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Reaction of Bis(diethylenetriamine)cobalt(III) with Formaldehyde and Ammonia

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Abstract

Condensation reactions of three isomers of bis(diethylenetriamine)cobalt(III) with formaldehyde and ammonia were studied. The *s-fac* isomer gave a main product containing two molecules of the cyclic amine, 1,3,5,8-tetraazacyclodecane. It was unstable in acidic solution to give several decomposition products. The encapsulated complex in which all the nitrogens were attacked by formaldehyde could not be obtained. The main product of the *u-fac* isomer was a half encapsulated complex, *i.e.*, three of the four primary amino groups reacted with formaldehyde and ammonia to produce a cobalt(III) complex of 3-(7-amino-2,5-diazaheptyl)-1,3,5,8-tetraazacyclodecane. The *mer* isomer gave a complex of 1,4,7,9,11,14,17-heptaazaheptadecane, together with the same reaction product as the one from the *u-fac* isomer.

Introduction

The formation of the encapsulated $[Co(sep)]^{3+}$ involves adding two $N(CH_2)_3$ caps to $[Co(en)_3]^{3+}$. Primary amines are involved in the condensation reaction with ammonia and formaldehyde. In principle secondary amines should be capable of entering into the condensation reaction if the N–H bonds are suitably oriented. This orientation, of course, is determined by the conformation of the chelate ring containing the coordinated NH.

The remarkable stability of the encapsulated complex $[Co(sep)]^{3+}$ suggests the route to other multidentate ligands from amines using the condensation reaction with formaldehyde and ammonia [1–4]. The three isomers of $[Co(dien)_2]^{3+}$ (dien = diethylenetriamine) offer an opportunity for evaluation of the scope of the capping reaction and for the synthesis of ligands that would be difficult to prepare by conventional routes.

Experimental

Preparation of s-fac-Bis(diethylenetriamine)cobalt(III) Phosphate Hexahydrate

Although the preparation of the *s-fac* isomer has already been reported [5], the method is not adequate for large scale preparation, because of the low yield of the desired isomer and also the necessity of using an SP-Sephadex column. The present method, based on the study reported by Keen and Searle [6], is suitable for the preferential synthesis of the *s-fac* isomer on a large scale.

A stream of air was passed through a mixture of $Co_3(PO_4)_2 \cdot 8H_2O$ (51.1 g, 0.1 mol), diethyelenetriamine (72 ml, 0.66 mol), K_2HPO_4 (63.2 g, 0.36 mol), and 500 ml of water in the presence of 6 g of Norit A for about 14 h. After about a half hour the cobalt phosphate was almost dissolved and yellow glittering crystals began to separate from the solution. The resulting slurry was filtered and washed with water repeatedly and then with ethanol. Yield (product plus charcoal): 127.3 g (86% without charcoal). *Anal.* for the recrystallized complex. Calc. for $[Co(dien)_2]PO_4 \cdot 6H_2O(C_8H_{38}N_6O_{10}PCo)$: C, 20.52; H, 8.18; N, 17.94. Found: C, 20.39; H, 7.92; N, 17.83%.

Conversion of the Phosphate to s-fac-Bis(diethylenetriamine)cobalt(III) Chloride Monohydrate

The above phosphate containing 6 g of charcoal (127.3 g, 0.26 mol) was put into 370 ml of 3 M HCl. The charcoal was filtered off and washed with water. The filtrate and washings were combined and evaporated almost to dryness in a vacuum evaporator. The resulting paste was transferred to a sintered glass filter and sucked dry. It was washed with 50 *v/v*% ethanol twice and then with 70% ethanol three times and finally with absolute ethanol. Yield, 81.3 g (80.6% based on the phosphate). From the combined filtrates, 11.9 g (11.8%) of further crystals were obtained. They were recrystallized by dissolving in 140 ml of 0.1 M HCl at 90 °C and by adding 330 ml of ethanol in small portions. Yield, 90.2 g (89.4% based on the phosphate).

