

A New Allosteric Bis Crown Ether Ligand that displays Negative Binding Co-operativity of the Diquat Dication by the Complexation of a Transition Metal Guest

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The synthesis of a new allosteric 2,2'-bipyridyl bis crown ether ligand (**3**) that binds the diquat dication is described; chelation of a transition metal at the allosteric bipyridyl site forces the bipyridyl function towards coplanarity, restricting the conformational freedom of the two benzo-15-crown-5 moieties in such a way as to disfavour the subsequent binding of diquat.

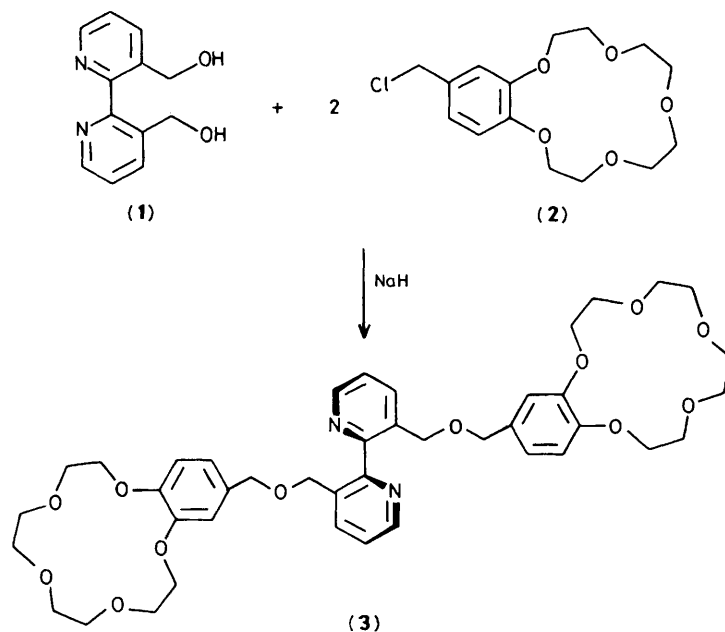
Macrocyclic molecules are able to provide suitable frameworks for the arrangement in space of several recognition sites, allowing the binding of several guest substrates.¹⁻⁴ Upon complexation these multisite receptors can act as models for demonstrating higher forms of molecular behaviour such as co-operativity, allostery, and regulation.^{1,5,7} This communication reports the synthesis of a novel allosteric bis crown ether ligand (**3**) containing a 2,2'-bipyridyl (bipy) fragment whose binding of the diquat dication (**4**) substrate is dependent upon the absence of a cobound transition metal guest at the bipyridyl allosteric site.

The condensation of 3,3'-bis(hydroxymethyl)-2,2'-bipyridine (**1**)⁸ and 2 equiv. of 4-chloromethylbenzo-15-crown-5 (**2**)⁹ in the presence of sodium hydride gave the bis crown ether ligand (**3**) in 77% yield. Its structure was verified by elemental analysis, mass spectrometry, and ¹H and ¹³C n.m.r. spectroscopy.

Upon mixing colourless equimolar acetonitrile solutions of (**3**) and (**4**) orange-yellow solutions are obtained instantaneously. Stoddart and co-workers¹⁰ have recently reported that similar colours result from (**4**) and dibenzo-crown ether mixtures. These colours are attributed to charge transfer between the electron-rich catechol units of the dibenzo-crown ether moieties and the electron deficient bipyridinium ring system of the diquat dication. Figure 1 shows the charge transfer absorption bands of (**4**) and its 1:1 complexes with (**3**) and selected crown ethers. Clearly the weak absorption band of (**4**) (λ_{max} ca. 400 nm in acetonitrile) is enhanced in the presence of (**3**). The isolation of a dark orange-red crystalline solid of (**3**)·(**4**) with 1:1 host-guest stoichiometry[†] was successfully achieved from an acetone/hexane solvent mixture of both compounds.

[†] Satisfactory elemental analyses and conductivity measurements were obtained for this complex. (**3**)·(**4**)·2PF₆⁻·H₂O requires C 51.1, H 5.2, N 4.4%. Found C 50.5, H 5.2, N 4.7%.

High field ¹H n.m.r. spectroscopy was used to study the binding of (**4**) by (**3**) in solutions of CD₃COCD₃. Table 1 reports the significant large upfield shifts for all the bipyridyl protons of the guest and the benzo-crown ether aromatic protons of the host.[‡] The sign and magnitude of these shifts suggest that the planar dicationic guest (**4**) intercalates between the two benzo-crown ether subunits of the host resulting in parallel stacking of the respective aromatic rings



[‡] No enhanced charge transfer band and $\Delta\delta$ chemical shifts were observed with (**1**) and (**4**).

