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The Stereochemistry of Amino Acid Rhodium(III) Complexes with Ethylenediamine-N,N'-di-S-α-Propionic Acid

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Substitution reactions of Δ-cis-α-[Rh(SS-EDDP)-Cl$_2$]$^-$ (SS-EDDP = ethylenediamine-N,N'-di-S-α-propionate) with R-alanine, S-alanine, R,S-alanine, and glycine yielded the corresponding amino acid rhodium(III) complexes of SS-EDDP with retention of configuration. Substitution reactions of Λ-cis-β-[Rh(SS-EDDP)Cl$_2$]$^-$ with amino acids, however, resulted in isomerization to the Δ-cis-α product or retention of configuration depending on the reaction condition. Electronic absorption, circular-dichroism, optical-rotatory-dispersion, and proton nuclear magnetic resonance spectra of those substitution products are reported.

Introduction

The (en)-cobalt(III) complexes of ethylenediamine-N,N'-di-S-α-propionic acid (SS-EDDP) yielded both the Δ- and Λ-*cis*-α isomers as well as the Δ-*cis*-β isomer out of the four possible isomers (Fig. 1) (en = ethylenediamine) [1]. In the dichloro rhodium(III) complexes, however, the ligand showed more pronounced stereospecificity and yielded only the Δ-*cis*-α and Λ-*cis*-β isomers [2]. As part of our continuing study of the stereochemistry of rhodium(III) complexes of the stereospecific tetradentate chelating agent, we have been interested in the substitution reactions of the dichloro rhodium(III) complexes of SS-EDDP with a series of amino acid. In this paper we wish to report the synthesis of the SS-EDDP-rhodium(III) complexes of R- or S-alanine, racemic alanine, and glycine as well as the CD and ^{1}H NMR spectra of those complexes.

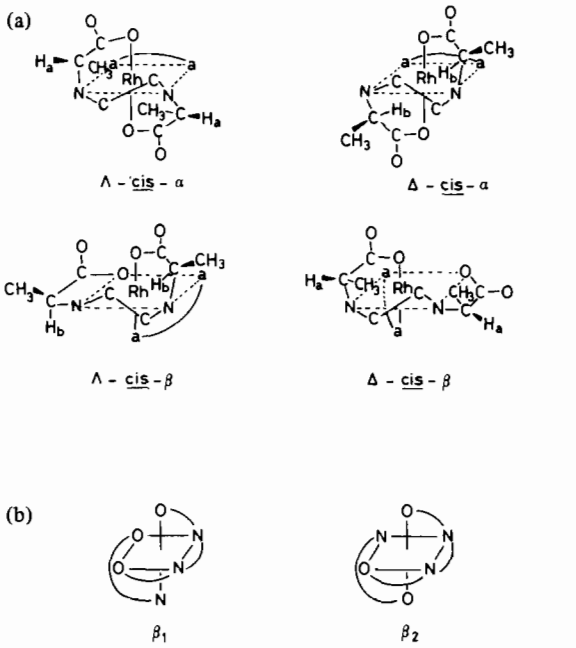

Fig. 1. (a) The four possible isomers of [Rh(SS-EDDP)(aa)] (aa = amino acid), and (b) the configurational isomers of *cis*-β-[Rh(SS-EDDP)(aa)] complexes.

Experimental

Physical Measurements

A Unicam SP 800 A spectrophotometer was used to obtain the electronic absorption spectra. ^{1}H NMR spectra were recorded on a Varian A-60 or a Brucker 90 mHz spectrometer. ORD and CD spectra were measured with a Jasco ORD/CD-5 spectrometer. Infrared spectra were taken with a Perkin-Elmer Model 337 spectrophotometer. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan.

Ethylenediamine-N,N'-di-S-α-propionic acid

This was prepared according to the reported method [1]. *Anal.* Calcd. for $C_8H_{16}N_2O_4$: C, 46.90; H, 7.89; N, 13.70. Found: C, 46.85; H, 7.92; N, 13.68.