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Preparation of u-fac- and mer-Bis(diethylenetriamine)cobalt(III) Chloride

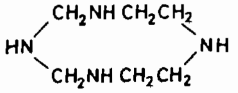
$[Co(dien)_2]PO_4 \cdot 6H_2O$ (30 g) was isomerized by heating at 80 °C for 4 h in the presence of 3 g of activated charcoal in 3 l of water. The charcoal was filtered off and the filtrate was concentrated to about 100 ml. The precipitated *s-fac* phosphate was filtered. A part of the resulting solution was charged on a column (5 X 50 cm) of SP-Sephadex C-25 and eluted with 0.1 M Na_3PO_4 and the isomers isolated by the reported method [5].

The *u-fac* isomer was optically resolved by the reported method [5].

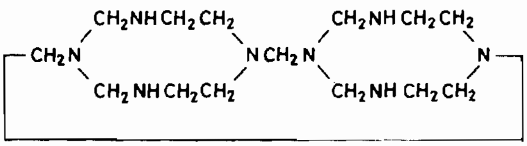
Condensation Reaction of the s-fac Isomer

The procedure of Harrowfield *et al.* [2] was repeated using an equimolar amount of *s-fac*-$[Co(dien)_2]Cl_3 \cdot H_2O$ instead of $[Co(en)_3]Cl_3 \cdot 3H_2O$ with slight modifications reducing the scale to 1/5 and using twice the amount of ammonia, *i.e.*, the molar ratio of ammonia and formaldehyde was 2:3, being the same ratio as the preparation of hexamethylenetetraamine. Thus, 1.95 g (5 mmol) of *s-fac*-$[Co(dien)_2]Cl_3 \cdot H_2O$ in 25 ml of water, 1.6 g of Li_2CO_3, 111 ml of 9 M NH_3, and 111 mol of 37% formaline were used.

The final solution was brick red. The solution was diluted to about ten times its volume and passed through a column (3 X 10 cm) of SP-Sephadex C-25. The column adsorbed yellow and dark red species and passed a pink species. The column was washed with a solution of 0.03 M NH_4Cl, which was slightly basic with NH_3. The yellow species on the column was eluted with 0.1 M $Na_4P_2O_7$. The eluate was acidified to pH less than 2 by dropwise addition of 6 M HCl. Yellow crystals, which separated from the solution, were filtered after 30 min. They were washed with water and then with ethanol. Yield, 1.74 g (47%). They were found to be mainly composed of the 1,3,5,8-tetraazacyclodecane (**Ia**) complex of cobalt(III), and were recrystallized by dissolving in a solution of $NaHCO_3$ followed by the addition of 3 M HCl. Yield, 1.36 g (37%). *Anal.* Calc. for $[Co(H\mathbf{Ia})_2]Cl(H_2P_2O_7)_2(C_{12}H_{38}N_8O_{14}ClP_4Co)$: C, 19.56; H, 5.20; N, 15.21. Found: C, 19.57; H, 5.34; N, 15.31%.



Ia



Ib

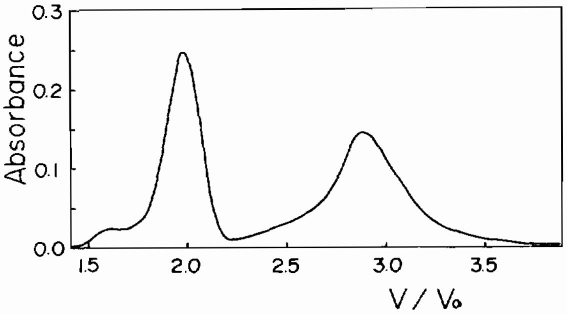


Fig. 1. Elution curve of the mother liquor from the recrystallization of $[Co(\mathbf{Ia})_2]HP_2O_7 \cdot 4.5H_2O$. Column, 2.9 X 40.5 cm SP-Sephadex C-25; eluent, 0.1 M $Na_2NH_4HP_2O_7$. The abscissa denotes the specific elution volume, *i.e.*, the ratio of the elution volume to the volume of the column.

