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# Synthesis and Complex-Forming Properties of Crown Ethers Incorporating Glucuronic Acid Moieties

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**Abstract.** Crown ethers **1** and **4** of the 18-crown-6 type containing two glucose units have been oxidised by $KMnO_4$ into mono- and dicarboxylic acid derivatives (**5** and **11**), and derivatives with different lipophilicities of the above crown ethers, namely the acetyl, benzyl and butyl derivatives (**8–10**, **13**, **14**) and methyl esters (**6** and **12**) have been synthesized.

The association constants ($K_a$) with Li, Na, K and $NH_4$ cations measured in $CHCl_3$ indicate that complexing ability increases on introduction of carboxy groups, and selectivity changes in favour of the Na cation. These compounds were able to transport alkyl-ammonium salts through a $CHCl_3$ liquid membrane, displaying, however, no chiral recognition ability.

**Key words:** Chiral crown ethers, complex formation, glucuronic acids.

## 1. Introduction

Following the pioneering publication of Cram [1], chiral crown ethers have been synthesised in great number, and their chiral recognition ability has been investigated on the enantiomers of organic ammonium salts [2–4]. Bradshaw *et al.* [5–8] determined the extent of chiral recognition from the kinetic and thermodynamic parameters of the complexes formed between chiral ligands containing pyridine units and the enantiomers of organic ammonium salts. This property can be utilised in the separation of enantiomers during transport through liquid membranes [9, 10].

One of the most important group of chiral crown ethers is the monosaccharide based compounds [11–21]. The preparation and complex-forming properties of crown ethers **1** and **4** of the 18-crown-6 type containing two glucose units have been published by us earlier [22, 23]. This work deals with changes in the complex-forming properties and chiral recognition abilities of these sugar-based macrocycles caused by the formation of carboxy groups via oxidation. Chiral crown ether carboxylic acids have been prepared from L-(+)-tartaric acid bis(*N*,*N*-dimethylamide), and their complex-forming properties investigated by Lehn *et al.* [24].

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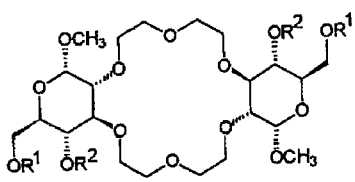
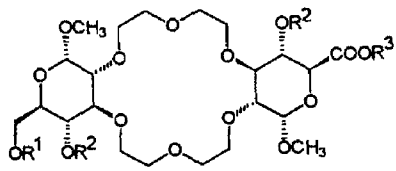
## 2. Experimental

$^1$H NMR spectra: Perkin Elmer R12 and Jeol FX-100 (in $CDCl_3$, TMS as internal standard, 80 MHz, ppm). IR spectra: Perkin Elmer 237 in KBr pellets. UV spectra: Hitachi-Perkin-Elmer 124. Polarimeter: Perkin-Elmer 241. M.p.: Büchi 510 (uncorrected). Elemental analysis: Perkin-Elmer 240 automatic analyser. TLC: Kieselgel 60 $F_{254}$ (Merck), eluent toluene-methanol mixtures (10 : 1–10 : 5), detection with Dragendorff's reagent. Column chromatography: Kieselgel 60 (0.2–0.063 mm, Merck).





**1** $R^1 = R^2 = H$

**2** $R^1 = R^2 = Ac$

**3** $R^1 = R^2 = Bu$

**4** $R^1 = H$, $R^2 = Bn$

**5** $R^1 = R^2 = H$, $R^3 = H$

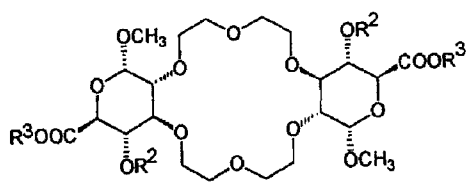
**6** $R^1 = R^2 = H$, $R^3 = Me$

**7** $R^1 = R^2 = H$, $R^3 = K$

**8** $R^1 = R^2 = Ac$, $R^3 = H$

**9** $R^1 = R^2 = Bu$, $R^3 = H$

**10** $R^1 = H$, $R^2 = Bn$, $R^3 = H$



**11** $R^2 = R^3 = H$

**12** $R^2 = H$, $R^3 = Me$

**13** $R^2 = Ac$, $R^3 = H$

**14** $R^2 = Bn$, $R^3 = H$

Ac = acetyl, Bu = butyl, Bn = benzyl, Me = methyl

*Methyl - 2,3 - dideoxy - α - D - glucopyranose[2,3 - b]methyl - 2,3 - dideoxy - α - D - glucurono - pyranose[2'3' - k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**5**)*

