An Investigation of the Kinetic and Thermodynamic Stability of a Tribenzomacrobicyclic Polyether Complex with Diquat in Acetone Solution

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Variable-temperature ^{1}H n.m.r. spectroscopic studies in CD_3COCD_3 and u.v. spectroscopic measurements in Me_2CO demonstrate that in the 1 : 1 complex, $[Diquat\cdot(\mathbf{1})]^{2+}$, the guest is encapsulated within the host and that the complexation strength ($\Delta G° = -7.4$ kcal mol^{-1}) is enhanced by the macrobicyclic cryptate effect.

Since *X*-ray crystallography has established[1] that the host (**1**) (Figure 1) encapsulates the Diquat dication, $[Diquat]^{2+}$, in the solid state in a particularly elegant fashion, it became necessary to establish the structure and stability of the 1 : 1

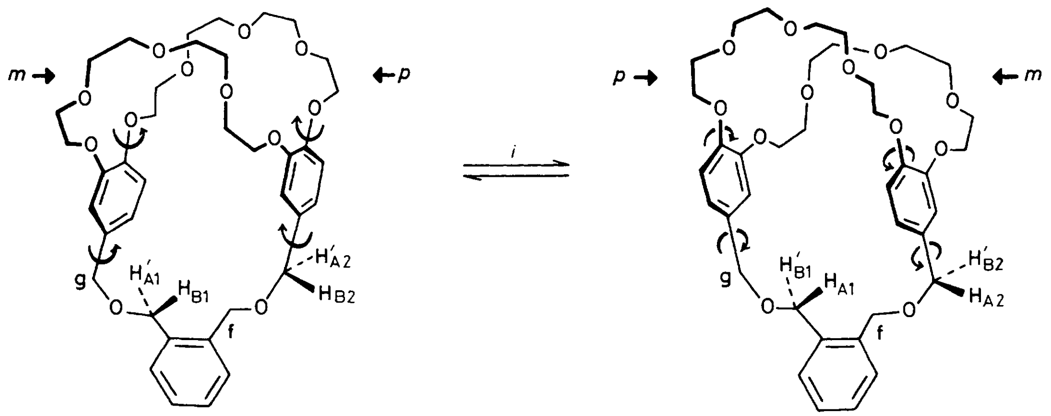

Figure 1. The degenerate conformational inversion (*i*) of the host (**1**), showing the site exchanges for the CH_2-f and CH_2-g protons (*m* ≡ *meta* and *p* ≡ *para* polyether chains).

Table 1. Temperature-dependent ^{1}H n.m.r. spectroscopic data and thermodynamic parameters for the host (**1**) and its 1 : 1 complex with Diquat bishexafluorophosphate.[a]

Species	^{1}H N.m.r. probe	Spectral changes[b]	T_c,±3 /°C	Δν(°C),±2 /Hz	J_{AB},±0.5 /Hz	k_c /s^{-1}	$\Delta G_c^‡$±0.3 /kcal mol^{-1}	Process
(**1**)	CH_2-f	A1/B1 → AB1	−78	85 (−95)	13	202	9.2	*i*
(**1**)	CH_2-g	A2/B2 → AB2	−78	48 (−95)	13	128	9.4	*i*
[Diquat·(**1**)][PF_6]$_2$	CH_2-f	A1/B1 → AB1	+10	124 (−30)	12	282	13.4	*d* + *i*
[Diquat·(**1**)][PF_6]$_2$	CH_2-g	A2/B2 → AB2	−5	39 (−30)	10.8	105	13.2	*d* + *i*
[Diquat·(**1**)]PF_6]$_2$	H-3	X/Y → XY	0	264 (−30)	—	587	12.5	*d*
[Diquat·(**1**)][PF_6]$_2$	H-4	X/Y → XY	0	384 (−30)	—	854	12.3	*d*
[Diquat·(**1**)][PF_6]$_2$	H-6	X/Y → XY	−13	80 (−30)	—	178	12.5	*d*

