Electronic Supplementary Information of

Thermosensitve Hydrogels Composed of Cyclodextrin Pseudorotaxanes. Role of [3]Pseudorotaxane in the Gel Formation

Toshiaki Taira, Yuji Suzaki, Kohtaro Osakada*

Chemical Resources Laboratory R1-3, Tokyo Institute of Technology, 4259 Nagatsuta, Midoriku, Yokohama 226-8503, Japan.
Fax: +81-45-924-5224; Tel: +81-45-924-5224
E-mail: kosakada@res.titech.ac.jp

Experimental Section

General. $Cl(CH_2)_{10}OC_6H_3$-3,5-$(OMe)_2$ was prepared by the literature method.[1] Other chemicals were commercially available. NMR spectra (^1H, $^{13}C\{^1H\}$) ware recorded on Varian MERCURY300 spectrometer, JEOL EX-400 spectrometer or JEOL JNM La-500 spectrometer. ^{13}C CP/MAS NMR spectra were recorded on JEOL JNM La-500. Fast atom bombardment mass spectra (FABMS) were obtained from a JEOL JMS-700 (matrix, (2-nitrophenyl)(n-octyl) ether (NPOE) or 3-nitrobenzyl alcohol (NBA)) spectrometer. Matrix assisted laser desorption ionization time of flight mass spectra (MALDI-TOFMS) were obtained from a Shimadzu AXIMA-CFR Plus (matrix, 2-hydroxy-5-methoxybenzoic acid (super DHB); cationization agent, silver trifluoroacetate) spectrometer. Elemental analyses were carried out with a Yanaco MT-5 CHN autorecorder. The absorption spectrum were recorded using JASCO V-530 UV/Vis spectrometer. Before measuring, the samples were stored at an adequate temperature using a JASCO EHC-477 peltire-type thermostated cell holder.

$Cl(CH_2)_8OC_6H_3$-3,5-$(OMe)_2$: A solution of 3,5-dimethoxyphenol (8.0 g, 52 mmol) and NaOH (3.2 g, 80 mmol) in DMF (35 mL) was stirred for 8 h at room temperature, followed by the addition of 1,8-dichlorooctane (18.0 mL, 95 mmol). The mixture was stirred for 24 h at 110 ^oC. The reaction was quenched by addition of 1 M HCl, and the organic product was extracted with CH_2Cl_2 and dried over $MgSO_4$. Evaporation of the solvent give a crude product which was

purified by SiO_2 column chromatography (hexane/CH_2Cl_2 = 5/1). Further purification of the product by recrystallization from solution at 3 ^oC and washing with cold hexane yield $Cl(CH_2)_8C_6H_3$-3,5-$(OMe)_2$ as white solid (1.67 g, 5.6 mmol, 11%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.24-1.57 (8H, CH_2), 1.69-1.85 (4H, CH_2), 3.54 (t, 2H, J = 7 Hz, $ClCH_2$), 3.77 (s, 6H, OCH_3), 3.91 (t, 2H, J = 6 Hz, OCH_2), 6.08 (3H, *ortho*-, *para*-C_6H_3). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 25.8 (CH_2), 26.7 (CH_2), 28.7 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 32.5 (CH_2), 44.9 ($ClCH_2$), 55.1 (OCH_3), 67.7 (OCH_2), 92.6 (C_6H_3), 93.1 (C_6H_3), 160.9 (C_6H_3), 161.3 (C_6H_3). Anal. calcd. for $C_{16}H_{25}ClO_3$: C, 63.88; H, 8.38; Cl, 11.79. Found: C, 63.59; H, 8.62; Cl, 12.08. FABMS: m/z = 301 $[M+H]^+$.

