CHEMISTRY LETTERS, pp. 101-104, 1994.

Highly Efficient Chromatographic Optical Resolution of *fac*-Tris(β-alaninato)cobalt(III) with an Optically Active ob_3 Isomer of Tris(*trans*-1,2-diaminocyclohexane)cobalt(III) Cation Adsorbed on a Cation-Exchange Resin

Tsutomu MIZUTA, Atsushi UCHIYAMA, Kazumasa UEDA, Katsuhiko MIYOSHI,* and Hayami YONEDA†
Department of Chemistry, Faculty of Science, Hiroshima University, 1-3-1, Kagamiyama, Higashi-Hiroshima 724

An extraordinarily high separation factor, amounting approximately to 7, was attained in the title system, where only the Λ enantiomer is strongly associated with the Δ-ob_3 isomer on the resin. The efficiency is explained in terms of the linearity of the triple hydrogen-bonds formed between the three lone-pairs of *fac*-$[Co(\beta\text{-ala})_3]$ and the three N-H groups of the Δ-ob_3-$[Co\{(+)\text{-chxn}\}_3]^{3+}$.

It is difficult to resolve racemic non-charged complexes into a pair of optically pure enantiomers, since they do not in general form diastereomeric crystals with an optically-active resolving reagent.1) Chromatography may serve as an effective means for this purpose. 2-5)

$[Co(\beta\text{-ala})_3]$ (β-ala = β-alaninato) is one of the neutral complexes whose optical resolution has been investigated in detail.6-8) Yoneda et al. demonstrated that *fac*-$[Co(\beta\text{-ala})_3]$ is separated into its pure enantiomers by means of a CM-Sephadex column using a solution of sodium *d*-tartrate in aqueous ethanol as an eluent.6) This chiral anion discriminates the chirality of the complex by making an intimate contact with the cationic triangular face composed of three amino groups of the complex. Since the complex has also an anionic triangular face composed of three carboxylate groups, its optical resolution may be also performed using a cationic resolving reagent which can interact with the anionic triangular face. Actually, optical resolution has been attempted on a column packed with SP-Sephadex (cation exchanger) on which is adsorbed an optically-active cation complex, Δ-$[Co(en)_3]^{3+}$, Δ-$[Co(sep)_3]^{3+}$, or Δ-lel_3-$[Co\{(-)\text{-chxn}\}_3]^{3+}$ (en = 1,2-diaminoethane, sep = 1,3,6,8,10,13,16,19-octaazabicyclo-[6,6,6]-eicosane, and chxn = 1,2-*trans*-diaminocyclohexane).9,10) The discrimination efficiency attained was, however, very low with any of these resolving reagents used.

---

† Present address: Department of Fundamental Natural Sciences, Okayama University of Science, Okayama 700.

Recently, we found that antimony *d*-tartrate anion, $[Sb_2(d\text{-tart})_2]^{2-}$ (*d*-tart = *d*-tartrate^{4-}), could discriminate the enantiomers of an ob_3 isomer of $[Co(chxn)_3]^{3+}$ more efficiently than those of a lel_3 isomer.11) A plausible association site of $[Sb_2(d\text{-tart})_2]^{2-}$ is a triangular face composed of the three oxygen atoms of a *d*-tart^{4-} fragment.12) Since the anionic face of *fac*-$[Co(\beta\text{-ala})_3]$ has a structural resemblance to the association site of $[Sb_2(d\text{-tart})_2]^{2-}$ regarding the arrangement of the three oxygen atoms, we expect that the racemic *fac*-$[Co(\beta\text{-ala})_3]$ is discriminated more efficiently with the optically active Δ-ob_3-$[Co\{(+)\text{-chxn}\}_3]^{3+}$ than with the Δ-lel_3-$[Co\{(-)\text{-chxn}\}_3]^{3+}$ previously investigated.9,10)

Δ-lel_3-$[Co\{(-)\text{-chxn}\}_3]^{3+}$ and Δ-ob_3-$[Co\{(+)\text{-chxn}\}_3]^{3+}$ were prepared by the literature method and their purity was checked by the circular dichroism (CD) spectra.13) These optically active complexes were adsorbed separately on the SP-Sephadex C-25 resin packed in a column with an appropriate size of 200 mm x 12 mm (I. D.). The columns were washed fully with water and then with an aqueous ethanol (30% v/v). A racemic *fac*-$[Co(\beta\text{-ala})_3]$ prepared by the literature method14) was loaded on the column and was eluted with aqueous ethanol at an elution rate of 0.3 ml/min. The eluates were fractionally collected, and the absorption and CD spectra were recorded for each fraction on a Shimadzu UV-160 spectrometer and a JASCO J-40CS spectropolarimeter.

