Synthetic, Kinetic, and Stereochemical Studies on the Copper(II), Nickel(II), and Cobalt(III) Complexes of 1,4,7,10,13-Penta-azacyclopentadecane

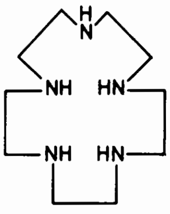
Robert W. Hay,* Ramesh Bembi, and (in part) W. Thomas Moodie and Paul R. Norman
Chemistry Department, University of Stirling, Stirling FK9 4LA

The preparation of the title quinquedentate macrocyclic ligand, L, is described. The complexes $[NiL(OH_2)][ClO_4]_2$, $[CuL][ClO_4]_2$, and $[CoLCl][ClO_4]_2$ have been prepared and characterised. The complexes can have three possible configurations as a result of the two chiral nitrogen centres; there are two N-*meso* diastereoisomers and one N-racemic diastereoisomer. Carbon-13 n.m.r. measurements establish that the Co^{III} complex is a mixture of the possible stereoisomers. The base hydrolysis of $[CoLCl]^{2+}$ is quite rapid with $k_{OH} = 2.45 \times 10^4$ dm^3 mol^{-1} s^{-1} at 30 °C and $I = 0.1$ mol dm^{-3}, which can be rationalised in terms of the *mer*-N_3 donor set. Acid aquation with $k_{aq} = 1.66 \times 10^{-4}$ s^{-1} at 50 °C is quite slow. The Cu^{II} and octahedral Ni^{II} complexes are labile in acidic solution, unlike the complexes of 1,4,8,11-tetra-azacyclotetradecane. The kinetics of the acid-catalysed dissociation have been studied in detail. For both complexes rate = k_H[complex]$[H^+]^2$, indicating the involvement of two protons in the transition state of the reaction. For $[CuL]^{2+}$, $k_H = 4.9 \times 10^{-2}$ dm^6 mol^{-2} s^{-1} and for $[NiL]^{2+}$, $k_H = 0.63$ dm^6 mol^{-2} s^{-1} at 25 °C and $I = 0.98$ mol dm^{-3}. The acid-catalysed dissociation of the Ni^{II} complex of 1,4,7,10,13,16-hexa-azacyclo-octadecane has also been studied in order to define the mechanism of these reactions. In this case, rate = k_H[complex]$[H^+]^3$. Possible mechanisms are considered in detail.

The Richman and Atkins [1] procedure allows the relatively simple and general synthesis of 9—21-membered rings containing three to seven heteroatoms. Although a very large volume of work has been published on 14-membered tetra-aza macrocyclic ligands and their complexes,[2] much less information is available on the larger ring systems. The present paper discusses various aspects of the co-ordination chemistry of 1,4,7,10,13-penta-azacyclopentadecane (L). Kodama *et al.*[3] determined formation constants for L with a variety of metal ions at 25 °C and $I = 0.2$ mol dm^{-3}; the log K_{ML} values are 18.1 (Ni^{II}), 28.3 (Cu^{II}), 19.2 (Cd^{II}), and 17.3 (Pb^{II}) and interestingly 28.5 for Hg^{II}. The high formation constants with the toxic metals, Cd^{II}, Hg^{II}, and Pb^{II}, suggest a potential application for the ligand in metal detoxification. Kinetic studies have also been reported [4] for the reaction of copper(II) with a number of macrocyclic penta-amine ligands including L. The cobalt(II) complex of L co-ordinates dioxygen [5] at pH ~5 to give the μ-peroxo-complex $[(CoL)_2O_2]^{4+}$. The additional nitrogen donor in the axial position promotes both the rates and equilibrium of O_2 uptake compared with 14-membered macrocyclic tetra-amines. In addition the quinquedentate macrocycles may serve as a model of the active site of the anticancer agent bleomycin which comprises five nitrogen donors around the central metal ion.[6—9]

Experimental

The ligand 1,4,7,10,13-penta-azacyclopentadecane pentahydrochloride (L·5HCl) was prepared as follows. *NN'N''N'''*-Tetratosyl-1,8-diamino-3,6-diazaoctane [10] (48 g, 0.075 mol) was dissolved in *dry* (molecular sieves) *NN*-dimethylformamide (500 cm^3). Sodium hydride (60% in paraffin oil, 24 g) was added in small portions to the reaction mixture which was kept under a stream of nitrogen. When effervescence ceased (*ca.* 2 h) the solution was warmed on a water-bath for *ca.* 45 min. The solution was cooled to room temperature and the excess sodium hydride filtered off. (At all stages the solution was kept under N_2 with the minimum exposure to the atmosphere.) The filtrate was transferred to a flask equipped with a thermometer, double-surface condenser, drying tube, N_2 inlet, and magnetic stirrer. *NOO'*-Tritosyldiethanolamine [10] (35 g, 0.075 mol) dissolved in dry *NN*-dimethylformamide (300 cm^3) was added dropwise and the mixture heated on an oil-bath for *ca.* 10 h at 110—120 °C with continuous stirring. The solution was cooled to room temperature and water (1 500 cm^3) added slowly with vigorous stirring. The solid product (which contains unreacted tosylates in addition to the required product) was washed with water and heated with formic acid. The pentatosylate of L is more soluble in formic acid than the reactants. Initial fractions were monitored by i.r. spectroscopy until the ν(NH) band at 3 280 cm^{-1} (due to the tetratosylate of 1,8-diamino-3,6-diazaoctane) was absent. Some 30 g of the required tosylate m.p. 278—280 °C (lit.[1] 278—280 °C) were obtained.



