

Highly Selective Monotetrahydropyranylation of Symmetrical Diols Catalysed by a Strongly Acidic Ion-exchange Resin

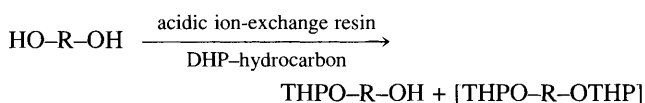
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Several primary and secondary symmetrical diols, ranging from propane-1,3-diol to decane-1,10-diol, are selectively monoprotected by monotetrahydropyranyl ether formation catalysed by a strongly acidic ion-exchange resin (Dowex 50w × 2, 50–100 mesh) in a 3,4-dihydro-2H-pyran–hydrocarbon mixture.

Methods for selective protection of multiple identical functional groups in a similar chemical environment are important in organic synthesis. Selective monoacylation of symmetrical diols has been well studied.^{1,2} Protection of hydroxy groups by etherification is quite common in organic syntheses³ and we have already reported the selective monotetrahydro-2H-pyranyl (THP) ether formation in the reaction of symmetrical diols in 3,4-dihydro-2H-pyran (DHP)–hexane catalysed by metallic sulfates supported on silica gel.⁴ Although maximum yields of the monoethers are high, the method has a serious disadvantage. The ditetrahydropyranyl ethers form very rapidly after most of the diols has been consumed.⁴ Therefore, attention must be paid as to when to terminate the reaction. Here we would like to report the reaction of symmetrical diols in DHP–hydrocarbon catalysed by a strongly acidic ion-exchange resin, in which the disadvantage described above is considerably reduced.



The selective monotetrahydropyranylation in this study was carried out by stirring a diol (1 mmol) and a sulfonic acid-type ion-exchange resin (Dowex 50w × 2, 50–100 mesh; 0.2 g) in DHP–toluene or DHP–hexane (6 ml) and monitoring by GLC. Most reactions were carried out at 30 °C in pursuit of good

reproducibility, although they proceeded at room temperature. Fig. 1 shows an example of the dependence of the product yield upon the reaction period in the etherification of hexane-1,6-diol at 30 °C in DHP–toluene (1 : 19). The yield of the diether was 3% when that of monoether reached 95%, and yields of both ethers did not vary greatly even after the yield of the monoether reached its maximum. This result shows that the reaction rate of the monoether is much lower than that of the diol and that the rate does not increase greatly even after most of the diol has been consumed. This result contrasts sharply with the result obtained in the reactions catalysed by silica gel-supported sulfates, in which the monoprotected substrates react much more rapidly in the absence of diols than in their presence.⁴ The result described above enhances the utility of the reaction catalysed by ion-exchange resins because the timing of the termination of the successive etherification is not so important in this reaction as in the reaction catalysed by the supported sulfates.

Table 1 shows that several primary and secondary symmetrical diols, ranging from propane-1,3-diol to decane-1,10-diol, have been monoprotected in high selectivity by tetrahydropyranyl ether formation catalysed by the strongly acidic ion-exchange resin in the DHP–hydrocarbon mixture. When butane-1,4-diol (1 mmol) and the catalyst (0.1 g) were stirred in DHP–toluene (2 : 3, 6 ml) at 30 °C for 2 h, 1.3 mmol of 2-hydroxytetrahydropyran was formed. It is inferred that this product was formed by the reaction between DHP and the water contained in the ion-exchange resin.

The R_f value by GLC of this product was equal to that of the monotetrahydropyranyl ether of butane-1,4-diol. Therefore, we used *cis*-but-2-ene-1,4-diol in place of butane-1,4-diol. 2-Hydroxytetrahydropyran was formed in any case. Cyclohexane-1,4-diol (a mixture of *cis*- and *trans*-isomers) gave the corresponding monoether in high yield. This result shows that secondary diols as well as primary diols undergo monotetrahydropyranylation selectively. In the reaction of decane-1,10-diol, yields of the monoether were lower under various reaction

