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# Novel, selective and co-operative assembly of cyclodextrins around [1,8-bis(pyridin-2-yl)-3,6-dithiaoctane]copper(II)

**Sivagnanam Usha and Mallayan Palaniandavar** *

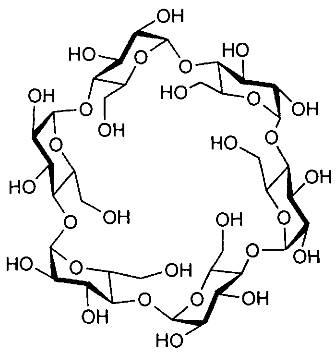
*Department of Chemistry, Bharathidasan University, Tiruchirapalli 620 024, India*

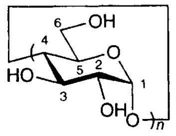
The redox chemistry of $[CuL]^{2+}$ [L = pdto = 1,8-bis(pyridin-2-yl)-3,6-dithiaoctane, bbdo = 1,8-bis(benzimidazol-2-yl)-3,6-dithiaoctane, pttn = 1,9-bis(pyridin-2-yl)-2,5,8-trithianonane or pttu = 1,11-bis(pyridin-2-yl)-3,6,9-trithiaundecane] in the presence of α-, β- and γ-cyclodextrins (cd) in aqueous solution has been extensively investigated by cyclic and differential pulse voltammetric techniques. The addition of cyclodextrins to the complexes results in a substantial decrease in peak currents rather than in peak potentials. The $i_{pa}$ rather than $i_{pc}$ or $\Delta E_p$ or $E_{\frac{1}{2}}$ is very sensitive to the variation in the cyclodextrin concentration. The couple $Cu^{II}$–$Cu^{I}$ of $[Cu(pdto)]^{2+}$ tends to become reversible, as shown by the decrease in $\Delta E_p$ and that of $i_{pa}/i_{pc}$ towards unity. Plots of $i_{pa}$, $i_{pc}$, $E_{pa}$ and $\Delta E_p$ *vs.* the number of moles of cyclodextrin show sharp inflections, interestingly at 5, 4 and 3 mol of α-, β- and γ-cd respectively. These limiting values do not correspond to the usual inclusion complex formation by cyclodextrins but to the formation of novel and regular arrays around the complex, the number of molecules in the array being dictated by the size of the cyclodextrin. This also illustrates the prevention of adsorption of $[Cu(pdto)]^{+}$ on the glassy carbon electrode. For the other complexes the changes in redox properties in the presence of cyclodextrins are not as regular and significant. Plots of changes in $i_{pa}$ and $i_{pc}$ *vs.* cyclodextrin concentration give Hill's coefficients greater than unity (1.3–2.1). The values of $K_{+}/K_{2+}$ for all the complexes and $K_a$ ($K_{2+}$) for the complex formation of $[Cu(pdto)]^{2+}$ with cyclodextrins have been determined and discussed. Significant reduction or enhancement in $\varepsilon_{max}$ values has been observed both for the ligand-field and charge-transfer bands in the presence of all three cyclodextrins.

Cyclodextrins are toroidally shaped polysaccharides made up of six (α-cd), seven (β-cd) and eight (γ-cd) D-glucose monomers, joined by α(1→4) bonds.[1] Owing to the hydrophobic nature of their inner cavities they act as hosts for many organic molecules,[2,3] inorganic ions[4–6] and organometallic compounds[7,8] and form inclusion complexes when the guest and cavity are of appropriate size.[9] They are the most important and widely studied examples of host molecules. The inclusion of bis(pyridin-2-ylmethanolato)copper(II) by cyclodextrins has been investigated[6] by EPR and CD spectroscopy. Recently the effect of α- and β-cyclodextrins on the ligand-substitution reactions of pentacyano(N-heterocycle)ferrate(II) complexes has been reported.[10] The electrochemical oxidation of ferrocenecarboxylic acid in the presence of β-cd has been investigated.[11,12] The second-sphere co-ordination of platinum and rhodium complexes bearing hydrophobic ligands, consisting of cyclodextrins, has been structurally characterized by Alston *et al.*[13–15] in the solid state using X-ray crystallography.

A cyclodextrin is also a well constructed miniature of an enzyme in the sense that it has a hydrophobic cavity of appropriate size, sites for introduction of catalytic groups at juxtapositions, and satisfactory water solubility.[16] The rate and stereochemical pathway of organic reactions are significantly changed by the inclusion complexation of substrates with cyclodextrins. Since the mechanisms of such reactions are very similar to those of enzymes or biological receptors, cyclodextrins have been regarded as good models for biopolymers and have been studied extensively as models for enzyme active sites.[17–19]

As we have been concerned in constructing models for and elucidating the novel electrochemical behaviour, high $Cu^{II}$–$Cu^{I}$ redox potentials and facile electron transfer, of blue copper proteins, the electrochemical behaviour of copper(II) complexes designed as models for these proteins in the presence of cyclodextrins was of interest. Inclusion complex formation by cyclodextrins, added in solution or bound to an electrode, has been shown to enhance the electrochemical reversibility of several organic guests.[20] We have chosen the biomimetic copper(II) complexes $[Cu(pdto)]^{2+}$ [pdto = 1,8-bis(pyridin-2-yl)-3,6-dithiaoctane],[21] $[Cu(bbdo)]^{2+}$ [bbdo = 1,8-bis(benzimidazol-2-yl)-3,6-dithiaoctane][22] $[Cu(pttn)]^{2+}$ [pttn = 1,9-bis(pyridin-2-yl)-2,5,8-trithianonane][23] and $[Cu(pttu)]^{2+}$ [pttu = 1,11-bis(pyridin-2-yl)-3,6,9-trithiaundecane][22] for the present investigation. The advantages associated with these complexes are their water solubility, known structures and well characterized intense S(σ)→$Cu^{II}$ charge-transfer (c.t.) band. Although there are a few reports on the inclusion complex formation of metal complexes with cyclodextrins,[12,24] that described in the present study is novel.

