# Association of Crown Ethers with Anilinium Ions in Methanol Solution and its Influence on Acid–Base Equilibria

By **Bernardo Masci**, Centro di Studio sui Meccanismi di Reazione del Consiglio Nazionale delle Ricerche, c/o Istituto di Chimica Organica, Università di Roma, 00185 Roma, Italy

The effect of adding toluene-*p*-sulphonic acid to *p*-nitroaniline and acetic acid to *p*-toluidine in methanol at 25.0 °C has been quantitatively studied by u.v.–visible spectrophotometry in the presence of 15-crown-5, 18-crown-6, and 21-crown-7. From the enhancement of the apparent basicity of the anilines due to complexation of the conjugate acids with crown ethers the association constants between crown ethers and anilinium ions were calculated. The order in the ability to associate, 18-crown-6 > 21-crown-7 > 15-crown-5, was the same in both series. A change of the anilinium ion substituent from *p*-$NO_2$ to *p*-$CH_3$ had little or no influence upon the association constants.

THE interaction of polyether ligands with cations may have as a consequence the perturbation of acid–base equilibria when either the cation, or the ligand, or both bear ionizable protons. A few examples have been reported recently. The degree of dissociation of polyoxyethylene-substituted alcohols [1] and phenols [2] in water or methanol solution is significantly enhanced in the presence of alkaline earth cations which complex the anionic form more strongly than the neutral form. Moreover, ammonia has been reported to completely convert a crown ether with an intra-annular phenolic function into the ammonium phenoxide.[3] Lately the pH increase of an alkylamine–alkylammonium ion mixture in water due to addition of 18-crown-6 has been used to determine the association constant between $RNH_3^+$ and the crown ether.[4]

The present study reports on the apparent basicity increase of *p*-nitroaniline and *p*-toluidine in methanol at 25.0 °C due to complexation of the corresponding anilinium ions with 15-crown-5 (15C5), 18-crown-6 (18C6), and 21-crown-7 (21C7). A u.v.–visible spectrophotometric analysis of the phenomenon allowed the determination of the association constants between the crown ethers and the anilinium ions.

Association between crown ethers and organic ammonium ions has been studied by several techniques both in chloroform [5] and in hydroxylic solvents,[4,6,7] but owing to the large number of host, guest, and medium parameters which must be varied, the picture is far from complete. As for aromatic ammonium ions, the only available association data refer to complexation of anilinium and methyl-substituted anilinium ions in methanol with 18C6. Relatively acidic ions, *e.g.* *p*-nitroanilinium ion, which are extensively dissociated in methanol, are not suitable for a quantitative study of association with crown ethers by titration calorimetry or any commonly used method. No such limit holds for the simple method described in the present work, based on the partial protonation of anilines. The method worked well both when an electron-releasing (*p*-$CH_3$) and when an electron-withdrawing substituent (*p*-$NO_2$) were present in the aniline ring.

As the desired degree of protonation can be obtained by using different acids independently of aniline base strength, the method is in principle of general applicability in the quantitative study of crown ether–anilinium ion association.

## RESULTS AND DISCUSSION

The effect of crown ethers on the acid–base equilibria of two anilines of largely different $pK_a$ values, namely *p*-nitroaniline and *p*-toluidine, was investigated in methanol solution at 25.0 °C.

The ratio $I$ between *p*-nitroanilinium ion and *p*-nitroaniline concentration was determined at various toluene-*p*-sulphonic acid concentrations by spectrophotometric measurement of the concentration of the base form. In the presence of fixed amounts of 15C5, 18C6, and 21C7 higher values for the $I$ ratio were observed. In all cases $I$ was found to be strictly linear with toluene-*p*-sulphonic acid concentration (Figure 1); these results are fully accounted for by the Scheme and equation (1), where CE refers to crown ether, $BH^+$ to

