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Article

Synthesis, Separation, and Assignment of the Seven Geometric Isomers of $[Co(dien)(ibn)Cl]^{2+}$

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All seven possible geometric isomers (four mer and three facial) for the $[Co(dien)(ibn)Cl]^{2+}$ system have been synthesized (dien = diethylenetriamine, ibn = 1,2-diamino-2-methylpropane). Their structures in dimethyl sulfoxide solution have been uniquely determined by two-dimensional NMR spectroscopy (DQCOSY and NOESY).

Introduction

In the $[Co(dien)(ibn)Cl]^{2+}$ system (dien = diethylenetriamine, ibn = 1,2-diamino-2-methylpropane), a gem dimethyl group has replaced the two methylene protons in $[Co(dien)(en)Cl]^{2+}$ but the chemistry should be generally similar to the ethylenediamine (en) analogues. However, the number of the geometric isomers is increased from four to seven (Figure 1) due to two possible end-to-end arrangements of the unsymmetrical ibn chelate, and this provides advantages in probing the mechanism of substitution reactions[1−3] as will be developed.

This system offers some particular advantages for a more detailed study of the base hydrolysis reaction.[3] First, due to the unsymmetric nature of ibn, there are two different paths for the reentering group Y in the common intermediate of the trigonal bipyramidal type believed[2,3] to arise in base hydrolysis (Figure 2). If each of the four stereochemically distinct mer reactants gave the same kinetic product distribution under the same reaction conditions, a case for such an intermediate would be particularly strong.

In another context, the interconversion of the isomers under nonbasic conditions, especially between the three facial isomers and between the mer and the facial isomers, can shed more light on the so-called edge displacement principle.[1,4] The *sec*-NH center directs the ways in which chelate arms move in net rearrangement processes, and there are only certain rearrangements possible for edge displacement. The newer concept of ligand folding[5] can be tested as a viable rearrangement pathway also (Figure 3).

Experimental Section

Instruments and Chemicals. All chemicals were analytical or an equivalent grade. ^{13}C NMR, ^{1}H NMR, and two-dimensional (2D) NMR spectra (DQCOSY and NOESY) were recorded on a Varian Unity Plus 400 MHz instrument at 25 °C. Solvents used were Me_2SO-d_6 with the central peak of the CD_3 septet as the reference (^{13}C, δ 39.37; ^{1}H, δ 2.50 ppm relative to $SiMe_4$). Full visible absorption spectra were obtained with use of a HP 8452A diode-array spectrophotometer thermostated to 25.0 ± 0.1 °C. Cation exchange media used were Dowex 50W×2 (H^+ form, 200−400 mesh; Bio-Rad) and SP-Sephadex C25 (Na^+ form; Pharmacia). The medium Biorex MSZ 50 (Na^+ form) was used for the chromatography of the acid sensitive azido complexes. Dowex was the most widely used, and 50 × 6 cm columns packed in 2 M HCl were employed. Elution profiles were obtained by evaporating numerous sequential fractions from the column, and weighing as the chloride salts. Isomeric compositions were determined by ^{13}C NMR spectroscopy.

Synthesis of the $[Co(dien)(ibn)Cl]^{2+}$ Isomers. The geometric isomers of $[Co(dien)(ibn)Cl]^{2+}$ were synthesized by a modification of the method described by Bosnich and Dwyer for the $[Co(dien)(en)Cl]^{2+}$ system;[6,7] $Co(dien)Cl_3$ (12.0 g) was suspended in 30 mL of water (pH ≈ 4), and isobutylenediamine (ibn, 3.94 g) was added. The mixture was stirred at room temperature for 1 h, during which time the pH dropped from ca. 9.5 to 6.4. The product mixture was acidified using 2 M HCl, filtered to remove residual $Co(dien)Cl_3$, and diluted and sorbed onto a Dowex column. Elution with HCl (2 M) separated a number of colored 2+ bands. A total of 8.0−10.0 g (chloride salts) of Co(III) complexes was obtained (yield: 50−70%).

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(1) Basolo, F.; Pearson, E. G. *Mechanisms of Inorganic Reactions*, 2nd ed.; Wiley: New York, 1967.

(2) Jackson, W. G.; Sargeson, A. M. In *Rearrangements in ground and excited states*; de Mayo, P., Ed.; 1980; Vol. 2; p 273.

(3) Tobe, M. L. *Adv. Inorg. Bioinorg. Mech.* **1983**, *2*, 1.

(4) Brown, D. D.; Ingold, C. K.; Nyholm, R. S. *J. Chem. Soc.* **1953**, 2673.

(5) Jackson, W. G.; Walsh, R. J. *Inorg. Chem.* **1991**, *30*, 4813.

(6) Bosnich, B.; Dwyer, F. P. *Aust. J. Chem.* **1966**, *19*, 2045.

(7) Couldwell, M. C.; House, D. A. *J. Inorg. Nucl. Chem.* **1991**, *33*, 2583.

