

Detection of Unpredictable Molecular Recognition through Carbonyl- π Interaction in Poly(methyl acrylate)-Silica Hybrids¹

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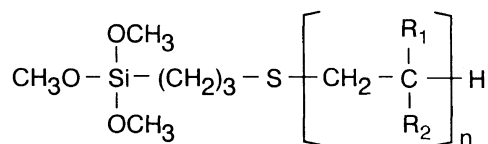
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ABSTRACT: It was detected through grafting onto silica that atactic poly(methyl acrylate) showed unpredictably specific retention selectivity against polycyclic compounds with π -electrons as if molecular-shape recognition was performed. This specificity was discussed with retention behaviors in several other polymer-grafted silicas and by proposing a parameter f to evaluate the contribution of π - π interaction.

KEY WORDS Graft Polymer / Silica / Organic-Inorganic Hybrids / π - π Interaction / Molecular Recognition / Liquid Chromatography /

It is well-known that “host-guest chemistry” is a very important field for understanding biofunctions at the molecular level and has also led to various developments in biomimetic applications such as artificial receptors for sensors, organic media for separation, and transducers for chemical signals. A few specialty polymers such as poly(α -amino acid)s have been focused as a polymer host molecule^{2–6} in order to reproduce biomimetic host-guest chemistry because of rigid and identical conformation in the main chain. On the contrary, atactic synthetic polymers such as poly(methyl acrylate) and polystyrene are recognized as general purpose polymers although we know that weak interactions such as π - π interaction derived from carbonyl and phenyl groups are one of the useful driving force for selective binding.^{7–9} However, nobody expects these atactic polymers to behave as host molecules, in spite of the fact that these are π -electron-rich polymers. In this paper, we describe on poly(methyl acrylate)-grafted silica to evaluate specific interaction ability and that unpredictably unique selectivity can be detected between poly(methyl acrylate) and polycyclic compounds with π -electrons through monitoring the retention time in high performance liquid chromatography process. We also discuss on semi-quantitative evaluation for π - π interaction.



$\text{R}_1 = -\text{H}$	$\text{R}_2 = -\text{COOCH}_3$ ($n = 21$)	Sil-MA ₂₁
$\text{R}_1 = -\text{CH}_3$	$\text{R}_2 = -\text{COOCH}_3$ ($n = 8$)	Sil-MMA ₈
$\text{R}_1 = -\text{H}$	$\text{R}_2 = -\text{CN}$ ($n = 21$)	Sil-AN ₂₁
$\text{R}_1 = -\text{H}$	$\text{R}_2 = -\text{phenyl}$ ($n = 16$)	Sil-St ₁₆
$\text{R}_1 = -\text{H}$	$\text{R}_2 = -\text{naphthyl}$ ($n = 30$)	Sil-VN ₃₀

Scheme 1.

EXPERIMENTAL

Materials

Poly(methyl acrylate), MA₂₁ with a trimethoxypropylsilyl group at one side of the terminal group was prepared by radical telomerization of methyl acrylate with 3-mercaptopropyltrimethoxysilane in ethanol according to previously reported method.^{10,11} A typical preparation procedure is as follows: methyl acrylate and 3-mercaptopropyltrimethoxysilane (30:1 in the molar ratio) were dissolved in ethanol. Azobisisobutyronitrile (0.1 wt% for the monomer) was added to the solution at 70°C. The mixture was stirred for 10 h at 70°C under N₂ gas atmosphere. The white precipitates were obtained *in vacuo*. The structure and polymerization degree of the polymer were determined by NMR spectroscopy. ¹H NMR chemical shifts of MA_n in CDCl₃ were as follows: $\delta = 0.8$ ppm (SiCH₂), $\delta = 1.8$ ppm (CHCO), $\delta = 3.5$ ppm (SiOCH₃), and $\delta = 3.6$ ppm (C(=O)OCH₃). The NMR spectrum showed that the degree of polymerization (n) was 21.

The polymer was readily immobilized onto porous silica (YMC 120-S5, diameter 5 μm , pore size 120 Å, specific surface area 300 cm² g⁻¹) by stirring the mixture in tetrachloromethane at reflux temperature. The resulted silica of successive washing with tetrachloromethane and ethanol provided no significant change in weight. IR spectrum showed a typical sharp absorption (near 1730 cm⁻¹) based on the carbonyl group. The amount of MA_n immobilized was determined as 21.3 wt% by elemental analysis.