L

The pentatosylate was hydrolysed with concentrated H_2SO_4 using a previously described procedure,[10] then converted to the free base, and finally to the pentahydrochloride. The ^{1}H n.m.r. spectrum of the amine pentahydrochloride in D_2O solution [sodium 4,4-dimethyl-4-silapentanesulphonate (dss) reference] showed the complete absence of tosyl groups and a single signal at δ 3.58 due to the equivalent CH_2 groups, m.p. 245—260 °C (decomp.) (Found: C, 30.50; H, 7.45; N, 17.60. Calc. for $C_{10}H_{30}Cl_5N_5$: C, 30.20; H, 7.60; N, 17.60%).

Aqua(1,4,7,10,13-*penta-azacyclopentadecane*)*nickel*(II) *Diperchorate*.—The ligand pentahydrochloride (0.2 g) was dissolved in water (15 cm^3) and treated with nickel(II) carbonate (0.35 g). The mixture was heated on a water-bath for 4 h, filtered hot, and $Na[ClO_4]$ (0.15 g) added to the purple filtrate. On standing (2—3 d) purple crystals deposited, which were filtered off, washed with propan-2-ol, then diethyl ether, and dried *in vacuo* (Found: C, 25.15; H, 5.25; N, 14.50. Calc. for $C_{10}H_{27}Cl_2N_5NiO_9$: C, 24.45; H, 5.15; N, 14.25%).

1,4,7,10,13-*Penta-azacyclopentadecanecopper*(II) *Diperchlorate*.—This complex was prepared as for the nickel(II) complex using copper(II) carbonate (Found: C, 25.15; H, 5.45; N, 14.70. Calc. for $C_{10}H_{25}Cl_2CuN_5O_8$: C, 25.15; H, 5.25; N, 14.65%).

Chloro(1,4,7,10,13-*penta-azacyclopentadecane*)*cobalt* (III) *Diperchlorate*.—The ligand pentahydrochloride (0.30 g) was dissolved in water (15 cm^3) and treated with freshly prepared $Na_3[Co(CO_3)_3]\cdot 3H_2O$ (0.30 g). The mixture was heated on a steam-bath for 1 h and filtered hot. To the deep red filtrate was added $Na[ClO_4]$ (0.15 g). On standing for 1—2 d the solution deposited reddish brown crystals which were filtered off, washed with propan-2-ol, then diethyl ether, and dried *in vacuo* (Found: C, 24.15; H, 5.10; N, 13.50. Calc. for $C_{10}H_{25}Cl_3CoN_5O_8$: C, 23.60; H, 4.95; N, 13.75%).

Aqua(1,4,7,10,13-*penta-azacyclopentadecane*)*cobalt* (III) *Triperchlorate*.—The chloro-complex (0.51 g) was dissolved in water (20 cm^3) and treated with $Ag[ClO_4]$ (0.22 g). The solution was warmed to *ca.* 60 °C and maintained at that temperature for 1 h and then cooled. The precipitated AgCl was filtered off and the excess Ag^I removed as AgCl by the careful addition of very dilute HCl. The solution was allowed to stand in the dark overnight and then filtered. The filtrate was evaporated to *ca.* 5 cm^3 on a steam-bath, cooled, and the reddish brown complex precipitated by the careful addition of ethanol. The complex was filtered off, and further purified by dissolving in the minimum volume of water, cooling in ice, and precipitating with ethanol (Found: C, 20.55; H, 4.35; N, 11.35. Calc. for $C_{10}H_{27}Cl_3CoN_5O_{13}$: C, 20.35; H, 4.60; N, 11.85%).

Kinetic Measurements.—The base hydrolysis of $[CoLCl]^{2+}$ was monitored spectrophotometrically at 300 nm. Plots of log $(A_\infty - A_t)$ *versus* time were linear for at least three half lives. Values of $k_{obs.}$ (the observed first-order rate constant at constant pH) were derived from the absorbance time using a PET Commodore microcomputer. The pH during the reaction was controlled by citrate buffers adjusted to $I = 0.1$ mol dm^{-3}. The hydroxide ion concentrations were derived from the pH using a molar activity coefficient of 0.770 and $pK_w = 13.833$ at 30 °C.[11] The acid dissociation kinetics of the nickel(II) and copper(II) complexes of L were determined using spectrophotometric monitoring (Gilford 2400S spectrophotometer). Reactions were carried out using perchloric acid solutions adjusted to $I = 0.98$ mol dm^{-3} with $Na[ClO_4]$. The dissociation of the nickel(II) complex was monitored at 225 nm and the copper(II) complex at 585 nm. Values of $k_{obs.}$ were determined as previously described.

The nickel(II) complex of 1,4,7,10,13,16-hexa-azacyclo-octadecane was prepared as previously described,[12] and the acid dissociation kinetics monitored at 212 nm using $HClO_4$ solutions adjusted to $I = 0.97$ mol dm^{-3}. The acid aquation of $[CoLCl]^{2+}$ was quite slow, and this reaction was studied using a sampling technique. The aquation reaction was studied at 50 °C using 0.1 mol dm^{-3} $HClO_4$ as solvent. Samples (3 cm^3) were withdrawn from the reaction flask, quenched in ice–water, and the absorbance immediately determined at 510 and 330 nm. Rate constants determined at both wavelengths were identical.

