Complexes between Disubstituted Benzo-15-Crown-5 Ligands and Sodium or Potassium Bromides[#]

MARTIN P. PAYNE and MARY R. TRUTER*
*Molecular Structures Department, Rothamstead Experimental Station, Harpenden, Herts.,
AL5 2JQ and Chemistry Department,* University College, 20 Gordon Street,
London, WC1H OAJ, U.K.

Abstract. Stability constants have been determined with ion selective electrodes for complexes between sodium or potassium bromide in methanol with each of four crown ethers, benzo-15-crown-5 (**Ia**), dibromobenzo-15-crown-5 (**Ib**), dimethoxybenzo-15-crown-5 (**Ic**) and di-*n*-butoxybenzo-15-crown-5 (**Id**). Those for (**Ib**) were significantly lower than the others. The stability constants for complexes between sodium bromide and (**Ia**) and (**Ib**) in dimethylformamide (DMF) were found to be about one fifth of the corresponding values in methanol. The conductivity method was used to measure the ion pairing in methanol of sodium bromide alone and in the presence of (**Ia**), (**Ib**), or (**Ic**). Ion pairing is increased on complexation, the association constants being $3.3 \, \text{mol}^{-1} \, \text{dm}^3$ for $Na^+ \, Br^-$ and $20\text{–}23 \, \text{mol}^{-1} \, \text{dm}^3$ for $Na(\textbf{Ia–c})^+ \, Br^-$. The syntheses of compounds (**Ic**) and (**Id**) are described.

Key words. Crown ethers, stability constants, ion pairing.

1. Retrospect

[#] This paper is dedicated to the memory of the late Dr C. J. Pedersen.
* Author and address for correspondence.

Obituary: Charles Pedersen

Nobel prize for a crowning achievement in chemistry

CHARLES. J. Pedersen, who has died in New Jersey at the age of 85, was awarded a Nobel Prize for Chemistry in 1987; the twenty-year delay between his first seminal publications and the award is an indication of the time required for something really new to be appreciated.

His father was Norwegian, his mother Japanese, and he was born in Korea. He studied chemistry in the University of Dayton, Ohio and at M.I.T., and he then joined du Pont at Wilmington, Delaware. He stayed there, becoming an American citizen in 1953, until his retirement in 1969. His status there from 1946 was that of research associate, a position of prestige which allowed him to do research free from managerial responsibility.

In 1961, after successful work in other fields, Pedersen started on the project which was to lead to his Nobel Prize. But his discoveries were entirely different from the intended objective. He set out to make compounds containing vanadium to act as catalysts for polymerization. He actually found, by mid-1962, that he had made a new kind of neutral organic compound capable of forming complexes with inorganic salts, such as sodium chloride, and extracting them into organic solvents.

During the next five years he worked with ever-increasing excitement and made sixty of these new compounds. He called them "crowns" because the systematic chemical names are very cumbersome and because with them the positive ions in the salts "could be crowned and uncrowned without physical damage to either, just like the heads of royalty". The surrounding of the positive ion by the organic crown molecule conferred new properties on it and also left the negative ion more reactive. Not all of the crowns were effective complexing agents. This allowed Pedersen to deduce the factors that were important, one of which was that the crown must be the correct size to encircle the ion. He found similar interactions (that is, without the formation or breaking of chemical bonds) to be possible between crowns and many metal salts and ammonium salts and also small organic molecules.

While individuals of vision in du Pont allowed him to continue his "blue skies" research, they did not allow it to be made public until 1967. Then he gave a talk at a meeting in Japan and as sole author he published one short and one full paper in the Journal of the American Chemical Society. The full paper described 49 new compounds which are difficult to make, and their interactions with various salts.

In all he published fewer than ten papers on crowns but these papers show amazing insights into future developments. The significance of his work was first realised only by a few people with prepared minds, notably biophysicists who were studying the transport of ions through biological membranes.

After his 1967 talk in Japan only two people came up to speak to him, one from a local pharmaceutical firm and the late Sir Ronald Nyholm, head of the chemistry department at University College, London. The latter was honorary director of the recently formed Agricultural Research Council's Unit of Structural Chemistry where the fundamental chemistry behind such "transport" was being investigated.

He invited Pedersen to work in the Unit for three months in 1969 and also arranged for samples of Pedersen's compounds to be studied by X-ray crystallography in the Unit. Results of the X-ray "pictures" showed that Pedersen's ideas about the crown sitting round the spherical positive ion were correct and also, that the uncomplexed crown molecule was a different shape in the absence of the ion so that the fit was more like that of a hood than of a rigid crown.

Two of the chemists who were among the first to appreciate Pedersen's work shared the Nobel Prize with him: Professors J-M Lehn of Strasbourg and D.J.Cram in California. They had in common that each led a large team, published several hundred papers and acknowledged a debt to Pedersen. They provided different, and brilliant, contributions to the field variously described as "molecular recognition" and "host-guest" chemistry. This — the ability deliberately to synthesise a larger host molecule to enclose selectively a chosen smaller guest — gives a new measure of control in a range of applications from pharmaceuticals to catalysts.

