Supplementary Materials: Effects of Alignment of Weak Interaction Sites in Molecular Shape Recognition High-Performance Liquid Chromatography

Hiroki Noguchi, Tianhang Liu, Makoto Takafuji and Hirotaka Ihara

1. Synthetic Scheme

General synthetic procedures were described in the main manuscript.

Figure S1. Synthetic scheme of amino acid derivatives for high-performance liquid chromatography (HPLC) organic phases.

2. Characterization

(1a) Yield: 72.3%; Melting point (m.p.): 88.0–90.1 °C; Fourier transform infrared (FT-IR) (KBr, cm⁻¹): 2928 (νC–H), 2853 (νC–H), 1770 and 1734 (νC=O, ester), 1541 (νC=O, amide); ¹H-NMR (400 MHz, CDCl₃): 0.88 (6H, t, CH₃), 1.26 (60H, br, CH₂), 1.52 (4H, m, COCH₂), 2.35 (3H, s, ArCH₃), 3.97 (4H, m, COCH₂); ³¹P-NMR (162 MHz, CDCl₃): 131.20 (s, P=O). Elemental analysis calcd (%) for CₓHᵧNₒOₚS: C 69.67, H 10.82, N 1.73; found C 69.25, H 10.62, N 1.75.

Figure S2. ¹H-nuclear magnetic resonance (NMR) of 1a.

(1b) Yield: 87.9%; m.p.: 62.4–64.0 °C; FT-IR (KBr, cm⁻¹): 2924 (νC–H), 2846 (νC–H), 1728 (νC=O, ester), 1473 (νC=O, amide); ¹H-NMR (400 MHz, CDCl₃): 0.88 (6H, t, CH₃), 1.26 (60H, br, CH₂), 1.60–1.65 (4H,
m, COCH₂CH₃); 2.66–2.82 (2H, dd, C*CH₂); 3.79–3.82 (1H, m, C*H); 3.97–4.10 (4H, m, COCH₂);
Elemental analysis calcd (%) for C₇H₉NO:S: C 75.3, H 12.48, N 2.20; found C 74.99, H 13.17, N 2.18.

Figure S3. ¹H–NMR of 1b.

(1c) Yield: 90.5%; m.p.: 68.1–68.8 °C; FT-IR (KBr, cm⁻¹): 3367 and 3331 (νN–H), 2912 and 2848 (νC–H), 1750 and 1734 (νC=O, ester), 1631 (δN–H, urea), 1572 (δN–H, urea); ¹H-NMR (400 MHz, CDCl₃): 0.62–0.66 (2H, t, SiCH₂) 0.88 (6H, t, CH₃), 1.26 (69H, br, CH₂ and CH₃CH₂O), 1.58–1.75 (6H, m, COCH₂CH₂ and SiCH₂CH₂), 2.80–3.03 (2H, dd, C*CH₂), 3.17–3.20 (2H, q, NHCH₂), 3.79–3.84 (6H, q, CH₃CH₂O), 4.05 (2H, t, OCH₂), 4.12 (2H, t, OCH₂), 4.59 (1H, t, NH), 4.72–4.84 (1H, m, C*H), 5.23–5.21 (1H, d, NH); Elemental analysis calcd (%) for C₅₀H₁₀₀N₂O₈Si: C 67.82, H 11.38, N 3.16; found C 67.23, H 11.94, N 3.16.

Figure S4. ¹H-NMR of 1c.

(2a) Yield: 78.0 %; m.p.: 70.6–71.4 °C; FT-IR (KBr, cm⁻¹): 2928 and 2049 (νC–H), 1741 and 1735 (νC=O, ester), 1541 (δNH³⁺), 1471 (δC–H); ¹H-NMR (400 MHz, CDCl₃): 0.88 (6H, t, CH₃), 1.14–1.36 (60H, br, CH₂), 1.50–1.59 (4H, m, COCH₂CH₂), 2.00–2.11 (2H, m, C*CH₂), 2.16–2.26 (2H, m, C*CH₂ CH₂), 3.82–4.03 (m, 4H, COCH₂), 7.10–7.85 (4H, d, ArH); Elemental analysis calcd (%) for C₇₉H₁₀₈N₂O₈S: C 69.94, H 10.88, N 1.70; found C 69.14, H 11.30, N 1.79.
Figure S5. $^1$H-NMR of 2a.