$Br(CH_2)_{12}OC_6H_3$-3,5-$(OMe)_2$: An acetone (30 mL) solution containing 3,5-dimethoxyphenol (4.1 g, 27 mmol), K_2CO_3 (3.4 g, 25 mmol) and 1,12-dibromododecane (17 g, 52 mmol) was refluxed for 21 h. Evaporation of the solvent give a crude product which was purified by SiO_2 column chromatography (hexane/CH_2Cl_2 = 2/1) to yields $Br(CH_2)_{12}OC_6H_3$-3,5-$(OMe)_2$ as white solid (6.0 g, 15 mmol, 56%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.19–1.51 (16H, CH_2), 1.76 (m, 2H, OCH_2CH_2), 1.85 (m, 2H, $BrCH_2CH_2$), 3.40 (t, 2H, J = 7 Hz, $ClCH_2$), 3.76 (s, 6H, OCH_3), 3.91 (t, 2H, J = 6 Hz, OCH_2), 6.08 (3H, *ortho*-, *para*-C_6H_3). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 26.0 (CH_2), 28.1 (CH_2), 28.7 (CH_2), 29.2 (2C, CH_2), 29.3 (CH_2), 29.4 (2C, CH_2), 29.5 (2C, CH_2), 32.8 (CH_2), 34.0 ($BrCH_2$), 55.2 (OCH_3), 67.9 (OCH_2), 92.7 (C_6H_3), 93.2 (C_6H_3), 161.0 (C_6H_3), 161.4 (C_6H_3). Anal. calcd. for $C_{20}H_{33}BrO_3$+0.25(H_2O): C, 59.18; H, 8.32; Br, 19.69. Found: C, 59.43; H, 8.39; Br, 19.48. FABMS: m/z = 401 $[M+H]^+$.

$[py$-*N*-$(CH_2)_8OC_6H_3$-3,5-$(OMe)_2]^+(Cl^-)$ (1a): A DMF solution (5 mL) of $Cl(CH_2)_8OC_6H_3$-3,5-$(OMe)_2$ (1.0 g, 3.3 mmol) and pyridine (1.3 mL, 16 mmol) was stirred at 110 ^oC for 27 h. The solution was poured into diethyl ether (200 mL). The precipitate was collected by filtration and washed with diethyl ether to yield **1a** as a white solid (1.27 g, 3.3 mmol, quant.). ^1H NMR (300 MHz, $CDCl_3$): δ 1.18–1.39 (8H, CH_2), 1.62 (m, 2H, CH_2), 1.95 (m, 2H, CH_2), 3.66 (s, 6H, OCH_3), 3.78 (t, 2H, J = 6 Hz, OCH_2), 4.88 (t, 2H, J = 7 Hz, NCH_2), 5.96 (3H, *ortho*-, *para*-C_6H_3), 8.07 (t, 2H, J = 7 Hz, C_5H_5N), 8.42 (t, 1H, J = 7 Hz, C_5H_5N), 9.44 (d, 2H, J = 7 Hz, C_5H_5N). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 25.6 (CH_2), 25.7 (CH_2), 28.7 (CH_2), 28.8 (CH_2), 28.9 (CH_2), 31.7 (CH_2), 55.1 (OCH_3), 61.7 (NCH_2), 67.6 (OCH_2), 92.6 (*ortho*-C_6H_3), 93.1 (*para*-C_6H_3), 128.3 (C_5H_5N), 144.9 (C_5H_5N), 145.0 (C_5H_5N), 160.7 (*meta*-C_6H_3), 161.2 (*ipso*-C_6H_3). Anal. calcd. for $C_{21}H_{30}ClNO_3$+(H_2O): C, 63.38; H, 8.11; N, 3.52; Cl, 8.91. Found: C, 63.45; H, 8.21; N, 3.59; Cl, 9.31. FABMS: m/z = 344 $[M-Cl]^+$.

