

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

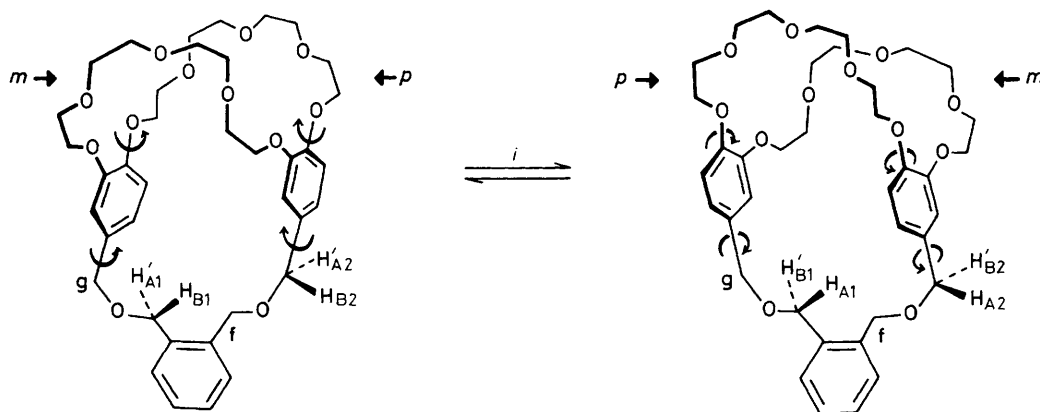
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Variable-temperature  $^1\text{H}$  n.m.r. spectroscopic studies in  $\text{CD}_3\text{COCD}_3$  and u.v. spectroscopic measurements in  $\text{Me}_2\text{CO}$  demonstrate that in the 1 : 1 complex,  $[\text{Diquat} \cdot (1)]^{2+}$ , the guest is encapsulated within the host and that the complexation strength ( $\Delta G^\circ = -7.4 \text{ kcal mol}^{-1}$ ) is enhanced by the macrobicyclic cryptate effect.

Since X-ray crystallography has established<sup>1</sup> that the host (1) encapsulates the Diquat dication,  $[\text{Diquat}]^{2+}$ , in the

solid state in a particularly elegant fashion, it became necessary to establish the structure and stability of the 1 : 1