Measurements

Silica-supported MA_n (Sil-MA_n) was packed into a stainless steel column (4.6 mm I.D. \times 250 mm) using a hexanol-chloroform (1:1) mixture and the liquid chromatographic property was examined using methanol or methanol-water as mobile phases. The chromatograph included a JASCO 880 PU pump, a Shimadzu UV-VIS photodiode array SPD-M6A and a Shodex refractometer SE-54. Five μl of the sample dissolved in methanol was injected through a Reodyne Model 7125 injector. Chromatography was carried out at flow-rate

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0.5 ml min⁻¹. The retention factor (k') was determined by $(t_e - t_0)/t_0$, where t_e and t_0 are retention time of samples and glycerol, respectively. The separation factor (α) was given by the ratio of retention factor.

Water-1-octanol partition coefficient ($\log P$) was determined by retention factor with octadecylated silica, ODS (Inertsil ODS, 4.6 × 300 mm, GL Science Co., Ltd.): $\log P = 3.262 + 4.208 \log k'$.¹²

Calculation of energy level of HOMO was carried out with CACHE-MOPAC 6.00 with PM3 option.

RESULTS AND DISCUSSION

Retention Behavior for Hydrophobic Compounds

Figure 1 shows the relationship between the retention factor ($\log k'$) and 1-octanol-water partition coefficient¹² ($\log P$) of alkylbenzenes as elutes with a Sil-MA₂₁ (the

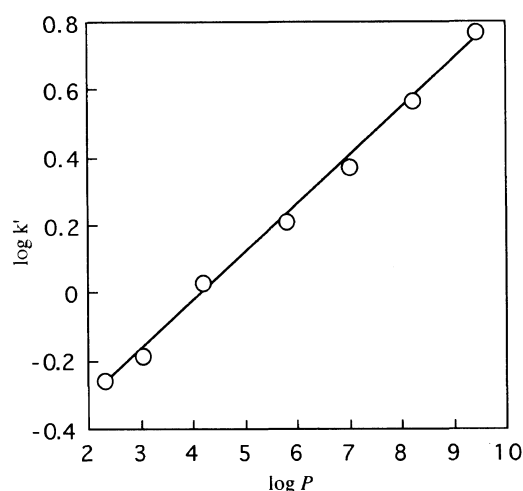


Figure 1. $\log k'$ - $\log P$ plots for alkylbenzenes with a Sil-MA₂₁ column. Samples are methyl-, ethyl-, butyl-, hexyl-, octyl-, decyl-, and dodecylbenzenes from the left in the figure. Mobile phase, methanol-water (7:3) at 25°C.

degree of polymerization, $n=21$) column and methanol-water as a mobile phase. $\log P$ value is often used as a hydrophobic parameter. As shown in Figure 1, the retention factor increases with increase in the alkyl length and the elution order is completely the same as that of usual hydrophobized silica such as ODS. This indicates that Sil-MA₂₁ can recognize molecular hydrophobicity like ODS. Such retention mode is generally recognized as reversed-phase liquid chromatography (RPLC). This indicates that MA₂₁ can behave as a hydrophobic organic phase. Perhaps, the main chain of MA₂₁ provides small hydrophobicity to recognize molecular hydrophobicity of alkylbenzenes.

Figure 2a also shows the relationship between $\log k'$ and $\log P$. The samples are polycyclic hydrocarbons with π -electrons but without alkyl group. If Sil-MA₂₁ has only hydrophobicity recognition ability, a linear correlation must be observed similarly to Figure 1. However, the plot rather seems to show that Sil-MA₂₁ instead recognizes the molecular size (the number of cyclic rings). Normal RPLC mode cannot explain this specificity.

