Base Hydrolysis of Amino-acid Esters and Amides in the Co-ordination Sphere of Cobalt(III). Part 3.[1] Hydrolysis of Methyl and Ethyl 4-Aminobutanoate

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The base hydrolysis of *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}]^{2+}$ (en = ethylenediamine) has been studied by pH-stat and stopped-flow spectrophotometry at 25 °C and I = 0.1 mol dm^{-3}. Two consecutive reactions are observed in the pH-stat measurements. Following loss of Cl$^-$ (k_{OH}^{Cl} 15.2 dm^3 mol^{-1} s^{-1}) a slower base hydrolysis of the ester function occurs (k_{OH} 0.72 dm^3 mol^{-1} s^{-1}). In the pH-stat measurements 2 mol of base are consumed per mol of complex and the final product of the reaction is the penta-amine hydroxo-complex which has been identified by visible spectra and potentiometric titration. In the stopped-flow measurements a single kinetic process is observed spectrophotometrically corresponding to chloride hydrolysis (k_{OH}^{Cl} 15.6 dm^3 mol^{-1} s^{-1}). For the analogous *cis*-$[CoBr(en)_2\{NH_2(CH_2)_3CO_2Me\}]^{2+}$, $k_{OH}^{Br} = 125 \pm 3$ dm^3 mol^{-1} s^{-1} and $k_{OH}^{Br} : k_{OH}^{Cl} = 8 : 1$. Complete base hydrolysis of the complex *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2\}]^+$ containing the *N*-co-ordinated amino-acid requires 1 mol of base (k_{OH}^{Cl} 10.4 dm^3 mol^{-1} s^{-1} determined by pH-stat; k_{OH}^{Cl} 9.83 dm^3 mol^{-1} s^{-1} determined spectrophotometrically at I = 0.1 mol dm^{-3} and 25 °C). For the unprotonated ester $NH_2(CH_2)_3CO_2Me$, lactamisation to give 2-pyrrolidinone competes with base hydrolysis, but k_{OH} for ester hydrolysis is *ca.* 0.1 dm^3 mol^{-1} s^{-1} at 25 °C. Thus a small enhancement (*ca.* 7.2 times) occurs for hydrolysis of the *N*-co-ordinated ester.

THERE has been considerable interest in the reactions of amino-acid esters and amides in the co-ordination sphere of metal ions and the subject has been recently reviewed.[2] 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] For the complexes $[CoX(en)_2\{NH_2(CH_2)_nCO_2R\}]^{2+}$ (en = ethylenediamine) containing *N*-co-ordinated amino-acid esters, the ester carbonyl group and solvent water can compete for the vacant site. Formation of the hydroxo-complex leads to the possibility of subsequent intramolecular nucleophilic attack by the co-ordinated hydroxo-group at the ester carbonyl group. The base hydrolysis of *cis*-$[CoX(en)_2(NH_2CH_2CO_2R)]^{2+}$ has been explored in detail by Buckingham *et al.*[8] A major product of the reaction is $[Co(en)_2(NH_2CH_2CO_2)]^{2+}$ containing chelated glycine. Tracer experiments with ^{18}O have established that the two main paths to the chelated glycine complex are (*a*) intramolecular nucleophilic attack by the bound hydroxide at the ester carbonyl group and (*b*) incorporation of the ester carbonyl group in the vacant

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[5] D. A. Buckingham, I. I. Olsen, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1967, **89**, 5129.

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[7] M. L. Tobe, *Accounts Chem. Res.*, 1970, **3**, 377.

[8] D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1969, **91**, 4102.

co-ordination site of the five-co-ordinate intermediate followed by attack by 'external' hydroxide ion.

Additional reaction paths can arise in these systems, since the amido-complex formed by reaction with base in the initial rapid pre-equilibrium step, before formation of the five-co-ordinate intermediate, can also react with the ester ligand. Thus the complex $[Co(NH_3)_5(NH_2CH_2CO_2Et)]^{3+}$ reacts in basic solution (pH 9—14) to give the expected $[Co(NH_3)_5(NH_2CH_2CO_2)]^{2+}$ containing *N*-co-ordinated glycine and also $[Co(NH_3)_4(NH_2CH_2CONH)]^{2+}$ containing deprotonated glycinamide chelated through both nitrogen atoms.[9]

Since 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. We have previously shown [10] that for the ε-amino-ester (methyl 6-aminohexanoate) the carbonyl group of the ester does not compete with water for the five-co-ordinate intermediate, presumably because this would require the formation of a nine-membered chelate ring. The present paper discusses the reactions of methyl 4-aminobutanoate which would involve a seven-membered ring. A subsequent paper will deal with the methyl β-alaninate system.