Routine and interval scan spectra were carried out with a Perkin-Elmer 402 spectrophotometer. Infrared spectra were determined using KBr discs. Hydrogen-1 and ^{13}C n.m.r. spectra were measured using a Bruker WP80 instrument with D_2O as solvent and dss as reference.

Table 1. Electronic spectra of the complexes

	λ/cm^{-1} (ε/dm^3 mol^{-1} cm^{-1}) [a]
$[NiL(OH_2)][ClO_4]_2$	45 870 (4 176)
	28 410 (14)
	19 230 (8)
	12 900 (18)
	12 050 (23)
$[CuL][ClO_4]_2$	47 170 (2 200)
	36 360 (5 500)
	17 095 (200)
$[CoLCl][ClO_4]_2$	43 290 (16 530)
	28 735 (sh) [b] (342)
	19 800 (253)
$[CoL(OH_2)][ClO_4]_3$	45 455 (19 434)
	22 220 (305)

[a] Water was the solvent used in all cases. [b] sh = Shoulder.

Results and Discussion

The ligand 1,4,7,10,13-penta-azacyclopentadecane (L) can be readily prepared by the reaction of the disodium salt of the tetratosylate of 1,8-diamino-3,6-diazaoctane with the tritosylate of diethanolamine in *NN*-dimethylformamide solution, followed by cleavage of the tosyl groups with concentrated sulphuric acid. The ligand pentahydrochloride reacts with nickel(II) carbonate to give a paramagnetic complex isolated as the perchlorate salt $[NiL(OH_2)][ClO_4]_2$ which displays a typical octahedral spectrum in aqueous solution. The $^3A_{2g}\rightarrow{}^3T_{1g}$ (*P*) band occurs at 28 410 cm^{-1} and the $^3A_{2g}\rightarrow{}^3T_{1g}$ (*F*) band at 19 230 cm^{-1}. Distinctive splitting of the $^3A_{2g}\rightarrow{}^3T_{2g}$ band occurs due to the lowered symmetry, Table 1.

The complex is a 2 : 1 electrolyte in aqueous solution (Λ_M = 204 S cm^2 mol^{-1} at 25 °C) but in nitromethane the conductivity approximates more closely to that of a 1 : 1 electrolyte (Λ_M = 73 S cm^2 mol^{-1} at 25 °C). In nitromethane solution it appears that the axial water ligand is displaced by a unidentate perchlorate anion. When a solution of the perchlorate salt in methanol is heated (70 °C) with $[NH_4][SCN]$ (1 : 1 mol ratio) for *ca.* 1 h, a violet crystalline complex containing co-ordinated thiocyanate (bands at 2 060 and 2 080 cm^{-1}) and ionic perchlorate can be isolated.

The copper(II) complex is blue with a single *d–d* band at 17 095 cm^{-1} (ε = 200 dm^3 mol^{-1} cm^{-1}) in aqueous solution. The high value of the absorption coefficient presumably results from the distorteds ite symmetry. The CuN_6 chromophores in complexes[12] such as $[Cu(haco)]^{2+}$ (haco = 1,4,7,10,13,16-hexa-azacyclo-octadecane) and $[Cu(dien)_2]^{2+}$ (dien = diethylenetriamine) absorb at 660 and 640 nm respectively. Clearly a very strong ligand field is exerted in the present complex. An aqueous solution of the perchlorate salt has Λ_M = 174 S cm^2 mol^{-1} at 25 °C consistent with a 2 : 1 electrolyte, but in nitromethane Λ_M = 125 S cm^2 mol^{-1} indicating a 1 : 1 electrolyte. On this basis it appears likely that both in the solid state and in non-co-ordinating solvents, a perchlorate anion occupies one axial site. The perchlorate ligand is replaced by a solvent donor in co-ordinating solvents such as water. The i.r. spectrum of the solid perchlorate salt provides some evidence for unidentate perchlorate. In addition, reaction of the perchlorate salt in methanol with $[NH_4][SCN]$ (1 : 1 mol ratio) gives a blue thiocyanate perchlorate containing co-ordinated thiocyanate (bands at 2 060 and 2 080 cm^{-1}).

Table 2. Base hydrolysis kinetics of $[CoLCl]^{2+}$ at 30 °C and pH 6.16

Time/s	Absorbance [a]	Calc. absorbance [b]
30	98.0	98.6
90	95.0	95.3
150	92.0	92.1
210	89.0	89.0
270	86.0	86.1
330	83.5	83.3
390	80.5	80.5
450	78.0	77.9
510	76.0	75.4
570	73.0	73.0
630	71.0	70.8
690	68.5	68.5
750	66.5	66.4
810	64.5	64.4
1 050	57.0	57.0
1 290	50.5	50.8
∞	15.5	

$k = 6.80 \times 10^{-4}\ s^{-1}$. Correlation coefficient = 0.999 85

[a] Arbitrary units. [b] Absorbances computed on the basis of $k = 6.80 \times 10^{-4}\ s^{-1}$.

