and the reaction was stirred overnight. The reaction mixture was filtered, and the filtrate was stripped to give an oil which was chromatographed on silica gel with chloroform to yield two products. The first product (an oil) corresponded to **2a**. The second product was recrystallized from benzene and petroleum ether to give a pure product (**2b**): 12 g (22%); mp 81–84 °C; NMR (Me_2SO-d_6) δ 1.4 (t, 1 H), 2.30 (s, 3 H), 3.53 (s, 3 H), 4.55 (q, 2 H), 7.5 (s, 1 H); ^{13}C NMR (Me_2SO-d_6) δ 163.61, 137.83, 136.14, 128.56, 59.33, 31.23, 14.47, 9.45. Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.65. Found: C, 56.90; H, 7.22; N, 16.66.

4(5)-Methyl-5(4)-(hydroxymethyl)imidazole (3). The HCl salt of **3** was prepared according to the procedure reported in the literature.[8] The free base was liberated by dissolving a sample of HCl salt in water which was basified to pH 9 and extracted with *n*-BuOH. The *n*-butanol solution was dried and concentrated to half of the original volume. Crystalline solid **3** (mp 129–132 °C, 80% recovery) was isolated: ^{13}C NMR (Me_2SO-d_6) δ 132.34, 129.68, 125.68, 52.84, 9.09. Anal. Calcd for $C_5H_8N_2O$: C, 53.56; H, 7.19; H, 7.19; N, 24.98. Found: C, 52.84; H, 7.13; N, 24.44.

Acknowledgment. We express our appreciation to Dr. L. Jackman, Dr. J. Stedman, and Dr. D. Daniel for their helpful discussions.

Registry No. 1a, 79731-12-7; **1b**, 79731-13-8; **2a**, 35445-32-0; **2b**, 74531-82-1; **3**, 29636-87-1; **3**·HCl, 38585-62-5; **4c**, 79731-14-9; **4a**·2HCl, 79731-15-0; **4b**, 79731-16-1; **4b**·2HCl, 79731-17-2; 4-methyl-5-carbethoxyimidazole, 51605-32-4; 4-methyl-5-chloromethylimidazole hydrochloride, 51605-33-5.

Crown Cation Complex Effects. 16. Solvent Dependence of the 15-Crown-5 and 18-Crown-6 Equilibria with Sodium Cation[1]

Dennis M. Dishong and George W. Gokel*

Department of Chemistry, University of Maryland, College Park, Maryland 20742

Received August 6, 1981

During the 14 years since Pedersen reported the first syntheses of the compounds he dubbed crown ethers,[2] a large number of binding constants have been reported. The data have often tended to apply to specific compounds and single solvents although a number of more detailed studies have recently appeared.[3] Lamb and co-workers have systematized a large number of binding constants in a recent monograph.[4] Despite these efforts, it is surprising to note that the solvent dependence of the binding data for two of the simplest crowns, 15-crown-5 and 18-crown-6, has not been reported.[5] Since such data are valuable for comparison with more elaborate macrocycles of interest to us,[6] we record here our own observations.

Table I. Sodium Cation Binding by 15-Crown-5 and 18-Crown-6

wt % of MeOH	mol fraction of MeOH	15-crown-5		18-crown-6	
		K_s	log K_s	K_s	log K_s
0	0	6.2	0.79	63 (6.3)[a]	1.80 (0.8)[a]
20	0.123	30.9	1.49	151	2.18
40	0.273	51.0	1.71	293	2.47
60	0.458	164	2.21	644	2.81
80	0.692	448	2.65	1759	3.25
90	0.835	926	2.97	5378	3.73
100	1.000	1780	3.25	22580	4.35

[a] Value from ref 10, see line B on Figure 1 and the text.

