CHEMISTRY LETTERS, pp. 1487 - 1490, 1984.

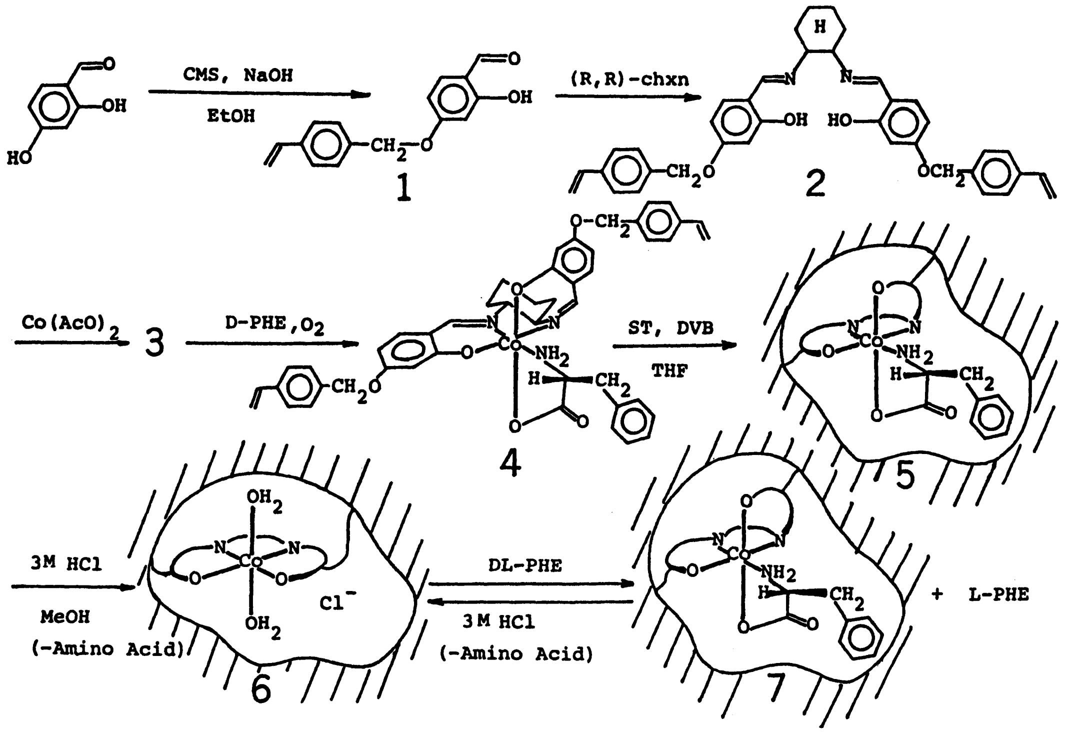
TEMPLATE SYNTHESIS OF POLYMER SCHIFF BASE COBALT(III) COMPLEX AND FORMATION OF SPECIFIC CAVITY FOR CHIRAL AMINO ACID

Yuki FUJII,* Katsuhiro KIKUCHI, Katsuhiro MATSUTANI, Koji OTA,
Masami ADACHI, Masato SYOJI, Ikuo HANEISHI, and Yasuo KUWANA
Department of Chemistry, Ibaraki University, Mito, Ibaraki 310

Template synthesis for Δ-β_2-[Co(Schiff base)(D-phe)] (Schiff base = 4-(p-vinylbenzyloxy)-sal$_2$-(R,R)-chxn) was carried out by copolymerizing the complex with styrene and divinylbenzene. After treating the formed polymer complex gel with HCl, the gel took in D-phe preferentially (maximum optical purity = 74%), when it reacted with an excess of DL-PHE.

Template synthesis of macromolecules is an attractive subject for preparing active site and/or specific cavity in the field of biomimetic and separation chemistry.[1-7] We applied the template synthesis to Co(III)-Schiff base complex with D-phe and succeeded in forming a polymer complex gel which discriminates the chirality of amino acid in high optical yield.

