polymer communications

New macromolecular ionophore: enantioselective membrane transport of racemic amino acid by poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol]

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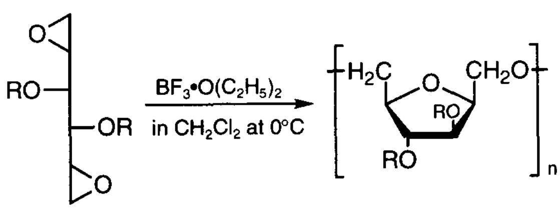
The chiral recognition property of poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol] (**2b**) towards racemic $RCH(CO_2CH_3)NH_3^+ \cdot X^-$ (3·HX) has been studied using a transport system involving an aqueous source and receiving phases separated by a chloroform phase containing **2b**. For HPF_6, $HClO_4$ and HCl salts of **3a** (R = Ph), the amount of **3a** transported into the receiving phase decreased in the order of $PF_6^- > ClO_4^- > Cl^-$, but the optical purities changed only slightly from 9.3 to 10.9%. The transport rates for aromatic guests, **3a** and **3b** ($R = CH_2Ph$), were faster than those for aliphatic ones, **3c** ($R = CH(CH_3)_2$) and **3d** ($CH_2CH(CH_3)_2$), using PF_6^- as the counterion. The optical purity was 10.9% for **3a** as a maximum value and decreased in the order of **3a** > **3c** > **3b** and **3d**. The formation of a complex between **2b** and **3a**·HX was confirmed by ^1H and ^{13}C n.m.r. spectral measurements.

(Keywords: membrane; transport; amino acid)

Introduction

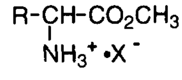
In host–guest chemistry, polymers with macrocyclic units, for example crown ether and azacrown, are generally known as host polymers having a recognition property towards guest molecules. However, there are a few limited studies describing other types of host polymers whose molecular recognition is not based on that of the macrocyclic structure. α,ω-Poly(cyclooxalkane)diyl[1] and poly(7-oxanorbornene)[2] exhibited a binding ability for various sizes of cations, such as Li^+, Ba^{2+}, methylene blue (MB), and rhodamine 6G (Rh6G). Recently, we reported that the cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannitol (**1a**) was regio- and stereospecific to give poly[(1→6)-2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol] (**2a**), which formed complexes with such organic cations as MB and Rh6G along with alkali metal picrates[3].

These polymers are supposed to form helical conformers capable of varying pitch and cavity size to optimize multidentate coordination with a given cation. This host–guest complexation mechanism is similar to that for naturally occurring acyclic ionophores which accommodate guest metal cations in their pseudocyclic cavities and transport a guest across the biomembrane. These polymers are therefore a new class of host polymers, namely, a macromolecular ionophore. Host polymer **2** consists of chiral constitutional repeating units, whose asymmetric character is distinct from the other macromolecular ionophores. Of greater interest, therefore, is the observation of the chiral recognition property of host polymer **2** toward a racemic guest.



1 **2**

1a, **2a**; $R=C_2H_5$, **1b**, **2b**; $R=CH_3$



$R{-}\underset{NH_3^+ \cdot X^-}{CH}{-}CO_2CH_3$

3·HX

3a, $R=C_6H_5$
3b, $R=C_6H_5CH_2$
3c, $R=(CH_3)_2CH$
3d, $R=(CH_3)_2CHCH_2$

In this paper, we report that the enantioselective transport of racemic methyl amino esters (**3**) was achieved using a system involving an aqueous source and receiving phases separated by a chloroform phase containing poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol] (**2b**).

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Experimental

Measurements. ^1H and ^{13}C n.m.r. spectra were recorded with a Bruker MSL 400 instrument. U.v. spectra were recorded on a Jasco 660 u.v./vis. spectrophotometer. The molecular weights of the resulting polymers were measured by gel permeation chromatography (g.p.c.) in tetrahydrofuran on a Waters M45 high-performance liquid chromatograph equipped with three polystyrene gel columns (Shodex KF-804L). Their number-average molecular weights were calculated on the basis of a polystyrene calibration.

Polymer synthesis. To a solution of **1b** in dichloromethane was added a solution of $BF_3{\cdot}OEt_2$ in dichloromethane at 0°C. After 24 h, the reaction mixture was poured into a large amount of ammonical methanol. The entire solution was then evaporated under reduced pressure. The residue was washed with n-hexane several times and then dried in vacuum to give polymer **2b**. The number-average molecular weight and the molecular weight distribution, determined by g.p.c. using polystyrene calibration, were 3800 and 2.0, respectively.

