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Cobalt(III) Complexes with *N*-Methylethane-1,2-diamine (meen). Synthesis and Characterization of the Isomers of $[Co(meen)_3]^{3+}$, $[Co(meen)_2(en)]^{3+}$ and $[Co(meen)(en)_2]^{3+}$

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Abstract

Of the twelve possible geometric isomers–diastereoisomers of $[Co(meen)_3]^{3+}$ (meen = *N*-methylethane-1,2-diamine), three isomers designated **A**, **B** and **C** according to their chromatographic elution order, have been detected from preparative mixtures. The highest yield and cleanest synthesis is $CoCl_2$ + 3meen + dimethylsulfoxide, which gives pure red **A**-$[Co(meen)_3]Cl_3$ as the crystallized product, and recrystallization of this from water or methanol gives pure orange–red **C**. Each isomer is robust in acid, but equilibrates in water to the mixture **A**:**B**:**C** = 3:1:2. These are therefore three N–H diastereoisomers of the same geometry with respect to the N–CH_3 groups, which is *mer* by ^{13}C NMR spectroscopy. This mixture can be separated by cation-exchange chromatography on SP-Sephadex by using acidic Na_2SO_4. A second synthesis method was aerial oxidation of Co(II) + 3meen + H^+ in aqueous solution with charcoal at 80 °C. The charcoal and oxygen caused some demethylation of coordinated Co–meen, and the crude yellow–orange isolated product was a mixture of isomers of $[Co(meen)_3]^{3+}$ (mostly **C**), $[Co(meen)_2(en)]^{3+}$ (three orange isomers **F**, **G**, **H**, of ten possible), $[Co(meen)(en)_2]^{3+}$ (one orange–yellow diastereoisomer **E** of two possible) and $[Co(en)_3]^{3+}$ (**D**). The en complex species were separated on Sephadex using Na_3PO_4 as eluent, and the designations **D** to **H** are in the elution order. Thus **F**, **G** and **H** are single diastereoisomers of the three different possible geometries (by ^{13}C NMR), and their ratios isolated *ca.* 5:1:36 should be approximately the equilibrium proportions.

Introduction

Complexes of *N*-methylethane-1,2-diamine (meen) have been of interest for many years, since the crude tris(meen) complexes $[Co(meen)_3]Cl_3$ and $[Ni(meen)_3]Br_2$ were first isolated by Keller and Edwards in 1952 [1]. The nickel(II) complex was further examined by Pavkovic and Meek in respect of the effect of N-substitution on spectroscopic properties [2], but the isomers of these tris(meen) complexes have never been separated or characterized. Particular isomers have, however, been isolated for several bis(meen) and mono(meen) complexes $[Co(meen)_2X_2]^+$ [3–7], $[Co(meen)(en)_2]^{3+}$ [8], $[Co(meen)(NH_3)_4]^{3+}$ [9, 10] and $[Co(meen)(CN)_4]^-$ [10], with their configurations being assigned from an X-ray crystal structure [7] and from electronic spectra, circular dichroism and NMR comparisons [6, 8], and by conformational analysis considerations [6, 10]. A prime interest in the studies with these complexes has been the effect of N-methyl substitution on various properties, including optical rotatory properties [6–8, 11, 12], kinetics of proton exchange and racemization [5, 9], conformational analysis by NMR [10], and reactivity and stabilities of some isomers [6].

Perhaps the most fundamental interest with Co–meen systems is in the stereospecificity which is imposed by the N-methyl substituent on the coordination of the ligand, which manifests in different stabilities of the isomers with some isomers being precluded [13]. The stereospecificity in the coordination of the C-methyl analogue propane-1,2-diamine (pn) and the stereochemistry of Co(pn) complex systems have been well clarified, largely through the separation, characterization and relative stabilities of the complexes $[Co(\pm pn)_3]^{3+}$, $[Co(\pm pn)_2(en)]^{3+}$ and $[Co(\pm pn)(en)_2]^{3+}$ by Corey and Bailar [14] and Dwyer and Sargeson and coworkers [15–20]. These results have played a significant role in our understanding of chelate ring conformations and in the development of conformational analysis of complex systems [14, 18].

Complex systems with meen are of comparable stereochemical interest, and in fact the stereochemistry is more complicated in these meen systems

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because the axial-equatorial character of N-methyl substituents is less pronounced than that of C-methyl substituents which are constrained to be equatorial in Co–pn. However, there have been no systematic studies of the experimental isomer possibilities in Co(meen) complexes, so that the stereochemistry in these systems is not well understood.

Before the availability of SP-Sephadex cation-exchange chromatography and ^{13}C NMR spectroscopy we [21] and MacDermott [22] obtained a partial separation of the crude red [Co(meen)$_3$]Cl$_3$ materials obtained from various preparations. With paper chromatography and thin layer chromatography, only two red bands separated with acidic eluents, although there are twelve geometric and diastereoisomeric possibilities for this system. Also, from the product synthesized over charcoal (following Keller and Edwards [1]), we separated a yellow material and believed this to be another [Co(meen)$_3$]$^{3+}$ geometric isomer. However, these materials could not be characterized at that time and the stereochemistry in [Co(meen)$_3$]$^{3+}$ has remained unsolved.

We have now achieved the separation of the various components in these [Co(meen)$_3$]Cl$_3$ materials by SP-Sephadex chromatography, and these isolations of some of the isomers of [Co(meen)$_3$]$^{3+}$, [Co(meen)$_2$(en)]$^{3+}$ and [Co(meen)(en)$_2$]$^{3+}$ are now described, along with some of their properties. We have found that under preparative conditions for [Co(meen)$_3$]$^{3+}$ involving charcoal and oxygen, some demethylation occurs to give complexes containing en. The separation and characterization of all these species gives insight into the stereospecificity of meen coordination, as the isomer proportions found for each complex system should correspond at least roughly to the thermodynamic stabilities. The bis(meen) and mono(meen) complexes reported previously and quoted above were not necessarily obtained under equilibrium conditions.

The stereochemistry involved in these meen complex systems is complicated, so that the isomeric possibilities for the various complexes and a nomenclature scheme are first elaborated.

Isomer Possibilities for [Co(meen)$_3$]$^{3+}$, and Nomenclature

There are twelve geometrically distinct forms if ring conformations are ignored, *i.e.* if the rings are taken to be flat or if the conformations are averaged. Consideration of the individual ring conformations gives a total of eightyeight conformational forms.

The isomerism arises from several sources:

(1) Alternative absolute configurations of the chelate rings about the cobalt, designated Λ and Δ according to the IUPAC scheme [23, 24], Fig. 1.

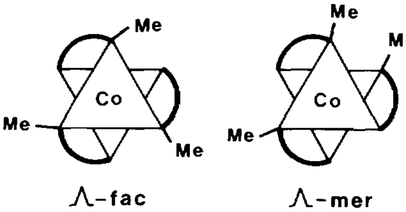

Fig. 1. Facial and meridional geometric (orientation) isomers, shown as projections down the pseudo-C_3 axes.

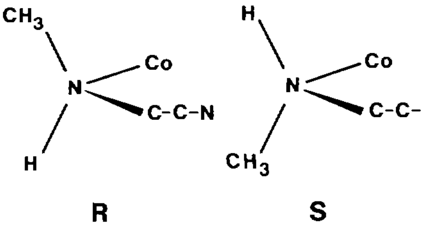

Fig. 2. Absolute configurations *R* and *S* about the coordinated *sec*-N in Co–meen.

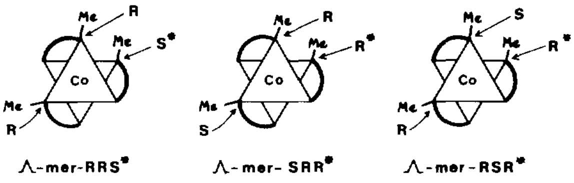

Fig. 3. Orientation isomers for Λ-*mer-RRS*-[Co(meen)$_3$]$^{3+}$. Stereochemistry parameters are listed for the rings clockwise around the pseudo-C_3 axis, when the single CH$_3$ is at the remote end of this axis. An asterisk denotes this single CH$_3$.

(2) The *R* or *S* absolute configuration of the substituents about the asymmetric nitrogen in each coordinated ligand, Fig. 2.

(3) Facial or meridional relative dispositions of the three methyl groups, giving rise to 'orientation isomers', Fig. 1.

(4) Further orientation isomers arise when the three chelate rings are distinguishable from each other, *i.e.* when the rings are differently orientated about the pseudo-C_3 molecular axis. This situation occurs for a *mer* arrangement of the methyl groups, where the rings are further distinguished by different absolute configurations at the nitrogens. For example the combination Λ-*mer-RRS* has three orientation isomers, Fig. 3.