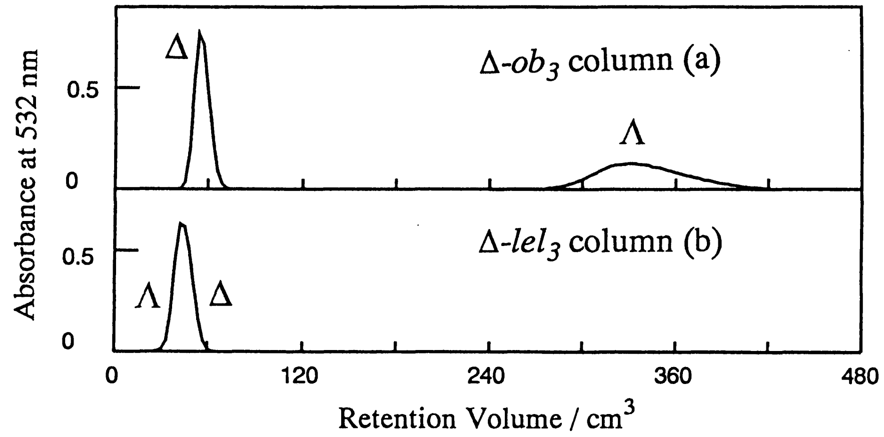


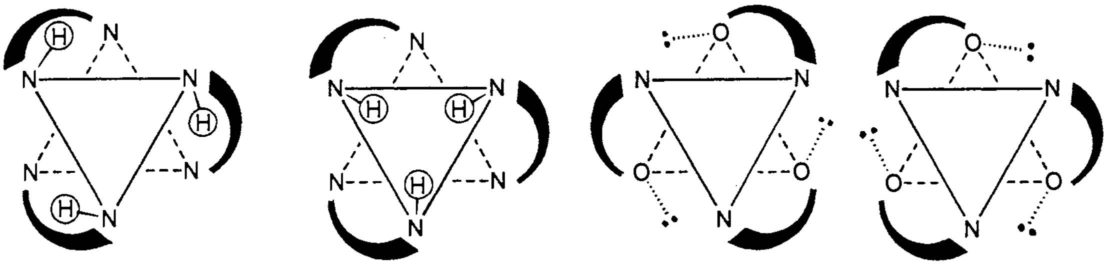
Fig. 1. Elution curves in the chromatographic resolution of *fac*-$[Co(\beta\text{-ala})_3]$ using the Δ-ob_3 column (a) and the Δ-lel_3 column (b).

A racemic *fac*-$[Co(\beta\text{-ala})_3]$ loaded on the top of a column which adsorbed Δ-ob_3-$[Co\{(+)\text{-chxn}\}_3]^{3+}$ (Δ-ob_3 column), was soon separated into two bands with elution. In Fig. 1-a are shown the elution curves obtained and the assignment of the absolute configuration7,8) for each band. A separation factor (α) is estimated to be approximately 7 from these elution curves. This value is surprisingly great compared with the previously reported value of 1.14, which was obtained using the *d*-tart^{2-} form of the anion-exchange resin.7,8)

On the other hand, when Δ-lel_3-$[Co\{(-)\text{-chxn}\}_3]^{3+}$ is used as a resolving reagent (Δ-lel_3 column), both enantiomers were eluted as a single band as shown in Fig. 1-b; a CD spectrum of a fraction at the front of the band showed that the Λ enantiomer was eluted slightly faster as previously reported.9,10)

To understand a mechanism which leads to such a drastic change in the discrimination efficiency, the elution curves shown in Fig. 1 are examined. A retention volume of Λ-*fac*-[Co(β-ala)$_3$] on the Δ-*ob*$_3$ column is much greater than those of other three combinations Δ-*fac*—Δ-*ob*$_3$, Λ-*fac*—Δ-*lel*$_3$, and Δ-*fac*—Δ-*lel*$_3$, meaning that the *fac*-[Co(β-ala)$_3$] is strongly associated with the chiral selector only in the combination of Λ-*fac*—Δ-*ob*$_3$. Therefore, we assume an extraordinarily attractive interaction present stereoselectively in this combination. Then, the molecular structures shown in Fig. 2 are considered for the elucidation of the specific interaction assumed. The most plausible association sites of the Δ-*ob*$_3$-[Co{(+)-chxn}$_3$]$^{3+}$ and the Δ-*lel*$_3$-[Co{(-)-chxn}$_3$]$^{3+}$ are the triangular faces which are composed of three N-H bonds directed along the three-fold axis of the complexes,15) as shown in Fig. 2. The same face is also present on the opposite side of each figure. The three N-H bonds of the Δ-*ob*$_3$ complex have a counterclockwise helicity when viewed from the front- to the back-side of the figure,16) while those of the Δ-*lel*$_3$ complex are oriented almost parallel to the three-fold axis and thus have no practical helicity. On the other hand, the association site of *fac*-[Co(β-ala)$_3$] is a triangular face composed of three carboxyl oxygen atoms coordinated to the Co(III). If we assume the sp^2 hybridization for these oxygen atoms, three lone-pairs are disposed on this triangular face so as to have a counterclockwise helicity for the Λ-*fac* complex and a clockwise helicity for the Δ-*fac* complex, as shown in Fig. 2. Since the three N-H bonds of the Δ-*ob*$_3$ complex have the same helicity as that of the three lone-pairs of Λ-*fac*-[Co(β-ala)$_3$], these N-H bonds are aligned nicely with the respective lone-pairs so as to hydrogen-bond strongly to them. In the combination of the Δ-*ob*$_3$ complex with the Δ-*fac* complex, on the other hand, no such strong hydrogen-bonds are formed, since each association site has an opposite helicity. The highly efficient optical resolution attained here is thus interpreted.

