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Host–guest assembly of ligand systems for metal ion complexation; synergistic solvent extraction of copper(II) ions by N_3O_2-donor macrocycles and carboxylic or phosphinic acids

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Host–guest formation between N_3O_2-donor macrocyclic hosts and lipophilic organic acid guests (that are themselves potential metal-ion ligands/extractants) has been investigated and the implications of formation of such ligand assemblies for the binding of metal ions have been probed. The formation of 2 : 1 (organic acid : macrocycle) assemblies has been demonstrated using NMR titration experiments in deuterochloroform for 4-*tert*-butylbenzoic, palmitic, phenylphosphinic, diphenylphosphinic and salicylic acids, with evidence for the additional formation of 1 : 1 intermediates in some cases. Molecular adducts of this type have been used in solvent extraction (water/chloroform) experiments to define the effect of assembly formation on metal ion binding. From entropy considerations it was anticipated that the formation of particular host–guest species of the above type might result in enhanced metal ion binding (and hence enhanced metal ion extraction) – a consequence of the fact that the components of the coordination sphere are, at least in part, assembled for complex formation. Using a range of assemblies of the above type, enhanced (synergistic) extraction of Cu(II) ions was confirmed in all cases. Adducts of 1,12,15-triaza-3,4:9,10-dibenzo-5,8-dioxacycloheptadecane and 1,12,15-triaza-3,4:9,10-bis(4′-*tert*-butylbenzo)-5,8-dioxacycloheptadecane with 4-*tert*-butylbenzoic acid and salicylic acid have been isolated and their solid-state structures (and 1 : 2 stoichiometries) confirmed by X-ray diffraction.

Introduction

Much recent attention has been given to the chemistry of synthetic receptors and molecular assemblies.[1] Recognition, complementarity, self assembly and preorganisation are all facets of this expanding field – the study of which continues to have implications for many areas of both chemistry and biochemistry. Thus, it has been realised for some time that the use of supramolecular ligand systems may assist a better control of the selectivity and efficiency of separation processes.[2]

In an earlier publication we considered the formation of host–guest adducts between organic moieties which are themselves potential metal-ion ligands and introduced the subtle concept of an 'assembly effect' involving metal-ion coordination by such ligand 'packages'.[3] The use of a discrete ligand package for metal complexation (where the package exists in solution in *equilibrium* with its corresponding metal complex) has the potential to result in enhanced complex stability. That is, the effect introduces an element of preorganisation between ligand components such that this may favourably influence metal complex formation, provided that the back equilibrium to the free (separated) ligands is unfavourable. The proposed effect is thus largely expected to be one of thermodynamic origin, leading to a favourable contribution to the overall entropy of the system.

The present paper deals with the application of ligand assemblies to the solvent extraction of metal ions in two-phase systems involving equilibria of the following types:

(i) Assembly of the ligand package by proton transfer from an organic acid to an amine macrocycle, followed by the formation of electrostatic and hydrogen bonds between the charged components,

$$L_{(org)} + n\,RXH_{(org)} \rightleftharpoons [LH_n(RX)_n]_{(org)}$$

(ii) Metal ion extraction, accompanied by displacement of protons from the package,

$$[LH_n(RX)_n]_{(org)} + M^{n+}{}_{(aq)} \rightleftharpoons [LM(RX)_n]_{(org)} + n\,H^+{}_{(aq)}$$

Clearly, a range of factors will influence the stability of the species involved in these equilibria; these include the stoichiometries of macrocycle (L) to acid (RXH) in the assemblies, the nature of the acid (lipophilicity, pK_a), the basicity and hydrophobicity of the macrocycle, the coordination requirements of the metal ion M^{n+}, the pH of the aqueous phase and the nature of the solvent employed.

Solvation/hydration of the ligand package or of the metal complex, *e.g.*

$$[LM(RX)_n]_{(org)} + m\,HRX_{(org)} + x\,H_2O_{(org)} \rightleftharpoons [LM(RX)_n]\cdot m\,HRX\cdot x\,H_2O_{(org)},$$

will also influence the equilibria and hence the efficiency of metal transport between phases. However, this is not the focus of the study now presented which deals with the relationship between ligand assembly and metal complex formation. Apart from its considerable intrinsic interest, the assembly concept has the exciting prospect of systematising a range of already reported metal-ion complexation behaviour as well as providing

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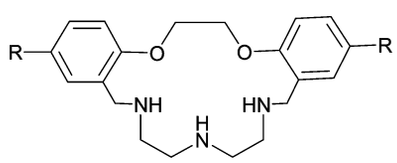
a basis for the rational design of improved metal uptake systems – especially for use in solvent extraction applications.

Whilst there are many reports of the use of synergistic combinations of metal solvent extractants,[4] rarely do these involve, as in the systems reported here, ligand packages with well defined stoichiometries which can be assembled and characterized in the absence of the metal ion. Nevertheless the formation of supramolecular assemblies has been recognised as a useful approach to the control of the selectivity and efficiency of metal-separation processes.[5] The benefit of using a combination of extractants to ensure the saturation of the coordination sphere of the extracted metal ion has been recorded, thus providing an explanation for the observed synergistic extraction by O- or S-donor macrocycles in the presence of carboxylic, phosphoric or sulfonic acids.[6] In this study the conclusions were supported by X-ray structure determinations of related complexes.[7]

There are fewer examples of the use of synergistic combinations of amine macrocycles and organic acid extractants in similar studies.[8] Mixtures of simple hydrophobic amines and organic acids, so-called 'acid–base couple' or 'binary extractants' have attracted more attention.[9]

We now present the results of an investigation of the effects of ligand self-assembly on the solvent extraction of Cu(II) by the mixed-donor macrocycles **1**–**3** in combination with selected carboxylic and phosphinic acids.