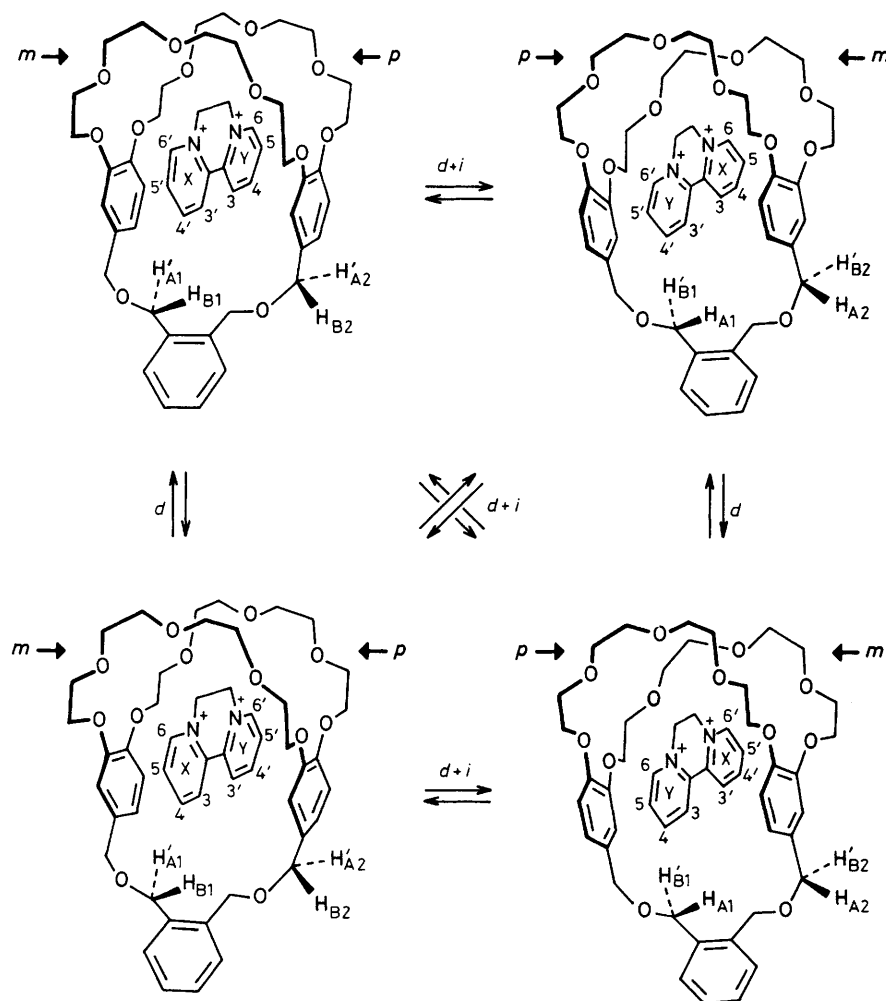


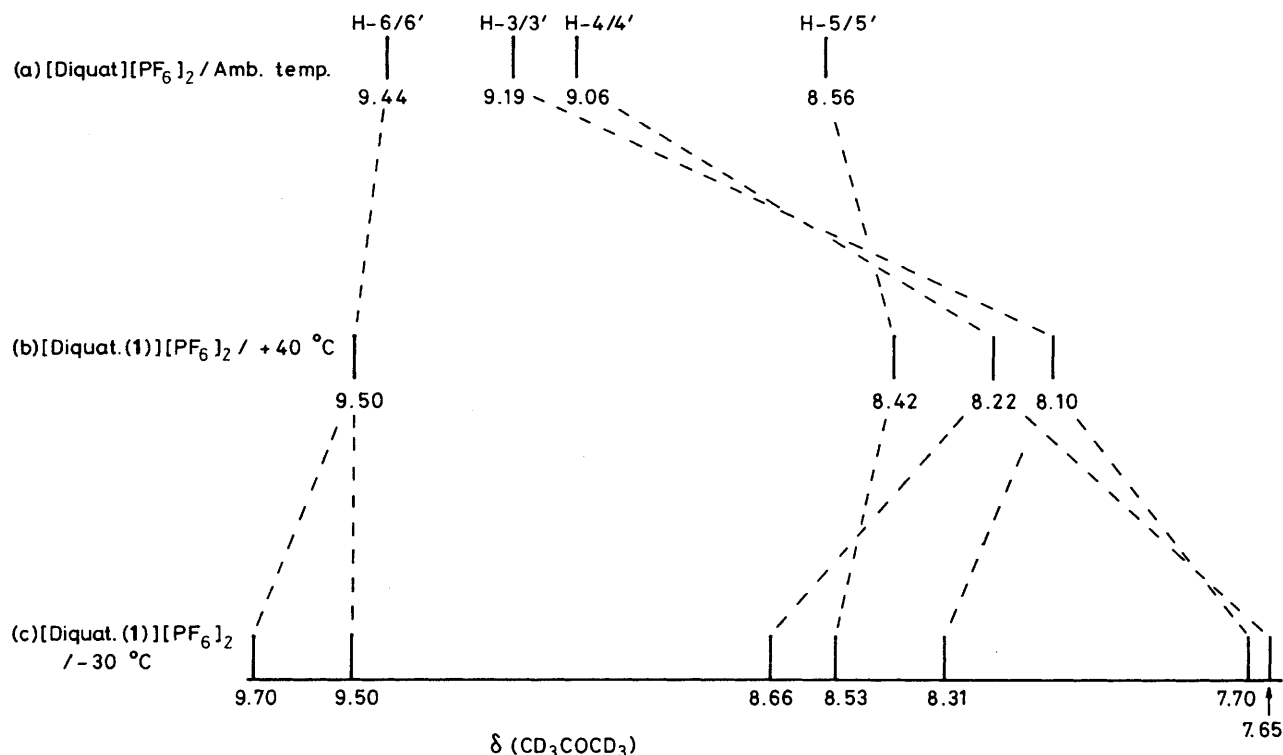
**Figure 1.** The degenerate conformational inversion (*i*) of the host (1), showing the site exchanges for the  $\text{CH}_2\text{-f}$  and  $\text{CH}_2\text{-g}$  protons (*m*  $\equiv$  meta and *p*  $\equiv$  para polyether chains).

**Table 1.** Temperature-dependent  $^1\text{H}$  n.m.r. spectroscopic data and thermodynamic parameters for the host (**1**) and its 1 : 1 complex with Diquat bishexafluorophosphate.<sup>a</sup>

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

<sup>a</sup> All spectra were recorded in  $\text{CD}_3\text{COCD}_3$  at 400 MHz on a Bruker WH400 spectrometer with  $\text{Me}_4\text{Si}$  as 'lock' and internal standard. Abbreviations used are:  $T_c$ , coalescence temperature;  $\Delta\nu$ , frequency separation for the appropriate  $^1\text{H}$  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,  $k_c = \pi[\Delta\nu^2 + 6J_{AB}^2]^{1/2}$  when the protons undergoing exchange between equally populated sites A and B are mutually coupled, and  $k_c = \pi\Delta\nu/2$  when the protons undergoing exchange between equally populated sites X and Y are not mutually coupled;  $\Delta G_c^{\ddagger}$ , free energy of activation at  $T_c$  calculated from the Eyring equation. <sup>b</sup> Sites are designated X/Y for uncoupled two-site systems. 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  $\text{CH}_2\text{-f}$  and  $\text{CH}_2\text{-g}$  protons and for the constitutionally homotopic protons on the bipyridinium ring of the Diquat dication are shown (*m*  $\equiv$  meta and *p*  $\equiv$  para polyether chain).



