Detection of Molecular-Shape Recognition for Polycyclic Aromatic Hydrocarbons by α-Helical Poly(L-Alanine) on Silica[1]

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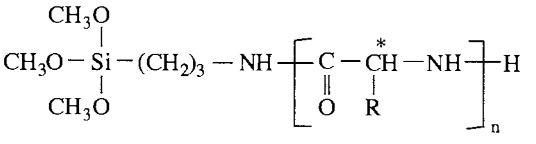
α-Helical poly(L-alanine) grafted onto porous silica particles with a reactive terminal trimethoxysilyl group showed a specific shape-selective retention for polycyclic aromatic hydrocarbons, recognizing their molecular linearities and slenderness. This selectivity is derived from the carbonyl groups on the rigid secondary structure and thus the poly(L-leucine) derivative having bulky residual groups showed almost no similar selectivity.

Poly(α-amino acid)s having ionic residual groups have been focused on host molecules for a host-guest chemistry because of homogeneity in the conformation of the main chain. For example, it is known that poly(L-lysine) provides specific binding sites for anionic dyes.[2-4] The residual ammonium groups work as a driving force for interaction and α-helical conformation provides chiral microenvironment. We have reported that this interaction can be accompanied by enantioselectivity.[4] In the present study, we wish to emphasize that poly(L-alanine) can behave as a specific host molecule for polycyclic aromatic guest molecules. We have an interest in this polymer because the main chain is always in α-helix regardless of pH and temperature and there is no functional group such as ionic and π-electronic groups for interaction in the side chain. Therefore, it would be easier to understand a role of the secondary structure for selective interaction.



$$(CH_3O)_3Si-(CH_2)_3-NH-[C(=O)-\overset{*}{C}H(R)-NH]_n-H$$

$R = -CH_3$ Sil-Ala$_n$ (n = 32)
$R = -CH_2CH(CH_3)_2$ Sil-Leu$_n$ (n = 27)

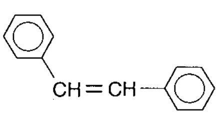
In this study, interaction between the polymer and the guest molecule was evaluated by the retention time using the column packed with the silica-supported poly(L-alanine). Therefore, poly(L-alanine) with a reactive trimethoxysilyl group at the one side of the main chain was prepared by polymerization of *N*-carboxyanhydride of L-alanine initiated by 3-aminopropyltrimethoxysilane and by following immobilization[5] of it onto porous silica particles using the reactive terminal group. We think that the grafting method provides few perturbation from silica. Poly(L-leucine)-grafted silica was also prepared according to the similar procedure. The ^{1}H-NMR and elemental analyses showed that the polymerization degrees and the amounts of immobilization were 32 and 15.0 wt% in the silica-supported poly(L-alanine) (Sil-Ala$_{32}$), and 27 and 14.5 wt% in the silica-supported poly(L-leucine) (Sil-Leu$_{27}$). IR spectroscopy showed that the both polymers (Ala$_{32}$ and Leu$_{27}$) before immobilization were in α-helices which were characterized by their specific absorption bands (amide V) at 620 cm^{-1}. Unfortunately, it was difficult to confirm the conformation of the polymers after immobilization because light scattering due to the silica particles prevented to detect the absorption based on the amide V.

When alkylbenzenes (n = 1 - 12 in C_6H_5-$(CH_2)_{n-1}CH_3$) were applied as guest molecules and a methanol-water mixture was used as a mobile phase, the retention factor[7] increased with increase of log P's[8] of the alkylbenzenes while the retention factor became higher in the order of Sil-Leu$_{27}$ > Sil-Ala$_{32}$. Since log P reflects the molecular hydrophobicity, these results indicate

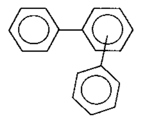
Table 1. Relative retention factor (separation factor) in polycyclic aromatic hydrocarbons

	Separation factor		
	Sil-Ala$_{32}$	Sil-Leu$_{27}$	ODS
cis-stilbene[a]	1	1	1
trans-stilbene	1.7	1.07	1.04
o-terphenyl[a]	1	1	1
m-terphenyl	1.5	1.5	1.4
p-terphenyl	7.2	1.7	1.5
chrysene[a]	1	1	1
benz(a)anthracene	0.81	1.02	1.03
naphthacene	6.0	1.2	1.2
benzene[a]	1	1	1
naphthalene	1.2	1.5	2.0
anthracene	2.8	2.4	3.5
naphthacene	37.5	4.5	7.8

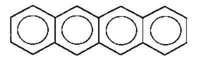
Mobile phases: 25 °C, methanol-water = 7 : 3 in Sil-Ala$_{32}$ and Sil-Leu$_{27}$, methanol-water = 9 : 1 in ODS.
[a] The separation factor corresponds to the relative retention factor based on the substances.
ODS: octadecylated silica.



