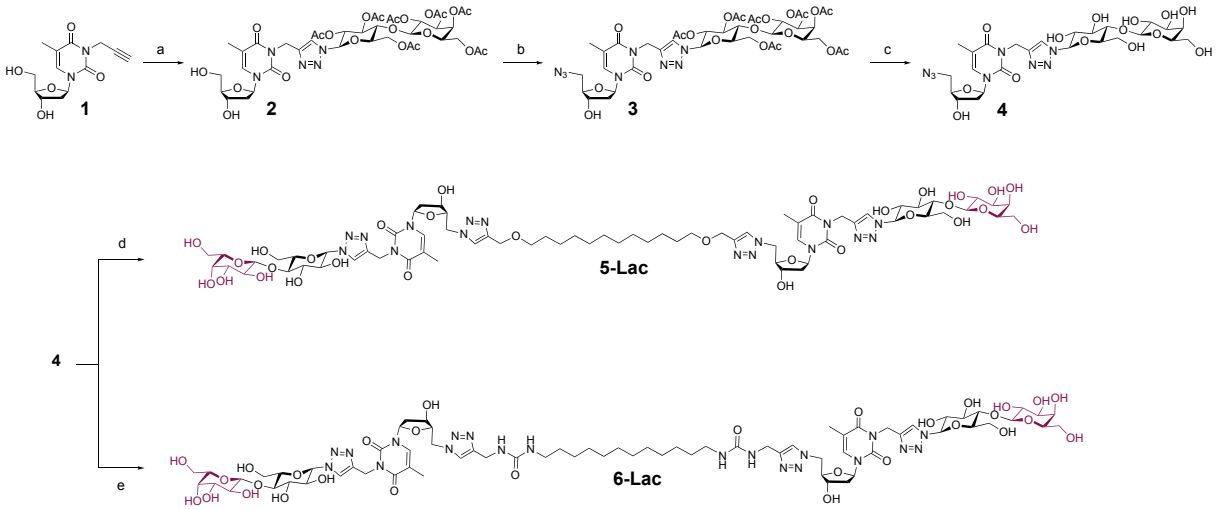
Supporting information

Synthesis

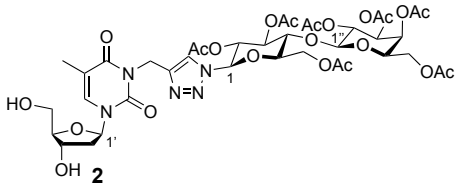
All commercially chemicals and solvents (Fluka, Sigma-Aldrich, Alfa-Aesar) were used without further purification. Reactions requiring anhydrous conditions were conducted with dry solvents under an inert atmosphere (argon). Analytical thin layer chromatography was performed using silica gel 60 F_{254} pre-coated plates (Merck). Detection was accomplished using UV light (254 nm), 10% conc. H_2SO_4 solution in ethanol or 1% aqueous $KMnO_4$ followed by heating. Column chromatography was performed on silica gel (0.043-0.063 mm). Compounds were characterized by ^1H, ^{13}C, COSY, HSQC experiments on Bruker Avance 300 (^1H: 300 MHz, ^{13}C: 75 MHz) and Bruker Avance DPX 500 (^1H: 500 MHz, ^{13}C: 125 MHz) spectrometers. Chemical shifts (δ) are given in parts per million (ppm) and coupling constants J in Hertz (Hz); peak multiplicity is reported as follow: s = singlet, bs = broad singlet, d = doublet, t = triplet, m = multiplet. High Resolution Mass Spectrometry was performed on a Waters Q-TOF 2 (IECB, Bordeaux, France) and a Thermo Fisher Q-Exactive (CRMPO, Rennes, France) spectrometers in the positive electrospray ionization (ESI) mode.

ß-galactosidase from *Aspergillus Oryzae* (12.1 units/mg, Sigma-Aldrich, France), Phosphate Buffered Saline (PBS) (Sigma Aldrich, France) and titrated HCl aqueous solution (0.1 M, Sigma Aldrich, France) were used as received for incubation experiments.



