Electronic Supporting Information

Enzymatic hydrolysis-induced degradation of a lactose-coupled supramolecular hydrogel

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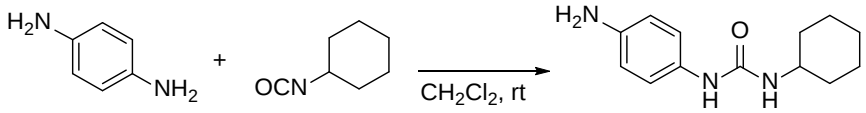
Contents

General

Chemicals and solvents required were obtained from commercial suppliers. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL AL-400 spectrometer. Mass spectra were measured on JMS-T100LC AccTOF (JEOL) or solariX FT-ICR-MS spectrometer (Bruker Daltonik GmbH) spectrometers. SEM studies were carried out on a JEOL JSM-6510LV spectrometer. Rheology measurements were performed by a TA Instruments DHR 2.

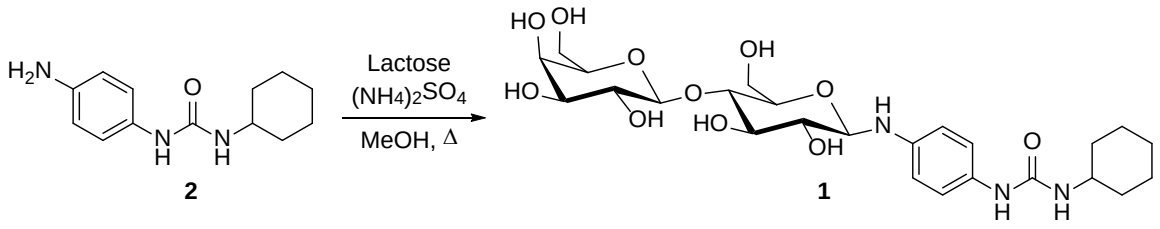
Synthesis and physical properties



2

Synthesis of 1-(4-aminophenyl)-3-cyclohexylurea (2). Cyclohexyl isocyanate (1.0 mL, 7.86 mmol) was added dropwise to a solution of 1,4-phenylenediamine (1.71 g 15.8 mmol) in CH_2Cl_2 (100 mL). The reaction mixture was stirred at room temperature for 14 h under argon atmosphere. Then the obtained solid was collected by filtration and washed with CH_2Cl_2. The crude product was purified by recrystallization (EtOAc). The desired product **2** was obtained as a white solid (1.61 g, 88%).

M.p. 199 °C; ^{1}H NMR (DMSO-d_6) δ 1.06-1.20 (m, 3H), 1.24-1.33 (m, 2H), 1.51-1.54 (m, 1H), 1.62-1.65 (m, 2H), 1.75-1.78 (m, 2H), 3.37-3.44 (m, 1H), 4.64 (brs, 2H), 5.79 (d, J = 7.8 Hz, 1H) 6.44 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 7.74 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 24.45, 25.31, 33.18, 47.56, 114.21, 120.04, 129.73, 143.26, 154.98; HRMS (ESI, M+Na^+) calcd for $C_{13}H_{19}N_3NaO$: 256.1420; found 256.1446.

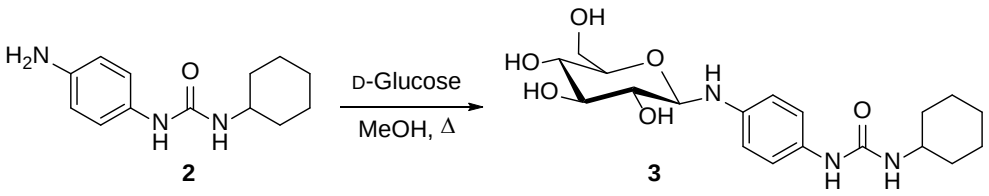


2 **1**

Synthesis of 1. A mixture of **2** (210 mg, 0.90 mmol), lactose monohydrate (326 mg, 0.91 mmol), and $(NH_4)_2SO_4$ (11.7 mg, 0.09 mmol) in MeOH (20 mL) was refluxed for 4 d under argon atmosphere.

The reaction mixture was cooled in ice bath and added H_2O (5 mL). The obtained solid was collected by filtration and washed with MeOH. The desired product **1** was obtained as white solid (458 mg, 89%).

