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Selective monotetrahydropyranylation of 1,*n*-diols catalyzed by aqueous acids

Takeshi Nishiguchi,[a,]* Seiji Hayakawa,[a] Yoshihiro Hirasaka[b] and Masahiko Saitoh[b]

[a]*Faculty of Agriculture, Yamaguchi University, Yamaguchi 753-5815, Japan*
[b]*Faculty of Education, Yamaguchi University, Yamaguchi 753-8513, Japan*

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Abstract

1,*n*-Diols with 3–12 carbon atoms gave selectively the corresponding monotetrahydropyranyl ethers in higher yields than 80% in the reaction catalyzed by hydrogen ion in the water layer which is in contact with DHP–toluene or DHP–hexane layer. © 2000 Elsevier Science Ltd. All rights reserved.

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Methods for the selective protection of one of two identical functional groups, which exist in symmetrical positions in a molecule, are important in organic synthesis.[1] Since the protection of hydroxyl groups by etherificaion is quite common in organic syntheses,[2] it will be worth developing the methods to obtain monohydroxyethers selectively from symmetrical diols. In some cases, the monoetherification of symmetrical diols can be achieved by Williamson reaction,[3] by the use of alumina and diazomethane,[4] and via cyclic compounds.[5] It has also been reported that the monotetrahydro-2*H*-pynanyl (THP) ether was obtained in 85% yield from 1,8-octanediol in the reaction catalyzed by iodine.[6] We have already reported the selective monotetrahydropyranylation of symmetrical diols in 3,4-dihydro-2*H*-pyran (DHP)–hydrocarbon catalyzed by metallic sulfates supported on silica gel[7] and by acidic ion-exchange resins which contain water.[8] In the former reaction diethers begin to form rapidly when diols have almost been consumed,[7] therefore close observation is required to decide when to terminate the reaction. This weak point is improved in the latter reaction.[8] However, the catalytic ion-exchange resins used in the reaction are expensive and the performance of the catalysts often changes as the reaction proceeds, because the amounts of water contained in the resins tend to decrease in the course of the etherification.

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* Corresponding author.

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Here we would like to report the selective monotetrahydropyranylation of 1,*n*-diols in which the disadvantages mentioned above are overcome. This reaction was carried out by stirring a diol, an acidic aqueous solution, and a mixture of DHP and a hydrocarbon.

$$\text{HO-(CH}_2)_n\text{-OH} \xrightarrow[\text{DHP–hydrocarbon}]{\text{H}_3\text{O}^+} \text{THPO-(CH}_2)_n\text{-OH} \xrightarrow[\text{DHP–hydrocarbon}]{\text{H}_3\text{O}^+} [\text{THPO-(CH}_2)_n\text{-OTHP}]$$

Fig. 1 shows an example of the dependence of the yields of the products on the reaction period in the etherification of 1,6-hexanediol (1 mmol) using aqueous $NaHSO_4$ (5 M, 0.2 ml) and DHP–toluene (5:95 (v/v), 6 ml). This reaction was followed by the use of GLC. The yield of the diether was 2% when that of the monoether reached 94%. The yield of the diether did not increase rapidly even after the yield of the monoether reached its maximum. The result described above enhances the value of this reaction because the timing to terminate the successive etherification is not so important in this reaction as in the reaction catalyzed by the supported sulfates.[7]

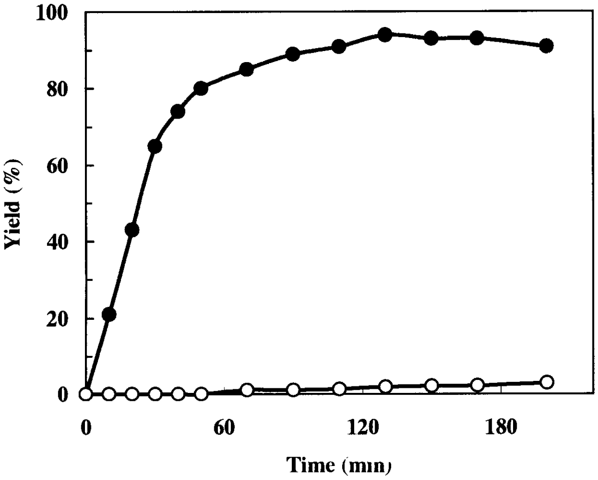

Figure 1. Yield of the monoether (●) and the diether (○) versus reaction time. 1,6-Hexanediol (1 mmol), aqueous $NaHSO_4$ (5 M, 0.2 ml) and DHP/toluene (5:95, 6 ml) were stirred at 30°C

The yield of 1,6-bis(tetrahydropyranyloxy)hexane in the reaction of 6-(tetrahydropyranyloxy)-1-hexanol, which was the starting material, was much lower than the yield of the monoether in the reaction of 1,6-hexanediol. The ratio of the reaction rate of the diether formation from the monoether to that of the monoether formation from the diol was roughly 1:80 under similar reaction conditions.

We presume that the selectivity for the monoether formation arises from the following assumed factors: (1) the percentage of the diol existing in the water layer is much higher than that of the monoether existing there; (2) the diol reacts in the aqueous layer which contains DHP and hydronium ion; (3) the formed monoether migrates from the aqueous layer into the surrounding aprotic organic layer which does not contain the catalytic species.