(2b) Yield: 80.0%; m.p.: 47.5 °C; FT-IR (KBr, cm$^{-1}$): 2922 (νC–H), 2843 (νC–H), 1738 (νC=O, ester), 1469 (δC–H); $^1$H-NMR (400 MHz, CDCl$_3$): 0.88 (6H, t, CH$_3$), 1.14–1.36 (60H, br, CH$_2$), 1.59–1.64 (4H, m, COCH$_2$CH$_2$), 1.79–2.15 (2H, m, C*CH$_2$), 2.44–2.47 (2H, m, C*CH$_2$CH$_2$), 3.44–3.48 (m, 1H, C*H), 4.05–4.12 (4H, m, OCH$_2$); Elemental analysis calcd (%) for C$_{37}$H$_81$NO$_4$: C 75.52, H 12.52, N 2.15; found C 75.24, H 13.03, N 2.20.

Figure S6. $^1$H-NMR of 2b.

(2c) Yield: 79.6%; m.p.: 65.5–68.0 °C; FT-IR (KBr, cm$^{-1}$): 3362 and 3337 (νN–H), 2918 and 2848 (νC–H), 1745 and 1729 (νC=O, ester), 1638 (νC=O, urea), 1578 (δN–H, urea), 1473 (δC–H); $^1$H-NMR (400 MHz, CDCl$_3$): 0.64–0.68 (2H, t, SiCH$_2$) 0.90 (6H, t, CH$_3$), 1.20–1.40 (69H, br, CH$_2$ and CH$_3$CH$_2$O), 1.62–1.66 (6H, m, COCH$_2$CH$_2$ and SiOCH$_2$CH$_2$), 1.95–2.19 (2H, m, C*CH$_2$), 2.37–2.46 (2H, m, C*HCH$_2$CH$_2$), 3.17–3.22 (2H, q, NHCH$_2$), 3.81–4.13 (6H, t, SiOCH$_2$CH$_3$), 4.05–4.13 (4H, m, OCH$_2$), 4.48–4.53 (1H, m, C*H), 4.61–4.62 (1H, m, NH), 4.92–4.94 (1H, d, NH); Elemental analysis calcd (%) for C$_{51}$H$_{102}$N$_2$O$_8$Si: C 68.10, H 11.43, N 3.11; found C 67.75, H 11.88, N 3.23.

Figure S7. $^1$H-NMR of 2c.
(3a) Yield: 75.6%; m.p.: 79.5–80.8 °C; FT-IR (KBr, cm⁻¹): 2921 and 2848 (νC–H), 1738 and 1734 (νC=O, ester), 1597 (δNH₃⁺), 1463 (δC–H); ¹H-NMR (400 MHz, CDCl₃): 0.88 (6H, t, CH₃), 1.14–1.36 (60H, br, CH₂), 1.54–1.76 (6H, m, COCH₂CH₃, C*CH₂), 1.86–1.88 (2H, m, C*CH₂CH₂), 2.17–2.20 (m, 2H, CH₂C(=O)), 2.35 (3H, s, ArCH₃), 3.94–4.12 (5H, m, OCH₂, C*H); Elemental analysis calcd (%) for C₄₉H₉₁NO₇S: C 70.20, H 10.94, N 1.67; found C 69.83, H 11.52, N 1.67.

Figure S8. ¹H-NMR of 3a.

(3b) Yield: 91.0%; m.p.: 42.9–43.8 °C; FT-IR (KBr, cm⁻¹): 2917 and 2849 (νC–H), 1725 (νC=O, ester), 1463 (δC–H); ¹H-NMR (400 MHz, CDCl₃): 0.88 (6H, t, CH₃), 1.14–1.36 (60H, br, CH₂), 1.58–1.78 (8H, m, OCH₂CH₃, C*CH₂CH₂, C*CH₂CH₂), 2.32–2.35 (m, 2H, CH₂C(=O)), 3.42–3.45 (1H, m, C*H), 4.04–4.12 (4H, m, OCH₂); Elemental analysis calcd (%) for C₄₂H₈₃NO₄: C 75.73, H 12.56, N 2.10; found C 75.23, H 13.16, N 2.20.

