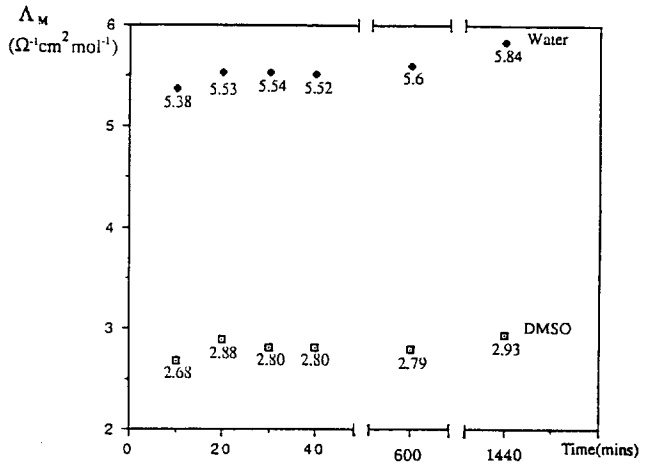

Figure 2. Molar conductance in water(◆) and dimethylsulfoxide (□) of *cis*-3-aminohexahydroazepine(1,1-cyclobutanedicarboxylato) platinum(II) at room temperature.

irrespective of time indicating the covalent nature of Pt-O bonds and the absence of separated ionic species even in DMSO solution in contrast to *cis*-$Cl_2(NH_3)_2Pt$[21]. In conclusion, the spectroscopic data together with conductance measurement are consistent with the stable molecular structure in the solid state for the title complex.

Acknowledgement. This research was supported by the Ministry of Science and Technology.

References

1. William, S. D.; Einhorn, L. H. in Prestayko, A. W.; Crooke, S. T.; Carter, S. K. Eds.; In *Cisplatin: Current Status and New Developments*; Academic Press: New York, 1980; p 323.
2. Leohrer, P. J.; Einhorn, L. H. *Ann. Intern. Med.* **1984**, *100*, 701.
3. Pouskouleli, G.; Kourounakis, P. *Biochem. Exp. Biol.* **1980**, *16*, 191.
4. Rosenberg, B. *Cancer Treat. Rep.* **1979**, *63*, 1433.
5. Rosenberg, B. *Interdisciplinary Science Reviews* **1978**, *3*, 134.
6. Von Hoff, D. D.; Schilsky, R.; Reichart, C. M. *Cancer Treat. Rep.* **1979**, *63*, 1439.
7. Krakoff, I. H. *Cancer Treat. Rep.* **1979**, *63*, 1523.
8. Kedar, A.; Cohen, M. E.; Freeman, A. I. *Cancer Treat. Rep.* **1978**, *62*, 819.
9. Burchenal, J. H.; Kalaher, K.; O'Toole, T.; Chisholm, J. *Cancer Res.* **1977**, *37*, 2455.
10. Eastman, A.; Bresnick, E. *Biochem. Pharmacol.* **1981**, *30*, 2721.
11. Barnard, C. F. J.; Cleare, M. J.; Hydes, P. C. *Chem., Bri.* **1986**, 1001.
12. Puniyani, S.; Srivastava, T. S. *Inorg. Chim. Acta.* **1987**, *131*, 95.
13. Gandolfi, O., Apfelbaum, H. C.; Blum, J. *Inorg. Chim. Acta.* **1987**, *135*, 27.
14. Bruck, M. A.; Ban, R.; Noji, M.; Inagaki, K.; Kidani, Y. *Inorg. Chim. Acta.* **1984**, *92*, 279.
15. Van Kralingen, C. G.; Reedijk, J.; Spek, A. L. *Inorg. Chem.* **1980**, *19*, 1481.
16. Keiichi, M.; Shimzo, I.; Masanori, M. Jpn. Kokai Tokkyo Koho JP 63,307,890, 1988.
17. Sheldrick, G. M. *SHELX-76: Program for Crystal Structure Determination*; University of Cambridge, England, 1976.
18. Neidle, S.; Ismail, I. M.; Sadler, P. J. *J. Inorg. Biochem.* **1980**, *13*, 205.
19. Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds, 4th Ed.*; John Wiley & Sons: New York, 1986; p 233.
20. Bitha, P.; Morton, G. O.; Dunne, T. S.; Delos Santos, E. E.; Lin, Y.; Boone, S. R.; Haltiwanger, R. C.; Pierpont, C. G. *Inorg. Chem.* **1990**, *29*, 645.
21. Watkins, D. M. *Biochimie.* **1978**, *60*, 835.