EXPERIMENTAL

Materials.—*trans*-Dichlorobis(ethylenediamine)cobalt(III) chloride was prepared as described by Bailar,[11] and *trans*-dibromobis(ethylenediamine)cobalt(III) bromide as described by Werner.[12] Methyl and ethyl 4-aminobutanoate hydrochlorides were prepared by Fischer–Speir esterification using standard methods.[13] The crude hydrochlorides were twice recrystallised from propan-2-ol–anhydrous diethyl ether. The methyl ester hydrochloride had m.p. 118—119 °C (lit.,[14] 118—120 °C) and the ethyl ester hydrochloride (hygroscopic) had m.p. 66—70 °C (lit.,[15] 65—72 °C).

The complex *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}]Cl_2$ containing the *N*-co-ordinated amino-acid ester was prepared essentially as described by Alexander and Busch [16] for the corresponding complex of methyl glycinate. The crude product was taken up in the minimum volume of hot water (60 °C), and crystallisation initiated by the addition of a few drops of hydrochloric acid (12 mol dm^{-3}). The complex was dried at 60 °C overnight *in vacuo* over P_4O_{10} (Found: C, 26.8; H, 6.65; N, 17.6. $C_9H_{27}Cl_3CoN_5O_2$ requires C, 26.9; H, 6.75; N, 17.4%). The complexes *cis*-$[CoBr(en)_2\{NH_2(CH_2)_3CO_2Me\}]Br_2$ and *cis*-$[CoBr(en)_2\{NH_2(CH_2)_3CO_2Et\}]Br_2$ were prepared similarly using *trans*-$[CoBr_2(en)_2]Br$ and the amino-acid ester hydrochloride. They were purified by methods previously described,[17] and were recrystallised from hot (60 °C) water and dried *in vacuo* (Found: C, 19.8; H, 5.2; N, 13.1. $C_9H_{27}Br_3CoN_5O_2$ (methyl ester) requires C, 20.15; H, 5.1; N, 13.1. Found: C, 21.0; H, 5.4; N, 12.9. $C_{10}H_{29}Br_3CoN_5O_2$ (ethyl ester) requires C, 20.8; H, 5.3, N, 12.7%).

The complex *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2H\}]Cl_2$ containing the *N*-co-ordinated amino-acid was prepared as follows. The amino-acid ester complex (chloro-derivative) (2 g) was shaken with HCl (25 cm^3, 4 mol dm^{-3}) for 24 h. Propan-2-ol (60 cm^3) and HCl (5 cm^3, 12 mol dm^{-3}) 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 cm^3, 12 mol dm^{-3}) was added and the solution allowed to cool. Crystallisation was initiated by the addition of propan-1-ol (Found: C, 24.9; H, 6.5; N, 18.0. $C_8H_{25}Cl_3CoN_5O_2$ requires C, 24.7; H, 6.5; N, 18.0%). The i.r. spectrum confirmed that the complex was anhydrous.

Kinetics and Measurements.—Ionisation constants and pH-stat kinetics were studied with a Radiometer TTTI automatic titrator, used in conjunction with a Radiometer PHA 63OT scale expander. A high-alkalinity glass electrode, type G202B, was used as indicator electrode and a saturated calomel electrode (s.c.e.) with diffusion filter, type K401, as reference electrode. The electrode system was standardised at 25.0 °C with 0.05 mol dm^{-3} potassium hydrogenphthalate (pH 4.005) and 0.01 mol dm^{-3} sodium tetraborate (pH 9.185) buffers. The general technique employed in the kinetic measurements has been outlined.[18] All the kinetic studies were carried out at $I = 0.1$ mol dm^{-3} (KCl) and 25 °C. Values of the hydroxide-ion concentrations were obtained from the pH, using a molar activity coefficient of 0.772,[19] and a pK_w value of 13.997 at 25 °C.[20]

Some kinetic measurements were carried out spectrophotometrically. In this case measurements were made with a Beckman Kintrac VII TM or Gilford 2400S instrument equipped with a thermostatted cell compartment. Base-hydrolysis studies were carried out at 25.0 ± 0.1 °C using sodium tetraborate buffers adjusted to $I = 0.1$ mol dm^{-3}. Chloride hydrolysis was monitored at *ca.* 508 nm corresponding to the absorption maximum of the product. Bromide hydrolysis was monitored at 315 nm. Reactions were normally followed for at least three half-lives. Linear plots of log $(A_\infty - A_t)$ or log $(A_t - A_\infty)$ *versus* time were observed in all cases.

