

Supporting Information

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Thixotropic Hydrogel Formation in Various Aqueous Solutions through Self-Assembly of an Amphiphilic Tris-Urea

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General

Chemicals and solvents required were obtained from commercial suppliers. ¹H and ¹³C NMR spectra were recorded on a JEOL JNM-ECA600 spectrometer. Mass spectra were measured on a JEOL JMS-T100LC AccTOF spectrometer. SEM studies were carried out on a JEOL JSM-6300 spectrometer.

Synthesis and physical properties



Synthesis of Tris-urea (5). To a solution of amine 2^1 (375 mg, 0.71 mmol) in 1,2-dichloroethane (1.5 mL) were added triphosgene (218 mg, 0.74 mmol) in 1,2-dichloroethane (1.5 mL) and Et₃N (220 µL, 1.56 mmol) successively under argon atmosphere at 0 °C. The reaction mixture was stirred at room temperature for 40 min. The low boiling point compounds were removed under reduced pressure and corresponding isocyanate was obtained as white solid. To the crude isocyanate were added 1,2-dichloroethane (2.9 mL) and 1,3,5-tris(aminomethyl)benzene $(3)^2$ (40 mg, 0.24 mmol) successively under argon atmosphere. The reaction mixture was stirred at 90 °C for 48 h and then cooled to room temperature and added saturated aqueous NH₄Cl solution. The aqueous layer was extracted with CH₂Cl₂. The combined organic layer was washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (SiO₂ acetone/ CH_2Cl_2 1/3 to 1/0). The desired product (5) was obtained as a white solid (347 mg, 78%). M.p. 165–166 °C; $[\alpha]_D^{26} = -16.7$ °(c = 1.0 in DMSO); ¹H NMR (600 MHz, DMSO-*d*₆) δ 1.93 (s, 9H), 1.97 (s, 9H), 1.98 (s, 9H), 2.01 (s, 9H), 3.54–3.62 (m, 6H), 3.63–3.70 (m, 9H), 3.80-3.83 (m, 3H), 4.00–4.03 (m, 12H), 4.17 (dd, J = 5.2, 12.0 Hz, 3H), 4.25 (d, J = 6.2 Hz, 6H), 4.76 (t, J = 8.9 Hz, 3H), 4.84 (d, J = 8.2 Hz, 3H), 4.89 (t, J = 9.6 Hz, 3H), 5.25 (t, J = 9.6 Hz, 3H), 6.49 (t, J = 5.8 Hz, 3H), 6.79 (d, J = 8.9 Hz, 6H), 7.10 (s, 3H), 7.27 (d, J = 8.9 Hz, 6H), 8.32 (s, 3H); ¹³C NMR (150 MHz, acetone-d₆) 20.66, 20.73, 20.78, 20.80, 44.23, 62.88, 68.65, 69.57, 69.91, 70.59, 71.09, 72.28, 72.48, 73.64, 101.51, 115.65, 121.53, 125.81, 134.54, 141.65, 155.25, 156.96, 169.90, 170.13, 170.43, 170.87; HRMS $(ESI, M+Na^{+})$ calcd for $C_{84}H_{108}N_6NaO_{39}$: 1847.6550; found 1847.6598.



S2

Synthesis of Tris-urea (1). A mixture of tris-urea **5** (593 mg, 0.32 mmol) and NaOEt (78 mg, 1.15 mmol) in ethanol (7.7 mL) was stirred at room temperature for 3 d. The reaction mixture was purified by membrane dialysis, and the solvent was removed under reduced pressure. The desired product **1** was obtained as pale brown solid (424 mg, 99%). M.p. 185–186 °C; $[\alpha]_D^{26} = -18.4 \circ (c = 1.0 \text{ in DMSO})$; ¹H NMR (600 MHz, DMSO-*d*₆) δ 2.92–2.99 (m, 3H), 3.01–3.05 (m, 3H), 3.07–3.10 (m, 3H), 3.11-3.14 (m, 3H), 3.41–3.45 (m, 3H), 3.60–3.66 (m, 12H), 3.72 (dd, *J* = 4.1, 5.5 Hz, 6H), 3.87–3.91 (m, 3H), 4.00 (t, *J* = 4.5 Hz, 6H), 4.16 (d, *J* = 8.2 Hz, 3H), 4.26 (d, *J* = 6.2 Hz, 6H), 4.49 (t, *J* = 5.8 Hz, 3H), 4.88 (d, *J* = 4.8 Hz, 3H), 4.92 (d, *J* = 4.8 Hz, 3H), 4.98 (d, *J* = 4.8 Hz, 3H), 6.49 (t, *J* = 5.8 Hz, 3H), 6.81 (d, *J* = 8.9 Hz, 6H), 7.11 (s, 3H), 7.28 (d, *J* = 8.9 Hz, 6H), 8.32 (s, 3H); ¹³C NMR (150 MHz, DMSO-*d*₆) 52.35, 70.63, 76.82, 77.42, 78.60, 79.38, 79.60, 82.94, 86.27, 86.41, 112.53, 124.10, 129.09, 134.05, 143.18, 150.18, 162.69, 164.96; HRMS (ESI, M+Na⁺) calcd for C₆₀H₈₄N₆NaO₂₇: 1343.5282; found 1343.5291.