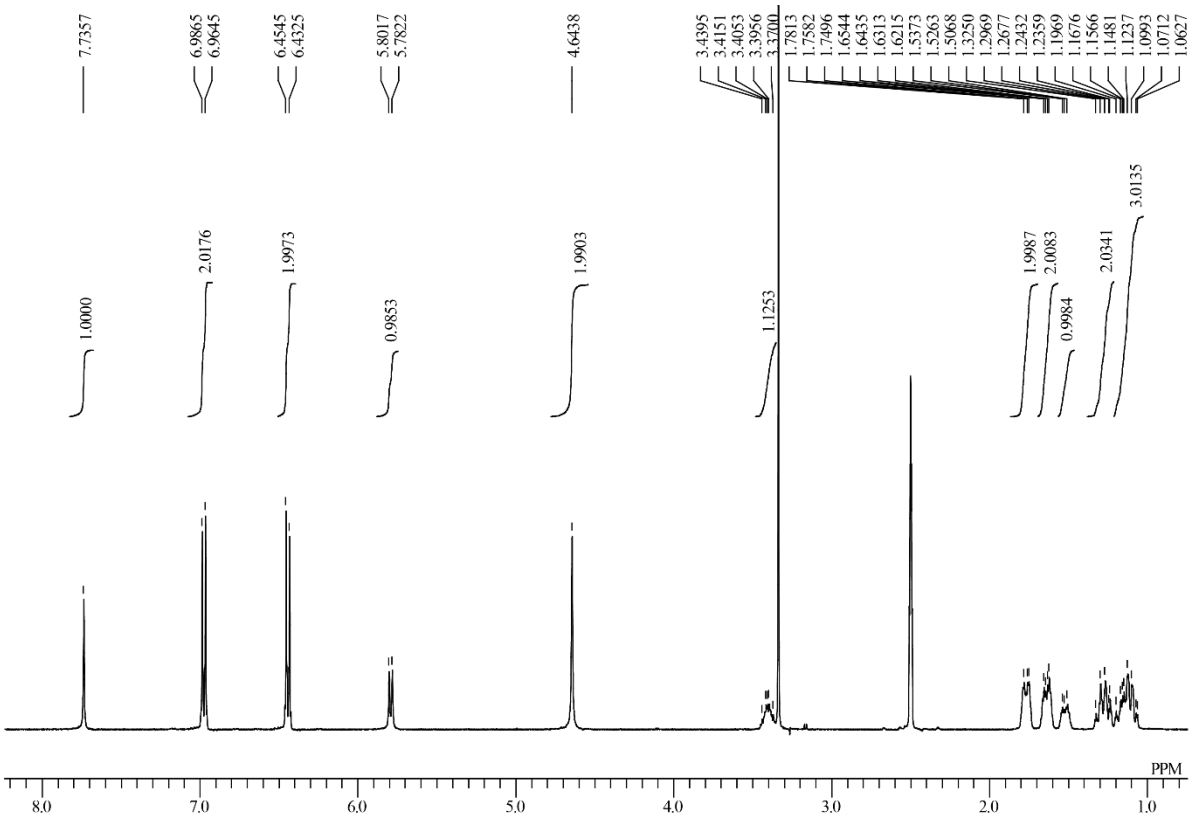
M.p. 173 °C (decomp.); ^{1}H NMR (DMSO-d_6) δ 1.03-1.20 (m, 3H), 1.24-1.33 (m, 2H), 1.51-1.54 (m, 1H), 1.62-1.66 (m, 2H), 1.76-1.79 (m, 2H), 3.19 (m, 1H), 3.33-3.62 (m, 11H), 3.67-3.71 (m, 1H), 4.23 (d, J = 6.8 Hz, 1H), 4.35 (t, J = 8.3 Hz, 1H), 4.51-4.56 (m, 2H), 4.68 (t, J = 5.4 Hz, 1H), 4.73 (s, 1H), 4.83 (d, J = 5.4 Hz, 1H), 5.00 (d, J = 5.4 Hz, 1H), 5.13 (d, J = 4.4 Hz, 1H), 5.85 (d, J = 7.8 Hz, 1H), 5.94 (d, J = 7.3 Hz, 1H), 6.58 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.8 Hz, 2H), 7.85 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 24.44, 25.31, 33.17, 47.55, 60.47, 60.53, 68.21, 70.63, 72.88, 73.27, 75.16, 75.55, 75.87, 80.98, 85.46, 103.86, 113.44, 119.56, 130.96, 141.86, 154.88; HRMS (ESI, M+Na$^+$) calcd for $C_{25}H_{39}N_3NaO_{11}$: 580.2477; found 580.2481.



