Optical Resolution of Anionic Complexes by a Chromatographic Column containing (β-Cyclodextrinato)bis(ethylenediamine)cobalt(III)(1+) Chloride

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Chromatographic columns prepared from SP-Sephadex C-25 resins and Δ- and Λ-(β-cyclodextrinato)-bis(ethylenediamine)cobalt(III)(1+) chloride have been successfully applied to the optical resolution of *cis*- and *trans*-(*RS*-amino acidato)(nitrilotriacetato)cobaltate(III)(1−) complexes.

Recently we prepared some $[Co(N)_4(O)_2]^+$ type complexes [(N) = *N*-bonded ligand; (O) = *O*-bonded ligand] containing α or β-cyclodextrin (α- or β-CDX), where CDX co-ordinates directly to a cobalt(III) ion through the two deprotonated secondary hydroxy groups of the same glucose unit.[1] These complexes have two kinds of chiral sources, one arising from the chelate ring arrangement around the cobalt(III) ion and the other from the chiral CDX. Since these CDX complexes also carry a positive charge, they can be easily adsorbed on cation exchange resins. The chromatographic column thus prepared

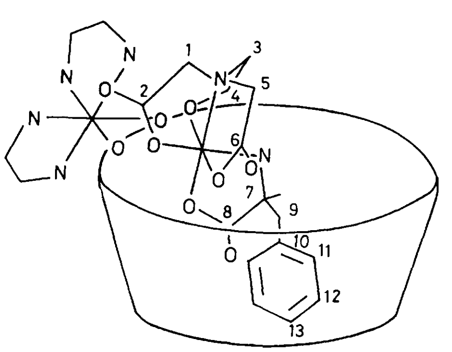

Figure 1. Proposed binding mode between Λ-[Co(β-CDX^{2-})(en)$_2$]$^+$ and *cis*-[Co(*S*-pheala)(nta)]$^-$.

Table 1. Optical resolution of anionic complexes by the chromatographic column containing Δ- or Λ-[Co(β-CDX^{2-})(en)$_2$]Cl.

	Column	
	Δ-β	Λ-β
Complex[a]	% E.e. (configuration)[b]	
cis-K[Co(*RS*-pheala)(nta)]	42% (*R*)	100% (*R*)
trans-K[Co(*RS*-pheala)(nta)]	13% (*R*)	35% (*R*)
cis-K[Co(*RS*-aoct)(nta)]	8% (*R*)	29% (*R*)
trans-K[Co(*RS*-aoct)(nta)]	3% (*R*)	2% (*R*)
cis-K[Co(*RS*-nleu)(nta)]	0%	0%
trans-K[Co(*RS*-nleu)(nta)]	0%	0%

[a] Abbreviations: amino acidato [NH$_2$CH(R)CO$_2$$^-$]: aoct = 2-amino-octanoato (R = [CH$_2$]$_5$Me), nleu = norleucinato (R = [CH$_2$]$_3$Me).
[b] Configuration of the first fractions.

from Δ- or Λ-(β-cyclodextrinato)bis(ethylenediamine)-cobalt(III) chloride[2] and SP-Sephadex C-25 resins have now been applied to the optical resolution of *cis*- and *trans*-K[Co(*RS*-am)(nta)] complexes[3] where *RS*-am and nta denote *RS*-amino acidato [NH$_2$CH(R)CO$_2$$^-$] and nitrilotriacetato [N(CH$_2$CO$_2$$^-$)$_3$], respectively. It is also advantageous that the resolution is possible by the use of only water as an eluent.

The column (80 cm × 1.5 cm i.d.) was packed first with SP-Sephadex C-25 (Na$^+$ form) resin up to a height of 15 cm and then with the resins prepared from Δ- or Λ-(β-cyclodextrinato)bis(ethylenediamine)cobalt(III) chloride and SP-Sephadex C-25 up to a height of 65 cm, the role of the former resin being to prevent the elution of the β-cyclodextrinato complexes. The racemic anionic complex (10 mg) dissolved in 1 cm^3 of water was placed on the top of the column and was eluted with distilled water at a rate of *ca.* 2 cm^3 min^{-1} at atmospheric pressure. The elution curve was obtained by measuring the absorbance of each fraction (1 cm^3) at the maximum wavelength of the first absorption band of the anionic complex. The first fractions showed CD spectra which were enantiomeric with respect to last fractions, though the band separation was not complete.

The results are shown in Table 1. In all experiments, the (*R*)-enantiomer is eluted before the (*S*)-enantiomer and the enantiomeric excess (e.e.) of the *cis*-isomer is higher than that of the corresponding *trans*-isomer. In general, the resolution trends in the Λ-β column are similar to those in the Δ-β column, though the resolution efficiency of the former is slightly higher than that of the latter. This means that the contribution of chirality due to the skew pairs of chelate rings is supplementary in the chiral recognition of the present system and the primary role is ascribed to the β-CDX molecules. Since the cavity of β-CDX is relatively wide, effective binding is possible for anionic complexes with large pendant groups such as a benzyl group or a long alkyl chain. The resolution percentages are higher for the complexes having such groups.

In order to determine the discriminating ability of the β-CDX complex, the ^{13}C NMR spectra were measured in the system Λ-[Co(β-CDX^{2-})(en)$_2$]Cl (en = ethylenediamine) and *cis*-K[Co(*RS*-pheala)(nta)] [pheala = phenylalaninato (R = CH$_2$Ph)].† In the nta moiety, two signals were observed only for each of the methylene (C-1) and the carbonyl (C-2) carbons of the out-of-the plane glycinate ring.[3] In the (*RS*)-pheala moiety, all carbons except for the methine carbon (C-7) and one carbon of the benzene ring (C-13) showed two split signals.‡ These splittings result from the difference in the induced shifts of the (*R*)- and (*S*)-enantiomers by the formation of diastereoisomeric host–guest complexes. Since such large splittings were not observed in the β-CDX and cis-K[Co(*RS*-pheala)(nta)] system, the co-ordination of β-CDX to a cobalt(III) ion enhances its chiral recognition capability.

A binding mode for the above system is proposed on the basis of the NMR spectra and the resolution experiments (Figure 1). This model explains the higher resolution percentages of the Λ-β column because in the system of Δ-[Co(β-CDX^{2-})(en)$_2$]$^+$ and *cis*-[Co(*RS*-pheala)(nta)]$^-$ the access of the nta moiety of the anionic complex to the positive centre is prevented by the arrangement of one of ethylenediamine chelate rings and consequently the electrostatic attraction will be reduced.

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References

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† Measured on a JEOL GSX400 spectrometer in D$_2$O. The concentrations of both complexes are *ca.* 0.05 mol dm^{-3}.

‡ δ(^{13}C): C-1 68.912, 68.853; C-2 183.265, 183.229; C-3 and C-5 69.999, 69.131; C-4 and C-6 181.572, 181.244; C-7 59.782; C-8 185.185, 185.031; C-9 38.634, 38.400; C-10 136.860, 136.612; C-11 and C-12 (130.161, 130.022), (129.650, 129.489); C-13 128.015.