Synthesis and Aquation Kinetics of the *cis*-Dichloro- and Three Diastereoisomeric *trans*-Dichloro-complexes of Cobalt(III) with the Macrocyclic Ligand C-*rac*-5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradecane

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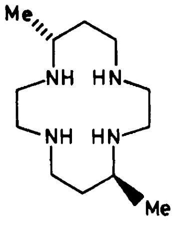
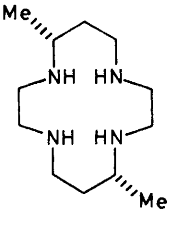
The synthesis and characterisation of *cis*-[$CoCl_2L$]Cl and three diastereoisomeric *trans*-[$CoCl_2L$]ClO_4 complexes [designated (B), (C), and (D)] are described (L = C-*rac*-5,12-dimethyl-1,4,8,11-tetra-azacyclotetradecane). Ten diastereoisomeric *trans*-[$CoCl_2L$]$^+$ complexes are in principle possible. Isomer (B) is pale green, is aquated without isomerisation ($k_{aq.}^{25} = 4.5 \times 10^{-5}$ s^{-1}), and has the *trans* III (*RSSR*) configuration of the chiral nitrogen centres, with one equatorial and one axial methyl substituent (confirmed by ^{1}H n.m.r. measurements). This isomer is comparable with the 'aquation-inert' [$CoCl_2$(cyclam)]$^+$ isomer (cyclam = 1,4,8,11-tetra-azacyclotetradecane). Isomer (C) is bright green, is aquated more rapidly than isomer (B) ($k_{aq.}^{25} = 6.5 \times 10^{-4}$ s^{-1}) to give a green chloroaqua-complex indicating retention of configuration, and could have a configuration with two equatorial methyl groups. Isomer (D), which is deep green, is prepared by isomerisation of *cis*-[$CoCl_2L$]Cl in HCl solution. Isomer (D) is aquated quite rapidly ($k_{aq.}^{25} = 9.0 \times 10^{-4}$ s^{-1}) with isomerisation to give a violet chloroaqua-species, and probably has a configuration with two equatorial methyl groups and two 'twist-boat' six-membered chelate rings. Activation parameters for aquation of the *cis* and *trans* complexes have been determined, and their relative reactivities are discussed. The ability of the macrocyclic ligand to fold in the transition state of a dissociative aquation reaction is shown to be important in determining the reactivities of the complexes.

The preceding paper [1] dealt with cobalt(III) complexes of the C-*meso* ligand (1). The present paper describes the synthesis and aquation kinetics of a number of cobalt(III) complexes of the C-*rac* ligand [L = (2)]. The complex *cis*-[$CoCl_2L$]Cl and three diastereoisomeric *trans*-[$CoCl_2L$]ClO_4 complexes [designated (B), (C), and (D)] have been prepared and their aquation kinetics studied, in an effort to determine the effects of chiral nitrogen centres on aquation rates. A subsequent paper will deal with complexes of the C-*rac* ligand with copper(II), nickel(II), and other ions.[2]



(1)

C-*meso*



(2)

C-*rac*

Experimental

5,12-Dimethyl-1,4,8,11-tetra-azacyclotetradeca-4,11-diene dihydroperchlorate was prepared as previously described.[3]

The ligands C-*meso*- and C-*rac*-5,12-dimethyl-1,4,8,11-tetra-azacyclotetradecane were prepared as follows.[4] The dihydroperchlorate salt of the diene (100 g) was dissolved in methanol–water (1 : 1 v/v, 500 cm^3) and $NaBH_4$ (20 g, excess) added in small amounts (*ca.* 0.5 g) with magnetic stirring over a period of *ca.* 1 h. The resulting solution was heated on a water-bath for *ca.* 1 h until evolution of H_2 ceased. The methanol was removed on a rotary evaporator and sodium hydroxide solution added to bring the pH to >14. The aqueous solution was then continuously extracted with benzene. The benzene extract was dried, and the mixture of C-*rac* and C-*meso* amines obtained by evaporation was separated by fractional crystallisation as previously described.[3] The ratio of C-*meso* to C-*rac* was *ca.* 6 : 1. The C-*rac* amine was recrystallised from diethyl ether, m.p. 105—106 °C (lit.,[3] 109 °C) (Found: C, 63.0; H, 12.2; N, 24.6. Calc. for $C_{12}H_{28}N_4$: C, 63.1; H, 12.35; N, 24.5%).

