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Supporting information

Uracile based Glycosyl-Nucleoside-Lipids as Low Molecular Weight OrganoGelators

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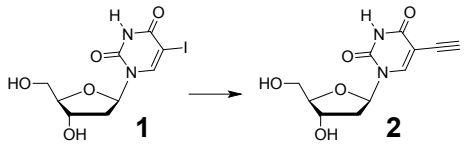
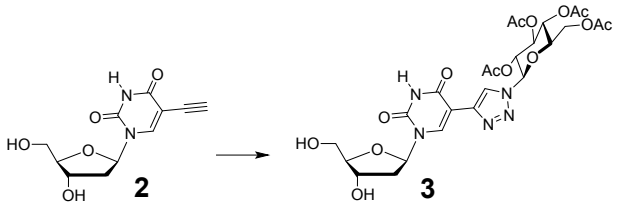
Synthesis

Materials

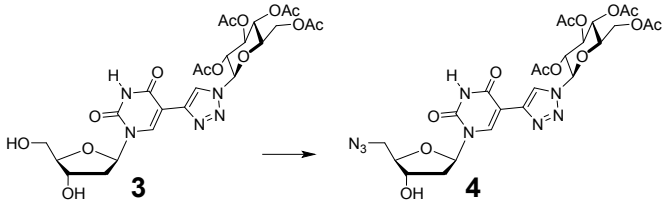
All commercially reagents and solvents (Fluka, Sigma-Aldrich, Alfa-Aesar) were used without further purification. For reactions requiring anhydrous conditions, dry solvents were used under inert atmosphere (nitrogen or argon). Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel F254 plates with fluorescent indicator (Merck). The detection of compounds was accomplished with UV light (254 nm). All compounds were characterized using ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectroscopy (Bruker Avance DPX-300 spectrometer, ^{1}H at 300.13 MHz and ^{13}C at 75.46 MHz). Assignments were made by ^{1}H-^{1}H COSY, DEPT and HSQC experiments. Chemical shifts (δ) are given in parts per million (ppm) relatively to tetramethylsilane or residual solvent peaks ($CHCl_3$: ^{1}H: 7.26, ^{13}C: 77.0). Coupling constants J are given in Hertz (Hz); peak multiplicity is reported as follows: s = singlet, bs = broad singlet, d = doublet, t = triplet, m = multiplet. High-resolution mass spectra (HRMS) were recorded with a Q-Exactive mass spectrometer (Thermo Fisher Scientific) in the electrospray ionisation (ESI) mode at the Centre Régional de Mesures Physiques de l'Ouest (CRMPO, Université de Rennes).



5-ethynyl-2'-deoxyuridine (**2**). To a solution of *5-iodo-2'-deoxyuridine* **1** (1 g, 2.82 mmol, 1.0 equiv) in anhydrous DMF (32 mL) was added *palladium tetrakis(triphenylphosphine)* (0.32 g, 0.28 mmol, 0.1 equiv), *copper iodide* (0.13 g, 0.68 mmol, 0.24 equiv), *triethylamine* (1.1 mL, 7.90 mmol, 2.8 equiv) and *trimethylsilylacetylene* (1.9 mL, 14.10 mmol, 5 equiv) in this order. The mixture was stirred at room temperature for 3.5 hours, then solvents were removed under reduced pressure. The resulting semi-liquid brown residue was submitted to column chromatography (10 % MeOH in DCM, Rf = 0.6) affording 1.3 g of brown foam. The latter was dissolved in THF (10.8 mL) and *TBAF 1 M in THF* (3.2 mL, 3.24 mmol, 1.15 equiv). After stirring at room temperature for 3 hours, the crude product was concentrated under reduced pressure. The product was purified by column chromatography on silica gel eluting with EtOAc/MeOH (80/20) to afford as a slightly yellow solid. Yield: 80 % (0.57 g). Rf = 0.8 (EtOAc/MeOH 80/20). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 2.11-2.14 (m, 2H, H-2'), 3.55-3.62 (m, 2H, H-5'), 3.78-3.81 (q, J = 3.11 Hz, 1H, H-4'), 4.11 (s, 1H, C≡CH), 4.20-4.24 (m, 1H, H-3'), 5.13-5.16 (t, J = 4.8 Hz, 1H, OH (5')), 5.24-5.26 (d, J = 4.2 Hz, 1H, OH (3')), 6.08-6.12 (t, J = 6.8 Hz, 1H, H-1'), 8.30 (s, 1H, H-6 uridine), 11.64 (bs, 1H, NH uridine). The NMR spectroscopic data agree with those described previously.[i]