The designations of such orientation isomers are not covered by the IUPAC rules [23, 24]. Further conventions are therefore necessary for specifying these isomers, and the following derive from proposals developed for the general case [M(AB)$_3$] by MacDermott [25, 26].

(a) An asterisk is used to indicate the ligand having the single methyl at one end of the pseudo-C_3 axis [25]. This procedure distinguishes particular isomers. For example the Λ-*mer-RRS** isomer is distinguished in the *RRS* combination, Fig. 3.

(b) For complete specification of the other two *RRS* isomers Λ-*mer-SRR** and Λ-*mer-RSR**, the rings have to be described (in terms of their *R* or *S* configurations at the asymmetric nitrogen) in a particular order, say clockwise [25, 26], in which they appear when the particular isomer is viewed along the pseudo-C_3 axis such that the single methyl substituent (whose description is asterisked) is situated at the remote end of this axis. We adopt a clockwise order as our convention. An analogous situation of three orientation isomers obtains for the combination Λ-*mer-RSS*.

(5) Asymmetry of the ring conformations, designated λ or δ by the IUPAC scheme [23, 24]. In general there are eight different combinations of the conformations of the three rings (δδδ, δδλ, δλδ, λδδ, δλλ, λδλ, λλδ, λλλ), and these are superimposed on the isomers arising from the other sources. In the situations *RRR* and *SSS* however, δδλ, δλδ and λδδ are identical, as are λλδ, λδλ and δλλ.

All the subsequent consideration of the stereochemistry will be with respect to one configuration Λ of the rings about the metal, for which the eighty-eight possible isomers arising from sources (2) to (5) are listed in Table 1.

While the Λ/Δ, *R*/*S* and λ/δ parameters, and the defined order of the listing of *R*/*S* and λ/δ around the three rings, uniquely define the isomers, there are two other descriptors of the stereochemistry which highlight the geometrical relationships in these structures. Each ring may also be described in terms of the approximately parallel (lel) or oblique (ob) inclination of the C–C axis to the pseudo-C_3 axis of the molecule, and also by the equatorial (eq) or axial (ax) disposition of each methyl substituent to its respective ring. The dependences of these factors on the previous stereochemical parameters are as follows.

TABLE 1. Isomers of Λ-[Co(meen)$_3$]$^{3+}$

Isomer	Conformers	Ring geometries	Methyl geometries	Conformers of C_3 symmetry
Λ-*fac-RRR*	δδδ	lel, lel, lel	eq, eq, eq	C_3
	δδλ	lel, lel, ob	eq, eq, ax	
	δλλ	lel, ob, ob	eq, ax, ax	
	λλλ	ob, ob, ob	ax, ax, ax	C_3
Λ-*fac-RRS*	δδδ	lel, lel, lel	eq, eq, ax	
	δδλ	lel, lel, ob	eq, eq, eq	
	δλδ	lel, ob, lel	eq, ax, ax	
	λδδ	ob, lel, lel	ax, eq, ax	
	δλλ	lel, ob, ob	eq, ax, eq	
	λδλ	ob, lel, ob	ax, eq, eq	
	λλδ	ob, ob, lel	ax, ax, ax	
	λλλ	ob, ob, ob	ax, ax, eq	
Λ-*fac-RSS*	Eight conformers designated δ/λ and lel/ob as above			
Λ-*fac-SSS*	δδδ	lel, lel, lel	ax, ax, ax	C_3
	δδλ	lel, lel, ob	ax, ax, eq	
	δλλ	lel, ob, ob	ax, eq, eq	
	λλλ	ob, ob, ob	eq, eq, eq	C_3
Λ-*mer-RRR**	δδδ*	lel, lel, lel*	eq, eq, eq*	
	δδλ*	lel, lel, ob*	eq, eq, ax*	
	δλδ*	lel, ob, lel*	eq, ax, eq*	
	λδδ*	ob, lel, lel*	ax, eq, eq*	
	δλλ*	lel, ob, ob*	eq, ax, ax*	
	λδλ*	ob, lel, ob*	ax, eq, ax*	
	λλδ*	ob, ob, lel*	ax, ax, eq*	
	λλλ*	ob, ob, ob*	ax, ax, ax*	

For Λ-*mer*, the other seven diastereoisomeric forms are

RRS, RSR*, SRR*, RSS*, SRS*, SSR*, SSS**

Each of these has eight conformers δ/λ and lel/ob as listed above for RRR* (but the eq/ax designations will be different).

$\Lambda\delta$ or $\Delta\lambda$ gives lel

$\Lambda\lambda$ or $\Delta\delta$ gives ob

$R\delta$ or $S\lambda$ gives eq

$R\lambda$ or $S\delta$ gives ax

These secondary descriptors lel/ob abd eq/ax are useful for understanding and checking the complicated stereochemistry in this system, and they are shown for some of the isomers in Table 1. Moreover, these geometrical factors would be expected to be significant in determining the relative stabilities of the isomers and this will be considered in subsequent work.

Thus for Λ-$[Co(meen)_3]^{3+}$, twelve geometric-diastereoisomeric forms arise from orientation isomerism and nitrogen asymmetry, four *fac* and eight *mer*. For each of these twelve 'isomeric' forms either eight or four conformer combinations are possible. Experimentally, the isomers should be separable from an equilibrium mixture into their geometric 'isomeric' forms (by chromatography or fractional crystallization), each as a racemic pair.

Designations of the Enantiomers

On forming the mirror image of a molecule, the chirality descriptors Λ/Δ, *R*/*S* and λ/δ become interchanged. Also, the ordering of the three rings about the pseudo-C_3 axis becomes reversed. Thus if the clockwise ring numbering convention is retained for both Λ and Δ configurations (with molecules always viewed with the single methyl at the remote end of the axis), the order of specifying the ring parameters becomes reversed in enantiomers. For example, the enantiomer of Λ-*mer-SRR**-$\delta\lambda\delta$ is Δ-*mer-S*SR*-$\lambda\delta\lambda$, or it can alternatively be written as Δ-*mer-SRS**-$\delta\lambda\lambda$.

Stabilities of the [Co(meen)$_3$]$^{3+}$ Isomers

Dreiding scale models show that in a Co(III)–meen ring the equatorial or axial character of an N-methyl substituent is not greatly marked, and that accordingly there is no obvious preference for an equatorial methyl since this is not directed away from the molecule as is the equatorial methyl in a Co(III)–pn ring. It is clear from the models however, that the dominating non-bonded interactions should be those of the N-methyl groups with neighbouring rings CH_3---CH_3, CH_3---ring, and CH_3---NH_2 or CH_3---NH, and that these should significantly influence the relative stabilities of the isomers. Inter-ring H---H interactions between NH and CH_2 groups of the type causing lel conformations to be preferred in $[Co(en)_3]^{3+}$ [14] may be of relatively less importance in these Co(meen) systems.

The *fac* isomers have the three methyl groups at one end of the (pseudo)-C_3 axis, whereas two methyls are together at one end of the axis in the *mer* isomers. Dreiding models show that for many of the conformers of the twelve geometric-diastereoisomers interactions between these *cis* methyls will be severe and will probably exclude the existence of some of these twelve forms. It can thus be predicted with some confidence that the Λ-*fac-RRR* and Λ-*fac-RRS* isomers will be excluded, but such semiquantitative estimates of non-bonded interactions do not indicate great differences between the other ten geometric-diastereoisomeric forms. Moreover, molecular potential energies have contributions from bond length deformations, valence angle deformations and torsional strains, as well as from non-bonded interactions, and all four effects are interdependent. A complete energy minimization analysis is therefore necessary to predict or explain the relative stabilities of isomers and conformers in this system, and this analysis is proceeding [27].

Differences in the Λ-[Co(meen)$_3$]$^{3+}$ and Λ-[Co($\pm$pn)$_3$]$^{3+}$ Systems

These systems are analogous in that they each have twelve distinct diastereoisomer species as possibilities. For a Co(meen) ring, both δ and λ conformers are possible, corresponding to axial and equatorial methyl dispositions, giving a total of eightyeight conformer possibilities (for one absolute configuration of the ligands about the metal, Δ or Λ). For any Co(pn) complex system, inter-ring non-bonded atomic interactions constrain the methyl substituent to be equatorial to its particular chelate ring, so that only the one conformational arrangement with all methyls equatorial is possible for each of the twelve 'isomeric forms' of a tris(pn) complex. Thus there is essentially complete conformational stereospecificity for a Co(pn) ring, such that the enantiomers of pn will always adopt particular chelate ring conformations on coordination, *i.e.* λ for Co-*R*(−pn) and δ for Co-*S*(+pn). The more stable isomers of $[Co(pn)_x(en)_{3-x}]^{3+}$ complexes are therefore predictable on the basis of non-bonded interactions [14]. In contrast, axial arrangements cannot necessarily be excluded from the experimental isomer possibilities for Co(meen) complexes.