10.1021/ic0202460 CCC: $25.00

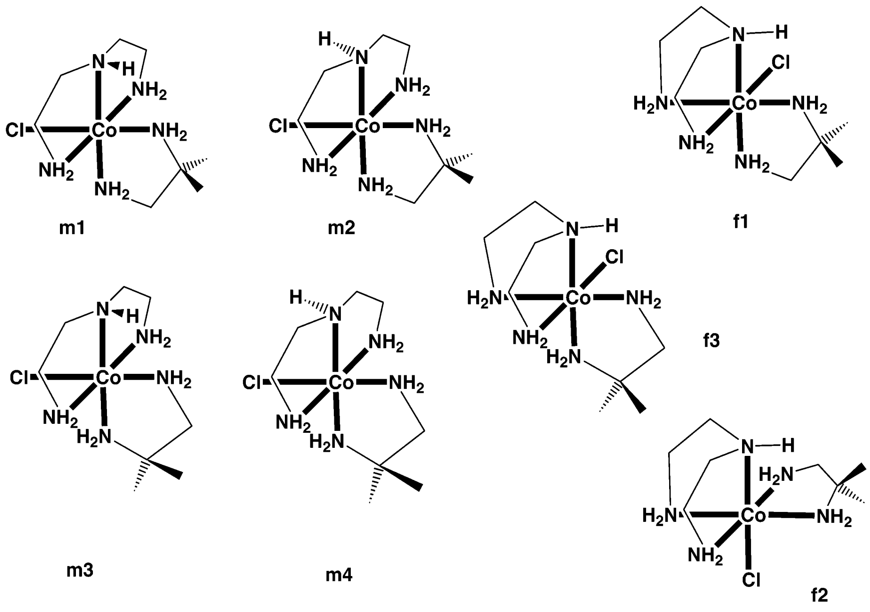

Figure 1. The seven geometric isomers for [Co(dien)(ibn)Cl]$^{2+}$.

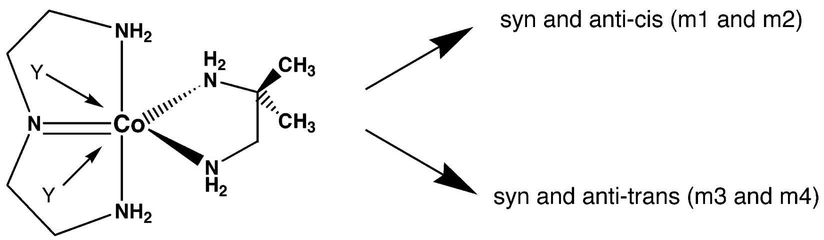

Figure 2. The deprotonated trigonal bipyramidal 5-coordinate intermediate.

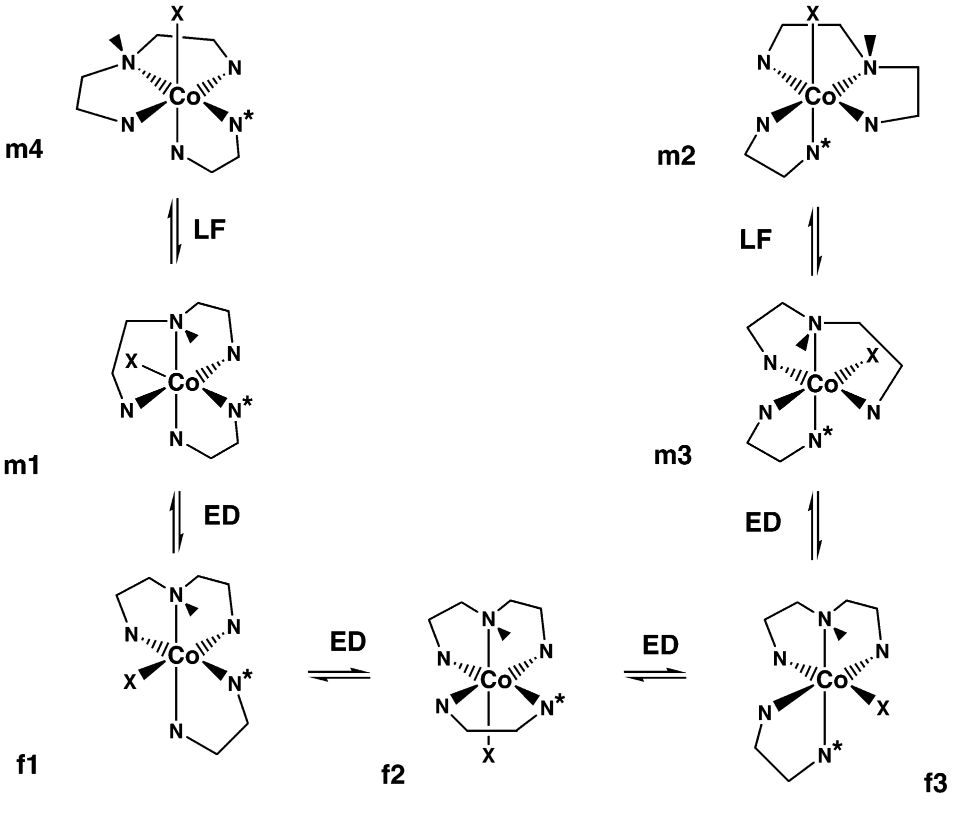

Figure 3. Edge displacement (ED) and ligand folding (LF) processes.