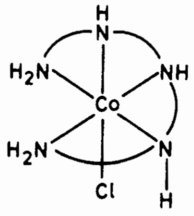
Table 3. Base hydrolysis of $[CoLCl]^{2+}$ in citrate buffers at 30 °C and $I = 0.1$ mol dm^{-3}

pH	$10^9[OH^-]$/ mol dm^{-3}	$10^4k_{obs.}/s^{-1}$	$10^{-4}k_{obs.}[OH^-]^{1}$/ dm^3 mol^{-1} s^{-1}
5.67	8.92	2.25	2.52
5.76	10.97	2.59	2.36
5.96	17.40	4.27	2.45
6.16	27.50	6.80	2.47
6.30	38.05	9.27	2.44

$k_{OH} = 2.45 \times 10^4$ dm^3 mol^{-1} s^{-1}

The complex $[CoLCl][ClO_4]_2$ is readily prepared by reacting $[Co(CO_3)_3]^{3-}$ with L·5HCl followed by addition of sodium perchlorate. The $^1A_{1g} \rightarrow {}^1T_{1g}$ transition occurs at 19 800 cm^{-1} ($\varepsilon = 253$ dm^3 mol^{-1} cm^{-1}) and the $^1A_{1g} \rightarrow {}^1T_{2g}$ transition as a shoulder at *ca.* 28 735 cm^{-1} ($\varepsilon = 342$ dm^3 mol^{-1} cm^{-1}), Table 1. The complex is a 2 : 1 electrolyte in aqueous solution (Λ_M = 230 S cm^2 mol^{-1} at 25 °C) and undergoes very slow acid aquation ($k_{aq} = 1.66 \times 10^{-4}$ s^{-1} at 50.0 °C in 0.1 mol dm^{-3} $HClO_4$).

The slow aquation rate (and the apparent lack of influence of the chiral nitrogen centres) probably arises due to the very rigid ligand system which occurs in $[CoLCl]^{2+}$. Ligand flexibility and the ability of a ligand to fold towards the leaving group are factors which have been observed to lead to rapid aquation rates.[13] The aquation of $\alpha\beta R$-$[CoL^1Cl]^{2+}$ (L^1 = 1,11-diamino-3,6,9-triazaundecane) with the configuration (I) *



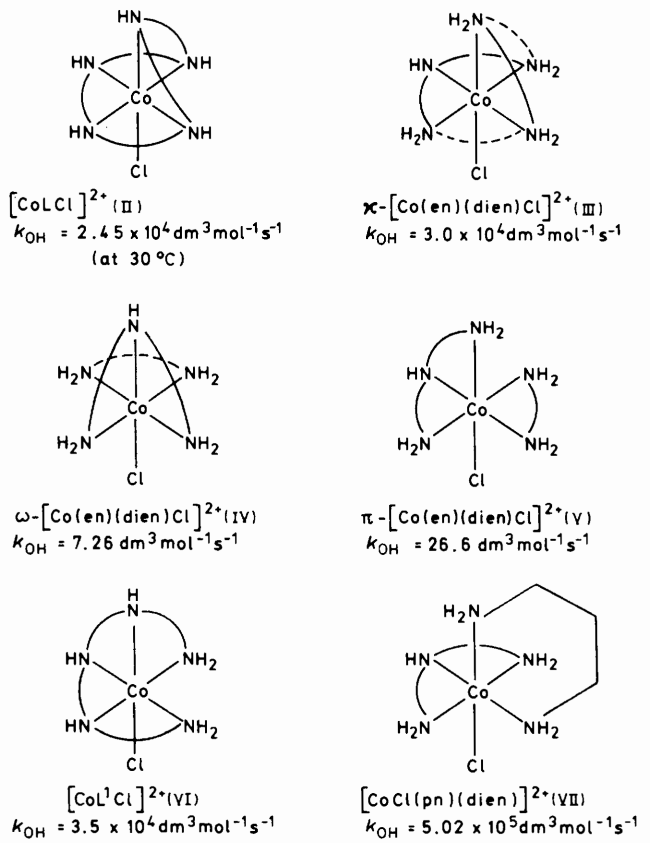
(I)

is also very slow with $k_{aq} = 3.2 \times 10^{-6}$ s^{-1} at 50 °C in 0.1 mol dm^{-3} $HClO_4$.[15] In this case, the single chiral nitrogen centre which leads to the $\alpha\beta R$ and $\alpha\beta S$ diastereoisomers has only a very minor effect on the aquation rates.