[py-*N*-$(CH_2)_{10}OC_6H_3$-3,5-$(OMe)_2$]$^+$(Cl^-) (1b): A DMF solution (10 mL) of $Cl(CH_2)_{10}OC_6H_3$-3,5-$(OMe)_2$ (2.1 g, 6.4 mmol) and pyridine (2.5 mL, 31 mmol) was stirred at 110 ^oC for 24 h. The solution was poured into diethyl ether (200 mL). The precipitate was collected by filtration and wash with diethyl ether to yield **1b** as a white solid (2.0 g, 4.9 mmol, 77%). ^1H NMR (300 MHz, DMSO-d_6): δ 1.20–1.42 (12H, CH_2), 1.65 (m, 2H, CH_2), 1.89 (m, 2H, CH_2), 3.68 (s, 6H, OCH_3), 3.88 (t, 2H, J = 6 Hz, OCH_2), 4.57 (t, 2H, J = 7 Hz, NCH_2), 6.05 (3H, *ortho*-, *para*-C_6H_3), 8.14 (t, 2H, J = 8 Hz, C_5H_5N), 8.59 (t, 1H, J = 8 Hz, C_5H_5N), 9.08 (d, 2H, J = 6 Hz, C_5H_5N). $^{13}C\{^1H\}$ NMR (75.5 MHz, DMSO-d_6): δ 25.5 (CH_2), 25.6 (CH_2), 28.5 (CH_2), 28.7 (CH_2), 28.8 ($2CH_2$), 28.9 (CH_2), 30.9 (CH_2), 55.2 (OCH_3), 60.6 (NCH_2), 67.4 (OCH_2), 92.7 (*ortho*-C_6H_3), 93.2 (*para*-C_6H_3), 128.1 (C_5H_5N), 144.9 (C_5H_5N), 145.5 (C_5H_5N), 160.6 (meta-C_6H_3), 161.2 (*ipso*-C_6H_3). Anal. calcd. for $C_{23}H_{34}ClNO_3$+1.3(H_2O): C, 64.04; H, 8.55; N, 3.25. Found: C, 63.95; H, 8.71; N, 3.32. FABMS: m/z = 372 $[M\text{-}Cl]^+$.

[py-*N*-$(CH_2)_{12}OC_6H_3$-3,5-$(OMe)_2$]$^+$(Br^-) (1c): A DMF solution (20 mL) of $Br(CH_2)_{12}OC_6H_3$-3,5-$(OMe)_2$ (3.0 g, 7.5 mmol) and pyridine (3.0 mL, 39 mmol) was stirred at 110 ^oC for 16 h. The solution was poured into diethyl ether (300 mL). The precipitate was collected by filtration and wash with diethyl ether to yield **1c** as a white solid (3.5 g, 7.3 mmol, 97%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.11–1.40 (16H, CH_2), 1.65 (m, 2H, CH_2), 1.97 (m, 2H, CH_2), 3.67 (s, 6H, OCH_3), 3.81 (t, 2H, J = 6 Hz, OCH_2), 4.91 (t, 2H, J = 7 Hz, NCH_2), 5.97 (3H, *ortho*-, *para*-C_6H_3), 8.09 (t, 2H, J = 7 Hz, C_5H_5N), 8.45 (t, 1H, J = 7 Hz, C_5H_5N), 9.50 (d, 2H, J = 6 Hz, C_5H_5N). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 25.7 (CH_2), 25.8 (CH_2), 28.8 (CH_2), 28.9 (CH_2), 29.1 (2C, CH_2), 29.2 (3C, CH_2), 31.8 (CH_2), 55.1 (OCH_3), 61.7 (NCH_2), 67.8 (OCH_2), 92.5 (*ortho*-C_6H_3), 93.1 (*para*-C_6H_3), 128.3 (C_5H_5N), 144.9 (2C, C_5H_5N), 160.8 (*meta*-C_6H_3), 161.2 (ipso-C_6H_3). Anal. calcd. for $C_{25}H_{38}BrNO_3$+0.25(H_2O): C, 61.91; H, 8.00; N,2.89; Br, 16.48. Found: C, 61.82; H, 8.11; N, 2.93; Br, 16.56. FABMS: m/z = 400 $[M\text{-}Br]^+$.