1, R = H
2, R = C(CH$_3$)$_3$
3, R = C$_9$H$_{19}$

Experimental

Where available, all reagents were of analytical grade and were used without further purification. The macrocyclic ligand **1** was prepared as described previously[10] while **2** was obtained by a similar procedure starting from 1,2-bis-(4-*tert*-butyl-2-formylphenoxy)ethane.[11] Macrocycle **3** was also prepared by an analogous procedure starting from 5-nonyl-2-hydroxybenzaldehyde.[12]

NMR Titrations

The NMR titration experiments were conducted on Bruker AM300 and AC200 NMR spectrometers at 297K. For the NMR titration studies, a weighed amount of acid was added incrementally to the respective macrocycles (typically ~0.07 mol dm^{-3}) dissolved in deuterated chloroform (0.5 cm^3) in the NMR tube; the amount added was determined by weight difference before and after each addition. Chemical shift changes in the ^{1}H and/or ^{13}C NMR spectra were recorded after each addition. All signals in deuterated chloroform were referenced to TMS. Induced chemical shifts were plotted as a function of the mole ratio of the carboxylic or phosphinic acid to macrocyclic ligand present at each titration point.

Solvent extraction

Individual solvent extraction experiments were performed in sealed glass vials containing an organic phase (5 cm^3) and an aqueous phase (5 cm^3). The preliminary experiments involving ligand 1 (see Results and discussion section) were performed with both metal ion and ligand concentrations of 10^{-2} mol dm^{-3}. For all other extraction experiments the aqueous phase consisted of a metal solution of concentration 10^{-3} mol dm^{-3} while the organic phase contained ligand at 10^{-3} mol dm^{-3} and known concentrations of carboxylic or phosphinic acid in chloroform (which had been presaturated with distilled water). In all experiments the aqueous phase was maintained at the chosen pH by the careful addition of dilute solutions of NaOH or HNO_3 (*via* a micropipette) with interspersed shaking until the required pH was obtained (and maintained). 'Control' experiments were performed in which the organic phase only contained the required concentration of carboxylic or phosphinic acid. Unless otherwise specified, all experiments involved shaking the extraction vial at 130 cycles/minute in a Haake SWB 20 oscillating shaker for a minimum of 4 h at 25 °C.

Metal ion concentrations in the respective phases were determined using atomic absorption spectroscopy. The fraction of metal extracted, F_m, was calculated as [moles of metal ion in the organic phase]/[total number of moles of the metal in both phases]. All extraction experiments were performed in duplicate with the relative error for the metal extraction being approximately ±10%.

Synthesis of adducts

[H$_2$1][4-*tert*-butylbenzoate]$_2$·CH$_3$CN·2H$_2$O. Slow crystallisation of an acetonitrile solution containing **1** and 4-*tert*-butylbenzoic acid in the ratio 2 : 1 yielded a crystalline 2 : 1 complex. These crystals were used directly for the X-ray structure determination without further characterisation.

[H$_2$2][salicylate]$_2$·H$_2$O. A hot solution of salicylic acid (0.03 g, 2×10^{-4} mol) in methanol (3 cm^3) was added dropwise to a hot stirred solution of **2** (0.04 g, 1×10^{-4} mol) in methanol (5 cm^3). A further 2 cm^3 of methanol was added. The solution was heated to boiling and its volume reduced by half. On standing, a white solid formed which was recrystallised from ethanol (5 cm^3) to give colourless prismatic crystals which were used for the crystallographic study (Found: C, 66.65; H, 7.64; N, 5.45. $C_{42}H_{55}N_3O_9$ requires C, 66.82; H, 7.48; N, 5.57%)

Single-crystal X-ray diffraction

Data for [H$_2$**1**][4-*tert*-butylbenzoate]$_2$·CH$_3$CN·2H$_2$O and [H$_2$**2**][salicylate]$_2$·H$_2$O were collected on CAD-4 and Bruker SMART 1000 CCD diffractometers respectively using graphite-monochromated Mo-Kα radiation generated from a sealed tube. ORTEP[13] depictions of the structures are provided in Figs. 1 and 2.[14] Crystallographic details are provided in Table 1. Cell constants were obtained by least squares refinement against