**Figure 3.** Partial  $^1\text{H}$  n.m.r. line spectra of (a)  $[\text{Diquat}][\text{PF}_6]_2$  at ambient temperature, (b)  $[\text{Diquat} \cdot (1)][\text{PF}_6]_2$  at  $+40^\circ\text{C}$ , and (c)  $[\text{Diquat} \cdot (1)][\text{PF}_6]_2$  at  $-30^\circ\text{C}$ .

complex formed in solution prior to crystallisation. Here, we discuss the temperature dependences of the  $^1\text{H}$  n.m.r. spectra, recorded in  $\text{CD}_3\text{COCD}_3$  at 400 MHz, (i) of the free host (1), (ii) of the 1:1 complex formed between (1) and  $[\text{Diquat}]^{2+}$  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  $^1\text{H}$  n.m.r. spectroscopic data and partial proton assignments for (1) at ambient temperature are listed in a footnote ( $\dagger$ ) in the preceding communication.<sup>1</sup> On cooling the  $\text{CD}_3\text{COCD}_3$  solution of (1) to  $-95^\circ\text{C}$ , the two  $4\text{H}$  singlets resonating at  $\delta$  4.50 ( $\text{CH}_2\text{-f}$ ) and 4.39 ( $\text{CH}_2\text{-g}$ ) 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<sup>2</sup> at the coalescence temperatures ( $T_c$ ), an average value for  $\Delta G_c^\ddagger$  of  $9.3 \text{ kcal mol}^{-1}$  ( $1 \text{ cal} = 4.184 \text{ J}$ ) emerged. We conclude that (1) is conformationally mobile on the  $^1\text{H}$  n.m.r. time scale above  $-78^\circ\text{C}$  as a result of a conformational inversion process involving passage $\ddagger$  (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  $\text{CH}_2\text{-f}$  between sites A1 and B1 and (ii) H and H' in  $\text{CH}_2\text{-g}$  between sites A2 and B2. Thus, the  $\Delta G_c^\ddagger$  value of  $9.3 \text{ kcal mol}^{-1}$  can be equated with the free energy of activation for the conformational inversion of the free host (1).

$\dagger$  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 consideration of the averaged  $C_s$  and  $C_{2v}$  molecular symmetries for (1) and  $[\text{Diquat}]^{2+}$ , respectively, reveals that in the 1:1 complex,  $[\text{Diquat} \cdot (1)]^{2+}$ , 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  $[\text{Diquat}]^{2+}$ , become heterotopic in  $[\text{Diquat} \cdot (1)]^{2+}$  and so should resonate with different chemical shifts under conditions of slow site exchange on the  $^1\text{H}$  n.m.r. time scale, reflecting slow dissociation of the 1:1 complex. The site exchanges ( $\text{A1} \rightleftharpoons \text{B1}$ ;  $\text{A2} \rightleftharpoons \text{B2}$ ;  $\text{X} \rightleftharpoons \text{Y}$ ) undergone by the pairs of protons  $\text{CHH}'\text{-f}$  and  $\text{CHH}'\text{-g}$  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  $[\text{Diquat} \cdot (1)]^{2+}$  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). $\ddagger$  The predictions made for the temperature dependence of the  $^1\text{H}$  n.m.r. spectrum of  $[\text{Diquat} \cdot (1)]^{2+}$  are demonstrated convincingly by the partial line spectrum shown in Figure 3.

Not only do the AB1 and AB2 singlets for  $\text{CH}_2\text{-f}$  and  $\text{CH}_2\text{-g}$  separate into two AB systems just below room temperature

$\ddagger$  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  $[\text{Diquat} \cdot (1)]^{2+}$ , the  $\Delta G_c^\ddagger$  values of 9.3, 12.4, and  $13.4 \text{ kcal mol}^{-1}$  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<sup>-1</sup>, 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<sup>-1</sup> 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)]<sup>2+</sup> 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<sup>5</sup> in [Diquat·dibenzo-30-crown-10]<sup>2+</sup>) 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)]<sup>2+</sup> 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<sup>7</sup> 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<sup>-1</sup>), then the value of 12.4 kcal mol<sup>-1</sup> obtained (Table 1) for the free energy of activation for the *d* process indicates that (1) must form a stronger complex with [Diquat][PF<sub>6</sub>]<sub>2</sub> than does dibenzo-30-crown-10. This has been confirmed by determining the association constant and derived free energy of complexation ( $\Delta G^\circ$ ) for the equilibrium (1) in acetone by a u.v. spectrophotometric method.<sup>5</sup> The value of -7.4 kcal mol<sup>-1</sup> obtained for  $\Delta G^\circ$  may be compared with the one of -5.79 kcal mol<sup>-1</sup> found<sup>5</sup> for [Diquat·dibenzo-30-crown-10][PF<sub>6</sub>]<sub>2</sub>.



Thus, we conclude that (i) the structure of [Diquat·(1)]<sup>2+</sup> in acetone solution is similar to that observed<sup>1</sup> in the solid state and that (ii) the macrobicyclic cryptate effect<sup>8</sup> leads to enhanced complexation of [Diquat]<sup>2+</sup> by (1) relative to dibenzo-30-crown-10.

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