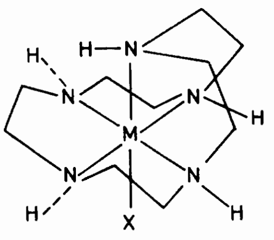
Base hydrolysis of $[CoLCl]^{2+}$ is quite rapid and was conveniently studied in the pH range 5.67—6.30 using citrate buffers adjusted to $I = 0.1$ mol dm^{-3}. Although ^{13}C n.m.r. measurements (see later) are consistent with the presence of the three possible diastereoisomers arising from the two chiral nitrogen centres, very ' clean ' first-order kinetics were observed at each pH, Table 2. Values of $k_{obs.}$ show a linear dependence on the hydroxide ion concentration, with k_{OH} = $k_{obs.}/[OH^-] = 2.45 \times 10^4$ dm^3 mol^{-1} s^{-1} at 30 °C and $I = 0.1$ mol dm^{-3}, Table 3. The results suggest that the three diastereoisomers undergo base hydrolysis at similar if not identical rates. Alternatively, a single diastereoisomer could be produced by base catalysed epimerisation in the pH range 5.7—6.3. Proton exchange of NH groups in cobalt(III) complexes is known to be rapid at pH > 4. In order to check this alternative explanation, a sample of $[CoLCl]^{2+}$ was subjected to base hydrolysis and the hydroxo-complex obtained isolated by evaporation of the solvent. The resulting solid was twice evaporated to dryness in the presence of concentrated hydrochloric acid to regenerate the chloro-complex, and the ^{13}C n.m.r. spectrum determined. The spectrum obtained was essentially identical to that shown in the Figure, with the proviso that some sharpening of signals occurred. These results suggest that base catalysed epimerisation does not occur and the three diastereoisomers have comparable thermodynamic stabilities. Cooksey and Tobe[16,17] have observed small variations (factors of *ca.* two-fold) in the base hydrolysis rates of different diastereoisomers of *trans*-$[Co(cyclam)Cl_2]^+$ and *trans*-$[CoL^2Cl_2]^+$ complexes (cyclam = 1,4,8,11-tetra-azacyclotetradecane and L^2 = 1,9-diamino-3,7-diazanonane). Thus the *R,S,S,R* diastereoisomer of $[Co(cyclam)Cl_2]^+$ has $k_{OH} = 6.5 \times 10^4$ dm^3 mol^{-1} s^{-1} while for the *R,R,R,R* diastereoisomer $k_{OH} = 1.57 \times 10^5$ dm^3 mol^{-1} s^{-1} at 25 °C. Little or no information is currently available on complexes containing larger macrocyclic rings, but the present results suggest that only very minor differences in values of k_{OH} may be expected. Henderson and Tobe[18] have considered the factors which influence the reactivity of chloropenta-amine complexes of cobalt(III) towards base hydrolysis. Deprotonation takes place at a nitrogen which is the middle member of a meridional set of three donors (called ' flat ' for convenience). The requirements for high lability towards base hydrolysis are (*i*) there should be a ' flat ' secondary nitrogen to form the amido-group, (*ii*) the amido-group must be *cis* to the leaving group, (*iii*) the plane of the amido-group in the intermediate should be able to lie perpendicular to the trigonal plane of the cobalt, (*iv*) there should be five-membered rings on either side of this group to hold it in position, and (*v*) there should be unidentate amines or a six-membered chelate occupying the remaining equatorial sites in the intermediate, so that there is minimal strain. It is of considerable interest to compare the reactivity of $[CoLCl]^{2+}$ towards base hydrolysis with that of the three $[Co(en)(dien)Cl]^{2+}$ (en = ethylenediamine) isomers,[19] Scheme 1. The values of k_{OH} for $[CoLCl]^{2+}$ and κ-$[Co(en)(dien)Cl]^{2+}$ are almost identical. These two complexes are structurally very similar and differ only in the two ethylenediamine bridges indicated by the dashed lines. The two isomers (ω and π) which have *fac* dien ligands have ' normal ' base hydrolysis rates. Increasing the flexibility of the axial–equatorial bridge as in $[CoCl(pn)(dien)]^{2+}$ (VII) (pn = propane-1,3-diamine) leads to a marked increase in the value of k_{OH}.[20] The complex[21] $[CoL^1Cl]^{2+}$ (VI) which is structurally somewhat similar to $[CoLCl]^{2+}$ and κ-[Co-

---

* For a discussion of the stereochemistry of these compounds see ref. 14.



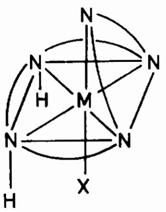
Scheme 1. Base hydrolysis rates of various chloropenta-amine complexes at 25 °C. L^1 = 1,11-diamino-3,6,9-triazaundecane



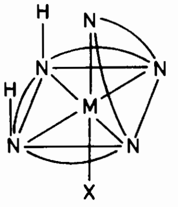
(VIII)

(en)(dien)Cl]$^{2+}$ with the *mer*-N_3 donor set has a very similar value of k_{OH}.

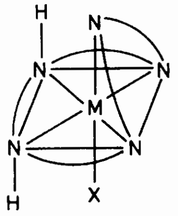
Stereochemical Considerations.—The gross stereochemistry of octahedral complexes of L can be represented as shown in (VIII). There are two chiral nitrogen centres (with dotted NH bonds), and the three possible diastereoisomers are shown diagramatically in (IX)—(XI). Molecular models show that none of the three possible stereoisomers is particularly strained. In principle the N-*meso* and N-*rac* diastereoisomers can be differentiated by the use of ^{13}C n.m.r. measurements. The copper(II) and nickel(II) complexes are paramagnetic, thus the measurements were made using the diamagnetic cobalt(III) complex. The N-*meso* diastereoisomers have a plane of symmetry and thus a maximum of five carbon signals should be seen. The N-racemic diasteroisomer should display a maximum of ten carbon signals. The ^{13}C spectrum of the cobalt(III) complex in D_2O is shown in the Figure. Clearly at least ten signals are observed with marked differences in their intensities. The intensity differences rule out the possibility of a pure N-*rac* diastereoisomer and the sample is apparently a mixture of the three possible diastereoisomers.