Stopped flow measurements were carried out with equipment of similar design to the Gibson–Milnes instrument.[21] The entire valve block, delivery block, drive syringes, and observation chamber were thermostatted at 25 ± 0.02 °C by circulating water.

Infrared spectra were determined on Nujol or hexachlorobutadiene mulls with a Perkin-Elmer 221 or Unicam SP 200 spectrophotometer. Visible-spectral measurements were made with a Perkin-Elmer 402 instrument using 1-cm cells. Hydrogen-1 n.m.r. spectra were determined at 60 Hz on a Hitachi–Perkin-Elmer R20 spectrometer. Solutions of the complexes were prepared in D_2O acidified where desired with D_2SO_4. Sodium 4,4-dimethyl-4-silapentanesulphonate was employed as internal reference.

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[10] R. W. Hay, R. Bennett, and D. J. Barnes, *J.C.S. Dalton*, 1972, 1524.

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[18] R. W. Hay, L. J. Porter, and P. J. Morris, *Austral. J. Chem.*, 1966, **19**, 1197.

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Thin-layer chromatography was carried out using glass plates coated with Kieselgel GF_{254}. The plates were eluted with (*a*) concentrated HCl in n-butanol saturated with water (5 cm^3 of concentrated HCl to 100 cm^3 of butanol) and (*b*) acetone–water–concentrated HCl (80 : 10 : 10 v/v).

RESULTS AND DISCUSSION

The *cis* configuration of the penta-amine halogeno-complexes was established by a variety of physical measurements. Nyholm and Tobe[22] have studied the visible-absorption spectra of *cis*- and *trans*-$[CoCl(en)_2(NH_3)]^{2+}$. For the *cis* isomer, $\lambda_{max.}$ 525 (ε 73) and 365 nm (ε 77 dm^3 mol^{-1} cm^{-1}); for the *trans* isomer, $\lambda_{max.}$ 525 (ε 47) and 367 nm (ε 53 dm^3 mol^{-1} cm^{-1}). The higher symmetry of the *trans* isomer leads to significantly lower absorption coefficients.

The visible spectra of the two penta-amine chloro-complexes $[CoCl(en)_2L]^{2+}$ (Table 1) compare favourably with the expected values for the *cis* configuration. In addition, the spectral parameters are almost identical to the values quoted by Alexander and Busch[16,23] 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.[16] For *cis*-$[CoBr(en)_2(NRH_2)]^{2+}$ complexes a single band is normally observed in the visible spectrum at 545 ± 5 nm with ε in the range 70—75 dm^3 mol^{-1} cm^{-1}, the higher-energy ${}^1A_{1g}\rightarrow{}^1T_{2g}$ transition being obscured by the charge-transfer band.[17] The i.r. spectra are also fully consistent with a *cis* configuration. In the CH_2-rocking region between 870 and 900 cm^{-1} the *cis* isomer normally has two weak bands and the *trans* isomer only one due to its higher symmetry.[24] Two bands are observed for the present complexes (Table 1). Thin-layer chromatography of the penta-amine chloro-complexes, using n-butanol–water–HCl as the eluting solvent, gave single-spot chromatograms. Similar conditions have been used to separate the *cis* and *trans* isomers of $[CoCl(en)_2(NH_3)]Cl_2$.

TABLE 1

Spectral characteristics of the penta-amine halogeno-complexes $[CoX(en)_2L]^{2+}$

(*a*) Visible spectra in aqueous solution

(Amino-acid or ester)	$\lambda_{max.}$/nm	ε/dm^3 mol^{-1} cm^{-1}
$NH_2(CH_2)_3CO_2Me$ [a]	528	77
	367	85
$NH_2(CH_2)_3CO_2H$ [a]	527	77
	366	84
$NH_2(CH_2)_3CO_2Me$	538	82
	427 ($\lambda_{min.}$)	23
$NH_2(CH_2)_3CO_2Et$ [b]	539	79
	426 ($\lambda_{min.}$)	22

(*b*) Infrared spectra (cm^{-1})

	ν(CO)	CH_2 rock
$NH_2(CH_2)_3CO_2Me$ [a]	1 734	899, 886
$NH_2(CH_2)_3CO_2Me$ [b]		
$NH_2(CH_2)_3CO_2Et$ [b]		
$NH_2(CH_2)_3CO_2H$ [a]	1 710	897, 872

[a] X = Cl. The reported values for *N*-co-ordinated glycine methyl ester are λ 526 (ε 77) and 367 nm (ε 82 dm^3 mol^{-1} cm^{-1}),[16] and for *N*-co-ordinated glycine are λ 527 (ε 77) and 366 nm (ε 84 dm^3 mol^{-1} cm^{-1}). [b] X = Br.

