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Diester-Calix[4]arenediquinone Complexation and Electrochemical Recognition of Group 1 and 2, Ammonium and Alkyl Ammonium Guest Cations.

Paul D.Beer*, Zheng Chen and Philip A.Gale.

Inorganic Chemistry Laboratory, University of Oxford, South Parks Road, Oxford, OX1 3QR.

Abstract : The synthesis, metal, ammonium and alkyl ammonium cation coordination chemistry and electrochemical recognition studies of a new diester-calix[4]arenediquinone receptor are described.

In recent years we[1] and others[2] have incorporated transition metal redox-active centres into a variety of crown ether, aza crown ether and cryptand macrocyclic structural frameworks and shown some of these host compounds to be selective and electrochemically responsive to the binding of cationic guest species. In addition redox responsive anion receptors based on cobalticinium[3], ruthenium (II) bipyridyl derivatives[4] and functionalised calix[4]arenes[5] have also been described. Although the synthesis[6,7] and electrochemical properties[8,9] of calix[4]arenequinones are known their potential use and application to amperometric sensor technology has not to our knowledge been utilised. We report here the first example of such an application in which a simple novel lower rim diester modified calix[4]arenediquinone L complexes and electrochemically recognises Group 1 and 2, ammonium and alkylammonium guest cations.

RESULTS AND DISCUSSION

Synthesis and Conformational Properties. Using the methodology of McKillop[10], which was applied to calixarenes by Gutsche and co-workers[7], the oxidation of p-tert-butylcalix[4]arene bis ethyl ester (1)[11] with thallium trifluoroacetate in trifluoroacetic acid for two hours at room temperature produced the new diester-calix[4]arenediquinone L as a yellow powder in 65% yield (Scheme 1). At room temperature the [1]H n.m.r. spectrum (CD_2Cl_2) of L exhibits the usual AB splitting pattern of the methylene protons consistent with a cone conformation for the calix. However, on cooling, the spectrum broadened and at the lowest temperature (191K) the pattern of the methylene proton splitting is consistent with the co-existence of cone and partial cone conformers (Fig.1). Interestingly, as can be seen from (Figure 1), the tertiary butyl resonance splits into two resonances at low temperatures also suggesting the presence of two species in solution. Whilst this work was in progress, a recent report by Casnati and co-workers[9] investigating the conformational properties of alkyl