Charlie Pedersen was a most delightful person, very modest and extremely kind and helpful to young people. He liked to work at the bench himself, always wearing his black beret, and chose not to have assistants. He was a keen fisherman and gardener with a happy home life. He and his wife, Sue, greatly enjoyed their stay in London, partly because they felt it was safe to walk about at night.

His later years were saddened by her death in 1983 and his own increasing physical disablement. By the time his belated award of the Nobel Prize arrived he was so frail that he was able to go to Stockholm only because du Pont provided a private aeroplane for him. But his physical disabilities did not affect his brain or personality. In a letter to me, dictated eight days before he died, he said, "Have you been doing any new work in crystallography? Please keep me informed!"

Mary R. Truter

Charles John Pedersen, born Pusan, March 19, 1904; died Salem, New Jersey, October 26, 1989.

2. Introduction

There is a delicate balance between ion-pairing, solvation and complex formation in the isolation of crystalline derivatives of alkali metal salts and crown ethers. Pedersen's [1] original samples were dried before being analysed or having their infrared spectra recorded. He was intrigued to learn that some of his crystalline complexes had been shown by crystal structure analysis to contain water, e.g. the complex between sodium iodide and benzo-15-crown-5, (**Ia**) [2]. After his retirement he worked for three months in the Agricultural Research Council Unit of Structural Chemistry (University College London). There, he ran his own infrared

spectra, modestly refuting a suggestion that this was a waste of his talent by saying "I see things when I do it myself."

Sodium bromide reacts with (**Ia**) to give a hydrated complex isomorphous with the iodide [3] i.e. containing $(NaH_2O(\mathbf{Ia}))^+$ whereas with the dimethoxy derivative (**Ic**) it gives an unsolvated complexed ion pair, (NaBr(**Ic**)) with an Na—Br bond length of 2.763(3) Å. We wondered if there might be a detectable difference in ion pairing in solution. We tried field desorption mass spectrometry [4]. From acetone solution the molecular ions $(Na\mathbf{Ia})^+$ and $(Na(\mathbf{Ic}))^+$ were obtained but not $(NaH_2O(\mathbf{Ia}))^+$ or $(NaBr(\mathbf{Ic}))^+$; however, the complex (NaBr(**Ic**)) gave Na_2Br^+ which might prove diagnostic for ion pairing.
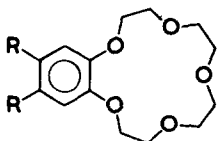
R = H   **Ia**
R = Br   **Ib**
R = OCH₃   **Ic**
R = OC₄H₉ **Id**

We now report investigations of solutions of sodium bromide or potassium bromide with benzo-15-crown-5 and three disubstituted compounds, (**Ib**), (**Ic**), and (**Id**). Stability constants were measured with ion selective electrodes in a system described previously [5]; our experiments using constant ionic strength conditions and earlier ones with tert-butylammonium bromide as an inert medium [6] had shown that it was reasonable to approximate ionic activities to concentrations so the stability constants are defined as:

$$K_1 = c(ML^+)/c(M^+) \cdot c(L) \tag{1}$$

$$K_2 = c(ML_2^+)/c(ML^+) \cdot c(L) \tag{2}$$

If ion pairing can be assumed to be negligible, e.g. for sodium tetraphenylborate, changes in conductivity may be used to determine stability constants. This technique was used by Smid and coworkers [7] to study complexes of benzo-15-crown-5 and its monosubstituted derivatives in acetone. In the present work we have used changes in conductivity to study ion pairing of $Na^+ Br^-$ or NaL^+Br^- and complex dissociation is an important complication. If K_1 is about 10^3 the complex will be dissociated to the extent of 30% at 10 mM and 60% at 1 mM. To reduce dissociation to less than 5% a 15–20 mM excess of ligand had to be used in conductivity experiments which were designed to determine the association constant of ion pairing defined as

$$K_A = c(MX)f_{mx}/c(M^+) \cdot c(X^-)f_m^+ \cdot f_x^- \tag{3}$$

$$= xf_{mx}/((1-x)^2 \cdot f_m^+ \cdot f_x^-) \tag{4}$$

Where c is the concentration, f_i are the activity coefficients and x is the fraction of ion associated.

3. Experimental

3.1. MATERIALS

Sodium bromide and potassium bromide were of A.R. quality (Aldrich), dried in a vacuum at 150°C for 2–3 h and stored in a desiccator.

For potentiometry, reagent grade DMF (Lancaster Synthesis) was purified by distillation at reduced pressure under a nitrogen atmosphere and A.R. grade methanol (Fisons) was used without further purification. For conductivity measurements fresh A.R. methanol (Fisons) was deionized by running through a 1 : 1 mixture of freshly activated cationic (IR 120) and anionic (IR A400) ion-exchange resins and stored in specially cleaned Pyrex distillation flasks. The specific conductivity of the deionized methanol was in the range $0.6–2.0 \times 10^{-6}$ ohm^{-1} cm^{-1}. The cleaning procedure consisted of coating the surfaces with freshly prepared chromic acid ($K_2Cr_2O_7$–60%H_2SO_4) for 30 min–1 h, followed by rinsing many times with distilled water, A.R. methanol and deionized methanol in that order until a negligible increase in the conductivity of the deionized methanol was observed. All glassware used in the titration, including the conductivity cell, was cleaned in a similar manner.

