Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 4107–4113

TETRAHEDRON: *ASYMMETRY*

A facile route into 6^A-mono-ω-alkenylcarbamido-6^A-deoxy-perfunctionalised cyclodextrin: key intermediate for further reactive functionalisations

Li-Feng Zhang, Lei Chen, Teck-Chia Lee and Siu-Choon Ng *

Department of Chemistry, National University of Singapore, 119260 Singapore

Received 17 August 1999; accepted 20 September 1999

Abstract

The Staudinger reaction was applied to the facile synthetic generation of a series of mono-6-alkylcarbamido-6-deoxy-perfunctionalised cyclodextrins and mono-6-ω-alkenylcarbamido-6-deoxy-perfunctionalised cyclodextrins. The latter compound with ω-alkenyl pendants was shown to be amenable to further reactive transformations as exemplified by a facile hydrosilylation with $(RO)_3SiH$ in the presence of platinum catalysts to afford reactive siloxane intermediates which can be immobilised onto silica gel for application as an efficient chiral stationary phase for enantioseparation applications.

1. Introduction

Chromatographic enantioseparation on chiral stationary phases (CSP) represents one of the most direct and facile approaches for the determination of enantiomeric purity[1] with strong potential for development into convenient bulk-phase industrial enantioseparation processes as exemplified in their application in the simulated counter-current production of enantiomerically pure drugs.[2] On the basis of previous work by the research groups of Okamoto[3] and Armstrong,[4] cyclodextrin has been successfully introduced into the chiral separation field with unique chiral separation ability. With a view of deriving a facile synthetic generation of novel CSP so as to afford low cost chiral packing materials, we have previously communicated on a straightforward immobilisation strategy for mono-6-azido-6-deoxy-perfunctionalised cyclodextrins onto aminised silica gel by application of a Staudinger reaction.[5] In this manuscript, we report our efforts to extend the Staudinger approach to the synthetic generation of mono-6-alkylcarbamido-6-deoxy-perfunctionalised cyclodextrins and mono-6-ω-alkenylcarbamido-6-deoxy-perfunctionalised cyclodextrins. Whilst the former compounds were used mainly in optimisation studies

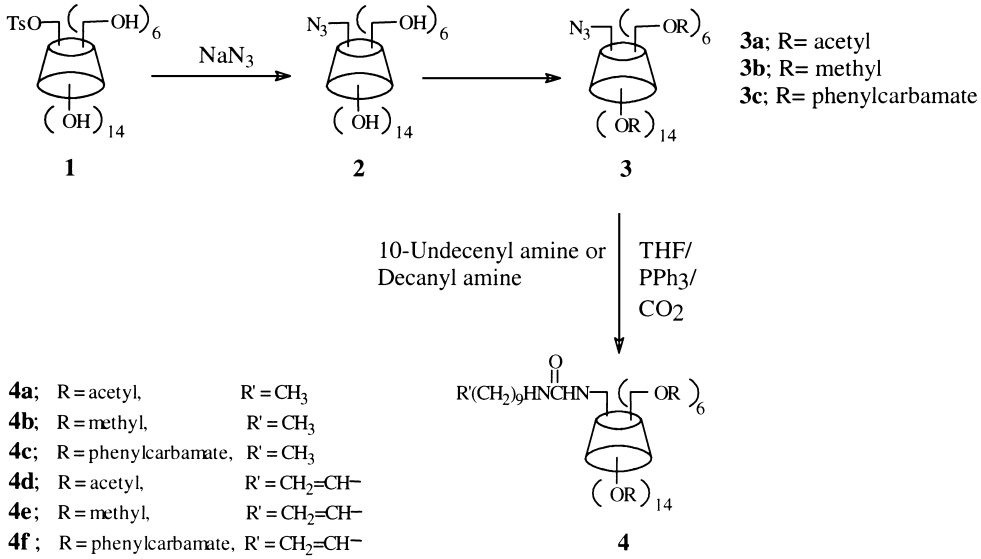
* Corresponding author. E-mail: chmngsc@leonis.nus.edu.sg

0957-4166/99/$ - see front matter
PII: S0957-4166(99)00435-8

for the synthesis route, the latter with ω-alkenyl pendants are anticipated to lend themselves to further reactive transformations into other useful functionalities. In particular, hydrosilylation with $(RO)_3SiH$ readily afforded reactive siloxanes which can be used for immobilisation onto polysiloxane for GC[6] or onto silica gel for HPLC[7] applications. Incidentally, the current approach afforded a facile entry into mono-6-functionalised-6-deoxy-perfunctionalised cyclodextrin, which is complementary to other somewhat more circuitous approaches.[8,9] Furthermore, the relatively mild reaction conditions used in the current synthetic route are tolerated by a wider range of the perfunctional moieties.

