

This article was downloaded by:

On: 23 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Journal of Coordination Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713455674>

Studies on copper(II) complexes of some polyaza macrocycles derived from 1,2-diaminoethane

Ankur Rastogi^a; Ram Nayan^a

^a Department of Chemistry, Hindu College, Moradabad-244001, India

To cite this Article Rastogi, Ankur and Nayan, Ram(2009) 'Studies on copper(II) complexes of some polyaza macrocycles derived from 1,2-diaminoethane', *Journal of Coordination Chemistry*, 62: 20, 3366 – 3376

To link to this Article: DOI: 10.1080/00958970903062046

URL: <http://dx.doi.org/10.1080/00958970903062046>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Studies on copper(II) complexes of some polyaza macrocycles derived from 1,2-diaminoethane

ANKUR RASTOGI and RAM NAYAN*

Department of Chemistry, Hindu College, Moradabad-244001, India

(Received 24 July 2008; in final form 3 April 2009)

Syntheses of copper(II) complexes of 20-membered and 15-membered aza macrocycles 1,3,6,8,11,13,16,18-octaaza-2,7,12,17-tetrachlorocycloicosane (OTCE, [20]-N₈) and 1,3,6,8,11,13-hexaazacyclopentadecane (HCPD, [15]-N₆) involving metal template condensation between 1,2-diaminoethane, trichloromethane and dichloromethane, respectively, are reported. Formulation of [Cu₄(OTCE)(H₂O)₈]Cl₈ and [Cu₃(HCPD)(H₂O)₆]Cl₆·2H₂O and the ligand hydrochlorides OTCE·8HCl and HCPD·6HCl are supported by elemental analyses, conductivity measurements, and spectral studies. For a comparative cavity size effect on the stability constant, potentiometric measurements on the copper complexes of the generated macrocycles [15]-N₆ and [20]-N₈ and the structurally related larger macrocycle 1,3,6,8,11,13,16,18,21,23-decaaza-2,2,7,7,12,12,17,17,22,22-decachlorocyclopentacosane (DDCP, [25]-N₁₀, prepared recently) have been performed in aqueous solution at 25°C ($\mu = 0.1 \text{ M KNO}_3$). Very high stability constants obtained for reaction $\text{Cu}^{2+} + \text{A} \rightleftharpoons \text{CuA}^{2+}$ (A = ligand, $\log K = 20.51$ and 25.87, respectively, for OTCE and DDCP systems) are a reflection on the folding of the ligand to provide a small cavity suitable for fitting of the copper ion. Further, a high equilibrium constant value for $\text{CuA}^{2+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_2\text{A}^{4+}$ (OTCE system, $\log K = 14.59$) or $\text{Cu}_2\text{A}^{4+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_3\text{A}^{6+}$ (DDCP system, $\log K = 16.69$) is due to suitable fitting of two and three copper ions in the 20-membered and 25-membered ring cavity of OTCE and DDCP, respectively.

Keywords: Aza macrocycles; Copper(II) complexes; 1,2-Diaminoethane; Dichloromethane; Trichloromethane; Solution study

1. Introduction

Cyclic ligands are able to bind increasing number of metal ions in relatively close proximity [1, 2], offering the prospect of generating unusual electronic and chemical properties [3–5]. Because of strong ligating of polyamine macrocyclic ligands, numerous metal-ion aza-macrocycles have been prepared. Recently, generation of 12-membered and 14-membered tetraaza macrocycles 1,4,7,10-tetraaza-2,3,8,9-tetrachlorocyclododecane (TTCD) [6], 1,3,7,9-tetraaza-2,2,8,8-tetrachlorocyclododecane (TTDE) [7], and 1,4,8,11-tetraaza-2,3,9,10-tetrachlorocyclotetradecane (TTTE) [7] have been reported in copper(II) template condensation between equimolar mixture of 1,1,2,2-tetrachloroethane and 1,2-diaminoethane, tetrachloromethane and 1,3-diaminopropane, and 1,1,2,2-tetrachloroethane and 1,3-diaminopropane, respectively. However, the mode of

*Corresponding author. Email: ramnayan_2003@yahoo.co.in

cyclization changes in a similar condensation between tetrachloromethane and 1,2-diaminoethane leading to a large macrocycle 1,3,6,8,11,13,16,18,21,23-decaaza-2,2,7,7,12,12,17,17,22,22-decachlorocyclopentacosane (DDCP, [25]-N₁₀) [6]. Thus, it is of interest to study template condensation reaction of 1,2-diaminoethane with other chlorocarbons derived from methane, like trichloromethane and dichloromethane, under similar reaction conditions. The different condensation mode of trichloromethane and dichloromethane includes their ability to generate new cyclic rings, 1,3,6,8,11,13,16,18-octaaza-2,7,12,17-tetrachlorocycloicosane (OTCE, [20]-N₈) and 1,3,6,8,11,13-hexaazacyclopentadecane (HCPD, [15]-N₆) (figure 1).

In this article we report the ring size effect on equilibrium constants for copper(II) complexes of DDCP, OTCE, and HCPD at 25°C ($\mu = 0.1 \text{ M KNO}_3$). In spite of a large flexible nature of DDCP or OTCE a very high value of the stability constant of its copper complex (CuA^{2+} , A = ligand) is a reflection on the conformational changes in the ligand where four N-atoms coordinated to copper are forced close to one another by folding of the ligand, and the copper ion thus fits in a small tetraaza cavity.