The complex $[Co(\mathbf{Ib})]^{3+}$ could not be detected in the solution of the reaction products.

Although the product gave a good analytical result, a chromatogram using SP-Sephadex and 0.1 M $Na_2NH_4HP_2O_7$, which was prepared by adding ammonia to a solution of $Na_2H_2P_2O_7$ and adjusting its pH to 8.0, revealed that it consisted of two species. The product was purified by dissolving in a minimum amount of 6 M NH_3 at a room temperature, and by leaving the resulting solution in a refrigerator overnight. From 2.21 g of the crude material, 0.41 g (23%) of pure crystals were obtained. *Anal.* Calc. for $[Co(\mathbf{Ia})_2]HP_2O_7 \cdot 4.5H_2O(C_{12}H_{42}N_8O_{11.5}P_2Co)$: C, 23.89; H, 7.02; N, 18.57. Found. C, 24.18; H, 6.93; N, 18.42%.

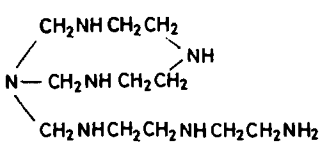
A byproduct or possibly a decomposition product of $[Co(\mathbf{Ia})_2]^{3+}$ was found to be $[Co(dien)(\mathbf{Ia})]^{3+}$ and was separated from the above mentioned filtrate. Figure 1 shows a chromatogram of the species contained in the NH_3 solution using a column of SP-Sephadex C-25 with 0.1 M $Na_2NH_4HP_2O_7$ as an eluent. The first fraction contained $[Co(dien)(\mathbf{Ia})]^{3+}$ and the second fraction, $[Co(\mathbf{Ia})_2]^{3+}$. The first fraction was diluted about ten times its volume and passed through a column (2 X 10) of SP-Sephadex C-25. The absorbed complex was washed with water and then removed by eluting with 0.1 M $Na_4P_2O_7$. The eluate was acidified to pH less than 2 with 3 M HCl and left in a refrigerator overnight. The yellow needles that formed were washed with water repeatedly and then with ethanol. *Anal.* Calc. for $[Co(dien)(H\mathbf{Ia})](H_2P_2O_7)_2 \cdot H_2O(C_{10}H_{36}N_7O_{15}P_4Co)$: C, 17.73; H, 5.36; N, 14.48. Found: C, 17.74; H, 5.37; N, 14.30%.

Condensation Reaction of the u-fac Isomer

The procedure employed for the reaction of the *s-fac* isomer was used without modification.

Since the product was stable in acidic media, it was adsorbed on a small column of SP-Sephadex, washed with 0.03 M NH_4Cl (slightly alkaline with

NH_3), and then eluted with 1 M HCl from the small column of SP-Sephadex. The residue, which was obtained by evaporating the eluate, was dissolved in a minimum amount of water. Orange crystals were obtained by the addition of ethanol to the solution. From 2.04 g (5 mmol) of *u-fac*-[Co(dien)$_2$]$Cl_3\cdot 2H_2O$, 1.63 g of the product was obtained. This contained a small amount of impurity, which was separated by a column of SP-Sephadex using 0.1 M $Na_2NH_4HP_2O_7$ as an eluent. The product was found to be a cobalt(III) complex of 3-(7-amino-2,5-diazaheptyl)-1,3,5,8-tetraazacyclodecane (**IIa**). *Anal.* Calc. for [Co(**IIa**)]$Cl_3\cdot H_2O$($C_{11}H_{31}N_7OCl_3Co$): C, 29.95; H, 7.08; N, 22.22; Co, 13.36. Found: C, 29.91; H, 7.05; N, 21.99; Co, 13.20%.



IIa

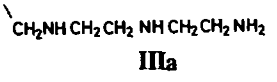
Reaction of the optically-active *u-fac*-isomer was carried out by the same procedure as that of the racemic isomer to give an optically active complex of **IIa**.