Table 1. $\Delta\delta$, ^1H n.m.r. chemical shift differences of guest (4) upon complexation with hosts (3) and (6) in CD_3COCD_3 ^a

	H(6), (6') ^b	H(3), (3') ^b	H(4), (4') ^b	H(5), (5') ^b	(NCH_2) ₂ ^b	Benzo-crown aromatic C ₆ H ₃ ^c	(3) (6)
(4)	9.51	9.25	9.10	8.61	5.70	6.80	6.81
(4)·(3)	9.35	9.02	8.95	8.49	5.62	6.71	—
$\Delta\delta$	-0.16	-0.23	-0.15	-0.12	-0.08	-0.09	—
(4)·(6)	9.49	9.20	9.07	8.59	5.69	—	6.81
$\Delta\delta$	-0.02	-0.05	-0.03	-0.02	-0.01	—	0.00

^a Spectra recorded at 400 MHz, ambient temperature with Me_4Si internal reference. ^b Guest (4) proton signals. ^c Host proton signals.

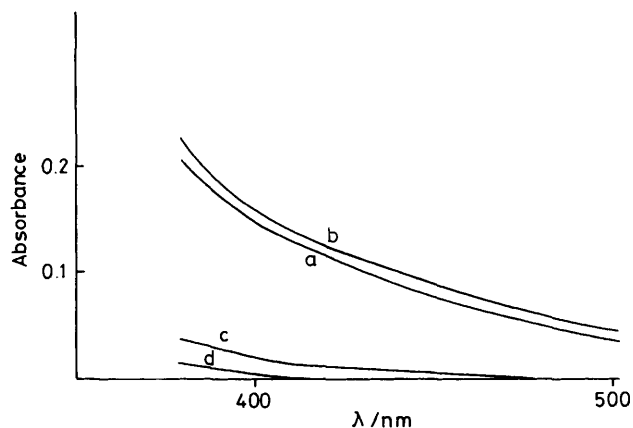
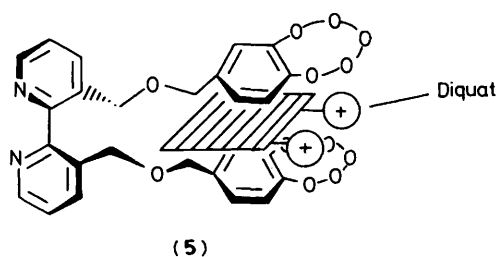
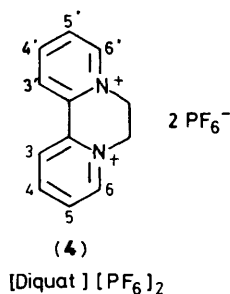
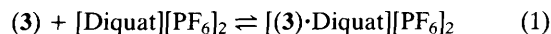


Figure 1. Charge-transfer absorption bands of (4) and its 1:1 complexes with (3) and benzo-crown ethers in acetonitrile (3×10^{-3} M; 1 cm cell). a, [Diquat]²⁺(3); b, [Diquat]²⁺ dibenzo-24-crown-8; c, [Diquat]²⁺ benzo-15-crown-5; d, [Diquat]²⁺.

(5). This solution host-guest orientation, similar to that found with (4) and dibenzo-30-crown-10,¹⁰ would cause the anisotropic diamagnetic susceptibility of one aromatic system to alter the local magnetic field which is experienced by ^1H nuclei attached to the other aromatic system. Further evidence for this proposed host-guest structure (5) in solution was obtained using nuclear Overhauser effect (n.o.e.) difference spectroscopy.¹¹ Irradiation of the (NCH_2)₂ protons of (4) resulted in significant changes in the intensities of the crown OCH_2 proton absorptions of (3) only. This result suggests the (NCH_2)₂ protons of (4) are involved in weak $\text{C-H} \cdots \text{O}$ hydrogen bonding with the oxygen donor atoms of the benzo-crown ether moieties.