2. Results and discussion

Scheme 1 depicts the synthetic route used. The starting material mono-6-deoxy-6-(*p*-tolysulfonyl)-β-cyclodextrin **1** was synthesised as reported previously.[10] This was converted to mono-6-azido-6-deoxy-β-cyclodextrin **2** by S_N2 reaction of **1** with excess sodium azide in DMF followed by purification by complex formation.[11]



Scheme 1. Synthetic route to mono-alkyl or ω-alkenyl-substituted perfunctionalised cyclodextrins via urethane linkage

The key intermediate **2** was converted into β-cyclodextrin derivatives with different substituted groups at the remaining 6-*O*, 2-*O* and 3-*O* positions in the following manner. Acetylation of **2** with acetic anhydride in pyridine afforded peracetylated mono-6-azido-6-deoxy-β-cyclodextrin **3a** in 82% yield. Methylation of **2** with sodium hydride and iodomethane in DMF gave permethylated 6-azido-6-deoxy-β-cyclodextrin **3b** with 82% yield. Treatment of **2** with phenyl isocyanate in pyridine afforded perphenylcarbamoylated mono-6-azido-6-deoxy-β-CD **3c** with 57% yield.[5]

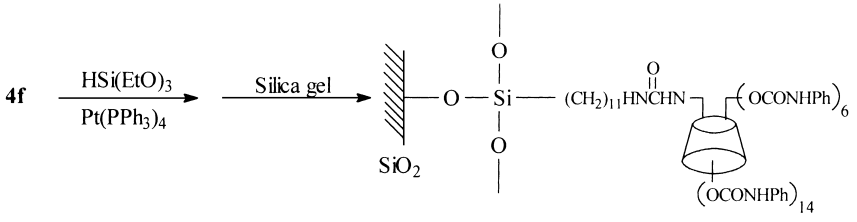
Thereafter, attachment of the alkyl/alkenyl pendant via the azido moiety was readily accomplished under very mild conditions by constant bubbling of CO_2 into a THF solution of *n*-decanylamine or ω-undecenylamine and the mono-azido-perfunctionalised β-CD **3a**–**c**. The Staudinger reaction was then initiated by injection of a solution of triphenylphosphine into the above mixture. The final products **4a**–**f** were obtained as white powders after purification by column chromatography in excellent yields (Table 1). The formation of the carbamido moiety in these compounds was evident from the ^{13}C NMR resonance band at ca. δ 157 ppm. The NMR, FT-IR spectra for all products were consistent with the

Table 1
6^A-Mono-decanyl- or undecenylcarbamido-6^A-deoxy-perfunctionalised cyclodextrins **4a–f** from **3**

Compounds	R	R'	Yields (%)	Mp (°C)	$[\alpha]_D^{25}$ (*c* 1.0, $CHCl_3$)
4a	Acetyl	n-decanyl	98	127-129	+107.7
4b	Methyl	n-decanyl	96	78-80	+126.0
4c	Phenylcarbamate	n-decanyl	96	206-209	+5.6
4d	Acetyl	10-undecenyl	97	115-117	+106.1
4e	Methyl	10-undecenyl	95	72-74	+132.9
4f	Phenylcarbamate	10-undecenyl	97	198-200	+8.5

proposed structures. The mild reaction conditions used in this approach are tolerated by the normally base- and acid- labile *O*-acetyl moiety in compounds **4a** and **d** which remained intact at the end of the Staudinger reaction.

We also investigated the possible hydrosilylation of the alkenyl-substituted β-cyclodextrins using a representative compound. Hence, **4f** was reacted with triethoxysilane in the presence of catalytic amounts of tetrakis(triphenylphosphine)platinum(0) and the labile reactive intermediate was further immobilised without further purification onto the surface of silica gel to directly afford the CSP **5** (Scheme 2).