Condensation Reaction of the mer Isomer

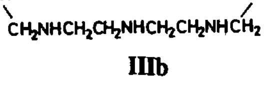
This isomer seems to be less reactive than the two facial isomers toward formaldehyde and ammonia. Thus, nearly half of the starting complex was recovered from the reaction mixture, together with two main products, under the same condition as the reaction of the *fac* isomers, and another condition using excess ammonia at nearly 40 °C.

The condensation reaction of the *mer* isomer gave a dark red solution, from which two main yellow products were obtained, at somewhat elevated temperature (55–60 °C), and using 2.08 g (5 mmol) of *mer*-[Co(dien)$_2$]$Cl_3\cdot 2.5H_2O$ in 25 ml of water, 1.6 g of Li_2CO_3, 114 ml of 8.77 M NH_3, and 114 ml of 37% formalin. The elution curves of these reaction products are shown in Fig. 2. The complex contained in band 1 was assigned as the same reaction product obtained from the *u-fac* isomer. Band 2 contained a cobalt(III) complex of 1,4,7,9,11,14,17-heptaazaheptadecane (**IIIa**). *Anal.* Calc. for [Co(**IIIa**)]$(ClO_4)_3\cdot H_2O$($C_{10}H_{31}N_7O_{13}Cl_3Co$): C, 19.29; H, 5.02; N, 15.75; Co, 9.46. Found: C, 19.34; H, 5.00; N, 15.94; Co, 9.38%.

The perchlorate of the complex contained in band 3 gave the following analysis. Found: C, 18.23; H, 4.52; N, 14.28; Co, 9.92%. The analysis corresponded to the composition, $C_9H_{27}N_6Co$. If this compound contains an oxygen, the calculated values for $C_9H_{27}N_6O_{13}Cl_3Co$ are C, 18.24; H, 4.59; N, 14.18; Co, 9.94% and if it contains one molecule of water, the calculated values for $C_9H_{29}N_6O_{13}Cl_3Co$ are C, 18.18; H, 4.92; N, 14.13; Co, 9.91%.



IIIa



IIIb

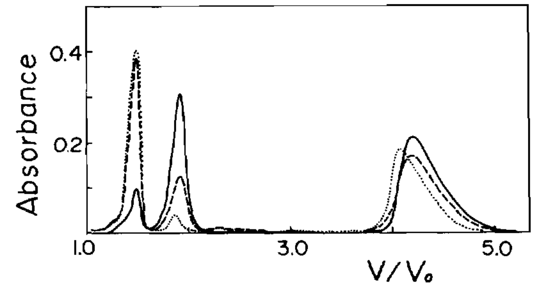


Fig. 2. Elution curve of the reaction product of *mer*-[Co(dien)$_2$]$^{3+}$. Solid line, the reaction products in excess of ammonia (Co:NH_3:HCHO = 1:251:300) at nearly 40 °C; dashed line, the reaction products under the condition of less ammonia (1:200:308) at nearly 40 °C; and dotted line, the reaction products under the condition (1:200:300) at 55–60 °C (see text). Column, 3.0 × 97 cm SP-Sephadex C-25; eluent, 0.1 M $Na_3HP_2O_7$. The band 3 of the dotted line consisted mainly of the reaction product, but the band 3 of the other two elution curves consisted mainly of the starting complex.

No signs of the formation of the complex [Co(**IIIb**)]$^{3+}$ were obtained in the chromatogram of the reaction products.

Physical Measurements

The electronic absorption spectra were obtained using a Shimadzu MPS-50L. The circular dichroism spectra were recorded using a Jasco J-500C spectropolarimeter. The ^{13}C NMR spectra were measured at 15.04 MHz on a JEOL JNM-FX60 spectrometer under the condition of noise-modulated proton decoupling.

Results and Discussion

The reaction product from the *s-fac* isomer seemed to be unstable in solution. In the early stage of this research, the product was treated with HCl as for the preparation of [Co(sep)]$^{3+}$. This treatment produces various kinds of species, most of which are yellow. Figure 3 shows a typical chromatogram of the product, which was initially adsorbed on a Dowex column, eluted with HCl followed by evaporating with a rotary evaporator. A solid compound was obtained from each band. However, most of them gave complex ^{13}C NMR spectra excepting for band 3 that contained the starting material.