The preparative scheme is shown below. 4-(p-Vinylbenzyloxy)salicylaldehyde **1** was prepared from 4-hydroxysalicylaldehyde and chloromethylstyrene (CMS) by employing a similar method to 4-benzyloxysalicylaldehyde.[8] Although m- and p-mixture (6:4) of CMS was used, p-vinylbenzyloxy-derivative **1** (mp = 102 °C) crystallized preferentially in about 16% yield and was characterized by ^{1}H and ^{13}C NMR spectra. Schiff base ligand **2** (mp = 205 °C) was prepared by the use of (1R,2R)-1,2-diaminocyclohexane (R,R-chxn).[9] Mixed ligand Co(III) complex **4** (dark green) was synthesized from Co(II)-Schiff base complex **3** and D-phenylalanine (D-PHE) under air oxidation conditions.[10,11] The Δ-β_2-structure of **4** was confirmed from electronic, CD, and ^{1}H NMR spectra.[10-12] The complex **4** (1.0 g) was then copolymerized with styrene (ST) and divinylbenzene (DVB) (the mol fraction of feed; **4**:ST:DVB = 1:20:4) in THF at about 63 °C for a day by the use of α,α'-azo-



bis(isobutyronitrile) (AIBN) as initiator. The polymer complex gel 5 thus formed was filtered, washed with THF and $CHCl_3$, and dried under vacuum. Yield, about 3.7 g. 5 is green in color and insoluble in THF, $CHCl_3$, CH_3OH, etc., whereas 4 is very soluble in the organic solvents; indicating that 1) radical polymerization occurs quite well in this system, though metal ions often inhibit the radical polymerization, 2) the complex part of 5 is bonded covalently to the polymer part, and 3) 5 is a crosslinked copolymer. From elemental analysis, the mol fraction of the copolymer 5 was estimated to be $(complex)_1(ST)_{20}(DVB)_4$.

When HCl (3 M, 3 cm^3) was added to the suspension of 5 (5.0 g) in CH_3OH (200 cm^3), the green color of 5 turned instantly to brown. The brown polymer complex gel 6 was filtered, washed with CH_3OH, and dried in vacuo. Yield, 4.86 g. The filtrate and washing solution were combined and evaporated to dryness to recover the D-phe dissociated from 5 as D-PHE·HCl. No racemization was confirmed from the optical rotation of the recovered D-PHE·HCl. The chemical properties of 6 are very resemble to those of trans-$[Co(sal_2en)(H_2O)_2]Cl$, and the elemental analysis of 6 corresponded to $([Co(Schiff\ base)(H_2O)_2]Cl)_1(ST)_{20}(DVB)_4$.

The polymer complex gel 6 (about 200 mesh, 3.5 g) was added to CH_3OH-$CHCl_3$ (1:1) solution (1400 cm^3) of DL-PHE (0.5 g) and the mixture was stirred for two days at room temperature. Whereby, the brown color of 6 turned to green within 10 min. The polymer complex gel 7 thus formed was filtered, washed with CH_3OH,

Table 1. Weight and Optical Purity (O.P.) of Recovered PHE·HCl

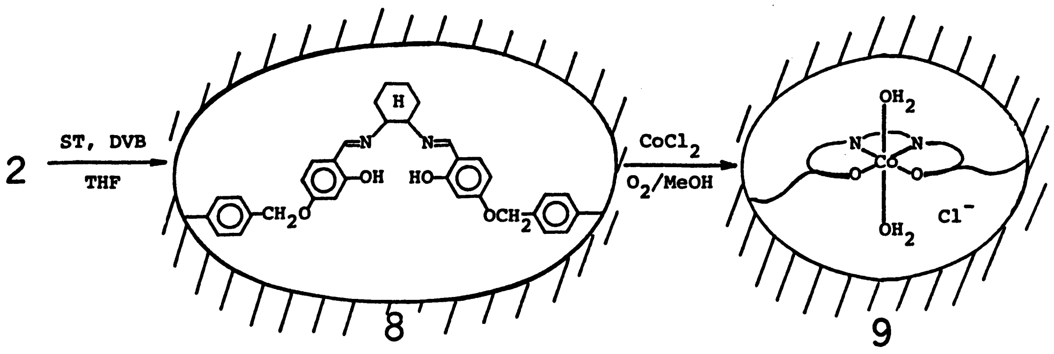
Complex	DL-PHE	Weight and O.P. of Recovered PHE·HCl From Reaction Soln.	 From Complex	$\text{O.P.}_{\max}$ a)
5 5.000 g	——	——	0.294 g (D, 100%)	——
6 3.500 g	0.500 g	0.488 g (L, 16%)	0.120 g (D, 65%)	74 ±1%
9 3.502 g	0.500 g	0.499 g (L, 9%)	0.111 g (D, 41%)	48 ±1%
10 1.000 g	1.000 g	1.015 g (L, 10%)	0.203 g (D, 50%)	57 ±2%