Benzo-15-crown-5(**Ia**),   4,5-dimethoxybenzo-15-crown-5   (**Ic**)   and   4,5-dibromobenzo-15-crown-5 (**Ib**) had been prepared by D. G. Parsons [8]. Benzo-15-crown-5 was formed by standard routes, for example coupling of the α,β-ditosylate of 1,11-dihydoxy-3,6,9-trioxyundecane with catechol, and the 4,5-dibromo derivative by the direct bromination of the unsubstituted crown. A similar synthesis of the dibromo compound has recently been published by other workers [9]. It was necessary to synthesize (**1c**) and dibutoxybenzo-15-crown-5 (**Id**) for the present work, success being achieved after considerable adaption from Ref. [8]. Details are given below.

3.2. SYNTHESIS OF DIMETHOXYBENZO-15-CROWN-5 Ic

There are four principal reaction steps, summarized in Scheme 1. Steps (i) and (ii) are based on the work of Dallacker and Lohnert [10] with minor modifications to reduce side-reactions. In step (i) the catechol in methanol was added over a period of about 2 hours, with vigorous stirring to keep the temperature below 20°C. Step (ii) was carried out under nitrogen to prevent aerial oxidation of the product.

(iii) 51.5 g, 1,11-dihydroxy-3,6,9-trioxyundecane (Aldrich) was dissolved in *ca.* 160 mL pyridine and *ca.* 130 g p-toluenesulphonyl chloride added with shaking over a period of 40 min and left at 0–5° for 3 h. The precipitated pyridinium hydrochloride was dissolved by stirring with 400 mL water and the pale yellow viscous oil which separated collected and washed with water (4 × 150 mL) and dried by addition of a little toluene and its subsequent removal as a toluene–water azeotrope under reduced pressure in a rotary evaporator. In the I.R. spectrum the strong doublet at 1190 cm^{-1} and 1175 cm^{-1} characteristic of p-toluenesulphonates and only a very weak OH stretch in the 3000–3500 cm^{-1} indicated the reaction to be practically complete. The yield of dried tosylate was approx. 50 g (38%).
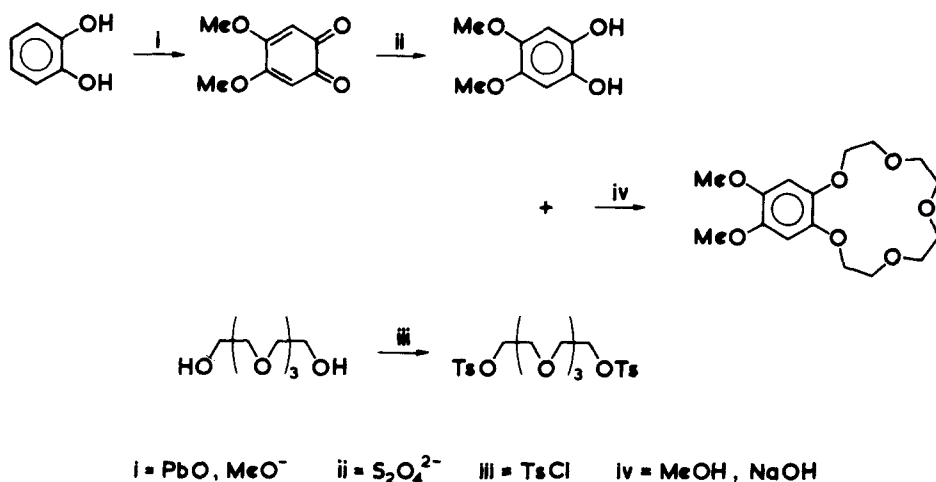
Scheme 1

(iv) A solution of 4,5-dimethoxycatechol (7.0 g, 0.0412 moles) in methanol (200 mL) was brought to reflux under a N_2 atmosphere, and 1,11-ditosyloxy-3,6,9-trioxaundecane (24.8 g, 0.0493 moles) added in one batch, and the mixture treated with sodium hydroxide pellets (4.9 g). Reaction occurred rapidly and the solution became dark green in colour. The addition of 10–20 mg sodium borohydride to prevent oxidation of the catechol resulted in the solution becoming pale orange-brown and it remained in this state throughout the refluxing period of $3\frac{1}{2}$ h.

The solution was allowed to cool to room temperature under the nitrogen atmosphere and a further 10 mg of sodium borohydride added to lessen the extent of oxidation during the subsequent workup. 20 mL aqueous 2M hydrochloric acid was added to neutralize the excess sodium hydroxide and the solution concentrated to ca. 50 mL by evaporation of solvent at reduced pressure, a solid (sodium tosylate) separated out. 200 mL H_2O was added and the solution extracted with CH_2Cl_2 (3 × 100 mL) and combined organic extracts washed with water (3 × 125 mL). Removal of the solvent under reduced pressure gave about 15 g of an oil dried by azeotropic distillation of added toluene (2 × 50 mL). This product was dissolved in ethyl acetate (40 mL) and a solution of lithium perchlorate (4 g) in ethanol (40 mL) added. On cooling to 0–5°C a fine white crystalline solid separated out, filtration, followed by drying using suction on a glass sinter gave 7.9 g of product.