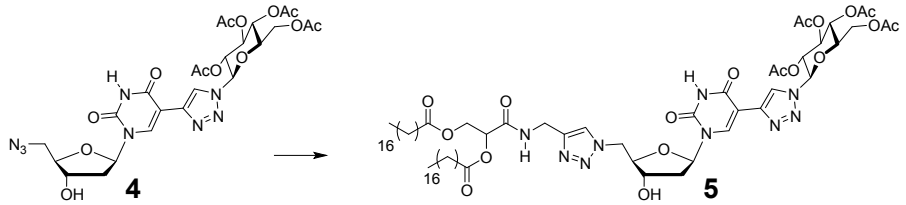


5-[1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl]-2'-deoxyuridine (**3**). To a solution of **2** (0.57 g, 2.26 mmol, 1.0 equiv) and *1-azido-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside* (0.84 g, 2.26 mmol, 1.0 equiv) in 66 mL of THF/H_2O (50/50) was added *copper sulfate pentahydrate* (57.4 mg, 0.23 mmol, 0.1 equiv) followed by *sodium ascorbate* (89.1 mg, 0.45 mmol, 0.2 equiv). The mixture was stirred at 65 °C for 20 hours. After cooling to room temperature, solvents were removed under reduced pressure. The resulting solid was washed with deionized water (150 mL) and absolute ethanol (50 mL). After drying, the resulting white solid was used in the next step without further purification. Yield: 64 % (0.91 g). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 1.81-2.03 (m, 12H, 4 CH_3 (OAc)), 2.16-2.20 (m, 2H, H-2'), 3.57-3.62 (m, 2H, H-5'), 3.83-3.86 (m, 1H, H-4'), 4.07-4.17 (m, 2H, H-6), 4.23-4.28 (m, 1H, H-3'), 4.31-4.37 (m, 1H, H-5), 5.04-5.07 (m, 1H, OH (5')), 5.22-5.30 (t, J = 9.7 Hz, 1H, H-4), 5.29-5.30 (m, 1H, OH (3')), 5.50-5.56 (t, J = 9.6 Hz, 1H, H-3), 5.72-5.79 (t, J = 9.4 Hz, 1H, H-2), 6.20-6.24 (t, J = 6.8 Hz, 1H, H-1'), 6.36-6.39 (d, J = 9.3 Hz, 1H, H-1), 8.61 (s, 1H, H-6 uridine), 8.66 (s, 1H, H triazole), 11.75 (bs, 1H, NH uridine). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 20.4-21.0 (CH_3 (OAc)), 40.2 (C-2'), 61.8, 62.4 (C-5', C-6), 68.0 (C-4), 70.4, 71.0 (C-2, C-3'), 72.7 (C-3), 73.7 (C-5), 84.3 (C-1), 85.2 (C-1'), 88.1 (C-4'), 105.0 (C-5 uridine), 121.6 (CH triazole), 137.0 (C-6 uridine), 140.0 (Cq triazole), 150.1 (C-2 uridine), 161.5 (C-4 uridine), 169.0, 169.8, 170.1, 170.5 (C=O acetate). HRMS (m/z): $[M+Na]^+$($C_{25}H_{31}N_5O_{14}Na$) 648.1758 (calculated 648.1760).

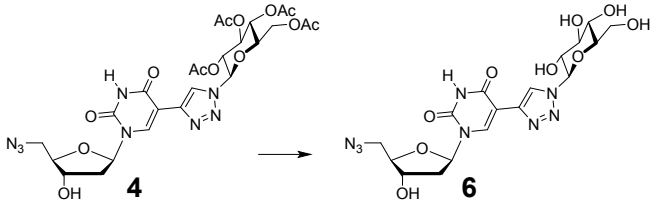


5-[1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl]-5'-azido-2'-deoxyuridine (**4**)**.** To a cold solution (0 °C) of **3** (0.91 g, 1.45 mmol, 1 equiv) in anhydrous pyridine (14 mL) was added dropwise (over 10 minutes) *methanesulfonyl chloride* (0.11 mL, 1.45 mmol, 1.0 equiv). The mixture was stirring at 0 °C for 4 hours. The solvent was removed under reduced pressure and a green semi liquid compound was obtained. Anhydrous DMF (40 mL) and *sodium azide* (3.77 g, 58.0 mmol, 40.0 equiv) were directly added to the residual residue and the reaction was stirring at 80 °C overnight. The solvent was removed *in vaccuo* and a yellow solid was obtained. It was dissolved in 30 mL of ethyl acetate and was washed twice with deonized water (30 mL). The organic phase was dried with Na_2SO_4 and concentrated under reduced pressure. The product was purified by column chromatography eluting with EtOAc to afford a white powder. Yield: 53 % (0.50 g). Rf = 0.4 (EtOAc)**.** ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.84-2.07 (m, 12H, 4 CH_3 (OAc)), 2.40-2.56 (m, 2H, H-2'),

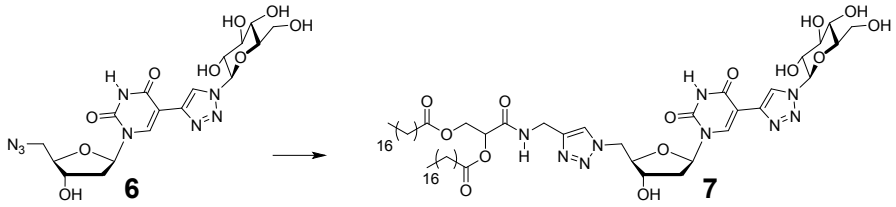
3.68-3.77 (m, 2H, H-5'), 4.03-4.06 (m, 1H, H-5), 4.12-4.19 (m, 2H, H-4', H-6A), 4.28-4.34 (m, 2H, H-6B), 4.53 (m, 1H, H-3'), 5.29-5.34 (t, J = 9.8 Hz, 1H, H-4), 5.42-5.47 (t, J = 9.3 Hz, 1H, H-3), 5.64-5.70 (t, J = 9.4 Hz, 1H, H-2), 5.90-5.95 (d, J = 9.1 Hz, 1H, H-1), 6.40-6.44 (t, J = 6.2 Hz, 1H, H-1'), 8.64 (s, 1H, H triazole), 8.71 (s, 1H, H uridine), 10.17 (bs, 1H, NH uridine). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 20.3-20.8 (CH_3 (OAc)), 40.3 (C-2'), 52.2 (C-5'), 62.4 (C-6), 68.0 (C-4), 70.4 (C-2), 71.9 (C-3'), 72.1 (C-3), 75.0 (C-5), 85.0 (C-4'), 85.8, 86.0 (C-1, C-1'), 106.0 (C-5 uridine), 121.3 (CH triazole), 137.1 (C-6 uridine), 139.8 (Cq triazole), 149.9 (C-2 uridine), 161.4 (C-4 uridine), 169.1, 169.8, 170.3, 170.9 (C=O acetate). HRMS (m/z): $[M+Na]^+$($C_{25}H_{30}N_8O_{13}Na$) 673.1823 (calculated 673.1824).



