Pergamon

Tetrahedron 58 (2002) 4319–4330

TETRAHEDRON

Enantioselective complexation of chiral linear hosts containing monosaccharide moieties with chiral organic amines

Motohiro Shizuma,[a,*] Munenori Ohta,[b] Hitoshi Yamada,[c] Yoshio Takai,[c] Takahiko Nakaoki,[b] Tokuji Takeda[a] and Masami Sawada[b,*]

[a]*The Technochemistry Department, Osaka Municipal Technical Research Institute, 1-6-50 Morinomiya, Joto-ku, Osaka 536-8553, Japan*
[b]*Faculty of Science and Technology, Ryukoku University, Seta, Otsu, Siga 520-2194, Japan*
[c]*Materials Analysis Center, The Institute of Scientific and Industrial Research, Osaka University, Ibaraki, Osaka 567-0047, Japan*

Received 11 January 2002; accepted 25 March 2002

Abstract—New chiral linear hosts (**1**–**3**, **a**: peracetylated derivatives, **b**: permethylated derivatives) containing monosaccharide end groups were designed on the basis of the structural features of permethylated 1^F-fructonystose (MeFruNys), which shows a remarkable chiral discrimination ability, and then synthesized. The chiral discrimination ability of their hosts toward chiral organic ammonium guests were evaluated using FAB mass spectrometry and ^{1}H NMR. Their hosts showed chiral discrimination for some guests. As the contrasting compounds (**4** and **5**) hardly showed any chiral discrimination, it was clarified that the structural features extracted from MeFruNys are very significant factors for chiral recognition. The ^{1}H NMR shift induced by adding a potassium ion (counter anion: SCN^-) in $(CD_3)_2CO$ suggested that the cation moiety of the chiral guests was located at the binding site consisting of the –O–C–C–O– units and the ring-oxygens of the saccharide moieties. The structure of the complex of host **1b** with 1-(1-naphthyl)ethylammonium ion (NEA^+) was estimated by the ^{1}H NMR induced shifts and the molecular dynamics simulation.

1. Introduction

Chiral recognition is one of the most fundamental and significant processes in living systems. Various chiral hosts such as chiral crown ether derivatives, etc., have been synthesized for chiral recognition.[1] Recently, dynamic molecular recognition has been paid great attention.[2] Their hosts drastically change the conformation of the skeleton or the branches depending on the chemical or physical environmental changes to recognize the functional molecules. Saccharide-chains binding to proteins or lipids play very important roles in molecular recognition on surface of cells or enzymes in vivo.[3] Molecular recognition by saccharides having highly flexible structures is one of the typical dynamic molecular recognition processes.

We have paid particular attention to the chiral molecular recognition of various permethylated oligosaccharides toward amino acid derivatives.[4] In the study, we found that linear *fructo*-oligosaccharides, which consist of β(2→1)-linked fructofuranoside and a reducing terminal monosaccharide moiety, had relatively high chiral discrimination abilities for some protonated amino acid esters in various permethylated oligosaccharides.[5] In particular, the permethylated 1^F-fructonystose (MeFruNys) showed a remarkable chiral discrimination ability, for example, $-\Delta\Delta G_{enan}=-1.2$ kcal mol^{-1}, with *S*-selectivity for Val-O-iPr$^+$. It was also clarified that the chiral recognition of MeFruNys was a dynamic mechanism with a drastic conformation change on based on evidence suggesting the 'induced-fitting theory'.[6]

In this paper, we describe the design and synthesis of new artificial linear hosts (Chart 1) based on the structural features of MeFruNys, the chiral discrimination ability toward protonated amino acid 2-propyl ester guests (Chart 2), and the structures of the host–guest complexes.

2. Results and discussion

2.1. Design and synthesis of chiral hosts

MeFruNys, which showed a remarkable chiral discrimination ability toward protonated amino acid ester guests, has the following structural features: (1) a linear structure which has flexibility for dynamic conformation changes during complexation with guests; (2) the –O–C–C–O– units (n=2 or 3) as a binding site for cation guests (via charge–dipole electrostatic interaction); (3) saccharide moieties as chiral origins (Scheme 1). Therefore, we

Keywords: amino acids and derivatives; enantioselection; host compounds; molecular recognition.
* Corresponding authors. Tel.: +81-6-6963-8023; fax: +81-6-6963-8040; e-mail: shizuma@omtri.city.osaka.jp

0040–4020/02/$ - see front matter
PII: S0040-4020(02)00351-4

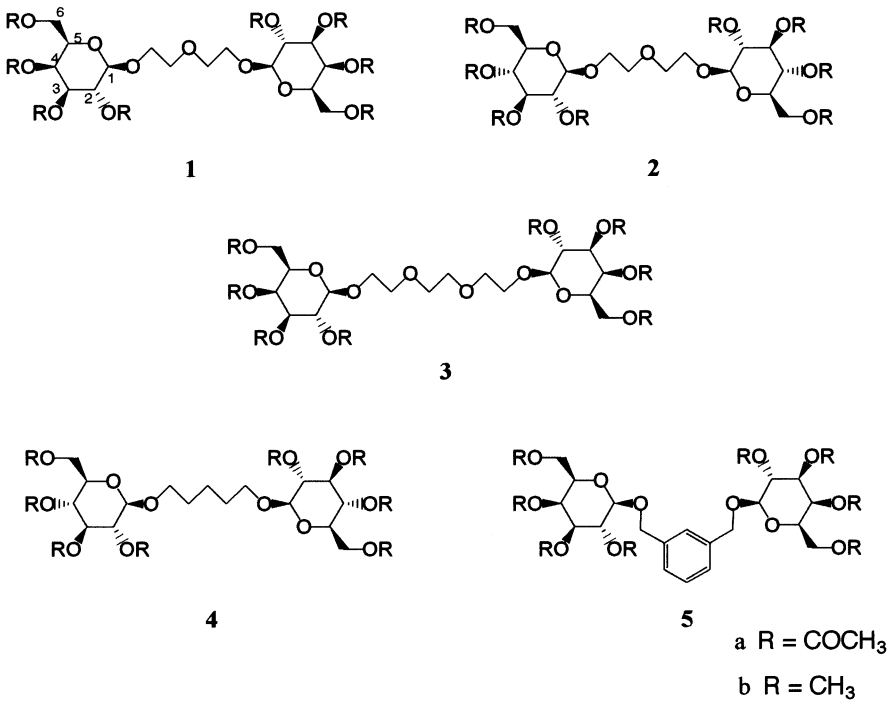


Chart 1. Chiral linear hosts.

designed new chiral hosts (**1**–**3**) based on the structural features of MeFruNys having four –O–C–C–O– units. All the hydroxyl groups of the monosaccharide moiety (D-galactose or D-glucose) were modified with acetyl groups (**a**) or methyl groups (**b**) which have an affinity for organic solvents in order to enhance the electrostatic interaction between the host and the guest cation by solvent effects. The new hosts were synthesized by the reaction pathways shown in Scheme 2. Some derivatives (**4a**, **4b**, **5a** and **5b**) without these structural features (the –O–C–C–O–) were also prepared for comparison with hosts **1**–**3** (**a** and **b**).

2.2. Chiral discrimination

2.2.1. FAB mass spectrometry. The chiral discrimination ability of hosts **1**–**5** (**a** and **b**) toward all the given guests at room temperature was evaluated using the FAB mass spectrometry/enantiomer labeled (FABMS/EL) guest

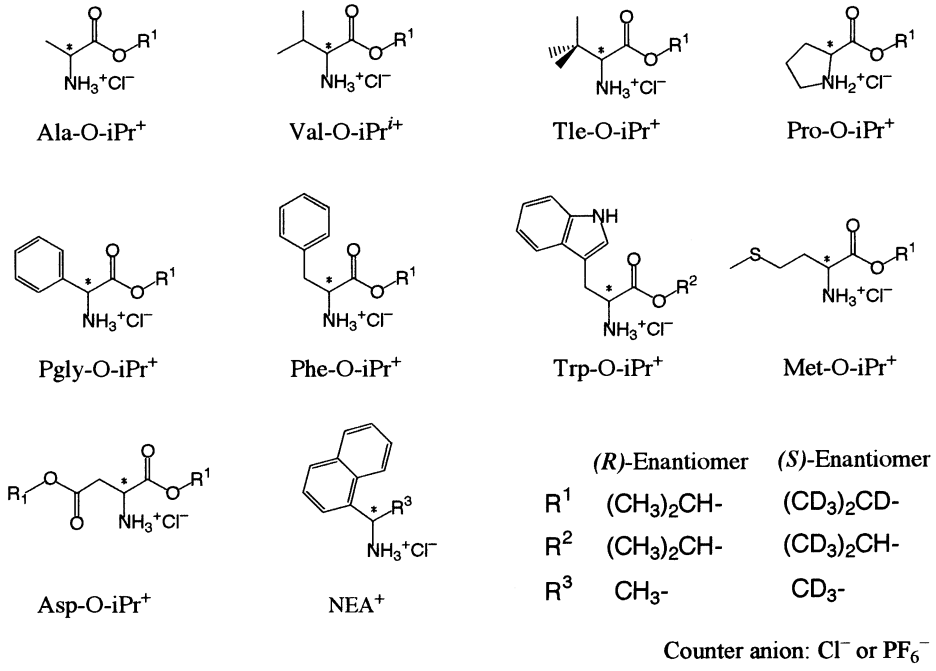
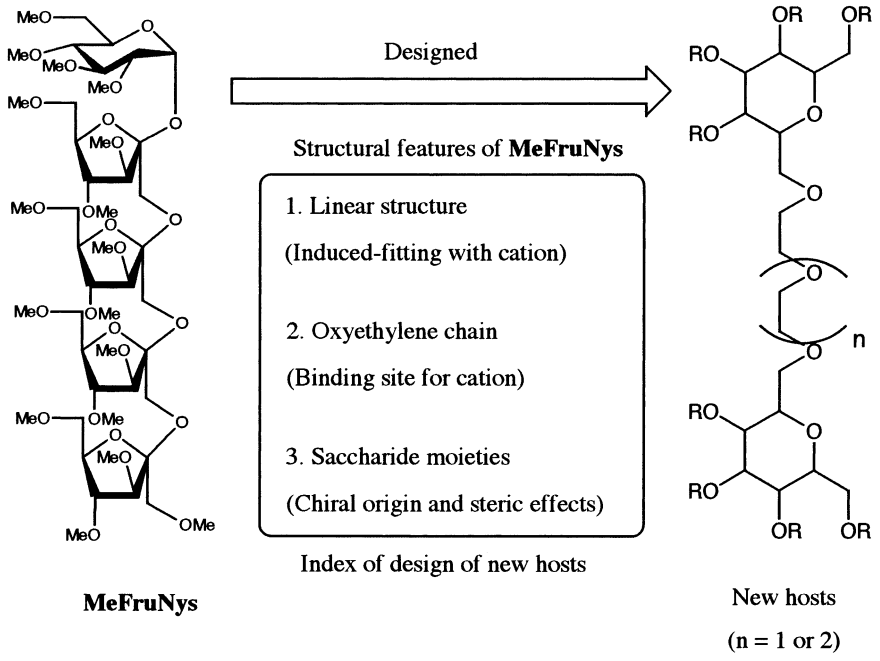


