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STUDIES IN COORDINATION CHEMISTRY

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To my parents, Sham, Ravita, Sonu,
Neelam, OP.
Not forgetting Late Goldy.

ACKNOWLEDGEMENTS

The author gratefully acknowledges assistance from the following people:

In particular, Dr. R. W. Hay for suggesting the topic of the thesis and stimulating discussions and for many helpful suggestions.

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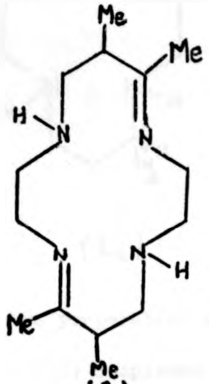
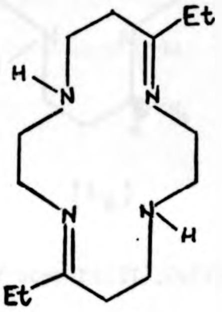
Mrs. E. Walker for preparing the manuscript with great attention and Miss Elspeth for general help.

ABSTRACT

Several new 14-membered tetradentate macrocyclic N_4 ligands and their metal complexes were synthesized. The macrocycles, 5,6,12,13 - Tetramethyl - 1,4,8,11 - tetra-azacyclotetradeca - 4,11 - diene dihydroperchlorate; $\mathrm{Me_4[14]diene.2HClO_4}$ (A) and 5,12 - Diethyl - 1,4,8,11 - tetra-azacyclotetradeca-4,11 - diene dihydroperchlorate; $\mathrm{Et_2[14]diene.2HClO_4}$ (B) were prepared by the reaction of 1,2 - diaminoethane monohydroperchlorate with methylisopropenyl ketone (MIK) and ethyl vinyl ketone (EVK) respectively.



(A)

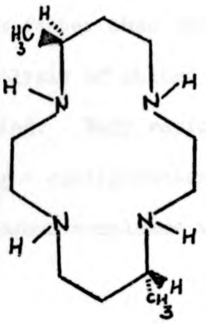


(B)

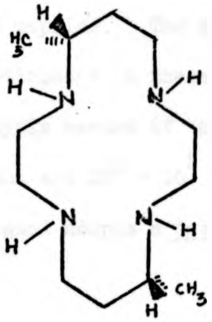
Both reactions appeared to be stereospecific giving the *transoid*-isomers (A) and (B) rather than the *cisoid*-isomers of the macrocycles.

Metal ion complexes of $\mathrm{Me_4[14]diene.2HClO_4}$ (A) of the general formulation $\mathrm{[M(Me_4[14]diene)](ClO_4)_2}$ ($M = Cu^{2+}, Ni^{2+}, Zn^{2+}$ and Hg^{2+}) were prepared and the studies extended to the isolation of $\mathrm{[Co^{III}(Me_4[14]diene)X_2]^{n+}}$ (where $X = Cl^-, Br^-, NO_2^-, SCN^-, N_3^-, CH_3CO_2^-, NH_3$) complexes. The structures of all compounds were confirmed by elemental analyses and by spectroscopic investigations. The spectroscopic properties of the complexes are consistent with a square planar geometry for the metal(II) perchlorate salts (M=Cu(II) and Ni(II)) and a *trans* - arrangement of the unidentate ligands in the octahedral cobalt(III) derivatives $\mathrm{[Co(Me_4[14]diene)X_2]^{n+}}$.

Reduction of the 5,12 - Dimethyl - 1,4,8,11 - tetra-azacyclotetradeca - 4,11 - diene dihydroperchlorate with Ni/Al alloy gave two [redacted] isomeric amines i.e C - *meso* - 5,12 - dimethyl - 1,4,8,11 - tetra-azacyclotetradecane (Isomer (a)) (L_A) and C - *rac* - 5,12 - dimethyl - 1,4,8,11 - tetra-azacyclotetradecane (Isomer (b)) (L_B).



(L_A)



(L_B)

The preparation and properties of some Ni(II),Cu(II),Zn(II),Mn(II),Rh(III), and Co(III) complexes of (L_A) and (L_B) are reported.

Methylation of the secondary nitrogen protons in several macrocyclic amine ligands yielded the corresponding N-tetramethyl derivatives.

The second section of the investigation dealt with the reactivity of octahedral complexes of cobalt(III) of the type *cis*-$[Co(en)_2(RNH_2)Br]Br_2$ (where R=H, CH_3,C_2H_5,n-C_3H_7,n-C_5H_{11},n-C_6H_{13}, aminoacetaldehyde dimethylacetal, cyclopropylamine, 3-amino-1-propanol, 6-amino-1-hexanol). All of these complexes were assigned *cis*-configurations on the basis of their spectral characteristics. The base hydrolysis kinetics for bromide release were studied spectrophotometrically at 25.0°C and I=0.10*M*. Loss of coordinated halide results in the formation of hydroxo product i.e. *cis* - $[Co(en)_2(RNH_2)OH]^{2+}$ with retention of configuration.

Some features of the base hydrolysis kinetics of amino acids and dipeptide esters coordinated to cobalt(III) were also studied. $[\mathrm{Co(dien)(aa)X}]^{n+}$ (X = Cl, NO_2; aa = glycinate anion, glycylglycine ethyl ester, glycinamide) complexes were prepared. The rate constant k_{OH} for peptide bond hydrolysis normally falls within the range 0.67 - 0.88 $M^{-1}s^{-1}$ at 25.0^{o} and I = 0.10*m*. Base hydrolysis of the complexed peptide is *ca* 2 X 10^{4} times faster than for the uncomplexed peptide. The kinetics of base hydrolysis of chloro - and nitro substituents in these complexes ~~was~~ were also studied. Very rapid chloride hydrolysis occurs if the dien ligand adopts a *mer* - configuration and the reactions are 10^{2} - 10^{4} times faster than for analogous complexes where the dien ligand adopts a *fac* - configuration.

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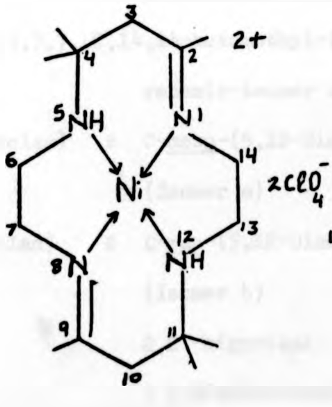
NOMENCLATURE

The definitive rules of nomenclature and abbreviations for Inorganic chemistry proposed by IUPAC[1] (International Union of Pure and Applied Chemistry) are used throughout this thesis. The tentative rules of IUPAC - IUB Commission on Biochemical nomenclature[2] were adopted when referring to reactions and complexes of peptides.

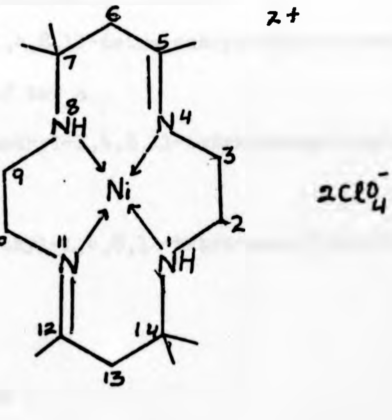
International union names based on the Chemical Society (London)[3(a)] and the American Chemical Society[3(b)] have been used for macrocyclic ligands. However, the former nomenclature is preferred in this work in which the nitrogen atoms are given the lowest numbers, i.e. the highest priority. Alternatively, adopting the American Chemical Society system double bonds are given the lowest numbers. For example, the nickel complex shown (I and II) can be named according to the Chemical Society as:

5,7,7,12,14,14-Hexamethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene nickel (II) Diperchlorate (1) or as:

2,4,4,9,11,11-Hexamethyl-1,5,8,12-tetra-azacyclotetradeca-1,8 diene nickel (II) Diperchlorate (II) according to the American Chemical Society system.



(II)



(I)

ABBREVIATIONS

Abbreviated names and notations have been used frequently for the sake of simplicity[4].

Bivalent metal complexes of tetra-azacyclotetradeca dienes with varying number of methyl substituents can be represented in general form as

$[M(II)(Me_x[14]diene)](ClO_4)_2$

M = First row transition metal and $x = 2,4,6$

The following trivial abbreviations have been used.

Me$_2$[14]diene.2HClO$_4$ ≡ 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene(II) dihydroperchlorate

Me$_4$[14]diene.2HClO$_4$ ≡ 5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene(II) dihydroperchlorate

Me$_6$[14]diene.2HClO$_4$ ≡ 5,7,7,12,14,14-Hexamethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene dihydroperchlorate

Et$_2$[14]diene.2HClO$_4$ ≡ 5,12-Diethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene(II) dihydroperchlorate

Ph$_2$Me$_2$[14]diene: 5,12-Dimethyl-7,14-diphenyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene

CYCLAM ≡ 1,4,8,11-tetra-azacyclotetradecane

tet a: *meso*-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetra-azacyclotetradecane

tet b: racemic-isomer of tet a

C-*meso*-(Me$_2$Cyclam) ≡ C-*meso*-(5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane) (Isomer a)

C-*rac*-Me$_2$(Cyclam) ≡ C-*rac*-(5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane (Isomer b)

bipy: 2,2'-bipyridal

en: 1,2-diaminoethane

dien 2,2'-diaminodiethylamine (diethylenetriamine)
trien: 1,2-di[aminoethylamino]-ethane
(triethylene tetramine)
dpt: Bis-(2-aminopropyl)-amine
(dipropylenetriamine)
2,3,2 tet: 1,4,8,11-tetra-azaundecane
trenen: 4-(aminoethyl)-1,4,7,10-tetra-azaundecane
tren: triamino triethylamine
tn: trimethylene diamine: $NH_2(CH_2)_3NH_2$
tep: ethylene bis(diethyl phosphine): $(C_2H_5)_2P.CH_2.CH_2.P(C_2H_5)_2$
MVK: Methyl vinyl ketone
EVK: Ethyl vinyl ketone
MIK: Methyl isopropenyl ketone
gly: NH_2CH_2CO
glyO: $NH_2CH_2CO_2^-$ (glycinate anion)
glyOR: $NH_2CH_2CO_2R$ (alkyl glycinate)
glyNH$_2$: $NH_2CH_2CONH_2$ (glycine amide)
glyglyOEt: $NH_2CH_2CONHCH_2CO_2Et$ glycyl glycine ethylester
Cyclen 1,4,7,10 - Tetraazacyclododecane

MATERIALS AND METHODS

Spectral measurements

Spectrophotometric kinetic measurements were made using a Gilford 2400S instrument. The cell compartment was thermostated to ± 0.1°C by water circulation from a 'Grant' constant temperature water bath. Base hydrolysis kinetics were carried out by dissolving a weighed quantity of the requisite complex in a 1cm matched cell filled with buffer previously equilib~~r~~rated at the appropriate temperature. Immediately, the cell was placed in a thermostated cell compartment and the absorbance monitored for 75-80% reaction. The product absorbance was determined after ten half lives.

Rate constants (k_{obs}) were evaluated from the slopes ($= - k_{obs}/2.303$) of plots of log $(A_t - A_\infty)$ or $\log(A_\infty - A_t)$ versus time.

All solutions were prepared with doubly distilled water. The water used for the borax buffers and standard sodium hydroxide solution was also degassed by boiling and cooled under nitrogen, to remove carbon dioxide.

Infrared spectra were recorded as KBr discs on a Perkin Elmer 457 and 577 Grating spectrophotometers. Precautions were taken to avoid contact of the discs with the moisture.

Electronic and visible spectra were recorded on Perkin Elmer 402 and Pye Unicam SP800 spectrophotometers with the appropriate solvent as blank.

N.M.R. spectra of the cobalt (III) complexes were recorded on a Perkin Elmer R10 spectrophotometer at 90 Mc/sec and ambient temperature with a 450 sec sweep rate in deutrated dimethyl sulphoxide(d_6-DMSO). Chemical shifts were measured relative to 3-(Trimethylsilyl)-propanesulphonic acid sodium salt (NaTMS) as internal standard and expressed in terms of δ(ppm) values.

A series of low ionic strength alkaline buffers suitable for spectrophotometric kinetic measurements were prepared from sodium tetraborate and boric acid or sodium hydroxide, using a modification of the method adopted by Perrin[5] to give an ionic strength, $I = 0.10M$. These buffers are nearly transparent in the ultraviolet region and were standardised on a pH meter. The standard buffers were stored under nitrogen and renewed frequently. Standard solutions of hydrochloric acid (0.10M) and sodium hydroxide (0.10M), and other similar reagents were prepared directly by dilution of BDH concentrated volumetric solutions.

The following buffer systems were used to cover various intervals of the pH scales. Acetic acid/Potassium hydroxide (4.5-5.5), 2,6-Lutidine/Hydrochloric acid (7.2-6.7), Sodium tetraborate/Boric acid (8.5-9.2), Sodium tetraborate/Potassium hydroxide (9.3-9.7), *n*-Butylamine/Hydrochloric acid (10.3-11.4) and Sodium hydroxide (0.1M) .

With two exceptions, all reagents were available as AnalaR grade and were used without further purification. The *n*-butylamine and 2,6-Lutidine were laboratory reagent grades, purified by fractional distillation; fractions between 78° and 146-8°C were collected respectively.
For acetic acid and potassium hydroxide cases, buffer solutions were made from stock solutions of 0.1M acetic acid and 0.1M KOH and 0.9M $NaClO_4$ solution to adjust the ionic strength to 0.1M. The *n*-butylaminehydrochloride buffers were made using stock solutions of *n*-butylamine(2M) and Hydrochloric Acid (1M).

Sodium tetraborate-boric acid buffers were made by dissolving 9.53g of sodium tetraborate (0.025M) and 6.18g of boric acid (0.1M) and diluting up to one litre with water. The final volume of the appropriate buffer was adjusted to 100cm^3 by addition of water. Great care was taken during the preparation of buffers as the accuracy of all pH measurements ultimately depends on the calibration accuracy of the pH meter which in turn depends on the accuracy of the buffer pH.

pH measurements were made with a Radiometer 26 pH meter equipped with a G202B high alkalinity glass electrode and a K401 calomel electrode. The scale expansion mode allowed the meter to be standardized to ± 0.005 units. The electrode assembly was standardized with both M/100 borax and M/20 oven dried (110°) potassium hydrogen phthalate. Normally, calibration was carried out daily when the meter was in use. The glass electrode was replaced periodically when it gave an unsatisfactory response to two buffers.

TABLE 1

The N.B.S. values[6] of the pH of the two Buffers are given below.

Temperature	M/100 Borax	M/20 Phthalate
0°	9.464	4.003
5	9.395	3.999
10	9.332	3.998
15	9.276	3.999
20	9.225	4.002
25	9.180	4.008
30	9.139	4.015
35	9.102	4.024
40	9.081	4.030
45	9.038	4.047

The hydroxyl ion activity coefficient y_1, was determined from the Davies equation[7] at I = 0.1 M and 25.0°, $y_1 = 0.772$.

$$-\log y_1 = A.Z^2\left(\frac{I^{\frac{1}{2}}}{1+I^{\frac{1}{2}}} - 0.2I\right) \qquad \ldots\ldots (1)$$

Z = valence of ions in solution
I = molar ionic strength

$$\text{Where } I = \tfrac{1}{2}\Sigma\, C_i Z_i^{\,2} \qquad \ldots\ldots (2)$$

Hydroxide ion concentrations were calculated from the pH according to the relation:

$$\mathrm{pH} = -\log a_{H^+}$$

and $pK_w = -\log a_{H^+} a_{OH^-} = 13.996$[8] at 25°

$$[OH^-] = a_{OH^-} / y_1$$

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$$[OH^-] = a_{OH^-}/y_1$$

TABLE 2

Hydroxide Ion concentrations calculated[9] using $pK_w = 13.996$, $I = 0{\cdot}10M$, $y_1 = 0.771$ at 25.0°C.

pH	$[OH^-] \times 10^{(14-x)}$ (Moles $litres^{-1}$)
X.00	1.307
X.10	1.645
X.20	2.071
X.30	2.607
X.40	3.282
X.50	4.132
X.60	5.201
X.70	6.549
X.80	8.243
X.90	10.380

Accepted values of pK_w[10], of the Debye-Hückel parameter A[11] and the calculated values of y_1 for a univalent ion at an ionic strength of 0.1M at a number of temperatures are given below.

TABLE 3

Temp°C	A	y_1(0.1M)	pK_w
15.0	0.5028	0.775	14.346
25.0	0.5115	0.772	13.997
35.0	0.5211	0.768	13.680
45.0	0.5317	0.764	13.396

Microanalysis for C, H, N and Cl were carried out by Strauss, Oxford.

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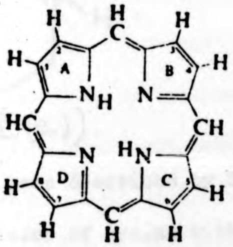
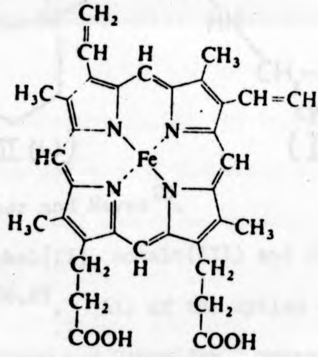
MACROCYCLES

1.1 INTRODUCTION

Organic macrocyclic quadridentate compounds of the pyrrole type have been known for many years and are derived from the single parent compound porphin (I). These naturally occurring macrocyclic compounds are highly unsaturated and substituted. Coordination compounds formed by phthalocyanine and other related types have been extensively studied[12]. Cobalt(III) complexes of various macrocyclic quadridentate amine ligands which can be considered as models for vitamin B_{12} have been studied[13,14].



Porphin I

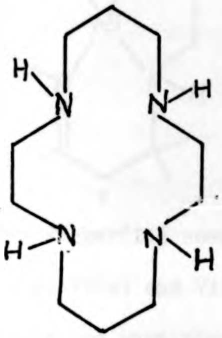


Heme II

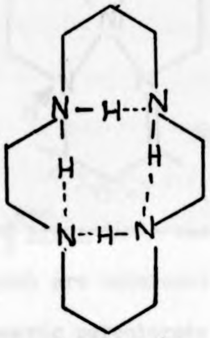
Several excellent reviews describing some important aspects of the coordination chemistry of macrocyclic ligands have been published[15-23].

The present studies are primarily concerned with some synthetic aspects of the tetra-azacyclotetradecadienes and the tetra-azacyclotetradecanes of the general type discovered by Curtis *et al*[29].

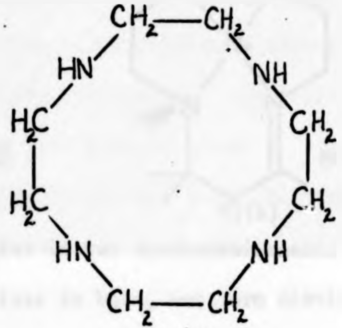
Van Alphen[24] first reported a relatively simple and saturated macrocyclic amine, 1,4,8,11-tetra-azacyclotetradecane 'CYCLAM' (III(a)) The cyclic amine (m.p. 185°C) is a non-hygroscopic crystalline compound and the intra-molecular hydrogen bonding between adjacent secondary amine groups is mainly responsible for these exceptional physical properties (III(b)). The preparation of a variety of cyclic tetra-amines by a purely organic route has been described by Stetter and Mayer[25].



(III(a))



(III(b))



cyclen

(IV)

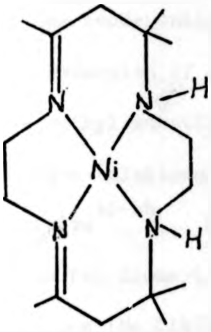
Complexes of cyclam with nickel(II), cobalt(III) and rhodium(III) were first described by Bosnich *et al*[26,27]. All of the cyclam complexes described have a *trans*-configuration. Collman and Schneider[28] prepared cobalt(III) and rhodium(III) complexes of Cyclen (IV), all these complexes have a *cis* - configuration.

One of the most studied group of synthetic macrocyclic ligands are those discovered by Curtis *et al*, who found that *"when tris ethylene diamine nickel(II) perchlorate is allowed to stand for several days in anhydrous acetone, the colour of the solution changes from blue-violet to yellow-brown"*[30]. The stoichiometry of the reaction can be represented as follows:

$$[Ni(NH_2.CH_2CH_2.NH_2)_3]^{2+} + 4CH_3COCH_3 \rightarrow [NiC_{16}H_{32}N_4]^{2+} + NH_2CH_2CH_2NH_2 + 4H_2O$$

i.e. the product is a nickel complex containing two diaminoethane residues and four acetone residues, condensed by elimination of four moles of water.

Curtis *et al* later successfully isolated two chemically distinct compounds from the tris (diaminoethane) nickel(II)/acetone condensation reaction and these were considered to be derivatives of the *cis* - and *trans*-dienes, *cis*, [Ni(*cis*(Me$_6$[14]diene)]$^{2+}$(V) and *trans* [Ni(*trans*(Me$_6$[14]diene)]$^{2+}$ (VI)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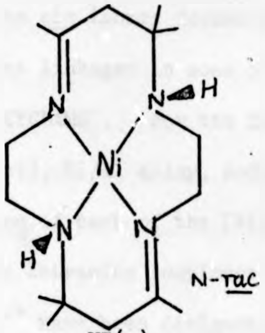
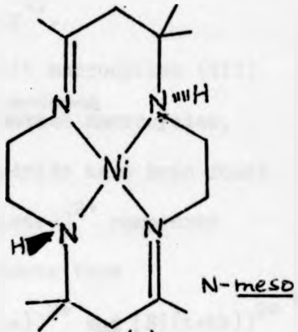


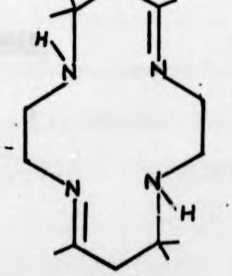
VI(a)



VI(b)

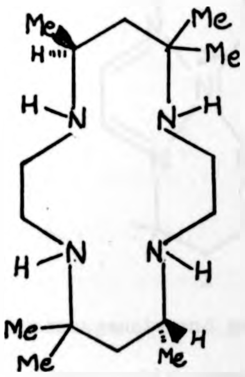
The nickel(II) complex of the *trans*-diene can exist in two diastereoisomeric forms VI(a) and VI(b) which are interconvertible in base, but form distinct salts, so that three isomeric perchlorate salts were isolated from the reaction[31]. The diastereoisomers arise from different configurations at the chiral nitrogen centres[32-36]. NMR and X-ray studies have shown that the 'orange' isomer resembles that of [Ni(*meso* *trans*-(Me$_6$[14]diene]$^{2+}$ and the yellow isomer resembles that of [Ni(*rac* *cis*-(Me$_6$[14]diene]$^{2+}$ [37,38]. The perchlorate complex of [Ni(*trans*(Me$_6$[14]diene)]$^{2+}$ isomer is least soluble and thus pure samples of diastereoisomers (VI(a)) and (VI(b)) can be obtained by fractional crystallisation using acetone, alcohol, water or their mixture as solvents[31].

Complexes of metal ions other than nickel(II) can readily be prepared from *trans*-Me$_6$[14]diene.2HClO$_4$ (VII) in methanol-water solution[39] and


VII

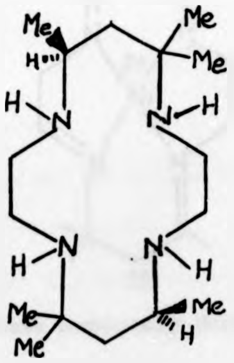
higher yields have been reported by reaction with metal acetates in methanol[40]. Cobalt(III) complexes have been prepared by reaction with $Na_3[Co(CO_3)_3]3H_2O$, and by oxidation of solutions prepared by reaction with cobalt(II) acetate or carbonate. Powell and coworkers have described Fe(II) and Zn(II) complexes of [<u>cis</u>-Me_6[14]diene)]$^{2+}$, since only for diaminoethane nickel(II))or copper(II))/ acetone condensation is the <u>cis</u> isomer formed exclusively[41].

Reduction of the imine linkages in some of the Curtis macrocycles (VII) give methyl substituted 'CYCLAMS'. For the fourteen ~~numbers~~ -membered macrocycles, hydrogen (platinum catalyst), Ni/Al alloy, sodium borohydride have been found effective[42-44]. Reduction of each of the [Ni(Me_6[14]diene)]$^{2+}$ complexes yields two isomeric cyclic tetramine complexes (the products from [Ni <u>trans</u> (Me_6[14]diene)]$^{2+}$ have been designated [Ni(teta)]$^{2+}$ and [Ni(tetb)]$^{2+}$ [42] and the pair from [Ni <u>cis</u>(Me_6[14]diene)]$^{2+}$, (Ni(tet c)]$^{2+}$ and [Ni(tet d)]$^{2+}$ [43]. The reduced ligands (VIII & IX) can be obtained from the respective nickel complex by reaction with cyanide to yield the free cyclic tetraamine plus the tetracyanonickelate ion[42,43].



tet <u>a</u> Or C-<u>meso</u>

VIII



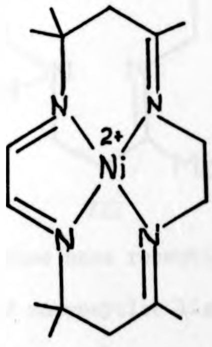
tet <u>b</u> or C-<u>racemic</u>.

IX

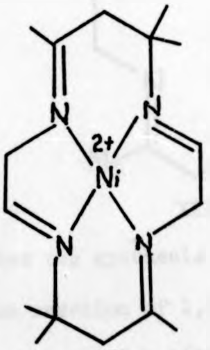
The relative yields of the two isomers varies with the reducing agent e.g. [Ni trans (Me$_6$[14]diene)]$^{2+}$, 22% [Ni(tet b)]$^{2+}$ was obtained with alkali and nickel-aluminium alloy, 33% with hydrogen and platinum catalyst[44]. The attribution of this isomerism to the introduction of two asymmetric carbon centres during reduction[42] has been confirmed by X-ray crystallography for the tet a - tet b pair, tet a being (C-meso trans Me$_6$[14] tetramine)(VIII) and tet b being (C-rac trans Me$_6$[14] tetramine)(IX).

Recently, Curtis and Hay have reported a convenient method to reduce 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene, Me$_6$[14]-diene.2HClO$_4$ to give the previously mentioned two diastereoisomeric hexamethyl tetra-azacyclotetradecanes[45] (VIII & IX).

The [Ni(Me$_6$[14]diene)]$^{2+}$ complexes are oxidised by nitric acid to give cyclictetra-imine "tetene" complexes [Ni trans Me$_6$[14] tetene)]$^{2+}$ (XI) and [Ni(cis[Me$_6$[14]tetene)]$^{2+}$ (X), although strong oxidising agents such as



X



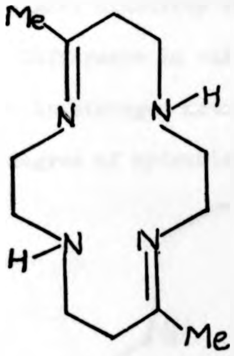
XI

acid permanganate and peroxydisulphate completely destroy the ligand of these macrocyclic complexes[46].

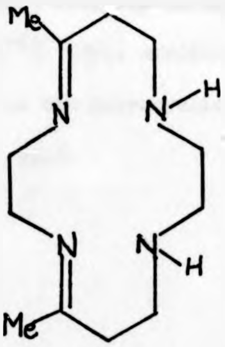
The imine groups of the macrocycle in trans-[Co(trans-Me$_6$[14]diene)Cl$_2$]$^+$ are reported to be slowly hydrolysed in hydrochloric acid solution[47].

Most of the work done in the past has dealt with one main macrocycle i.e. trans-Me$_6$[14]diene^{2+}(VII). Kolinski and coworkers have extended these studies to prepare a similar macrocycle, 5,12-dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene dihydroperchlorate (XII), by the reaction of methyl vinylketone (MVK) with 1,2-diaminoethane monohydroperchlorate[48]. This synthesis is originally an extension of the method described by Curtis and Hay for the preparation of Me$_6$[14]diene.2HClO$_4$[49].

Generally, the reaction of 1,2-diamino ethane with α, β- unsaturated carbonyl compounds appears to be stereospecific and the trans-isomer of the Me$_6$[14]diene is obtained exclusively[49]. Korybut-Daszkiewicz's provisional assignment of the trans-imine structure to Me$_2$[14]diene.2HClO$_4$ (XII) rather than the cis form (XIII) has been confirmed by recent X-ray crystallographic studies[50].



XII



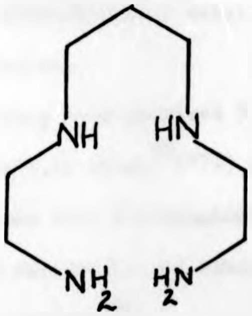
XIII

Myers and Rose have recently described the synthesis of an analogous[51] 16-membered macrocyclic ligand by the reaction of 1,3-diaminopropane and methyl vinyl ketone in the presence of both nickel(II) and hydrogen ions, which has the cis-configuration[52]. As the nickel complex isolated represented only 33% of the total nickel present it is possible that the trans - isomer also occurs in this reaction.

The use of the Schiff base reaction plays a central role in these processes via nucleophilic attack by the amine nitrogen on the carbon of the carbonyl group to yield a carbinol-amine intermediate and normally the reaction is acid-catalyzed. (See section 1.3.1).

A large number of metal(II) ion ($M=Ni^{2+}, Cu^{2+} Zn^{2+}, Co^{2+}$) complexes of the $Me_2[14]diene.2HClO_4$ (XII)macrocyclic ligand, and a new series of trans - $[Co^{III}(Me_2[14]diene)(L_2)]^{n+}$ (where L = $Cl^-, Br^-, NO_2^-, SCN^-, NH_3$); cis - $[Co^{III}(Me_2[14]diene)(aa)]^{n+}$ (aa = acetylacetonate; CO_3^{2-}) have recently been prepared[53].

Margerum *et al*[54] have studied the thermodynamic stability of metal complexes of macrocyclic ligands and have found the stability of macrocyclic complexes compared with that of open chain ligands of the same denticity (eg 2,3,2-tet (XIV)) is greatly enhanced. Busch has called this effect "multiple juxtapositional fixedness" while Margerum has used the term "macrocyclic effect". New equilibrium and calorimetric results by Hinz and Margerum[a] for the formation of nickel(II) complexes of cyclam and 2,3,2-tet reveal that the higher stability of the former rests entirely in the enthalpy term (the difference in -ΔH is *ca*. 60kJmol^{-1}). This striking effect has its origin not in stronger metal-ligand bonds in the macrocyclic complex but in a smallerdegree of hydration of the free ligand.



2,3,2-tet

XIV

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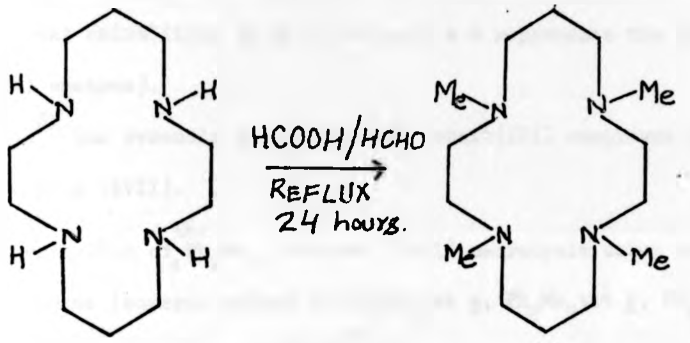
[a] F.P. Hinz and D.W. Margerum *J. Amer. Chem. Soc.*, 1974, 96, 4993

A new class of saturated 14-membered macrocyclic ligands with tertiary nitrogen donors has recently been reported[56] by methylating 'Cyclam' in order to study the redox chemistry of nickel(III) complex avoiding the following reaction processes:

$$\mathrm{Ni^{III}{-}N{-}H \quad + B \rightarrow Ni^{II}{-}N\cdot \quad + BH^{+}}$$

These tetra-N-methylated 14-membered macrocyclic ligands differ significantly compared with the unsubstituted macrocycles as far as metal complex

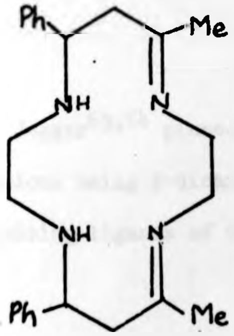


III(a)

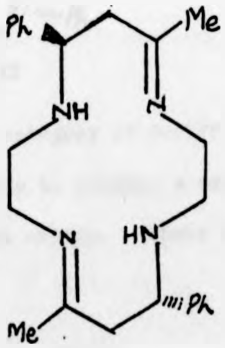
XV

stereochemistry is concerned. This is apparent from the studies made by Kaden[57] who describes ~~for the preparation o~~f metal complexes in solution which are reported to be penta-coordinate.

Lloyd and Hideg characterised 5,12-Dimethyl-7,14-diphenyl-tetraazacyclotetradeca-4,11 diene[58](XV1) macrocyclic ligand by the reaction of benzylidene-acetone with 1,2-diaminoethane and assigned the cis-diimine structure to the macrocycle and subsequently provided mass spectral evidence to support this structure[59].



XVI

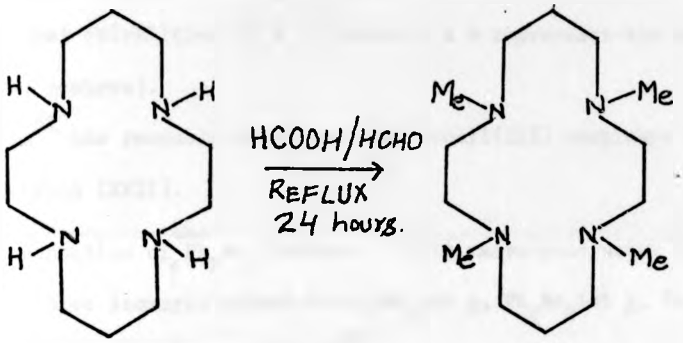


XVII

A new class of saturated 14-membered macrocyclic ligands with tertiary nitrogen donors has recently been reported[56] by methylating 'Cyclam' in order to study the redox chemistry of nickel(III) complex avoiding the following reaction processes:

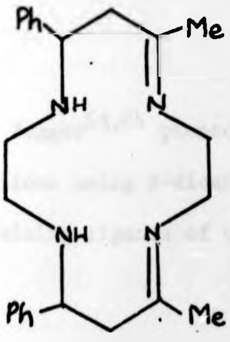
$$Ni^{III}\text{-}N\text{-}H \quad + B \rightarrow Ni^{II}\text{-}N\cdot \quad + BH^{+}$$

These tetra-N-methylated 14-membered macrocyclic ligands differ significantly compared with the unsubstituted macrocycles as far as metal complex stereochemistry is concerned. This is apparent from the studies made by Kaden[57] who describes. ~~for the preparation of~~ metal complexes in solution which are reported to be penta-coordinate.

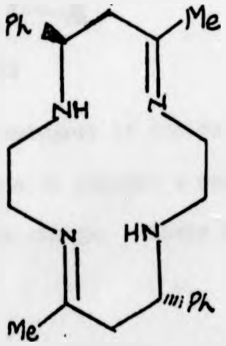


III(a) XV

Lloyd and Hideg characterised 5,12-Dimethyl-7,14-diphenyl-tetra-azacyclotetradeca-4,11 diene[58] (XV1) macrocyclic ligand by the reaction of benzylidene-acetone with 1,2-diaminoethane and assigned the <u>cis</u>-diimine structure to the macrocycle and subsequently provided mass spectral evidence to support this structure[59].



XVI

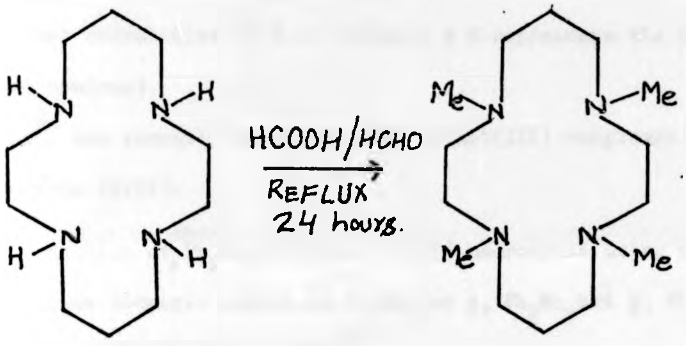


XVII

A new class of saturated 14-membered macrocyclic ligands with tertiary nitrogen donors has recently been reported[56] by methylating 'Cyclam' in order to study the redox chemistry of nickel(III) complex avoiding the following reaction processes:

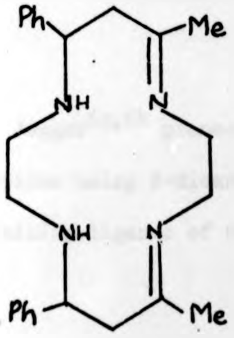
$$Ni^{III}-\overset{/}{\underset{\backslash}{N}}-H \quad +B \quad \rightarrow \quad Ni^{II}-\overset{/}{\underset{\backslash}{N}}\cdot \quad +BH^{+}$$

These tetra-N-methylated 14-membered macrocyclic ligands differ significantly compared with the unsubstituted macrocycles as far as metal complex stereochemistry is concerned. This is apparent from the studies made by Kaden[57] who describes. ~~for the preparation~~ of metal complexes in solution which are reported to be penta-coordinate.

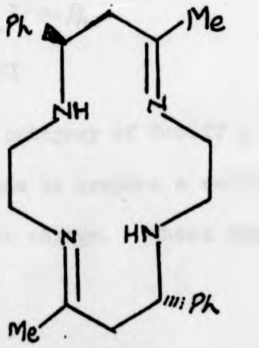


III(a) XV

Lloyd and Hideg characterised 5,12-Dimethyl-7,14-diphenyl-tetra-azacyclotetradeca-4,11 diene[58] (XV1) macrocyclic ligand by the reaction of benzylidene-acetone with 1,2-diaminoethane and assigned the <u>cis</u>-diimine structure to the macrocycle and subsequently provided mass spectral evidence to support this structure[59].