Methyl 4-aminobutanoate hydrochloride has a strong i.r. band at 1 728 cm^{-1} assigned to ν(CO) of the ester. This band occurs at a higher frequency for methyl glycinate hydrochloride [ν(CO) at 1 748 cm^{-1}], and methyl α-alaninate hydrochloride [ν(CO) at 1 735 cm^{-1}], but is similar to the value observed for methyl 6-aminohexanoate (1 726 cm^{-1}). The carbonyl frequencies decrease as the chain length increases, reflecting the weaker $-I$ effect of the NH_3^+ group. For the complex $[CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}]^{2+}$ the carbonyl-stretching frequency occurs at 1 734 cm^{-1} suggesting 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 1 710 cm^{-1} confirming the presence of an unco-ordinated carboxyl group.

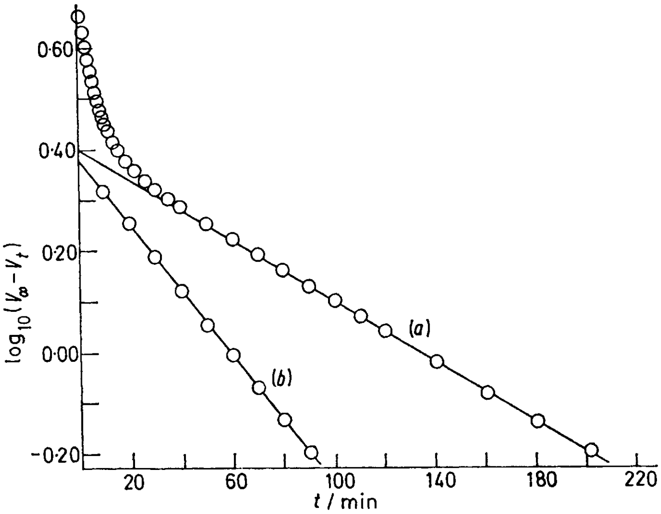

FIGURE 1 (*a*) Plot of log ($V_\infty - V_t$) against time for the base hydrolysis of *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}]^{2+}$ at pH 10.10. If the linear portion of the 'slow' reaction is extrapolated to the ordinate (t = 0) and this value of $V_\infty - V_t$ *subtracted* from the $V_\infty - V_t$ data of the original curve then a corrected plot (*b*) for the 'fast' reaction is obtained

The *cis* configuration of the complexes is also confirmed by the ^1H n.m.r. spectra. The methylene protons of the en chelate ring occur at *ca.* δ 2.85 p.p.m. for a *cis* configuration and at >3.0 p.p.m. for a *trans* configuration, the signal position being essentially independent both of the solvent used for the measurements and the ligand-field strength of the additional ligands.[17] All the present complexes have the methylene proton signal at *ca.* 2.8 p.p.m.

Kinetics.—The base hydrolysis of *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}]^{2+}$ was monitored by a pH-stat. Plots of log ($V_\infty - V_t$) against time, where V_∞ is the final volume of base consumed and V_t the volume at time t, showed marked initial curvature, becoming linear at high values of t (Figure 1). In addition, 2 mol of base were consumed per mol of complex (experimentally, 1.97 ± 0.02 mol).

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[22] R. S. Nyholm and M. L. Tobe, *J. Chem. Soc.*, 1965, 1707.

[23] M. D. Alexander and D. H. Busch, *Inorg. Chem.*, 1966, **5**, 1590.

[24] M. E. Baldwin, *J. Chem. Soc.*, 1960, 4369.