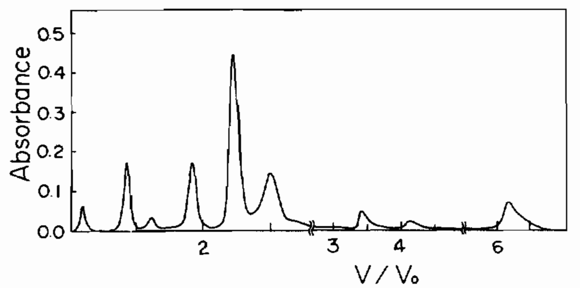


Fig. 3. Elution curve of the reaction product of the *s-fac* isomer treated in acidic conditions (see text). Column, 3.0 X 97 cm SP-Sephadex C-25; eluent, 0.1 M $Na_3HP_2O_7$.

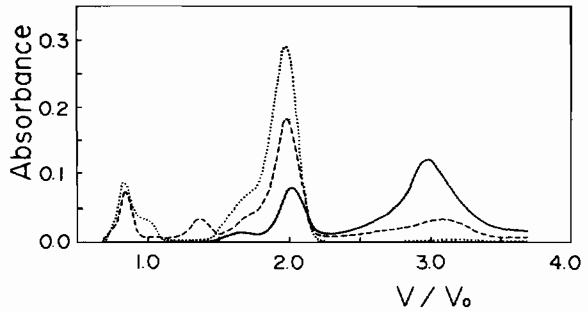


Fig. 4. Elution curve of $[Co(HIa)_2]Cl(H_2P_2O_7)_2$ dissolved in sodium carbonate solution. Solid line, eluted just after the dissolution; dashed line, after four days; and dotted line, after 39 days. Column, 2.0 X 40.5 cm SP-Sephadex C-25; eluent, 0.1 M $Na_2NH_4HP_2O_7$.

The product was unstable even in neutral or basic solution. Figure 4 illustrates the instability of the product. Most of the species thus formed could not be isolated from solution without decomposition. The solid compounds obtained showed electronic absorption spectra which were different from the ones in the eluates.

However, some of the products were stable and their structures could be assigned. Thus, band 2 with specific elution volume of *ca.* 1.0 was found to consist of the starting material. The species contained in the last band (band 6) was assigned the structure shown in Fig. 5(a). They were assigned mainly from their analytical results and ^{13}C NMR spectra, which are shown in Fig. 6.

The main product, $[Co(\mathbf{Ia})_2]^{3+}$, forms a least soluble salt with diphosphate ions of the composition, $[Co(\mathbf{Ia})_2]Cl(H_3P_2O_7)_2$, which may be formulated as $[Co(H\mathbf{Ia})_2]Cl(H_2P_2O_7)_2$. This salt contained appreciable amount of byproduct, $[Co(dien)(\mathbf{Ia})]^{3+}$, even after recrystallization four times by dissolving the salt in $NaHCO_3$ solution followed by precipitation with HCl. This was easily purified, however, by dissolving the salt in a minimum amount of 6 M NH_3, followed by leaving the solution in a refrigerator. The crystals thus obtained had a composition of $[Co(\mathbf{Ia})_2]HP_2O_7 \cdot 4.5H_2O$.

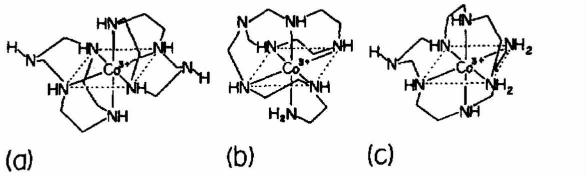


Fig. 5. Presumed structure of the reaction products. (a) $[Co(Ia)_2]^{3+}$ from *s-fac*-$[Co(dien)_2]^{3+}$; (b) $[Co(IIa)]^{3+}$ from *u-fac*-$[Co(dien)_2]^{3+}$; (c) $[Co(IIIa)_2]^{3+}$ from *mer*-$[Co(dien)_2]^{3+}$.

