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TEMPERATURE DEPENDENCE OF TEMPLATE EFFECT IN THE SYNTHESIS OF CROWN ETHERS

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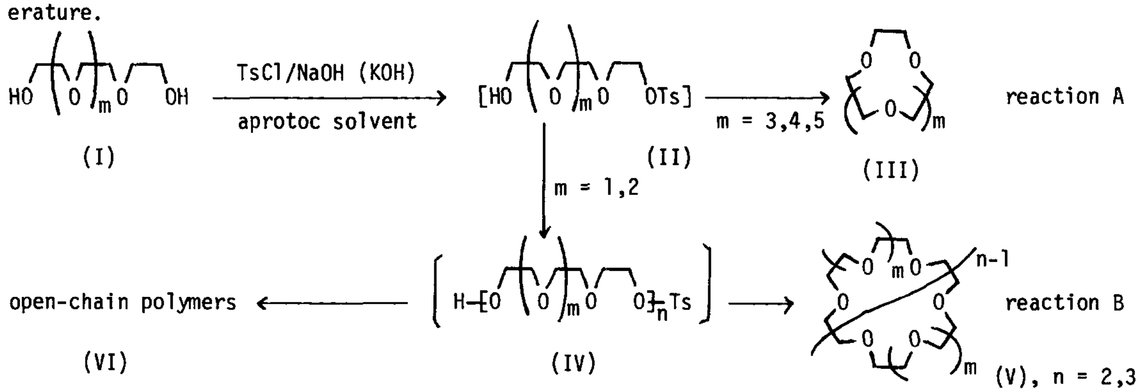
It is well known that the yields of crown ethers depend strongly on the metal template used in the modified Williamson synthesis between oligoethylene glycol or catechol and oligoethylene glycol dichlorides or ditosylates[1-7]. Solvents may play an important roll in some cases[3,4], but no report has reffered to the effect of temperature in the crown ether synthesis.

Recently we reported a new preparation method of crown compounds from oligoethylene glycols and sulfochlorides via the *in situ* formation of oligoethylene glycol monotosylates (II) (reaction A,B)[9,10]. During the course of investigation of reaction conditions, we found that the cyclization step of (II) to the corresponding crown ethers was affected considerably by temperature.



Thus, in reaction A (I, m=3,4,5) and B (I, m=1), a solution of glycol (1.0g) and equimolar amounts of p-toluenesulfonyl chloride in 30 ml of solvent was slowly added dropwise with stirring to a suspension of four molar equivalent of powdered alkali metal hydroxide in 30 ml of solvent over a period of two hours. Dioxane was used as solvent in most of the reactions but monoglyme (0°C) and diglyme (100°, 120°C) were also employed, since no appreciable differences in the yields of crown ethers among solvents (dioxane, monoglyme, diglyme and THF) was observed in the reaction at 40° and 80°C.

In reaction C, triethylene glycol (0.5 g, 3.3 mmol) and triethylene glycol ditosylate (1.53g, 3.3 mmol) were stirred in 30 ml of dioxane for two hours in the presence of powdered potassium hydroxide (0.9g, 14 mmol).

The results of synthesis of crown ethers in various temperatures are tabulated in the Table.

Table. Synthesis of Crown Ethers.

Reaction type	Product	Alkali metal hydroxide	Temp.(°C) 0	Yield of Crown Ethers (GLC, %)[1)] 20	40	60	80	100	120
A	15-crown-5	NaOH	31	70	81	82	79	80	59
"	"	KOH	26	37	53	57	54	52	48
"	18-crown-6	NaOH	—	44	57	71	70	67	50
"	"	KOH	—	77	95	98	94	89	84
B	" 2)	"	—	48	67	72	70	61	58
C	"	"	—	38	50	65	59	—	—
A	21-crown-7	NaOH	—	19	28	38	36	36	32
"	"	KOH	—	48	73	79	80	73	62

1) Average values of 2 to 5 runs. 2) 27-crown-9 which was formed from the trimerized intermediate (IV, m=1, n=3) was detected by GLC.

As shown in the Table, sodium hydroxide is preferable to potassium hydroxide for the preparation of 15-crown-5, while the reverse is the case with 18-crown-6 supporting the reported effect of the template atoms[1-8]. Potassium hydroxide was found as much more effective than sodium hydroxide for the synthesis of 21-crown-7, but other alkali or alkaline earth metal hydroxides such as lithium hydroxide (for 12-crown-4) and barium hydroxide[8] (for 18-crown-6) were found as ineffective.

On the other hand, an apparent temperature effect was also noticed. In almost all reactions the maximum yield was obtained at the temperature around 60°C. Although the reactions proceeded effectively at the lower and the higher temperatures as indicated by the complete consumption of glycol, the open-chain polymers were liable to be formed. The intermediate (II) is organized in a conformation suitable for ring formation by metal template and the reacting ends ($-O^-$ and CH_2OTs) may further be brought together to the preferable position for substitution at the optimum temperature.

References

1) C.J.Pedersen, J. Am. Chem. Soc., 89, 7017 (1967).
2) J.Dale, P.O.Kristiansen, J. Chem. Soc., Chem. Commun., 670 (1971).
3) R.N.Greene, Tetrahedron Lett., 1793 (1972).
4) F.L.Cook, T.C.Caruso, M.P.Byrne, C.M.Bowers, D.H.Speck, and C.L.Liotta, Tetrahedron Lett., 4029 (1974).
5) K.Madan, D.J.Cram, J. Chem. Soc., Chem. Commun., 437 (1975).
6) G.Jones, C.J.Ransom, and C.B.Reese, Synthesis, 515 (1975).
7) D.N.Reinhoudt, R.T.Grey, J.C.Smit, and I.Veenstra, Tetrahedron, 32, 1161 (1976).
8) L.Mandolini, B.Masci, J. Am. Chem. Soc., 99, 7709 (1977).
9) P.-L.Kuo, M.Miki, and M.Okahara, J. Chem. Soc., Chem. Commun., 504 (1978).
10) P.-L.Kuo, M.Miki, I.Ikeda, and M.Okahara, Tetrahedron Lett., 4273 (1978).

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