Powdered $KMnO_4$ (0.12 g) was added to a stirred solution of **1** (0.5 g) in dry $CHCl_3$ (20 mL). After 4 h of stirring at room temperature further $KMnO_4$ (0.12 g) was added and the mixture was stirred for a further 18 h. The brown precipitate was filtered off by sintered glass filter, was suspended in water (20 mL), heated to boiling (to compress $MnO_2$), and, after recooling, $MnO_2$ was filtered off and washed with water. The combined filtrates and washes were stirred with Varion KS cation exchange resin (4 mL). The aqueous solution filtered off the resin was evaporated in vacuo, the residue was dried in a vacuum desiccator over $P_2O_5$, and then crystallised from an ethanol–petroleum ether mixture. *Yield* 0.35 g (68%) of **5**; m.p.: 78–80 °C, $[\alpha]_D^{22} = +77.8$ ($c = 1$ in $CHCl_3$). $^1$H-NMR: 3.40 (s, 6H, 2 × $OCH_3$), 3.6–4.0 (m, 30H, $CH_2$ and CH groups), 4.83 (d, 2H, $J = 3.5$ Hz, anomeric H). *Elemental anal.: Calc.* for $C_{22}H_{38}O_{15}$; C 48.71, H 7.01. *Found;* C 48.50, H 7.20.

On titration with 0.1 N NaOH standard solution in the presence of phenolphthalein indicator, an equivalent amount (18.5 mL NaOH/g product) of alkali was consumed.

*Methyl - 2,3 - dideoxy - α - D - glucopyranose[2,3 - b]methyl - 2,3 - dideoxy - α - D - methyl - glucuronopyranose[2'3' - k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**6**)*

An ethereal solution (16 mL) of diazomethane (5 mmol) was added dropwise to a solution of **5** (0.54 g) in $CH_2Cl_2$ (10 mL) under stirring. After completing the reaction the excess of diazomethane was decomposed with 10% acetic acid solution. The $CH_2Cl_2$ phase was washed with 10% aqueous $Na_2CO_3$ solution and with water, and then, after drying over $MgSO_4$, it was evaporated. The raw product was chromatographed on Kieselgel (40 g) column (300 × 20 mm) with toluene–MeOH (10 : 2) as eluent. *Yield* 0.37 g (66.5%) of **6** (yellow syrup), $[\alpha]_D^{22} = +72.8$ ($c = 1$ in $CHCl_3$). $^1$H-NMR: 3.38 (s, 3H, $COOCH_3$), 3.44 (s, 6H, 2 × $OCH_3$), 3.60–4.30 (m, 29H, $CH_2$ and CH protons), 4.82 (d, 2H, $J = 3.5$ Hz, anomeric H). *Elemental anal.: calc.* for $C_{23}H_{40}O_{15}$; C 49.64, H 7.19. *Found:* C 49.35, H 7.10.

Potassium salt of **5**: prepared in the same way as **5**, but without the treatment on the cation exchange resin. Yield: 0.39 g (71.1%). M.p.: 110 °C (from ethanol), $[\alpha]_D^{22} = +66.7$ ($c = 1$, $H_2O$).