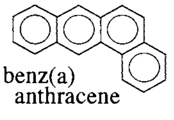
trans- and *cis*-stilbenes



o-, *m*- and *p*-terphenyls



naphthacene



benz(a) anthracene

chrysene

that the polymers provide hydrophobic binding sites and the hydrophobicities become higher in the order of Leu_{27} > Ala_{32} because the silica provides only hydrophilicity. This order is understandable by the difference of their molecular hydrophobicities derived from the residual isobutyl and methyl groups.

Unusual retention behavior was observed when polycyclic aromatic hydrocarbons were applied as guest molecules. Table 1 includes the separation factors between or among the isomers of polycyclic aromatic hydrocarbons. The remarkably high separation factors[7] were obtained only in Sil-Ala_{32}. For example, the separation factor between *p*-terphenyl and *o*-terphenyl was 7.2 in Sil-Ala_{32} while 1.33 in Sil-Leu_{27}. It should be noted that the small separation factors in Sil-Leu_{27} are closed to those observed with simply-hydrophobized silica, ODS.[8] Since ODS has no functional group, the small selectivity due to Sil-Leu_{27} is on the basis of hydrophobic property. As supported this, the isomers have similar log P's each others: for example, chrysene (5.51); benz(a)anthracene (5.54); naphthacene (5.82). These results indicates that Sil-Ala_{32} has specific molecular recognition ability. Here, we know that *trans*-stilbene, *p*-terphenyl and naphthacene have higher molecular linearlity and slenderness than the corresponding isomers: *cis*-stilbene and *o*-terphenyl are bulky compounds with bending structures and chrysene is more cubic compared with naphthacene. In addition, it should be noted that the separation factor between naphthacene and anthracene is remarkably higher in Sil-Ala_{32} (13.4 = 37.5 / 2.8) than in Sil-Leu_{27} (1.9 = 4.5 / 2.4). These facts strongly suggest that Ala_{32} recognizes both molecular-slenderness and -length.

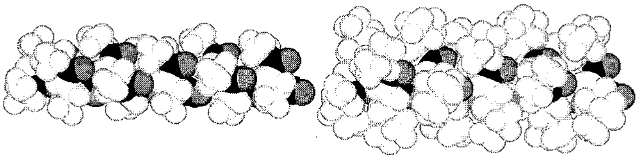


Figure 1. CPK models of right-handed α-helical Ala_{18} (left) and Leu_{18} (right) derived from the PEPCON.[9] The black- and gray-colored atoms present carbonyl carbons and oxygenes, respectively. The carbonyl groups of Leu_{18} are covered with their isobutyl residual groups.

In conclusion, we estimate that the molecular recognition ability due to Sil-Ala_{32} is derived from the highly-oriented carbonyl groups on the rigid main chain. This estimation is supported by following facts: (1) in general, a carbonyl-π interaction is much stronger than a CH-π interaction.[5] The Ala_{32} has many carbonyl groups in the main chain. When acetone was added as an inhibitor for this interaction to a mobile phase, the selectivity of Sil-Ala_{32} decreased remarkably although 2-propanol did not showed almost no significant effect. (2) When the experiment was carried out in hexane to remove hydrophobic effect, the retention ability of Sil-Ala_{32} for polycyclic aromatic hydrocarbons was almost maintained while disappeared in both Sil-Leu_{27} and ODS. This indicates that the hydrophobicity is not essential for the selective retention. (3) According to the CPK model[9] (Figure 1), the carbonyl groups are uncovered with the residual methyl groups in poly(L-alanine). In addition, their carbonyl groups are conformationally fixed through a rigid secondary structure. Therefore, a slender compound such as naphthacene can be easily incorporated into the carbonyl area. On the other hand, the bulky isobutyl groups in poly(L-leucine) prevent such approach to work only as hydrophobic functional groups. In addition, naphthacene has a lot of π-electrons for the carbonyl-π interaction. Probably, the highly-oriented carbonyl groups interact with the π-electrons on slender aromatic hydrocarbons such as naphthacene and *p*-terphenyl to produce multiple interactions more efficiently than with the π-electrons on chrysene as a cubic compound and on *o*-terphenyl as a bending compound. As supported this estimation, we confirmed that the most linear isomer showed the highest retention factor in the four kinds of five-ring polycyclic aromatic hydrocarbons. The details will be discussed elsewhere.

References and Notes

1 Part 3. Excavation and amplification of potential functions of polymers. See reference 5 for Part 2.

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6 Fuji Silysia Super Micro Bead silica gel, diameter 5 μm, pore size 146 Å, specific surface area 330 cm^2g^{-1}.

7 Water-1-octanol partition coefficient (log P) was determined by retention factor with octadecylated silica, ODS (Inertsil ODS, 4.6 x 300 mm, GL Science Co., Ltd.): log P is presented by 3.262 + 4.208 log k'.[5]

8 The retention factor (k') was determined by $(t_r - t_0) / t_0$ where t_r and t_0 are retention time of samples and methanol, respectively. The separation factor was given by the ratio of retention time.

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