Important differences experimentally between the Co(pn) and Co(meen) systems are the following:

(1) Studies of Co(pn) complexes have been aided by the use of optically resolved *R*(−)pn in the syntheses, which limits the isomeric possibilities and defines the absolute stereochemistry (as *R*) at the carbon centres. The various complexes separated are optically active, so that optical rotatory properties can be employed to characterize these species. By comparison, asymmetry in the Co(meen) complexes occurs at the methylated nitrogen centres and arises only on coordination of the ligands ('donor atom asymmetry'). It is thus not possible to use the optically active ligand to simplify elucidation

of the stereochemistry in Co(meen) complexes by restricting the isomer possibilities.

(2) Moreover, optical rotatory parameters cannot be employed to characterize the separated Co(meen) species. The separations on Sephadex are obtained by exploiting geometric differences, and the separated species are racemates.

(3) Further complications in investigations of Co(meen) systems are the possible equilibrations between the NH diastereoisomers through N–H exchange (base-catalyzed) at the asymmetric donor-nitrogen atoms, and the lower stabilities of complexes with the secondary amine meen than with pn.

Isomer Possibilities for $[Co(meen)_2(en)]^{3+}$

For $[Co(meen)_2(en)]^{3+}$ three possible geometries arise from the *cis* or *trans* relative positions of the NH_2 and CH_3 groups in the two meen ligands. Each geometry has several possible diastereoisomers, giving in all ten geometrically distinct forms for each absolute configuration of the complex. All these diastereoisomeric forms for the Λ complex configuration are shown in Fig. 4, along with their designations.

Each of these ten diastereoisomer forms has four conformer combinations for the Co(meen) rings: δδ, δλ, λδ, λλ. As previously, these different conformations of the meen rings will have different dispositions of the methyl groups, equatorial or axial, so that the non-bonded interactions from the methyl groups should differ markedly in these four conformers.

Of the forty total conformers developed so far, the following particular conformers have C_2 symmetry:

Λ-*cis*-CH_3,*trans*-NH_2-*RR*,	δδ and λλ conformers
Λ-*cis*-CH_3,*trans*-NH_2-*SS*,	δδ and λλ conformers
Λ-*trans*-CH_3,*cis*-NH_2-*RR*,	δδ and λλ conformers
Λ-*trans*-CH_3,*cis*-NH_2-*SS*,	δδ and λλ conformers

Assuming conformational mobility of all chelate rings in solution, these four diastereoisomer forms would be expected to show effective C_2 symmetry in their ^{13}C NMR spectra and give four carbon

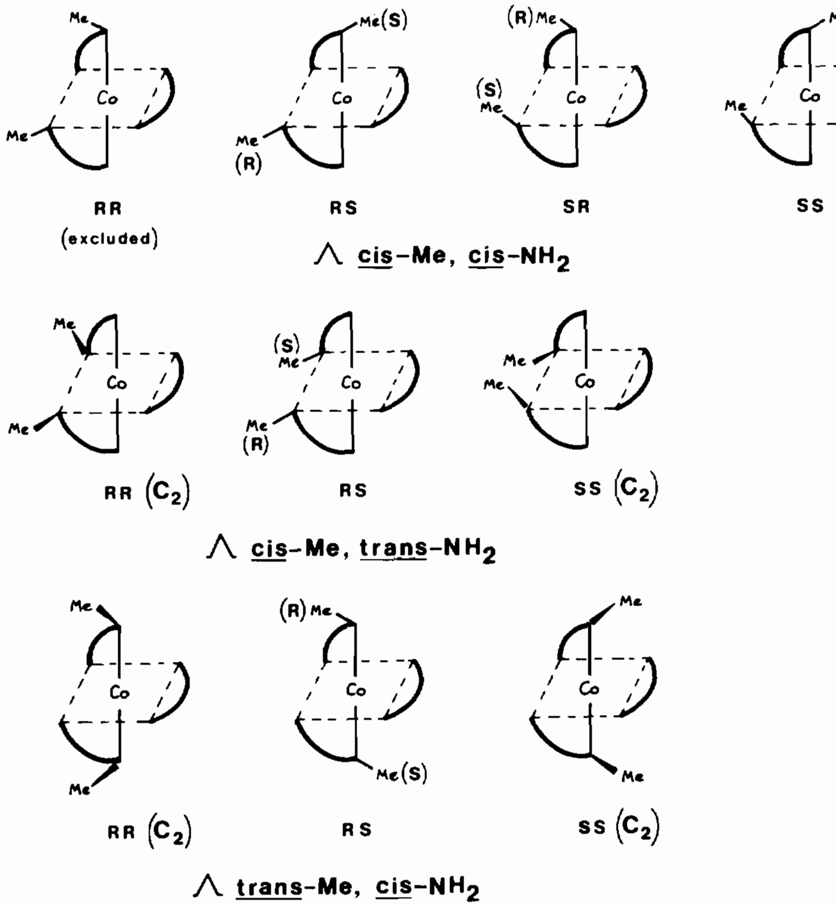

Fig. 4. Possible geometric isomers–diastereoisomers for Λ-$[Co(meen)_2(en)]^{3+}$. The four forms with effective C_2 symmetry are noted. For each of the geometries Λ-*cis*-CH_3,*trans*-NH_2 and Λ-*trans*-CH_3,*cis*-NH_2, the *RS* and *SR* forms are identical.

resonances, three from Co(meen) and one from Co(en). The other six diastereoisomer forms have C_1 symmetry and should give eight carbon resonances.

The alternative possible conformations of the Co(en) ring δ or λ will double the number of total conformer combination possibilities to eight for each diastereoisomeric form. Although the non-bonded interactions of the methyl substituents should not be greatly affected by these alternative Co(en) ring conformations, both of the en conformer possibilities will have to be considered in a complete analysis of the system. One of the diastereoisomers, Λ-*cis*-CH_3,*cis*-NH_2-*RR* (which corresponds to the least likely and excluded $[Co(meen)_3]^{3+}$ diastereoisomer), can be reasonably excluded on the basis of the methyl interactions which are indicated by models to be severe in all of the conformers. However, assessment of the stability order for the other nine forms requires a complete energy minimization analysis [27].

Isomer Possibilities for $[Co(meen)(en)_2]^{3+}$

Two diastereoisomers are possible for each configuration Λ or Δ, Fig. 5, and each diastereoisomer has alternative conformations of the Co(meen) ring. Thus the conformers are Λ-*R*-δ (eq, lel); Λ-*R*-λ (ax, ob); Λ-*S*-δ (ax, lel); Λ-*S*-λ (eq, ob).

The two diastereoisomers are in principle separable chromatographically. All the conformers have C_1 symmetry, so that with conformational averaging of all chelate rings in solution seven ^{13}C NMR resonances could be expected from each diastereoisomer in solution.

The non-bonded interactions from the methyl would seem to be lowest for the Λ-*R*-δ conformer where the methyl lies between the two en rings, suggesting that the Λ-*R* should be the more stable diastereoisomer, as considered previously by Sargeson [18].

For each diastereoisomer and Co(meen) conformer, four conformer combinations for the $Co(en)_2$ rings are possible, δδ, δλ, λδ, and λλ. Thus there are sixteen conformers in all for each configuration Λ or Δ.

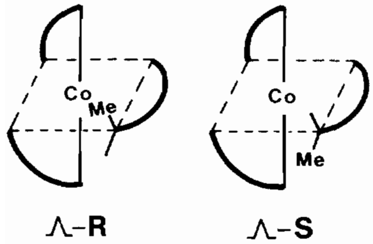

Fig. 5. Diastereoisomers of Λ-$[Co(meen)(en)_2]^{3+}$. Λ-*R* is predicted to be the more stable.

Results and Discussion

Syntheses for $[Co(meen)_3]^{3+}$

Several methods were examined for the preparation of $[Co(meen)_3]^{3+}$, in anticipation that different non-equilibrium syntheses might yield some different isomers.

Two main methods were employed. Oxidation of a mixture of $CoCl_2$ + 3meen in dimethylsulfoxide, with Me_2SO functioning as both solvent and oxidant [28], yielded a clean red product $[Co(meen)_3]Cl_3$ in high yield. This solid was one isomer **A**, but it was subsequently shown to isomerize rapidly in water to an equilibrium mixture of three isomers designated **A**, **B** and **C**. These designations refer to their chromatographic elution order. Aerial oxidation of Co(II) with meen in aqueous solution, in the presence of charcoal, was carried out at 80 °C as used by Keller and Edwards [1]. This method yielded a yellow–orange product, which was a mixture of $[Co(meen)_3]Cl_3$ as one isomer **C** (which equilibrates in water to the **A**, **B**, **C** mixture), three isomers of $[Co(meen)_2(en)]^{3+}$ designated **F**, **G** and **H**, one isomer of $[Co(meen)(en)_2]^{3+}$ **E**, and $[Co(en)_3]^{3+}$ **D**. Demethylation is thus a significant process during the aerial oxidation at 80 °C, and it must involve charcoal and probably the oxygen also.