5

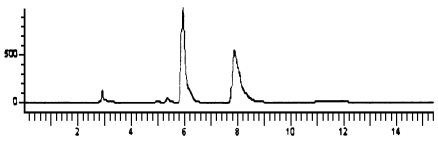
Scheme 2. Synthetic route to the chiral stationary phase (CSP)

A successful immobilisation was evident from the weak but characteristic FT-IR vibrational bands in the derivatised silica, particularly in the 1800–1400 cm^{-1} region, reminiscent of those present in the precursor compound **4f**. The higher carbon content in elemental analyses for **5** as of the presence of determined surface concentration of CD derivatives on the silica gel to the extent of ca. 0.39 μmol m^{-2}, further corroborated the success of the immobilisation approach.

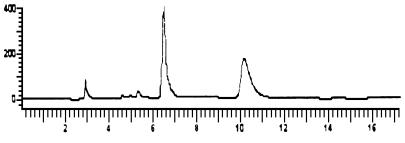
After compound **5** was packed into a stainless HPLC column (Ø 4.6×250 mm) as a CSP, the chromatographic properties were tested with a wide range of structurally diverse racemic compounds and drugs, with representative chromatograms depicted in Fig. 1. Details of these analytical results will be reported elsewhere.

3. Experimental

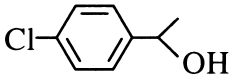
Structures of all compounds were assigned by ^1H NMR and ^{13}C NMR spectra obtained on a Bruker ACF300 FT-NMR spectrometer. FT-IR spectra were performed on a Bio-Rad TFS156 instrument using KBr pellets. Elemental microanalyses were determined on a Perkin–Elmer 2400 CHN analyser. The



α = 1.63 Rs = 4.60



α = 2.02 Rs = 6.2



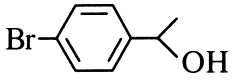


Figure 1. HPLC separation of the enantiomers on a stainless column (Ø 4.6×250 mm) packed with **5**. Mobile phase: hexane:isopropanol (90:10). Flow rate: 1 ml/min. UV detector: λ=254 nm

optical rotations of new compounds were measured on a Perkin–Elmer 241 polarimeter. The chromatographic system used consisted of a Perkin–Elmer series 200 LC pump under the control of a computer equipped with Turbochrom software, and eluted compounds were detected by a 785A UV–vis detector at λ=254 nm. CSP packaging was accomplished using an Alltech pneumatic HPLC pump (Alltech Associates Inc.). Standard empty stainless steel columns from Phenomenex (Ø 4.6×250 mm) were used. β-Cyclodextrin was purchased from Fluka. The silica gel used was Hypersil 5μ silica gel (pore size 120 Å, surface area 170 m^2/g). CO_2 (99.9% pure) was purchased from National Oxygen Pte Ltd, Singapore. Mono-6-(*p*-tolysulfonyl)-6-deoxy-β-cyclodextrin **1**,[10] mono-6-azido-6-deoxy-β-cyclodextrin **2**,[11] mono-6-azido-6-deoxy-perfunctionalised β-cyclodextrin **3a**–**c**[5] and 10-undecenylamine[12] were prepared as reported in the literature as referenced.

*3.1. (6^A-Decanylcarbamido-6^A-deoxy) heptakis(2,3-di-*O*-acetyl)-6^B,6^C,6^D,6^E,6^F,6^G-hexakis-*O*-acetyl-β-cyclodextrin **4a***