Scheme SI1. Synthetic route leading to enzyme-sensitive bolaamphiphiles **5-Lac** and **6-Lac**.

***N*3-[(1-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-D-lactopyranosyl)-1*H*-1,2,3-triazol-4-yl)methyl]thymidine (2)**



Chemical Formula: $C_{39}H_{51}N_5O_{22}$
Molecular Weight: 941,85

Propargylthymidine **1** (900 mg, 3.21 mmol) and 1-deoxy-1-azido-2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-D-lactopyranose[1] (2.33 g, 3.53 mmol, 1.1 equiv) were first dissolved in 20 mL of ^{t}BuOH/H_2O (1:1). Copper sulfate pentahydrate (80 mg, 0.32 mmol, 0.1 equiv) and sodium ascorbate (127 mg, 0.64 mmol, 0.2 equiv) were successively added and the mixture was stirred at 65 °C for 15 hours. Solvents were removed under reduced pressure and the resulting solid was washed with water until washings were colorless. The crude product was purified by flash chromatography on silica gel eluting with EtOAc/MeOH (90:10) to provide the title compound as a white solid (1.94 g, 64 %).

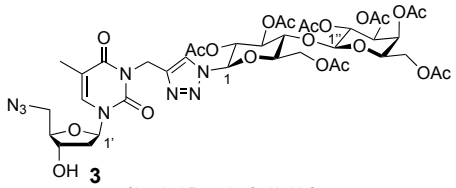
Rf: 0.40 (EtOAc/MeOH 90:10)

^{1}H NMR (300 MHz, acetone-*d6*) δ (ppm): 1.77 (s, 3H, OAc), 1.85 (d, *J*= 1.1 Hz, 3H, CH_3 thymine), 1.91 (s, 3H, OAc), 2.01-2.09 (m, 12H, OAc), 2.13 (s, 3H, OAc), 2.22-2.30 (m, 2H, H-2'), 3.75-3.83 (m, 2H, H-5'), 3.95 (AB system, *J*= 5.3 Hz, 1H, H-4'), 4.10-4.24 (m, 5H, H-4, H-5", H-6a, H-6"), 4.24-4.33 (m, 2H, H-5, OH), 4.39-4.59 (m, 3H, H-3', H-6b, OH), 4.90 (d, *J*= 7.4 Hz, 1H, H-1"), 5.03-5.13 (m, 2H, H-2", H-3"), 5.13-5.26 (m, 2H, NCH_2 triazole), 5.35-5.39 (m, 1H, H-4"), 5.41-5.50 (m, 1H, H-3), 5.55 (dd, *J*= 9.2, 9.5 Hz, 1H, H-2), 6.16 (d, *J*= 9.1 Hz, 1H, H-1), 6.36 (apparent t, *J*= 6.6, 6.9 Hz, 1H, H-1'), 7.85-7.90 (m, 1H, H-6 thymine), 8.00-8.05 (m, 1H, CH triazole).

^{13}C NMR (75 MHz, acetone-*d6*) δ (ppm): 13.3 (CH_3 thymine), 20.3, 20.6-20.8, 20.9 (OAc), 36.7 (NCH_2 triazole), 41.3 (C-2'), 61.9 (C-6"), 62.8 (C-5'), 63.1 (C-6), 68.1 (C-4"), 70.0 (C-2" or C-3"), 71.5 (C-2 or C-3, C-5), 71.8 (C-2" or C-3"), 72.1 (C-3'), 73.6 (C-2 or C-3), 76.4, 76.9 (C-4, C-5"), 85.7 (C-1), 86.5 (C-1'), 88.7 (C-4'), 101.8 (C-1"), 109.9 (C-5 thymine), 123.5 (CH triazole), 135.9 (C-6 thymine), 144.9 (C-4 triazole), 151.6, 163.5 (C=O thymine), 169.4, 169.8, 170.2, 170.3, 170.7, 170.8, 170.9 (C=O acetyl).