5'-[(4-((1,2-Distearoyl-sn-glycer-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-5-(1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl)]-2'-deoxyuridine (**5**). To a solution of **4** (0.31 g, 0.48 mmol, 1 equiv) and *(S)-4-Oxo-4-(prop-2-ynylamino)butane-1,2-diyl dioctadecanoate* (0.33 g, 0.48 mmol, 1 equiv) in 20 mL of *tert*-butanol/H_2O (1:1) was added *copper sulfate pentahydrate* (12.0 mg, 0.048 mmol, 0.1 equiv) followed by *sodium ascorbate* (19.0 mg, 0.096 mmol, 0.2 equiv). After stirring at 75 °C for 20 hours, solvents were removed under reduced pressure. The resulting solid was dissolved in CH_2Cl_2 (120 mL) and washed twice with water (40 mL). The organic phase was dried with Na_2SO_4 and concentrated under reduced pressure. The product was purified by column chromatography eluting with EtOAc/MeOH (100/0 then 97/3) to afford a white powder. Yield: 67 % (0.43 g). Rf = 0.6 (EtOAc/MeOH 97/3). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.84-0.89 (t, J = 6.9 Hz, 6H, 2 CH_3 of the stearic chain), 1.16-1.26 (m, 56H, 28 CH_2 of the stearic chain), 1.54-1.59 (m, 4H, 2 C**H$_2$**CH_2C=O), 1.87-2.08 (m, 12H, 4 CH_3 (OAc)), 2.24-2.29 (m, 5H, 2 CH_2C=O of the stearic chain, H-2'A), 2.41-2.43 (m, 1H, H-2'B), 2.54-2.56 (d, J = 6.0 Hz, 2H, CH_2C=O), 4.07-4.14 (m, 2H, H-5, OC**H'**H''), 4.17-4.34 (m, 4H, H-6, H-4', OCH'**H''**), 4.45-4.47 (m, 3H, NCH_2 triazole, OH(3')), 4.51 (m, 1H, H-3'), 4.70 (m, 2H, H-5'), 5.29-5.36 (t, J = 9.8 Hz, 1H, H-4), 5.39-5.53 (dd, 1H, CH), 5.44-5.50 (t, J = 9.5 Hz, 1H, H-3), 5.61-5.67 (t, J = 9.3 Hz, 1H, H-2), 5.94-5.97 (d, J = 9.2 Hz, 1H, H-1), 6.20-6.24 (t, J = 6.5 Hz, 1H, H-1'), 7.13-7.16 (bs, 1H, NH amide), 7.73 (s, 1H, H triazole), 8.03 (s, 1H, H uridine), 8.54 (s, 1H, H triazole), 9.75 (bs, 1H, NH uridine). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 14.2 (CH_3 of the stearic chain), 20.3-20.8 (CH_3 (OAc)), 22.8 (**C**H_2CH_3), 25.0, 25.1 (CH_2CH_2), 29.2-29.8 (CH_2 of the stearic chain), 32.0 (**C**$H_2CH_2CH_3$), 34.2, 34.4 (CH_2C=O of chain), 35.0 (NCH_2 triazole), 37.7 (C-2'), 39.1 (C-2′), 51.0 (C-5'), 61.8 (C-6), 64.6 (OCH_2), 67.9, 68.7 (C-4, CH), 70.5, 71.2 (C-2, C-3'), 72.9 (C-3), 75.1 (C-5), 84.1 (C-4'), 85.7 (C-1), 86.8 (C-1'), 105.9 (C-5 uridine), 121.7, 124.2 (CH triazole), 137.2 (C-6 uridine), 139.6, 145.1 (Cq triazole), 149.5 (C-2 uridine), 161.1 (C-4 uridine), 169.1, 169.2, 169.6, 170.2, 170.8 (C=O amide/acetate), 173.4, 173.7 (-O-C=O). HRMS (m/z): $[M+Na]^+$($C_{68}H_{109}N_9O_{18}Na$) 1362.7783 (calculated 1362.7783).

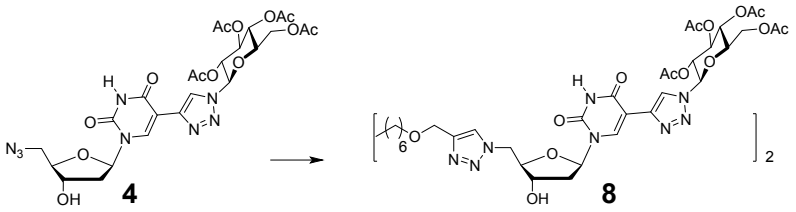


5-[1-(β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl]-5'-azido-2'-deoxyuridine (**6**). A solution of sodium methoxide (1 M in MeOH, 0.4 mL) was added dropwise to a solution of **4** (0.52 g, 0.80 mmol, 1 equiv) in 10 mL of anhydrous methanol at room temperature. The complete deprotection of hydroxide groups was checked by TLC in EtOAc/MeOH, 80/20. After 3 hours stirring, *amberlite IRC-50* was added to convert Na^+ to H^+ ions. After 30 minutes at the same temperature, the resin was removed by hot filtration and washed with MeOH (100 mL). The filtrate was concentrated and purified by column chromatography eluting with EtOAc/MeOH (100/0, then 80/20). Yield: 73 % (0.28 g). Rf = 0.3 (EtOAc/MeOH 80/20). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 2.19-2.37 (m, 2H, H-2'), 3.22-3.51 (m, 4H, H-3, H-4, H-5, H-6A), 3.59-3.79 (m, 4H, H-2, H-5', H-6B), 3.89-3.93 (m, 1H, H-4'), 4.23-4.29 (m, 1H, H-3'), 4.64-4.68 (d, J = 5.7 Hz, 1H, OH(6)), 5.17-5.19 (d, J = 5.3 Hz, OH(4)), 5.26-5.28 (d, J = 4.8 Hz, 1H, OH(3)), 5.42-5.44 (d, J = 5.9 Hz, 1H, OH(2)), 5.50-5.51 (d, J = 4.4 Hz, 1H, OH(3')), 5.58-5.61 (d, J = 9.5 Hz, 1H, H-1), 6.22-6.26 (t, J = 6.5 Hz, 1H, H-1'), 8.42 (s, 1H, H triazole), 8.49 (s, 1H, H uridine), 11.75 (bs, 1H, NH uridine). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 39.1 (C-2'), 51.5 (C-5'), 60.8 (C-6), 69.5, 70.4 (C-4, C-3'), 72.2 (C-2), 77.0, 80.0 (C-3, C-5), 84.6, 85.0 (C-1', C-4'), 87.5 (C-1), 105.2 (C-5 uridine), 121.3 (CH triazole), 136.1 (C-6 uridine), 138.7 (Cq triazole), 149.6 (C-2 uridine), 161.1 (C-4 uridine). HRMS (m/z): $[M+Na]^+$($C_{17}H_{22}N_8O_9Na$) 505.1402 (calculated 505.1405).

