Base Hydrolysis of Amino-acid Esters and Amides in the Co-ordination Sphere of Cobalt(III). Part I. Hydrolysis of Methyl 6-Aminohexanoate

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The base hydrolysis of *cis*-$\{Co(en)_2Cl[NH_2(CH_2)_5CO_2Me]\}^{2+}$ has been studied by pH-stat and stopped-flow spectrophotometric techniques at 25 °C and $I = 0{\cdot}1$M. Two consecutive reactions occur in base. Following loss of Cl^- ($k_{OH} = 12{\cdot}8$ l mol^{-1} s^{-1} by pH-stat, $k_{OH} = 13{\cdot}6 \pm 1$ l mol^{-1} s^{-1} by stopped flow), a slower base hydrolysis of the ester function occurs ($k_{OH} = 0{\cdot}22$ l mol^{-1} s^{-1}). In the pH-stat measurements 2 moles of base are consumed per mole of complex and the final product of the reaction is the hydroxypenta-ammine which has been identified by visible spectra and potentiometric titration. Base hydrolysis of the complex *cis*-$\{Co(en)_2Cl[NH_2(CH_2)_5CO_2]\}^+$ containing the *N*-co-ordinated amino-acid requires 1 mole of base for complete hydrolysis ($k_{OH} = 9{\cdot}5$ l mol^{-1} s^{-1} for loss of chloride by pH-stat, $k_{OH} = 9{\cdot}2$ l mol^{-1} s^{-1} determined spectrophotometrically in borax buffers at $I = 0{\cdot}1$M and 25 °C). For base hydrolysis of the unprotonated form of the free ester, $NH_2(CH_2)_5CO_2Me + OH^- \longrightarrow NH_2(CH_2)_5CO_2^- + MeOH$ in the pH range 11·0—11·5 the value of $k_{OH} = 0{\cdot}148$ l mol^{-1} s^{-1}. Thus a slight rate enhancement (*ca.* 1·5 times) occurs for hydrolysis of the *N*-co-ordinated ester. Such an effect is understandable owing to the length of the alkyl chain separating the cobalt(III) centre from the ester function. The present results establish a further hydrolytic pathway for *N*-co-ordinated amino-esters in halogenopenta-ammine complexes of cobalt(III), quite different from the reactions of glycine esters where intramolecular pathways occur.

RECENTLY there has been considerable interest in the hydrolysis of glycine esters in complexes of the type *cis*-$[Co(en)_2X(glyOR)]^{2+}$ (R = Me, Et, or Pr^i; X = Cl or Br; glyOH = unidentate $NH_2{\cdot}CH_2{\cdot}CO_2H$; gly = chelated $NH_2{\cdot}CH_2{\cdot}CO_2^-$). The Hg^{II}- and HOCl-induced removal of bromide ion from $[Co(en)_2Br(glyOR)]^{2+}$ has been shown [1] to proceed *via* the chelated ester intermediate $[Co(en)_2(glyOR)]^{3+}$ previously suggested by Alexander and Busch.[2]

The base hydrolysis of the complexes is of interest as the co-ordinated amino-acid remains bound in solution and considerably more mechanistic information can be obtained than in the kinetically labile Ni^{II} and Cu^{II} systems. The complexes are also of interest as models for the metal-activated esterases.

It is generally considered that in the base hydrolysis of complexes of the type $[CoN_5X]^{2+}$ (X = Cl or Br; N_5 = a system of five nitrogen donors) a five-co-ordinate intermediate occurs.[3-7] In the ester complexes the possibility arises that the ester carbonyl group and solvent water compete for the vacant site. Formation of the hydroxo-complex leads to the possibility of subsequent internal nucleophilic displacement of the ester group by the bound hydroxide ion. The base hydrolysis of the $[Co(en)_2X(glyOR)]^{2+}$ ions have been explored in detail by Buckingham, Foster, and Sargeson.[8] The ion $[Co(en)_2(gly)]^{2+}$ is formed primarily, along with numerous side products, some of which have not yet been characterised. Tracer experiments with ^{18}O have established that the two main pathways to the chelated glycine complex are (*a*) internal nucleophilic attack of the bound hydroxide ion and (*b*) incorporation of the ester carbonyl group into the vacant co-ordination site of the five-co-ordinate intermediate (II) (Scheme).