XVI



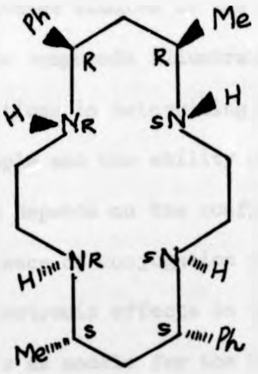
XVII

The preparation of 5,12-dimethyl-7,14-diphenyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene (XVI) is believed to involve Michael addition to give the β-amino ketone. Dimerisation of two β-amino ketone residues by Schiff base condensation gives the macrocyclic diene.

Cook, Curtis and Hay[60] prepared a variety of nickel(II) and copper(II) complexes of the ligand and on the basis of n.m.r. work and comparisons with other macrocyclic ligands of known structure suggested that the ligand has the trans -C-meso-diimine structure (XVII) in which the two carbon centres have different chiralities (R & S) (where R & S represents the configuration of the chiral centres).

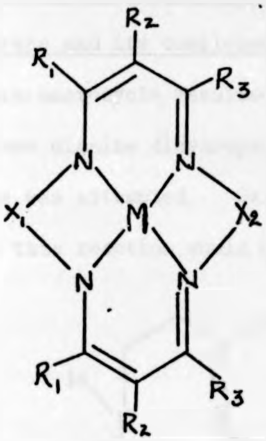
Curtis[61] has recently described some cobalt(III) complexes of the Ph_2Me_2[14]diene macrocycle (XVII).

Reduction of the Ph_2Me_2[14]diene (XVII) macrocycle using sodium borohydride gives three isomeric amines as Ph_2Me_2tet a, Ph_2Me_2tet b, Ph_2Me_2tet c in the ratio 75%. 20%, 5% respectively[62]



XVIII

Jagger[63,64] pioneered a second category of Schiff's base condensation reactions using β-dicarbonyl compounds to prepare a series of complexes containing ligands of doubly negative charge. These complexes are of the following general type (XIX), where X_1 and X_2 are either or both $-(CH_2)_3-$ or o-phenylene.



XIX

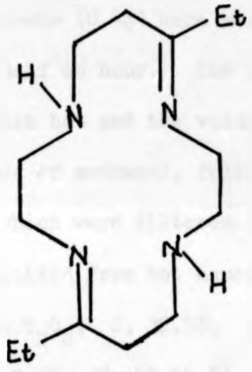
M = Ni or Cu.

The recent success in the synthesis of a great many macrocyclic amine ligands by metal-template reactions has stimulated the present investigation so as to provide a series of compounds in which ring size, degree of unsaturation and ring substituents can be varied. The macrocyclic moiety is non labile and facilitates studies of the reactivity at additional coordination sites. The compounds illustrate the importance of stereochemical considerations in determining the properties of complexes of macrocycles, for example and the ability of the macrocycle to buckle to accommodate a chelate depends on the configuration about coordinated amine centres. The absence of conjugation involving the donor atom and their inability to transmit electronic effects in these tetra-azacyclo macrocycles restrict their usefulness as models for the biological systems.

1.2 EXPERIMENTAL

1.2.1 Synthesis of 5,12-Diethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene Dihydroperchlorate and its complexes with nickel(II), copper(II) and zinc(II).

As a tetra-aza-macrocycle resulted from the reaction of methyl vinyl ketone with ethylene diamine dihydroperchlorate, the analogous reaction with ethyl vinyl ketone was attempted. Using the procedures of Curtis and Hay[49], it was hoped that this reaction would give the diethyl substituted macrocycle(XX).



XX

5,12-Diethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene Dihydroperchlorate; $Et_2[14]diene.2HClO_4$. -

1,2-Diaminoethane monohydroperchlorate ($28cm^3$, 50% ethylene diamine and $28cm^3$, 50% $HClO_4$) in situ was transferred to a three necked flask and stirred in an ice bath with methanol ($300cm^3$) under nitrogen. Ethyl vinyl ketone (EVK) ($12.5cm^3$) in methanol ($100cm^3$) was added dropwise over a period of two hours. The temperature was maintained below -5°C throughout the addition. Finally, the reaction mixture was stirred for a period of eight hours at room temperature and the yellow suspension placed in a refrigerator. The white crystalline product which separated was filtered off, washed with ethanol then ether and finally dried in vacuo.

yield ~ 16g. m.p. 115.5-116°C.

(Calc. for $C_{14}H_{30}N_4Cl_2O_8$; C, 37.09; H, 6.66; N, 12.35;
Found C, 37.30; H, 6.64; N, 12.34,%).

Metal Complexes:

5,12-Diethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene copper (II) Diperchlorate; $[Cu(Et_2[14]diene)](ClO_4)_2$.

Equivalent amounts of copper(II) carbonate (0.35g) and the macrocyclic ligand dihydroperchlorate (0.4g) were mixed in methanol (30 cm^3) and heated on a water bath for half an hour. The reaction mixture became purple-red and was filtered whilst hot and the volume reduced to about $5cm^3$. Addition of appropriate volumes of methanol, followed by ether and cooling in ice gave purple-red crystals which were filtered off and washed with ethanol. The product was recrystallised from hot aqueous methanol and dried in vacuo.

(Calc. for $C_{14}H_{28}N_4CuCl_2O_8$; C, 32.78; H, 5.11; N, 10.92;
Found C, 32.47; H, 5.38; N, 10.45,%).

5,12-Diethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene nickel(II) Diperchlorate; $[Ni(Et_2[14]diene](ClO_4)_2$.

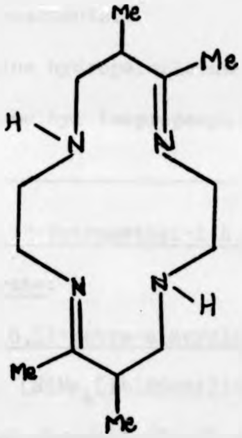
Nickel(II) carbonate (0.4g) was heated in methanol water (300 cm^3, 1:1 v/v) with a slight excess of $Et_2[14]diene.2HClO_4$ (0.45g) on a water bath for 30 minutes. The yellow solution was filtered whilst hot and the filtrate concentrated to about $2cm^3$ on a rotary evaporator. Methanol ($10cm^3$) was added and the yellow-orange product crystallised after cooling in an ice bath for several hours. The complex was filtered off and washed with a little cold methanol then ether and finally dried in vacuo.

(Calc. for $C_{14}H_{28}N_4NiCl_2O_8$: C, 32.96; H, 5.53; N, 10.98;
Found C, 32.56; H, 5.46; N, 10.62,%).

5,12-Diethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene.
zinc(II) Diperchlorate (hydrated); $[Zn(Et_2[14]diene])ClO_4)_2.X\ H_2O$. -

Zinc(II) perchlorate hexahydrate (0.5g) was dissolved in water ($10cm^3$) and to this solution was added the macrocyclic ligand (0.45g) in methanol. The reaction mixture was heated on a water bath for 0.5 hr and filtered whilst hot. The filtrate was evaporated to half its volume. Attempts to obtain a pure product were only partially successful owing to its hygroscopic nature.

1.2.2 5,6,12,13-Tetra methyl-1,4,8,11-tetra-azacyclotetradeca-4-11-diene Dihydrogenperchlorate; $Me_4[14]diene.\ 2HClO_4$. -



XXI

The ligand was prepared by Kolinski's[48] method with slight modifications. Aqueous perchloric acid ($165cm^3$, 72%. 2 moles) was added dropwise with continuous stirring to a cooled (card ice bath) methanolic solution of 1,2-diaminoethane ($134cm^3$, 10%, v/v, 2 moles). After complete addition, the reaction mixture was transferred to a three necked round bottom flask equipped with a stirrer, N_2-gas inlet and a dropping funnel. The reaction solution was immersed in an ice bath and the flask purged with nitrogen. Methyl isopropenyl ketone (MIK) ($196cm^3$, 2 moles) was diluted with an equal volume of methanol and added slowly over a period of two hours while maintaining the reaction temperature between 0-5°C.

The resulting reaction mixture was then stirred for four hours and the temperature was allowed to rise slowly to room temperature. The suspension was stored overnight in a refrigerator. The milky white product was filtered off and washed several times with methanol then ether and finally dried in vacuo. yield ∿ 310g m.p. 132-4°C.

(Calc. for $C_{14}H_{30}N_4Cl_2O_8$: C, 37.09; H, 6.67; N, 12.36;
Found C, 36.77; H, 6.48; N, 12.35,%)

Notes: 1. The temperature (0 to -5°C)should be maintained during the addition of reactants.

2. Ethylenediamine hydroperchlorate was made in situ and reacted with methyl isopropenyl ketone.

Metal Complexes of 5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene Dihydroperchlorate:

5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene nickel(II) Diperchlorate; $[NiMe_4[14]diene)](ClO_4)_2$. -

Nickel(II) acetate tetrahydrate (0.4g) was heated in methanol-water solution (300 cm^3, 1:1 v/v) with a slight excess of $Me_4[14]diene.2HclO_4$ ligand (0.5g) on a water bath for an hour and the solution filtered whilst hot. This yellow filtrate was concentrated to a small volume on a rotary evaporator and to this 20 cm^3 of methanol added; on cooling, orange-yellow crystalline product was filtered off, washed with little ice-cold methanol then ether and finally dried in vacuo.

(Calc. for $C_{14}H_{28}N_4NiCl_2O_8$: C, 32.86; H, 5.35; N, 10.79;
Found C, 32.96; H, 5.53; N, 10.98%)

5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca zinc(II) Diperchlorate; $[Zn(Me_4[14]diene)](ClO_4)_2$. -

Zinc(II) perchlorate hexahydrate (0.5g) was dissolved in water ($10cm^3$) and added to a methanol solution of the macrocyclic ligand (0.55g). The reaction mixture was heated on a water bath for 30 minutes and filtered whilst hot. Excess solvent was removed on a rotary evaporator, addition of methanol and subsequent cooling gave white crystals, which were filtered off and washed with ethanol then ether and finally dried in vacuo.

(Calc. for $C_{14}H_{28}N_4ZnCl_2O_8$: C, 32.53; H, 5.46; N, 10.84;
Found C, 32.85; H, 5.26; H, 10.64%)

5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene copper(II) Diperchlorate; $[Cu(Me_4[14]diene)](ClO_4)_2$. -

Copper(II) carbonate (0.5g) was suspended in water ($20cm^3$) and $Me_4[14]$-diene.$2HClO_4$ macrocyclic ligand (0.6g) in aqueous methanol added to it. The resulting mixture heated on a water bath for half an hour and the red-purple solution filtered whilst hot. The crude complex obtained on concentration of the red filtrate on an evaporator was washed with ethanol, then ether and finally recrystallised from hot methanol.

(Calc. for $C_{14}H_{28}N_4CuCl_2O_8$: C, 32.65; H, 5.48; N, 10.88;
Found C, 32.54; H, 5.31; N, 10.92%

This preparation was repeated using copper(II) nitrate hexahydrate for suitable crystals, but attempts were unsuccessful.

(Calc. for $C_{14}H_{28}N_4CuCl_2O_8$: C, 32.65; H, 5.48; N, 10.88;
Found C, 32.64; H, 5.30; N, 11.02,%)

5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene mercuric Diperchlorate Pentahydrate: $[Hg(Me_4[14]diene)](ClO_4)_2 \cdot 5H_2O$. -

Mercuric Chloride (0.3g) was dissolved in 10 cm^3 of water and added to a slight excess of macrocyclic ligand (0.45g), and warmed on a water bath for 20 minutes. The reaction mixture was then filtered whilst hot on a sintered glass cruicible and reduced its volume to about $5cm^3$. Addition of appropriate amounts of methanol then ether and subsequent cooling caused the crystallisation of the complex. Pale white hygroscopic crystals were filtered off and dried in vacuo for several hours. (Calc. for $C_{14}H_{28}N_4HgCl_2O_8 \cdot 5H_2O$: C, 22.51; H, 4.79; N, 7.67; Found C, 22.66; H, 5.16; N, 7.55,%).

Trans - dichloro-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene) cobalt(III) perchlorate; trans -$[CoMe_4[14]diene)Cl_2]ClO_4$. -

A solution of sodium tris-carbonato cobaltate trihydrate (0.8g)$(Na_3(Co(CO_3)_3) \cdot 3H_2O$ and $Me_4[14]diene.2HClO_4$ (0.8g) was made in $30cm^3$ of aqueous methanol and heated on a warm bath until effervescence ceased (20 minutes). The resulting red solution was filtered whilst hot and concentrated hydrochloric acid (15 cm^3) added to it and volume reduced on a water bath. The shining green plates obtained on cooling, were filtered off and dried at 110°C and recrystallised from hot methanol, washed with ethanol then ether and finally dried in vacuo. (Calc. for $C_{14}H_{28}N_4CoCl_3O_4$: C, 34.90; H, 5.85; N, 11.63; Found C, 34.58; H, 6.12; N, 11.36,%)

Trans - dibromo-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene) cobalt(III) Perchlorate Dihydrate:

trans $\mathrm{[Co(Me_4[14]diene)Br_2]ClO_4.2H_2O}$:

trans $\mathrm{[Co(Me_4[14]diene)Cl_2]ClO_4}$(0.25g) was dissolved in 25 cm^3 of 10% methanolic solution of hydrobromic acid and evaporated to dryness on a rotary evaporator. The bright green product obtained on evaporation was recrystallised from a small amount of hot ethanol, washed with ethanol then ether and finally dried in vacuo.

(Calc. for $\mathrm{C_{14}H_{32}N_4CoCl_2O_6Br_2}$: C, 27.71; H, 5.31; N, 9.23;
Found C, 27.23; H, 5.11; N, 8.96%)

Trans - dinitro-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene) cobalt(III) Perchlorate Monohydrate;

trans - $\mathrm{[CoMe_4[14]diene\ (NO_2)_2]ClO_4.H_2O}$. -

A solution of trans - $\mathrm{[Co(Me_4[14]diene)Cl_2]ClO_4}$ (0.24g, 5mmol) in methanol (40 cm^3) was heated with(0.069g) of sodium nitrate on a water bath for half an hour. The pale brown solution filtered whilst hot and orange-yellow crystals obtained on cooling, filtered off and washed with methanol then ether and finally dried in vacuo. (Yield = 0.3g)

Calc. for $\mathrm{C_{14}H_{30}N_6CoClO_9}$: C, 32.38; H, 5.80; N, 16.13;
Found C, 32.66; H, 5.65; N, 15.99%)

Trans diazido-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene) cobalt(III) Perchlorate;

trans - $\mathrm{[Co(Me_4[14]diene)(N_3)_2]ClO_4}$. -

trans - $\mathrm{[Co(Me_4[14]diene)Cl_2]ClO_4}$ (0.4g) was dissolved in 20 cm^3 of water and sodium azide (0.7g) added to it. The colour of the resulting solution changed immediately from green to blue-violet on warming on a water bath for 20 minutes. The solution on standing gave shining blue-violet crystals

Trans - dibromo-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca -4,11 diene) cobalt(III) Perchlorate Dihydrate;

trans $[Co(Me_4[14]diene)Br_2]ClO_4.2H_2O$:

trans $[Co(Me_4[14]diene)Cl_2]ClO_4$(0.25g) was dissolved in 25 cm^3 of 10% methanolic solution of hydrobromic acid and evaporated to dryness on a rotary evaporator. The bright green product obtained on evaporation was recrystallised from a small amount of hot ethanol, washed with ethanol then ether and finally dried in vacuo.

(Calc. for $C_{14}H_{32}N_4CoCl_2O_6Br_2$: C, 27.71; H, 5.31; N, 9.23;
Found C, 27.23; H, 5.11; N, 8.96%)

Trans - dinitro-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca--4,11 diene) cobalt(III) Perchlorate Monohydrate;

trans - $[CoMe_4[14]diene (NO_2)_2]ClO_4.H_2O$. -

A solution of trans - $[Co(Me_4[14]diene)Cl_2]ClO_4$ (0.24g, 5mmol) in methanol (40 cm^3) was heated with(0.069g) of sodium nitrate on a water bath for half an hour. The pale brown solution filtered whilst hot and orange-yellow crystals obtained on cooling, filtered off and washed with methanol then ether and finally dried in vacuo. (Yield = 0.3g)

Calc. for $C_{14}H_{30}N_6CoClO_9$: C, 32.38; H, 5.80; N, 16.13;
Found C, 32.66; H, 5.65; N, 15.99%)

Trans diazido-(5.6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca -4,11-diene) cobalt(III) Perchlorate;

trans - $[Co(Me_4[14]diene)(N_3)_2]ClO_4$. -

trans - $[Co(Me_4[14]diene)Cl_2]ClO_4$ (0.4g) was dissolved in 20 cm^3 of water and sodium azide (0.7g) added to it. The colour of the resulting solution changed immediately from green to blue-violet on warming on a water bath for 20 minutes. The solution on standing gave shining blue-violet crystals which were filtered off and washed with ethanol then ether and finally dried in *vacuo*.

A second crop of the crystalline product can be obtained by adding more sodium azide and subsequent cooling for several days.

(Calc. for $C_{14}H_{28}N_{10}CoCl_4{}^{OH}$: C, 33.97; H, 5.70; N, 28.31;
Found C, 33.49; H, 5.75; N, 28.77,%).

Trans - di-isothiocyanato-(5,6,12,13-tetramethyl-1,4,8,11- - tetra-azacyclotetradeca-4,11-diene) cobalt(III) Thiocyanate Tetrahydrate; *trans* - $[CoMe_4[14]diene)(SCN)_2]SCN.4H_2O$. -

trans - $[Co(Me_4[14]diene)Cl_2]ClO_4$ (0.3g) was dissolved in hot aqueous methanol (25 cm^3) and to this added an excess of solid potassium thiocyanate.

The reaction mixture was then heated on a water bath for 15 minutes during which the color of the solution changed from green to red and filtered whilst hot. The red filtrate was cooled in a refrigerator for a couple of days. The shining red crystalline complex was then filtered off and washed with ethanol then ether and finally dried in *vacuo*.

The i.r. of the complex showed no bands due to perchlorate, but very strong absorption peaks due to ionic thiocyanate group were observed.

(Calc. for $CoC_{14}H_{36}N_7S_3O_4$: C, 36.61; H, 6.50; N, 17.58.
Found C, 36.77; H, 6.25; N, 18.09,%).

Trans -diammine-(5,6,12,13-tetra-methyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene) cobalt(III) Chloride Diperchlorate;

trans - $[CoMe_4[14]diene)(NH_3)_2]Cl.(ClO_4)_2$. -

To a solution of *trans* - $[Co(Me_4[14]diene)Cl_2]ClO_4$(0.4g) in minimum volume of hot acetonitrile added a few drops of concentrated ammonia (ρ = 0.88) and the colour of the solution gradually changed from green to orange-red after 20 minutes of stirring. Ethanolic lithium perchlorate addition (2 cm^3) to this orange-red solution, followed by cooling in ice gave orange-yellow product. The crude complex was recrystallised from hot water and dried in *vacuo*.

Calc. for $C_{14}H_{34}N_6CoCl_3O_8$: C, 29.00 H, 5.9; N, 14.49

Found C, 28.22; H, 5.69; N, 14.80%)

Trans - diacetato-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetrade-4,11 diene) cobalt(III) Perchlorate;

trans - $[Co(Me_4[14]diene)(CH_3COO)_2]ClO_4$. -

A solution of *trans*-$[Co(Me_4[14]diene)Cl_2]ClO_4$ (1.0g) was made in hot methanol and to this sodium acetate (0.75g) followed by few drops of glacial acetic acid were added. The reaction mixture was then warmed on a water bath for half an hour. The purple-pink solution thus obtained on standing gave a pink crystalline product and was recrystallised from hot aqueous methanol and dried in *vacuo*.

(Calc. for $CoC_{18}H_{34}N_4ClO_8$: C, 40.87; H, 6.47; N, 10.59;

Found C, 41.20; H, 6.70; N, 10.84,%)

Attempted Synthesis of Cis - Acetylacetanato-(5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene) cobalt(III) Perchlorate; *cis* - $[\mathrm{Co(Me_4[14]diene)(acac^-)}]\mathrm{ClO_4}$. -

trans - $[\mathrm{Co(Me_4[14]diene)Cl_2}]\mathrm{ClO_4}$ (0.3g) was dissolved in 30 $\mathrm{cm^3}$ of hot methanol and to this (0.2g) acetylacetone added followed by few drops of concentrated aqueous ammonia solution. The resulting solution was heated on a water bath for 40 minutes during which time the colour of the solution changed from green to red. ~~and made~~ The solution was made neutral with perchloric acid (1M) and filtered whilst hot. Slow evaporation of methanol and gentle cooling to obtain crystalline complex were unsuccessful, but oily product obtained on several occasions. The reaction seems slow and reversible.

Cis- Carbonato - (5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca tetra deca-4,11 diene) cobalt(III) Perchlorate; Dihydrate; *cis* - $[\mathrm{Co(Me_4[14]diene)(CO_3)}]\mathrm{ClO_4.2H_2O}$. -

Trisodium tris carbonato cobaltate(III) (0.8g) and the macrocyclic ligand $\mathrm{Me_4[14]diene.2HClO_4}$ (0.9g) were mixed together in methanol-water solution (5 $\mathrm{cm^3}$) and warmed on a water bath for 20 min. till the $\mathrm{CO_2}$ evolution ceased. The red solution was filtered whilst hot and concentrated to about 10 $\mathrm{cm^3}$ on an evaporator. Addition of a few $\mathrm{cm^3}$ of methanol and standing overnight at 4°C gave dark red crystals, which were recrystallised from minimum volume of hot water and dried in *vacuo* for several hours.

(Calc. for $\mathrm{CoC_{15}H_{32}N_4ClO_7}$: C, 35.54; H, 6.36; N, 11.05;
Found C, 35.20; H, 6.50; N, 11.40,%).

Trans - Chloronitro (5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene) cobalt(III) Perchlorate;

trans - $[\mathrm{Co(Me_4[14]diene)Cl(NO_2)]ClO_4}$. -

The complex was prepared by stirring trans-$[\mathrm{Co(Me_4[14]diene)Cl_2]ClO_4}$ (0.48g) in hot 95% methanol (50 $\mathrm{cm^3}$) with one molar equivalent (0.062g) of sodium nitrite. After heating for about half an hour, the red-brown solution was filtered whilst hot, and cooled in an ice-bath. The resulting orange-red precipitate was then filtered off, washed with ice cold ethanol then ether and dried in *vacuo*. A second fraction was obtained by the addition of ether to the filtrate, and further cooling in an ice-bath. (Calc. for $\mathrm{C_{14}H_{28}N_5CoCl_2O_6}$: C, 34.15; H, 5.73; N, 14.22; Found C, 33.93; H, 5.51; N, 14.51,%).

The complex has absorption maxima values at 355 nm ($\varepsilon = 2.1 \times 10^3$) and 506 nm ($\varepsilon = 110$), measured in dry acetonitrile.

Trans - diazido - 5,12 - dimethyl-1,4,8,11-tetra-azacyclotetradeca tetradeca - 4,11-diene) cobalt(III) Perchlorate;

trans - $[\mathrm{Co(Me_2[14]diene)(N_3)_2]ClO_4}$. -

trans - $[\mathrm{Co(Me_2[14]diene)Cl_2]ClO_4}$[53] (0.4g) was dissolved in 10 $\mathrm{cm^3}$ of water and an excess sodium azide was added to it. The colour of the resulting solution changed immediately from green to blue-violet on warming on a water bath for half an hour. This solution on standing gave shining blue-violet crystals, which were filtered off and washed with ethanol then ether and finally dried in *vacuo*.

(Calc. for $\mathrm{CoC_{12}H_{24}N_{10}ClO_4}$: C, 30.80; H, 5.18; N, 30.01; Found C, 30.56; H, 5.28; N, 29.94,%).

Cis - dichloro - (5,6,12,13-tetramethyl-1,4,8,11-tetra-azacyclotetradeca--4,11 diene) Rhodium Perchlorate Monohydrate;

cis-[Rh(Me$_4$[14]diene)Cl$_2$]ClO$_4$. -

A solution of Me$_4$[14]diene.2HClO$_4$ (1.72g, 3.8mM) ~~ligand~~ and rhodium trichloride trihydrate (0.75g, 2.8mM) was made in methanol-water solution. The resulting red solution was heated under reflux for five hours during which time the colour gradually changed to yellow. Perchloric acid (5cm^3, 70%) was added to precipitate the product and the yellow product was recrystallized from hot water-methanol, dried in *vacuo*.

(Calc. for $C_{14}H_{30}N_4RhCl_3O_5$: C, 30.92; H, 5.56; N, 10.30; Found C, 30.73; H, 5.49; N, 9.83,%).

1.2.3 Isomeric 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecanes

(i.e. C-*meso*-Me$_2$Cyclam and C-*rac*-Me$_2$Cyclam amines)

The macrocyclic amines were prepared by the method first described by Kolinski *et al*[48]. The C-*meso* and C-*rac* forms of Me$_2$Cyclam correspond to the Me$_2$Cyclam isomers *a* and *b* respectively. Configurations were assigned tentatively by comparison of melting points and other physical properties with the analogous tet *a* and tet[65]. This point is dealt with in some detail under Results and Discussion.

5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene nickel(II) perchlorate (48.2g, 0.1mole) was dissolved in water 500cm^3 at 50°C with continuous stirring[48]. Sodium hydroxide pellets (13g) and powdered Ni-Al alloy (50% Nickel, 15g) were added in small proportions over a period of two hours; keeping the addition of sodium hydroxide slightly ahead of alloy. The resulting mixture was heated for another hour and celite (filtering aid) 10g was added to precipitate aluminium as hydroxide, followed by addition of concentrated hydrochloric acod until pH 8-9† was reached.

The unreacted alloy and aluminium hydroxide precipitate was then filtered off and filtrate evaporated to half its volume.*

Ethanol (450 cm^3) and sodium cyanide (29.4g, 0.6moles) were added and the reaction mixture refluxed for 4 hours. Finally, ethanol was distilled off and the water solution extracted with benzene in a continuous manner (Liquid-Liquid Extraction) for two days. The benzene extract was evaporated to dryness and fractional crystallisation from xylene yielded two amines.

C-meso-(Me_2Cyclam)(Isomer a).

The crude product(i.e. mixture of two isomers) was dissolved in the minimum amount of hot xylene, on cooling, white needles were obtained ~~then~~ which were filtered off and dried in vacuo for several hours.

m.p. 137.9°C (Reported 144°C) Calc. for $C_{12}H_{28}N_4$: C, 63.11; H, 12.35; N, 24.55; Found C, 62.85; H, 12.50; N, 24.30,%)

C-rac-(Me_2Cyclam) (Isomer b):

The residue from xylene crystallisation was evaporated to dryness and white crystalline plates of Isomer b amine were obtained and recrystallised from dry ether.

m.p. 108.5-109°C (Reported 109.5°C)

NOTES:

† Under acidic conditions (pH-2,3) octahedral nickel(II) complex of the mixture of amine has been isolated and later established independently.

* Suitable evaporation (about half or one third volume gave rise to the crystallisation of the nickel(II) complex of one of amines. In the present case red crystalline complex isolated.

(Calc. for $C_{12}H_{28}N_4NiCl_2O_8$: H, 5.81; N, 11.53;
Found H, 6.12; N, 12.00,%).

Modified Synthesis of 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane (Sodium Borohydride Reduction) . -

A convenient method has been ~~reported~~ developed to reduce 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene dihydroperchlorate i.e. $Me_2[14]diene.2HClO_4$ using sodium borohydride. The reaction period could be shortened in this manner and provides one exclusive isomer a or C-meso-(Me_2Cyclam).

5,12-dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene dihydroperchlorate (30g) was dissolved in 300 cm^3 methanol-water solution (1:1, $^v/_v$) and to this added a slight excess of sodium borohydride (> 2moles) in small portions over a period of an hour with continuous stirring. The resulting solution was warmed on a water bath for 20 minutes, till the effervescence ceased completely and allowed to stand at room temperature for a while. Instant crystallisation followed which grew as the solution was concentrated on a water bath, the resulting white solid was then filtered off and dissolved in aqueous methanol. The solution was made alkaline to about pH 12 and evaporation of this solution gave crude amine and recrystallised from xylene. On cooling, white needles were obtained, filtered and dried in vacuo.

m.p. 144.5°C (Reported C-meso-(Me_2Cyclam) 144.5-145°C)[48]

Calc. for ($C_{12}H_{28}N_4$: C, 63.11; H, 12.35; N, 24.53;

Found C, 62.78; N, 24.62; H, 12.11,%).

Metal Complexes:

C-*meso*-(5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane) copper(II) Diperchlorate; $[Cu[C\text{-}meso\text{-}(Me_2Cyclam)](ClO_4)_2$. -

Copper(II) perchlorate hexahydrate (0.3g) was dissolved in 10 cm^3 of water and (0.4g) C-*meso*-(Me_2Cyclam) amine in 30 cm^3 methanol added to it. The mixture was heated on a water bath for 30 minutes and filtered whilst hot. The resulting solution was concentrated on a rotary evaporator and the crude product was dissolved in a minimum amount of hot methanol. Cooling in ice, gave shining purple-red plates which were filtered off, washed with a little ice cold methanol, then ether and finally dried in *vacuo*.

(Calc. for $C_{12}H_{28}Cl_2CuN_4O_8$: C, 29.87; H, 5.75; N, 11.41;
Found C, 29.51; H, 5.28; N, 11.26,%).

C-*rac*-(5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane) copper(II) Diperchlorate; $[Cu(C\text{-}rac\text{-}(Me_2Cyclam)](ClO_4)_2$. -

The above procedure was repeated using isomer *b* and the crude complex was recrystallised from hot methanol. The purple-red plates of the complex thus obtained on cooling were filtered off and dried in *vacuo*.

(Calc. for $C_{12}H_{28}Cl_2O_8$: C, 29.87; H, 5.75; N, 11.41;
Found C, 30.13; H, 6.14; N, 11.18,%).

C-*rac*-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecadecane copper(II) Dinitrate; $[Cu(C\text{-}rac\text{-}(Me_2Cyclam))](NO_3)_2$. -

The main purpose of preparing this complex has been to obtain suitable crystals for X-ray crystallographic study and thus definitive assignment of the configuration for the two amine Isomers.

Cupric nitrate trihydrate (0.3g) and Me_2Cyclam amine (isomer b) were dissolved in 30 cm^3 of methanol and warmed on a water bath for 20 minutes. Purple-red crystallisation occurred as the solution was concentrated and these were filtered off. The crude complex was recrystallised from a minimum volume of hot methanol. On slow cooling at room temperature a crystalline product was obtained, filtered and dried in vacuo.
(Calc. for $CuC_{12}H_{28}N_6O_6$: H, 6.78; N, 20.20;
Found H, 6.41; N, 20.02,%).

C-meso-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane nickel(II) Diperchlorate; $[Ni(C\text{-}meso\text{-}Me_2Cyclam))](ClO_4)_2$. -

A solution of nickel(II) perchlorate (0.3g) and Me_2Cyclam amine (isomer b) (0.4g) was made in methanol-water (300 cm^3, 1:1, v/v) and warmed on a water bath for an hour. The resulting orange-yellow solution was filtered whilst hot and concentrated to about 2 cm^3 on a rotary evaporator. Addition of methanol (15 cm^3) followed by subsequent cooling in ice gave orange-yellow crystals, which were filtered off. The crude product was recrystallised from hot aqueous methanol, cooled and dried in vacuo.
(Calc. for $C_{12}H_{28}N_4NiCl_2O_8$: C, 29.70; H, 5.81; N, 11.55;
Found C, 29.59; H, 5.92; N, 11.24,%).

C-meso and C-rac - 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca zinc(II) Diperchlorate complexes;

(i) Zinc(II) perchlorate hexahydrate (0.4g) was dissolved in water (10 cm^3) and a slight excess of Me_2Cyclam (amine a) (0.45g) in 30 cm^3 methanol solution added to it. The mixture was heated on a water bath for half an hour and filtered whilst hot and solvent removed on a rotary evaporator. The white crystalline product obtained on cooling was recrystallised from minimum amount of hot methanol. The white product was washed with little ice cold methanol and dried in vacuo.

(Calc. for $C_{12}H_{28}N_4ZnCl_2O_8$: C, 29.30; H, 5.73; N, 11.39;
Found C, 29.72; H, 5.95; N, 11.45,%).

(ii) The above procedure was repeated using isomer b of Me_2Cyclam. The crude complex was recrystallised from aqueous methanol and the white crystalline complex obtained washed with methanol and dried in vacuo.

Calc. for $ZnC_{12}H_{28}N_4Cl_2O_8$: C, 29.30; H, 5.73; N, 11.39;
Found C, 29.65; H, 6.00; N, 11.67,%)

C-meso-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca lead(II) Dinitrate Sesquihydrate; [Pb (C-meso-(Me_2Cyclam)]$(NO_3)_2 1.5H_2O$. -

An aqueous solution of lead nitrate (0.3g, 0.001mole) was added to a methanolic solution of Me_2Cyclam (amine a) and the resulting solution was stirred at 50° for half an hour. Finally, the mixture was heated on a water bath for half an hour and filtered whilst hot. Excess solvent was evaporated off on a rotary evaporator followed by addition of appropriate amount of dry ether; on cooling, cream coloured crystalline complex separated, filtered, washed with little cold methanol then ether and dried in vacuo.

(Calc. for $Pb^{II}C_{12}H_{31}N_6O_9$: C, 24.56; H, 5.32; N, 14.32;
Found C, 24.30; H, 4.82; N, 13.99,%)

C-meso-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane-manganese (II) Dichloride (Hydrated); [Mn(C-meso-(Me_2Cyclam)Cl_2] . -

Manganese(II)chloride dihydrate (0.25g) was dissolved in methanol (10 cm^3) and to this added an equivalent amount of Me_2Cyclam (amine a) solution in methanol. The resulting green solution was then heated on a water bath for half an hour whilst hot. The light green product obtained on cooling was recrystallised from hot methanol and dried in vacuo.

(Calc. for $C_{12}H_{33}N_4MnCl_2$: C, 36.09; H, 8.33; N, 14.03;
Found C, 36.07; H, 7.43; N, 13.78,%).

Trans - 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecanes nickel(II) Dichloride; trans-[Ni(C-meso-(Me_2Cyclam)Cl_2] . -

(Indirect route)

This blue complex of nickel(II) with mixed amines has been isolated just by accident during the reduction of precursor nickel(II) diene complex for Isomeric amines. After the addition of Ni-Al alloy is over, under high acidic conditions (pH 3 ∿ 4), blue crystalline product started separating. The crude complex was recrystallised from hot methanol

(Calc. for $C_{12}H_{28}N_4NiCl_2$: C, 40.25; H, 7.88; N, 15.65;
Found C, 40.12; H, 7.73; N, 15.55,%)

(Direct Preparation)

The above complex has been prepared (independently) in order to confirm its identity by the following method.

Nickel(II) chloride hexahydrate (0.49) was dissolved in water (20 cm^3) and Me_2Cyclam (amine a) (0.5g) solution in methanol added to this green solution, followed by the addition of excess lithium chloride and digested the solution for 10 minutes. The solution on standing gave purple-blue product which was then filtered off and recrystallised from aqueous methanol.

(Calc. for $C_{12}H_{28}N_4NiCl_2$: C, 40.25;; H, 7.88; N, 15.65
Found C, 40.64; H, 7.46; N, 15.30,%)

C-meso-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca complex with Hg(II):
$[Hg^{II}(C\text{-}\underline{meso}\text{-}(Me_2Cyclam)\text{-}2H]^{o}$. -

Aqueous solution of Mercuric chloride (0.45g) was added to a methanolic solution of Me_2Cyclam (amine a) (0.5g) and heated on a steam bath for an hour. The resulting solution was then filtered whilst hot and concentrated to about 5 cm^3, followed by addition of appropriate amounts of ethanol, then ether and cooled. Grey-white crystalline complex was filtered off and recrystallised from hot aqueous methanol and dried in vacuo.

($[Hg^{II}(L\text{-}2H)]^{o}$ Where L stands for C-meso-Me_2Cyclam
Calc. for $HgC_{12}H_{26}N_4$: C, 33.75; N, 13.12; H, 6.14;
Found C, 33.68; N, 12.94; H, 7.08,%).

Trans - dichloro-C-meso-(5,12-dimethyl-1,4,8,11-tetra-azacyclotetradecane cobalt(III) Chloride Dihydrate; trans - $[Co^{III}(C\text{-}\underline{meso}(Me_2Cyclam)Cl_2]Cl2H_2O$. -

Sodium tris carbonato cobaltate(III) trihydrate[66] (0.8g) and an equivalent amount of Me_2Cyclam (isomer a) macrocycle were mixed together in methanol-water (50 cm^3; 1:1, (v/v)and heated on a water bath for 30 min. The resulting red solution was filtered whilst hot. Concentrated hydrochloric acid (25 cm^3) was added to the red solution and reduced the volume of the reaction mixture to about 10 cm^3. The green product started separating as the solution was concentrated, cooling in ice gave crude complex, which was then filtered off and recrystallised from hot 6M HCl and finally from methanol. Shining green needles thus obtained were washed with a little ice cold methanol then ether and dried in vacuo.

(Calc. for $CoC_{12}H_{32}N_4Cl_3O_2$: C, 33.53; H, 7.50; N, 13.03;
Found C, 33.94, H, 6.91; N, 13.08,%).

Trans - diazido-C-*meso*-(5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane) cobalt(III) Azide;

trans -[Co(C-*meso*-Me$_2$Cyclam)(N$_3$)$_2$]N$_3$. -

trans -[Co(C-*meso*-(Me$_2$Cyclam)Cl$_2$]Cl.2H$_2$O (0.3g) was dissolved in methanol (20cm^3) and sodium azide (0.4g) was added and the mixture stirred. The dark green solution which turned bluish-violet immediately was allowed to boil for half an hour. On cooling, bluish-violet crystals of the diazido azide separated and were then filtered off. The crystalline product was washed with alcohol then ether and recrystallized from minimum volume of hot water. The yield could be increased further by adding more sodium azide to the mother liquour. Yield = (0.3g).

(Calc. for [CoC$_{12}$H$_{28}$N$_{13}$: C, 34.86; H, 6.82; N, 44.05;
Found C, 34.67; N, 44.00; H, 6.8,%).