Transport experiment. In a U-tube (i.d. 14 mm) was placed 10 ml of chloroform with $2\,g\,l^{-1}$ of the host polymer **2b**. Water, 0.08 M in HCl (5 ml) containing 0.02 M guest amine salt, was placed in the α-arm (the source phase). The β-arm (the receiving phase) contained 5.0 ml of 0.10 M HCl solution in water. The chloroform phase was mixed using a small magnetic stirrer at a constant rate. The transported guest salts were followed by measuring the u.v. absorbance at 272 nm for the solution in the β-arm. The optical purity was determined by h.p.l.c. using Crownpak CR(+) (Daicel Chemical Industries, Ltd) as the optical resolution column and aq. $HClO_4$ (pH 2.0) as the eluent.

Results and discussion

Typical results are summarized in *Table 1*. The effect of the counteranion (X^-) on the transport experiment was examined using HPF_6, $HClO_4$ and HCl salts of phenylglycine methyl ester (**3a**). The amount of **3a** transported to the receiving phase was 31.5% for PF_6^- and decreased in the order of $PF_6^- > ClO_4^- > Cl^-$. This result indicates that the lipophilicity of the counterions affects the formation of the host–guest complex and the transport rate of the complex through the chloroform membrane. On the other hand, the optical purities had values of 9.3–10.9%, and this slight change means that X^- is not an important factor affecting the chiral recognition property of **2b**. The structural effect of a guest on transport was elucidated using HPF_6 salts of methyl amino esters ($3{\cdot}HPF_6^-$). The transport rates for the aromatic guests, **3a** and **3b**, were faster than those for the aliphatic ones, **3c** and **3d**. The optical purity was 10.9% for **3a** as a maximum value and decreased in the order of **3a**>**3c**>**3b** and **3d**. This order conforms to the character of the R group of $RCH(CO_2CH_3)NH_3^+{\cdot}PF_6^-$ in the following sense: the greater the steric requirements of this group in the vicinity of the chiral centre of the guest, the higher the chiral recognition. The characteristic of the chiral recognition of **2b** is very similar to that of the chiral crown ethers incorporating 1,1'-binaphthyl units reported by Lingenfelter *et al.*[4]. For all the host–guest systems, the faster moving enantiomer was the L-form.

The formation of a host–guest complex was observed by n.m.r. spectral measurements, when the transport experiments were carried out in $CDCl_3$ under the same condition as described in *Table 1*. *Figure 1* shows the ^{13}C

Table 1 Enantioselective transport of DL-$RCH(CO_2CH_3)NH_3^+{\cdot}X^-$ (3·HX) by poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol] (**2b**)

		Guest in receiving phase (β-arm)		
3 (R)	X^-	Transported (%)[a]	Optical purity (%)[b]	Faster moving enantiomer
3a (C_6H_5)	PF_6^-	31.5	10.9	L
	ClO_4^-	9.4	10.7	L
	Cl^-	2.1	9.3	L
3b ($C_6H_5CH_2$)	PF_6^-	30.9	2.3	L
3c ($(CH_3)_2CH$)	PF_6^-	17.8	7.3	L
3d ($(CH_3)_2CHCH_2$)	PF_6^-	16.7	2.3	L

[a] Transported after 120 h

[b] Analysed by h.p.l.c. when 30% of guest was transported from source phase to receiving phase