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Δ-cis-α-H[Rh(SS-EDDP)Cl$_2$]·H$_2$O and Λ-cis-β-H[Rh(SS-EDDP)Cl$_2$]·3H$_2$O

These were prepared by the method reported [2]. *Anal.* Calcd. for *cis-α*-$RhC_8H_{15}N_2O_4Cl_2 \cdot H_2O$: C, 24.30; H 4.30; N, 7.09. Found: C, 24.27; H, 4.33; N, 7.05. Calcd. for *cis-β*-$RhC_8H_{15}N_2O_4Cl_2 \cdot 3H_2O$: C, 22.27; H, 4.87; N, 6.49. Found: C, 22.22; H, 4.83; N, 6.52.

Δ-cis-α-[Rh(SS-EDDP)(S-ala)]

To 0.197 g of *Δ-cis-α*-H[Rh(SS-EDDP)Cl$_2$]·H$_2$O dissolved in freshly distilled DMF was added 0.046 g of S-alanine. The mixture was refluxed for 6 to 8 hours and then cooled in an ice bath for several hours. The creamy white product was filtered and washed with ethanol and ether. Yield was 0.06 g (31%). *Anal.* Calcd. for $RhC_{11}H_{20}N_3O_6$: C, 33.59; H, 5.09; N, 10.69. Found: C, 33.62; H, 5.18; N, 10.71.

Δ-cis-α-[Rh(SS-EDDP)(R-ala)]

The same procedure was employed to prepare the R-alanine adduct as in the S-alanine, using R-alanine (0.046 g) in place of S-alanine. Yield was 0.07 g (35%). *Anal.* Found: C, 33.47; H, 5.18; N, 10.61.

Δ-cis-α-[Rh(SS-EDDP)(R,S-ala)]

The same procedure was followed to make the racemic alanine adduct as in the S-alanine using racemic alanine in place of S-alanine. *Anal.* Found: C, 33.60; H, 5.14; N, 10.66.

Δ-cis-α-[Rh(SS-EDDP)(gly)]

This was prepared by the same method as that used for S-alanine complex using glycine in place of S-alanine. *Anal.* Calcd. for $RhC_{10}H_{18}N_3O_6 \cdot 2/3H_2O$: C, 30.69; H, 4.94; N, 10.74. Found: C, 30.56; H, 4.84; N, 10.72.

Λ-cis-β-[Rh(SS-EDDP)(S-ala)]

A solution of 0.216 g of *Λ-cis-β*-[Rh(SS-EDDP)Cl$_2$]·3H$_2$O dissolved in pure DMF was refluxed with 0.046 g of S-alanine for 8 hours. The creamy white product was filtered, washed with ethanol and ether and dried in an oven at 70 °C for two hours. *Anal.* Calcd. for $RhC_{11}H_{20}N_3O_6 \cdot 2/3H_2O$: C, 32.59; H, 5.26; N, 10.37. Found: C, 32.49; H, 5.28; N, 10.35.

Results and Discussion

All the amino acid complexes have been prepared *via* the substitution reactions with the *Δ-cis-α-* or *Λ-cis-β*-[Rh(SS-EDDP)Cl$_2$]$^-$, the absolute configurations of which have been charaterized previously [2]. The substitution of R-, S-, and racemic alanine, and glycine in the *Δ-cis-α*-[Rh(SS-EDDP)Cl$_2$]$^-$ complex yields the *cis-α* products with retention of configuration. The ORD, CD, and ^{1}H NMR spectra all indicate the *Δ-cis-α* absolute configuration.

The absolute configuration assignments of these isomers concur with the assignments made by Hall and Douglas [3, 4] from the CD spectra of a series of resolved Rh(en)$_2$amino acid^{2+} complexes. Although the en complexes showed a positive rotation at the sodium D line, and the *cis-α*-SS-EDDP-ala complexes were negative at the sodium D line, the absolute configuration assignments are still the same: $(-)_D$-*cis-α*-[Rh(SS-EDDP)(S-ala)] is Δ and $(+)_D$-[Rh(en)$_2$-(S-ala)]$^{2+}$ is also Δ. The optical activity of the tetradentate ligand may be responsible for the change of sign of rotation at the Na_D line.