Preparation of Cobalt(III) *Complexes.*—The C-*rac* ligand (0.90 g) was dissolved in methanol (50 cm^3) and cobalt(II) chloride hexahydrate (0.92 g) in methanol (20 cm^3) added to give a deep brown solution. A rapid stream of air was bubbled through the solution for 2 h. Concentrated HCl (3 cm^3) was then added to give a green solution, and the methanol was evaporated under an air stream. Violet crystals of the *cis* isomer (A) (300 mg) were deposited on evaporation to half volume and these were removed by filtration and washed with water, ethanol, then ether, and air dried. The green filtrate was diluted with water (*ca.* 25 cm^3) and concentrated perchloric acid (3 cm^3, 70%) added. Green crystals of the isomer (B) (500 mg) rapidly deposited which were filtered off, washed with ethanol then ether, and dried. This isomer is soluble in MeCN and dimethyl sulphoxide (dmso). The filtrate, which was still green, was evaporated to half volume on a steam-bath and the small quantity of green complex obtained on cooling was rejected [a mixture of isomers (B) and (C)]. The filtrate was further concentrated to half volume and cooled overnight to give the bright green isomer (C) (*ca.* 100 mg) which was filtered off, washed with ethanol then ether, and dried. Isomer (C) is soluble in water, MeCN, and dmso.

Isomer (D) was obtained as follows. The violet *cis* isomer (A) (100 mg) was dissolved in hot water (25 cm^3) and dilute hydrochloric acid (*ca.* 5 cm^3) added, followed by a few drops of concentrated $HClO_4$. The solution was heated at *ca.* 60 °C for 1 h, and then set aside. Deep green crystals of isomer (D) (*ca.* 50 mg) slowly deposited from the violet solution. This isomer is soluble in water, MeCN, and dmso. Analytical data for the various isomers are summarised in Table 1. Isomer (B) is pale green, isomer (C) green, and isomer (D) deep green.

Table 1. Analytical data

Complex	Analysis (%) * C	H	N
cis-[$CoCl_2L$]Cl	36.2 (36.6)	7.1 (7.2)	14.0 (14.2)
trans-[$CoCl_2L$]ClO_4 (B)	31.3 (31.5)	6.0 (6.2)	12.0 (12.2)
trans-[$CoCl_2L$]ClO_4 (C)	31.7	6.1	12.0
trans-[$CoCl_2L$]ClO_4 (D)	31.2	6.0	12.2

* Calculated figures in parentheses.

Table 2. Electronic spectra

Complex	$\lambda_{max.}$/nm	ε/dm^3 mol^{-1} cm^{-1}
cis-[$CoCl_2L$]Cl [a]	534	77
	390	102
	238	15 650
trans-[$CoCl_2L$]ClO_4 (B) [b]	625	31
	455 (sh)	34
	400 (sh)	60
	322	778
trans-[$CoCl_2L$]ClO_4 (C) [b]	630	34
	450 (sh)	48
	320 (sh)	1 500
	254	20 550
trans-[$CoCl_2L$]ClO_4 (D) [b]	606	31
	365 (sh)	183
	264	30 500
	260	27 200

[a] In H_2O. [b] In MeCN.

Kinetic Measurements.—The aquation kinetics were monitored spectrophotometrically with a Gilford 2400S spectrophotometer which was interfaced with an Apple II computing system. All the aquation studies were carried out using 0.097 mol dm^{-3} HNO_3 as solvent. Aquation of the *cis* complex was monitored at 335 nm where an absorbance decrease occurs. Loss of the second chloride ligand leads to an absorbance increase at this wavelength. Aquation of isomer (B) was monitored at 307 nm, isomer (C) at 330 nm, and isomer (D) at 290 nm. Excellent first-order plots were obtained in all cases, consistent with a high degree of isomeric purity.

Routine and interval-scan electronic spectra were measured using a Perkin-Elmer 402 spectrophotometer. I.r. spectra were determined as discs in KBr, using a Perkin-Elmer 457 instrument. ^{1}H N.m.r. spectra were determined using $(CD_3)_2SO$ or CD_3CN as solvent with tetramethylsilane as internal reference. Measurements were made with a Bruker WP80 instrument.