The following syntheses did not yield any different isomers of the above complexes. From aerial oxidation carried out in methanol at 45 °C and without charcoal, the red product which precipitated was $[Co(meen)_3]Cl_3$ as isomer **C** only. Apparently **C** is the least soluble isomer as the chloride salt in water and methanol, whereas **A** is the least soluble chloride in dimethylsulfoxide, and syntheses in these different media yield these different solid isomers because of rapid equilibration. Accordingly, recrystallization of the **A** $[Co(meen)_3]Cl_3$ product from water gave pure **C** isomer, so that both of the main isomers can be readily obtained from the dimethylsulfoxide synthesis.

Substitution reactions $[Co(NH_3)_5(H_2O)]^{3+}$ + 3meen in water at 80 °C without charcoal gave $[Co(meen)_3]^{3+}$ in **A**, **B**, and **C** isomers as from the dimethylsulfoxide oxidation. However if charcoal was present this substitution reaction yielded yellow demethylated complexes. These substitution reactions produced numerous by-products and were not useful.

Sephadex Separation of the $[Co(meen)_3]^{3+}$ *Isomers from the Dimethylsulfoxide Oxidation Synthesis*

Sephadex chromatography indicated that all the various $[Co(meen)_3]Cl_3$ products behaved identically. With the acidic eluent 0.2 M Na_2SO_4/H_2SO_4 pH 2, two orange–red bands separated (1), first eluted, and (2), and these were in the amount ratio (1)/(2) *ca.* 2. The complexes in the eluted bands were isolated by using a cation-exchange process: they were eluted off a resin column by either HBr or HCl, then obtained by evaporation of the HX eluent. The ^{13}C NMR spectra in D_2O/HBr (see below) showed that the band (1) product contained two isomers **A** and **B** in the mole amount ratio **A**/**B** *ca.* 3, and that the band (2) product consisted only of a single isomer **C**. The ratios of these $[Co(meen)_3]^{3+}$ isomers are thus **A**:**B**:**C** = 3:1:2, and no other isomers have been detected.

These isomers were the most satisfactorily crystallized as the bromide salts. Slow crystallization of the solutions gave large crystals of **A** and **C**. Isomer **B** could not be crystallized separately from the band (1) material as the bromide. However, on careful crystallization all of **A** could be removed pure as the bromide to leave only **B** in the mother liquor, from which **B** could be obtained as the nitrate or perchlorate salts (using conversion on Dowex resin).

With 0.1 M Na_3PO_4 eluent, the various $[Co(meen)_3]^{3+}$ isomers moved together as a pink–red band because they rapidly equilibrate in the basic conditions of the eluent. This $[Co(meen)_3]^{3+}$ band was preceded immediately by a purple smear. This purple must have contained hydrolysed species, probably $[Co(meen)_3(OH)]^{2+}$, which arose in the basic conditions, since on changing the eluent to NaCl the hydrolysis ceased and the purple was then eluted out ahead of the remaining orange $[Co(meen)_3]^{3+}$ band.

Distinction of $[Co(meen)_3]^{3+}$ Isomers by ^{13}C NMR Spectra and Chromatography

There are twelve geometrically distinct forms possible for $[Co(meen)_3]^{3+}$ (geometric isomers and N–H diastereoisomers), and each can exist in a number of conformers, giving eightyeight conformers in all for each configuration of the ligands about the cobalt as elaborated above. In solution the conformers of each 'geometric' form should rapidly equilibrate, so that the ^{13}C NMR spectra should show the highest conformational symmetry of the particular 'geometric' form by rapid conformational averaging. Two of the twelve geometric forms have C_3-symmetry conformers (Table 1) so that these geometric forms Λ-*fac-RRR* and Λ-*fac-SSS* should show effective C_3 symmetry and give three carbon resonances. All conformers of the other ten 'geometric' forms have C_1 symmetry, so that nine ^{13}C NMR resonances will be expected for each of these forms, three from each chemically distinct carbon type.

The three resonances from meen·2HCl are assigned as δ 45.9, MeN^+H_2–C; δ 35.8, C–N^+H_3; δ 33.8, CH_3. (These assignments follow from the off-resonance spectrum, and from comparisons with the spectra of en·2HCl (δ 36.9) and dien·3HCl (δ 45.0 and 35.8) [29].) The isomers of $[Co(meen)_3]^{3+}$, and also those of $[Co(meen)_2(en)]^{3+}$ and $[Co(meen)(en)_2]^{3+}$, each show resonances in three regions corresponding to these three different carbon types in meen·2HCl (Fig. 6). The signals from the complexes are downfield from those in the protonated amine, but the relative order of the chemical shifts of the three carbon types is unchanged [29, 30].

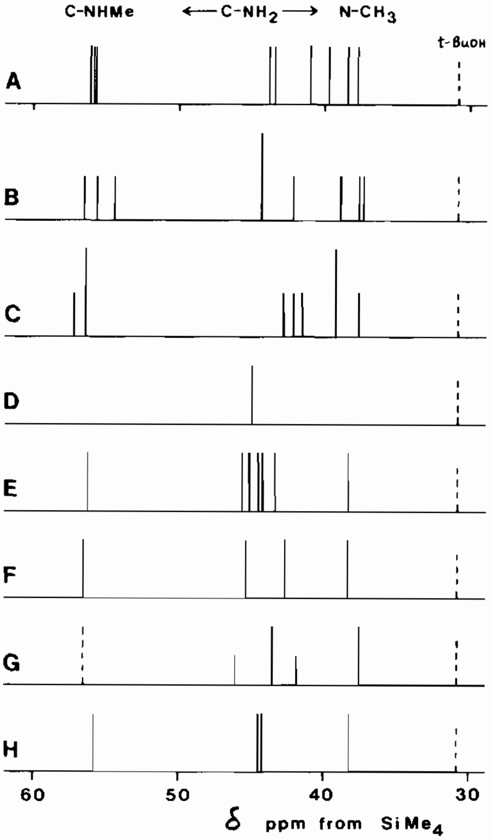

Fig. 6. 20.1 MHz ^{13}C NMR spectra of Co(meen) complexes as bromide salts in D_2O/HBr (t-butyl alcohol capillary reference, δ 30.79 ppm from $SiMe_4$). A–C, $[Co(meen)_3]^{3+}$ isomers, all C_1 symmetry; D, $[Co(en)_3]^{3+}$; E, $[Co(meen)(en)_2]^{3+}$; F and H, $[Co(meen)_2(en)]^{3+}$ isomers with C_2 symmetry; G, $[Co(meen)_2(en)]^{3+}$ isomer with C_1 symmetry.

Inversions of configurations at the asymmetric nitrogens of the individual ligands of $[Co(meen)_3]^{3+}$ will be expected to occur, through proton-exchange, as in the racemization of $[Co(NH_3)_4(meen)]^{3+}$ [9]. This base-catalyzed process should lead to equilibration between diastereoisomeric forms which differ only in N-configurations, *i.e.* between the four Λ-*fac* forms, and between the eight Λ-*mer* forms. Such equilibrations are slower than the NMR time scale however, so that the NMR resonances from the individual 'geometric' forms should be recorded. This N–H isomerization has been recorded previously in some N_4 macrocycle systems with nickel(II)

[31], and with the complex system [Co(hexacyclen)]$^{3+}$, hexacyclen = 1,4,7,10,13,16-hexaazacyclooctadecane [32], and resonances of the individual NH diastereoisomers are observed from the equilibrium mixture of each system.

The ^{13}C NMR spectra of the isomers **A**, **B** and **C**, run in acid to inhibit hydrolysis, are quite similar (Fig. 6), each showing nine different carbon atoms (in 9 or 8 peaks) which give the symmetry of each as C_1.

The twelve 'geometric' forms are in principle distinguishable chromatographically, provided that the interconversions between these forms are much slower than the time required for a chromatographic separation. These interconversions should be precluded in the acidic conditions of the eluent Na_2SO_4/H_2SO_4 in chromatography. If equilibrations occur within the separation time, as in a basic eluting medium such as Na_3PO_4, only two bands corresponding to the *mer* diastereoisomer mixture and the *fac* diastereoisomer mixture would be expected if only N–H isomerizations were involved (and if both *mer* and *fac* forms could exist). If equilibration between *mer* and *fac* forms occurred during the chromatography, only one band would be obtained.