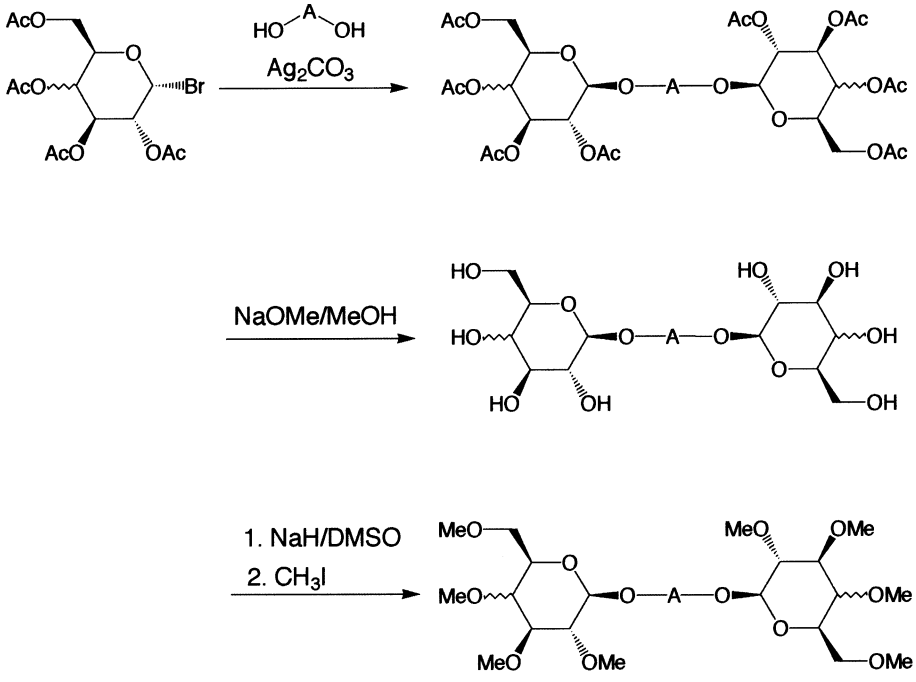
Chart 2. Chiral organic ammonium guest (counter anion: chloride or hexafluorophosphate).



Scheme 1. Design of new chiral recognition compounds on the basis of the structural features of MeFruNys.

method (nitrobenzyl alcohol (NBA) matrix).[7] The FABMS/EL guest method has many advantages such as an easy, short-time, and direct measurement compared with other evaluation methods of chiral discrimination ability. In this method, the FAB mass spectra of three component samples in a solution (NBA matrix) of a host (H) and a 1:1 mixture of the *S*-amino acid ester salt labeled with deuteriums ($G_{S\text{-dn}}^{+}$) and the unlabeled *R*-amino acid ester salt (G_R^{+}) were measured at room temperature, and the two diastereomeric 1:1 complex ion peaks differing in molecular weight ($\Delta MW=n$, n: number of deuteriums) were compared in intensity in order to estimate the chiral discrimination ability (see Section 4). The relative peak intensity $[I(H+G_R)^{+}/I(H+G_{S\text{-dn}})^{+}=I_R/I_{S\text{-dn}}]$ values are summarized in Table 1.

The 1:1 complex ion peaks of their hosts with all the given amino acid ester salts were observed in the FAB mass spectra. Typical FAB mass spectra are shown in Fig. 1. The chiral discrimination of hosts **1**–**3** (**a** and **b**) was



Scheme 2. Synthetic schemes.

Table 1. Chiral discrimination ability ($I_R/I_{S\text{-dn}}$) values in the FABMS/EL guest method) of hosts (**1**–**5**) toward organic ammonium ionic guests

Host	Guest									
	Ala-O-iPr$^+$	Val-O-iPr$^+$	Tle-O-iPr$^+$	Pro-O-iPr$^+$	Pgly-O-iPr$^+$	Phe-O-iPr$^+$	Trp-O-iPr$^+$	Met-O-iPr$^+$	Asp-O-iPr$^+$	NEA$^+$[a]
1a	0.84	0.82	0.98	0.91	1.5	1.1	1.1	0.93	1.1	0.73
1b	0.94	0.90	1.1	0.86	1.0	0.58	0.45	0.87	1.1	1.4
2a	1.1	0.88	1.1	1.1	0.84	0.95	1.2	0.97	1.2	0.96
2b	0.83	0.83	0.97	0.95	0.75	0.49	0.43	0.72	1.3	1.5
3a	0.83	0.98	1.1	0.74	1.1	0.63	0.57	0.87	1.3	1.4
4a	0.95	1.0	0.98	1.0	1.0	1.0	0.97	1.0	1.1	1.0
4b	0.92	0.93	0.94	1.0	0.86	0.87	0.87	0.92	0.99	1.2
5a	0.98	0.86	1.1	1.0	1.0	0.99	0.96	0.94	1.1	–
5b	0.93	0.95	1.1	1.0	0.89	0.86	0.83	0.98	1.1	1.1
18C6	1.0	0.99	1.00	1.0	0.99	1.0	1.0	1.0	1.0	1.0

[a] FAB mass spectra were measured under different concentration condition from the other (see Section 4). 18C6=18-crown-6 as an achiral host. Errors of the $I_R/I_{S\text{-dn}}$ values were ca. 1.0±0.04.

observed for some given guests. Hosts **4**, **5** (**a** and **b**) hardly showed any chiral discrimination abilities.

2.2.2. Binding ability. The association constants (K) of host **1a**, **1b**, **2a**, and **2b** with some guests were determined in $(CD_3)_2CO$ at 298 K by the NMR titration method (Table 2). The ratio of the association constants (K_R/K_S), i.e. the chiral discrimination ability, were in good agreement with the $I_R/I_{S\text{-dn}}$ values using the FABMS/EL guests method. In the permethylated oligosaccharides and chiral crown ether derivatives, it has been reported that the K_R/K_S values were in good agreement with the $I_R/I_{S\text{-dn}}$ values for the different solvents.[7] The chiral discrimination ability in an organic solvent such as $(CD_3)_2CO$ may be in agreement with that in NBA using the FABMS/EL method, because the ability was represented as the ratio values to offset most of the solvent effects.

2.2.3. Chiral discrimination and the structure of the hosts. The acetyl derivatives **1a** showed *R*-selectivity. However, host **2a** showed little enantioselectivity. On the other hand, the methyl derivatives **1b**, **2b**, and **3b** showed similar enantioselectivities for the given guests, for example, the *S*-selectivity for Phe-O-iPr$^+$ and Trp-O-iPr$^+$, and the *R*-selectivity for NEA$^+$. The chiral discrimination ability hardly depended on the number of –O–C–C–O– units (2 or 3 units). As hosts **4** and **5** having no –O–C–C–O– units hardly showed any enantioselectivity ($0.83<I_R/I_{S\text{-dn}}<1.08$), the structural features of MeFruNys were suggested to be required for chiral discrimination. For the chiral discrimination of permethylated hosts **1b**, **2b**, and **3b** toward Phe-O-iPr$^+$, Trp-O-iPr$^+$, and NEA$^+$, the configuration of C-4 of the monosaccharide moieties seems not to be important. However, for the chiral discrimination of the peracetylated hosts, the configuration of C-4 of the monosaccharide moieties would be very important.