On the other hand, in the case of Δ-*lel*$_3$-[Co{(-)-chxn}$_3$]$^{3+}$ as a selector, the fitness of the orientation of the N-H bonds to the lone-pairs is bad to a similar extent for both enantiomers of *fac*-[Co(β-ala)$_3$], because the three N-H bonds have no practical helicity. Thus, the Δ-*lel*$_3$ complex on the resin can neither discriminate *fac*-[Co(β-ala)$_3$], nor hold it strongly through the hydrogen-bonds. In practice, the Δ-*lel*$_3$ complex prefers the Δ-*fac*



Δ-*ob*$_3$-[Co{(+)-chxn}$_3$]$^{3+}$ Δ-*lel*$_3$-[Co{(-)-chxn}$_3$]$^{3+}$ Λ-*fac*-[Co(β-ala)$_3$] Δ-*fac*-[Co(β-ala)$_3$]

Fig. 2. Schematic drawings of the association sites of the complexes.

complex slightly to the Λ-*fac* complex, and so the inverted selectivity is obtained, which has been interpreted in terms of a small steric repulsion arising between the chxn and β-ala chelate rings in the hetero-chiral combination (Λ-*fac*—Δ-lel_3).9,10) The similar steric repulsion may also operate in the case of the Δ-ob_3 complex as a selector, but its contribution is considered much smaller.

Finally, optical resolution of *fac*-[Co(β-ala)$_3$] attained here on the Δ-ob_3 column is so efficient that we are now investigating the optical resolution of structurally-related complexes with chiral selectors having helically-disposed N-H groups and the application of these systems to stereoselective electron-transfer reactions.

References

1) To our knowledge, two examples have been reported in which an electrically neutral metal complex is resolved via diastereomeric crystal formation; M. Kita, K. Yamanari, K. Kitahama, and Y. Shimura, *Bull. Chem. Soc. Jpn.*, **54**, 2995 (1981); A. F. Drake, J. M. Gould, S. F. Mason, C. Rosini, and F. J. Woodley, *Polyhedron*, **2**, 537 (1983).
2) H. Yoneda, *J. Liq. Chromatogr.*, **2**, 1157 (1979); H. Yoneda, *J. Chromatogr.*, **313**, 59 (1984).
3) Y. Okamoto, S. Honda, E. Yashima, and H. Yuki, *Chem. Lett.*, **1983**, 1221.
4) H. Yoneda, T. Yukimoto, Y. Kushi, and H. Nakazawa, *J. Liq. Chromatogr.*, **9**, 573 (1986).
5) H. Nakazawa, H. Ohtsuru, and H. Yoneda, *Bull. Chem. Soc. Jpn.*, **60**, 525 (1987).
6) H. Yoneda and T. Yoshizawa, *Chem. Lett.*, **1976**, 707.
7) S. Yamazaki, T. Yukimoto, and H. Yoneda, *J. Chromatogr.*, **175**, 317 (1979).
8) T. Yukimoto and H. Yoneda, *J. Chromatogr.*, **210**, 477 (1981).
9) U. Sakaguchi, I. Yamamoto, S. Izumoto, and H. Yoneda, *Bull. Chem. Soc. Jpn.*, **56**, 153 (1983).
10) K. Miyoshi, Y. Sakamoto, A. Ohguni, and H. Yoneda., *Bull. Chem. Soc. Jpn.*, **58**, 2239 (1985).
11) T. Mizuta, K. Sasaki, and K. Miyoshi, manuscript in preparation.
12) K. Miyoshi, S. Izumoto, and H. Yoneda, *Bull. Chem. Soc. Jpn.*, **59**, 3475 (1985).
13) S. E. Harnung, B. S. Sorensen, I. Creaser, H. Maegaard, U. Pfenninger, and C. E. Schaffer, *Inorg. Chem.*, **15**, 2123 (1976); P. Osvath and G. Lappin, *Inorg. Chem.*, **26**, 195 (1987).
14) M. B. Celap, S. R. Niketic, T. J. Janjic, and V. N. Nikolic, *Inorg. Chem.*, **6**, 2063 (1967).
15) The presence of a cyclohexane group on each chelate ring will block the access of *fac*-[Co(β-ala)$_3$] along the C_2 axis. In addition, three N-H groups are available for the hydrogen-bonds along the C_3 axis, whereas only two would be available along the C_2 axis. Thus, the association along the C_3 axis is the most likely.
16) T. Mizuta, K. Toshitani, and K. Miyoshi, *Inorg. Chem.*, **30**, 572 (1991).

(Received October 12, 1993)