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Liquid Chromatographic Resolution of Both π-Acidic and π-Basic Analytes on a Chiral Stationary Phase Derived from (S)-Tyrosine

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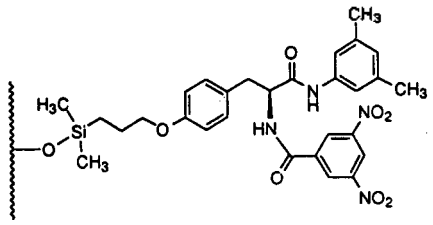
Received July 26, 1996

Chiral recognition models for resolving π-basic N-acyl-α-(1-naphthyl)alkylamines and π-acidic N-(3,5-dinitrobenzoyl)-α-amino alkyl esters on a (S)-tyrosine-derived chiral stationary phase (CSP) containing both π-basic and π-acidic interaction site have been proposed. In the models, the CSP was supposed to interact with the analytes through the π-π interaction between the 3,5-dinitrophenyl or the 3,5-dimethylphenyl group of the CSP and the 1-naphthyl or the 3,5-dinitrophenyl group of the analyte, and through the hydrogen bonding interaction between the appropriate N-H hydrogen of the CSP and the appropriate carbonyl oxygen of the analyte. In this instance, the alkyl substituent of the pertinent enantiomer of the analyte was found to intercalate between the adjacent strands of the bonded phase and consequently control the trends of the separation factors.

Introduction

Liquid chromatographic resolution of enantiomers on CSPs has been known to be one of the most accurate and convenient means in determining the enantiomeric composition of chiral compounds.[1] Therefore, there have been significant efforts for developing efficient CSPs for the liquid chromatographic resolution of enantiomers and various CSPs derived from optically active natural or synthetic chiral compounds are now available.[2] Among various CSPs, Pirkle-type CSPs have been known to separate two enantiomers by forming energetically different two transient diastereomeric π-π complexes with two enantiomers. For example, CSPs containing π-acidic aryl functional group have been applied for resolving π-basic racemates.[3] Similarly, CSPs containing π-basic aryl functional group have been used for resolving π-acidic racemates.[4] In this context, CSPs containing both π-acidic and π-basic aryl functional groups are very interesting in that they can resolve either π-basic or π-acidic racemates. However, up to now, only a few CSPs containing both π-acidic and π-basic aryl functional groups have been reported.[5]

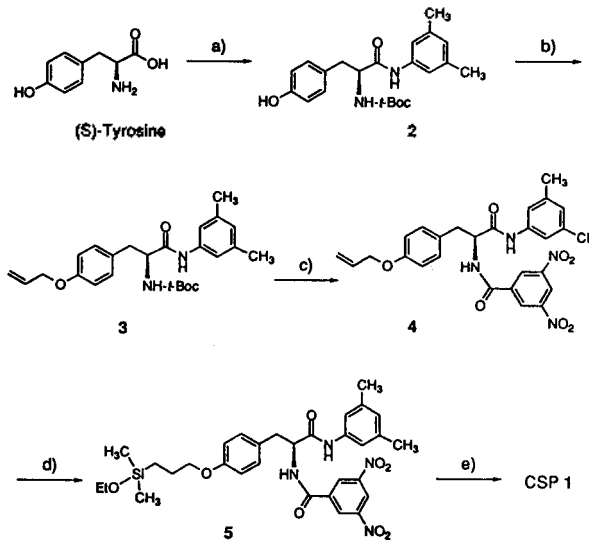
Recently, we reported in a short communication that CSP **1** prepared by grafting simple achiral 3,5-dimethylaniline to (S)-N-(3,5-dinitrobenzoyl)tyrosine unit can be successfully used in resolving either π-basic or π-acidic racemates or in



CSP **1**

separating simultaneously π-basic and π-acidic racemates.[6] However, the detailed synthetic procedure for CSP **1** and the chiral recognition mechanism have not been reported. In this study, we wish to report the detailed synthetic procedure for CSP **1**. In addition, we wish to propose chiral recognition models which can be applied for rationalizing the resolution behaviors of representative π-acidic and π-basic racemates on CSP **1**.

Experimental



Scheme 1. (a) (1) Di-*tert*-butyl dicarbonate, triethylamine, H_2O/1,4-dioxane, room temperature, 3 hr. (2) 3,5-Dimethylaniline, EEDQ, CH_2Cl_2, room temperature, 3 hr. (b) (1) NaH, DMF, 2 hr. (2) Allylbromide, DMF, room temperature, 18 hr. (c) (1) HCl, 1,4-dioxane, room temperature, 24 hr. (2) 3,5-Dinitrobenzoyl chloride, triethylamine, CH_2Cl_2, room temperature, 4 hr. (d) (1) Dimethylchlorosilane, $H_2PtCl_6 \cdot 6\ H_2O$, CH_2Cl_2, reflux, 2 hr. (2) EtOH/triethylamine (1 : 1, v/v). (e) 5 μm Rexchrom silica gel, Dean-Stark trap, toluene, reflux.