Such behaviour is consistent with two consecutive first-order reactions at constant pH, as shown in equations (1) and (2). The data were analysed as illustrated in Figure 1. Other workers have used a similar approach.[25] However, this type of kinetic analysis strictly applies only to concurrent first-order reactions.

$$\textit{cis}\text{-}[\mathrm{CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}}]^{2+} + [\mathrm{OH}]^- \xrightarrow{k_{\mathrm{OH}}^{\mathrm{Cl}}} [\mathrm{Co(en)_2(OH)\{NH_2(CH_2)_3CO_2Me\}}]^{2+} + \mathrm{Cl}^- \quad (1)$$

$$[\mathrm{Co(en)_2(OH)\{NH_2(CH_2)_3CO_2Me\}}]^{2+} + [\mathrm{OH}]^- \xrightarrow{k_{\mathrm{OH}}^{\mathrm{ester}}} [\mathrm{Co(en)_2(OH)\{NH_2(CH_2)_3CO_2\}}]^{+} + \mathrm{MeOH} \quad (2)$$

We consider that the present approach is valid *in this case* since (*a*) the ratio of the two rate constants is *ca.* 20 : 1, so that linear extrapolation is a reasonably valid approximation, and (*b*) the reaction is followed by base consumption, which avoids the difficulties which arise from differing absorption coefficients of the various species in the case of spectrophotometric monitoring. The pH-stat kinetic data are summarised in Table 2.

TABLE 2

pH-Stat rate constants for the base hydrolysis of *cis*-$[\mathrm{CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}}]^{2+}$ at 25 °C and I = 0.1 mol dm^{-3} *

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

pH	$10^3k_{\mathrm{obs.}}$/s^{-1}	k_{OH}/dm^3 mol^{-1} s^{-1}
9.90	1.59	15.3
10.00	1.97	15.1
	2.00	15.3
	2.02	15.4
10.10	2.48	15.1
10.20	3.05	14.8

$k_{\mathrm{OH}}^{\mathrm{Cl}}$ = 15.2 ± 0.2 dm^3 mol^{-1} s^{-1}

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

pH	$10^4k_{\mathrm{obs.}}$/s^{-1}	k_{OH}/dm^3 mol^{-1} s^{-1}
9.90	0.74	0.72
10.00	0 92	0.70
	0.95	0.73
	0.96	0.73
10.10	1.17	0.71
10.20	1.43	0.69

$k_{\mathrm{OH}}^{\mathrm{ester}}$ = 0.72 ± 0.02 dm^3 mol^{-1} s^{-1}

* 1.97 ± 0.02 mol of base were consumed per mol of complex in the reaction.

The initial rapid hydrolysis of chloride is consistent with the spectrophotometric data (see later). Thus $k_{\mathrm{OH}}^{\mathrm{Cl}}$ = 15.2 dm^3 mol^{-1} s^{-1} and $k_{\mathrm{OH}}^{\mathrm{ester}}$ = 0.72 dm^3 mol^{-1} s^{-1} at 25 °C and I = 0.1 mol dm^{-3} (Table 2). The observed first-order constants $k_{\mathrm{obs.}}$ are related to k_{OH} by the expression $k_{\mathrm{OH}} = k_{\mathrm{obs.}}/[\mathrm{OH}^-]$. The average value of $k_{\mathrm{OH}}^{\mathrm{Cl}}$ = 15.2 dm^3 mol^{-1} s^{-1} is very similar to that previously obtained[26] for the base hydrolysis of *cis*-penta-aminechloro-complexes of the type *cis*-$[\mathrm{CoCl(en)_2(NRH_2)}]^{2+}$ (R = a primary alkyl group) ($k_{\mathrm{OH}}^{\mathrm{Cl}}$ = 12.7 dm^3 mol^{-1} s^{-1} at 25 °C and I = 0.1 mol dm^{-3}).

Conversion of the penta-aminechloro- into the penta-aminehydroxo-complex leads to significant visible spectral changes owing to an alteration of the ligand field about the cobalt(III) ion. Thus an $\mathrm{N_5Cl}$ donor system has $\lambda_{\mathrm{max.}}$ at *ca.* 527 ± 3 nm for the lowest-energy ligand-field band.[26] Hydrolysis of the ester should have no effect on the electronic spectrum since the ligand field is unaltered. Measurements in sodium tetraborate 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 = 0.1 mol dm^{-3}, and 485 nm. The kinetic data obtained are summarised in Table 3. The average value of k_{OH} = 15.6 dm^3 mol^{-1} s^{-1} is the same within experimental error as the ' fast ' pH-stat rate constant, confirming that the initial fast reaction does indeed apply to chloride hydrolysis.