To recover the free crown, 7.8 g lithium perchlorate complex were dissolved in 50 mL water and the solution extracted with dichloromethane (3 × 50 mL), the combined organic extract was washed with water (4 × 50 mL). The aqueous washings were extracted with CH_2Cl_2 (2 × 50 mL) and the combined organic extracts evaporated to dryness, producing a buff coloured oil which on cooling and seeding with a few crystals of the previously prepared crown crystallized to give 4.8 g of a buff coloured solid.

A 85% petroleum ether (b.p. 80–100°), 15% ethyl acetate mixture proved suitable for recrystallization giving 2.0 g of creamy white crystals, m.p. 80–81°C, *found*: C 58.48, H 7.45% *calc*. for $C_{16}H_{24}O_7$, C 58.52, H 7.37%. The IR spectrum of this product was identical with that of the sample used to make the 4,5-dimethoxybenzo-15-crown-5 sodium bromide complex [3]. The IR active C—O—C stretching bands give rise to strong bands at 1220, 1200 and 1140 cm^{-1}. The ^1H NMR spectrum in $CDCl_3$ showed multiplets due to methylene resonances at 4.14(4H), 3.92(4H) and 3.75(8H) ppm in addition to a singlet due to aromatic protons at 6.60 ppm and the methoxy methyl groups at 3.83 ppm, fully consistent with the above formulation.

3.3. SYNTHESIS OF 4,5-DIBUTOXYBENZO-15-CROWN-5 (Id)

Our first attempts to make 4,5-dimethoxybenzo-15-crown-5 were modelled on the conditions employed for the original synthesis of benzo-15-crown-5 itself (Pedersen [1]), coupling of 1,11-dichloro-3,6,9-trioxaundecane in *n*-butanol with 4,5-dimethoxycatechol. This method, however, resulted in exchange of aromatic ring substituent methoxy groups with butoxy groups to give 4,5-dibutoxybenzo-15-crown-5, as shown in Scheme 2. The mechanism probably involves oxidation to the quinone followed by nucleophilic attack by the butanol oxygen with simultaneous or subsequent elimination of methoxy groups.

(iii') 1,11-dichloro-3,6,9-trioxyundecane was prepared by the chlorination of the dihydroxy compound with purified thionyl chloride using pyridine to remove the HCl produced. After work up the product was purified by extraction with benzene and vacuum distillation b.p. 130–135°C, 0.2 mm Hg.

(iv') This dichloro compound and 4,5-dimethoxycatechol were dissolved in equimolar proportions (38 g and 28 g respectively) in 400 mL *n*-BuOH. The mixture was heated to reflux (110°C) and 10% excess of KOH added. The reaction mixture turned dark brown in colour. After 3 h gently refluxing, a small sample was
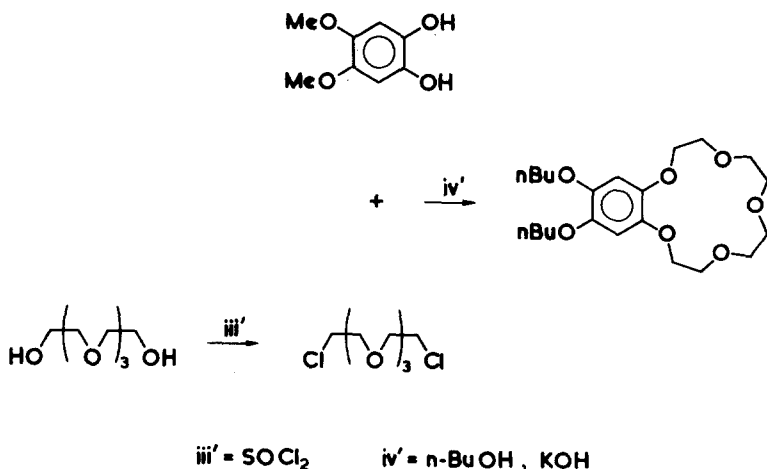
Scheme 2

worked up as described below, and an IR spectrum run on the resulting dark brown oil. The absence of bands at 660 cm^{-1} and 740 cm^{-1} due to C—Cl stretch indicated that all the dichloro compound had reacted. On cooling the reaction mixture was extracted with chloroform (3 × 150 mL), washed with water (3 × 100 mL), dried with anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure giving approx. 40 g of a dark brown oil. In an attempt to remove some highly oxidized dark materials, the oil was dissolved in ethyl acetate and passed through a layer of alumina on a Grade 2 glass sinter funnel. Only a small proportion of the dark material was retained by the alumina. The ethyl acetate solution was evaporated to dryness, the brown oil redissolved in *ca.* 100 mL methanol and the solution left overnight at 0–5° in a refrigerator. Successively over a few days two white solids separated, the first melting sharply at 132–134°C. and the second over the range 106°–116°C. Neither could be identified from their IR and NMR spectra. The filtrate was evaporated to dryness and the resulting dark brown viscous oil (35–40 g) was distilled under reduced pressure. The main product was obtained at 210–240°C and redistilled, the fraction b.p. 210–240°C (0.2 mm Hg) was collected. Its ^{1}H NMR spectrum was consistent with 4,5-di-*n*-butoxybenzo-15-crown-5 as the major product. In CDCl$_3$: $\delta 0.96(t)$, 1.48(m), 1.73(m), 3.88(m), 3.93(t), 4.10(m), 6.57(s) ppm. Recrystallization of *ca.* 5.2 g of this crude product in 40 mL petrol (b.p. 80–100°) gave 1.1 g of almost colourless (very pale creamy yellow-brown) crystals, m.p. 44–47°C.