General

^{1}H NMR spectra were recorded on a Varian Gemini 200 spectrometer. IR spectra were measured on a Mattson Polaris FT-IR spectrometer. Melting points were taken on a Rigaku TAS 100 thermal analyzer. Elemental analyses were performed at the OCRC, Sogang University, Seoul.

(S)-Tyrosine was obtained from Aldrich Chemical Co. Racemic and optically active analytes used in this study were available from previous study.[5c] Solvents for HPLC analysis were of HPLC grade. All reagents were of reagent grade and used without further purification unless otherwise indicated.

Chromatography was performed on an HPLC system consisting of a Waters model 510 pump, a Rheodyne model 7125 injector with a 20 μ sample loop, a Youngin model 710 absorbance detector with a 254 nm UV filter and a Youngin D520B computing integrator.

Preparation of CSP 1

CSP 1 was prepared starting from (S)-tyrosine as shown in Scheme 1. All reactions were carried out under an argon atmosphere.

(S)-N-(*tert*-Butyloxycarbonyl)tyrosine 3,5-Dimethylanilide 2. (S)-N-(*tert*-Butyloxycarbonyl)tyrosine (4.90 g, 17.44 mmole) and 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ, 4.74 g, 19.16 mmole) were dissolved in 100 mL of methylene chloride and the resulting solution were stirred for 20 min. at room temperature. 3,5-Dimethylaniline (2.17 mL, 17.40 mmole) was added to the solution and the mixture was stirred for 3 hr at room temperature. The reaction mixture was evaporated under a reduced pressure and the residue was dissolved in ethyl acetate. The ethyl acetate solution was washed with 2 N HCl solution and then water. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (ethyl acetate/hexane : 1/8, v/v) to afford **2** (4.83 g, 72.1% yield) as a white crystalline solid. The enantiomeric purity of **2** was found to be greater than 98% by analysis on a CSP described previously.[7] mp 213-222 ℃. ^{1}H NMR (DMSO-d_6) δ 1.32 (s, 9H), 2.23 (s, 6H), 2.66-2.88 (m, 2H), 4.17-4.25 (m, 1H), 6.65 (d, 2H), 6.69 (s, 1H), 6.96 (d, 1H), 7.09 (d, 2H), 7.21 (s, 2H), 9.19 (s, 1H), 9.80 (s, 1H). IR ($CHCl_3$, NaCl) cm^{-1} 3322, 2979, 2920, 1698, 1674.

(S)-N-(*tert*-Butyloxycarbonyl) O-Allyltyrosine 3,5-Dimethylanilide 3. Compound **2** (3.85 g, 10.01 mmole) was dissolved in 40 mL of DMF. To the stirred solution was slowly added NaH (0.47 g, 11.80 mmole, 60% in mineral oil) dispersed in 20 mL of DMF at 0 ℃ under an argon atmosphere. After stirring the mixture at room temperature for 2 hrs, allylbromide (0.85 mL, 9.82 mmole) was added and then the whole mixture was stirred for 18 hrs. After checking the complete disappearance of the starting material by TLC, water (10 mL) was added to the reaction mixture. The whole reaction mixture was concentrated and then the residue was dissolved in ethyl acetate. The ethyl acetate solution was dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (ethyl acetate/hexane : 1/8, v/v) to afford **3** (3.68 g, 86.6% yield) as a white crystalline solid. The enantiomeric purity of **3** was found to be greater than 98% by analysis on a CSP described previously.[7] mp 113-117 ℃. ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 9H), 2.24 (s, 6H), 3.05-3.07 (m, 2H), 4.47-4.50 (m, 3H), 5.25-5.44 (m, 3H), 5.98-6.11 (m, 1H), 6.72 (s, 1H), 6.84 (d, 2H), 7.02 (s, 2H), 7.15 (d, 2H), 7.91 (broad s, 1H). IR ($CHCl_3$, NaCl) cm^{-1} 3301, 2979, 2920, 1666, 1618.

(S)-N-(3,5-Dinitrobenzoyl) O-Allyltyrosine 3,5-Dimethylanilide 4. Compound **3** (3.82 g, 9.0 mmole) was dissolved in 90 mL of 1,4-dioxane. The solution was saturated with HCl gas and then was stirred for 24 hrs at room temperature. After checking the complete disappearance of the starting material by TLC, the solution was evaporated under reduced pressure. The residue and triethylamine (3.13 mmole, 22.45 mmole) were dissolved in 90 mL of methylene chloride. To the stirred solution was slowly added dinitrobenzoyl chloride (2.07 g, 8.98 mmole) dissolved in 30 mL of methylene chloride over 20 min at 0 ℃. And then the whole mixture was stirred for 4 hrs at room temperature. The reaction mixture was evaporated and the residue was dissolved in ethyl acetate. The ethyl acetate solution was washed with water, dried over anhydrous $MgSO_4$, filtered and concentrated. Finally the residue was crystallized from *n*-hexane to afford **4** as a white crystalline solid (4.2 g, 91.6%). The enantiomeric purity of **4** was found to be greater than 98% by the analysis on a CSP described previously.[7] mp 183-188 ℃. ^{1}H NMR (DMSO-d_6) δ 2.23 (s, 6H), 2.99-3.17 (m, 2H), 4.48 (d, 2H), 4.87-4.94 (m, 1H), 5.18-5.37 (m, 2H), 5.93-6.06 (m, 1H), 6.70 (s, 1H), 6.85 (d, 2H), 7.23 (s, 2H), 7.31 (d, 2H), 8.94 (s, 1H), 9.05-9.06 (m, 2H), 9.55 (d, 1H), 10.13 (s, 1H). IR ($CHCl_3$, NaCl) cm^{-1} 3309, 3094, 2922, 1644.