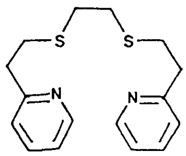




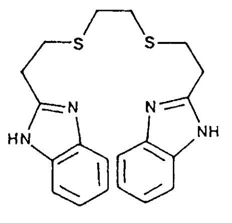
## Experimental

### Materials

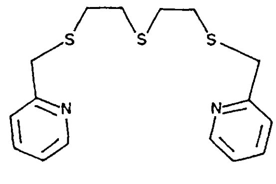
The cyclodextrins were generous gifts from American Maize-Products Co. 2-Vinylpyridine, ethane-1,2-dithiol, bis(2-sulfanylethyl) sulfide and copper(II) perchlorate hexahydrate were from Aldrich and used as such.



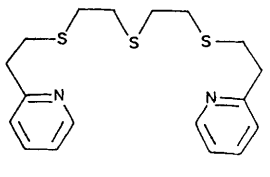
pdto



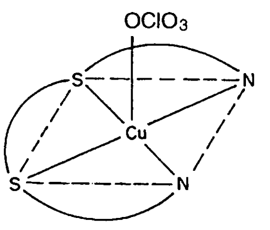
bbdo



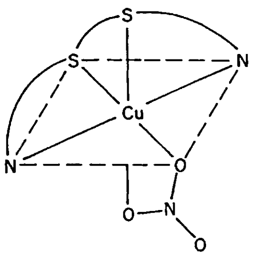
pttn



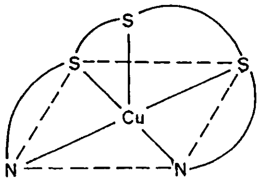
pttu



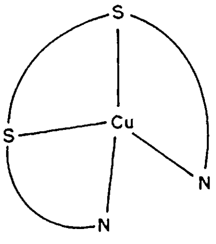
$[Cu(pdto)(OClO_3)]^+$



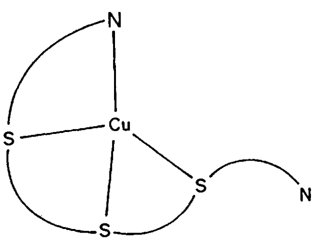
$[Cu(bbdo)(NO_3)]^+$



$[Cu(pttn)]^{2+}$



$[Cu(pdto)]^+$



$[Cu(pttu)]^+$

### Syntheses

The compounds pdto, bbdo, pttn and pttu and their $Cu(ClO_4)_2$ complexes were prepared as described previously.[21–23] **CAUTION**: [1,8-bis(pyridin-2-yl)dithiaoctane]copper(II) perchlorate is a contact explosive. Brubaker[21] was deafened for several months by the explosion of about 1 g of the perchlorate which detonated while being transferred from a sintered glass funnel. No such incident occurred during this work. However, $[Cu(pttu)][ClO_4]_2$ exploded when transferred from a sintered glass crucible.

### Physical measurements

The reflectance and solution spectra were recorded on a Hitachi U-3400 double-beam UV/VIS/NIR spectrophotometer, EPR spectra on a Varian E-112 X-band spectrometer, the field being calibrated with diphenylpicrylhydrazyl (dpph). The values of $g_0$ and $A_0$ were measured at ambient temperature and $g_{\parallel}$ and $A_{\parallel}$ at 77 K. Cyclic voltammetry and differential pulse voltammetry on a glassy carbon or platinum-sphere electrode were performed at 25.0 ± 0.2 °C. A three-electrode cell configuration was used, the reference electrode being a saturated calomel electrode (SCE). The temperature of the electrochemical cell was maintained by a cryocirculator (Haake D8 G). The solutions were deoxygenated by bubbling a stream of nitrogen gas through them and an atmosphere of nitrogen was maintained over solutions during measurements. The instruments utilized included an EG&G PAR 273 potentiostat/galvanostat and an IBM PS-2 computer; EG&G M270 software was employed to carry out the experiments and to acquire the data. A HP plotter (DMP 40) was used to plot out the voltammograms. The $E_{\frac{1}{2}}$ value observed under identical conditions for (hydroxymethyl)ferrocene in aqueous 0.1 mmol $dm^{-3}$ $NaClO_4$ solution was 0.176 V *vs.* SCE and $\Delta E_p^0$ ($\Delta E_p$ at zero scan rate) was 73 mV.

## Results and Discussion

Several intermolecular interactions have been proposed and discussed as being responsible for the formation of cyclodextrin inclusion complexes in aqueous solution.[16,18,23,26] They are hydrophobic, van der Waals, hydrogen bonding, the release of high-energy water from a cyclodextrin–water adduct, together with the formation of a hydrogen-bonding network around the O(2), O(3) (secondary hydroxyl groups) side of the torus of the cyclodextrin macrocycle, upon substrate inclusion. Recently the second-sphere co-ordination of transition-metal complexes bearing hydrophobic ligands by cyclodextrins has been characterized structurally in the solid state by X-ray crystallography.[13–15] In these adducts the hydrophobic ligand of the complex penetrates the cavity of the cyclodextrin *via* the wider aperture of the receptor associated with the face bearing the secondary hydroxy groups. Thus in the crystal structure[14] of the 1 : 1 adduct of *trans*-$[Pt(PMe_3)(NH_3)Cl_2]$ with β-cd the $PMe_3$ ligand is inserted into and bound to the narrow primary hydroxy-group-bearing face of the β-cd torus. Further, a severely disordered surface forms a lid on the wider secondary hydroxy-group-bearing face of the β-cd torus and the complex lies within this surface. In the present study we have successfully employed electrochemical techniques to discern the selective and co-operative assembly of cyclodextrins around $[Cu(pdto)]^{2+}$ in aqueous solution.