3.4. MEASUREMENTS OF STABILITY CONSTANTS

Stability constants were measured by potentiometry using the apparatus and methods described previously [5]. The titration vessel was kept at 25.0 ± 0.2°C, the ion selective electrodes were ORION for sodium and Electronic Instruments Ltd for potassium cations. The reference electrode was an Ag/AgCl type filled with a solution of the alkali metal chloride in the current solvent. Before use in methanol or DMF the electrodes were immersed in *ca.* 10 mM solutions of NaBr or KBr in the solvent for at least 48 h then rinsed with the solvent.

The electrodes were calibrated with solutions of known concentration. Decade shifts in methanol were close to 59.2 mV as predicted for Nernstian response; they were checked before each tritration and the actual values used. For DMF, the anomalously high value of 65 ± 1 mV was found, for two titrations for each of Na$^+$, K$^+$, Rb$^+$ and Cs$^+$.

For methanol, titrations were carried out with salt solution (1–5 mM) in the 'pot' and 25 to 30 aliquots of crown solution were added the e.m.f. being measured when it had steadied after each addition. The titrations were repeated several times with different concentrations of solutions. For DMF, the solid addition method was used; it required 250 mg of benzo-15-crown-5 (**Ia**) to produce a change of 24 mV.

3.5. CONDUCTIVITY MEASUREMENTS

Electrical conductances were measured using a WPA CMD 400 digital conductance meter. The conductance cell was of traditional design, made of Pyrex glass with brightly platinized electrodes.

The extent of ion-pairing of simple 1 : 1 salts with single charged ions in methanol is small at the millimolar concentration level, requiring an accuracy of better than *ca.* 1% for a reliable comparison of association constants.

The conductivity cell was in a water bath thermostatically regulated to *ca.* 0.2° between 24.5 and 25.5°C. The cell was fitted with a cork top with two bored holes into which the tapered tip of the precision burette (10 mL, 0.005 mL graduations, Pyrex Grade A) and a soft glass air leak were inserted. The air leak was made with the narrowest possible capillary consistent with a reasonable rate of delivery of titrant (*ca.* 1–2 mL/minute). The temperature of the water bath was recorded using a thermometer accurate to 0.1°.

In the titrations *ca.* 10 mM NaBr in 20 mM crown solution was employed as titrant and *ca.* 20 mM crown solution as titrand. The former was generally made up from *ca.* 10 mM salt solution and a known mass of crown. The crown compounds despite recrystallization were slightly contaminated with salt producing a small but significant contribution (*ca.* 5×10^6 ohm^{-1}) to the conductance throughout the titration. Correction for this 'background' was carried out by subtraction of the initial conductance of titrand from the subsequent values. To allow the accurate determination of initial titrand volumes and estimates of evaporation losses from weighings the densities of both solutions were determined using a pyknometer previously calibrated with distilled water.

At the beginning of each titration the conductance cell was weighed in air and filled to a volume of *ca.* 7.5–8.0 mL with titrand and re-weighed allowing the initial volume to be precisely determined. The initial volume employed was *ca.* 50% greater than that required to submerge the electrodes completely.

The cell was left in the water bath for 30 min–1 h for thermal equilibrium to be established, the conductivity was recorded and the first addition of titrant (0.1–0.5 mL) made. The cell was gently agitated in the bath allowing mixing and thermal equilibrium to be established and the steady value of the conductivity obtained after 3–5 min recorded. The additions of titrant and conductivity readings were continued until the cell was nearly full and the concentration had risen to *ca.* 4 mM. Between twenty and thirty additions were made in total. The cell was then re-weighed allowing the volume of evaporation occurring over the course of the titration (DV) to be estimated by subtraction of the addition volume indicated from the readings of a calibrated burette. An approximate volume correction was applied on the assumption that the total volume of evaporation increased linearly with the volume of titrant added.

The effective cell constant was measured over a range of concentrations by means of a conductometric titration solution as titrant at *ca.* 25°C using a method essentially the same as the main experiment. The molar conductance of aqueous KCl at 25°C has been shown [11] to follow the equation:

$$\Lambda = 149.873 - 95.01c^{1/2} + 38.48c \log c + 183.1c - 176.4c^{3/2} \tag{5}$$

where c is the molality (mol/kg). Coefficients of this equation for conductivites at 18°, 10° and 0° were also given in the same paper.

Since the temperature of the bath could not be easily adjusted to exactly 25°C small corrections were required. An interpolation procedure was employed.