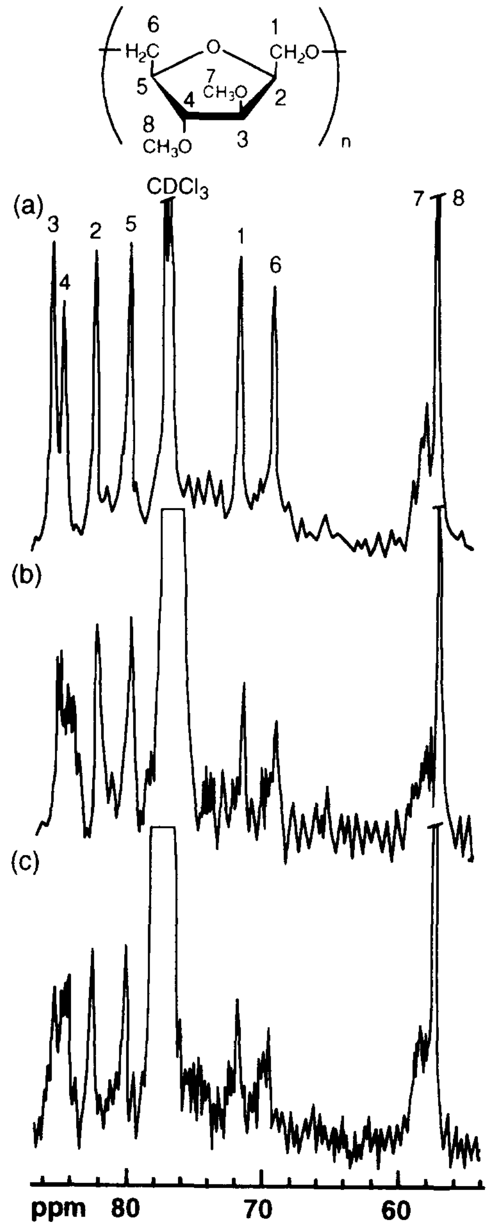

Figure 1 ^{13}C n.m.r. spectra of **2b** before (a) and after the complexation with D- or L-$3a{\cdot}PF_6^-$: (b) **2b**/D-isomer; (c) **2b**/L-isomer

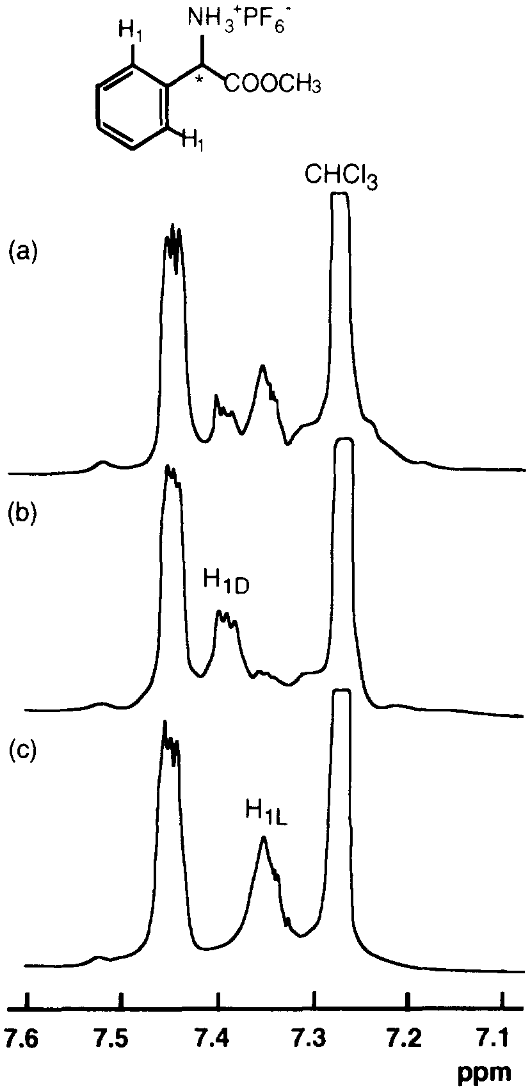

Figure 2 ^{1}H n.m.r. spectra of the aromatic protons of **3a** for the transport experiments of DL-, D or L-**3a**·PF_6^- using **2b**: (a) DL-; (b) D-; (c) L-**3a**·PF_6^-

n.m.r. spectra of **2b** before and after the complexation with D- or L-**3a**·PF_6^-. The absorptions at 84.7, 85.4 and 69.3 ppm due to the C3, C4 and C6 carbons in 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units were singlet before the host–guest complexation. On the other hand, the absorptions at the C3, C4 and C6 split into multiplets after the complex formation between **2b** and D-**3a**·PF_6^-, and those at C4 and C6 between **2b** and L-one. This result indicates that the oxygens attached to the C3, C4 and C6 carbons act as a donor atom for the host–guest complexation.

Figure 2 shows the ^{1}H n.m.r. spectra of guests for the transport experiments using D-, L- or DL-**3a**·PF_6^-. The broad absorptions at 7.36 and 7.42 ppm due to the *ortho* protons (H_1) were observed for the transport system using DL-**3a**·PF_6^-. The former (H_{1L}) and the latter (H_{1D}) agreed with the absorption for L-**3a** and for D-**3a** in the host–guest complexation, respectively. The H_{1L}/H_{1D} areal ratio was 1.35, a value close to the L-**3a**/D-**3a** ratio of 1.25 (optical purity, 10.9%) in *Table 1*. These results indicate that the coordination environment of **2b** with L-**3a** differs from that of D-**3a**, and the **2b**-L-**3a** complex is more stable than the **2b**-D-**3a** one. Consequently, this difference in stability causes the predominant transport of the L-isomer to **2b**.

We are now studying the effect of alkyl groups at the C3 and C4 positions on the chiral recognition property of host polymer **2** in connection with the mechanism of the host–guest complexation.

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