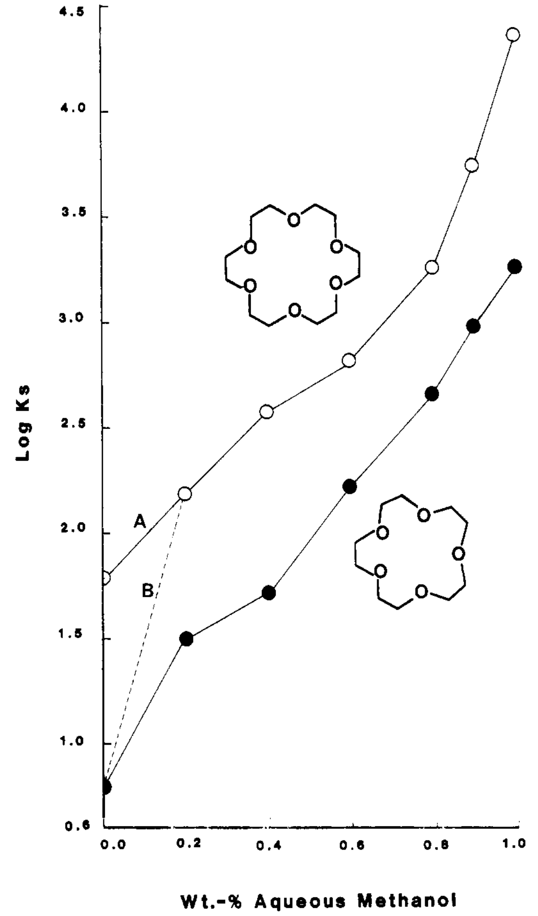

Figure 1. Solvent dependence of Na^+ binding by 15-crown-5 and 18-crown-6.

In Table I are collected the binding constants[7] for the reaction illustrated in eq 1. The two crowns studied are

$$\text{crown} + \text{Na}^+ \overset{K_s}{\rightleftharpoons} (\text{crown}\cdot\text{Na})^+ \qquad (1)$$

15-crown-5 and 18-crown-6. The solvents chosen for these studies are methanol–water mixtures. The percentages reported are by weight at 25 °C. The corresponding mole fractions were calculated. Whenever possible, calibration was attempted with literature values. For example, our value of log K_s for 15-crown-5 in pure water was 0.79 and the reported value is 0.70.[9] The binding constant for

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(1) Previous paper in this series: Ahern, M. F.; Leopold, A.; Beadle, J. R.; Gokel, G. W. *J. Am. Chem. Soc.*, in press.

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(5) Binding data are available for a number of cations in a number of solvents, but differences in methods, solvents, and other variables complicate comparisons. Kolthoff[2c] has recently reported on binding constants for 18-crown-6 and Na^+ in six different solvents but no mixtures.

(6) Schultz, R. A.; Dishong, D. M.; Gokel, G. W., *Tetrahedron Lett.*, **1981**, 2623 and references therein.

(7) Binding constants were measured in the designated weight-percent solvent at 25.0 ± 1.0 °C, using a Corning Model 476210 electrode and an Orion Model 501 or 701 "Ionalyzer" millivolt meter according to the procedure of Frensdorff.[8] All apparatus was contained in a N_2-flushed drybox and solution temperature was maintained by using circulating di-*n*-butyl phthalate as a heat-transfer fluid.

0022-3263/82/1947-0147$01.25/0

18-crown-6 and sodium in methanol (log K_s) is 4.35 and the reported value is 4.36.[10] Our log K_s value for 18-crown-6 in water is 1.80 ($K_s = 63$). This value is considerably higher than the calorimetrically determined value of 0.8 ($K_s = 6.3$)[10] or the conductometric value of 0.3.[8] The experimental error in these values determined by either method should be considerably less than an order of magnitude. Note, however, that the binding is quite weak and the sensitivity of these measurements will be lower in water than for any methanol mixture. Further note that binding constants between sodium and four other 18-crown-6 molecules have been measured. These are: cyclohexano-18-crown-6 ($K_s = 0.8$),[11] dicyclohexano-18-crown-6 ($K_s = 0.69$),[9] di-*tert*-butyldicyclohexano-18-crown-6 ($K_s = 1.42$),[11] and dibenzo-18-crown-6 (log $K_s = 1.16$).[12] The first two values noted above were determined calorimetrically and the latter two conductometrically and spectroscopically, respectively.