Assumption (1) is supported by the result that 6-(tetrahydropyranyloxy)-1-hexanol hardly existed in the water layer, while 1,6-hexanediol existed mainly there when (1 mmol) stirred well along with water (0.6 ml) and DHP–toluene (6 ml) at 30°C (Fig. 2).

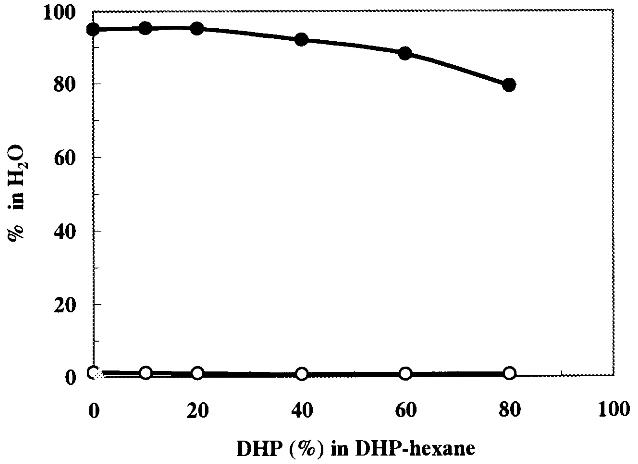

Figure 2. The percentage of 1,6-hexanediol (●) and 6-(tetrahydropyranyloxy)-1-hexanol (○) in the water layer (0.6 ml) which was kept in contact with DHP–toluene (6 ml) at 30°C

Tetrahydropyranyl ethers are usually hydrolyzed to the corresponding alcohols in dilute aqueous acids.[2] However, the yield of the monoether is high in this reaction, probably because the monoether, even if its amount is small in the acidic water layer, moves into the surrounding organic layer immediately after its formation, as inferred by Fig. 2.

Table 1 shows that some 1,*n*-diols with 3–12 carbon atoms gave the corresponding mono-tetrahydropyranyl ethers in higher yields than 80% in the reaction catalyzed by aqueous $NaHSO_4$. In the reaction of 1,10-decanediol using DHP–toluene, the yield of the monoether was low. The yield was increased by changing DHP–toluene into DHP–hexane and by adding DMSO (0.2 ml). In the reaction of 1,12-dodecanediol, the yield of the monoether was somewhat lower than the yields of the monoethers in the reactions of the diols with not more than 10 carbon atoms.

Table 1
Selective monotetrahydropyranyration of HO-$(CH_2)_n$-OH with DHP catalyzed by aqueous $NaHSO_4$[a]

n	$NaHSO_4$ (ml)	DHP (vol.%)	Temp. (°C)	*T* (min)	Yield (%)[b]	
					Monoether	Diether
3	0.2	40	30	50	93	2
6	0.2	5	30	130	92	2
10	0.2	3	30	480	66	26
10	1.0	3	40	960	81	11
10[c]	1.0	3	40	720	83	9
10[c,d]	1.0	3	40	300	88	4
12[c,d]	1.0	5	50	420	80	3

[a] Diol (1.0 mmol), aqueous $NaHSO_4$ solution (5 M), and DHP–toluene (6 ml) were stirred.
[b] GLC yields obtained by the use of internal standards.
[c] The solvent was a DHP–hexane mixture.
[d] DMSO (0.2 ml) was added.

Each diol had a particular DHP/hexane or DHP/toluene ratio that gives the highest selectivity. In the reaction of 1,6-hexanediol, the percentages of DHP at which the highest selectivity was realized were about 5 and 60% in the reaction in DHP–toluene and DHP–hexane, respectively. The highest yield of the monoether from 1,6-hexanediol in the reaction of DHP–toluene was higher than in the reaction of DHP–hexane. In the reaction of 1,10-decanediol, the selectivity for the monoether was higher when the percentage of DHP in DHP–hexane was 3% than when it was 5%. When the number of carbon atoms of the diols is large, the organic layers whose ability to dissolve diols must be low to realize the high selectivity.

As described previously, the addition of DMSO increased the selectivity in the reaction of 1,10-decanediol. The increase of the selectivity may be explained by the presumption that the strongly polar additive is distributed mainly in the water layer and that the dissolving power of the water layer for the diol is enhanced by the addition to a greater extent than for the monoether.[8] For catalysts, aqueous NH_4HSO_4, $KHSO_4$ and $Fe_2(SO_4)_3$, and diluted hydrochloric acid (0.2 M) were as effective as aqueous $NaHSO_4$.

This method of selective etherification is suitable for large-scale preparations because the catalysts described above are inexpensive and harmless to a natural environment, and the experimental operation in this method is quite simple. Further, the reproducibility of results in this reaction is much higher than that in the reactions catalyzed by acidic ion-exchange resins,[8] in which amounts of water contained in the catalysts are not always settled even when the resins are purchased and change in the course of the reaction.

Supplementary material: An example of monoetherification of 1,*n*-diols. The etherification of hexane-1,6-diol is typical. A mixture of hexane-1,6-diol (0.118 g, 1 mmol), aqueous 5 M $NaHSO_4$ (02 ml), 1-octadecene (GLC internal standard, 40 μl), and 5:95 (vol/vol) DHP–toluene (6 ml) was stirred at 30±1°C. Samples of the supernatant liquid were then removed periodically and analyzed by GLC. The retention times of the monoether and the diether were identical to those of authentic samples prepared by the conventional method described in the previous paper.[6,7] The yields of monoethers at a particular yield of diethers were derived from plots of product yield versus time, such as those shown in Fig. 1.

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