Cis - dichloro-(C-*meso*-(5,12-dimethyl-1,4,8,11-tetra-azacyclotetradecane)) rhodium(III) Chloride; *cis* -[Rh(C-*meso*-(Me$_2$Cyclam))Cl$_2$]Cl . -

Rhodium trichloride trihydrate (0.75, 2.8mM) and Me$_2$Cyclam (Isomer *a*) (0.96g, 3.8mM) were dissolved in methanol (250 cm^3) and heated under reflux for four hours, during which the red colour of the solution changed to pale yellow. The resulting solution was filtered whilst hot and concentrated to about 10cm^3. Fine yellow crystalline complex thus obtained on cooling was washed with ethanol then ether and dried in *vacuo* for several hours.

(Calc. for C$_{12}$H$_{28}$N$_4$RhCl$_3$; C, 32.93; H, 6.44; N, 12.80.
Found C, 33.16; H, 6.58; N, 12.63,%).

1.2.4 Synthesis of 1,4,8,11-Tetramethyl-5,12-dimethyl-1,4,8,11-tetra-azacyclotetradecanes Tetra-hydrochloride Monohydrate;

C-meso and C-rac(Me_2Cyclam)$(HCl)_4H_2O$:

Tetra-N-methyl-C-meso-(Me_2Cyclam)$(HCl)_4.H_2O$. -

A solution consisting of 5mmoles of C-meso(Me_2Cyclam), 5cm^3 (90%) formic acid and 2cm^3 35% formaldehyde was refluxed for 24 hours. Concentrated hydrochloric acid (5cm^3) was then added to this pale yellow solution and evaporated to dryness. The crude product was recrystallized from aqueous ethanol, filtered off and dried in *vacuo*. m.p. 296-8^o (slow decomposition) (Calc. for Tetra N-methyl-C-meso-(Me_2Cyclam)$(HCl)_4H_2O$;$C_{16}H_{42}N_4OCl_4$: C, 42.85; H, 9.44; N, 12.49; Found C, 43.10; H, 9.42; N, 12.44,%).

Tetra-N-methyl-C-rac-(Me_2Cyclam)$(HCl)_4.H_2O$

Above procedure was repeated to prepare this tetra-N-methyl substituted macrocyclic ligand using C-rac-(Me_2Cyclam) and the crude product recrystallized from minimum volume of aqueous ethanol and dried in *vacuo*. m.p. 280^{o}C.

The above ligands were synthesized essentially by the method described by Kaden and coworkers[57] with slight modifications.

Metal complexes of Tetra N-methyl-C-meso-(Me_2Cyclam) tetra hydrochloride Monohydrate macrocycle:

(i) 1,4,8,11-Tetramethyl-C-meso-(5,12-dimethyl-1,4,8,11-tetra-azacyclotetra-decane) zinc(II) Diperchlorate Monohydrate. -

An aqueous solution of zinc perchlorate hexahydrate (0.5g) in cm^3 water was mixed with 0.4g) of the title ligand in ethanol (15 cm^3). The white crystalline complex thus obtained was filtered off, washed with a little ice cold methanol and recrystallized from aqueous methanol and dried in *vacuo*.

(Calc. for $C_{16}H_{38}N_4ZnCl_2O_9$; C, 33.90; H, 6.75; N, 9.88
Found C, 33.32; H, 6.90; N, 9.57,%).

(ii) 1,4,8,11-Tetramethyl-C-meso-(5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane) copper(II) Diperchlorate Monohydrate:

Copper(II) perchlorate hexahydrate (0.4g) dissolved in water (10 cm^3) was added to a methanolic solution of the tetra-N-methyl-C-meso-(Me_2Cyclam) (0.5g in 30 cm^3). The resulting blue solution was concentrated to a small volume with a slow current of air. During this period a light green crust appeared along the sides of the evaporating basin which eventually became violet and was filtered off. The Pure light blue complex thus obtained on recrystallization from minimum volume of water-methanol, filtered and dried in *vacuo*.

(Calc. for $C_{16}H_{38}N_4CuCl_2O_9$: C, 34.01; H, 6.77; N, 9.91
Found C, 33.38; H, 7.02; N, 9.63,%).

Synthesis of 1,4,8,11-Tetramethyl-C-rac-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetra-azacyclotetradecane Tetrahydrochlorate Tetrahydrate . -

5mmoles of the unsubstituted macrocyclic ligand 5 cm^3 formic acid (90%) and 2 cm^3 of 35% formaldehyde were slowly heated on a water bath until the CO_2 evolution stopped. The resulting mixture was then refluxed for 20 hours. After the addition of 5 cm^3 concentrated hydrochloric acid, the solution was evaporated to dryness on a rotary evaporator and the crude product was recrystallised from ethanol-water solution m.p. 297-8°C.

Calc. for $C_{20}H_{56}N_4Cl_4$: C, 43.01; H, 10.10; N, 10.03;
Found C, 43.12; H, 9.24; N, 10.37%)

Synthesis of 1,4,8,11-Tetramethyl- 5,12-dimethyl-7,14-diphenyl-1,7,8,11-tetra-azacyclotetradecane) Tetrahydrochloride Hydrated (Isomer a) .-

The macrocyclic amine C-*meso*-Ph_2Me_2teta$(HCl)_4$(1g) was dissolved in 5ml of formic acid (90%) and to this added formaldehyde (35%, 2 cm^3). The pale coloured solution was then refluxed for 24 hours on a water bath. Concentrated hydrochloric acid (5 cm^3) was added to this mixture and evaporated to dryness. The crude product was recrystallised slowly from aqueous methanol followed by addition of appropriate amount of ether; on cooling dull white moisture sensitive product obtained; filtered and dried in vacuo for several hours.

(Calc. for $C_{28}H_{53}N_4Cl_4(1.5)H_2O$: C, 53.58, H, 7.87; N, 8.92
Found C, 52.89; H, 7.59; N, 9.57%).

Synthesis of 1,4,8,11-Tetramethyl-C-rac-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetra-azacyclotetradecane Tetrahydrochlorate Tetrahydrate . -

5mmoles of the unsubstituted macrocyclic ligand 5 cm^3 formic acid (90%) and 2 cm^3 of 35% formaldehyde were slowly heated on a water bath until the CO_2 evolution stopped. The resulting mixture was then refluxed for 20 hours. After the addition of 5 cm^3 concentrated hydrochloric acid, the solution was evaporated to dryness on a rotary evaporator and the crude product was recrystallised from ethanol-water solution m.p. 297-8°C.

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The macrocyclic amine C-*meso*-$Ph_2Me_2teta(HCl)_4$(1g) was dissolved in 5ml of formic acid (90%) and to this added formaldehyde (35%, 2 cm^3). The pale coloured solution was then refluxed for 24 hours on a water bath. Concentrated hydrochloric acid (5 cm^3) was added to this mixture and evaporated to dryness. The crude product was recrystallised slowly from aqueous methanol followed by addition of appropriate amount of ether; on cooling dull white moisture sensitive product obtained; filtered and dried in vacuo for several hours.

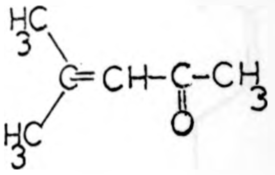
(Calc. for $C_{28}H_{53}N_4Cl_4(1.5)H_2O$: C, 53.58, H, 7.87; N, 8.92

Found C, 52.89; H, 7.59; N, 9.57%).

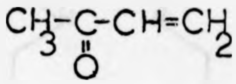
1.3 RESULTS AND DISCUSSION

1.3.1 Ligand synthesis

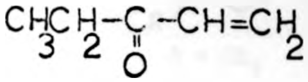
Curtis and Hay[49] first reported that the monohydroperchlorate salt of 1,2-diaminoethane reacted with mesityl oxide (A) to give Me$_6$[14]diene (VII)



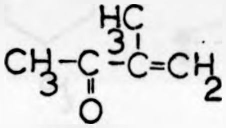
(A)



(B)



(C)



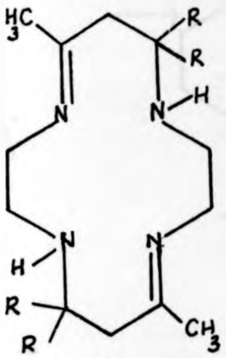
(D)

Kolinski and Korybut-Daszkiewicz subsequently prepared Me$_2$[14]diene by the reaction of en.HClO$_4$ with methyl vinyl ketone (B) and prepared the nickel(II) complex. Hay and Lawrence[53] have studied the coordination chemistry of Me$_2$[14]diene in detail and X-ray crystallography has confirmed the trans-diimine structure[50]. In this thesis the reaction of en.HClO$_4$ with ethyl vinyl ketone (C) and methyl isopropenyl ketone (D) has been studied.

Cyclisations around a metal ion as originally described by Curtis give mixtures of the cis and trans - diimines, however, the en.HClO$_4$ reactions appear to be completely stereospecific giving only the trans-diimine.

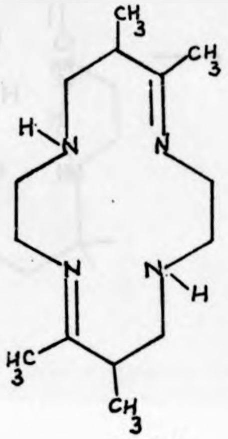
The reaction of methyl isopropenyl (MIK) (D) with 1,2-diamino-ethane dihydroperchlorate gives high yields of 5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene dihydroperchlorate macrocycle (XXI). Recent crystallographic studies and similar preparative methods for the analogous macrocycles (VII) and (XIII) has now supported the view that

5,6,12,13-Tetra methyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene dihydroperchlorate also has the transoid-imine

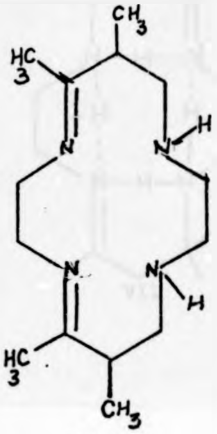


$R = CH_3$ VII

R = H XII



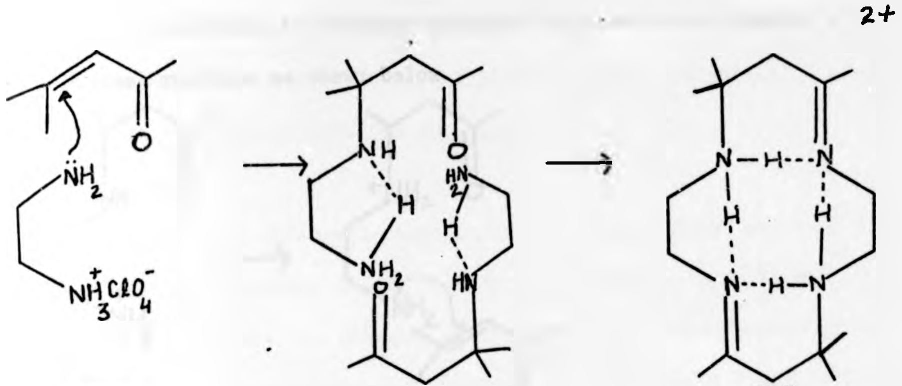
XXI(a)



XXI(b)

structure (XXI(a)) rather than the cisoid structure (XXI(b)). Two possible mechanisms have been considered for the macrocycle synthesis.

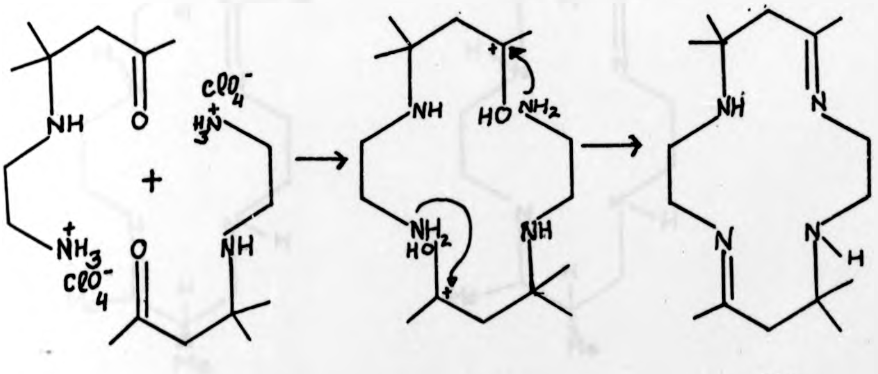
Hay and Curtis[45] suggested that the reactions proceed as shown below. The first step of the cyclisation involves a Michael addition of the non protonated amine to the double bond of mesityl oxide to yield the β-amino ketone (XXII). The protonation of the second amine group is presumed to block its participation in a similar reaction.



XXII VII

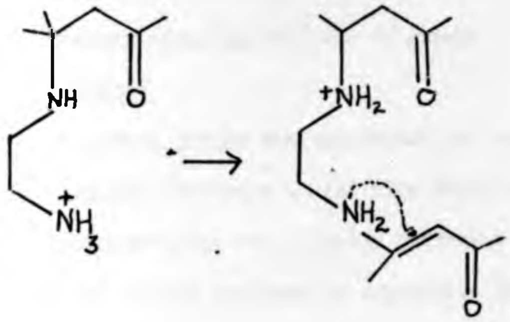
Two molecules of the β-aminoketone then cyclise by ketimine formation to give the macrocycle (VII).

Lloyd[67] has suggested that an intramolecular proton transfer to oxygen may occur after the initial Michael reaction.



XXII XXIII VII

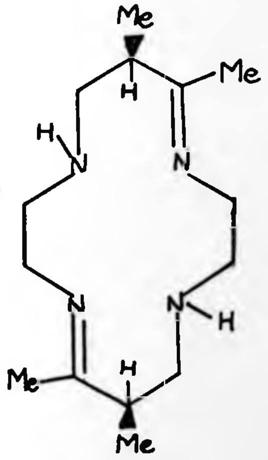
The second route seems more favourable because such a transfer would set up just the right reacting species required for cyclisation of the β-amino ketone. In the case of a nitrogen to nitrogen exchange this could also promote a further Michael reaction as shown below



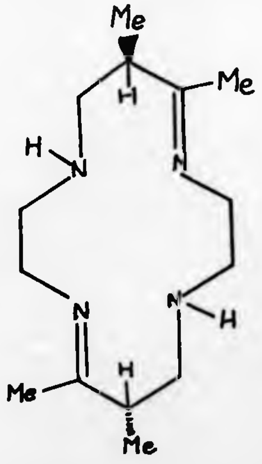
It is reasonable to extend the above arguments to the Me_4[14]diene macrocycle.

Nuclear Magnetic Resonance Spectra

The n.m.r. spectrum of Me_4[14]diene.$2HClO_4$ in perdeutrated DMSO at 220 MHz suggested that two stereoisomers (XXIV) and (XXV) are possible due to the presence of two chiral carbon centres in the ligand.



XXIV



XXV

The most prominent features of the spectrum are resonances due to the ring and imino methyl protons of the ligand.

Ring methyl protons

Two overlapping doublets are observed in the spectrum which can be assigned to the ring methyls coupling with the CH group.

Imino methyl protons

The imino methyl groups are equivalent in structures (XXIV) and (XXV) but a doublet of unequal intensity in the high field region has been observed. This could be attributed to the two slightly different sets of imino methyl groups.

The reminder of the spectrum is assignable to the methylenic and NH proton resonances.

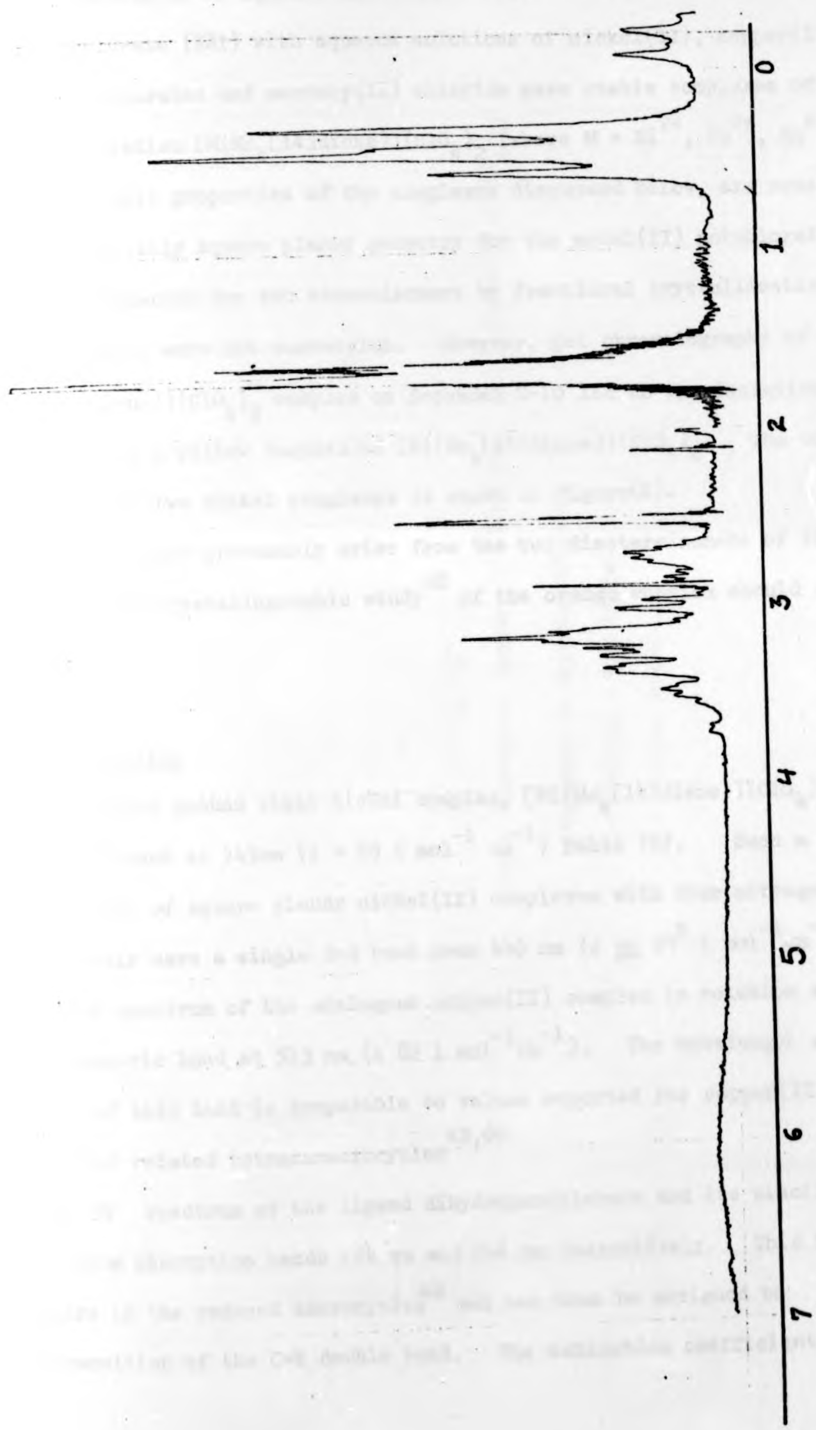


FIGURE 1 N.M.R. spectra of 5,6,12,13 - tetramethyl - 1,4,8,11 - tetraaza - cyclotetradeca - 4,11, diene dihydroperchlorate.

220 Mc / sec.

1.3.2 Metal Complexes of $Me_4[14]diene.2HClO_4$. -

The reaction of an aqueous-methanolic solution of the macrocyclic ligand dihydroperchlorate (XXl) with aqueous solutions of nickel(II), copper(II) and zinc(II) perchlorates and mercury(II) chloride gave stable complexes of the general formulation $[M(Me_4[14]diene)](ClO_4)_2$ (where $M = Ni^{2+}$, Cu^{2+}, Zn^{2+}, Hg^{2+}). The spectroscopic properties of the complexes discussed below, are consistent with an essentially square planar geometry for the metal(II) perchlorate salts. Attempts to separate the two stereoisomers by fractional crystallisation of the ligand (XXI) were not successful. However, gel chromatography of the $[Ni(Me_4[14]diene)](ClO_4)_2$ complex on Sephadex G-10 led to the isolation of an orange-red and a yellow complex of $[Ni(Me_4[14]diene)](ClO_4)_2$. The visible spectra of the two nickel complexes is shown in Figure(2).

These two complexes presumably arise from the two diastereisomers of the ligand. A current X-ray crystallographic study[68] of the orange complex should confirm this point.

Electronic spectra

The singlet ground state nickel complex, $[Ni(Me_4[14]diene)](ClO_4)_2$, has a single d-d band at 445nm (ε = 88 l mol^{-1} cm^{-1}) Table (4). Such a band is characteristic of square planar nickel(II) complexes with four nitrogen donors which normally have a single d-d band near 440 nm (ε ca 10^2 l mol^{-1}cm^{-1})[60]

The visible spectrum of the analogous copper(II) complex in solution shows a nearly symmetric band at 513 nm (ε 82 l mol^{-1}cm^{-1}). The wavelength and intensity of this band is comparable to values reported for copper(II) complexes of related tetrazamacrocycles[42,69].

The UV spectrum of the ligand dihydroperchlorate and its zinc(II) complex show absorption bands 224 nm and 246 nm respectively. This band disappears in the reduced macrocycles[48] and can thus be assigned to $n \rightarrow \pi^*$ transition of the C=N double bond. The extinction coefficients

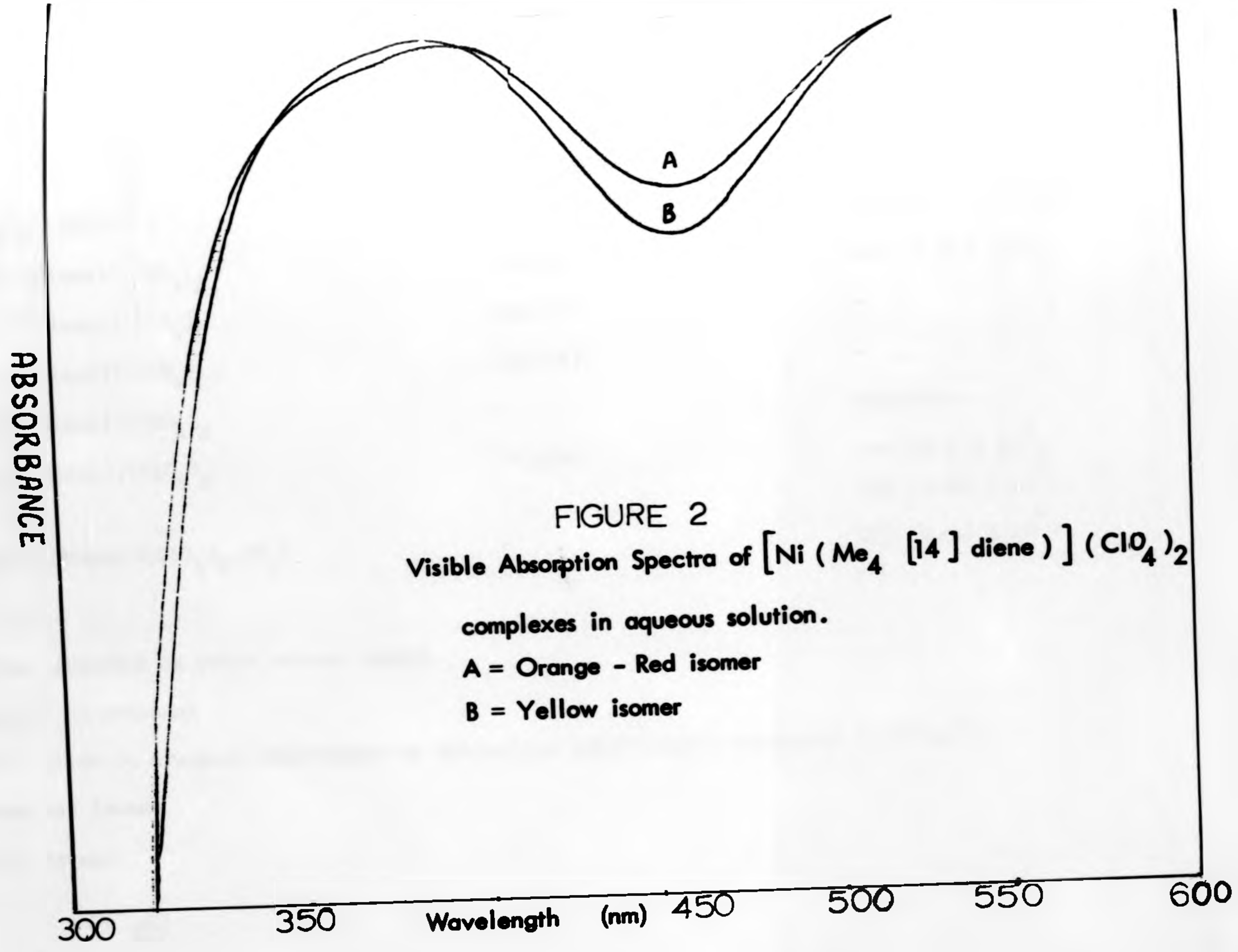


FIGURE 2

Visible Absorption Spectra of $[\mathrm{Ni(Me_4\ [14]\ diene)}](\mathrm{ClO_4})_2$ complexes in aqueous solution.

A = Orange - Red isomer

B = Yellow isomer

TABLE 4

Electronic Absorption Spectra of Bivalent Transition metal complexes[X] with $Me_4[14]diene.2HClO_4$ macrocycle

Complex	d-d(transitions)	Charge transfer transitions
$Me_4[14]diene.2HClO_4$ †	-	224(990), 208(980)*
$[Ni(Me_4[14]diene)](ClO_4)_2$	445(88)	283 (6.5×10^3)
Δ$[Ni(Me_4[14]diene)](ClO_4)_2$	439(61)	-
∇$[Ni(Me_4[14]diene)](ClO_4)_2$	442(75)	-
$[Zn(Me_4[14]diene)](ClO_4)_2$	-	246(660)
$[Cu(Me_4[14]diene)](ClO_4)_2$	513(82)	245 (9.5×10^3) 194 (3.96×10^4)
$[Hg^{II}(Me_4[14]diene)](ClO_4)_2.5H_2O$	-	203 (1.93×10^4)

X Spectra recorded in water unless stated

† Measured in methanol

* Values given in brackets correspond to Extinction coefficients expressed in $M^{-1}cm^{-1}$

Δ Orange red isomer

∇ Yellow isomer

and wave lengths of the visible and UV absorption maxima of the metal complexes of the macrocyclic ligand (XXl(a)) are recorded in Table (4).

Infrared spectra:

The i.r. spectra of the ligand dihydroperchlorate and its metal complexes are listed in Table (5). All the complexes show bands assignable to νN-H *ca*.3200 cm^{-1}, δNH *ca*.1460 cm^{-1} and νC=N 1660 cm^{-1}. Complexes formulated with perchlorate anions show the characteristic broad band at about 1100 cm^{-1} and a very intensive peak at 625 cm^{-1}. For Hg(II) complex, a broad band due to νOH and δ(HOH) absorption is observed and νN-H frequency is displaced to a lower value, because secondary amine groups are involved in hydrogen bonding[60].

TABLE 5

Characteristic Infrared bands (cm^{-1}) of the complexes of the type $[M(Me_4[14]diene](ClO_4)_2$ (where $M=Ni^{2+}, Cu^{2+}, Zn^{2+}$ and Hg^{2+})

Complex	νC=N	νClO_4^-	νN-H	Ligand bands
$Me_4[14]diene.2HClO_4$	1669s	1095vs,br 625vs	3170s	3095m,2960s,2795s,1457br,1385s,775vs,865s.
$[Ni(Me_4[14]diene)](ClO_4)_2$	1660s	1100br,625vs	3210vs	3005w,2987s,1455s,sp,1213s,851vs,772w
$[Cu(Me_4\ [14]diene)](ClO_4)_2$	1665vs	1105s,br 626vs	3240vs	2985m,2890w,1455m,1208s,1008s,895s,935m.
$[Zn(Me_4[14]diene)](ClO_4)_2$	1668vs	1115s,br 630vs	3250vs	2987m,2892w,1455sp,1354m,1205s,995s,889vs,774w.
$[Hg^{II}(Me_4[14]diene)](ClO_4)_2.5H_2O$	1664s,br	1090br 628vs	3190br	2985br,m; 1452s,1381w,818m.

s = strong; vs = v strong; sp = split; m = medium; br = broad; w = weak

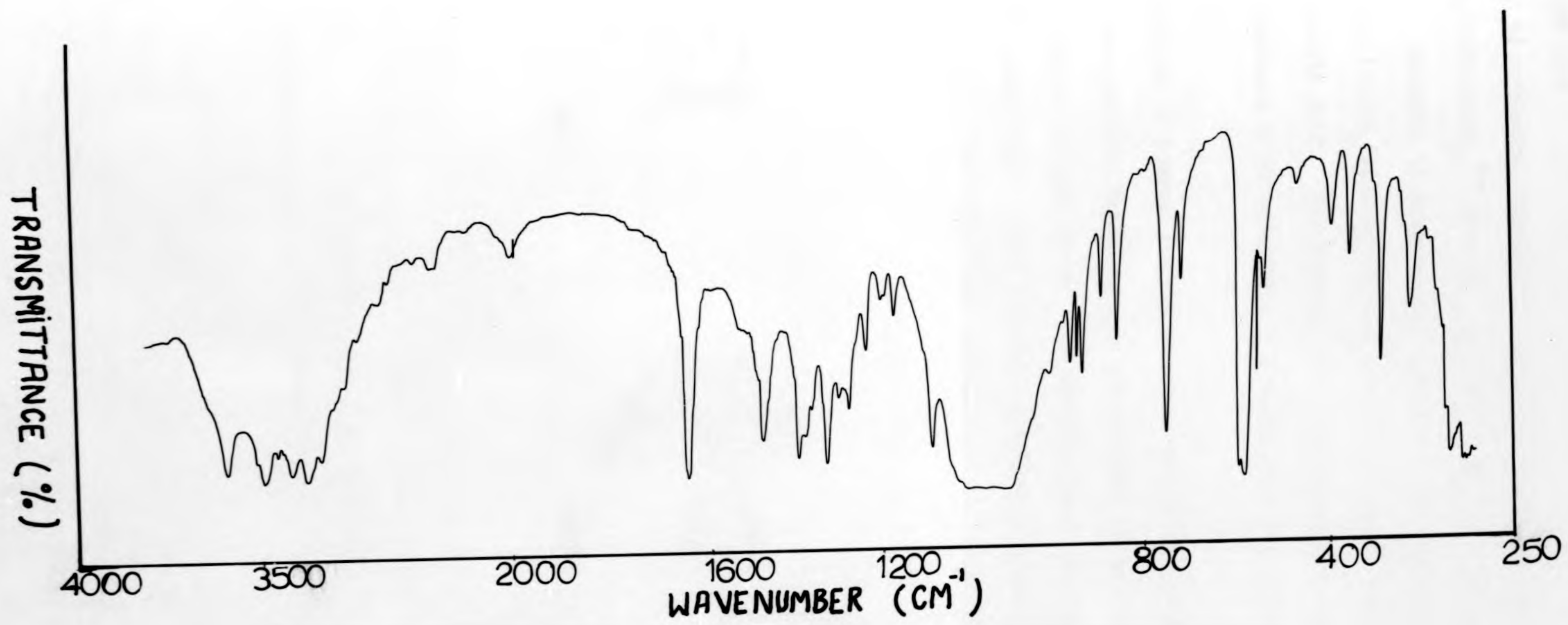


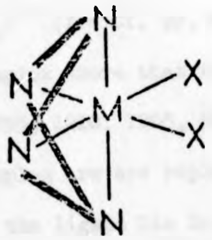
Figure 3 Infrared Spectrum of 5,6,12,13-Tetramethyl-1,4,8,11-tetra-azacyclotetradeca-4,11,diene dihydroperchlorate; $Me_4[14]diene.2HClO_4$ macrocycle.

Cobalt(III) Complexes

A variety of octahedral cobalt(III) complexes of the general type *trans* -$[Co(Me_4[14]diene)X_2]^{n+}$ (X = Cl^-, Br^-, NO_2^-, NH_3, N_3^- and $CH_3CO_2^-$) have been prepared. Attempts to prepare *cis* - complexes were unsuccessful and the carbonato species $[Co(Me_4[14]diene)CO_3]ClO_4$ has been isolated confirming that the ligand will fold. The reaction with acetylacetonate (acac$^-$) was very slow and appeared to be reversible indicating that the ligand only folds with difficulty.

On coordination to a metal ion two interconvertible diastereoisomers (*rac* and *meso*) are possible depending upon the relative disposition of the N-H bonds with respect to each other. In addition, each of these diastereoisomers could adopt either a planar or folded geometry on coordination to a metal ion (XXVI) and (XXVII).

XXVI



XXVII

Infrared spectra:

Apart from the bands due to the anionic ligands the spectra of all the cobalt(III) complexes of the type trans -[$CoMe_4$[14]diene)X_2]$^{n+}$ show a strong band in the region 3200 cm^{-1} assigned to the N-H stretching vibration. This band occurs in almost the same position for analogous copper(II), nickel(II), zinc(II) complexes[39].

Lowering of the νN-H frequencies by about 40 cm^{-1} occurs between different anions of the same complex, for example: νN-H(3180 cm^{-1}) value for the nitrito complex (perchlorate anion) drops to 3120 cm^{-1} in case of diisothiocyanato complex (thiocyanate anion)[70].

The isothiocyanato structure in trans -[Co(Me_4[14]diene)$(SCN)_2$]$^{+}$ is consistent with the observed C-N, C-S frequencies[71,72].

The skeltal vibrations of the macrocyclic ligand in the region 750-1450cm^{-1} are very important in reflecting the changes in the geometry of the ligand absorption spectra of the macrocycle. A comparison of the ligand absorption spectra of the trans -[Co(Me_4[14]diene)X_2]$^{n+}$ (X = Cl, Br, NO_2, etc.,) with the cis -[Co(Me_4[14]diene)CO_3]$^{n+}$ complex shows that the bands which appear for the former complex at 1235, 1295, 1210, 1005, 900 cm^{-1} are either too weak to be observed in the latter complex are are replaced by new bands. This suggests that the nitrogen atoms of the ligand lie in the same plane for the trans -[Co(Me_4[14]diene]X_2]$^{n+}$ complexes whereas macrocycle is believed to be folded in case of cis -[Co(Me_4[14]diene)Co_3]$^{n+}$ complex[53,73]. Bands observed for the isothiocyanato and dinitrito complexes have absorptions at 2039 and 1315 cm^{-1} respectively and are consistent with the absorptions due the ionic C≡N and νNO_2 symmetric vibrations[72]. The principal i.r. absorption bands in trans -[Co(Me_4[14]diene)X_2]$^{n+}$ complexes are listed in Table (6).

TABLE 6

Infrared frequencies of the complexes of the type [$CO^{III}(Me_4(14)diene)X_2]^{n+}$

Complex	ν_{N-H}	$\nu_{C=N}$ νN-H	νClO_4^-	Ligand absorption bands
trans-[$Co(Me_4[14]diene)Cl_2]ClO_4$	3205s	1647s	1096vs 624s	1456s,1427s,1371m,1209w,1030m,890m
trans-[$Co(Me_4[14]diene)Br_2]ClO_4$	3214s	1648vs	1100vs 623vs	1452s,1435s,1375m.1210m,1035s,900s
trans-[$Co(Me_4[14]diene)(NO_2)_2]ClO_4$	3185m	1646s	1098s	1465w,1415sh,1393s,1212w,1040m,896m
trans-[$Co(Me_4[14]diene)(N_3)_2]ClO_4$	3210s	1645s	1090br	1450br,1370m,1285vs,1208w,900s
trans-[$Co(Me_4[14]diene)(SCN)_2]SCN.4H_2O$	3110br	1645s	-	1448m,1425sp,1289m,1207w,1136s,1079,1044s, 898s,840s
trans-[$Co(Me_4[14]diene)(NH_3)_2]Cl.(ClO_4)_2$	3230br	1642s	1100v.br 630vs	3480ν(OH)br ν2040 ionic(C=N) 1472w,1429w,1292sh,1210sh,9405,900s
trans-[$Co(Me_4[14](diene)(CH_3COO)_2]ClO_4$	3100br	1650s	1095vs	1580s,1456m,1382s,1330vs,1210m,1180s,1020sh, 900s,786s,552m,420m
cis-[$Co(Me_4[14]diene)(CO_3)]ClO_4.H_2O$	3160br	1629s	623vs	1450m,1360br,834s,750m,700sh

Abbreviations: S-strong, w-weak, br-broad, sh-shoulder, m-medium, sp-split, vs-very strong

Visible and UV Spectra

The dihalogeno complexes of cobalt(III) exhibit three low-intensity absorption bands in the visible region characteristic of *trans* -[CoN_4X_2]$^{n+}$ chromophore[74]. Such complexes have a basic D_{4h} symmetry, with the $^1A_{1g}$ → $^1T_{1g}$ (O_h) transition into two components a$^1A_{1g}$ → ^1E_g (D_{4h}) and a$^1A_{1g}$ → $^1A_{2g}$ (D_{4h}) transition[74,75]. Where the tetragonal splitting is not very large as in the *trans* -[Co(Me_4[14]diene)X_2]$^{n+}$ complexes (where X = NH_3,NO_2^-,NCS^-) only a single absorption band is observed under the $^1A_{1g}$ → $^1T_{1g}$ (O_h) envelope. Energies and intensities observed for these complexes are very similar to the spectra of *trans* -[Co(Me_2[14]diene]X_2]$^{n+}$ type complexes[53] and thus support the assignment of *trans* structures to the cobalt(III) diacido compounds of Me_4[14]diene^{2+} macrocycle. The wavelength values and extinction coefficients of the visible and ultraviolet absorption maxima of the cobalt(III) complexes are presented in Table (7).

TABLE 7

Electronic absorption spectra of *trans*-[CO^{III}(Me$_4$[14]diene)X$_2$]$^+$ (X=$\bar{\text{Cl}}$, $\bar{\text{Br}}$, $\bar{\text{NO}}_2$, $\bar{\text{N}}_3$, SC$\bar{\text{N}}$,NH$_3$) complexes.

