DALTON
FULL PAPER

Polydentate ligand construction: a re-examination of an intramolecular condensation reaction †

Julian M. W. Browne, Jan Wikaira and Richard M. Hartshorn *

Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch, New Zealand. E-mail: r.hartshorn@chem.canterbury.ac.nz

Received 6th June 2001, Accepted 18th September 2001
First published as an Advance Article on the web 14th November 2001

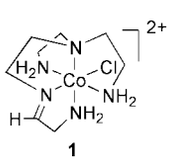
The intramolecular condensation reaction of coordinated aminoacetaldehyde and 1,4,7,10-tetraazadecane (trien) has been reinvestigated. The structure of the product, an imine-containing cobalt(III) complex, has been corrected, and this, together with the isolation and characterisation of carbinolamine intermediates, has allowed a modified mechanism to be proposed for the reaction. The isolated carbinolamines result from condensation of the aldehyde with the most acidic coordinated amine (*trans* to the chloride ligand). The carbinolamines are unable to dehydrate to form an imine product until after they have undergone a rearrangement of the coordination sphere to a geometry that will allow a planar imine to form.

Introduction

Photodecarboxylation reactions of amino acids coordinated to cobalt(III) have been shown to give rise to metallacyclic products.[1,2] Unfortunately, the low stability of many of the resulting complexes has prevented detailed study of their chemistry. We have shown recently that incorporation of the initial amino acid fragment into a polydentate ligand leads to metallacycles of enhanced stability being produced in the photolysis reactions.[2j] We have therefore undertaken a series of studies with the aim of synthesising cobalt(III) complexes of polydentate amino acids. These complexes would be good candidates for the photochemical preparation of cobalt complexes containing relatively stable three-membered Co–N–C metallacycles.

One of the proposed synthetic routes to the polydentate complexes makes use of intramolecular condensation reactions between a polyamine ligand and a keto acid ligand such as pyruvate. Reduction of the resulting imino acid complexes should produce amino acid complexes of the kind desired. A condensation reaction of coordinated pyruvate has been reported, but this involved reaction with an ammine ligand rather than a polyamine.[3] There are also a number of examples reported in which other carbonyl containing ligands have undergone condensation reactions with a polyamine ligand.[4]

In particular, Sargeson's group have reported the synthesis of a range of polydentate ligands *via* condensation reactions with aminocarbonyl ligands.[4d,e] This work was an extension of the chemistry first developed with the synthesis of $[Co(trenenim)Cl]^{2+}$ (**1**).[4a] These latter reactions demonstrated that high regioselectivity can be obtained. Such selectivity would be highly desirable in our systems, in order to reduce the number of isomers that might be produced.



1

The observed regioselectivity was attributed to the difference in the acidity of protons on the coordinated primary amines.[4a] In the synthesis of **1**, the condensation occurred only with the primary amine *trans* to the chloride ligand. The protons on the coordinated amine *trans* to the chloride ligand are more acidic than those on the other coordinated primary amines. The nucleophile resulting from this deprotonation will therefore have a greater opportunity to trap the carbonyl group.

We considered also that the preferred planarity of the resulting imine group might prevent the formation of some stereoisomers in our systems, as the imine donor should enforce meridional coordination on the imine and the two adjacent donor atoms. In such cases the elimination of water from the intermediate carbinolamine would be a facile process. A carbinolamine complex might be the expected product from systems where the intramolecular reaction does occur but where the subsequent elimination of water is prevented. Such a product has been seen from this kind of condensation reaction.[4b]

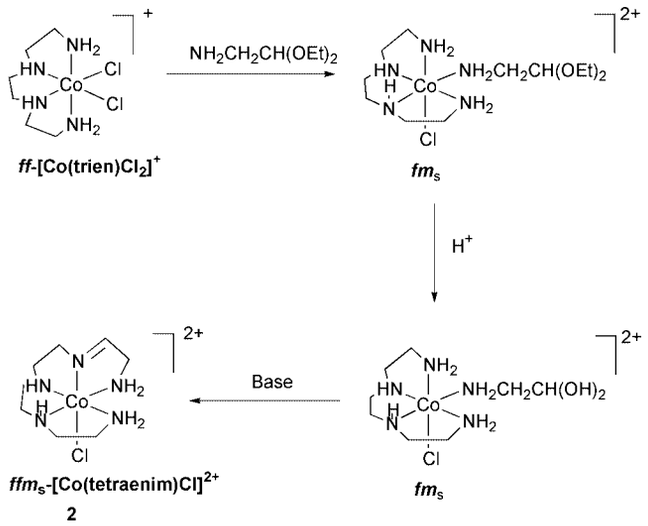
The reported isolation of a complex, **2**, in which the imine nitrogen atom and the two adjacent amine donors were proposed to adopt a facial geometry, appeared to be a counterexample.[4e] This complex resulted from an intramolecular condensation reaction between one of the primary amines of the trien ligand (1,4,7,10-tetraazadecane) and coordinated aminoacetaldehyde (Scheme 1).

The structural assignment of this complex was based on several factors: comparison of its spectral data with those of the limited number of related compounds; identification of the known polyamine complexes that resulted from the borohydride reduction of the imine complex; and consistency of the structural assignment with the proposal that such condensations should occur with the coordinated amine that is *trans* to the chloride ligand. The indirect nature of the evidence on which the structural assignment was based, together with the importance of the stereochemical consequences for the keto acid condensation reactions that we wished to study, lead us to conclude that this system warranted reinvestigation.

A large number of stereoisomers may exist for many of the compounds described in this paper. The stereoisomers are identified using the nomenclature of Hartshorn and House,[10] in which the descriptors that define the wrapping of polydentate ligands around an octahedral metal are given as prefixes. The descriptors *m* and *f* indicate meridional and facial ligand segments respectively, while a and s (as subscripts) indicate the

† Electronic supplementary information (ESI) available: crystal data tables. See http://www.rsc.org/suppdata/dt/b1/b104976n/

DOI: 10.1039/b104976n



Scheme 1

location of substituents on coordinating atoms (*anti* or *syn* to other donor atoms of the polydentate ligand).