2.3. Structures of diastereomeric host–guest complexes

2.3.1. Position of cation moiety in guests. In order to determine the position of the cation moiety of the guest in the host–guest complex, the ^{1}H NMR shifts induced by adding a simple potassium ion (K$^+$) instead of the ammonium moiety of the chiral guests to hosts **1a**, **1b**, **2a**, and **2b** were measured in $(CD_3)_2CO$ at 298 K. For example, the spectra of complexation of host **1b** with K$^+$ are shown in Fig. 2. In the methylated host, the protons of the oxyethylene chain, H1 and H-5, showed relatively large downfield shifts. The association constants (K) of the complexation were determined from the spectral changes. The K values of hosts **1a**, **1b**, **2a**, and **2b** with K$^+$ were 97, 15, 67, and 18 (M^{-1}), respectively. The limiting shifts, which are corresponding to the chemical shifts of the complexed hosts, were calculated from the K values, the initial concentration of the host and the guest, and the observed shifts. The limiting downfield shifts are summarized in Table 3. In the case of **2b**, these protons also showed the limiting downfield shifts. In acetylated hosts, the H-5 and the oxyethylene protons showed the limiting downfield shifts. The specific shifts of these hosts suggest that the cation is located at the binding site which consists of the –O–C–C–O– units and the ring oxygens (O-5) of the saccharide moieties.

2.3.2. Position of substituents of asymmetric carbon in guests. In order to clarify the position of the substituents of the asymmetric carbon in the guests, the ^{1}H NMR shifts induced by adding NEA$^+$ to host **1b** were measured in $CDCl_3$ at 298 K (Fig. 3). The naphthyl group induces upfield shifts of the adjacent protons due to the shield effects of the π-electron conjugation systems. In the case of (*S*)-NEA$^+$, the upfield shifts of H-2 were observed. On the other hand, the upfield shifts of H-1 and the protons of the oxyethylene chain was observed in (*R*)-NEA$^+$. Thus, the naphthyl groups in the complexes of host **1b** with each enantiomeric guest are suggested to be located near their protons of hosts **1b**.

2.3.3. Expected structure of host 1b–NEA$^+$ complex by MD. The dynamic structure of the host **1b**–NEA$^+$ complex were simulated using the molecular dynamics (MD) program. The most stable structure of the complex is not easy to determine by molecular simulation methods such as the molecular orbital (MO) and the molecular mechanics (MM) calculations due to the high flexibility of the conformations of the linear host. Therefore, the MD simulation was applied in order to evaluate the average structure of the various conformations. The equilibrated structures simulated by the MD are shown in Fig. 4. In both complexes with (*R*)-NEA$^+$ and with (*S*)-NEA$^+$, host **1b** had a pseudo-ring structure, and the cation was located at the

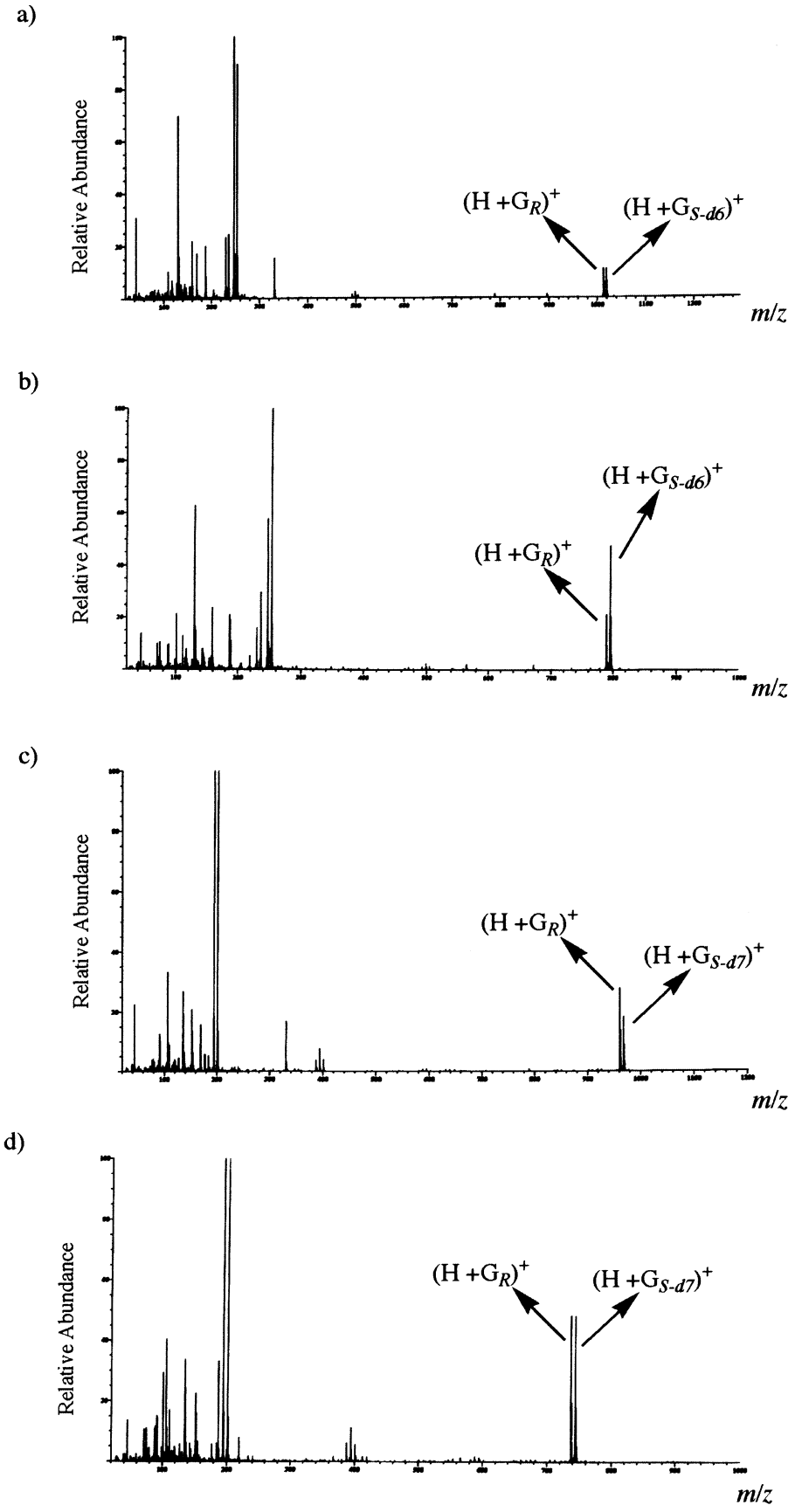


Figure 1. Typical mass spectra in the FABMS/EL guest method. (a) Host: **1a**, guest: Trp-O-iPr$^+$, $(H+G_R)^+$ *m/z* 1013, $(H+G_{S\text{-}d6})^+$ *m/z* 1019; (b) host: **1b**, guest: Trp-O-iPr$^+$, $(H + G_R)^+$ *m/z* 789, $(H + G_{S\text{-}d6})^+$ *m/z* 795; (c) host: **1a**, guest: Pgly-O–iPr$^+$, $(H + G_R)^+$ *m/z* 960, $(H + G_{S\text{-}d7})^+$ *m/z* 967; (d) host: **1b**, guest: Pgly-O–iPr$^+$, $(H + G_R)^+$ *m/z* 736, $(H + G_{S\text{-}d7})^+$ *m/z* 743.

Table 2. Association constants (K) of chiral linear hosts with chiral organic ammonium ion in $(CD_3)_2CO$ at 298 K (counter anion: PF_6^-)

Host	Guest	K (M^{-1})	K_R/K_S
1a	(*R*)-Phe-O-iPr$^+$	3.3×10	0.85 (1.1)
1a	(*S*)-Phe-O-iPr$^+$	3.9×10	
1a	(*R*)-Pgly-O-iPr$^+$	1.0×10^3	1.2 (1.5)
1a	(*S*)-Pgly-O-iPr$^+$	8.2×10^2	
1b	(*R*)-Trp-O-iPr$^+$	3.0×10^2	0.66 (0.45)
1b	(*S*)-Trp-O-iPr$^+$	4.5×10^2	
2a	(*R*)-Trp-O-iPr$^+$	5.9×10^2	1.3 (1.2)
2a	(*S*)-Trp-O-iPr$^+$	4.6×10^2	
2a	(*R*)-Phe-O-iPr$^+$	4.4×10^2	0.86 (0.95)
2a	(*S*)-Phe-O-iPr$^+$	5.1×10^2	
2b	(*R*)-Trp-O-iPr$^+$	4.1×10^2	0.47 (0.43)
2b	(*S*)-Trp-O-iPr$^+$	8.8×10^2	

The corresponding $I_R/I_{S\text{-dn}}$ values are shown in parentheses.

Table 3. ^{1}H NMR downfield limiting shifts (ppm) induced by K^+ (SCN^-) in $(CD_3)_2CO$ at 298 K

Protons	Host			
	1a	**1b**	**2a**	**2b**
H-1	0.03	0.08	0.03	0.06
H-2	0.04	0.05	0.03	0.03
H-3	0.01	0.07	0.01	0.05
H-4	0.01	–	0.01	0.04
H-5	0.05	0.08	0.05	0.06
H-6	0.03	0.07	0.03	0.05
H-6′	0.01	0.01	0.01	0.00
Oxyethylenes	0.06	0.07	0.07	0.07
	0.04	0.04	0.04	

Acetyl and methyl protons of hosts could not be assigned. All the acetyl and methyl protons showed small downfield shifts. The limiting shifts were calculated from the association constants, initial concentration of the hosts and the guests, and the observed shifts.

binding site consisting of the –O–C–C–O– units and the ring oxygens of the saccharide moiety. The naphthyl group is not located at the open-ring part of the host. For the complex with (*R*)-NEA$^+$, the naphthyl group was located above H-1 and the averaged distance from the center of the naphthyl group, which was the shortest distance between the naphthyl group and the other host protons, was ca. 5 Å. For the complex with (*S*)-NEA$^+$, the naphthyl group was located above H-2 and the averaged distance from the center of the naphthyl group was also ca. 5 Å. The positions of the cation and the naphthyl group of NEA$^+$ guest suggested by the ^{1}H NMR induced shifts were in good agreement with the structures of the complexes expected by the MD simulation.