*Methyl - 2,3 - dideoxy - 4,6 - O - diacetyl - α - D - glucopyranose[2,3 - b]methyl - 2,3 - dideoxy - 4 - O - acetyl - α - D - glucuronopyranose[2'3' - k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**8**)*

The potassium salt **5** (2.3 g) was dissolved in a mixture of pyridine (10 mL) and acetic anhydride (10 mL), and heated on a steam bath for 15 h. After cooling, the reaction mixture was evaporated in vacuo, the residue was dissolved in $CHCl_3$ (20 mL) and filtered through a filter paper. The filtrate was washed thrice with water and then stirred for 30 min with a little amount of water and Varion KS cation exchange resin (4 mL). After filtering off the resin, the chloroform phase was dried over $MgSO_4$ and then evaporated. *Yield* 1.6 g (61%) of **8**, m.p.: 119–122 °C (acetone–water 5 : 1), $[\alpha]_D^{22} = +50.2$ ($c = 1$, $CHCl_3$). $^1$H-NMR: 2.0 (s, 9H, 3 × OAc), 3.40 (s, 6H, 2 × $OCH_3$), 3.3–4.5 (m, 27H, $CH_2$ and CH protons), 4.81 (d, 2H $J = 3.5$ Hz, anomeric H). *Elemental anal.: calc.* for $C_{28}H_{44}O_{18}$; C 50.29, H 6.58. *Found:* C 50.08, H 6.43.

*Methyl - 2,3 - dideoxy - 4,6 - O - dibutyl - α - D - glucopyranose[2,3 - b]methyl - 2,3 - dideoxy - 4 - O - butyl - α - D - glucuronopyranose[2'3' - k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**9**)*

The potassium salt **5** (1.74 g) was stirred with a mixture of butyl bromide (22 mL) and 50% NaOH (15 mL) for 70 h at 40 °C. The organic phase was evaporated in vacuo, the residue was dissolved in $CH_2Cl_2$ (25 mL), washed with water, and then stirred for 30 min with a mixture of a little water and cation exchange resin. After filtration and separation the organic phase was washed again with water, dried over $MgSO_4$, and then evaporated to yield a yellow syrup of **9**. Yield 1.52 g (71.3%), $[\alpha]_D^{22} = +34.6$ ($c = 1$, $CHCl_3$). $^1$H-NMR: 0.89 (t, 9H, 3 × $CH_3$), 1.11–1.89 (m, 18H, butyl-$CH_2$), 3.33 (s, 6H, 2 × $OCH_3$), 3.40–4.30 (m, 26H, $CH_2$ and CH protons), 4.77 (d, $J = 3.5$ Hz, 2H, anomeric H). *Elemental anal.: calc.* for $C_{34}H_{62}O_{15}$; C 57.46, H 8.73. *Found:* C 57.24, H 8.62.

*Methyl - 2,3 - dideoxy - 4 - O - benzyl - α - D - glucopyranose[2,3 - b]methyl - 2,3 - dideoxy - 4 - O - benzyl - α - D - glucuronopyranose[2'3'-k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**10**)*

Powdered $KMnO_4$ (0.26 g) was added to a solution of **4** (1.6 g) in dry $CHCl_3$ (20 mL) under stirring, and after 8 h of stirring at room temperature additional $KMnO_4$ (0.26 g) was added, and the mixture was stirred for a further 17 h. The precipitate was filtered off and washed twice with $CHCl_3$. The combined chloroform phases were washed three times with water (6 mL) each, and then stirred for 20 min with a mixture of water (5 mL) and cation exchange resin (5 mL). After filtering, the $CHCl_3$ phase was dried over $MgSO_4$, evaporated, and the residue was purified on a Kieselgel column (70 g, 350 × 25 mm, eluent: toluene–methanol 10 : 3) to give amorphous, white **10**. *Yield* 1.07 g (65.6%), $[\alpha]_D^{22} = +72.5$ ($c = 1$, $CHCl_3$). $^1$H-NMR: 3.42 (s, 3H, $OCH_3$), 3.50 (s, 3H, $OCH_3$), 3.4–4.2 (m, 30H, $CH_2$ and CH protons), 4.85 (d, 2H, $J = 3.5$ Hz, anomeric H), 7.23 (s, 10H, aromatic protons),

9.44 (broad, 1H, COOH). *Elemental anal.: calc.* for $C_{36}H_{50}O_{15}$; C 59.83, H 6.92. *Found:* C 59.59, H 6.79.