calixarenediquinones noted a similar dynamic process which was rationalised by considering the mobility of the quinone groups. At room temperature the quinone moieties can rotate through the calix cavity whilst the aromatic
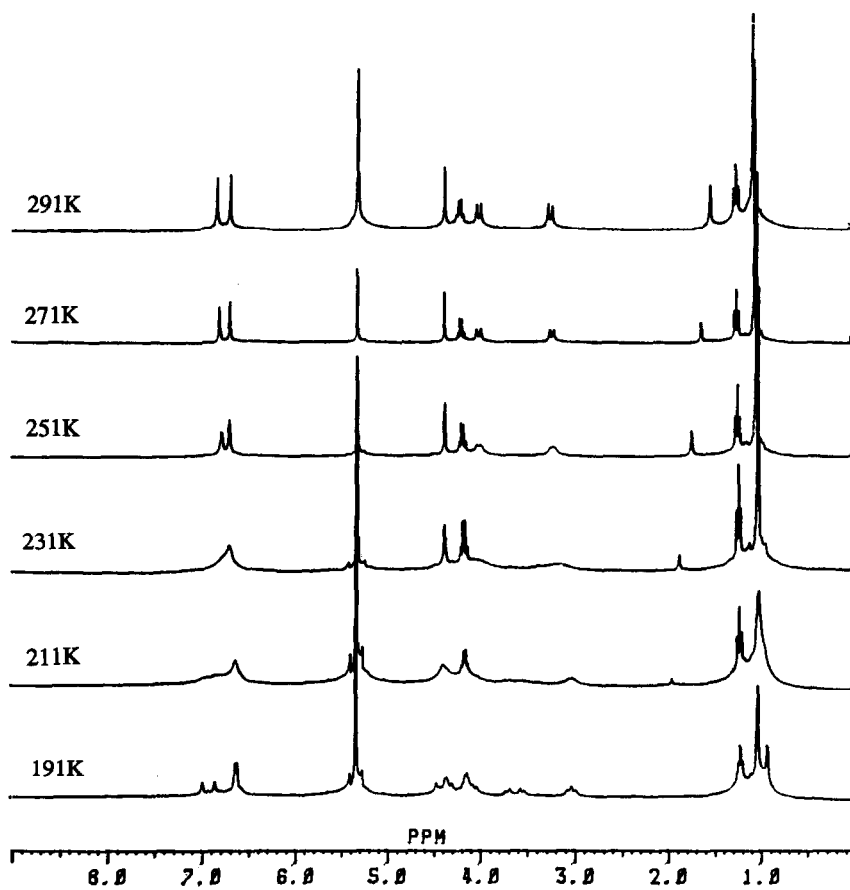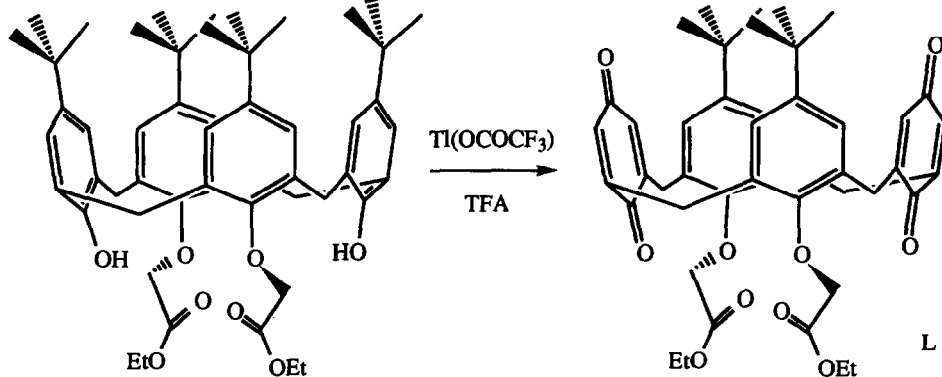

Scheme 1

Fig.1.   The n.m.r. spectrum of L from 291K to 191K

rings stay fixed relative to one another. At low temperatures this dynamic process is slowed on the n.m.r. timescale and the quinone moieties adopt fixed cone and partial cone conformations. Relative integration of the methylene proton resonances suggest L, at 191K, exists in CD_2Cl_2 solution as a 50 : 50 mixture of cone and partial cone conformers.

COORDINATION STUDIES

[1]H n.m.r. Titrations. For comparison purposes the [1]H n.m.r. solution complexation studies with Group 1 and 2, ammonium and butyl ammonium cations were carried out with L and the known dimethylether calix[4]arenediquinone (2)[7].
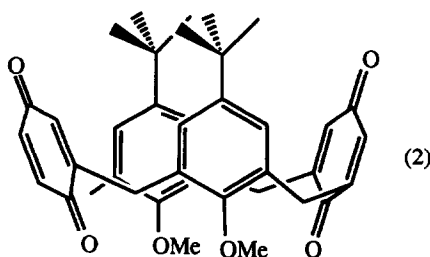

Fig.2. The model compound (2)[7].

In a typical titration experiment the stepwise addition of a concentrated solution of a cation salt in 40:60 (v/v) deuterated chloroform/acetonitrile to a dilute solution of L in the same deuterated solvent mixture resulted in either large significant downfield shifts of the receptor protons or the evolution of a new set of resonances corresponding to a complexed species. This most notably occurred with Ba^{2+} (Figure 3).