(S)-N-(3,5-Dinitrobenzoyl) O-(3-Ethoxydimethylsilyl-

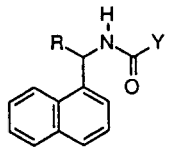
propyl)tyrosine 3,5-Dimethylanilide 5. O-Allyltyrosine derivative **4** (4.0 g, 7.71 mmole) was dissolved in 120 mL of methylene chloride. To this solution were added dimethylchlorosilane (50 mL) and $H_2PtCl_6 \cdot 6\ H_2O$ (*ca.* 10 mg) dissolved in 1 mL of dry tetrahydrofuran. The reaction mixture was heated to reflux for 4 hrs. After checking that there was no starting material in the reaction mixture, methylene chloride and excess dimethylchlorosilane were removed by simple distillation and then under reduced pressure. The residue was dissolved in 50 mL of dry methylene chloride and then 10 mL of triethylamine-absolute ethanol (1 : 1, v/v) was added slowly with stirring. The mixture was stirred at room temperature for 30 min, concentrated and subjected to flash column chromatography on silica gel (ethyl acetate/hexane : 1/8, v/v) to afford hydrosilylated compound **5** (3.07 g, 63.9%) as a yellowish oily material. The enantiomeric purity of **5** was found to be greater than 98% by the analysis on a CSP described previously.[7] ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 6H), 0.62-0.71 (m, 2H), 1.18 (t, 3H), 1.70-1.85 (m, 2H), 2.16 (s, 6H), 3.25 (d, 2H), 3.66 (q, 2H), 3.82 (t, 2H), 5.11-5.21 (m, 1H), 6.67 (s, 1H), 6.78 (d, 2H), 6.88 (s, 2H), 7.22 (d, 2H), 8.43 (broad s, 1H), 8.64 (d, 1H), 8.91-8.97 (broad s, 3H). IR ($CHCl_3$, NaCl) cm^{-1} 3289, 3096, 2895, 1646, 1544.

Preparation of CSP 1 and HPLC column packing. A 250-mL flask equipped with a Dean-Stark trap, a condenser and a magnetic stirring bar was charged with Regis Rexchrome silica gel (5 μm, 4.5 g) and toluene (100 mL). The mixture was heated to reflux until the complete azeotropic removal of water. To the heterogeneous solution was added silyl compound **5** (3.0 g, 4.81 mmole) dissolved in 20 mL of toluene. The whole mixture was heated to reflux for 50 hrs. The modified silica gel was filtered, washed successively with toluene, ethyl acetate, methanol, acetone, diethyl ether and hexane and then dried under high vacuum. Elemental analysis of the modified silica gel (Found: C, 4.90; H, 0.70; N, 0.87) showed a loading of 0.14 mmoles of selector (based on C) or 0.15 mmoles of selector (based on N) per gram of stationary phase. The modified silica gel was slurried in methanol and packed into a 250 mm×4.6 mm I.D. stainless-steel HPLC column using a conventional slurry packing method with an Alltech slurry packer. After washing the HPLC column thus packed with 100 mL of methylene chloride, a solution of 2 mL of hexamethyldisilazane in 50 mL of methylene chloride was eluted through the column to protect the residual silanol groups and then methylene chloride was eluted to wash out unreacted hexamethyldisilazane.

Results and Discussion

CSP **1** was prepared as shown in Scheme 1. To summarize, (S)-tyrosine was converted into the *t*-buthoxycarbonyl derivative, (S)-N-(*tert*-butyloxycarbonyl)tyrosine, and then treated with 3,5-dimethylaniline in the presence of 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ) in methylene chloride to afford 3,5-dimethylanilide derivative **2** of (S)-N-(*tert*-butyloxycarbonyl)tyrosine. Treatment of compound **2** with NaH in DMF and then with allylbromide at room temperature afforded O-allyl tyrosine derivative **3**. The *tert*-butyloxycarbonyl group of compound **3** was then removed by treating with HCl gas in dioxane and the resulting compound was treated with 3,5-dinitrobenzoyl chloride in the presence of triethylamine to give (S)-N-(3,5-dinitrobenzoyl) O-allyltyrosine 3,5-dimethylanilide **4**. Finally, hydrosilylation of compound **4** and then treatment of the resulting hydrosilylated compound **5** with 5 mm Rexchrom silica gel afforded CSP **1**. In each step, no racemization was detected by HPLC analysis on a known CSP.[7]