Since viscosity variation is the main source of the temperature dependence of conductivities the coefficients at the above four temperatures were fitted to simple functions of the viscosity. E.g.

$$\Lambda_o = 135.454\,(10^3\eta)^{-0.8708} \quad (R^2 = 0.9999988) \tag{6}$$

Viscosities were estimated from the empirical relation [12],

$$\log(\eta T/\eta 20°) = (1.3272(20-T) - (0.001053(T-20)^2/(T+105) \tag{}$$

with $\eta 20°(H_2O) = 1.002 \times 10^{-3}\,N\,s\,m^{-2}$. The error in the conductivity produced by this method is negligible compared with that resulting from the uncertainty in the temperature ($\pm 0.1°$).

3.6. ANALYSIS OF CONDUCTANCE DATA

The development of conductivity theory for electrolytes in solution has been reviewed extensively [e.g. 13, 14]. Although a wide variety of equations are available only the most theoretical treatments, requiring considerable computing power, yield reasonably consistent K_A values when association is small, e.g. in methanol or water. In view of this and the comparative nature of the present study, we have used the simpler and more convenient Shedlovksy analysis [15]. It is based on a modification of the 1933 Fuoss Equation [16], i.e.

$$\Lambda = y(\Lambda_0 - (A + B\Lambda_0)(yc)^{1/2}) \tag{7}$$

in which the second term in the fraction dissociated, $y = 1 - x$, is replaced by the experimental factor Λ/Λ_0:

$$\Lambda = y\Lambda_0 - (A + B\Lambda_0)\Lambda/\Lambda_0(yc)^{1/2} \tag{8}$$

A and B are functions of the solvent viscosity (η_0), dielectric constant (D) and temperature (T) ($A = 82.5/\eta_0(DT)^{1/2}$, $B = 8.204 \times 10^5/(DT)^{3/2}$ [17]. Rearrangement of (8) gives:

$$\Lambda = y\Lambda_0/(1 + (A + B\Lambda_0)(yc)^{1/2}/\Lambda_0) \tag{9}$$

Solution of the Shedlovsky equation proceeds as follows. Equation (9) is a quadratic in $y^{1/2}$, giving:

$$y = \Lambda/\Lambda_0(z/2 + (1 + (z/2)^2)^{1/2})^2 = S(z)\Lambda/\Lambda_0 \tag{10}$$

where $z = (A + B\Lambda_0)\,(\Lambda c)^{1/2}/\Lambda_0^{3/2}$. $1/S(z)$ is the fractional decrease in conductivity predicted due to ionic (asymmetry and electrophoretic) effects in the absence of association. Considering the ion-pair equilibrium:

$$M^+ + X^- \leftrightarrows MX$$
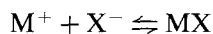
$$K_A = a(MX)/a(M^+)\cdot a(X^-) = (1 - y)\cdot f/f_\pm^2\cdot y^2\cdot c \tag{4}$$

where c = molar concentration of MX and f = activity coefficient. The mean ionic activity coefficients ($f_\pm$) were evaluated in the present work using the extended Debye–Hükel Equation [18].

$$\ln(f_\pm) = \alpha c^{1/2}/(1 + \beta Rc) \tag{11}$$

where

$$\alpha = e^3 (2.10^3 N_A)^{1/2} / (2.303.8\pi (\varepsilon_0 D K_b T)^{3/2}) \tag{12}$$

$$\beta = (2.10^3 N_A e^2 / \varepsilon_0 D K_b T)^{1/2} \tag{13}$$

and $R =$ the 'ion-size parameter'. Following the recommendations of Justice [19] we employ $R = q =$ the Bjerrum distance $(e^2/4\pi\varepsilon_0 D K_b$, 858 pm in methanol). Substitution of Equation (10) into (4) gives:

$$1/\Lambda S(z) = 1/\Lambda_0 + K_A \Lambda S(z)\, cf_{\pm}^2 / \Lambda_0^2 \tag{14}$$

A plot of $1/\Lambda S(z)$ vs. $\Lambda S(z) cf_{\pm}^2 / \Lambda_0^2$ gives an intercept $1/\Lambda_0$ and slope K_A. A first estimate of $\Lambda_0 = 100$ was employed for the initial evaluation of $S(z)$ and in the first Shedlovsky plot. From the latter a more accurate value of Λ_0 was obtained for use in subsequent iterations. Only four or five cycles of refinement were required for successive Λ_0 values to differ by less than 0.1%. The calculation was easily handled by a small computer or programmable calculator. For the present purposes a programm 'KIPFIT' was written [20] in BASIC for operation on a Tektronix 4051 including corrections for complex dissociation and viscosity changes described below.

3.6.1. Viscosity Corrections

Since conductance measurements on the complexes have been carried out in solutions approx. 20 mM in crown ligand the viscosity of the medium is significantly greater than that of the pure solvent and the conductances accordingly reduced.