Results and Discussion

Aeration of methanolic solutions of the ligand and cobalt(II) chloride hexahydrate followed by treatment with HCl gives initially the violet complex *cis*-[$CoCl_2L$]Cl. Addition of perchloric acid followed by fractional crystallisation gives initially the pale green *trans*-[$CoCl_2L$]ClO_4 isomer (B), followed by the bright green *trans*-[$CoCl_2L$]ClO_4 isomer (C). Isomerisation of *cis*-[$CoCl_2L$]$^+$ in HCl solution followed by addition of $HClO_4$ gives the deep green *trans*-[$CoCl_2L$]ClO_4 isomer (D). The electronic spectra (Table 2) are fully consistent with the assigned configurations. The three diastereoisomeric *trans* complexes have significant differences in their i.r. spectra in the 1 200—1 400 cm^{-1} region (Figure 1), which are useful for identification purposes. The *cis* isomer is readily distinguished as it has two ν(NH) bands at 3 145 and 3 225 cm^{-1}, the first band being more intense than the second. The three *trans* isomers have a single ν(NH) band near 3 200 cm^{-1}. They can also be distinguished by their ^{1}H n.m.r. spectra. The two ring-methyl groups can be diaxial, diequatorial, or axial–equatorial depending upon the configuration of the chiral nitrogen centres. Isomer (B) has two methyl doublets at δ 1.39 (J = 7.0 Hz) and 1.22 (J = 7.2 Hz) indicating equatorial and axial groups (Table 3). Isomer (C) has a single methyl doublet at δ 1.40 (J = 7 Hz). Isomer (D) also has a single methyl doublet at δ 1.37 (J = 7.2 Hz). Isomer (B) is aquated slowly with retention of configuration, (C) is aquated more rapidly to give a green chloroaqua-complex indicating no isomerisation, while (D) is aquated rapidly to give a violet chloroaqua-species indicating isomerisation.