Xerogel of 1b and α-CD: A H_2O solution (5 mL) of **1b** (220 mg, 0.5 mmol) and α-CD (1.0 g, 1.0 mmol) was stirred at 70 ^oC for 20 min. The solution was cooled to 4 ^oC for 32 h gave hydrogel. Addition of acetone (5 mL) to the hydrogel formed white precipitate. The precipitate was collected by filtration and washed with acetone (30 ml) to yield xerogel as a white solid. The xerogel was also obtained by slow evaporation of the hydrogel.

The reaction of urea with hydrogel containing 1b and α-CD: Heating of an aqueous solution of **1b** (14 mg, 0.04 mmol) and α-CD (68 mg, 0.07 mmol) at 60 ^oC and subsequent cooling to room temperature gave hydrogel. Addition of urea (64 mg, 1.1 mmol) to the hydrogel and heating at 60 ^oC. The solution was cooled to room temperature to gave transparent solution.

1. ^{13}C CP/MAS NMR spectra of Xerogel of 1b and α-CD

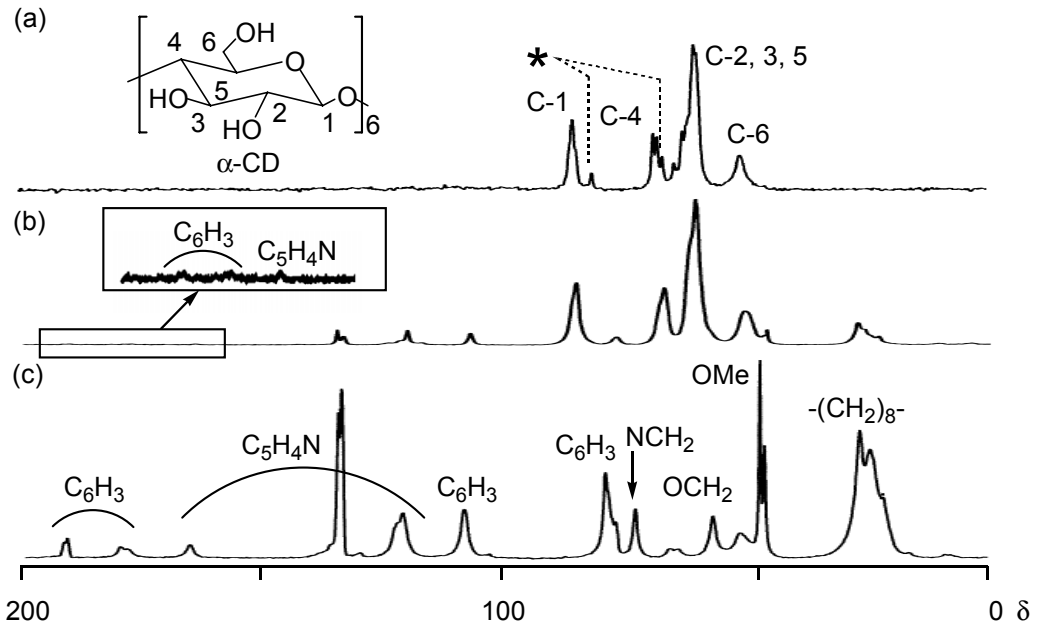

Figure S1. ^{13}C CP/MAS NMR spectra (100 MHz, RT) of (a) α-CD, (b) xerogel of **1b** and α-CD, and (c) **1b**. Peaks with an asterisk are assigned to C-1 and C-4 with a conformationally strained glycoside linkage.