A solution of *n*-decanylamine (0.08 g, 0.50 mmol) and 6^A-mono-azido-6^A-deoxy-peracetylated β-CD **3a** (0.90 g, 0.45 mmol) in 5 ml dry THF was stirred under a constant passage of dry CO_2 at room temperature. After 2 min, a solution of PPh_3 (0.12 g, 0.45 mmol) in 5 ml dry THF was added. The mixture was allowed to react until TLC revealed that the starting material **3a** had been consumed. After evaporation of the solvent, the product was purified by column chromatography using $CHCl_3$:ethyl acetate (4:1) as the mobile phase to afford the title compound as a white powder (0.95 g, 98%). Mp: 127–129°C; $[\alpha]_D$ +107.7 (*c* 1.0, $CHCl_3$); IR (cm^{-1}): 3431 (N–H str), 2937, 2856 (C–H str), 1752 (C=O str, acetyl), 1663 (C=O str, urea), 1235, 1045 (C–O–C str); ^{1}H NMR ($CDCl_3$, TMS) δ (ppm): 5.33–5.27 (m, 7H, H3), 5.15–5.06 (m, 7H, H1), 5.02–4.79 (m, 2H, N*H*), 4.82–4.79 (m, 7H, H2), 4.55–4.51 (d, 6H, J=10.8 Hz, Hb6), 4.35–4.26 (m, 6H, J=12.6 Hz, Hb6′), 4.20–4.05 (m, 7H, H5), 3.75–3.70 (m, 7H, H4), 3.57–3.51 (m, 1H, Ha6), 3.49–3.32 (m, 1H, Ha6′), 3.30–3.16 (m, 1H, NCH_2R), 3.11–3.00 (m, 1H, NCH_2′R), 2.18–2.00 (several s, 60H, CH_3CO), 1.46–1.26 (m, 16H, (CH_2)$_7$), 0.88 (t, 3H, J=6.6 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 25°C) δ (ppm): 171.2–169.2 (CH_3*C*O), 158.0 (NH-*C*O-NH), 97.1–96.4 (C1), 78.3–75.9 (C4), 70.7–69.5 (C2, C3, C4), 62.4 (Cb6), 41.3 (Ca6), 40.2 (NH*C*H_2R), 31.7–22.4 ((CH_2)$_8$), 20.5 (*C*H_3CO), 13.9 (R*C*H_3). Microanalysis for $C_{93}H_{132}N_2O_{55}$: calcd C, 51.76%; H, 6.12%; N, 1.30%. Found C, 51.22%; H, 6.10%; N, 1.30%.

3.2. (6^A-Decanylcarbamido-6^A-deoxy) heptakis(2,3-di-O-methyl)-6^B,6^C,6^D,6^E,6^F,6^G-hexakis-O-methyl-β-cyclodextrin **4b**

A similar procedure to the one used for the synthesis of compound **4a** using ω-decanylamine (0.08 g, 0.500 mmol) and 6^A-mono-azido-6^A-deoxy-permethylated β-CD **3b** (0.65 g, 0.45 mmol) afforded **4b** (0.69 g, 96%). Mp: 78–80°C; $[\alpha]_D$ +126.0 (*c* 1.0, $CHCl_3$); IR (cm^{-1}): 3400 (N–H str), 2928 (C–H str), 1651 (C=O str, urea), 1038 (C–O–C str); ^{1}H NMR ($CDCl_3$, TMS) δ (ppm): 5.13–5.03 (m, 9H), 3.95–3.05 (m, 104H), 1.50–1.20 (m, 16H), 0.92 (t, 3H); ^{13}C NMR ($CDCl_3$, 25°C) δ (ppm): 158.5, 98.6, 81.6, 80.8, 70.6, 63.0, 61.2, 58.9, 58.4, 41.4, 40.4, 31.0, 30.5, 29.6, 28.0, 22.2, 14.0. Microanalysis for $C_{73}H_{132}N_2O_{35}$: calcd C, 54.89%; H, 8.33%; N, 1.75%. Found C, 54.91%; H, 8.21%; N, 1.69%.

3.3. (6^A-Decanylcarbamido-6^A-deoxy) heptakis(2,3-di-O-phenylcarbamate)-6^B,6^C,6^D,6^E,6^F,6^G-hexakis-O-phenylcarbamate-β-cyclodextrin **4c**

A similar procedure to the one used for the synthesis of compound **4a** using ω-decanylamine (0.08 g, 0.500 mmol) and 6^A-mono-azido-6^A-deoxy-perphenylcarbamoylated β-CD **3c** (1.59 g, 0.45 mmol) afforded **4c** (1.60 g, 96%). Mp: 206–209°C; $[\alpha]_D$ +5.6 (*c* 1.0, $CHCl_3$); IR (cm^{-1}): 3400, 3319 (N–H str); 3145, 3064 (arom C=C ring str); 2936, 2862 (C–H str); 1732 (C=O str); 1604, 1537, 1443 (arom C=C ring str); 1227, 1053 (C–O–C str); 750 (C–H arom op bend); ^{1}H NMR ($CDCl_3$, TMS) δ (ppm): 7.70–6.60 (m, 120H), 5.65–3.00 (m, 53H), 1.25–1.15 (m, 16H), 0.9 (t, 3H); ^{13}C NMR ($CDCl_3$, 25°C) δ (ppm): 153.9–152.7, 137.6–136.9, 128.7–128.4, 123.4, 119.8–118.9, 98.8, 78.8, 73.5, 69.7, 67.8, 62.0, 60.3, 31.8, 29.5–29.3, 25.5, 22.6, 20.9, 14.1. Microanalysis for $C_{193}H_{192}N_{22}O_{55}$: calcd C, 62.66%; H, 5.23%; N, 8.33%. Found C, 61.94%; H, 5.38%; N, 7.89%.