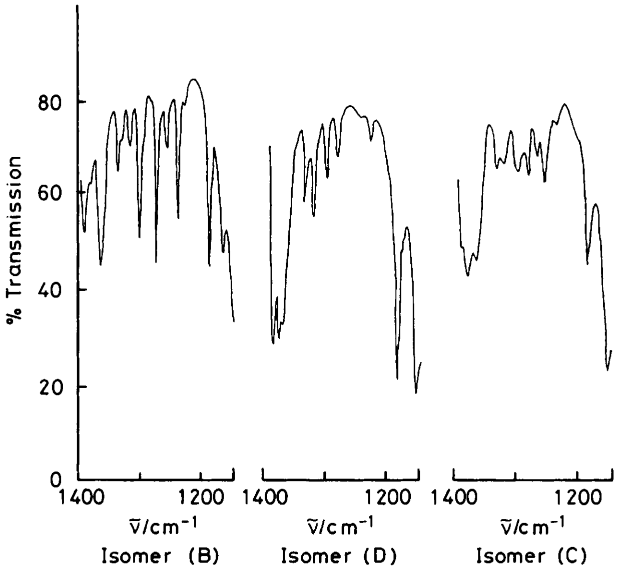


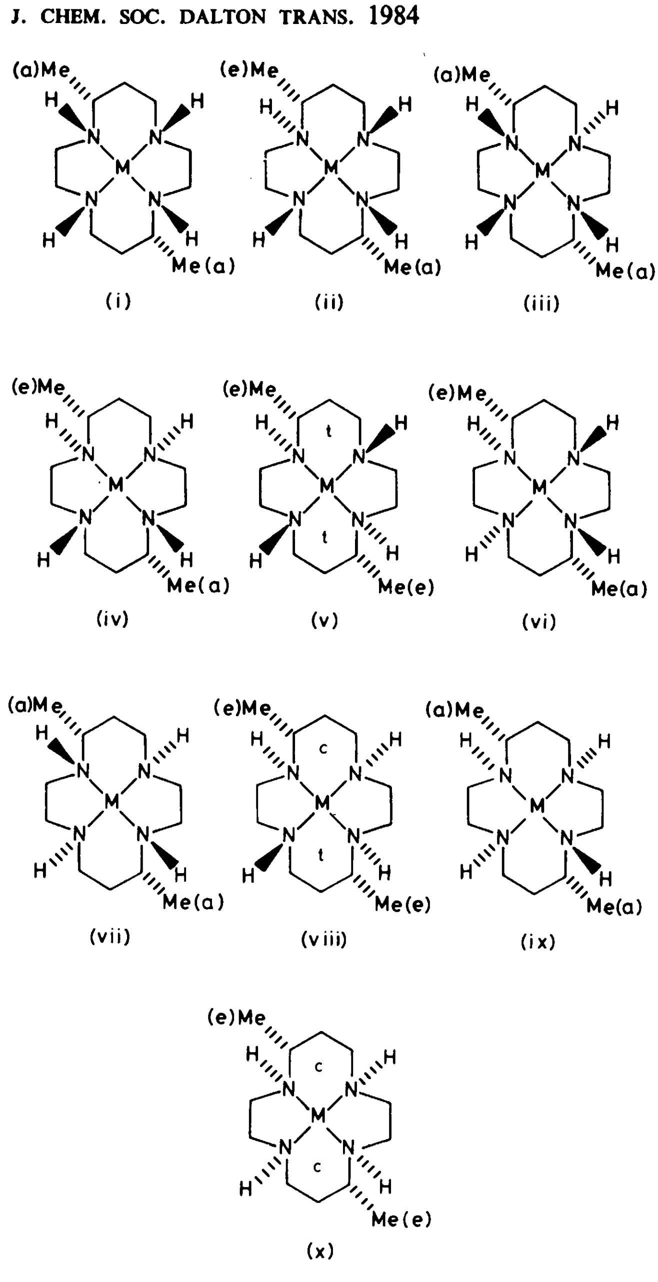
Figure. I.r. spectra of the three *trans*-diastereoisomers in the 1 400—1 250 cm^{-1} region (KBr discs)

Table 3. ^{1}H N.m.r. spectra of the diastereoisomeric *trans*-[$CoCl_2L$]-ClO_4 complexes in $(CD_3)_2SO$ with $SiMe_4$ as reference

Isomer	δ/p.p.m. CH$_3$	NH
(B)	1.39 (d, J = 7.0 Hz), 1.22 (d, J = 7.2 Hz)	6.62, 6.37, 5.40
(C)	1.40 (d, J = 7.0 Hz)	6.62, 5.55
(D)	1.37 (d, J = 7.2 Hz)	6.40, 5.76

Stereochemical Considerations.—The structures of the ten possible diastereoisomeric complexes of the C-*rac* ligand are summarised in Scheme 1. An examination of molecular models indicates that a diequatorial arrangement of the ring-methyl substituents occurs in structures (v), (viii), and (x). The arrangement in (i), (iii), and (vii) is diaxial, and diastereoisomers (ii), (iv), (vi), and (ix) have one axial and one equatorial methyl substituent.

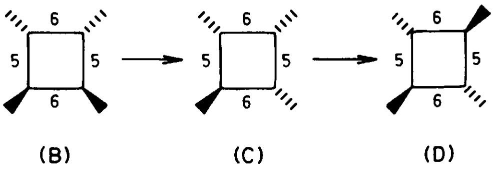
The thermodynamically stable *trans* III [5] (*RSSR*) configuration of the chiral secondary NH centres is only found in structure (iv). This configuration has been assigned to the



Scheme 1. Configurations of diastereoisomers with the *C-rac* ligand. Isomer (B) has structure (iv), isomer (D) structure (v), and isomer (C) structures (viii) or (x). a = Axial; e = equatorial; c = chair six-membered ring; t = twist-boat ring

non-labile diastereoisomer of *trans*-[CoCl$_2$(cyclam)]$^+$,[6-8] and we also assign this configuration to the *trans* isomer (B). This view is consistent with the ^{1}H n.m.r. data which indicate one axial and one equatorial methyl group.

Isomer (D) is obtained by isomerisation of the folded *cis*-[CoCl$_2$L]$^+$ cation in acidic solution which should not allow inversion of the secondary NH centres. Crystallographic work on *cis*-[Co(cyclam)(en)]Cl$_3$·3H$_2$O[9] (en = ethylenediamine; cyclam = 1,4,8,11-tetra-azacyclotetradecane) and *cis*-[CoCl$_2$(cyclam)]Cl[10] has established the nitrogen configuration V (see Scheme 1, preceding paper) which allows two fold lines. The nitrogen configuration II appears to occur in the *cis*-dichloro-complex of the *C-meso* ligand which allows only one fold line. We feel it most probable that *cis*-[CoCl$_2$L]$^+$ has nitrogen configuration V which is found in structures (v) and (vii) of Scheme 1. The diastereoisomer (v) has two equatorial methyl groups and (vii) two axial methyl groups.