The relative viscosity of electrolyte solutions as a function of concentration is given to a first approximation by the Jones–Dole equation [21]:

$$\eta/\eta_0^0 = 1 + A'c^{1/2} + B'c \tag{15}$$

Where $A' =$ Debye–Falkenhagen constant, an ion–ion interaction term expressible as a function of solvent properties, and $B' = $ a factor directly proportional to the molecular volume of the solute in solution.

Flow times in an Ostwald viscometer were measured for the pure solvent, 20 mM crown solutions and solutions 20 mM in crown and ca. 10 mM in salt. Determinations of the densities of these solutions using a pyknometer precalibrated with distilled water allowed the conversion of the kinematic viscosities thus derived into absolute viscosities. The results may be expressed by the following approximate relations in which the viscosity is assumed to be a linear function of total ligand and salt concentrations:

$$\eta/\eta_0 = 1 + 0.41[\mathbf{Ia}]_{TOT} + 0.69[NaBr]_{TOT} \tag{16}$$

$$\eta/\eta_0 = 1 + 0.70[\mathbf{Ic}]_{TOT} + 0.49[NaBr]_{TOT} \tag{17}$$

$$\eta/\eta_0 = 1 + 0.77[\mathbf{Ib}]_{TOT} + 0.98[NaBr]_{TOT} \tag{18}$$

The molar conductivities derived for each titration point were corrected for viscosity effects by applying Walden's rule [22].

$$\Lambda_2 = \Lambda_1 (\eta/\eta_0) \tag{19}$$

in conjunction with Equations (16)–(18).

3.6.2. Temperature Corrections

The temperature of the water bath was set as close as possible to 25°C. Small deviations (up to 0.3°) were observed. The factors A and B in Equation (8) were corrected for direct temperature dependence and for the effect of temperature on the viscosity and dielectric constant of methanol from the empirical relations [12]:

$$\eta T = \eta 25°C - 8.7 \times 10^{-3}(T\text{-}25) + 0.26 \times 10^{-3}(T\text{-}25)^2 \tag{20}$$

$$\log D_T = \log D_{25}^0 - 0.0026(T\text{-}25) \tag{21}$$

The effect of these corrections on derived association constants was very minor ($\ll 1K_A$ unit).

From expressions for the ionic mobility based on a spherical ion model the temperature dependence of Λ resides principally in the variation of the viscosity of the solvent. Thus:

$$\Lambda_0 \alpha \, 1/\eta_T$$

Use of this relation allowed approximate correction of derived Λ_0 values for the small temperature variations. Such corrections were in no case greater than 0.5% of the total conductivity.

3.6.3. Complex Dissociation Corrections

Further corrections to the conductivities were made to allow for complex dissociation by the calculation of the percentage dissociation and assuming additivity of the conductivities of free and complexed ions. Stability constants for each complex are in Table I and the extent of dissociation (x') was estimated from the equation:

$$K_1 \approx c(ML^+)/c(M^+) \cdot c(L) = (1 - x')/x' \cdot (c°(L) - (1 - x')c°(M)) \tag{1'}$$

Table I. Mean stability constants from potentiometric titrations in methanol and DMF at $25.0 \pm 0.2°$.

Ligand	n	MX	$\log K_1$	$(\pm)$	n	MX	$\log K_1$	$(\pm)$	$\log K_2$	$(\pm)$
In MeOH		25–30 data points per titration								
Ia	3	NaBr	2.94	(1)	5	KBr	2.88	(4)	3.15	(4)
Ib	3	NaBr	2.32	(2)	3	KBr	2.39	(3)	3.01	(1)
Ic	6	NaBr	2.87	(3)	3	KBr	2.80	(2)	3.23	(2)
Id	3	NaBr	2.81	(3)	4	KBr	2.76	(9)	3.35	(2)
In DMF		15–20 data points per titration								
Ia	2	NaBr	1.38	(5)						
Ib	2	NaBr	0.82	(3)						

n number of titrations.
$(\pm)$ error in the least significant digit.

The superscript $°$ denotes total concentrations of crown and metal ions, free or complexed. Rearrangement and solution of the resulting quadratic in x' gives Equation (23):

$$x' = [- (K_1(c°(L) - c°(Na)) + 1) + (K_1(c°(L) - c°(Na)) + 1)^2$$
$$+ 4c°(Na) \cdot K_1)^{1/2}]/2 \cdot c°(Na) \cdot K_1 \tag{23}$$

Since to a very good approximation

$$\Lambda_2 = (1 - x')\Lambda NaL^+Br^- + x'\Lambda Na^+Br^- \tag{24}$$

$$\Lambda_3 = \Lambda NaL^+Br^- = (\Lambda_2 - x' \cdot \Lambda Na^+Br^-)/(1 - x') \tag{25}$$

where Λ_3 is now the molar conductivity corrected for both viscosity and complex dissociation effects. ΛNa^+Br^- was estimated from the Shedlovsky Equation (9).

4. Results

From the e.m.f. titrations the stability constants and mass balances were calculated with the program MINIQUAD 75 [23] modified by Dr. J. D. Owen to run interactively on a Prime 750 computer. Rapid convergence was obtained with the stoichiometries 1 : 1 for sodium complexes and 1 : 1 plus 1 : 2 for potassium complexes. Results are in Table I, the estimates of error are derived from the independent experiments not the standard deviations calculated by MINIQUAD for individual values.