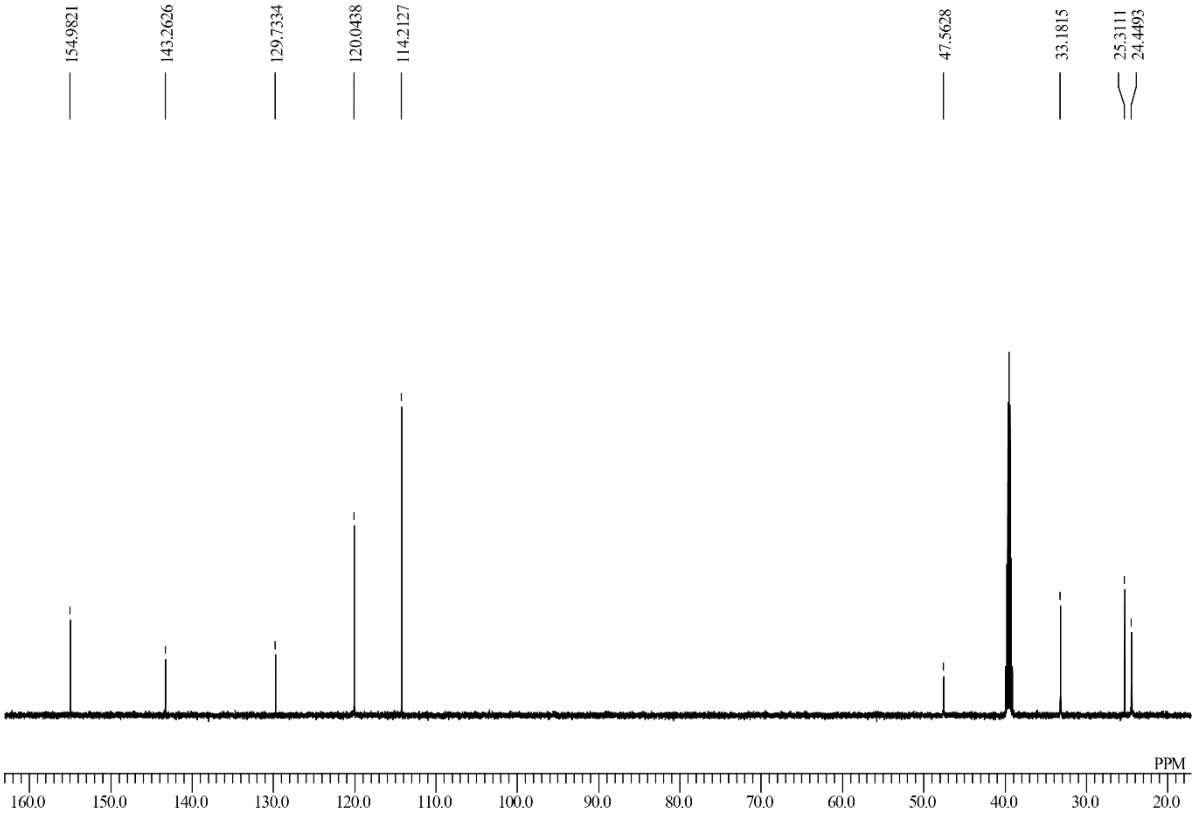
Synthesis of 3. A mixture of **2** (101 mg, 0.43 mmol) and D-glucose (77.3 mg, 0.43 mmol) in MeOH (3.0 mL) was refluxed for 24 h under argon atmosphere. The obtained solid was collected by filtration and washed with ice cold water and MeOH. The desired product **3** was obtained as white solid (79.5 mg, 47%).

M.p. 174-175 °C; ^{1}H NMR (DMSO-d_6) δ 1.08-1.20 (m, 3H), 1.24-1.33 (m, 2H), 1.51-1.54 (m, 1H), 1.63-1.66 (m, 2H), 1.76-1.79 (m, 2H), 3.07-3.26 (m, 4H), 3.38-3.45 (m, 2H), 3.62-3.66 (m, 1H), 4.26 (t, J = 8.1 Hz, 1H), 4.43 (t, J = 5.9 Hz, 1H), 4.83 (d, J = 4.9 Hz, 1H), 4.88 (d, J = 5.4 Hz, 1H), 4.96 (d, J = 4.9 Hz, 1H), 5.84 (t, J = 7.3 Hz, 2H), 6.57 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 8.8 Hz, 2H), 7.84 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 24.43, 25.30, 33.16, 47.52, 61.02, 70.29, 73.15, 77.24, 77.70, 85.82, 113.44, 119.51, 130.91, 142.00, 154.84; HRMS (ESI, M+Na$^+$) calcd for $C_{19}H_{29}N_3NaO_6$: 418.1949; found 418.1936.

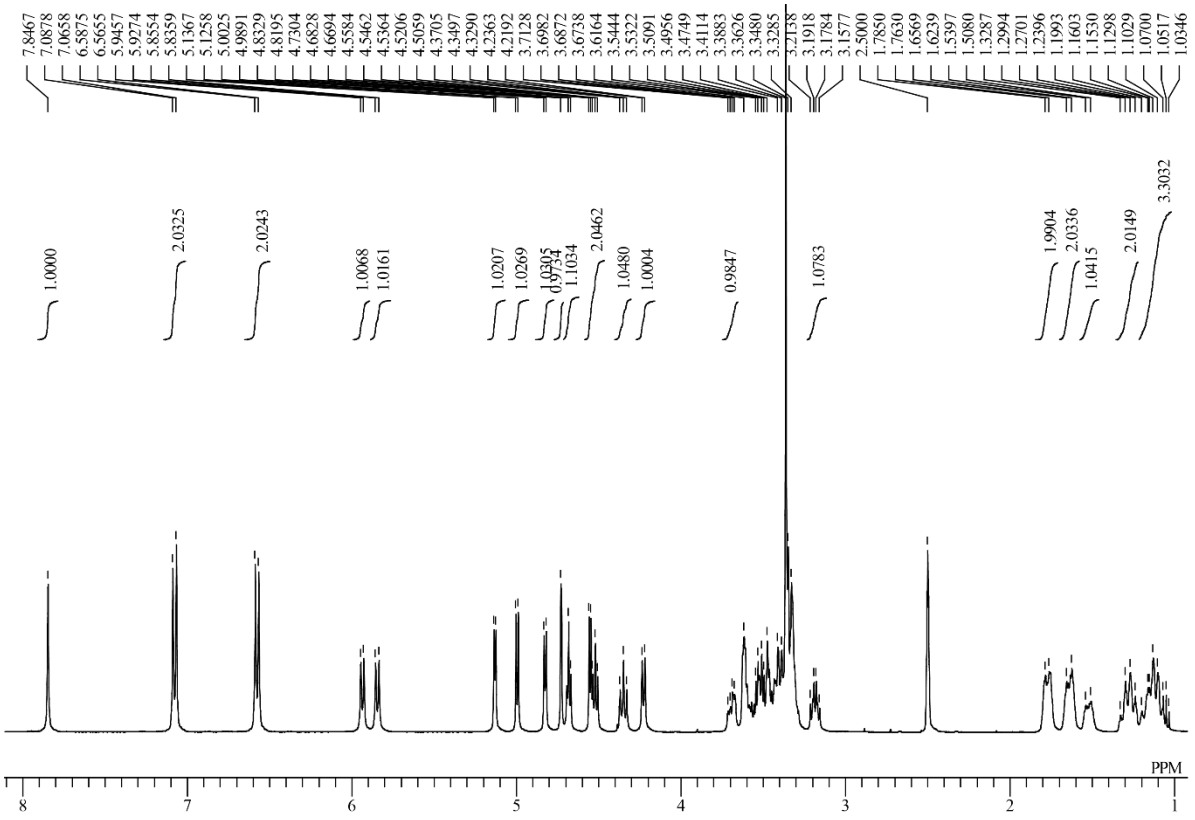
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **2**