Figure S9. ¹H-NMR of 3b.

(3c) Yield: 83.0%; m.p.: 58.8–59.7 °C; FT-IR (KBr, cm⁻¹): 3365 and 3341 (νN–H), 2916 and 2849 (νC–H), 1734 (νC=O, ester), 1630 (νC=O, urea), 1567 (δN–H, urea); ¹H-NMR (400 MHz, CDCl₃): 0.64–0.68 (2H, t, SiCH₂), 0.88 (6H, t, CH₃), 1.20–1.40 (69H, br, CH₂ and CH₃CH₂O), 1.59–1.67 (8H, m, C*CH₂, C*H₂CH₃, COCH₂CH₃ and SiOCH₂CH₂), 2.32–2.33 (2H, m, CH₂C(=O)), 3.15–3.20 (2H, q, NHCH₂), 3.79–3.84 (9H, q, SiOCH₂CH₃), 4.02–4.12 (4H, m, OCH₂), 4.46–4.53 (2H, m, C*H, NH), 4.80–4.82 (1H, d, NH); Elemental analysis calcd (%) for C₅₂H₁₀₄N₂O₈Si: C 68.37, H 11.48, N 3.07; found C 67.96, H 11.88, N 3.07.
Figure S10. $^1$H-NMR of 3c.

(TES-Asp-2C$_1$) Yield: 96.2%; Mp 51.3–51.8 °C; FT-IR (KBr, cm$^{-1}$): 3367 and 3331 (νN–H), 2912 and 2848 (νC–H), 1750 and 1734 (νC=O, ester), 1631 (νC=O, urea), 1572 (δN–H, urea); $^1$H-NMR (400 MHz, CDCl$_3$): 0.62–0.66 (2H, t, SiCH$_2$), 0.88 (6H, t, CH$_3$), 1.26 (69H, br, CH$_2$ and CH$_3$CH$_2$O), 1.58–1.75 (6H, m, COCH$_2$CH$_2$ and SiCH$_2$CH$_2$), 2.80–3.03 (2H, dd, C*CH$_2$), 3.17–3.20 (2H, q, NHCH$_2$), 3.79–3.84 (6H, q, CH$_3$CH$_2$O), 4.05 (2H, t, OCH$_2$), 4.12 (2H, t, OCH$_2$), 4.72–4.84 (1H, m, C*H), 5.23–5.21 (1H, d, NH); Elemental analysis calcd (%) for C$_{50}$H$_{100}$N$_2$O$_8$Si: C 67.82, H 11.38, N 3.16; found C 67.23, H 11.94, N 3.16.

Figure S11. $^1$H-NMR of Dimethyl ((3-(triethoxysilyl)propyl)carbamoyl)-l-aspartate (TMS-Asp-2C$_1$).
**TGA**

![TGA Graph](image)

Sil-Glu-2C\textsubscript{18}: 18.2%
Sil-Adi-2C\textsubscript{18}: 22.1%
Sil-Asp-2C\textsubscript{18}: 23.0%
Sil-Asp-2C\textsubscript{1}: 26.2%

Figure S12. Thermogravimetric curves of amino acid derivatives immobilized silica.

**HPLC**

![HPLC Graph](image)

Figure S13. Relationship between the log $k$ and log P of various polyaromatic hydrocarbons (PAHs) (open circle) and alkyl benzenes (filled circle) with amino acid derivatives bonded silica and octadecyl silica (ODS). Mobile phase: methanol-water (9:1), Flow rate: 1.0 mL·min$^{-1}$, Column temperature: 20 °C.
Table S1. Retention factors of Phenol, Resorcinol, and Phloroglucinol with Dimethyl ((3-(triethoxysilyl)propyl)carbamoyl)-l-aspartate bonded silica (Sil-Asp-2C1).

<table>
<thead>
<tr>
<th>Analyte</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenol</td>
<td>0.11</td>
</tr>
<tr>
<td>Resorcinol</td>
<td>0.27</td>
</tr>
<tr>
<td>Phloroglucinol</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Mobile phase: acetonitrile-10 mM ammonium acetate (9:1), flow rate: 1.0 mL·min⁻¹, Column temperature: 10 °C.

© 2016 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC-BY) license (http://creativecommons.org/licenses/by/4.0/).