Intuitively, it seems that the binding between sodium cation and 18-crown-6 should be stronger than for 15-crown-5 just because additional solvation can be provided by the extra oxygen. The crystal structure of such a complex suggests this.[13] Note that the two lines (Figure 1) approximately parallel each other, but binding with sodium cation is stronger for 18-crown-6 in all solvent mixtures than it is with 15-crown-5. Although size correlations have received considerable attention in the past, the relatively small and hard sodium cation does not seem to fit as well[4] into such systematizations. In any event, we have included in Figure 1, both our (line A) and Lamb's[9] (line B) values. Slope calculations are presented below for both.

Statistical analyses of the 18-crown-6 (A and B) and 15-crown-5 lines show that each may be approximated as linear with reasonable confidence. The slopes[15] and correlation factors (r) are as follows: 15-crown-5, slope = 2.34, $r = 0.995$; 18-crown-6 (line A), slope = 2.32, $r = 0.968$; 18-crown-6 (line B), slope = 2.99, $r = 0.969$.

A visual examination corroborates that neither 18-crown-6 line fits as well as the 15-crown-5 data, although the correlation factors are not significantly different. It is interesting to note that Izatt et al.[14] have reported calorimetrically determined K_s values for reaction of benzo-15-crown-5 in aqueous methanol mixtures. He reports log K_s values of 0.72, 1.17, 1.64, 1.99, and 2.26 in 20%, 40%, 60%, 70%, and 80% methanol, respectively. The calculated slope of this line is 2.57 and $r = 0.997$. This accords reasonably well with our own data for the parent system.

Although the primary purpose of this communication is to record the K_s solvent dependences for 15-crown-5 and 18-crown-6, it is interesting to note that the nitrogen lariats[6] exhibit a similar rise in the ordinate value as polarity declines. Thus *N*-methoxyethylmonoaza-15-crown-5 binds Na^+ (log K_s) as follows: 1.36, 2.13, 2.56, 3.24, 3.66, and 3.97 in water, 40%, 60%, 80%, 90%, and 100% methanol, respectively. The slope of the best straight line is 2.63 and $r = 0.988$. The solvent trends therefore seem to be typical of a number of simple as well as more complex systems.

Experimental Section

15-Crown-5 was obtained from the Aldrich Chemical Co. and was distilled before use. 18-Crown-6 was prepared by our previously reported procedure.[16] Analytical reagent grade methanol was used for all solvent compositions and mixtures were made by combining the appropriate weights of methanol and water at 25 °C. Binding constants were recorded as described in ref 7. Linear regressions were calculated with a hand calculator equipped with the appropriate program.

Acknowledgment. We warmly thank the NIH for a grant (GM 29150) which partially supported this work.

Registry No. 15-Crown-5, 33100-27-5; 18-crown-6, 17455-13-9; sodium cation, 17341-25-2.

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Carbon-13 Nuclear Magnetic Resonance Chemical Shifts of Chlorinated and Fluorinated Phthalic Anhydrides and Acids

M. J. Fifolt, S. A. Sojka,* and R. A. Wolfe

Hooker Chemicals & Plastics Corp., Research Center, Grand Island Complex, Niagara Falls, New York 14302

Received June 16, 1981

The theory and practice of carbon-13 NMR spectroscopy has progressed, in part, by the systematic analysis of substituent effects in classes of organic compounds.[1] Aromatic substituent effects have been extensively studied in the case of simple benzene derivatives.[2] However, more functionalized aromatic derivatives have received less attention.[3–5] In order to partially fill this gap, we report the results of our systematic study on chlorine- and fluorine-substituted phthalic anhydrides and acids.

Experimental Section

All materials were commercially available or synthesized by literature procedures. Compounds **1**, **12**, **14**, **16**, and **22** were purchased from Aldrich Chemical Co. The remaining compounds were synthesized by using the procedures in the indicated references: **2**,[6] ,**3**[7] **4**,[8] **5**,[9] **6**,[6] **7**,[10] **8**,[11] **9**,[12] **10**,[13] **11**,[14] **13**,[15] **15**,[16] **17**,[17] **18**,[11]

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