Additional complexities can arise in such systems, since the amido-complex (I) formed by reaction with base in the initial equilibrium step can also react with the ester ligand. Thus the complex $[Co(NH_3)_5NH_2{\cdot}CH_2{\cdot}CO_2Et]^{3+}$ reacts in basic solution (pH 9—14) to give the expected $[Co(NH_3)_5NH_2{\cdot}CH_2{\cdot}CO_2]^{2+}$ containing *N*-co-ordinated glycine and also $[Co(NH_3)_4NH_2{\cdot}CH_2{\cdot}CONH]^{2+}$ containing deprotonated glycine amide chelated through both nitrogen atoms.[9] *N*-Co-ordinated aziridines also occur in the base hydrolysis of $[Co(en)_2Br(NH_2{\cdot}CH_2{\cdot}CH_2Br)]^{2+}$ by a similar intramolecular pathway.[10]

As previous investigations have been limited to glycine esters, we have studied the base hydrolysis of similar complexes derived from β-, γ-, and ε-amino-esters. In the case of the γ- and ε-amino-acid esters, it would be expected that the carbonyl group of the ester would not compete effectively with water for the five-co-ordinate intermediate as this would involve the formation of 7- and 9-membered rings respectively. The present paper discusses the reactions of the ε-amino-ester (methyl 6-aminohexanoate).

EXPERIMENTAL

Materials.—*trans*-Dichlorobis(ethylenediamine)cobalt(III) chloride was prepared as described by Bailar.[11]

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[1] D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1968, **90**, 6032.
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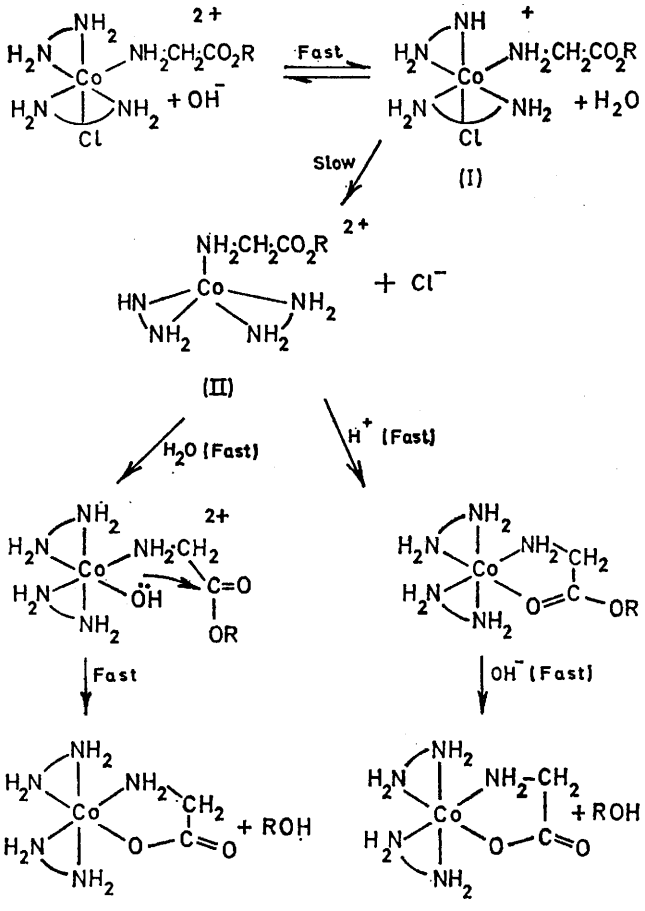
[7] D. A. Buckingham, I. I. Olsen, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1968, **90**, 6654.
[8] D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1969, **91**, 4102.
[9] D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1969, **91**, 3451.
[10] D. A. Buckingham, C. E. Davis, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1970, **92**, 6159.
[11] J. C. Bailar, *Inorg. Synth.*, 1946, **2**, 222.

Methyl 6-aminohexanoate monohydrochloride was prepared by Fischer–Speir esterification by standard methods.[12] The crude product was twice recrystallised from propan-2-ol–anhydrous ether and had m.p. 121—122° (lit.,[13,14] 121—122°).

cis-{Co(en)$_2$Cl[NH$_2$(CH$_2$)$_5$CO$_2$Me]}Cl$_2$ containing the *N*-co-ordinated amino-acid ester was prepared essentially as described by Alexander and Busch [15] for the corresponding complex of methyl glycinate. *trans*-Dichlorobis(ethylenediamine)cobalt(III) chloride (5·71 g, 0·02 mol) and the