Interestingly the difference in chemical shift between the AB pair of doublets of the methylene protons increases from 0.35ppm to 0.76ppm on the addition of 1.0 equivalents of Ba^{2+} (Figure 3). This observation may be attributed to the Ba^{2+} cation locking the calixarene into a cone conformation by complexing not only the ester carbonyl oxygen donor atoms but also interacting with the quinone carbonyl moieties. This mode of metal cation coordination would have the effect of inhibiting the quinone calix-ring inversion process and consequently rigidifying the receptor into a cone conformation. Indeed, in support of this hypothesis a low temperature [1]H n.m.r. spectrum of L in the presence of Ba^{2+} exhibited exclusively one pair of doublets for the methylene protons. The resulting [1]H n.m.r. titration curves with L suggested 1:1 solution stoichiometry with Na^+, K^+, NH_4^+ and $^nBuNH_3^+$ guest cations, in which the ammonium cations are probably stabilised primarily through favourable hydrogen bonding interactions with the quinone and ester carbonyl groups (Figure 4). The importance of these hydrogen bonding interactions can be highlighted when considering the observation that (2) containing no ester moieties gave no evidence for complexing NH_4^+ or $Bu^nNH_3^+$. Consequently these ammonium cationic guest species do not appear to inhibit the room temperature dynamic quinone-calix ring inversion process of the methyl ether receptor (2).

UV/VIS Spectroscopic Investigations - Association Constant Determinations. UV/VIS spectroscopic titrations (See Experimental) were used to determine association constant data for L and (2) with the metal and ammonium cations and the results are summarised in Table 1 .

Table 1 . The Association Constants of L and (2) with various Cations.

Cation	L : Association Constant	(2) : Association Constant
Na^+	(a)	(b)
K^+	7.2 ($\pm$1.3)x10^4	1.9 ($\pm$0.3)x10^4
Ba^{2+}	4.8 ($\pm$0.2)x10^5	5.3 ($\pm$0.2)10^3
NH_4^+	1.1 ($\pm$0.2)x10^4	(b)
$Bu^nNH_3^+$	6.6 ($\pm$2.5)x10^3	(b)

(a) The association constant is too high for the curve fitting program used to calculate.

(b) No evidence of binding was seen.

In the case of L, Ba^{2+} forms a very stable complex, at least an order of magnitude greater than K^+, NH_4^+ and $Bu^nNH_3^+$. This is not surprising considering the charge difference between these guests. The association constant with Na^+ unfortunately could not be elucidated, however the results of a fast atom bombardment mass spectrometry (FABMS) competition experiment suggested an association constant for Na^+ in excess of the K^+ value. FABMS has been used to study the selectivity of crown ethers for Group 1 metal cations in competition experiments[12]. The FABMS competition experiment of L ($5x10^{-3}$M, 0.5ml CH_2Cl_2) with the hexafluorophosphate salts of sodium, potassium and ammonium ($5x10^{-3}$M,0.5ml CH_3CN) gave gas phase complex ions of $[L+Na]^+$ ion (m/z 759) and a minor peak $[L+K]^+$ ion (m/z 775) exclusively (Figure 5). The relative peak intensities suggest a selectivity order of $Na^+>>K^+>>NH_4^+$.