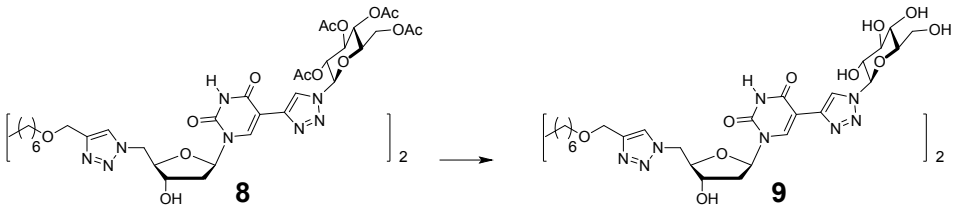


5'-[(4-((1,2-Distearoyl-sn-glycer-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-5-(1-(β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl)]-2'-deoxyuridine (**7**). To a solution of **6** (0.15 g, 0.31 mmol, 1 equiv) and *(S)-4-Oxo-4-(prop-2-ynylamino)butane-1,2-diyl dioctadecanoate* (0.21 g, 0.31 mmol, 1 equiv) in 20 mL of *tert*-butanol/H_2O (50/50) was added *copper sulfate pentahydrate* (7.7 mg, 0.031 mmol, 0.1 equiv) followed by *sodium ascorbate* (12.3 mg, 0.062 mmol, 0.2 equiv). The mixture was stirred at 65 °C for 20 hours. After cooling to room temperature, solvents were removed under reduced pressure. The resulting solid was washed with deionized water (100 mL), absolute ethanol (100 mL) and DCM (100 mL). After drying, the resulting white solid was purified by column chromatography eluting with EtOAc/MeOH (80/20). Yield: 33 % (0.12 g). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 0.83-0.87 (t, 6H, 2

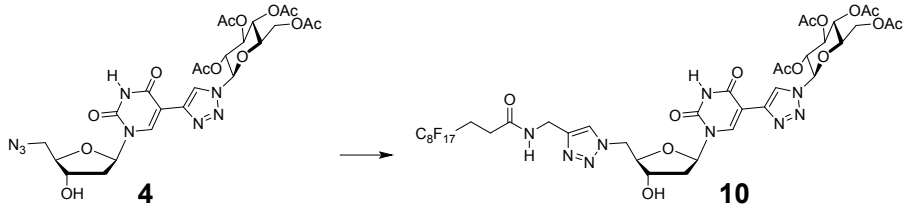
CH_3 of the stearic chain), 1.15-1.23 (m, 56H, 28 CH_2 of the stearic chain), 1.42-1.48 (m, 4H, 2 C**H$_2$**CH_2C=O), 2.15-2.26 (m, 5H, 2 CH_2C=O of the stearic chain, H-2'A), 2.34-2.51 (m, 1H, H-2'B, 2 CH_2C=O), 3.26-3.47 (m, 4H, H-3, H-4, H-5, H-6A), 3.66-3.80 (m, 2H, H-2, H-6A), 3.97-4.04 (m, 1H, OC**H'**H''), 4.09-4.14 (m, 1H, H-4') 4.25-4.29 (m, 4H, H-3', NCH_2 triazole, OCH'**H''**), 4.56-4.75 (m, 3H, H-5', OH(6)), 5.21 (bs, 1H, OH(4)), 5.27-5.34 (m, 2H, CH, OH (3)), 5.48 (bs, 1H, OH(2)), 5.55 (bs, 1H, OH(3')), 5.59-5.63 (d, J = 9.2 Hz, 1H, H-1), 6.19-6.23 (t, J= 7.0 Hz, 1H, H-1'), 7.96 (s, 1H, H triazole), 8.24 (s, 1H, H uridine), 8.44 (bs, 1H, NH amide, H triazole), 11.78 (bs, 1H, NH uridine). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 13.3 (CH_3 of the stearic chain), 21.6 (**C**H_2CH_3), 24.0, 24.1 (CH_2CH_2), 28.0-28.6 (CH_2 of the stearic chain), 30.9 (**C**$H_2CH_2CH_3$), 33.1, 33.3 (CH_2C=O of chain), 33.9 (NCH_2 triazole), 36.3 (C-2'), 38.3 (CH_2C=O), 51.1 (C-5'), 60.6 (C-6), 63.8 (OCH_2), 68.1 (CH), 69.5 (C-4), 70.8 (C-3'), 72.1 (C-2), 76.5, 79.6 (C-3, C-5), 84.3 (C-4'), 85.4 (C-1'), 87.4 (C-1), 105.1 (C-5 uridine), 121.0, 123.0 (CH triazole), 135.9 (C-6 uridine), 144.3, 148.4 (Cq triazole), 149.1 (C-2 uridine), 160.1 (C-4 uridine), 167.8 (C=O amide), 171.5, 172.0 (-O-C=O). HRMS (m/z): $[M+Na]^+$($C_{68}H_{90}N_{16}O_{28}Na$) 1601.6003 (calculated 1601.6003). HRMS (m/z): $[M+Na]^+$($C_{60}H_{101}N_9O_{14}Na$) 1194.7360 (calculated 1194.7361).



1,12-bis-dodecanyl-5'-[(4-oxymethyl)-1H-1,2,3-triazol-1-yl)]-N3-[1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl)]-2'-deoxyuridine (**8**). To a solution of **4** (1.16 g, 1.78 mmol, 2 equiv) and *1,12-dipropargyloxydecane* (0.30 g, 1.07 mmol, 1.2 equiv) in 50 mL of *tert*-butanol/H_2O (50/50) was added *copper sulfate pentahydrate* (44.9 mg, 0.18 mmol, 0.2 equiv) followed by *sodium ascorbate* (71.3 mg, 0.36 mmol, 0.4 equiv). The mixture was stirred at 65 °C for 20 hours. After cooling to room temperature, solvents were removed under reduced pressure. The resulting solid was washed with deionized water (200 mL). After drying, the resulting white solid was purified by column chromatography eluting with EtOAc/MeOH (100/0, then 95/5) to afford a white powder. Yield: 65 % (0.91 g). Rf = 0.3 (EtOAc/MeOH 95/5). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 1.18 (m, 16H, CH_2), 1.39-1.42 (m, 4H, 2 C**H$_2$**CH_2O), 1.81-2.08 (m, 12H, 4 CH_3 (OAc)), 2.15-2.34 (m, 4H, 2 H-2'), 3.29-3.33 (t, J = 6.5 Hz, 4H, 2 CH_2O), 4.01-4.21 (m, 6H, 2 H-4', H-6), 4.26-4.31 (m, 2H, 2 H-3'), 4.33-4.37 (m, 2H, 2 H-5), 4.40 (s, 4H, 2 triazole CH_2O), 4.61-4.79 (m, 4H, 2 H-5'), 5.24-5.30 (t, 2H, J = 9.7 Hz, H-4), 5.52-5.58 (m, 4H, 2 H-3, 2 OH(3')), 5.74-5.80 (t, J = 9.4 Hz, 2H, 2 H-2), 6.17-6.20 (t, J = 6.8 Hz, 2H, 2 H-1'), 6.39-6.42 (d, J = 9.2 Hz, 2 H, H-1), 8.11 (s, 2H, 2 H triazole), 8.24 (s, 2H, 2 H-6 uridine), 8.69 (s, 2H, 2 H triazole). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 20.0-20.5 (CH_3 (OAc)), 25.7-29.1 (CH_2), 38.4 (C-2'), 51.1 (C-5'), 62.1-63.1 (C-6, triazole CH_2O), 67.6 (C-4), 69.4 (C-2), 70.0 (CH_2O), 70.9, 72.2, 73.3 (C-3', C-3, C-5), 84.0 (C-1'), 84.6 (C-4'), 85.5 (C-1), 104.8 (C-5 uridine), 121.2, 124.8 (CH triazole), 136.6 (C-6 uridine), 139.4, 144.1 (Cq triazole), 149.5 (C-2 uridine), 161.0 (C-4 uridine), 168.6, 169.4, 169.7, 170.1 (C=O acetate). HRMS (m/z): $[M+Na]^+$($C_{68}H_{90}N_{16}O_{28}Na$) 1601.6003 (calculated 1601.6003).