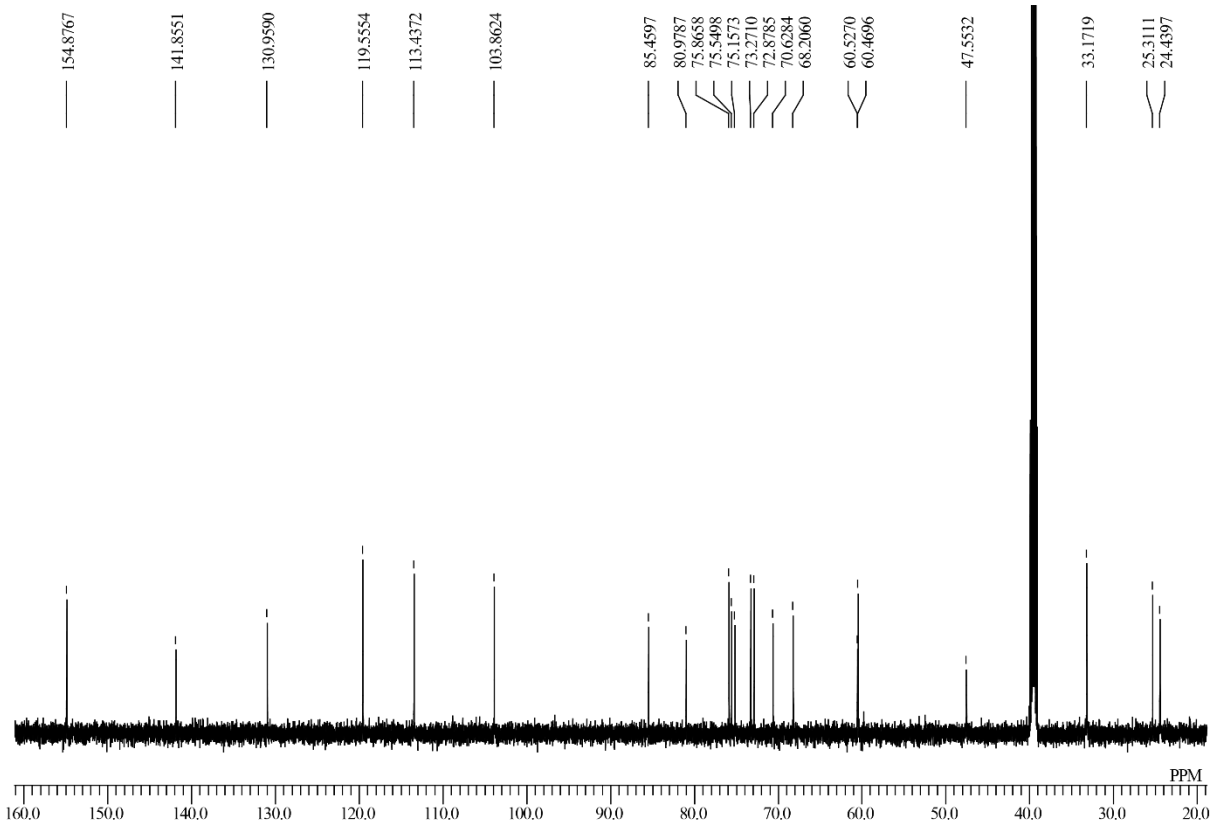
^{13}C NMR spectrum (100 MHz, $CDCl_3$, 298 K) of **2**