### Electronic and EPR spectra

In aqueous solution all the present copper(II) complexes exhibit one (16 700 $cm^{-1}$) or two (16 700, 11 200 $cm^{-1}$) intense ligand-field bands as well as a highly intense $S(\sigma)\rightarrow Cu^{II}$ charge-transfer band (29 300–28 100 $cm^{-1}$) (Table 1, Fig. 1).[22,23,27] For almost all the complexes no change in the position of the bands is discernible on the addition of an excess (0.010 mol $dm^{-3}$) of α-, β- and γ-cd in aqueous solution (Table 1, Fig. 1); however, there is a small but significant reduction or enhancement in molar absorption coefficient for both these bands. This is similar to the observation made in acetonitrile solution, suggesting that the binding of cyclodextrins to the complex is not sufficiently strong to perturb the primary co-ordination sphere. This inference is supported by the absence of any change in either $g_{\parallel}$ or $A_{\parallel}$ in the presence of an excess of cd (2% aqueous solution).

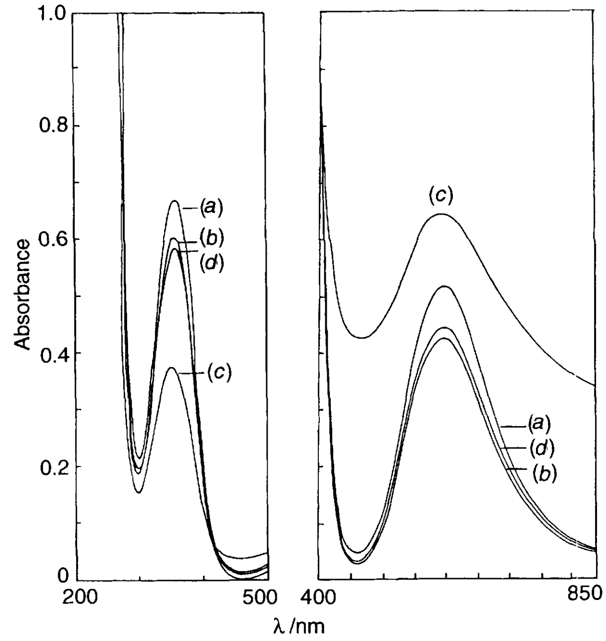


**Fig. 1** Charge-transfer (200–500 nm) and ligand-field (400–850 nm) spectra of $[Cu(pdto)]^{2+}$ (0.001 mol $dm^{-3}$) in aqueous (*a*) and aqueous α-cd (0.010 mol $dm^{-3}$) (*b*), β-cd (0.010 mol $dm^{-3}$) (*c*) and γ-cd (0.010 mol $dm^{-3}$) (*d*) solutions

**Table 1** Electronic spectral data for copper(II) complexes[a] in the presence of an excess[b] of cyclodextrin

| | | $\tilde{\nu}_{max}/cm^{-1}$ ($\varepsilon_{max}/dm^3\ mol^{-1}\ cm^{-1}$) | |
|---|---|---|---|
| Complex | Medium | Ligand field | Charge transfer |
| $[Cu(pdto)]^{2+}$ | Water | 16 800 (494) | 28 600 (3210) |
| | MeCN | 16 900 (743) | 28 000 (4660) |
| | α-cd | 16 800 (408) | 28 600 (2900) |
| | β-cd | 16 800 (619) | 28 600 (1800) |
| | γ-cd | 16 800 (426) | 28 600 (2795) |
| $[Cu(bbdo)]^{2+}$ | Water | 16 700 (168) | 29 300 (3760) |
| | | 11 400 (189) | 24 700 (1420) |
| | MeCN | 16 900 (220) | 28 700 (2810) |
| | | 11 600 (210) | |
| | α-cd | 16 700 (172) | 29 300 (1990) |
| | | 11 300 (189) | 24 700 (680) |
| | β-cd | 16 700 (173) | 29 300 (2070) |
| | | 11 300 (192) | 24 700 (680) |
| | γ-cd | 16 700 (187) | 29 300 (2000) |
| | | 11 400 (186) | 24 700 (640) |
| $[Cu(pttn)]^{2+}$ | Water | 16 700 (411) | 28 100 (3590) |
| | | 11 200 (179) | |
| | MeCN | 16 700 (450) | 27 700 (4760) |
| | | 11 200 (190) | |
| | α-cd | 16 700 (392) | 28 300 (3100) |
| | | 11 200 (168) | |
| | β-cd | 16 700 (375) | 28 300 (3420) |
| | | 11 200 (160) | |
| | γ-cd | 16 800 (384) | 28 300 (3400) |
| | | 11 200 (165) | |
| $[Cu(pttu)]^{2+}$ | Water | 16 700 (296) | 26 400 (1910) |
| | MeCN | 16 300 (490) | 26 100 (3280) |
| | | 11 100 (100) | |
| | α-cd | 16 700 (196) | 26 400 (1580) |
| | β-cd | 16 600 (517) | 28 400 (2015) |
| | γ-cd | 16 800 (356) | 28 400 (2080) |

[a] Concentration of the complex 0.001–0.0015 mol $dm^{-3}$. [b] Concentration of α-cd, 0.010; β-cd, 0.010; γ-cd, 0.010 mol $dm^{-3}$.

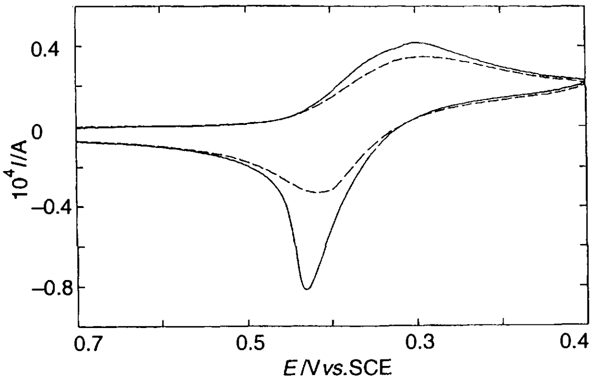


**Fig. 2** Cyclic voltammograms of $[Cu(pdto)]^{2+}$ (0.001 mol $dm^{-3}$) in aqueous solution (0.1 mol $dm^{-3}$ $NaClO_4$) in the absence (——) and presence of 0.010 mol $dm^{-3}$ β-cd (– – – –) at 50 mV $s^{-1}$ scan rate