TABLE 3

Stopped-flow studies of the base hydrolysis of *cis*-$[\mathrm{CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}}]^{2+}$ at 25 °C and I = 0.1 mol dm^{-3} *

$[\mathrm{OH}^-]$/mol dm^{-3}	$k_{\mathrm{obs.}}$/s^{-1}	k_{OH}/dm^3 mol^{-1} s^{-1}
0.100	1.58	15.8
	1.53	15.3
0.075	1.06	14.1
	1.29	17.2
	1.17	15.6
0.050	0.772	15.4
0.025	0.368	14.7
	0.385	15.4

$k_{\mathrm{OH}}^{\mathrm{Cl}}$ = 15.6 dm^{-3} mol^{-1} s^{-1}

* Monitoring wavelength, 485 nm; [complex] = 1.0 × 10^{-3} mol dm^{-3}.

TABLE 4

Base hydrolysis of *cis*-$[\mathrm{CoBr(en)\{NH_2(CH_2)_3CO_2R\}}]^{2+}$ at 25 °C and I = 0.1 mol dm^{-3} *

pH	$10^5k_{\mathrm{obs.}}$/s^{-1}	$10^{-2}k_{\mathrm{OH}}$/dm^3 mol^{-1} s^{-1}
(*a*) R = Me		
8.57	0.633	1.32
8.78	1.00	1.29
8.98	1.51	1.23
9.12	2.08	1.22
9.38	3.83	1.20
9.50	5.00	1.22
9.57	5.65	1.17
$k_{\mathrm{OH}}^{\mathrm{Br}}$ = 123 ± 6 dm^3 mol^{-1} s^{-1}		
(*b*) R = Et		
8.65	0.73	1.27
8.95	1.43	1.25
9.14	2.33	1.31
9.38	4.05	1.30
9.57	6.18	1.28
$k_{\mathrm{OH}}^{\mathrm{Br}}$ = 128 ± 3 dm^3 mol^{-1} s^{-1}		

* Reactions monitored spectrophotometrically at 315 nm, [complex] = *ca.* 10^{-3} mol dm^{-3}.

Base hydrolysis of the analogous penta-aminebromo-complexes *cis*-$[\mathrm{CoBr(en)_2\{NH_2(CH_2)_3CO_2R\}}]^{2+}$ (R = Me or Et) was also studied spectrophotometrically at 315 nm using buffer solutions (Table 4). The methyl ester has $k_{\mathrm{OH}}^{\mathrm{Br}}$ = 123 ± 6 dm^3 mol^{-1} s^{-1} and the ethyl ester $k_{\mathrm{OH}}^{\mathrm{Br}}$ = 128 ± 3 dm^3 mol^{-1} s^{-1}. Methyl esters normally undergo base hydrolysis approximately twice as fast as ethyl esters, so that the equivalence of the two rate constants provides additional evidence for bromide

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[25] K. R. Ashley and R. E. Hamm, *Inorg. Chem.*, 1966, **5**, 1645; B. Chakravorty and A. K. Sil, *Inorg. Chim. Acta*, 1977, **24**, 105.

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

hydrolysis. The ratio $k_{Br}^{OH} : k_{Cl}^{OH} = 125 : 15.6 = 8.0 : 1$ is comparable with values for similar penta-amine halogeno-complexes of this type.[17] Figure 2 illustrates the visible spectral changes observed on base hydrolysis of *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}]^{2+}$. These changes are fully consistent with the conversion of the penta-aminechloro- into the penta-aminehydroxo-complex. Back titration with acid of the products obtained on complete base hydrolysis revealed a group at $pK_a^P = 6.13$ and another group at $pK_a^P = 3.94$. (pK_a^P Is the practical ionisation constant involving the activity of the hydrogen ion and the concentration of the other species.)