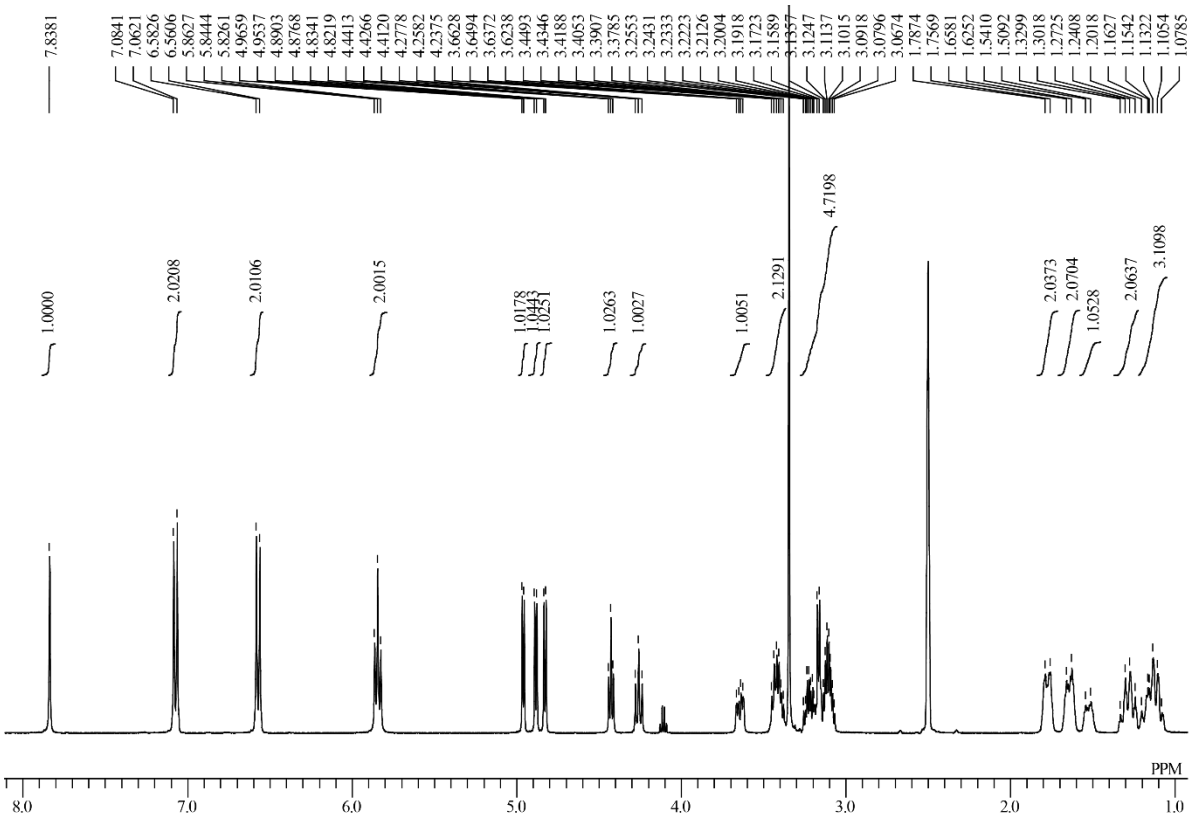
^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of **1**



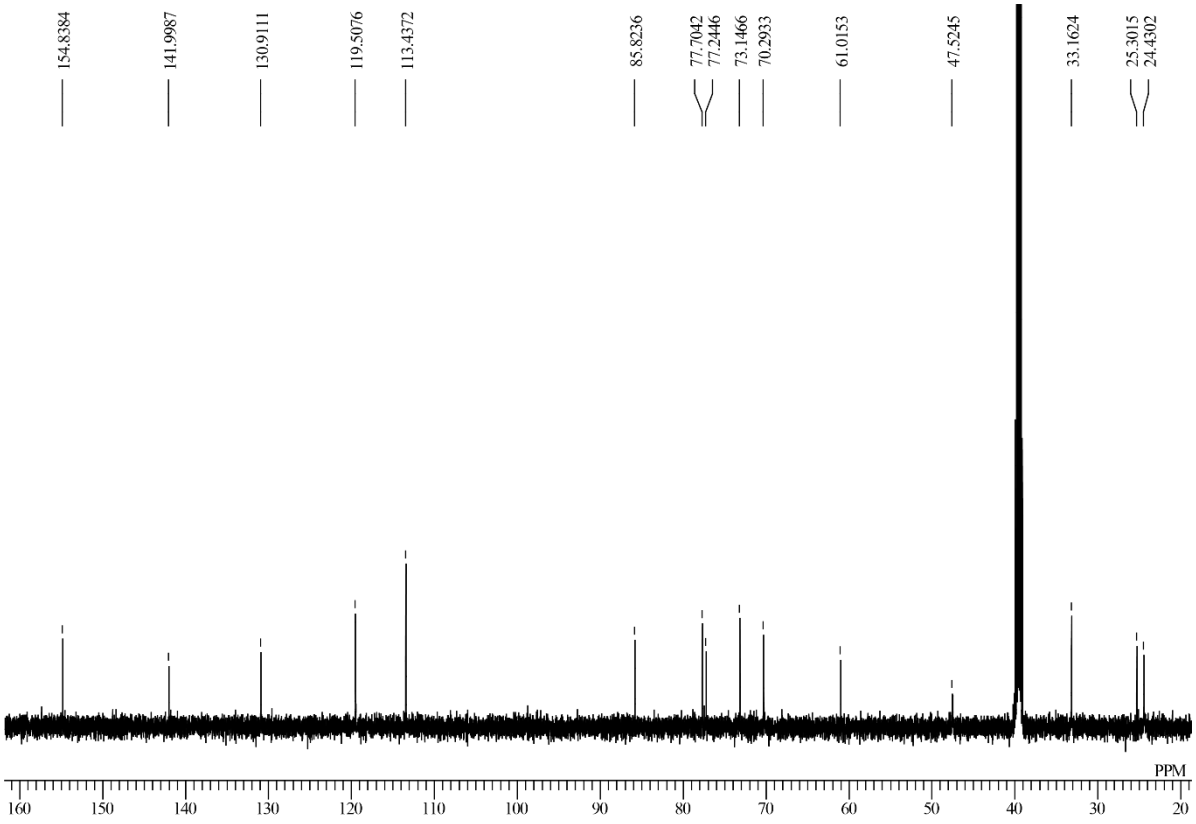
^{13}C NMR spectrum (100 MHz, DMSO-d_6, 298 K) of **1**