Use of Lanthanide Metal Ions in Chiral Ligand Exchange Chromatography

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Received August 6, 1993

Chiral ligand exchange chromatography has been extensively used for resolving racemic α-amino acids without derivatization.[1] Transition metal ion complexes of optically pure α-amino acids have been usually applied as chiral mobile phase additives[2] or chiral stationary phases[3] after binding to solid column support such as silica gel or polymer in chiral ligand exchange chromatography. The most frequently used transition metal ion in chiral ligand exchange chromatography is Cu^{2+}. Other transition metal ions such as Zn^{2+}, Co^{2+}, Ni^{2+}, Cd^{2+} and Hg^{2+} have also been rarely adopted in chiral ligand exchange chromatography.[1] However, lanthanide metal ions have not been selected previously in chiral ligand exchange chromatography.[4] In our recent study,[5] we demonstrated that lanthanide metal ions form 1 : 1 complex with optically active L-proline. It was reported, in that study, that the heterocyclic nitrogen atom and the carboxylate of L-proline are involved in the chelate formation and the thermodynamic constants for the complexation of L-proline with lanthanide metal ions are similar to those with Cu^{2+} and Zn^{2+}. Based on these results, the possibility of the use of lanthanide metal ions in chiral ligand exchange chromatography was proposed in that paper.[5] To elucidate the proposal, we report the examples for the use of lanthanide metal ions in chiral ligand exchange chromatography.

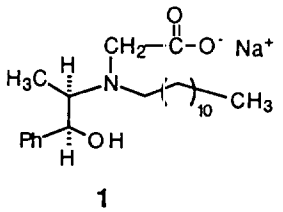
Recently, we showed that a dynamic chiral stationary phase containing Cu^{2+} complex with (1S, 2R)-N,N-carboxymethyldodecylnorephedrine monosodium salt **1** tentatively

Table 1. Resolution of Racemic α-Amino Acids on (1S, 2R)-Norephedrine Derivative **1** Loaded onto a Commercial Octadecyl-Silica Gel Column[a]

