COMPLEXATION OF DIQUAT BY DISUBSTITUTED DIBENZO-30-CROWN-10 DERIVATIVES
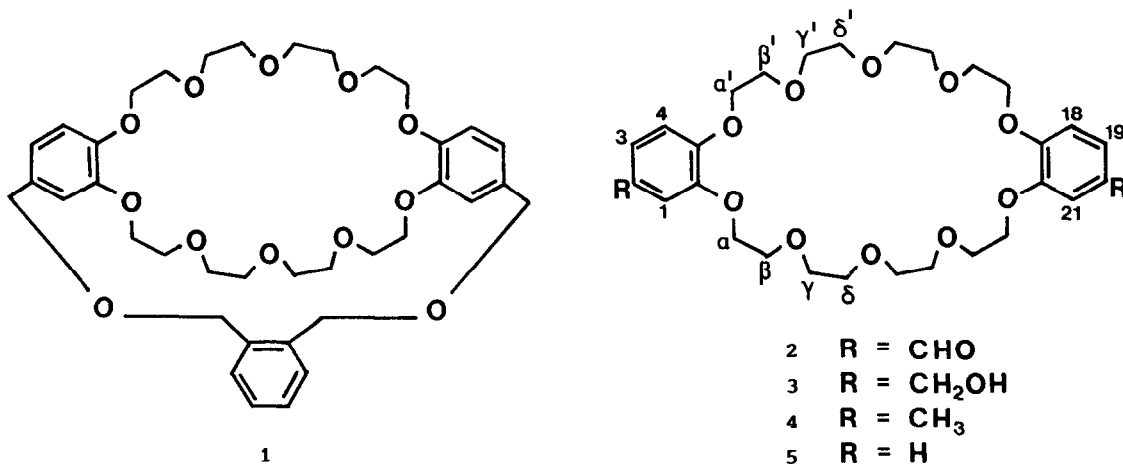
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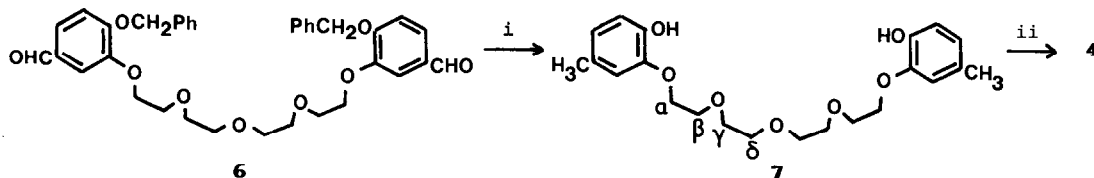Department of Chemistry, The University, Sheffield S3 7HF

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*X-Ray structural investigations of the 1:1 crystalline complexes formed
between [Diquat][PF$_6$]$_2$ and (i) the bisformyl dibenzo-30-crown-10 deriv-
ative 2 and (ii) the dimethyl dibenzo-30-crown-10 derivative 4 reveal
that in both cases, charge transfer, as well as electrostatic binding
and weak [C—H···O] hydrogen bonding combine to give the complexes their
remarkable stabilities; in acetone solution, the stability constants
for the 1:1 complexes involving 2, 3, and 4 are 2100, 50000, and 48000
M^{-1}, respectively.*

Recently, we described [2] an eight-step synthesis of the macrobicyclic receptor molecule
1 and showed that this host molecule encapsulates the diquat [3] dication in both the solid state
and in solution [2,4]. Two disubstituted dibenzo-30-crown-10 derivatives, **2** and **3** (*i.e.* the
2,20-bisformyl and 2,20-bishydroxymethyl derivatives, respectively) were isolated and charact-
ised *en route* to **1**. Here, we report on (**i**) the regioselective synthesis [5] of the 2,20-di-
methyl derivative **4**, (**ii**) the X-ray structural analyses [6] that have been successfully carried
out on 1:1 complexes of **2** and **4** with diquat bishexafluorophosphate, [Diquat][PF$_6$]$_2$ [7], and (**iii**)
measurements of stability constants in acetone solution [8] for 1:1 complex formation between
[Diquat][PF$_6$]$_2$ and all three 2,20-disubstituted dibenzo-30-crown-10 derivatives, namely **2**, **3**,
and **4**.