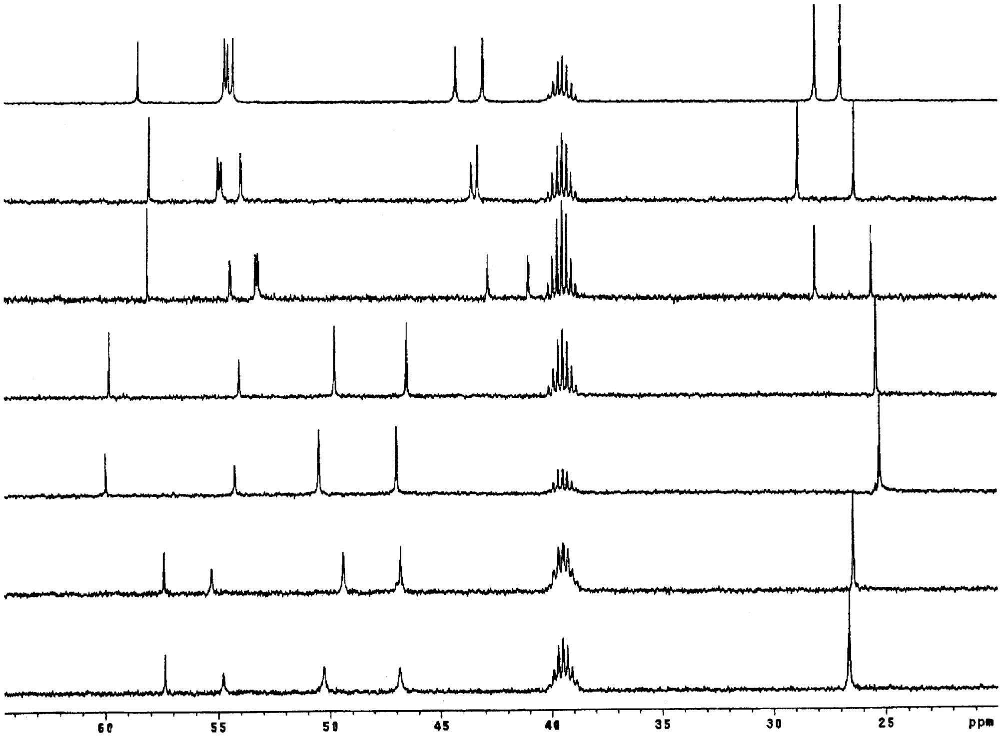

Figure 4. ^{13}C NMR spectra of the seven geometric isomers of [Co(dien)(ibn)Cl]$ZnCl_4$ in Me_2SO-d_6 (top to bottom: f3, f2, f1, m4, m3, m2, m1).

Separation of the [Co(dien)(ibn)Cl]$^{2+}$ Isomers. It is difficult to fully separate all seven isomers by using column chromatography on Dowex. Using a 50 cm × 5.5 cm column, only m4 can be isolated cleanly. Generally the isomers were collected in groups (m1, f1; and f3, f2, m3). The solubilities of the chlorides within the groups were such that the isomers could be separated by fractional crystallization (m3 was much less soluble than f3 or f2). Using these solubility differences, the m3, f3, and f2 chloride salts could be enriched in the desired isomer by repeated refractionation (from water/HCl/MeOH/Me_2CO) and finally recrystallized to purity. The perchlorate salt of the m3 isomer was much less soluble than the f3 or f2 isomers, and this fact was utilized in the final purification step to remove residual f2 and f3, which remained in solution. The elution curves show the residual f2 and f3 species can be separated by column chromatography. The separation of the f1 and m1 isomers was particularly difficult by physical methods. However, it is comparatively easy to separate the f1 and m1 isomers by controlled base hydrolysis due to a significant difference in their rates of base hydrolysis: k_{OH}(mer)/k_{OH}(facial) is about 1000. Thus, excess NaOH (0.5 M) was added rapidly to a solution containing a mixture of the f1 and m1 isomers, followed by quenching immediately with excess HCl (2 M) and separating by using column chromatography on Dowex. Isomers m2 and m4 were also conveniently synthesized from their corresponding azido complexes, which are the predominant kinetic products in the reaction between any of the mer chloro isomers and NaN_3 at relatively short reaction times (see below). The azido species are converted quantitatively into the chloro ions (with retention) on reaction with excess $NaNO_2$/11 M HCl and heating.

Each of the isomers was characterized as chloride, perchlorate, and tetrachlorozincate salts; the latter two salts were obtained from concentrated solutions of the chlorides using one-fifth volume of the appropriate precipitant (70% $HClO_4$ or 2 M "H_2ZnCl_4" (2 M $ZnCl_2$ in 5 M HCl)). Anal. Calcd for [Co(dien)(ibn)Cl]$ZnCl_4$: C, 19.49; H, 5.11; N, 14.21. Found: C, 19.33; H, 4.83; N, 14.08 (m3).