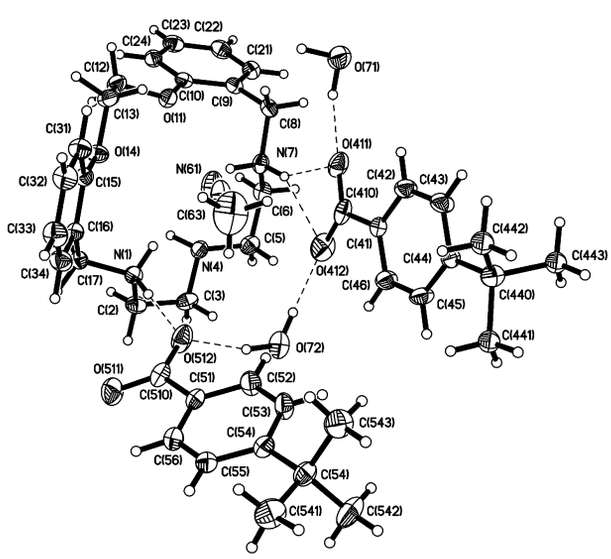


Fig. 1 ORTEP depiction of the solid-state structure of [H$_2$**1**][4-*tert*-butylbenzoate]$_2$·CH$_3$CN·2H$_2$O showing the hydrogen bonds between the benzoate oxygen atoms and the benzylammonium groups N1 and N7 and the waters of crystallisation O71 and O72. Rotational disorder about C(44)–C(440) is not shown.

Table 1 Crystallographic data

Parameter	$[H_2\mathbf{1}]$[*tert*-butylbenzoate]$_2\cdot 2H_2O$	$[H_2\mathbf{2}]$[salicylate]$_2\cdot H_2O$
Formula	$C_{44}H_{62}N_4O_8$	$C_{42}H_{56}N_3O_9$
M_r	774.98	746.90
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/n$ (no. 14)	$P2_1/c$ (no. 14)
a/Å	17.606(2)	18.638(10)
b/Å	15.587(2)	12.575(7)
c/Å	18.288(2)	19.075(10)
β/°	118.01(2)	113.528(9)
V/Å^3	4430.9(9)	4099(4)
D_c/g cm^{-3}	1.162	1.210
Z	4	4
Crystal size/mm	0.08 × 0.13 × 0.40	0.478 × 0.465 × 0.237
Crystal colour	Colourless	Colourless
Crystal habit	Lath	Prism
T/K	296(2)	150(2)
λ(Mo-Kα)/Å	0.71073	0.71073
μ(Mo-Kα)/mm^{-1}	0.08	0.085
T(Gaussian)$_{min,max}$	Not measured	0.957, 0.981
$2\theta_{max}$/°	49.96	56.50
hkl Range	−2 20, 0 18, −21 19	−24 24, −15 15, −24 24
N	8173	35320
N_{ind} (R_{merge})	7783 (0.0335)	9213 (0.0290)
N_{obs} ($I > 2\sigma(I)$)	2540	6981
N_{var}	517	531
Residuals $R1(F)$, $wR2(F^2)$	0.0413, 0.1564[a]	0.0533, 0.1299[a]
GoF (all)	0.95	1.301
Residual extrema/e Å^{-3}	−0.187, 0.24	−0.289, 0.522

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ for $F_o > 2\sigma(F_o)$; $wR2 = (\Sigma w(F_o^2 - F_c^2)^2/\Sigma(wF_c^2)^2)^{1/2}$ (all reflections); $w = 1/[\sigma^2(F_o^2) + (AP)^2 + BP]$ where $P = (F_o^2 + 2F_c^2)/3$ and $A = 0.0721$ and $B = 0$ for $[H_2\mathbf{1}]$[4-*tert*-butylbenzoate]$_2\cdot 2H_2O$, and A = 0.04 and B = 1.0 for $[H_2\mathbf{2}]$[salicylate]$_2\cdot H_2O$.