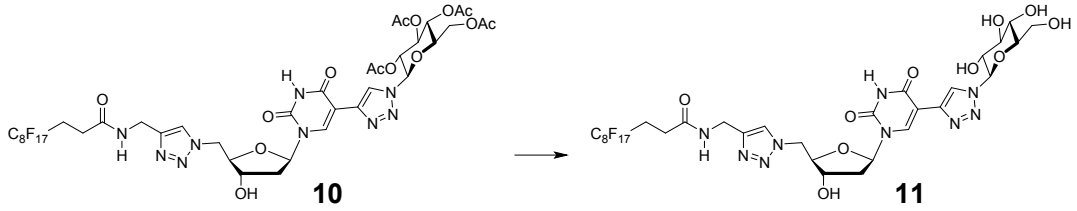


1,12-bis-dodecanyl-5'-[(4-oxymethyl)-1H-1,2,3-triazol-1-yl)]-N3-[1-(β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl)]-2'-deoxyuridine (**9**). A solution of *sodium methoxide* (1 M in MeOH, 0.2 mL) was added dropwise to a solution of **8** (0.40 g, 0.25 mmol, 1 equiv) in 20 mL of anhydrous methanol. The complete deprotection of hydroxide groups was checked by TLC in EtOAc/MeOH, 90/10. After heating for 1.5 hours at 50 °C, *amberlite IRC-50* was added to convert Na^+ to H^+ ions. After 20 minutes at the same temperature, the resin was removed by filtration and washed with hot MeOH (30 mL). The filtrate was concentrated and the product was washed with CH_2Cl_2 (30 mL) then water (90 mL). The product was then dried under reduced pressure to afford a white powder. Yield: 64 % (0.20 g). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 1.20 (m, 16H, CH_2), 1.42-1.46 (m, 4H, 2 C**H$_2$**CH_2O), 2.15-2.38 (m, 4H, 2 H-2'), 3.22-3.39 (m, 10H, 2 CH_2O, 2 H-3, 2 H-4, 2 H-5), 3.43-3.49 (m, 2H, 2 H-6A), 3.67-3.80 (m, 4H, 2 H-2, 2 H-6B), 4.12-4.17 (m, 2H, 2 H-4'), 4.28-4.31 (m, 2H, 2 H-3'), 4.64 (s, 2H, 2 triazole CH_2O), 4.59-4.77 (m, 6H, 2 H-5', 2 OH(6)), 5.18-5.29 (d, J = 5.2 Hz, 4H, 2 OH(3/4)), 5.45-5.43 (d, J = 6.0 Hz, 2H, 2 OH(2)), 5.55-5.56 (d, J = 4.3 Hz, 2H, 2 OH(3')), 5.60-5.63 (d, J = 9.2 Hz, 2H, 2 H-1), 6.18-6.23 (t, J = 7.0 Hz, 2H, 2 H-1'), 8.13 (s, 2H, 2 H triazole), 8.24 (s, 2H, 2 H-6 uridine), 8.44 (s, 2H, 2 H triazole), 11.78 (s, 2H, 2 NH uridine). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 25.7-29.1 (CH_2), 38.4 (C-2'), 51.2 (C-5'), 60.8 (C-6), 63.1 (triazole CH_2O), 69.5 (CH_2O), 71.0 (C-3'), 72.2 (C-2), 69.5, 77.0, 80.0 (C-3, C-4, C-5), 84.6 (C-4'), 85.5 (C-1'), 87.5 (C-1), 105.3 (C-5 uridine), 121.5, 124.7 (CH triazole), 136.4 (C-6 uridine), 138.6, 144.1 (Cq triazole), 149.6 (C-2 uridine), 161.1 (C-4 uridine). HRMS (m/z): $[M+Na]^+$($C_{52}H_{74}N_{16}O_{20}Na$) 1265.5156 (calculated 1265.5157).



5'-[4-((1H,1H,2H,2H-perfluoroundecanamide)methyl)-1-H-1,2,3-triazol-1-yl)-5-(1-(1-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl]-2'-deoxyuridine (**10**). To a solution of **4** (0.30 g, 0.46 mmol, 1 equiv) and *N-propargyl-2H,2H,3H,3Hperfluoroundecanamide* (0.29 g, 0.55 mmol, 1.2 equiv) in 20 mL of *tert*-butanol/H2O (50/50) was added *copper sulfate pentahydrate* (11.5 mg, 0.046 mmol, 0.1 equiv) and *sodium ascorbate* (18.2 mg, 0.092 mmol, 0.2 equiv). The mixture was stirred at 65 °C for 20 hours. The solvent was removed under reduced pressure and the residual solid was washed with water (200 mL). After drying, the crude product was purified by column