SCHEME Pathways to [Co(en)$_2$gly]$^{2+}$

amino-acid ester hydrochloride (3·64 g, 0·02 mol) were ground together in a mortar and water (4 ml) added to give a paste. Triethylamine (2·8 ml, 0·02 mol) was syringed in small portions into the mixture with continuous grinding. The colour of the paste rapidly changed from green to the characteristic purple-red colour of the chloropenta-ammine and coagulation occurred. Methanol–acetone (10 : 1, 20 ml) was then added and the crude product filtered off on sintered glass. The solid was washed successively with methanol, ethanol, and acetone. The crude material was air-dried then recrystallised from the minimum of water (60 °C). Crystallisation was initiated by addition of a few drops of hydrochloric acid (12M). The *complex* was dried overnight *in vacuo* at 60 °C over P_2O_5 (Found: C, 30·3; H, 7·0; N, 16·5. $C_{11}H_{31}Cl_3CoN_5O_2$ requires C, 30·7; H, 7·25; N, 16·3%). The i.r. spectrum established that the compound was anhydrous.

cis-{Co(en)$_2$Cl[NH$_2$(CH$_2$)$_5$CO$_2$H]}Cl$_2$,H$_2$O containing the *N*-co-ordinated amino-acid was prepared essentially as described by Alexander and Busch for the *N*-co-ordinated glycine complex.[16] The amino-acid ester complex (2·15 g, 0·005 mol) was shaken with hydrochloric acid (4M, 25 ml) for 24 h. Propan-2-ol (60 ml) and hydrochloric acid (12M, 5 ml) were then added causing extensive crystallisation. The mixture was cooled overnight in a refrigerator, and the ruby-red crystalline product filtered off. The complex was dissolved in the minimum of hot water (*ca.* 70 °C). Hydrochloric acid (1 ml, 12M) was added and the solution allowed to cool. The recrystallised *material* was filtered off, washed with ethanol and acetone, and dried overnight *in vacuo* (KOH) at 60 °C (Found: C, 27·8; H, 7·1; N, 16·4. $C_{10}H_{31}Cl_3CoN_5O_3$ requires C, 27·7; H, 7·2; N, 16·2%). The i.r. spectrum confirmed that the compound was hydrated.

Kinetics and Measurements.—Ionisation constants and kinetics were measured with a Radiometer TTT1 automatic titrator, used in conjunction with a Radiometer PHA 630T scale expander. A high-alkalinity glass electrode, type G 202B, was used as indicator electrode and a saturated calomel electrode with diffusion filter, type K401, as reference electrode. The electrode system was standardised at 25·0 °C with 0·05M-potassium hydrogen phthalate (pH = 4·005) and sodium tetraborate (pH = 9·185) buffers. The general technique employed in the kinetic measurements has been outlined.[17] All kinetic studies were carried out at I = 0·1M (KCl) and 25 °C. Values of the hydroxide-ion concentrations were obtained from the pH, by use of a molar activity coefficient of 0·772,[18] and a value of pK_w = 13·9965 at 25 °C.[19]

Visible spectral measurements were made with a Perkin-Elmer 402 u.v.-visible recording spectrophotometer with 1-cm cells. Measurements were made on *ca.* 0·01M solutions.

Some kinetic measurements were carried out spectrophotometrically. In this case a Beckman Kintrac V11 TM recording spectrophotometer was employed. Base hydrolysis studies were carried out 25·0 ± 0·1 °C in a series of borax-based buffers adjusted to an ionic strength of 0·1M. The reactions were followed at *ca.* 508 nm corresponding to the absorption maximum of the product. Reactions were followed to 75—80% completion and the 'infinity' absorbances determined after ten half-lives. Stopped-flow measurements were carried out with equipment of similar design to the Gibson–Milnes instrument.[20] The reaction chamber was constructed of lucite and the mixing jet and flow control valves of stainless steel. The observation chamber had a 1-cm light path, 3 mm in diameter

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[15] M. D. Alexander and D. H. Busch, *Inorg. Chem.*, 1966, **5**, 602.
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[17] R. W. Hay, L. J. Porter, and P. J. Morris, *Austral. J. Chem.*, 1966, **19**, 1197.
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[20] Q. H. Gibson and L. Milnes, *Biochem. J.*, 1964, **91**, 161.

with a Teflon-gasketed lucite window. A Unicam SP 500 monochromator was employed and the light intensity measured with an IP-28A photomultiplier tube, the output of which was fed into a 2A63 Tektronix differential amplifier. The kinetic trace was displayed on a Tektronix oscilloscope, type 564, and photographed with a Polaroid camera. The entire valve block, delivery block, driving syringes, and observation chamber were thermostatted at 25 ± 0·02 °C by circulating water. Each kinetic trace required *ca.* 0·5—1·0 ml of solution. A total of *ca.* 15 ml of each reactant solution was generally sufficient for flushing and several measurements.