^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of **3**



^{13}C NMR spectrum (100 MHz, DMSO-d_6, 298 K) of **3**



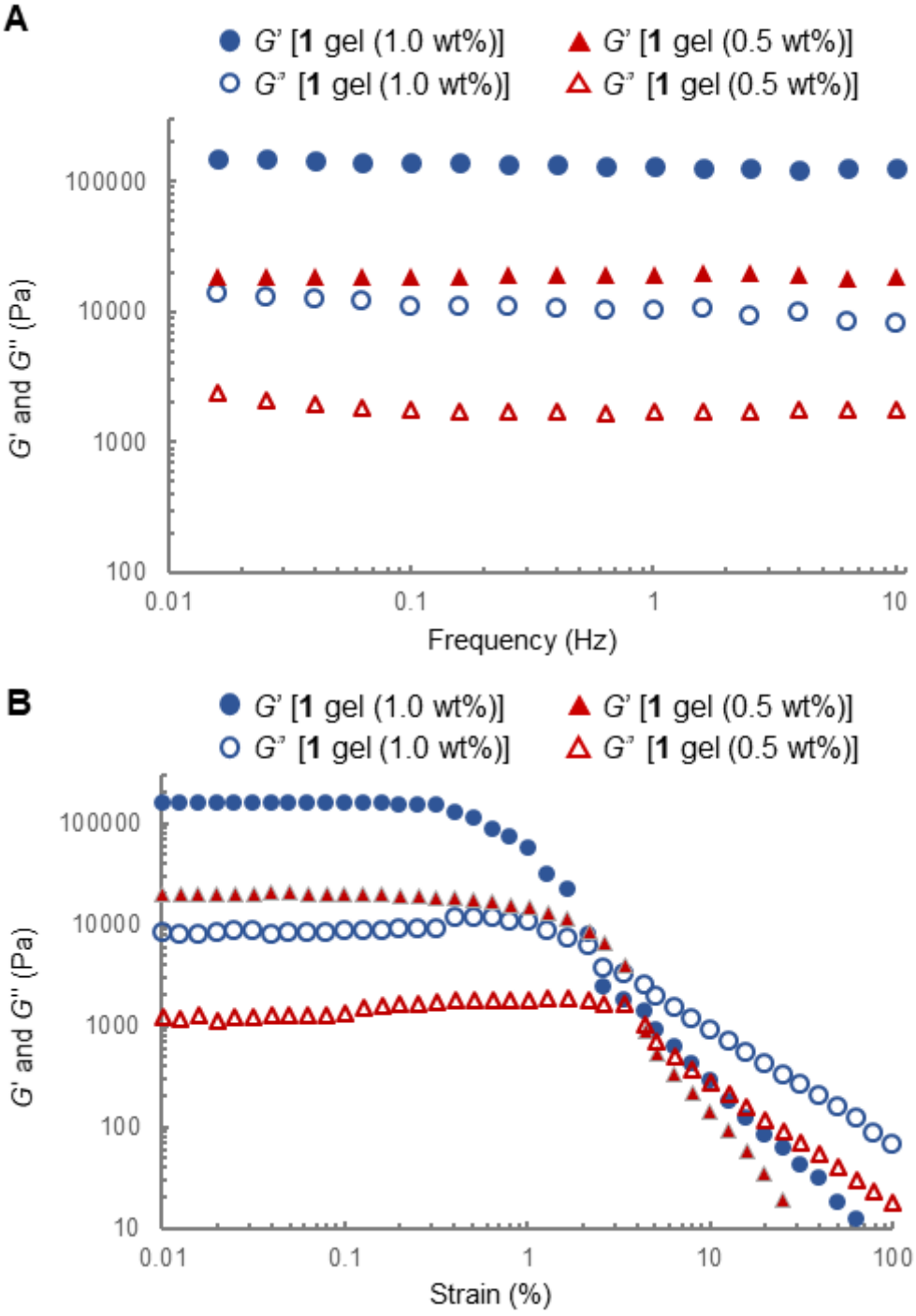


Fig. S1 *G*'and *G*'' values of supramolecular hydrogel of **1** (0.5 wt% and 1.0 wt%) via a) frequency sweep at 0.1% strain; and b) strain sweep at 1.0 Hz.

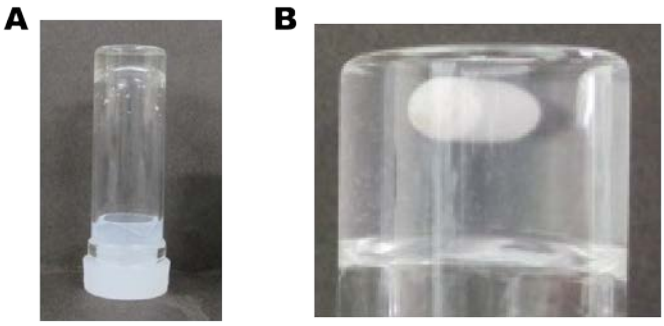


Fig. S2 Photographs of supramolecular hydrogel of **1** prepared from (a) stirring a mixture using vortex mixer (2500 rpm); (b) injecting DMSO solution of **1** into pure water.

