A Convenient One-step Preparation of Oxacyclanes by Dehydration of Diols over Alumina

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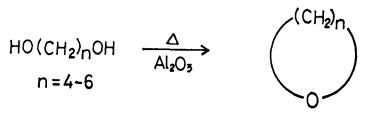
Synopsis. Dehydration of 1,4-, 1,5-, or 1,6-alkanediols over alumina at 220—250 °C in a distillation apparatus gave the corresponding 5- to 7-membered oxacyclanes in good yield of 51—71%. Diethylene glycol also gave 1,4-dioxane in 49% yield, whereas attempted one-step synthesis of crown ethers from polyethylene glycols in a similar manner resulted in the predominant formation of 1,4-dioxane without any trace of crown ether.

Most aliphatic ethers are prepared by the removal of water from alcohol under acidic conditions.[1] However, this method has not been used extensively and is actually unsuccessful as a general method for the preparation of oxacyclanes from α,ω-alkanediols.[2,3] Oxacyclanes have been synthesized so far from diols *via* many steps.[4-6] Recently, the synthesis of oxacyclanes has been accomplished by the use of dimethyl sulfoxide,[7] sulforane,[8] or carbodiimide,[9] but these syntheses require the use of relatively inaccessible reagents and do not give satisfactory yield for the synthesis of larger-sized oxacyclanes. The use of alumina as a dehydrating agent appears to be well established for the preparation of tetrahydrofuran derivatives from 1,4-diols.[10,11] An attempted extension of the method to prepare smaller-sized oxacyclanes has been unsuccessful[11] and further attempts have not been made so far.

We wish now to present a convenient one-step method for preparing 5- to 7-membered oxacyclanes from diols and also an attempted one-step synthesis of crown ethers from polyethylene glycols. The use of alumina in liquid phase makes the method easy to use and gives good yields.



In a typical experiment, a diol was mixed with an equal weight of activated alumina and the mixture was heated up to 220—250 °C in a distillation apparatus fitted with a heating mantle until distillation ceased (*ca.* 5—30 h) to give a corresponding oxacyclane and water as an azeotropic distillate. Dehydration by alumina of 1,4-, 1,5-, or 1,6-alkanediol, *i.e.* **3**, **5**, **7**, or **9**, afforded the oxacyclane, *i.e.* **4**, **6**, **8**, or **10**, in 51—71% isolated yield, although 1,3-butanediol failed to give 2-methyloxetane in a satisfactory yield, probably due to the strain of the four-membered ring. The introduction of other functional group, *i.e.* an additional hydroxyl group or a double bond, resulted in diminished yield of 18—25%.

We also carried out the dehydration of polyethylene glycol by alumina, since this method seemed quite attractive as a simple method for preparing crown ethers. Although the reaction of diethylene glycol over alumina gave 1,4-dioxane in good yield, similar treatment with tri- or tetraethylene glycol resulted in the predominant formation of 1,4-dioxane without any trace of crown ether.

TABLE 1. DEHYDRATION OF DIOLS OVER ALUMINA AT 220—250 °C

Diol		Reaction time/h	Product		(% yield)	Bp/°C
1,4-Butanediol	**3**	20		**4**	(71)	65—66
2,5-Hexanediol	**5**	6	a)	**6**	(58)	92—94
1,5-Pentanediol	**7**	5		**8**	(52)	87—88
1,6-Hexanediol	**9**	18		**10**	(53)	112
1,2,6-Hexanetriol	**11**	30	OH	**12**	(18)	187
3-Hexene-2,5-diol	**13**	12	a)	**14**	(25)	73—75
1,3-Butanediol	**1**	20		**2**	(0.8)[b]	—
Diethylene glycol	**15**	21		**16**	(49)	98—100

a) From ^{13}C NMR spectrum, this ether is shown to be a 1:1 mixture of *cis*- and *trans*-isomers. b) Yield determined by GLC.

We may conclude this method offers a simple and convenient procedure especially for the preparation of 5- to 7-membered oxacyclanes and its alkyl derivatives.

Experimental

All the diols were commercially available and fractionally distilled prior to use. Commercial alumina for chromatography of 200 mesh (Nakarai Chimicals Co.) was used as a dehydration catalyst after dried for 10 h in an oven at 200 °C.

Dehydration of Diols ***1***, ***3***, ***5***, ***7***, ***9***, ***11***, *and* ***13***. Preparation of oxacyclanes, **2**, **4**, **6**, **8**, **10**, **12**, or **14**, was accomplished in a distillation apparatus by heating a diol with an equal weight of activated alumina at 220—250 °C. The product ether and water was distilled as an azeotropic mixture. The distillate was saturated with salt, and the organic layer was dried, filtered and then fractionally distilled to give the product oxacyclane. The isolated yield and boiling point of the

product are presented in Table. The product ethers (95—99% pure by GLC on polyethylene glycol-20M column) were identified by IR, ^{13}C NMR and, if needed, mass spectra and GLC comparison with the authentic samples.

1,4-Dioxane (16). Dehydration of diethylene glycol (20 g) over alumina (12 g) and the subsequent work-up gave 8.1 g (49%) of 1,4-dioxane. The IR and NMR spectra and GLC retention time were identical with those of the authentic dioxane.

Attempted Synthesis of Crown Ether. The facile preparation of 1,4-dioxane from diethylene glycol prompted us to the one-step synthesis of crown ethers from polythylene glycols. Dehydrations of tri- and tetraethylene glycols over alumina were performed merely to give 1,4-dioxane as a major dehydration product in both cases. Repeated attempts at a reduced pressure also gave dioxane; no cyclic polyethers, *e.g.* 9-crown-3 or 12-crown-4, were produced in any cases.

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