Synthesis of the [Co(dien)(ibn)(N_3)]$^{2+}$ Isomers. A chloride salt of [Co(dien)(ibn)Cl]$^{2+}$ (any isomer, or an isomer mixture) was dissolved in 10 times its weight of water, and an equal volume of 2 M NaN_3 was added. After an appropriate time, depending upon which isomer was required as the major product, the reaction was quenched with "H_2ZnCl_4" (2 M) and dark pink crystals containing at least three of the four mer isomers formed immediately. To separate the isomers, the product mixture (from 5 g of starting material) was dissolved in a minimal amount of water and loaded onto a Dowex column (50 × 6 cm) and eluted with 2 M HCl in the dark. Four bands developed. The first and the last bands were well separated, while the middle two bands were barely separated. The order of isomers eluting from the column was found to be very similar to that for the chloro species. [The azido complexes in this system are surprisingly quite stable in acid: even after heating in concentrated HCl for 1 h on the steam bath, there remains appreciable azido complex.] The acid eluates were quickly rotaevaporated at <50 °C without detectable formation of chloro complex impurity. The individual azido complexes were recrystallized from water as perchlorate or tetrachlorozincate salts as described above for the chloro ions.

The azido complexes were characterized by NMR and by chemical correlation with the aqua complexes (nitrosation in acid) and the chloro species (anation in strong HCl); both reactions proceed with retention.

Results and Discussion

NMR Spectroscopy. Figure 4 shows the ^{13}C NMR spectra for the seven geometric isomers in Me_2SO-d_6. 2D NMR spectra (DQCOSY, NOESY) were also recorded for Me_2SO-d_6 as solvent; these are considered later, together with the one-dimensional (1D) ^{1}H spectra.

The carbon spectra are clearly different and come in two sets. The four mer iomers each have a plane of symmetry

Table 1. Visible Absorption Spectral Data [λ/nm (ϵ/mol^{-1} cm^{-1})] for the [Co(dien)(ibn)Cl]Cl$_2$ Isomers in 0.01 M HClO$_4$ at 25 °C

isomer	max	min	max	min
m1	484 (80.5)	418 (37.0)	368 (81.0)	334 (52.0)
m2	514 (70.5)	422 (26.0)	366 (78.0)	334 (55.5)
m3	486 (95.5)	416 (41.5)	*a*	*a*
m4	492 (745)	418 (27.0)	354 (88.0)	336 (85.0)
f1	536 (560)	420 (12.0)	362 (59.5)	330 (32.5)
f2	520 (62.5)	412 (17.0)	356 (74.0)	330 (32.5)
f3	524 (110.0)	408 (49.0)	*a*	*a*

[a] These are obscured by intrusive UV absorption.

and show five lines each (3 × 2C + 2 × 1C); the tertiary C is of diminished intensity, as is usual (0 nOe). The three facial isomers are asymmetric, and each shows eight lines. It is also evident from the spectra that one isomer is not an impurity in another. Note that some line broadening in these spectra is matched by the broadening in the Me$_2$SO-d_6 reference, and is therefore only a resolution problem.

Electronic Absorption Spectra. The vis/UV spectra are characteristic of the [CoN$_5$Cl] chromophore; the data are presented in Table 1.

Separation of the Geometric Isomers of [Co(dien)(ibn)-Cl]$^{2+}$. All seven geometric isomers in this system have been synthesized without resort to specialized kinetic methods. Gainsford and House have also prepared some isomers in this system.[8] There is no marked difference in stabilities between the mer and facial isomers, although corresponding fac (e.g., f3 vs m3) species were generally more abundant. Much the same holds for the closely analogous [Co(dien)-(en)Cl]$^{2+}$ system. The anti-mer species were also more stable than corresponding syn isomers (e.g., m1 vs m2), and this seems to be universally true in [Co(dien)(diamine)Cl]$^{2+}$ systems. Isomers differing only in the position of the gem dimethyl group on the backbone of the bidentate (cis vs trans) were comparable in energy, which is hardly surprising.

The separation of some mer/fac mixture isomers required a special technique. The mer chloro species are much more reactive in base hydrolysis than the facial isomers, the difference being over 500-fold.[9] Utilizing this fact, a mixture of the mer and facial chloro species was dissolved in a buffer (pH 8−9, 20 °C), and quenched with hydrochloric acid after about 30 s. The facial isomers remained unchanged while the mer isomers were converted to the 3+ aqua species. This mixture of 2+ and 3+ cations was then separated easily by chromatography, and the mer aqua species were converted back to the chloro ions with retention by heating in HCl. This method was used where the mer isomers could not otherwise be separated from the facial isomers directly. The disadvantage was that a mixture of mer isomers was obtained in the selective base hydrolysis step, and the different mer forms then required a further separation step. From Figure 5, one can see that it is difficult to separate these mer chloro isomers, but it could be achieved by converting the mixed mer ions to their azido species, whence they could be separated by direct chromatography.