As found previously [24] the initial addition of crown ether did not produce as great a change in e.m.f as that calculated from the overall stability constant. We think this may be a surface effect on the electrode.

The Shedlovsky plots of corrected Δ_3 vs. $c^{1/2}$ were linear over the concentration range 0.6 to 2.5 mM and gave the results in Table II. For Na^+Br^- the mean association constant is in good agreement with that $[K_A = 3.7 \text{ mol dm}^{-3}]$ calculated by our method from the conductivity measurements given by Jervis et al. [25] but our Λ_0 is slightly lower than theirs $[101.5 \text{ ohm}^{-1} \text{ mol}^{-1} \text{ dm}^3]$. Results of our comparative study are clear cut. The mobility of the sodium ion in methanol solution is reduced on complexation with benzo-15-crown-5 and to a greater degree with the dibromo- and dimethoxy-crown compounds as expected from their greater molar volumes.

Although there is considerable variation in the association constants for different runs, it is clear that K_A is significantly higher for crown complexed than for uncomplexed sodium bromide. At the highest concentrations reached in the titrations (ca 2.5 mM) the complexes are estimated to be present as ion-pairs to the extent of 5%, cf. less than 1% for uncomplexed NaBr.

5. Discussion

Our value of log K_1 for NaBr with benzo-15-crown-5, 2.94, is intermediate between that obtained previously by the same method in the same laboratory [26], 3.05, and in a different laboratory [27], 2.87. Even larger variations are recorded if different methods are used [28], e.g. 3.37 by the conductivity method for this system and 4.03

Table II. Analysis of conductivity measurements for NaBr in methanol, alone and complexed with crown ethers.

Expt.	n^a	$\Lambda_0(25°)$ ohm^{-1} mol^{-1} dm^3	K_A mol^{-1} dm^3	$\delta(\Lambda)^b$
Na$^+$Br$^-$				
1	18	98.48	1.7	0.08
2	18	98.61	3.6	0.13
3	18	99.35	4.7	0.29
Mean		98.9 ± 0.4	3 ± 2	
Na(Ia)$^+$Br$^-$				
1	25	94.82	19.2	0.19
2	21	95.44	22.2	0.16
3	24	95.25	18.8	0.13
Mean		95.1 ± 0.3	20 ± 1	
Na(Ib)$^+$Br$^-$				
1	22	90.84	22.6	0.13
2	21	90.42	21.9	0.15
3	18	91.04	26.6	0.14
Mean		90.8 ± 0.3	24 ± 2	
Na(Ic)$^+$Br$^-$				
1	18	90.17	19.4	0.12
2	26	91.10	23.0	0.17
3	19	89.96	24.0	0.15
4	23	89.58	20.4	0.24
5	12	89.02	15.0	0.16
Mean		90.0 ± 0.7	20 ± 3	

[a]No. of points.
[b]Standard deviation from calculated and experimental conductivites $(\Sigma(\Lambda_i^{obs.} - \Lambda_i^{calc.})^2(n-1))^{1/2}$.

to 4.50 for Na with benzo-18-crown-6 in methanol. Our value of $\log K_1$ for NaBr with benzo-15-crown-5 in DMF is in reasonable agreement with that, 1.6, obtained by NMR methods [29]. Lower values in DMF than methanol are to be expected from the donor numbers of the solvents, 26 and 18, respectively.

Comparison of **Ib** and **Ia** shows that for Na$^+$ and K$^+$, the former in methanol or DMF, there is a significant reduction in $\log K_1$, 0.6 for Na$^+$ and ~0.5 for K$^+$ on dibromination; this is compatible with lower electron density on the aromatic oxygen atoms with electron-withdrawing substituents. Smid and coworkers [7] found a similar effect for monosubstituted bromobenzo-15-crown-5 in acetone. The effect of dibromination on K_1 is less for potassium than for sodium and very small for K_2. This is probably because the K$^+\cdots$0 distances are greater in the 1 : 2 complexes than in the 1 : 1 and K$^+\cdots$0 is longer than Na$^+\cdots$0. The dimethoxy and di-n-butoxy substitutions give reductions in K_1 on the margin of significance by this method and further discussion is deferred until the results of NMR studies are presented [30].

Previous investigation of ion pairing in complexes of simple salts with various 18-crown-6 derivatives in coordinating solvents by Kolthoff and coworkers [31] indicated that the extent of ion-pairing in the complex is either similar to or less than that in the free salt; increases in ionic association on complexation were found only for potassium picrate and potassium tetraphenylborate with di-*tert*-butyldibenzo-18-crown-6 in methanol. Unfortunately crystal structures corresponding exactly to those MXL systems are not yet available. Measurements of ionic association for cryptate-222 complexes with sodium or potassium halides show increased ion-association in the complexes in solution in methanol [32] while there is no ion-pairing in the crystals of the corresponding iodides [33]. We have not found significantly greater association for the system which gives crystals containing complexed ion pairs [3]. We do not consider that measurement of conductivities, however carefully carried out, would enable us to predict the nature of the entities giving crystalline products.

Acknowledgements

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