ELECTROCHEMICAL STUDIES

The electrochemical properties of L and (2) were investigated in dichloromethane 10% / acetonitrile 90% solvent mixture using cyclic voltammetry with $(Bu^n)_4NBF_4$ as the supporting electrolyte. (2) exhibited two reversible reduction waves corresponding to the respective formation of a radical anion and diradical dianion[9] (Figure 6). For L, the main reduction waves were very similar to that of (2) except that the corresponding re-oxidation current formed only a single peak. The small pre-reduction waves are possibly due to a small amount of Na^+L complex present in the sample. Cyclic voltammograms were also recorded after progressively adding stoichiometric equivalents of the cation guest to the electrochemical solutions of L and (2) and the results are summarised in Tables 2 and 3. The largest magnitude of anodic perturbation for both calix[4]arenediquinones is observed with Ba^{2+} which possesses the largest charge to radius ratio. In the case of L much stronger anodic perturbations of the reduction couples were observed with all cations than with (2). This can be explained by considering the source of the anodic perturbations. In the case of L, the cation is bound at the lower rim recognition site. Upon reduction binding is enhanced by a cation-radical anion interaction[9]. Comparison with the NMR measurements and the UV/VIS titration curves shows that there is no interaction between ammonium and nbutylammonium cations and (2). Therefore the anodic perturbations in these cases is due to the cation-radical anion interaction so revealing the precedent of alkyl ammonium cation complexation and electrochemical recognition by L.
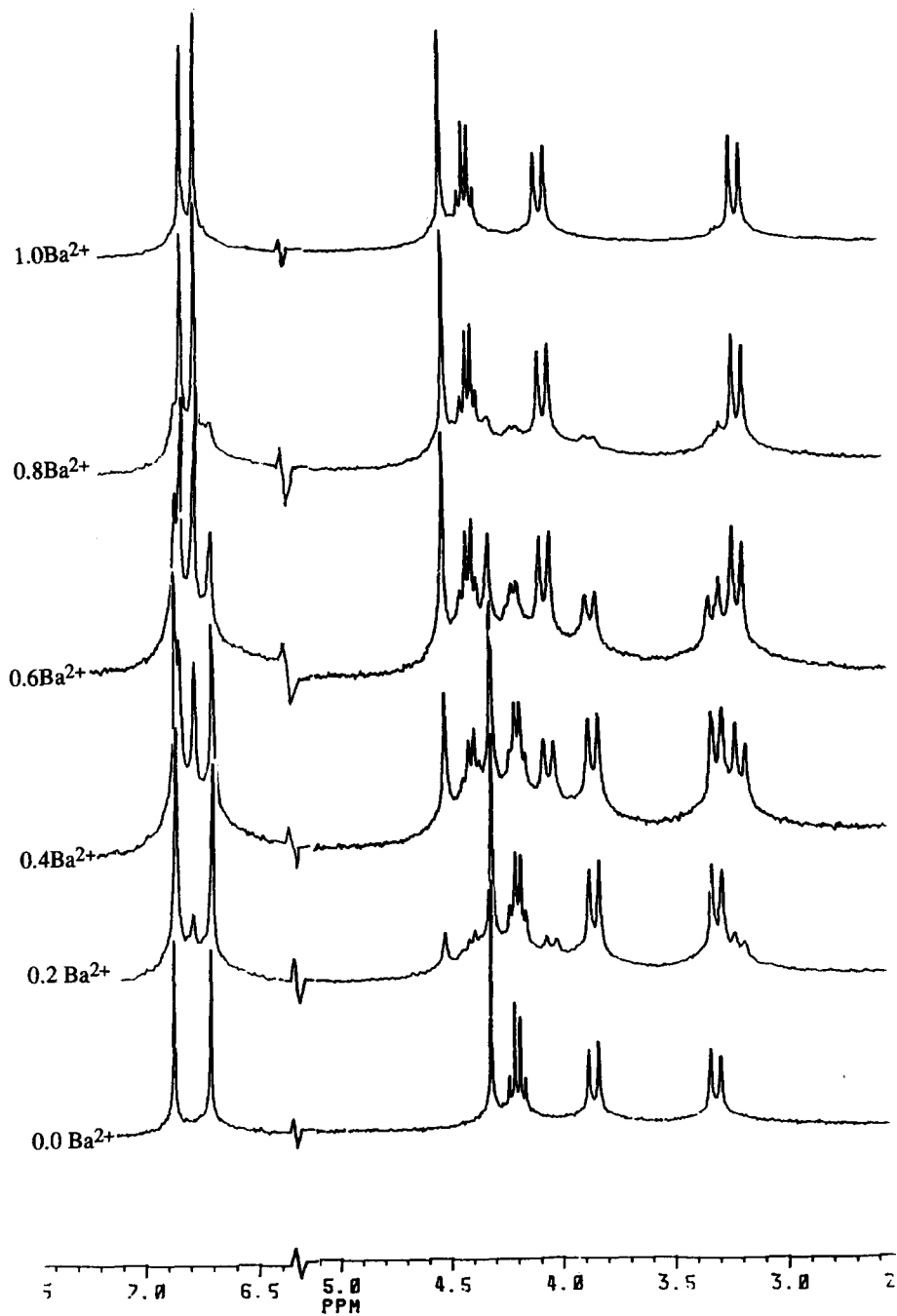
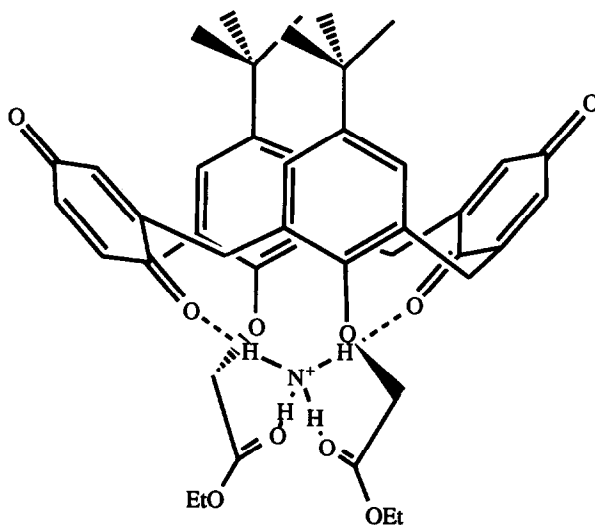Fig.3. The n.m.r. spectrum of L upon addition of barium cations
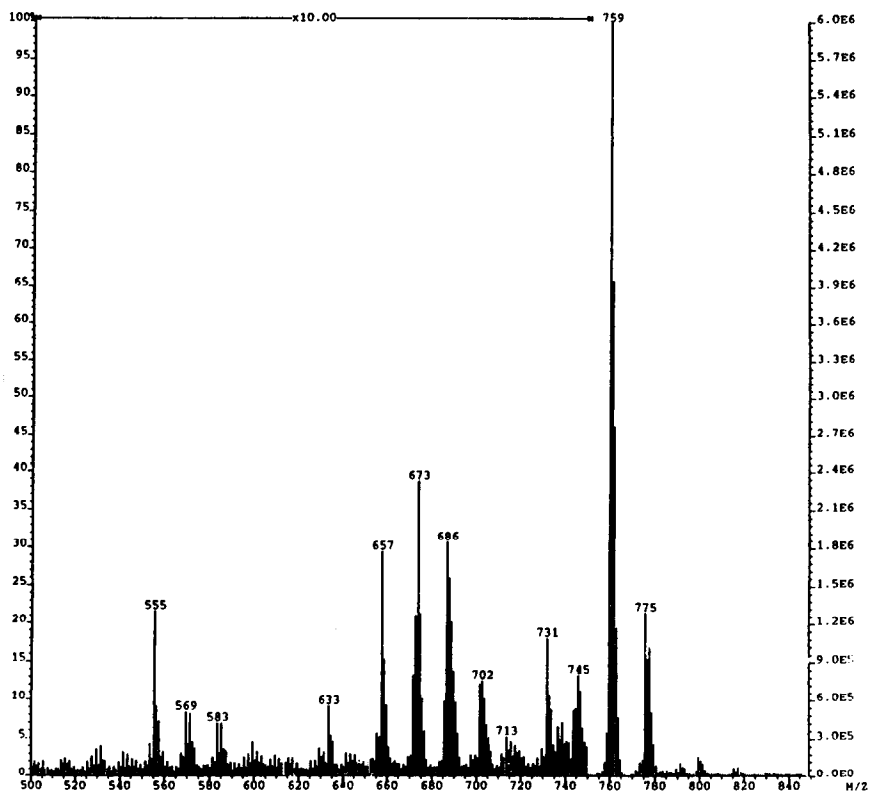
Fig. 4. The tetrahedral binding site in L
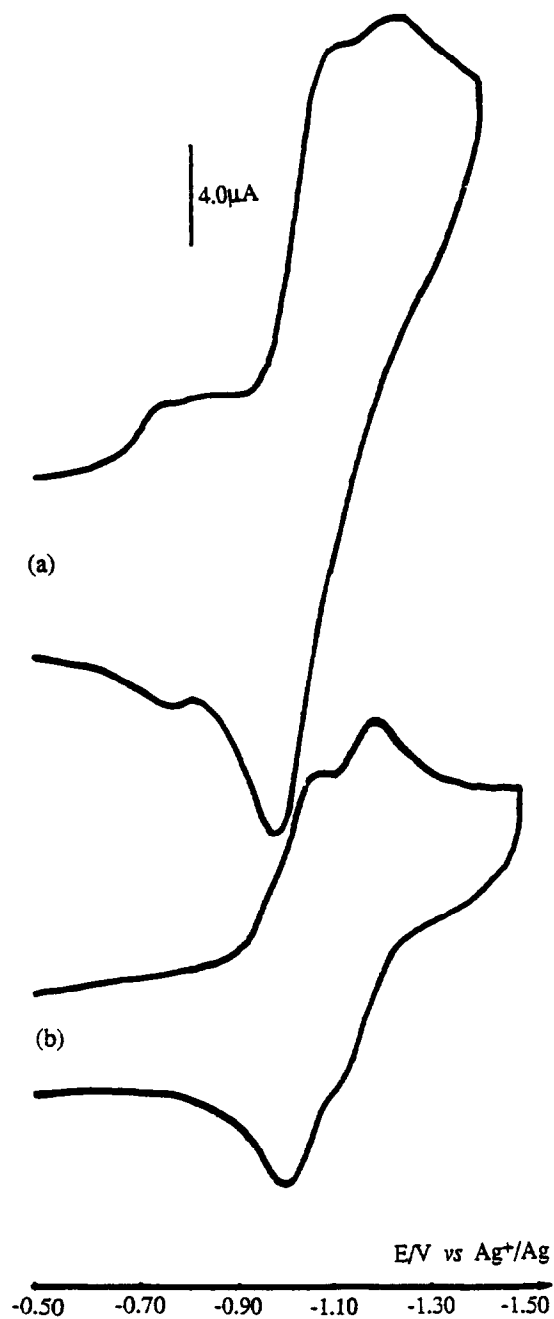