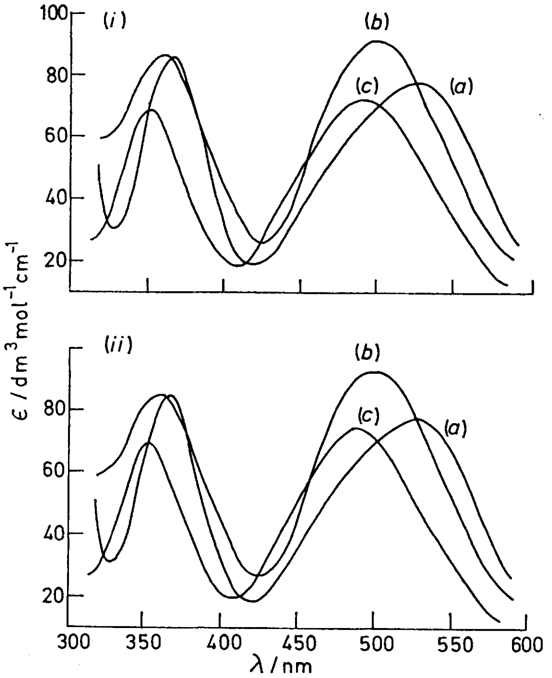


FIGURE 2 (*i*) Electronic spectra of *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2Me\}]^{2+}$ (*a*) and the products of base hydrolysis at pH 9.2 (*b*) and subsequent acidification to pH 2.5 (*c*). (*ii*) Electronic spectra of *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2H\}]^{2+}$ and the products of base hydrolysis and subsequent acidification. Details as in (*i*)

$$[Co(en)_2(OH)\{NH_2(CH_2)_3CO_2\}]^{+} + H^{+} \rightleftharpoons [Co(en)_2(OH_2)\{NH_2(CH_2)_3CO_2\}]^{2+} \quad (3)$$

$$[Co(en)_2(OH_2)\{NH_2(CH_2)_3CO_2\}]^{2+} + H^{+} \rightleftharpoons [Co(en)_2(OH_2)\{NH_2(CH_2)_3CO_2H\}]^{3+} \quad (4)$$

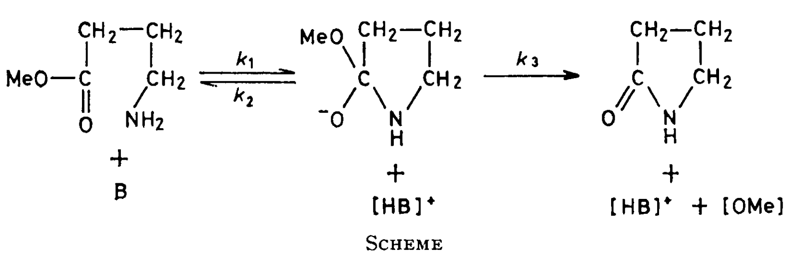
These pK_a values are consistent with the protonation equilibria (3) and (4). Thus the pK_a^P of *cis*-$[Co(en)_2(NMeH_2)(OH_2)]^{3+}$ is 6.5 at 25 °C and $I = 0.1$ mol dm^{-3}. No attempt was made to determine the configuration of the products formed on base hydrolysis; however, the relatively high absorption coefficients and the data available from similar penta-aminechloro-complexes[26] suggest that the *cis* configuration is predominantly retained. The visible spectra of the products are listed in Table 5.

TABLE 5

Visible spectra of the products of base hydrolysis of $[CoCl(en)_2L]^{2+}$

	After base hydrolysis		After back titration	
Ligand L	λ/nm	ε/dm³ mol⁻¹ cm⁻¹	λ/nm	ε/dm³ mol⁻¹ cm⁻¹
$NH_2(CH_2)_3CO_2Me$	501	88	488	71
	358	83	351	68
$NH_2(CH_2)_3CO_2H$	501	91	489	74
	361	86	352	70

One of us has previously studied[27] the base hydrolysis of methyl 4-aminobutanoate. For this ester, intramolecular aminolysis (lactamisation) competes with base hydrolysis (Scheme). The reaction is first order in the concentration of hydroxide ion when no other base is present, but is also subject to general base catalysis. A detailed analysis of the kinetics of base hydrolysis has shown that at pH >9.7 lactamisation is the predominant reaction path (>95%). Rate constants have been obtained[27] for the base hydrolysis of the unprotonated ester (E) and for the protonated ester $[HE]^+$. At 25 °C and $I = 0.1$ mol dm^{-3} the rate constants are 0.1 dm³ mol⁻¹ s⁻¹ (E) and 2.08 dm³ mol⁻¹ s⁻¹ (HE^+). Detailed studies[28] of the rates of base hydrolysis of the protonated and unprotonated forms of α-amino-acid methyl esters have shown that values of $k_{OH}(HE^+)/k_{OH}(E)$ are *ca.* 100, whereas for β-alanine methyl ester this quotient decreases to 51; for methyl 4-aminobutanoate it is *ca.* 21. As expected, removal of the ammonium group from the reaction centre decreases the difference between $k_{OH}(HE^+)$ and $k_{OH}(E)$. For the base hydrolysis of the *N*-co-ordinated methyl ester in the cobalt(III) complex $k_{OH} = 0.72$ dm³ mol⁻¹ s⁻¹ so that the reaction is *ca.* 7 times faster than for the free ester. The protonated ester is some three times more reactive to base hydrolysis than the metal-complexed ester. A further point of importance is that metal complexation prevents the ring-closure reaction from occurring.