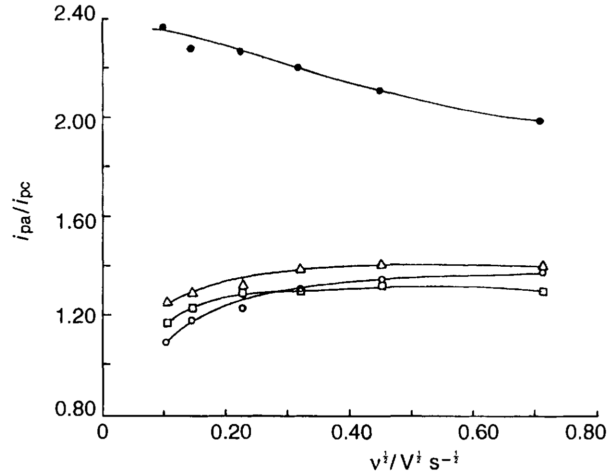


**Fig. 3** Plots of $i_{pa}/i_{pc}$ *vs.* $v^{\frac{1}{2}}$ for $[Cu(pdto)]^{2+}$ in the absence (●) and presence of α-cd (△), β-cd (○) and γ-cd (□) solutions

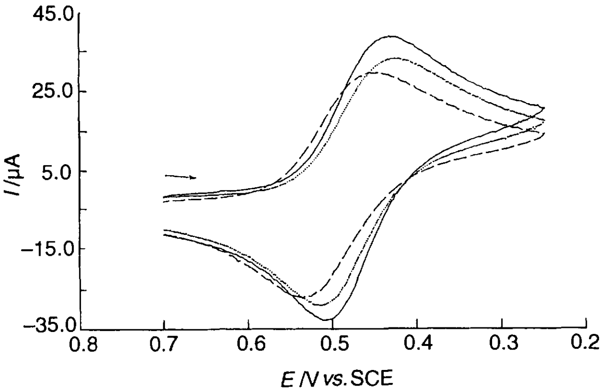


**Fig. 4** Cyclic voltammograms of $[Cu(pttu)]^{2+}$ (0.001 mol $dm^{-3}$) in aqueous solution (0.1 mol $dm^{-3}$ $NaClO_4$) in the absence (——) and presence of 0.010 mol $dm^{-3}$ α-cd (· · ·) and 0.01 mol $dm^{-3}$ γ-cd (– – – –) at 50 mV $s^{-1}$ scan rate

## Electrochemical behaviour of complexes

The cyclic voltammogram of $[Cu(pdto)]^{2+}$ in aqueous solution at a glassy carbon electrode at 50 mV $s^{-1}$ shows that the $Cu^{II}$–$Cu^{I}$ couple is irreversible (Fig. 2), as evident from the very high values of $\Delta E_p$ and peak current ratio ($i_{pa}/i_{pc}$) (Table 2; $\Delta E_p$ = 59 mV and $i_{pa}/i_{pc}$ = 1 for a reversible one-electron transfer). The weak adsorption of the product of reduction, $[Cu(pdto)]^+$, is revealed by the symmetrical anodic peak at high current and the shape of the plot of $i_{pa}/i_{pc}$ *vs.* $v^{\frac{1}{2}}$ (Fig. 3).[28] The adsorption of $[Cu(phen)_2]^+$ (phen = 1,10-phenanthroline) containing aromatic rings on the surface of a glassy carbon electrode has been previously noted.[29] The redox cycle of $[Cu(pdto)]^{2+}$ is quasi-reversible ($\Delta E_p$ 126 mV) at a platinum-sphere electrode and the $i_{pa}/i_{pc}$ value is near to unity suggesting no adsorption

**Table 2** Redox properties of copper(II) complexes (0.001 mol dm$^{-3}$) in aqueous solution (0.1 mol dm$^{-3}$ $NaClO_4$) in the presence of cyclodextrins[a] at a glassy carbon electrode, scan rate 50 mV s$^{-1}$

| Complex | Cyclodextrin | $E_{pc}$/V | $E_{pa}$/V | $i_{pc}$/μA | $i_{pa}$/μA | $\Delta E_p$/mV | $E_{\frac{1}{2}}$/V CV | $E_{\frac{1}{2}}$/V DPV[b] | $i_{pa}/i_{pc}$[c] | $10^6 D$/cm$^2$ s$^{-1}$ | $K_+/K_{2+}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $[Cu(pdto)]^{2+}$ | None | 0.304 | 0.430 | 40.0 | 79.4 | 126 | 0.367 | 0.369 | 2.3 | 2.82 | |
| | α | 0.296 | 0.418 | 34.3 | 33.1 | 122 | 0.357 | 0.367 | 1.4 | 2.23 | 0.68 |
| | β | 0.318 | 0.424 | 33.9 | 29.8 | 106 | 0.371 | 0.371 | 1.2 | 2.23 | 0.52 |
| | γ | 0.286 | 0.442 | 33.8 | 30.5 | 156 | 0.364 | 0.375 | 1.3 | 1.97 | 0.63 |
| $[Cu(bbdo)]^{2+}$ | None | 0.428 | 0.552 | 23.8 | 58.2 | 124 | 0.490 | 0.457 | 2.8 | 1.29 | |
| | α | 0.394 | 0.551 | 13.7 | 45.5 | 157 | 0.473 | 0.449 | 3.8 | 0.29 | 0.86 |
| | β | 0.412 | 0.530 | 18.6 | 59.9 | 118 | 0.471 | 0.443 | 3.6 | 0.77 | 0.48 |
| | γ | 0.400 | 0.520 | 14.7 | 39.9 | 120 | 0.460 | 0.433 | 3.1 | 0.40 | 0.36 |
| $[Cu(pttn)]^{2+}$ | None | 0.288 | 0.372 | 54.6 | 131 | 84 | 0.330 | 0.303 | 2.9 | 5.12 | |
| | α | 0.280 | 0.364 | 50.6 | 92.6 | 84 | 0.322 | 0.294 | 2.2 | 4.79 | 0.89 |
| | β | 0.276 | 0.362 | 49.8 | 106 | 86 | 0.319 | 0.297 | 2.5 | 4.47 | 0.65 |
| | γ | 0.272 | 0.358 | 43.8 | 83.8 | 86 | 0.315 | 0.295 | 2.3 | 3.24 | 0.56 |
| $[Cu(pttu)]^{2+}$ | None | 0.434 | 0.512 | 38.9 | 31.8 | 78 | 0.473 | 0.475 | 1.1 | 1.20 | |
| | α | 0.428 | 0.512 | 36.0 | 28.0 | 84 | 0.470 | 0.471 | 1.1 | 2.02 | 0.96 |
| | β | 0.436 | 0.522 | 29.9 | 24.0 | 86 | 0.479 | 0.477 | 1.1 | 1.40 | 1.26 |
| | γ | 0.458 | 0.542 | 28.6 | 24.7 | 84 | 0.500 | 0.504 | 1.1 | 2.02 | 3.10 |

