

Microwave-Mediated Selective Monotetrahydropyranylation of Symmetrical Diols Catalyzed by Iodine

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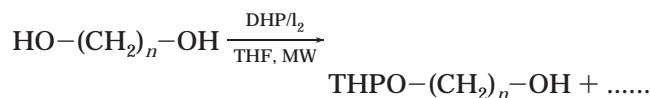
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Selective protection of one hydroxyl group as its tetrahydropyranyl ether in 1,*n*-symmetrical diol is achieved by iodine-catalyzed reaction of the diol with dihydropyranyl ether under microwave irradiation.

Protection of hydroxyl groups by the preparation of tetrahydropyranyl ethers is quite common and an advantageous reaction in organic synthesis.¹ Although several reagents are available¹ for protection of alcohols as their tetrahydropyranyl ethers, the selective protection of one of two identical hydroxyl groups in a symmetrical molecule is very limited. Only a few recent reports from Nishiguchi et al. have described the use of metallic sulfate supported on silica gel² or some acidic ion-exchange resins³ as suitable catalyst for this purpose. In general monoetherification of symmetrical diol is achieved by the Williamson synthesis,⁴ by the use of alumina and diazomethane⁵ or via cyclic acetals in a two-step procedure.⁶ In the acetal-opening process the reaction needs to be done at very low temperature (−78 °C), and the yield is also low. The process involving metallic sulfate supported on silica gel² has the drawback as to when to terminate the reaction for getting optimum yield. Herein we report a microwave-mediated reaction for selective protection of one hydroxyl as a tetrahydropyranyl ether in a symmetrical 1,*n*-diol. During the course of our studies⁷ on iodine-catalyzed reactions in organic synthesis we have observed that iodine is a very good catalyst for tetrahydropyranylation of hydroxyl groups under microwave irradiation.⁸



In the present method, the diol in dry THF was irradiated in a microwave oven in the presence of 3,4-dihydro-2*H*-pyran and catalytic amount of iodine to afford

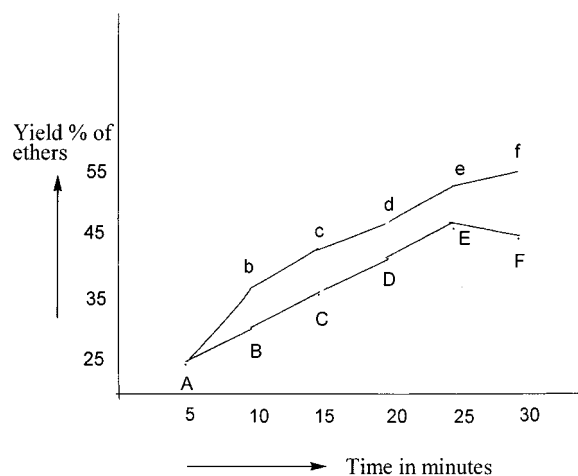


Figure 1. Yield vs reaction time. Reaction of ethane-1,2-diol with DHP under reflux in THF. Curve A–B is for diether and A–B–C–D–E–F is for monoether.

Table 1. Monoprotection of 1,*n*-Diols

substrate	power (W)	time (s)	temp (°C)	yield (%) of monoether	diether
ethane-1,2-diol	600	150	67	78	17
propane-1,3-diol	600	150	67	77	17
butane-1,4-diol	600	160	67	75	16
hexane-1,6-diol	600	160	67	76	16
cyclohexane-1,4-diol	600	170	67	77	15

75% or greater isolated yield of the monoprotected diol within 3 min. When the same reaction was carried out under reflux, the conversion was quantitative within 30 min, but selectivity was very poor. The isolated yield of the monoether was 43% and that of the diether was 51%. Even at room temperature the reaction proceeded slowly without any selectivity (product ratio monoether:diether 1:1). Figure 1 depicts the progress of the reaction of ethane-1,2-diol with DHP under reflux in THF.

Table 1 presents our observations along with the optimum parameters for obtaining the best yields of monotetrahydropyranylated diol.

