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DIAZADIBENZO-30-CROWN-10 DERIVATIVES AS RECEPTORS FOR DIQUAT

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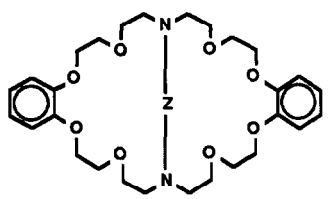
*In acetone-d_6 solution, ^1H n.m.r. spectroscopy reveals that receptors **4-9**, prepared from the readily-synthesised diazadibenzo-30-crown-10derivative **1**, form strong 1:1 molecular inclusion complexes with Diquat, which, although present mainly as the dication, is accompanied by trace amounts of the radical cation.*

Our observation[2] that dibenzo-30-crown-10 (**DB30C10**) forms a strong 1:1 complex in organic solvents with [Diquat][PF_6]$_2$ led[3] to the synthesis of bicyclic **DB30C10** derivatives which exhibited only slightly better receptor properties than **DB30C10** itself. Another means[4] by which the complexation of substrates containing hydrogen bond donors might be enhanced would be to replace some O atoms in the polyether chains by NR groups. Here, we report on *(i)* the stepwise synthesis of the diazadibenzo-30-crown-10 derivative **1**, *(ii)* the characterisation[5] of the *N,N*-disubstituted derivatives **2-7** and the cryptands **8** and **9**, and *(iii)* some spectroscopic investigations on the structures and strengths of their 1:1 complexes formed with [Diquat]$^{2+}$ in solution. In addition to providing the basis for a comparison between O- and NR-containing receptors, the presence of N atoms in **1** allows side arms, incorporating additional binding sites[6], to be introduced. This synthetic modification could be used to locate two anionic binding sites in a receptor that might exhibit aqueous solubility[7] whilst still complexing with [Diquat]$^{2+}$.

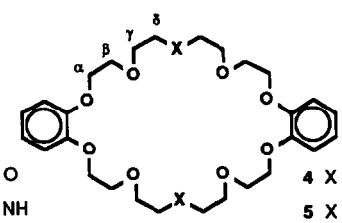
Alkylation of *p*-toluenesulphonamide (K_2CO_3, DMF, 100°C, 48 h) with 2-(2-chloroethoxy)ethanol gave (SiO_2/EtOAc) **10** (68%, oil), which was converted (TsCl, C_5H_5N, 0°C) into **11** (95%, oil). Reaction (^{t}BuOK, THF, reflux, 18 h) of **11** with monobenzylcatechol[2] afforded [SiO_2/Et_2O-light petroleum (1:1, v/v)] **12** [74%, m.p. 87-88°C (MeOH-CH_2Cl_2)]. Hydrogenolysis (Pd/C, MeOH-CH_2Cl_2) gave **13** (~100%, m.p. 63-64°C), which, in a subsequent reaction (^{t}BuOK, THF, reflux, 40 h) with **11** yielded (SiO_2/5% EtOH-Et_2O) **2** [23%, m.p. 117-118°C (MeOH-CH_2Cl_2), single crystals suitable[8] for *X*-ray



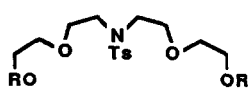
Z

8 CH_2-*p*-$C_6H_4CH_2$

9 CH_2-p-C_6H_4O(α′ β′ γ′ δ′ ε′)OC_6H_4-p-CH_2



DB30C10 X = O
1 X = NH
2 X = NTs
3 X = NCO_2Et
4 X = NMe
5 X = NCH_2CO_2Et
6 X = NCH_2Ph
7 X = NCH_2-*o*-C_6H_4OMe



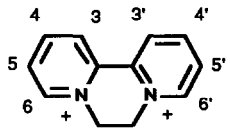
10 R = H **12** R = *o*-$C_6H_4OCH_2Ph$
11 R = Ts **13** R = *o*-C_6H_4OH