I.r. spectra were determined on Nujol or hexachlorobutadiene mulls with a Perkin-Elmer 221 spectrophotometer or a Unicam SP 200 spectrophotometer. ^{1}H N.m.r. spectra were determined at 60 MHz on a Hitachi–Perkin-Elmer R20 spectrometer. Solutions of the complexes were prepared in D_2O acidified where desired with D_2SO_4. Sodium 2,2-dimethyl-2-silapentane-5-sulphonate was employed as internal reference.

Microanalyses were by Dr. A. D. Campbell, Chemistry Department, University of Otago, Dunedin.

RESULTS AND DISCUSSION

The *cis*-configuration of the chloropenta-ammines was established by a variety of physical measurements. Nyholm and Tobe [21] prepared both the *cis*- and *trans*-isomers of $[Co(en)_2ClNH_3]^{2+}$ and studied their visible absorption spectra. For the *cis*-isomer, $\lambda_{max.}$ 525 nm (ε 73) and 365 nm (ε 77); for the *trans*-isomer, $\lambda_{max.}$ 525 nm (ε 47) and 367 nm (ε 53). Although the wavelengths of maximum absorption are essentially the same for both isomers, the intensities of the bands are much greater for the *cis*-isomer.

The visible spectra of the two chloropenta-ammines (Table 1) compare favourably with Nyholm and Tobe's results for a *cis*-configuration. The spectral parameters are also almost identical to the figures quoted by Alexander and Busch [15,16] for the analogous glycine and glycine ester complexes. The *cis*-configurations of the ethyl glycinate and isopropyl glycinate complexes have been confirmed by optical resolution.[15]

Baldwin [22] has shown that the most consistent difference in the i.r. spectra of *cis*- and *trans*-isomers of bis(ethylenediammine)cobalt(III) complexes occurs in the CH_2-rocking region between 870 and 900 cm^{-1}. In this region the *cis*-isomer commonly shows two bands and the *trans*-isomer only one. The splitting is due to the lower symmetry of the *cis*-derivatives. Both chloropenta-ammines show two bands in this region (Table 1).

Methyl 6-amino-n-hexanoate hydrochloride has a strong i.r. band at 1726 cm^{-1} attributable to νCO (ester). This band occurs at a higher frequency in methyl glycinate hydrochloride (νCO 1748 cm^{-1}) and methyl α-alaninate hydrochloride (νCO 1735 cm^{-1}). The lowering of νCO as the protonated amino-group is withdrawn along the carbon chain reflects the weaker $-I$ effect of the NH_3^+ group. In the complex $\{Co(en)_2Cl[NH_2(CH_2)_5CO_2Me]\}^{2+}$ the carbonyl stretching vibration occurs at 1726 cm^{-1} indicating that the inductive effect of the cobalt(III) ion is similar to that of the proton. The amino-acid complex has a strong band at 1707 cm^{-1} confirming the presence of the unco-ordinated carboxyl group.

TABLE 1

Spectral properties of the chloropenta-ammines

(*a*) Visible spectra [a]

Amino-acid or ester	$\lambda_{max.}$/nm	ε/mol^{-1} cm^{-1}
$NH_2(CH_2)_5CO_2Me$	528	78
	366	87
$NH_2(CH_2)_5CO_2H$	527	78
	365	86

(*b*) Infrared spectra

	νCO/cm^{-1}	CH_2 rock/cm^{-1}
$NH_2(CH_2)_5CO_2Me$	1726	898, 883
$NH_2(CH_2)_5CO_2H$	1707	896, 874

(*c*) N.m.r.[b]

$NH_2(CH_2)_5CO_2Me$-complex

OCH_3 3·68 δ (3H); $NH_2CH_2CH_2NH_2$ 2·87 δ (8H); $NH_2CH_2CH_2NH_2$ 4·21 δ (4H) and 5·13 δ (4H); $NH_2(CH_2)_5CO_2Me$ 4·64 δ (2H)

$NH_2(CH_2)_5CO_2H$-complex

$NH_2CH_2CH_2NH_2$ 2·85 δ (8H)
$NH_2CH_2CH_2NH_2$ 4·27 δ (4H) and 5·33 δ (4H)
$NH_2(CH_2)_5CO_2H$ 4·65 δ (2H)

[a] The reported values for glycine methyl ester are λ 526 nm (ε 77) and λ 367 nm (ε 82) and for *N*-co-ordinated glycine λ 527 (ε 77) and 366 nm (ε 84). [b] The integrals for the amino-protons are approximate, since the signals are in the region of the HOD resonance.