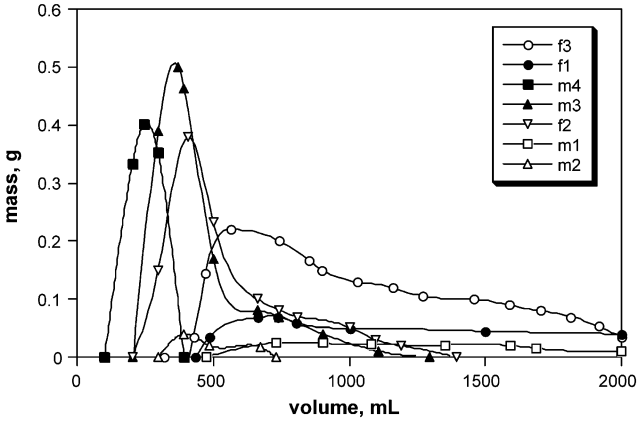

Figure 5. Elution profiles for [Co(dien)(ibn)Cl]$^{2+}$.

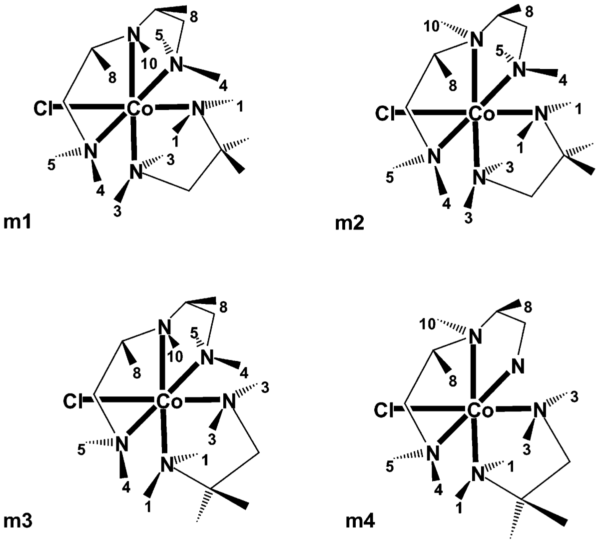

Figure 6. Short-range (<0.5 nm) through-space interactions for the four *mer*- [Co(dien)(ibn)Cl]$^{2+}$ isomers.

From the pure azido isomers, the corresponding chloro isomers of the same configuration were easily generated, and also the corresponding pure aqua isomers:

$$[\mathrm{Co(triamine)(diamine)N_3}]^{2+} + \mathrm{NO_2}^- + 2\mathrm{H}^+ \rightarrow [\mathrm{Co(triamine)(diamine)OH_2}]^{3+} + \mathrm{N_2}\uparrow + \mathrm{N_2O}\downarrow$$

$$[\mathrm{Co(triamine)(diamine)OH_2}]^{3+} + \mathrm{Cl}^- \rightarrow [\mathrm{Co(triamine)(diamine)Cl}]^{2+} + \mathrm{H_2O}$$

For the first of these two reactions in water, the product was the aqua species. In the concentrated HCl, the major product was the chloro species formed directly by Cl$^-$ capture.

Identification of the Geometric Isomers of [Co(dien)-(ibn)Cl]$^{2+}$. While it is important to synthesize all of the isomers in a system if one is to fully interpret the kinetics and stereochemistry, it is equally important to unambiguously identify these isomers. There are a number of methods to identify the isomers, some chemical, some spectroscopic. Two kinds of 2D NMR spectra have been utilized routinely. These are the DQCOSY and NOESY experiments. DQ-

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(8) House, D. A.; Gainsford, A. R. Unpublished work (doctoral dissertation of A. R. Gainsford).

(9) Zhu, T.; Jackson, W. G. Results to be published, 2003.