Previously, we have reported [2] that under carefully controlled conditions (i in Scheme 1,
but only for 3.5 h), hydrogenolysis of the benzyl ether protecting groups in **6** can be effected
prior to the onset of extensive reduction of the CHO groups. However, on prolonged exposure

2   R = CHO
3   R = CH$_2$OH
4   R = CH$_3$
5   R = H

OCH$_2$Ph PhCH$_2$O OH HO

OHC CHO H$_3$C CH$_3$ ii → 4

6 7

i → ii →

Scheme 1. Reagents and conditions: i, H$_2$ (atmos. press.), 10% Pd/C, CH$_2$Cl$_2$, RT, 36 h; ii, Ts[OCH$_2$CH$_2$]$_4$OTs, NaH, THF, reflux, 24 h.

(36 h) of **6** to H$_2$ under the same catalytic conditions, not only does hydrogenolysis of the benzyl ether protecting groups occur, but so also does the hydrogenation-hydrogenolysis sequence, CHO → CH$_2$OH → CH$_3$, associated with **6** → **7** in Scheme 1. The acyclic polyether **7** can be isolated in 98% yield as an oil. Base-promoted reaction (ii in Scheme 1) with Ts[OCH$_2$CH$_2$]$_4$OTs[9] afforded **4**, m.p. 72-75°C (ex. MeOH), in 44% yield after SiO$_2$ chromatography (CHCl$_3$-MeOH).

The vapour diffusion method[10] was employed successfully in three separate experiments[11] with **2**, **3**, and **4** to obtain 1:1 crystalline complexes with [Diquat][PF$_6$]$_2$. Although, in all three instances, the single crystals were of suitable quality for X-ray structural investigations, in the case of [Diquat.**3**][PF$_6$]$_2$, the determination of the structure is proving to be particularly demanding because of the presence of two crystallographically independent molecules in a non-centrosymmetric space group ($P222_1$) and the consequent requirement to determine the positions of a minimum of 140 non-hydrogen atoms. The structural analyses of [Diquat.**2**][PF$_6$]$_2$ (Figure 1) and [Diquat.**4**][PF$_6$]$_2$ (Figure 2) demonstrate forcibly the elegant complexing ability of the dibenzo-30-crown-10 moiety with the diquat dication despite the addition of substituents on to the benzo rings. The conformations of the polyether chains in both molecules differ little from those observed[2,8] for [Diquat.**1**][PF$_6$]$_2$ and [Diquat.**5**][PF$_6$]$_2$. There is appreciable thermal anisotropy in the C(3) to C(9) and in the C(20) to C(24) portions of the macrocycle in [Diquat.**4**] [PF$_6$]$_2$; this thermal motion is less pronounced in [Diquat.**2**][PF$_6$]$_2$. In both cases, binding of the dication is by a combination of (**i**) [C—H···O] hydrogen bonding, (**ii**) electrostatic bonding between the nitrogen atoms and the catechol oxygen atoms, and (**iii**) charge transfer interactions between the almost parallel π-electron-rich benzo-rings and the π-electron-deficient bipyridinium dication.

