Stereospecificity and Diastereoselectivity in Mixed Ligand Complexes of Amino Acid Derivatives

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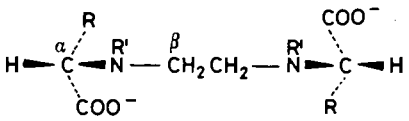
The problem of stereoselectivity in coordination compounds is very often related to the well-known stereochemical specificity of biological systems. We hope to shed some light onto this problem by studying the formation of simple ternary complexes composed of one metal ion and two different ligands. We have started to study the stereochemistry of the Co(III) ternary complexes with synthetic amino acids EDDA-type, I:



I

R′ = R = H (EBG) [1]
R′ = H, R = CH_3 (SS–EBA) [2]
R′ = H, R = i-C_3H_7 (SS–EBV) [3]
R′–R = –$(CH_2)_3$– (SS–EBP) [4]

The linear tetradentate ligands SS–EBA, SS–EBV, and SS–EBP are optically-active analogs of prochiral EBG. The tris chelated $[Co(EBAA)en]^+$ of a tetradentate ligand EBAA [5] can exist in four isomers (Fig. 1). Because of the tetrahedral stereochemistry of four-covalent nitrogen, the puckered chelate rings

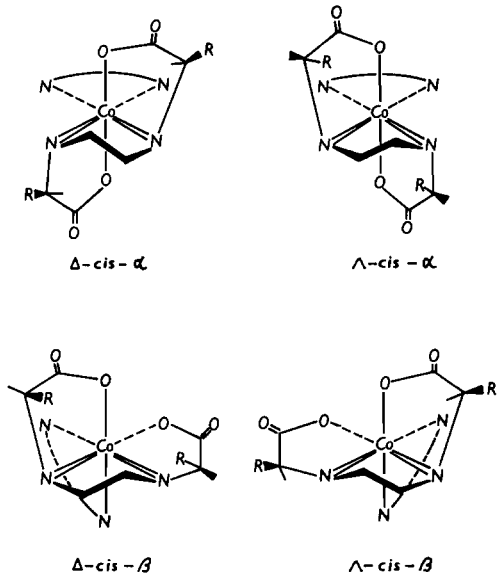


Fig. 1. The four possible isomers of $[Co(EBAA)en]^+$ ion.

in the *cis*-β isomer are somewhat strained and slightly distorted from the plane containing the donor N and O atoms, so that this isomer might be expected to be less stable than the *cis*-α one.

The complexes were prepared by oxidation of Co(II) in the presence of desired ligands using active carbon as a catalyst which would result in equilibrium. Separation and isolation of isomers were carried out either by column chromatography on ion-exchange resin [2, 6–8], or by fractional crystallization [4]. The absolute configurations of these isomers were assigned by considering ^1H and ^{13}C NMR, absorption and CD spectra, and the known configurations of some ligands. The yields of the diastereoisomers are listed in Table I. When Co(III)–EBAA complexes are synthesized under the above-mentioned conditions, the *cis*-α compound is essen-

TABLE I. Diastereoselectivity of Mixed Co(III) Complexes (in w.%).

Complex	Diastereoisomer				Ref.
	Δ-*cis*-α	Λ-*cis*-α	Δ-*cis*-β	Λ-*cis*-β	
$[Co(EBG)en]^+$	50	22	7	–	7, 8
$[Co(SS–EBA)en]^+$	36	30	10	–	2
$[Co(SS–EBV)en]^+$	83	–	<0.5	–	6
$[Co(SS–EBP)en]^+$	62	–	20	–	4
$[Rh(SS–EBA)en]^+$	80	–	–	–	9

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TABLE II. Comparison of V_W for Alkyl Substituents on C_α (in cm^3 mol^{-1}).

Parent amino acid	R	V_W
glycine	H	3.45[a]
α-alanine	CH_3	13.67[b]
α-amino butyric acid	C_2H_5	23.91[a]
valine	i-C_3H_7	34.13[a]
leucine, isoleucine	i-C_4H_9	44.35[c]

[a]Calculated from data in [12, 13]. [b]Ref. [12]. [c]Ref. [13].

tially obtained [7, 10, 11]. *Cis-β* complex can also be obtained, most favorably as mixed ligand complexes with a bidentate ligand *e.g.* carbonate, oxalate or 1,2-diamines [2, 4, 8]. In all cases known it is the *cis-α* isomer which is formed in a greater amount. Replacement of the hydrogen atom on the C_α by a methyl group introducing two asymmetric centers on the other hand produces only small stereoselectivity concerning the absolute configuration of the complex. In the Rh(III) complexes, however, the ligand showed more pronounced stereospecificity and yielded only the Δ-*cis-α* isomer [9]. The higher yield of the *cis-α* isomer supported the observation from molecular models that the direct intramolecular interligand interactions of the amine protons of the en with EBAA backbone are significantly greater in the *cis-β* isomer.

The two acidate arms are equivalent in the *cis-α* isomer. In the Δ enantiomer both R groups point away from the central chelate ring (C_β) while in the Λ isomer both point toward the central chelate ring backbone. The arms are non-equivalent in the *cis-β* isomer: one is in the plane formed by the cobalt atom and the backbone chelate ring, and the second is out-of-plane. Bulky substituent R produces rather large steric non-bonded repulsion between that and the central chelate ring backbone, and make the structure unstable. As a measure volume or bulk of substituents we considered van der Waals volume, V_W (Table II). Thus, the stereospecific formation of the Δ enantiomer may be postulated for substituents greater than C_2H_5. When SS–EBP coordinates as a tetradentate, only configuration of the asymmetric N can coordinate for a particular configuration of the asymmetric C_α atom. The factors determining stereospecific coordination in studied complexes seem to be mainly the steric non-bonded repulsion. Such steric repulsion, however, cause not only stereospecificity but also diastereoselectivity, with direct intramolecular interligand interactions and differences in the strain of the chelate rings being responsible.

There are examples where the diastereoselectivity of a multidentate optically-active ligand becomes important without the introduction of a second optically-active ligand into the coordination entity either. It seems therefore that the introduction of bulky substituents in the glycinic chelate rings of EBAA is sufficient to determine the absolute configuration of a ternary complex.

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5 Abbreviations used: EBAA, ethylenebisamino acid; EBG, ethylenebisglycinate = EDDA, ethylenediamine–N,N′–diacetate; SS–EBA, ethylenebis–S–α-alaninate; SS–EBV, ethylenebis–S–valinate; SS–EBP, ethylenebis–S–prolinate; en, ethylenediamine.
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