In the host–guest complexes, the structure of the host was estimated to be the pseudo-ring conformation. The drastic conformation change from linear to the pseudo-ring structure suggests a dynamic chiral discrimination mechanism.

2.4. Comparison between new hosts and MeFruNys

Permethylated hosts in new designed hosts showed high chiral discrimination. The chiral discrimination abilities of hosts **1b** and **2b** toward Trp-O-iPr$^+$ ($-\Delta\Delta G_{enen}$=0.5 kcal $^{-1}$) were the same level as that of MeFruNys ($-\Delta\Delta G_{enen}$= 0.5 kcal mol^{-1}). However, in most cases, the chiral discrimination ability was smaller than that of MeFruNys. For example, the chiral discrimination abilities of hosts **1b** and **2b** were $-\Delta\Delta G_{enen}$=0.4 kcal mol^{-1} toward Phe-O-iPr$^+$. While, that of MeFruNys was $\Delta\Delta G_{enen}$=1.0 kcal mol^{-1}. MeFruNys has the spiro-attached fructofuranose rings to the oxyethylene chain. The fructofuranose rings, which are rigid and steric, may be one of significant factors in high chiral discrimination. The introduction of rigid substituents into the oxyethylene chain may be required in order to develop new chiral hosts which has further large chiral recognition.

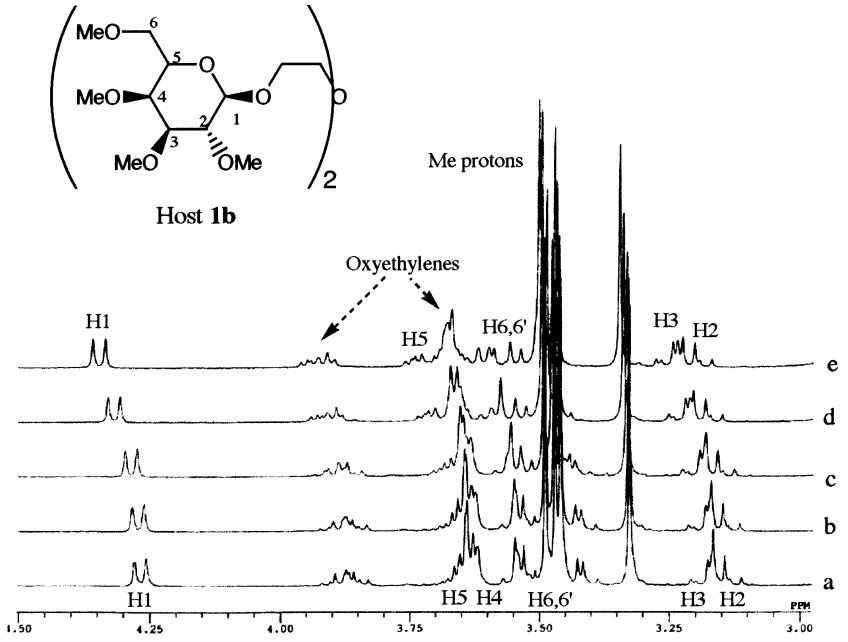


Figure 2. ^{1}H NMR (270 MHz) spectral changes of host **1b** with added K^+ (SCN^-) in $(CD_3)_2CO$ at 298 K ($[H]_0$=2.59 mM). Ratio of concentration [H]/[G]: (a) 0, (b) 1.07, (c) 5.30, (d) 20.6, (e) 39.9.

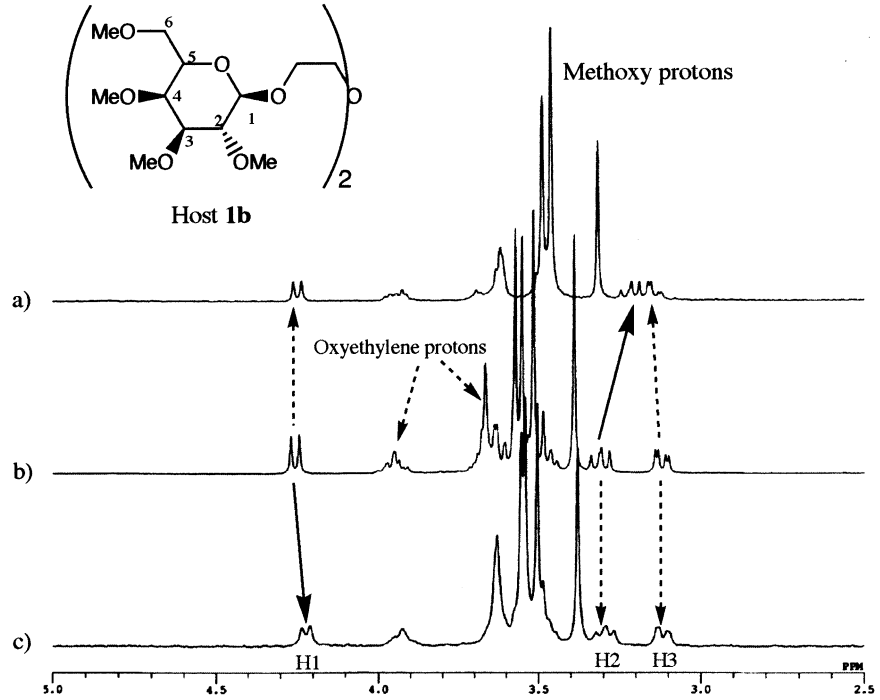


Figure 3. ^{1}H NMR spectral change of host **1b** with added NEA$^+$(PF_6^-) in $CDCl_3$ at 298 K ($[H]_0$=2.2 mM). Ratio of concentration [H]/[G]=2.0. (a) **1b** with (*S*)-NEA$^+$(PF_6^-); (b) free **1b**; (c) **1b** with (*R*)-NEA$^+$(PF_6^-).

3. Summary

These new flexible linear hosts were designed on the basis of the features of remarkable chiral recognition of the oligosaccharide derivatives. They were then synthesized and the structures of the complexes with chiral organic ammonium ions were clarified. The permethylated linear hosts showed a relatively higher chiral recognition via dynamic complexation. Our strategy to develop new chiral recognition hosts using the FABMS/EL guest method may be useful for studying the chiral stationary phase in liquid or gas chromatography[8] and the chiral selector in capillary electrophoresis.[9]

4. Experimental

^{1}H (270 MHz) and ^{13}C NMR (70 MHz) spectra were taken with a JEOL JNM EX-270 spectrometer. TMS was used as the internal standard. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectra were taken with a JEOL JNM 600 spectrometer. FAB mass spectra were measured by using a JEOL JMS-600 mass spectrometer. FT-IR spectra were taken with a Shimadzu FT-IR 8100 spectrophotometer. Elemental analyses were performed using a Perkin–Elmer 2400. Liquid column chromatography for the isolation and the purification of hosts was carried out on a Yamazen LC apparatus with an RI detector under appropriate medium pressure. Melting points were measured with a Yanaco micro-melting point apparatus.

4.1. Materials

18-Crown-6 was used as a commercial product (Aldrich) without further purification. Potassium thiocyanate (Wako) was used without purification after drying under reduced pressure with vacuum pump at 100°C over 8 h. $CDCl_3$ (Aldrich, 99.9 at.% D) and $(CD_3)_2CO$ (Aldrich, 99 at.% D) were used as solvents for NMR measurement without purification. 3-Nitrobenzyl alcohol (Aldrich) was used as FABMS matrix without purification.

4.2. Synthesis of hosts

A series of the peracetylated linear hosts (**1a–5a**) was synthesized by peracetylation,[10] halogenation[11] and Koenigs–Knorr glycosidation.[12] After their deacetylation, a series of the permethylated linear hosts (**1b–5b**) was synthesized by Hakomori method.[13]

4.2.1. 2,2′-Oxydiethyl bis-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside) (1a). Under nitrogen in darkness, 1-bromo-2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (2.60 g, 6.32 mmol), diethylene glycol (0.32 g, 3.04 mmol), silver carbonate (2.60 g, 9.42 mmol) and molecular sieves 4A (11 g) were stirred in dichloromethane (20 mL) at room temperature overnight. The reaction mixture was filtered through celite and the filtrate was evaporated and purified by liquid chromatography (silica gel 60, ethyl acetate/*n*-hexane=1:1, v/v). The eluted fraction was evaporated under vacuum to yield pure products as a white powder (1.01 g, 39%). Mp 40–41°C; $[\alpha]_D^{20}=-4.7$ (*c*=0.2, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.39 (*dd*, 2H, $^3J_{H\text{-}4,H\text{-}5}$=1.0 Hz, $^3J_{H\text{-}3,H\text{-}4}$=3.3 Hz, H-4), 5.21 (*dd*, 2H, $^3J_{H\text{-}2,H\text{-}3}$=10.4 Hz, $^3J_{H\text{-}1,H\text{-}2}$=7.8 Hz, H-2), 5.04 (*dd*, 2H, $^3J_{H\text{-}3,H\text{-}4}$=3.5 Hz, $^3J_{H\text{-}2,H\text{-}3}$=10.4 Hz, H-3), 4.56 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, H-1), 4.19 (*dd*, 2H, $^2J_{H\text{-}6,H\text{-}6'}$=11.2 Hz, $^3J_{H\text{-}5,H\text{-}6}$=6.9 Hz, H-6), 4.12 (*dd*, 2H, $^2J_{H\text{-}6,H\text{-}6'}$=11.2 Hz, $^3J_{H\text{-}5,H\text{-}6'}$=3.3 Hz, H-6′), 3.92 (*m*, 4H, H-5, Gal-O–CH_aH$_b$–CH$_2$–O–), 3.63 (*m*, 6H, Gal-O–CH$_a$$H_b$–C$H_2$–O–),