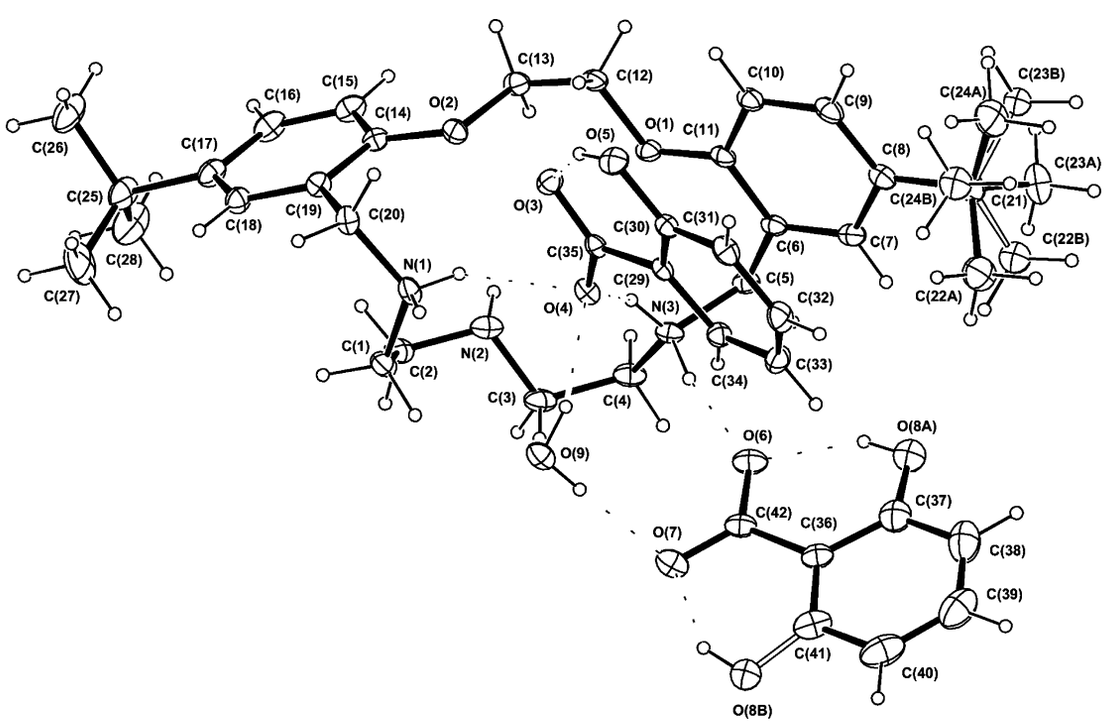


Fig. 2 ORTEP depiction of $[H_2\mathbf{2}]$[salicylate]$_2\cdot H_2O$ with 20% displacement elliposids. Hydrogen bond interactions are indicated with dotted lines and the unfilled non-hydrogen bonds signify the disorder described in the Experimental section.

25 and 972 reflections located between 20–28 and 4.5–55° 2θ respectively.

For $[H_2\mathbf{1}]$[4-*tert*-butylbenzoate]$_2\cdot CH_3CN\cdot 2H_2O$, data reduction and the solution and refinement of the structure in space group $P2_1/n$ were carried out as described previously[15] using SHELX-86[16] and SHELXL-97.[17] The C(440) *tert*-butyl groups is rotationally disordered over three sites, with occupancies of 0.397, 0.301 and 0.301. With the exception of the disordered *tert*-butyl methyl groups C-atoms all non hydrogen atoms were refined with anisotropic displacement parameters and a riding atom model was used for the hydrogen atoms.

For $[H_2\mathbf{2}]$[salicylate]$_2\cdot H_2O$, the data integration and reduction were undertaken with SAINT and XPREP,[18] and subsequent computations were carried out with the teXsan[19] and WinGX[20] graphical user interfaces. A Gaussian absorption correction was applied to the data,[18,21] and the data reduction included the application of Lorentz and polarisation corrections. The structure was solved in the space group $P2_1/c$ (no. 14) by direct methods with SIR97,[22] and extended and refined with SHELXL-97.[17] One *tert*-butyl group (C21–C24) is slightly rotationally disordered over two positions in a 9 : 1 ratio for the A and B components (Fig. 2). Two sites were also located for

Table 2 Observed endpoints for the ^{1}H NMR titrations of macrocycles **1**–**3** with the various carboxylic and phosphinic acids shown in $CDCl_3$

Acid	**1**	**2**	**3**
4-*tert*-Butylbenzoic	1 : 2	1 : 2	1 : 1[a] 1 : 2[a]
Palmitic	1 : 2	1 : 2	1 : 1 1 : 2
Phenylphosphinic		1 : 2	1 : 2
Diphenylphosphinic		1 : 2	1 : 2
Salicylic		1 : 2	1 : 2

[a] Also observed in deuterohexane.

the hydroxyl group O(8) in one of the salicylate units, and these sites were assigned complementary occupancies, refined and then fixed at 0.75 and 0.25. With the exception of C(22B), C(23B), C(24B) and O(8B), all non-hydrogen atoms were refined with anisotropic displacement parameters and a riding atom model was used for the hydrogen atoms. The hydrogen atoms of the water, the protonated amines and the O(5) hydroxyl group were identified from difference Fourier maps and modelled with isotropic displacement parameters.

CCDC reference numbers 207755 and 207756.

See http://www.rsc.org/suppdata/dt/b3/b303825d/ for crystallographic data in CIF or other electronic format.

Results and discussion

Formation of ligand adducts in $CDCl_3$

In our previous investigations[3,23] NMR titrations proved to be a valuable tool for detecting host–guest formation between potential ligands in solution, as well as yielding the stoichiometry of the resulting assemblies and defining the nature of the host–guest interaction sites. In these studies it was demonstrated that a range of both polyamine and mixed-donor macrocycles readily form 1 : 1 and/or 2 : 1 adducts with 4-*tert*-butylbenzoic or palmitic (hexadecanoic) acid in $CDCl_3$.[3,23,24] Overall, it was concluded that the maximum stoichiometry of the respective adducts in $CDCl_3$ corresponds to the number of amine sites in the host ligand that have (log) protonation constants equal to or greater than 6–7 in aqueous or aqueous–methanol media.

In the present study, the results from NMR titrations (Table 2) provide evidence for the formation of ligand assemblies between the macrocycles **1**–**3** and 4-*tert*-butylbenzoic, palmitic, phenylphosphinic, diphenylphosphinic and salicylic acid. The titrations involved the incremental addition of the respective acids to the chosen macrocycle in $CDCl_3$ contained in an NMR tube while the ^{1}H or ^{13}C NMR spectrum was monitored. Clear formation of host–guest assemblies was observed in all cases. For example, addition of palmitic acid to **1** gave induced shifts (in the range 0.3–0.6 ppm) for the signals corresponding to the methylene protons adjacent to the nitrogen donors. This implies that there is a relatively strong interaction between the NH groups and palmitic acid. A large induced shift was also observed for the NH signal (~7 ppm). Parallel behaviour was observed for the signals of the corresponding methylene carbons in the ^{13}C NMR spectrum. In contrast, both the proton and carbon signals for the methylene groups adjacent to the ether oxygens are associated with negligible shifts, in keeping with there being little host–guest interaction at these sites. A similar situation was observed for the addition of phenylphosphinic acid to **2** (see Fig. 3).