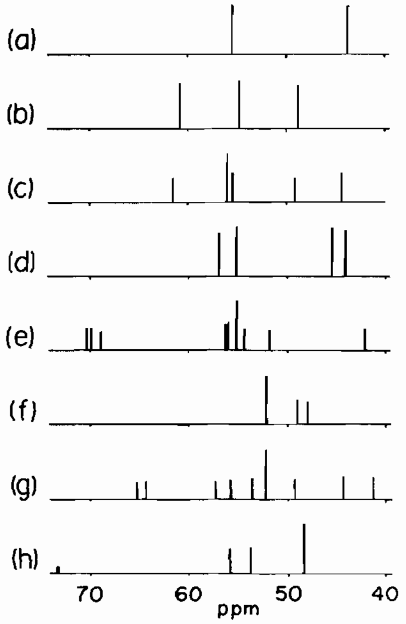


Fig. 6. Schematic representation of the ^{13}C NMR spectra of the starting materials and their reaction products. (a) *s-fac*-$[Co(dien)_2]^{3+}$ in water; (b) $[Co(Ia)_2]^{3+}$ in NH_3–NH_4^+ (pH 8); (c) $[Co(dien)(Ia)]^{3+}$ in NH_3–NH_4^+ (pH 8); (d) *u-fac*-$[Co(dien)_2]^{3+}$ in water; (e) $[Co(IIa)]^{3+}$ in water; (f) *mer*-$[Co(dien)_2]^{3+}$ in water; (g) $[Co(IIIa)]^{3+}$ in water; (h) the complex obtained from the band 3 of the reaction product of the *mer* isomer. The resonance lines are plotted from external TMS.

The byproduct $[Co(dien)(\mathbf{Ia})]^{3+}$ was obtained also as crystalline diphosphate from the eluent (band 5 with specific elution volume of *ca.* 2.0 in Fig. 4). The salt should be formulated as $[Co(dien)(H\mathbf{Ia})](H_2P_2O_7)_2 \cdot H_2O$.

The fully capped species $[Co(\mathbf{Ib})]^{3+}$ could not be obtained from the solution of the reaction product. In order to explain the elution order of the three isomers of $[Co(dien)_2]^{3+}$, the ion association of the *s-fac* isomer with a phosphate ion was assumed through the interaction among three hydrogens of amino groups and three oxygen atoms of the phosphate ion [7, 8]. This kind of ion association bears a close resemblance to the encapsulation by three molecules of HCHO and a molecule of ammonia.

However, for the *s-fac* isomer this is not the case. The Stuart model showed that severe distortion occurred when the fully encapsulated complex, [Co(**Ib**)]$^{3+}$, was formed from the *s-fac* isomer.

The reaction product from the *u-fac* isomer was stable even in acidic solution. Thus, the main product was obtained from the reaction mixture by the same procedure as isolation of [Co(sep)]$^{3+}$. A trace amount of impurity present in the chloride of the main product was easily separated by column-chromatography on SP-Sephadex C-25 using 0.1 M $Na_2NH_4HP_2O_7$ as an eluent.

Reduction of [Co(H**IIa**)$_2$]$^{5+}$ or [Co(**IIa**)]$^{3+}$ with zinc dust and HCl resulted in the decomposition of the complex and the formation of hydrated cobalt(II) ion. No reversible oxidation–reduction seemed to take place in contrast to the behavior of [Co(sep)]$^{3+}$ [3, 4].

The reaction products from the *mer* isomer were not simple. Only the complex with the 'half connected' ligand, [Co(**IIIa**)]$^{3+}$, was obtained under mild conditions, and no signs of the formation of the complex with both ligands connected, [Co(**IIIb**)]$^{3+}$, was found in the reaction product even under more severe conditions. A Stuart model showed that strained chelate-rings resulted in [Co(**IIIb**)]$^{3+}$.