Complex	d-d transitions	Charge transfer
trans-[CoMe$_4$[14]dieneCl$_2$]ClO$_4$ ^{X}	624(25); 434sh(35)	238 (1.93 X 10^4)$^\Delta$ 207(1.47 X 10^4)
**trans*-[Co(Me$_4$[14]diene)Br$_2$]ClO$_4$.2H$_2$O	642(43) 378(100)	272 (2.52 X 10^4) 307sh (1.9- X 10^4) 235 (~ 10^5)
†*trans*-[Co(Me$_4$[14]diene)(NO$_2$)$_2$]ClO$_4$	440(166)	258 (3.6 X 10^4) 357 (4.3 X 10^3) 215 (~ 10^5)
trans-[Co(Me$_4$[14]diene)(SCN$_2$]SCN.4H$_2$O	518(195)	229sh (~ 10^4)
trans-[Co(Me$_4$[14]diene)(NH$_3$)$_2$]Cl(ClO$_4$)$_2$	446(75), 333(118)	220(3.0 X 10^4)
cis-[Co(Me$_4$[14]diene)CO$_3$]ClO$_4$.H$_2$O	506(126),364(176)	235 (2.1 X 10^7)

X Spectra measured in 1M aq. HCl

* " " " dry acetonitrite

† " " " water

Δ Values in brackets correspond to Extinction coefficients expressed in 1 M^{-1}cm^{-1}

1.3.3 Metal Complexes of 5, 12-Diethyl-1, 4, 8, 11 -tetra-azacyclotetradeca- - 4, 11 diene dihydroperchlorate . -

The macrocyclic tetra-aza ligand 5, 12 - Diethyl - 1, 4, 8, 11 - tetra-azacyclotetradeca - 4, 11-diene dihydroperchlorate; $Et_2[14]diene.2HClO_4$ has been prepared by the reaction of 1, 2 - diamino ethane monohydroperchlorate with ethyl vinyl ketone (EVK) and the reaction appears to be essentially stereospecfiic giving only the trans - macrocyclic diimine.

The macrocycle dihydroperchlorate can be kept for months in a dessicator, provided that the material is pure. Impure samples decompose quite readily possibly by a retro-Michael reaction or by hydrolysis of the imine linkage. A number of metal(II) complexes $[M(Et_2[14]diene)]ClO_4)_2$. , (M = Ni^{2+}, Cu^{2+} and Zn^{2+}) have been prepared by the reaction of equimolar aqueous methanolic solutions of the ligand dihydroperchlorate with the corresponding metal perchlorate. The metal(II) complexes are four coordinate and the spectral properties discussed below, are consistent with an square-planar geometry.

Electronic spectra

The visible spectra on nickel(II) and copper(II) complexes show a single d-d band at 446 nm (ε = 65 l $mol^{-1}cm^{-1}$) and 514 nm ($\varepsilon \sim$ 85 l $mol^{-1}cm^{-1}$) respectively. The wavelengths and intensities of the bands are quite comparable to the values reported for analogous nickel(II), copper(II) complexes of related macrocycles[53] and is characteristic of square-planar geometry of complexes with four nitrogen donors[60]. The zinc(II) complex has a band in the ultraviolet spectrum at ca.235 nm and is probably due to the $n\rightarrow\pi^*$ transition in the C=N bond.

Infrared spectra

The i.r. spectra of the macrocycle dihydroperchlorate (XX) shows bands at 1658 (νC=N), 1100 and 625 cm^{-1} (νClO_4^-) Table (8)

The i.r. spectra of the metal complexes give bands assignatle to νN-H ca. 3200cm^{-1} and νC=N at ca. 1655 cm^{-1}. The additional ligand bands appear at frequencies similar to the parent macrocycle. However, the zinc(II) complex shows a broad band at 3450 cm^{-1} due to ν(OH) and the νN-H stretching frequencies are masked by the water bands of the hydrated complex.

TABLE 8

Prominent Bands in the infrared spectra of the $Et_2[14]diene.2HClO_4$ macrocycle and its metal complexes (in cm^{-1})

Complex	νN-H	νC=N	Anion modes (ClO_4)	Other ligand bands
$Et_2[14]diene.2HClO_4$	3195m.br	1658vs	1100br 625vs	1519,1420br 1330s,1255s, 1233s,927vs 828s,765vs
$[Cu(Et_2[14]diene)](ClO_4)_2$	3218s	1659vs	1085v.br 623vs	3160s,2940m,sp 14655,1410w, 1300m,1270w, 822m.
$[Ni(Et_2[14]diene)](ClO_4)_2$	3220s	1672vs	1080br 625vs	1460m,1405w. 1298w,958m 832s.
$[Zn(Et_2[14]diene)](ClO_4)X.H_2O$	masked	1670vs	1110v,br	840s, 1460m, 1305sh.

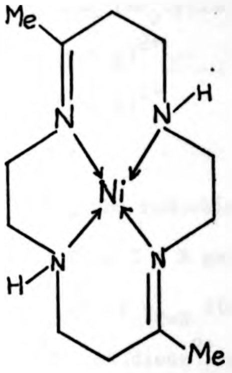
s-strong, w-weak, m-medium, sh-shoulder, m,sp-medium split,
vs-very strong, br-broad.

1.3.4 Reduction products of 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca 4,11 diene dihydroperchlorate . -

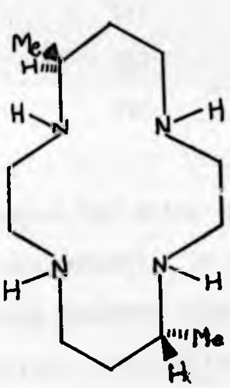
The nickel (II) complex of the macrocyclic ligand, 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene dihydroperchlorate (XXVIII) can be reduced with hydrogen to give a mixture of two complexes.

The free isomeric amines (XXIX) and (XXX) can be isolated by treating the mixture with sodium cyanide which removes the nickel(II) as Ni(CN)$_4^{2-}$.

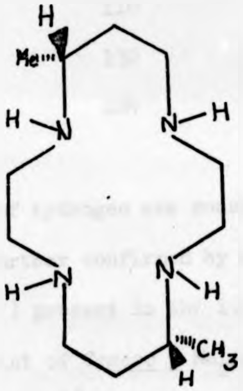
A recent X-ray crystallographic[68] investigation will establish the configuration of the two diastereoisomers (rac or meso).



XXVIII



XXIX

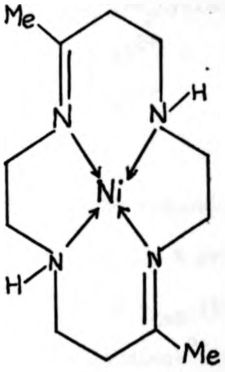


XXX

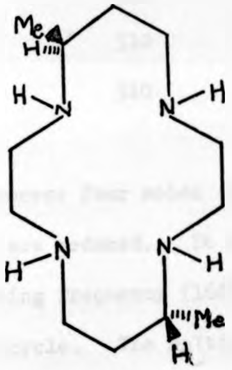
Margerum et al[65] have tentatively assigned rac versus meso configurations on the basis of melting points and the similarity of the physical properties of the relative molar absorptivities of the copper complexes with the tet a versus tet b Table (9).

1.3.4 Reduction products of 5,12-Dimethyl-1.4,8,11-tetra-azacyclotetradeca 4.11 diene dihydroperchlorate . -

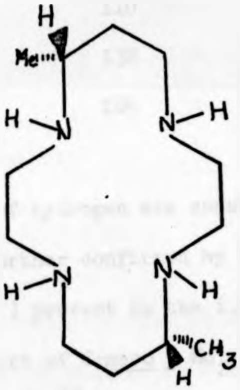
The nickel (II) complex of the macrocyclic ligand, 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene dihydroperchlorate (XXVIII) can be reduced with hydrogen to give a mixture of two complexes.
The free isomeric amines (XXIX) and (XXX) can be isolated by treating the mixture with sodium cyanide which removes the nickel(II) as $Ni(CN)_4^{2-}$.
A recent X-ray crystallographic[68] investigation will establish the configuration of the two diastereoisomers (rac or meso).



XXVIII



XXIX



XXX

Margerum et al[65] have tentatively assigned rac versus meso configurations on the basis of melting points and the similarity of the physical properties of the relative molar absorptivities of the copper complexes with the tet a versus tet b Table (9).

TABLE 9

	m.p.
C-*meso* - Me$_2$Cyclam	144.5 - 145°
C-*rac* - Me$_2$Cyclam	109.5 - 110°
tet *a* (*meso*)	146-148°
tet *b* (*rac*)	97 - 105°

Spectral data

	λ/nm	ε/(l mol^{-1}cm^{-1})
Cu[C-*meso*-(Me$_2$Cyclam)]$^{2+}$	518	88
Cu[C-*rac*-(Me$_2$Cyclam)]$^{2+}$	513	110
Cu(tet *a*)$^{2+}$	510	132
Cu(tet *b*)$^{2+}$	510	184

During the reduction process four moles (2H$_2$) of hydrogen are consumed indicating that both C = N groups are reduced. It was further confirmed by the absence of $\nu_{C=N}$ stretching frequency (1660 cm^{-1}) present in the i.r. spectra of Me$_2$[14]diene^{2+} macrocycle. The melting point of C-*meso* - Me$_2$cyclam (137°C) is slightly lower than the reported value (144.5°C)[48] even after repeated recrystallisations but corresponds fairly well with the other physical properties.

The macrocyclic amine 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane can also be prepared by a relatively shorter and modified route by the reaction of Me$_2$[14]diene.2HClO$_4$ with sodium borohydride in methanol-water solution. This method provides a single isomer with melting point 144°C very similar to the one obtained by the nickel-aluminium reduction method.

Infrared spectra:

The i.r. spectra of 5,12,Dimethyl-1,4,8,11-tetra-azacyclotetradecane amines Isomers a and b have been listed in Table 10

TABLE 10

Isomer	νN-H	νNH...N	$\nu N^{+}H$	Ligand bands
*C-*meso*-Me_2Cyclam	3210s,3245vs 3190m,3250m	2805m	2650m 2690w	1485m,1155m, 1130s,850s,815s
C-*meso*-Me_2Cyclam	3290sp	2800m	2660w 2690sh	1235vs,1480m, 1150sp,1100s 855s,818s
C-*rac*-Me_2Cyclam	3250m 3210s	2790m	2595w	1485s,sp,1365 1135s,1245s 1005m,808s,840m

s-strong, m-medium, w-weak, vs-very strong, sp-split.

*Prepared by Modified Synthesis.

The bands due to νN-H remains sharp but as the secondary amine groups are involved in hydrogen bonding interaction, bands due to νNH-N are moderately weakened.

1.3.5 Metal Complexes of 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecanes;

The macrocyclic (XXIX) C-meso or C-rac (XXX) amines act as tetradentate ligands. Only the nickel(II) complexes have been previously reported.[48] The reaction of aqueous or methanolic solutions of the macrocyclic amines (XXIX)or (XXX) with aqueous solutions of nickel(II) copper(II), zinc(II) perchlorates, lead(II) nitrate, manganese(II) and mercury(II) chlorides give orange-yellow, red-violet, colourless and green coloured (Mn(II)) complexes respectively. These complexes were isolated as their perchlorate salts and recrystallized from aqueous methanol. The metal(II) perchlorates have the general formulation $[M(L](ClO_4)_2$ ($M = Ni^{2+}, Cu^{2+}, Zn^{2+}, Mn^{2+}, Pb^{2+}, Hg^{2+}$ and L = C-meso or C-rac-Me_2(Cyclam).

The structures of all complexes are four coordinate and a square planar geometry was established for the nickel(II) and copper(II) complexes on the basis of spectroscopic measurements. The nickel(II) complexes of (XXIX) and (XXX) are thermodynamically stable and the nickel is removed only by treatment with an excess of cyanide ion.

During the reduction of 5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca-4-11-diene nickel(II) diperchlorate, with Ni/Al alloy, an orange-red crystalline nickel(II) complex of Me_2Cyclam was isolated. This occurred if the volume of the solution was reduced to about one-third volume before decomposition with NaCN).
With HCl at pH (2 ∿ 3), it was possible to isolate a blue-violet octahedral nickel(II) complex from the reduced macrocyclic amines mixture. Both these complexes have been verified by direct preparation methods and spectroscopic measurements.

The complex $[Co(C\text{-}meso\text{-}(Me_2Cyclam)Cl_2]Cl.2H_2O$ was prepared by the reaction of C-meso-Me_2Cyclam and two equivalents of HCl with $Na_3[Co(CO_3)_3]3H_2O$ in methanol solution. The corresponding diazido complex, $[Co(C\text{-}meso\text{-}(Me_2Cyclam)\text{-}(N_3)_2]N_3$ was prepared from the dichloro complex by reaction with sodium azide in aqueous solution. The complexes are octahedral with a trans-arrangement of the acido ligands. The dichloro complex is bright green and the azido complex is deep blue.

Visible and ultraviolet spectra of the complexes of C-meso and C-rac(Me_2cyclam).-

The visible and UV spectra of copper(II), nickel(II), zinc(II) manganese(II) and cobalt(III) complexes of C-meso and C-rac-Me_2Cyclam in aqueous solution are recorded in Table (ii).

The absorption spectra of nickel(II) complexes of c-meso and c-rac - Me_2Cyclam) are quite similar. Thus [Ni C-meso-(Me_2Cyclam)]$(ClO_4)_2$ has λmax 451 (ε=86) and [Ni(C-rac-(Me_2Cyclam)]$(ClO_4)_2$ has λmax 456 (ε = 72) characteristic of square planar geometry. Square planar nickel(II) complexes with four nitrogen donors usually have a d-d band at 445 nm ($\varepsilon \sim 100$ $l mol^{-1} cm^{-1}$)[60].

The visible spectra of copper(II) complexes show a broad symmetric band at 510 nm similar to analogous square planar copper(II) compounds[69]. The copper(II) complexes have similar UV bands to those of nickel(II), but the relative position of the bands are shifted about 20 nm to shorter wavelengths with the nickel(II) complex. The zinc(II) complex has a band at about 225 nm ($\varepsilon \sim 600$ $l\ mol^{-1} cm^{-1}$) which can probably be assigned to the $n \rightarrow \pi^*$ transition of the C = N double bond.

The dichloro complex of cobalt(III) exhibit three low-intensity absorption bands in the visible region (see section 1.3.2) characteristic of the trans - $[CoN_4X_2]^{n+}$ chromophore[74] and only a single absorption band at 564 nm is observed under the $1\ A_{1g} \rightarrow 1\ T_{2g}$ (O_h) envelope in the trans-[Co(C-meso-Me_2Cyclam)$(N_3)_2$]N_3 complex.

Infrared Spectra

The i.r. spectra of the complexes are listed in Table (12). Apart from the bands due to the anionic ligands, the spectra of copper(II), nickel(II), zinc(II) and lead(II) complexes show a strong sharp band at about 3230 cm^{-1} assigned to the N-H stretch. The νN-H stretching frequency of trans-[Co C-meso-(Me_2Cyclam)Cl_2]Cl.$2H_2O$ complex absorbs at 3200 cm^{-1}. Differences

TABLE 11

Visible and Ultraviolet Spectra* of Bivalent Transition metal complexes of C-meso and C-rac-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecanes, Isomers (a and b).

Complex	d-d transition	Charge transfer
$[Cu(C\text{-}meso\text{-}(Me_2Cyclam)](ClO_4)_2^{a}$	510 (86)	259(3.52 X 10^3)
$[Cu(C\text{-}rac\text{-}Me_2Cyclam](ClO_4)_2$	512 (98)	260(2.86 X 10^3)
$[Ni(C\text{-}\overset{rac}{meso}\text{-}Me_2Cyclam](ClO_4)_2$	451 (86)	223 (1.28 X 10^4),207sh
$[Ni(C\text{-}Meso\text{-}Me_2Cyclam](ClO_4)_2$	456 (72)	220 (1.19 X 10^4)
$[Zn(C\text{-}meso\text{-}Me_2Cyclam)](ClO_4)_2$	-	227 (6.20 X 10^2)
$[Zn(C\text{-}\overset{rac}{meso}\text{-}Me_2Cyclam)](ClO_4)_2$	-	221 (5.96 X 10^2)
$[Ni(C\text{-}meso\text{-}(Me_2Cyclam)Cl_2]^{\Delta}$	457 (79), 338	($\sim 10^5$)
^{b}trans-$[Co^{III}(C\text{-}meso\text{-}(Me_2Cyclam)Cl_2]Cl\cdot 2H_2O$	623 (30) 317 (213)	259 (L.10 X 10^5) 212(3.6 X 10^4)
trans-$[Co^{III}(C\text{-}meso\text{-}Me_2Cyclam)(N_3)_2]N_3$	564 (330) 478 (42)	344 (1.29) X 10^4) (216 2.69 X 10^4)

NOTES: *Band maxima in nm; Extinction coefficients (1 $Mol^{-1}cm^{-1}$) in parentheses:

^{a}= Spectra recorded in aqueous solution

^{b}= Measured in 1M HCl

$^{\Delta}$= Assignments uncertain

TABLE 12

Characteristic Infrared frequencies (incm^{-1}) of transition metal complexes of C-meso and C-rac-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecanes, (Isomers a and b).

Complex	νN-H	νClO$_4^-$	Other ligand bands
[Cu(C-meso(Me$_2$Cyclam)](ClO$_4$)$_2$	3238s	1097s,br 627s	1435s,1465s,990m
[Cu(C-rac-(Me$_2$Cyclam)](ClO$_4$)$_2$	3236s	1100s,br 629s	1432m,995m
[Ni(C-meso-[Me$_2$Cyclam)](ClO$_4$)$_2$	3206s	1100s,br 628s	1440m,1470m
[Ni(C-rac-(Me$_2$Cyclam)](ClO$_4$)$_2$	3180	1090br 624s	1437s,1000w,846m
[Zn(C-meso-(Me$_2$Cyclam)](ClO$_4$)$_2$	3210s	1098br,626s	1440m,840m
[Zn(C-rac-(Me$_2$Cyclam)](ClO$_4$)$_2$	3230s	1102br,626s	1445m
[Pb(C-meso-(Me$_2$Cyclam)](No$_3$)$_2$.1.5H$_2$O	3220s	-	2930s,2965s,1380br,1150s,1095m,775s,3465br(νOH$^-$)
[Mn^{II}(C-meso-(Me$_2$Cyclam)]Cl$_2$.2.5H$_2$O	3145s	-	2930w,1604m,1100vs,1025sp,840s,798m,353m(νOH$^-$)
[Hg^{II}(C-meso-Me$_2$Cyclam-2H)]^0	3230br	-	1560br,1430br,1335m,1283m,1150s,1122s,885m
trans-[CO^{III}(C-meso-Me$_2$Cyclam)Cl$_2$]Cl.2H$_2$O	3200s	-	3095w, 1428m, 1110s, 1029s
trans-[Co^{III}(C-meso-(Me$_2$Cyclam)(N$_3$)$_2$]N$_3$	3185m	-	2000vs ν(N$_3^-$).

of more than 40 cm^{-1} are often observed in νN-H frequencies between different salts of the same complex amine[70]. Complexes formulated with perchlorate anions show the characteristic broad band at about 1100 cm^{-1} and a very intense peak at 625 ± 5 cm^{-1}. A strong band at 2000 cm^{-1}[47] confirms the presence of an azido group in the *trans* - [Co-(C-*meso*-(Me$_2$Cyclam)(N$_3$)$_2$]N$_3$ complex. Complexes formulated as hydrates show typical ν(OH) and δ(HOH) bands.

1.3.6 Some Rhodium(III) complexes of C-*meso*-(Me$_2$Cyclam) and 5,6,12,13 - Tetramethyl - 1,4,8,11 - tetra - azacyclotetradeca - 4,11-diene dihydroperchlorate (Me$_4$[14]diene.2HClO$_4$) . -

The complexes of rhodium(III) with the cyclic tetramines, C-*meso*-(Me$_2$Cyclam) and Me$_4$[14]diene. 2HClO$_4$ have been prepared and assigned *cis* or *trans* - configurations on the basis of infrared and UV-visible spectra. The rhodium-halogen stretching frequencies in the i.r. and the spin allowed d-d transitions are identified.

The preparation of the dichloro complex from rhodium(III)chloride trihydrate and C-*meso* - (Me$_2$Cyclam) in water gives predominantly the *cis*-isomer. However, the analogous reaction with Cyclam in methanol solution, the *trans*-isomer predominated (60% *trans*, 30% *cis*)[76]. The *trans* - [Rh(Me$_4$[14]diene)Cl$_2$]ClO$_4$.H$_2$O complex was prepared from RhCl$_3$.3H$_2$O and Me$_4$[14]diene in methanol.

Rhodium(III) d-d Spectra

The visible spectra (Table (13)) of these cyclic tetra-amine complexes resemble these of previously reported rhodium(III) tetra-amine complexes of Cyclam. The characteristic differences between *cis* and *trans*-complexes (higher extinction coefficients and lowest energy band shifted to higher frequency for *cis*-complexes compared with the analogous *trans*-complex) were used for the confirmation of the assigned structures[76]. Table (13) shows that this prediction is consistent with the assignment of stereoisomers for the present complexes.

TABLE 13

Electronic absorption spectra of some [Rh(amine)Cl$_2$]$^+$ complexes

	Complex	λ/(nm)	ε/l mol^{-1} cm^{-1}	Ref
	trans-[Rh(en)$_2$Cl$_2$]$^+$	406	75	77
	Cis-[Rh(Cyclam)Cl$_2$]$^+$	354	223	76
	trans-Rh(Cyclam)Cl$_2$]$^+$	406	78	76
*	*cis*-[Rh(C-*meso*-(Me$_2$Cyclam))Cl$_2$]$^+$	356* 305 209	258 340 $\sim 10^3$	-
*	*trans*-[Rh(Me$_4$[14]diene)Cl$_2$]ClO$_4$.H$_2$O	395 216	51 1.77X10^4	-

* Present Studies

An increase in steric constraint would be expected to cause greater distortions and thereby greater intensities in the visible absorption spectra of the complexes. Collman and Schneider discuss this principle with respect to a cis[Rh(amine)X_2]$^+$ series. The centre of symmetry is removed in a cis-isomer relative to a trans, (considering the primary effects of the N-donors and ignoring the secondary effects of the ethylene linkages[28,76]). As a result larger extinction coefficients are predicted for the cis-isomers.

Infrared Spectra

The i.r. spectra Table (14) of the complexes resemble those of their analogous cyclam complexes[76] and also provide evidence for the increased distortion of the octahedral field in the cis series. The ν(N-H) and ν(Rh-N) modes and the CH_2 rocking modes appear as single bands in the trans and double bands in the cis-isomers.

The spectral bands assignable to the anions support the formulations given. The rhodium-halogen and other ligand bands have been assigned (Table (14)).

TABLE 14

Prominent infrared absorption frequencies (cm^{-1}) of diacido amine rhodium(III) Complexes.

Complex	ν(N-H)	ν(CH_2)	ν(Rh-N)	ν(Rh-Cl)	Other ligands bands
trans-[Rh(en)$_2$$Cl_2$]$ClO_4$	-	-	-	344vs†	142m, 260vs 314m
*cis-[Rh(Cyclam)Cl_2]$^+$	30605 31755	840m 855m	505 459	- -	-
*trans-[Rh(Cyclam)Cl_2]$^+$	31055	875m	493	-	-
cis-[Rh(C-meso-(Me$_2$Cyclam)Cl_2]$^+$	3165	871vs 835vs	501s	301vs	1445vs, 1286vs, 1028br, 784s
trans-[Rh(Me$_4$[14]diene)Cl_2]$^+$	3140s	881s	500w	338m	νOH3450 νClO_4-1098s 629vs νC=N 1650

* Ref 76 † Ref 78

An increase in steric constraint would be expected to cause greater distortions and thereby greater intensities in the visible absorption spectra of the complexes. Collman and Schneider discuss this principle with respect to a cis[Rh(amine)X_2]$^+$ series. The centre of symmetry is removed in a cis-isomer relative to a trans, (considering the primary effects of the N-donors and ignoring the secondary effects of the ethylene linkages[28,76]). As a result larger extinction coefficients are predicted for the cis-isomers.

Infrared Spectra

The i.r. spectra Table (14) of the complexes resemble those of their analogous cyclam complexes[76] and also provide evidence for the increased distortion of the octahedral field in the cis series. The ν(N-H) and ν(Rh-N) modes and the CH_2 rocking modes appear as single bands in the trans and double bands in the cis-isomers.

The spectral bands assignable to the anions support the formulations given. The rhodium-halogen and other ligand bands have been assigned (Table (14)).

TABLE 14

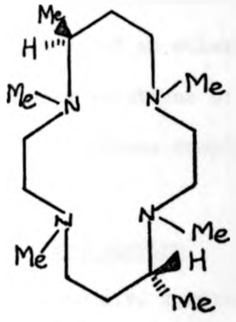
Prominent infrared absorption frequencies (cm^{-1}) of diacido amine rhodium(III) Complexes.

Complex	ν(N-H)	ν(CH_2)	ν(Rh-N)	ν(Rh-Cl)	Other ligands bands
trans-[Rh(en)$_2$Cl$_2$]ClO$_4$	-	-	-	344vs†	142m, 260vs 314m
*cis-[Rh(Cyclam)Cl$_2$]$^+$	30605 31755	840m 855m	505 459	- -	-
*trans-[Rh(Cyclam)Cl$_2$]$^+$	31055	875m	493	-	-
cis-[Rh(C-meso-(Me$_2$Cyclam)Cl$_2$]$^+$	3165	871vs 835vs	501s	301vs	1445vs, 1286vs, 1028br, 784s
trans-[Rh(Me$_4$[14]diene)Cl$_2$]$^+$	3140s	881s	500w	338m	νOH345o νClO$_4$-1098s 629vs νC=N 165o

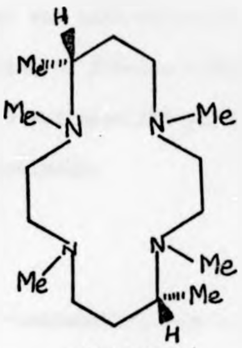
* Ref 76 † Ref 78

1.3.7 Synthesis of N-tetra methyl substituted 1,4,8,11-tetra-aza-cyclotetradecanes.

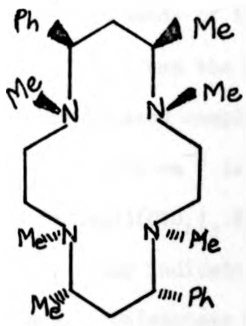
The following N-tetramethyl macrocycles



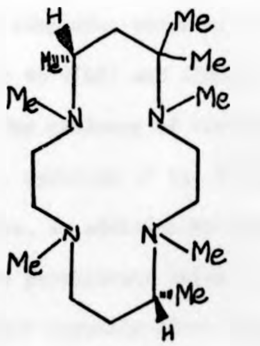
(XXXI)



(XXXII)



(XXXIII)



(XXIV)

have been prepared by direct methylation of the appropriate tetraazacyclotetradecane using formic acid and formaldehyde essentially by the method described by Kaden et al[57] for the Me_2Cyclam macrocycle. The preparation and spectral properties of copper(II), zinc(II) complexes of N-tetra methyl derivative of C-meso-(Me_2Cyclam) (XXlX) are discussed.

Barefield and Wagner[56] have recently published the preparation and discussed some of the properties of the Ni(II), Cu(II) and Zn(II) complexes of N-tetra methyl Cyclam. Kaden et al[57] have studied the complexation kinetics of nickel(II), copper(II) and cobalt(II) with several N-tetra methyl macrocycles, however no attempt was amde made to isolate the complexes. The reaction of an ethanolic solution of N-tetra methyl-C-meso(Me_2Cyclam) with aqueous solutions of copper(II) and zinc(II) perchlorates gave blue-violet and colourless complexes respectively.

Infrared spectra

The i.r. spectra of the N-tetramethyl substituted tetra-azacyclotetradecanes show, as expected, no NH stretching frequencies. The principal absorption bands of the metal complexes occur in the region 900-1100 cm^{-1}. The $\nu(ClO_4^-)$ and the bands due to $\nu(OH)$ and $\delta(HOH)$ vibrations are observed in the hydrated complexes. The presence of two well defined bands at 1118 and 1076 cm^{-1} in the i.r. spectrum of the [Cu(N-tetramethyl-C-meso (Me_2Cyclam)]$(ClO_4)_2 \cdot H_2O$ complex, in addition to strong bands at 932 and 623 cm^{-1} may indicate that the perchlorate anion is acting as a unidentate ligand. Unidentate perchlorate normally gives bands at 1120, 1063 and 935 [79] cm^{-1}.

Visible spectrum of [Cu(N-Tetramethyl-C-meso-(Me_2Cyclam)]$(ClO_4)_2 \cdot H_2O$. -

The visible absorption spectrum of the copper(II) complex, [Cu(N-Tetramethyl-C-meso-(Me_2Cyclam)]$(ClO_4)_2 \cdot H_2O$ has $\lambda max = 595nm$ and closely resembles the analogous copper(II) complex of N-Tetramethyl Cyclam with $\lambda max = 583$ nm[56]. This latter complex is considered to be five coordinate. The visible spectrum of [Cu(N-Tetramethyl C-meso-(Me_2Cyclam)]$^{2+}$ complex slowly shifts to $\lambda max = 620nm$, Figure (4) suggesting that some type of stereochemical change is occurring in solution. Additional work on this system is required.

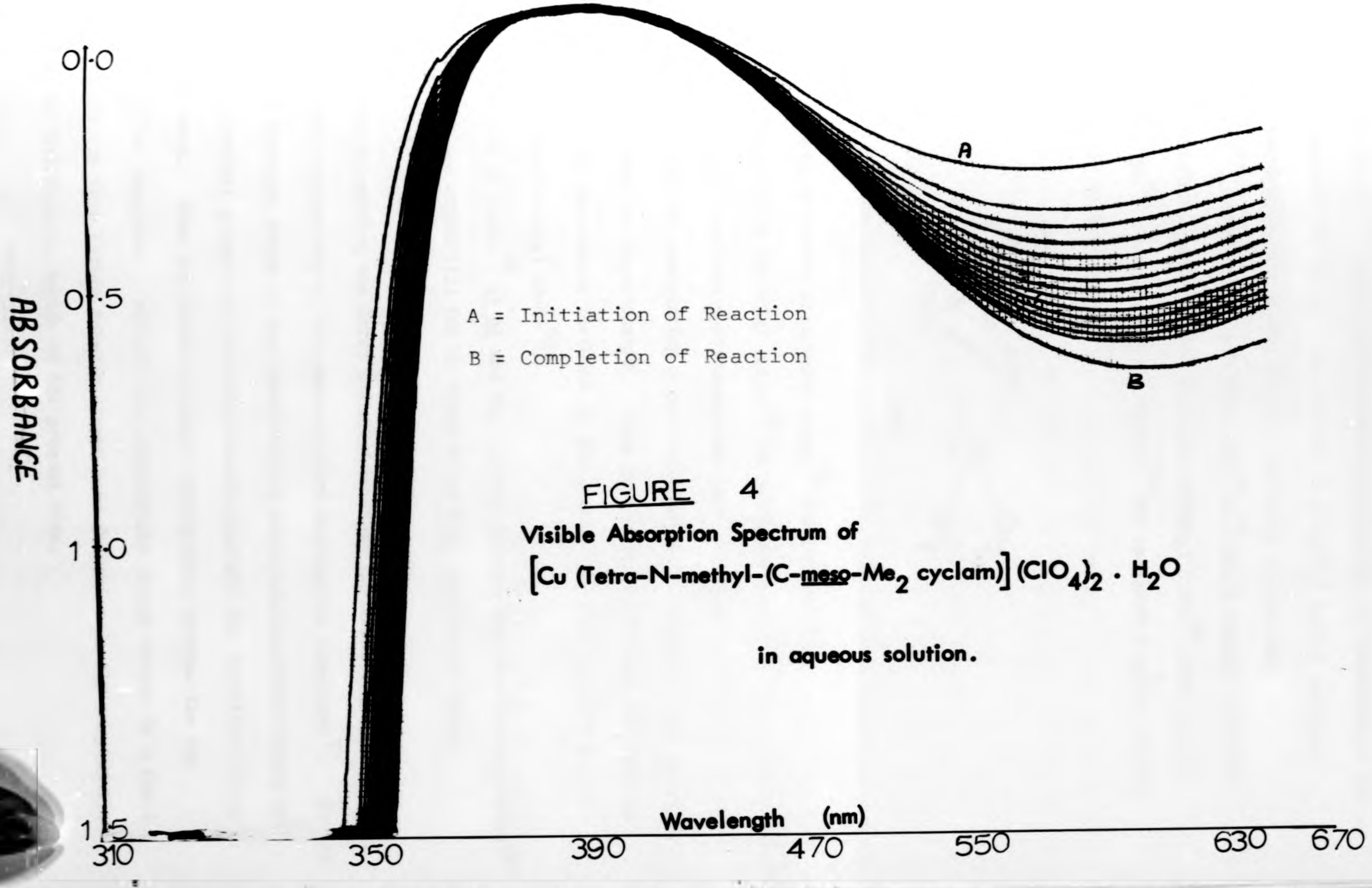


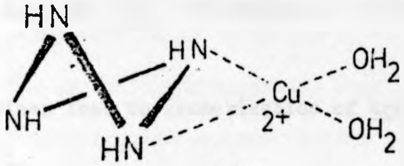
FIGURE 4

Visible Absorption Spectrum of

$[Cu\ (Tetra\text{-}N\text{-}methyl\text{-}(C\text{-}\underline{meso}\text{-}Me_2\ cyclam)]\ (ClO_4)_2 \cdot H_2O$

in aqueous solution.

Margerum *et al*[54,80] have investigated the kinetics of formation of the copper(II) complexes of tet *a*. In neutral or slightly acidic solution copper(II) reacts with the ligand to give initially a blue complex Cu(teta)(blue)$^{2+}$, (λmax 620nm, ε = k93 l mol^{-1}cm^{-1} which readily converts to a more thermodynamically stable red form Cu(tet*a*) (red)$^{2+}$ λmax, 520 nm ε = 140 l mol^{-1}cm^{-1}) at higher pH. Curtis[19] has assigned a square planar configuration to Cu(tet*a*) (red)$^{2+}$.



XXXV

From the results of recent structural study[81] Buxtorf and Kaden have inferred that copper(II) ion in Cu(tet*a*) (blue)$^{2+}$ is pentacoordinate[82]. The rate of interconversion of the blue pentacoordinate into red square planar end product has been explained by postulating a pre-equilibrium to conjugate base in which a coordinate group is deprotonated. This inversion at nitrogen followed by rearrangement of the carbon backbone of the ligand can occur to give a more stable red form Cu(tet*a*) (red)[83].

Recent results of Clark[84] *et al* and the visible spectra data for Cu(tet*a*)(blue)$^{2+}$ suggest that the copper(II) ion is bound by an N_2O_2 sequence of donor atoms (XXXV).

The previous assumption was later extended to study the reactivity of N-tetramethyl derivatives of the unsubstituted macrocyclic complexes[57]. As the four amino hydrogen atoms of the unsubstituted tetra-azacyclotetradecanes are replaced by methyl groups and this replacement prevents the formation of the conjugate base. Thus the pentacoordinate intermediate becomes the end product of the reaction. Whether the conformation change occurs in a rapid pre-equilibrium step before metal-nitrogen bond formation in the complexation process is difficult to decide at the present time.

HALOPENTAMMINES OF COBALT(III)

2.1 INTRODUCTION

The reaction of amines with *cis* and *trans* $-[Co(en)_2Cl_2]Cl$ has been studied by various groups[85-92]. Bailar and Clapp[93] made the following generalisations:

(a) Aniline and more strongly basic amines coordinate with both *cis* and *trans* $-[Co(en)_2Cl]Cl$ to give the *cis* - chloro(amine) bis(ethylene diamine) cobalt(III) complexes.

(b) Less basic amines lead to isomerisation of *trans* $-[Co(en)_2Cl_2]Cl$ to *cis* $-[Co(en)_2Cl_2]Cl$.

In addition, some disproportionation of the starting complex to $[Co(en)_3]^{3+}$ occurs.

The hydrolysis of halopentammines of cobalt(III), $[CoN_5X]^{2+}$, $(X = Cl,Br)$ obey the rate expression[92].

Rate = $k_{aq}[CoN_5X] + k_{OH}[CoN_5X][OH^-]$ where k_{aq} and k_{OH} are constants referring to aquation (acid hydrolysis) and base hydrolysis respectively.

Aquation is one of the most extensively studied reactions of cobalt(III) complexes[94-98]. All the available experimental data correlating various effects on the rates are compatible with the assignment of an S_N1 mechanism[92,99]. Factors affecting the aquation rate include:

(i) chelation which retards the rate of acid hydrolysis[100]. Accordingly, the rates of aquation decrease in the series[101,102]

trans $-[Co(Cyclam)Cl_2]^+$ (1) < *trans* $-[Co(en)_2Cl_2]Cl^+$(30) -

\- < *trans* $-[Co(en)(NH_3)_2Cl_2]^+$ (230) < *trans* $-[Co(NH_3)_4Cl_2]^+$ (1800).

(ii) Increased positive charge on the complex which retards the rate of acid hydrolysis e.g. $[Co(en)(dien)Cl]^{2+}$ (1) trans $-[Co(en)_2Cl_2]^+$[102] (60).

The base hydrolysis of cobalt(III) complexes has recently been reviewed by Tobe[103], Poon[104] and Edwards et al[105]. These reactions involve replacement of halide ion ($\bar{X}$) by hydroxide ion, viz.,

$$[Co(en)_2(NH_2R)X]^{2+} + OH^- \rightarrow [Co(en)_2(NH_2R)(OH)]^{2+} + X^-$$

and are usually quite rapid. Four different mechanisms have been proposed to account for the base hydrolysis of cobalt(III) halopentammines[106-110].