Separation Behavior for Geometrical Isomers

In order to understand the unbelievable result of Figure 2a, we investigated with retention selectivity for geometrical isomers of stilbenes. The mobile phase was a methanol-water (7:3) solution at 15°C. Sil-MA₂₁ provided a higher separation factor ($\alpha=1.61$, the ratio of retention capacities between *trans*- and *cis*-stilbenes) than that ($\alpha=1.20$) of octadecylated silica (ODS¹³). The small separation factor in ODS indicates that the hydrophobicity difference between the geometrical isomers is very small, and thus the higher selectivity in Sil-MA₂₁ is not attributable to hydrophobic effect of immobilized MA₂₁. Essential difference in the immobilized phases between Sil-MA₂₁ and ODS is characterized by a carbonyl group of MA₂₁ moiety. Therefore, we estimate that the carbonyl group provides unexpectedly effective interaction with π -electrons of elutes. This estimation is

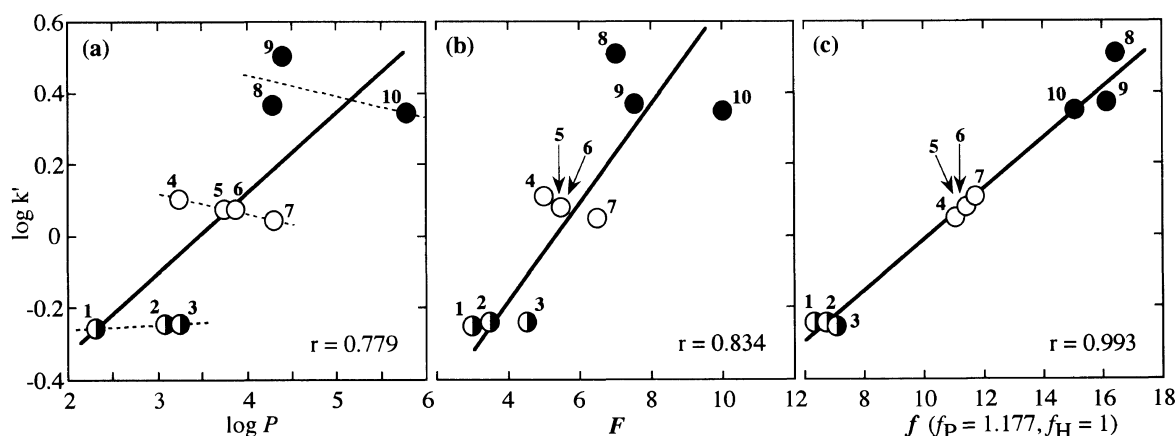
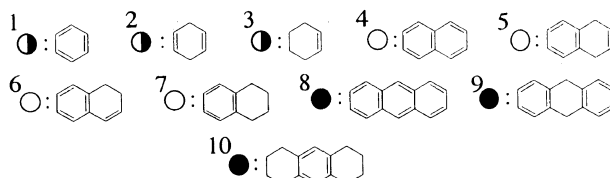


Figure 2. Plots of $\log k'$ - $\log P$, $\log k'$ - F , and $\log k'$ - f in retention behavior for polycyclic compounds with π -electrons through a Sil-MA₂₁ column using methanol-water (7:3) as mobile phase at 25°C. The elutes are given below:



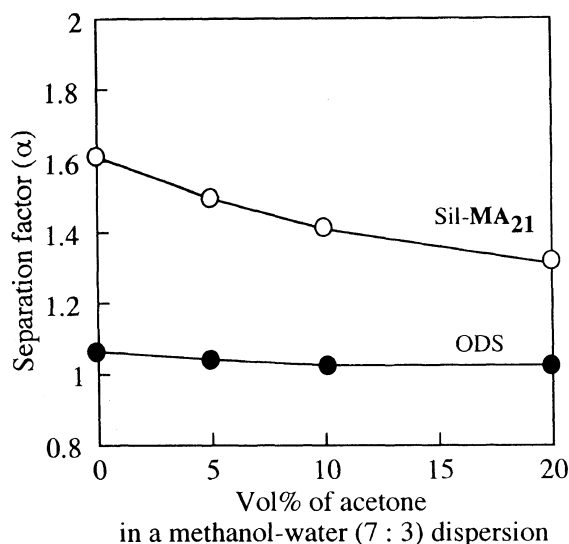
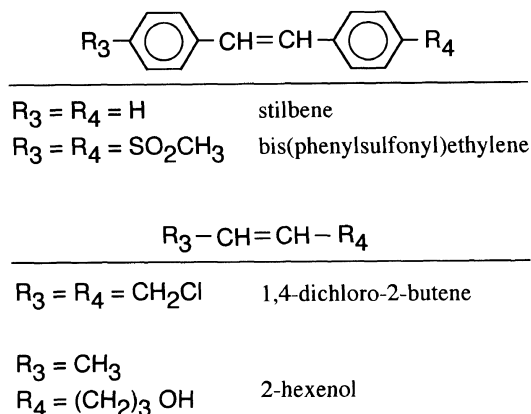