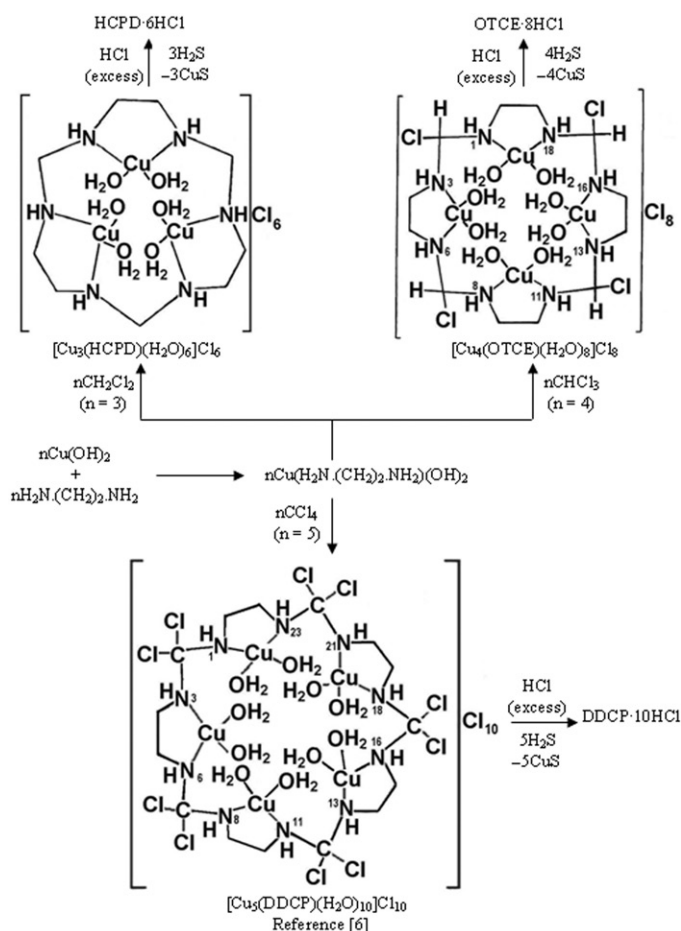


Figure 1. Reaction scheme.

Accommodation of two or three copper ions in the [20]-N₈ and [25]-N₁₀ cavities, respectively, is also favored in solution. The equilibrium constant for $\text{CuA}^{2+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_2\text{A}^{4+}$ ($\log K = 14.59$, OTCE system) or $\text{Cu}_2\text{A}^{4+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_3\text{A}^{6+}$ ($\log K = 16.69$, DDCP system) is due to suitable fitting of more than one copper ion in the large cavity.

2. Experimental

2.1. Chemicals and reagents

Solvents and reagents used were of reagent grade and used without purification. Solutions of 0.1770 N NaOH, 0.02159 N HNO₃, and 1.0 M KNO₃ were prepared using G.R. grade chemicals. Copper(II) nitrate solution prepared in aqueous medium was estimated by EDTA titrations [8]. Aqueous solutions of DDCP · 10HCl, OTCE · 8HCl, and HCPD · 6HCl were prepared by direct weighing.

2.2. Physical and chemical measurements

Elemental analyses were performed by the Central Drug Research Institute, Lucknow. Ionizable chlorides in the sample were determined by conductometric titrations [6]. The metal complexes were decomposed and copper(II) content was estimated by complexometric titration. A DDR conductivity meter (Type 304) was employed for conductivity measurements. Infrared spectra (FTIR) from 4000 to 350 cm⁻¹ were recorded on a Shimadzu 820 IPC spectrophotometer using KBr disks. ¹H NMR spectra were run on a Bruker DRX 300 (300 MHz FT) in D₂O solution using DSS as an internal standard. Mass spectra (EIMS) were recorded on a D-300 spectrometer. For FABMS, a Jeol SX 102/DA-600 spectrometer/data system using argon/xenon (6 KV, 100 mA) as the FAB gas was employed. The accelerating voltage was 10 KV and the spectra were recorded at room temperature. *m*-Nitrobenzyl alcohol was used as the matrix. The ESMS was recorded on a MICROMASS QUATTRO II Triple Quadrupole Mass Spectrometer. The sample dissolved in water was introduced into the ESI source through a syringe pump at the rate of 5 μL min⁻¹. The ESI capillary was set at 3.5 KV and the cone voltage was 40 V. The spectrum was collected in 6 s scans and the printouts are average of 6–8 scans. LCMS samples were introduced through JASCO HPLC under the conditions indicated.

2.3. Potentiometric titrations

The following mixtures: (i) 0.002159 N HNO₃; (ii) 0.0005 M DDCP · 10HCl/OTCE · 8HCl/HCPD · 6HCl + (i); (iii) 0.0005 M copper nitrate + (ii); (iv) 0.001 M copper nitrate + (ii); (v) 0.0015 M copper nitrate + (ii) (DDCP system) prepared in 50 mL were titrated pH-metrically at 25°C and an ionic strength of 0.1 M KNO₃ using an EC 5656 pH-meter with combined electrode system. From the experimental data titration curves (pH vs. *a*) were plotted and analyzed [9, 10] for obtaining information on the existing metal-ligand equilibria.