AA[b]	0.2 mM $LaCl_3$			0.2 mM $CeCl_3$			0.2 mM $PrCl_3$			0.2 mM $GdCl_3$			0.2 mM $HoCl_3$		
	k_1'[c]	k_2'[d]	α[e]	k_1'[c]	k_2'[d]	α[e]	k_1'[c]	k_2'[d]	α[e]	k_1'[c]	k_2'[d]	α[e]	k_1'[c]	k_2'[d]	α[e]
Ala	2.89(L)	4.29(D)	1.48	1.56(L)	2.26(D)	1.45	2.75(L)	3.82(D)	1.39	2.17(L)	3.23(D)	1.49	1.30(L)	1.86(D)	1.43
Val	7.18(L)	9.77(D)	1.36	3.25(L)	4.24(D)	1.30	4.92(L)	6.73(D)	1.37	3.20(L)	4.51(D)	1.41	2.70(L)	3.65(D)	1.35
Leu	14.00(L)	24.30(D)	1.74	6.61(L)	11.28(D)	1.71	9.08(L)	15.75(D)	1.73	9.56(L)	15.90(D)	1.66	5.38(L)	9.32(D)	1.73
Pro	3.29(D)	5.55(D)	1.69	2.70(L)	4.33(D)	1.60	3.02(L)	5.10(D)	1.69	2.15(L)	3.50(D)	1.63	2.40(L)	3.93(D)	1.64
Met	14.57(L)	22.08(D)	1.52	6.74(L)	9.16(D)	1.36	9.78(L)	14.16(D)	1.45	9.93(L)	13.77(D)	1.39	6.05(L)	8.48(D)	1.40
Phegl	14.86(L)	24.62(D)	1.66	9.40(L)	15.08(D)	1.60	11.60(L)	18.40(D)	1.59	14.01(L)	22.79(D)	1.63	8.69(L)	13.81(D)	1.59
Asp	1.64(D)	2.55(L)	1.66	0.79	0.79	no	1.47	1.47	no	1.98	1.98	no	1.61(D)	1.96(L)	1.22
His	5.84	5.84	no	4.32(D)	4.87(L)	1.13	5.07	5.07	no	5.85	5.85	no	3.49(D)	3.89(L)	1.11
Gln	3.28	3.28	no	3.15(L)	3.81(D)	1.21	3.29(L)	4.04(D)	1.23	3.17(L)	4.35(D)	1.37	2.63(L)	3.20(D)	1.22
Glu	2.26	2.26	no	1.70(L)	2.07(D)	1.22	2.78	2.78	no	2.95	2.95	no	2.40(L)	2.84(D)	1.18
Arg	7.95(L)	9.74(D)	1.23	6.46	6.46	no	7.02	7.02	no	7.56(L)	8.83(D)	1.17	4.91(L)	5.51(D)	1.12
Ser	3.05	3.05	no	2.61	2.61	no	2.86	2.86	no	3.07	3.07	no	2.67	2.67	no
Thr	4.24	4.24	no	3.17	3.17	no	2.80	2.80	no	3.47	3.47	no	2.77	2.77	no
Cys	1.41	1.41	no	1.33	1.33	no	1.27	1.27	no	1.23	1.23	no	1.44	1.44	no

[a] Chromatography was performed with an instrument consisted of a Waters Model U6K Liquid Chromotograph Injector, a Waters Model 441 Absorbance Detector (254 nm UV) and a Waters Model 740 Data Module Recorder. All data were obtained by using a mixed solvent of acetonitrile and water (10/90, v/v) containing lanthanide metal trichloride (2×10^{-4} M) such as $LaCl_3$, $CeCl_3$, $PrCl_3$, $GdCl_3$, or $HoCl_3$ as a mobile phase with flow rate of 0.8 ml/min at room temperature. [b] Full names of amino acids are as following. Ala: Alanine, Val: Valine, Leu: Leucine, Pro: Proline, Met: Methionine, Phegl: Phenylglycine, Asp: Aspartic acid, His: Histidine, Gln: Glutamine, Glu: Glutamic acid, Arg: Arginine·HCl, Ser: Serine, Thr: Threonine, Cys: Cysteine. [c] Capacity factor for the first eluted enantiomer. Absolute configuration of the first eluted enantiomer is in the parenthesis. [d] Capacity factor for the second eluted enantiomer. Absolute configuration of the second eluted enantiomer is in the parenthesis. [e] Separation factor. No resolution was denoted by no.

loaded onto a C_{18}-silica gel column can be used for resolving underivatized racemic α-amino acids.[6,7] To test the possibility of the use of lanthanide metal ions in chiral ligand exchange chromatography for resolving underivatized α-amino acids, a dynamic chiral stationary phase was prepared as described previously[6,7] by tentatively loading **1** onto a C_{18}-silica gel column (Waters μ Bondapak™ C_{18}, 3.9×300 mm column). To resolve racemic α-amino acids on the dynamic chiral stationary phase prepared, 10% acetonitrile solution in water containing lanthanide metal trichloride such as $LaCl_3$, $CeCl_3$, $PrCl_3$, $GdCl_3$, or $HoCl_3$ (2×10^{-4} M) was eluted through the column until the baseline (254 nm UV monitor) became stable and then, racemic α-amino acid samples were injected.



