The Complexing Ability of Crown Ethers Incorporating Glucose

PETER BAKÓ, LÁSZLÓ FENICHEL and LÁSZLÓ TÔKE*
Department of Organic Chemical Technology, Technical University of Budapest, H-1111 Budapest, Müegyetem rkp. 3, Hungary.

Abstract. The complexing (in $CHCl_3$) and extracting abilities of 18-crown-6 type compounds (**1–15**) were measured with Li, Na, K and NH_4 cations. The substituents on the sugar part affected these properties significantly ($K_a = 10^3$–10^7). Some substituents, like acetyloxy groups (**3**) decreased whereas others, like tosyloxy groups (**10, 11**) significantly increased the complexing ability and thus changed the selectivity. The compound with four tosyloxy groups (**11**) shows an excellent picrate salt extracting ability in a CH_2Cl_2-water system.

Key words: Crown ether, complex formation, extraction ability.

1. Introduction

A variety of monosaccharides has been used as starting material for the synthesis of several types of chiral crown ethers [1, 2], and the stabilities of their complexes with metal and ammonium cations have been determined, mainly in a binary $CDCl_3$-water system [1, 3, 4].

In the case of metal, ammonium, methylammonium and *t*-butyl ammonium picrates, the values of the association constants (K_a) were determined by UV spectrophotometry, following the extraction of the aqueous solution of the picrate salt of the crown ether with deutero chloroform [1, 4]. The complexing ability of sugar crowns toward ammonium ions was measured with *t*-butyl ammonium thiocyanate by ^{1}H NMR spectroscopy [5, 6].

2. Experimental

The synthesis of the sugar-based crown ethers **1–15** has been described by us previously [7–10]; the dibenzo-18-crown-6 used for comparison is a Merck product. The complexing constants of the compounds with Li, Na, K and ammonium picrates were measured in chloroform, by UV spectrometry, using the method of Cram [4]. Most of the crown ethers were insoluble in water: solubilities were 0.5% of the total used. The distribution constants of the water-soluble crown ethers between water and chloroform were determined in independent experiments and these constants

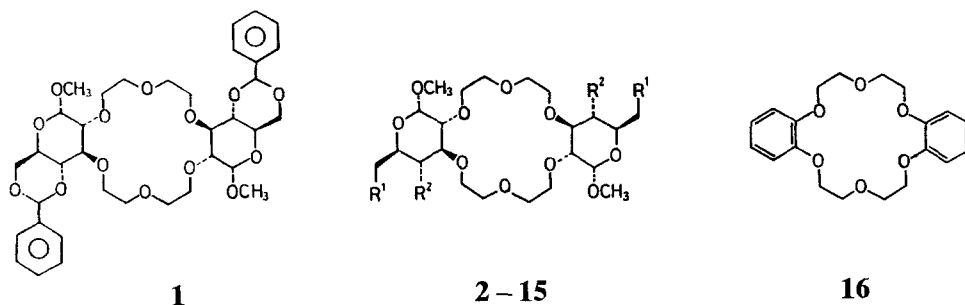---

* Author for correspondence.

Fig. 1.

were taken into consideration in the calculations of K_a values [14, 15]. Although the host-guest stoichiometric ratio in the solution was unknown, for the similar 18-crown-6 type sugar crowns the literature describes 1 : 1 complexes only [1], and our calculations were based on this stoichiometry.

The complex forming ability of some glucopyranoside compounds having benzylidene, benzyloxy, acetoxy, and tosyloxy substituents was measured with metal picrates under the same conditions as in the case of the crown ethers. It has been found that these groups are not able to form complexes with alkali metal and ammonium picrates.

The alkali metal and ammonium picrates were prepared and purified by the method of Wong [11].