$$I = [H^+](1 + K_{CE}[CM])/K_a \qquad (1)$$

anilinium ion, $CE{\cdot}BH^+$ to associated anilinium ion, B to aniline, and $H^+$ to $CH_3OH_2^+$. Under the assumption that the same activity coefficient may be assigned to the three positively charged species, $K_a$ and $K_{CE}$ in equation (1) may be regarded as thermodynamic equilibrium constants. The slope of the straight lines in Figure 1 obtained in the presence of crown ethers, $(1 + K_{CE}[CE])/K_a$, divided by the slope obtained in the absence of crown ethers, $1/K_a$, gives the apparent basicity-enhancing factor for *p*-nitroaniline $(1 + K_{CE}[CE])$, which increases without limit with increasing crown concentration. The results are presented in the Table as log $K_{CE}$ values. The value obtained for $1/K_a$ was $26.6 \pm 0.11$, an average of six determinations; this corresponds to a $pK_a$ value of 1.42 which may be compared to the literature value of 1.28.[8]

As conceivable interfering phenomena, protonation of crown ethers, which has been reported to occur in apolar solvents,[9] and complexation of $CH_3OH_2^+$ with crown ethers must be considered for the acid solution.

The absence of systematic deviations from linearity with increasing acid concentration up to $1 \times 10^{-2}$M and the invariance of the $K_{CE}$ values with crown concentration suggest these factors to be unimportant under the conditions of the present investigation. Moreover, no

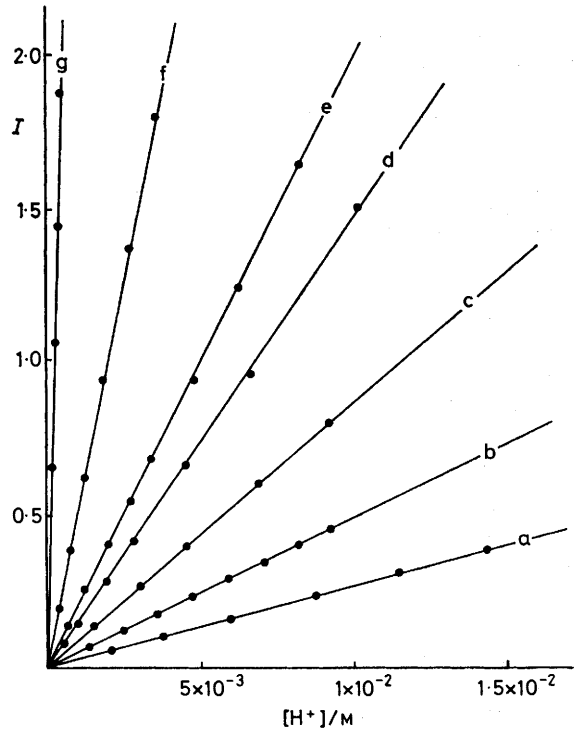
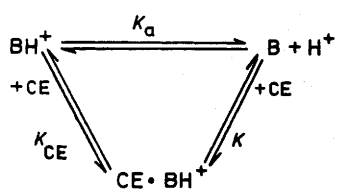



FIGURE 1 Representative linear plots of $I = [BH_{tot}^+]/[B]$ for *p*-nitroaniline in methanol at 25.0 °C *versus* toluene-*p*-sulphonic acid concentration in the presence and in the absence of crown ethers: a, no crown ether added; b, 15C5 $1.07 \times 10^{-2}$M; c, 21C7 $4.40 \times 10^{-3}$M; d, 15C5 $5.35 \times 10^{-2}$M; e, 21C7 $1.08 \times 10^{-2}$M; f, 18C6 $2.36 \times 10^{-3}$M; g, 18C6 $2.36 \times 10^{-2}$M

change was observed in the u.v. spectrum of benzo-18-crown-6 in the presence of $1 \times 10^{-2}$M-$HClO_4$ in methanol solution, whereas significant spectral changes of benzo-crown ethers usually accompany all kinds of complexation including protonation.[10]




SCHEME

When the acidity of the ammonium ions is low enough not to give appreciable dissociation in the medium, other methods, such as calorimetric titration [7] or potentiometric techniques,[6] may be used to determine complexation constants in solvents such as methanol. By the present approach weak acids must be used with more basic anilines in order partially to protonate the base and allow the crown ether to influence the acid–base equilibrium.