The *cis*-configuration of the complexes is also confirmed by the n.m.r. spectra (Table 1). The methylene protons of the ethylenediamine chelate ring absorb at *ca.* 2·85δ for a *cis*-configuration and at >3·0δ for a *trans*-configuration.[23] In addition the amino-protons of ethylenediamine are non-equivalent in the unsymmetrical *cis*-isomer and give rise to two [24] or three [25] peaks. In the symmetrical *trans*-isomer a single NH_2 signal is observed.

The ionisation constant for the equilibrium (1) was

$$cis\text{-}\{Co(en)_2Cl[NH_2(CH_2)_5CO_2H]\}^{2+} \overset{K_a}{\rightleftharpoons} cis\text{-}\{Co(en)_2Cl[NH_2(CH_2)_5CO_2]\}^{+} + H^+ \quad (1)$$

determined potentiometrically at $I = 0{\cdot}1$M and 25 °C. The practical ionisation constant is $pK_a^P = 4{\cdot}39 \pm 0{\cdot}04$ while the thermodynamic constant is $pK_a^T = 4{\cdot}27$.

The thermodynamic constant of 4·17 is similar to the value of 4·37 reported for the thermodynamic constant of the amino-acid at 25 °C and $I = 0{\cdot}05$M.[26] The effect of the cobalt(III) ion is therefore similar to that of a proton as previously noted by Alexander and Busch [16]

[21] R. S. Nyholm and M. L. Tobe, *J. Chem. Soc.*, 1956, 1707.
[22] M. E. Baldwin, *J. Chem. Soc.*, 1960, 4369.
[23] J. R. Lantzke and D. W. Watts, *Austral. J. Chem.*, 1967, **20**, 35.
[24] P. Clifton and L. Pratt, *Proc. Chem. Soc.*, 1963, 339.
[25] S. L. Spees, L. J. Durham, and A. M. Sargeson, *Inorg. Chem.*, 1966, **5**, 12.
[26] E. R. B. Smith and P. K. Smith, *J. Biol. Chem.*, 1942, **146**, 187.

in the analogous glycine system. The visible spectra of the acid and its conjugate base were identical.

Kinetics.—The base hydrolysis of *cis*-$[Co(en)_2Cl(hexOMe)]^{2+}$ [hex = $NH_2(CH_2)_5CO$] was followed by use of a pH-stat. Two consecutive or possibly concurrent reactions (2) and (3) could occur in base. Consistent

$$cis\text{-}[Co(en)_2Cl(hexOMe)]^{2+} + OH^- \xrightarrow{k_{Cl}} [Co(en)_2OH(hexOMe)]^{2+} + Cl^- \quad (2)$$

$$[Co(en)_2OH(hexOMe)]^{2+} + OH^- \xrightarrow{k_{ester}} [Co(en)_2OH(hexO)]^{+} + MeOH \quad (3)$$

with a kinetic scheme of this type it was found that two moles of base were consumed per mole of the complex. Initial hydrolysis of the chloride rather than the ester is consistent with the spectrophotometric kinetics (see later). Base hydrolysis of the ester is relatively slow; $[k_{OH}(Cl^-)/k_{OH}(ester)] = 58$ at 25 °C and $I = 0{\cdot}1$M. It was therefore possible to study both processes in isolation. Chloride hydrolysis was studied in the pH range 9·40—10·00, and the rate constants obtained are shown in Table 2. At constant pH, controlled by the use of a pH-stat, the reaction is of pseudo-first order in the complex and the observed pseudo-first-order rate constant k_{obs} is related to k_{OH} (the second-order rate constant) by the expression, $k_{obs} = k_{OH}[OH^-]$. Values of $[OH]^-$ were obtained from the pH as described in the Experimental section. The average value for $k_{OH}(Cl^-)$ is 12·8 ± 0·1 l mol^{-1} s^{-1} at $I = 0{\cdot}1$M and 25 °C. This rate constant is very similar to that previously obtained [27] for base hydrolysis of *cis*-chloropenta-ammines of the type *cis*-$[Co(en)_2ClNH_2R]^{2+}$ where R is a primary alkyl group (k_{OH} = 12·7 l mol^{-1} s^{-1} at 25 °C and I = 0·1M). As the second hydrolytic step was rather too slow to follow by pH-stat in the pH range 9·4—10·0, the pH was therefore raised to 11·0—11·4 after consumption of one mole of base. The rate constants obtained in the second hydrolysis step (ester hydrolysis) are shown in Table 2. The average value for k_{OH}(ester) is 0·22 l mol^{-1} s^{-1} at 25 °C and $I = 0{\cdot}1$M.