(IX)
N-*meso*



(X)
N-*meso*



(XI)
N-*rac*

Acid Dissociation Kinetics.—The copper(II) and nickel(II) complexes of L are quite labile in acidic solution. The kinetics of these acid dissociation reactions of complexes of macrocyclic ligands has attracted considerable interest over recent years in an attempt to understand the unusual thermodynamic and kinetic properties of these complexes.[22] The acid dissociation of tetra-azacycloalkane complexes is extremely slow [23,24] and attention has focused on more labile systems including N_2O_2, N_2S_2, S_4, and N_3 macrocyclic systems.[25–31]

The kinetics of the acid catalysed dissociation of $[CuL]^{2+}$ was studied using $HClO_4$ solutions in the range 0.19—0.58 mol dm^{-3} adjusted to I = 0.98 mol dm^{-3} with Na[ClO$_4$]. The reactions are first order in the complex and values of $k_{obs.}$ at various hydrogen ion concentrations are listed in Table 4. A plot of $k_{obs.}$ *versus* $[H^+]$ indicates that the reaction does not show a first-order dependence on $[H^+]$, but a second-order dependence on $[H^+]$. Values of $k_H = k_{obs.}[H^+]^{-2}$ are quite constant giving $k_H = 4.9 \times 10^{-2}$ dm^6 mol^{-2} s^{-1}, Table 4.

Similar measurements with $[NiL(OH_2)]^{2+}$ also established a second-order dependence on $[H^+]$, with k_H = 0.63 dm^6 mol^{-2} s^{-1} at 25 °C, Table 4. To our knowledge, this appears to be the first example of a second-order dependence on $[H^+]$ for the acid dissociation of macrocyclic complexes. The transition state of the reaction must involve the complex and two protons and it seems probable that one protonation site is the single axial nitrogen while the other is one of the equatorial nitrogens. We have recently reported [12] the preparation of the nickel(II) and copper(II) complexes of the sexidentate ligand 1,4,7,10,13,16-hexa-azacyclo-octadecane (XII) where the nickel(II) complex has the unsymmetrical topology (XIII). The copper(II) and nickel(II) complexes are quite labile under acid conditions. Dissociation of the copper(II) complex is very rapid even at pH 4, while that of the nickel(II) complex is considerably slower. These complexes contain two axial nitrogen donors, and as a result, it might be expected that the reaction would involve a third-order dependence on $[H^+]$ due to protonation of two axial nitrogens and one equatorial nitrogen. Acid dissociation of the nickel(II) complex does indeed show a dependence on $[H^+]^3$ with $k_H = 2.58 \times 10^2$ dm^9 mol^{-3} s^{-1} at 25 °C, Table 4.

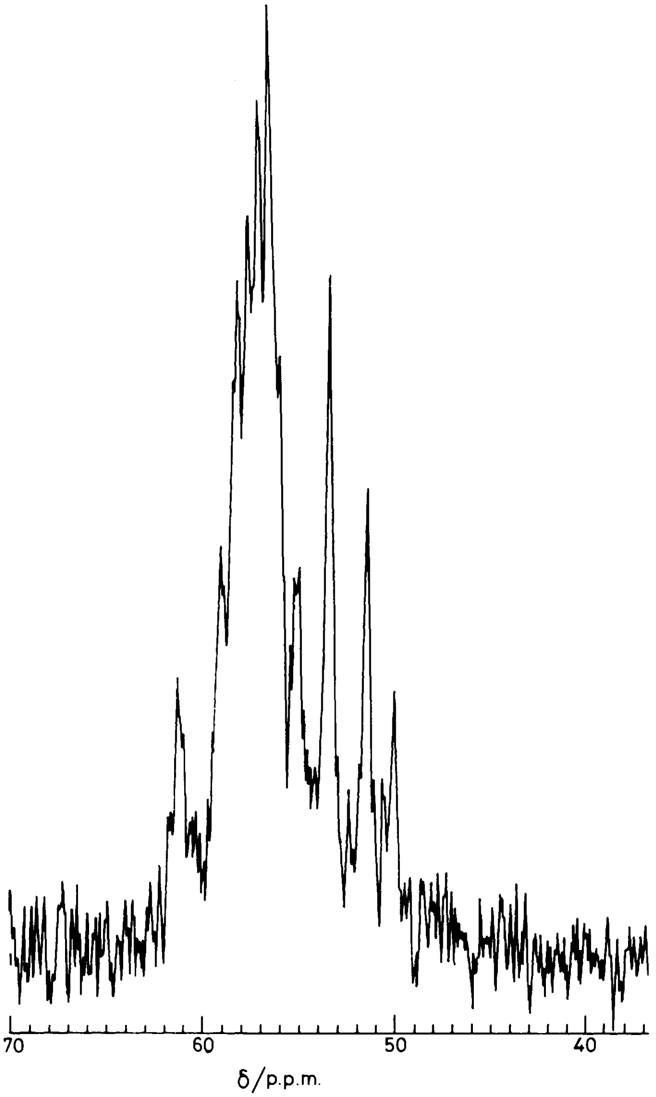


Figure. The ^{13}C n.m.r. spectrum of $[CoLCl]^{2+}$ in D_2O with dss as reference. The spectrum shown is the summation of two spectra of 139 000 scans and 49 000 scans weighted in the ratio 3 : 1 respectively. There is a small dss peak at 56.6 p.p.m.

