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HYDROXYMETHYL 18-CROWN-6 AND HYDROXYMETHYL [2.2.2]CRYPTAND: VERSATILE DERIVATIVES FOR BINDING THE TWO POLYETHERS TO LIPOPHILIC CHAINS AND TO POLYMER MATRICES

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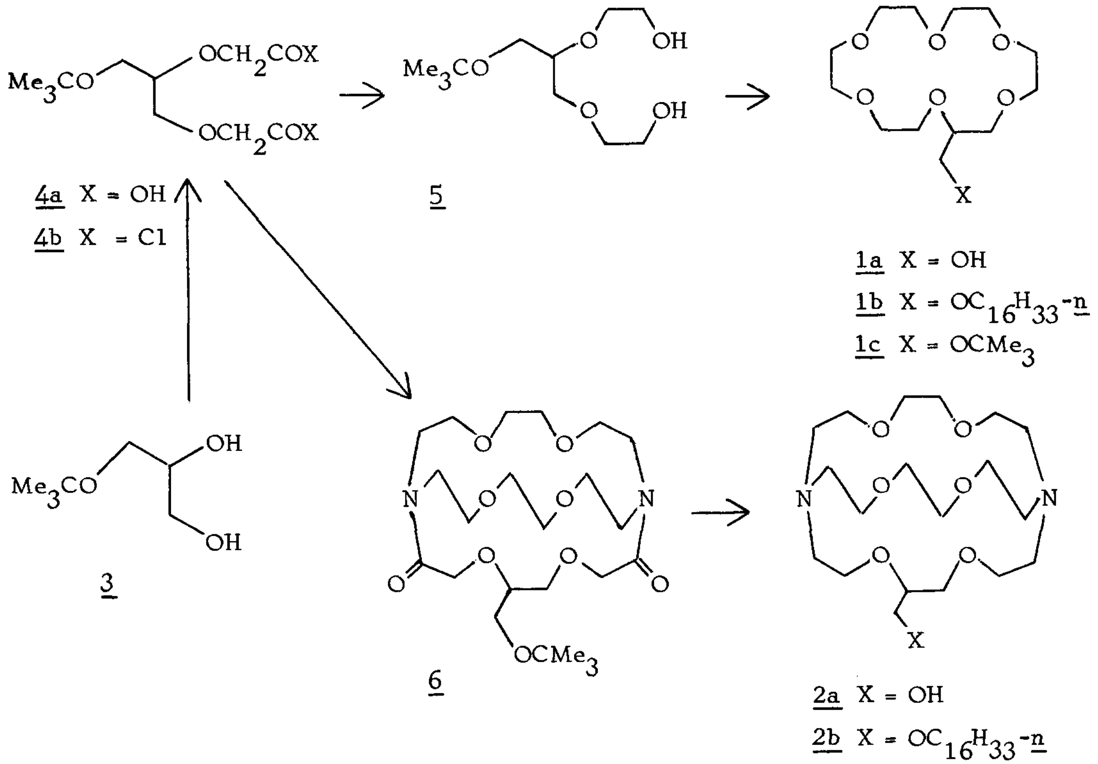
Summary: The presence of the hydroxymethyl group allows facile functionalisation of 18-crown-6 and of [2.2.2]cryptand. A variety of lipophilic and polymer-supported macrocyclic polyethers is thus available . They are efficient and easily recyclable phase-transfer catalysts.

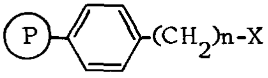
Multidentate macrocyclic and macrobicyclic polyethers have aroused increasing interest in recent years, dating from the pioneering studies of Pedersen and Lehn.[1] However use of most of them, expecially macrobicyclic derivatives (cryptands), is severely limited by the necessity of multistep syntheses and the difficulties of recovery. More versatile systems are obtained by introducing alkyl chains to afford solubility in low polarity organic media,[2,3] or by anchoring to polymer supports.[4,5]

This report describes the synthesis of polyethers 1 and 2: the hydroxymethyl group affords the simplest way to attach 18-crown-6 and [2.2.2]cryptand both to lipophilic chains and to a variety of polymer matrices.

3-t-Butoxy-1,2-propanediol 3 was obtained from t-butyl glycidyl ether[6] by treatment with formic acid and then with 50% aqueous sodium hydroxide: 88%, bp 115-117°C (16 mm). Condensation with chloroacetic acid in t-BuOH-t-BuOK afforded 3,6-dioxa-4-t-butoxymethylene-1,8-octanedicarboxylic acid 4a, which was directly reduced to diol 5 with LiAlH$_4$ in THF: 74%, bp 127-130°C (0.3 mm). Reaction of 5 with triethyleneglycol ditosylate (potassium hydroxide in 10:1 aqueous THF, reflux, 3h) gave crown-ether 1c (alumina, chloroform; isolated as KBF$_4$ complex, 38%, mp 125-126°C), then converted with HBF$_4$ in methylene chloride into hydroxymethyl-18-crown-6 1a: KBF$_4$ complex, 91%,mp 144-145°C from methylene chloride-ethyl ether.