[a] All spectra were recorded in CD_3COCD_3 at 400 MHz on a Bruker WH400 spectrometer with Me_4Si as 'lock' and internal standard. Abbreviations used are: T_c, coalescence temperature; Δν, frequency separation for the appropriate ^{1}H n.m.r. probe with the temperature at which it was measured indicated in parentheses; J_{AB}, geminal coupling constant between two mutually coupled protons undergoing exchange between equally populated sites A and B; k_c, exchange rate constant at T_c calculated from the approximate expressions, $k_c = \pi[\Delta\nu^2 + 6J_{AB}^2]^{\frac{1}{2}}/2^{\frac{1}{2}}$ when the protons undergoing exchange between equally populated sites A and B are mutually coupled, and $k_c = \pi\Delta\nu/2^{\frac{1}{2}}$ when the protons undergoing exchange between equally populated sites X and Y are not mutually coupled; $\Delta G_c^‡$, free energy of activation at T_c calculated from the Eyring equation. [b] Sites are designated X/Y for uncoupled two-site sytems. Sites that represent two time-averaged signals are designated XY. Sites are designated A1/B1 and A2/B2 for coupled AB systems. Sites that represent two time-averaged signals from these AB systems are designated AB1 and AB2.

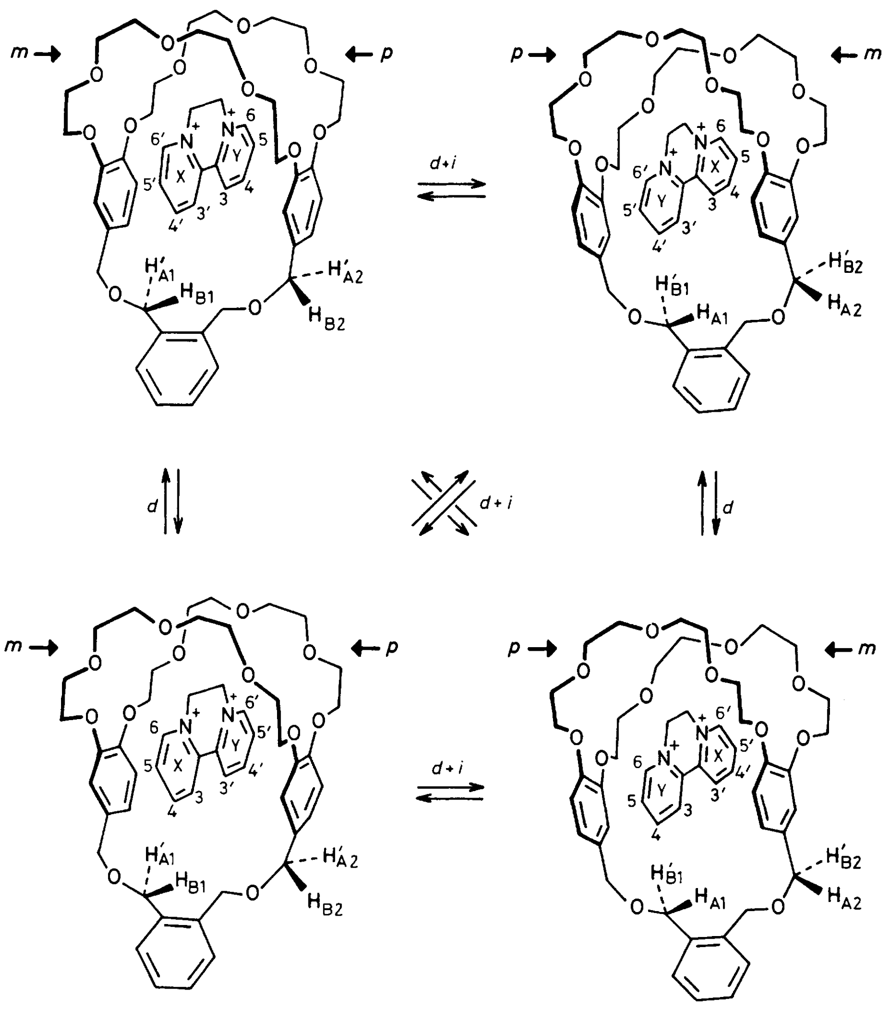

Figure 2. Conformational inversion of the host (**1**) and guest–host exchange processes (*d* and *d* + *i*) for the Diquat dication with (**1**). The site exchanges for CH_2-f and CH_2-g protons and for the constitutionally homotopic protons on the bipyridinium ring of the Diquat dication are shown (*m* ≡ *meta* and *p* ≡ *para* polyether chain).

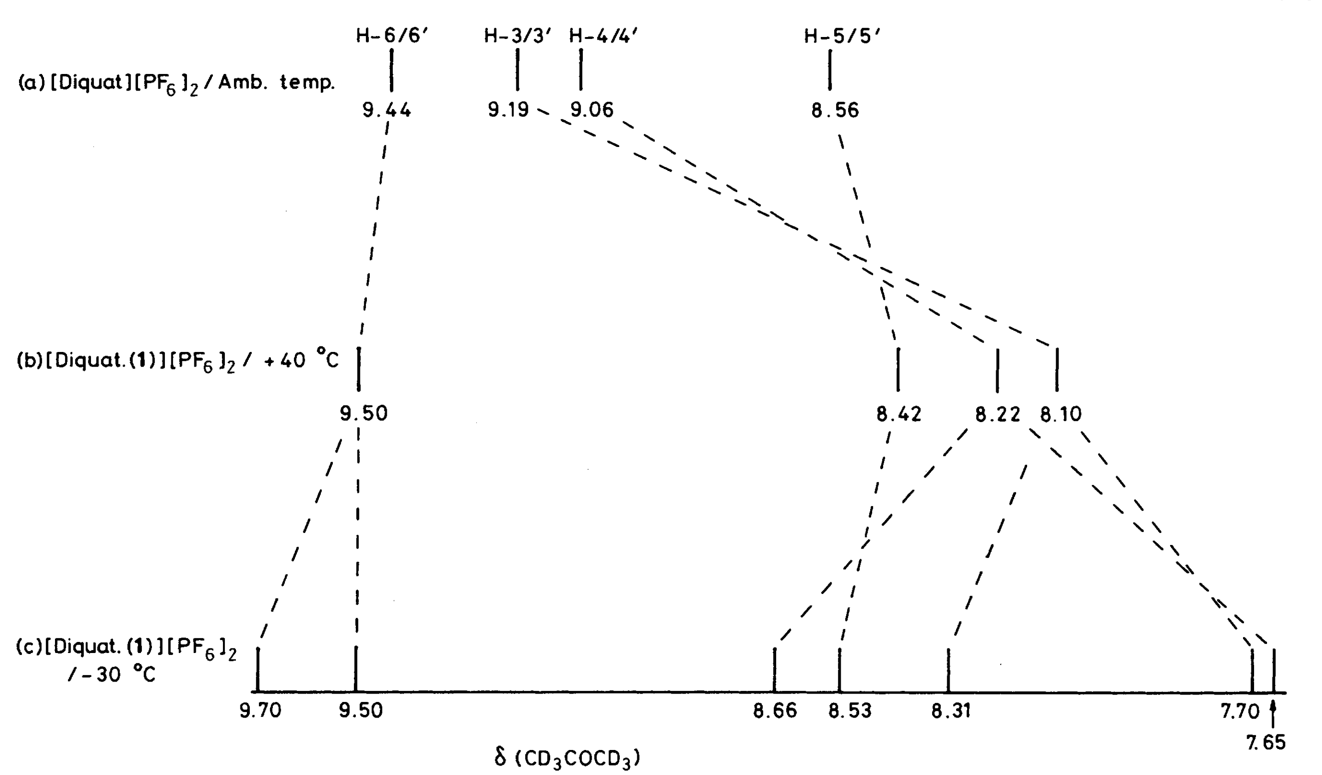

Figure 3. Partial ^1H n.m.r. line spectra of (a) [Diquat][PF_6]$_2$ at ambient temperature, (b) [Diquat·(**1**)][PF_6]$_2$ at +40 °C, and (c) [Diquat·(**1**)][PF_6]$_2$ at −30 °C.