crystallography]; detosylation ($LiAlH_4$, THF, reflux, 12 days) gave **1** (66%, m.p. 85-87°C ($CHCl_3$-light petroleum)]. Reaction (Et_3N, $CHCl_3$-Et_2O, rt, 24 h) of **1** with ethyl chloroformate afforded (neutral Al_2O_3/5% EtOAc-$CHCl_3$) **3** (65%, oil) which was reduced ($LiAlH_4$, THF, reflux, 60h) to yield **4** [76%, m.p. 74-75°C (Me_2CO-$^nC_5H_{12}$)]. Alkylation (Na_2CO_3, MeCN, rt, 4 days) of **1** with ethyl bromoacetate gave (neutral Al_2O_3/10% EtOAc-$CHCl_3$) **5** (60%, m.p. 40-42°C). Alkylation (Na_2CO_3, MeCN, reflux, 48 h) of **1** with: (a) benzyl bromide gave [SiO_2/$CHCl_3$-EtOAc (1:1, v/v) **6** (64%, oil); (b) *p*-methoxybenzyl chloride afforded (SiO_2/EtOAc) **7** (71%, oil); (c) α,α'- dibromo-*p*-xylene gave (neutral Al_2O_3/10% EtOAc- $CHCl_3$) **8** [12%, m.p. 84-86°C (Me_2CO-$^nC_5H_{12}$)]; (d) 1,14-bis[4-bromoethyl)phenoxy]-3,6,9,12-tetraoxadecane[9] gave (neutral Al_2O_3/EtOAc) **9** (5%, oil).

The diazadibenzo-30-crown-10 derivatives **1**-**9** were evaluated as complexing agents for both $[Diquat]^{2+}$ and $[Paraquat]^{2+}$ by comparing ^1H n.m.r. spectra recorded in CD_3COCD_3 solutions for *(a)* the free receptors, *(b)* the free substrates, as their bishexafluorophosphates, and *(c)* 1:1 molar ratios of receptor:substrate mixtures. The results of these experiments were supported by following colour changes in solution arising from π–π charge transfer interactions between the π-electron rich receptors and π-electron deficient substrates, and also by attempting to isolate coloured crystalline complexes[10]. In addition to these charge transfer interactions, the intermolecular forces implicated in this type of complexation involve hydrogen bonding, Coulombic attractions, and dispersion forces. Possibly as a consequence of the combined electronic and steric characteristics associated with the amide N atoms in **2** and **3**, all of the potential non-covalent bonding interactions appear to be impaired to the extent that these receptors do not complex with either $[Diquat]^{2+}$ or $[Paraquat]^{2+}$. On the other hand, in the presence of equimolar amounts of $[Diquat][PF_6]_2$, the receptors **4**-**9** gave rise[11] to orange solutions, undoubtedly indicating charge transfer complex formation; this observation is reflected in the significant ^1H n.m.r. chemical shifts (Table 1) exhibited by the resonances[12] in [Diquat.**4**-**9**][PF_6]$_2$ compared with those observed for $[Diquat][PF_6]_2$. In common with [Diquat.**DB30C10**][PF_6]$_2$, the signals for both H-3/3' and H-4/4' in [Diquat.**4**-**9**][PF_6]$_2$ experience substantial upfield shifts suggesting that both the bipyridinium ring protons lie within the paratropic regions of the catechol rings. However, the signals for H-5,5' and H-6,6' behave quite differently in the complexes of the polyether (**DB30C10**) and diazapolyether (**4**-**9**) receptors; a consideration of the structural features present within these complexes suggests the following possible explanations: *(a)* the *N*-substituents in **4**-**9** might be influential; *(b)* the different hydrogen bonding characteristics could be responsible; *(c)* the stacking geometries of the aromatic rings could be dissimilar. Interestingly, the $(NCH_2)_2$ signal is shifted upfield by 0.23 ppm in [Diquat.**8**][PF_6]$_2$, indicating the location of this portion of the substrate within the shielding zone of the bridging xylyl unit of **8**. Receptor **10** was designed so that the chain Z might encircle the bound $[Diquat]^{2+}$ substrate: alas, the ^1H n.m.r. chemical shift data (Table 1) do not support the realisation of this stereochemical expectation.