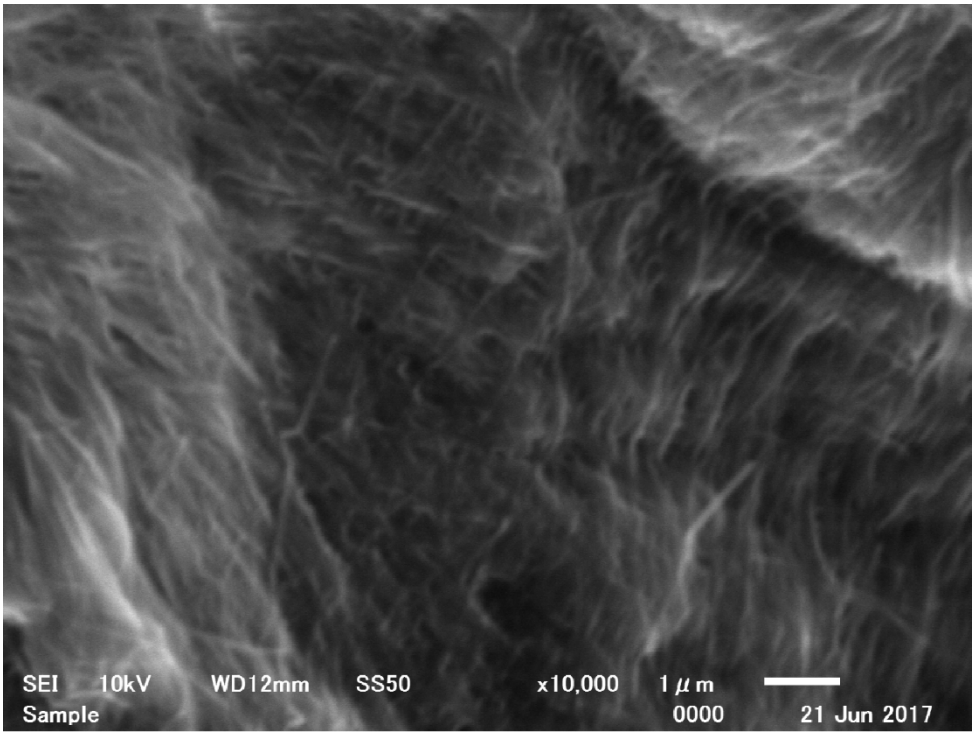


Fig. S3 SEM image of a sample prepared from liquid containing precipitate obtained from a mixture of supramolecular hydrogel of **1** and β-Gal.

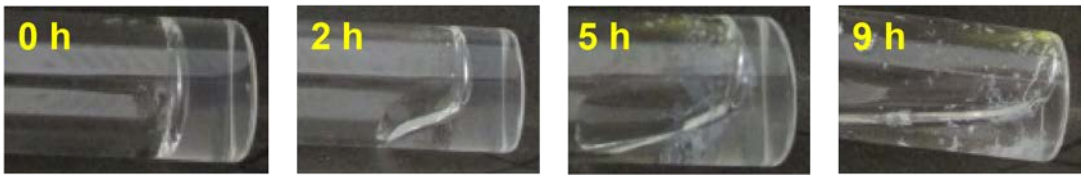


Fig. S4 Photographs of time course of mixture of supramolecular hydrogel (0.5 wt% of **1**, 500 μL) and β-Gal (10 units, 50 μL).