*Bis(methyl - 2,3 - dideoxy - α - D - glucuronopyranose)[2,3 - b][2'3' - k] - 14,7,10,13,16 - hexaoxacyclooctadecane (**11**)*

Compound **1** (0.5 g) was dissolved in $CH_3CN$ (15 mL), and $KMnO_4$ (0.3 g) was added. The mixture was stirred for 9 h, and after the introduction of an additional amount of $KMnO_4$, (0.3 g) for a further 9 h. The reaction mixture was processed by the method described for **5**. White, amorphous **11** was obtained with a yield of 0.42 g (80%). $[\alpha]_D^{22} = +92.3$ ($c = 1$, water). IR: 3380–3300, 2850, 1740, 1430, 1385, 1170–1010, 750 $cm^{-1}$. $^1$H-NMR ($D_2O$): 3.40 (s, 6H, 2 × $OCH_3$), 3.30–4.48 (m, 28H, $CH_2$ and CH protons), 4.99 (d, 2H, $J = 5.1$ Hz, anomeric H). *Elemental anal.: calc.* for $C_{22}H_{36}O_{16}$; C 47.48, H 6.47. *Found:* C 47.29, H 6.39.

Alkali consumption in titration: 35.9 ml of 0.1 N NaOH/g of product (as expected).

*Bis(methyl - 2,3 - dideoxy - α - D - methylglucuronopyranose)[2,3 - b][2'3' - k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**12**)*

A procedure similar to the preparation of **6** was applied. A yellow syrup of **12** was obtained with a yield of 77%. $[\alpha]_D^{22} = +48.8$ ($c = 1.2$, $CHCl_3$). $^1$H-NMR: 3.38 (s, 6H, 2 × $COOCH_3$), 3.44 (s, 6H, 2 × $OCH_3$), 3.35–4.56 (m, 26H, $CH_2$ and CH protons), 4.81 (d, 2H, $J = 3.5$ Hz, anomeric H). *Elemental anal.: calc.* for $C_{24}H_{40}O_{16}$; C49.31, H6.84. *Found:* C 49.12, H 6.70.

*Bis(methyl - 2,3 - dideoxy - 4 - O - acetyl - α - D - glucuronopyranose)[2,3 - b][2'3' - k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**13**)*

A procedure similar to the preparation of **8** was applied. An amorphous yellow product of **13** was obtained with a yield of 33%. $[\alpha]_D^{22} = +82.7$ ($c = 1$, $CHCl_3$). $^1$H-NMR: 2.0 (s, 6H, 2 × OAc), 3.35 (s, 6H, 2 × $OCH_3$), 3.30–4.35 (m, 26H, $CH_2$ and CH protons), 4.75 (d, 2H, $J = 3.5$ Hz, anomeric H). IR: 3380–3300, 2850, 1740, 1430, 1360, 1230, 1175–1020, 755 $cm^{-1}$. *Elemental anal.: calc.* for $C_{26}H_{40}O_{18}$; C 48.77, H 6.25. *Found:* C 48.62, H 6.29.

*Bis(methyl - 2,3 - dideoxy - 4 - O - benzyl - α - D - glucuronopyranose)[2,3 - b][2'3' - k] - 1,4,7,10,13,16 - hexaoxacyclooctadecane (**14**)*

A procedure similar to the preparation of **10** was applied. Compound **14** was obtained as an amorphous solid with a yield of 68.3%. $[\alpha]_D^{22} = +90.0$ ($c = 1$, $CHCl_3$). $^1$H-NMR: 3.40 (s, 6H, 2 × $OCH_3$), 3.48–4.10 (m, 24H, $CH_2$ and CH protons), 4.47 (s, 4H, 2 × $CH_2Ph$), 4.81 (d, 2H, $J = 3.5$ Hz, anomeric H), 7.28 (s,

10H, 2 × Ph), 9.23 (s, 2H, 2 × COOH). *Elemental anal.: calc.* for $C_{36}H_{48}O_{16}$; C 58.69, H 6.52. *Found:* C 58.47, H 6.50.