3.4. (6^A-(10′-Undecenylcarbamido)-6^A-deoxy)heptakis (2,3-di-O-acetyl)-6^B,6^C,6^D,6^E,6^F,6^G-hexakis-O-acetyl-β-cyclodextrin **4d**

A similar procedure to the one used for the synthesis of compound **4a** using ω-undecenylamine (0.086 g, 0.50 mmol) and 6^A-mono-azido-6^A-deoxy-peracetylated β-CD **3a** (0.90 g, 0.45 mmol) afforded **4d** (0.95 g, 97%). Mp: 115–117°C; $[\alpha]_D$ +106.1 (*c* 1.0, $CHCl_3$); IR (cm^{-1}): 3427 (N–H str), 2937, 2859 (C–H str), 1744, 1663 (C=O str), 1227, 1042 (C–O–C str); ^{1}H NMR ($CDCl_3$, TMS) δ (ppm): 5.85–5.76 (m, 1H, C=C*H*R), 5.38–5.21 (m, 7H, H3), 5.16–5.05 (m, 7H, H1), 5.02–4.94 (m, 4H, C=CH_2 and N*H*), 4.84–4.68 (m, 7H, H2), 4.58–4.50 (d, 6H, J=12 Hz, Hb6), 4.35–4.26 (d, 6H, J=12.7 Hz, Hb6′), 4.24–4.05 (m, 7H, Ha5), 3.78–3.64 (m, 7H, H4), 3.57–3.51 (m, 1H, Ha6), 3.49–3.35 (m, 1H, Ha6′), 3.30–3.18 (m, 1H, NCH_2R), 3.11–3.00 (m, 1H, NCH_2′R), 2.18–2.00 (several s, 60H, CH_3CO), 1.46–1.19 (m, 16H, (CH_2)$_8$); ^{13}C NMR ($CDCl_3$, 25°C) δ (ppm): 170.6–169.3 (CH_3*C*O), 158.0 (NH-*C*O-NH), 139.1 (CH_2=*C*R), 113.9 (*C*H_2=CR), 96.6–96.4 (C1), 77.4–76.5 (C4), 70.7–69.5 (C2, C3, C4), 62.4 (Cb6), 41.2 (Ca6), 40.3 (NH*C*H_2R), 33.7–26.8 ((CH_2)$_8$), 20.62 (*C*H_3CO). Microanalysis for $C_{94}H_{132}N_2O_{55}$: calcd C, 52.01%; H, 6.13%; N, 1.29%. Found C, 51.72%; H, 6.30%; N, 1.20%.

3.5. (6^A-(10′-Undecenylcarbamido)-6^A-deoxy) heptakis(2,3-di-O-methyl)-6^B,6^C,6^D,6^E,6^F,6^G-hexakis-O-methyl-β-cyclodextrin **4e**

A similar procedure to the one used for the synthesis of compound **4a** using ω-undecenylamine (0.086 g, 0.50 mmol) and 6^A-mono-azido-6^A-deoxy-permethylated β-CD **3b** (0.65 g, 0.45 mmol) afforded **4e** (0.69 g, 95%). Mp 72–74°C; $[\alpha]_D$ +132.9 (*c* 1.0, $CHCl_3$); IR (cm^{-1}): 3406 (N–H str), 3084 (C=C str),

2976, 2922, 2855 (C–H str), 1651 (C=O str, urea), 1160, 1032 (C–O–C str); ^{1}H NMR ($CDCl_3$, TMS) δ (ppm): 5.82–5.76 (m, 1H), 5.14–5.01 (m, 11H), 3.85–3.15 (m, 104H), 1.28–1.24 (m, 16H); ^{13}C NMR ($CDCl_3$, 25°C) δ (ppm): 159.0, 139.0, 114.0, 99.2–98.8, 81.9–79.8, 71.4–70.85, 61.4–61.2, 59.1–58.3, 42.1, 42.0, 40.4, 33.6–26.9. Microanalysis for $C_{74}H_{132}N_2O_{35}$: calcd C, 55.22%; H, 8.26%; N, 1.74%. Found C, 55.15%; H, 8.26%; N, 1.66%.