Table 4. Kinetics of the acid catalysed dissociation of the copper(II) and nickel(II) complexes at 25 °C and I = 0.98 mol dm^{-3}

(*a*) $[CuL]^{2+}$

$[H^+]$/ mol dm^{-3}	$10^2[H^+]^2$/ mol^2 dm^{-6}	$10^3k_{obs.}$/s^{-1}	$10^2k_{obs.}[H^+]^{-2}$/ dm^6 mol^{-2} s^{-1}
0.193	3.74	1.92	5.13
0.290	8.41	3.71	4.41
0.387	14.95	7.72	5.16
0.483	23.36	10.99	4.70
0.580	33.64	17.43	5.18

$k_H = 4.9 \times 10^{-2}$ dm^6 mol^{-2} s^{-1}

(*b*) $[NiL]^{2+}$

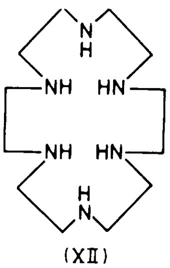
$10^2[H^+]$/ mol dm^{-3}	$10^3[H^+]^2$/ mol^2 dm^{-6}	$10^3k_{obs.}$/s^{-1}	$k_{obs.}[H^+]^{-2}$/ dm^6 mol^{-2} s^{-1}
4.80	2.30	1.32	0.57
7.73	5.98	3.73	0.62
9.67	9.40	6.09	0.64
11.60	13.50	9.11	0.67
14.51	21.03	14.03	0.66

k_H = 0.63 dm^6 mol^{-2} s^{-1}

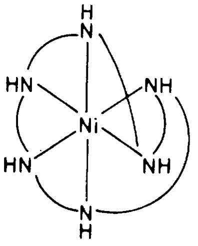
(*c*) $[Ni(haco)]^{2+}$

$10^3[H^+]$/ mol dm^{-3}	$10^5[H^+]^3$/ mol^3 dm^{-9}	$10^3k_{obs.}$/s^{-1}	$10^{-2}k_{obs.}[H^+]^{-3}$/ dm^9 mol^{-3} s^{-1}
9.6	0.09	0.227	2.52
20.3	0.84	2.14	2.54
30.9	2.95	7.54	2.55
38.7	5.80	15.60	2.69
48.3	11.27	28.46	2.59

$k_H = 2.58 \times 10^2$ dm^9 mol^{-3} s^{-1}



(XII)



(XIII)

The kinetic behaviour of $[CuL]^{2+}$ in acidic solution can be described in terms of the equations (1)—(3). Monoprotonation

$$[CuL]^{2+} + H^+ \underset{}{\overset{K_1}{\rightleftharpoons}} [Cu(HL)]^{3+} \qquad (1)$$

$$[Cu(HL)]^{3+} + H^+ \overset{K_2}{\rightleftharpoons} [Cu(H_2L)]^{4+} \qquad (2)$$

$$[Cu(H_2L)]^{4+} \xrightarrow{k} Cu^{2+}(aq) + H_2L^{2+} \qquad (3)$$

of $[CuL]^{2+}$ to $[Cu(HL)]^{3+}$ is expected to involve protonation at the apical nitrogen atom, since the axial copper–nitrogen bond is expected to be weaker as a result of Jahn–Teller distortion. The subsequent steps in the reaction are outlined in Scheme 2. Species (2) is introduced since it is improbable that a proton can attack a fully co-ordinated nitrogen. Arguments in favour of a partly bonded species, as opposed to a species in which the bond is completely broken but the nitrogen is still in close proximity to the metal ion, have been discussed elsewhere.[32] Species of the type $[Cu(HL)]^{3+}$ have often been reported in potentiometric studies of copper(II) polyamine complexes. For example, the copper complex of *N*-(2-aminoethyl)butane-1,4-diamine has a log K_{CuHL} = 6.4 (ref. 33) and the copper complex[34] of *N*-(2-aminoethyl)propane-1,3-diamine has log K_{CuHL} = 3.14.

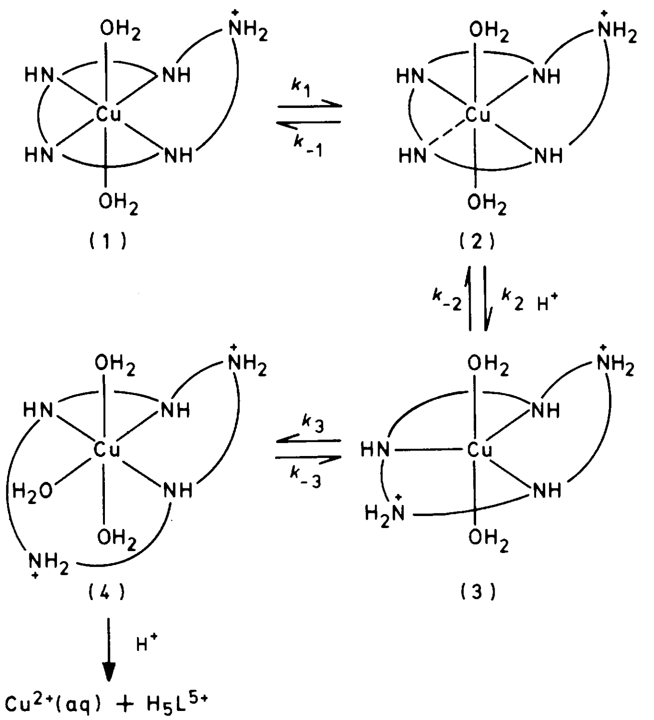
It can be readily shown using equations (1)—(3) that the rate law (4) holds. Under the conditions of the present

$$\text{Rate} = \frac{k_1K_1K_2[CuL^{2+}][H^+]^2}{1 + K_1[H^+] + K_1K_2[H^+]^2} \qquad (4)$$

experiments $K_1[H^+] + K_1K_2[H^+]^2 \ll 1$ and $k_H = kK_1K_2$, since rate = $k_H[CuL^{2+}][H^+]^2$.