Experimental

Materials and methods

ff-[Co(trien)Cl_2]Cl was prepared according to literature methods.[5] Reagent grade reagents and solvents were obtained from commercial sources and used without further purification for all syntheses unless stated. Dowex 50WX2-400 cation exchange resin was used for chromatographic separations. Column dimensions are given as height × diameter. Concentration of solutions by removal of solvent was carried out at reduced pressure in a Büchi rotary evaporator equipped with a water aspirator and water bath (<40 °C).

Measurements

^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR300 spectrometer using 3-(trimethylsilyl)propane-1-sulfonic acid, TMPS (^{1}H, δ 0), or 1,4-dioxane (^{13}C, δ 67.19) as an internal standard and dilute DCl (≈0.01 M, 99% D) as the solvent. Infrared spectra were run on a Shimadzu FTIR-8201PC using KBr disks. A Hewlett Packard 8452A spectrophotometer was used to record the UV-visible spectra in 1 mM HCl and the data are reported as λ_{max}/nm (ε_{max}/L mol^{-1} cm^{-1}). Elemental analyses were performed by the University of Otago Microanalytical Service.

Syntheses

***fms*-[Co(trien)($NH_2CH_2CH(OCH_2CH_3)_2$)Cl]Br_2·0.5H_2O.** This complex was prepared according to the literature method.[4e] ^{13}C NMR spectrum: δ 101.1 (CH), 65.0 (CH_2CH_3), 64.7 (CH_2CH_3), 54.7, 54.3, 51.4, 50.6 (CH_2NHC), 47.7 ($CH_2CH_2NH_2$), 46.2 (CH_2CH), 41.6 ($CH_2CH_2NH_2$), 15.0 (2×) (CH_3).

***fms*-[Co(trien)($NH_2CH_2CH(OH)_2$)Cl]Cl_2.** This complex was prepared according to the literature method.[4e] ^{13}C NMR in dilute DCl: δ 88.6 (CH), 54.8, 54.4, 51.6, 50.6 (CH_2NHC), 49.0 (CH_2CH), 47.7 ($CH_2CH_2NH_2$), 41.9 ($CH_2CH_2NH_2$).

Preparation of *mff*-[Co(tetraenim)Cl]$^{2+}$ and carbinolamine complexes. *fms*-[Co(trien)($NH_2CH_2CH(OH)_2$)Cl]Cl_2 (6.25 g) was dissolved in H_2O (120 mL) and the resulting solution was maintained at pH 6.2 ± 0.1 for four hours, using aqueous pyridine (0.1 M), according to the literature method.[4e] The volume was made up to 500 mL with H_2O and adsorbed onto an H^+-form Dowex 50WX2-400 column (14 × 3 cm). The column was initially eluted with aqueous hydrochloric acid (0.5 M) to remove cobalt(II). The elution regime of the literature method was then followed to remove a red band and an orange band, with some decomposition material remaining on the column. These bands were taken to dryness on a rotary evaporator at 80 °C, in accordance with the literature method. The residues from both bands were mixed and made up to 1 L with aqueous hydrochloric acid (0.01 M). This solution was adsorbed onto an H^+-form Dowex 50WX2-400 column (41 × 5.5 cm) and eluted with aqueous hydrochloric acid (1 M). Two red bands eluted. The second band (**B**) contained a significant majority (>95%) of the material. Both bands were taken to dryness on a rotary evaporator and shown to be mixtures (by NMR spectroscopy). The residue from the second band (**B**) was dissolved in aqueous hydrochloric acid (0.01 M, 600 mL) and adsorbed onto an SP Sephadex C25 column (128 × 3.5 cm) prewashed in aqueous hydrochloric acid (0.01 M). Elution with aqueous acidified Na_2SO_4 {Na_2SO_4 (0.1 M) + HCl (0.01 M)} developed three red bands (**B1**, **B2** and **B3**), followed by an orange band (**B4**). These bands were collected, adsorbed separately on short H^+-form Dowex 50WX2-400 columns, eluted with HCl, and taken to dryness. This procedure separated the complexes from the Na_2SO_4. Anation of the orange band (**B4**) by removing the HCl at 80 °C using a rotary evaporator gave material that was spectroscopically identical to that obtained from **B3**. The yield of the imine complex, *mff*-[Co(tetraenim)Cl]Cl_2, obtained from **B3** and **B4**, was ≈80%. The yield of the major carbinolamine **B2**, *exo-ffms*-[Co(tetraenol)Cl]Cl_2, was ≈15%. The residues from bands **A** and **B1** accounted for the remaining 5% of material. ^{13}C NMR spectroscopy on the residue from band **A** revealed that several compounds were present. Attempts to separate the compounds present in the small quantity of residue proved unsuccessful. Comparison of the NMR data with the results obtained from subsequent experiments revealed the major component of the residue obtained from band **A** to be *exo-ffm*$_a$-[Co(tetraenol)Cl]Cl_2. Both *exo-ffms*-[Co(tetraenol)Cl]Cl_2 and *mff*-[Co(tetraenim)Cl]Cl_2 could be obtained as their $[ZnCl_4]^{2-}$ salts by dissolution in 1 M HCl, addition of 1 equivalent of $ZnCl_2$ and then reducing the volume of the solution.

*exo-ffms-[Co(tetraenol)Cl]$ZnCl_4$·2H_2O (**B2**).* UV/vis: 364 (127), 476 (118), 532 (118). Anal. calcd. for $C_8H_{23}N_5Cl_5CoOZn$·2H_2O: C, 17.70; H, 5.01; N, 12.90%. Found: C, 17.95; H, 5.01; N, 12.61%. ^{1}H NMR in dilute DCl (1 M): δ 2.65 (m, 2H), 2.95 (m, 4H), 3.15 (m, 5H), 3.4 (m, 2H), 3.65 (m, 1H), 4.55 (d, 1H), 4.65 (br, 1H), 5.54 (br, 1H), 5.80 (br, 2H), 6.10 (br, 1H), 6.60 (br, 1H), 7.05 (br, 1H). ^{13}C NMR in dilute DCl (10 mM): δ 92.9 (CHOH), 55.2, 54.1, 51.1, 50.4, 48.7, 48.6, 48.4 (CH_2N).