X-Ray diffraction analysis

Solvated crystalline adducts of macrocycles **1** and **2** with 4-*tert*-butylbenzoic acid and salicylic acid respectively were isolated on evaporation of an acetonitrile solution for the former and an ethanol solution for the latter containing the component species in a 1 : 2 (macrocycle : acid) ratio, respectively. Single-crystal X-ray diffraction structure determinations confirm the 1 : 2 stoichiometry of these adducts in the solid state and also that transfer of two acid protons (to the benzylamino nitrogen atoms in each case, see Figs. 1 and 2) has occurred. Such a formulation is in agreement with the NMR titration studies and pK_a data[25–31] (see Tables 2 and 3) which indicate that the strong interactions between the adduct components in solution involve the more basic secondary amine groups. In the case of the adduct with macrocycle **1**, a molecule of acetonitrile is also present, located centrally over the cavity of the macrocycle (see Fig. 1).

The water molecules present in the lattices of both adducts provide hydrogen-bonding bridges between the carboxylate groups. As a consequence, the solid-state structures do not necessarily provide good models for these assemblies dissolved in hydrophobic solvents of the type used for the extraction studies (see below). However, they do indicate that proton transfer has occurred in the solid and indicate that a combination of electrostatic forces and hydrogen bonding occurs, leading to a substantial interaction between the secondary ammonium groups of the macrocycle and the carboxylate anions. The situation is similar to the proton transfer that occurs in the 2 : 1 adduct between cyclam and benzoic acid described previously and characterised by X-ray and neutron diffraction in combination with density functional computations.[24] Recently a comparable result has been obtained for 7,16-diaza-18-crown-6 and *p*-aminobenzene sulfonic acid.[32]

Table 3 pK_a values for macrocycles **1**–**3** (in 95% methanol at 25 °C, I = 0.1 Et_4NClO_4) and organic acids [in H_2O, I = 0.1 (H,Na)ClO_4] used in this study

Macrocycle	pK_{a1}	pK_{a2}	pK_{a3}	Ref.
1	9.69	8.45	~2	25
2	9.65	8.33	~2	25
3	9.65	8.32	~2	25

Organic acid	pK_a	Ref.
4-*tert*-Butylbenzoic	4.40	26
Palmitic	[a]	
Phenylphosphinic	1.75	27
Diphenylphosphinic	1.72	28
Salicylic	2.72	29

[a] The insolubility in water and complex behaviour of palmitic acid in two-phase systems (see, for example, Ouimet *et al.*[30] and references therein) makes it inappropriate to quote a value for comparison with those of the other acids listed. Aliphatic carboxylic acids with different alkyl chain lengths have pK_a values in the range 4.7–4.9.[31]

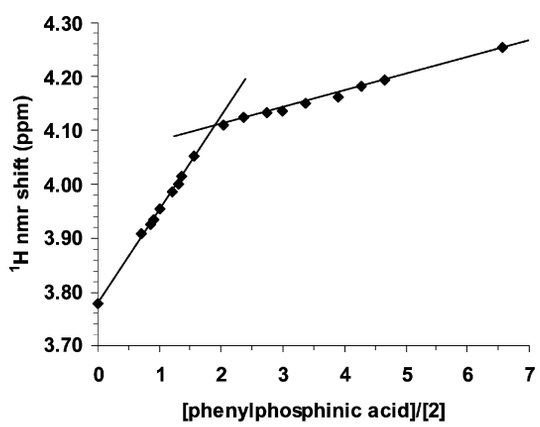


Fig. 3 ^{1}H NMR titration data corresponding to addition of phenylphosphinic acid to **2** in deuterochloroform.

Solvent extraction studies

Having confirmed that the ligand 'packages' form in $CDCl_3$, a study was undertaken to assess the efficacy of the different packages in transporting metals from aqueous solution into chloroform. With this ultimate aim, preliminary experiments were carried out using **1** to establish appropriate conditions. It was immediately apparent on contacting a Cu(II) nitrate solution with **1** alone in chloroform that there is a tendency for this macrocycle to transfer to the aqueous phase. Thus, treatment of the chloroform solution of **1** with aqueous Cu(II) solution leads to the generation of a deep blue colouration in the aqueous phase. This is consistent with the transfer of ligand across the organic/aqueous boundary to form hydrated Cu(II) complexes of **1**. Such ligand 'bleeding' almost certainly involves a cationic complex but may also involve cationic (protonated) forms of the ligand. In view of this it was anticipated that the introduction to the organic phase of a lipophilic anion might increase the lipophilicity of any cationic species by generating either host–guest or ion-pair 'charge neutralised' assemblies. Accordingly, a slight excess of palmitic acid was added to the organic phase in the above experiment. This resulted, on shaking, in a dramatic change in which the deep blue colour of the copper solution was largely transferred to the chloroform phase, consistent with copper complex formation now predominating in this phase. In the light of this result, Cu(II) extraction experiments were performed in the presence of various ratios of palmitic acid to macrocycle **1**; for each ratio a series of individual experiments was carried out over a pH range of 1–6, with the aqueous phase containing Cu(II) nitrate (0.01 mol dm^{-3}) and the chloroform phase containing **1** (0.01 mol dm^{-3}). Equal volumes of both phases were employed. The results are shown in Fig. 4. For this system a pH at equilibrium of 5.0 and a palmitic acid to macrocycle ratio of 4 : 1 provides efficient (~90%) extraction of copper. In contrast, at pH 3.0 approximately 90% of the copper remains in the aqueous phase. It should be noted that a pH of 5.0 falls below the region where metal hydrolysis might interfere with the extraction process. The observation that an acid to macrocycle ratio greater than that needed for adduct formation (2 : 1) leads to somewhat increased copper transfer is consistent with neutral carboxylic acid molecules forming outer-sphere complexes, and acting as 'solvating extractants'.† Alternatively, the efficacy of formulations with high acid to macrocycle ratios may simply be a reflection that excess acid is needed to drive the equilibrium for formation of the 2 : 1 assembly to completion under the conditions employed. With respect to this, macrocycle **1** has a substantial tendency to bleed into the aqueous phase – an equilibrium process that is significantly reversed in the presence of excess palmitic acid (see earlier discussion).