Figure 2 shows the dependence of the product yield on the microwave power in the monotetrahydropyranylation of ethane-1,2-diol at a reaction period of 120 s. It may be seen that above 40% (180 W) of power output the yield remains between 60 and 65%. At higher energy the yield of monoether is a little less due to the formation of the

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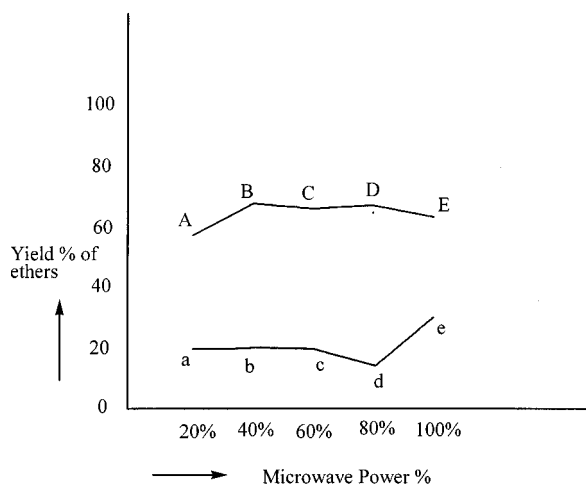


Figure 2. Yield vs microwave power. Reaction of ethane-1,2-diol with DHP carried out for 120 s at different level. Graph ABCDE for monoether. Graph abcde for diether.

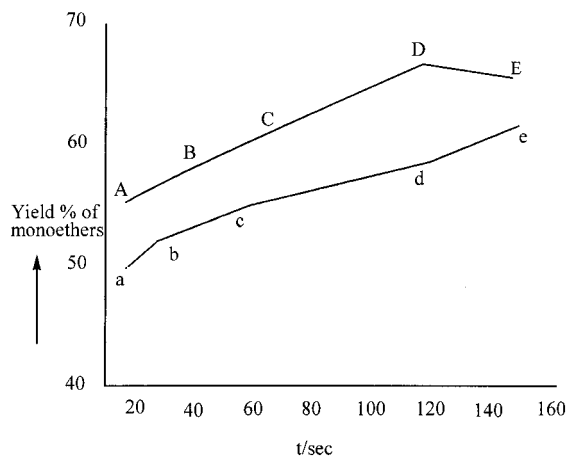


Figure 3. Yield vs reaction time. Reaction of ethane-1,2-diol with DHP at constant power. Graph ABCDE at 800 W power and Graph abcde at 90 W power.

corresponding diethers. In all the cases, the reactions are not complete and around 10% of the diol remains unreacted. Figure 3 shows the variation of product yield at different reaction times at a particular power of 20% (90 W) and 100% (800 W), respectively. At 90 W of power the reaction remains incomplete, and the yields are also low. Even at the highest power (800 W) the product yield varies with time.

Table 2 shows the temperature of the reaction mixture corresponding to a range of power of the microwave oven for a given period of time.

Table 2. Correlation of Reaction Temperature with Time at Specified Power

time (s)	power (W)	temp (°C)
20	90	36
30	90	50
60	90	52
120	90	58
120	180	65
120	360	67
120	600	67
120	800	68

From Figures 1–3 as well as the Tables 1 and 2, it can be inferred that the product yields and selectivities of the reactions are microwave-specific and depend on both the power of the microwave oven selected and the total reaction time. These two factors in turn determine the temperature of the reaction mixture. At lower temperature the yield of the monoether is less in comparison to the yield at higher temperature. Interestingly the yield of the diether varies around 15 to 20% in all the reactions.

Experimental Section

In a typical reaction, a solution of 1 mmol (62 mg) of ethane-1,2-diol in dry THF (0.8 mL) was mixed with 1.25 mmol (106 mg) of 3,4-dihydro-2*H*-pyran and 0.2 mmol of iodine. The mixture was added to a 50 mL conical flask, and a small funnel was placed over it to reduce any possible evaporation of solvent (**CAUTION**).⁹ The flask as such was placed in a microwave oven (kitchen type, Brand LG, Model 'Multiwave' MS-283MC) and irradiated at 600 W of power for 150 s. Immediately on completion, the flask was taken out, and the temperature of the mixture was recorded with a thermometer. The mixture was diluted with chloroform (50 mL) and washed with a dilute solution of sodium thiosulfate followed by water. The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. Purification by column chromatography (1:2 EtOAc:hexane) gave 78% (114 mg) of the monoether along with 17% (39 mg) of the diether. All the products are already known in the literature² and were characterized by spectral analysis and by comparing with authentic material prepared by reported methods.

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(9) **CAUTION:** Fire may break out when organic solvents, especially flammable ones, are heated in a domestic microwave oven. Of course, in the present setup in small scale the reaction proceeded without any mishaps.