TABLE 2

pH-Stat rate constants for the base hydrolysis of *cis*-$\{Co(en)_2Cl[NH_2(CH_2)_5CO_2Me]\}^{2+}$ at 25 °C and $I = 0{\cdot}1$M

(*a*) First hydrolysis step (chloride hydrolysis)

pH	10^4k_{obs}/s^{-1}	k_{OH}/l mol^{-1} s^{-1}
9·40	4·17	12·70
9·40	4·20	12·76
9·70	8·38	12·80
10·00	16·80	12·87
10·00	16·78	12·85

$k_{OH}(Cl^-)$ = 12·8 ± 0·1 l mol^{-1} s^{-1}.

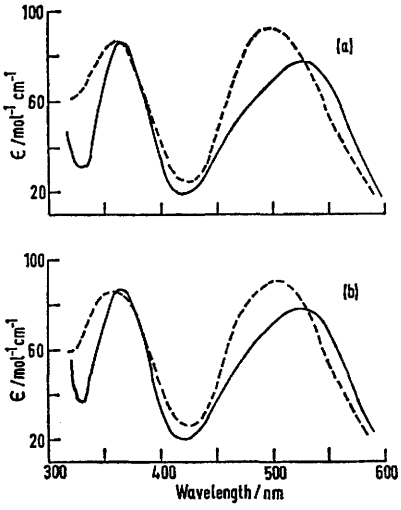
(*b*) Second hydrolysis step (ester hydrolysis)

11·00	2·85	0·218
11·00	2·82	0·217
11·20	4·60	0·222
11·40	7·33	0·223
11·40	7·30	0·222

k_{OH}(ester) = 0·22 ± 0·005 l mol^{-1} s^{-1}.

Conversion of the chloropenta-ammine into the hydroxypenta-ammine leads to significant visible spectral changes owing to an alteration of the ligand field about the cobalt(III) ion. Thus an N_5Cl donor system has $\lambda_{max.}$ at *ca.* 527 ± 3 nm for the lowest-energy ligand-field band,[27] compared with $\lambda_{max.}$ *ca.* 504 ± 3 nm for the $N_5(OH)$ donor system. Hydrolysis of the ester should have no effect on the electronic spectrum as the ligand field is unaltered.

The Figure illustrates the spectral changes observed on base hydrolysis of $\{Co(en)_2Cl[NH_2(CH_2)_5CO_2Me]\}^{2+}$. These changes are fully consistent with the conversion of the chloropenta-ammine into the hydroxypenta-ammine.



Visible spectra of the chloropenta-ammines and the products of base hydrolysis in borax buffer (pH 9·2). The products are indicated by the broken lines: (a) $\{Co(en)_2Cl(NH_2(CH_2)_5CO_2]\}^{+}$; (b) $\{Co(en)_2Cl[NH_2(CH_2)_5CO_2Me]\}^{2+}$

Measurements in borax buffer solutions indicated that a single rate process accounted for the visible spectral changes. Stopped-flow spectrophotometric measurements were carried out at 25 °C, $I = 0{\cdot}$M, and 485 nm. Excellent pseudo-first-order plots were obtained at constant hydroxide-ion concentrations. The rate constants obtained are summarised in Table 3. The average value of k_{OH} = 13·6 ± 1 l mol^{-1} s^{-1} is the same within experimental error as the ' fast ' pH-stat constant,

TABLE 3

Base hydrolysis of *cis*-$\{Co(en)_2Cl[NH_2(CH_2)_5CO_2Me]\}^{2+}$ studied by stopped flow at 25 °C and $I = 0{\cdot}1$M

$[OH^-]$	k_{obs}/s^{-1}	k_{OH}/l mol^{-1} s^{-1}
0·100	1·43	14·3
0·100	1·41	14·1
0·075	1·03	13·7
0·050	0·701	14·0
0·050	0·621	12·4
0·025	0·331	13·2

k_{OH} = 13·6 ± 1 l mol^{-1} s^{-1}.

[27] R. W. Hay and P. L. Cropp, *J. Chem. Soc.* (*A*), 1969, 42.

$k_{OH} = 12{\cdot}8$ l mol^{-1} s^{-1}, confirming that the first hydrolytic step applies to loss of chloride.