CSP **1** thus prepared was successfully applied in resolving either π-basic or π-acidic racemates.[6] As described in the introduction section, however, the chiral recognition mechanism has not been reported. As an effort to elucidate the chiral recognition mechanism manifested by CSP **1**, in this study, we resolved a homologous series of N-acyl-α-(1-naphthyl)alkylamine **6** and a homologous series of N-(3,5-dinitrobenzoyl)-α-amino alkyl ester **7** as representative π-basic and π-acidic racemates respectively on CSP **1**. The use of homologous series of analytes has been often utilized as mechani-



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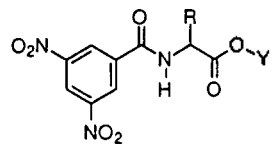

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Table 1. Resolution of N-acyl-α-(1-naphthyl)alkylamine **6** on CSP **1**

Analytes	Y	R	k_1'[a]	k_2'[b]	α[c]	Conf.[d]
6 a	CH_3	CH_3	3.44	3.78	1.10	S
b	CH_2CH_3	CH_3	2.66	3.81	1.43	S
c	$(CH_2)_2CH_3$	CH_3	2.41	3.31	1.37	
d	$(CH_2)_3CH_3$	CH_3	2.30	3.21	1.40	S
e	$(CH_2)_5CH_3$	CH_3	2.14	2.87	1.34	
f	$(CH_2)_6CH_3$	CH_3	2.08	2.75	1.32	
g	$(CH_2)_8CH_3$	CH_3	1.90	2.45	1.29	
h	$(CH_2)_{10}CH_3$	CH_3	1.79	2.24	1.25	
i	$(CH_2)_{11}CH_3$	CH_3	1.72	2.09	1.22	
j	$(CH_2)_{14}CH_3$	CH_3	1.62	1.93	1.19	S
k	$(CH_2)_{16}CH_3$	CH_3	1.53	1.81	1.18	S
l	CH_3	CH_2CH_3	2.67	3.39	1.27	
m	CH_3	$(CH_2)_2CH_3$	2.34	3.15	1.35	
n	CH_3	$(CH_2)_3CH_3$	2.27	3.06	1.35	
o	CH_3	$(CH_2)_4CH_3$	2.05	2.86	1.40	
p	CH_3	$(CH_2)_6CH_3$	1.82	2.59	1.42	
q	CH_3	$(CH_2)_8CH_3$	1.61	2.43	1.51	
r	CH_3	$(CH_2)_{12}CH_3$	1.38	2.22	1.61	
s	CH_3	$(CH_2)_{14}CH_3$	1.26	2.08	1.65	

All data have been collected using 10% 2-propanol in hexane at the flow rate of 2.0 mL/min. Void volumes were measured using 1,3,5-tri-*tert*.-butylbenzene. [a]Capacity factors of the first eluted enantiomers. [b]Capacity factors of the second eluted enantiomers. [c]Separation factors. [d]Absolute configuration of the second eluted enantiomers. For blanks, the elution orders have not been established.

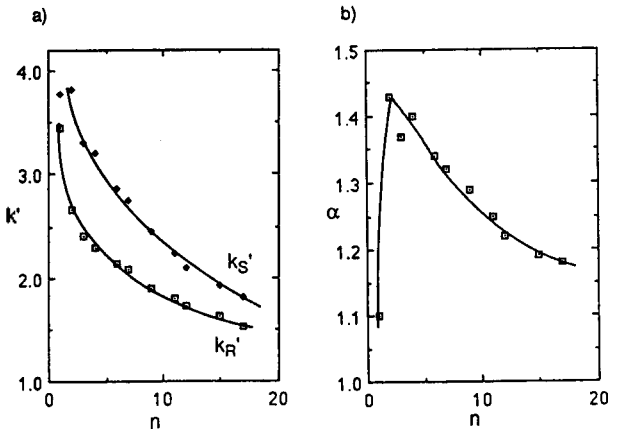

Figure 1. Trends in (a) the capacity factors of the two enantiomers and in (b) the separation factors for resolving N-acyl-α-(1-naphthyl)ethylamines **6** (R=CH_3) on CSP **1**. The length of the acyl chain [Y : -$(CH_2)_nH$] of the analyte is denoted by *n* on the abscissa. For the chromatographic conditions, see Experimental and the footnote to Table 1.

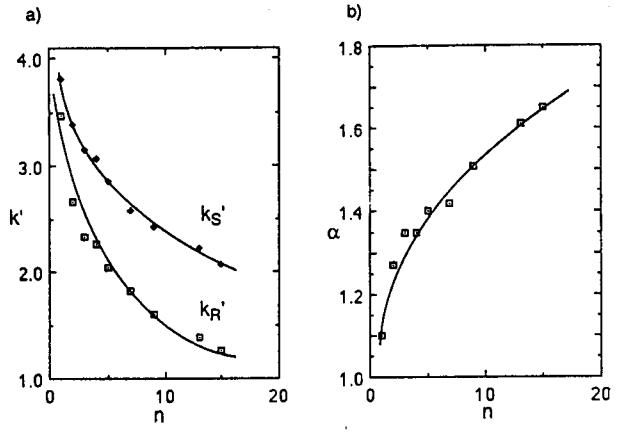

Figure 2. Trends in (a) the capacity factors of the two enantiomers and in (b) the separation factors for resolving N-acetyl-α-(1-naphthyl)alkylamines **6** (Y=CH_3) on CSP **1**. The length of the alkyl chain [R : -$(CH_2)_nH$] at the chiral center of the analyte is denoted by *n* on the abscissa. For the chromatographic conditions, see Experimental and the footnote to Table 1.