2.4. Synthesis of the copper(II) complex of HCPD

Dichloromethane (6.97 g, 82.06 mmol) was added to a blue stirred solution of copper hydroxide (8.00 g, 82.00 mmol) in 1,2-diaminoethane (4.93 g, 82.03 mmol) containing 200 mL *n*-butanol. After being refluxed, the solution changed to green, greenish-violet, and violet after 15 min, 30 min, and 1 h and 30 min, respectively. The violet solution was further refluxed for 5 h during which the color of the solution did not change. The content was cooled to room temperature (25°C), dissolved in 50 mL water and filtered. The negligible amount of blackish-brown residue was rejected. The filtrate contained two layers, a violet aqueous layer and a wine-red nonaqueous layer. The aqueous layer containing the macrocyclic complex was separated by a separating funnel. Concentration and refrigeration of the aqueous layer yielded violet crystals associated with some sticky materials. The sticky impurity insoluble in ether, benzene, butanol, etc. was removed by treating the crude product with a mixture of benzene and petroleum ether (1 : 1). The solvent mixture was added to the crude product placed on filter paper. Violet spots appeared on the filter paper due to absorption of the impurity. Taking fresh paper and the same solvent mixture, the process was repeated till the filter paper was found spot-free. The product was recrystallized from a methanol : acetone mixture (1 : 1) and the crystals were purified by filter paper treatment using benzene : ether mixture as described above. The yield of the violet crystals is 1.3 g.

2.5. Synthesis of the copper(II) complex of OTCE

A quantity of 9.79 g (85.01 mmol) of chloroform was added to a stirred mixture containing 8.00 g (82.00 mmol) of copper hydroxide and 4.93 g (82.03 mmol) of 1,2-diaminoethane in 200 mL of methanol. The deep blue mixture containing ~50% undissolved copper hydroxide was heated for 15 min with constant stirring, during which time the mixture turned into a light violet turbid solution. Subsequently, it was refluxed for 4 h and 45 min. The turbidity completely disappeared after 1 h and the mixture turned violet. There was no further change in violet color during additional heating for 3 h and 45 min. The mixture was then cooled, stirred for ~10 min with 100 mL of water and filtered. A small amount of a blackish-green residue was rejected. Concentration and refrigeration of the violet solution yielded violet crystals. The crystals were washed 2–3 times each with methanol and petroleum ether (b.p. 40–60°C); yield 1.68 g.

2.6. Preparation of the metal-free macrocycles

Aqueous solution of the copper(II) complexes of HCPD and OTCE in 100 mL water were prepared by dissolving 1.00 g (1.32 and 0.90 mmol, respectively). These solutions were acidified with conc. HCl (5 mL, 12 N) and H₂S gas was passed into these solutions for about 15 min. The black CuS was separated by filtration and the presence of Cu(II) ion in filtrate was checked by again passing H₂S gas. The filtrate was further boiled for 2–3 min in order to remove the dissolved H₂S gas. The resulting solutions containing hydrochlorides of the macrocycles were concentrated and kept at room temperature (25°C, for 15 days) for crystallization. The crystallized products HCPD · 6HCl (needle

shaped, white crystals) and OTCE · 8HCl (fine white crystals) were washed with ether and dried under reduced pressure in yields of 0.50 and 0.40 g, respectively.

3. Results and discussion

3.1. Synthesis

The reaction of equimolar amounts of 1,2-diaminoethane, chlorocarbon (trichloromethane and dichloromethane) and copper hydroxide initially leads to the formation of a blue metal-ammine complex. On refluxing the reaction mixture, condensation of the coordinated amine and chlorocarbon proceeds, followed by a color change yielding polynuclear complexes. Thus, 20-membered and 15-membered ring products 1,3,6,8,11,13,16,18-octaaza-2,7,12,17-tetrachlorocycloeicosane (OTCE) and 1,3,6,8,11,13-hexaazacyclopentadecane (HCPD) are generated in condensation of 1,2-diaminoethane with trichloromethane and dichloromethane, respectively. Cyclization, through template condensation, yielding a product with one molecule of each reactant (1,2-diaminoethane and trichloromethane or dichloromethane), is unlikely to occur as the resulting smallest cavity of the product cannot accommodate copper(II). Thus, the ring size expands by condensation of three and four molecules of the reactants in dichloromethane and trichloromethane systems, respectively. The template condensation of equimolar amounts of copper hydroxide, 1,2-diaminoethane and tetrachloromethane, reported earlier [6], yields pentanuclear copper complex of DDCP ($[\text{Cu}_5(\text{DDCP})(\text{H}_2\text{O})_{10}]\text{Cl}_{10} \cdot 4\text{H}_2\text{O}$). Five molecules of each reactant are involved in condensation. The ring size order DDCP > OTCE > HCPD is probably associated with the number of Cl atoms of the chlorocarbons. Probably, the ring expands to reduce crowding in the cavity by large Cl atoms.

Elemental analyses, conductivity measurements, and molecular weights by mass spectrometry support the formulation of the new macrocyclic compounds (table 1). Structures of the macrocycles have been confirmed by the infrared and proton magnetic

Table 1. Analytical and physical data for the copper(II) complexes of OTCE and HCPD.