*mff-[Co(tetraenim)Cl]$ZnCl_4$ (**B3** and **B4**).* UV/vis: 356 (116), 476 (128) (lit.,[4e] 350 (128); 474 (127). IR ν(C=N) 1678 cm^{-1} (lit.,[4e] 1680 cm^{-1}). Anal. calcd. for $C_8H_{21}N_5Cl_5CoZn$: C, 19.65; H, 4.33; N, 14.33%. Found: C, 19.76; H, 4.54; N, 14.14%. ^{1}H NMR: δ 2.68 (m, 2H), 3.1 (m, 5H), 3.3 (m, 1H), 3.52 (m, 1H), 3.97 (m, 1H), 4.16 (m, 1H), 4.28 (m, 1H), 4.39 (m, 2H), 5.2 (br, 2H), 5.5 (br, 1H), 5.8 (br, 1H), 6.5 (br, 1H), 6.6 (br, 1H), 8.14 (s, 1H). ^{13}C NMR: δ 183.4 (CH=N), 58.6, 57.1, 56.2, 55.7, 55.5, 55.4, 45.0 (CH_2N).

Preparation of carbinolamines. *fms*-[Co(trien)($NH_2CH_2CH(OCH_2CH_3)_2$)Cl]Cl_2 (3.00 g) was dissolved in aqueous hydrochloric acid (1 M, 50 mL) and left to stand at room temperature for 24 hours. Aqueous NaOH (1 M, 45 mL) was added slowly with stirring. The pH was adjusted to 6.2 ± 0.1 by dropwise addition of aqueous NaOH (0.1 M). After 15 minutes the reaction was quenched by addition of aqueous hydrochloric acid (0.1 M, 100 mL). This solution was adsorbed directly onto an H^+-form Dowex 50WX2-400 column (14 × 3 cm) that had been prewashed with aqueous hydrochloric acid (1 mM). The column was eluted with aqueous hydrochloric acid (0.5 M) to remove cobalt(II), and then with aqueous hydrochloric acid (1.0 M) to remove a broad red band from the column. This

band was collected in fractions. Each fraction was taken to dryness on a rotary evaporator and the mixtures characterised using ^{13}C NMR spectroscopy. Five compounds were present: *exo-ffm*$_s$-[Co(tetraenol)Cl]Cl_2; *exo-ffm*$_a$-[Co(tetraenol)Cl]Cl_2: ^{13}C NMR: δ 93.5 (CHOH), 59.4, 55.8, 52.7, 52.2, 51.6, 49.2, 46.6 (CH_2NH_2); ^{13}C NMR resonances were assigned to three other compounds: δ 91.8 (CHOH), 61.5, 57.3, 56.5, 55.7, 51.8, 45.4 (CH_2NH_2), 41.7 (CH_2NH_2); 85.8 (CHOH), 55.5, 55.1, 50.7, 50.6, 48.8, 44.2 (CH_2NH_2), 40.5 (CH_2NH_2); 85.4 (CHOH). (No other resonances could be observed due to spectral congestion.)

Resubmission of *exo-ffm*$_s$-[Co(tetraenol)Cl]$ZnCl_4$ to reaction conditions. *exo-ffm*$_s$-[Co(tetraenol)Cl]$ZnCl_4$ (0.20 g, 0.4 mmol) was dissolved in H_2O (20 mL). The pH was adjusted and maintained at 6.2 ± 0.1 with aqueous pyridine (0.1 M) for three hours. The reaction mixture was diluted to 100 mL with aqueous hydrochloric acid (10 mM). The solution was then adsorbed onto an H^+-form Dowex 50WX2-400 column (14 × 5.5 cm) which had been pre-washed with aqueous hydrochloric acid (10 mM). The column was washed with HCl (0.5 M, 300 mL), followed by HCl (1.0 M, ≈2 L), during which time three bands were eluted. The first band (red) was spectroscopically identified as the *exo-ffm*$_a$-[Co(tetraenol)Cl]$^{2+}$ ion. The second band (red) was spectroscopically identical to the starting material, *exo-ffm*$_s$-[Co(tetraenol)Cl]$^{2+}$. The third band (orange) was taken to dryness on a rotary evaporator at 80 °C. HCl (1.0 M) was added and the solution was again taken to dryness at 80 °C. The residue from the third band was found to contain two compounds (by ^{13}C NMR) which were spectroscopically identical to the starting material and the imine *mff*-[Co(tetraenim)Cl]$^{2+}$. The ratio of the two compounds in the third band was determined by integration of NMR spectra. Yields (crude): *exo-ffm*$_a$-[Co(tetraenol)Cl]Cl_2: 0.01 g, 6%; *exo-ffm*$_s$-[Co(tetraenol)Cl]Cl_2: 0.12 g, 75%; *mff*-[Co(tetraenim)Cl]Cl_2: 0.03 g, 19%. A small amount of the *exo-ffm*$_a$-[Co(tetraenol)Cl]$^{2+}$ ion was obtained as its $[ZnCl_4]^{2-}$ salt, but this was only sufficient for characterisation by NMR, and attempted crystallography (see below).