Equilibration Between the [Co(meen)$_3$]$^{3+}$ Isomers

Equilibration between the three [Co(meen)$_3$]$^{3+}$ isomers occurs readily even in neutral water. Thus the ^{13}C NMR spectra of **A** or **C** bromides in D_2O (pH *ca.* 5.5) accumulated up to one hour from dissolution showed resonances from all three isomers. The spectra obtained by further accumulations (over 2–9 h from dissolution) were essentially the same, so that equilibration must have been reached within about one hour at 25 °C. The equilibrium isomer ratio as estimated from the relative peak ratios (3:1:2) agrees with that assessed from the chromatography.

These various equilibrated solutions from the pure **A** or **C** isomers were re-separated on Sephadex with Na_2SO_4/H^+ elution into the two orange–red bands of (**A** + **B**) and **C**, to give the same ratios of the three complexes as previously. This ratio, **A**:**B**:**C** = 3:1:2, is therefore the equilibrium ratio at room temperature.

The rapid equilibration is also demonstrated in Sephadex chromatography, where elution with Na_2SO_4 in water, pH 5.5, gave less separation than with the eluent acidified to pH 2. Thus to avoid isomerization, the complexes must be chromatographed and manipulated in acidic solution, pH ≤ 2.

The facility of interconversion between the 'geometric' forms of [Co(meen)$_3$]$^{3+}$ contrasts markedly with the robustness towards racemization and isomerization of other cobalt(III)–hexamine complexes such as [Co(en)$_3$]$^{3+}$ and [Co(dien)$_2$]$^{3+}$ [33]. Also, the isolated 'geometric' forms of [Co(meen)$_2$(en)]$^{3+}$ **F** and **H** are robust in base, being separated chromatographically using Na_3PO_4 (see later). Thus the isomerization of [Co(meen)$_3$]$^{3+}$ cannot involve rearrangement of chelate rings, but must be due to N–H inversions at the asymmetric nitrogen centres. This N–H isomerization, occurring in neutral conditions, is more facile however than in Ni(II)–macrocycle systems (where basic conditions 0.1 M NaOH over some hours were used to effect equilibration) [31] and in [Co(hexacyclen)]$^{3+}$ [32].

Thus the three isomers **A**, **B**, **C** must be diastereoisomers of the one geometry, and the similarity in the ^{13}C NMR spectra is consistent with this. This geometry is most probably *mer*, as some of the *fac* forms have been excluded on the basis of large nonbonded interactions, and also because the C_3 symmetries of some *fac* conformers should have reflected in the ^{13}C NMR spectra.

The two red bands separated previously by paper and thin layer chromatography [21, 22] must have been the major isomers **A** and **C**.

Aerial Oxidation Synthesis for [Co(meen)$_3$]$^{3+}$ with Charcoal at 80 °C, and Characterization of the Products

This synthesis follows the conditions as first used by Keller and Edwards [1]. With the solution stoichiometry

$$CoCl_2 + (5/2)\text{meen} + (1/2)(\text{meen}\cdot 2HCl) + (1/4)O_2 \longrightarrow [Co(\text{meen})_3]Cl_3 + (1/2)H_2O$$

and charcoal present, aeration was carried out at 80 °C for 2 h then continued at room temperature for two days. The crude product was obtained by precipitation, and the low yield (50%) reflected the lower stabilities of complexes with N-substituted-en than those with en [34], but was due also to the high solubility of the complex mixture. This product could be fractionally crystallized from water fairly cleanly into two portions: the less soluble fraction, yellow, contained complexes with en ligands which must have arisen by demethylation of meen. The more soluble red portion predominated and contained [Co(meen)$_3$]$^{3+}$. This red material was largely complex **C** (by ^{13}C NMR in acid) as the least soluble [Co(meen)$_3$]$^{3+}$ isomer from water, with a little demethylated complex (**H**) also present.

The yellow materials were separable by Sephadex chromatography using Na_3PO_4 elution into four yellow–orange bands of CoN_6 complexes (Fig. 7). The complexes in these bands are designated **D**, **E**, **F** + **G**, and **H** according to their elution order, and were isolated using cation-exchange.

These complexes were characterized by ^{13}C NMR spectra (Fig. 6), and the chemical forms were confirmed by elemental analyses. **D** was [Co(en)$_3$]$^{3+}$,

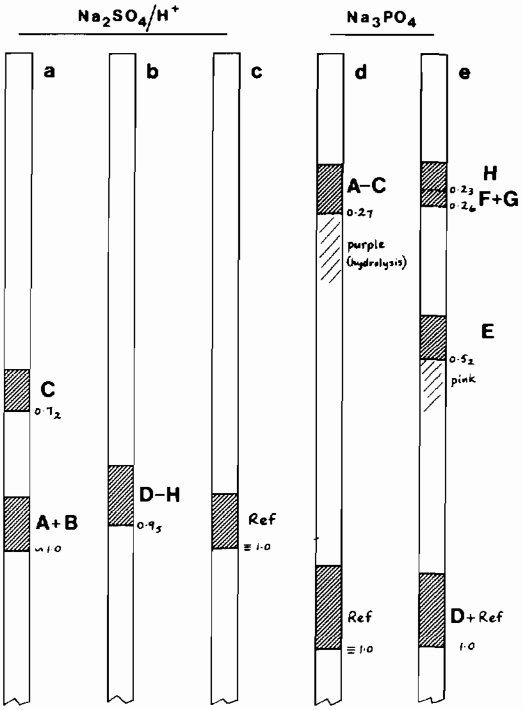

Fig. 7. Chromatographic separations on SP-Sephadex columns with different eluents 0.2 M Na_2SO_4/H_2SO_4 pH 2 and 0.1 M Na_3PO_4: columns (a) and (d), the red $[Co(meen)_3]^{3+}$ products **A**–**C** of the dimethylsulfoxide oxidation synthesis; columns (b) and (e), the less soluble yellow demethylated products **D**–**H** of the oxygen oxidation synthesis with charcoal. $[Co(en)_3]^{3+}$ has been added to columns (c), (d) and (e) as a reference. The figures are R_x values relative to $[Co(en)_3]^{3+}$.

being identical to the authentic complex (by ^{13}C NMR single resonance, and Sephadex elution).

Complex **E** showed seven approximately equal ^{13}C NMR peaks, consistent with one of the two possible diastereoisomers of $[Co(meen)(en)_2]^{3+}$.

The material from the orange third Sephadex band contained two complexes **F** and **G**, with the eight ^{13}C NMR resonances being in two sets of unequal intensities. The major component **F** was obtained pure by careful crystallization and showed four equal ^{13}C NMR peaks, identifying it as a C_2-symmetry isomer of $[Co(meen)_2(en)]^{3+}$. The other four peaks in the mixture spectrum, apparently unequal, are from **G**, which cannot be crystallized separately. The general pattern of these ^{13}C NMR resonances, together with **G** chromatographing coincidently with **F** and satisfactory elemental analyses, indicate that **G** is another $[Co(meen)_2(en)]^{3+}$ isomer. However, the three unequal resonances in the H_2N–C– region show that **G** would have C_1 symmetry and the peak assignments from the eight different carbons in $[Co(meen)_2(en)]^{3+}$ would then have to be: a resonance from two MeHN–C– carbons coincident with and obscured by the peak δ 56.5 from complex **F**; peaks 1:2:1 from H_2N–C– carbons; and the upfield peak δ 37.5 from the two methyl carbons coincidently.

H was the main yellow product. With four ^{13}C NMR peaks and eluting closely behind **F** + **G**, it is another C_2 isomer of $[Co(meen)_2(en)]^{3+}$.

The product ratios were determined semiquantitatively as **D**:**E**:**F**:**G**:**H** = 2:12:5:1:36 by visual assessment of the Sephadex bands, and from the ratio **F**/**G** determined from the ^{13}C NMR spectrum of the evaporated mixture from the orange third Sephadex band. The extent of the demethylation and hence the proportions of the different complex systems would be expected to vary with the preparative conditions (charcoal, air or oxygen, temperature, time) so there would be little significance in the ratios of these, **D**:**E**:**F** + **G** + **H** = 1:6:21, except that the ratios indicate that demethylation takes place sequentially and not stereoselectively from one of the $[Co(meen)_3]^{3+}$ complexes to give **E**. However, the ratios of the isomers within each system are meaningful as the isomers should be in equilibrium on the charcoal, and these experimental ratios can be compared with those calculated from energy minimizations. The useful figures are: for $[Co(meen)(en)_2]^{3+}$, one isomer **E** formed essentially stereospecifically; for $[Co(meen)_2(en)]^{3+}$, **F**:**G**:**H** *ca.* 5:1:36.