It is now generally accepted that the bulk of these reactions proceed by S_N1CB (Substitution Nucleophilic Unimolecular Conjugate base) mechanism which involves deprotonation of an amine ligand (eq 1) followed by a dissociative aquation of the amido conjugate base. Usually, the proton transfer is a reversible process and much faster than the overall base hydrolysis. This reaction scheme[100] can be illustrated as follows:

$$[Co(NH_3)_5Cl]^{2+} + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Co(NH_3)_4(NH_2)Cl]^+ + H_2O \qquad \ldots\ldots (1)$$

$$[Co(NH_3)_4(NH_2)Cl]^+ \xrightarrow[slow]{k_2} [Co(NH_3)_4(NH_2)]^{2+} + Cl^- \qquad \ldots\ldots (2)$$

$$[Co(NH_3)_4(NH_2)]^{2+} + H_2O \xrightarrow{fast} [Co(NH_3)NH_2(H_2O)]^{2+} \qquad \ldots\ldots (3)$$

$$[Co(NH_3)_4(NH_2)H_2O]^{2+} \xrightarrow{fast} [Co(NH_3)_5OH]^{2+} \qquad \ldots\ldots (4)$$

The general kinetic expression for the base hydrolysis reactions of cobalt(III) complexes can be derived as follows:

$$\text{Complex} + OH^- \xrightarrow{K} \text{Amido} + H_2O \qquad \ldots\ldots (5)$$

$$\text{Amido} \xrightarrow{k_2} \text{Products} \qquad \ldots\ldots (6)$$

At constant pH if k_2 is the rate determining step, then

$$\text{Rate} = k_{obs}[\text{Total complex}] \qquad \ldots\ldots (7)$$

$$= k_2\,[\text{Amido}] \qquad \ldots\ldots (8)$$

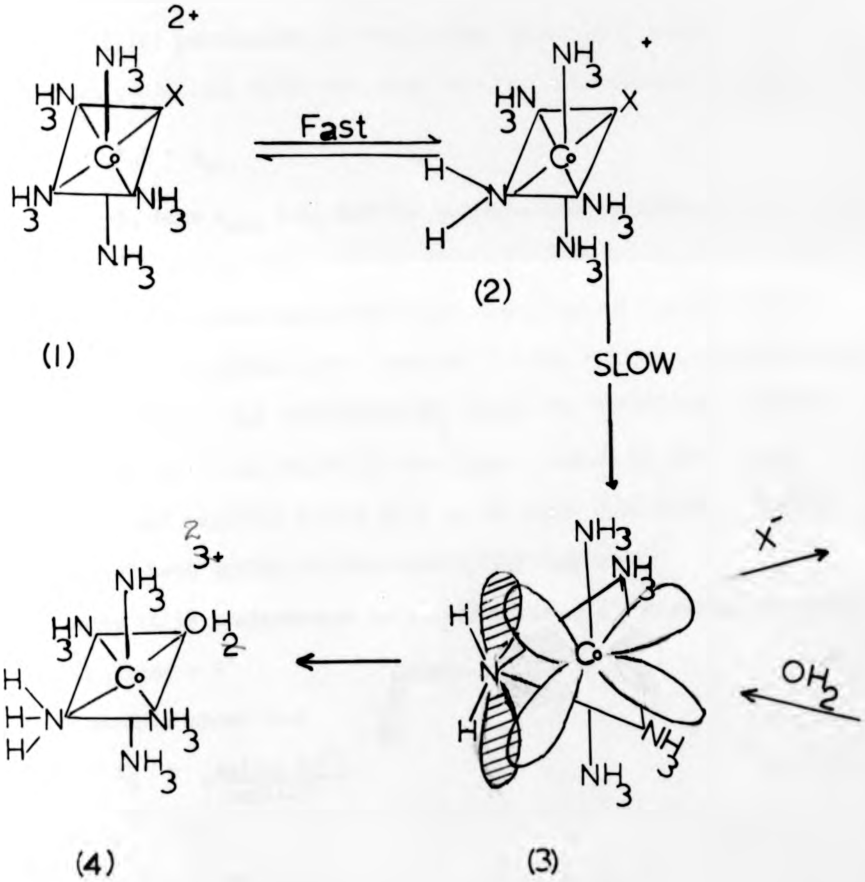
(Where [Total complex] = [Amido] + [Complex])

$$\text{Hence } k_{obs} = \frac{k_2[\text{Amido}]}{[\text{Total complex}]} \qquad \ldots\ldots (9)$$

$$K = \frac{[\text{Amido}]}{[\text{Complex}]\,[OH^-]} \qquad \ldots\ldots (10)$$

FIGURE 5

$S_N1C.B.$ MECHANISM



or [Amido] = K[complex] $[OH^-]$

9

Substitute for [Amido] and [Total complex] terms in eq (10)

$$k_{obs} = \frac{k_2[\text{complex}]\,[OH^-]}{[\,[\text{complex}] + [\text{Amido}]\,]}$$

or

$$k_{obs} = \frac{k_2K[\text{complex}]\,[OH^-]}{[\text{Complex}] + K[\text{complex}]\,[OH^-]\,]}$$

$$k_{obs} = \frac{k_2K[OH^-]}{1 + K[OH-]} \qquad \ldots\ldots (11)$$

Since cobalt(III) pentammines are weak acids (pKa > 15), under most experimental conditions K[OH] <<1, then equation (11) becomes $k_{obs}=k_2K[OH^-]$

or $\frac{k_{obs}}{[OH^-]} = k_2K = k_{OH}$.

If $K[OH^-]$ >>1, then $k_{obs} = k_2$ and the reaction becomes independent of the hydroxide ion concentration.

The absence of departure of the base hydrolysis of $[Co(NH_3)_5Cl]^{2+}$ from first order dependence, even when $[OH^-]$ = 0.1 → 1.0M , suggests that K < 0.05. Erickson[111] has determined pK_a values for Pt(II)-amine complexes from dependence of ^1H nmr shifts of the ligand protons on the concentration of strong alkali and reported values of K in the range 0.01-0.20. However, this method has not been applied to the cobalt(III) complexes.

In many cases it is preferential to consider the acid ionisation equilibria

$$\text{Complex} \overset{Ka}{\rightleftharpoons} \text{Amido} + H^+ \qquad \ldots\ldots (12)$$

It can be readily shown that

$$\text{if} \quad K_a = \frac{[\text{Amido}]\,[H^+]}{[\text{complex}]} \qquad \ldots\ldots (13)$$

$$K_a = kK_w$$

$$\text{hence } k_{obs} = \frac{k_2K_a[OH^-]}{(k_w + [OH^-]\,)} \qquad \ldots\ldots (14)$$

Where K_a is the acid dissociation constant of the complex substrate and K_w is the ionic product of water. Although K_a values for aquo complexes are easily determined by standard methods[112], attempts to determine K_a for amine complexes of Co(III) have been unsuccessful.

As S_N1CB mechanism requires the formation of an amido conjugate base and it has been observed that complexes lacking amino protons such as trans - $[Co(bipy)_2Cl_2]^+$ [113] and trans - $[Co(tep)_2Cl_2]$ [92] are insensitive to base hydrolysis.

Since the equilibrium concentration of the amido conjugate base equation (12) is a function of the acidity of the amino proton of the complex, it would be expected that for complexes containing acidic amines, base hydrolysis might be observed at low pH. Base hydrolysis of cis - $[Co(en)_2L(Cl]^{2+}$, where L represents a series of substituted anilines has been observed at pH values as low as 1 by Nanda et al[114] and by Chan[115].

Pearson and Edgington have provided an interesting evidence for the conjugate base mechanism from their study of the activity of peroxide ion in the base hydrolysis of $[Co(NH_3)_5NO_3]^{2+}$ and $[Co(NH_3)_5Cl]^{2+}$ complexes[116]. As peroxide ion is a weaker base but a stronger nucleophile than hydroxide ion, the base hydrolysis in the presence of peroxide ion should then proceed more slowly in case of an S_N1CB reaction and more rapidly in an S_N2 reaction. The results obtained are consistent with the S_N1CB process. In this reaction π-bonding by the amido group stabilises the 5-coordinate intermediate,

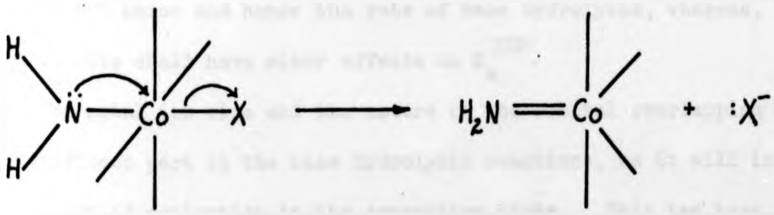


Figure (6) showing dissociation of ligand X by an amido group.

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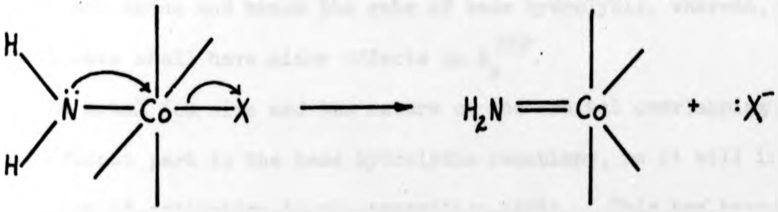


Figure (6) showing dissociation of ligand X by an amido group.

Buckingham et al have suggested that the labilizing effect of the amido group operates through the N - Co σ bond and a cis - amido group is necessary for effective hydrolysis in $[Co(trenen)\ X]$[117] complexes (where $X = Cl, N_3^-\ OH_2$)

The isotopic exchange experiments of Green and Taube[118] showed that O^{16} ^{16}O to O^{18} ratio in the hydroxo product of the base hydrolysis of $[Co(NH_3)_5X]^{2+}$ (where $X = Cl^-, Br^-, NO_3^-$) was constant and consistent with the value expected for water to be the entering group. This observation strongly suggests that the hydroxide ion only acts as a catalyst and a common five coordinate intermediate is involved in these reactions. However, the isotopic evidence cannot be generalised as found by Dolbear et al[119].

The dissociative nature S_N1CB mechanism has been examined in terms of activation parameter studies[120]. A positive Δs^* value is predicted for an S_N1CB reaction and the bulk of the experimental values for Δs^* lie between + 20 and + 40 cal $mole^{-1}$ deg^{-1}[105].

All the above cumulative evidence is highly favourable of the amido conjugate base being the reactive species in the base hydrolysis of cobalt(III) halopentammines.

Branching of the chain in the non-participating amine normally leads to a marked acceleration in the rate of base hydrolysis presumable due to steric acceleration of the dissociative mechanism[121]. Experiments of Palmer and Basolo have shown that increasing N-alkyl chelation will increase acid constant (K_a) of the amine and hence the rate of base hydrolysis, whereas, C-alkyl substituents shall have minor effects on K_a[122].

The metal ion size and the nature of the orbital overlapping also plays a significant part in the base hydrolysis reactions, as it will in turn effect the energy of activation in the transition state. This has been shown by studying the base hydrolysis reactions of $[Rh(NH_3)_5Br]^{2+}$ and $[Co(NH_3)_5Br]^{2+}$ complexes. The greater the number of d-electrons on the central metal atom, the faster its conjugate base must react (cobalt (III) faster than chromium)[123,124].

Earlier experiments have revealed that the rate of base hydrolysis of halopentammines of cobalt(III) at ionic strength 0.1M remains unaffected within the experimental error by the ionic species used to maintain the ionic strength[121].

The present work extends the scope of base hydrolysis and the characterisation of several chloro as well as an$\overset{a}{o}$lgous bromo straight chain and sterically congested amine complexes of cobalt(III).

2.2 EXPERIMENTAL

2.2.1 Preparation of Compounds

Trans-dichloro-bis(ethylenediamine)Cobalt(III) Chloride . -

This compound was prepared by Bailar's procedure[125]; better yields of the product can be obtained in less reaction period by a more recent method[126] [trans - $[Co(en)_2Cl_2]Cl$; requires Cl, 37.34;

Found Cl, 37.8%

Trans-dibromo-bis(ethylene diamine)Cobalt(III) Bromide . -

The method described by Werner[86] has been slightly modified to prepare this compound.

Cobalt (II) bromide hexahydrate[127] (156g) was dissolved in water (100 cm^3) and 1,2-diaminoethane (480 cm^3, 10%)was added very slowly with continuous stirring over a period of two hours. The reaction mixture was cooled to 0°C and hydrogen peroxide (90 cm^3, 30%) added slowly with stirring maintaining the temperature below 10°C. The resulting solution was warmed on a water bath (60°) for 30 minutes and hydrobromic acid (100 cm^3, 48%) added, followed by evaporation to dryness on an evaporator. This procedure was repeated at least three times and finally, bright green product was recrystallised from the minimum amount of acidified (HBr) hot water and dried in an oven at 110° yield ∿ 210g (69%).

(Calc. for $C_4H_{16}N_4CoBr_3$; C, 11.47; H, 3.85; N = 13.38;
Found C, 11.80; H, 4.12; N, 13.67%)

2.2.2 Preparation of Complexes

(a) Primary amines

is - bromoamine bis(ethylenediamine) cobalt(III) Dibromide;

cis - $[Co(en)_2(NH_2R)Br]Br_2$. -

(R = C_2H_5, n-C_3H_7, n-Bu, n-amyl, n-hexyl)

These complexes were prepared by the Bailar and Clapp[93] method and purified by Gel-filtration technique as described slightly later.

Trans - $[Co(en)_2Br_2]Br$ (4.18g, 0.01 moles) was ground into a paste in water ($2cm^3$) and a small excess of the appropriate amine was added to it. The colour of the paste rapidly changed from bright green to the characteristic purple-red of the bromopentammine cobalt(III) complexes. After half an hour, the coagulated mixture was filtered on a sintered glass funnel and the product washed with methanol until washings were colourless. The crude complex was purified and recrystallised from the minimum amount of hot water and purple-red crystalline complex obtained on cooling, was filtered off and dried in vacuo.

cis - $[Co(en)_2NH_3(Br)]Br_2$

The above procedure was repeated using aqueous ammonia solution(ρ=0.88) and recrystallised from hot water, dried in vacuo. yield ~ 60%

cis - $[Co(en)_2(MeNH_2)Br]Br_2$

The method of preparation was identical to that used in the ethylamine case except appropriate amount of aqueous methyl amine (30%). The crude product was recrystallised from hot water and dried in vacuo.

TABLE 15

Analytical Figures for the Bromopentammines

Cis - $[Co(en)_2(NH_2R)Br]Br_2$

R	Calculated			Found		
	% C	% H	% N	% C	% H	% N
H	11.02	4.39	16.06	10.80	4.64	15.79
Me	13.28	4.68	15.49	13.06	4.85	15.26
Et	15.46	4.98	15.03	15.47	5.19	14.96
n-Pr	17.55	5.48	14.62	17.48	5.40	14.56
n-Bu	19.53	5.54	14.23	19.76	5.66	14.31
n-amyl	21.35	5.77	13.84	21.47	5.87	13.72
n-hexyl	23.09	6.00	13.46	23.23	6.04	13.27

Cis -Aquo(n-butylamine) bis (ethylene diamine) Cobalt(III) Nitrate Monohydrate;

cis -$[Co(en)_2(NH_2Bu^n)H_2O](NO_3)_3.H_2O$. -

The compound was prepared essentially by the method of Chan and Leh[128]

Mercuric nitrate (36g) in 100 cm^3 of nitric acid (2M) was added to a suspension of *cis* -$[Co(en)_2(NH_2Bu^n)Br]Br_2$ (5g) in 100 cm^3 of 2M nitric acid at 60°C. The resulting solution was stirred for 15 minutes and filtered whilst hot. Ethanol-ether (200 cm^3, 1:1 v/v) mixture was added and the solution left in a refrigerator overnight to crystallize. The orange-red crystals were filtered, purified by gel-filtration and recrystallised from nitric acid (1M) at 60°C.

(Calc. for $CoC_8H_{22}N_8O_{11}$; C, 20.65; H, 4.76; N, 24.08;
Found C, 20.81; H, 4.92; N, 24.5)

Visible spectrum

The visible spectrum was recorded at pH 1 (0.1M HCl) and pH 14 (0.1M NaOH).

This was to allow for the two extremes of the equilibrium, Figure (7).

$$[Co(en)_2(NH_2C_4H_9(OH_2)_2]^{3+} \rightleftarrows [Co(en)_2(NH_2C_4H_9)OH]^{2+} + H^+$$

Acid Base

Cis - Chloro(aminoacetaldehyde dimethylacetal)bis(ethylene diamine) cobalt(III) Dichloride; *cis* -$[Co(en)_2(NH_2CH_2CH(OMe)_2Cl]Cl_2$. -

2.86g of *trans* -$[Co(en)_2Cl_2]Cl$ was ground to a paste with 3cm^3 of water and an equimolar amount of amino acetaldehyde dimethylacetal was added dropwise with continuous grinding for 30 minutes. The coagulated product was crystallized on addition of methanol (30cm^3) and purified by gel-filtration, the pure complex was recrystallized from hot water.

(Calc. for $C_8H_{28}N_5CoCl_3O_2$; C, 24.59; H, 6.96; N, 17.92;
Found C, 24.27; H, 6.90; N, 18.06%,)
Visible spectrum: 528(ε = 78) and 368 nm (ε = 90).

Cis - bromo(amino acetaldehyde dimethylacetal)bis(ethylenediamine) cobalt(III) dibromide;
cis -$[Co(en)_2(NH_2CH_2CH(OMe)_2Br]Br_2$. -

The above procedure was repeated and the crude complex was recrystallized from hot water and dried in *vacuo*.

(Calc. for $C_8H_{28}N_5CoBr_3O_2$: C, 18.33; H, 5.19; N, 13.36;
Found C, 18.50; H, 5.44; N, 13.80%).
Visible spectrum: 546 nm (ε = 79).

(b) alicyclic amines and amino alkanols

Cis - Bromo(cyclopropylamine)bis(ethylenediamine)cobalt(III) Dibromide; cis -$[Co(en)_2C_3H_7N)Br]Br_2$. -

trans - dibromo bis(ethylenediamine) cobalt(III) complex(4.18g, 0.01 moles) was finely powdered and equimolar amount of cyclopropylamine syringed into this green product with 3 cm^3 of water. The green paste was ground for an hour occasionally during which period the colour changed from green to purple-red. The crude product was filtered off and purified by the method used for analogous alkylamine complexes.

(Calc. for $C_5H_{15}N_3CoBr_3$: C, 17.66; H, 4.87; N, 14.71;

Found C, 17.38; H, 4.86; N, 14.49%)

Visible spectral data: λmax = 548 nm (ε = 81)

Cis -Chloro(cyclopropylamine) bis(ethylenediamine)cobalt(III) Dichloride Monohydrate;

cis -$[Co(en)_2\ (C_3H_7N)Cl]Cl_2.H_2O$. -

This complex was prepared by following Chan's method[129] and the crude complex was purified and recrystallized from hot water (60°). Brick-red product obtained on cooling, filtered and dried in vacuo.

(Calc. for $C_5H_{17}N_3CoCl_3O$: C, 23.31; H, 6.98; N, 19.42;

Found C, 23.66; H, 6.85; N, 19.49%)

visible spectral data: λmax 527(ε 73) and 348nm (ε=82).

Cis - Bromo(3-amino-1-propanol)bis(ethylenediamine) cobalt(III)Dibromide; cis -$[Co(en)_2(NH_2CH_2CH_2CH_2OH)Br]Br_2$. -

trans -$[Co(en)_2Br_2]Br$ (4.18g, 0.01 moles) and 3-amino-1-propanol (0.75g, 0.01 moles) were ground together in a pestle and mortar with 2-3cms^3 of water for 30 minutes. The colour of the paste slowly changed from green to purple-red followed by coagulation on long standing. The crude product was filtered off and purified by chromatographic filtration. Fine purple-red crystalline complex obtained on recrystallisation from hot water.

(Calc. for $C_7H_{25}N_5CoBr_3O$: C, 17.01; H, 5.10; N, 14.17;
Found C, 17.11; H, 5.11, N, 14.05%)

Visible spectral data in aqueous solution gives λ max 547 (ε = 84)

Cis - Bromo(6-amino-1-hexanol)bis(ethylenediamine) cobalt(III) Dibromide; *cis* -$[Co(en)_2(NH_2(CH_2)_6OH)Br]Br_2$. -

The complex was prepared by repeating the above method using 6-amino-1-hexanol and recrystallized from the minimum amount of hot water. (Calc. for $C_{10}H_{31}N_5CoBr_3O$: C, 22.40, H, 5.82; N, 13.06; Found C, 22.16; H, 5.82; N, 12.96%)

Visible spectra: λmax 545 nm (ε = 76).

2.2.3 Purification of Cis -$[Co(en)_2NH_2R)Br]Br_2$ complexes.

(R = H, Me, Et, n-pr, n-Bu, n-amyl, n-hexyl)

Gel chromatography has been extensively used as a biochemical separation technique[130,131] and more recently to separate cobalt(III) complexes[132]. The white colour of the matrix and no contamination of the products makes visual detection and separation of the fractions easy.

The type of G-10 Sephadex (SP) was used in gel chromatography filtrations because the molecular weights of cobalt complexes were of the order of 500 with cms X 1.5cm column dimensions.

The following method has been used to obtain pure Bromopentammine complexes of cobalt(III).

The crude complex was dissolved in minimum amount of hot water (6C°C) and pipetted in to the G-10 Sephadex Column. On elution, with slightly acidified water, two major bands were obtained.

The first and faster moving orange-yellow band was ascribed to tris-ethylenediamine cobalt(III) confirmed by visible spectra and discarded.

The second purple-red band of the desired complex was collected and concentrated on a rotary evaporator to about 5cm^3. Pure purple-red crystalline products obtained on cooling, filtered and recrystallized from the minimum amount of hot water.

2.2.4 Base Hydrolysis of Cobalt Bromopentammines of the type $[Co(en)_2(NH_2R)Br]Br_2$

These compounds were hydrolysed within the pH range 8.50 to 9.50 in aqueous media at an ionic strength of 0.1M ($NaClO_4$). Reactions were followed spectrophotometrically on a Gilford 2400S instrument by adopting the following method.

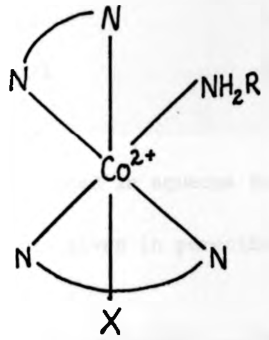
A known amount of the substrate was dissolved by rapidly inverting the stoppered cell three to four times before measurements were begun. Pseudo first order rate constants were obtained from the plots of log $[OD_t-OD_\infty]$ or log $[OD_\infty-OD_t]$ against time. Kinetic data giving rise to plots which were not linear over at least 3 reaction half lives were rejected. Normally, the cell compartment temperature was monitored periodically during the course of a kinetic run. A temperature deviation of greater than ± 0.2° was considered unacceptable. The pH of the kinetic solutions was determined prior to the completion of reaction.

2.3 RESULTS AND DISCUSSION

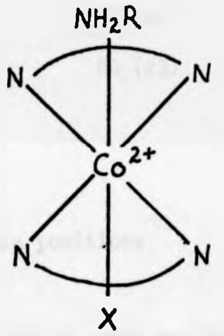
The reaction of aliphatic amines with trans-$[Co(en)_2X_2]^+$ (X=Cl,Br) has been used to prepare several halopentammines of the type $[Co(en)_2(RNH_2)X]^{2+}$ (RNH_2 = normal straight chain and branched chain amines, amino alkanols, cyclopropylamine; X=Cl,Br).

2.3.1 Configuration of Reactant Complexes

The halopentammine cobalt(III) complexes can exist as the cis or trans isomers.



cis I



trans II

All the complexes have been assigned a cis - configuration on the basis of a variety of spectroscopic measurements

2.3.2 Spectral Measurements

(i) Electronic Visible Spectra: The visible absorption spectra of the cobalt(III)-bromopentammines prepared are given in Table (16). Two spin allowed d-d transitions are commonly observed for octahedral cobalt(III) complexes i.e. a band at longer wavelength assigned to the $^1A_{1g} \rightarrow {}^1T_{1g}$ transition and one at shorter wavelength assigned to the $^1A_{1g} \rightarrow {}^1T_{2g}$ transition The visible spectra of cis and trans $-[Co(en)_2(NH_3)Cl]Cl_2$ shows that the absorption maxima in these two isomers are essentially the same, but the intensities of the cis-isomer are much greater than those of the trans-isomer

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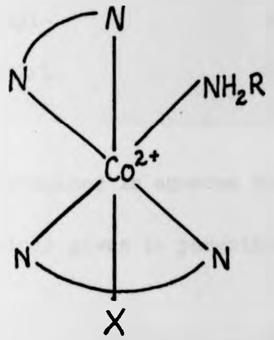

cis I

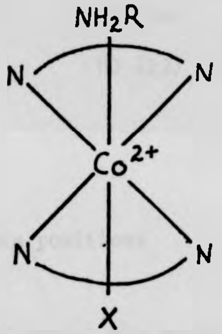

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TABLE 16

Visible spectra[†] of cis -$[Co(en)_2(RNH_2)Br]Br_2$ complexes

(R=)	λmax(nm)	ε/(l mol^{-1}cm^{3})
H	544 (425)[*]	75 (18)[*]
Me	548 (431)	71 (20)
Et	547 (429)	72 (22)
n.Pr	549 (430)	81 (23)
n-Bu	546 (428)	78 (21)
n-amyl	546 (431)	79 (24)
n-hexyl	545 (429)	80 (23)

[†] determined in aqueous solutions

[*] values given in parentheses correspond to λmin positions

For the cis-isomer λmax 525(ε=73) and 365 nm (ε=77); for the trans-isomer λmax 525(ε=47) and 367 nm (ε=53). However, for bromopentammines (CoN_5Br), one major band[133] at 546 ± 2 nm in the visible spectrum is observed with molar extinction coefficients in the range 70-75. The shorter wavelength band in bromopentammines is obscured by the charge transfer band in the ultraviolet which carries over into the visible region.

From the data of Table (16) it is clear that the spectra of all the complexes are very similar and there is a close resemblance between the bromopentammines and chloroamine complexes of cobalt(III). This strongly suggests the cis configuration (I) for the complexes.

(ii) Infrared spectra: Additional evidence for the cis-configuration of the complexes comes from infrared studies.

TABLE 17

Some characteristic Infrared stretching frequencies (cm^{-1}) of the cobalt-ethylene diamine rings of some cis-$[Co(en)_2(RNH_2)Br]Br_2$ complexes

Amine (RNH_2)	CH_2 rocking^{-1}, frequencies	NH_2 bending frequencies (cobalt-ethylenediamine ring)
Ethyl amine	892s, 876s	1573s,sp, 1618w
n-Propylamine	894s, 873s	1559s, sp, 1613w
n-Butylamine	902s, 894s	1578sp, 1594w
n-Amylamine	896s, 872m	1580sp, 1608w
H-hexylamine	895m, 877m	1582s, 1609sh
Methyamine	890s, 878s	1587, 1610s

s-strong, sp-split, m-medium, sh-shoulder, w-weak, br-broad.

The splitting of the δ(NH) bands of the NH_2 groups of the ethylenediamine chelate rings into two peaks at ca. 1612(w) and $1574cm^{-1}$(vs) is consistent with a cis-configuration. Trans-complexes generally show no splitting in this region[134], due to the higher symmetry of the complexes.

Baldwin has shown that the infrared spectra of cis and trans - isomers of bis(ethylenediamine) cobalt(III) complexes differ in the CH_2 rocking region ($880-900cm^{-1}$). In this region, the cis-isomer, due to the lower symmetry shows two bands and the trans-isomer only one band[135]. All of the complexes show two bands in this region.

In addition, Bailar et al suggested that cis and trans configuration of cobalt(III) bis(ethylenediamine) complexes may be distinguished in the region ($1100-1200cm^{-1}$). In this region two bands are observed in the cis-complexes, and only one band in the trans-complexes[71].

Finally, Hughes and McWhinnie have observed four bands in cis-complexes and three in the trans-complexes in the region $510-600cm^{-1}$[136]. Most of the complexes have three bands in this region.

The infrared data is summarised in Table Table (17).

(iii) N.M.R. Spectra

Clifton and Pratt[137] have shown that for the n.m.r. spectra of amine and ethylenediamine cobalt(III) complexes in D_2O, the nitrogen protons exhibit a chemical shift dependent on the geometry of the complex. Protons attached to a nitrogen atom trans to a chloro ligand in either a pentammine or bis ethylenediamine cobalt(III) complex resonated at higher field strength than the protons bonded to a nitrogen atom cis to these ligands. The cis - bis-(ethylenediamine) cobalt(III) complexes reported have two peaks attributed to nitrogen protons, while the trans-isomers displayed a single peak. This has been verified by Buckingham et al[138] though they claim that cis-isomers have three NH peaks.

TABLE 18

Chemical shifts of ethylenediamine (CH_2), NH protons and alkylamine proton resonances of cis-[Co(en)$_2$(RNH_2)Br_2 complexes

(in perdeutro Dimethyl Sulphoxide)

	Alkylamine		Ethylenediamine	
RNH_2	CH_3 triplet	Methylene proton	CH_2 protons	NH proton resonances
NH_2	-	-	2,85,2.56,2.46	5.78,5.30,5.02,4.63
$MeNH_2$	2.19	-	2.53,2.61,2.72,2.83	5.88,5.48,5.18,4.69
$EtNH_2$	1.29,1.21,1.15	-	2.80,2.67,2.58,2.49	5.75,5.40,4.98,4.50
n-$PrNH_2$	1.00,0.92,0.84	1.70,1.65,1.48	2.85,2.65,2.56,2.57	5.74,5.40,4.75,4.30
n-$BuNH_2$	0.98,0.90,0.83	1.72,1.64,1.47,1.40	2.80,2.65,2.55	5.74,5.40,4.75,4.30
n-$AmylNH_2$	0.90,0.85,0.76	1.64,1.58,1.50	2.79,2.62,2.55,2.45	5.69,5.34,4.71,4.33
n-$HexylNH_2$	0.94,0.89,0.83	1.82,1.72,1.69,1.59	2.80,2.65,2.55,2.46	5.71,5.32,4.69,4.35

Lantzke and Watts[139] have investigated a number of bis (ethylenediamine) cobalt(III) complexes, and thereby have found a relationship between the configuration of the complex and (a), the chemical shifts for the carbon proton resonances and (b), the band widths at half-height ($w_{\frac{1}{2}}$) for nitrogen protons of ethylenediamine. All the cis-complexes gave signals below 3.00δ (with a mean value of 2.88δ) whereas the trans-isomers exhibited signals at a value greater than 3.00δ.

For the present studies the spectra were recorded in perdeutro DMSO as exchange of the nitrogen protons does not occur in DMSO as in D_2O. NaTMS was used as internal reference. In general, all the spectra show,

(1) A characteristic broad and complex band at 2.75 ± 0.05 δ due to the NCH_2CH_2N protons consistent with a cis-stereochemistry.

(2) Four broad peaks due to the NH protons at approximately (4.50 to 5.80 ± 0.2)δ Table (18) also consistent with a cis -stereochemistry.

Additional signals also occur in the expected position for the primary amine ligand.

2.3.3 Stereochemistry

The base hydrolysis of cobalt(III) chloropentammines has been shown to occur with retention of configuration[121,128].

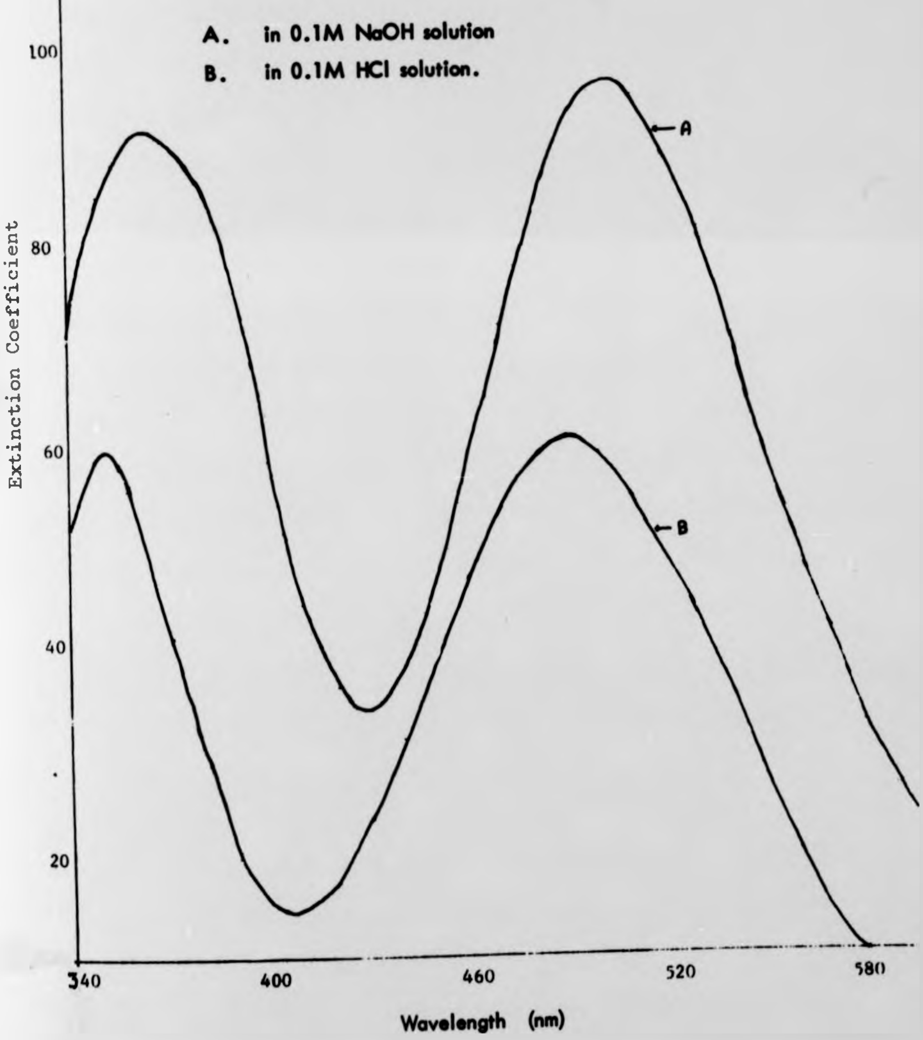
Experiments were carried out to confirm that a similar stereochemical result occurred with the bromopentammines of cobalt(III).

A sample of cis-aquo (n-butylamine) bis(ethylenediamine) cobalt(III) nitrate was prepared by mercury(II) catalysed aquation of the bromopentammine complex. It has been established that mercury(II) catalysed aquations occur with retention of configuration[96,102]. The spectrum of the hydroxy-pentammine obtained by base hydrolysis of cis-bromo (n-butylamine) bis(ethylenediamine) cobalt(III) has λmax 504 (ε=114) and 358 nm (ε = 101). This spectrum is almost identical to that of cis-aquo(n-butylamine) bis(ethylenediamine) cobalt(II) determined in 0.1M sodium hydroxide, λmax 501 (ε=113) and 354 nm (ε=109).

FIGURE 7

Visible Absorption Spectrum of

cis - $[Co(en)_2(n\text{-}BuNH_2)H_2O](NO_3)_3 \cdot H_2O$



The CoN_5O chromophore normally has λmax 505 nm[121]. Thus unless the spectra of cis and trans -aquopentammines are virtually identical, it appears that base hydrolysis occurs with essentially complete retention of configuration.

$$cis\text{-}[Co(en)_2(RNH_2)Br]^{2+} + OH^- \rightarrow cis\text{-}[Co(en)_2)(NH_2R)OH]^{2+} + Br^-$$

The visible spectra of the products obtained on base hydrolysis of the other bromopentammines were fully consistent with the formation of hydroxy pentammines.

2.3.4 Kinetic Studies

The rate law for the base hydrolysis of cobalt(III) halopentammines has been established for a wide variety of complexes[92]

$$\frac{-d[\text{complex}]}{dt} = k_{OH}[\text{complex}][OH^-]$$

At constant pH, controlled by the use of a pH-stat or spectrophotometrically, the reaction becomes pseudo-first order in complex. The observed pseudo-first order rate constant k_{obs} is related to k_{OH} (the second order rate constant) by the expression, $k_{obs} = k_{OH}[OH^-]$, (See Section 2.1). Values of $[OH^-]$ are obtained from the pH ($= -\log\{H^+\}$), where braces represent activities, using activities coefficients calculated from Davies equation[7]. The base hydrolysis of the halopentammines may be summarised by the equation:

cis $-[Co(en)_2(NH_2R)X]^{2+} + OH^- \rightarrow [Co(en)_2(NH_2R)OH]^{2+} + X^-$ (where $X=Cl^-, Br^-$).

Hay and Cropp[121] have studied the base hydrolysis of several straight chain amine derivatives of the type cis $-[Co(en)_2(RNH_2)Cl]^{2+}$ (R = Me, Et, n-Pr, n-Bu) and found that these complexes hydrolysed at essentially the same rate with $k_{OH} = 1.2 \times 10^1 M^{-1}s^{-1}$ at 25.0°C and I = 0.1M. This result is inconsistent with the previous data of Chan[141], who found a significant variation in rate constants at 0°C, Table (19).

TABLE 19

Base hydrolysis kinetics* of cobalt(III) halopentammines at 25.0° and I=0.1M.

R	Cis $-[Co(en)_2(RNH_2)Cl]Cl_2$		Cis $-[Co(en)_2(RNH_2)Br]Br_2$	
Me	12.0^{a}	$^{\Delta}7.1^{c}$	$^{\dagger}71.8^{b}$	$^{\Delta}50^{c}$
Et	12.0	6.5^{c}	70.9^{b}	47^{c}
n-Pr	12.0	11.1^{c}	-	273^{c}

* $M^{-1}s^{-1}$ Δ at 0°C † average of two values (pH-stat)

a = ref 121 b = ref 140 c = ref 141

In addition, Chan and Leh[90] have reported that for the base hydrolysis of $[Co(NH_3)_5Cl]^{2+}$ and $[Co(NH_3)_5Br]^{2+}$ at high base concentrations a deviation from a first order dependence on $[OH^-]$ occurred.
Buckingham and Sargeson have been unable to reproduce this work[142]. Similar conclusions have also been reached by Hay and Barnes[143].

In the present investigations a wide range of *cis*-$[Co(en)_2(amine)Br]^{2+}$ type complexes have been studied since Chan has claimed that the rate of base hydrolysis of these complexes is dependent upon the nature of the primary amine ligand. Very preliminary work by Cropp[140], Table (19) did not support this view and as a result a detailed study of these reactions was undertaken.

(a) *Cis* -$[Co(en)_2(NH_2R)Br]Br_2$. -

The base hydrolysis of *cis* -$[Co(en)_2(NH_2R)Br]Br_2$ (R=H, Me, Et, *n*-Pr, *n*-Bu, *n*-amyl, *n*-hexyl) complexes was studied spectrophotometrically on a Gilford 2400S spectrophotometer in the pH-range 8.50 - 9.50. All kinetic measurements were carried out at 25.0°C and I = 0.1*M*. The data in Table (20) includes the observed first-order rate constants (k_{obs}) and the second order rate constant (k_{OH}) values.