The association constants of the compounds with Li, Na, K and ammonium picrates were measured in $CHCl_3$, by UV spectrometry, using the method of Cram [25]. Most of the crown ethers were insoluble in water: solubilities were 1–2% of the total used. The distribution constants of the water-soluble crown acids between water and $CHCl_3$ were determined in independent experiments and these constants were taken into consideration in the calculations of $K_a$ values.

Transport experiments were carried out in a conventional cell apparatus [9] consisting of an outer cylindrical glass vessel (46 mm i.d.) and a central glass tube (24 mm i.d.). The 0.01 M $CHCl_3$ solution (30 mL) of the host separated the inner aqueous phase (0.1 M HCl or NaOH, 8 mL) and the outer aqueous phase (0.08 M HCl, 15 mL) which contained $LiPF_6$ (0.4 M) and the racemic guest (0.08 M). The organic layer was stirred at a constant speed (60 r.p.m.), and transport was followed by monitoring the absorbance at 262 nm.

A 10% error was estimated in the transport experiments. The optical purity in the receiving phase was determined polarimetrically. The distribution of the water (NaOH) soluble crown acids between the water phase (NaOH) and $CHCl_3$ was determined polarimetrically.

## 3. Results and Discussion

### 3.1. SYNTHESIS

Tetrahydroxy crown ether **1** appeared to be suitable for the preparation of carboxylic acids by the oxidation of their hydroxymethyl groups. As oxidant, $KMnO_4$ was chosen since this reagent provides a mild oxidation condition in both neutral and alkaline media. The oxidation of **1** could be expected to yield two products: monocarboxylic acid **5** and dicarboxylic acid **11**. Pure monocarboxylic acid could not be prepared in water, acetonitrile etc., since under widely varying reaction conditions mixtures containing the starting substance or dicarboxylic acid were obtained. (The primary analysis of reaction products was performed by TLC and alkaline titration.) However, a uniform product could be obtained in the presence of dry $CHCl_3$ or $CH_2Cl_2$ as solvent, in solid–liquid phase transfer reaction.

This form of the reaction was interesting because only the starting crown ether could be dissolved in these solvents while $KMnO_4$ was insoluble, but the latter could be solubilised by the effect of the crown ether. Therefore, in this reaction, the crown ether was not only a substrate but a catalyst as well. We assumed that in dilute solution the primary product of oxidation is the potassium salt of the monocarboxylic acid, which is poorly soluble in $CHCl_3$ or $CH_2Cl_2$, and thus precipitates during the reaction. This led us to find the reaction conditions under which the main product is the monocarboxylic acid, **5**. In $CH_2Cl_2$ (with a substrate: $KMnO_4$ ratio of 1 : 1.5) a monocarboxylic acid yield of 87% was obtained after 5 h

of stirring and refluxing, whereas in $CHCl_3$ the yield was 68% after 18 h of stirring at room temperature. At the end of processing the reaction product, the free acid was released from the potassium salt by means of a cation exchange resin.

The synthesis of dicarboxylic acid **11** was easier to perform: crown ether **1** was treated with an excess of $KMnO_4$ (6.7 mole equivalents in water, 2.8 in acetonitrile) at room temperature for 18 to 20 h, to yield 80–84% of bis-glucuronic acid. Both products (**5** and **11**) could be titrated with 0.1 NaOH standard solution in the presence of phenolphthalein indicator, and an equivalent amount of alkali solution (18.4 mL/g and 35.9 mL/g, respectively) was consumed. In the $^1$H-NMR spectrum the signal of acidic protons could not be assigned. In the IR spectra the carboxylic groups produced strong bands in the 1740–1745 $cm^{-1}$ region. As a further confirmation of the structure, the reaction of monocarboxylic acid **5** with diazomethane (in ethanol–ether mixture) yielded monoester **6**, whereas that of **11** under similar conditions led to dimethyl ester **12**.

Uronic acid crown ethers **5** and **11** dissolve well in water, but are poorly soluble in chloroform (in fact, **11** is insoluble, and thus its complex forming properties could not be determined in chloroform). From the aspects of further investigations it appeared to be useful to convert **5** and **11** chemically into more lipophilic forms and to prepare derivatives that are soluble in chloroform.

