

LARIAT ETHERS. 2.¹ THE REMARKABLE SOLVENT DEPENDENCE OF BINDING CONSTANTS
IN MACROCYCLIC POLYETHERS BEARING SECONDARY DONOR GROUPS ON FLEXIBLE ARMS

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Abstract: Certain hydroxylated macrocyclic polyethers are found to have considerably diminished binding constants in polar solvents, even when the sidearm does not appear to be large enough to hinder the crown hole.

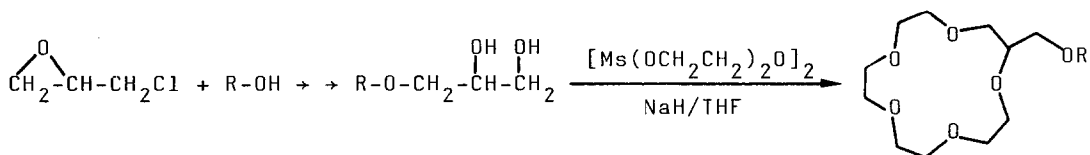
We have previously reported enhanced cation binding for certain macrocyclic polyethers which have secondary donor groups on flexible arms that can overlay the macroring in such a way that axial solvation is provided to a complexed cation.² We have called such compounds "lariat ethers" because of the conceptual similarity between them and the lassoes which are used to rope and tie animals. The studies noted above were conducted in a two-phase system of CH_2Cl_2 and H_2O and binding was assessed by the picrate extraction technique.³ We have now examined a number of related compounds which are soluble in aqueous methanolic solution (often by virtue of a hydroxyl group) and found that these compounds exhibit binding constants in aqueous methanol which are somewhat different from what might have been anticipated.

The K_s values presented here are equilibrium binding constants. Although K_s is the ratio k_f/k_r for complexation, we have not determined the values herein from these rate constants, but rather using an ion selective electrode and millivolt meter. Because of the large differences in binding constants among macrocyclic polydentate compounds and even for the same compound in different solvents, it has been common practice to express K_s as its decadic logarithm (i.e., $\log K_s$). To our knowledge, there is no theoretical reason for this since K_s is unitless. The convenience of using $\log K_s$ rather than K_s should therefore defer to clarity when the compressing effect of logarithms might obscure otherwise interesting data. Since binding constants are generally lower in more polar solvents, and since the simple solvent effect may be huge compared to differences due to structural effects in

closely related compounds, we have chosen to emphasize K_s values here rather than to use the perhaps more common log values.

It is well-established that cation binding properties for macrocyclic polyether ligands differ substantially in solvents of differing polarities.⁴ For example, dibenzo-18-crown-6 binds K^+ in H_2O with an equilibrium constant (K_s) of 47 ($\log K_s = 1.67$)⁵ and in anhydrous MeOH, $K_s = 100,000$ ($\log K_s = 5.00$).⁶ 18-Crown-6, a compound which should be a better K^+ binder, has the following constants: $K_s(H_2O) = 107$ ($\log K_s = 2.03$)⁷ and $K_s(MeOH) = 1,120,000$ ($\log K_s = 6.05$).⁸ Note that the binding constant is lower in H_2O , an inherently better cation solvating medium than MeOH. In both cases, however, 18-crown-6 is, as expected, a better cation binder than dibenzo-18-crown-6.³ This relationship of binding constants is presumably due to the diminished basicity of the four sp^2 oxygens bound to the aromatic rings in dibenzo-18-crown-6.

The compounds described herein were all prepared as described previously and shown in the equation below.^{2,9} Hydroxymethyl-15-crown-5 was prepared by hydrogen-

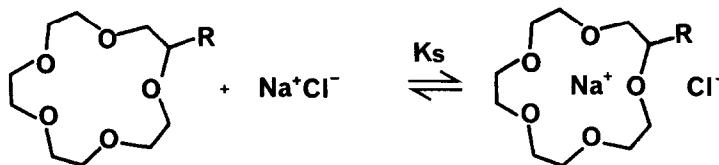


ation of benzyloxymethyl-15-crown-5 which we² and others¹⁰ have previously reported. The other hydroxyl-containing compounds were prepared by oxymercuration¹¹ of the precursor alkanes.

A perusal of the data in the table suggests several interesting facts. With the exceptions of **6** and its analog, **8**, all of the compounds bearing side-arms exhibit significantly lower Na^+ binding than does 15-crown-5 (**1**). This stands in remarkable contrast to the relationship of extraction constants which we have previously reported.² 15-Crown-5 (**1**) extracted 7.6% of the available Na^+ picrate from H_2O into CH_2Cl_2 , whereas **6** extracted twice as much (15.7%). In 90% aq. MeOH, binding constants for **1** and **6** do not appear to differ significantly. Moreover, the extraction constant for **4** was found to be 18% in CH_2Cl_2 and in 90% MeOH, it is a significantly poorer binder than **1**.

Were it not for the identity of binding constants for **1**, **6**, and **8**, one might surmise that addition of any side-arm diminishes the binding ability of these materials. The reason for the contrast between the extraction constant and equilibrium binding constant data is not entirely clear. A possible explanation is that the side-arms may be heavily hydrogen bonded in 90% MeOH and the combination of the solvation shell and side-arm partially block the crown hole. This explanation is tentative at best and the phenomena underlying these remarkable differences

Table: Binding Constants for Lariat Ethers



Cpd. No.	R ^a	Binding Constants ^b	
		K _s	Log K _s
1		5.01; ^{c,d} 926±32 ^e	0.70; ^{c,d} 0.73 ^d
2		555	2.74
3		556	2.75
4		669	2.83
5		666	2.82
6		927	2.97
7		364	2.56
8		843	2.93

a. Corresponds to the side chain in a substituted 15-crown-5. All compounds are colorless to pale yellow oils. New compounds were pure by gas chromatographic analysis and gave satisfactory C, H analyses as well as acceptable IR and NMR spectra. b. Measured in 90% (w/w) aq. MeOH at 25.0±1.0°C using a Corning 476210 electrode and an Orion model 501 "ionalyzer" meter. c. See ref. 7. d. Value determined in water. e. A standard deviation of ±3.5% was determined for 15-crown-5 in 90% MeOH by conducting 11 determinations of K_s on mixtures from 0.50-6.80 mM in ligand and 1.00-2.00 mM in NaCl. Frensdorff (ref. 3a) has suggested that systematic errors may make such electrochemical measurements as uncertain as ±10%.

are currently under investigation.

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Notes and References

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