The CD spectra of the *cis-α* rhodium(III) complexes of SS-EDDP and alanine are substantially more complicated than the spectra of [Rh(en)$_2$-(amino acid)]$^{2+}$ complexes. While only two components were noted with the latter series, there are four distinct components in the *cis-α*-ala CD spectrum in the region 210–450 nm (Fig. 2). The low frequency band in the bis(en)-amino complexes has been assigned to the $^1A_1 \rightarrow {}^1E^a$ transition since the E^a peak is generally dominant in the first band region [3, 5, 6]. The high frequency band around 240 nm has been assigned to the $^1A_1 \rightarrow {}^1E^a$ transition. Only in the bis(en)-methionine complex was there any indication of the presence of another peak in the region of the low energy band, which has been assigned to the $^1A_1 \rightarrow {}^1A_2$ transition [3, 4].

By analogy with $(+)_D$-[Rh(en)(S-met)]$^{2+}$, the long wavelength absorption at 360 nm observed in this work is assigned to the $^1A_1 \rightarrow {}^1E^a$ transition. The high energy broad absorption at 270 nm is assigned to the $^1A_1 \rightarrow {}^1E^b$ transition. As in the bis(en)-methionine complex, the absorption at 310 nm is assigned to the $^1A_1 \rightarrow {}^1A_2$ transition. The highest energy CD band at 225 nm is as yet assigned. The tetragonal splitting is obviously much larger in the case of the rhodium(III) tetradentate complexes. The greater ring conformational effects from the tetradentate ligand should be responsible for the complexity of the CD spectra.

The molecular rotation of the *Δ-cis-α*-S-ala complex has the greatest magnitude while the racemic alanine complex is approximately the average of the S-ala and R-ala spectra. The preparation of the *Δ-cis-α*-glycine complex allowed the vicinal effect of the optically active alanine to be observed. The S-ala complex has increased the molecular rotation of the complex to approximately the same degree that the R-ala complex has reduced it, so that in the *Δ-cis-α* series it is seen that the S-alanine has a positive vicinal effect and the R-alanine a negative vicinal effect.

The ^{1}H PMR spectra characterize the *cis-α* isomers of the S-, R-, and racemic alanine complexes

TABLE I. Absorption, ORD, and CD Spectral Data of Δ-*cis*-α- and Λ-*cis*-β-[Rh(SS-EDDP)(amino acid)].

Complex	Absorption		ORD		CD	
	λ(nm)	ε	λ(nm)	[M]	λ(nm)	Δε
Δ-*cis*-α-[Rh(SS-EDDP)(S-ala)]	350(br)	196	395	−2,114	360	−5.15
	283	232	328	+18,290	308	+0.87
					270	−0.98
Δ-*cis*-α-[Rh(SS-EDDP)(R-ala)]	350(br)	188	395	−3,305	360	−3.92
	283	214	328	+14,647	308	+0.89
					270	−0.76
Δ-*cis*-α-[Rh(SS-EDDP)(R,S-ala)]	350	188	390	−4,023	360	−4.66
	283	213	328	+17,320	310	+0.94
					270	−0.94
Δ-*cis*-α-[Rh(SS-EDDP)(gly)]	360	321	395	−4,061	360	−4.11
	290	255	322	+17,004	308	+0.71
					270	−1.44
Λ-*cis*-β-[Rh(SS-EDDP)(S-ala)]	348	202	326	−7,047	346	+1.25
	283	261			306	−0.82

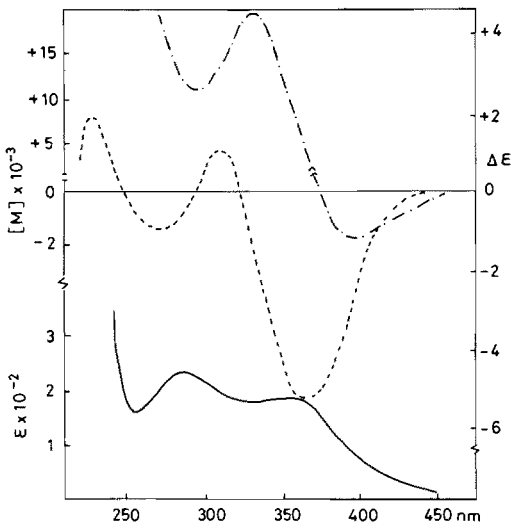

Fig. 2. The electronic absorption (——), ORD (— · —), and CD (- - - -) spectra of Δ-*cis*-α-[Rh(SS-EDDP)(S-ala)].

