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AN INVESTIGATION BY HIGH RESOLUTION ^{1}H NMR SPECTROSCOPY OF THE KINETIC STABILITIES OF SOLUTION COMPLEXES OF DIQUAT WITH DISUBSTITUTED DIBENZO-30-CROWN-10 DERIVATIVES

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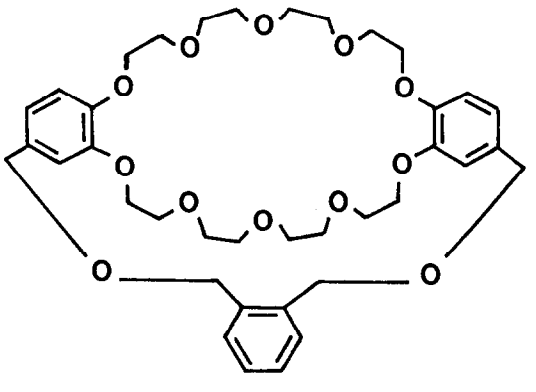
Dynamic ^{1}H n.m.r spectroscopy reveals that the disubstituted derivatives **2** *-* **4** *of dibenzo-30-crown-10 (***5***) form strong 1:1 complexes in CD_3COCD_3 solution with the diquat dication. Desymmetrisation of the guest by the bound host provides the key to a novel application of this form of spectroscopic analysis to molecular receptor chemistry.*

In the preceding communication,[2] it was demonstrated that the 2,20-bisformyl, -bis-hydroxymethyl, and -dimethyl derivatives (**2**, **3**, and **4**, respectively) of dibenzo-30-crown-10 (**5**) all form 1:1 complexes with [Diquat][PF_6]$_2$ both in the solid state and in solution. Since the corresponding 1:1 complex with the macrobicyclic receptor molecule **1** exhibited [3] sufficient kinetic stability in acetone solution for conducting a study by dynamic ^{1}H n.m.r. spectroscopy, we were prompted to extend the investigation to the 1:1 complexes, [Diquat.**2**][PF_6]$_2$, [Diquat.**3**][PF_6]$_2$, and [Diquat.**4**][PF_6]$_2$, in CD_3COCD_3. We were pleasantly surprised to discover that these three complexes all have kinetic stabilities such that they can be probed and measured by variable temperature ^{1}H n.m.r. spectroscopy at 400 MHz. Here, we report our results and compare them with the thermodynamic stabilities found [2] for these complexes. Finally, a comparison is drawn (**i**) with the kinetic and thermodynamic stabilities of [Diquat.**1**][PF_6]$_2$, and (**ii**) with the thermodynamic stability [4] of [Diquat.**5**][PF_6]$_2$. All the quantitative data have been obtained in either acetone or CD_3COCD_3 solutions.

If the diquat dication is complexed in a 'face-to-face' manner (*cf.* the *X*-ray crystal structures of the 1:1 complexes [2]) with the receptor molecules **2** - **4**, as shown in Figure 1,



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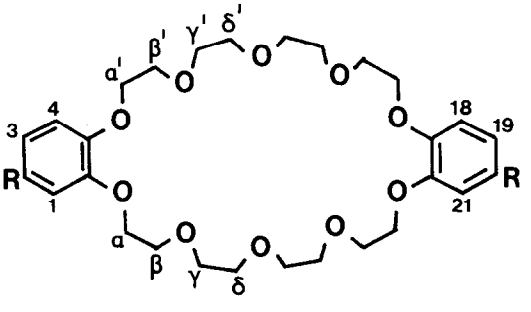