Synthesis of Tris-urea (4). A mixture of 1 (20 mg, 15 µmol) and 6 M HCl (0.44 mL) was heated on a hot plate for 10 min. The obtained hydrogel was purified by membrane dialysis, and the solvent was removed under reduced pressure. The tris-urea 4 was obtained as pale brown solid (12 mg, 95%). M.p. 224–226 °C; ¹H NMR (600 MHz, DMSO- d_6) δ 3.46–3.48 (m, 6H), 3.50-3.52 (m, 6H), 3.70 (t, *J* = 4.8 Hz, 6H), 4.00 (t, *J* = 4.8 Hz, 6H), 4.26 (d, *J* = 6.2 Hz, 6H), 4.61 (t, *J* = 5.5 Hz, 3H), 6.50 (t, *J* = 5.8 Hz, 3H), 6.80 (d, *J* = 8.9 Hz, 6H), 7.11 (s, 3H), 7.27 (d, *J* = 8.9 Hz, 6H), 8.32 (s, 3H); ¹³C NMR (150 MHz, DMSO- d_6) 42.80, 60.25, 67.32, 69.03, 72.46, 114.55, 119.53, 124.51, 133.66, 140.65, 153.16, 155.40; HRMS (ESI, M+Na⁺) calcd for C₄₂H₅₄N₆NaO₁₂: 857.3697; found 857.3690.

¹H NMR spectrum (600 MHz, DMSO-*d*₆) of tris-urea **5**



 13 C NMR spectrum (150 MHz, acetone- d_6) of tris-urea **5**



¹H NMR spectrum (600 MHz, DMSO-*d*₆) of tris-urea **1**



¹³C NMR spectrum (150 MHz, DMSO-*d*₆) of tris-urea **1**



¹H NMR spectrum (600 MHz, DMSO-*d*₆) of tris-urea **4**



¹³C NMR spectrum (150 MHz, DMSO-*d*₆) of tris-urea **4**





Figure S1. Storage modulus (G') and loss modulus (G'') of hydrogel (1.0 wt% of **1**): a) frequency sweep at the strain of 0.1%, b) strain sweep at the frequency of 1.0 Hz.



Figure S2. Photograph and SEM image of disassembled hydrogel of 1 (1.0 wt%) by mechano-stress.

solution	pН	MGC (wt%)	photograph
Glycine-HCl buffer	3.0	0.25	
Phosphate–NaOH buffer	6.9	0.25	
HEPES buffer	7.0	0.25	
Tris-HCl buffer	7.4	0.25	
Tris–Borate–EDTA buffer	8.3	0.25	
Glycine–NaOH buffer	9.0	0.25	
Borate–NaOH buffer	9.1	0.25	HE P
PBS	9.4	0.25	
D-MEM	7.2	0.25	

HEPES: 4-(2-hydroxyethyl)-1	-piperazineethanesulfonic	acid, Tris: tris(hydro	oxymethyl)aminomethane,	

EDTA: ethylenediaminetetraacetic acid, PBS: phosphate buffered saline, D-MEM: Dulbecco's modified Eagle medium

 Table S1. Gelation experiments of buffers by amphiphilic tris-urea 1.



Figure S3. Photographs and SEM images of 0.25 wt% of **1** and 700 equivalents of a) NaF (gel), b) NaCl (gel), c) NaBr (gel), and d) NaI (sol).



Figure S4. Thixotropic properties of a) sat. NaCl gel of 1 (1.0 wt%), b) 8 M HCl gel of 1 (4.0 wt%), and c) 7 M KOH gel of 1 (2.0 wt%).

References

- S. Yamamichi, Y. Jinno, N. Haraya, T. Oyoshi, H. Tomitori, K. Kashiwagi, M. Yamanaka, *Chem. Commun.* 2011, 47, 10344–10346.
- (2) a) W. Kiggen, F. Voegtle, S. Franken, H. Puff, Tetrahedron 1986, 42, 1859-1872; b) A. Granzhan, C.

Schouwey, T. Riis-Johannessen, R. Scopelliti, K. Severin, J. Am. Chem. Soc. 2011, 133, 7106-7115.