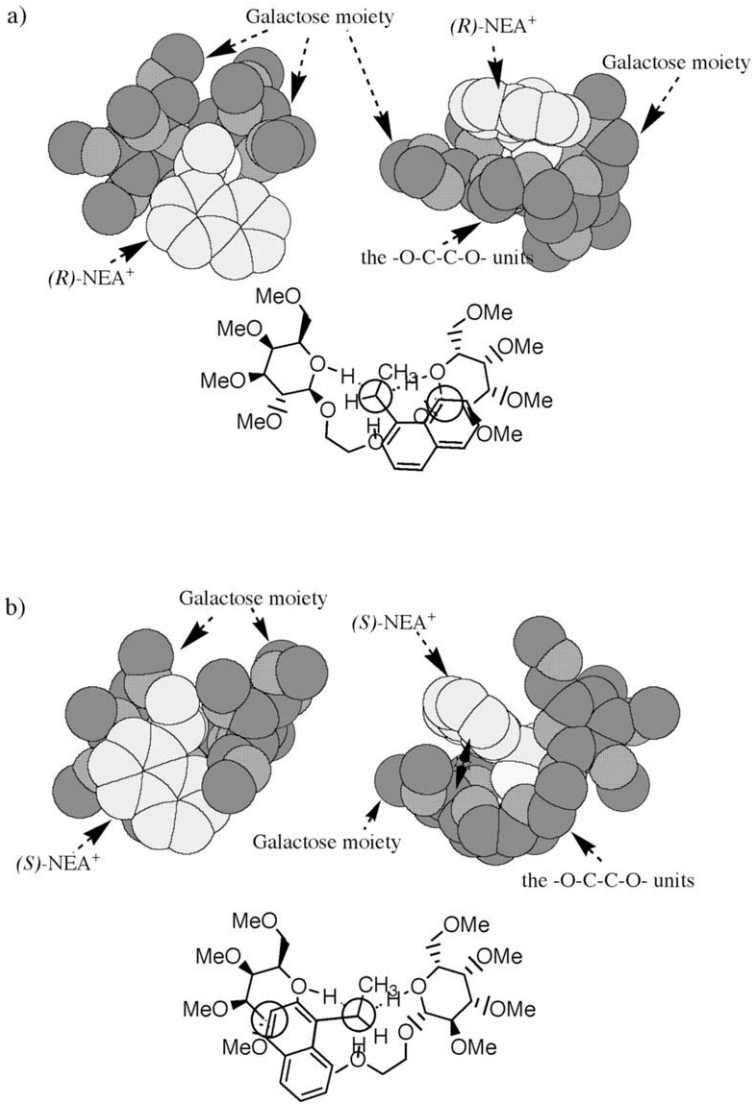


Figure 4. Averaged structures of complexes of **1b** with NEA^+ simulated by the MD. (a) Guest: (*R*)-NEA^+, (b) guest: (*S*)-NEA^+.

2.15 (*s*, 6H, acetyl), 2.06 (*s*, 6H, acetyl), 2.05 (*s*, 6H, acetyl), 1.99 (*s*, 6H, acetyl); ^{13}C NMR (70 MHz, $CDCl_3$) δ 170.4, 170.2, 170.1, 169.4, 101.4, 70.9, 70.7, 70.4, 69.0, 68.8, 67.1, 61.3, 20.7, 20.7, 20.7, 20.6; FT-IR (KBr-disk, cm^{-1}) 2944, 2886 (C–H), 1738 (C═O), 1462, 1436 (H–C–H, H–C–C), 1252, 1175, 1136, 1059 (ester, ether), 756; FABMS *m/z* 805 $(M+K)^+$. Anal. calcd for $C_{32}H_{46}O_{13}$: C, 50.13; H, 6.05. Found: C, 50.14; H, 6.02.

4.2.2. 2,2′-Oxydiethyl bis-(2,3,4,6-tetra-*O*-methyl-β-D-galactopyranoside) (1b). 1a (0.34 g, 0.45 mmol) was stirred with 0.05N sodium methoxide in methanol (5 mL) at room temperature overnight. The solution was neutralized with H-formed cation exchange resin (Amberlite AG IR-120B) which was well washed with methanol before using. After filtration to remove the resin, the filtrate was evaporated to give quantitatively the deacetylated host. This was reacted at room temperature for 4 h with dimethylsulfinyl carbanion which was prepared from sodium hydride (50 mg) and dimethyl sulfoxide (8 mL), added dropwise methyl iodide (5 mL) keeping ca. 10°C and stirred overnight. After extraction with chloroform, the organic layer was washed three times with sat. $Na_2S_2O_3$ aq. and water, respectively, and dried over anhydrous magnesium sulfate. After filtration, the filtrate was evaporated to give a white solid which was recrystallized from diethyl ether to yield 0.19 g colorless crystal (79%). Mp 60–62°C; $[\alpha]_D^{20}=-5.2$ (c=0.2, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 4.26 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.6 Hz, H-1), 3.95 (*m*, 2H, Glc-O–C*H*′–C), 3.72–3.44 (*m*, 14H, ethylenes, H-4, H-5, H-6, H-6′), 3.58 (*s*, 6H, –OMe), 3.55 (*s*, 6H, –OMe), 3.52 (*s*, 6H, –OMe), 3.39 (*s*, 6H, –OMe), 3.31 (*dd*, $^3J_{H\text{-}1,H\text{-}2}$=7.6 Hz, $^3J_{H\text{-}2,H\text{-}3}$= 9.9 Hz, H-2), 3.12 (*dd*, $^3J_{H\text{-}2,H\text{-}3}$=9.6 Hz, $^3J_{H\text{-}3,H\text{-}4}$=3.0 Hz, H-3); ^{13}C NMR (70 MHz, $CDCl_3$) δ 103.9, 83.8, 80.5, 74.8, 73.0, 70.7, 70.2, 68.7, 61.2, 60.7, 59.2, 58.4; FT-IR (KBr-disk, cm^{-1}) 2926, 2878 (C–H), 1474, 1445 (H–C–H, H–C–C), 1179, 1150, 1105, 1080 (ether); FABMS *m/z* 581 $(M+K)^+$. Anal. calcd for $C_{24}H_{46}O_{13}$: C, 53.12; H, 8.54. Found: C, 53.13; H, 8.51.)

4.2.3. 2,2′-Oxydiethyl bis-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside) (2a). White powder; mp 97–98°C; ^1H NMR (270 MHz, $CDCl_3$) δ 5.22 (*dd*, 2H, $^3J_{H\text{-}2,H\text{-}3}$=9.6 Hz, $^3J_{H\text{-}3,H\text{-}4}$=9.2 Hz, H-3), 5.09 (*dd*, 2H, $^3J_{H\text{-}3,H\text{-}4}$=9.2 Hz,

$^3J_{H\text{-}4,H\text{-}5}$=9.9 Hz, H-4), 4.99 (*dd*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, $^3J_{H\text{-}2,H\text{-}3}$=9.6 Hz, H-2), 4.59 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, H-1), 4.27 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6}$=4.6 Hz, $^2J_{H\text{-}6,H\text{-}6'}$=12.2 Hz, H-6), 4.14 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6'}$=2.6 Hz, $^2J_{H\text{-}6,H\text{-}6'}$=12.2 Hz, H-6′), 3.93 (*m*, 2H, Glc-O–C*H*H′–C), 3.66 (*m*, 8H, H-5, Glc-O–CH*H*′–CH_2–O), 2.09 (*s*, 6H, –OAc), 2.04 (*s*, 6H, –OAc), 2.03 (*s*, 6H, –OAc), 2.01 (*s*, 6H, –OAc); ^{13}C NMR (70 MHz, $CDCl_3$) δ (ppm) 20.6, 20.6, 20.6, 20.7, 62.0, 68.4, 69.1, 70.3, 71.8, 72.8, 100.9, 169.3, 169.4, 170.3, 170.6; FT-IR (KBr-disk, cm^{-1}) 2944, 2886 (C–H), 1738 (C=O), 1462, 1436 (H–C–H, H–C–C), 1252, 1175, 1136, 1059 (ester, ether), 756; FABMS *m/z* 805 $(M+K)^+$. Anal. calcd for $C_{32}H_{46}O_{21}$: C, 50.13; H, 6.05. Found: C, 50.30; H, 6.27.

4.2.4. 2,2′-Oxydiethyl bis-(2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside) (2b). Colorless crystal; mp 66–67.5°C; $[\alpha]_D^{20}$=−5.0 (*c*=0.2, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.20 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.6 Hz, H-1), 3.89 (*dt*, 2H, ^3J=6.3 Hz, ^2J=9.6 Hz, Glc-O–C*H*H′–C), 3.62 (*s*, 6H, –OMe), 3.56 (*s*, 6H, –OMe), 3.52 (*s*, 6H, –OMe), 3.39 (*s*, 6H, –OMe); ^{13}C NMR (70 MHz, $CDCl_3$) δ 59.3, 60.3, 60.3, 60.7, 68.9, 70.2, 71.4, 74.6, 79.3, 83.6, 86.3, 103.5; FT-IR (KBr-disk, cm^{-1}) 2935, 2897 (C–H), 1474, 1451 (H–C–H, H–C–C), 1152, 1105, 1080, 1059 (ether); FABMS *m/z* 581 $(M+K)^+$. Anal. calcd for $C_{24}H_{46}O_{13}$: C, 53.12; H, 8.54. Found: C, 53.26; H, 8.42.