Fig.5 . The FABMS competition experiment

Fig.6 . Cyclic voltammograms of (a) L (1.7x10^{-4} M) and (b) (2) (1.0x10^{-4} M) in 10% CH$_2$Cl$_2$ and 90% CH$_3$CN
Scan rate: 50 mV/sec

Table 2 . A Summary of the Maximum Anodic Shifts Seen upon the Addition of Cations to the Electrochemical
Solution of L. Scan Rate = 50mV/sec, Reference Ag^+/Ag.

Cation Added to L	Radical Anion	Diradical Dianion
Na^+	300mV	(a)
K^+	180mV	(a)
Ba^{2+}	600mV	(a)
NH_4^+	430mV	(a)
$Bu^nNH_3^+$	420mV	(a)

(a)   The two peaks have merged into one (shifts are then quoted with respect to the mono radical-mono anion peak in the free
ligand).

Table 3 . A Summary of the Maximum Anodic Shifts Seen upon the Addition of Cations to the Electrochemical
Solution of (2).Scan Rate = 50mV/sec, Reference Ag^+/Ag..

Cation Added to (2)	Radical Anion	Diradical Dianion
Na^+	100mV	(a)
K^+	50mV	<5mV
Ba^{2+}	520mV	(a)
NH_4^+	260mV	(a)
$Bu^nNH_3^+$	170mV	(a)

(a)   The two peaks have merged into one (shifts are then quoted with respect to the mono radical-mono anion peak in the free
ligand).