*3.6. (6^A-(10′-Undecenylcarbamido)-6^A-deoxy) heptakis(2,3-di-O-phenylcarbamate)-6^B,6^C,6^D,6^E,6^F,6^G-hexakis-O-phenylcarbamate-β-cyclodextrin **4f***

A similar procedure to the one used for the synthesis of compound **4a** using ω-undecenylamine (0.086 g, 0.50 mmol) and 6^A-mono-azido-6^A-deoxy-perphenylcarbamoylated β-CD **3c** (1.59 g, 0.45 mmol) afforded **4f** (1.61 g, 97%). Mp: 198–200°C; $[\alpha]_D$ +8.5 (*c* 1.0, $CHCl_3$); IR (cm^{-1}): 3401, 3315 (N–H str); 3145, 3059 (arom C=C ring str); 2930, 2862 (C–H str); 1733 (C=O str); 1598, 1533, 1447 (arom C=C ring str); 1227, 1049 (C–O–C str); 749 (C–H arom op bend); ^{1}H NMR ($CDCl_3$) δ (ppm): 7.38–6.56 (m, 120H), 5.90–5.80 (m, 1H), 5.56–3.60 (m, 55H), 1.30–1.20 (m, 16H); ^{13}C NMR ($CDCl_3$, 25°C) δ (ppm): 153.7–152.7, 137.0–136.8, 128.7–128.4, 123.6, 119.7–118.8, 114.0, 98.8, 78.8, 73.5, 69.7, 67.8, 62.0, 60.3, 33.7–20.9. Microanalysis for $C_{194}H_{192}N_{22}O_{55}$ (3711.77): calcd C, 62.78%; H, 5.21%; N, 8.31%. Found C, 61.94%; H, 5.38%; N, 7.89%.

*3.7. Hydrosilylation and immobilisation procedure for **4f***

(6^A-(10′-Undecenylcarbamido)-6^A-deoxy) heptakis(2,3-di-*O*-phenylcarbamate)-6^B,6^C,6^D,6^E,6^F,6^G-hexakis-*O*-phenylcarbamate-β-cyclodextrin **4f** (1.5 g) was stirred with 5 ml triethoxysilane and 10 mg of tetra(triphenylphosphine)platinum(0) at 70°C. After 72 h, the mixture was adsorbed onto silica gel in a Buchner funnel and eluted out quickly by addition of 100 ml of diethyl ether. After removal of solvent, the residue was dissolved in 50 ml of anhydrous toluene and 20 ml of THF, followed by addition of 4.0 g of silica gel (dried at 180°C/0.5 mmHg for 6 h). The mixture was then stirred for 8 h, whence 1 ml of water was added, and the mixture was stirred at 80°C for an additional 3 h. After filtration, the residue was heated to 200°C for 5 h. The final product **5** was purified by continuous extraction with acetone in a Soxhlet apparatus for 24 h. Microanalysis for **5**: C, 14.60%; H, 1.85%; N, 1.91%.

According to the microanalysis data, the surface concentration of CD derivatives on the silica gel was about 0.39 μmol m^{-2}.

3.8. Preparation of HPLC column

The slurry method (using CCl_4/dioxane) was employed for column preparation with acetone as the packing solvent. After the silica gel was suspended in CCl_4/dioxane and sonicated for 0.5 h, the silica gel was packed into the stainless steel column (Ø 4.6×250 mm) with standing at the maximum pressure of 7500 psi for 10 min before a gradual release of pressure. The column was conditioned with the mobile phase before use.

Acknowledgements

Funding from NUS in support of this project (RP982752) is gratefully acknowledged. L. Chen is grateful to NUS for the award of a research scholarship.