The ratios are also expected to vary to some extent with the manner of isolation, which was precipitation of crude total complex from the reaction mixture, followed by fractional recrystallization to obtain the less soluble yellow material. Clearly some other minor isomers which were formed would have remained in the mother liquors, but more important is the possible loss of isomers of higher solubility which might have been present in reasonable amounts in the equilibrium. We feel that the various isomers of each complex would not range so greatly in solubility as to cause the ratios obtained in the isolated solid to be markedly different from the equilibrium values, and thus we take the above ratios for the systems $[Co(meen)_2(en)]^{3+}$ and $[Co(meen)(en)_2]^{3+}$ to represent roughly the equilibrium ratios.

Equilibrations between the Demethylated Complexes and Deductions of Stereochemistry

For $[Co(meen)(en)_2]^{3+}$, the two N–H diastereoisomers possible (Fig. 5) will interconvert rapidly in base by proton exchange, so that the material isolated from the Na_3PO_4 effluent should contain these isomers in equilibrium proportions. As with the $[Co(meen)_3]^{3+}$ system, the two N–H diastereoisomers should also interconvert in neutral water, when the separate forms should be evident in the ^{13}C NMR spectrum run under such conditions. That only one isomer **E** has been observed indicates the high stereospecificity in this mono(meen) system.

For the C_2-symmetry isomers **F** and **H** of [Co(meen)$_2$(en)]$^{3+}$ there are four possibilities (Fig. 4). That **F** and **H** do not interconvert in weak base (during the separation with Na_3PO_4, pH 12) shows that they are not diastereoisomers of the same geometric isomer. Thus they must be the most stable diastereoisomers in the different geometric isomer systems, *cis*-CH_3,*trans*-NH_2 and *trans*-CH_3, *cis*-NH_2. The stereospecificity within each geometry is apparently high, as only the one N–H diastereoisomer in each system has been observed, *i.e.* *RR* or *SS*, but not *RS*.

Complex **G** involves some uncertainty. The band (3) material containing **F** and **G** was in only small proportion, and from this only a small quantity of **F** has been isolated, and **G** has been observed only in solution with **F**. We were unable to carry out extensive equilibration trials, but a solution of **F** (pure by ^{13}C NMR in D_2O/HBr) after basifying with NaOH to pH 12.5 gave no indication of the resonances from **G** when the ^{13}C NMR spectrum was re-recorded (albeit only weak resonances expected). This suggests that **F** and **G** do not interconvert, which would exclude **G** as the **RS** diastereoisomer (C_1 symmetry) of the same geometry as **F**. Since **G** and **H** do not interconvert, **G** would then be the stable diastereoisomer of the third possible geometry for [Co(meen)$_2$(en)]$^{3+}$,*cis*-CH_3,*cis*-NH_2.

Work is in progress to determine the structures of these isolated complexes by single crystal X-ray analysis [35].

The Mechanism of Demethylation

Demethylation clearly occurred during the aerial oxidation synthesis of [Co(meen)$_3$]$^{3+}$ with charcoal at 80 °C, but the yellow demethylated complexes were not evident from a similar aerial oxidation preparation at 20 °C. Demethylated complexes were also produced in a substitution synthesis [Co(NH$_3$)$_5$Cl]Cl$_2$ + 3meen at 80 °C with charcoal, but not from a similar synthesis without charcoal. Thus demethylation occurs only with charcoal and at elevated temperatures, but the possible involvement of oxygen is unclear from these results.

Such demethylation processes have been observed previously in some other Co(III) systems. N–C cleavage was first demonstrated in the oxygen oxidation preparation at elevated temperature of [Co(etolen)$_3$]$^{3+}$ [etolen = 2-(2′-aminoethylamino)ethanol] when by-products [Co(en)$_3$]$^{3+}$, ammonia and formaldehyde were observed. No [Co(en)$_3$]$^{3+}$ was found from the substitution preparation [Co(NH$_3$)$_6$]$^{3+}$ + 3etolen with charcoal [36–38], but dealkylation was observed from [Co(etolen)$_3$]Cl$_3$ in water with charcoal and air. Thus charcoal and oxygen both have essential roles in these cleavage reactions [37–39].

Demethylation from *s-fac*-[Co(medien)$_2$](ClO$_4$)$_3$ [medien = 4-methyldiethylenetriamine] in water with charcoal (90 °C, 3 days) was substantial to give *s-fac*-[Co(dien)(medien)]$^{3+}$ as the main product (11%), and some *mer*-[Co(dien)$_2$]$^{3+}$ was also formed. Oxygen was shown to be necessary for this process also [40]. This work, like the [Co(etolen)$_3$]$^{3+}$ reactions, demonstrated that N–C cleavage is not of necessity associated with formal Co(II) + O_2 oxidation processes but can also occur from Co(III) species with charcoal present. However these Co(III) reactions may in fact involve Co(II) species behaving as catalysts, and these could presumably be generated by reduction on the charcoal. Evidence for such Co(II) involvement has been provided from detailed studies of the following systems in which demethylation occurred:

Co(II) + etolen + charcoal + O_2

[Co(etolen)$_3$]Cl$_3$ + charcoal + O_2

In each system the Co(II) concentration reached a steady state value, but only if charcoal was present [39].

The demethylation in the present [Co(meen)$_3$]$^{3+}$ system was further examined by heating solutions of pure **A**-[Co(meen)$_3$]Br$_3$ in D_2O at 80 °C for three hours under the following conditions:
(i) with oxygen bubbling;
(ii) with added freshly ground charcoal and oxygen bubbling;
(iii) with added charcoal, but with nitrogen bubbling.

The ^{13}C NMR spectrum from (i) showed an equilibrium mixture of the [Co(meen)$_3$]$^{3+}$ isomers **A**, **B** and **C**. The deep-red solutions from (ii) and (iii) after filtering off the charcoal gave similar ^{13}C NMR spectra. These were complicated, and they showed several new peaks and some peaks enhanced from (i) consistent with the appearance of demethylated products **E**, **F** and **H**, and a decrease in some peaks from (i) consistent with a decrease of **A** and **C**. The experiment (iii) is inconclusive about the role of oxygen, as traces of oxygen might be difficult to exclude. We could not detect by ^{13}C NMR any expected monocarbon products from the demethylation (HCO_2H, HCHO, MeOH), although these could have been removed with the charcoal. These product solutions were also examined by Sephadex chromatography on small columns using Na_3PO_4 and Na_2SO_4/H^+ eluents. The bands separating from reaction mixtures (ii) and (iii) were similar, and consistent with substantial demethylation to **F** and **H**, although (with sulfate elution) bands corresponding to **A** and **C** were evident. A purple band of hydrolyzed species was also present.

Similar experiments starting from meen or meen·2HCl (in D_2O with added charcoal and oxygen, 80 °C for 8 h) showed that no demethylation occurred from the uncoordinated amine.

These present results reinforce the conclusions about the demethylations in Co(III) systems observed previously. All the various observations on the three systems indicate that the oxidative N–C cleavage reactions involve free radicals. A plausible radical mechanism has been proposed (particularly for dealkylation in the oxygen oxidation synthesis of $[Co(etolen)_3]^{3+}$) in which an initial addition product of Co(II) with molecular oxygen goes to a Co(III)–superoxide intermediate. This oxide nucleophile can then attack a carbon, leading on to N–C scission [39].

Nickel peroxide is a standard free-radical oxidizing agent [41], and has been found to effect radical demethylations of *N*-methylamides [42]. However, the reagent did not effect demethylation of A-$[Co(meen)_3]Br_3$ (in D_2O at room temperature for 4 h).

Sephadex Chromatography Behaviour of the Various Complexes

The chromatographic separations on SP-Sephadex cation-exchange resin columns of the various complexes and isomers from the two main preparations are represented in Fig. 7. The separations are quantified in terms of R_x values (relative R_F) relative to $[Co(en)_3]^{3+}$ as the reference complex, obtained by using small amounts of complexes on small columns [43, 44], and these values are shown on the diagrams.

It is notable that the eluent SO_4^{2-}/H^+ gives almost no discrimination between the various demethylated products in the less soluble yellow material from the aerial oxidation synthesis $[Co(en)_3]^{3+}$ (**D**), $[Co(meen)(en)_2]^{3+}$ (**E**) and the isomers of $[Co(meen)_2(en)]^{3+}$ (**F**), (**G**), (**H**). However, with a third methyl substituent a reasonable separation between the $[Co(meen)_3]^{3+}$ isomers **A** and **C** is obtained with this eluent.