Figure 3. Effect of acetone on the separation factor between *trans*- and *cis*-stilbenes with Sil-MA₂₁ and ODS columns. Mobile phase, methanol-water (7:3) at 25°C.



Scheme 2.

encouraged by the calculation result on interaction between benzene and formic acid reported by Bredás and Street.¹⁴ As shown in Figure 3, we observed that the geometrical selectivity in Sil-MA₂₁ decreased remarkably when acetone with a carbonyl group was added to the mobile phase ($\alpha = 1.61, 1.49, 1.41,$ and 1.31 at 0, 5, 10, and 20 vol% at 15°C, respectively), but the addition of 2-propanol without a carbonyl group had no significant change. This fact strongly suggests that π - π interaction through carbonyl groups plays an essential role in geometrical selectivity against stilbenes. Similarly, good selectivity was observed in the geometrical isomers of bis(phenylsulfonyl)ethylene, but not observed in those of neither 1,4-dichloro-2-butene nor 2-hexenol ($\alpha < 1.1$). These results strongly showed that the geometrical selectivity is much dependent on the detailed chemical structure of the samples. Also it is clear that the 1,4-dichloro-2-butene and 2-hexenol are non-conjugating with substituent groups. If π - π (carbonyl- π) interaction includes charge transfer interaction, energy level of HOMO must be a very useful parameter to estimate it. As supported this, MOPAC calculation^{15,16} showed that energy level of HOMO of both stilbene and bis(phenylsulfonyl)ethylene provided large differences in their

geometrical isomerism, but those of neither 1,4-dichloro-2-butene nor 2-hexenol provided significant difference: for example, $-8.63 \text{ eV}/-9.06 \text{ eV}$ and $-9.59 \text{ eV}/-9.60 \text{ eV}$ for *trans/cis*-isomers of stilbene and 2-hexenol, respectively.

Discussion on Retention Mode

In order to evaluate the contribution of π - π interaction in the specific retention for the polycyclic compounds with π -electrons, we propose a new parameter f , because the conventional $\log k' - \log P$ plot is not applicable for Sil-MA₂₁ (a correlation coefficient, r is only 0.78 in Figure 2a). Although Schabron *et al.* propose an F parameter considering the contribution of double bonds of elutes, which is given by the following equation: $F =$ the number of double bonds + the number of primary and secondary carbon atoms $- 0.5$ for a nonaromatic ring,¹⁷ which has been often used to characterize retention behavior for π -electron-containing compounds,¹⁸ the $\log k' - F$ plot provided still very small correlation coefficient ($r = 0.83$) shown in Figure 2b. On the other hand, our f parameter is presented as follows:

$$f = f_{\text{H}} \text{ for the number of } sp^3 \text{ carbon atoms} + f_{\text{P}} \text{ for the number of } sp^2 \text{ carbon atoms}$$

$$\beta = f_{\text{P}}/f_{\text{H}}$$

where f_{P} and f_{H} values are defined to give the highest correlation coefficient (r) and a parameter f does not characterize the absolute chemical potential of a solute but is used to estimate what degree interacts with stationary phase. Therefore, a parameter of β (the ratio of f_{P} and f_{H}) in f provides the most significant information to understand retention mechanism. If stationary phase has no specific interaction such as π - π interaction with sp^2 carbon atoms of samples, β value will become below 1 because sp^2 carbon atoms behave as more polar moiety than sp^3 carbon atoms in RPLC. As shown in Figure 2c, the $\log k' - f$ plot for Sil-MA₂₁ provided a much better linearity ($r = 0.99$ in $\beta = 1.18$) than those of the $\log k' - \log P$ and $\log k' - F$.