References

1. (a) Allenmark, S. G. *Chromatographic Enantioseparation Methods and Application;* Ellis Horwood: New York, 1988. (b) Welch, C. J. *J. Chromatogr., A* **1994**, *666*, 3. (c) Zief, M.; Crane, L. *Chromatographic Chiral Separation*; Marcel Dekker: New York, 1988. (d) Pirkle, W. H.; Pochapsky, T. C. *Chem. Rev*. **1989**, *89*, 347.
2. (a) Ching, C. B.; Lim, B. G.; Lee, E. J. D.; Ng, S. C. *J. Chromatogr*. **1993**, *634*, 215. (b) Lim, B. G.; Ching, C. B.; Tan, R. B. H.; Ng, S. C. *Chem. Eng. Sci*. **1995**, *50*, 2289.
3. (a) Hargitai, T.; Okamoto, Y. *J. Liq. Chromatogr*. **1993**, *16*, 843. (b) Hargitai, T.; Kaida, Y.; Okamoto, Y. *J. Chromatogr*. **1993**, *628*, 11.
4. (a) Armstrong, D. W.; Ward, T. J.; Armstrong, R. D.; Beesley, T. E. *Science* **1986**, *232*, 1132. (b) Armstrong, D. W.; Jin, H. L. *Chirality* **1989**, *1*, 27. (c) Armstrong, D. W.; Stalcup, A. M.; Hilton, M. L.; Duncan, J. D.; Faulkner, J. R.; Chang, S. C. *Anal. Chem*. **1990**, *62*, 1610. (d) Berthod, A.; Chang, S.; Armstrong, D. W. *Anal. Chem*. **1990**, *64*, 395. (e) Armstrong, D. W.; Chang, C. D.; Lee, S. H. *J. Chromatogr*. **1991**, *539*, 83.
5. Zhang, L. F.; Wong, Y. C.; Chen, L.; Ching, C. B.; Ng, S. C. *Tetrahedron Lett*. **1999**, *40*, 1815.
6. (a) Bradshaw, J. S.; Chen, Z.; Yi, G. L.; Rossiter, B. E.; Malik, A.; Pyo, D. J.; Yun, H.; Black, D. R.; Zimmerman, S. S.; Lee, M. L.; Tong, W. D.; D'Souza, V. T. *Anal. Chem*. **1995**, *67*, 4437. (b) Malik, A.; Yun, H.; Yi, G. L.; Bradshaw, J. S.; Rossiter, B. E.; Markides, K. E.; Lee, M. L. *J. Microcolumn Sep*. **1995**, *7*, 91–105. (c) Jung, M.; Schurig, V. *J. Microcolumn Sep*. **1993**, *5*, 11.
7. (a) Ciucanu, I.; Konig, W. A. *J. Chromatogr., A* **1994**, *685*, 166. (b) Tanaka, M.; Yoshinaga, M.; Ito, M.; Ueda, H. *Anal. Sci*. **1995**, *11*, 227.
8. Khan, A. R.; Forgo, P.; Stine, K. J.; D'Souza, V. T. *Chem. Rev*. **1998**, *98*, 1977.
9. (a) Yi, G. L.; Bradshaw, J. S.; Rossiter, B. E.; Malik, A.; Li, W. B.; Lee, M. L. *J. Org. Chem*. **1993**, *58*, 4844.
10. (a) Zhong, N.; Byun, H. S.; Bittman, R. *Tetrahedron Lett*. **1998**, *39*, 2921. (b) Petter, R. C.; Salek, J. S.; Sikorski, C. T.; Kumaravel, G.; Lin, F. T. *J. Am. Chem. Soc*. **1990**, *112*, 3860. (c) Gibson, A. R.; Melton, L. D.; Slessor, K. N. *Can. J. Chem*. **1974**, *52*, 3905. (d) Matsui, Y.; Okimoto, A. *Bull. Chem. Soc. Jpn*. **1978**, *51*, 3030. (e) Parrot-Lopez, H.; Galons, H.; Coleman, A. W.; Mahuteau, H.; Miocque, M. *Tetrahedron Lett*. **1992**, *33*, 209.
11. Melton, L. D.; Slessor, K. N. *Carbohydr. Res*. **1971**, *18*, 29.
12. (a) Dobashi, Y.; Hara, S. *J. Org. Chem*. **1987**, *52*, 2490. (b) Boyer, B.; Durand, S.; Lamaty, G.; Moussanou-Missima, J. M.; Pavia, A. A. *J. Chem. Soc., Perkin Trans*. **1991**, *8*, 1311.