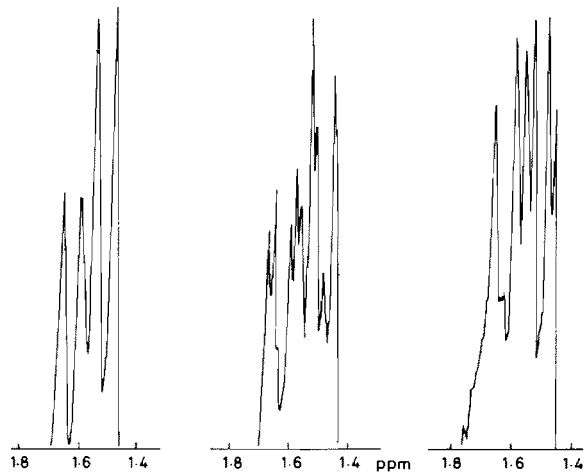

Fig. 3. The methyl region of the 90 mHz PMR spectra of: Δ-*cis*-α-[Rh(SS-EDDP)(R-ala)], left; Δ-*cis*-α-[Rh(SS-EDDP)-(RS-ala)], middle; and Δ-*cis*-α-[Rh(SS-EDDP)(S-ala)], right.

completely. The methyl regions of these complexes are shown in Fig. 3. The R-alanine complex shows two methyl doublets with a 2:1 intensity. This indicates that the C_2 axis of symmetry of the *cis*-α isomer still holds and the propionate arms are equivalent. The doublet at 1.62 ppm is distinctive of the R-alanine methyl group in these *cis*-α isomers. In the S-alanine adduct this symmetry axis has been destroyed and three separate methyl doublets can be seen. The doublet at 1.64 ppm is characteristic of the S-alanine methyl group. It is interesting to note that coordination of an alanine group shifts the methyl doublet from the free alanine resonance at 1.48 ppm to 1.62–1.64 ppm. Coordination of the alanine has thus reduced the electron density around the methyl protons, *i.e.*, had a positive shielding effect.

Dreiding models of the two alanine complexes show only minor stereochemical differences between them. In the S-alanine complex the methyl and carbonyl groups of the alanine lie in approximately the same plane. The R-alanine methyl function is at about a 30° angle with the plane of the carbonyl bond. This slight shift in position of the methyl group between the R-alanine and the S-alanine is sufficient to destroy the pseudo C_2 axis of the *cis*-α complex of the latter amino acid.

The methyl region of the spectrum of the racemic alanine adduct is essentially a mixture of the spectra of the S- and R-alanine species. The doublets at 1.48 and 1.52 ppm are assigned to the ligand methyl doublets due to *cis*-α-S-ala complex, while the doublet at 1.49 ppm is assigned to the ligand methyl doublet of the *cis*-α-R-ala complex. The two methyl doublets from the coordinated alanine resonate exactly as they did in their respective S- and R-ala isomers, *i.e.*, 1.64 and 1.62 ppm. Although the proton quartets still resonate in the H_b region (Fig. 1), they are slightly split since the H_b protons are not all equivalent.

Figure 4 shows the ORD, CD, and absorption spectra of Λ-*cis*-β-[Rh(SS-EDDP)(S-ala)]. The dominant positive band in the CD spectrum concurs with the Λ absolute configurational assignment. The PMR spectrum of this complex was very complex and the orientation of the coordinated amino acid, whether β_1 or β_2 (Fig. 1), could not be determined from either PMR or infrared spectra. The *cis*-β_2 configuration is predicted to be more stable isomer by conformational energy calculations [7].