chromatography eluting with EtOAc/MeOH (100/0 then 90/10) to afford a white solid. Yield: 57 % (0.31 g). Rf = 0.7 (EtOAc/MeOH 90/10). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 1.81-2.03 (m, 12H, 4 CH_3 (OAc)), 2.18-2.22 (m, 2H, H-2'A), 2.36-2.42 (m, 5H, H-2'B, CH_2CH_2CO), 4.10-4.18 (m, 2H, H-4', H-6), 4.28-4.38 (m, 4H, H-3', H-5, $NHCH_2$ triazole), 4.57-4.67 (m, 2H, H-5'), 5.24-5.30 (t, J = 9.7 Hz, 1H, H-4), 5.51-5.58 (t, J = 9.5 Hz, 1H, H-3), 5.74-5.80 (t, J = 9.4 Hz, 1H, H-2), 6.18-6.22 (t, J = 6.92 Hz, 1H, H-1'), 6.38-6.41 (d, J = 9.2 Hz, 1H, H-1), 7.99 (s, 1H, H triazole), 8.26 (s, 1H, H-6 uridine), 8.51 (s, 1H, NH amide), 8.69 (s, 1H, H triazole), 11.80 (s, 1H, NH uridine). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 20.0-20.5 (CH_3(C=O)), 25.6-25.8 (CH_2CH_2CO), 34.2 ($NHCH_2$ triazole), 38.3 (C-2'), 51.2 (C-5'), 62.0 (C-6), 67.6 (C-4), 70.0 (C-2), 70.9 (C-3' or C-5), 72.2 (C-3), 73.3 (C-3' or C-5), 84.0 (C-1), 84.5 (C-4'), 85.7 (C-1'), 104.8 (C-5 uridine), 121.3-123.6 (CH triazole), 136.8 (C-6 uridine), 139.4-149.5 (Cq triazole), 149.5 (C-2 uridine), 161.0 (C-4 uridine), 168.6, 169.2, 169.4, 169.6, 170.1 (C=O acetate, C=O amide). HRMS (m/z): $[M+H]^+$($C_{39}H_{39}N_9O_{14}F_{17}$) 1180.2332 (calculated 1180.2339).



5'-[4-((1H,1H,2H,2H-perfluoroundecanamide)methyl)-1-H-1,2,3-triazol-1-yl)-5-(1-(1-((β-D-glucopyranoside)-1H-1,2,3-triazol-4-yl]-2'-deoxyuridine (**11**). A solution of *sodium methoxide* (1M in MeOH, 0.2 mL) was added dropwise to a solution of **10** (0.21 g, 0.18 mmol, 1 equiv) in 15 mL of anhydrous methanol. After heating for 3 hours at 70 °C, *amberlite IRC-50* was added to convert Na^+ to H^+ ions. After 30 minutes at the same temperature, the resin was immediately removed by filtration and washed with hot MeOH (200 mL). The filtrate was concentrated and the product was washed with cold MeOH (50 mL). Yield : 0.10 g (55%). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 2.16-2.20 (m, 2H, H-2'A), 2.34-2.44 (m, 5H, H-2'B, CH_2CH_2CO), 3.22-3.50 (m, 4H, H-3, H-4, H-5, H-6A), 3.65-3.80 (m, 2H, H-2, H-6B), 4.10-4.15 (m, 1H, H-4'), 4.29-4.30 (m, 3H, H-3', $NHCH_2$ triazole), 4.57-4.75 (m, 3H, H-5', OH(6)), 5.17-5.19 (d, J = 5.2 Hz, 1H, OH(4)), 5.26-5.28 (d, J = 4.7 Hz, 1H, OH(3)), 5.42-5.44 (d, J = 5.8 Hz, 1H, OH(2)), 5.54-5.55 (d, J = 4.0 Hz, 1H, OH(3')), 5.59-5.62 (d, J = 9.2 Hz, 1H, H-1), 6.19-6.23 (t, J = 6.8 Hz, 1H, H-1'), 8.00 (s, 1H, H triazole), 8.24 (s, 1H, H-6 uridine), 8.44 (s, 1H, H triazole), 8.51 (bs, 1H, NH amide), 11.78 (s, 1H, NH uridine). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 25.5-25.8 (CH_2CH_2CO), 34.3 ($NHCH_2$ triazole), 38.3 (C-2'), 51.3 (C-5'), 60.8 (C-6), 69.5 (C-4), 71.0 (C-3'), 72.2 (C-2), 77.0, 80.0 (C-3, C-5), 84.6 (C-4'), 85.5 (C-1'), 87.5 (C-1), 105.3 (C-5 uridine), 121.5-123.6 (CH triazole), 136.4 (C-6 uridine), 138.6-144.5 (Cq triazole), 149.5 (C-2 uridine), 161.1 (C-4 uridine), 169.3 (C=O amide). HRMS (m/z): $[M+Na]^+$($C_{31}H_{30}N_9O_{10}F_{17}Na$) 1034.1732 (calculated 1034.1736).

Physicochemical assays

Gelation test / Critical Concentration Gelation (CCG)

Various solvents containing U-GNLs were heated until dissolution in a test-tube and gradually allowed to cool to room temperature unless otherwise stated. If the sample does not flow under its own weight when the tube is turned upside-down, it is recognized as a gel. The Critical Gelation Concentration (CCG) was assessed using the tube-inverting method. The gel was repeatedly diluted with absolute ethanol, heated and sonicated until no formation of gel.

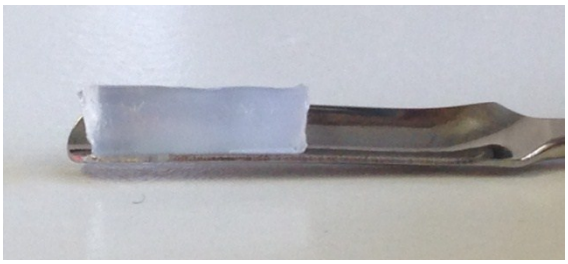


Fig. SI1. Alcogel **5** at 1 % w/v in absolute ethanol.

Gel-Sol transition temperature

For the alcogel **5**, a Gel-Sol transition of 55 °C was measured by gradually heating the sample (2°C steps) with a Thermomixer compact (Eppendorf, Hauppauge, NY, USA).