Compound	Yield (%) color	Color at D.P. (m.p. °C)	Λ_M ($\text{Ohm}^{-1}\text{cm}^2$ mol^{-1})	% Found (Calcd)					Molecular weight found (Calcd)
				C	H	N	Cu	Cl ^a	
$[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8]\text{Cl}_8$	7.4	black	736	13.14	4.02	10.14	22.83	25.48	1106
$\text{Cu}_4\text{C}_{12}\text{H}_{44}\text{N}_8\text{O}_8\text{Cl}_{12}$	violet	(210) ^b		(13.09)	(4.01)	(10.10)	(22.91)	(25.57)	(1109.3)
OTCE · 8HCl	95.2	—	—	20.03	5.05	15.65	—	39.64	466
$\text{C}_{12}\text{H}_{28}\text{N}_8\text{Cl}_4 \cdot 8\text{HCl}$	white	(142)		(20.07)	(5.06)	(15.61)		(39.50)	(718.0)
$[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_6]$	6.2	black	540	14.20	5.30	10.98	24.88	27.80	704
$\text{Cl}_6 \cdot 2\text{H}_2\text{O}$	violet	(210) ^b		(14.15)	(5.29)	(11.00)	(24.95)	(27.85)	(763.9)
$\text{Cu}_3\text{C}_9\text{H}_{40}\text{N}_6\text{O}_8\text{Cl}_6$									
HCPD · 6HCl	87.7	—	—	24.92	6.98	19.25	—	48.96	286
$\text{C}_9\text{H}_{24}\text{N}_6 \cdot 6\text{HCl}$	white	(170)		(24.84)	(6.96)	(19.31)		(48.88)	(435.2)

Notes: ^aionizable chloride ion; ^bdecomposition point.

resonance spectra. The IR bands are strongly suggestive of the cyclic nature of the macrocycles, there being an absence of the bands due to coordinated or free-NH₂ groups [11–14]. Large stability constants obtained for the complexes in solution are due to cyclic structure of the ligands.

3.2. Infrared spectra

3.2.1. OTCE system. The presence of coordinated water in the copper–OTCE complex is indicated by bands at 3219 (weak but very sharp), 704 (medium, broad), and 642 cm⁻¹ (very weak) assigned to stretching, rocking, and wagging vibrations, respectively. A medium but very sharp band at 524 cm⁻¹ is due to $\nu(\text{Cu-O})$. Characteristic strong/medium bands at 2958, 2889 cm⁻¹ and very strong but sharp band at 1384 cm⁻¹ are attributed to C–H asymmetric, symmetric stretching, and scissoring vibrations, respectively. A very strong and sharp $\nu(\text{C-N})$ appears at 1043 cm⁻¹. The weak but sharp band for N–H stretch is at 3141 cm⁻¹ while the bending vibration is at 1587 cm⁻¹. A weak but very sharp band at 426 cm⁻¹ indicates that copper coordinates to ligand through nitrogen.

The $\nu(\text{N-H})$ and $\delta(\text{N-H})$ modes of secondary amines in OTCE · 8HCl appear at 3186 and 1600 cm⁻¹, respectively. Weak bands at 2501, 2416, and 2337 cm⁻¹ (sharp) and a medium but very sharp band at 2052 cm⁻¹ are associated with NH₂⁺Cl⁻ group. There is no band that could be assigned to a NH₂ group.

3.2.2. HCPD system. Absorptions at 3122 and 1580 cm⁻¹ (assigned to $\nu(\text{N-H})$ and $\delta(\text{N-H})$, respectively, of secondary amine group) for the copper–HCPD complex suggests that HCPD is a completely condensed macrocyclic ligand. Coordinated water is indicated by a band at 3300 cm⁻¹ (strong and broad), assigned to stretching vibrations and by other peaks at 690 (strong but broad) and 520 cm⁻¹ (strong but very sharp), attributed to O–H rocking and Cu–O stretch, respectively. A weak band at 440 cm⁻¹ is due to $\nu(\text{Cu-N})$. The $\nu(\text{C-N})$ is at 1080 cm⁻¹ (medium but broad).

1,3,6,8,11,13-Hexaazacyclopentadecane hydrochloride exhibits very weak bands at 2922 and 2800 cm⁻¹ assigned to asymmetric and symmetric C–H stretching vibrations, respectively, and C–H scissoring peak at 1385 cm⁻¹. Medium but sharp N–H stretching vibration for secondary amine is at 3200 cm⁻¹. A medium but sharp peak at 1600 cm⁻¹ may be attributed to $\delta(\text{N-H})$. The $\nu(\text{C-N})$ is at 1082 cm⁻¹. The C–H, C–N, or N–H vibration frequency is at higher energy than corresponding frequency in Cu–HCPD complex. The weak or very weak bands at 2588, 2501, 2414, and 2335 cm⁻¹ are associated with the amine hydrochloride.