Back titration with acid of the products obtained on complete base hydrolysis revealed a group of $pK_a^P = 6{\cdot}1$ and a further group with a pK_a^P of *ca.* 4·4. These pK_a values are consistent with the protonation equilibria (4) and (5).

$$\{Co(en)_2[NH_2(CH_2)_5CO_2]OH\}^+ + H^+ \rightleftharpoons \{Co(en)_2[NH_2(CH_2)_5CO_2]OH_2\}^{2+} \quad (4)$$

$$\{Co(en)_2[NH_2(CH_2)_5CO_2]OH_2\}^{2+} + H^+ \rightleftharpoons \{Co(en)_2[NH_2(CH_2)_5CO_2H]OH_2\}^{3+} \quad (5)$$

Thus the pK_a^P of *cis*-$[Co(en)_2(NH_2Me)OH_2]^{3+}$ is 6·5 at $I = 0{\cdot}1$M.[27] The acid consumption data and visible spectral changes on acidification (Table 4) are quite consistent with the suggested kinetic scheme. No attempt was made to determine the actual configuration of the products formed on base hydrolysis.

TABLE 4

Visible spectra of products after base hydrolysis of the chloropenta-ammines

	After base hydrolysis [a]		After back titration [b]	
Ligand	λ/nm	ε/mol^{-1} cm^{-1}	λ/nm	ε/mol^{-1} cm^{-1}
$NH_2(CH_2)_5CO_2Me$	501	90	489	70
	359	86	352	64
$NH_2(CH_2)_5CO_2H$	499	93	489	68
	362	87	352	62

[a] Determined in borax buffer, the values of ε are ±2 mol^{-1} cm^{-1} and of λ ±2 nm. [b] Complete base hydrolysis on a pH-stat followed by back titration with acid. Owing to the more dilute solutions, the extinction coefficients are probably ±5 mol^{-1} cm^{-1}.

The base hydrolysis of the unco-ordinated ester was also studied in the pH range 11·0—11·50 by pH-stat. At high pH it is possible to study the process (6) in

$$NH_2(CH_2)_5CO_2Me + OH^- \longrightarrow NH_2(CH_2)_5CO_2^- + MeOH \quad (6)$$

isolation without significant contributions from the base hydrolysis of the protonated species $^+NH_3(CH_2)_5CO_2Me$. The pK_a for the equilibrium (7) is 10·3 at 25 °C.[28] The

$$^+NH_3(CH_2)_5CO_2Et \rightleftharpoons NH_2(CH_2)_5CO_2Et + H^+ \quad (7)$$

rate constants obtained for base hydrolysis of the unprotonated ester are summarised in Table 5.

The average value of k_{OH} is 0·148 ± 0·003 l mol^{-1} s^{-1} at 25 °C and $I = 0{\cdot}1$M. Thus a slight rate enhancement (*ca.* 1·5 times) occurs for hydrolysis of the *N*-co-ordinated ester ($k_{OH} = 0{\cdot}22 \pm 0{\cdot}005$ l mol^{-1} s^{-1}) compared with the unco-ordinated ester. This small effect is understandable in view of the length of the alkyl chain separating the cobalt(III) centre and the ester function. Buckingham, Foster, and Sargeson have studied the reactions of the complex $[Co(NH_3)_5NH_2{\cdot}CH_2{\cdot}CO_2Et]^{3+}$ in base.[9] For the ester hydrolysis pathway, $k_{OH} = 50$ l mol^{-1} s^{-1} at 25 °C and $I = 0{\cdot}1$M. For base hydrolysis of $NH_2{\cdot}CH_2{\cdot}CO_2Et$ (E) and $^+NH_3{\cdot}CH_2{\cdot}CO_2Et$ (EH^+) the values of k_{OH} are 0·635 [29] and 23 l mol^{-1} s^{-1} [30] respectively at 25 °C and $I = 0{\cdot}1$M. In this case a considerably larger rate acceleration (*ca.* 80-fold) occurs for base hydrolysis of the *N*-co-ordinated ester compared with the unprotonated ester E. Such a result is expected since the ester function is located close to the positively charged (3+) cobalt ion.

TABLE 5

Base hydrolysis of methyl 6-amino-n-hexanoate at 25 °C $I = 0{\cdot}1$M

pH	$10^4 k_{obs}$/s^{-1}	k_{OH}/l mol^{-1} s^{-1}
11·00	1·92	0·147
11·10	2·50	0·152
11·20	3·10	0·150
11·30	3·93	0·151
11·40	4·77	0·145
11·50	6·03	0·146

$k_{OH} = 0{\cdot}148 \pm 0{\cdot}003$ l mol^{-1} s^{-1}.

The effect of charge on the base hydrolysis of carboxylic esters has been extensively studied.[31-33] Generally the rate of base hydrolysis of the positively charged form of an ester is *ca.* 10^2—10^3 times greater than that of its neutral form (assuming that the positive charge is located near the reaction centre). This effect has been attributed to the fact that a reaction between oppositely charged ions has, for electrostatic reasons, an abnormally high collision factor.