CONCLUSIONS

A new diester-calix[4]arenediquinone receptor molecule has been prepared and shown to complex Group 1
and 2 metal, ammonium and alkylammonium cations with association constants of up to 4.80×10^5 with Ba^{2+}.
This receptor also electrochemically recognises cationic guests and is, to our knowledge, the first class of redox-
active ionophore to amperometrically sense an alkyl ammonium cationic guest species.

EXPERIMENTAL

Solvent and Reagent Pretreatments. Where necessary solvents were purified and dried prior to use using standard
procedures.

Unless otherwise stated commercial grade chemicals were used without further purification.

Instrumental methods. The melting point was recorded on a Gallenkamp melting point apparatus in open capillaries and is uncorrected.

NMR spectra were recorded on a Brüker AM 300 instrument.

IR spectra were recorded on a Perkin Elmer 1710 IR FT spectrometer.

UV spectra were recorded on a Perkin-Elmer Lambda 6 spectrometer.

Electrochemical measurements were conducted on a Princeton Applied Research Potentiostat/Galvanostat Model 273.

Fast atom bombardment mass spectra were performed at University College, Swansea by the S.E.R.C. mass spectrometry service.

All elemental analyses were carried out by the Inorganic Chemistry Laboratory, Oxford.

SYNTHESIS

5,17-Di-tert-butyl-26,28,-bis-(carboethoxymethyl)-calix[4]-25,27-diquinone L.

Para-tert-butylcalix[4]arene bis ethyl ester (0.82g, 1mmol) was stirred in TTFA/TFA solution (6.8ml, 6mmol) for two hours in the dark. The TFA was then removed *in vacuo* and the residue poured onto ice/water (50ml). The product was then extracted into chloroform(100ml), separated and the organic layer washed with water (100ml). The organic layer was then dried over $MgSO_4$ and reduced *in vacuo*. The residue was purified by column chromatography on silica gel eluting with chloroform/methanol 90:10 (v/v). The product was collected and triturated with methanol to give a yellow powder (0.48g, 65%).

Analysis calcd. for $C_{44}H_{48}O_{10}.H_2O$: C, 70.0; H, 6.7

Found: C, 70.0; H, 6.7

^1H NMR (CD_2Cl_2 300MHz) 1.10 (s, 18H, $(CH_3)_3C$), 1.28 (t, J=7.1Hz, 6H, CH_2CH_3), 1.58 (s,2H,H_2O), 3.27 (d, J=13.3Hz, 4H, $ArCH_2Ar$), 4.02(d, J=13.3Hz,4H,$ArCH_2Ar$), 4.23(q, J=7.1Hz, 4H, CH_2CH_3),4.39(s, 4H, OCH_2), 6.71(s, 4H, C=CH), 6.85 (s,4H,ArH).

^{13}C NMR (CD_2Cl_2 75.42MHz) 14.10(CH_3CH_2) , 31.27($(CH_3)_3C$), 32.71($ArCH_2Qu$), 33.88($(CH_3)_3C$), 61.35(CH_2O), 71.29(CH_2O), 126.81($CH=C$), 128.36, 132.88(ArH), 146.61,147.86, 169.26(C=O), 185.40(C=O), 188.57(C=O).

IR : 1760.0cm^{-1},1733.9cm^{-1}, 1654.8cm^{-1} (Carbonyl stretches)

FAB MS : m/z 738 ((M+H)$^+$ 737)

M.P. 235°C (dec)

UV/VIS SPECTRA EXPERIMENTS FOR DETERMINING ASSOCIATION CONSTANTS

Titrations. The titrations were conducted by progressively adding a cation solution (0.1M in CH_3CN), using a 10μl syringe, to the cuvette containing 3.0 ml of the compound solution (5 x 10^{-5}M in CH_2Cl_2/CH_3CN 4:21 (v/v)). The maximum addition for all the cations was less than 150μl to minimise the change of the solution volume. The spectrum was recorded after each addition. The added equivalents of the cation were then plotted against the absorption intensity change at a certain wave length around the absorption peak on the spectrum (310nm-370nm) . This was repeated at three different wave lengths.