Scheme 2. Possible interconversions of diastereoisomers (the numbers indicate the size of the chelate rings)

The ^{1}H n.m.r. spectrum of isomer (D) has a single methyl doublet at δ 1.37 indicating two equatorial methyl groups consistent with structure (v).

Isomer (C) has a single methyl doublet at δ 1.40 indicating a diequatorial arrangement of the methyl substituents found in diastereoisomers (v), (viii), and (x). If isomer (D) has structure (v), (C) must be one of the set (viii) and (x). The diastereoisomer (viii) has one potential fold line while (x) has two potential fold lines. Two chair (C) six-membered rings occur in structure (x) and there is one chair and one twist-boat (t) six-membered ring in (viii).

Aquation Kinetics.—Aquation rates for the four dichloro-complexes at various temperatures are summarised in Table 4. Activation parameters and aquation rates at 25 °C are collated in Table 5. For aquation reactions of cobalt(III) polyamine complexes proceeding *via* a dissociative mechanism it is generally observed that stereochemical retention is associated with negative values of $\Delta S^‡$ and stereochemical change with positive $\Delta S^‡$ values.[11-13] This view is endorsed by the present results. Isomer (D) is aquated with stereochemical change to give a violet chloroaqua-complex ($\Delta S^‡ = +22$ J K^{-1} mol^{-1}), and *cis*-[CoCl$_2$L]$^+$ ($\Delta S^‡ = +12$ J K^{-1} mol^{-1}) can be isomerised under acidic conditions to give isomer (D).

As previously observed with cyclam (Table 6),[6] and the *C-meso* derivative of L,[1] rapid aquation of the *cis*-dichloro-complexes is observed with a factor of *ca.* 10^3 between the relative aquation rates of the *cis* isomer and the inert *trans* isomer (B). This *trans* isomer has the nitrogen configuration III, and lacks any fold lines.

For aquation of *cis*-[CoCl$_2$(cyclam)]$^+$, $k_{aq.}^{25} = 1.6 \times 10^{-2}$ s^{-1} (ref. 6) which is comparable with $k_{aq.}^{25} = 5.5 \times 10^{-2}$ s^{-1} observed with *cis*-[CoCl$_2$L]$^+$. The aquation of the (*RSSR*) diastereoisomer of *trans*-[CoCl$_2$(cyclam)]$^+$ which has the nitrogen configuration III ($k_{aq.}^{25} = 1.1 \times 10^{-6}$ s^{-1})[7] takes place somewhat more slowly than that of isomer (B) ($k_{aq.}^{25} = 4.5 \times 10^{-5}$ s^{-1}) with the same nitrogen configuration. This result may be due to some steric acceleration by the ring-methyl substituents in the latter complex.

Isomers (C) and (D) have comparable aquation rates, but markedly different values of $\Delta S^‡$, consistent with retention of configuration with isomer (C) ($\Delta S^‡ = -35$ J K^{-1} mol^{-1}) and inversion with (D) ($\Delta S^‡ = +22$ J K^{-1} mol^{-1}). Isomer (D) has two potential fold lines with two twist-boat six-membered rings in a *trans* complex and isomerisation to a folded *cis* complex is thus probable in aquation.

Isomer (C) could have structure (viii) with one fold line or structure (x) with two potential fold lines. Folded *cis* derivatives have not been observed with the nitrogen configuration found in (x). This nitrogen configuration I (*RSRS*) is observed in complexes of *NN'N''N'''*-tetramethyl-substituted cyclam which are often five-co-ordinate.[14,15] Structure (viii) would be expected to lead to quite rapid aquation, but not necessarily with inversion of configuration to give a *cis* species, and may well be the correct representation of isomer (C). The interconversion (B) ⟶ (C) ⟶ (D) could involve a single nitrogen inversion at each step (Scheme 2).