Reduction of [Co(tetraenim)Cl]$ZnCl_4$ with $NaBD_4$. [Co(tetraenim)Cl]$ZnCl_4$ (0.20 g, 0.4 mmol) was dissolved in carbonate buffer (100 mL, 1.0 g Na_2CO_3, 1.0 g $NaHCO_3$) and stirred for 2 minutes. $NaBD_4$ (0.20 g, 4.8 mmol) was added to the solution and stirring was continued for a further 2.5 minutes. The resulting orange solution was adsorbed onto a Na^+-form Dowex 50WX2-400 column (10 × 10 cm) under suction. The column was washed with H_2O (≈2 L), aqueous hydrochloric acid (0.5 M, ≈2 L), and finally eluted with aqueous hydrochloric acid (3.0 M) to remove an orange band. The orange band was taken to dryness on a rotary evaporator at 35 °C under vacuum. The orange-red residue contained multiple isomers, however the major two compounds were identified as *ffm*$_s$-[Co(tetraenD_1)Cl]$^{2+}$ and *ffm*$_s$-[Co(tetraenD_1)(OH_2)]$^{3+}$.

ffm$_s$-[Co(tetraenD_1)(OH_2)]$^{3+}$. ^{13}C NMR: δ 60.9, 57.8, 57.1, 56.2, 52.6 (small br peak), 51.4, 50.9, 43.5 (lit.,[6] for *ffm*$_s$-[Co(tetraen)(OH_2)]$^{3+}$: δ 61.0, 57.8, 57.1, 56.2, 52.6, 51.5, 51.0, 43.6).

ffm$_s$-[Co(tetraenD_1)Cl]$^{2+}$. ^{13}C NMR: δ 60.1, 57.8, 57.3, 55.1, 52.8 (small br peak), 52.3, 50.7, 44.3 (lit.,[6] for *ffm*$_s$-[Co(tetraen)Cl]$^{2+}$: 60.1, 57.8, 57.3, 55.2, 52.9, 52.4, 50.8, 44.3).

Crystal structure determinations

The X-ray data were collected on a Siemens P4 four circle diffractometer, using a Siemens SMART 1K CCD area detector and irradiating the sample with graphite monochromated Mo-K_α (λ = 0.71073 Å) X-rays. The crystal was mounted 5.5 cm from the detector. The data were collected by the SMART program[7] and processed with the help of SAINT[8] to apply Lorentz and polarisation corrections to the diffraction spots (integrated 3 dimensionally). SADABS[9a] was used to scale the diffraction data, apply empirical absorption corrections and to apply decay corrections if required. The structures were refined by direct methods using the SHELXTL program.[9b] Hydrogen atoms were calculated at ideal positions and refined using a riding model unless otherwise stated in the text.

Crystallographic data are shown in Table 1.

CCDC reference numbers 165266–165268.

See http://www.rsc.org/suppdata/dt/b1/b104976n/ for crystallographic data in CIF or other electronic format.

***mff*-[Co(tetraenim)Cl]$ZnCl_4$.** Crystals of [Co(tetraenim)Cl]-$ZnCl_4$ (red plates) were grown by vapour diffusion of methanol into a solution of [Co(tetraenim)Cl]$ZnCl_4$ in aqueous hydrochloric acid (0.1 M).

***fm$_s$*-[Co(trien)$(NH_2CH_2CH(OEt)_2)$Cl]Br_2.** Red needles were grown by vapour diffusion of acetone into a solution of [Co(trien)$(NH_2CH_2CH(OEt)_2)$Cl]Br_2 in aqueous hydrochloric acid (1 mM).

***exo-ffm$_s$*-[Co(tetraenol)Cl]$ZnCl_4$.** Red blocks were grown by vapour diffusion of ethanol into a solution of *exo-ffm*$_s$-[Co(tetraenol)Cl]$ZnCl_4$ in aqueous hydrochloric acid (1 mM).

***exo-ffm$_a$*-[Co(tetraenol)Cl]$ZnCl_4$.** Crystals of *exo-ffm*$_a$-[Co(tetraenol)Cl]$ZnCl_4$ (overlapping red plates) were grown by vapour diffusion of ethanol into a solution of *exo-ffm*$_a$-[Co(tetraenol)Cl]$ZnCl_4$ in aqueous hydrochloric acid (1 mM). The crystals proved to be twinned. Analysis of the data allowed us to identify the isomer that was present (from the positions of the non-hydrogen atoms), but a complete solution of the structure was not possible.

Results and discussion

The intramolecular condensation of coordinated aminoacetaldehyde with trien was proposed by Engelhardt *et al.*[4e] to generate the novel "angular" imine structure, [Co(tetraenim)Cl]$^{2+}$ (**2**, Scheme 1). This reaction was part of a multi-step synthesis of the *ffm*$_s$-[Co(tetraen)Cl]$^{2+}$ and *ffm*$_a$-[Co(tetraen)Cl]$^{2+}$ complexes.[4e,10]

The structural assignment of the intermediates was based upon UV-visible data. In particular, the diethyl acetal intermediate was assigned the *fm* (or β) configuration because the visible absorption spectrum was much closer in appearance to the spectra of related complexes with the *fm* configuration than to those with the *ff* (or α) configuration.[4e] ^{1}H NMR data lead to the proposal that the acetal complex was the *fm*$_s$ isomer, where the proton on the meridional nitrogen donor points towards the axial nitrogen donor, and away from the chloride ligand. Deprotection of the acetal gave a diol complex that was assigned the same *fm*$_s$ configuration, based on spectral data that was essentially identical to that of the acetal.

Base treatment of the diol complex gave a [Co(tetraenim)-Cl]$^{2+}$ complex, which was reduced, and then anated, to give predominantly the *ffm*$_s$-[Co(tetraen)Cl]$^{2+}$ complex, together with a small amount of the *ffm*$_a$-[Co(tetraen)Cl]$^{2+}$ complex. The structures of both of these complexes have been established unequivocally.[11] There was little characterisation of the imine intermediate, but the *ffm*$_s$-[Co(tetraenim)Cl]$^{2+}$ structure was proposed, primarily because it is the structure that would be expected if the intramolecular reaction of the carbonyl had occurred with the coordinated amine *trans* to chloride. Reduction of the imine group in the proposed structure would give the observed tetraen complexes.