HRMS (ESI): (M+Na) Calcd. 964.2918, Found 964.2923.

5'-azido-*N*3-[(1-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-D-lactopyranosyl)-1*H*-1,2,3-triazol-4-yl)methyl]-5'-deoxythymidine (3)



Chemical Formula: $C_{39}H_{50}N_8O_{21}$
Molecular Weight: 966,86

Compound **2** (1.88 g, 2.00 mmol) was first dissolved in anhydrous DMF (20 mL). Then, triphenylphosphine (630 mg, 2.40 mmol, 1.2 equiv), sodium azide (650 mg, 10.00 mmol, 5 equiv) and carbon tetrabromide (796 mg, 2.40 mmol, 1.2 equiv) were successively added. The reaction mixture was stirred at room temperature for 24 hours and then treated with 50 mL of a 5 % w/v $NaHCO_3$ aqueous solution. After stirring for a further 30 minutes, the mixture was extracted with CH_2Cl_2 and the organic phase washed with water. After drying over Na_2SO_4 the solvents were removed under reduced pressure. The resulting solid was purified by flash chromatography on silica gel eluting with a step gradient of MeOH starting from 1 % to 5 % v/v in CH_2Cl_2 to provide the title compound as a white solid (1.17 g, 61 %).

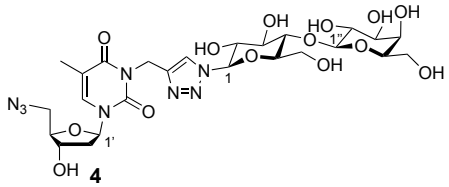
Rf: 0.20 (CH_2Cl_2/MeOH 95:5)

^{1}H NMR (300 MHz, acetone-*d6*) δ (ppm): 1.77 (s, 3H, OAc), 1.89 (d, *J*= 1.2 Hz, 3H, CH_3 thymine), 1.91 (s, 3H, OAc), 2.03 (s, 3H, OAc), 2.04 (s, 6H, OAc), 2.05 (s, 3H, OAc), 2.13 (s, 3H, OAc), 2.26-2.41 (m, 2H, H-2'), 3.59-3.78 (m, 2H, H-5'), 3.98-4.06 (m, 1H, H-4'), 4.11-4.25 (m, 5H, H-4, H-6a, H-5", H-6"), 4.25-4.32 (m, 1H, H-5), 4.40-4.48 (m, 1H, H-3'), 4.51-4.58 (m, 1H, H-6b), 4.63 (d, *J*= 4.3 Hz, 1H, OH-3'), 4.90 (d, *J*= 7.6 Hz, 1H, H-1"), 5.04-5.15 (m, 2H, H-2", H-3"), 5.15-5.27 (m, 2H, NCH_2 triazole), 5.38 (dd, *J*= 1.2, 3.2 Hz, 1H, H-4"), 5.46 (dd, *J*= 8.2, 9.6 Hz, 1H, H-3), 5.55 (apparent t, *J*= 9.1, 9.6 Hz, 1H, H-2), 6.16 (d, *J*= 9.1 Hz, 1H, H-1), 6.38 (t, *J*= 6.8 Hz, 1H, H-1'), 7.58 (d, *J*= 1.2 Hz, 1H, H-6 thymine), 8.01-8.05 (m, 1H, CH triazole).

^{13}C NMR (75 MHz, acetone-*d6*) δ (ppm): 13.3 (CH_3 thymine), 20.3, 20.6-20.8, 21.0 (OAc), 36.8 (NCH_2 triazole), 40.2 (C-2'), 53.1 (C-5'), 61.9 (C-6"), 63.1 (C-6), 68.1 (C-4"), 70.0 (C-3"), 71.5 (C-2), 71.8 (C-5), 72.3 (C-3', C-2"), 73.6 (C-3), 76.4, 76.9 (C-5", C-4), 85.7 (C-1), 86.0 (C-4'), 86.4 (C-1'), 101.8 (C-1"), 109.9 (C-5 thymine), 123.6 (CH triazole), 135.4 (C-6 thymine), 144.9 (C-4 triazole), 151.6, 163.5 (C=O thymine), 169.4, 169.8, 170.2, 170.3, 170.7, 170.8, 170.9 (C=O acetyl).