The eluent PO_4^{3-} is usually considerably more discriminating than SO_4^{2-} [43], and it effects a good separation between the differently demethylated complexes in the present work. The complexes elute progressively more slowly (lower R_x) with increasing methyl substituents:

$$[Co(en)_3]^{3+} > [Co(meen)(en)_2]^{3+} > [Co(meen)_2(en)]^{3+} \approx [Co(meen)_3]^{3+}$$

This is clearly attributable to decreasing numbers of N–H sites for association to the PO_4^{3-} anions, and perhaps also to increasing conformational rigidity caused through the steric interactions of the methyls which might hinder the optimal development of the N–H---O hydrogen bonds. There is little discrimination between the three geometric isomers of $[Co(meen)_2(en)]^{3+}$ and the single geometry (*mer*) of $[Co(meen)_3]^{3+}$, so that some saturation condition seems to be reached with two methyl substituents.

The NH diastereoisomers of the one geometry (*mer*) of $[Co(meen)_3]^{3+}$ interconvert rapidly even in neutral solution, so that they elute as one band with PO_4^{3-}, presumably corresponding to the NH diastereoisomer and conformer forming the optimum hydrogen bonding with that eluting anion [45]. The diastereoisomers of the other complexes should behave in the same manner. However SO_4^{2-} does effect separations between the NH diastereoisomers of $[Co(meen)_3]^{3+}$ (in acidic conditions), and this is surprising in view of the failure of SO_4^{2-} to separate the different methylated complexes where the differences would be expected to be less subtle.

The elution order for the three $[Co(meen)_2(en)]^{3+}$ isomers, (**F** + **G**)>**H**, or more precisely for the geometries of which they are the isolated diastereoisomers, can now be rationalized on the basis of the structure known for **F** by X-ray analysis [35] and the tentative structures deduced for **G** and **H** from the ^{13}C NMR spectra and their non-equilibrations in base. The geometry *cis*-CH_3,*cis*-NH_2, which has been assigned to **G**, provides one set of three primary amine groups, at one end of the pseudo-C_3 axis in each of the three diastereoisomers *RS*, *SR* and *SS*, which should be suitable for hydrogen-bonding to a PO_4^{3-} anion (diastereoisomer *RR* has been excluded). The geometry *trans*-CH_3,*cis*-NH_2, of complex **F** [35], has a set of three N–H bonds at each end of the pseudo-C_3 axis in the *SS* diastereoisomer, although each of these sets involves a (coordinated) secondary amine function. With the third geometry *cis*-CH_3,*trans*-NH_2, there is one set only of three N–H bonds, and one of these is from a secondary amine group. This geometry appears to present the least favourable hydrogen bonding conditions, and the assignment of this third geometry to the remaining complex **H** is consistent with this isomer being the slowest eluting.

Experimental

^{13}C NMR Spectra

20.1 MHz ^{13}C NMR spectra in D_2O, broad-band proton decoupled, were recorded on a Bruker WP80-DS spectrometer locked to deuterium. An 8192 data table was used. For spectra in D_2O, a capillary of t-butyl alcohol provided a reference signal at 618.9 Hz, δ 30.79 ppm for CH_3 downfield from $SiMe_4$. (This reference signal was measured for a t-butyl alcohol capillary in $CDCl_3$ against $SiMe_4$ as internal reference.)

As with other cobalt(III) (3+)-charged complexes previously studied, the chemical shifts of the resonances of the $[Co(meen)_3]^{3+}$ isomers show little variation with different anions. Any such variation is similar to that found between different recordings of the same complex, generally 0.1 in δ.

The integrated intensities of proton-decoupled ^{13}C resonances may not in general be proportional to the number of carbon nuclei in each peak due to varying nuclear Overhauser enhancements and differences of the spin-lattice relaxation times [46, 47]. However, we have found that ^{13}C NMR peak areas of CH_2 and $N{-}CH_3$ carbons from a number of polyamine complexes of cobalt(III) do reflect carbon concentrations to within 20%, and frequently better [29, 45]. A similar situation obtains with the ^{13}C peak ratios of the complexes in the present work, and the ratios quoted have been rounded to integral values.

The amine meen (Fluka purum) was used as supplied. Its high purity was confirmed by the ^{13}C NMR spectrum run in D_2O (δ 52.9, 40.0, 34.8 ppm) when the en resonance (δ 43.2) was completely absent, and also by the spectrum of meen·2HCl (δ 45.9, 35.8, 33.8) when en·2HCl (δ 36.9) was absent.

Some of the amine was converted to meen·2HCl by addition of stoichiometric HCl in a methanol solution, filtering off the precipitated product, and washing with methanol.

Synthesis of $[Co(meen)_3]Cl_3$ by Dimethylsulfoxide Oxidation

$CoCl_2 \cdot 6H_2O$ (9.52 g, 0.04 mol) was dissolved in Me_2SO (20 ml, BDH Analar). The solution was heated to boiling and maintained for 5 min (140–160 °C) to remove much of the water, then cooled to 70 °C. A solution of meen (7.35 g, 0.10 mol) and meen·2HCl (2.94 g, 0.02 mol) in Me_2SO was prepared with warming in the minimum volume of the solvent (14 ml). The warm cobalt solution was added to the stirred amine solution whereupon reaction ensued within seconds: the temperature rose, the colour changed from blue to dark brown, a sulfide odour signified reduction of Me_2SO, and the $[Co(meen)_3]Cl_3$ product commenced to separate. The mixture was maintained at about 70 °C for 5 min, then allowed to cool to room temperature.

The fine reddish crystalline product was filtered off, washed with ethanol and acetone, and air-dried. Yields were variable, up to 14.5 g, 93%. *Anal.* Calc. for $[Co(C_3H_{10}N_2)_3]Cl_3$: C, 27.9; H, 7.8; N, 21.7. Found: C, 27.5; H, 8.0; N, 21.5%. This material was essentially pure isomer **A**, but on recrystallization from water with ethanol pure isomer **C** was obtained (^{13}C NMR spectra in D_2O/HCl). Both of these solids separated into two red components by thin layer chromatography (TLC) (sec-butanol/water/conc. HCl eluent on cellulose).

Sephadex Chromatographic Separation of the $[Co(meen)_3]^{3+}$ Isomers and their Characterization

A solution of $[Co(meen)_3]Cl_3$ from the above (1.0 g in 60 ml water) was applied to a large column (4.5 diam × 40 cm) of SP-Sephadex C-25 cation-exchange resin, and washed on with water. The column was eluted with 0.2 M Na_2SO_4/H_2SO_4 to pH 2, and the two orange–red bands which separated were collected. All samples of $[Co(meen)_3]Cl_3$, and also mother liquors, gave the same two bands only, and always in the same ratio: first eluted (1)/second eluted (2) *ca.* 2, assessed visually. (1) contained **A** + **B**, with **A**/**B** *ca.* 3 by ^{13}C NMR, and (2) contained **C**.

In isolation of the complexes, solutions were kept acidic to avoid isomerization. The two band effluents were diluted and applied to small columns (1.2 × 10 cm) of Dowex 50W-X2 cation-exchange resin, 200–400 mesh, H^+ form. The columns were washed first with 0.1 M HBr to remove all Na^+ (otherwise NaBr may crystallize subsequently), then the complexes were eluted off with 3 M HBr. These effluents were each rotary-evaporated to a sludge, and further HBr was removed by drawing air through the flask.

Each sludge was dissolved in 0.01 M HBr (*ca.* 4 ml) and the solution was left to crystallize in a vacuum desiccator. The mother liquor was sucked off and the deep-red crystals were air-dried on filter paper. The crystals obtained from band (1) were pure isomer **A**. *Anal.* Calc. for $[Co(C_3H_{10}N_2)_3]Br_3 \cdot 2H_2O$: C, 19.4; H, 6.1; N, 15.1; Br, 43.0. Found: C, 19.4; H, 6.1; N, 15.0; Br, 43.7%. ^{13}C NMR peaks: δ 56.1, 55.9, 55.7, 43.8, 43.4,* 41.0,* 39.7,* 38.4,* 37.7 ppm. **A** could be crystallized pure to leave **B** predominating in the HBr mother liquor, and further careful crystallization of **A** left essentially only **B** in the mother liquor as shown by its ^{13}C NMR spectrum: δ 56.5, 55.6, 54.4,* 44.3 (2 carbons),* 42.1, 38.9,* 37.6, 37.3,* (* are unique and distinctive peaks of the particular isomer). **B** could not be crystallized as bromide, but it could be isolated as the nitrate salt (from Dowex/1 M HNO_3) and as the perchlorate salt (from Dowex/3 M HCl, followed by concentrated $HClO_4$).

The crystals from band (2) were pure isomer **C**. *Anal.* Calc. for $[Co(C_3H_{10}N_2)_3]Br_3 \cdot H_2O$: C, 20.0; H, 6.0; N, 15.6; Br, 44.5. Found: C, 20.1; H, 6.0; N, 15.5; Br, 43.8%. ^{13}C NMR δ 57.2,* 56.4 (2 C), 42.8,* 42.1, 41.5* 39.2 (2 C),* 37.6 ppm. Resonances from the chloride salts were generally identical (±0.1 δ) to those of the bromides, except that the signals giving the double peak in the bromide of (C) (δ 56.4) were resolved into separate peaks in the chloride (δ 56.7, 56.4).