Calculation of the Association Constants. A self-written non-linear curve fitting computer program was used to fit the experimental titration curves using the equation for a 1:1 complex:

$$\alpha = (I-I_f{}^0)/(I_c{}^0-I_f{}^0) + (I-I_f{}^0)/[C_f{}^0K(I_c{}^0-I)] \tag{1}$$

where α is the added equivalents of cations, $I_f{}^0$, I and $I^0{}_c$ are absorption intensities of the free ligand, the ligand plus α equivalents of cations and the ligand plus large excess cation solutions, $C_f{}^0$ is the concentration of the free ligand and K is the association constant. The fitting procedure was repeated for each cation for all the three titration curves at different wave lengths and the averaged value of K is reported.

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REFERENCES

1(a)   Beer, P.D. *Chem. Soc. Rev.*, **1989**,18,409.

1(b)   Beer, P.D. *Adv. Inorg. Chem.*, **1992**, 39,79.

2(a)   Hall, C.D., Sharpe, N.W., Danks I.P. and Sang Y.P. *J.Chem.Soc.Chem.Commun.*, **1989**,419.

2(b)   Fu, E., Green, M.L.H., Lowe, V.J. and Marder, S.R. *J.Organometal.Chem.*,**1988**, 341, C39.

2(c)   Green, M.L.H., Heiser, W.B. and Saunders, G.C. *J.Chem.Soc.Dalton Trans.*, **1990**, 3789.

2(d)   Lowe, N.D. and Garner D.C. *J.Chem.Soc.Dalton Trans.*,**1993**, 2197.

2(e)   van Veggel, F.C.J.M., Harkema, S., Bos, M., Verboom, W., Klein, G., Woolthius, G. and Reinhoudt, D.N. *J.Org.Chem.*, **1989**, 54, 2351.

3   Beer, P.D., Hesek, D., Hodacova, J. and Stokes, S.E. *J.Chem.Soc.Chem.Commun.*, **1992**, 270.

4   Beer, P.D., Dickson, C.A.P., Fletcher, N., Goulden, A.J., Grieve, A., Hodacova, J. and Wear, T. *J.Chem.Soc.Chem.Commun.*, **1993**, 828.

5   Beer, P.D., Drew, M.G.B., Hazlewood, C., Hesek, D. and Stokes, S.E. *J.Chem.Soc.Chem.Commun.*, **1993**, 229.

6(a)   Morita, Y., Agawa, T., Kai, Y., Kanehisa, N., Kasai, N., Nomura, E. and Taniguchi, H. *Chem.Lett.*, **1989**, 1349.

6(b)   Morita, Y., Agawa, T., Nomura, E. and Taniguchi, H. *J.Org.Chem.*, **1992**, 57, 3658.

7   Reddy, P.A., Kashyap, R.P., Watson, W.M. and Gutsche, C.D., *Isr.Journ.Chem.*, **1992**, 32, 89.

8   Suga, K, Fujihira, M., Monta, Y. and Agawa, T. *J.Chem.Soc.Faraday Trans.*, **1991**, 87, 1575.

9   Casnati, A., Comelli, E., Fabbi, M., Bucchi, V., Mori, G., Ugozzoli, F., Lanfredi, A.M.M., Puchini, A., and Ungaro, R. *Recl.Trav.Chim.Pays-Bas.*, **1993**, 112, 384.

10   McKillop, A., Swann, B.P., and Taylor, E.C., *Tetrahedron*, **1970**, 26, 4031.

11   Collins, E.M., McKervey, M.A., Madigan, E., Moran, M.B., Owens, M., Ferguson, G., and Harris, S.J. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 12, 3137.

12   Johnstone, R.A.W. and Rose M.E., *J.Chem.Soc.Chem.Commun.* **1983**,1268.