A similar kinetic treatment can be applied to the nickel(II) complex of 1,4,7,10,13,16-hexa-azacyclo-octadecane. In this case it is necessary to introduce a further equilibrium (5), and $k_H = kK_1K_2K_3$.

$$[Ni(H_2L)]^{4+} + H^+ \overset{K_3}{\rightleftharpoons} [Ni(H_3L)]^{5+} \qquad (5)$$



Scheme 2. Acid catalysed dissociation of $[Cu(HL)]^{3+}$

Acknowledgements

We thank Miss F. McLaren for carrying out preliminary work on the preparation of 1,4,7,10,13-penta-azacyclopentadecane and the S.E.R.C. for financial support and for the award of a postdoctoral fellowship (to R. B.).

References

1 J. E. Richman and T. J. Atkins, *J. Am. Chem. Soc.*, 1974, **96**, 2268.
2 See, for example, 'Coordination Chemistry of Macrocyclic Compounds,' ed. G. A. Melson, Plenum Press, New York, 1979.
3 M. Kodama, E. Kimura, and S. Yamaguchi, *J. Chem. Soc., Dalton Trans.*, 1980, 2536.
4 M. Kodama and E. Kimura, *J. Chem. Soc., Dalton Trans.*, 1978, 104.
5 M. Kodama and E. Kimura, *Inorg. Chem.*, 1980, **19**, 1871.
6 Y. Sugiura and Y. Mino, *Inorg. Chem.*, 1979, **18**, 1336.
7 T. Takita, Y. Muraoka, T. Nakatani, A. Fuji, Y. Iitaka, and H. Umezawa, *J. Antibiot.*, 1978, **31**, 1073.
8 R. D. Bereman and M. E. Winkler, *J. Inorg. Nucl. Chem.*, 1980, **42**, 1797.
9 Y. Sugiura, *J. Am. Chem. Soc.*, 1980, **102**, 5216.
10 R. W. Hay and P. R. Norman, *J. Chem. Soc., Dalton Trans.*, 1979, 1441.
11 R. A. Robinson and R. H. Stokes, 'Electrolyte Solutions,' 2nd edn., Butterworths, London, 1959.
12 R. W. Hay, B. Jeragh, S. F. Lincoln, and G. H. Searle, *Inorg. Nucl. Chem. Lett.*, 1978, **14**, 435.
13 R. W. Hay, P. R. Norman, D. A. House, and C.-K. Poon, *Inorg. Chim. Acta*, 1981, **48**, 81.
14 M. R. Snow, D. A. Buckingham, P. A. Marzilli, and A. M. Sargeson, *Chem. Commun.*, 1969, 891; M. R. Snow, *J. Chem. Soc., Dalton Trans.*, 1972, 1627.
15 T-L. Ni and C. S. Garner, *Inorg. Chem.*, 1967, **6**, 1071.
16 C. J. Cooksey and M. L. Tobe, *Inorg. Chem.*, 1978, **17**, 1558.
17 C. J. Cooksey and M. L. Tobe, *Inorg. Chem.*, 1978, **17**, 2442.
18 R. A. Henderson and M. L. Tobe, *Inorg. Chem.*, 1977, **16**, 2576.
19 R. W. Hay and K. B. Nolan, *J. Inorg. Nucl. Chem.*, 1976, **38**, 2118.
20 L. S. Dong and D. A. House, *Inorg. Chim. Acta*, 1976, **19**, 23.
21 T. L. Ni and C. S. Garner, *Inorg. Chem.*, 1967, **6**, 1071.
22 See for example, R. W. Hay, and P. R. Norman, *Inorg. Chim. Acta*, 1980, **45**, L139, and refs. therein.
23 D. K. Cabbiness and D. W. Margerum, *J. Am. Chem. Soc.*, 1970, **92**, 2151.
24 L. Hertli and T. A. Kaden, *Helv. Chim. Acta*, 1974, **57**, 1328.
25 A. Anderegg, A. Ekstrom, L. F. Lindoy, and R. J. Smith, *J. Am. Chem. Soc.*, 1980, **102**, 2670.
26 C. S. Kallianor and T. A. Kaden, *Helv. Chim. Acta*, 1979, **62**, 2562.
27 L. L. Diaddario, L. L. Zimmer, T. E. Jones, L. S. W. Sokol, R. B. Cruz, E. L. Yee, L. A. Ochrymowycz, and D. B. Rorabacher, *J. Am. Chem. Soc.*, 1979, **101**, 3511.
28 T. J. Riedo and T. A. Kaden, *Helv. Chim. Acta*, 1979, **62**, 1089.
29 L. J. Murphy and L. J. Zompa, *Inorg. Chem.*, 1979, **18**, 3278.
30 L. F. Lindoy and R. J. Smith, *Inorg. Chem.*, 1981, **20**, 1314.
31 P. G. Graham and D. C. Weatherburn, *Aust. J. Chem.*, 1981, **34**, 291.
32 D. W. Margerum, G. R. Gayley, D. C. Weatherburn, and G. K. Pagenkopf in 'Coordination Chemistry,' ed. A. E. Martell, vol. 2, A.C.S. Monograph No. 174, American Chemical Society, Washington, 1978.
33 M. Gold and H. K. J. Powell, *J. Chem. Soc., Dalton Trans.*, 1976, 230.
34 R. Barbucci, L. Fabrizzi, and P. Paoletti, *Inorg. Chim. Acta*, 1973, **7**, 157.

Received 9th July 1981; *Paper* 1/1088