Rheology

Dynamic viscoelastic properties of organogels were evaluated using a Kinexus® Pro+ rheometer (Malvern Instruments Ltd., United Kingdom), with a cone plate geometry (diameter: 40 mm, angle: 1 °). The lower plate is equipped with a Peltier temperature control system, and all samples were studied at 25 ± 0.01 °C unless indicated otherwise. The gel was heated at 70 °C and the liquid resulting was placed into the rheometer and subjected to sinusoidal oscillations. Shear strain (0.01 % - 100 %) was applied to determine the Linear Viscoelastic Region (LVR), the region in which the stress is linearly related to the strain. Elastic (G') and viscous (G") moduli were then determined by performing a frequency sweep from 0.63 to 62.83 rad/s with an applied strain of 0.03 % (which was within the LVR of samples). Note that the material maintained its structure until a strain of about 1 %. At least three replicates were measured for each sample.

Transmission Electron Microscopy (TEM)

TEM microscopy experiments were performed with a Hitachi H 7650 (negative staining with Uranyle acetate 2.5 % in water, Ni carbon coated grids). Samples containing **5** U-GNL were obtained from the mixtures of 2 mg/mL in ethanol and methanol. Before TEM imaging, the sample was dried on the grids at room temperature.

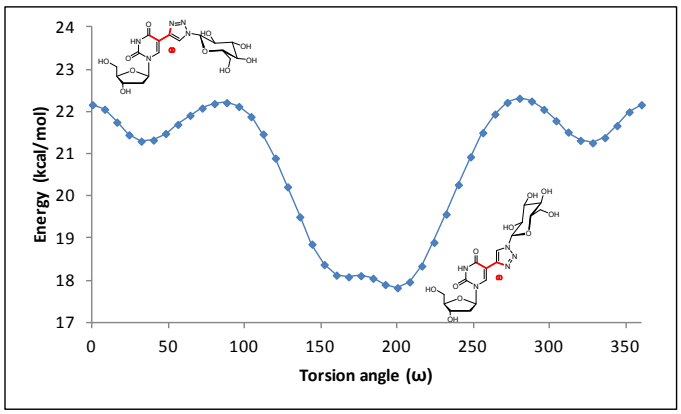


Fig. SI2 Conformational analysis of *5-[1-(β-D-glucopyranoside)-triazol-4-yl]-2'-deoxyuridine.*

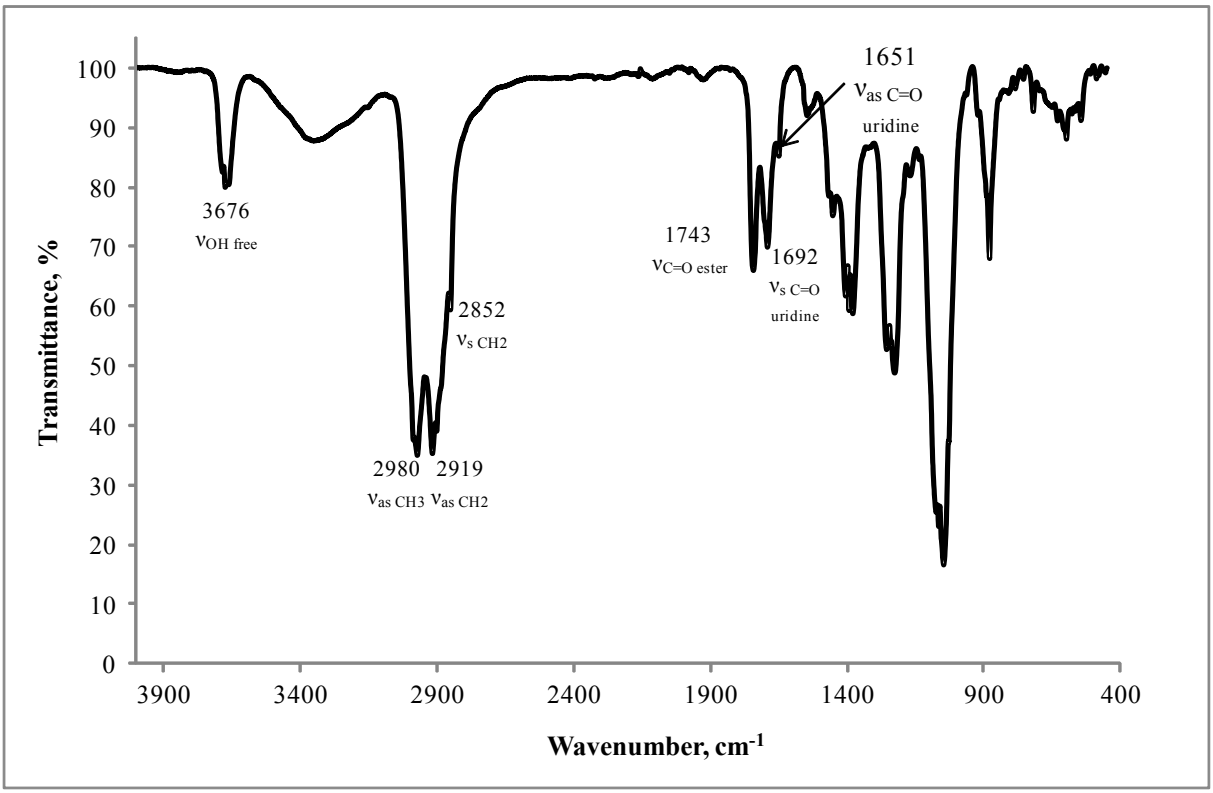


Fig. SI3 ATR FTIR spectrum of U-GNL **5** based alcogel in ethanol (5% w/v)