3.2.3. Comparison of copper(II) complexes of HCPD and OTCE. In copper complexes of HCPD and OTCE, the Cu–N stretching frequency order is HCPD > OTCE. Poor coordinating power of OTCE in comparison to HCPD may arise from electron-withdrawing nature of four Cl-atoms in the ligand. The nitrogen atoms of HCPD, being stronger donors than those of OTCE, may increase electron density on the coordinated copper ion, and the Cu–O (H₂O) bond order follows the trend OTCE > HCPD. The trend may also be associated with the ligand ring size. Eight waters in the OTCE cavity are expected to be more comfortably fitted than the six water molecules in the

HCPD cavity. Much lowering of $\nu(\text{N-H})$ in $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_6]\text{Cl}_6 \cdot 2\text{H}_2\text{O}$ from HCPD as compared to that in $[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8]\text{Cl}_8$ from OTCE also supports stronger coordination by HCPD.

3.3. Mass spectra

Determination of molecular weight by mass spectra of the compounds HCPD \cdot 6HCl, OTCE \cdot 8HCl (EIMS), $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_6]\text{Cl}_6$ (FABMS), and $[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8]\text{Cl}_8$ (ESMS) has been very useful in completing the characterization. The highest m/z peaks in HCPD \cdot 6HCl, $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_6]\text{Cl}_6$, and $[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8]\text{Cl}_8$ are very close to their molecular ions. The slightly low m/z values in these systems may be associated with the mass lost (H, H_2O or HCl) due to fragmentation of the molecular ions. The mass spectrum of the metal-free ligand hydrochloride HCPD \cdot 6HCl shows that the highest m/z value of the product deviates from its calculated molecular ion weight (table 1). The mass loss corresponds to the sum of the masses of the few H atoms and four molecules of HCl attached with the macrocycles through weak coordinate bonds. The isotope peaks reflecting Cl atoms in the mass spectra of the ligand hydrochlorides are not seen, probably due to spurious contributions to the isotope peak intensities from the molecular ion and from weak background peaks [15]. The representative mass spectrum and fragmentation pattern of HCPD \cdot 6HCl is provided in Supplementary material.

The mass spectra of $[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8]\text{Cl}_8$ and $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_6]\text{Cl}_6$ have been further analyzed on the basis of isotopic abundance of different nuclei, particularly those of copper and chlorine. The fragments of various ionic species arising from the thermal cleavage of the macrocycles are supported by the presence of the isotopic peaks. The representative mass spectrum and fragmentation pattern of $[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8]\text{Cl}_8$ is shown in Supplementary material. The spectrum shows m/z peak at 1106 (0.03%) attributable to $[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8 - 2\text{H}]^+$ ion. As the relative abundance of the peak is very low, the isotopic distribution is not seen. But, in other fragments the isotopic peaks are seen. For example, a peak at m/z 960 (12.3%) attributable to $[\text{Cu}_4(\text{OTCE})\text{Cl}_8 - 4\text{H}]^+$ show isotopic peaks at m/z 954, 956, 958, 960, 962, 964, 966, 968, and 970. The spectrum of $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_6]\text{Cl}_6$ exhibits a peak at m/z 704 (0.3%) assignable to $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_5\text{Cl}_6 - \text{H}]^+$ ion with isotopic peaks at m/z 700, 702, and 706. The number of isotopic peaks for $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})\text{Cl}_6 - 4\text{H}]^+$ ion spans from m/z 629 to 641.

Both complexes show peaks corresponding to metal-free macrocycles, at m/z 432 (48.8%) for $[\text{OTCE} + 6\text{H}]^+$ and 214 (6.2%) for $[\text{HCPD} - 2\text{H}]^+$, respectively, which further confirm formation of macrocyclic complexes [16–18].

3.4. ^1H NMR spectra

Additional structural evidence for OTCE has been obtained from the ^1H NMR spectrum of its hydrochloride. A sharp peak at 3.44 ppm expected for methylene protons is observed. Also, a broad band singlet at 4.95 ppm may be assigned to $(\text{CH} + \text{NH}_2^+)$ proton resonances.

3.5. Solubility, conductivity, and other data

All the products are highly soluble in water due to their ionic nature. Their solubility is reduced in other polar solvents like methanol, ethanol, DMF, DMSO, etc. The molar conductances ($\text{Ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$) obtained for $[\text{Cu}_3(\text{HCPD})(\text{H}_2\text{O})_6]\text{Cl}_6 \cdot 2\text{H}_2\text{O}$ (540) and $[\text{Cu}_4(\text{OTCE})(\text{H}_2\text{O})_8]\text{Cl}_8$ (736) in aqueous solution are consistent with formulation of these complexes. Weight loss equivalent to two molecules of H_2O in the HCPD complex below 120°C shows that these molecules are not coordinated to copper(II). No weight loss below this temperature was observed for OTCE complex. The violet crystals of OTCE and HCPD complexes decompose to black solid at 210°C . But, white crystals of the ligand hydrochlorides $\text{OTCE} \cdot 8\text{HCl}$ (fine) and $\text{HCPD} \cdot 6\text{HCl}$ (needle shape) melt at 142 and 172°C , respectively.

3.6. Solution study

3.6.1. DDCP system. Dissociation of all protons associated with the 10 aza groups of the ligand below $\text{pH} \sim 11.0$ is evident from the titration curve (Supplementary material). The curve also shows weak, very weak, and steep inflections at $a = 1, 4,$ and $10,$ respectively. The equilibrium constants for the proton-ligand reactions are reported in table 2.

Table 2. Equilibrium constant for copper(II) complexes of the macrocycles DDCP, OTCE, and HCPD at 25°C ($\mu = 0.1 \text{ M KNO}_3$).