2. 2D ROESY ^{1}H NMR Spectrum of 1b and α-CD

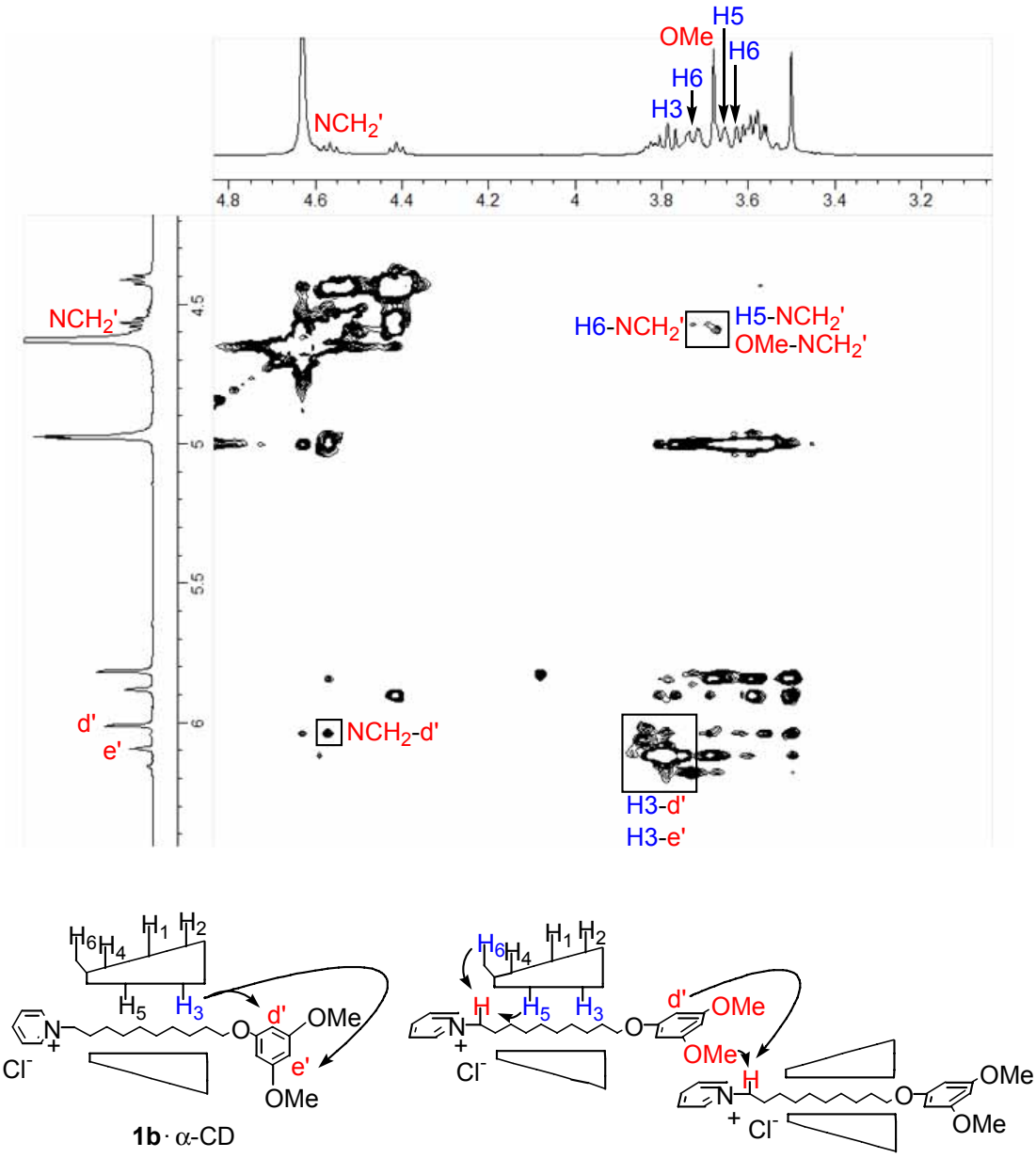

Figure S2. 2D ROESY ^{1}H NMR spectrum (500 MHz, 30 °C) of **1b** (100 mM) and α-CD (50 mM) in D_2O (mixing time = 400 ms).

Reference

[1] Y. Suzaki, T. Taira and K. Osakada, *Dalton Trans*., 2006, 5345.