

The Reduction of Crown Lactones to Crown Ethers

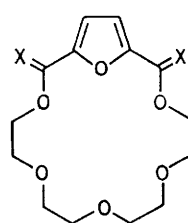
David J. Ager* and Ian O. Sutherland*

Department of Organic Chemistry, Robert Robinson Laboratories, University of Liverpool,
P.O. Box 147, Liverpool L69 3BX, U.K.

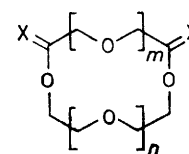
Crown lactones may be reduced to crown ethers using lithium aluminium hydride.

A recently described method¹ for reducing the crown lactone (**1a**) to the crown ether (**1b**) involves conversion of the lactone into the thioester (**1c**) followed by reduction with Raney nickel to the ether. This procedure gives a low (12%) overall yield for the process (**1a**) → (**1b**) and fails for the simple dilactone (**2a**) which could not be converted into the corresponding thioester. We describe a direct high-yielding procedure for reducing crown lactones to crown ethers which may have a general application.

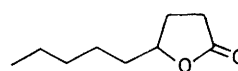
Lactones are generally reduced by lithium aluminium hydride to the corresponding diol^{2,3} although a limited amount of the reducing agent (0.25 mol. equiv.) gives⁴ the hydroxyaldehyde. The reduction of lactones with lithium aluminium hydride in the presence of boron trifluoride–diethyl ether gives cyclic ethers,⁵ however, and this result suggests that a direct reduction of the readily available crown lactones⁶ into ethers should be possible. The series of lactones (**2a**)—(**7a**) was prepared by reaction of the appropriate diacid chlorides and diols under high dilution in toluene to give the yields reported in Table 1. In some cases these yields were increased by distillation of the residues in a mixture with magnesium chloride hexahydrate according to an established procedure.⁷ The reduction of the dilactone (**2a**) with lithium aluminium hydride in boiling tetrahydrofuran gave a mixture



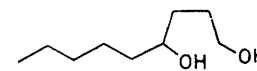
(1)



	<i>m</i>	<i>n</i>
(2)	1	3
(3)	2	2
(4)	3	1
(5)	4	0
(6)	1	2
(7)	0	4



(8)



(9)

In (1)–(7): a, X = O; b, X = H₂; c, X = S

Table 1. Preparation and reduction of crown lactones.

Lactone	Yield of lactone/% ^a	Yield of crown ether/% ^b
(2a)	48 (76) ^c	89 (68 ^d , 87 ^e)
(3a)	34	92
(4a)	39	83
(5a)	33	77
(6a)	31	79
(7a)	41	0

^a After recrystallization from light petroleum. ^b Isolated by quenching the reaction mixture with water, filtration and evaporation, and recrystallization of the residual solid for cases (2a)—(5a). Lactones (2a)—(5a) gave 18-crown-6 and lactone (6a) gave 15-crown-5. ^c Total yield after pyrolysis of residual material with magnesium chloride. ^d Yield obtained from a reduction of 15 g of the lactone (2a); other yields are based upon the reduction of 1—2 g of the lactone. ^e Yield obtained from a reduction in the presence of boron trifluoride-diethyl ether.

of diols as expected. However, reduction to give the crown ether (2b) could be achieved in high yield by the addition of the dilactone (2a) in tetrahydrofuran to a suspension of lithium aluminium hydride in the same solvent at 0 °C over 1.5—2 h. The dilactones (3a)—(6a) could be reduced by the same procedure to give good yields of the corresponding crown ethers [18-crown-6 from (3a)—(5a) and 15-crown-5 from (6a)].

This procedure may provide a useful method for the preparation of crown ethers in cases where the usual Williamson ether synthesis is difficult to carry out. The scope of the

reaction is indicated by Table 1 and we note only one case in which the reaction failed; the reduction of the dilactone (7a), derived from oxalic acid, gave a mixture of products with ring cleavage as the major pathway. The mechanism of the reduction is not clear but it is possible that lithium complexes⁸ are involved since the reduction of the γ -butyrolactone (8), using lithium aluminium hydride and similar reaction conditions, gave the diol (9), suggesting that the crown ether system is required for ether formation.

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