Evidence for the stoicheiometry of the solution complexes, together with measurements of their stability constants (K_a) and derived free energies of complexation ($\Delta G°$) for the equilibria, [Diquat][PF$_6$]$_2$ + **2**,**3**,or **4** $\rightleftharpoons$ [Diquat.**2**,**3**,or **4**][PF$_6$]$_2$, were obtained from a treatment[8] of the dependence on concentrations of the absorption bands at 400 nm in acetone for 1:1 mixtures of [Diquat][PF$_6$]$_2$ with **2**, **3**, or **4**. For **2**, **3**, and **4**, respectively, K_a = 2100, 50000, and 48000 dm^3 mol^{-1} corresponding to $\Delta G°$ = -4.5, -6.4, and -6.4 kcal mol^{-1}. These values should be compared[8] with K_a and $\Delta G°$ values of 17500 dm^3 mol^{-1} and -5.8 kcal mol^{-1} for [Diquat.**5**][PF$_6$]$_2$ in acetone. The order (**3** $\cong$ **4** > **5** > **2**) of stabilities of the 1:1 complexes involving the receptor molecules **2** - **5** is in accord with expectation.[12] Just as the presence of electron-withdrawing CHO groups at the 2 and 20 positions of the catechol rings should decrease their π-donor capabilities, so the presence of electron-donating CH$_3$ groups in these positions should enhance the ability of the catechol rings to act as π-donors towards the π-electron deficient bipyridinium dication. It is unlikely, however, that the explanation of the relative stabilities of
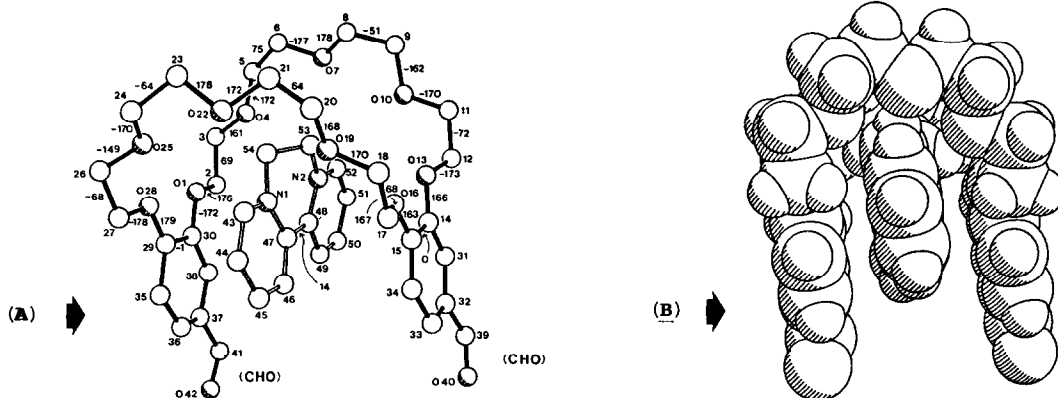
Figure 1. The solid state structure in both framework (A) and space-filling (B) representations of the 1:1 complex formed between the diquat dication and the bisformyl dibenzo-30-crown-10 derivative **2**. Torsional angles (°) (O—C—C—O and C—C—O—C) associated with the 30-membered ring are shown beside the relevant C—C and C—O bonds on the framework representation (A). Selected hydrogen contact distances, $R[C\cdots O]$, $R[H\cdots O]$ (Å), angles (°) between COC planes and HO vectors, C—H$\cdots$O angles (°) at H atoms assuming normal trigonal and tetrahedral geometry: [C(43)$\cdots$O(22)], 3.20, [H(43)$\cdots$O(22)], 2.26, 41, 165; [C(52)$\cdots$O(7)], 3.37, [H(52)$\cdots$O(7)], 2.48, 42, 153; [C(52)$\cdots$O(10)], 2.99, [H(52)$\cdots$O(10)], 2.28, 9, 130. Separation (Å) between pyridinium ring N in guest and phenolic O in host: N(1)$\cdots$O(28), 3.41; N(2)$\cdots$O(13), 3.19. Twist angle between the pyridinium rings in the guest: 14°. Separation between the benzo rings in the host of 6.92 Å with a 3.8° departure from parallel alignments of their mean planes.
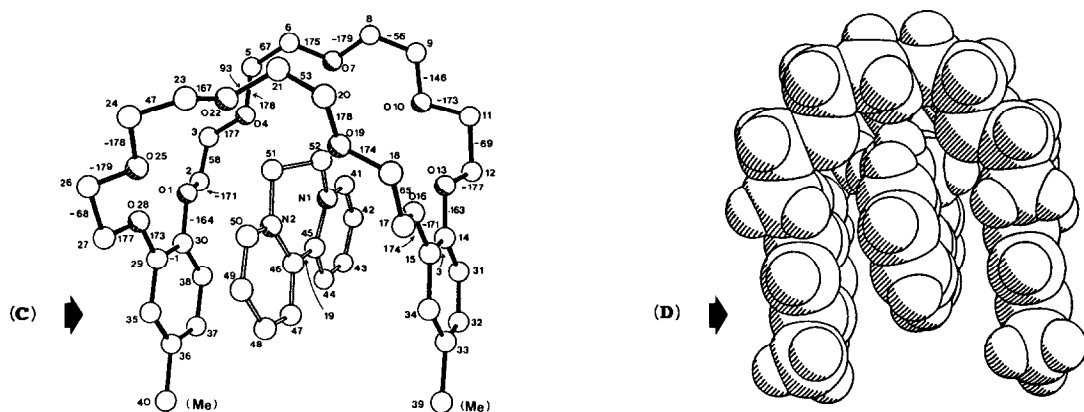