Six possible structures for the [Co(tetraenim)Cl]$^{2+}$ intermediate exist (Fig. 1) if the orientation of the protons on meridional nitrogen atoms and the absolute configuration of the complex are ignored. During the reduction of the imine derived

Table 1 Crystallographic data

Compound	*mff*-[Co(tetraenim)Cl]$ZnCl_4$	*fm*$_s$-[Co(trien)($NH_2CH_2CH(OEt)_2$)Cl]Br_2	*exo-ffm*$_s$-[Co(tetraenol)Cl]$ZnCl_4$
Formula	$C_8H_{21}Cl_5CoN_5Zn$	$C_{12}H_{33}Br_2ClCoN_5O_2$	$C_8H_{23}Cl_5CoN_5OZn{\cdot}CH_3CH_2OH$
M	488.88	533.63	552.92
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_1/c$	$Pna2_1$	$P2_1/c$
a/Å	10.752(5)	14.618(7)	10.548(3)
b/Å	9.510(4)	18.114(9)	8.838(2)
c/Å	17.268(7)	7.712(4)	22.210(6)
β/°	91.095(5)		98.980(4)
V/Å^3	1765.5(1)	2041.9(16)	2045.1(9)
Z	4	4	4
T/K	163(2)	163(2)	163(2)
μ/mm^{-1}	3.05	4.899	2.651
Reflections	22056	22915	15317
Independent	3597	3577	4154
Observed	2910	2751	3273
Parameters refined	184	209	219
R [*I* > 2*σ*(*I*)]	0.022	0.045	0.027
Rw [*I* > 2*σ*(*I*)]	0.053	0.114	0.059

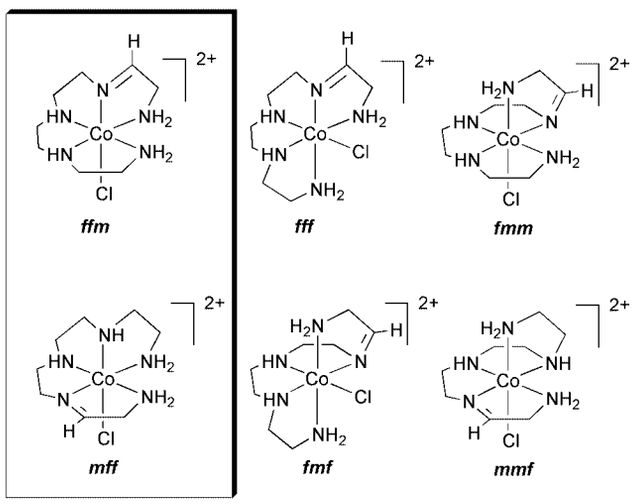


Fig. 1 The six possible structures for the [Co(tetraenim)Cl]$^{2+}$ intermediate.

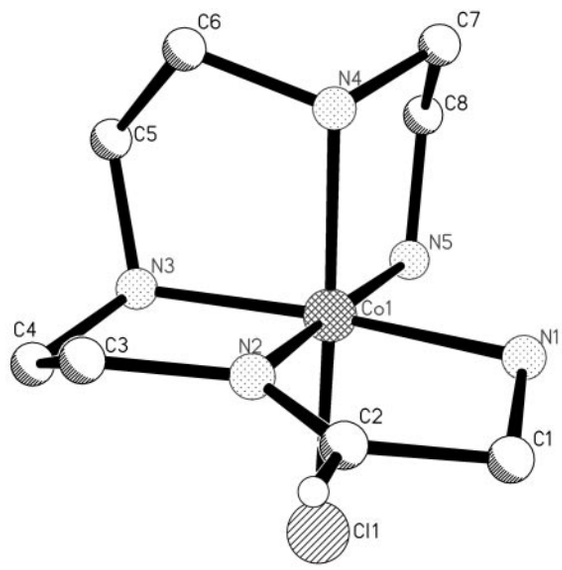


Fig. 2 X-Ray crystal structure of the *mff*-[Co(tetraenim)Cl]$^{2+}$ cation. The $[ZnCl_4]^{2-}$ has been omitted, as have most of the hydrogen atoms, for clarity. Selected atomic distances (Å): Co1–N1 1.9741(18), Co1–N2 1.8842(19), Co1–N3 1.9509(18), Co1–N4 1.9628(17), Co1–N5 1.9645(18), Co1–Cl1 2.2517(9), N2–C2 1.262(3), other N–C 1.47–1.50. Selected bond angles (°): C2–N2–C3 125.2, C2–N2–Co1 118.3, C3–N2–Co1 116.1, N2–C2–C1 116.2. Selected torsion angles (°): C3–N2–C2–C1 174.7, Co1–N2–C2–C1 1.4.

from the *fm*$_s$ intermediate, base hydrolysis of the chloride ligand meant that the final products could not be directly correlated to the imine from which they were derived. To solve this problem Engelhardt *et al.*[4e] substituted the Cl^- ligand with an NO_2^- ligand, with apparent retention of stereochemistry. Reduction of this imine led to formation of *ffm*-[Co(tetraen)$(NO_2)]^{2+}$ isomers, with no apparent base hydrolysis of the NO_2^- ligand. From this result it can be concluded that the [Co(tetraenim)Cl]$^{2+}$ moiety must have an identical back-bone to the *ffm*-[Co(tetraen)X]$^{n+}$ product. The "angular" *ffm*-[Co(tetraenim)X]$^{n+}$ imine and the "planar" *mff*-[Co(tetraenim)X]$^{n+}$ imine (the two boxed isomers in Fig. 1) are the two isomers that have this backbone structure. The imine complex was assigned the first of these structures, based on the idea that the condensation would occur *trans* to the Cl^- ligand.

We have used two methods to test the accuracy of the structural assignment: deuterium labelling in the reduction step, and single crystal X-ray structure determination of the imine.

The [Co(tetraenim)Cl]$^{2+}$ complex was obtained using the method of Engelhardt *et al.*[4e] The complex was isolated as the tetrachlorozincate salt rather than as the perchlorate salt that is described in the literature, but the NMR, UV-visible, and IR data were very similar to those described in the literature.

X-Ray quality crystals of the [Co(tetraenim)Cl]$ZnCl_4$ complex were grown by vapour diffusion of methanol into an acidified solution of the complex, and the resulting structure is shown in Fig. 2. The most significant feature of this structure is that it is the *mff* isomer, with a meridional "planar" imine, and not the "angular" imine proposed in the literature.[4e] The significantly shorter length of the N2–C2 bond (1.262(3) Å) with respect to the other N–C bonds (1.47–1.50 Å) identifies this as the imine group. The three angles around the N2 atom sum to ≈360°, and the torsion angles Co1–N2–C2–C1 (1.4°) and C3–N2–C2–C1 (174.7°) are all consistent with the imine being approximately planar. The single hydrogen atom attached to carbon C2 was found in the electron difference map and refined using a riding model.