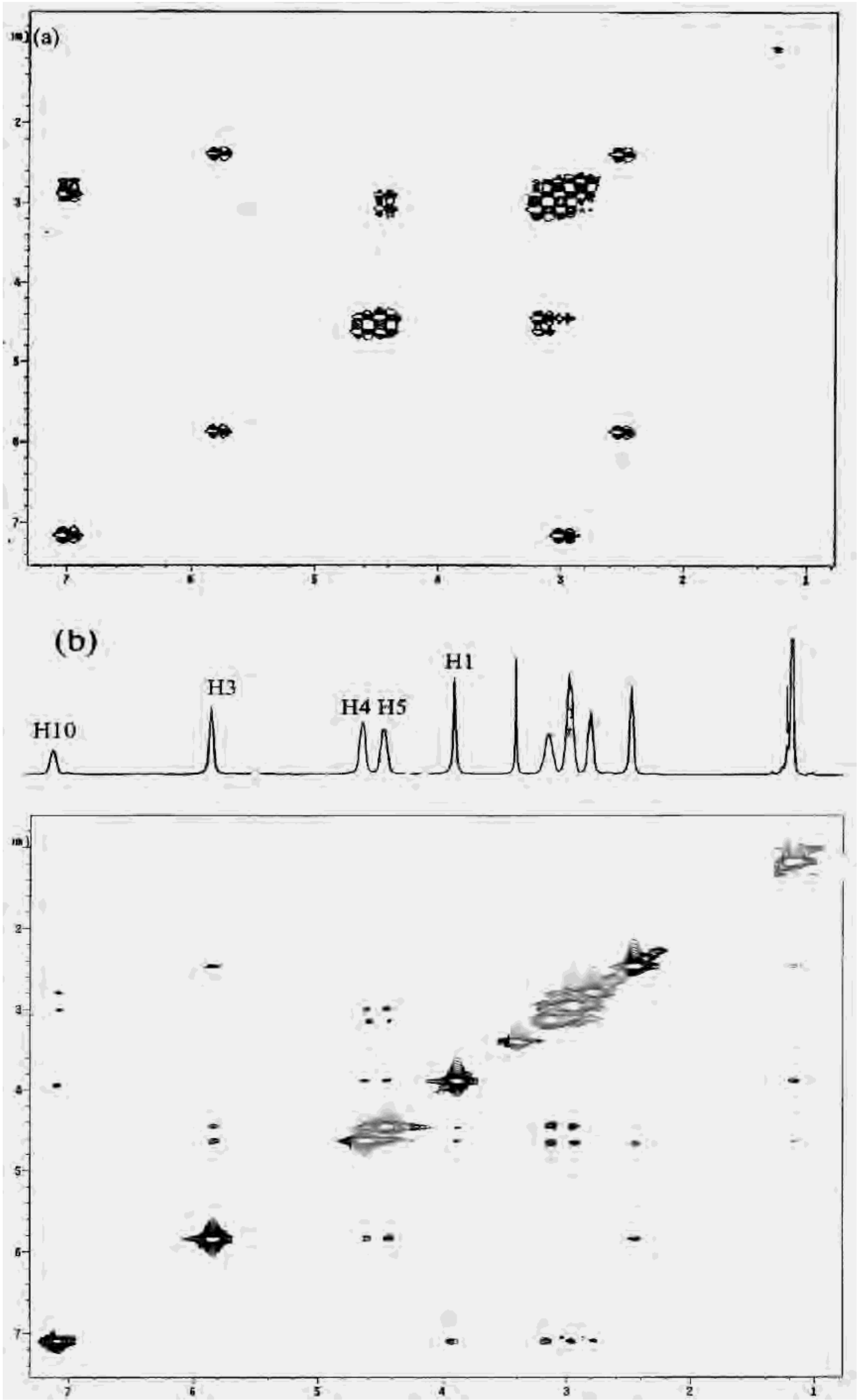

Figure 7. (a) DQCOSY, (b) ^{1}H NMR, and (c) NOESY spectra of m1-[Co(dien)(ibn)Cl]$ZnCl_4$ in Me_2SO-d_6.

COSY NMR correlates the resonances of hydrogens which are scalar (*J*) coupled and suppresses uncoupled protons,[10−12] while NOESY NMR correlates the resonances of hydrogens which are physically close in space ($<$5 Å).[13−15] DQCOSY NMR reveals the connectivity of gem and vicinal hydrogen atoms in a compound; the patterns are similar within each series of mer or fac complxes. However, each geometric isomer has its unique topological structure, and the NOESY NMR spectrum exposes these differences. Thus, together, the two kinds of NMR experiment permitted the unambiguous assignment of all seven configurations.

Figure 6 shows the numbering scheme for the mer structures. Some of the important through-space ^{1}H−^{1}H correlations in each isomer are as follows. Protons H8 and H10 are correlated with H1 (m1) or H3 (m3) in the anti isomers while in the syn isomers H10 is remote and the correlation with these protons is absent. Similarly, the protons on the N trans to Cl$^-$ (H1 in the m1, m2 isomers and H3 in the m2, m4 species) are correlated with the nearer amine proton H4 of dien, whereas where these H protons are on the nitrogen cis to Cl$^-$ (H3 in the m1, m2 and H1 in the m2, m3) they correlate with *both* the dien terminal protons H4 and H5. These sets of correlations therefore completely distinguish the four mer isomers.

Although the DQCOSY spectra cannot pinpoint which isomer is which, they were essential for identifying key protons such as H1, H3, H4, and H5. In the ibn ligand, H1 protons do not correlate with any other protons, because they are α to the C(Me)$_2$ group, whereas H3 has a clear correlation with the α-CH$_2$.

In the DQCOSY spectrum (Figure 7a), H10 is at δ 10.1, H3 is at δ 5.85, H1 is at δ 3.90, and the pair of amine protons H4, H5 is at δ 4.63 and 4.47 ppm. From the NOESY spectrum (Figure 7c), the cross-peaks at 7.10, 3.90 show the correlation of H10 with H1, clearly identifying this isomer as m1.

The spectra for the remaining three mer isomers are all in the Supporting Information. In the DQCOSY spectrum (Figure 8Sa) for another mer isomer, proton H10is at δ 6.69, H3 is at δ 5.92, H1 is at δ 4.26, and the pair of amine protons H4, H5 is at δ 4.86 and 4.57 ppm. From the NOESY spectrum (Figure 8Sc), there is no correlation of H3 with H4, H5 of dien while the correlations of H1 with these same protons reveal that this isomer is m2.