When a series of control experiments were carried out under similar conditions to the above but in the absence of **1** (with the palmitic acid concentration maintained at 0.04 mol dm^{-3}), no copper extraction occurred when the pH was 3.0 and also when it was adjusted to 4.1, while at higher pH values a third (solid) phase was observed to form. Interestingly, such behaviour contrasts with the situation discussed above

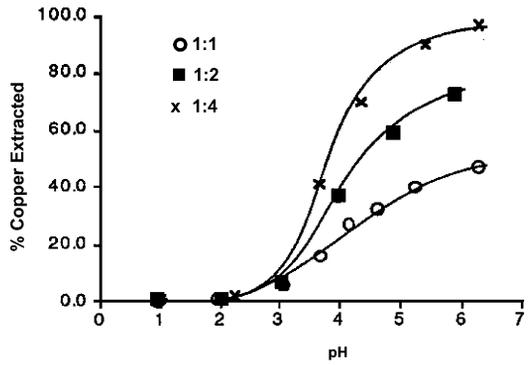


Fig. 4 The pH-dependence of extraction of Cu(II) into a chloroform solution of **1** (10^{-2} mol dm^{-3}) and palmitic acid (1×10^{-2}, 2×10^{-2} or 4×10^{-2} mol dm^{-3}) after equilibration with an equal volume of an aqueous solution of $Cu(NO_3)_2$ solution (10^{-2} mol dm^{-3}).

where macrocycle **1** (at 0.01 mol dm^{-3}) was also present in the chloroform phase and no third phase formed. Further, it is clear that for a pH of <4.1 (at least), extraction by palmitic acid alone is insignificant.

In order to investigate material balances in systems of the present type, a further experiment was carried out using a chloroform solution containing **1** (0.01 mol dm^{-3}) and palmitic acid (0.04 mol dm^{-3}), with copper concentrations being monitored in both the aqueous and chloroform phases after equilibration over a range of pH values from 1 to 6. The result (Fig. 5) indicates that good copper mass balances were achieved and hence that no third phase containing copper was formed. Under these conditions the pH for 50% copper-loading of the organic phase ($pH_{1/2}$) was 3.8. Similar 'S-curve' plots were obtained for Co(II) and Ni(II) although, as expected, displacement of the curves relative to each other was evident, with the observed $pH_{1/2}$ values being 5.6 and ~4.4, respectively. The extraction efficiencies thus follow the Irving–Williams stability order of Co(II) < Ni(II) < Cu(II).[35] However, further study of the cobalt and nickel systems were not pursued here since Ni(II) showed a very slow approach to equilibrium (>24 h) and also because the $pH_{1/2}$ (for >90%) transfer of Co(II) is sufficiently high that there were concerns that precipitation of hydroxides might be induced and/or that oxidation to Co(III) might occur.

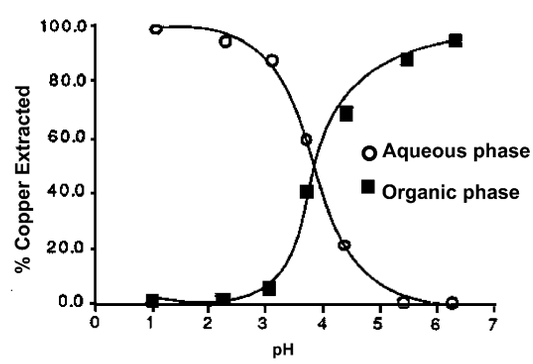


Fig. 5 The pH-dependence and material balance for extraction of Cu(II) into a chloroform solution of **1** (10^{-2} mol dm^{-3}) and palmitic acid (4×10^{-2} mol dm^{-3}) after equilibration with an equal volume of an aqueous solution of $Cu(NO_3)_2$ solution (10^{-2} mol dm^{-3}).