1

The chromatographic results for resolving various racemic α-amino acids on the dynamic chiral stationary phase prepared are summarized in Table 1. As shown in Table 1, various racemic α-amino acids are resolved with reasonable separation factors with a few exceptions. The five lanthanide metal ions used in this study do not show any notable differences in resolving α-amino acids as shown in Table 1. Among others, $HoCl_3$ seems to be more general in resolving α-amino acids as evidenced by the number of amino acids resolvable (11 amino acids are resolved) with this metal compound. D-Enantiomers are usually retained longer than L-enantiomers on the column for α-amino acids having a simple α-alkyl side chain such as alanine, valine, and leucine, etc. However, for α-amino acids having hydrophilic side chain such as aspartic acid and histidien, L-enantiomers elute second. These elution orders are exactly consistent with those obtained using Cu^{2+}.[6,7]

The elution orders obtained using Cu^{2+} have been explained by the chiral recognition model proposed previously.[6,7] The diastereomeric ternary complex formed from the fixed ligand, (D)-α-amino acid and Cu^{2+} was presumed to be more stable than that from the fixed ligand, (L)-α-amino acid and Cu^{2+} because the α-alkyl substituent of simple (D)-α-amino acids is hydrophobically attracted by the octadecyl chains of silica gel while that of (L)-α-amino acid is directed into the bulk of aqueous mobile phase and provides some instability. The rapid and reversible formation of energetically different two diastereomeric complexes from the fixed ligand (chiral selector), two enantiomers of α-amino acids and lanthanide metal ion is also expected to result in the separation of two enantiomers. However, it should be noted that the structure of the diastereomeric complex formed from the ligand, α-amino acid and lanthanide metal ion may be quite different from that of the corresponding Cu^{2+} complex; the lanthanide metal ions employed in this work are larger in size, higher in nuclear charge, and have higher coordination numbers than Cu^{2+} ion. The higher nuclear charge and the

higher coordination numbers of the lanthanide metal ions may be also responsible for the increased capacity factors denoted by k_1' or k_2' in Table 1 as compared to those with Cu^{2+}.[6,7]

It is well known that ligand field stabilization energies are very small for the lanthanide metal ions and the thermodynamic properties of the lanthanide complexes can be fairly accurately correlated by the electrostatic consequences of charge and size.[8] If the interaction between lanthanide metal ion and resolving α-amino acid is mainly electrostatic, one can expect the steady increase in the capacity factors as the atomic number of lanthanide increases. However, the variation in the capacity factors according to the lanthanide metal ions does not show any notable trend. This may stem from the fact that the considerable change in size of the lanthanide ions from La^{3+} (1.17 Å) to Ho^{3+} (1.04 Å) might result in appreciably different structure among homologous lanthanide complexes with α-amino acids as suggested by other workers.[9]

In conclusion, we elucidated that lanthanide metal ions can be used to form energeticaly different two diastereomeric complexes with the fixed chiral ligand (chiral selector) and the two enantiomers of mobile recemic α-amino acid for the resolution of α-amino acids without derivatization in chiral ligand exchange chromatography. The use of lanthanide metal ion instead of Cu^{2+} ion was found to increase the capacity factors. However, any trend in the capacity factors according to the lanthanide metal ions was not observed. The higher nuclear charge, higher coordination numbers of lanthanide metal ions and the variation in the structure of homologous lanthanide complexes originated from appreciably different radii of lanthanide ions were presumed to be responsible for the increased capacity factors without any notable trend.

Acknowledgement. This work was supported by the grants from the Basic Science Research Program, Ministry of Education, Korea (BSRI-93-307) and by the grants from the Organic Chemistry Research Center sponsored by the Korea Science and Engineering Foundation.