All hydrolyses exhibited a first-order dependence on hydroxide ion as indicated by sensibly constant values of k_{OH}, Table (21), as the primary alkyl group is varied in agreement with the observations of Hay and Cropp[121] for the analogous chloro derivatives. Some typical plots for the base hydrolysis of *cis* -$[Co(en)_2(n\text{-}PrNH_2)Br]Br_2$ complex are shown in Figure (7).

The bromo complexes undergo base hydrolysis five to six times more rapidly than the chloro complexes. Long *et al* have reported a similar rate enhancement for $[Co(en)_2(NH_3)Br]^{2+}$ relative to $[Co(en)_2(NH_3)Cl]^{2+}$ [96,144] complex. The values of k_{OH} for the chloro and bromopentammines of cobalt(III) are summarised in Table (21).

TABLE 20

Rate constants for the base hydrolysis of Bromopentammines of the type cis - $[Co(en)_2(RNH_2)Br]Br_2$ determined spectrophotometrically at 25.0 ± 0.2°C and I = 0.10M ($NaClO_4$) λ = 315 nm

	pH	$10^3k_{obs}/s^{-1}$	$10^{-1}k_{OH}/M^{-1}s^{-1}$
R=H	9.59	3.56	7.06
	9.35	1.89	6.53
	9.18	1.41	7.23
	9.18	1.30	6.68
	8.98	0.831	6.81
	8.77	0.510	6.68
	8.59	0.371	7.36
R=Me	9.38	2.55	8.20
	9.19	1.60	8.23
	8.98	0.990	7.96
	8.79	0.663	8.31
	8.59	0.418	8.30
R=Et	9.57	3.72	7.70
	9.30	1.95	7.58
	9.19	1.63	8.13
	8.98	0.923	7.86
	8.73	0.525	7.56
	8.54	0.368	8.20

Table 20 (Contd.).

R	pH	$10^{3}k_{obs}$ s^{-1}	$10^{-1}k_{OH}$ $M^{-1}s^{-1}$
R=n-Pr	9.57	3.87	8.05
	9.32	2.21	8.18
	9.32	2.23	8.26
	9.17	1.48	7.76
	8.97	0.970	7.85
	8.73	0.548	7.88
	8.53	0.338	7.70
R=n-Butyl	9.57	3.95	8.18
	9.32	2.11	7.81
	9.18	1.51	7.75
	8.73	0.571	8.20
	8.53	0.363	8.26
	9.01	1.12	8.46
R=n-amyl	9.58	4.18	8.50
	8.99	2.00	8.31
	9.27	1.12	8.80
	8.55	0.328	8.25
	8.55	0.391	8.50
R=n-hexyl	9.59	4.40	8.73
	9.58	4.06	8.05
	9.27	2.60	8.30
	8.98	1.12	8.80
	8.74	0.575	8.26
	8.56	0.383	8.33

Table 21

Summary of Base hydrolysis Rate constants (k_{OH}) of Cobalt(III) halopentammines of the type cis-$[Co(en)_2(NH_2R)X]^{2+}$ at 25.0° and I = 0.1M (where X = Cl,Br)

Amine	pK_a of amine* at 25.0°C	$k_{OH}^{Br}(M^{-1}s^{-1})$	$k_{OH}^{Cl}(M^{-1}s^{-1})$†	k_{OH}^{Br}/k_{OH}^{Cl}
NH_3	9.27	70.2 ± 3.5	8.08	8.7
Me	10.67	82.0 ± 2.0	12.75	6.4
Et	10.67	78.3 ± 3.0	12.83	6.1
n-Pr	10.69	79.0 ± 1.5	12.75	6.2
n-Bu	10.66	81.1 ± 2.5	12.75	6.4
n-Amyl	10.64	84.7 ± 2.0	-	-
n-Hexyl	10.64	84.8 ± 3.0	-	-

*Ref No (146) †Ref No (121)

Table 21

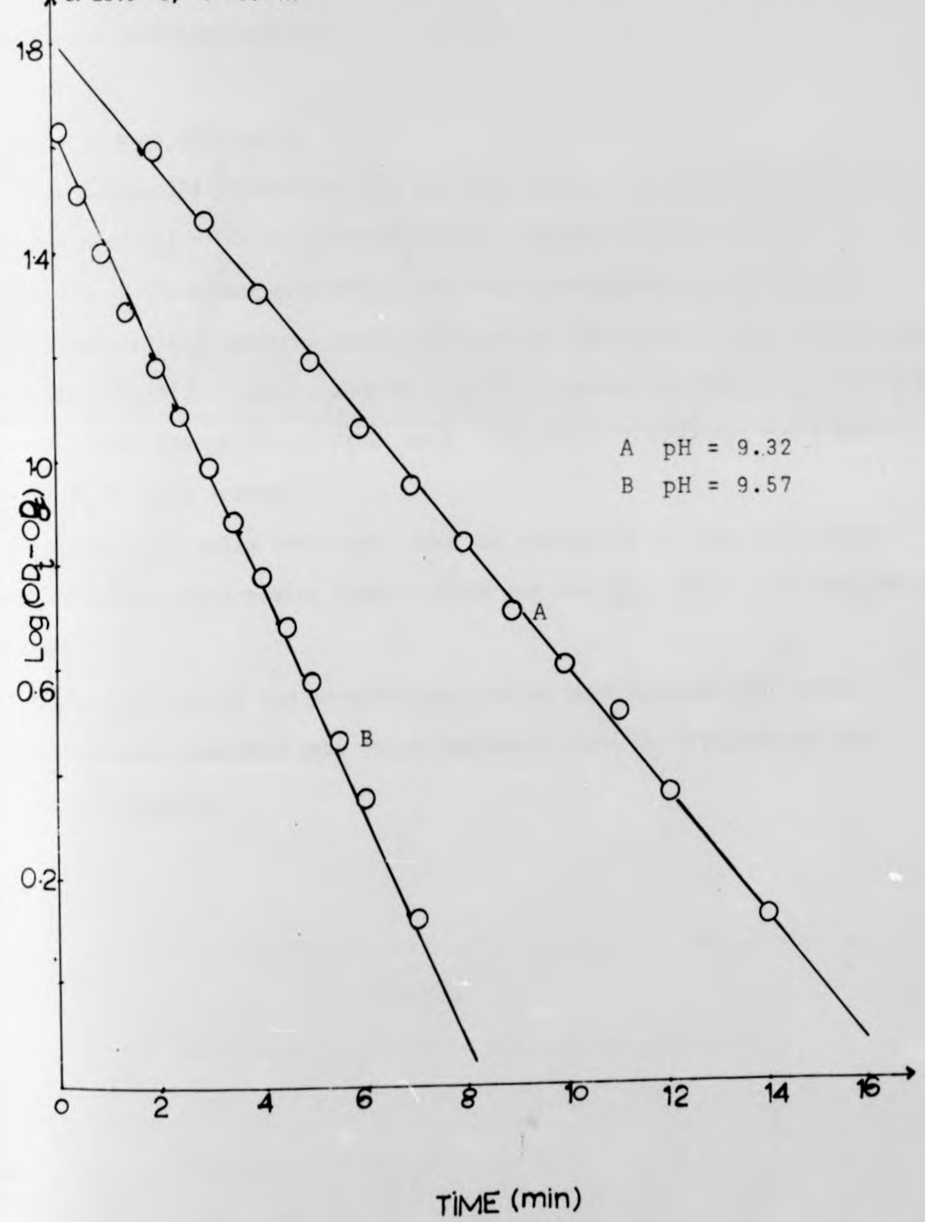
Summary of Base hydrolysis Rate constants (k_{OH}) of Cobalt(III) halopentammines of the type cis-$[Co(en)_2(NH_2R)X]^{2+}$ at 25.0° and I = 0.1M (where X = Cl,Br)

Amine	pK_a of amine* at 25.0°C	$k_{OH}^{Br}(M^{-1}s^{-1})$	$k_{OH}^{Cl}(M^{-1}s^{-1})$†	k_{OH}^{Br}/k_{OH}^{Cl}
NH_3	9.27	70.2 ± 3.5	8.08	8.7
Me	10.67	82.0 ± 2.0	12.75	6.4
Et	10.67	78.3 ± 3.0	12.83	6.1
n-Pr	10.69	79.0 ± 1.5	12.75	6.2
n-Bu	10.66	81.1 ± 2.5	12.75	6.4
n-Amyl	10.64	84.7 ± 2.0	-	-
n-Hexyl	10.64	84.8 ± 3.0	-	-

*Ref No (146) †Ref No (121)

FIGURE 8

Kinetic plots for the Base hydrolysis of cis - $[Co(en)_2(n\text{-}Pr\,NH_2)Br]Br_2$ at 25.0 °C, I = 0.1 M



The electron donating (+I) effect of the alkyl group leads to a small but significant increase in the rate of base hydrolysis[145] which is not unexpected since an electron releasing group would be expected to stabilise the 5-coordinate intermediate.

Products of base hydrolysis

The figure (8) illustrates the spectral changes observed on base hydrolysis of cis - $[Co(en)_2(n\text{-}BuNH_2)Br]Br_2$ complex in borax buffer. Conversion of the bromopenta-ammine into the hydroxypenta-ammine leads to a significant visible spectral change owing to an alteration of the ligand field about the cobalt(III) ion. Thus an N_5Br donor system has λmax at ca. 546 ± 2nm for the lowest energy ligand field band, compared with λmax ca. 504 ± 3nm for the N_5OH donor system[147].

These changes are fully consistent with the conversion of bromo-pentammine into the hydroxypenta-ammine (λmax = 505nm for the cis - $[Co(en)_2(n\text{-}BuNH_2)Br]Br_2$ complex]

The visible spectra of the products obtained on base hydrolysis of other bromopentammine complexes were fully consistent with the formation of the hydroxypenta-ammine.

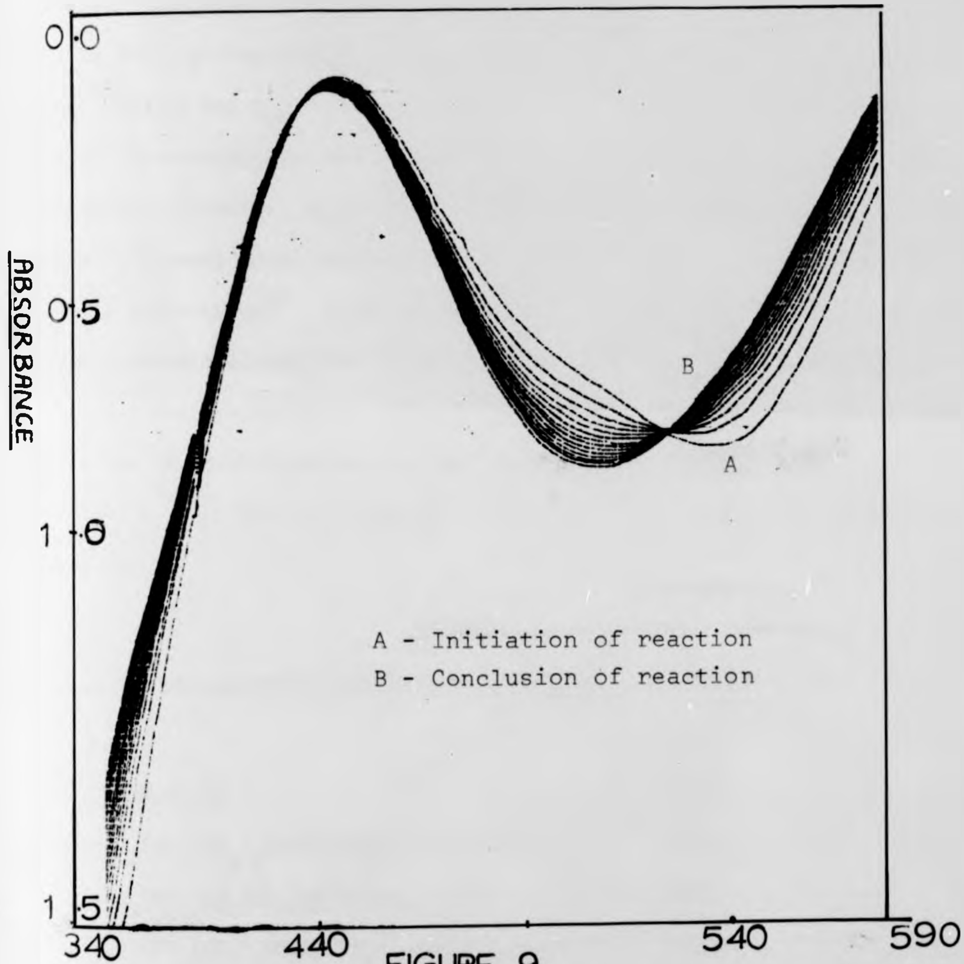


FIGURE 9

Visible spectra obtained during the course of Base hydrolysis of cis – $[Co(en)_2(Bu^n NH_2)Br]Br_2$ in Borax buffer. (pH 9.18)

(b) cis - $[Co(en)_2(NH_2(CH_2)_nOH)Br]Br_2$ (where n = 3.6)

A kinetic study was also carried out on the base hydrolysis of complexes of the type cis - $[Co(en)_2NH_2(CH_2)_nOH)Br]^{2+}$ (where n = 3,6) at 25.0° and I = 0.10M. The spectrophotometric rate constants k_{obs} are summarised in the Table (23), giving a value of $k_{OH} = 1.50 \pm 0.04 X 10^2 M^{-1} s^{-1}$ for 3-amino-1-propanol complex and $k_{OH} = 1.08 \pm 0.04 X 10^2 M^{-1} s^{-1}$ for the 6-amino-1-hexanol complex. These constants are similar to the rate constants reported for the ethanolamine derivative, ($k_{OH} = 1.45 X 10^2 M^{-1} s^{-1}$) [148]. Hydrolysis of the penta-amino alkanol bromo complex is about twice as rapid as the corresponding alkylamine derivatives,[121] a result which has been commented on by Chan and Leh[149].

The bromoaminoalkanol bis (ethylenediamine) cobalt(III) bromide complexes have a cis - configuration, as shown by the i.r. data e.g. the presence of two bands in the CH_2 rocking region of the ethylenediamine chelate rings (870-900cm^{-1})[135]. The i.r. data due to νOH in these complexes is summarised in Table 22.

TABLE 22

νOH(cm^{-1}) of some aliphatic alcohols and cobalt(III) complexes

CH_3OH	3645	a
$CH_3CH_2CH_2CH_2OH$	3636	b
cis-$[Co(en)_2(NH_2(CH_2)_3OH)Cl](NO_3)_2$	3571	c
cis-$[Co(en)_2(NH_2(CH_2(CH_2)OH)Br]Br_2$	3360	*
cis-$[Co(en)_2(NH_2(CH_2)_6OH)Br]Br_2$	3430	*

* Present studies a = ref (150), b = ref (151), c = ref (149)

Although the absorption range for the OH stretching frequencies of a free hydroxyl group is usually quoted as being 3700-3500 cm^{-1}[152] the overall range is actually much smaller within any single class of compounds.

TABLE 23

Spectrophotometric Rate Constants for the Base hydrolysis of *cis* -$[Co(en)_2(NH_2(CH_2)_nOH)Br]Br$

	pH	$10^3 k_{obs} s^{-1}$	$10^{-2} k_{OH} M^{-1} s^{-1}$
n=3			
	9.39	4.81	1.51
	9.31	3.86	1.46
	9.18	3.05	1.55
	8.97	1.76	1.46
	8.77	1.16	1.52
	8.64	0.86	1.53
n=6			
	9.44	4.08	1.14
	9.44	3.86	1.10
	9.03	1.55	1.11
	8.83	0.95	1.08
	8.53	0.45	1.03
	8.53	0.47	1.07

(c) Alicyclic and Hindered Amines

Aminoacetaldehyde dimethylacetal and cyclopropylamine derivatives: These are relatively bulky amines where some steric acceleration might be expected if a dissociative mechanism operates. The base hydrolysis rate constants (k_{OH}) for the chloro and bromoaminoacetaldehyde dimethylacetal complexes at 25.0° and I=0.1M are $8.2 \times 10^{1} M^{-1} s^{-1}$ and $1.67 \times 10^{3} M^{-1} s^{-1}$ respectively. Table (25).

These rate constants are significantly greater than these for the corresponding chloro-n-butylamine ($1.28 \times 10^{1} M^{-1} s^{-1}$)[121], bromo-n-butylamine ($8.11 \times 10^{1} M^{-1} s^{-1}$), and chloro-isopropylamine ($5.16 \times 10^{1} M^{-1} s^{-1}$)[121] complexes. This increased substitution results in a 20 fold increase for the release of bromide ion in the bromo complex of aminoacetaldehyde-dimethylacetal compared with corresponding straight chain bromopentammine complex of cobalt(III).

This rate enhancement is attributed to the relief of steric strain, as the reactant proceeds through the activated complex to the relatively stabilized five-coordinate intermediate following the loss of the halide ion. Buckingham and coworkers[153] have observed a marked acceleration ($> 10^{5}$) during the base hydrolysis of a series of pentakis alkylamine complexes of the type $[CoA_5Cl]^{2+}$ (A = CH_3CH_2, $n\text{-}C_3H_7NH_2$, $i\text{-}C_4H_9NH_2$). compared with $[Co(en)_2RNH_2)Cl]^{2+}$ complexes.

The infrared and visible spectra of the chloro and bromo-aminoacetaldehyderide dimethylacetal complexes of cobalt(III) are very similar to the analogous cis - haloammine bis-(ethylenediamine) cobalt(III). This confirms that the present complexes have a cis - configuration.

The rates of base hydrolysis of the chloro and bromo complexes of cyclopropylamine are summarised in Table (25). A ten fold increase in the rate of base hydrolysis <u>cis</u>-$[Co(en)_2$ (cyclopropylamine)$Cl]^{2+}$ complex (k_{OH}= 1.28 ± 0.05 X $10^2M^{-1}s^{-1}$ is observed compared with the chloro-n-propylamine) analogue where k_{OH} = 1.27 X $10^{-1}M^{-1}s^{-1}$[121].

A comparison of the rate constants for base hydrolysis, Table (24) reveals a distinct increase in the rate of base hydrolysis on changing the alicyclic ligands from cyclopropylamine to cyclohexylamine. These observations are in direct contrast with the results of Chan et al[129] who reported no variation in the rate constants as the alicyclic amine was varied.

<u>TABLE</u> 24

<u>Summary of second order rate constants for the base hydrolysis of the coordinated halide in</u> <u>cis</u>-$[Co(en)_2(amine)X]^{2+}$ ions at 0°C and I=0.1M; ($X=Cl^-,Br^-$)

<u>Amine</u>	<u>X</u>	k_{OH} $M^{-1}s^{-1}$	Ref
Cyclopropylamine	Cl	1.20	129
"	Cl	1.28 X 10^{2*}	-
"	Br	5.78 X 10^{2*}	-
Cyclohexylamine	Cl	2.50	154
"	Cl	1.23	129
"	Br	8.90	154
Methylamine	Cl	0.17	90
Isopropylamine	Cl	0.40	90

*Present work 25.0°C

Recently, Nanda and Nanda in discussing the base hydrolysis of the cyclohexylamine derivative have suggested that the high value of k_{OH} can be rationalised on the basis of a dissociative mechanism[154]. The cyclohexyl group is much bulkier than the methyl, ethyl or the isopropyl group. <u>Cis</u> S_N2 attack by hydroxide ion at the cobalt(III) centre would be expected to lead to slower rates, which has not been observed by these workers.

TABLE 25

Spectrophotometric Rate Constants for the base hydrolysis of *cis* - $[Co(en)_2(RNH_2)X]^{2+}$type complexes at 25.0°, I = 0.1M

RNH_2=Cyclopropylamine

	pH	$10^3 k_{obs}\ s^{-1}$	$10^{-2} k_{OH}\ M^{-1}s^{-1}$
X=Cl	9.37	3.80	1.25
	9.28	3.23	1.31
	9.08	1.96	1.27
	8.52	0.56	1.30
X=Br	9.28	12.6	5.02
	8.97	7.20	5.80
	8.75	4.31	5.91
	8.55	2.48	5.40

RNH_2=Aminoacetaldehydedimethylacetal

	pH	$10^3 k_{obs}\ s^{-1}$	$10^{-2} k_{OH}\ M^{-1}s^{-1}$
X=Cl	9.54	3.55	0.78
	9.37	2.75	0.90
	9.17	1.71	0.90
	8.98	0.87	0.70
X=Br	8.98	20.1	16.3
	8.66	9.71	16.3
	8.33	5.16	18.5
	7.98	1.96	16.0

The data in Tables (20,23,25) thus strongly support the view that these reactions occur by an S_N1CB mechanism. Additional evidence for this view comes from the activation parameters Table (26). It appears that the five coordinated intermediate has a trigonal bipyrimidal geometry in keeping with the observation that base hydrolysis is often accompanied by stereochemical change and that cis - and trans isomers do not differ enormously in their reactivity. The experimental Δs^* values for S_N2 and S_N1CB mechanisms lie between -62.70 and +167.20 $kJ^oK^{-1}mol^{-1}$ respectively[105].

TABLE 26

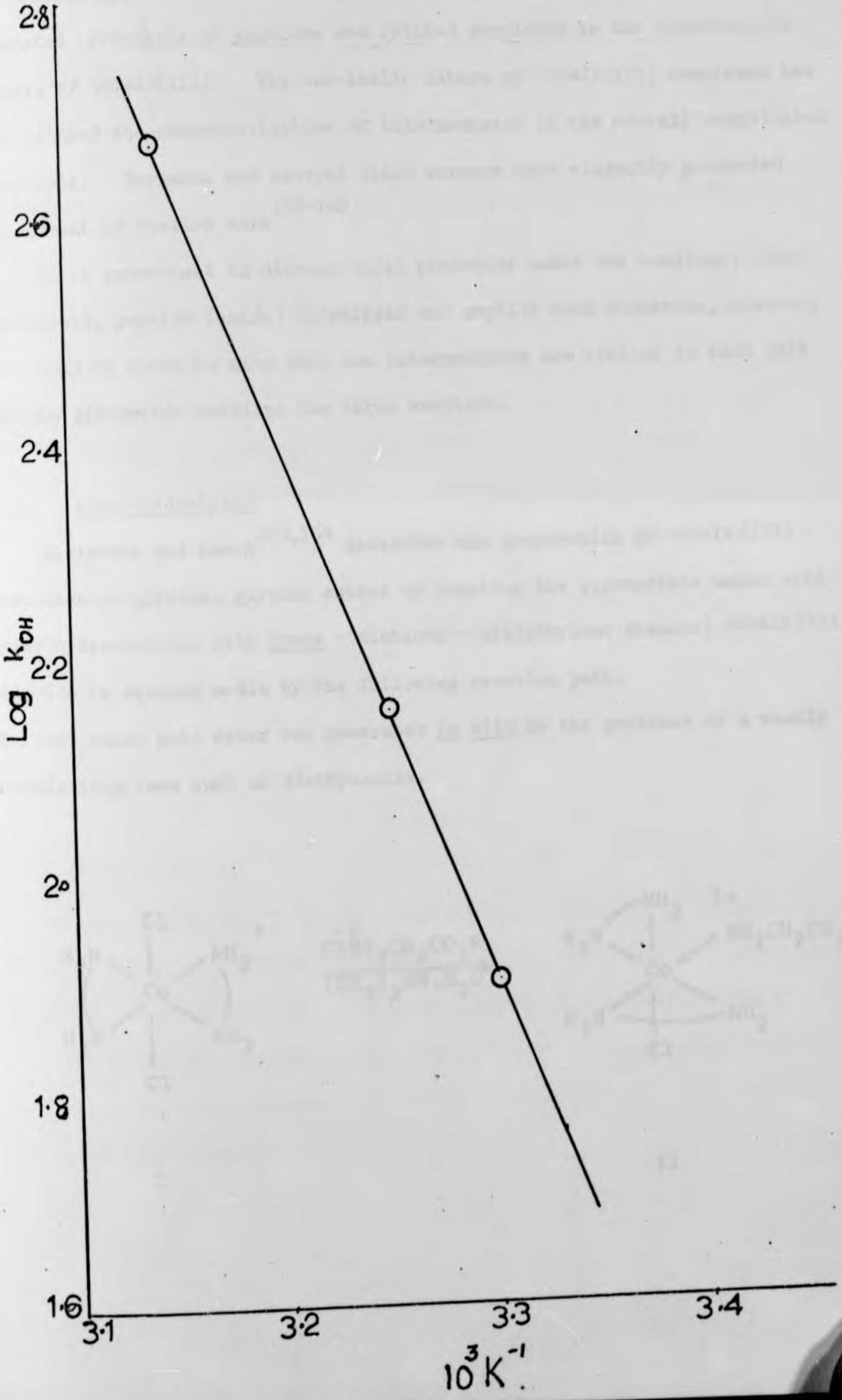
Comparison of the activation parameters of base hydrolysis of cis -$[Co(en)_2(NH_2R)X]^{2+}$ complexes.

Amine	X	ΔH $kJMol^{-1}$	$\Delta s^* kJ^oK^{-1}mol^{-1}$
NH_3^{Δ}	Cl	115.36	94.80
NH_3^{Δ}	Br	119.90	96.10
$EtNH_2^{\Delta}$	Cl	98.20	100.30
NH_2-n-Pr^{Δ}	Cl	97.80	103.66
†NH_2-n-Pr	Br	88.90	96.14

†Present work. Δ = data from ref 105

The activation parameters for the cis -$[Co(en)_2(n\text{-}PrNH_2)Br]Br_2$ Table (26) bear a close resemblance to other related systems.

Figure 10. Arhenius Plot for the Base hydrolysis of <u>cis</u> -$[Co(en)_2(NH_2Pr^n)Br]Br_2$ complex, 25.0°, I = 0.1$\underline{M}$



3.1 INTRODUCTION

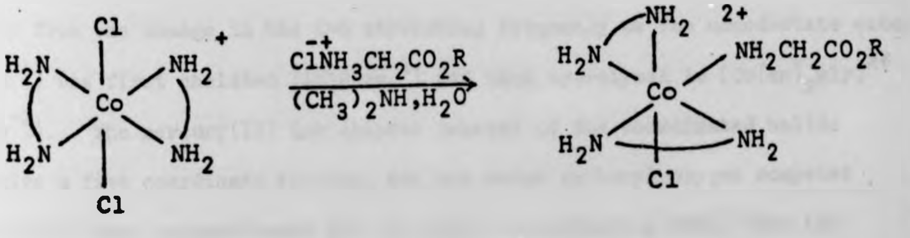
Recently, a number of groups[155-157] have studied the metal ion promoted hydrolysis of peptides and related complexes in the coordination sphere of cobalt(III). The non-labile nature of cobalt(III) complexes has facilitated the characterisation of intermediates in the overall complicated reactions. Fernando and several other workers have elegantly presented an account of earlier work[158-162].

It is convenient to discuss these processes under the headings, ester hydrolysis, peptide (amide) hydrolysis and peptide bond formation, however, it should be borne in mind that the intermediates are similar in each case and the discussion overlaps the three sections.

3.1.1 Ester hydrolysis

Alexander and Busch[163,164] described the preparation of cobalt(III) complexes of glycine, glycine esters by reacting the appropriate amino acid ester hydrochloride with trans - dichloro - bis(ethylene diamine) cobalt(III) chloride in aqueous media by the following reaction path.

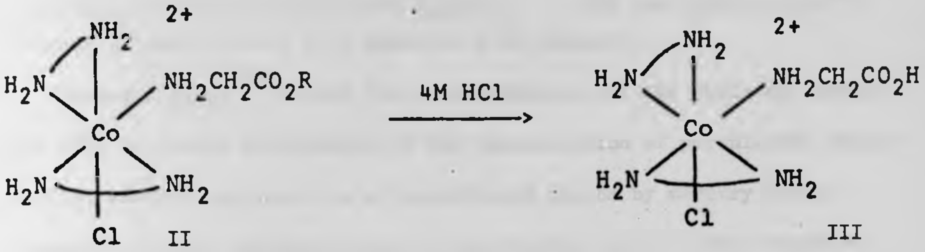
The free amino acid ester was generated *in situ* by the presence of a weakly coordinating base such as diethylamine.



I

II

The N-coordinated aminoacid derivatives (III) could be prepared by acid hydrolysis of the ester function,



II

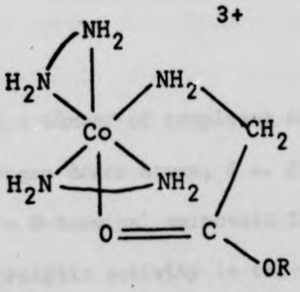
III

Busch and Coworkers.[165,166] studied the Hg^{2+} promoted hydrolysis of <u>cis</u> - $[Co(en)_2\ X\ (glyoR)]^{2+}$ ion in acid solution,

$$[Co(en)_2X(glyoR)]^{2+} + Hg^{2+} + H_2O \rightarrow [Co(en)_2(gly)]^{2+} + ROH + H^+ + HgX^+$$

$$(X = Cl,\ Br;\ \ R = CH_3,\ C_2H_5, i\text{-}C_3H_7)$$

and proposed that a chelated ester species $[Co(en)_2(glyOR)]^{3+}$ (IV) was the reactive intermediate in the Hg^{2+} promoted reaction[167]. Evidence for such a species was obtained



IV

primarily from the change in the C=O stretching frequency as the monodentate ester (1735 cm^{-1}) was first chelated (1610 cm^{-1}) and then hydrolysed to $[Co(en)_2gly]^{2+}$ (1640 cm^{-1}). The mercury(II) ion assists removal of the coordinated halide ion to give a five coordinate species, and the ester carbonyl oxygen competes so effectively with solvent water for the vacant coordination site, that the chelated ester is formed exclusively.

The base hydrolysis of $[Co(en)_2\ X(glyOR)]^{2+}$ ions have been studied in detail by Buckingham, Foster and Sargeson[168], (where X = Cl, Br; R = CH_3, $(C_2H_5)(CH_3)_2CH, CH_3(CH_2)_3(CH_3)C$ and $C_6H_5CH_2$). The ion $[Co(en)_2(gly)]^{2+}$ is formed primarily along with numerous side products .

Kobayashi *et al*[169] showed that the hydrolysis of the chelated glycine ester (IV) is rather independent of the concentration of perchlorate ion in solution, whereas the reaction of coordinated halide by mercury ion is accelerated in high concentrations of perchlorate ion with the formation of an inert intermediate aquo complex, *cis* - $[Co(en)_2(H_2O)(NH_2CH_2COOR)]^{2+}$

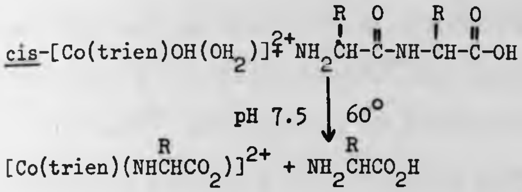
Base hydrolysis of *cis* - $[Co(en)_2Cl(NH_2(CH_2)_5COOMe)]^{2+}$ has recently been investigated[147]. Two consecutive reactions occur in base. Following loss of chloride ion, a slower base hydrolysis of the ester function occurs. The final product of the reaction is the hydroxy pentammine and the reaction is free from the intra molecular effects observed with the glycine esters.

3.1.2 Peptide Hydrolysis

It has been found that a number of complexes of the type $[CoN_4(OH)(OH_2)]^{2+}$ (N_4 = a system of four nitrogen donor atoms, i.e. 2 en, trien or tren) stochiometrically cleave the N-terminal aminoacid from di- or tri-peptides. A necessary feature for hydrolytic activity in the cobalt complex is the availability of at least two *cis* - sites in the octahedral coordination sphere, the remaining sites being filled by non-labile ligands. The peptide cleavage reactions are stoichiometric rather than catalytic.

Collman and coworkers proposed *cis* - $[Co\ trien\ (OH)(OH_2)]^{2+}$ as a model-metallo-enzyme[170,171]. The similarities between the complex and Mn^{2+}, Mg^{2+} containing leucine-amino peptidase are that both require chelation to promote hydrolysis[172] and selectively cleave the N-terminal peptide bond. The model complex of Collman, however, differs from the enzyme in reacting stoichiometrically with peptide to form irreversibly a stable chelate with the aminoacid residue formed by the chelate.

Dipeptide is quantitatively degraded by cis $-[Co(trien)OH(OH_2)]^{2+}$ under mild conditions at pH 7.5 in aqueous solution.



$$\underline{cis}\text{-}[Co(trien)OH(OH_2)]^{2+} + NH_2\overset{R}{C}H\text{-}\overset{O}{C}\text{-}NH\text{-}\overset{R}{C}H\text{-}\overset{O}{C}\text{-}OH \xrightarrow[pH\ 7.5]{60^\circ} [Co(trien)(NH\overset{R}{C}HCO_2)]^{2+} + NH_2\overset{R}{C}HCO_2H$$

From the above reaction scheme, it is clear that a free N-terminal group is necessary, because an N-protected peptide or diketopiperazine does not react with cis $-[Co(trien)OH(OH_2)]^{2+}$ complex.

However, problems arise due to the equilbrium,

$$[Co(trien)(H_2O)]^{3+} \underset{pK_a\ 5.27}{\overset{H^+}{\rightleftharpoons}} [Co(trien)OH(H_2O)]^{2+} \underset{pK_a\ 7.59}{\overset{-H^+}{\rightleftharpoons}} [Co\ trien(OH)_2]^{+}$$

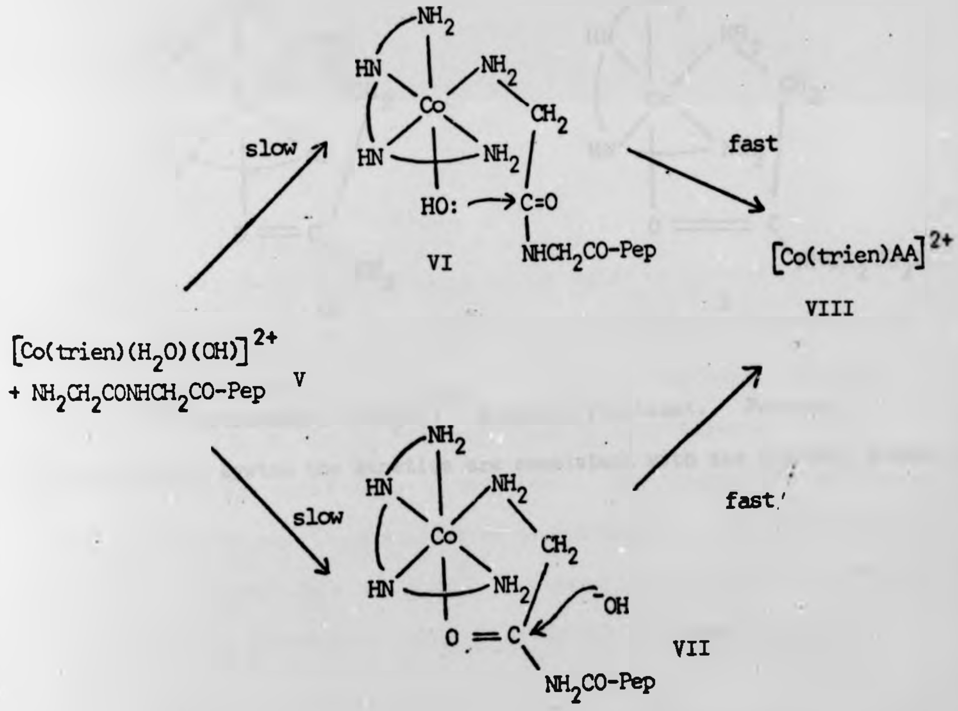
By the coordination of water molecules to cobalt(III) the acidity increases, a H^+ is liberated in the neutral pH range and more than an equivalent amount of the nucleophilic reagent OH^- is coordinated around the metal ion. (This hydroxide ion has recently been proved to play an important role in the hydrolysis of amides and related complexes of cobalt(III)[173]).

A study of the reactions of aminoacid esters and peptides with cis $-[Co(en)_2OH(H_2O)]^{2+}$[174] and $[Co(tren)(OH)(H_2O)]^{2+}$ have also been made[175] Amide hydrolysis is usually accompanied by ligand disproportionation leading to a mixture of products. The N-terminal aminoacid of a peptide in $[Co(tren)OH(H_2O]^{2+}$ complex is selectively removed as $[Co(trien)AA]^{2+}$ (where AA = NH_2CHRCO_2H) and only a trace of the C-terminal aminoacid complex is detected in few cases. The reactions are, however, much slower than the corresponding peptide cleavage reactions of trien, probably due to slower water exchange rates in the tren complex.

Very recently, Kimura[176], Bentley and Creaser[177] have studied the hydrolysis of several polypeptides with cis-β-Hydroxoaquo (triethylene tetramine) cobalt(III) ion and established the quantitative nature of the reactions. The cleavage of the diethylester of L-aspartic acid and dipeptides containing aspartic acid, glutamic acid by $[Co(dien)OH(H_2O)]^{2+}$ complex with the formation of $[Co(dien)(L\text{-}Aspc)]^+$ has also been studied[178].

Cyclen[28] and complexes of diethylenetriamineacetic acid[179] have been prepared as possible peptide cleaving agents.

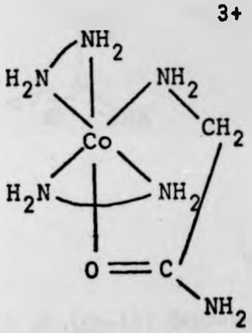
The proposed mechanisms for the hydrolysis are shown in scheme (A)



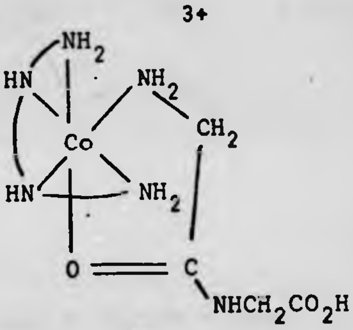
Scheme A

Collman and Kimura[180] first isolated the carbonyl bonded species illustrated in (VII), and this complex is considered to be the intermediate involved in the peptide hydrolysis. The preparation of the peptide reagent <u>cis</u> - $[Co(trien)(OH)(H_2O)](ClO_4)_2$ has been described[181].