[a] Concentration of α-, β- and γ-cd, 0.005 mol dm$^{-3}$. [b] Scan rate for differentical pulse voltammetry 0.001 V s$^{-1}$ pulse height 50 mV. [c] Calculated as $\{[(i_{pa})_0 + 0.485(i_{sp})_0]/i_{pc}\} + 0.086$.

of copper(I) species. The entirely different crystal structures[23] of $[Cu(pdto)(ClO_4)]^+$ (square pyramidal) and $[Cu(pdto)]^+$ (tetrahedral) species mean that significant configurational changes accompany the heterogeneous electron-transfer reaction.[30] This leads to a large reorganizational energy which is reflected in the decreased rate of electron transfer and hence the higher $\Delta E_p$ value observed for the $Cu^{II}$–$Cu^I$ couple. The benzimidazole analogue of the pdto complex, $[Cu(bbdo)]^{2+}$, also shows irreversible redox behaviour with high $i_{pa}/i_{pc}$ and $\Delta E_p$ values because of adsorption of copper(I) species. In contrast, $[Cu(pttu)]^{2+}$, the homologue of $[Cu(pdto)]^{2+}$, displays nearly reversible redox behaviour (Fig. 4) in aqueous solution, as verified by the constancy of $i_{pc}/v^{\frac{1}{2}}$, low $\Delta E_p$ values and an $i_{pa}/i_{pc}$ value of unity (Table 2).

**Dithioether complexes in the presence of cyclodextrins.** The incremental addition of α-, β- and γ-cd to $[Cu(pdto)]^{2+}$ in aqueous solution diminishes the anodic peak current considerably and there is a substantial cathodic shift in the anodic peak potential. However, the changes in current and potential of the cathodic peak are comparatively small. Thus on the addition of α- and β-cd the $Cu^{II}$–$Cu^I$ redox cycle tends to become diffusion controlled and reversible, as inferred from the linear plot of $i_{pc}$ *vs.* $v^{\frac{1}{2}}$ passing through the origin (Fig. 5), the decrease in $\Delta E_p$ and the approach of $i_{pa}/i_{pc}$ values to unity (Table 2).

When the cyclodextrin concentration is increased the values of both the anodic and cathodic peak currents decrease to a certain concentration and then remain constant, suggesting completion of adduct formation with the copper complex (Table 2). Plots of $i_{pa}$ [Fig. 6(*a*)–(*c*)], $E_{pa}$ and $\Delta E_p$ *vs.* cyclodextrin concentration show inflection points at approximately 5 for α-, 4 for β- and 3 mmol dm$^{-3}$ for γ-cd, with the limiting concentrations corresponding to adduct formation of $[Cu(pdto)]^{2+}$ with α-, β- and γ-cd in the mole ratios 1:5, 1:4 and 1:3 respectively. The observed stoichiometries depend, interestingly, upon the size of the cyclodextrin molecules and hence the number of D-glucose monomers. The observation of such saturation points has often proved difficult or impossible.[11] However, Yokoi *et al.*[6] used EPR spectroscopy to observe the inclusion of one and two molecules of bis(pyridin-2-ylmethanolato)copper(II) with α- and γ-cd respectively. Harada and Takahashi[24] found that ferrocene needs two molecules of α-cd and one of γ-cd to form inclusion complexes. However, no such regular array of cyclodoxtrins around even organic substrates has been observed previously. It has been shown that modified or substituted β-cd forms an aggregate, specifically with 4-nitrophenol and not with other substrates.[12]

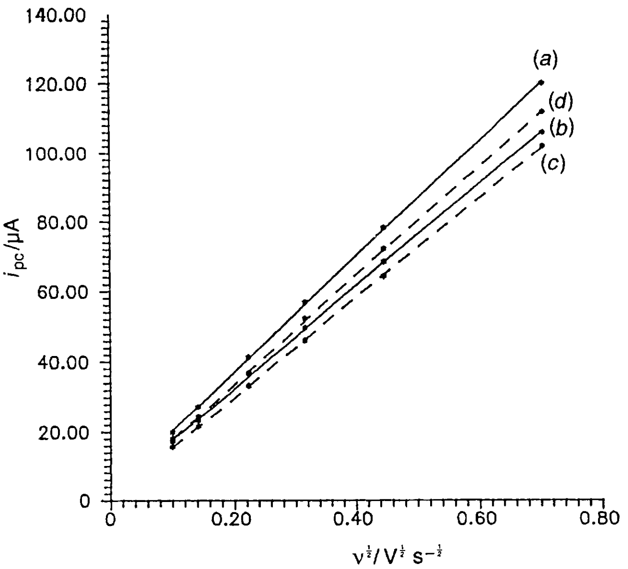


**Fig. 5** Plots of $i_{pc}$ *vs.* $v^{\frac{1}{2}}$ for $[Cu(pdto)]^{2+}$ (0.001 mol dm$^{-3}$) in the absence (*a*) and presence of α-cd (0.005 mol dm$^{-3}$) (*b*), β-cd (0.004 mol dm$^{-3}$) (*c*) and γ-cd (0.003 mol dm$^{-3}$) (*d*)