As mentioned already, the lipophilicities of the ligand assemblies and their metal complexes will influence the efficiency of metal extraction. Accordingly, the incorporation of *tert*-butyl or branched-nonyl substituents into **1** was observed to increase metal transfer in chloroform extractions. This effect is manifest in different ways. Under a given set of conditions, for example, with the same concentration of macrocycle and

† Generally, extraction of metal ions with monocarboxylic acids (HA below) can be represented by the following equation:

$$M^{n+}_{(aq)} + p\,H_2O_{(aq)} + (n/2 + m/2)(HA)_{2(org)} \rightleftharpoons 1/x(MA_n{\cdot}mHA{\cdot}pH_2O)_{x(org)} + n\,H^+_{(aq)}.$$

Depending upon the experimental conditions, different species have been identified; in the case of Cu(II), for example, monomeric $[CuA_2]$, $[CuA_2{\cdot}HA]$, $[CuA_2{\cdot}2HA]$, $[CuA_2{\cdot}4HA]$ and dinuclear $[CuA_2]_2$, $[(CuA_2{\cdot}HA)_2]$, $[(CuA_2{\cdot}2HA)_2]$ species have all been observed.[33] In the case of Fe(III) the trinuclear hydrated species $[(FeA_3{\cdot}H_2O)_3]$was also one of the species found.[34]

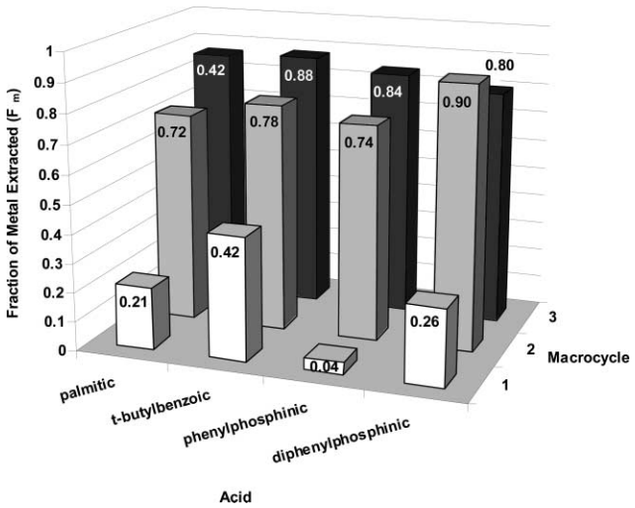


Fig. 6 The effect of lipohilicity of the macrocycles **1**–**3** on Cu-extraction into a chloroform solution (10^{-3} mol dm^{-3}) containing either palmitic, 4-*tert*-butylbenzoic, phenylphosphinic or diphenylphosphinic acids (2×10^{-3} mol dm^{-3}) from an aqueous solution (pH 5.0) of $Cu(NO_3)_2$ at (10^{-3} mol dm^{-3}).

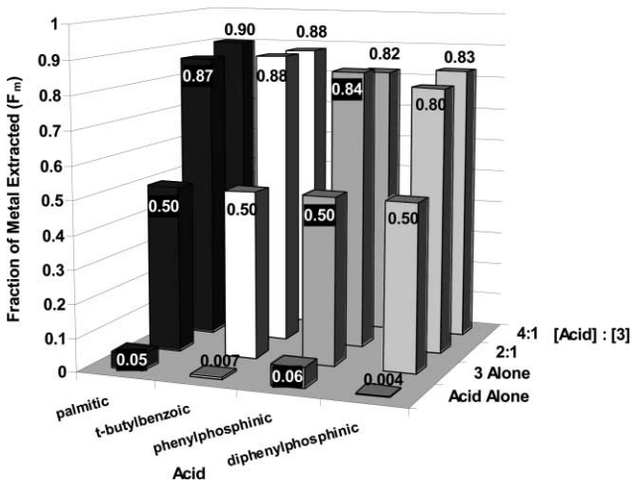


Fig. 7 Synergistic copper extraction into a chloroform solution containing the macrocycle **3** (10^{-3} mol dm^{-3}) and either palmitic, 4-*tert*-butylbenzoic, phenylphosphinic or diphenylphosphinic acid (2 or 4×10^{-3} mol dm^{-3}) from an aqueous solution (pH 5.0) of $Cu(NO_3)_2$ at (10^{-3} mol dm^{-3}). The values for the acid alone extractions (4×10^{-3} mol dm^{-3}) are all within experimental error of zero but we show them here to emphasise the synergism exhibited by these acid components after the addition of **3**.

the same molar ratio of acid to macrocycle the metal transfer varies in the order **1** < **2** < **3**, see Fig. 6.‡

The dependence of copper extraction on the nature of the organic acid component of the ligating packages was investigated for the five acids listed in Table 3. For the equilibration pH-values chosen, the acid alone extracted no copper within the limits of experimental error of the analyses. At the same extraction pH, the addition of the acid to one of the macrocycles **1**–**3** in every case gave a higher copper loading than the macrocycle alone, confirming synergism of extraction by the acid–macrocycle assemblies. Results for 4-*tert*-butylbenzoic, palmitic, phenylphosphinic and diphenylphosphinic acids are presented in Fig. 7 for extractions carried out at pH 5. For salicylic acid, extractions were performed at an equilibrium pH of 3.8, at which the acid alone showed negligible copper uptake (at higher pH values extraction did occur); hence at this pH any observed synergism will not be clouded by the occurrence of simultaneous extraction by salicylic acid alone. In this context, the need for a pH lower than 5 employed for the parallel studies involving the other carboxylic and phosphinic acids, is undoubtedly a reflection of the expected stronger binding for Cu(II) in the case of this potentially bidentate ligand. The results shown in Fig. 8 again confirm that