In contrast with results obtained previously[2] for [Diquat.**DB30C10**][PF_6]$_2$, the ^1H n.m.r. spectra of the 1:1 complexes formed between $[Diquat][PF_6]_2$ and the diazadibenzo-30-crown-10 derivatives **4** and **6**-**9** exhibit[13] an interesting phenomenon: freshly prepared CD_3COCD_3 solutions of these complexes give rise to ^1H n.m.r. spectra in which the resonances for all the protons in $[Diquat]^{2+}$ are significantly broadened whilst all the signals for the protons in the receptors are well resolved. After standing for 2-4 h, the CD_3COCD_3 solutions employed to record the spectra of [Diquat.**4**][PF_6]$_2$ and [Diquat.**8**][PF_6]$_2$ exhibit sharp resonances for the substrate protons. However, even after standing for 16 h, the CD_3COCD_3 solutions of [Diquat.**6**][PF_6]$_2$, [Diquat.**7**][PF_6]$_2$, and [Diquat.**9**][PF_6]$_2$ afforded spectra where resonances for the substrate protons other than H-6/6' were still quite broad[14]. Most likely, the phenomenon arises[15] from the complexation of very small amounts (<0.01%)[16] of the paramagnetic radical cation – $[Diquat]^{+\cdot}$ – present initially and undergoing electron transfer with $[Diquat]^{2+}$. The presence of a radical cation, which is clearly quenched[17] by oxygen in the atmosphere, has been supported by recording the u.v. spectrum of [Diquat.**1**][PF_6]$_2$ in Me_2CO every 10 mins following preparation of the sample: an absorption at λ 380 nm, which has been assigned[18] to $[Diquat]^{+\cdot}$ disappears during 30 mins. Two interesting questions are raised: (1) why is $[Diquat]^{+\cdot}$ only observed when

Table 1. ^{1}H N.m.r. chemical shift data [δ values (Δδ values)][a] for solutions in CD_3COCD_3



PF_6^{2-}

	H-3/3'	H-4/4'	H-5/5'	H-6/6'	$^{+}(NCH_2)_2$
[Diquat][PF_6]$_2$	9.19	9.06	8.56	9.44	5.66
[Diquat.**4**][PF_6]$_2$[b]	8.29 (-0.90)	8.67 (-0.39)	8.47 (-0.09)	9.87 (+0.43)	5.75 (+0.09)
[Diquat.**5**][PF_6]$_2$[c]	8.47 (-0.72)	8.78 (-0.28)	8.53 (-0.03)	9.85 (+0.41)	5.68 (+0.02)
[Diquat.**6**][PF_6]$_2$[d]	← 8.98-9.07[f] →		8.58 (+0.02)	9.61 (+0.17)	5.72 (+0.06)
[Diquat.**7**][PF_6]$_2$[d]	← 8.98-9.08[f] →		8.58 (+0.02)	9.62 (+0.18)	5.72 (+0.06)
[Diquat.**8**][PF_6]$_2$[b]	8.73 (-0.41)	8.78 (-0.28)	8.54 (-0.02)	9.57 (+0.13)	5.43 (-0.23)
[Diquat.**9**]PF_6]$_2$[d]	← 9.01-9.06[f] →		8.59 (-0.34)	9.58 (+0.14)	5.75 (+0.09)
[Diquat.**DB30C10**][PF_6]$_2$[e]	8.59 (-0.60)	8.40 (-0.66)	8.22 (-0.34)	9.46 (+0.02)	5.72 (+0.06)

[a] Spectra were recorded at ambient temperature on a Bruker AM250 spectrometer using CD_2HCOCD_2H as reference. [b] Spectrum recorded 4 h after preparation of the sample. [c] Spectrum recorded immediately after preparation of the sample. [d] Spectrum recorded 16 h after preparation of the sample. [e] Values quoted from ref 2. [f] The broad line widths of the resonances does not allow an assignment to be made.

diazadibenzo-30-crown-10 derivatives are the receptors, and (2) why does the radical remain localised[19] in the substrate and not become delocalised through electron transfer to the receptors **4** and **6-9**?