We emphasize applicability of this simple parameter to other π -electron-containing polymers. Table I summarizes the comparison on correlation coefficients with three kinds of parameters, $\log P$, F and f . Only the $\log k' - f$ plot provided good linearities for all of Sil-MMA₈,¹⁹ Sil-AN₂₁,²⁰ Sil-St₁₆,¹¹ and Sil-VN₃₀,¹⁹ where poly(methyl methacrylate), poly(acrylonitrile), poly(styrene), and poly(vinylnaphthalene), respectively, instead of MA₂₁ were grafted onto silica, respectively. However, the $\log k' - \log P$ and $\log k' - F$ plots provided a very small correlation coefficient for Sil-MMA₈ and Sil-AN₂₁ as well as Sil-MA₂₁. This indicates that the retention factor (k') in these polymers is not understandable without considering π - π interaction. On the other hand, the polymers, St₁₆ and VN₃₀ provide relatively high correlation coefficients in the plots of $\log k' - \log P$ ($r = 0.91$ and 0.93 , respectively) although these values are smaller than those in the $\log k' - f$ plot. This can be explained by their stronger hydrophobicity than those of MA₂₁, MMA₈, and AN₂₁.

In addition, we also emphasize that the β value includes significant information to understand the retention

Table I. Comparison of correlation coefficient (r) in the plots of $\log k' - \log P$, $\log k' - F$, and $\log k' - f$.

Bonded phase		Correlation coefficient (r)			
		$\log P$	F	f	β
Sil-MA ₂₁	Poly(methyl acrylate)	0.78	0.83	0.99	1.18
Sil-MA ₂₁ ^a	Poly(methyl acrylate)	—	—	0.97	400
Sil-MMA ₈	Poly(methyl methacrylate)	0.84	0.89	0.99	0.98
Sil-AN ₂₁	Poly(acrylonitrile)	0.57	0.62	0.97	2.07
Sil-St ₁₆	Poly(styrene)	0.91	0.96	0.99	0.79
Sil-VN ₃₀	Poly(vinyl naphthalene)	0.93	0.97	0.99	0.75
ODS ^b	Octadecyl	—	0.98	0.98	0.51

^a Mobile phase: methanol: water = 7:3 except for Sil-MA₂₁ (hexane) and ^bODS (methanol: water = 9:1); samples which were given in Figure 3 were used; 25°C.

mode. For example, MMA₈ is very similar to MA₂₁ in the chemical structure, but the β value (0.98) in Sil-MMA₈ is smaller than that (1.18) in Sil-MA₂₁. This can be explained by larger hydrophobicity derived from an α -methyl group of a MMA moiety. Higher hydrophobicity in MMA than MA reduces f_P/f_H value with increase of f_H value. This estimation is supported by following results: when hexane was used as a mobile phase instead of a methanol-water mixture, $\log k' - f$ plot for Sil-MA₂₁ provided extremely large β value (nearly 400) as shown in Table I. This strongly indicates that hydrophobic effect of MA₂₁ moiety almost disappeared in hexane and the main driving force for selective retention is absolutely induced by $\pi - \pi$ (carbonyl- π) interaction. On the other hand, ODS provided the smallest β value (0.51 in Table I) in a methanol-water solution. This small value indicates that ODS has almost no π -electron-recognition ability. However, it should be noted that β value does not become zero even in ODS. Perhaps, the value of 0.51 means that an sp^2 carbon behaves as a hydrophobic moiety with a half of hydrophobicity for an sp^3 carbon.

At last, we introduce a typical example showing sp^2 carbon recognition with Sil-MA₂₁. ODS had no separation ($\alpha = 1.00$) for a mixture of cyclohexene and naphthalene, in spite of their remarkable difference in the chemical structures. This is because hydrophobicity difference of these samples is extremely small. On the other hand, Sil-MA₂₁ which showed the largest f_P/f_H value (400 in hexane) provided the largest separation

factor ($\alpha = 6.60$) of all the silica-polymer hybrids used in this study.

In conclusion, we succeeded to excavate potential molecular recognition ability of general purpose polymers such as poly(methyl acrylate). This success was supported through hybridization of polymers with silica and through establishment of a new parameter f for evaluation of $\pi - \pi$ interaction, and these applicabilities were also proved.

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