4.2.5. 2,2′-(1,2-[Diethoxy]-ethanediyl) bis-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside) (3a). Colorless powder; ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.39 (*d*, 2H, $^3J_{H\text{-}3,H\text{-}4}$= 3.3 Hz, H-4), 5.21 (*dd*, 2H, $^3J_{H\text{-}2,H\text{-}3}$=10.2 Hz, $^3J_{H\text{-}1,H\text{-}2}$= 7.9 Hz, H-2), 5.02 (*dd*, 2H, $^3J_{H\text{-}2,H\text{-}3}$=10.2 Hz, $^3J_{H\text{-}3,H\text{-}4}$= 3.3 Hz, H-3), 4.56 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, H-1), 4.18 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6}$=6.8 Hz, $^2J_{H\text{-}6,H\text{-}6'}$=11.2 Hz, H-6), 4.12 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6'}$=6.3 Hz, $^2J_{H\text{-}6,H\text{-}6'}$=11.2 Hz, H-6′), 3.95 (*m*, 4H, H-5, methylene protons), 3.70 (*m*, 10H, methylene protons), 2.06 (*s*, 6H, –OAc), 2.05 (*s*, 6H, –OAc), 1.99 (*s*, 6H, –OAc), 1.99 (*s*, 6H, –OAc); ^{13}C NMR (70 MHz, $CDCl_3$) δ 170.4, 170.2, 170.1, 169.4 (carbonyls), 101.3 (C-1), 70.9, 70.7, 70.6, 70.2, 69.1, 68.8, 67.1, 61.3 (C–O), 20.7, 20.6, 20.6, 20.5 (methyl); FABMS *m/z* 849 $(M+K)^+$.

4.2.6. 2,2′-(1,2-[Diethoxy]-ethanediyl) bis-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside) (3a). Colorless syrup; $[\alpha]_D^{20}$=−19.9 (*c*=0.2, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.26 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.6 Hz, H-1), 3.97 (*m*, 2H, Glc-O–C*H*H′–C), 3.72–3.47 (*m*, 18H, ethylenes, H-4, H-5, H-6, H-6′), 3.58 (*s*, 6H, –OMe), 3.56 (*s*, 6H, –OMe), 3.52 (*s*, 6H, –OMe), 3.39 (*s*, 6H, –OMe), 3.31 (*dd*, $^3J_{H\text{-}1,H\text{-}2}$=7.3 Hz, $^3J_{H\text{-}2,H\text{-}3}$=9.6 Hz, H-2), 3.12 (*dd*, $^3J_{H\text{-}2,H\text{-}3}$=9.9 Hz, $^3J_{H\text{-}3,H\text{-}4}$=3.0 Hz, H-3); ^{13}C NMR (70 MHz, $CDCl_3$) δ 58.3, 59.2, 60.7, 61.2, 68.7, 70.2, 70.6, 70.7, 72.9, 74.8, 80.5, 83.7, 103.9; FT-IR (KBr-disk, cm^{-1}) 2930, 2836 (C–H), 1458, 1451 (H–C–H, H–C–C), 1204, 1111, 1078, (ether); FABMS *m/z* 625 $(M+K)^+$. Anal. calcd for $C_{26}H_{50}O_{14}$: C, 53.23; H, 8.59. Found: C, 53.10; H, 8.69.

4.2.7. 1,5-Pentandiyl bis-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside) (4a). Colorless crystal; mp 105–106°C; $[\alpha]_D^{20}$=−12.4 (*c*=0.2, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.20 (*dd*, 2H, $^3J_{H\text{-}3,H\text{-}4}$=9.6 Hz, $^3J_{H\text{-}2,H\text{-}3}$=9.2 Hz, H-3), 5.08 (*dd*, 2H, $^3J_{H\text{-}4,H\text{-}5}$=9.9 Hz, $^3J_{H\text{-}3,H\text{-}4}$=9.5 Hz, H-4), 4.97 (*dd*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, $^3J_{H\text{-}2,H\text{-}3}$=9.2 Hz, H-2), 4.49 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, H-1), 4.27 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6}$= 4.6 Hz, $^3J_{H\text{-}6,H\text{-}6'}$=12.2 Hz, H-6), 4.13 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6'}$= 2.3 Hz, $^3J_{H\text{-}6,H\text{-}6'}$=12.2 Hz, H-6′), 3.86 (*dt*, 2H, ^2J=9.6 Hz, ^3J=6.3 Hz, G-O–C*H*H′–C), 3.69 (*m*, 2H, $^3J_{H\text{-}4,H\text{-}5}$=9.9 Hz, $^3J_{H\text{-}5,H\text{-}6}$=4.6 Hz, $^3J_{H\text{-}5,H\text{-}6'}$=2.3 Hz, H-5), 3.47 (*dt*, 2H, ^2J= 9.6 Hz, ^3J=6.9 Hz, Glc-CH*H*′–C), 2.09 (*s*, 6H, –OAc), 2.04 (*s*, 6H, –OAc), 2.02 (*s*, 6H, –OAc), 2.01 (*s*, 6H, –OAc), 1.58 (*m*, 4H, Glc-O–C–CH_2–C–), 1.35 (*m*, 2H, ^3J=7.3 Hz, –C–CH_2–C–); ^{13}C NMR (70 MHz, $CDCl_3$) δ 20.6, 20.6, 20.6, 20.7, 22.2, 29.0, 62.0, 68.5, 69.9, 71.3, 71.8, 72.9, 100.8, 169.2, 169.4, 170.3, 170.7; FT-IR (KBr-disk, cm^{-1}) 2944, 2872 (C–H), 1759, 1744 (C=O), 1456 (H–C–H, H–C–C), 1238, 1223 (esters), 1171, 1132, 1090, 1040 (ether); FABMS *m/z* 803 $(M+K)^+$. Anal. calcd for $C_{33}H_{46}O_{20}$: C, 51.83; H, 6.33. Found: C, 51.59; H, 6.54.

4.2.8. 1,5-Pentandiyl bis-(2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside) (4b). Colorless crystal; mp 66–67.5°C; $[\alpha]_D^{20}$=−5.2 (*c*=0.2, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.20 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.6 Hz, H-1), 3.89 (*dt*, 2H, ^3J=6.3 Hz, ^2J=9.6 Hz, O–C*H*H′–CH_2–O), 3.94–2.94 (*m*, 12H, H-2, H-3, H-4, H-6, H-6′, methylenes), 3.62 (*s*, 6H, –OMe), 3.56 (*s*, 6H, –OMe), 3.52 (*s*, 6H, –OMe), 3.39 (*s*, 6H, –OMe), 3.25 (*m*, 2H, H-5), 1.58 (*m*, 4H, Glc-O–C–CH_2–C–), 1.45 (*q*, 2H, ^3J=7.3 Hz, –C–CH_2–C–); ^{13}C NMR (70 MHz, $CDCl_3$) δ 2.5, 29.4, 59.3, 60.4, 60.4, 60.8, 69.7, 71.4, 74.6, 79.5, 83.8, 86.4, 103.4; FT-IR (KBr-disk, cm^{-1}) 2938, 2832 (C–H), 1473, 1458 (H–C–H, H–C–C), 1128, 1080 (ether); FABMS *m/z* 579 $(M+K)^+$. Anal. calcd for $C_{25}H_{48}O_{12}$: C, 55.54; H, 8.95. Found: C, 55.30; H, 8.88.

4.2.9. 1,3-Bis-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylmethyl) benzene (5b). White crystal; mp 29–31°C; $[\alpha]_D^{20}$=−6.0 (*c*=0.2, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.37–7.23 (*m*, 4H, aromatic protons) 5.40 (*dd*, 2H, $^3J_{H\text{-}3,H\text{-}4}$=3.3 Hz, $^3J_{H\text{-}4,H\text{-}5}$=0.7 Hz, H-4), 5.27 (*dd*, 2H, $^3J_{H\text{-}2,H\text{-}3}$=10.6 Hz, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, H-2), 5.01 (*dd*, 2H, $^3J_{H\text{-}2,H\text{-}3}$=10.6 Hz, $^3J_{H\text{-}3,H\text{-}4}$=3.3 Hz, H-3), 4.91 (*d*, 2H, ^2J=12.2 Hz, Ph-C*H*H′–), 4.63 (*d*, 2H, ^2J=12.2 Hz, Ph-CH*H*′–), 4.54 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.9 Hz, H-1), 4.22 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6}$=6.6 Hz, $^2J_{H\text{-}6,H\text{-}6'}$=11.2 Hz, H-6), 4.14 (*dd*, 2H, $^3J_{H\text{-}5,H\text{-}6'}$=6.9 Hz, $^2J_{H\text{-}6,H\text{-}6'}$=10.2 Hz, H-6′), 3.92 (*dt*, 2H, $^3J_{H\text{-}5,H\text{-}6}$=1.0 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$=6.6 Hz, H-5), 2.16 (*s*, 6H, –OAc), 2.07 (*s*, 6H, –OAc), 2.01 (*s*, 6H, –OAc), 1.98 (*s*, 6H, –OAc); ^{13}C NMR (70 MHz, $CDCl_3$) δ 20.5, 20.6, 20.6, 61.3, 67.1, 68.9, 70.5, 70.7, 70.9, 99.9, 127.0, 127.3, 128.7, 137.1, 169.3, 170.1, 170.2, 170.4; FT-IR (neat, cm^{-1}) 2984, 2942, 2886 (C–H), 1744 (C=O), 1638 (C=C), 1489, 1433, 1372 (C–C–H, H–C–H), 1221 (ester), 1078, 1053 (ether) 957, 901; FABMS *m/z* 837 $(M+K)^+$. Anal. calcd for $C_{36}H_{46}O_{20}$: C, 54.13; H, 5.80. Found: C, 54.00; H, 5.90.