2 R = CHO
3 R = CH_2OH
4 R = CH_3
5 R = H

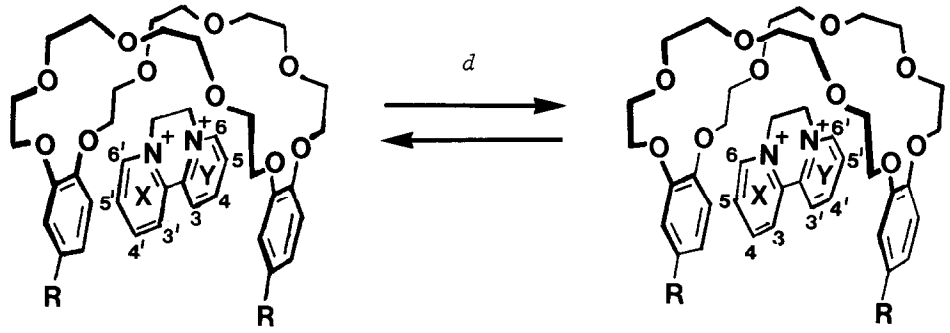

Figure 1. The dissociation-recombination process (*d*) for the diquat dication with molecular receptors **2** - **4**. The site exchanges of the constitutionally homotopic pairs of protons (H-3/3'; H-4/4'; H-5/5'; H-6/6') between sites X and Y, that give rise to the temperature dependent ^{1}H n.m.r. spectra (see Table 1) are indicated for one of the 'face-to-face' complexes.

then the averaged $\mathbf{C}_{2v}$ symmetry of the former is obliged to commute with the averaged $\mathbf{C}_s$ symmetry of the latter in their complexing conformations. The consequent loss by the diquat dication of its C_2 axis, along with the σ plane perpendicular to the mean plane of the tricyclic system allows the identification of sites X and Y for the pyridinium rings depending on whether they are *syn* or *anti* respectively to the R substituents on the benzo rings of **2** - **4**.[5] The resulting exchanges of H-3, H-4, H-5, and H-6 with H-3', H-4', H-5', and H-6', respectively between sites X and Y can be probed by low temperature ^{1}H n.m.r. spectroscopy in CD_3COCD_3 (Table 1).[6] In [Diquat.**2**]$^{2+}$, only H-3/3' exhibits peak separations , whereas, in [Diquat.**3**]$^{2+}$, all pairs of constitutionally homotopic protons, with the exception of H-6/6', separate into equal intensity signals. In [Diquat.**4**]$^{2+}$, H-3/3', H-4/4', H-5/5', and H-6/6' all provide (see Figure 2) suitable low temperature probes for the dissociation-recombination process (*d*) illustrated in Figure 1. From the appropriate analyses [7] of the low temperature ^{1}H n.m.r. spectroscopic data, average $\Delta G_c^{\ddagger}$ values of 9.4, 9.4, and 9.8 kcal mol^{-1} are obtained (Table 1) for process *d* involving the 1:1 complexes of **2**, **3**, and **4**, respectively. A comparison with the free energies of complexation (see the $\Delta G°$ values in Table 2 for [Diquat.**2**][PF_6]$_2$, [Diquat.**3**][PF_6]$_2$, and [Diquat.**4**][PF_6]$_2$ in acetone indicates that the association of the 1:1 complexes is close to being diffusion controlled (*i.e.* $\Delta G_a^{\ddagger}$ = *ca.* 3 kcal mol^{-1}) at least [8] in the case of the molecular