The value of $I$ was determined for *p*-toluidine at various acetic acid concentrations both in the presence and in the absence of crown ethers. Equation (1) still holds but obviously non-linear plots were obtained for the relationship between $I$ and acetic acid concentration. By expressing $[H^+]$ as a function of the concentration ($c_a$) and the dissociation constant ($K_a'$) of acetic acid,

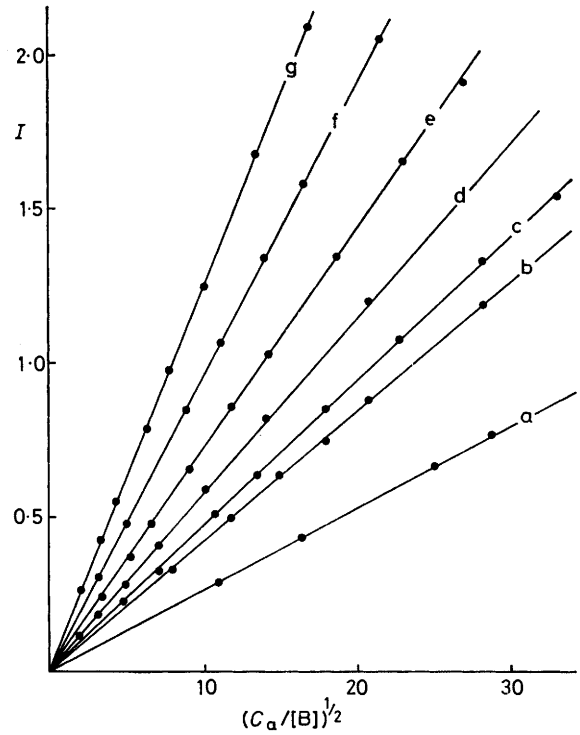



FIGURE 2 Representative linear plots of $I = [BH_{tot}^+]/[B]$ for *p*-toluidine in methanol at 25.0 °C *versus* the square root of the ratio between added acetic acid concentration and base form concentration in the presence and in the absence of crown ethers: a, no crown ether added; b, 15C5 $3.60 \times 10^{-2}$M; c, 21C7 $5.17 \times 10^{-3}$M; d, 15C5 $8.72 \times 10^{-2}$M; e, 21C7 $1.50 \times 10^{-2}$M; f, 18C6 $1.62 \times 10^{-3}$M; g, 18C6 $3.22 \times 10^{-3}$M

equation (2) is obtained from equation (1). Figure 2 shows representative linear plots of $I$ *versus* $(c_a/[B])^{\frac{1}{2}}$ with

$$I = \left[\frac{c_a K_a'(1 + K_{CE}[CE])}{[B]K_a}\right]^{\frac{1}{2}} \qquad (2)$$

15C5, 18C6, 21C7, and no crown added. From the slopes the log $K_{CE}$ values were calculated (Table). In the absence of crown ethers the value for the slope, $(K_a'/K_a)^{\frac{1}{2}} = 2.64 \pm 0.04 \times 10^{-2}$, an average of three determinations, was obtained, in good agreement with the value of $2.26 \times 10^{-2}$ calculated from literature data (acetic acid $pK_a$ 9.63;[11] *p*-toluidine $pK_a$ 6.34[8]).

The trend of $K_{CE}$ values in the two series 18C6 > 21C7 > 15C5 is the same as that found for $Bu^tNH_3^+$–benzo-crown ethers in $CDCl_3$,[12] the association constants being 2—3 powers of ten lower in methanol, which is a better solvating agent for both cation and ligand oxygen atoms. The marked preference for the hexaco-ordinate ligand is probably due to a good arrangement in which a symmetrical array for the three hydrogen bonds is pos-

sible with oxygens alternately displaced on one side of the mean plane of the ring.[13,14]

The log $K_{CE}$ values reported in the Table for the two anilinium ions are also for two different counterions, namely acetate and toluene-*p*-sulphonate. As no drift was observed in the plots in Figures 1 and 2 both in the presence and in the absence of crown ethers, on increasing the anion concentration, significant association

log $K_{CE}$ values for the association of anilinium ions and crown ethers in methanol at 25.0 °C

| | 15C5 | 18C6 | 21C7 |
|---|---|---|---|
| *p*-Nitroanilinium | 1.92 ± 0.04 [a] | 3.88 ± 0.02 [b] | 2.77 ± 0 02 [e] |
| *p*-Toluidinium | 1.69 ± 0.04 [d] | 3.85 ± 0.02 [e] | 2.61 ± 0.03 [f] |

