Novel Catalytic Resolution and Asymmetric Transformation of α-Dichloro(triethylenetetra-amine)cobalt(III) Dichloride†

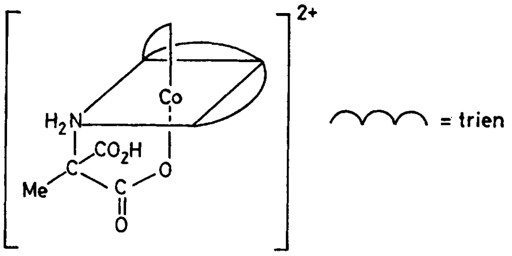
By Robert C. Job

(Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523)

Summary Reaction of racemic [α-(trien)$CoCl_2$] Cl with α-amino-α-methylmalonic acid in refluxing methanol, in the presence of triethylamine and catalytic amounts of naturally occurring chiral acids, produces high optical yields of a single enantiomeric product.

Gillard *et al.* have achieved a kinetic resolution of the $[(en)_2Co^{III}]^{3+}$ unit by isolation of a diastereomeric product with (*S*)-glutamic acid.[1] The $[(trien)Co^{III}]^{3+}$ unit has been resolved similarly using (*S*)-proline.[2] A second-order asymmetric transformation[3] of $[(en)_3Co^{III}]^{3+}$ utilizing 1 equiv. of (+)-tartaric acid has been reported.[4] A one-to-one ratio of chiral agent to metal complex was used in each of the above examples. This communication reports the first case of a *catalytic* resolution and asymmetric transformation of a cobalt(III) co-ordination complex.

When racemic α-dichloro(trien)cobalt(III) chloride (3·0 mmol) and α-amino-α-methylmalonic acid (3·0 mmol) are refluxed in methanol for 18—40 h with triethylamine (6 equiv.) and a chiral acid (0·01 equiv.), an orange crystalline precipitate, $(-)_{436}$-Λ-β_2-(trien)-(*R*)-aminomethylmalonatocobalt(III) dichloride (**1**) is formed in high optical purity.‡ The c.d. spectrum of (**1**) is nearly identical to that of a similar Λ-β_2 complex, with malonate bound in the *pro-R* configuration, the structure of which has been the subject of an *X*-ray determination.[5] The complex (**1**) was purified to constant rotation by fractional crystallization as the perchlorate salt {$[M]_{436}$ −4609° (1M HCl)}. It has been shown that acid-catalysed decarboxylation of aminomethylmalonate bound to tetra-aminocobalt(III) leads to an alanine



(1)

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† Abbreviations used: trien = triethylenetetra-amine; mam = α-amino-α-methylmalonate; en = ethylenediamine. For information on the α and β, and Δ and Λ nomenclature systems, see footnote 1 of ref. 7.

‡ Satisfactory elemental analyses were obtained. Compound (**1**) exhibits the expected methyl n.m.r. singlet at δ −1·80 *vs.* sodium dimethylsilapentanesulphonate.

complex.[6] The c.d. spectrum of the expected alanine complex formed upon acid-catalysed decarboxylation of (**1**) is identical to the published spectrum of Λ-β_2-(trien)Co^{III}-(alanine)$^{2+}$ with $[\theta]_{490}$ 7250°.[2] The location of the c.d. maxima and the i.r. spectrum in the 980—1100 cm^{-1} region further established the complex as β_2.[7]

TABLE. Results from various chiral agents.

Chiral agent	% Yield of (**1**)	% Λ-(**1**)	% Isolated yield of Λ-(**1**)
(*S*)-Phenylalanine (5·5 mg)	69·2	91·7	63·5
(*S*)-Phenylalanine (50 mg)	54·7	90·1	49·3
(+)-Tartaric acid (6·3 mg)	51·1	98·5	50·3
(*S*)-Glutamic acid (5·7 mg)	56·8	96·8	55·0
(*S*)-Aspartic acid (6·6 mg)	68·6	78·5	53·9
(*S*)-Alanine (6·8 mg)	53·0	68·9	36·5
None	59·7	50·1	29·9

The results of experiments with several naturally occurring chiral acids are summarized in the Table. In most cases the isolated yield of Λ products exceeds the 50% expected of a simple resolution, indicating that an asymmetric transformation has taken place. This point is strengthened upon examination of the mother liquors. Analysis of the fractions obtained from cation-exchange chromatography of the mother liquors from several experiments, using known ellipticities and absorption coefficients, reveals that approximately equal amounts of Δ and Λ species are present. Thus the overall yield of Λ products in a typical reaction is *ca.* 60—80%. Each of the four possible β_2 diastereomers§ is present to some extent [Λ-β_2-(trien)Co-(*R*-mam)$^{2+}$ (0·091 mmol), Λ-β_2-(trien)Co-(*S*-mam)$^{2+}$ (0·240 mmol), Δ-β_2-(trien)Co-(*R*-mam)$^{2+}$ (0·060 mmol), and Δ-β_2-(trien)Co-(*S*-mam)$^{2+}$ (0·269 mmol)]¶ along with some product representing decarboxylation into alanine complexes.

Independent confirmation of the lability of both the tetra-amine and malonate ligands was obtained by observing the racemization of pure (**1**) in methanol with triethylamine and sufficient water to effect solution. The half-life for disappearance of all optical activity was 7·8 h at 63 °C. The absorption spectrum remained essentially constant in character and magnitude during the course of the experiment.

A mass balance on the product analysis of the above mother liquor reveals the following total amounts of products: Λ-β 0·331 mmol, Δ-β 0·329 mmol, (*S*)-malonate 0·509 mmol, and (*R*)-malonate 0·151 mmol. While both Λ and Δ products are present in the mother liquor in equal amounts, the amount of total bound (*S*)-malonate far exceeds that of (*R*)-malonate. Thus, after precipitation of the Λ-β-(*R*)-malonate complex, and by the time the mother liquor has been analysed, the remaining tetra-amine ligand has already isomerized to an equal Δ,Λ mixture, whereas the bound (*R*)-malonate is still in a depleted state. This implies that the Δ–Λ equilibration proceeds significantly more readily than the malonate equilibration.

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§ Considering only (*S*,*S*) and (*R*,*R*) configuration about the secondary amine nitrogen atoms. No (*R*,*S*) or (*S*,*R*) isomers were observed (ref. 6).

¶ Obtained as the unipositive ions upon cation exchange chromotography of the mother liquor and identified by c.d. measurements.

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