Extraction ability was measured by the method of Kimura *et al.* [12] with the above mentioned picrates in a CH_2Cl_2-water system, by means of UV spectrometry (using a Hitachi Perkin-Elmer 124 spectrometer).
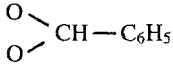
3. Results and Discussion

3.1. COMPLEXING ABILITY

In all the compounds investigated (1–15), the ring is always of the 18-crown-6 type, and the substituents on the sugar part vary (R^1 denotes the substituents on the two primary carbons, R^2 those on the two secondary carbons: Figure 1). Consequently, in this case one can study the effect of substituents on complexing ability (or salt extracting ability), i.e. the so-called lateral discrimination. The lateral groups may have a secondary interaction with the guest molecules. This interaction is a result of several factors: they may be steric effects or hydrophilic and hydrophobic effects (the crown ether also encounters water molecules during the measurement). These effects occur in a complex way, strengthening or weakening one another, and thus it is hard to predict scientifically the values of the resulting complexing constants.

We examined C.P.K. space-filling molecular models of the crown ethers substituted by different groups. The substituents were changed only on the 4C and 6C

TABLE I.   Association constants of crown compounds (1–15) (log K_a in chloroform at 22°C.[a]

Crown compd.	R^1	R^2	log K_a			
			Li^+	Na^+	K^+	NH_4^+
1	O–CH—C_6H_5 (O)		4.14	4.05	5.04	4.12
2	OH	OH	4.04	4.50	4.85	4.01
3	OAc	OAc	3.57	3.20	4.46	3.58
4	Br	OBz	3.68	4.38	4.16	3.96
5	H	OH	4.75	5.05	4.78	4.56
6	Br	OH	3.57	3.95	4.40	3.53
7	OH	OBn	3.58	4.76	4.70	4.38
8	OTr	OAc	4.15	4.80	4.47	3.67
9	OH	OAc	3.75	3.62	4.37	3.59
10	OTs	OH	5.70	5.40	5.45	5.64
11	OTs	OTs	6.17	6.23	6.00	5.81
12	OMs	OH	4.47	4.16	4.65	4.33
13	OMe	OMe	3.18	4.21	4.35	3.91
14	OBu	OBu	4.25	4.33	4.38	3.82
15	OBn	OBn	3.56	4.01	4.09	3.72
16	dibenzo-18-crown-6		4.08	4.44	7.85	5.96

Ac = acetyl, Bz = benzoyl, Tr = trityl, Ts = tosyl, Ms = mesyl, Me = methyl, Bu = butyl, Bn = benzyl

[a] Aqueous phase (0.5 mL); [picrate] = 0.15 M; organic phase (CHCl$_3$, 0.2 mL); [crown ether] = 0.075 M; Ref. [4].

atoms of the pyranose residues (1–15). We found that these substituents did not induce conformational changes on the sugar ring and on the crown ring.

As a comparison, the properties of dibenzo-18-crown-6 (16) were also measured. As can be seen from Table I, the substituents found on the sugar parts affect the complexing ability significantly: the association constants, K_a, are in the 10^3–10^7 range. The weakest complexing ability is shown by the substances bearing two or four acetyloxy groups (3, 9), bromine and benzoyloxy groups (4, 6), four methoxy groups (13) or four benzyloxy groups (15).

Tetrabutoxy (14) and hexamethoxy ethers (13) have nearly identical properties, except that the lithium complex of 14 is an order of magnitude stronger than that of 13.

There are substituents which promote complex formation with all cations: the presence of two tosyloxy groups (10) increases this ability by 1–1.5 orders of magnitude; that of four tosyloxy groups (11) by two orders of magnitude with respect to the benzylidene derivative (1).

As is known, the size of the 18-ring corresponds (on the basis of ion radii) to a selectivity sequence of $NH_4^+ \approx K^+ > Na^+ > Li^+$. This tendency also holds for our compounds: the majority forms the strongest complex with K^+. There are, however, substituents which change this characteristic sequence of the basic crown: the bromobenzoyloxy derivative (4), the unsubstituted (5), the benzyloxy (7), the trityloxy-acetyloxy (8) and the tetratosyloxy (11) derivatives all form the most stable complex with sodium. A comparison of the behaviour of 4 and 6 suggests that the crown ether becomes sodium selective on addition of benzoyloxy groups. A comparison of 8 and 9 indicates that the trityloxy groups increase the stability of the sodium complex by more than one order of magnitude.