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References and Footnotes

1. On leave of absence from Centro CNR, "Sintesi e Stereochimica di Speciali Sistemi Organici", Milano, Italy.
2. H.M. Colquhoun, E.P. Goodings, J.M. Maud, J.F. Stoddart, J.B. Wolstenholme, and D.J. Williams, *J. Chem. Soc. Perkin Trans.* 2, 1985, 607 and references therein.
3. B.L. Allwood, F.H. Kohnke, J.F. Stoddart, and D.J. Williams, *Angew. Chem. Int. Ed. Engl.*, 1985, **24**, 581 and references therein.
4. Aza-crowns have been shown (S.J. Leigh and I.O. Sutherland, *J. Chem. Soc. Chem. Commun.*, 1975, 414; J.F. Stoddart, *Chem. Soc. Rev.*, 1979, **8**, 85) to form stronger complexes with RNH_3^+ ions than the corresponding all-oxygen macrocycles.
5. All new compounds gave satisfactory analytical and ^{1}H n.m.r. spectroscopic data; δ (250 MHz, CD_3COCD_3) for **1** : 2.75 (8H, t, NCH_2), 3.61 (8H, t, γ-CH_2), 3.77 (8H, m, β-CH_2), 4.11 (8H, m, α-CH_2), 6.86-6.94 (8H, m, C_6H_4); for **2** : 2.35 (6H, s, Me), 3.42 (8H, t, NCH_2), 3.68 (8H, t, γ-CH_2), 3.70 (8H, m, β-CH_2), 4.03 (8H, m, α-CH_2), 6.86-6.92 (8H, m, C_6H_4), 7.30 & 7.72 (8H, AA'XX' system, $MeC_6H_4SO_2$); for **3** : 1.18 (6H, t, Me), 3.51 (8H, t, NCH_2), 3.67 (8H, t, γ-CH_2), 3.77 (8H, m, β-CH_2), 4.05 (4H, q, CO_2CH_2), 4.11 (8H, m, α-CH_2), 6.84-6.96 (8H, m, C_6H_4); for **4** : 2.29 (6H, s, Me), 2.61 (8H, t, NCH_2), 3.65 (8H, t, γ-CH_2), 3.78 (8H, m, β-CH_2), 4.10 (8H, m, α-CH_2), 6.84-6.96 (8H, m, C_6H_4); for **5** : 1.16 (6H, t, Me), 2.92 (8H, t, NCH_2), 3.54 (4H, s, NCH_2CO), 3.65 (8H, t, γ-CH_2), 3.78 (8H, m, β-CH_2), 4.05

(4H, q, CO_2CH_2), 4.10 (8H, m, α-CH_2), 6.84-6.96 (8H, m, C_6H_4); for **6** : 2.75 (8H, t, NCH_2), 3.66 (8H, t, γ-CH_2), 3.73 (4H, s, NCH_2Ph), 3.76 (8H, m, β-CH_2), 4.10 (8H, m, α-CH_2), 6.83-6.95 (8H, m, C_6H_4), 7.17-7.37 (10H, m, Ph); for **7**: 2.72 (8H, t, NCH_2), 3.64 (12H, t & s, γ-CH_2 & NCH_2Ar), 3.72 (6H, s, OMe), 3.76 (8H, m, β-CH_2), 4.10 (8H, m, α-CH_2), 6.79 & 7. 25 (8H, AA'XX' system, *p*-C_6H_4), 6.84-6.96 (8H, m, C_6H_4); for **8** : 2.67 (8H, t, NCH_2), 3.53 (8H, t, γ-CH_2), 3.65 (4H, s, NCH_2Ar), 3.68 (8H, m, β-CH_2), 4.01 (8H, m, α-CH_2), 6.77-6.89 (8H, m, *o*-C_6H_4), 7.37 (4H, s, *p*-C_6H_4); for **9** : 2.72 (8H, t, δ-CH_2), 3.57-3.65 (24H, m, γ-, γ'-, δ'-, ε'-CH_2 & NCH_2Ar), 3.74-3.79 (12H, m, β- & β'-CH_2), 4.00-4.04 (4H, m, α'-CH_2), 4.07-4.11 (12H, m, α-CH_2), 6.79 & 7.24 (8H, AA'XX' system, *p*-C_6H_4), 6.84-6.95 (8H, m, C_6H_4).