stic probes to investigate the origins of enantioselectivity exerted by a certain Pirkle-type CSP. For example, increasing or decreasing trends in the separation factors of a homologous series of analytes with the variation of the length of the substituent have been used as evidences for the intercalation of alkyl substituents of analytes between the adjacent strands of the bonded phase during the chiral recognition.[8]

Table 1 summarizes the results for resolving a homologous series of π-basic N-acyl-α-(1-naphthyl)alkylamine **6** on CSP **1**. The elution orders shown in Table 1 were determined by injecting configurationally known samples. As shown in Table 1, the separation factor, α, decreases continuously as the acyl chain (denoted by Y) of the analyte increases in length while that increases continuously as the alkyl chain (denoted by R) at the chiral center of the analyte increases

Table 2. Resolution of N-(3,5-dinitrobenzoyl)-α-amino alkyl ester **7** on CSP **1**

Analytes	R	Y	k_1'[a]	k_2'[b]	α[c]	Conf.[d]
7 a	$CH_2CH(CH_3)_2$	CH_3	2.43	5.41	2.23	S
b	$CH_2CH(CH_3)_2$	CH_2CH_3	2.13	5.03	2.36	S
c	$CH_2CH(CH_3)_2$	$(CH_2)_2CH_3$	1.99	4.67	2.35	S
d	$CH_2CH(CH_3)_2$	$(CH_2)_3CH_3$	1.87	4.32	2.31	S
e	$CH_2CH(CH_3)_2$	$(CH_2)_5CH_3$	1.71	3.60	2.11	S
f	$CH_2CH(CH_3)_2$	$(CH_2)_7CH_3$	1.56	3.14	2.01	S
g	$CH_2CH(CH_3)_2$	$(CH_2)_9CH_3$	1.43	2.80	1.96	S
h	$CH_2CH(CH_3)_2$	$(CH_2)_{11}CH_3$	1.32	2.54	1.92	S
i	$CH_2CH(CH_3)_2$	$(CH_2)_{13}CH_3$	1.23	2.31	1.88	S
j	$CH_2CH(CH_3)_2$	$(CH_2)_{15}CH_3$	1.15	2.15	1.87	S
k	CH_3	CH_2CH_3	2.52	4.72	1.89	S
l	$(CH_2)_2CH_3$	CH_2CH_3	2.26	4.61	2.04	
m	$(CH_2)_4CH_3$	CH_2CH_3	2.20	4.72	2.15	
n	$(CH_2)_6CH_3$	CH_2CH_3	2.17	4.64	2.14	
o	$(CH_2)_7CH_3$	CH_2CH_3	2.15	4.66	2.17	

All data have been collected using 10% 2-propanol in hexane at the flow rate of 2.0 mL/min. Void volumes were measured using 1,3,5-tri-*tert.*-butylbenzene. [a]Capacity factors of the first eluted enantiomers. [b]Capacity factors of the second eluted enantiomers. [c]Separation factors. [d]Absolute configuration of the second eluted enantiomers. For blanks, the elution orders have not been established.

in length. These trends are more clearly illustrated with the trends in the capacity factors of the two enantiomers in Figure 1 and 2.

From Figure 1, it is clearly recognized that the capacity factor of the more retained (S)-enantiomer decreases more rapidly than that of the less retained (R)-enantiomer as the acyl chain (denoted by Y) of the analyte increases in length and, in consequence, the separation factor, which is defined as the ratio of the capacity factor of the second eluted enantiomer to that of the first eluted enantiomer, decreases continuously. The maximum in the separation factor at n=2 noted in Figure 1 may originate from conformational reasons as described previously.[9] On the contrary, from Figure 2, the capacity factor of the less retained (R)-enantiomer is recognized to decrease more rapidly than that of the more retained (S)-enantiomer as the the alkyl chain (denoted by R) at the chiral center of the analyte increases in length and consequently the separation factor increases continuously.

From the trends of the capacity factors shown in Figure 1, it might be expected that the acyl chain of the more retained (S)-enantiomer of N-acyl-α-(1-naphthyl)alkylamine **6** intercalates between the adjacent strands of the connecting tether of the CSP during the chiral recognition and the intercalation process experiences difficulty more and more as the acyl chain increases in length. Similarly, from the trends of the capacity factors shown in Figure 2, the alkyl chain at the chiral center of the less retained (R)-enantiomer is expected to intercalate between the adjacent strands of the connecting tether of the CSP during the chiral recognition.