The peak-current ratio in the presence of α-, β- and γ-cd increases only slightly with increase in scan rate suggesting that the copper(I) species is very slightly adsorbed on the surface of the electrode,[29] in contrast to the cd-free solutions in which it is weakly adsorbed. In the $Cu^{II}$–$Cu^I$ redox potential range the coverage of the electrode by cd molecules is greater[31] or their orientation is adequate to form a more compact layer; this may also lead to the prevention of adsorption and explain the reduction in peak-current value and observed reversibility. However, the addition of D-glucose, even at higher concentrations, did not confer reversibility. So it is clear that only adduct formation renders the redox behaviour diffusion controlled and reversible. We have shown that inclusion complex formation of methyl viologen dication 1,1′-dimethyl-4,4′-bipyridinium by β-cd is an effective and selective method to reduce adsorption and hence to confer reversibility on the electroactive species.[20] For $[Cu(pdto)]^{2+}$ a similar inclusion

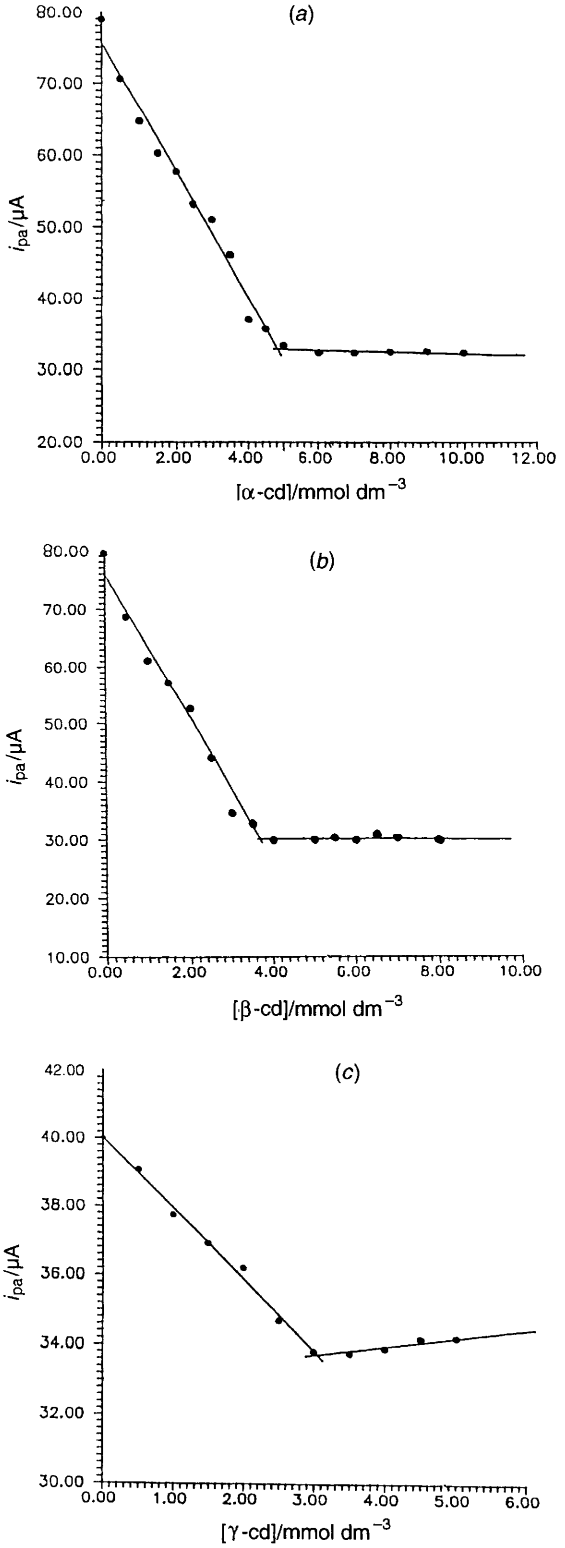


**Fig. 6** Plots of (*a*) observed anodic peak current *vs.* concentration of α-cd added, (*b*) observed anodic peak current *vs.* concentration of β-cd added and (*c*) observed cathodic peak current *vs.* concentration of γ-cd added, for $[Cu(pdto)]^{2+}$ (0.001 mol dm$^{-3}$)

phenomenon is not obviously involved, as the sizes of the cd cavities are much smaller than that of the complex.

The interaction of the present complexes with cyclodextrins may involve expulsion of a few water molecules or the partial inclusion of the pyridine or benzimidazole ring into the primary or secondary hydroxy-group-bearing face of the cd. The expulsion of the enthalpy-rich[32] water molecules enclosed within the uncomplexed cd cavity into bulk water upon substrate inclusion results in a negative enthalpy change, together with a positive entropy change, leading to stronger interaction. An X-ray crystallographic study of β-cd dodecahydrate[33] has shown that 6.5 water molecules within the cavity are disordered over eight sites and display extensive thermal motion. Also there may be hydrogen-bonding interactions of the benzimidazole NH group of co-ordinated bbdo with hydroxyl groups of the cyclodextrins.

$$\begin{tikzcd}
Cu^{2+} + e^- \arrow[r, shift left, "E_f^\circ"] \arrow[d, shift left] & Cu^+ \arrow[l, shift left] \arrow[d, shift left] \\
Cu^{2+}\text{-cd} + e^- \arrow[u, shift left, "K_{2+}"'] \arrow[r, shift left, "E_b^\circ"] & Cu^+\text{-cd} \arrow[l, shift left] \arrow[u, shift left, "K_+"']
\end{tikzcd}$$

**Scheme 1**

From the slope of the plots of $i_{pc}$ *vs.* $v^{\frac{1}{2}}$ plot the values of the diffusion coefficient ($D$) were calculated using Sevcik's equation.[34] In the presence of α-, β- and γ-cd the slope is suppressed and thus there is always a decrease in $D$ (Table 2) suggesting that the copper(II) complex diffuses slowly to the electrode mainly in a cyclodextrin-bound form. The diffusion coefficients of the cd-bound complexes ($D_c$) calculated from the $i_{pc}$ values at the limiting cyclodextrin concentrations (Table 2), at which adduct formation is complete, are also typical[33] of one-electron transfer.