Tosyloxy groups (10, 11) not only enhance the complexing ability but also change the selectivity sequence, preferring primarily lithium and sodium, respectively.

In the case of the tetrasubstituted derivatives ($R^1 = R^2$), the stability of the complex with respect to K^+ decreases in the sequence of OTs > OCHPh > OH > OAc > OBu > OMe > OBn (Figure 2). Compared to the values measured with Na^+, some selectivity is shown by 1 and 3 (OCHPh and OAc), inasmuch as there is a 1–1.2 order of magnitude difference between the K_a values obtained with Na^+ and K^+ ions.

The stability of the disubstituted compounds ($R^2 = OH$) with respect to K^+ decreases in the sequence of OTs > OH > H > OMs > Br (Figure 3), and compared to the Na^+ values none of the compounds shows significant selectivity.

As can be seen, tosyloxy groups increase the stability of complexes with all cations, but suppress the differences thereby decreasing the selectivity.

We investigated the lipophilicity of compounds 1–15 by reverse- phase TLC on a silica gel plate modified by octadecyltrimethylsilane, with an ethanol-water (7 : 3) eluent. In this system the R_f values are characteristic of the lipophilicity of the crown ethers. We did not find any general connection between the lipophilicity and association constants (e.g. the order of lipophilicity is 1 > 10 > 3 but that of the K_a values is 10 > 1 > 3).

3.2. EXTRACTION ABILITY

Table II shows the extraction ability of picrate salts of compounds 1, 2, 3, 4, 7, 10, 11 and 16 in the CH_2Cl_2-water system. The tendencies are similar to those of complex formation; substituents affect the extraction ability to a great extent depending on the type of ions. Dibenzo-18-crown-6 (16) used as reference shows a notable selectivity with potassium ions.
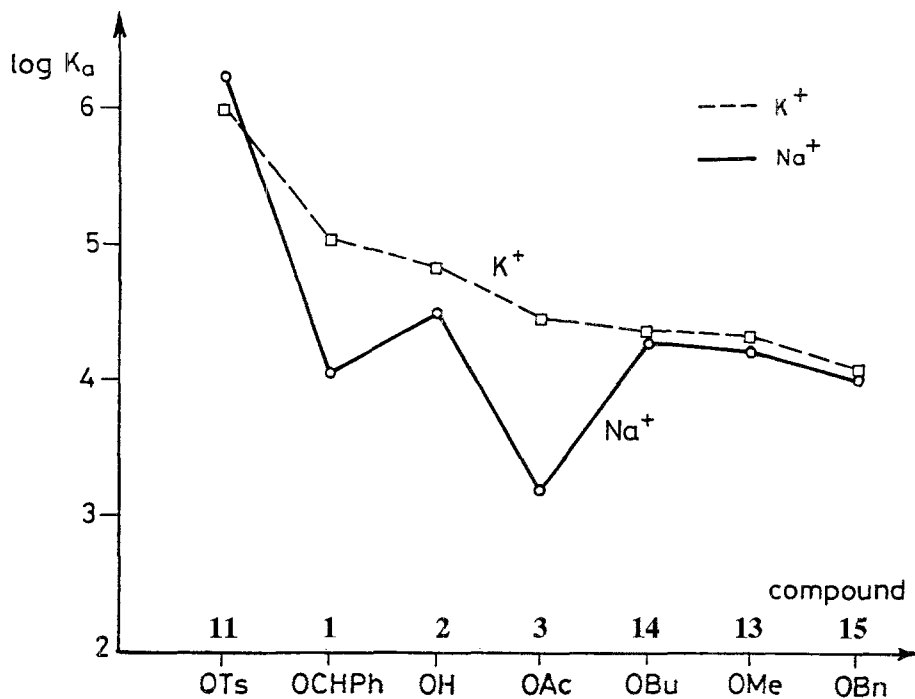
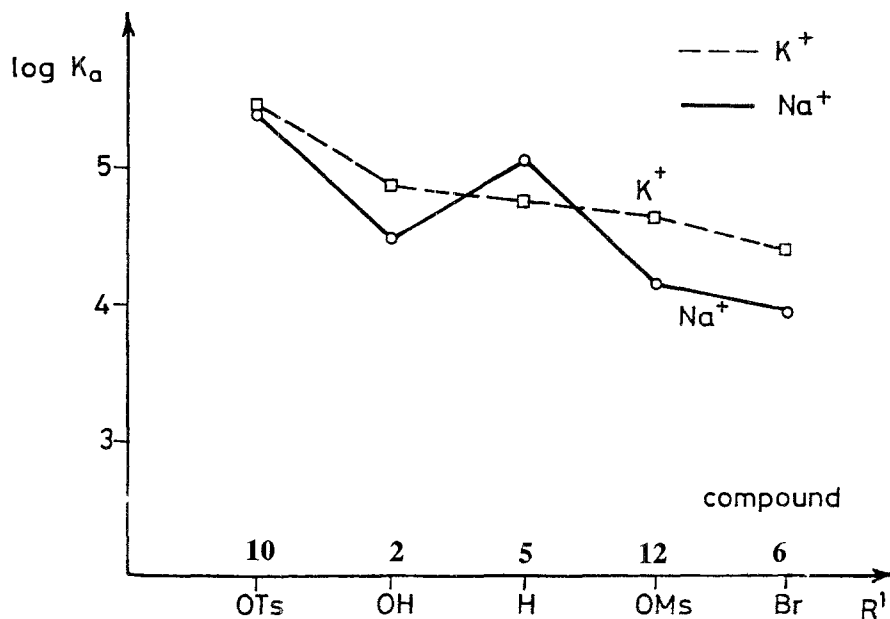Fig. 2.   Log K_a values for tetrasubstituted derivatives.