Table 4. Aquation of the dichloro-complexes at various temperatures in 0.097 mol dm^{-3} HNO_3

(*a*) *cis*-$[CoCl_2L]Cl$		(*b*) *trans*-$[CoCl_2L]ClO_4$ isomer (B)		(*c*) *trans*-$[CoCl_2L]ClO_4$ isomer (C)		(*d*) *trans*-$[CoCl_2L]ClO_4$ isomer (D)	
θ_c/°C	$10^3k_{aq.}/s^{-1}$	θ_c/°C	$10^4k_{aq.}/s^{-1}$	θ_c/°C	$10^3k_{aq.}/s^{-1}$	θ_c/°C	$10^3k_{aq.}/s^{-1}$
10.5	9.5	25.0	0.45	25.0	0.65	25	0.9
13.0	11.35	33.5	1.3	34.0	1.7	30.5	1.8
16.0	17.4	39.0	2.6	37.0	2.4	34.0	3.1
19.5	25.8	44.0	5.0			37.0	4.1
25.0	54.6						

Table 5. Aquation rates at 25 °C and the activation parameters *

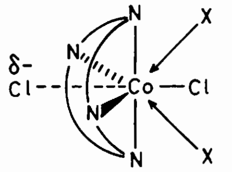
Complex	$k_{aq.}^{25}/s^{-1}$	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$/J K^{-1} mol^{-1}
cis-$[CoCl_2L]Cl$	5.5×10^{-2}	83.9 ± 4	12 ± 4
trans-$[CoCl_2L]ClO_4$ (B)	4.5×10^{-5}	96.7 ± 2	-4 ± 4
trans-$[CoCl_2L]ClO_4$ (C)	6.5×10^{-4}	80.6 ± 2	-35 ± 6
trans-$[CoCl_2L]ClO_4$ (D)	9.0×10^{-4}	96.9 ± 5	22 ± 6

* Activation parameters determined from the least-squares slope and intercept of the Eyring plots. The values of $k_{aq.}^{25}$ calculated from the quoted activation parameters are as follows: 5.2×10^{-2} for the *cis* isomer, 4.4×10^{-5} for the *trans* isomer (B), 6.5×10^{-4} for the *trans* isomer (C), 9.0×10^{-4} s^{-1} for the *trans* isomer (D).

Table 6. Aquation rates and activation parameters for *cis*- and *trans*-$[CoCl_2(cyclam)]^+$ complexes [a]

Isomer	$k_{aq.}^{25}/s^{-1}$	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$/J K^{-1} mol^{-1}	% Steric change
cis-RRRR V [b]	1.6×10^{-2}	76.6	−25	0
trans-RRRR V [b]	1.75×10^{-3}	101.3	+42	25
trans-RSSR III [b]	1.10×10^{-6}	103	−12	0

[a] Data taken from ref. 3. [b] The roman numerals correspond to the configurations given in ref. 5.



(3)

Conclusions

The present results, and those obtained with the *C-meso* ligand,[1] complement the observations of Poon and Tobe that *trans* complexes of cyclam with the nitrogen configuration III (*RSSR*) are aquated slowly [7] while *cis* and *trans* complexes [6] with the nitrogen configuration V (*RRRR* or *SSSS*) are aquated quite rapidly.

The presence of potential fold lines in the ligand can lead to high reactivity in aquation and we have previously presented evidence that the ligand should be capable of folding towards the leaving group.[6] Aquation is a dissociative process involving a five-co-ordinate intermediate. In the present macrocyclic complexes, the intermediate is not a regular square pyramid, but a trigonal bipyramid or distorted square pyramid with the cobalt atom lying out of the plane of the four nitrogen atoms. The macrocycle folds towards the leaving group as shown diagrammatically in structure (3). If the macrocycle cannot fold, presumably the intermediate more closely resembles a square pyramid, the attainment of which requires a higher free energy of activation. If the intermediate is of the trigonal-bipyramidal type the entering group X can retrace the pathway of the leaving group to give the *trans* complex or can take the pathways indicated by the arrows in structure (3) to give a *cis* complex and lead to inversion of configuration.

In the *cis* complex, dissociation of the halide ligand can lead directly to structure (3) without any additional flexing of the macrocycle and so rapid aquation occurs. There can be little doubt that a certain degree of folding of the macrocycle is required to reach the transition state for aquation. The presence of a fold line allows the transition state to be reached more readily and thus leads to rapid aquation.

Acknowledgements

We thank the S.E.R.C. for financial support and the award of a postdoctoral fellowship (to R. B.).

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Received 3rd *May* 1983; *Paper* 3/707