The stoichiometry of the solution (3)·(4) complex was found to be 1:1 with an association constant (K_a) of $400 \text{ dm}^3 \text{ mol}^{-1}$ and calculated free energy of complexation (ΔG°) of $-3.6 \text{ kcal mol}^{-1}$ (equation 1) ($1 \text{ cal} = 4.184 \text{ J}$). These values, although smaller in magnitude, compare well with

those of the (4) dibenzo-crown ether complexes reported by Stoddart.¹⁰

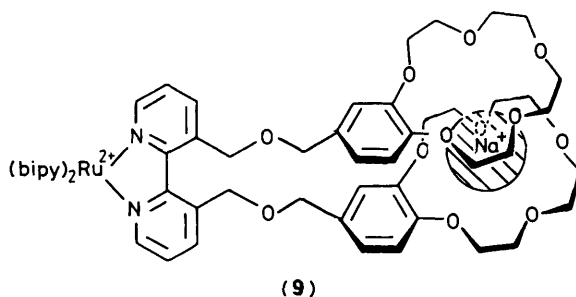
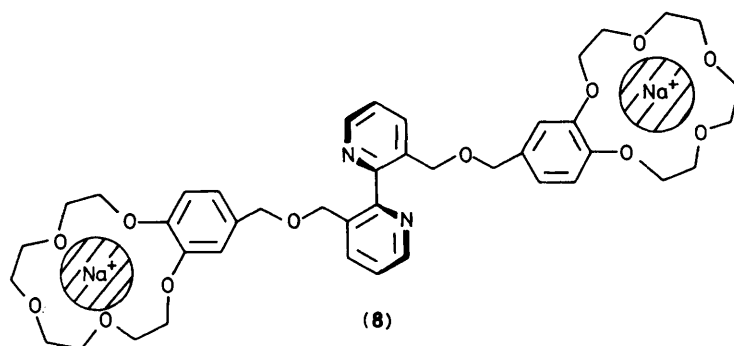


Molecular models (Corey-Pauling-Koltun) of (3) indicated that chelation of a transition metal at the bipyridyl nitrogens would force the bipyridyl function towards coplanarity resulting in the restriction of conformational freedom of the two benzo-crown ether groups. It was of interest therefore to study this effect of allosteric transmission of binding information from one co-ordinating site to another on the complexation of (4). The reaction of (3) with $(\text{bipy})_2\text{RuCl}_2 \cdot 2\text{H}_2\text{O}$ followed by NH_4PF_6 gave $[(\text{bipy})_2\text{Ru}(3)](\text{PF}_6)_2$ (6) as an orange crystalline solid (λ_{max} , 456 nm, ϵ $1.57 \times 10^4 \text{ mol}^{-1} \text{ cm}^{-1}$). Subsequent ^1H n.m.r. binding studies of (6) with diquat (4) in CD_3COCD_3 revealed only very small upfield shifts for the bipyridyl protons of the guest (maximum shift observed -0.05 p.p.m. Table 1) and the absence of a charge transfer band at $\lambda = 425 \text{ nm}$.[§] Analogous findings were also obtained with the chromium complex $[(\text{CO})_4\text{Cr}(3)]$ (7).

These results imply that the presence of a transition metal at the allosteric bipyridyl nitrogens site of (3) leads to a rigid conformation of the two benzo-crown ether moieties which is not favourable for the subsequent binding of (4).

To rationalise this allosteric effect further, complexation studies of (3) and (6) with the spherical sodium cationic guest were undertaken. Refluxing a methanolic solution of (3) with excess of NaPF_6 led to the successful isolation of a crystalline complex $(3) \cdot 2\text{NaPF}_6$ (8). In contrast, the reaction of (6) with NaPF_6 gave $[(\text{bipy})_2\text{Ru}(3)\text{Na}](\text{PF}_6)_3$ (9). These observed stoichiometries, all confirmed by elemental analyses and conductivity measurements suggest that the sodium guest cation only forms an intramolecular sandwich complex with the two benzo-crown ether groups in the presence of Ru^{II}

[§] No spectroscopic evidence for the existence of a charge transfer complex resulting from (6) itself or equimolar mixtures of (6) and $\text{Ru}(\text{bipy})_3^{2+}$ or (6) and benzo-crown ethers was found, negating the possibility of co-ordination-induced-self-complexation (second sphere co-ordination)¹² of (6) reducing the affinity of binding for diquat.



(6) = (9) without Na⁺

chelated at the bipyridyl function. Thus, the probable rigid solution conformation of (6) has the two benzo-crown ether moieties held in close proximity, cofacial to each other, disfavoured the intercalation of the planar diquat dication, but favouring the formation of intramolecular sandwich complexes with spherical alkali metal cationic guests.

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