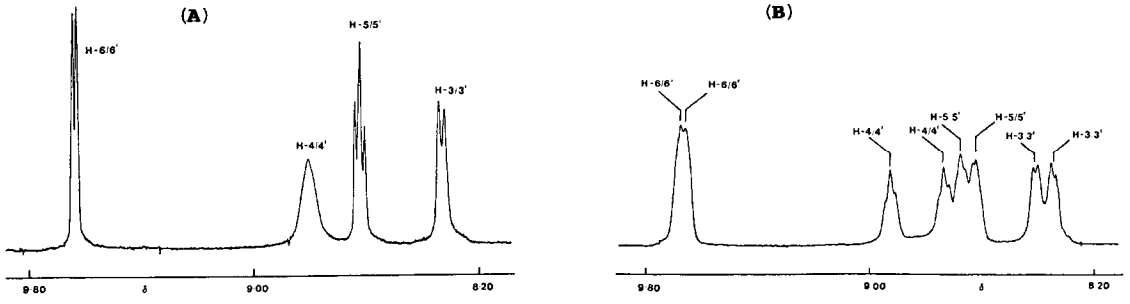

Figure 2. Partial ^{1}H n.m.r. spectra for [Diquat.**4**][PF_6]$_2$ recorded on a Bruker WH 400 Spectrometer at (**A**) -60°C and (**B**) -84°C in CD_3COCD_3. Only the signals for the protons on the pyridinium rings of the diquat dication are shown.

Table 1. Temperature dependent ^{1}H n.m.r. spectroscopic data and thermodynamic parameters for 1:1 complexes formed between diquat bishexafluorophosphate and the molecular receptors **2** - **4**. [a]

1:1 Complex [b]	^{1}H N.m.r. probe	T_c, ±3 (°C)	Δν, ±2 (°C) (Hz)	k_c (s^{-1})	$\Delta G_c^{\ddagger}$, ±0.3 (kcal mol^{-1})
[Diquat.**2**][PF_6]$_2$	H-3/3'	-71	132 (-97)	293	9.4
[Diquat.**3**][PF_6]$_2$	H-3/3'	-74	64 (-91)	142	9.5
[Diquat.**3**][PF_6]$_2$	H-4/4'	-83	32 (-100)	71	9.3
[Diquat.**3**][PF_6]$_2$	H-5/5'	-84	24 (-100)	53	9.4
[Diquat.**4**][PF_6]$_2$	H-3/3'	-76	24 (-84)	53	9.8
[Diquat.**4**][PF_6]$_2$	H-4/4'	-70	72 (-81)	160	9.7
[Diquat.**4**][PF_6]$_2$	H-5/5'	-78	24 (-96)	53	9.7
[Diquat.**4**][PF_6]$_2$	H-6/6'	-81	8 (-96)	18	9.9

[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 parenthesis; k_c, exchange rate constant at T_c calculated from the approximate expression, $k_c = \pi\Delta\nu/(2)^{\frac{1}{2}}$, for protons undergoing exchange (Figure 1) between equally populated sites X and Y which are not mutually coupled; $\Delta G_c^{\ddagger}$, free energy of activation at T_c from the Eyring equation.

[b] At ambient temperature, the chemical shifts (δ) for H-3/3' (d), H-4/4' (t), H-5/5' (t), and H-6/6' (d), respectively were as follows: in [Diquat][PF_6]$_2$, 9.19, 9.06, 8.56, 9.44; in Diquat.**2**][PF_6]$_2$, 8.55, 8.79, 8.59, 9.63; in [Diquat.**4**][PF_6]$_2$, 8.24, 8.64, 8.42, 9.46. At the time of writing this communication, chemical shift data for [Diquat.**3**][PF_6]$_2$ recorded at 400 MHz at ambient temperature were not available.

receptors **3** and **4**. These results suggest that, although the bicyclic receptor molecule **1** binds the diquat dication more strongly than **2** - **5**, the thermodynamic stability [9] ($\Delta G°$ = -7.4 kcal mol^{-1}) falls short of that expected on the basis of its kinetic stability [3] ($\Delta G_d^{\ddagger}$ = 12.4 kcal mol^{-1}). Hence, a $\Delta G_a^{\ddagger}$ value of *ca.* 5 kcal mol^{-1} suggests that an energy demanding conformational change within **1** must precede its association with the diquat dication. The data recorded in Table 2 confirm the existence of a macrobicyclic cryptate effect [10] for [Diquat.**1**][PF_6]$_2$, which leads [3] to enhance complexation of $[Diquat]^{2+}$ by **1** relative to that by dibenzo-30-crown-10 (**5**) and its 2,20-bisformyl, -bishydroxymethyl, and -dimethyl derivatives, **2**, **3**, and **4**.