Reaction	$\log K^a$		
	DDCP	OTCE	HCPD
$\text{H}_{10}\text{A}^{10+} \rightleftharpoons \text{H}_9\text{A}^{9+} + \text{H}^+$	-6.25	-	-
$\text{H}_9\text{A}^{9+} \rightleftharpoons \text{H}_8\text{A}^{8+} + \text{H}^+$	-6.85	-	-
$\text{H}_8\text{A}^{8+} \rightleftharpoons \text{H}_7\text{A}^{7+} + \text{H}^+$	-7.20	-6.74	-
$\text{H}_7\text{A}^{7+} \rightleftharpoons \text{H}_6\text{A}^{6+} + \text{H}^+$	-7.75	-7.20	-
$\text{H}_6\text{A}^{6+} \rightleftharpoons \text{H}_5\text{A}^{5+} + \text{H}^+$	-8.20	-7.72	-6.48
$\text{H}_5\text{A}^{5+} \rightleftharpoons \text{H}_4\text{A}^{4+} + \text{H}^+$	-8.65	-8.50	-7.60
$\text{H}_4\text{A}^{4+} \rightleftharpoons \text{H}_3\text{A}^{3+} + \text{H}^+$	-9.10	-9.55	-9.35
$\text{H}_3\text{A}^{3+} \rightleftharpoons \text{H}_2\text{A}^{2+} + \text{H}^+$	-9.50	-10.08	-10.61
$\text{H}_2\text{A}^{2+} \rightleftharpoons \text{HA}^+ + \text{H}^+$	-9.95	-10.52	-
$\text{HA}^+ \rightleftharpoons \text{A} + \text{H}^+$	-10.25	-10.95	-
$\text{Cu}^{2+} + \text{H}_6\text{A}^{6+} \rightleftharpoons \text{CuH}_6\text{A}^{8+}$	14.01	-	-
$\text{CuH}_6\text{A}^{8+} \rightleftharpoons \text{CuH}_5\text{A}^{7+} + \text{H}^+$	-5.10	-	-
$\text{CuH}_5\text{A}^{7+} \rightleftharpoons \text{CuH}_4\text{A}^{6+} + \text{H}^+$	-5.89	-	-
$\text{CuH}_4\text{A}^{6+} \rightleftharpoons \text{CuH}_3\text{A}^{5+} + \text{H}^+$	-6.70	-6.85	-
$\text{CuH}_3\text{A}^{5+} \rightleftharpoons \text{CuH}_2\text{A}^{4+} + \text{H}^+$	-7.45	-8.20	-
$\text{CuH}_2\text{A}^{4+} \rightleftharpoons \text{CuHA}^{3+} + \text{H}^+$	-8.90	-9.62	-9.30
$\text{CuHA}^{3+} \rightleftharpoons \text{CuA}^{2+} + \text{H}^+$	-9.75	-10.50	-
$\text{Cu}^{2+} + \text{H}_4\text{A}^{4+} \rightleftharpoons \text{CuH}_4\text{A}^{6+}$	-	14.58	-
$\text{Cu}^{2+} + \text{H}_2\text{A}^{2+} \rightleftharpoons \text{CuH}_2\text{A}^{4+}$	-	-	17.15
$\text{Cu}^{2+} + \text{A} \rightleftharpoons \text{CuA}^{2+}$	25.87	20.51	-
$\text{CuH}_3\text{A}^{4+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_2\text{A}^{4+} + 2\text{H}^+$	-	-	-10.12
$\text{CuA}^{2+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_2\text{A}^{4+}$	5.27	14.59	-
$\text{Cu}_2\text{H}_2\text{A}^{6+} \rightleftharpoons \text{Cu}_2\text{HA}^{5+} + \text{H}^+$	-9.65	-	-
$\text{Cu}_2\text{HA}^{5+} \rightleftharpoons \text{Cu}_2\text{A}^{4+} + \text{H}^+$	-10.25	-	-
$\text{Cu}_2\text{A}^{4+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_3\text{A}^{6+}$	16.69	-	-
$\text{Cu}_3\text{A}^{6+} + \text{OH}^- \rightleftharpoons \text{Cu}_3\text{A}(\text{OH})^{5+}$	7.40	-	-
$\text{Cu}_3\text{A}(\text{OH})^{5+} + \text{OH}^- \rightleftharpoons \text{Cu}_3\text{A}(\text{OH})_2^{4+}$	6.35	-	-

A = ligand; ^avalues are ± 0.02 – 0.26 .

The values are consistent with those of tetraaza ligands [16]-N₄ and [17]-N₄ [19] and tricyclic ligands 1,4,7,10,12,15,17,20,23,26,27,30-dodecaazadispiro[10.4.10.4]triacontane (DDST) and 2,5,7,10,13,15,18,21,23,26,29,32-dodecaazatricyclo[20.10.0.0^{6,17}]dotriacontane (DOCD) [20]. The 1 : 1, copper-DDCP · 10HCl titration curve shows an inflection at $a = 4$ (pH ~4.8) indicating formation of CuH₆A⁸⁺ species involving four aza donors (1, 3, 6, and 23). The formation of the protonated species is also supported by the gradual increase in intensity of a bluish-green color at pH ~4.0 in the titration mixture, up to pH ~4.8. The color or its intensity does not change beyond this pH, but dissociation of protons from the protonated complex is shown by the titration curve. There are two additional inflections in the curve at $a = 8$ and 10. The equilibrium constant related to the 1 : 1, copper : ligand reactions are given in table 2.