complex formed in solution prior to crystallisation. Here, we discuss the temperature dependences of the ^1H n.m.r. spectra, recorded in CD_3COCD_3 at 400 MHz, (i) of the free host (**1**), (ii) of the 1 : 1 complex formed between (**1**) and [Diquat]$^{2+}$ and (iii) employ the spectroscopic data, along with (iv) a supporting association constant determination in acetone by u.v. spectroscopy, to assess the kinetic and thermodynamic stabilities of the 1 : 1 complex.

The full ^1H n.m.r. spectroscopic data and partial proton assignments for (**1**) at ambient temperature are listed in a footnote (†) in the preceding communication.[1] On cooling the CD_3COCD_3 solution of (**1**) to −95 °C, the two 4H singlets resonating at δ 4.50 (CH_2-f) and 4.39 (CH_2-g) separated into two AB systems, referred to as A1/B1 and A2/B2 in Table 1. From the rate constants (k_c), calculated by an approximate treatment[2] at the coalescence temperatures (T_c), an average value for $\Delta G_c^\ddagger$ of 9.3 kcal mol^{-1} (1 cal = 4.184 J) emerged. We conclude that (**1**) is conformationally mobile on the ^1H n.m.r. time scale above −78 °C as a result of a conformational inversion process involving passage† (Figure 1) of one of the polyether chains through the centre of the macrobicyclic ring incorporating the diether bridge and the other polyether chain (*cf.* refs. 3 and 4). This degenerate process *i* exchanges the pairs of diastereotopic protons (i) H and H′ in CH_2-f between sites A1 and B1 and (ii) H and H′ in CH_2-g between sites A2 and B2. Thus, the $\Delta G_c^\ddagger$ value of 9.3 kcal mol^{-1} can be equated with the free energy of activation for the conformational inversion of the free host (**1**).

A consideration of the averaged C_s and C_{2v} molecular symmetries for (**1**) and [Diquat]$^{2+}$, respectively, reveals that in the 1 : 1 complex, [Diquat·(**1**)]$^{2+}$, the guest must experience the lower averaged molecular symmetry (C_s) of the host. It follows that protons (*e.g.* H-3 and H-3′) which are constitutionally homotopic in [Diquat]$^{2+}$, become heterotopic in [Diquat·(**1**)]$^{2+}$ and so should resonate with different chemical shifts under conditions of slow site exchange on the ^1H n.m.r. time scale, reflecting slow dissociation of the 1 : 1 complex. The site exchanges (A1 $\rightleftarrows$ B1; A2 $\rightleftarrows$ B2; X $\rightleftarrows$ Y) undergone by the pairs of protons CHH′-f and CHH′-g in the host and by the pairs of protons H-3,3′, H-4,4′, H-5,5′, and H-6,6′ in the complexed guest of [Diquat·(**1**)]$^{2+}$ are illustrated in Figure 2 for (i) the process *d* involving dissociation (and rapid recombination) of the complex *without* inversion of (**1**) and (ii) the process *d* + *i* involving dissociation (and rapid recombination) of the complex *with* inversion of (**1**).‡ The predictions made for the temperature dependence of the ^1H n.m.r. spectrum of [Diquat·(**1**)]$^{2+}$ are demonstrated convincingly by the partial line spectrum shown in Figure 3.