HRMS (ESI): (M+Na) Calcd. 989.2983, Found 989.2988.

5'-azido-*N*3-[(1-(β-D-lactopyranosyl)-1*H*-1,2,3-triazol-4-yl)methyl]-5'-deoxythymidine (4)



4

Chemical Formula: $C_{25}H_{36}N_8O_{14}$
Molecular Weight: 672,61

Compound **3** (1.00 g, 1.03 mmol) was stirred in 15 mL of anhydrous MeOH until complete dissolution. Acetyl chloride (144 µL, 2.06 mmol, 2 equiv) was added and stirring was continued for a further 48 hours. A white precipitate was observed and TLC (CH_2Cl_2/MeOH 70:30) showed complete conversion. Solvents were evaporated under reduced pressure and the resulting solid was purified by flash chromatography on silica gel eluting with CH_2Cl_2/MeOH (70:30) to provide the title compound as a white solid (567 mg, 82 %).

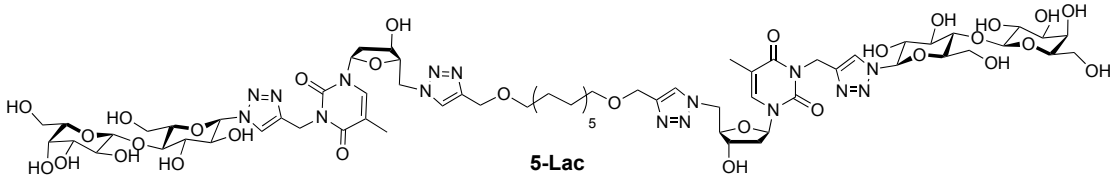
Rf: 0.20 (CH_2Cl_2/MeOH 70:30)

^{1}H NMR (300 MHz, D_2O) δ (ppm): 1.87 (s, 3H, CH_3 thymine), 2.25-2.47 (m, 2H, H-2'), 3.44-4.06 (m, 15H, H-4', H-5', H-2, H-3, H-4, H-5, H-6, H-2", H-3", H-4", H-5", H-6"), 4.39-4.45 (m, 1H, H-3'), 4.45-4.49 (m, 1H, H-1"), 5.17 (s, 2H, NCH_2 triazole), 5.70 (d, *J*= 9.1 Hz, 1H, H-1), 6.24 (t, *J*= 6.6 Hz, 1H, H-1'), 7.53 (s, 1H, H-6 thymine), 8.14 (s, 1H, CH triazole).

^{13}C NMR (75 MHz, D_2O) δ (ppm): 12.2 (CH_3 thymine), 36.2 (NCH_2 triazole), 37.7 (C-2'), 51.5, 59.7, 61.0, 68.5, 70.8, 70.9, 71.9, 72.5, 74.4, 75.4, 77.2, 77.6, 84.5 (C-5', C-6", C-6, C-4", C-3", C-2, C-5, C-3', C-2", C-3, C-4, C-5", C-4'), 86.2 (C-1), 87.2 (C-1'), 102.9 (C-1"), 110.8 (C-5 thymine), 123.7 (CH triazole), 135.9 (C-6 thymine), 143.1 (C-4 triazole), 151.4, 164.9 (C=O thymine).

HRMS (ESI): (M+Na) Calcd. 695.2243, Found 695.2249.