[a] Five determinations, [CE] $9.04 \times 10^{-3}$—$1.03 \times 10^{-1}$M. [b] Six determinations [CE] $9.05 \times 10^{-4}$—$2.36 \times 10^{-2}$M [c] Three determinations, [CE] $4.40 \times 10^{-3}$—$1.45 \times 10^{-2}$M. [d] Three determinations, [CE] $3.60 \times 10^{-2}$—$8.72 \times 10^{-2}$M. [e] Three determinations, [CE] $1.62 \times 10^{-3}$—$3.22 \times 10^{-3}$M. [f] Four determinations, [CE] $5.17 \times 10^{-3}$—$2.11 \times 10^{-2}$M.

with anions for complexed and uncomplexed cations is unlikely. The absence of any significant ion pairing effect for ammonium salts and their 18C6 complexes in methanol has already been noted by Izatt *et al.*:[7] this point is further confirmed by the very good agreement between the value reported in that work for the association of 18C6 with *p*-toluidinium bromide (log $K_{CE}$ 3.82 ± 0.04) and the value of 3.85 ± 0.02 found by the present method for *p*-toluidinium acetate.

The slight difference in log $K_{CE}$ for 15C5 and 21C7 observed for the two anilinium salts is probably due to the different cation structure. Although the trend is that expected on the basis of substituent electronic effects, with the electron-withdrawing *p*-nitro-substituent, reinforcing the positive charge on the ammonium group, the effects are so small that no speculation on their origin is safe; in fact no effect at all is observed within experimental error for 18C6.

No significant effect was noted by Izatt *et al.*[7] on comparing the complexation ability of anilinium ion and *m*- and *p*-methyl-substituted anilinium ions toward 18C6. From the present analysis, extended to various crown ethers and to the *p*-nitro-substituent, the general conclusion may be drawn that electron-releasing or electron-withdrawing substituents on the aromatic ring have little or no influence upon the strength of crown ether–anilinium ion association.

## EXPERIMENTAL

Methanol (Erba RP) was distilled over 2,4-dinitrobenzoic acid in order to remove basic volatile impurities and then dried by a further distillation over magnesium. 15C5 (Aldrich), 18C6 (Aldrich), and acetic acid (Erba RP) were used as received. 21C7 was prepared as previously described [1] and further purified by vacuum distillation. *p*-Toluidine (Eastman) and *p*-nitroaniline (Fluka) were recrystallized from ethanol–hexane. Anhydrous toluene-*p*-sulphonic acid was obtained by vacuum distillation of the monohydrate (Erba RP). The absence of significant amounts of acid or base impurities in the methanol–crown ether solution is demonstrated by straight lines passing through the origin in Figures 1 and 2. In preliminary experiments with *p*-toluidine in commercial methanol, non-zero intercepts were observed, although the $K_{CE}$ values obtained were in full agreement with those obtained in the purified solvent.

U.v.–visible measurements were run either on a Beckman DB GT spectrophotometer using 4.00-cm quartz cuvettes or on a Varian DMS 90 spectrophotometer using 1.00-cm quartz cuvettes. The absorbance at 375 nm for 1—1.4 × $10^{-5}$M-*p*-nitroaniline or at 293 nm for 0.85—1.2 × $10^{-4}$M-*p*-toluidine, was recorded at 25.0 °C after at least 10 min, to allow for thermal equilibration; calculated amounts of the proper acid solution (4M-acetic acid and 0.3—1.5M-toluene-*p*-sulphonic acid) were then added by SGE microsyringes and absorbance recorded after allowing *ca.* 4 min for temperature equilibration.

With $A$ being the absorbance value after each acid addition and $A_0$ the initial absorbance value corrected for dilution, $I$ values were calculated as $(A_0 - A)/A$.