Only the *mer* isomer gave the reaction product of its isomerized form, [Co(**IIa**)]$^{3+}$. The isomerization of the *mer* isomer to the two *fac* isomers was examined under similar conditions as the encapsulated reaction except that formaldehyde was absent. Thus, in the presence of 0.7 g of lithium carbonate, 0.13 g of ammonium chloride in 50 ml of 0.2 M ammonia, 0.42 g of *mer*-[Co(dien)$_2$]$Cl_3 \cdot 2.5H_2O$ gave 0.83% of the *s-fac* isomer and 7.63% of the *u-fac* isomer for 2 h at 70 °C, which is a somewhat higher temperature than the encapsulated reactions. At 55–60 °C for 2 h, which was employed under severe encapsulated reactions, it gave 0.05% of the *s-fac* isomer and 0.72% of the *u-fac* isomer. Under mild encapsulated reaction conditions, 40–45 °C for 2 h, it does not isomerize to the *fac* isomers. This fact clearly indicates that the encapsulated reaction enhances the isomerization to the *fac* isomer, and preferentially produces the isomerization product of only one form, [Co(**IIa**)]$^{3+}$. It is difficult to understand, at present, why the complex [Co(**Ia**)$_2$]$^{3+}$ or its decomposition products could not be detected in the solution of the reaction products.

Figure 6 shows the ^{13}C NMR spectra of the reaction products together with those of the starting materials. The symmetry of each complex is reflected in the NMR spectrum. Three resonance lines observed at 68.9–70.3 ppm in the spectrum of [Co(**IIa**)]$^{3+}$ are assigned to $N(\underline{C}H_2NH)_3$ carbons. They are quite close to that observed at 66.5 ppm for [Co(sep)]$^{3+}$ [3]. The $NH(\underline{C}H_2NH)_2$ carbons seem to resonate at higher field than the $N(\underline{C}H_2NH)_3$ carbons. Thus, the resonance line observed at 60.8 ppm in [Co(**Ia**)$_2$]$^{3+}$ and those observed at 65.8 and 64.8 ppm in [Co(**IIIa**)]$^{3+}$ are assigned to these carbons.

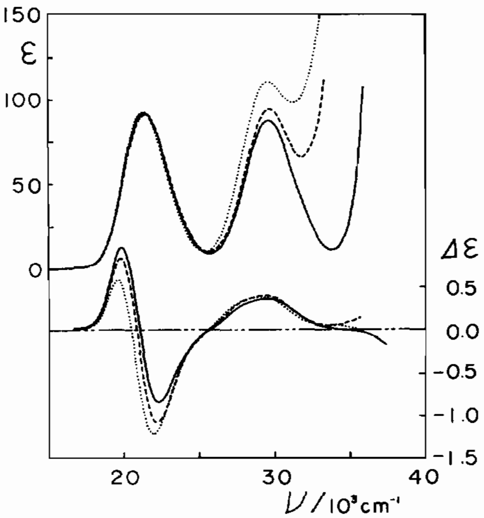


Fig. 7. AB and CD spectra of (a) (+)$_{589}$-*u-fac*-[Co(dien)$_2$]$^{3+}$ in water (solid lines); (b) (+)$_{589}$-*u-fac*-[Co(dien)$_2$]$^{3+}$ in 0.1 M Na_3PO_4 (dashed lines); (c) its reaction product, (−)$_{589}$-[Co(**IIa**)]$^{3+}$ in water (dotted lines).

The CD spectra of the *u-fac* isomer and its reaction product are shown in Fig. 7. The effect of adding PO_4^{3-} to the solution of the *u-fac* isomer is similar to that for the capped product [Co(**IIa**)]$^{3+}$, but the change is greater for [Co(**IIa**)]$^{3+}$. The similar changes are consistent with the assumed structure of the reaction product involving the capping of a face with three primary amine groups. This is the expected approach of PO_4^{3-} through hydrogen bonding [9]. The effects of capping [Co(en)$_3$]$^{3+}$ on the CD spectrum was shown to be similar to the interaction with PO_4^{3-} [10].

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