The anodic and cathodic peak currents of $[Cu(bbdo)]^{2+}$ decrease and the peak-current ratio slightly increases when the concentration of α-, β- and γ-cd is increased; however, no inflections are observed. The $\Delta E_p$ value decreases slightly for all the three cyclodextrins, suggesting that the copper(II) species is not stabilized in cd solutions.

**Trithioether complexes in the presence of cyclodextrins.** Addition of the cyclodextrins in steps to aqueous $[Cu(pttn)]^{2+}$ and $[Cu(pttu)]^{2+}$ has little effect on the $Cu^{II}$–$Cu^{I}$ redox process (Table 2, Fig. 4). Thus the values of $\Delta E_p$ and $E_{\frac{1}{2}}$ remain unaffected; however, the peak currents decrease with or without any change in $i_{pa}/i_{pc}$ values, suggesting that the complexes interact with the cyclodextrins appreciably. Addition of β- and γ-cd to $[Cu(pttn)]^{2+}$ decreases $E_{\frac{1}{2}}$ as well as the peak-current ratio (Table 2) suggesting that adsorption of copper(I) species formed on reduction is not completely prevented. For the addition of β- and γ-cd to $[Cu(pttu)]^{2+}$ there is a slight increase in $E_{\frac{1}{2}}$ (see below). Thus, unlike $[Cu(pdto)]^{2+}$, no interesting changes in electrochemical properties were observed on adding the cyclodextrins; this suggests that the interaction of $[Cu(pdto)]^{2+}$ with cyclodextrins is selective, probably because the complex is square planar. Further, there is no cleavage of a metal–ligand bond but a stereochemical rearrangement from a square-planar to a tetrahedral geometry occurs on electron transfer; on the other hand for the non-planar trithioether complexes cleavage of at least one M–L bond and hence break up and reforming of the assembly of cyclodextrins around the redox-active species occurs. The presumably five-co-ordinate $[Cu(pttu)]^{2+}$, like its homologue[23] $[Cu(pttn)]^{2+}$, would lead to the formation of four-co-ordinate $[Cu(pttu)]^{+}$ in which one of the $Cu$–$N_{py}$ bonds is broken.[22]

## Changes in redox potentials

From the shifts in redox potentials observed on the addition of cyclodextrins the ratio of the formation constants $K_+/K_{2+}$ was calculated, assuming reversible electrode reaction as well as reversible binding of copper-(II) and -(I) species to the cyclodextrins (Scheme 1) and using the general formula[20] (1)

$$E_b^\circ - E_f^\circ = 0.059 \log(K_+/K_{2+}) \qquad (1)$$

where $E_b^\circ$ and $E_f^\circ$ are the formal potentials of the redox couple (+2/+1) in the bound and free forms respectively and $K_{2+}$ and

**Table 3** Hill coefficient ($h$) and $K_a$* using $i_{pa}$ and $i_{pc}$ values for the interaction of $[Cu(pdto)]^{2+}$ with cyclodextrins

| Parameter | α-cd | | β-cd | | γ-cd | |
|---|---|---|---|---|---|---|
| used | $h$ | $K_a$/dm$^3$ mol$^{-1}$ | $h$ | $K_a$/dm$^3$ mol$^{-1}$ | $h$ | $K_a$/dm$^3$ mol$^{-1}$ |
| $i_{pa}$ | 2.09 | 3680 | 1.87 | 4730 | 1.44 | 900 |
| $i_{pc}$ | 1.47 | 1450 | 1.25 | 2130 | 1.49 | 920 |

* $K_a$ values are 1/[intercept] and $h$ values are the slopes of the plots of ln $[Y/(1 - Y)]$ *vs.* ln $X$ (Fig. 7).

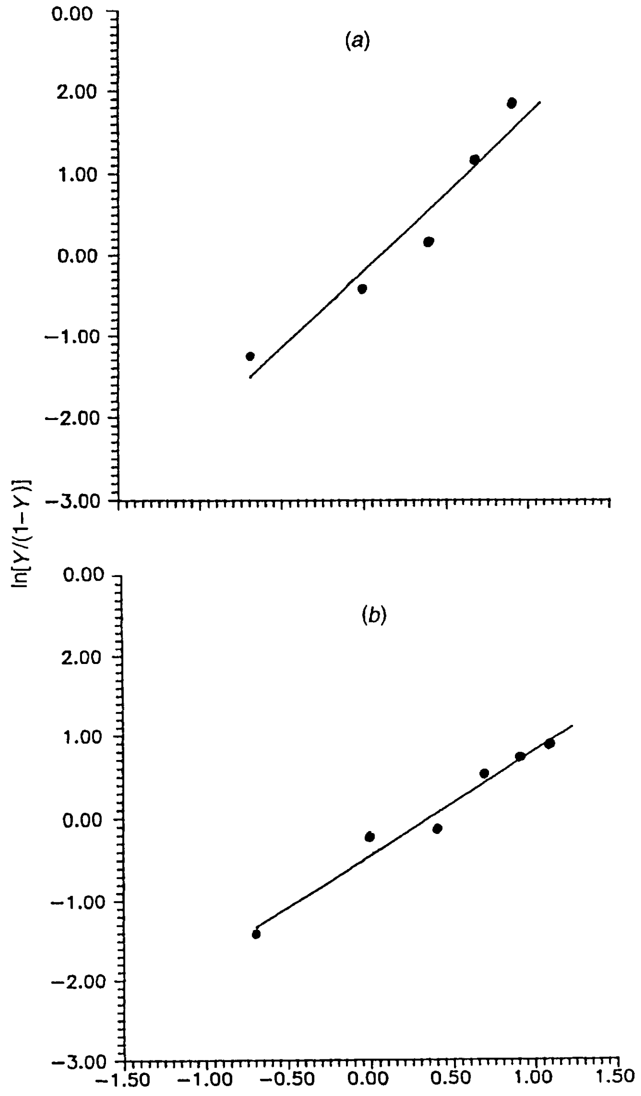


**Fig. 7** Plots of ln$[Y/(1 - Y)]$ *vs.* ln $X$ using the cathodic peak current (*a*) and the anodic peak current (*b*) of $[Cu(pdto)]^{2+}$ in the presence of β-cd