Condensation of acid dichloride 4b with 1,10-diaza-18-crown-6 under high dilution conditions,[7] subsequent reduction of the bicyclic diamide 6 with B$_2$H$_6$ in THF, and hydrolysis with 6N HCl afforded hydroxymethyl derivative 2a, isolated as NaBF$_4$ cryptate: 44%, mp 200°C, dec., from methylene chloride-ethyl ether.





9a n = 1 X = 18-crown-6
9b n = 6 X = 18-crown-6
10a n = 1 X = [2.2.2]cryptand
10b n = 6 X = [2.2.2]cryptand

By reaction with n-hexadecyl bromide in t-BuOK-t-BuOH, hydroxymethyl derivatives 1a and 2a gave n-hexadecyl ethers 1b (92%, mp 38-39°C) and 2b (68%, mp 47°C), respectively.[8]

Heating 1a and 2a for 7h at 80°C with chloromethyl polystyrene 7 (1% crosslinking with p-divinylbenzene, 1.25 mequiv Cl/g) in the presence of t-BuOK in diglyme or DMF, gave polymer-supported crown-ether 9a and cryptand 10a, respectively. Analogous condensations with macroporous polystyrene 8, containing ω-bromohexyl chains (1.2 mequiv. Br/g) and prepared as previously described,[9] gave resins 9b and 10b, respectively. Yields in immobilized crown ethers and cryptands 9, 10, were in the range 50 to 95%, as determined by the observed variations in weight and by titration with potassium picrate.[10,11]

Ethers 1b, 2b are practically insoluble in water but soluble in non-polar organic media, and can be used as efficient phase-transfer catalysts. Their behaviour is identical to that of the previously studied alkyl substituted crown ethers[2a,b] and cryptands.[3]

As already found for quaternary ammonium and phosphonium salts anchored to polymer supports,[12] Table - Reaction of n-octyl bromide with KI and KCN under phase-transfer conditions: catalytic efficiency of alkoxy-substituted and polymer-supported crown-ethers and cryptands.[a]

Catalyst	$t^{1/2}$, min.[b] KI	KCN
1b	27	
2a	250	
2b	16	27
9a[c]	29	55
9b[c]	22	97
10a[c]	123	17
10b[c]	45	14

[a] n-Octyl bromide (2 mmol), KI or KCN (5 mmol) and catalyst (0.02 mmol) in toluene (1.04 mL) -water (0.65 mL) at 90°C; stirring speed 1300 rpm. [b] Measured by GLC analysis (SE-30, 3% over chromosorb at 120°C). [c] Conditioned for 12 h in toluene water at 90°C.

use of highly porous resins reduces difficulties associated with diffusive and fluidodynamic factors. This is particularly valid for 9b and 10b, in which the high porosity of the polymer matrix and the presence of lipophilic spacer chains[12,13] makes these polymer-supported crown-ethers and cryptands very similar in reactivity to the corresponding free, soluble systems. Indeed, they are efficient phase-transfer catalysts, and aliphatic nucleophilic substitutions can be carried out in the presence of 0.01 molar equiv. of crown-ether or cryptand (Table).[14]

The ability of polymer supported crown-ethers 9 and cryptands 10 to efficiently extract cations from aqueous solutions is an important property in the case of dangerous or expensive materials.[15] Appropriate cations are extracted from a dilute aqueous solution with a slight excess of resin swelled in toluene or methylene chloride and recovered by washing the resin with acetone-water.[16]

The versatility of intermediates 1 and 2, which may be anchored to any kind of chain, and the possibility of indefinite recycling of polymer-bound derivatives 9 and 10, allow much wider use of crown ethers and cryptands.

References and Notes

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11) In the case of 10a and 10b the titration was run by stirring a $1.1\text{x}10^{-3}$M solution of potassium picrate in 0.1 N aqueous potassium hydroxide with 5-10 mg of resin swelled in 10 mL of methylene chloride. The residual picrate in the aqueous phase was determined by u.v. spectroscopy. Titration of [2.2.2, C_{14}] cryptand according to this method gave quantitative results. In the case of crowns 9a and 9b a value of 95% of that calculated from weight increase and elemental data was obtained with 10 molar equiv. of picrate.

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14) More informations are required for better evaluation of factors responsible for the different efficiency of catalysts 1, 2, 9 and 10: microenvironments at the catalytic site, diffusion phenomena, complexation constants, etc... .

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16) This property may be used to return to the normal ^{1}H NMR spectrum of an organic compound after measurements in the presence of lanthanide shift reagents. As an example, normal chemical shifts of ^{1}H NMR spectrum of $PhCH_2OH$ in $CDCl_3$ were re-established in about 1 min by simple addition of resins 9 or 10 to the solutions containing $Eu(fod)_3$ or $Pr(fod)_3$. This method allows facile recovery of the already analyzed organic sample.

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