Figure 2. The solid state structure in both framework (C) and space-filling (D) representations of the 1:1 complex formed between the diquat dication and the dimethyl dibenzo-30-crown-10 derivative **4**. Torsional angles (°) (O—C—C—O and C—C—O—C) associated with the 30-membered ring are shown beside the relevant C—C and C—O bonds on the framework representation (C). Selected hydrogen contact distances, $R[C\cdots O]$, $R[H\cdots O]$ (Å), angles (°) between COC planes and HO vectors, C—H$\cdots$O angles (°) at H atoms assuming normal trigonal and tetrahedral geometry: [C(41)$\cdots$O(10)], 3.11, [H(41)$\cdots$O(10)], 2.40, 7, 130; [C(50)$\cdots$O(25)], 3.14, [H(50)$\cdots$O(25)], 2.44, 0, 130; [C(51)$\cdots$O(1)], 3.32, [H(51)$\cdots$O(1)], 2.42, 49, 156; [C(51)$\cdots$O(22)], 3.42, [H(51)$\cdots$O(22)], 2.50, 11, 159; [C(52)$\cdots$O(16)], 3.33, [H(52)$\cdots$O(16)], 2.45, 39, 153. Separation (Å) between pyridinium ring N in guest and phenolic O in host: N(1)$\cdots$O(13), 3.21; N(2)$\cdots$O(28), 3.41. Twist angle between the pyridinium rings in the guest: 19°. Separation between the benzo rings in the host of 6.92 Å with a 4.7° departure from parallel alignments of their mean planes.

the 1:1 complexes is as straightforward as this: the stabilising pole-dipole intermolecular interactions are probably also influenced by the nature of the substituents at C-2 and C-20.

The following communication reveals that the thermodynamic stabilities of the 1:1 complexes involving molecular receptors **2 – 4** are also reflected in their kinetic stabilities as determined by [1]H n.m.r. spectroscopy.

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

2. B.L. Allwood, F.H. Kohnke, A.M.Z. Slawin, J.F. Stoddart, and D.J. Williams, *J. Chem. Soc., Chem. Commun.*, 1985, 000.

3. The systematic name for diquat is 6,7-dihydrodipyrido[1,2-a:2',1'-c]pyrazinediium. For a recent review of the chemistry of diquat, see L.A. Summers, 'The Bipyridinium Herbicides,' Academic Press, London, 1980.

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

5. Both new compounds gave satisfactory analytical and [1]H n.m.r. spectroscopic data: for **7**, δ ($CDCl_3$-D_2O, 220 MHz) 2.20 (6H, s, 2xCH_3), 3.60-3.75 (8H, m, γ- and δ-OCH_2 protons), 3.75-3.84 (4H, m, β-OCH_2 protons), 4.07-4.17 (4H, m, α-OCH_2 protons), and 6.50-6.80 (6H, m, aromatic protons); for **4**, δ ($CDCl_3$, 220 MHz) 2.22 (6H, s, 2xCH_3), 3.61-3.70 (8H, m, δ- and δ'-OCH_2 protons), 3.70-3.80 (8H, m, γ- and γ'-OCH_2 protons), 3.80-3.90 (8H, m, β- and β'-OCH_2 protons), 4.05-4.15 (8H, m, α- and α'-OCH_2 protons), 6.65 and 6.75 (4H, AB system, J_{AB} = 8 Hz, H-3, H-4, H-18, and H-19), and 6.77 (2H, s, H-1 and H-21).