Based on the intercalation processes expected from the

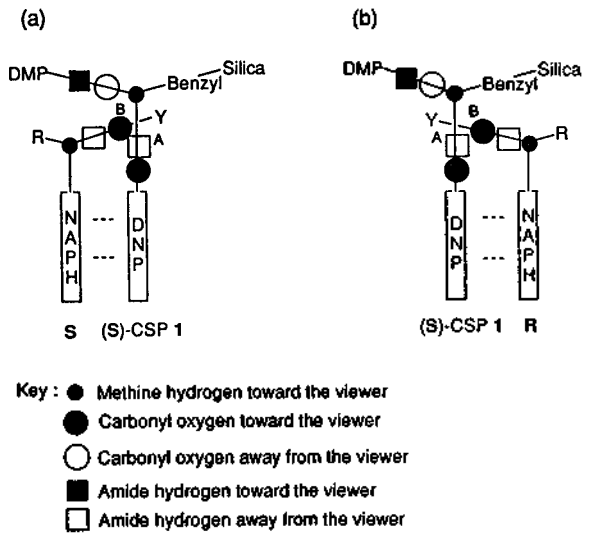

Figure 3. Proposed chiral recognition model for resolving N-acyl-α-(1-naphthyl)alkylamines **6** on CSP **1**. The acyl chain (denoted by Y) of the (S)-analyte is located behind the CSP and is directed to intercalate between the adjacent strands of the bonded phase as shown in (a) while the alkyl chain (denoted by R) at the chiral center of the (R)-analyte is directed to intercalate between the adjacent strands of the bonded phase as shown in (b).

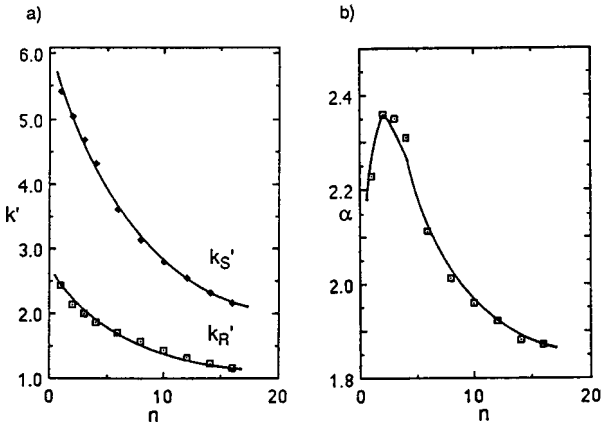

Figure 4. Trends in (a) the capacity factors of the two enantiomers and in (b) the separation factors for resolving N-(3,5-dinitrobenzoyl)leucine alkyl ester **7** (R=isobutyl) on CSP **1**. The length of the ester alkyl chain [Y : -$(CH_2)_n$H] of the analyte is denoted by *n* on the abscissa. For the chromatographic conditions, see Experimental and the footnote to Table 2.

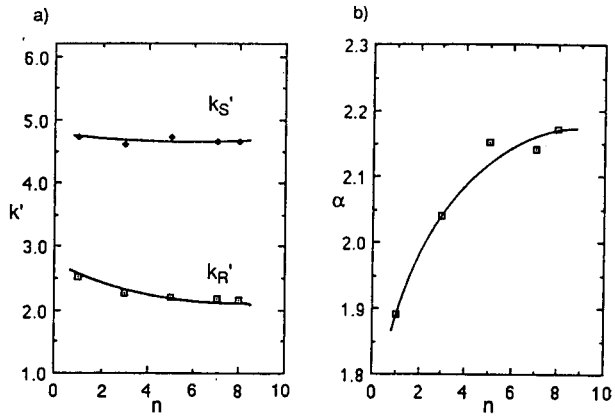

Figure 5. Trends in (a) the capacity factors of the two enantiomers and in (b) the separation factors for resolving N-(3,5-dinitrobenzoyl)-α-amino ethyl ester **7** (Y=ethyl) on CSP **1**. The length of the alkyl chain [R : -$(CH_2)_n$H] at the chiral center of the analyte is denoted by *n* on the abscissa. For the chromatographic conditions, see Experimental and the footnote to Table 2.

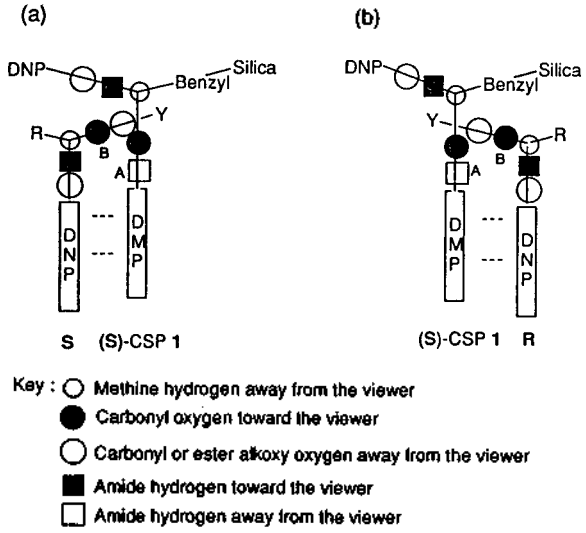

Figure 6. Proposed chiral recognition model for resolving N-(3,5-dinitrobenzoyl)-α-amino alkyl ester **7** on CSP **1**. The ester alkyl chain (denoted by Y) of the (S)-analyte is located behind the CSP and is directed to intercalate between the adjacent strands of the bonded phase as shown in (a) while the alkyl chain (denoted by R) at the chiral center of the (R)-analyte is directed to intercalate between the adjacent strands of the bonded phase as shown in (b).