Not only do the AB1 and AB2 singlets for CH_2-f and CH_2-g separate into two AB systems just below room temperature

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† In Figure 1, *m* and *p* refer to the polyether chains that are respectively *meta* and *para* to the diether bridge in (**1**). In order for (**1**) to invert, the *m*-polyether chain has to pass through a 29-membered ring and/or the *p*-polyether chain has to pass through a 27-membered ring. The third possibility, namely the passage of the diether bridging unit through a 30-membered ring, can be discounted.

‡ A number of examples of face-to-face crown ether complexes have been reported (J. C. Metcalfe, J. F. Stoddart, G. Jones, W. E. Hull, A. Atkinson, I. S. Kerr, and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1980, 540; J. Krane and O. Aune, *Acta Chem. Scand., Sect. B*, 1980, **34**, 397; J. A. A. de Boer, J. W. H. M. Uiterwijk, J. Geevers, S. Harkema, and D. N. Reinhoudt, *J. Org. Chem.*, 1983, **48**, 4821) in which conformational inversion of the host can occur in a 1 : 1 complex *without* prior dissociation of the guest. In the case of [Diquat·(**1**)]$^{2+}$, the $\Delta G_c^\ddagger$ values of 9.3, 12.4, and 13.4 kcal mol^{-1} for the *i*, *d*, and *d* + *i* processes, respectively, indicate that conformational inversion of (**1**) can only take place following partial if not complete dissociation.

affording (Table 1) an average $\Delta G_c^{\ddagger}$ value of 13.4 kcal mol^{-1}, which can be associated with the *d* + *i* process, but also three of the signals (XY) for the guest protons, namely, H-3/3′ H-4/4′, and H-6/6′, separate into pairs of signals X and Y, affording (Table 1 and Figure 3) an averaged $\Delta G_c^{\ddagger}$ value of 12.4 kcal mol^{-1} for the *d* process. In the case of H-3/3′ and H-4/4′, the relatively large $\Delta\nu$ values of 264 and 384 Hz reflect their proximity (*cf.* ref. 1) in [Diquat·(**1**)]$^{2+}$ to both the oxygen atoms and the benzo ring in the diether bridge of the host. Figure 3 also shows that the time-averaged signals for H-3/3′ and H-4/4′ observed at +40 °C are shifted dramatically upfield (*cf.* the situation[5] in [Diquat·dibenzo-30-crown-10]$^{2+}$) presumably on account of the other two benzo rings with their approximately parallel alignments to the bipyridinium ring system. Significantly, the most exposed protons (*i.e.* H-5/5′) on the guest in [Diquat·(**1**)]$^{2+}$ exhibit little change in their chemical shift(s) as the temperature is lowered (Figure 3).

Assuming the exchange processes depend entirely (*cf.* ref. 6) upon a unimolecular dissociation–recombination mechanism[7] and that the free energy of activation for recombination is close to if not actually diffusion-controlled (*i.e.* $\Delta G_a^{\ddagger}$ = *ca.* 3 kcal mol^{-1}), then the value of 12.4 kcal mol^{-1} obtained (Table 1) for the free energy of activation for the *d* process indicates that (**1**) must form a stronger complex with [Diquat][PF$_6$]$_2$ than does dibenzo-30-crown-10. This has been confirmed by determining the association constant and derived free energy of complexation (ΔG°) for the equilibrium (1) in acetone by a u.v. spectrophotometric method.[5] The value of −7.4 kcal mol^{-1} obtained for ΔG° may be compared with the one of −5.79 kcal mol^{-1} found[5] for [Diquat·dibenzo-30-crown-10][PF$_6$]$_2$.

$$[\text{Diquat}]^{2+} + (\mathbf{1}) \rightleftharpoons [\text{Diquat}\cdot(\mathbf{1})]^{2+} \qquad (1)$$

Thus, we conclude that (i) the structure of [Diquat·(**1**)]$^{2+}$ in acetone solution is similiar to that observed[1] in the solid state and that (ii) the macrobicyclic cryptate effect[8] leads to enhanced complexation of [Diquat]$^{2+}$ by (**1**) relative to dibenzo-30-crown-10.

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