References

1. (a) Davankov, V. A.; Navratil, J. D.; Walton, H. F. *Ligand Exchange Chromatography*; CRC Press: Boca Raton, Florida, 1988; (b) Lam, S. In *Chiral Liquid Chromatography*; Lough, W. J. ed.; Blackie, Glasgow and London: 1989, chap. 5; (c) Davankov, V. A. In *Chiral Separation by HPLC: application to pharmaceutical compounds*; Krstulović, A. M., ed.; Ellis Horwood, Chichester: 1989, chap. 15.
2. Hare, P. E.; Gil-Av, E. *Science* **1979**, *204*, 1226.
3. (a) Gübitz, G. *J. Liq. Chromatogr.* **1986**, *9*, 519; (b) Jin, R.; He, B. *J. Liq. Chromatogr.* **1989**, *12*, 501.
4. Cation-exchange resins loaded with lanthanum ions have been used as selective sorbents for anions of aromatic acids and amino acids. Otto, J.; De Hernandez, C. M.; Walton, H. F. *J. Chromatogr.* **1982**, *247*, 91.
5. Choi, I.-Y., Kim, Y.-I., Choi, S.-N.; Hyun, M. H. *J. Kor. Chem. Soc.* **1993**, *37*, 105.
6. Hyun, M. H.; Lim, N.-E.; Choi, S.-N. *Bull. Kor. Chem. Soc.* **1991**, *12*, 594.
7. Hyun, M. H.; Ryoo, J.-J.; Lim, N.-E. *J. Liq. Chromatogr.* **1993**, *16*, 3249.
8. Bratsch, S. G.; Lagowski, J. J. *J. Chem. Phys.* **1985**, *89*, 3310.
9. (a) Kanno, H.; Hiraishi, J. *J. Phys. Chem.* **1982**, *86*, 1488; (b) Johnson, G.; Wakita, H. *Inorg. Chem.* **1985**, *24*, 3047; (c) Huheey, J. D.; Keiter, E.; Keiter, R. *Inorganic Chemistry*; Harper-Collins: 1993.

Comparison of Liquid Crystalline Behavior of *N*-(4-n-Alkyloxybenzylidene)-4′-n-butylanilines and *N*-(4-n-Alkyloxybenzylidene)-4′-*p*-aminocinnamates

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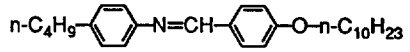
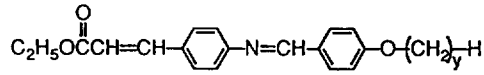
Received August 11, 1993

There have been much efforts to establish structure-property relationship of low molar mass thermotropic compounds.[1-4] While we have been conducting an investigation on the mesomorphic properties of dimesogenic and multimesogenic compounds,[5-8] we have found that the following three compounds have not been yet reported. Therefore, we became interested in their synthesis and comparing the liquid crystalline properties thereof.



I - 10



II - 5 (y=5) , II - 10 (y=10)

N-(4-n-Pentyloxybenzylidene)-4′-n-butylaniline(**I-5**) was reported earlier by Smith and coworkers.[9]

Results and Discussion

Thermal transition behavior of compounds **I-5**(*N*-(4-n-pentyloxybenzylidene)-4′-n-buthylaniline), **I-10**, **II-5** and **II-10** are summarized in Table 1 together with the nature of mesophases they reveal. The data for **I-5** are quoted from reference 9. Identification of the mesophases formed by these compounds was performed by the examination of their optical textures observed through a cross-polarized microscope equipped with a hot-stage.[10,11] The DSC thermograms of **II-5** and **II-10** are shown in Figure 1. The thermograms were obtained at the heating and cooling rates of 10℃/min. All of the present compounds are enantiotropically thermotropic and did not form any additional monotropic phase on cooling, see Figure 1. One interesting observation made on the crystallization behavior of the compounds is that the compound