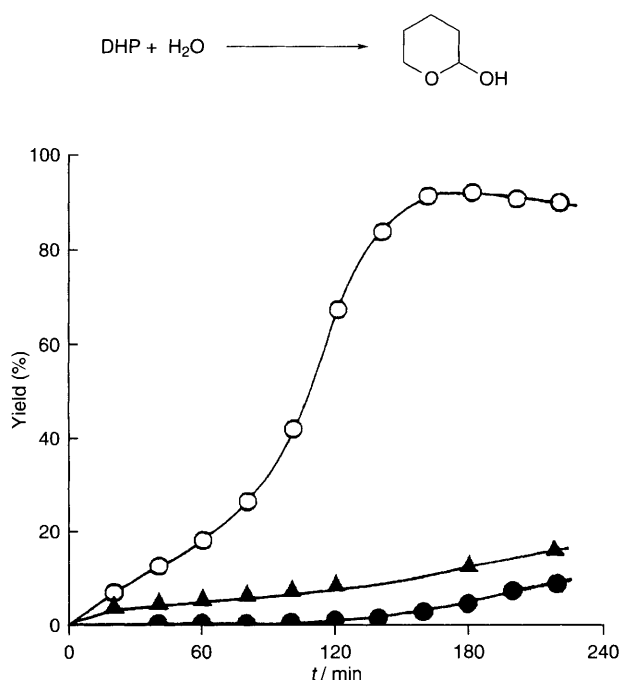


Fig. 1 Yields vs. reaction time. Hexane-1,6-diol or 6-(tetrahydropyranyloxy)hexane-1-ol (1 mmol) and Dowex 50W × 2 (50–100 mesh) (0.2 g) were stirred at 30 °C in DHP–toluene (1 : 19, 6 ml): monoether (○) and diether (●) from the diol; and the diether (▲) from the monoether.

Table 1 Selective monotetrahydropyranylation of symmetrical diols with DHP catalysed by an ion-exchange resin^a

| Diol | DHP (%) | T/min | Yield (%) | |
|-----------------------------------|---------|-------|------------|---------|
| | | | mono-ether | diether |
| Propane-1,3-diol | 80 | 30 | 78 | 3 |
| Propane-1,3-diol ^b | 40 | 220 | 81 | 3 |
| <i>cis</i> -But-2-ene-1,4-diol | 80 | 10 | 80 | 3 |
| Hexane-1,6-diol | 5 | 210 | 95 | 3 |
| Hexane-1,6-diol ^c | 60 | 40 | 85 | 5 |
| Cyclohexane-1,4-diol | 40 | 90 | 95 | 3 |
| Octane-1,8-diol | 3 | 270 | 95 | 2 |
| Decane-1,10-diol ^{c,d} | 3 | 300 | 74 | 9 |
| Decane-1,10-diol ^{c,d,e} | 3 | 355 | 87 | 8 |

^a Diol (1.0 mmol) and Dowex 50W × 2 (50–100 mesh) (0.2 g) were heated at 30 °C in DHP–toluene (6 ml). ^b Amount of catalyst used was 0.04 g. ^c The solvent was a DHP–hexane mixture. ^d Reaction temperature was 40 °C. ^e *N,N*-Dimethylformamide (0.1 ml) was added.

conditions, but increased by the addition of *N,N*-dimethylformamide (0.1 ml).[†]

The graph in Fig. 1 also shows the yields of 1,6-bis(tetrahydropyranyloxy)hexane. This diether was formed when 6-(tetrahydropyranyloxy)hexan-1-ol and the catalyst were stirred under the same conditions as in the reaction of hexane-1,6-diol noted in Fig. 1. The yields of the diether obtained in the reaction of the monoether without the diol are much lower than the yields of the monoether obtained in the reaction of the diol. This result shows that the selectivity of the monoether formation results from the fact that the reactivity of the diol is much higher than that of the monoether.

We presume that the monoether selectivity arises from a number of factors. Generally, sulfonic acid-type ion-exchange resins contain 50–80% water (suppliers catalogue). In fact, Dowex 50w × 2, (50–100 mesh) lost 26% of its weight by drying over P₂O₅ for 7 d. This result suggests a strongly acidic aqueous layer is formed on the surface of the resin. When this dried catalyst was used, the selectivity for the monoether formation was low and the diether began to form at once. A partition equilibrium between the aqueous layer and the aprotic DHP–hydrocarbon layer would be set-up, and diols have higher partition coefficients than the product monoethers. Etherification of alcohols occurs in the aqueous layer and/or at the interface between the aqueous and the nonaqueous liquid layer, while the formed monoethers move out of the aqueous layer into the aprotic layer, through a process resembling continuous extraction, and remain there without reacting further.

The selectivity and initial rates of formation of the monoether depend on the nature and composition of the solvents used. Each diol has particular DHP–hydrocarbon ratios for which the highest selectivities are obtained. Generally, the larger the hydrocarbon portion of the diol becomes, the smaller the DHP ratio needed. However, the selectivity and rates of reaction do

not depend on the DHP–hydrocarbon ratio to the same extent as the reaction catalysed by metallic sulfates supported on silica gel. This dull response of the selectivity to reaction conditions is also an advantage of this reaction system. A smaller DHP ratio delays the etherification and necessitates the use of a larger amount of the catalyst. Therefore, amounts of the catalyst vary in Table 1. As the use of a solid reagent has obvious advantages during set-up and work-up, this method of selective etherification is both simple and practical. Preliminary studies show that most of sulfonic acid-type ion-exchange resin work as well as Dowex 50w.

Received, 21st July 1995; Com. 5/04817F

Footnote

[†] Addition of *N,N*-dimethylformamide improved the selectivity of the reaction of decane-1,10-diol, whose solubility in water in the ion-exchange resin is low, but hardly affected the selectivity of the reaction of octane-1,8-diol, which has a higher solubility.

References

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