Table 2. A comparison of the thermodynamic and kinetic stabilities of the 1:1 complexes formed between diquat bishexafluorophosphate and molecular receptors **1** - **5**.

Molecular receptor	**1**	**2**	**3**	**4**	**5**
$\Delta G°$ (kcal mol^{-1})	-7.4 [a]	-4.5 [b]	-6.4 [b]	-6.4 [b]	-5.8 [c]
$\Delta G_d^{\ddagger}$ (kcal mol^{-1})	12.4 [a]	9.4 [d]	9.4 [d]	9.8 [d]	-

[a] See ref 3. [b] See ref 2. [c] See ref 4.

[d] Average values obtained from Table 1. $\Delta G_c^{\ddagger}$ can be equated with $\Delta G_d^{\ddagger}$ in this instance.

Although considerable progress has been made towards designing a tailor-made receptor molecule for the diquat dication, we regard the macrobicyclic host **1** as only a first generation receptor: the challenge now is to synthesise a receptor molecule with a rigidly defined cavity of the appropriate size and shape, both sterically and electronically, to encapsulate $[Diquat]^{2+}$. The importance of this objective resides in the potentially interesting and significant properties of the complexes themselves: in particular, their redox behaviour and photochemical characteristics are likely to be worthy of detailed investigation.

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1. On leave of absence from Dipartimento di Chimica Organica e Biologica, Università di Messina, Messina, Italy.

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3. F.H. Kohnke and J.F. Stoddart, *J. Chem. Soc., Chem. Commun.*, 1985, 000.

4. H.M. Colquhoun, E.P. Goodings, J.M. Maud, J.F. Stoddart, D.J. Williams, and J.B. Wolstenholme, *J. Chem. Soc., Chem. Commun.*, 1983, 1140; *J. Chem. Soc., Perkin Trans. 2*, 1985, 000.

5. The **desymmetrisation** of the diquat dication can be expressed in another way with reference to sites X and Y occupied by the pyridinium rings: the polyether chain (*i.e.* the one with the α-β-γ-δ-OCH_2 group sequence), which is *meta* to the R substituents, is *syn* to site X and *anti* to site Y: the polyether chain (*i.e.* the one with the α'-β'-γ'-δ'-OCH_2 group sequence), which is *para* to the R substituents, is *anti* to site X and *syn* to site Y.

6. Unlike $[Diquat.\mathbf{1}]^{2+}$ where the conformational inversion (*i*) of **1** is a relatively slow process, in the case of the 1:1 complexes involving **2** - **4**, the ring inversion of the molecular receptors is fast on the ^1H n.m.r. time scale and $\Delta G_d^{\ddagger} > \Delta G_{d+i}^{\ddagger} > \Delta G_i^{\ddagger}$.

7. We have assumed that the exchange process *d* is governed (*cf.* M.R. Johnson, I.O. Sutherland, and R.F. Newton, *J. Chem. Soc., Perkin Trans. 1*, 1979, 357) by a unimolecular dissociative-recombination mechanism (F. de Jong, D.N. Reinhoudt, C.J. Smit, and R. Huis, *Tetrahedron Lett.*, 1976, 4783; F. de Jong, D.N. Reinhoudt, and R. Huis, *Tetrahedron Lett.*, 1977, 3985; F. de Jong and D.N. Reinhoudt, *Adv. Phys. Org. Chem.*, 1980, **17**, 279).

8. The $\Delta G_d^{\ddagger}$ value of 9.4 kcal mol^{-1} for $[Diquat.\mathbf{2}][PF_6]_2$ is unexpectedly high beside the $\Delta G°$ value of -4.5 kcal mol^{-1}. This would imply that association is considerably slower than diffusion-controlled for this 1:1 complex. If this is so, the reason for it is unclear.

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