## APPENDIX

Equation (1) is easily obtained by combining equations (4)—(6) with (3), if $\gamma_{H^+} = \gamma_{BH^+} = \gamma_{CE\cdot BH^+}$.

$$I = [BH_{tot}^+]/[B] \quad (3)$$

$$[BH_{tot}^+] = [BH^+] + [CE\cdot BH^+] \quad (4)$$

$$K_{CE} = [CE\cdot BH^+]\gamma_{CE\cdot BH^+}/[CE][BH^+]\gamma_{BH^+} \quad (5)$$

$$K_a = [B][H^+]\gamma_{H^+}/[BH^+]\gamma_{BH^+} \quad (6)$$

In order to obtain equation (2) equations (7)—(9) may be written. $[AcO^-]$ in equation (8) and $[CH_3O^-]$ in (9) may be

$$[H^+]\gamma_{\pm}^2 = K_a'[AcOH]/[AcO^-] \quad (7)$$

$$[AcOH] = c_a - [AcO^-] \quad (8)$$

$$[AcO^-] = [BH^+] + [CE\cdot BH^+] + [H^+] - [CH_3O^-] \quad (9)$$

safely neglected. The approximate forms of equations (8) and (9), when combined with (4)—(7), lead to (10). As

$$[H^+]^2\gamma_{\pm}^2 = K_a'c_a/\{1 + ([B]/K_a)(1 + K_{CE}[CE])\} \quad (10)$$

*p*-toluidine concentration was varied from $1 \times 10^{-4}$ to $3 \times 10^{-5}$M during experiments and $K_a = 4.6 \times 10^{-7}$,[8] 1 may be neglected with respect to $([B]/K_a)(1 + K_{CE}[CE])$ in all cases (even when $[CE] = 0$). The further approximation $\gamma_{\pm}^2 = 1$ was assumed, as at the highest attained ionic strength ($[BH_{tot}^+]$ *ca.* $7 \times 10^{-5}$M) $\gamma_{\pm}$ calculated by the Debye–Hückel limiting law was 0.97. When the approximate form of equation (10) is combined with (1), (2) is obtained.

I thank Professors G. Illuminati and L. Mandolini for helpful discussions.

[1/098 *Received*, 22*nd January*, 1981]

## REFERENCES

[1] L. Mandolini and B. Masci, *Synth. Commun.*, 1979, **9**, 851.
[2] G. Ercolani, L. Mandolini, and B. Masci, *J. Am. Chem. Soc.*, in the press.
[3] M. A. McKervey and D. L. Mulholland, *J. Chem. Soc., Chem. Commun.*, 1977, 438.
[4] J. L. Roberts, L. E. McClintock, Y. El-Omrani, and J. W. Larson, *J. Chem. Eng. Data*, 1979, **24**, 79.
[5] For a review, see D. N. Reinhoudt and F. de Jong, in 'Progress in Macrocyclic Chemistry' eds. R. M. Izatt and J. J. Christensen, Wiley, New York, 1979, vol. 1.

[6] J. P. Behr, J. M. Lehn, and P. Vierling, *J. Chem. Soc., Chem. Commun.*, 1976, 621.
[7] R. M. Izatt, J. D. Lamb, N. E. Izatt, B. E. Rossiter, J. J. Christensen, and B. L. Haymore, *J. Am. Chem. Soc.*, 1979, **101**, 6273.
[8] Taken from the compilation in J. E. Leffler and E. Grunwald, ' Rates and Equilibria of Organic Reactions ', Wiley, New York, 1963, p. 268.
[9] N. Nae and J. Jagur-Grodzinski, *J. Am. Chem. Soc.*, 1977, **99**, 489.
[10] B. Masci, unpublished observations.
[11] T. Shedlovsky and R. L. Kay, *J. Phys. Chem.*, 1956, **60**, 151.
[12] F. de Jong, D. N. Reinhoudt, and R. Huis, *Tetrahedron Lett.*, 1977, 3985; ref. 5, p. 199.
[13] J. M. Timko, S. S. Moore, D. M. Walba, P. C. Hiberty, and D. J. Cram, *J. Am. Chem. Soc.*, 1977, **99**, 4207.
[14] J. F. Stoddart, in ' Enzymic and Non-enzymic Catalysis ', eds. P. Dunnill, A. Wiseman, and N. Blakebrough, Ellis Horwood, Chichester, 1980.