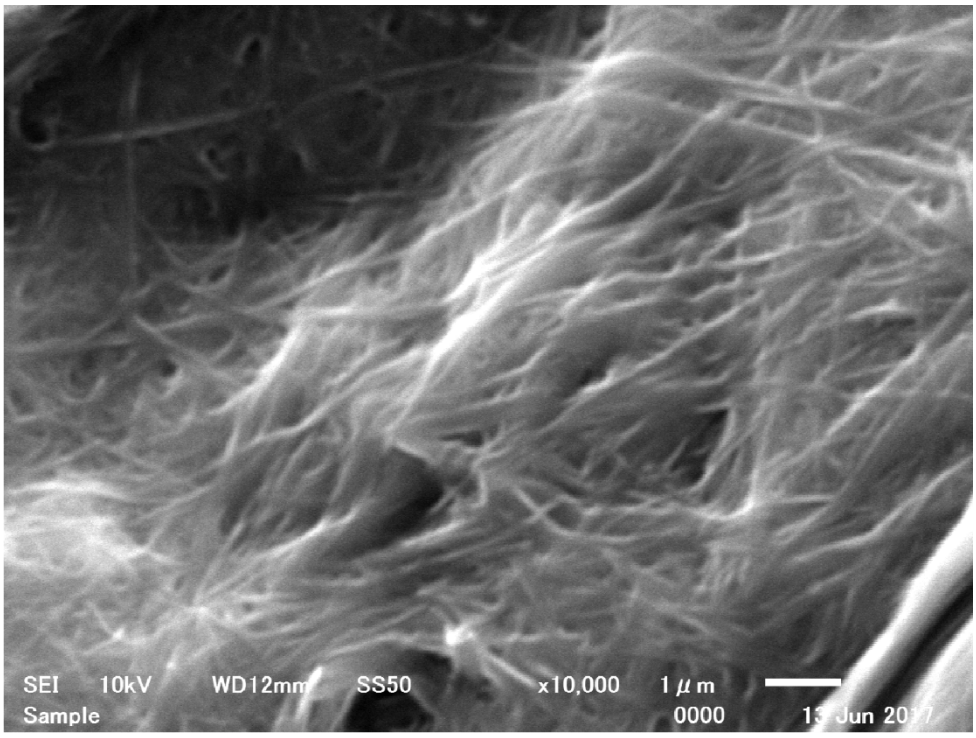


Fig. S5 SEM image of a mixture of **3** water.

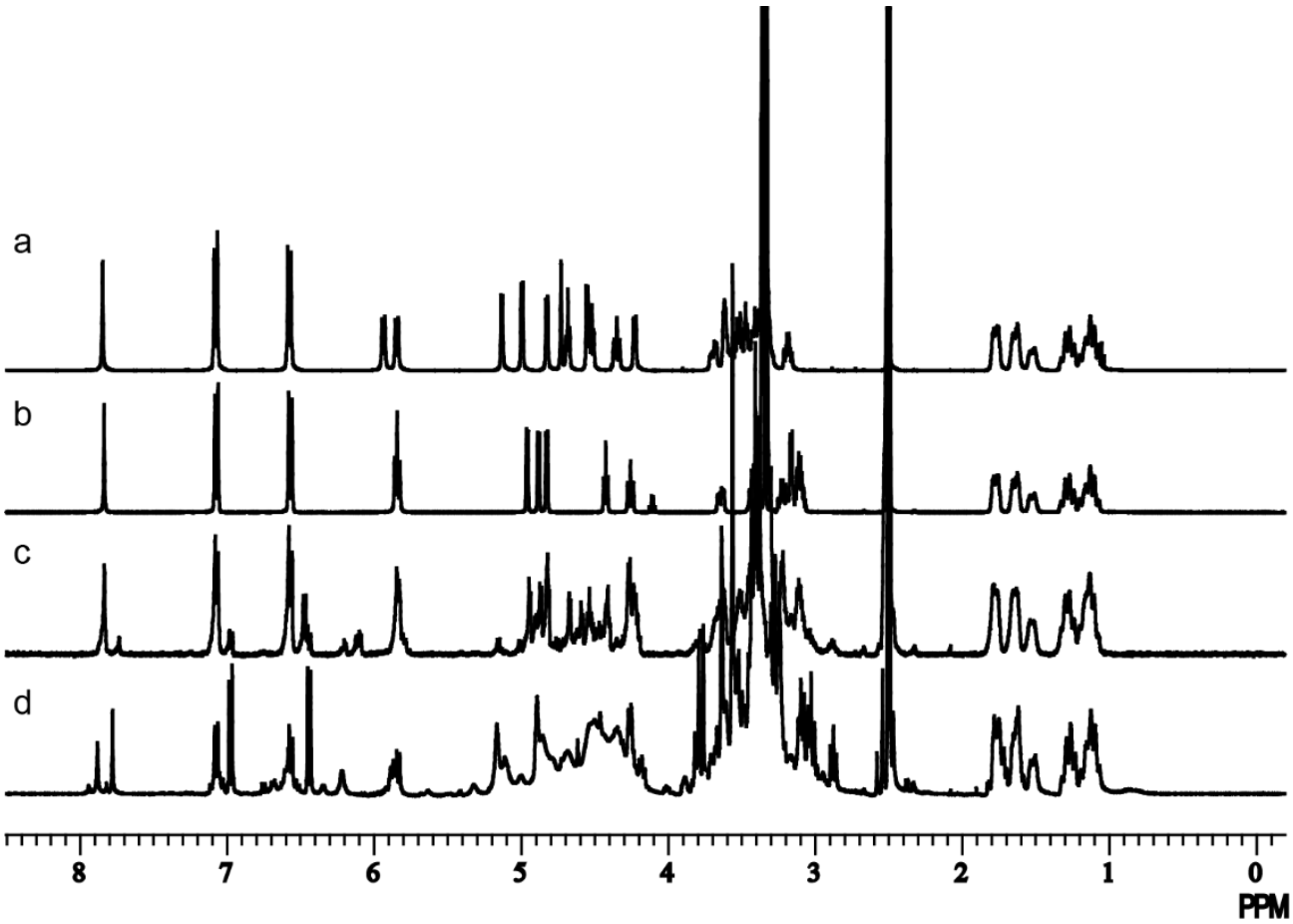


Fig. S6 ^{1}H NMR spectra (DMSO-d_6, 298 K) of a) **1**; b) **3**; c) mixture of supramolecular hydrogel (0.5 wt% of **1**, 500 μL) and β-Gal (100 units) after 6 h; d) mixture of supramolecular hydrogel (0.5 wt% of **1**, 10 mL) and kiwifruit (1.5 g) after 24 h.