chromatographic resolution trends shown in Figure 1 and 2 and the elution orders shown in Table 1, a chiral recognition model is proposed from the study of CPK molecular models as shown in Figure 3. In that chiral recognition model shown in Figure 3, the CSP and the analyte are schematically represented in conformations which are presumed to be in their lowest energy and hence preferentially populated as described previously.[5e,8b] In Figure 3a, the (S)-analyte approaches to (S)-CSP **1** from the side of the 3,5-dimethylphenyl (DMP) amide of the CSP and eventually interacts with the CSP through the π-π interaction between the π-acidic 3,5-dinitrophenyl (DNP) of the CSP and the π-basic 1-naphthyl (NAPH) group of the analyte and through the hydrogen bonding interaction between the amide N-H hydrogen (labeled as A) of the CSP and the carbonyl oxygen (labeled as B) of the analyte. In this instance, the acyl chain (denoted by Y) of the (S)-analyte is oriented alongside the direction of the connecting tether of the CSP and finally intercalates between the adjacent strands of the bonded phase. On the other hand, in Figure 3b, the (R)-analyte approaches to (S)-CSP

1 from the side of the *p*-alkoxybenzyl connecting tether of the CSP and interacts with the CSP through the π-π interaction and through the hydrogen bonding interaction, which are very similar to those shown in Figure 3a. In this instance, the alkyl chain at the chiral center of the (R)-analyte is oriented to intercalate between the adjacent strands of the bonded phase.

From the elution order shown in Table 1, it is expected that the (S,S)-diastereomeric complex shown in Figure 3a is more stable than the (R,S)-diastereomeric complex shown in Figure 3b. However, the reason why the (S,S)-diastereomeric complex is more stable than the (R,S)-diastereomeric complex is not clear yet. One thing to mention is that the amide functionality is generally considered to be sterically less demanding than the simple alkyl functionality[4a] and consequently the 3,5-dimethylanilide part of the CSP is considered to be sterically less demanding than the *p*-alkoxybenzyl part of the CSP. Based on the steric reason, the (S,S)-diastereomeric complex might be considered to be more stable than the (R,S)-complex. In this instance, increasing the length of the acyl chain (denoted by Y) of the analyte decreases the stability of the (S,S)-diastereomeric complex more rapidly than that of the (R,S)-diastereomeric complex because of the intercalation of the acyl chain between the strands of the bonded phase and consequently diminishes the difference between the stability of the (S,S)- and (R,S)-diastereomeric complex. Consequently, the separation factor decreases continuously as the acyl chain increases in length. In contrast to this, increasing the length of the alkyl chain (denoted by R) at the chiral center of the analyte decreases the stability of the (R,S)-diastereomeric complex more rapidly than that of the (S,S)-complex because of the intercalation of the alkyl chain at the chiral center of the analyte between the adjacent strands of the bonded phase and consequently increases the difference between the stability of the (S,S)- and (R,S)-diastereomeric complex. Consequently, the separation factor increases continuously as the alkyl chain at the chiral center of the analyte increases in length. All of these expected from the chiral recognition mechanism shown in Figure 3 are exactly consistent with the chromatographic resolution results shown in Table 1.

The results for resolving a homologous series of π-acidic N-(3,5-dinitrobenzoyl)-α-amino alkyl ester **7** on CSP **1** are summarized in Table 2. The elution orders shown in Table 2 are again determined by injecting configurationally known samples. The trends in the capacity factors and the separation factors shown in Table 2 are illustrated graphically in Figure 4 and 5. As shown in Figure 4, the capacity factor of the more retained (S)-enantiomer decreases more rapidly than that of the less retained (R)-enantiomer and consequently the separation factor, α, decreases continuously as the ester alkyl chain (denoted by Y) increases in length. However, as shown in Figure 5, the capacity factor of the less retained (R)-enantiomer decreases more rapidly than that of the more retained (S)-enantiomer and consequently the separation factor, α, increases continuously as the alkyl chain (denoted by R) at the chiral center increases in length. To rationalize these resolution trends, we propose, from the study of CPK space filling molecular models, a chiral recognition model which is shown in Figure 6. The conformations of the CSP **1** and the analyte shown in the schematic presentation in Figure 6 are presumed to be in their lowest energy as described previously.[5e,8b]

In Figure 6, CSP **1** interacts with both of the (S)- and (R)-analyte through the π-π interaction between the π-basic 3,5-dimethylphenyl (DMP) group of the CSP and the 3,5-dinitrophenyl (DNP) group of the analyte. In addition, CSP **1** interacts from its 3,5-dinitrophenyl (DNP) site with the (S)-analyte through the hydrogen bonding interaction between the amide N-H hydrogen (labeled as A) of the 3,5-dimethylanilide group of the CSP and the ester carbonyl oxygen (labeled as B) of the analyte as shown in Figure 6a. In this instance, the ester alkyl chain (denoted by Y) of the (S)-analyte is oriented to intercalate between the strands of the *p*-alkoxybenzyl connecting tether of the CSP. CSP **1** also interacts from its *p*-alkoxybenzyl site with the (R)-analyte through the same hydrogen bonding interaction. In this event, the alkyl chain (denoted by R) at the chiral center of the analyte is directed to intercalate between the strands of the bonded phase.