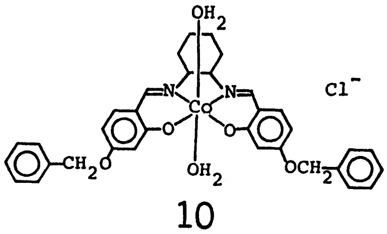
a) Estimated optical purity of coordinated amino acid to complex (calculated value), when a large excess of racemic amino acid is used for reaction. This value is the measure of chiral discrimination of complex, because the system is thermodynamic in origin and the O.P. of amino acid varys depending on the reaction mol ratio between complex and racemic amino acid.[10]

and dried in vacuo. A small amount of HCl (6 M) was added to the mixture of the filtrate and washing solution, and the solution was evaporated to dryness to recover unreacted PHE as hydrochloride salt. On the other hand, 7 was treated with HCl (3 M) in CH_3OH, and PHE·HCl and brown polymer complex 6 were recovered by the same method for 5. The weight and optical purity of recovered PHE·HCl are listed in Table 1. The reaction between 6 and DL-PHE was repeated twice, but the results were invariable within the experimental error.

In order to evaluate the template effect, non-template polymer complex 9 and monomer complex 10 were prepared and their chiral recognition was tested by the use of the similar method to 6. The preparative method of 9 is shown below. The mol fraction of feed; 2:ST:DVB = 1:20:4. The chemical properties of 9 and 10 were very similar to those of 6, except for 10 being soluble in $CHCl_3$. It should be noted that the reaction of 9 with DL-PHE is much slower than that of 6. The results of chiral discrimination for 9 and 10 are also listed in Table 1.

Table 1 indicates that 1) the selectivity for chiral recognition ($\text{O.P.}_{\max}$) of





10

the template polymer complex 6 is higher than that of the monomer complex 10, 2) the selectivity of 10 is almost the same as that of trans-[Co(sal$_2$-(R,R)-chxn)(H$_2$O)$_2$]Cl[10]; suggesting the effect of 4-benzyloxy group is quite small, and 3) the selectivity of non-template polymer complex 9 is lower than that of 10. Therefore, these results clearly indicate that template effect operates quite effectively in this system. We are now undertaking the study of colum chromatographic use of the polymer Schiff base Co(III) complex for the separation of DL-amino acids.

The authors wish to thank Prof. Yoshimi Kurimura and Dr. Yoshihito Osada of Ibaraki University, for their helpful discussion. This study was supported in part by a Grant-in-Aid for Scientific Research (No. 59470032) from the Ministry of Education, Science and Culture, to whom the authors are grateful.

References

1) K. J. Shea, E. A. Thompson, S. D. Pandy, and P. S. Beauchamp, J. Am. Chem. Soc., 102, 3149 (1980).
2) G. Wulff, A. Sarhan, and K. Zabrochi, Tetrahedron Lett., 44, 4329 (1973).
3) G. Wulff and W. Verper, J. Chromatogr., 167, 171 (1978).
4) G. Wulff, R. Kemmerer, J. Vietmeier, and H. G. Poll, Nouv. J. Chim., 6, 681 (1982).
5) H. Nishide and E. Tsuchida, Makromol. Chem., 177, 2295 (1976).
6) H. Nishide, J. Deguchi, and E. Tsuchida, J. Poly. Sci., Polym. Chem. Ed., 15, 3023 (1977).
7) S. N. Gupta and D. C. Neckers, J. Polym. Sci., Polym. Chem. Ed., 20, 1609 (1982).
8) J. Daly, L. Horner, and B. Witkop, J. Am. Chem. Soc., 83, 4787 (1961).
9) R. G. Asperger and C. F. Liu, Inorg. Chem., 4, 1492 (1965).
10) Y. Fujii, M. Sano, and Y. Nakano, Bull. Chem. Soc. Jpn., 50, 2609 (1977).
11) Y. Fujii, M. Matsufuru, A. Saito, and S. Tsuchiya, Bull. Chem. Soc. Jpn., 54, 2029 (1981).
12) Y. Kushi, T. Tada, Y. Fujii, and H. Yoneda, Bull. Chem. Soc. Jpn., 55, 1834 (1982).

(Received May 21, 1984)