6. Crown ethers and aza-crown ethers bearing side-arms with additional donor atoms - the so-called lariat ethers - have been synthesised and widely used for complexing inorganic cations: see V.J. Gatto, K.A. Arnold, A.M. Viscariello, S.R. Miller, C.R. Morgan, and G.W. Gokel, *J. Org. Chem.*,1986, **51**, 5373 and references therein. For a review on aza-macrocycles with pendant arms, see T.A. Kaden, *Topics Curr. Chem.*, 1984, **121**, 157.
7. Crown ethers bearing ionisable groups have geen used in aqueous solution for the complexation of inorganic cations [see, for example, M. Takagi and K. Ueno, *Topics Curr. Chem.*, 1984, **121**, 39 and references therein; F. de Jong, A. van Zon, D.N. Reinhoudt, G.J. Torny, and H.P.M. Tomassen, *Rec. Trav. Chim. Pays-Bas.*, 1983, **102**, 164] and organic cations such as methyl viologen, *i.e.* Paraquat [see M. Dahenens, L.Lacombe, J.M. Lehn, and J.P. Vigneron, *J. Chem. Soc. Chem. Commun.*, 1984, 1097; J. Jazwinski, J.M. Lehn, R. Méric, J.P. Vigneron, M. Cesario, J. Guilhem, and C. Pascard, *Tetrahedron Lett.*, 1987, **28**, 3489].
8. The *X*-ray crystal structure of **2** is reported in the third communication in this series.
9. The dibromide was obtained from reaction (^{t}BuOK, ^{t}BuOH, reflux, 48 h) of *p*-hydroxybenzyl alcohol with penta-ethyleneglycol bistosylate (ref 1); this reaction gave (SiO_2/EtOAc) 1,14-bis[4-(hydroxymethyl)phenoxy]3,6,9,12-tetraoxadecane [44%, m.p. 71-72°C (C_6H_6)] which was brominated (PBr_3, PhMe-Et_2O, rt, 18 h) to afford (SiO_2/20% EtOAc-$CHCl_3$) the dibromide [69%, m.p. 57-59°C (C_6H_{12}-C_6H_6)].
10. From 1:1 molar equivs of [Diquat][PF_6]$_2$ and receptors **5**-**8**, the following complexes were isolated as orange-red crystals: [Diquat.**5**][PF_6]$_2$ [m.p. 122-125°C (Me_2CO-MeOH; crystals suitable for *X*-ray crystallography - see following communication in this series]; [Diquat.**6**][PF_6]$_2$ [m.p. 125-127°C (Me_2CO-Et_2O)]; [Diquat.**7**][PF_6]$_2$ [m.p. 98-101°C (Me_2CO-$^nC_5H_{12}$)]; [Diquat.**8**][PF_6]$_2$ [m.p. 169-171°C (Me_2CO-Et_2O)].
11. Receptors **4**-**9** are selective for [Diquat]$^{2+}$: they interact only very weakly with [Paraquat]$^{2+}$; 1:1 molar solutions in CD_3COCD_3 are pale yellow and exhibit less than 0.1 ppm shifts for the [Paraquat]$^{2+}$ signals in their proton n.m.r. spectra.
12. As a consequence of the 1:1 complex formation, some of the signals for the receptors are also significantly shifted. A general trend is observed for the bridging polyether chains with up-field shifts for the α- and β-CH_2 protons and downfield shifts for the γ-CH_2 and NCH_2 protons.
13. Fully-resolved resonances for both the receptor and the substrate are observed in the ^{1}H n.m.r. spectrum of [Diquat.**5**][PF_6]$_2$ recorded immediately after the preparation of the equimolar solution.
14. The ^{1}H n.m.r. spectrum of a solution containing equimolar amounts of **1** and [Diquat][PF_6]$_2$ in CD_3COCD_3 shows very broad signals for the receptor: the substrate resonances are much broadened.
15. We thank Dr. Brian E . Mann for helpful discussions.
16. J.K.M. Saunders and B.K. Hunter, "Modern NMR Spectroscopy. A Guide for Chemists", Oxford University Press, Oxford, 1987, p. 221.
17. Use of degassed CD_3COCD_3 for the ^{1}H n.m.r. spectroscopic studies delays quenching of the radical cation: flushing solutions with oxygen enhances the rate of quenching of the radical cation.
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