

Intracomplex Macrocyclization: a Novel Approach to Effective Synthesis of Cryptands

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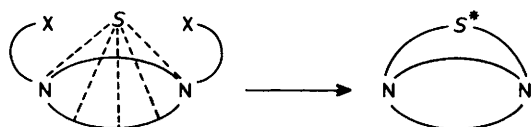
Dihydroxycryptands are formed in good yield by the reactions of *N,N'*-bis(oxiranylmethyl)diazacrown ethers with amines.

Crown ethers bearing appropriate functional groups in side chains may bind a substrate, react with it with high chemo- and regio-selectivity, and release the products.^{1,2} It seemed promising to study the use of this phenomenon for an effective synthesis of cryptands as shown in Scheme 1.

For realization of this reaction the substrate must form a complex with a crown ether and interact irreversibly with the two functional groups X. In this connection we have studied the reaction of the bis(oxiranylmethyl)diazacrown ethers (1) and (2)³ with the amines (3)—(5). The latter are known to be able to form complexes with crown ethers and interact readily

with epoxy groups. The reactions of equimolar amounts of the crown ethers (1) and (2) with the amines (3)—(5) were carried out in boiling ethanol for 8—10 h. The solvent was evaporated off and the residue was purified by chromatography on alumina (chloroform–benzene–propan-2-ol as eluant). In all cases the cryptands (7) were the main products, their yields reaching 73—92%.

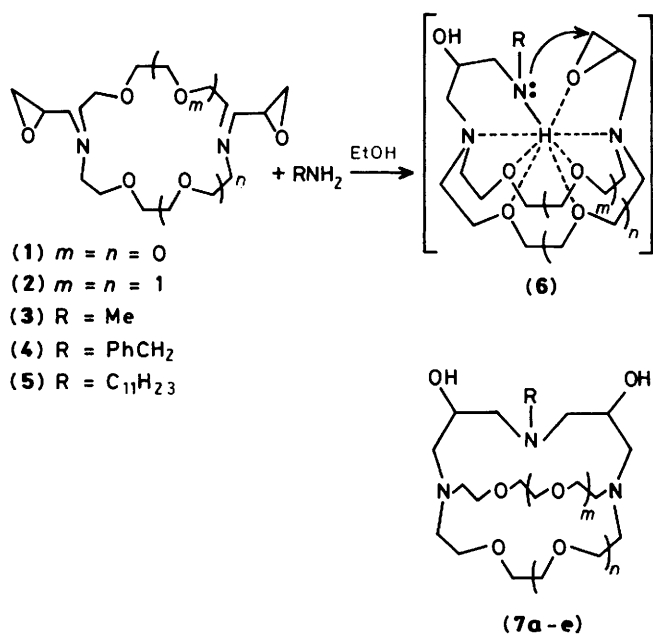
The cryptands (7a—e) were isolated as mixtures of *meso*- and (\pm)-stereoisomers. Their analytical and spectral data are in good agreement with the suggested structures.



Scheme 1. X = functional group able to interact with a substrate; S* = chemically transformed substrate.

Table 1. Yields of cryptands (7).

	R	m	n	%		R	m	n	%
(7a)	Me	0	0	92	(7d)	CH ₂ Ph	1	1	85
(7b)	Me	1	1	73	(7e)	C ₁₁ H ₂₃	1	1	79
(7c)	CH ₂ Ph	0	0	83					



Scheme 2

A choice between the formation of linear and cyclic products is controlled by the possibility of inter- or intramolecular addition of the second epoxy group to the substrate. In this connection, the high yield of the cryptands (7) is unexpected, as the reaction was not carried out under high dilution conditions (reagent concentrations $5 \times 10^{-2} \text{ mol l}^{-1}$), and there was no template cation present. We suggest that the high yields are due to the formation of the intermediate (6), in which the favourable steric arrangement of reaction centres is determined by the binding of the substrate to the macrocycle (Scheme 2). This suggestion is consistent with the high yield of the cryptand (7d) (91%) in the reaction of the diepoxy diazacrown ether (2) with benzylamine at molar ratio 1:2.

We hope that the principle of intracomplex cyclization will open up new possibilities for the effective one-step synthesis of macroheterocyclic compounds.

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References

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