Monocarboxylic acid **5** could not be acetylated either in acetic anhydride-pyridine or with acetic anhydride in the presence of $ZnCl_2$ catalyst. The desired result was obtained, however, by acetylating the potassium salt **7** of the monocarboxylic acid with acetic anhydride in pyridine (16 h, 90 °C) and liberating the acid on a cation exchange resin after processing the reaction product. Triacetate **8** was obtained with a yield of 61%, and, as expected, the product was soluble in chloroform.

Diacetate derivative **13** was obtained in a similar manner with a yield of 33% by acetylating the potassium salt of dicarboxylic acid **11**.

The tributyl ether of **5** was prepared in THF with an excess of butyl bromide in the presence of 50% sodium hydroxide solution. In the two-phase system the crown ether substrate itself played the role of phase transfer catalyst. The syrupy tributyl ether derivative **9** was obtained with a yield of 73% after 50 h stirring at 40 °C.

In certain cases a reverse order of synthesis proved to be more successful, according to which the substituent is built into the molecule first and then the product is oxidised into the corresponding uronic acid derivative. The previously described [22] 4,4′-di-*O*-benzyl crown ether **4** appeared to be suitable for the preparation of lipophilic crown-carboxylic acid derivatives that dissolve well in organic solvents, via the oxidation of its hydroxymethyl groups. Benzylated monocarboxylic acid **10** could be prepared with a yield of 65% in dry chloroform with 1.43 mole equivalents of $KMnO_4$ (25 h, room temperature), whereas the dicarboxylic acid derivative **14** was prepared in acetonitrile with a large excess of $KMnO_4$ (by refluxing for 18 h) with a yield of 83%. The products were not crystalline (syrup), and well soluble,

Table I. Association constants of chiral crown compounds (log $K_a$ in $CHCl_3$, at 22 °C).

| | 1[a] | 2[a] | 3[b] | 4[b] | 5 | 8 | 9 | 10 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $Li^+$ | 4.04 | 3.57 | 4.25 | 3.57 | 4.39 | 4.11 | 4.30 | 5.25 | 4.15 | 4.23 | 5.04 |
| $Na^+$ | 4.50 | 3.20 | 4.33 | 4.20 | 5.50 | 5.13 | 4.57 | 5.97 | 5.15 | 4.74 | 5.45 |
| $K^+$ | 4.85 | 4.46 | 4.38 | 4.70 | 5.37 | 4.83 | 4.48 | 5.62 | 4.97 | 4.60 | 5.17 |
| $NH_4^+$ | 4.01 | 3.58 | 3.82 | 4.34 | 5.19 | 4.54 | 4.00 | 5.44 | 4.87 | 4.26 | 4.89 |

Aqueous phase (0.5 mL); [picrate] = 0.15 M; organic phase ($CHCl_3$, 0.2 mL); [crown ether] = 0.075 M; determination by UV spectroscopy: Ref. [25].
Error limit: ±0.03; the results are the average of triplet runs.
[a] Ref. [17]; [b] Ref. [22].

as expected, in chloroform and insoluble in water. The signals of the acidic protons in the $^1$H-NMR spectra of both compounds appeared at $\delta$ 9.94 ppm.

### 3.2. COMPLEX FORMATION

The association constants ($K_a$) of glucuronic acid crown ethers obtained by oxidation were determined by the method of Cram [25] in chloroform, at room temperature, applying Li, Na, K and ammonium picrates as guest molecules. Table I shows the log $K_a$ values of the above molecules together with those of starting substances **1** and **4** and of tetrasubstituted derivatives **2** and **3**, taken for comparison [17, 22, 23].

On comparing the $K_a$ values of starting substance **1** and monocarboxylic acid **5**, it can be seen that the introduction of a carboxy group into the molecule increases the complex formation ability with respect to all cations, to the greatest extent with $NH_4^+$ and $Na^+$. A similar tendency can be observed from a comparison of tetraacetate **2** and triacetate monocarboxylic acid derivative **8**: the complex formation constant with respect to $Na^+$ has increased by nearly two orders. On the other hand, the $K_a$ values of dicarboxylic acid diacetate **13** are lower than those of monocarboxylic acid **8**.

