Asymmetric Synthesis of Threonine and Allo-threonine *via* Stereochemically Inert Dissymmetric Complexes of Cobalt(III)

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Summary The glycine fragments of the optically active cobalt(III) complexes (Ia and b), (IIa and b), and (IIIa and b) condense with acetaldehyde in water at pH 11, and decomposition of the resulting complexes gives a mixture of asymmetric threonine and allo-threonine.

TABLE

Enantiomeric composition of the mixture of amino-acids[a] obtained from the reaction of Λ- or Δ-complexes with acetaldehyde in water at pH 11·0—11·6; reaction times 40 min—3 h; glycine–acetaldehyde ratio 1:100; under Ar.

				Asymmetric yield		Enantiomeric composition of valine in final mixture	
		T/°C	Threo–allo ratio	Threonine	Allothreonine	%R	%S
(Ia)	Λ-[Co(Sal-Gly$_2$]	25	1·5:1	27·0% *R*	64·3% *R*		
(Ib)	Δ-[Co(Sal-Gly)$_2$]	11·5	1·2:1	46% *S*	55% *S*		
(IIa)	Λ-[Co(3-MeSal-Gly)$_2$] ..	25	2:1	70·0% *S*	16% *S*		
(IIIa)	Λ-[Co(Sal-*S*-Val)(Sal-Gly)] ..	17[b]	2:1	26·2% *R*	74% *R*	40·03	50·97
(IIIa)	"	17	2:1	3·8% *R*	62·8% *R*	17·0	83·0
(IIIb)	Δ-[Co(Sal-*S*-Val)(Sal-Gly)] ..	17	2·2:1	82·0% *S*	63·2% *S*	11·0	89·0

[a] G.l.c. analysis (S. Makaparksin, P. Birrel, and E. Gil-Av, *J. Chromatography Sci.*, 1970, **8**, 177). [b] At pH 12·2.

WE report here on the condensation of the glycine fragments of potassium Λ- and Δ-bis-(*N*-salicylideneglycinato)-cobaltate(III) (Ia and b), potassium Λ- and Δ-bis-(*N*-3-methylsalicylideneglycinato)cobaltate(III) (IIa and b), and diastereoisomers of potassium Λ- and Δ-(*N*-salicylideneglycinato-*N*-salicylidene-*S*-valinato)cobaltate(III)† (IIIa and b) with acetaldehyde, which, after decomposition of the complexes, yields a mixture of asymmetric threonine and allo-threonine. Salicylaldehyde in these complexes behaves as a pyridoxal analogue, increasing the mobility of the α-proton of glycine. The Co^{3+} complexes retain their dissymmetry during the reaction,[2] thus permitting imitation of the chiral environment of the active centre of pyridoxal-dependent enzymes. Projections of Dreiding models of (IIa) and (Ib) (Λ and Δ) are in the Figure.

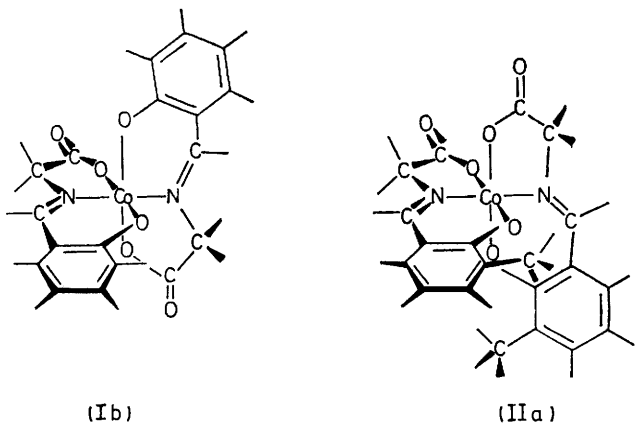
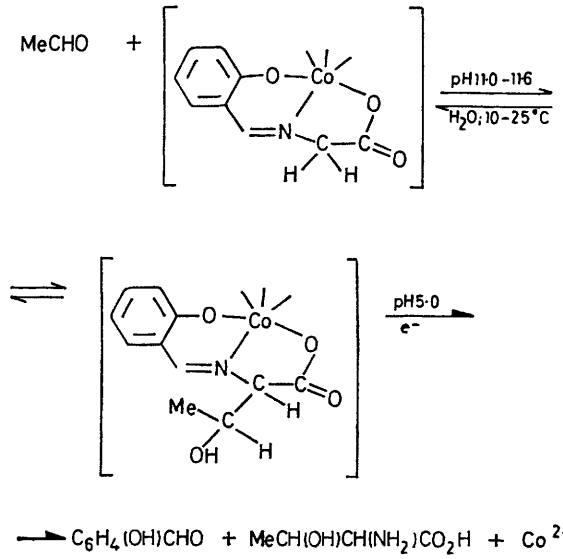


FIGURE. Projections of Dreiding models of potassium Λ-bis-(*N*-3-methylsalicylideneglycinato)cobaltate (IIa) and potassium Δ-bis-(*N*-salicylideneglycinato)cobaltate (Ib).

The protons of the glycine fragments in compounds (I)—(III) are diastereoisotopic and labile. They easily exchange with solvent under the influence of OH^- ions, and under similar conditions the glycine fragment undergoes condensation with acetaldehyde. After electrochemical decomposition of the mixture of diastereoisomeric complexes and removal of Co^{2+} ions a mixture of optically active threonines is isolated with a chemical yield of 80—90%. The results obtained are in the Table.



Compounds (Ia) and (IIIa) with the Λ absolute configuration give *R*-threonines, whereas compounds (Ib) and (IIIb) with the opposite configuration (Δ) give *S*-threonines. In the case of (III) the asymmetric yield varies depending on the degree of epimerization of the *S*-valine fragment. This testifies to the strong mutual influence of the asymmetric centres in these dissymmetric complexes. Condensation of (IIa) with acetaldehyde yields an excess of *S*-threonine rather than *R*-threonine. In other words, introduction of a methyl group into position 3 of the phenyl ring reverses the stereoselectivity in the series under investigation. This effect is to be expected taking into account the steric screening of the *pro*-*R*-protons of the glycine fragment by the methyl group of the neighbouring ligand in (IIa) (see Figure).

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† The absolute configuration Λ or Δ, of the complex corresponds to the left-hand or right-hand helicity of the ligands with respect to the C_2 axis of symmetry of the complexes, as in ref. 1.

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[2] D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1967, **89**, 5133; R. C. Job and T. C. Bruice, *ibid.*, 1974, **96**, 3809; R. G. Asperger and Ch.F. Liu, *Inorg. Chem.*, 1967, **6**, 796; M. Marakami and K. Takahashi, *Bull. Chem. Soc. Japan*, 1959, **32**, 308; Yu. N. Belokon', S. V. Vitt, M. M. Dolgaya, V. M. Belikov, and P. V. Petrovskii, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1972, 2776.