6. Crystal data: for [Diquat.**2**][PF_6]$_2$.0.75 CH_3CN, $C_{43.5}H_{54.25}O_{12}N_{2.75}P_2F_{12}$, M = 1087, orthorhombic, space group $P2_1cn$, a = 11.445(2), b = 20.417(4), c = 21.397(5) Å, U = 5000 Å^3, Z = 4, D_c = 1.45 g cm^{-3}. R = 0.115, R_w = 0.118 for 2338 independent observed reflections [θ ≤ 55°, $|F_o|$ > 3σ($|F_o|$)]; for [Diquat.**3**][PF_6]$_2$, orthorhombic, space group $P222_1$, a = 11.342(4), b = 22.064(6), c = 39.40(2), U = 9859 Å^3, Z = 8; for [Diquat.**4**][PF_6]$_2$.H_2O, $C_{42}H_{58}O_{11}N_2P_2F_{12}$, M = 1057, monoclinic, a = 11.698(2), b = 19.112(4), c = 22.182(5) Å, β = 97.32(2)°, U = 4919 Å^3, space group $P2_1/n$, Z = 4, D_c = 1.43 g cm^{-3}. R = 0.122, R_w = 0.126 for 3602 independent observed reflections [θ ≤ 50°, $|F_o|$ > 3σ($|F_o|$)]. In all cases, data were measured on a Nicolet R3m diffractometer with graphite monochromated Cu-K$_\alpha$ radiation using the ω-scan routine. The structures of [Diquat.**2**][PF_6]$_2$.0.75 CH_3CN and [Diquat.**4**][PF_6]$_2$.H_2O were solved by direct methods and the non-hydrogen atoms refined anisotropically. E-Maps computed for the phase solutions with the highest figures of merit gave plausible solutions for 21 of the 73 non-hydrogen atoms in the first structure and 43 of the 69 non-hydrogen atoms in the second. The remaining atoms were located in subsequent ΔF maps. In each structure, both PF_6^- groups were refined as rigid bodies. Thermal motion in the structures was high, being particularly pronounced in the PF_6^- groups and in portions of the polyether chains. The atomic coordinates are available from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratories, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation of this communication.

7. C.M. Elliot and E.J. Hershenhart, *J. Am. Chem. Soc.*, 1982, **104**, 7519.

8. 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, 0000.

9. J. Dale and P.O. Kristiansen, *Acta Chem. Scand.*, 1972, **26**, 1471.

10. P.G. Jones, *Chem. Brit.*, 1981, **17**, 222.

11. Experimental: [Diquat.**2**][PF_6]$_2$.0.75 CH_3CN:- [Diquat][PF_6]$_2$ (24 mg, 0.050 mmol) and **2** (30 mg, 0.050 mmol) were dissolved in CH_3CN (*ca.* 1 ml) and deep orange crystals, m.p. 138-140°C, were obtained after 24 h by vapour diffusion with Et_2O-CH_3CN. [Diquat.**3**][PF_6]$_2$:- [Diquat][PF_6]$_2$ (24 mg, 0.050 mmol) and **3** (30 mg, 0.050 mmol) were dissolved in CH_3OH (1 ml)-CH_3COCH_3 (0.5 ml) by warming and deep red crystals, m.p. 161-162.5°C, were obtained after 24 h by vapour diffusion with heptane-light petroleum. [Diquat.**4**][PF_6]$_2$.H_2O:- [Diquat][PF_6]$_2$ (25 mg, 0.053 mmol) and **4** (30 mg, 0.053 mmol) were dissolved in CH_3OH (1 ml)-CH_3COCH_3 (0.3 ml) by warming and deep red crystals, m.p. 149-153°C, were obtained after 24 h by vapour diffusion with light petroleum. All three complexes afforded satisfactory results for their elemental analyses.

12. R. Foster, 'Organic Charge-Transfer Complexes', Academic Press, London, 1969, p. 179-215.