Reduction of [Co(tetraenim)Cl]$^{2+}$ with $NaBD_4$ gave a mixture of compounds. The dominant species in the mixture were the *ffm*$_s$-[Co(tetraenD_1)$(OH_2)]^{3+}$ and *ffm*$_s$-[Co(tetraenD_1)Cl]$^{2+}$ complexes. Only one resonance in each of the ^{13}C NMR spectra for the *ffm*$_s$-[Co(tetraenD_1)$(OH_2)]^{3+}$ and *ffm*$_s$-[Co(tetraenD_1)-Cl]$^{2+}$ complexes exhibited diminished intensity by comparison with the same peak in the NMR spectra of the $NaBH_4$ reduction products.

The ^{13}C NMR spectrum was complicated by the presence of small amounts of *ffm*$_a$-[Co(tetraenD_1)X]$^{n+}$ isomers in the deuteride reduced product. Furthermore deuteride addition to the imine carbon atom introduces another stereogenic centre, and results in a mixture of isomers being produced. The introduction of additional chirality will produce subtly different

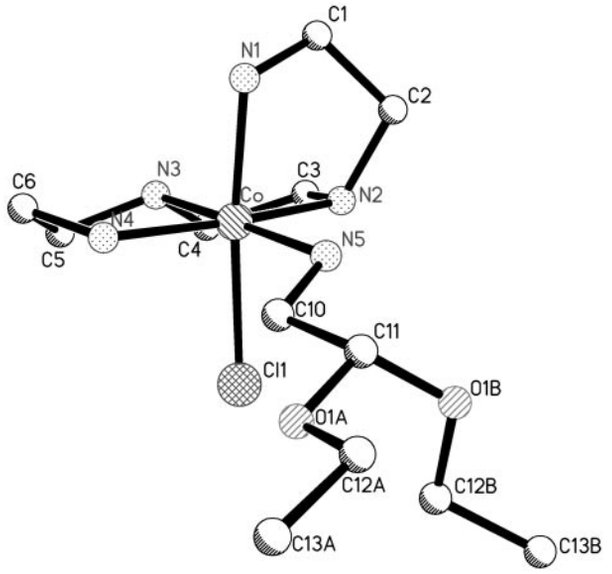


Fig. 3 X-Ray crystal structure of the *fm*$_s$-[Co(trien)(NH_2CH_2CH-$(OEt)_2$Cl]$^{2+}$ cation. Hydrogen atoms and the two bromide anions have been omitted for clarity. Selected atomic distances (Å): Co–N1 1.965(6), Co–N2 1.950(6), Co–N3 1.937(6), Co–N4 1.966(7), Co–N5 2.010(6), Co–Cl1 2.296(2).

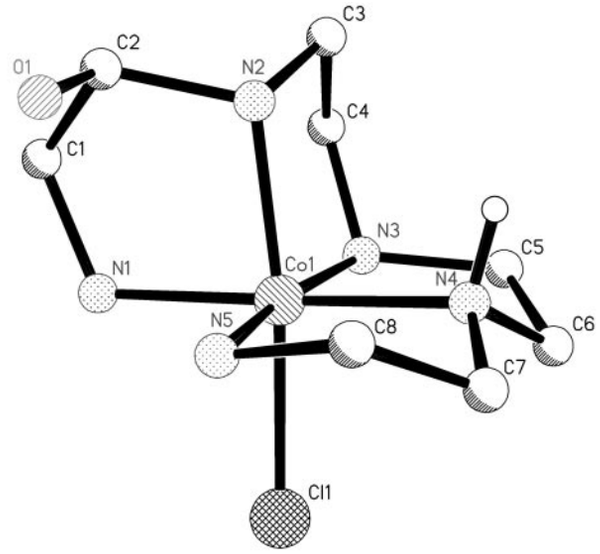


Fig. 4 X-Ray crystal structure of the *exo-ffm*$_s$-[Co(tetraenol)Cl]$^{2+}$ cation. The $[ZnCl_4]^{2-}$ anion, the ethanol of crystallisation and most of the hydrogen atoms have been omitted for clarity. Selected atomic distances (Å): Co1–N1 1.974(2), Co1–N2 1.966(2), Co1–N3 1.970(2), Co1–N4 1.939(2), Co1–N5 1.968(2), Co1–Cl1 2.2664(8), O1–C2 1.397(3), N2–C2 1.508(3), other N–C 1.47–1.52.

chemical shifts for each diastereoisomer, with the chemical shift of the deuterated carbon atom being most affected. The resulting overlap of the signals assigned to the deuterated carbon atom, and overlap with other signals in the spectrum, precluded the straight-forward determination of the ^{13}C–^{2}H coupling constants. However, Jackson's assignment[6] of the ^{13}C NMR spectrum for the *ffm*$_s$-[Co(tetraen)(OH_2)]$^{3+}$ complex allowed us to identify the site of deuteration as the carbon atom adjacent to the meridional amine. This result, obtained for the bulk sample, is consistent with the imine location derived from the X-ray diffraction experiments on the single crystal.

The structure determination demonstrates that the portion of the imine ligand that was derived from the initial trien ligand adopts the *ff*-configuration around the metal ion. This is the same configuration as that of the original starting material, *ff*-[Co(trien)Cl_2]$^+$, but the intermediate acetal complex was assigned the *fm*-configuration in the earlier work. This means that either the structural assignment of the acetal intermediate is incorrect, or that the polyamine ligand wrapping undergoes at least two rearrangements during the reaction sequence.

Considerable effort was spent in attempts to grow X-ray quality crystals of the known [Co(trien)($NH_2CH_2CH(OEt)_2$)-Cl]Br_2 complex. Success was ultimately achieved by vapour diffusion of acetone, into an acidified solution of the complex. The resulting fine needles were only just large enough for the purpose. The result of the structure determination is shown in Fig. 3. The most significant feature of this structure is the wrapping of the trien backbone, which is the same as that proposed by Engelhardt *et al.*[4e] Thus, it appears that the polyamine backbone does indeed rearrange at least twice during the reaction sequence.