A number of N-O chelated glycine amide and peptide complexes of the type $[Co(N_4glyNR_1R_2)]^{2+}$ have been prepared[182]. Typical complexes are shown in (IX) and (X). The kinetics of the base hydrolysis have been studied in order to establish if the C=O chelated species was the reactive intermediate

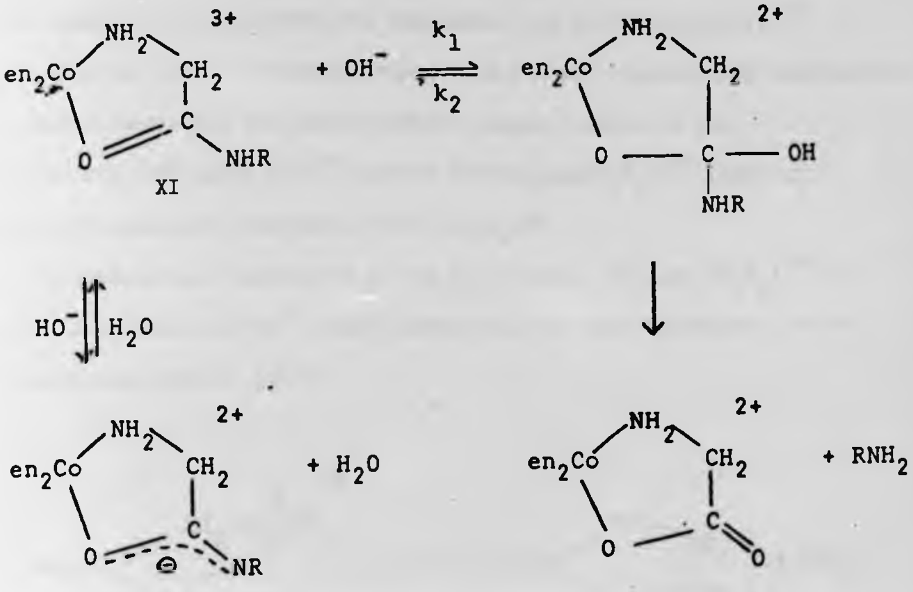


1X



X

in the $[Co^{III}(tetraamine)\ OH(H_2O)]^{2+}$ promoted reactions. For the ethylenediamine system the kinetics are consistent with the reaction Scheme (B).



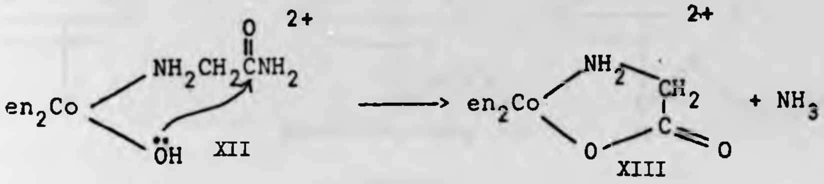
Scheme B

At high pH (*ca*.11) deprotonation of the amide or peptide nitrogen occurs. Such deprotonated species do not undergo base hydrolysis. For the carbonyl bonded species (XI) rate constants for hydroxide ion attack vary from 1 to $25M^{-1}s^{-1}$ at 25° corresponding to rate enhancements of *ca* 10^4-10^6 over the uncoordinated substrates. The biological implications of these reactions have been considered by Buckingham *et al*[182]. The Zn(II) activated carboxypeptidase A and Mn^{II} leucine amino peptidase have rates some 10-10^4 times faster than obtained by Co(III) activation of the carbonyl group.

Buckingham *et al* have studied the intramolecular and intermolecular hydrolysis reactions in detail[173].

Base hydrolysis of the *cis*-$[Co(en)_2Br(glyNR_1R_2)]^{2+}$ over the pH range 9-14 results in two pathways for the production of $[Co(en)_2(gly)]^{2+}$. Following the loss of bromide, competition for the 5-coordinate intermediate by solvent water and the amide carbonyl oxygen results in the *cis*-$[Co(en)_2(OH)(glyNR_1R_2)]^{2+}$ and the $[Co(en)_2glyNR_1R_2)]^{3+}$ (carbonyl chelated) species in the ratio 54:46 (R_1=R_2=H).

Intramolecular hydrolysis in the *cis*-$[Co(en)_2(OH)(gly\ NR_1R_2)]^{2+}$ ion (XII) is at least 10^7-10^{11} times faster than the base hydrolysis of the uncoordinated glycine amide.

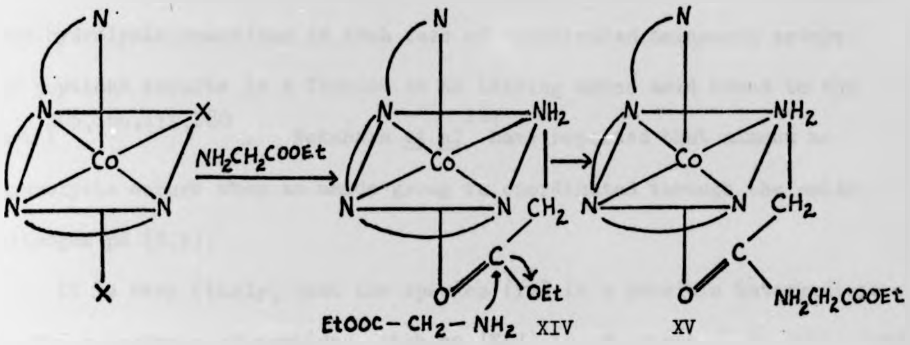


Such a mechanism provided a pathway for hydrolysis which is decidedly more efficient than that provided by direct metal-ion polarisation of the carbonyl function. Divalent metal ions compare favourably with cobalt(III) in promoting hydrolysis in model systems and it seems likely that such mechanisms will operate in the labile metal-ion reactions[157].

3.1.3 Peptide bond formation

The formation of glycine peptide esters in the presence of copper(II) has recently been studied[183]. Treatment of glycine esters with copper(II) in a non-aqueous solvent at room temperature gave di-, tri-, and tetraglycine peptide esters.

Buckingham et al published a scheme of reactions[184] that can be assumed to be general; When the species [Co trien X_2]$^+$ reacts with the ethyl ester of glycine in anhydrous conditions (DMSO or DMF), the corresponding complex of the ethylester of glycylglycine is obtained. The peptide ester is coordinated through the terminal amino group and the carbonyl oxygen atom of the same aminoacid residue.



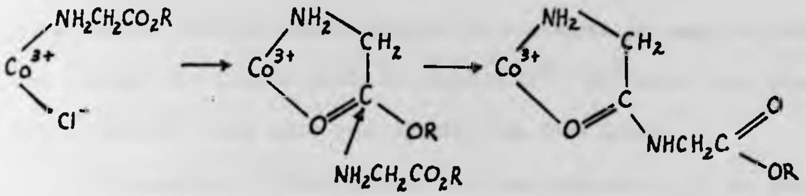
Scheme C

The above reaction scheme (C) has been established through the isolation of (XIV) which, when treated with ethylglycinate gives (XV)[185]. This latter complex can be isolated, but when treated with water in basic conditions, the dipeptide hydrolyzes yields the cobalt complex of ethyl glycinate.

Collman and Kimura obtained similar results in the case of $[Co(en)_2X_2]^+$. They pointed out that in similar conditions, but in the absence of the metal complex, the reaction does not take place[180].

More recently Wu and Busch[186] showed that the reaction of $[Co(dien)X_3]$ complex ($X=Cl,NO_2$) with glycine esters and glycylglycine ester gives $[Co(dien)(glyglyOR)X]^{2+}$ and $[Co(dien)(glyglyglyglyOR)]^{2+}$ complexes respectively.

In all these cases the peptide bond is formed in the coordination sphere of the Co(III) ion; presumably the coordination of the ester, through the carbonyl oxygen, causes bonds polarization, thus activating the carbonyl carbon and facilitating nucleophilic attack by the amino group of another ester molecule.



XVI

The hydrolysis reactions in each case of coordinated aminoacid esters or peptides results in a fashion so as leaving amino acid bound to the metal[165,166,171,180]. Nakahara *et al*[187] have reported that almost no hydrolysis occurs when an amide group is coordinated through the amide nitrogen pH (8.5).

It is very likely, that the species (XV) is a possible intermediate in the hydrolysis of peptides, such as (XIV) is of esters. In other words, (XIV) can react with any nucleophile such as water or, in anhydrous conditions, with another molecule of ester as already mentioned, the same applies to (XV). The former reaction leads to hydrolysis, the latter to peptide bond formation.

Hay *et al*[188] have studied the base hydrolysis of peptide bond in the glycylglycine complex of *cis*-$\beta_2[Co(trien)]^{3+}$ and showed that the reaction rate at pH ~ 11 equals $k_1[CoHA] + k_2[CoA^-][OH^-]$, where CoHA = the dipeptide complex;

CoA^- = deprotonated dipeptide complex, $k_1 = 2.70\ M^{-1}s^{-1}$ and $k_2 = 1.43\ M^{-1}s^{-1}$ (at 25°C). The rate constant of the alkaline hydrolysis of free glycylglycine, however is $4.0 \times 10^{-5} M^{-1}s^{-1}$ (at 26°), and thus it has been established that the peptide bond activated by coordination to Co^{3+} is cleaved about 6.5×10^4 times more readily.

Buckingham et al later determined the hydrolysis rate of amide and ester in a similar ethylenediamine complex in a neutral pH range and showed that the readily coordinated amide is cleaved 10^5 - 10^6 times less readily than the ester, but 10^6 times more readily than the free amide[182].

In the present investigation, the base hydrolysis of the peptide bond and of the ligand X (Cl,NO_2) in the cobalt(III) complexes containing glycine, glycinamide and dipeptide esters have been studied.

3.2 EXPERIMENTAL

3.2.1 Materials

Glycine, glycine ethylester hydrochlorate, glycylglycine were obtained from BDH chemicals (England); glycylglycine ethylester hydrochloride, glycinamide hydrochloride and β-alanine were purchased from SIGMA chemicals and Koch-light chemicals. Dipropylene triamine was obtained from K & K Laboratories; Inc. Plainview, New York. The chemicals were of high purity and were used without further purification.

3.2.2 Preparation of Compounds

Trinitro(diethylenetriamine) Cobalt(III); $[Co(dien)(NO_2)_3]$. -

This compound was prepared by the method described by Crayton and Mattern[189]

Calc. for $CoC_4H_{13}N_6O_6$; C, 16.85; H, 4.33; N, 28.90;
Found C, 16.60; H, 4.50; N, 28.20,%).

Trichloro (diethylenetriamine) Cobalt(III); $[Co(dien)Cl_3]$. -

A solution of diethylenetriamine (10.3g, 0.1 mole) in water (50 cm^3) was added dropwise, with stirring, to a solution of cobalt(II) chloride hexahydrate (24.1g, 0.1 mole) in water (100 cm^3). The resulting mixture was oxidised by dropwise addition of hydrogen peroxide (30%, v/v, 105cm^3). Concentrated hydrochloric acid (100 cm^3, 1.2 moles) was then added and the solution concentrated on a rotary evaporator to half its volume. On cooling fine brown crystals were obtained which were washed with alcohol then ether and finally dried in vacuo. Yield = 12g
(Calc. for $CoC_4H_{13}N_3Cl_3$; C, 17.87; H, 4.87; N, 16.20;
Found C, 17.57; H, 4.71; N, 16.46, %).

The above method was slightly modified from that described by House et al[190].

Trichloro(dipropylenetriamine)Cobalt(III); $[CodptCl_3]$. -

An improved synthesis has been described below[191] to prepare this compound. cobalt(II) chloride hexahydrate (24.0g,0.1 moles) was dissolved in water and mixed with dipropylenetriamine (13,0.1 mole). Hydrogen peroxide (100 cm^3, 30% v/v) was added slowly with continuous stirring then concentrated hydrochloric acid (100 cm^3). The solution volume was reduced on a water bath to *ca*. 100 cm^3 and cooled. The amorphous dull green product was filtered off washed with ethanol then ether and finally dried in *vacuo*.

yield ~ 13g.

(Calc. for $CoC_6H_{17}N_3Cl_3$; C, 24.30; H, 5.88; N, 14.20;

Found C, 24.09; H, 5.95; N, 13.97; Cl, 36.32, %).

The possibility of chloride group aquation is minimised in this manner.

Glycyl-β-alanine Methylester Hydrobromide . -

β-Alanine methyl ester hydrochloride (3.21g, 0.023 moles), N-Carbobenzyloxyglycine and dry dichloromethane (300 cm^3) was placed in a three necked flask equipped with a reflux condenser, dropping funnel and a N_2 inlet tube. The resulting suspension was stirred for an hour, then triethylamine (2.33g) was added dropwise. Dicyclohexyl carbodiimide (5.8g) in dichloromethane (20 cm^3) was then added and the solution kept overnight at room temperature. Addition of glacial acetic acid (0.5ml) caused the precipitation of dicyclohexyl urea which was filtered off. The dichloromethane layer was washed successively with hydrochloric acid (2M), sodium bicarbonate solution then water. Three washings were carried out in each case and CH_2Cl_2 layer dried over anhydrous sodium sulphate. The dichloromethane was removed on a rotary evaporator, giving an oily residue, which was then treated with CH_3COOH/HBr solution (20 cm^3) and stirred. Addition of the appropriate volume of ether then ethanol, caused the crystallisation of Glycyl-β-alanine ethyl ester hydrobromide. The white crystalline product was filtered off and finally dried overnight in *vacuo*

Trichloro(dipropylenetriamine)Cobalt(III): [$CodptCl_3$] . -

An improved synthesis has been described below[191] to prepare this compound. cobalt(II) chloride hexahydrate (24.0g,0.1 moles) was dissolved in water and mixed with dipropylenetriamine (13,0.1 mole). Hydrogen peroxide (100 cm^3, 30% v/v) was added slowly with continuous stirring then concentrated hydrochloric acid (100 cm^3). The solution volume was reduced on a water bath to ca. 100 cm^3 and cooled. The amorphous dull green product was filtered off washed with ethanol then ether and finally dried in vacuo.

yield ~ 13g.

(Calc. for $CoC_6H_{17}N_3Cl_3$; C, 24.30; H, 5.88; N, 14.20;

Found C, 24.09; H, 5.95; N, 13.97; Cl, 36.32, %).

The possibility of chloride group aquation is minimised in this manner.

Glycyl-β-alanine Methylester Hydrobromide . -

β-Alanine methyl ester hydrochloride (3.21g, 0.023 moles), N-Carbobenzyloxyglycine and dry dichloromethane (300 cm^3) was placed in a three necked flask equipped with a reflux condenser, dropping funnel and a N_2 inlet tube. The resulting suspension was stirred for an hour, then triethylamine (2.33g) was added dropwise. Dicyclohexyl carbodiimide (5.8g) in dichloromethane (20 cm^3) was then added and the solution kept overnight at room temperature. Addition of glacial acetic acid (0.5ml) caused the precipitation of dicyclohexyl urea which was filtered off. The dichloromethane layer was washed successively with hydrochloric acid (2M), sodium bicarbonate solution then water. Three washings were carried out in each case and CH_2Cl_2 layer dried over anhydrous sodium sulphate. The dichloromethane was removed on a rotary evaporator, giving an oily residue, which was then treated with CH_3COOH/HBr solution (20 cm^3) and stirred. Addition of the appropriate volume of ether then ethanol, caused the crystallisation of Glycyl-β-alanine ethyl ester hydrobromide. The white crystalline product was filtered off and finally dried overnight in vacuo

(Calc. for $C_7H_{15}BrN_2O_3$; C, 32.9, H, 5.9; N, 10.8;
Found C, 32.7; H, 5.9; N, 10.8%).

3.2.3 Reaction of [Co(dien)X_3] (where X = NO_2Cl) with amino acids and dipeptide ester hydrochlorides .-

A general method described by Wu and Busch[186] and Fujita[192] was used to prepare this series of complexes.

[Co(dien)(glyO)X]ClO_4; (X = NO_2,Cl)

These complexes were prepared essentially as described by Busch et al[186]

([Codien(glyO)Cl]ClO_4; Calc. for $CoC_6H_{19}N_4Cl_2O_6$; C, 19.40; H, 4.62; N, 15.10
Found C, 19.28; H, 5.14; N, 14.91,%)

([Co(dien)(glyO)NO_2]ClO_4; Calc. for $CoC_6H_{19}N_5ClO_6$; C, 18.88; H, 4.49;
N, 18.35;
Found C, 18.68; H, 4.88; N, 18.42,%).

[Co(dien)(gly NH_2)Cl]$(ClO_4)_2$. -

The method employed to prepare glycinato complex was used substituting glycine by glycine amide hydrochloride. Free amino acid amide was generated by reacting with equimolar amount of weak base (diethylamine).

(Calc. for $CoC_6H_{19}N_5Cl_3O_9$; C, 15.32; H, 4.07; N, 14.89;
Found C, 15.62; H, 4.50; N, 14.71,%).

[Co(dien)(glyglyOEt)Cl]$(ClO_4)_2$. -

The complex was prepared in aqueous solution as hygroscopic products were obtained in non-aqueous solvents such as DMF, DMSO and these products proved difficult to purify.

Equimolar quantities of [Co(dien)Cl_3] (1.34g, 5mmol) and glycylglycine ethylester hydrochloride were made into a paste with 5 cm^3. Diethylamine (0.5 cm^3) was added to the above suspension and the mixture ground for 0.5 hours.

The residual paste was filtered off on a sintered glass and washed with water ($10cm^3$). A few drops of concentrated perchloric acid (60%) were added to the combined filtrate and washings. The resulting solution was concentrated, initially on a rotary evaporator and then on a dish under a slow stream of air till the complex crystallised. The crude complex was washed with ethanol then ether and recrystallized from minimum volume of hot water. Fine purple-grey crystals were obtained on cooling, were filtered off and finally dried over silica gel in vacuo.

(Calc. for $CoC_{10}H_{26}N_5Cl_3O_{10}$; C, 21.57; H, 4.53; N, 12.58; Cl, 19.11;
Found C, 21,52; H, 4.70; N, 12.75; Cl, 19.41,%).

$[Co(dien)(glyglyOEt)\ (NO_2](ClO_4)_2$. -

This complex has been prepared by the method described to prepare $[Co(dien)(glyO)NO_2]ClO_4$, substituting glycylglycine ethylester hydrochloride for glycine. The orange-yellow crystalline product was recrystallised from the minimum amount of hot water and dried in vacuo.

(Calc. for $CoC_{10}H_{25}N_6O_{13}Cl_2$; C, 21.20; H, 4.44; N, 14.80
Found C, 21.13; H, 4.64; N, 14.71,%).

$[Co(dien)(glyglyOH)NO_2]Cl_2$. -

Acid hydrolysis of the above complex was carried out by adopting Alexander and Busch method[164]. Glycylglycine ethylester complex, $[Co(dien)(glyglyOEt)NO_2]^{2+}$ was stirred with $50cm^3$ of 3N Hydrochloric acid for 24 hours. Acetone ($200cm^3$) was added to this mixture and cooled in ice for several hours. The yellow product thus obtained was filtered off and washed successively with acetone, ether and dried in vacuo.

(Calc. for $CoC_8H_{21}N_5O_5Cl_2$; C, 23.36; H, 5.14; N, 20.44
Found C, 23.57; H, 5.38; N, 20,70,%).

$[Co(dien)(glyglyglyO)NO_2]^+$. -

This complex as a glass was kindly supplied by Dr Paul R Mitchell, Chemistry Department, University of Kent at Canterbury (England). The compound gave a satisfactory analysis.

3.2.4 Kinetic measurements

The base hydrolysis kinetic studies were made spectrophotometrically using a Gilford-2400S instrument. A solution of the appropriate reaction mixture (2.5 cm^3) in a 1 cm path length silica cell was equilibrated in the spectrophotometer cell compartment for 20 minutes. The reaction was then initiated by the addition of a known amount of the substrate.

All reactions were carried out under pseudo first order conditions. In some cases rate constants were evaluated from computer extrapolated infinity plot using data collected over the first two reaction half lives. The computer programme used was of the generalized least squares types based on the letagrop programmes of Šillen[193].

All pH measurements were made at the temperature of the kinetic studies using a Radiometer-26pH meter. Hydroxide ion concentrations were calculated using the appropriate molar activity coefficients and values of pKw listed in General Section.

3.3 RESULTS AND DISCUSSION

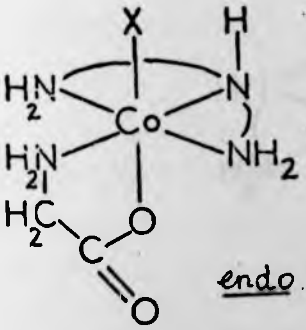
The reaction of $[Co(dien)X_3]$, (where X = Cl,NO_2) with glycine and several other related compounds gives $[Co(dien)(glyO)X]^+$, $[Co(dien)(glyglyOR)X]^{2+}$ complexes[186]. The $[Co(dien)]^{3+}$ moiety serves to block three of the six sites on the cobalt(III), making it a three functional site reagent. These complexes can be maintained in aqueous solution, at low pH < 6 for several hours without appreciable hydrolysis of the peptide or the ester group.

The formation of the dipeptide proceeds, from either GlyOR or GlyglyOR, by activation of the glycine ester group by coordination of the carbonyl oxygen to cobalt. Nucleophilic attack at the carbonyl carbon by the amino group of a second amino acid or peptide reagent[186] then occurs (see section 3.1.3).

3.3.1 Stereochemistry of the Complexes

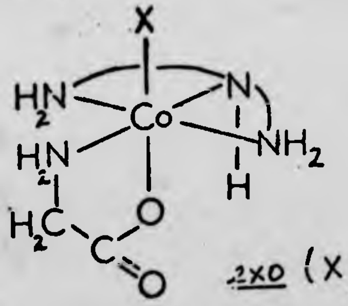
The complexes are considered to have the dien ligand in a meridional configuration with a trans - (O,X) arrangement of the additional ligands and can be represented by the structures (XVII-XX).

Wu and Busch[186] have provided n.m.r. and electronic spectral evidence to support structures of this type. Ohkawa, Fujita and Shimura[192] have characterised a variety of trans(O,X) - $[Co X(aminoacidato) (dien)]^+$ complexes with X = CN^-, NO_2^- or Cl^- and have confirmed by n.m.r. spectroscopy the existence of exo and endo conformational isomers (XXI-XXII) in the cyanoderivative due to chiral secondary nitrogen centres.



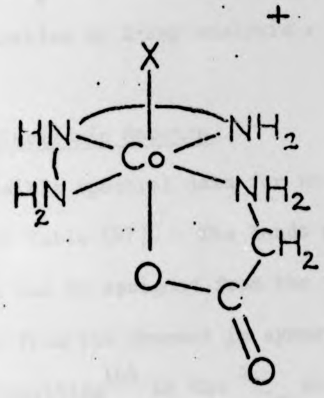
endo (X,NH)

XXI

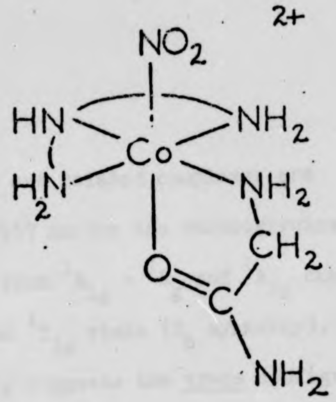


exo (X,NH)

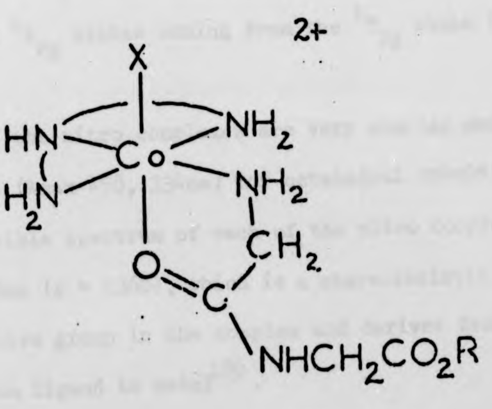
XXII



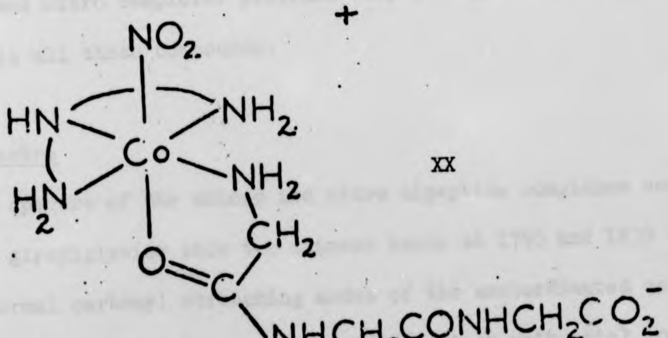
XVII



XVIII



XIX



XX

However, Yamagucchi and Ooi[194] have shown that the trans(O,Cl)-$[CoClglyO]$ $(dien)]ClO_4$ and the trans (O,NO_2)-$[CoNO_2(glyO)dien]Cl.H_2O$ have the endo configuration by X-ray analysis .

(a) Electronic Spectra

Visible spectral data for the dipeptide and related complexes are given in Table (27). The bands at 562 and 457 nm for the chloroglycine complex can be assigned from the transition from $^1A_{1g} \rightarrow {}^1E_g$ and $^1A_{2g}$ components derived from the descent in symmetry from the $^1T_{1g}$ state (O_h symmetry). This large splitting[195] in the $^1T_{1g}$ state strongly suggests the trans configuration for the chloro complex for only in such a structure are the two weaker field donor atoms trans to each other. The absorption band at shorter wavelengths (373nm or 364nm) may be assigned to the unresolved transitions from the $^1A_{1g}$ ground state to ^1E_g and $^1B_{2g}$ states coming from the $^1T_{2g}$ state (for octahedral symmetry)[196].

The spectra of all the nitro complexes are very similar and two spin allowed d-d transitions (λmax 458, 334nm) for octahedral cobalt(III) complexes are observed in the visible spectrum of each of the nitro complexes. The intense band at 335 ± 3nm ($\varepsilon = 1360$), which is a characteristic band indicative of the presence of a nitro group in the complex and derives from a charge transfer transition from ligand to metal[189].

The close similarity in the electronic absorption spectra values of the glycinato chloro and nitro complexes provides very strong evidence for a similar geometry in all these compounds.

(b) Infrared spectra

The infrared spectra of the chloro and nitro dipeptide complexes containing the ethylester of glycylglycine show two intense bands at 1740 and 1235 cm^{-1} assigned to the normal carbonyl stretching modes of the uncoordinated ester group[197]. These values indicate little or no interaction with metal ion because

TABLE 27

Electronic Scectra Data for Dipeptide and Related Complexes

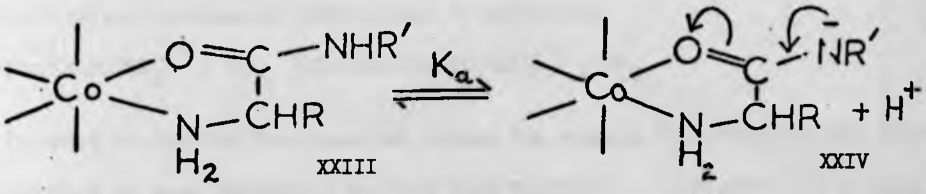
Complex	λmax nm (± 2)	$\varepsilon_{coeff}(l\ mol^{-1}cm^{-1})$
$[Co(dien)gly(NO_2)]ClO_4$[a]	457, 332	164, 1360
$[Co(dien)gly(Cl)]ClO_4$[b]	558, 457, 359	76, 85
$[Co(dien)(glyNH_2)Cl]ClO_4)_2$[b]	573, 455, 373	75, 84, 145
$[Co(dien)(glyglyOEt)No_2](ClO_4)_2$[a]	457, 333	198, 1560
$[Co(dien)(glyglyOEt)Cl]$[b]$(ClO_4)_2$	572, 458, 349	62, 86

a = measured in water b = measured in methanol.

they are quite near the intense bands at 1745 and 1245cm^{-1} for free glycylglycine ester hydrochloride. The only bands showing significant differences in these two complexes occur at 1426 and 1337 cm^{-1} and are assigned to the asymmetric and symmetric stretching modes of NO_2^- [198]. An intense band occurring at 1631 cm^{-1} is assigned to the coordinated amide group[180]. The infrared spectra of the glycine amide complex shows similar features. A strong band at 1657 cm^{-1} due to carbonyl stretch in the infrared spectra of the coordinated glycinate complexes, while for the uncoordinated glycine hydrochloride the high frequency carbonyl stretching band is found at 1600cm^{-1} [164].

3.3.2 Kinetics

The relatively non-labile character of coordinated NO_2^- in basic solution makes trans - (O,NO_2)-[Co(dien)(glyglyOEt)NO_2]$(ClO_4)_2$ complex a useful substrate for studies of the hydrolysis of the bidentate chelated dipeptide ligands. Carbonyl bonded amide and peptide complexes of cobalt(III) are quite acidic[180,182]



XXIII

XXIV

Wu and Busch[186] have reported a pK_a value of 9.89 for $[Co(dien)(glyglyOR)NO_2]^{2+}$ while $[Co(dien)(glyglyOH)NO_2]^{2+}$ has pKa1 2.86 and pKa2 11.1. This result establishes amide hydrogen which is made more acidic by coordination of the amide carbonyl group. The pK_a of the complex, cis -$[Co(trien)(glyglyOR)]^{3+}$, prepared by Collman and Kimura[180] is 9.4 which is slightly lower than the pK_a value obtained from $[Co(dien)(glyglyOC_2H_5)NO_2]^{2+}$($pK_a$ 9.89). The strongly electron withdrawing alkoxycarbonyl group leads to a marked increase in acidity of the carbonyl bonded peptide.

Spectrophotometric studies of the base hydrolysis of $[Co(dien)(glyglyOEt)NO_2]^{2+}$ indicated that two consecutive reactions were occurring. The first reaction was studied in the pH range 10.49-11.36 using n-butylamine/HCl buffers at I = 0.1M and 25.1°C. The results obtained are summarised in Table (28). The values of $k_{obs}/[OH^-]$ are constant and thus confirming a first order dependence on the hydroxide ion concentration with $k_{OH} = 0.68M^{-1}s^{-1}$. This reaction can be assigned to the peptide bond cleavage (as ester hydrolysis should not give any change in the visible spectrum since the ligand field around cobalt atom does not alter). Base hydrolysis of the nitrodipeptide complex at pH ∿ 10 gives the glycinato complex (eq 1). The visible spectrum of this product is

$$[Co(dien)(NH_2CH_2CONHCH_2CO_2Et)NO_2]^{2+} \xrightarrow{\sim pH\ 10} [Co(dien)(NH_2CH_2CO_2^-)NO_2]^+ \quad . . . (1)$$

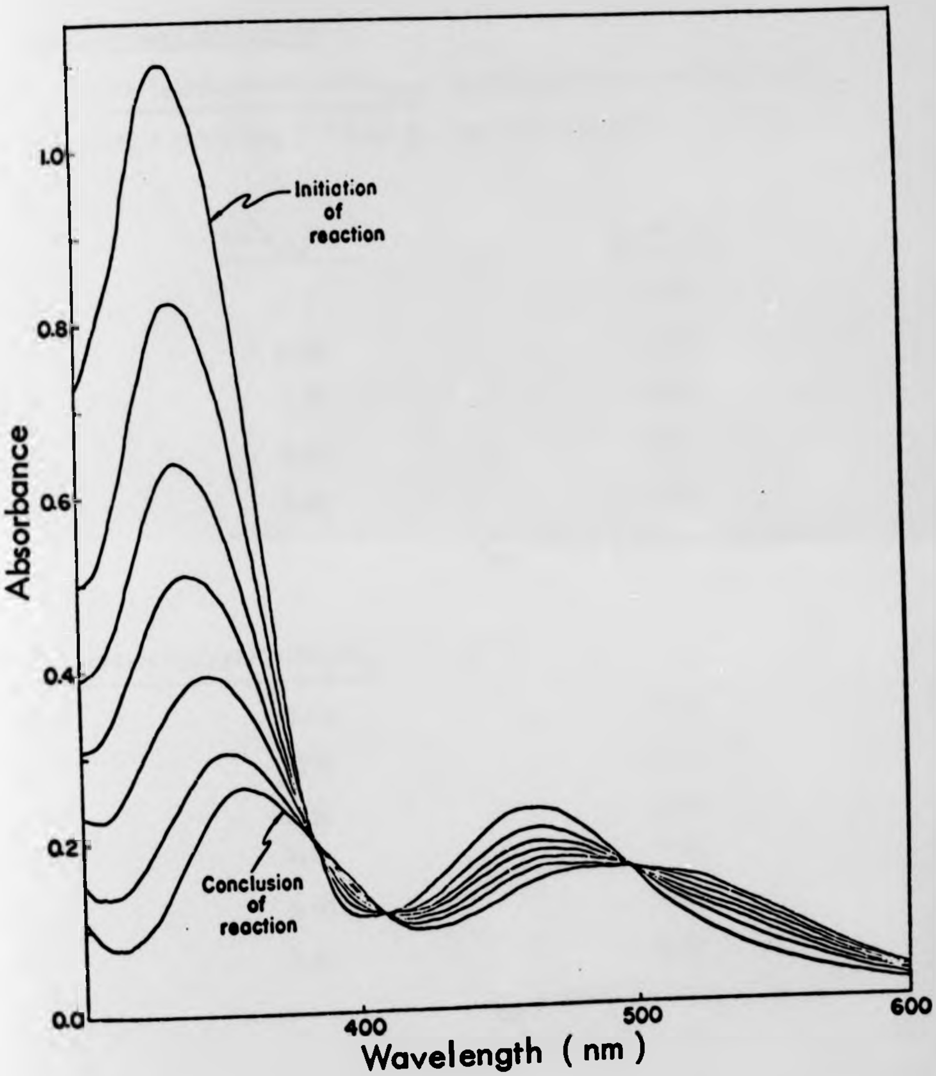
identical with that prepared from the reaction of $[Co(dien)(NO_2)_3]$ with glycine.

The second slower reaction, the substitution of NO^-_2 by $\overline{OH}$ was studied in 0.1M NaOH and the mean value of k_{obs} (three runs) was $2.52 \times 10^{-3}s^{-1}$ giving a value of $k_{\underset{OH}{obs}} = 2.83 \times 10^{-2}M^{-1}s^{-1}$ at 25.0°C. It is important to note that the hydrolysis of the peptide bond in 0.1M NaOH is much faster than the substitution reaction of nitro group by hydroxide.

$$[Co(dien)(glyO)NO_2]^+ + \overline{OH} \quad [Co(dien)(glyO)(OH)]^+ + NO_2 \quad . . . . (2)$$

In order to confirm this reaction scheme the complex $[Co(dien)(glyO)NO_2]ClO_4$ was subjected to base hydrolysis in 0.1M NaOH solution. In Figure (11) spectra are presented taken at various times during the course of hydrolysis of the nitro-glycine complex in 0.1M alkaline solution. Three isobestic points are observed and thus indicating the presence of only two uniquely absorbing species (within experimental error) during the course of hydrolysis[133]. The value of k_{OH} obtained was $2.88 \times 10^{-2}M^{-1}s^{-1}$ at 25.0°C in agreement with the previous data. Wu has reported a value of $k_{OH} = 1.3 \times 10^{-2}M^{-1}s^{-1}$ at 25.0°C and I = 0.6M. A negative salt effect would be expected for this reaction[199].

FIGURE 11



Visible spectra obtained during the course of hydrolysis of $[Co(dien)(glyO)NO_2]^+$ in 0.1 M NaOH.

Table 28

Base hydrolysis kinetics of dipeptide and related complexes of Cobalt(III)

(a) Peptide bond hydrolysis

(i) $[Co(dien)(glyglyOEt)NO_2](ClO_4)_2$; n-Butylamine-hydrochloric acid buffers, λ = 334 nm, I = 0.10 M, Temp = 25.0±0.2°C.

pH	$10^4 k_{obs}/s^{-1}$	$k_{OH}/M^{-1}s^{-1}$
11.36	19.2	0.65
11.00	8.83	0.69
10.86	6.72	0.72
10.65	3.63	0.64
10.49	2.68	0.69

$k_{OH} = (6.8 \pm 0.3) \times 10^{-1} M^{-1} s^{-1}$

(ii) $[Co(dien)(glyglyOH)NO_2]Cl_2$

10.93	10.23	0.93
10.72	5.77	0.85
10.59	4.60	0.84
10.59	4.25	0.91
10.51	3.60	0.84
10.43	3.10	0.89

$k_{OH} = (8.8 \pm 0.4) \times 10^{-1} M^{-1} s^{-1}$

(iii) $[Co(dien)(glyglyglyO)NO_2]^+$

11.10	10.10	0.62
10.80	5.20	0.63
10.51	2.80	0.68
10.20	1.50	0.73

$k_{OH} = (6.7 \pm 0.4) \times 10^{-1} s^{-1}$

(iv) Peptide bond hydrolysis of $[Co(dien)(glyglyOEt)OH]^{2+}$ at λ = 310 nm, n-butylamine-HCl buffers, I = 0.10 M Temp 25.0°C.

pH	$10^3k_{obs}/s^{-1}$	$k_{OH}/M^{-1}s^{-1}$
10.65	4.1	7.1
10.65	4.0	7.0
10.28	1.71	6.95
10.40	2.33	7.16
10.28	1.70	6.86

$k_{OH} = (7.01 \pm 0.2)\ M^{-1}s^{-1}$

(b) Chloride hydrolysis

(i) $[CoCl(dien)(glyO)]ClO_4$; 2-6, Lutidine HCl Buffers, λ = 505 nm
I = 0.1 M, Temp 25.0°C

pH	$10^3k_{obs}/s^{-1}$	$10^{-4}k_{OH}/M^{-1}s^{-1}$
7.46	4.70	1.28
7.26	3.23	1.35
7.02	1.83	1.36
6.83	1.09	1.27
6.77	0.96	1.28

$k_{OH}^{Cl} = (1.30 \pm 0.05) \times 10^4 M^{-1}s^{-1}$

(ii) $[CoCl(dien)glyglyOEt)](ClO_4)_2$; acetic acid - Potassium hydroxide (0.1MKOH) buffers, λ = 307 nm, I = 0.1M, Temp 25.0 ± 0.2°C.

pH	$10^4k_{obs}/s^{-1}$	$10^{-6}k_{OH}/M^{-1}s^{-1}$
5.13	18.45	1.08
4.74	7.25	1.04
4.56	5.18	1.12
4.32	2.98	1.12
4.07	1.65	1.10

$k_{OH}^{Cl} = (1.09 \pm 0.05) \times 10^6 M^{-1}s^{-1}$

(iii) $[CoCl(dien)(glyNH_2)]^{2+}$; Acetic acid - KOH buffers, I = 0.1M, λ = 307 nm, Temp = 25.0°C.

pH	$10^4k_{obs}/s^{-1}$	$10^{-5}k_{obs}/[OH^-]/M^{-1}s^{-1}$
5.17	10.67	5.67
4.97	6.78	5.70
4.70	3.57	5.47
4.49	2.33	5.93
4.21	1.33	6.47

$k_{OH}^{Cl} = (5.85 \pm 0.5 \times 10^5 M^{-1}s^{-1}$

The hydrolysis of $[Co(dien)(glyglyOH)NO_2]Cl_2$ was also studied in the pH-range 10.43-10.93 in n-butylamine buffers. At this pH the only hydrolytic reaction of significance is hydrolysis of the peptide bond. The values of $k_{obs}/[O\bar{H}]$ are constant, Table (28) giving a value of $k_{OH} = 0.88\ M^{-1}s^{-1}$ at 25.0° and I = 0.1M, a rate constant similar to that observed with the corresponding ester complex.