The dimethyl ester **12** and triacetate monocarboxylic acid derivative **8** show practically identical complexing properties with the small $Li^+$ and $Na^+$ ions, but the values of **12** are higher with $K^+$ and $NH_4^+$ having a larger ionic diameter.

An increase of 1 to 1.8 orders in the association constants can be observed with dibenzyl derivative **4** on the introduction of one carboxy group (**10**), but a decrease on the introduction of a second carboxy group (**14**) with respect to **10**. Note that with butyl substituted crown ether **3** the $K_a$ values hardly increase on the introduction of a carboxy group (**9**).

As expected, the introduction of carboxy groups enhances the complex formation abilities of crown ethers in all cases with respect to all ions investigated. Lehn *et al.* established that the carboxylate groups in the crown ether increase the complex stability with cations and especially when they are close to the ring. It may be due

in part to two effects: the ion-pair interaction and electrostatic interaction between the carboxylate groups and the cations. The selectivities of complexation display electrostatic and hydrophobic effects [24]. In our compounds the carboxylic groups are further from the crown ring, so the interactions are weaker but the effect of the lateral discrimination of side chain carboxylic groups are perceptible. The relatively more modest increase in the complex formation abilities of dicarboxylic acids (**13**, **14**) with respect to monoacids (**8**, **10**) may be due to a mutual (intermolecular) hydrogen bonding among the carboxy groups.

It is worth noting that oxidation also affects the selectivities of crown ethers: whereas derivatives **1–4** form the strongest complexes with K ions (the ionic diameter of $K^+$ corresponds to the inner dimensions of the 18-crown-6 ring) the oxidised derivatives prefer Na ion complex formation. Generally for our uronic crowns the selectivity sequence is $Na^+ > K^+ > NH_4^+ > Li^+$.

### 3.3. CHIRAL RECOGNITION

Chiral recognition of crown ether derivatives can be investigated in the transport processes of racemic ammonium hydrochlorides through liquid membranes [9, 26]. In this work the transport of racemic phenylethylamine hydrochloride and phenylglycine methyl ester hydrochloride through chloroform membrane was measured by using the carboxy derivatives in question. Measurements were performed in a coaxial cylinder cell apparatus with the method of Cram [9].

These measurements are generally carried out in acidic media. Our transport experiments were performed also in acidic conditions using aqueous HCl as a receiving phase. In these cases the compounds **8**, **9**, **10**, **13** and **14** remained completely in the $CHCl_3$ phase and so they did not disturb the UV determination of the transported amine salts. One of the aims of our synthetic work was to increase the lipophilicity of the crown acids by alkylation, acylation and aralkylation of the free hydroxyl groups, hoping that they remain in the organic phase. This was successful in the case of aqueous HCl receiving phase. These compounds were able to carry the above ammonium salts from the source phase to the aqueous acidic phase through the $CHCl_3$ membrane. Unfortunately, chiral recognition could not be observed: the receiving phase always contained a racemic mixture.

The methyl phenylglycinate salt was found to be better transported than the phenylethylamine salt by all crown acids. Good transporting abilities were found for these crown compounds. The percentage of the amine transported into the receiving phase related to the original source phase for methyl (±)-phenylglycinate * HCl (determined by UV) after 5 h, are: **8** (23.2%), **9** (19.6%), **10** (28.8%), **13** (22.5%) and **14** (22.0%).

The transporting capacities of crown ethers appear to be approximately proportional to their complex formation abilities; the greatest amounts of amine were transported by dibenzyl monocarboxylic acid derivative **10**, which forms the strongest complex with the ammonium ion. However, the crown carboxylic

acids with lipophilic groups allow acid-to-alkali transport (against pH) to occur, which may often be more selective [9]. Unfortunately the results of the transport experiments in the $CHCl_3$–aqeuous NaOH (receiving phase) system were not appreciable because of the solubility of the crown acids in aqueous NaOH.

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