It is noted that, while the substitution reactions of the Δ-*cis*-α-$[Rh(SS\text{-}EDDP)Cl_2]^-$ with alanine in DMF gave products with retention of configuration, those of the Λ-*cis*-β-$[Rh(SS\text{-}EDDP)Cl_2]^-$ with alanine resulted in isomerization to the Δ-*cis*-α product except one occasion in which we obtained Λ-*cis*-β-[Rh(SS-EDDP)(S-ala)]. Refluxing a solution containing Λ-*cis*-β-$[Rh(SS\text{-}EDDP)Cl_2]^-$ and optically active or racemic alanine or glycine in DMF has yielded Δ-*cis*-α-[Rh(SS-EDDP)(amino acid)] product. The Δ-*cis*-α-[Rh(SS-EDDP)(R-ala)] obtained in this fashion showed a molar rotation about 1000° higher than the standard Δ-*cis*-α-[Rh(SS-EDDP)(R-ala)] complex which was produced from the reaction of Δ-*cis*-α-$[Rh(SS\text{-}EDDP)Cl_2]^-$ and R-alanine in DMF. Both products showed the same ir and ^1H NMR spectra. While the Δ-*cis*-β-R-ala compound obtained from the Λ-*cis*-β-Cl_2 complex analyzed with one water molecule, the standard Δ-*cis*-α-R-ala complex was anhydrous. When a solution of Λ-*cis*-β-$[Rh(SS\text{-}EDDP)Cl_2]^-$ complex and a two-fold excess of racemic alanine in DMF was refluxed, the CD spectrum of the product showed complete isomerization to the Δ-*cis*-α-[Rh(SS-EDDP)(R,S-ala)].

The isomerization of the *cis*-β-$[Co(EDDA)X_2]^-$ complex (EDDA = ethylenediamine-N,N′-diacetic acid, $X_2 = (H_2O)_2$, oxalate or malonate) to the more stable *cis*-α form has been reported [8–11]. Molecular models indicate that cumulative ring strain is more appreciable in the *cis*-β isomer than in the *cis*-α isomer. Thus, the stereochemical inversion of the Λ-*cis*-β isomer to the Δ-*cis*-α isomer observed in this work is not unreasonable. Further study about the mechanism of the substitution and isomerization reactions observed in this work will be published elsewhere.

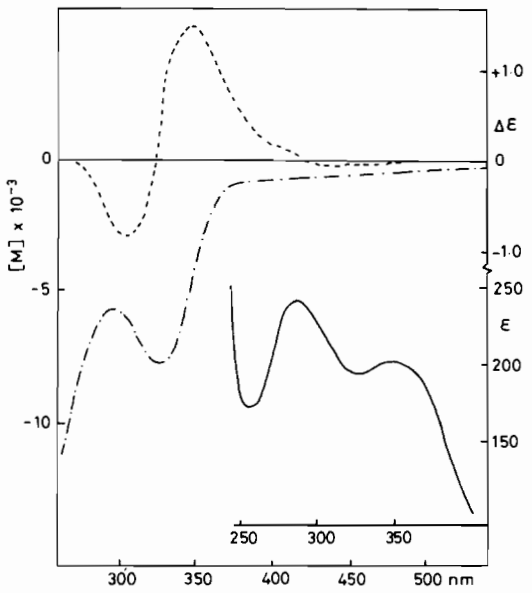

Fig. 4. The electronic absorption (———), ORD (– · –), and CD (- - -) spectra of Λ-*cis*-β-[Rh(SS-EDDP)(S-ala)].

Acknowledgements

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References

1 L. N. Schoenberg, D. W. Cooke and C. F. Liu, *Inorg. Chem.*, *7*, 2386 (1968).
2 Preparation of dichloro rhodium(III) complexes is to be published elswhere.
3 S. K. Hall and B. E. Douglas, *Inorg. Chem.*, *7*, 530 (1968).
4 S. K. Hall and B. E. Douglas, *ibid.*, *7*, 533 (1968).
5 A. J. McCaffery, S. F. Mason and R. B. Ballard, *J. Chem. Soc.*, 2883 (1965).
6 J. H. Dunlop, R. D. Gillard and N. C. Payne, *ibid.*, *(A)* 1469 (1967).
7 L. G. Marzilli and D. A. Buckingham, *Inorg. Chem.*, *6*, 1042 (1967).
8 C. W. Van Saun and B. E. Douglas, *ibid.*, *8*, 115 (1969).
9 P. J. Harnett, D. W. Watts and J. I. Legg, *ibid.*, *8*, 2534 (1969).
10 J. I. Legg, D. W. Cooke and B. E. Douglas, *ibid.*, *6*, 700 (1967).
11 J. I. Legg, *Chem. Commun.*, 675 (1967).