Potentiometric titration of $[Co(dien)glyglyOH)NO_2]^{2+}$(II) at I = 0.1M gave a value of $pK_a = 10.9 \pm 0.1$ for ionisation of the peptide hydrogen (pK_a^P is a practical ionisation constant involving the hydrogen ion activity and the concentration of the other species), although this constant is in reasonable agreement with the value of 11.1 quoted by Wu and Busch[186]. It is possible that it is a 'mirage' or false constant[200] and the true value is somewhat higher. Potentiometric measurements with glass electrodes give unreliable pK_a values above pK_a 11[200].

It is well established[182,201] that the deprotonated peptide is inert to base hydrolysis, however values of $\frac{k_{obs}}{[OH^-]}$ are constant up to pH 10.9. At this pH appreciable amounts of the deprotonated peptide complex should exist. The kinetic measurements thus suggest that the potentionetric measurements are unreliable.

Similar kinetic measurements were carried out with the complex

$[Co(dien)(glyglyglyO)[NO_2]^+$ (XX)

Peptide bond hydrolysis was studied at 330nm using *n*-butylamine-HCl buffers, Table (28). Values of $k_{obs}[OH^-]$ are constant over the pH range 10.20-11.0 with $k_{OH} = 0.67\ M^{-1}s^{-1}$ at 25° and I = 0.1*M*. Thus for peptide bond hydrolysis in the three nitro complex falls within the range 0.67 - 0.88 $M^{-1}s^{-1}$ at 25°C. For base hydrolysis of glycylglycine, k_{OH} is *ca.* $4 \times 10^{-4} M^{-1}s^{-1}$ at 26°C (determined in 2M - sodium hydroxide) so that the peptide bond hydrolysis is some 2×10^4 times faster in the metal complex. Similar rate enhancements

TABLE 29

Summary of kinetic data at I = 0.1M and 25.0°C

	$k_{OH}^{Peptide}$ $(M^{-1}s^{-1})$	$k_{OH}^{NO_2}$ $(M^{-1}s^{-1})$	k_{OH}^{Cl} $(M^{-1}s^{-1})$
$[Co(dien)(glyglyOEt)](ClO_4)_2$	0.65	2.5×10^{-2}	-
$[Co(dien)(glyglyOH)NO_2]Cl_2$	0.88		-
$[Co(dien)(glyglyglyO)NO_2]^+$	0.67		-
$[Co(dien)(glyO)NO_2]ClO_4$	-	2.45×10^{-2}	-
$[Co(dien)(glyO)Cl]ClO_4$	-		1.3×10^{4}
$[Co(dien)(glyglyOEt)Cl](ClO_4)_2$	7.0	-	1.1×10^{6}
$[Co(dien)(glyNH_2)Cl](ClO_4)_2$	-	-	5.85×10^{5}

TABLE 29

Summary of kinetic data at I = 0.1M and 25.0°C

	$k_{OH}^{Peptide}$ $(M^{-1}s^{-1})$	$k_{OH}^{NO_2}$ $(M^{-1}s^{-1})$	k_{OH}^{Cl} $(M^{-1}s^{-1})$
$[Co(dien)(glyglyOEt)](ClO_4)_2$	0.65	2.5×10^{-2}	-
$[Co(dien)(glyglyOH)NO_2]Cl_2$	0.88		-
$[Co(dien)(glyglyglyO)NO_2]^+$	0.67		-
$[Co(dien)(glyO)NO_2]ClO_4$	-	2.45×10^{-2}	-
$[Co(dien)(glyO)Cl]ClO_4$	-		1.3×10^4
$[Co(dien)(glyglyOEt)Cl](ClO_4)_2$	7.0	-	1.1×10^6
$[Co(dien)(glyNH_2)Cl](ClO_4)_2$	-	-	5.85×10^5

have been observed in cis β_2 -$[Co(trien)(glyglyOR)]^{3+}$ and related complexes. Base hydrolysis of oxygen bonded $[Co(NH_3)_5DMF]^{3+}$ (DMF = N,N - dimethyl formaniside) is accelerated $\geq 10^4$ fold compared with the hydrolysis of the uncoordinated amide[202]. In this latter reaction the rate acceleration is due exclusively to a much more positive entropy of activation ($\Delta S^* = + 67\ J^o\ K^{-1} mol^{-1}$).

One chloro-peptide complex $[CoCl(dien)(glyglyOEt].(ClO_4)_2$ was studied. Base hydrolysis of chloride is very rapid and this reaction can be studied in isolation in the pH range 4-5 since peptide bond hydrolysis is not significant at pH values < 10. Values of $k_{obs}/[OH^-]$ are constant with $k_{OH}^{Cl} = 1.1 \times 10^6\ M^{-1}s^{-1}$ at 25.0°C and I = 0.1M, Table (28). Peptide bond hydrolysis was studied in the pH range 10.18 - 10.65 and refers to the complex $[Co(dien)(glyglyOEt)OH)^{2+}$. In this case k_{OH} is $7.0 \pm 0.1\ M^{-1}s^{-1}$ at 25.0°, the reaction is some ten times faster than for the nitro derivatives. If the *trans* (O,X)- configuration is retained on base hydrolysis, nucleophilic and/or general base catalysis by the Co-OH group would not be expected, however, the *cis* (O,X) - configuration would allow catalysis of this to occur[173].

In Figure (12) spectra are presented taken at various times during the course of base hydrolysis of $[Co(dien)(glyO)Cl]ClO_4$ in 2,6-Lutidine-HCl buffer (pH ~ 6.95). The rapid base hydrolysis rates of $[CoCl(dien)(glyO)]^+$, $[Co(dien)Cl(glyglyOEt)]^{2+}$ and $[CoCl(dien)(glyNH_2)]^{2+}$, Tables (28,29) are fully consistent with the *mer* - configuration of the dien-ligand in these complexes. Very recently, it has been noted that *mer*-dien complexes of cobalt(III) containing chloro-ligands undergo base hydrolysis 10^2-10^4 times faster than analogous complexes in which the dien ligand is facial[203]. Thus for the series of three isomeric $[CoCl(dien)(en)]^{2+}$ complexes (XXV-XXVII) the values of k_{OH} are $7.26\ M^{-1}s^{-1}(\omega)$, $26.6\ M^{-1}s^{-1}(\pi)$ and $3.0 \times 10^4\ M^{-1}s^{-1}$ (κ) at 25.0° and I = 0.1M, while for *trans* (O,Cl) - $[CoCl(dien)(glyO)]^+$ $k_{OH} = 1.3 \times 10^4\ M^{-1}s^{-1}$.

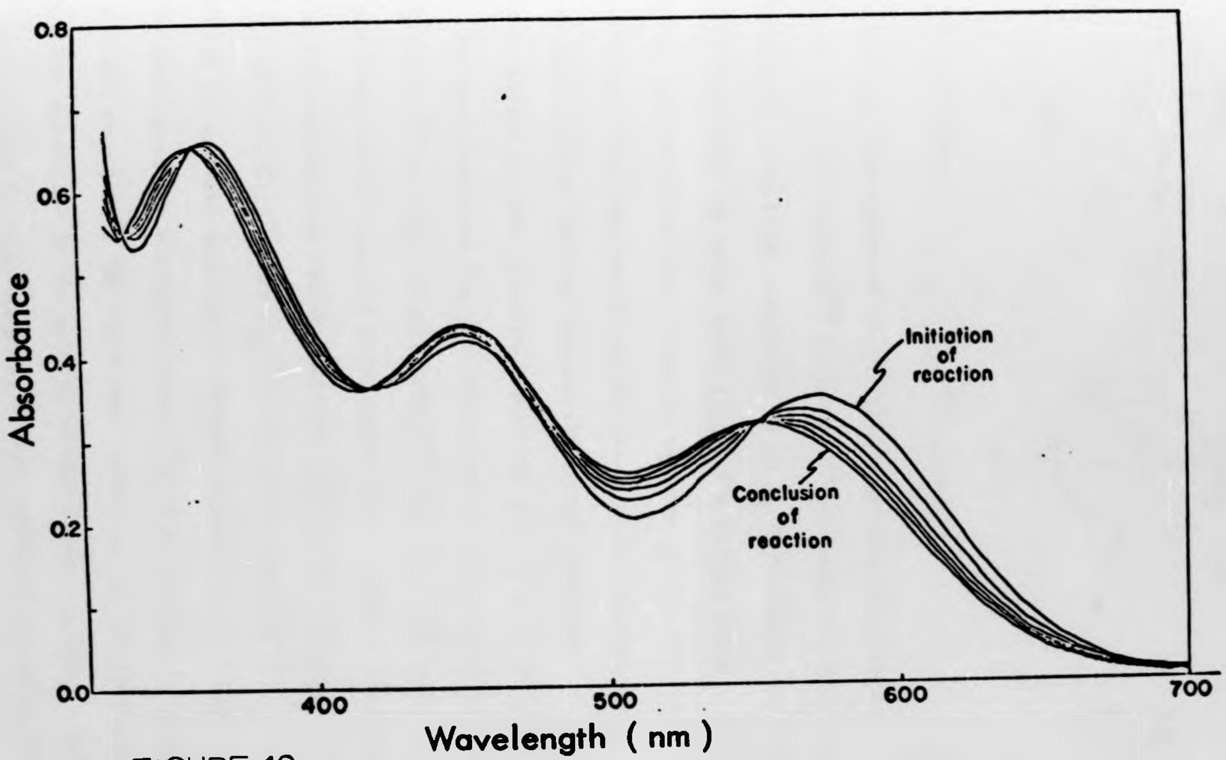
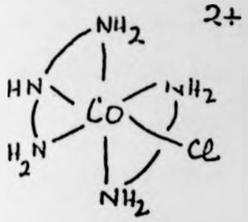


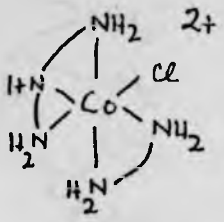
FIGURE 12

Visible spectra obtained during the course of Base hydrolysis of $[Co(dien)(glyO)Cl]ClO_4$ in 2,6, - Lutidine. (pH ~ 6.95)

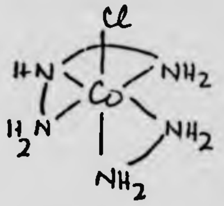
Table (28). The mer complex hydrolyse some 10^3 faster than ω and π - isomers with the fac - configuration.


XXV

ω-isomer


XXVI

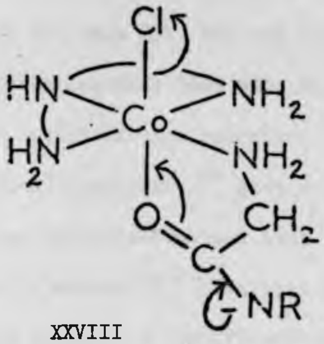
π-isomer


XXVII

κ-isomer

The base hydrolysis of cobalt(III) complexes is generally accepted to occur by an S_N1CB mechanism[103]. Nordmeyer[204] has suggested that in the base hydrolysis of cobalt(III) complexes by an S_N1CB mechanism the labile conjugate base is that with the amido group cis to the leaving group. The secondary nitrogen proton of the dien ligand is the most acidic site and thus if the ionisation of the most acidic proton leads to the formation of an active amido species(which may not necessarily be the case) the π - isomer should be more active in base hydrolysis than the ω-isomer, as is observed.

The rate constants for base hydrolysis of chloride in [CoCl(dien)-(glyglyOEt)]$^{2+}$ and [CoCl(dien)(glyNH$_2$)]$^{2+}$ are 1.1 X 10^6 and 5.8 X 10^5 $M^{-1}s^{-1}$ respectively at 25°C and I = 0.1M, Table (29). These reactions are extremely rapid and considerably faster than base hydrolysis of trans - (RS) - [Co(2,3,2 - tet)Cl$_2$]$^+$ where k_{OH}^{Cl} = 6.1 X 10^4 at 25.0°C[205]. In this latter reaction it has been possible to observe general base catalysis since deprotonation of the substrate becomes the rate determining step in the base hydrolysis reaction. The rapid base hydrolysis of the amide and peptide complexes may be due to the acidity of the - CONH - proton. The conjugate base(XXVIII)could provide adequate π- bond stabilisation of the 5-coordinate intermediate. Rapid base hydrolysis of cis - [Co(Cl)(en)$_2$(amine)]$^{2+}$ complexes (amine = aniline, p-toluidine) has been observed[115,206] and has been attributed to the high acidity of the coordinated aromatic amine[103].



XXVIII

3.3.3 Products of base hydrolysis

Villas-Boas[207] has isolated $[Co(dien)(glyO)(OH_2)](ClO_4)_2.H_2O$ and determined its absorption spectrum. In acid solution the complex has λmax 356(ε103) 452(ε 78) and 520 nm (ε 78) and 520 nm (ε 61) while the hydroxy complex obtained in basic solution has λmax 363(ε 132) and 500 nm (ε 95). The pK_a for the ionisation

$[Co(dien)(glyO)(OH_2)] \rightleftarrows [Co(dien)(glyO)(OH)^+ + H$

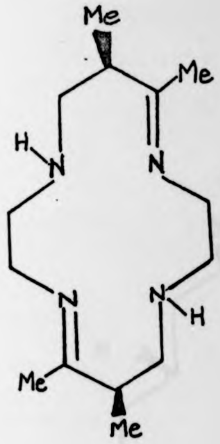
was determined spectrophotometrically to be 5.8 (measurements at 500 nm) and 5.9 by potent~~/~~iometric titration. As the visible spectrum of $[Co(dien)(glyO)(H_2O)]^{2+}$ shows splitting of the absorption band at ∿ 500 nm the two oxygen donors are probably trans to each other.

Base hydrolysis of trans (O,Cl) -$[CoCl(dien))glyO)]^+$ borax buffer (pH 9.18) gave a product with λmax 357 and 483 nm values which on acidification to convert to the aquo species had λmax 349, $\overset{4}{7}51$ and 523 nm in good agreement with the reported values for trans(O,O) - $[Co(dien)$-(glyO-$(glyO)(OH_2)]^{2+}$.

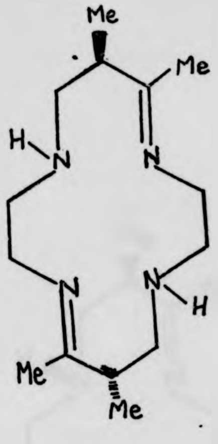
Mercury(II) catalysed aquation (mercury(II) nitrate in 0.1M HNO_3) of $[CoCl(dien)(glyO))]^+$ gave an aquo species with λmax 352, 453 and 519 nm. Since this latter reaction should occur with retention of configuration, it appears that base hydrolysis of trans (O,Cl) -$[CoCl(dien)(glyO)]^+$ occurs predominantly with retention of configuration. Base hydrolysis of trans (O,Cl) -$[CoCl(dien)(glyNH_2)]^{2+}$ gave a product λmax 353 and 483nm which on an acidification had λmax 351, 449 and 526 nm. Mercury(II) catalysed aquation gave an aquo complex with λmax 350, 451 and 527 nm so that retention of configuration also occurs in this reaction. Base hydrolysis of trans (O,Cl) -$[CoCl(dien)(glyglyOEt)]^{2+}$ gave an hydroxo species with λmax 344 and 472 nm which on acidification had λmax 339, 448 and 532 nm, while the aquo species obtained by mercury(II) catalysed aquation has λmax 342, 450 and 546 nm. In this case there is a significant shift of the lowest energy ligand field band suggesting that some isomerisation occurs during base hydrolysis which may explain the significantly higher rates of peptide bond hydrolysis observed with this complex.

Appendix I

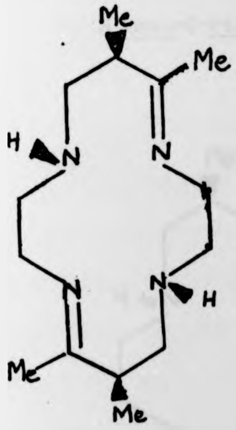
1.1 Possible structural forms of 5,6,12,13-Tetra-methyl-1,4,8,11-tetra-azacyclotetradeca-4,11 diene dihydroperchlorate; Me$_4$[14]diene.2HClO$_4$. -



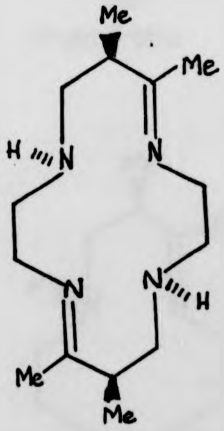
C-rac



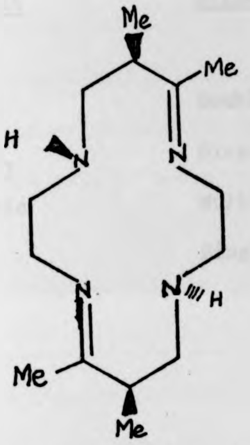
C-meso



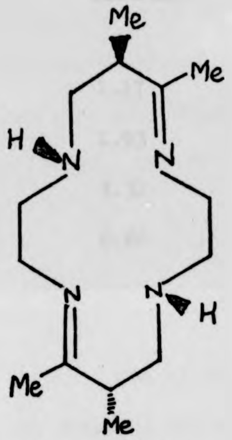
N-rac-C-rac



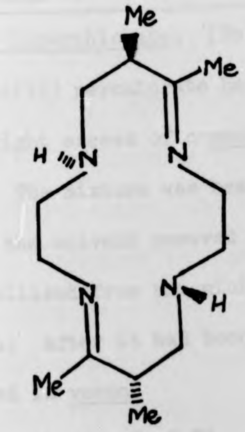
N-rac-C-rac



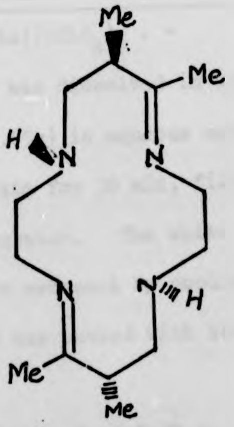
N-meso-C-rac



N-rac-C-meso



N-meso-C-meso



N-meso-C-meso

Two all meso forms + 4 racemic mixtures

TABLE 30

1.2 NMR spectral data for the 5,6,12,13- Tetramethyl -1,4,8,11- -tetra-azacyclotetradecadeca-4,11-diene dihydroperchlorate macrocycle (in perdeutro DMSO, δ(p.p.m) downfield from internal standard NaTMS, 90 MHz)

Assignment	Signal shape	Chemical	Rel. Intesities
Ring CH_3	Doublet*	1.17	6
Imino CH_3	Singlet	1.93	6
methylenic	Multiplet	3.31	-
NH	Singlet	6.66	2

*Two singlets of unequal intensities.

1.3 C-meso-5,12-Dimethyl-7,14-Diphenyl-1,4,8,11-tetra-azacyclotetradecane zinc(II) Diperchlorate; $[Zn(C\text{-}meso\text{-}Ph_2Me_2teta)](ClO_4)_2$. -

Zinc(II) perchlorate hexahydrate (0.5g) was dissolved in water ($10cm^3$) and a slight excess of c-mesoPh$_2$Me$_2$teta[62] (0.65g) in aqueous methanol ($30cm^3$) added. The mixture was heated on a water bath for 30 min, filtered whilst hot and the solvent removed on a rotary evaporator. The white product was recrystallised from the minimum volume of hot methanol by cooling on an ice bath; after it had been filtered off it was washed with ice-cold methanol and dried in *vacuo*.

(Found C, 44.17; H, 5.71; N, 8.45 Calc. for $C_{24}H_{36}N_4ZnCl_2O_8$. C, 44.69; H, 5.69; N, 8.69).

2.1 Reaction of cis-(Aminopropionitrile)bis(ethylenediamine)chloride cobalt(III) complex in Aqueous Solution . -

Introduction

In recent years there has been considerable interest in hydrolysis of nitriles in the coordination sphere of metal ions[208]. Breslow *et al* found that 1:1 complex of nickel(II) and 2-cyano-1,10-phenathroline is hydrolysed 10^7 faster than the uncomplexed substrate[209] Coordinated nitriles of the type $[Co(NH_3)_5N{\equiv}C\text{-}Ar]^{3+}$ are hydrolysed rapidly in base to give corresponding nitrogen carboxamido complexes[210,211]. The rate accelerations of *ca.* 2×10^6 observed in these systems are similar with that reported for the base hydrolysis of the acetonitrile complex $[Co(NH_3)_5N{\equiv}C;CH_3]^{3+}$ 212.

Experimental

Preparation of cis-$[Co(en)_2(NH_2CH_2CH_2CN)Cl]Cl_2.H_2O$. -

The complex was prepared essentially as described by Chan and Lee[213] and recrystallised from the minimum volume of hot water to which a few drops of concentrated hydrochloric acid had been added. The purple-red crystals of the complex separated from the cooled solution. The product was washed with ethanol then ether and dried in *vacuo* over silica gel.

(Found C, 22.56; H, 6.41; N, 22.39 Calc. for $C_7H_{24}N_6CoCl_3O$; C, 22.50; H, 6.47; N, 22.49%)

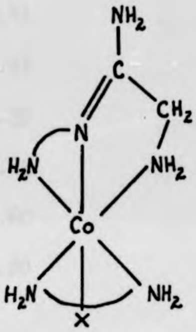
The i.r. spectrum of the complex was identical with that of analogous chloro-penta-ammine cobalt(III) complexes except for a strong band at 2250 cm^{-1} assigned to ν(CN) of the NH_2 coordinated nitrile. In addition CH_2 rocking vibrations occur at 875-895 cm^{-1}. In this region *cis*-bis(ethylenediamine) cobalt(III) complexes normally give two bands due to the lower symmetry of the *cis*-derivatives and the *trans*-isomer only one[135].

The visible absorption spectrum (λmax 528 (ε 83) and 368nm (ε 93)) is consistent with a *cis*-configuration[96].

Kinetics and Measurements

Visible spectral measurements were made with a Perkin Elmer 402 spectrophotometer. Spectrophotometric kinetics were carried out using a Gilford 2400S spectrophotometer. The spectrophotometric kinetic data is summarised in Table(31).

In near neutral or basic solution, the ions $[Co(en)_2X(NH_2CH_2CN)]^{2+}$ (X = Cl, Br) undergo rapid base-catalysed ring closure to give purple $[Co(en)_2[NH_2\overset{CH_2}{{}_\wedge}.C(NH_2):NCH_2.CH_2\overset{NH_2}{{}_\wedge}]X]^{2+}$, (I), containing a tridentate amidine ligand[214].



I

It was found that the product of base hydrolysis of cis-chloro aminopropionitrile bis(ethylenediamine) cobalt(III) complex [λmax 504 and 359nm] in a borax buffer was almost identical with the formation of hydroxypenta-ammine[147].

In the present case it appears that steric factors retard the cyclisation reaction considerably and the hydrolytic reaction of significance is the hydrolysis of chloride ligand. This conclusion must be regarded as somewhat tentative as amidine formation reaction might be very slow.

TABLE 31

Cis $-[Co(en)_2(NCCH_2CH_2NH_2)Cl]Cl_2$; λ = 330nm, I = 0.1M

Temp 25.0°C Boric acid/Borate Buffers

pH	$10^4 k_{obs}/s^{-1}$	$10^{-1} k_{OH}/M^{-1}s^{-1}$
8.67	3.41	5.63
8.77	3.93	5.15
8.98	4.39	3.54
9.18	3.83	1.93
9.38	3.60	1.11
9.54	3.20	0.74

2.2 Kinetic Data from Spectrophotometric Studies

2.2.1 cis-$[Co(en)_2(EtNH_2)Br]Br_2$, λ = 315 nm, I = 0.1M,

pH = 9.57 Temp 25.0°C OD_∞ = 45.10

Time	OD_t	(OD_t-OD_∞)	$\log(OD_t-OD_\infty)$
0.0	89.8	43.7	1.6405
0.5	83.9	38.8	1.5888
1.0	79.5	34.4	1.5366
1.5	75.6	30.5	1.4843
2.0	72.5	27.4	1.4378
2.5	69.4	24.3	1.3856
3.0	67.1	22.0	1.3424
3.5	64.9	19.8	1.2967
4.0	62.9	17.8	1.2504
4.5	61.0	15.9	1.2014
5.0	59.4	14.3	1.1553
5.5	57.9	12.8	1.1072
6.0	56.2	11.1	1.0453
6.5	54.8	9.7	0.9868
7.0	53.4	8.3	0.9191

Calculations: pH = 9.57

$[\bar{OH}] = 4.82 \times 10^{-5}$ moles

$$\text{Slope} = \begin{array}{r} 1.5366 \\ \underline{1.3424} \\ 0.1942 \end{array}$$

Slope = 0.0971

$$k_{obs} = \frac{2.303 \times 0.0971}{60} = 3.72 \times 10^{-3}\ s^{-1}$$

$$\frac{k_{obs}}{[OH^-]} = \frac{3.72 \times 10^{-3}}{4.82 \times 10^{-5} \times 60} = 7.70 \times 10^{1}\ M^{-1}s^{-1}$$

2.2.2 <u>Cis</u>-$[Co(en)_2(n\text{-}PrNH_2)Br]Br_2$ at pH = 9.57 OD_∞ = 38.0

Time	OD_t	(OD_t-OD_∞)	$\log(OD_t-OD_\infty)$
0.0	89.9	51.9	1.7152
0.5	83.3	45.3	1.6561
1.0	77.8	39.8	1.5999
1.5	73.3	35.3	1.5478
2.0	69.0	31.0	1.7918
2.5	65.8	27.8	1.4440
6.0	62.8	24.8	1.3945
3.0	60.0	22.0	1.3424
3.5	57.5	19.5	1.2900
4.0	55.3	17.3	1.2380
4.5	53.4	15.4	1.1875
5.0	51.6	13.6	1.1335
5.5	49.9	11.9	1.0755
7.0	47.1	9.1	0.9590
8.0	44.9	6.9	0.8388
9.0	42.7	4.7	0.6721

Calculations: pH = 9.57

$[O\bar{H}]$ = 4.81 X 10^{-5} moles

$$\text{Slope} = \begin{array}{r} 1.6561 \\ \underline{1.4440} \\ 0.2121 \end{array}$$

Slope = 0.1010

$$k_{obs} = \frac{2.303 \text{ X } 0.1010}{60} = 3.87 \text{ X } 10^{3} \text{ s}^{-1}$$

$$\frac{k_{obs}}{[OH^-]} \quad \frac{3.87 \text{ X } 10^{3}}{4.81 \text{ X } 10^{-5}} = 8.05 \text{ X } 10^{1} \text{ M}^{-1} \text{ s}^{-1}$$

2.2.3 <u>Cis</u>-$[Co(en)_2(n\text{-}BuNH_2)Br]Br_2$ at pH = 9.01 OD_∞ = 25.60

Time	OD_t	(OD_t-OD_∞)	$\log(OD_t-OD_\infty)$
0	88.10	62.5	1.7959
2	78.8	53.2	1.7259
4	71.50	45.9	1.6618
6	65.0	39.4	1.5955
8	59.8	34.2	1.5340
10	55.3	29.7	1.4728
12	51.9	26.3	1.4200
14	48.3	22.7	1.3560
16	45.5	19.9	1.2989
18	42.9	17.3	1.2380
20	40.9	15.3	1.1847
22	39.1	13.5	1.1303
24	37.3	11.7	1.0682
26	36.0	10.4	1.0170
28	34.9	9.3	0.9685

Calculations: pH = 9.01 log (OH^-) = 5.01 $[OH^-] = 1.33 \times 10^{-5}$ moles

$$\text{Slope} = \begin{array}{r} 1.4200 \\ \underline{1.1847} \\ 0.2353 \end{array}$$

Slope = 0.0294

$$k_{obs} = \frac{2.303 \times 0.0297}{60} = 1.12 \times 10^{-3}\ s^{-1}$$

$$\frac{k_{obs}}{[OH^-]} = \frac{1.12 \times 10^{-3}}{1.33 \times 10^{-5}} = 8.46 \times 10^{-}\ M^{-1}\ s^{-1}$$

2.3.1 Cis-$[Co(en)_2(n\text{-}PrNH_2)Br]Br_2$; λ=315nm,

Temp = 39.8°C OD_∞ 25.60 pH = 8.38 I = 0.1M

Time	OD_t	$OD_t - OD_\infty$	$\log(OD_t - OD_\infty)$
0.0	89.5	63.9	1.8055
0.5	82.5	56.9	1.7551
1.0	75.8	50.2	1.7007
1.5	69.7	44.1	1.6444
2.0	64.3	38.7	1.5877
2.5	59.4	33.8	1.5289
3.0	55.1	29.5	1.4698
3.5	50.9	25.3	1.4031
4.0	47.7	22.1	1.3444
4.5	44.9	19.3	1.2856
5.0	42.4	16.8	1.2253
5.5	40.2	14.6	1.1644
6.0	38.4	12.8	1.1072
6.5	36.3	10.7	1.0294
7.0	34.9	9.3	0.9685

2.3.2 Cis-$[Co(en)_2(n\text{-}PrNH_2)Br]Br_2$; λ = 315nm pH = 8.38 OD_∞ = 37.01

I = 0.1M Temp 39.8°C.

Time	OD_t	OD_t-OD_∞	$\log(OD_t-OD_\infty)$
0.0	91.2	54.2	1.7340
0.5	85.3	48.3	1.6839
1.0	79.9	42.9	1.6325
1.5	74.8	37.8	1.5775
2.0	70.2	33.2	1.5211
2.5	66.3	29.3	1.4669
3.0	62.8	25.8	1.4116
3.5	60.1	23.1	1.3636
4.0	57.1	20.1	1.3032
4.5	55.0	18.0	1.2553
5.0	52.6	15.6	1.1931
5.5	51.1	14.1	1.1492
6.0	49.4	12.4	1.0934
6.5	47.9	10.9	1.0374
7.0	46.7	9.7	0.9868

2.3.3 Cis-$[Co(en)_2(n\text{-}PrNH_2)Br]Br_2$; λ = 315nm

Temp 30.1°C pH = 8.40 I = 0.1M OD_∞ = 25.10

Time	OD_t	$OD_t - OD_\infty$	$\log(OD_t - OD_\infty)$
0.0	95.3	70.2	1.8463
2.0	87.5	62.4	1.7952
4.0	80.0	54.9	1.7396
6.0	73.6	48.5	1.6857
8.0	67.7	42.6	1.6294
10.0	62.8	37.7	1.5763
12.0	58.3	33.2	1.5211
14.0	54.5	29.4	1.4683
16.0	51.0	25.9	1.4133
18.0	48.1	23.0	1.3617
20.0	45.4	20.3	1.3075
22.0	42.9	17.8	1.2504
24.0	40.9	15.8	1.1987

Appendix III

3.1 Chloride Hydrolysis

3.1.1 Base hydrolysis of $[Co(dien)(glyO)Cl]ClO_4$; λ = 505 nm, pH = 7.26, I = 0.1M, Temp 25.0°C, Lutidine- HCl Buffers OD_∞ = 71.7

Time (minutes)	OD_t	$(OD_\infty - OD_t)$	$\log(OD_\infty - OD_t)$
0.0	30.9	40.8	1.6107
0.5	34.6	37.1	1.5694
1.0	37.9	33.8	1.5289
1.5	41.0	30.7	1.4871
2.0	43.8	27.9	1.4456
2.5	46.5	25.2	1.4014
3.0	48.3	23.4	1.3692
3.5	50.8	20.9	1.3201
4.0	52.6	19.1	1.2810
4.5	54.5	17.2	1.2355
5.0	56.2	15.5	1.1903
5.5	57.7	14.0	1.1461
6.0	58.8	12.9	1.1106
6.5	60.0	11.7	1.0682

3.1.2 $[Co(dien)(glyNH_2)Cl](ClO_4)_2$; λ 307 nm, I = 0.1M, CH_3COOH/KOH Buffers, Temp 25.0°C, OD_∞ = -9.5 pH = 4.97

Time (minutes)	OD_t	$(OD_t - OD_\infty)$	$\log(OD_t - OD_\infty)$
0	87.2	96.7	1.9854
2	80.1	89.6	1.9523
4	73.5	83.0	1.9191
6	65.9	75.7	1.8774
8	61.6	71.1	1.8519
10	56.5	66.0	1.8195
12	52.1	61.6	1.7896
16	44.0	53.5	1.7284
20	36.5	76.0	1.6628
24	29.9	39.4	1.5955
28	24.6	34.1	1.5328
32	20.1	29.6	1.4713
36	16.3	25.8	1.4116
40	13.1	22.6	1.3541
44	10.2	19.7	1.2945

3.1.3 $[Co(dien)(glyglyOEt)Cl](ClO_4)_2$; λ = 307 nm, I = 0.1M, pH = 4.07

CH_3COOH/KOH Buffers, OD_∞ = -28.8 Temp = 25.0°C

Time (minutes)	OD_t	$(OD_t - OD_\infty)$	$\log(OD_t - OD_\infty)$
0	98.6	127.4	2.1052
9	94.5	123.3	2.0909
8	90.1	118.9	2.0752
12	85.9	114.7	2.0595
16	81.5	110.3	2.0425
20	77.0	105.8	2.0250
24	72.8	101.6	2.0067
28	68.5	97.3	1.9881
32	64.5	93.3	1.9669
36	60.9	89.7	1.9528
40	57.3	86.1	1.9350
44	53.8	82.6	1.9170
48	50.5	79.3	1.8993
52	47.5	76.3	1.8825
56	44.8	73.6	1.8669
60	41.9	70.7	1.8494
67	39.3	68.1	1.8331
68	36.5	65.3	1.8149
72	34.0	62.8	1.7980
76	31.5	60.3	1.7803
80	29.0	57.8	1.7619
84	26.6	55.4	1.7435
88	24.3	53.1	1.7251
92	22.3	51.1	1.7084
96	20.2	49.0	1.6902

3.2 Peptide hydrolysis

$[Co(dien)(glyglyOEt)NO_2](ClO_4)_2$; λ = 334 nm pH = 10.86, I = 0.1M,
OD∝ = 32.69 Temp 24.8°C

Time (minutes)	OD_t	$(OD_t - OD_\infty)$	$\log(OD_t - OD_\infty)$
0	95.4	62.71	1.7974
2	91.5	58.81	1.7695
4	86.9	54.21	1.7341
6	83.0	50.31	1.7017
8	78.9	46.21	1.6647
10	75.4	42.71	1.6305
12	71.9	39.21	1.5934
14	68.6	35.91	1.5552
16	65.9	33.21	1.5212
18	63.4	30.71	1.4872
20	61.0	28.31	1.4520
24	57.0	24.31	1.3858
28	53.0	20.31	1.3077
32	50.2	17.51	1.2433
36	47.4	14.71	1.1676
40	45.4	12.71	1.1041
47	43.2	10.51	1.0216
48	42.7	9.11	0.9595
52	40.6	7.91	0.8982
56	39.2	6.51	0.8136
60	38.2	5.51	0.7412

3.3 Base hydrolysis of [Co(dien)(glyO)]ClO_4; λ = 505 nm, I = 0.2M 2,6 - lutidine - HCl Buffers, Temp 25.0°C.

The kinetics of the base hydrolysis were monitored spectrophotometrically with a Gilford 2400 S spectrophotometer. Chloride hydrolysis was studied using 2,6 - Lutidine - HCl buffers, the ionic strength being adjusted to I = 0.2M with $NaClO_4$ In each case the volume was made up to 100 cm^3. In each case the volume was made up to 100 cm^3.

3.3.1 (20 cm^3 of 2M lutidine + 20 cm^3 of 1MHCl, NO $NaClO_4$)

pH	10^3k_{obs} s^{-1}	$10^{-4}k_{OH}$ $M^{-1}s^{-1}$
6.64	1.71	3.03
6.64	1.66	2.93
6.65	1.38	2.38

3.3.2 (10 cm^3 of 2M lutidine + 10 cm^3 of 1M HCl + 0.10 moles of $NaClO_4$)

7.06	2.50	1.68
7.06	2.98	2.00
7.06	3.03	1.37

3.3.3 (5 cm^3 of 2M - lutidine + 5 cm^3 of 1M HCl + 0.15 moles of $NaClO_4$)

7.27	4.20	1.86
7.24	4.20	1.91

3.3 Base hydrolysis of [Co(dien)(glyO)]ClO_4; λ = 505 nm, I = 0.2M 2,6 - lutidine - HCl Buffers, Temp 25.0°C.

The kinetics of the base hydrolysis were monitored spectrophotometrically with a Gilford 2400 S spectrophotometer. Chloride hydrolysis was studied using 2,6 - Lutidine - HCl buffers, the ionic strength being adjusted to I = 0.2M with $NaClO_4$ In each case the volume was made up to 100 cm^3.

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pH	$10^3 k_{obs}$ s^{-1}	$10^{-4} k_{OH}$ $M^{-1}s^{-1}$
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7.24	4.20	1.91

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