Fig. 3.   Log K_a values for disubstituted derivatives.

TABLE II. Extraction of alkali metal and ammonium picrates.[a]

Derivatives of bis(glucopyrano-sido)-18-crown-6	Extractability (%) [b]			
	Li^+	Na^+	K^+	NH_4^+
4,6-O-benzylidene- (1)	5.9	14.8	9.6	14.9
tetrahydroxy- (2)	6.7	4.4	7.1	12.9
4,4',6,6'-tetra-O-acetyl- (3)	6.3	11.8	14.7	14.1
4-O-benzoyl-6-bromo- (4)	3.9	21.5	14.2	21.6
4,4'-di-O-benzyl- (7)	28.3	15.5	32.0	35.1
6,6'-di-O-tosyl- (10)	6.9	1.4	14.8	20.6
4,4',6,6'-tetra-O-tosyl- (11)	99.5	93.2	98.5	99.6
dibenzo-18-crown-6 (16)	14.0	2.1	56.7	33.5

[a] Temperature 25°C; aqueous phase (10 mL); [picrate] =
5×10^{-3}M; organic phase (CH_2Cl_2, 10 mL); [crown ether] =
1×10^{-2}M.
[b] Defined as % picrate extracted into the organic phase.
Determined by UV spectroscopy.

The dibenzyloxy derivative (7) is worth noting since its Li, Na and NH₄ picrate extraction ability is better than that of 16, but shows only insignificant selectivity. The most interesting is a comparison of the ditosyloxy (10) and tetratosyloxy (11) derivatives: the modest extraction ability of the former changes dramatically on the introduction of two further tosyloxy groups (11), increasing it to an extremely large value: 11 takes up to 1.7 times larger amount of potassium picrate, 3 times more ammonium picrate, 7 times more lithium picrate, and finally, 44 times more sodium picrate into the organic phase than compound 16. A probable explanation is that the polar Ar-SO₂ groups, being capable of secondary interactions, increase the stablity toward cations. These factors give us a chiral crown ether of outstanding extraction ability.

4. Conclusions

We have found that, by changing the subtituents found on the sugar parts only, the complexing ability and selectivity of crown ethers can be influenced significantly. By applying four tosyloxy substituents, a compound (11) was prepared which can be conceived to behave as a good phase transfer catalyst in the liquid-liquid phase, and this may play an important role in stereoselective syntheses. To demonstrate this assumption, further research is required.

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