4.2.10. 1,3-Bis-(2,3,4,6-tetra-*O*-methyl-β-D-galactopyranosylmethyl) benzene (5b). Colorless syrup; $[\alpha]_D^{20}$=−39.8 (*c*=0.2, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.30 (*m*, 4H, aryl protons) 4.92 (*d*, 2H, ^2J= 11.9 Hz, Ph-C*H*H′–), 4.60 (*d*, 2H, ^2J=12.2 Hz, Ph-CH*H*′–), 4.33 (*d*, 2H, $^3J_{H\text{-}1,H\text{-}2}$=7.6 Hz, H-1), 3.67–3.46 (*m*, 8H, H-4, H-5, H-6, H-6′), 3.59 (*s*, 6H, –OMe), 3.57 (*s*, 6H, –OMe), 3.52 (*s*, 6H, –OMe), 3.42 (*s*, 6H, –OMe), 3.39 (*dd*, 2H,

$^3J_{H\text{-}2,H\text{-}3}$=9.9 Hz, $^3J_{H\text{-}1,H\text{-}2}$=7.6 Hz, H-2), 3.13 (*dd*, 2H, $^3J_{H\text{-}2,H\text{-}3}$=9.6 Hz, $^3J_{H\text{-}3,H\text{-}4}$=3.0 Hz, H-3); ^{13}C NMR (70 MHz, $CDCl_3$) δ 58.3, 59.2, 60.8, 61.2, 70.6, 70.7, 73.0, 74.9, 80.7, 83.8, 102.6, 126.9, 127.0, 128.3, 137.7; FT-IR (KBr-disk, cm^{-1}) 2998 (=C–H), 2932, 2836 (C–H), 1750, 1717 (C=C), 1489, 1456 (H–C–H, H–C–C), 1105, 1078 (ether); FABMS *m/z* 813 $(M+K)^+$. Anal. calcd for $C_{28}H_{46}O_{12}$: C, 58.52; H, 8.07. Found: C, 58.50; H, 8.11.

4.2.11. Preparation of organic ammonium salts. Amino acid 2-propyl ester hydrochlorides were synthesized according to the standard esterification method from commercial D- [or (*R*)-] amino acid and L- [or (*S*)-] amino acid (Aldrich, Sigma, Tokyo Kasei, and Wako) with $(CD_3)_2CDOD$ (99+ at.% D, Aldrich).[14] (*S*)-Tryptophan-2-propyl-d_6 ester hydrochlorides was prepared by esterification with $(CD_3)_2CHOH$, (99.5 at.% D, CDN isotope, Canada) to avoid H/D exchange of the indole moiety. The proportion of the deuterium-labeled amino acid ester hydrochlorides depends on that of the alcohol. The deuterium content of the labeled amino acid hydrochlorides was >99%. The above products were dried in vacuo at 40°C before the FABMS measurements.

Organic ammonium hexafluorophosphate were prepared according to the anion exchange method between the corresponding organic ammonium chloride and $AgPF_6$ (Aldrich).[15] Typical procedures and the characterization were as follows: (*R*)-1-(1-naphthyl)-ethylammonium hexafluorophosphate [(*R*)-NEA^+ (PF_6^-)]. 1-(1-Naphthyl)-ethylamine (165 mg, 0.96 mmol) was dissolved in dichloromethane, and the solution was bubbled with dry HCl gas. The precipitate was filtrated, washed with dichloromethane, and dried at 60°C in vacuo overnight. The obtained chloride (200 mg, 0.96 mmol) was dissolved into a 5 mL of water. While, the equimolar $AgPF_6$ (243 mg) was also dissolved into a 5 mL of water. The aqueous solutions were mixed, and the produced precipitate (AgCl) was removed by filtration. The water was removed from the filtrate with frozen drier. The quantitatively obtained white powder was further dried in vacuo before the ^{1}H NMR experiments. Anal. calcd for $C_{12}H_{14}F_6NP$: C, 45.44; H, 4.45; N, 4.42. Found: C, 46.92; H, 4.52; N, 4.59. (*S*)-NEA^+(PF_6^-), anal. calcd for $C_{12}H_{14}F_6NP$: C, 45.44; H, 4.45; N, 4.42. Found: C, 46.97; H, 4.52; N, 4.59.

4.3. The FABMS/EL guest method

(a) *Measurement conditions in FAB mass spectra*. FAB mass spectra (positive mode) were measured with a JEOL JMS-600 mass spectrometer operating at an accelerating voltage of 6 kV with a mass range of *m/z* 20–2300. The instrument was equipped with a standard JEOL FAB source and an ion gun. Xenon was used as the atom beam with an emission current of 0.5 mA and an acceleration of 3 kV. The ion source pressure was typically ca. 2×10^{-6} Torr. The spectra were obtained with a magnet scan rate of 5 s per scan (to *m/z* 2300) and the data were processed with a JEOL JMA data processing system on a Microsoft Windows 98. The calibration was carried out with CsI.

(b) *Preparation of sample solutions*. A sample solution was prepared by mixing three solutions under two conditions as follows: microsyringes and a vibrator were used. FABMS measurements were performed, after the solution stood overnight, with a deposit of a 1 μL aliquot of the mixed solution on a FAB probe tip. *Condition A*: (1) 10 μL of a 0.67 M MeOH solution of a 1:1 mixture of (*R*)-unlabeled and (*S*)-labeled guests ($[G_R^+]=[G_{S\text{-dn}}^+]$=0.33 M); (2) 5 μL of a 0.20 M $CHCl_3$ host solution; (3) 15 μL of NBA matrix. The last concentrations in NBA were calculated to [H]= 0.067 M, [G]=0.45 M. *Condition B* (in NEA^+): (1) 5 μL of a 0.30 M MeOH solution of a 1:1 mixture of (*R*)-unlabeled and (*S*)-labeled guests ($[G_R^+]=[G_{S\text{-dn}}^+]$= 0.15 M); (2) 5 μL of a 0.05 M $CHCl_3$ host solution; (3) 15 μL of NBA matrix. In these concentration conditions after evaporation of MeOH and $CHCl_3$ solvents in the ion source, the concentrations in NBA were calculated to [H]=0.0167 M, [G]=0.10 M ($[H]/[G_R^+]/[G_{S\text{-dn}}^+]$=1:3:3). ($[H]/[G_R^+]/[G_{S\text{-dn}}^+]$=1:3.3:3.3).

4.4. ^{1}H NMR experiments

(a) *The K values and the limiting shifts with organic guest and potassium cations*. The induced shifts of proton peaks of the host by adding stepwise organic guest cations (counter anion: PF_6^-) or potassium ion (counter anion: SCN^-) were monitored at 298 K, and from the spectral changes the *K* values were determined using the 1:1 non-linear method.[17] The stoichiometry of their hosts with the guests was assumed as 1:1 complexation because of no observation of the other complex ion peaks (for example, 1:2 complex) in FAB mass spectra. A typical example was as following: 0.6 mL of a 2.59 mM host **1b** $(CD_3)_2CO$ solution was prepared in 5 mm NMR tube with a septa cap. ^{1}H NMR spectra were measured at 298 K by step of adding six portions of KSCN $(CD_3)_2CO$ solution to the host solution. The molar ratio [G]/[H] was 0, 0.36, 1.07, 2.49, 5.30, 10.49, 20.6 and 39.9, respectively. The signals of H-1, H-2, H-3, and four OMe's protons were followed, and the *K* values were calculated from their shift changes by means of the typical 1:1 non-linear method, respectively. The averaged *K* value was 15.0 M^{-1}, and the σ value was 2.1.

In the case of a 1:1 complexation equilibrium, the following equation holds:[16]

$$[H] = [(K[G]_0 + K[H]_0 + 1) - \{(K[G]_0 + K[H]_0 + 1)^2 - 4K[H]_0\}^{1/2}]/2K \quad (1)$$

Here [H] represents the host concentration in the equilibrium. $[H]_0$, $[G]_0$ and *K* were the initial concentration of the host and the guest, and the association constant, respectively. The limiting shift (δ_{lim}) is represented by the following equation:

$$\delta_{lim} = ([H]_0\delta_{obs} - [H]\delta_0)/([H]_0 - [H]) \quad (2)$$

Here δ_{obs} and δ_0 represent the observed shift and the initial shift, respectively. Therefore, the limiting shifts are calculated from Eqs. (1) and (2).

(b) *Induced shifts by organic ammonium hexafluorophosphates*. Until no or little shifts were observed, the

organic ammonium salt $CDCl_3$ solution (2.2 mM) was added into the host $CDCl_3$ solution in a 5 mm NMR tube keeping room temperature, and then, the induced shifts were measured. In the case of host **1b** with (*R*)- and (*S*)-NEA^+ (PF_6^-), the molar concentration ratio [G]/[H] was 2.0. $CDCl_3$ were selected as solvent because larger induced shifts were observed compared with in $(CD_3)_2CO$.