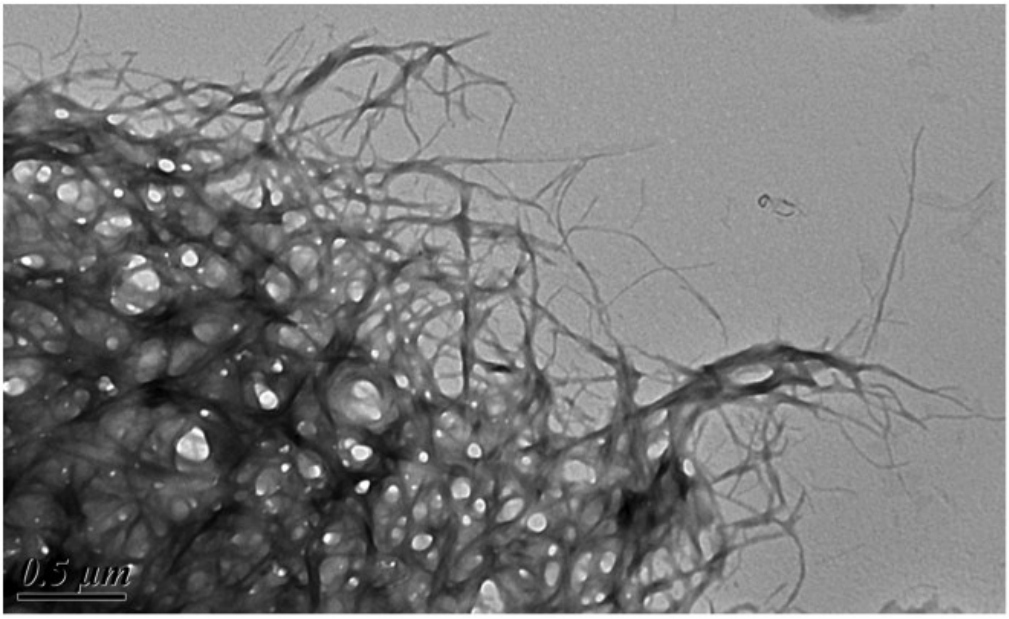


Fig. SI4. TEM image of U-GNL **5** in Ethanol (2 % w/v)

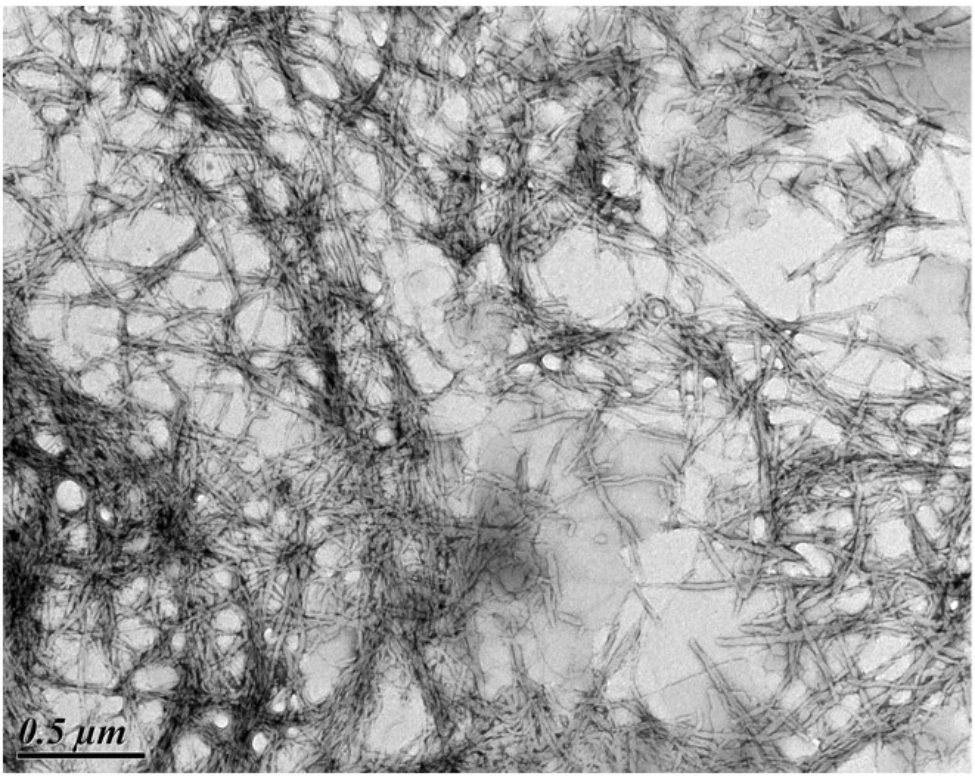


Fig. SI5. TEM image of U-GNL **5** in Methanol (2 % w/v)

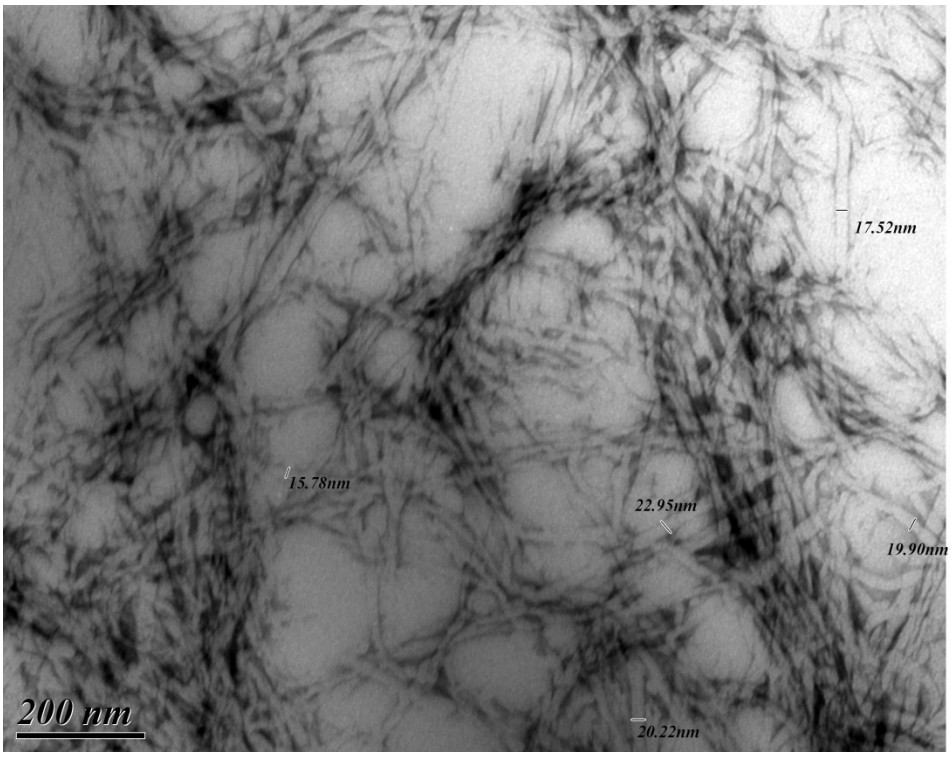


Fig. SI6. TEM image of U-GNL **5** in Methanol (2 % w/v)

[i] C. S. Yu, F. Oberdorfer, *Synlett,* 2000, **1**, 86-88.