Stability constant in a macrocyclic complex is related to ring size, donor atoms, and ligand conformational changes. As ring size increases, the constraints of the ring diminish, with a consequent decrease in the macrocyclic effect. Kodama and Kimura [21] in their studies on copper complex of 1,4,8,12-tetraazacyclopentadecane ([15]-N₄) reported a stability constant at 25°C (log $K = 24.4$). Despite large cavity size and presence of 10 electron-withdrawing chlorines, a high value of stability constant (log $K = 25.87$) is obtained for the DDCP system due to conformational changes in the macrocycle. The four nitrogens coordinated to copper are forced close to one another by folding of the ligand, providing a suitable smaller cavity for the copper ion.

A steep inflection at $a = 8$ (pH ~7.0) in pH *versus a* curve of 2 : 1, Cu : DDCP · 10HCl system, indicates that the corresponding species Cu₂H₂A⁶⁺ is independently formed in the second step where four aza groups 8, 11, 13, and 16 or 11, 13, 16, and 18 or 13, 16, 18, and 21 coordinate the second copper ion. A very low value of stability constant (log $K = 5.27$) for the reaction $\text{CuA}^{2+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_2\text{A}^{4+}$ indicates that during coordination of the second copper ion the macrocycle becomes unfolded (as in original state), and the two copper ions are accommodated in the same large cavity. Beyond $a = 8$ deprotonation of the diprotonated complex takes place where the corresponding two equilibria exist in solution. The color change in the reaction mixture is almost comparable with that of 1 : 1, copper : ligand system.

The color change in the titration mixture of 3 : 1, copper : ligand system is again comparable to that of 1 : 1 or 2 : 1, metal : ligand system. Considerable lowering of the titration curve from that of 2 : 1 system and a steep inflection at $a = 10$ (pH ~6.0, a pH lower than that in the 2 : 1 system at $a = 8$) indicate suitable fitting of the three copper ions in the large cavity involving all the nitrogens in bond formation. It appears that the third copper ion is coordinated to only two aza groups, and in spite of suitable fitting of the three copper ions a very low value for reaction $\text{Cu}_2\text{A}^+ + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_3\text{A}^{6+}$ is expected; a high value for this reaction (log $K = 16.69$) is probably due to structural rearrangement during association of the third copper ion by coordination of three aza groups 8, 11, 13 and 16, 18, 21 to second and third copper ions, respectively. Further, formation of two hydroxo species Cu₃A(OH)⁵⁺ and Cu₃A(OH)₂⁴⁺ are expected due to association of one OH⁻ to each copper (second and third coordinated to macrocycle). The titration curve again shows a weak inflection at $a = 11$ and a very steep inflection at $a = 12$.

3.6.2. OTCE system. Dissociation of eight protons from the hydrochloride OTCE · 8HCl below pH 11.0 is indicated by its pH *versus a* curve. The corresponding proton dissociation constants (table 2) are in agreement with those for DDCP.

The titration curve for 1:1, copper:OTCE mixture shows a steep inflection at $a=4$ (pH ~ 6.0), followed by two weak inflections at $a=5$ (pH ~ 7.6) and $a=6$ (pH ~ 9.0). The initial greenish-blue solution gradually changes to violet between pH 4.5 and 5.6 (between $a=0.7$ and 3.9). The steep inflection and the color change indicate formation of violet $\text{CuH}_4\text{A}^{6+}$ involving coordination of four aza groups of position 1, 3, 6, and 18 to copper(II). The four protons of $\text{CuH}_4\text{A}^{6+}$ further dissociate between $a=4$ and 8, but the violet color remains unchanged beyond $a=4$.

A high equilibrium constant value for $\text{Cu}^{2+} + \text{A} \rightleftharpoons \text{CuA}^{2+}$ ($\log K=20.51$) is due to folding of the ligand along C(7)–N(8) and N(16)–C(17) to provide a smaller cavity suitable for fitting a single copper ion as discussed in the DDCP system. The value is low compared to the copper–DDCP complex which is more flexible and contains additional electron-withdrawing chlorines. In view of the high equilibrium constant value for the DDCP system, the copper ion is more effectively fitted in a smaller cavity and folding of DDCP to provide such a cavity is favored by an increase in its ring size.

A very steep inflection at $a=8$ (pH ~ 7.1) shown by the titration curve of 2:1, copper:OTCE system (Supplementary material) indicates formation of nonprotonated Cu_2A^{4+} where four aza donors of position 8, 11, 13, and 16 coordinate the second copper ion. The greenish-blue initial solution turned to a mixture of violet and greenish-blue due to the presence of $\text{CuH}_4\text{A}^{6+}$ and the free Cu^{2+} ion at pH ~ 5.6 ($a=5.5$). The color further, gradually, changes to violet at pH ~ 6.7 ($a=7.8$). The equilibrium constant value ($\log K \sim 15$) for reaction $\text{CuA}^{2+} + \text{Cu}^{2+} \rightleftharpoons \text{Cu}_2\text{A}^{4+}$ in the OTCE system is close to that of recently reported [20] copper complexes of DDST and DOCD ($\log K \sim 16$), although the second copper ion in these systems is accommodated in a separate ring cavity ([10]-N₄ or [12]-N₄).