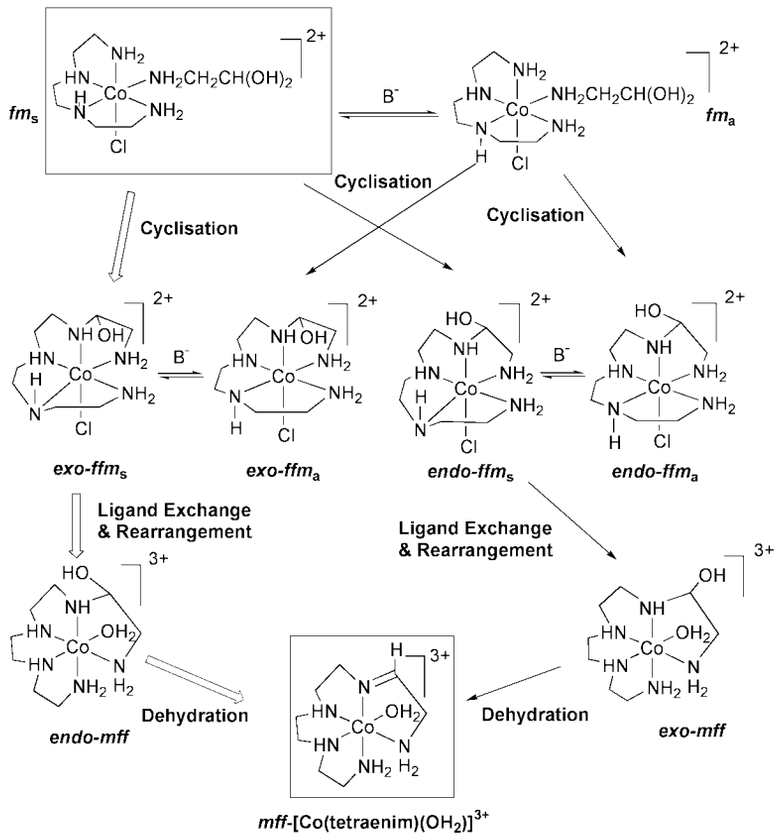
The observation of several minor bands during the ion exchange chromatographic purification of the imine complex and the isolation of a new carbinolamine complex from one of them lead us to consider the possibility of being able to isolate intermediates from the condensation reaction. Quenching the reaction after short reaction times demonstrated that the carbinolamines were a major component of the reaction mixture prior to formation of significant amounts of the imine complex. These are complexes that have been prepared for the first time.

The structure of the major carbinolamine, *exo-ffm*$_s$-[Co-(tetraenol)Cl]$ZnCl_4$, was determined by X-ray techniques and is shown in Fig. 4. This is one of the carbinolamines that would result from the reaction of the carbonyl group (that would be present in small amounts as a result of dehydration of the diol) with the primary amine coordinated *trans* to the chloride ligand in the starting material. Other carbinolamines would result from the primary amine approaching the other face of the carbonyl group, from epimerisation of the meridional secondary amine, and from reaction of the carbonyl group with the secondary amine that is also coordinated *cis* to the amino-acetaldehyde ligand. ^{13}C NMR signals that can be assigned to such molecules were detected in spectra of mixtures that were obtained from ion exchange chromatographic experiments.

Subjecting the isolated carbinolamine complex to the reaction conditions resulted in the production of some of the known imine complex, *mff*-[Co(tetraenim)Cl]$^{2+}$, and some of the N–H epimeric carbinolamine, *exo-ffm*$_a$-[Co(tetraenol)Cl]$^{2+}$, but approximately 75% of the material was recovered unchanged. It was noted that the imine complex was only present in the aquated material that was removed from the column in the second band and subsequently anated. We infer from this that a ligand exchange reaction may be required during the rearrangement of the polyamine backbone to give the final product. This would be consistent with the edge displacement mechanism for ligand rearrangement reactions.[12]

The carbinolamine is clearly a competant intermediate for the reaction, but the rate of the reaction would appear to be somewhat less than that of the deprotected acetal. We attribute this to the presence or absence of cobalt(II) in the reaction mixtures. Cobalt(II) was detected following ion exchange chromatography of the acetal reaction mixture, but not following the resubmission experiment. The cobalt(II) ions may catalyse the rearrangement that is required to form the imine complex, probably by enhancing the rates of ligand exchange reactions. We speculate that the cobalt(II) ions that we detected in the acetal reaction mixture are the result of redox chemistry of the pendant aldehyde that will be present in small amounts following deprotection of the acetal. Such reactivity would not be expected in the case of the carbinolamine complex.

The second carbinolamine was identified as the N–H epimer of the starting material through an incomplete X-ray structure determination. Twinning of the crystals prevented a complete solution being obtained, but the relative positions of the non-hydrogen atoms were established, and we believe that this,



Scheme 2

together with the NMR data, is sufficient to identify the compound. Production of the N–H epimer is not surprising given that the reaction conditions are such that the amine protons would exchange with solvent and, in doing so, provide a mechanism by which inversion at nitrogen could occur. The NMR data allowed us to establish that this compound was also present in small amounts in the original imine synthesis.

We believe that the isolation and characterisation of these carbinolamine intermediates puts us in a position to propose a mechanism by which the *mff*-[Co(tetraenim)Cl]$^{2+}$ complex may be formed from the isolated acetal complex. The *fm*$_s$-acetal complex is deprotected stereoretentively, and the resulting diol dehydrates, producing an aldehyde that is able to undergo a condensation reaction with the coordinated amines. The proposed mechanism is shown in Scheme 2. The predominant pathway (identified by the broad arrows) is condensation with the primary amine *trans* to the chloride ligand to give the *exo-ffm*$_s$-[Co(tetraenol)Cl]$^{2+}$ complex, since the protons on this amine will be more acidic than those on the other coordinated amines. It is quite likely that at least some reaction occurs through addition of the amine to the opposite face of the carbonyl group, generating the *endo-ffm*$_s$-[Co(tetraenol)Cl]$^{2+}$ complex. Epimerisation of the meridional nitrogen donor would give rise to the two *ffm*$_a$-complexes. There is some prospect that a small amount of condensation occurs with the secondary amine that is *cis* to the aminocarbonyl ligand, possibly in the case where chloride ligand exchange precedes the condensation reaction. This is not shown in Scheme 2, but there is precedent for this in the literature.[4d]