4.5. Molecular simulation

All molecular model simulation were calculated with a software Cerius^2 (MSI, ver. 4.2) on a Silicon Graphic workstation unix system (octane). The initial molecular structures were constructed with a 3D-Sketcher software module in Cerius^2 and the molecular structures were optimized with an MM (force field: PCFF).[17] The MD of the permethylated oligosaccharides were simulated using a canonical (NTV) ensemble (T=298 K), and the temperature was controlled by the Hoover dynamics method.[18] One step of the calculation is 1 fs. Calculation was repeated over 100,000 steps (100 ps). The properties which are an averaged molecular length, a radius of gyration, and a self-diffusion coefficient were evaluated from last 30,000 steps (30 ps).

Acknowledgements

We are grateful to Mrs Fusako Fukuda, deceased (Material Analysis Center, The Institute of Scientific and Industrial Research, Osaka University) for elemental microanalyses.

References

1. (a) de Jong, F.; Siegel, M. G.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1975**, 551–553. (b) Kyba, E. P.; Timko, J. M.; Kaplan, L. J.; de Jong, F.; Gokel, G. W.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 4555–4568. (c) Peacock, S. C.; Domeier, L. A.; Gaeta, F. C. A.; Helgeson, R. C.; Timko, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 8190–8202. (d) Newcomb, M.; Toner, J. L.; Helgeson, R. C.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 4941–4947. (e) Sogah, G. D. Y.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3035–3042. (f) Peacock, S. C.; Walba, D. M.; Gaeta, F. C. A.; Helgeson, R. C.; Cram, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 2043–2052. (g) Lingenfelter, D. S.; Helgeson, R. C.; Cram, D. J. *J. Org. Chem.* **1981**, *46*, 393–402. (h) Knobler, C. B.; Gaeta, F. C. A.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1988**, 330–331. (i) Cram, D. J.; Sogah, G. D. Y. *J. Chem. Soc., Chem. Commun.* **1981**, 625–626. (j) Cram, D. J.; Sogah, G. D. Y. *J. Am. Chem. Soc.* **1985**, *107*, 8301–8302.
2. (a) Spisni, A.; Corradini, R.; Marchelli, R.; Dossena, A. *J. Org. Chem.* **1989**, *54*, 684–688. (b) Kato, Y.; Conn, M.; Rebek, Jr., J. *J. Am. Chem. Soc.* **1994**, *116*, 3279–3285. (c) Jansen, R. J.; de Gelder, R.; Rowan, E. A.; Scheeren, H. W.; Nolte, R. J. *J. Org. Chem.* **2001**, *66*, 2643–2653. (d) Cabell, L. A.; Best, M. D.; Lavigane, J. J.; Schneider, S. E.; Perreault, D. M.; Monahan, M.-K.; Anslyn, E. V. *J. Chem. Soc., Perkin Trans. 2* **2001**, 315–323. (e) Wang, X.; Erickson, S. D.; Iimori, T.; Still, W. C. *J. Am. Chem. Soc.* **1992**, *114*, 4128–4137. (f) Benito, J. M.; Gômez-Garcia, M.; Jimènez Blanco, J. L.; Mellet, C. O.; Garcia Fernàndez, J. M. *J. Org. Chem.* **2001**, *66*, 1366–1372. (g) Vögle, F.; Weber, E. *Angew. Chem. Int. Ed.* **1979**, *18*, 753–776. (h) Suzuki, Y.; Morozumi, T.; Nakamura, H.; Shimomura, M.; Hayashita, T.; Bartsh, R. A. *J. Phys. Chem. B* **1998**, *102*, 7910–7917.
3. (a) Drichamer, K. *Nature* **1992**, *360*, 183–186. (b) Williams, D. H.; Bardsley, B. *Angew. Chem. Int. Ed.* **1999**, *38*, 1172–1193.
4. (a) Sawada, M.; Shizuma, M.; Takai, Y.; Adachi, H.; Takeda, T.; Uchiyama, T. *Chem. Commun.* **1998**, 1453–1454. (b) Shizuma, M.; Adachi, H.; Amemura, A.; Takai, Y.; Takeda, T.; Sawada, M. *Tetrahedron* **2001**, *57*, 4567–4578. (c) Shizuma, M.; Adachi, H.; Takai, Y.; Hayashi, M.; Tanaka, J.; Takeda, T.; Sawada, M. *Carbohydr. Res.* **2001**, *335*, 275–281.
5. Shizuma, M.; Adachi, H.; Kawamura, M.; Takai, Y.; Takeda, T.; Sawada, M. *J. Chem. Soc., Perkin Trans. 2* **2001**, 592–601.
6. Kawai, Y.; Matsuo, T.; Ohno, A. *J. Chem. Soc., Perkin Trans. 2* **2000**, 887–891.
7. (a) Sawada, M.; Takai, Y.; Yamada, H.; Hirayama, S.; Kaneda, T.; Tanaka, T.; Kamada, K.; Mizooku, T.; Takeuchi, S.; Ueno, K.; Hirose, K.; Tobe, Y.; Naemura, K. *J. Am. Chem. Soc.* **1995**, *117*, 7726–7736. (b) Sawada, M. *Mass Spectrom. Rev.* **1997**, *16*, 73–90. (c) Sawada, M. *J. Mass Spectrom. Soc. Jpn* **1997**, *45*, 439–458. (d) Shizuma, M. *J. Mass Spectrom. Soc. Jpn* **1998**, *46*, 211–218. (e) Sawada, M.; Takai, Y.; Yamada, H.; Nishida, J.; Kaneda, T.; Arakawa, R.; Okamoto, M.; Hirose, K.; Tanaka, T.; Naemura, K. *J. Chem. Soc., Perkin Trans. 2* **1998**, 701–710. (f) Sawada, M.; Harada, T.; Takai, Y.; Nakano, K.; Kuroda, M.; Arakawa, R. *J. Mass Spectrom. Soc. Jpn* **2000**, *48*, 141–144.
8. (a) Sand, D. M.; Schlenk, H. *Anal. Chem.* **1961**, *33*, 1624–1625. (b) Schurig, V.; Nowotny, H.-P. *Angew. Chem. Int. Ed.* **1990**, *29*, 939–957. (c) Berthod, A.; Chang, S.-C.; Armstrong, D. W. *Anal. Chem.* **1990**, *64*, 395–404. (d) Armstrong, D. W.; Stalcup, A. M.; Hilton, M. L.; Duncan, J. D.; Faulkner, Jr., J. R.; Chang, S.-C. *Anal. Chem.* **1990**, *62*, 1610–1615. (e) Yi, G.; Bradshaw, J. S.; Rossiter, B. E.; Malik, A.; Li, W.; Lee, M. L. *J. Org. Chem.* **1993**, *58*, 4844–4850. (f) Yi, G.; Bradshaw, J. S.; Rossiter, B. E.; Reese, S. L.; Pertersson, P.; Markides, K. E.; Lee, M. L. *J. Org. Chem.* **1993**, *58*, 2561–2565.
(g) Hargitai, T.; Kaida, Y.; Okamoto, Y. *J. Chromatogr.* **1993**, *628*, 11–22.
9. (a) Fanali, S. *J. Chromatogr.* **1989**, *474*, 441–446. (b) Kuhr, W. G.; Monnig, C. S. *Anal. Chem.* **1992**, *64*, 389R–407R. (c) Kano, K.; Tamiya, Y.; Otsuki, C.; Shimomura, T.; Ohno, T.; Hayashida, O.; Murakami, Y. *Supramolecular Chem.* **1992**, *2*, 137. (d) Chien, R. L.; Burghi, D. S. *Anal. Chem.* **1992**, *64*, 489A–496A. (e) Quang, C.; Khaledi, M. G. *Anal. Chem.* **1993**, *65*, 3354–3358. (f) Stalcup, A. M.; Gahm, K. H. *Anal. Chem.* **1996**, *68*, 1360–1368.
10. Hudson, C. S.; Dale, J. K. *J. Am. Chem. Soc.* **1915**, *37*, 1264–1270.
11. Pittman, Jr., C. U.; McManus, S. P.; Larsen, J. W. *Chem. Rev.* **1972**, *72*, 357–438.
12. Glaudemans, C. P. J.; Zissis, E.; Jolley, M. *Carbohydr. Res.* **1974**, *40*, 129–135.
13. (a) Hakomori, S. *J. Biochem. (Tokyo)* **1964**, *55*, 205–208. (b) Conard, H. E. *Method in Carbohydrate Chemistry*; Whister, R. L., Bemiller, S. N., Eds.; Academic: New York, 1972; Vol. 6, p. 361. (c) Melton, L. D.; McNeil, M.; Darvill, A. G.; Albersheim, P.; Dell, A. *Carbohydr. Res.* **1986**, *146*, 279–285.

14. Kyba, E. P.; Timko, J. M.; Kaplan, L. J.; de Jong, F.; Gokel, G. W.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 4555–4568.
15. Sousa, L. R.; Sogah, G. D. Y.; Hoffman, D. H.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 4569–4576.
16. (a) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703–2707. (b) Hu, S. I.; Goldberg, E.; Miller, S. I. *Org. Magn. Reson.* **1972**, *4*, 683–693. (c) Connors, K. A. *Binding Constants. The Measurement of Molecular Complex Stability*; Wiley: New York, 1987; Chapter 5, pp. 187–215.
17. Sun, H.; Ren, P.; Fried, J. P. *Comput. Theor. Polym. Sci.* **1998**, 229–246.
18. Hoover, W. G. *Computational Statistical Mechanics*; Elsevier: Amsterdam, 1990.