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[27] R. W. Hay and P. J. Morris, *J.C.S. Perkin II*, 1972, 1021.
[28] R. W. Hay and P. J. Morris, *J. Chem. Soc.* (*B*), 1970, 1577.

The base hydrolysis of the amino-acid complex *cis*-$[CoCl(en)_2(NH_2CH_2CO_2)]^+$ was also studied by pH-stat and spectrophotometrically. In the pH-stat runs it was found that 1 mol of base was consumed per mol of complex, consistent with equation (5). The kinetic data

$$cis\text{-}[CoCl(en)_2\{NH_2(CH_2)_3CO_2\}]^+ + [OH]^- \longrightarrow [Co(en)_2(OH)\{NH_2(CH_2)_3CO_2\}]^+ + Cl^- \quad (5)$$

obtained by pH-stat are summarised in Table 6. Excellent first-order plots were obtained at constant pH, giving $k_{OH} = 10.4$ dm^3 mol^{-1} s^{-1} at 25 °C and $I = 0.1$ mol dm^{-3}. A series of rate measurements was also carried out spectrophotometrically with sodium tetraborate buffers adjusted to $I = 0.1$ mol dm^{-3} (Table 6). The spectrophotometric rate constant $k_{OH} = 9.8$ dm^3 mol^{-1} s^{-1} is in close agreement with the pH-stat rate constant. The visible spectral changes observed on base hydrolysis in sodium tetraborate buffer are essentially identical to those observed with the ester complex (Figure 2). Scan spectra of the base hydrolysis in tetraborate buffer at various time intervals showed three isosbestic points (528, 378, and 319 nm) indicating the presence of two uniquely absorbing species. Back titration of the products with acid revealed two pK_a^P values (6.12 and 4.0) which can be assigned to the aqua $\rightleftharpoons$ hydroxo equilibrium and to protonation of the carboxyl group of the *N*-co-ordinated amino-acid.

TABLE 6

Rate constants for the base hydrolysis of *cis*-$[CoCl(en)_2\{NH_2(CH_2)_3CO_2\}]^+$ at 25 °C and $I = 0.1$ mol dm^{-3}

(*a*) pH-Stat rate constants

pH	$10^4k_{obs.}$/s^{-1}	Ratio *	k_{OH}/dm^3 mol^{-1} s^{-1}
9.30	2.70	0.98	10.35
	2.72	0.99	10.40
9.60	5.42	0.98	10.40
9.90	10.83	0.95	10.43
	10.88	0.97	10.48

$k_{OH} = 10.4 \pm 0.1$ dm^3 mol^{-1} s^{-1}

(*b*) Spectrophotometric rate constants

pH	$10^4k_{obs.}$/s^{-1}	k_{OH}/dm^3 mol^{-1} s^{-1}
8.91	1.07	10.15
9.11	1.67	9.82
9.37	3.00	9.77
9.53	4.23	9.55

$k_{OH} = 9.8 \pm 0.4$ dm^3 mol^{-1} s^{-1}

* Moles of base consumed per mol of complex.

The ionisation constant for equilibrium (6) was determined potentiometrically at $I = 0.1$ mol dm^{-3} and 25 °C: pK_a^P 4.14 and pK_a^T 4.02 (the thermodynamic constant). Significantly, the ionisation constant is similar to the thermodynamic constant of the amino-acid at 25 °C and $I = 0.05$ mol dm^{-3}, for which the quoted value is 4.03.[29] As has been previously noted, co-ordination of the amino-group to cobalt(III) leads to a similar field effect as protonation of the amino-group.

$$cis\text{-}[CoCl(en)_2\{NH_2(CH_2)_3CO_2H\}]^{2+} \xrightleftharpoons{K_a} cis\text{-}[CoCl(en)_2\{NH_2(CH_2)_3CO_2\}]^+ + H^+ \quad (6)$$

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[29] E. J. King, *J. Amer. Chem. Soc.*, 1954, **76**, 1006.