Based on the elution order shown in Table 2 and on the steric reason described above, the (S,S)-diastereomeric complex shown in Figure 6a is presumed to be more stable than the (R,S)-diastereomeric complex shown in Figure 6b. In this instance, increasing the ester alkyl chain (denoted by Y) of the (S)-analyte decreases the stability difference between the (S,S)- and the (R,S)-complex because of the intercalation of the ester alkyl chain between the adjacent strands of bonded phase and consequently decreases the separation factor continuously. In contrast to this, increasing the alkyl chain (denoted by R) at the chiral center of the (R)-analyte increases the stability difference between the (S,S)- and the (R,S)-complex because of the intercalation of the alkyl chain at the chiral center between the adjacent strands of bonded phase and consequently increases the separation factor. All of these are exactly consistent with the observed chromatographic resolution trends summarized in Table 2.

In summary, CSP **1** prepared from (S)-tyrosine was found to be effective in resolving either π-basic or π-acidic racemates. Based on the chiral resolution trends for resolving a homologous series of N-acyl-α-(1-naphthyl)alkylamine **6** and a homologous series of N-(3,5-dinitrobenzoyl)-α-amino alkyl ester **7** as representative π-basic and π-acidic racemates respectively on CSP **1** and from the study of CPK molecular models, we proposed chiral recognition models shown in Figure 3 and 6. In resolving π-basic N-acyl-α-(1-naphthyl)alkylamine **6**, CSP **1** was proposed to utilize its N-(3,5-dinitrobenzoyl) group as a π-acidic interaction site and the N-H hydrogen of its N-(3,5-dinitrobenzoyl) group as a hydrogen bonding donor as shown in Figure 3. In this instance, the acyl chain of the (S)-analyte and the alkyl chain at the chiral center of the (R)-analyte were directed to intercalate between the strands of the bonded phase, control the stability difference between the two diastereomeric (S,S)- and (R,S)-complex and consequently govern the trends of the resolution. Similarly, in resolving π-acidic N-(3,5-dinitrobenzoyl)-α-amino alkyl ester **7**, CSP **1** was proposed to utilize its 3,5-dimethylphenyl (DMP) group as a π-basic interaction site and the N-H hydrogen (labeled as A) of its 3,5-dimethylanilide group as a hydrogen bonding donor as shown in Figure

6. In this event, the ester alkyl chain of the (S)-analyte and the alkyl chain at the chiral center of the (R)-analyte were oriented to intercalate between the adjacent strands of the bonded phase, influence the stability difference between the two diastereomeric (S,S)- and (R,S)-complex and consequently control the separation factor according to the length of the ester alkyl chain and to the length of the alkyl chain at the chiral center of the analyte. The chromatographic resolution trends for resolving a homologous series of N-acyl-α-(1-naphthyl)alkylamine **6** and a homologous series of N-(3, 5-dinitrobenzoyl)-α-amino alkyl ester **7** expected from the chiral recognition models shown in Figure 3 and 6 were found to be exactly consistent with those observed. Therefore it might be concluded that the chiral recognition models proposed in this study are quite convincing. However, it should be noted that the chiral recognition models proposed in this study might be modified or improved as more data relevant to the chromatographic resolution are collected.

Acknowledgment. This work was supported by OCRC-KOSEF and Basic Science Research Institute Program (BSRI-96-3410).

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Synthesis, Crystal Structure, and Magnetic Properties of RbV_2SeO_7 as Compared with KV_2SeO_7

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Received August 1, 1996

Crystalline compound RbV_2SeO_7, a Rb analogue of KV_2SeO_7, was synthesized from a hydrothermal reaction of V_2O_5, V_2O_3, SeO_2, and Rb_2CO_3 in the mole ratio 3 : 1 : 15 : 6 (in millimoles) at 230 ℃. RbV_2SeO_7 crystallizes in an orthorhombic space group *Pnma* (No. 62) with $a=18.444(8)$, $b=5.415(3)$, $c=7.070(4)$ Å, $Z=8$. The two structures of KV_2SeO_7 and RbV_2SeO_7 are almost the same except that bond lengths in the latter are slightly longer than in the former. The magnetic susceptibility measurement for RbV_2SeO_7 in the temperature range 4-300 K showed an antiferromagnetic ordering with $T_N=45$ K, higher than that for KV_2SeO_7 of 27 K. The origin of the magnetic coupling and the different ordering temperatures in the two phases are discussed in relation to the crystal structures.

Introduction

Recently, one can find increasing number of publications on the hydrothermal reactions applied to synthesize novel inorganic compounds.[1] This technique is considered as one of the low-temperature synthesis techniques from which compounds with interesting structures and physical properties are often obtained.

During our investigation into the hydrothermal reactions in the vanadium selenite system, we have synthesized a mixed valent layered compound KV_2SeO_7.[2] This compound showed an antiferromagnetic ordering at 27 K whose susceptibility