In the DQCOSY spectrum (Figure 9Sa), H10 is at δ 7.51, H1 is at δ 5.48, H3 is at δ 4.49, and the pair of amine protons H4, H5 are superimposed at δ 4.38. From the NOESY (Figure 9Sc), the cross-peaks at 7.51, 4.49 and absence of others show the specific correlation of H10 with H3. These uniquely define the m3 configuration.

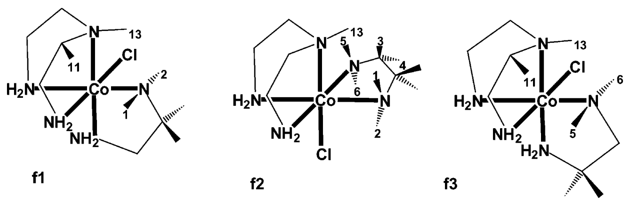

Figure 11. Short-range through-space proton interactions for the three facial isomers.

For the mer isomer which was ultimately identified as m4, the unique *sec*-NH (H10) is seen at δ 6.54 (1H). H1 is a singlet at δ 5.46; H3 at δ 4.60 is also a singlet, but correlates with the methylene protons in the DQCOSY spectrum. This therefore permits the distinction between H1 and H3. The pair of amine proton signals H4 or H5 at δ 4.86 and 4.55 are gem, from the DQCOSY spectrum (Figure 10Sa). From the NOESY spectrum (Figure 10Sc), there are no correlations of H10 with H1 or H3, indicating the syn (m2 or m4) configuration, but there are correlations of H1 with both H4 and H5, uniquely defining the isomer as m4.

In summary, the 2D NMR spectra allowed the definitive assignment of the four mer-isomer configurations.

Due to the asymmetry of the facial isomers, there are more signals and cross-peaks than for the mer isomers, but specific correlations exist to easily enable isomer distinctions. The numbering scheme for the short ($<$2.5 nm) through-space interactions is shown in Figure 11; each is observed in the corresponding NOESY spectrum. Thus, the specific correlations for the f1 isomer are seen as the cross-peaks of H13 with H1 and H2; those for f3, cross-peaks of H13 with H5 and H6; and those for f2, cross-peaks of H13 with one set of methyl protons in ibn.

In the DQCOSY spectra, there are apparently several pairs of geminal (CH$_2$, NH$_2$) and vicinal (CHCH, CHNH) protons, and each pair exhibits cross-peaks. The NH and CH protons are readily distinguished by their chemical shifts, low and high field respectively, and through characteristic ^{14}N broadening. Further, the unique NH (H13) shows no NH−NH cross-peaks. The protons H1 and H2 on N1 are remote and are uniquely correlated, unlike the protons on N2, N3, and N5 which also correlate with CH protons, and these NH protons are therefore readily identified. The NH proton H13 correlates only with the methylenes H11 and H14, which are at higher field. To identify H5, H6, and others, the NOESY spectra were used in conjunction with the DQCOSY spectra. The correlations of H13 with H1, H2, H5, and H6 are observed for the particular isomers shown.

On the basis of the above analysis, the specifics are given below.

The DQCOSY spectrum for the f2 isomer (Figure 12a) reveals H13 (uncorrelated) at δ 6.07 and H13 at δ 1.29 and 1.33. In the NOESY spectrum (Figure 12c), H13 correlates with the methyl protons at δ 1.29 consistent with the f2 configuration.

The other facial isomer spectra are all in Supporting Information. In the DQCOSY spectrum of the f1 isomer (Figure 13Sa), H13 is clearly at δ 7.04. The unique correlations at δ 5.05 and 4.51 reveal that they correspond

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(10) Maudsley, A. A.; Ernst, R. R. *Chem. Phys. Lett.* **1977**, *50*, 368.
(11) Douglas, A.; et al. *J. Nat. Prod.* **1986**, *49*, 456.
(12) Derome, A. E. *Modern NMR Techniques for Chemistry Research*; Pergamon Press: New York, 1987.
(13) Macura, S.; Ernst, R. R. *Chem. Phys. Lett.* **1980**, *41*, 95.
(14) Wagner, G.; Kumar, A.; Wuthrich, K. *Eur. J. Biochem.* **1981**, *114*, 375.
(15) Wagner, G.; Wuthrich, K. *J. Mol. Biol.* **1982**, *155*, 347.