In all of these cases the resulting carbinolamine is unable to dehydrate to form an imine, either because the preferred planar geometry cannot be achieved (due to the location of the donor atoms adjacent to the carbinolamine nitrogen atom), or because the nitrogen atom lacks a proton that can be removed in the elimination of water. Edge displacement isomerisation can occur *via* ligand exchange pathways, and this, together with epimerisation of the meridional secondary amine, allows each of the secondary carbinolamines to achieve a geometry in which elimination of water can occur. This results in the *mff*-[Co(tetraenim)(OH$_2$)]$^{3+}$ imine complex, which is then anated during the workup procedure. These ligand exchange reactions would be catalysed by the presence of cobalt(II) ions, thereby explaining the slower reaction rates that were observed in the resubmission experiments.

Conclusion

Engelhardt *et al.*[4e] may have misidentified one of the imine complexes that they synthesised, but the key principles that they put forward are still valid, and indeed the somewhat more complex mechanism that we propose for the formation of the imine complex is entirely consistent with their thesis. The condensation reaction does indeed appear to proceed predominantly with the amine bearing the most acidic protons (provided it is coordinated *cis* to the carbonyl containing ligand). The key corollary that we would like to add to this is that the dehydration to form the imine will only occur if the resulting imine can adopt a planar geometry. If the geometry of the carbinolamine is such that the dehydration is prevented, the complex will undergo backbone rearrangements in order to reach a geometry in which the dehydration reaction can occur.

References

1 For reviews of early work see: (*a*) V. I. Pavlovskii and A. L. Poznyak, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 789; (*b*) J. Sykora and J. Sima, *Coord. Chem. Rev.*, 1990, **107**, 1; (*c*) V. I. Pavlovskii and A. L. Poznyak, *Z. Chem.*, 1989, **29**, 6.

2 For examples see: (*a*) V. V. Pansevich and A. L. Poznyak, *Russ. J. Inorg. Chem. (Transl. of Zh. Neorg. Khim.)*, 1991, **36**, 1425; (*b*) A. L. Poznyak and V. E. Stelímashok, *Metalloorg. Khim.*, 1992, **5**, 611; (*c*) A. L. Poznyak and L. V. Stopolyanskaya, *Russ. J. Inorg. Chem. (Transl. of Zh. Neorg. Khim.)*, 1995, **40**, 1080; (*d*) T. Ama, H. Kawaguchi, K. Okamoto, T. Yasui, T. Yonemura and M. Yoshida,

Bull. Chem. Soc. Jpn., 1995, **68**, 874; (*e*) T. Yonemura, H. Kawaguchi, K. Shibuya, K. Murakami, T. Yasui, K. Okamoto and J. Hidaki, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 2287; (*f*) M. Kojima, F. MD. Akhter, K. Nakajima and Y. Yoshikawa, *Bull. Chem. Soc. Jpn.*, 1996, **69**, 2889; (*g*) D. M. Tonei, L. J. Baker, P. J. Brothers, G. R. Clark and D. C. Ware, *Chem. Commun.*, 1998, 2953; (*h*) T. Yonemura, K. Shibuya, T. Ama, H. Kawaguchi, K. Okamoto, J. Hidaka and T. Yasui, *Inorg. Chem.*, 1999, **38**, 3244; (*i*) R. M. Hartshorn and S. G. Telfer, *J. Chem. Soc., Dalton Trans.*, 1999, 3217; (*j*) R. M. Hartshorn and S. G. Telfer, *J. Chem. Soc., Dalton Trans.*, 2000, 2801.

3 J. McB. Harrowfield and A. M. Sargeson, *J. Am. Chem. Soc.*, 1974, **96**, 2634.

4 (*a*) B. T. Golding, J. McB. Harrowfield and A. M. Sargeson, *J. Am. Chem. Soc.*, 1974, **96**, 3003; (*b*) J. D. Bell, A. R. Gainsford, B. T. Golding, A. J. Herlt and A. M. Sargeson, *J. Chem. Soc., Chem. Commun.*, 1974, 980; (*c*) A. R. Gainsford and A. M. Sargeson, *Aust. J. Chem.*, 1978, **31**, 1679; (*d*) A. R. Gainsford, R. D. Pizer, A. M. Sargeson and P. O. Whimp, *J. Am. Chem. Soc.*, 1981, **103**, 792; (*e*) L. M. Engelhardt, A. R. Gainsford, G. J. Gainsford, B. T. Golding, J. McB. Harrowfield, A. J. Herlt, A. M. Sargeson and A. H. White, *Inorg. Chem.*, 1988, **27**, 4551.

5 A. M. Sargeson and G. H. Searle, *Inorg. Chem.*, 1967, **6**, 787.

6 W. G. Jackson, *Inorg. Chem.*, 1991, **30**, 1570.

7 SMART Version 5.045, Data Collection Software, Siemens Analytical Instruments Inc., Madison, WI, 1998.

8 SAINT Version 5.01, Data Integration Software, Siemens Analytical Instruments Inc., Madison, WI, 1998.

9 (*a*) G. M. Sheldrick, SADABS Version 5.01, Program for Empirical Absorption Correction of Area Detector Data, University of Göttingen, Germany, 1996; (*b*) G. M. Sheldrick, SHELXTL, Structure Determination Program, Version 5.03, University of Göttingen, Germany, 1990.

10 The nomenclature used for identifying isomers of the compounds described in this paper is described in R. M. Hartshorn and D. A. House, *J. Chem. Soc., Dalton Trans.*, 1998, 2577.

11 M. R. Snow, D. A. Buckingham, P. A. Marzilli and A. M. Sargeson, *Chem. Commun.*, 1969, 891.

12 D. D. Brown, C. K. Ingold and R. S. Nyholm, *J. Chem. Soc.*, 1953, 2673.