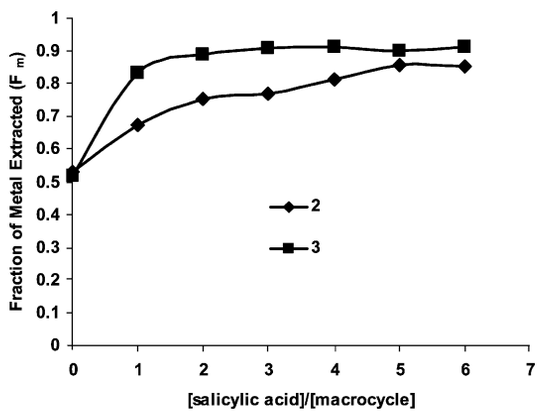


Fig. 8 Copper extraction into chloroform solutions containing the macrocycles **2** or **3** (10^{-3} mol dm^{-3}) and different concentrations of salicylic acid (zero to 6×10^{-3} mol dm^{-3}) from an aqueous solution (pH 3.8) of $Cu(NO_3)_2$ at (10^{-3} mol dm^{-3}).

synergism occurs for salicylic acid in combination with either **2** or **3**.

For the extractions illustrated in Figs. 7 and 8 and for all the other permutations of acids and macrocycles investigated in this work there are relatively small differences between the synergistic benefits of using 4-*tert*-butylbenzoic, palmitic, phenylphosphinic or diphenylphosphinic at the same molar ratio in combination with one of the macrocycles chosen from **1**–**3**. Thus, for a given macrocycle with a particular ratio of acid to macrocycle greater than 2 : 1 (namely, the ratio required to yield the 'ideal' package for forming charge neutral copper complexes) the differences in copper loadings using different acids fall within experimental error of each other. The absence of major variations is not unexpected, given that the packages have only minor differences in their donor sets (carboxylate oxygen atoms *vs.* phosphinate oxygen atoms) and that the pK_a values of the acid components (see Table 3) are sufficiently low that formation of the 2 : 1 salts with the macrocycles will be a favourable process in all cases.

The assembly effect

As discussed earlier, enhanced metal complex formation and metal extraction by ligand 'packages' derived from **1**–**3** can be ascribed to the operation of an 'assembly effect'[3] in which the ligand components of a coordination shell assemble

‡ The provision of a lipophilic anion RX^- in the ligand packages containing **1**–**3** ensures that extraction of metal cations into the organic phase by the 'ion exchange' reaction

$$[LH_n(RX)_n]_{(org)} + M^{n+}{}_{(aq)} \rightleftharpoons [LM(RX)_n]_{(org)} + nH^+{}_{(aq)}$$

can occur without co-extraction of anions to preserve charge neutrality in the organic phase. In the absence of such organic-soluble anions provided by the assemblies, the metal extraction requires dehydration and transport of both the metal cation and its attendant anion(s) to the organic phase:

$$L_{(org)} + M^{2+}{}_{(aq)} + 2X^-{}_{(aq)} \rightleftharpoons [MLX_2]_{(org)}.$$

Consequently, in contrast to the systems described in this paper, the efficiency of metal extraction will be very dependent on the hydration energy of the anion and on the nature and strength of its bonding to the metal centre or other functions in the metal–macrocycle complex. While such effects fall outside the programme reported here, it should be noted that they are of major significance in developing systems specifically designed to transport metal salts in hydrometallurgical circuits.[36] In the present study, for the packages of **1**–**3** containing two mol of organic anion per mol of macrocycle, as expected, the uptake of copper shows very little dependence on whether the nitrate or sulfate salt is used as a copper source in the aqueous phase.

spontaneously in the absence of a metal ion. In the presence of a complexing metal ion, the assembled adduct will exist in equilibrium with its metal complex and, for this situation, the formation of the metal complex from the assembled adduct is expected to be more favourable than from the separated ligand components due to entropy effects.§ Namely, there is less loss of disorder on complexation on employing the adduct than there would be if complex formation involved the non-assembled ligands.

Further, the formation of self-assembled ligand systems employing electrostatic and hydrogen bonding interactions will generally show considerable synthetic advantage over preparing structural analogues of the lariat azacrown ether type incorporating *covalently* attached pendant carboxylic or phosphinic acid arms.[37]

Concluding remarks

The assembly effect, which spans the areas of supramolecular host–guest chemistry and classical metal coordination chemistry, clearly has implications for the design of new reagents for use in metal ion solvent extraction systems. It also points the way for rationalising many of the examples of synergism previously reported in the solvent extraction literature. More generally, an appreciation of this effect has the potential to provide an additional guide to the subtleties of metal complex formation alongside other well-established 'effects' in coordination chemistry.

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§ Metal complexation by the adducts may also be favoured on enthalpy grounds if the adducts contain ligand–ligand hydrogen-bonds which are retained in the metal complex because such attractive interactions compensate for the donor–donor atom repulsion energy terms associated with generating the coordination sphere. Such ligand–ligand secondary bonding is thought to contribute to the 'strength' of simple bidentate commercial extractants such as the phenolic oximes which have been shown to pre-assemble in non-polar solvents.[36]

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