Aerial Oxidation Synthesis for [Co(meen)$_3$]$^{3+}$ with Charcoal

(a) At 80 °C

A solution of $CoCl_2 \cdot 6H_2O$ (19.0 g, 0.08 mol), meen·2HCl (5.9 g) and meen (14.8 g) in water (40 ml), with activated charcoal (2 g), was aerated while being heated (80 °C) over a steam bath for 2 h. Aeration was then continued at room temperature for 2 days. The charcoal was filtered off, and the volume was reduced. Ethanol was added carefully, to precipitate an orange solid. This was filtered off, washed with ethanol and acetone, and air-dried. Yield 16 g, 52%. No further tris(diamine) product crystallized on addition of $NaClO_4$ to the red–violet mother liquor, but small amounts of violet and subsequently green complexes were obtained, which were probably the isomers of $[Co(meen)_2Cl_2]ClO_4$.

The orange hexamine complex product was fractionally recrystallized from water by addition of ethanol. The first fractions obtained were yellow, and the later more soluble fractions red, and the red material predominated. The yellowish fractions were collectively recrystallized to remove any red material; this purification was necessary as the complexes within the yellow material are not separable from those in the red material by Sephadex chromatography as used subsequently (Fig. 7).

The hexamine component complexes **D**, **E**, **F**, **G**, **H** of the yellow material were not separable by TLC. Careful fractional recrystallization gave some of the major component **H** pure (^{13}C NMR) in a first fraction. *Anal.* Calc. for $[Co(C_3H_{10}N_2)_2(C_2H_8N_2)]Cl_3 \cdot 1.5H_2O$: C, 24.0; H, 7.8; N, 21.0. Found: C, 24.1; H, 7.8; N, 21.0%. However, the subsequent yellow fractions were mixtures, so that all the complexes were best obtained by Sephadex chromatography (see below).

The red solid fractions were largely isomer **C** of $[Co(meen)_3]Cl_3$, but contained a little demethylated complex **H** (by ^{13}C NMR in acid), with **H** decreasing along the fractions. All the red fractions were chromatographically identical to the red $[Co(meen)_3]Cl_3$ product from the dimethylsulfoxide oxidation synthesis, giving two red bands by TLC, and two bands on Sephadex chromatography with Na_2SO_4/H^+.

(b) At 20 °C

A preparation similar to that above, but with aeration carried out entirely at room temperature gave only red material (*ca.* 35% yield). No discrimination was effected on fractional recrystallization, all fractions giving two red components presumably **A** and **C** on TLC or Sephadex.

Sephadex Separation of Products from the Aerial Oxidation Synthesis

The yellow material (combined fractions) from the aerial oxidation synthesis at 80 °C was applied to columns 4.5 × 40 cm of SP-Sephadex, 1.6 g over two columns. The columns were eluted with 0.1 M Na_3PO_4, when bands separated as follows: (1) pale yellow, first eluted, containing complex **D**; (2) pink–violet; (3) orange–yellow, containing **E**; (4) orange, containing **F** as major component and **G** minor; (5) orange, containing complex **H**. Bands (4) and (5) were not cleanly separated. The relative amounts of the complexes (visually estimated) were **D**:**E**:(**F** + **G**):**H** *ca.* 1:6:3:18. The complexes were isolated by applying each effluent to a column of Dowex 50W-X2 cation-exchange resin, 200–400 mesh, H^+ form. After washing with 0.1 M HBr to remove all Na^+, the complex was eluted with 3 M HBr, and the effluent was evaporated to near dryness. Bands (4) and (5) were each rechromatographed down a Sephadex column 4.5 × 40 cm when each was then obtained cleanly. To the evaporated HBr effluents ethanol was added, and the complexes were then recovered by filtration, washing with ethanol and acetone, and air-drying to constant weight. The amounts thus obtained were **D**, 0.03 g; **E**, 0.34 g; **F** + **G**, 0.13 g; **H**, 0.70 g; and these corresponded to the visually estimated relative amounts. **F** was subsequently obtained pure by recrystallization of the **F** + **G** mixture from 0.01 M HBr.

The ^{13}C NMR spectra in D_2O/HBr gave resonances as follows: **D**, $[Co(en)_3]Br_3$, δ 44.9; **E**, $[Co(meen)(en)_2]Br_3$, δ 56.2, 45.6, 45.1, 44.5, 44.2, 43.3, 38.3 (approximately equal intensities); **F**, $[Co(meen)_2(en)_2]Br_3$, δ 56.2, 45.3, 42.6, 38.3 (equal intensities); **G**, $[Co(meen)_2(en)]Br_3$, in mixture with **F**, δ 46.0, 43.5, 41.8, 37.5 (not equal), probably another resonance coincident with 56.5 of complex **F**; ratio **F**:**G** *ca.* 5:1; **H** $[Co(meen)_2(en)]Br_3$, δ 55.6, 44.0, 43.7, 38.0 (equal intensities).

Anal. Calc. for $[Co(C_3H_{10}N_2)(C_2H_8N_2)_2]Br_3 \cdot 2H_2O$: C, 15.9; H, 5.7; N, 15.9; Br, 45.3. Found for **E**: C, 15.8; H, 5.5; N, 15.2; Br, 43.9%. Calc. for $[Co(C_3H_{10}N_2)_2(C_2H_8N_2)]Br_3 \cdot H_2O$: C, 18.3; H, 5.8; N, 16.0. Found for **F** + **G**: C, 18.4; H, 5.7; N, 15.9%. Calc. for $[Co(C_3H_{10}N_2)_2(C_2H_8N_2)]Br_3 \cdot 2H_2O$: C, 17.7; H, 5.9; N, 15.5; Br, 44.2. Found for **H**: C, 17.9; H, 5.7; N, 15.3; Br, 44.6%.

The complexes were also isolated as perchlorate salts by addition of $HClO_4$ to evaporated solutions of HCl eluates from Dowex resins. *Anal.* Calc. for $[Co(C_3H_{10}N_2)(C_2H_8N_2)_2](ClO_4)_3 \cdot H_2O$: C, 14.8; H, 5.0; N, 14.7; Cl, 18.7. Found for **E**: C, 14.6; H, 5.1; N, 14.5; Cl, 18.7%. Calc. for $[Co(C_3H_{10}N_2)_2(C_2H_8N_2)](ClO_4)_3 \cdot H_2O$: C, 16.5; H, 5.2; N, 14.4; Cl, 18.2. Found for **F** + **G**: C, 16.3; H, 5.1; N, 14.1; Cl, 18.0%.

Aerial Oxidation Synthesis in Methanol

meen (1.85 g) and meen•2HCl (0.74 g) were dissolved in methanol (50 ml), and anhydrous $CoCl_2$ (1.30 g, 0.01 mol) was added. The solution was aerated at 45 °C for 6 h, then aeration was continued at room temperature for 1 day. The resulting red powder was filtered off, washed with methanol and acetone, and air-dried. Yield 2.5 g, 63%. This product was essentially pure isomer **C**, by the ^{13}C NMR spectrum in D_2O/HCl. Sephadex chromatography with Na_2SO_4/H^+ gave two red bands, due to equilibration of **C** in water during application. The methanol mother liquor gave no other bands corresponding to other CoN_6^{3+} species.

Substitution Synthesis for $[Co(meen)_3]^{3+}$

A solution of $[Co(NH_3)_5(H_2O)](ClO_4)_3$ (2.30 g, 0.005 mol) and meen (1.3 g) in water (50 ml) was heated on a steam bath with occasional stirring for 3 h. The resulting solution was first absorbed on Dowex and eluted off with 3 M HBr, then chromatographed down columns of SP-Sephadex with 0.2 M Na_2SO_4/H_2SO_4 pH 2 eluent. Hydrolysis and bromo by-products were substantial in several bands, and the $[Co(meen)_3]^{3+}$ complex eluted as two orange bands. These were collected and worked up on Dowex/3 M HCl, and they were identified by ^{13}C NMR spectra of the evaporated effluents as isomers **A** + **B** in ratio 3:1, and **C**. No *fac* isomers were detectable from this preparation. Elution down Sephadex with 0.1 M Na_3PO_4 gave only one band of $[Co(meen)_3]^{3+}$, and yellow bands of demethylated complexes were absent.

In another substitution synthesis charcoal was used, and the crude product was precipitated with ethanol. Yield 30%. Sephadex chromatography with Na_3PO_4 gave yellow bands corresponding to the demethylated complexes **E**, **F** and **H**.

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