$K_+$ are the equilibrium constants for the binding of cd to the copper-(II) and -(I) complexes, respectively. The formation and dissociation of the adducts are expected to be fast enough to maintain an equilibrium on the time-scale of the cyclic voltammetry experiment. The values of $K_+/K_{2+}$ (Table 2) illustrate that the copper-(II) rather than -(I) forms of almost all the complexes interact strongly with all the cyclodextrins; however, the values are greater than unity for $[Cu(pttu)]^{2+}$ in the presence of β- and γ-cd suggesting that the copper-(I) rather than -(II) form interacts strongly.

### Is the binding of cyclodextrins co-operative?

Allosteric regulation of binding and catalysis is a common feature in the regulation of enzymes by molecular effectors. When the affinity of an enzyme for a substrate increases with increasing effector concentration the allostery is termed positive co-operativity, and the transition from the inactive to the active state of the protein is the allosteric transition. Positive co-operativity in the binding of inorganic guests to synthetic hosts has been observed in dicoronands linked by a biphenyl,[36] gable porphyrins,[37] porphyrin dimers,[38] and crystalline haem models.[39] It has been reported also in micelle-catalysed reactions.[40,41] Titrations of $[Cu(pdto)]^{2+}$ with cyclodextrins led to sigmoidal rather than hyperbolic curves. Replotting of the titration data according to the Hill equation [12,40] (2) where

$$\ln[Y/(1 - Y)] = h \ln X - \ln K_d \qquad (2)$$

$X$ = concentration of cyclodextrin added, $Y$ = ratio of the observed change in the value of $i_{pa}$ or $i_{pc}$ of the complex on adding the cd to the maximum change in the respective electrochemical property, $h$ = the Hill coefficient and $K_d$ = overall dissociation constant, gave straight lines (Fig. 7) the slope of which is defined as the Hill coefficient ($h$), which is construed as an index of co-operativity. Non-co-operative systems exhibit $h \approx 1.0$, positively co-operative systems $h > 1.0$ and negatively co-operative systems $h < 1.0$. As a point of reference, haemoglobin has $h = 2.8$, while myoglobin has $h = 1.0$ towards binding of oxygen.

For the binding of $[Cu(pdto)]^{2+}$ to cyclodextrins the $h$ values calculated using $i_{pc}$ and $i_{pa}$ are collected in Table 3. For all three cyclodextrins the value of $h$ is greater than unity (1.3–2.1). Hill coefficients greater than unity are the experimental hallmark of positive co-operativity,[12] in which initial binding events render subsequent binding events more favourable. Thus the present study shows that the binding of cyclodextrins to $[Cu(pdto)]^{2+}$ is co-operative. The analysis of $i_{pa}$ and $i_{pc}$ data gave values of the association constant $K_a$ ($1/K_d$) which are of the same order of magnitude for all the cyclodextrins. These values suggest that the stability of $[Cu(pdto)]^{2+}$ adducts varies in the order β-cd > α-cd > γ-cd. For several organic substrates β-cd has been shown to exhibit selective inclusion complex formation. For the present complex selectivity is not achieved obviously because inclusion is not involved; however, the stability is still the highest. It appears that uncomplexed β-cd includes a number of high-energy water molecules, a higher number than those of uncomplexed α-cd.[33,42] So, if the major part of the binding energy for the present complex is derived from the release of these water molecules, β-cd should lead to a more negative enthalpy of complexation and hence a higher association constant than would α-cd. In contrast, the values of $\Delta H^\circ$ and $\Delta S^\circ$ for the formation of inclusion complexes of β-cd with *p*-nitrophenol,[43] *p*-nitrophenylglycosides,[43] and *m*- and *p*-disubstituted benzenes[44] are considerably less negative than those for the corresponding α-cd complexes.

The association constant $K_a$ for the interaction of an organic host molecule with $n$ cyclodextrin molecules has been calculated using the diffusion coefficient of the free complex ($D_c$) and the observed diffusion coefficients ($D_{obs}$) at various cyclodextrin concentrations using the relationship[43] (3). However, the

$$D_{obs} = \{(D_f - D_{obs})/K_a[cd]^n\} + D_c \qquad (3)$$

present adduct-formation data failed to fit this relationship for the observed values of $n = 5$, 4 and 3 for α-, β- and γ-cd respectively. This suggests that complete adduct formation occurs only at the saturation points prior to which the co-operative adduct formation occurs.

## Conclusion

The present voltammetric study reveals that the $Cu^{II}$–$Cu^{I}$ redox couple of $[Cu(pdto)]^{2+}$ becomes free from adsorption effects and tend to enhance its reversibility in the presence of five, four and three equivalents of α-, β- and γ-cd respectively. These limiting concentrations decrease with increasing size of the cyclodextrin molecules and are consistent with the formation of arrays of cyclodextrins around the copper(II) complex. However, for other copper(II) complexes no significant changes in redox properties have been observed. Thus the binding of cyclodextrins to $[Cu(pdto)]^{2+}$ tends to be selective and β-cd exhibits a stronger binding than α- and γ-cd.

Cyclodextrins have been reported to be effective hosts for many molecules by inclusion complex formation but the present assembly of cyclodextrins around the redox-active species can be regarded as a new and multifunctional model for the biological systems involved in molecular recognition.[32]

The self-assembly of cyclodextrin molecules to form functional aggregates like micelles illustrates the principle of co-operativity in enzymes. The positive co-operativity observed for the binding of all the three cyclodextrins with $[Cu(pdto)]^{2+}$ implies the stimulation of the interaction of additional substrate molecules upon interaction of the first molecule with the enzyme.[12]

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