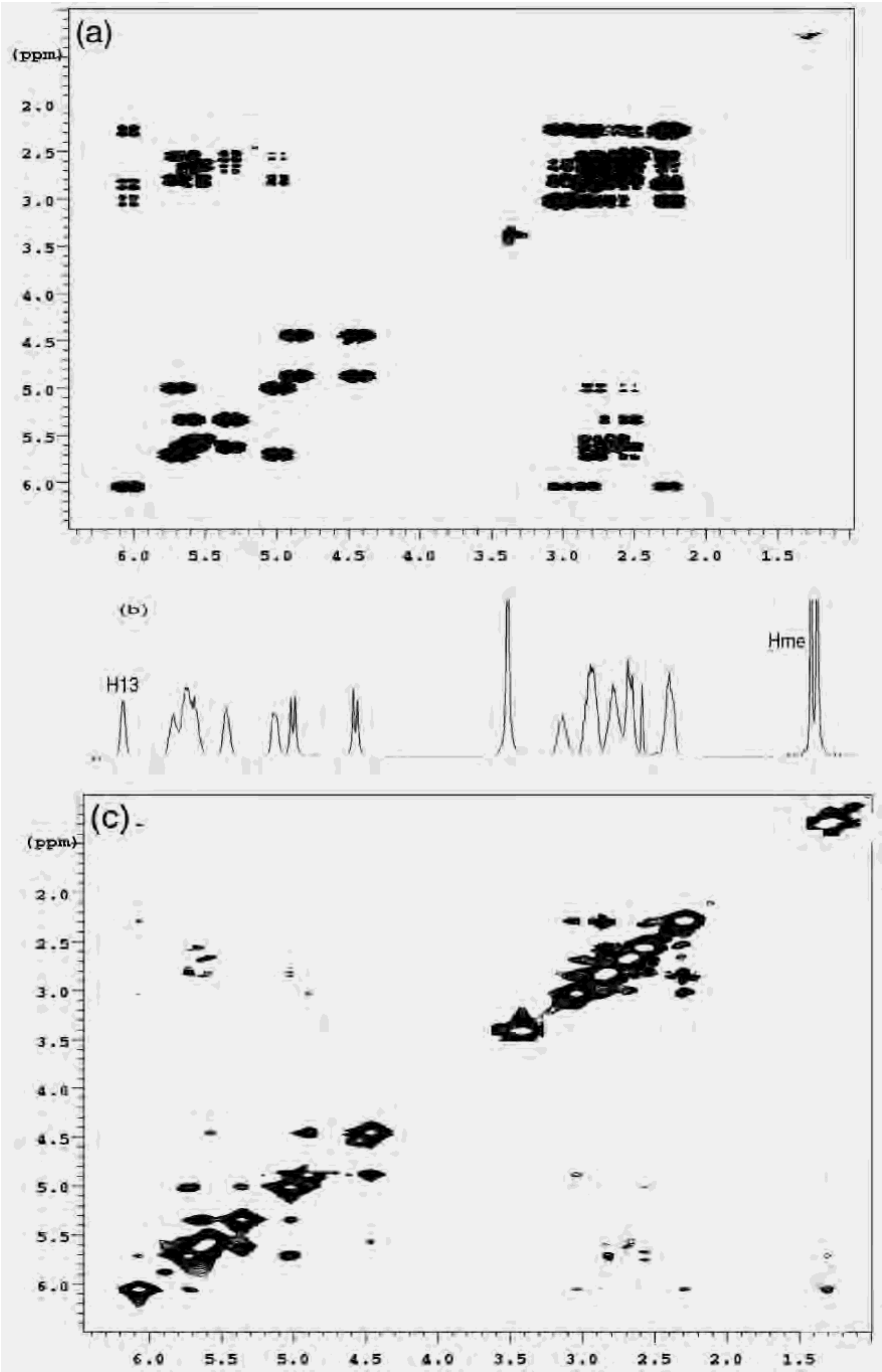

Figure 12. (a) DQCOSY, (b) ^{1}H NMR, and (c) NOESY spectra of f2-[Co(dien)(ibn)Cl]ZnCl$_4$ in Me$_2$SO-d_6.

to H1 and H2. In the NOESY spectrum (Figure 13Sc), H13 correlates with one of the pair of proton(s) at δ 4.51 (H2). The isomer is therefore f1 or f2, but because f2 has been identified (above), it is f1.

In the DQCOSY spectrum of the f3 isomer (Figure 14Sa), H13 is clearly at δ 7.02 and H1/H2 is at δ 5.50 and 5.04 (multiplet). The large multiplet (4H) around 5.0 ppm (components 5.00 (2H), 5.01, and 5.03 from the DQCOSY spectrum) and another at 5.12 (2H) make it hard to distinguish the protons within the multiplets. In the NOESY spectrum (Figure 14Sc), the methyl protons (δ 1.21/1.28) correlate with H3 and H4 (at δ 2.52/3.90), which in turn correlate with H5 and H6 (at δ 5.94/5.04); thus we recognize the two NH protons of ibn adjacent to the methylene. One of the protons in the H1/H2 and H5/H6 pairs is overlapped, but one of the them does correlate with H13. The f1 configuration has been assigned; in that isomer H1 correlates with H13. Since H1 and H6 are almost coincident, the correlation here must be between H6 and H13, unique to the f3 isomer.

Conclusions

All seven [Co(dien)(ibn)Cl]$^{2+}$ isomeric complexes have been synthesized and characterized. 2D NMR techniques allow definitive structural assignments. X-ray structures for several of the isomers are reported elsewhere, as well as the base hydrolysis kinetics and stereochemistry and rearrangements under other conditions to demonstrate the edge displacement and ligand folding processes.

Acknowledgment. W.G.J. is grateful to the Australian Research Council for financial support.

Supporting Information Available: Figures 8S, 9S, 10S, 13S, and 14S (DQCOSY, 1D ^{1}H, and NOESY spectra for the m2, m3, m4, f1, and f2 isomers). This material is available free of charge via the Internet at http://pubs.acs.org.

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