Detailed studies [34] of the rates of base hydrolysis of the protonated (EH^+) and unprotonated (E) forms of α-amino-acid methyl esters have indicated that values of $k_{OH}(EH^+)/k_{OH}(E)$ are *ca.* 100, whereas for β-alanine methyl ester the ratio falls to 51. Thus, as expected, removal of the ammonium group from the reaction centre decreases the difference between $k_{OH}(EH^+)$ and $k_{OH}(E)$. Further withdrawal to the ε-position as in lysine methyl ester, reduces k_{EH^+}/k_E to 2·7.[35]

The base hydrolysis of the amino-acid complex *cis*-$\{Co(en)_2Cl[NH_2(CH_2)_5CO_2]\}^+$ was also studied by pH-stat and spectrophotometrically. The visible spectral changes observed on base hydrolysis in borax buffer are essentially identical to those observed with the ester complex (Figure). In the pH-stat runs, it was found

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that one mole of base was consumed per mole of complex, consistent with the stoicheiometry (8).

$$cis\text{-}\{Co(en)_2Cl[NH_2(CH_2)_5CO_2]\}^+ + OH^- \longrightarrow \{Co(en)_2OH[NH_2(CH_2)_5CO_2]\}^+ + Cl^- \quad (8)$$

The rate data obtained by pH-stat are summarised in Table 6, giving $k_{OH} = 9{\cdot}5 \pm 0{\cdot}5$ l mol^{-1} s^{-1} at 25 °C and $I = 0{\cdot}1$M. A series of rate measurements was also carried out spectrophotometrically with borax buffers adjusted to $I = 0{\cdot}1$M (Table 6). The spectrophotometric rate constant $k_{OH} = 9{\cdot}2 \pm 0{\cdot}5$ l mol^{-1} s^{-1} is in close agreement with the pH-stat constant.

TABLE 6

Rate constants for the base hydrolysis of *cis*-$\{Co(en)_2Cl[NH_2(CH_2)_5CO_2]\}^+$ at 25 °C and $I = 0{\cdot}1$M

(*a*) pH-Stat constants

pH	$10^4 k_{obs}$/s^{-1}	Ratio [a]	k_{OH}/l mol^{-1} s^{-1}
9·3	2·35	0·98	9·00
9·3	2·41	1·02	9·25
9·6	5·18	0·95	9·95
9·6	5·00	0·92	9·57
9·9	10·00	0·96	9·60
9·9	10·25	1·01	9·87

$k_{OH} = 9{\cdot}5 \pm 0{\cdot}5$ l mol^{-1} s^{-1}.

[a] Moles of base consumed per mole of complex.

(*b*) Spectrophotometric constants

pH	$10^4 k_{obs}$/s^{-1}	k_{OH}/l mol^{-1} s^{-1}
8·91	1·02	9·60
9·11	1·54	9·32
9·37	2·82	9·13
9·53	3·90	8·78

$k_{OH} = 9{\cdot}2 \pm 0{\cdot}5$ l mol^{-1} s^{-1}.

Back titration with acid revealed a group of $pK_a^P = 6{\cdot}1$ (protonation of the hydroxyl group) and a further pK_a^P of *ca.* 4·3 (protonation of the carboxyl ion). The titration data and visible spectral data (Table 4) are thus consistent with the formation of a hydroxypentaammine $\{Co(en)_2OH[NH_2(CH_2)_5CO_2]\}^+$ as the final product of base hydrolysis of both the amino-acid ester and amino-acid complex. The somewhat larger rate constant for chloride hydrolysis of the ester derivative (12·8 l mol^{-1} s^{-1}) than for the carboxylic acid derivative (9·5 l mol^{-1} s^{-1}) is probably due to the higher positive charge carried by the ester complex. The present results provide an example of a base-hydrolysis pathway involving the unidentate ester. The $Co(en)_2Cl^{2+}$ and $Co(en)_2OH^{2+}$ moieties appear to play a somewhat similar role to H^+. For example, the ionisation constants for the species $\{Co(en)_2Cl[NH_2(CH_2)_nCO_2H]\}^{2+}$ and $^+NH_3(CH_2)_nCO_2H$ for glycine, β-alanine,[36] 4-aminobutyric acid,[36] and 6-aminohexanoic acid are very comparable. The pK_a of a proton attached to a metal–oxygen centre $[Co(en)_2(NH_2Me)OH_2]^{3+}$ (pK_a *ca.* 6) is vastly different from that of the protonated species H_3O^+ ($pK_a = -1{\cdot}74$). The different effects are probably due to the distance between the protonated or co-ordinated centre and the reactive site.

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