catalytic amount of hydrochloric acid[6].



These results involve intervention of the protonated form of DMSO[7] which would play the part of a convenient and mild catalyst[8~9~10~11]. Owing to its strong basicity, moreover, DMSO would prevent secondary reactions from the protonated intermediate 6

The formation of THP ethers takes place readily in the presence of DMSO and hydrochloric acid, and is accompanied by few rearranged products (2 + 3 < 5%). With an excess of THP[6], conversion of 1 is nearly quantitative (ratio 4 to 5 = 0 3) with stoechiometric amount of THP, 1 leads to a conversion of about 75% (ratio 4 to 5 = 3.8).

The advantages of the use of our system DMSO/HCl for the selective protection of 1,3-butanediol over described methods , have been outlined more selectivity, high yields. Owing to the solubility of carbohydrates in DMSO, the stage is thus set for the synthesis of partially alkylated sugars from partially tetrahydropyranylated intermediates[1] .

Acknowledgement · we thank Professors J-M Surzur and C. Roussel for helpfull discussions, and Centre National de la Recherche Scientifique for financial support (ASPn°77).

References and Notes

1 To be published.

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4 When pure 3 is stirred with Dowex 50 in MeOH at 50°C, 4 hours, only 2 is obtained and not 1, consistent with the proposed structure for 3 and the proposed selective[12] removal of THP groups with retention of alkylidene group

5 Two equivalents of 2-methoxypropene are used (yield 98%). 7 is an isopropylideneketal also obtained from 1 by acid catalysed exchange with 2,2-dimethoxypropane[13] The obtention of 7 involves the same protonated intermediate from both routes.

6 DHP (50 or 120 mmol) in DMSO (25ml) is slowly added to a stirred solution of 1 (50 mml) in DMSO (25ml) and acid catalyst (3 mmol) at room temperature Reaction time 4 hours. Immediately after reaction, solid K_2CO_3 is added to neutralize HCl and avoid rearrangements when the solvent is distilled off. When K_2CO_3 is omitted, a great proportion of rearranged 2 is observed.

7 The equilibrium $(CH_3)_2SO + HCl \rightleftharpoons (CH_3)_2\overset{+}{S}OHCl^-$ has been studied by I.M. Kolthoff and T.B. Reddy, Inorg Chem. 1, 189, 1962.

8 The use of a mild catalyst, pyridinium p-toluene sulfonate PPTS[9] is highly efficient in $CHCl_3$ for the fully tetrahydropyranylation of 1 (94% yield of 5). For the synthesis of mono THP ethers, however, the use of this catalyst showed a lack of selectivity, some rearrangement occurred (16%) and yields were low (41%)

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10 The reaction takes place much more slowly if Macroreticular ion exchange resin, recognized however, as a useful mild catalyst[11] , is used (In $CHCl_3$ conversion after 24h 50% ratio 2/4 = 0.4. In DMSO conversion 6% 4 = 100%)

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(Received in France 21 April 1982)