3.6.3. HCPD system. Four out of six protons of the ligand hydrochloride dissociate between pH ~ 5.0 and 11.0. The corresponding proton-ligand dissociation constants are reported in table 2. The pH *versus* a curve for the 1:1, copper:HCPD system showing very steep inflection at $a=4$ (pH ~ 6.0) indicates formation of diprotonated $\text{CuH}_2\text{A}^{4+}$ involving four aza donors coordinated to copper. A gradual color change from greenish-blue to violet between pH ~ 4.7 and 6.0 ($a=0.4$ and 3.9) also supports the formation of violet $\text{CuH}_2\text{A}^{4+}$. No further color change is observed up to pH 11.0 but, an increase in a up to 5 (at pH 11.0) indicates dissociation of one proton from the diprotonated complex.

The 2:1, copper:HCPD curve shows two steep inflections at $a=4$ (pH ~ 5.8) and 7 (pH ~ 8.5). The first inflection is due to formation of $\text{CuH}_2\text{A}^{4+}$, the violet species as in 1:1, copper:HCPD system. An increase in a value and violet color intensity of the reaction mixture between $a=4$ and 6 indicates formation of Cu_2A^{4+} where the second copper is probably coordinated to the two remaining aza groups. A greenish-blue turbidity appears in the titration mixture at pH ~ 7.5 ($a=6$). The second inflection at $a=7$ (in the turbidity region) is due to decomposition of Cu_2A^{4+} into CuHA^{3+} and $\text{Cu}(\text{OH})_2$. Displacement of the second copper ion as its hydroxide is expected because of the small cavity ligand where the second metal ion is not well fitted, and also, coordination of the second copper ion to ligand through only two aza groups.

Acknowledgements

The Regional Sophisticated Instrumentation Centre, Central Drug Research Institute, Lucknow, is to be thanked for recording the infrared, ^1H NMR, and mass spectra and microanalyses of the compounds.

References

- [1] J.D. Charters, L.F. Lindoy, G.V. Meehan. *Coord. Chem. Rev.*, **216–217**, 249 (2000).
- [2] S. Brooker, J.D. Ewing, J. Nelson. *Inorg. Chim. Acta*, **317**, 53 (2001).
- [3] L. Broge, U. Pretzmann, N. Janesen, I. Stofte, C.E. Olsen, J. Springberg. *Inorg. Chem.*, **40**, 2323 (2001).
- [4] E. Colacio, J.M. Dominguez-Vera, M. Ghazi, R. Kivekas, J.M. Moreno, A. Pajunen. *J. Chem. Soc., Dalton Trans.*, 505 (2000).
- [5] E.V. Rybak-Akimova, N.W. Alcock, D.H. Busch. *Inorg. Chem.*, **37**, 1563 (1998).
- [6] M. Singh, R. Nayan. *Synth. React. Inorg. Met.-Org. Chem.*, **27**, 619 (1997).
- [7] M. Singh, R. Nayan. *Synth. React. Inorg. Met.-Org. Chem.*, **28**, 87 (1998).
- [8] J. Bassett, R.C. Denny, G.H. Jeffery, J. Mendham. *Vogel's Text Book of Quantitative Inorganic Analysis*, 4th Edn, Longman Group Ltd., London (1978).
- [9] R. Nayan, A.K. Dey. *Indian J. Chem.*, **14A**, 892 (1976).
- [10] R. Nayan. *J. Inorg. Nucl. Chem.*, **43**, 3283 (1981).
- [11] S.C. Jackels, K. Farmery, E.K. Barefield, N.J. Rose, D.H. Busch. *Inorg. Chem.*, **11**, 2893 (1972).
- [12] M.S. Holtman, S.C. Cummings. *Inorg. Chem.*, **15**, 660 (1976).
- [13] M. Singh, R. Nayan. *Indian J. Chem.*, **35A**, 239 (1996).
- [14] M. Singh, R. Nayan. *Synth. React. Inorg. Met.-Org. Chem.*, **29**, 1395 (1999).
- [15] B.S. Furniss, A.J. Hannaford, V. Rogers, P.W.G. Smith, A.R. Tatchell. *Vogel's Text Book of Practical Organic Chemistry including Qualitative Organic Analysis*, 4th Edn, ELBS and Longman Group Ltd., London (1978).
- [16] D.H. Cook, D.E. Fenton. *J. Chem. Soc., Dalton Trans.*, 810 (1979).
- [17] N.J. Long, D.G. Parker, P.R. Speyer, A.J.P. White, D.J. Williams. *J. Chem. Soc., Dalton Trans.*, 2142 (2002).
- [18] R.N. Prasad, A. Jain. *Indian J. Chem.*, **46A**, 1782 (2007).
- [19] R.M. Izatt, J.S. Bradshaw, S.A. Nielson, J.D. Lamb, J.J. Christensen, D. Sen. *Chem. Rev.*, **85**, 271 (1985).
- [20] Anurag, A.K. Pandey, R. Nayan. *J. Coord. Chem.*, **59**, 1963 (2006).
- [21] M. Kodama, E. Kimura. *J. Chem. Soc., Dalton Trans.*, 2269 (1977).