1,12-bis{((1-(*N*3-[(1-(β-D-lactopyranosyl)-1*H*-1,2,3-triazol-4-yl)methyl]thymidin-5'-yl)-1*H*-1,2,3-triazol-4-yl)methyl)oxy}dodecane (5-Lac)



5-Lac

Chemical Formula: $C_{68}H_{102}N_{16}O_{30}$
Molecular Weight: 1623,65

Compound **4** (260 mg, 0.39 mmol) and 1,12-dipropargyloxydodecane[2] (58 mg, 0.21 mmol, 0.55 equiv) were dissolved in 10 mL of ^{t}BuOH/H_2O (1:1). Copper sulfate pentahydrate (10 mg, 0.04 mmol, 0.1 equiv) and sodium ascorbate (16 mg, 0.08 mmol, 0.2 equiv) were successively added and the mixture was heated at 65 °C for 15 hours. After cooling to room temperature, solvents were removed under reduced pressure and the resulting green solid was purified by flash chromatography on silica gel eluting with CH_2Cl_2/MeOH/H_2O (70:40:6) to provide the title compound as a white solid (225 mg, 71 %).

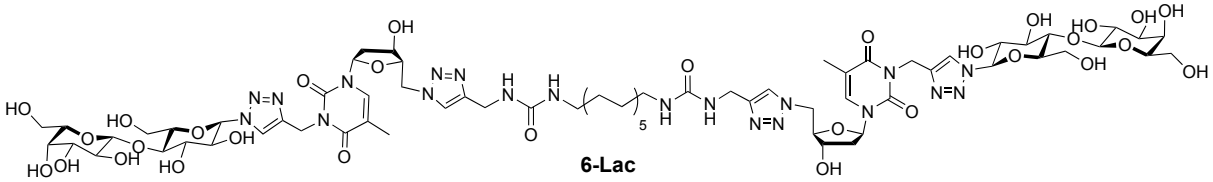
Rf: 0.20 (CH_2Cl_2/MeOH/H_2O 70:40:6)

^{1}H NMR (500 MHz, DMSO-*d6*) δ (ppm): 1.16-1.30 (m, 16H, CH_2), 1.41-1.54 (m, 4H, C**H**$_2$CH$_2$O), 1.87 (s, 6H, CH_3 thymine), 2.09-2.26 (m, 4H, H-2'), 3.27-3.67 (m, 26H, H-3, H-4, H-5, H-6a, H-2", H-3", H-4", H-5", H-6", CH_2O, OH), 3.71-3.80 (m, 2H, H-6b), 3.80-3.89 (m, 2H, H-2), 4.07-4.15 (m, 2H, H-4'), 4.24 (d, *J*= 7.1 Hz, 2H, H-1"), 4.26-4.33 (m, 2H, H-3'), 4.44-4.49 (m, 4H, OCH_2 triazole), 4.57 (d, *J*= 4.5 Hz, 2H, OH), 4.59-4.67 (m, 2H, OH), 4.67-4.76 (m, 6H, H-5', OH), 4.80-4.91 (m, 4H, OH), 5.05 (AB system, *J*= 13.6 Hz, 4H, NCH_2 triazole), 5.15 (d, *J*= 4.2 Hz, 2H, OH), 5.55 (d, *J*= 5.7 Hz, 2H, OH C-3'), 5.59 (d, *J*= 9.3 Hz, 2H, H-1), 6.22 (apparent t, *J*= 6.8, 7.0 Hz, 2H, H-1'), 7.45 (s, 2H, H-6 thymine), 8.08 (s, 2H, CH triazole), 8.13 (s, 2H, CH triazole).

^{13}C NMR (125 MHz, DMSO-*d6*) δ (ppm): 12.8 (CH_3 thymine), 25.7 (CH_2), 29.0-29.1 (CH_2, **C**H_2CH$_2$O), 36.2 (NCH_2 triazole), 38.1 (C-2'), 51.1 (C-5'), 60.0, 60.5 (C-6, C-6"), 63.3 (OCH_2 triazole), 68.2, 70.6, 70.7, 73.3, 75.2, 75.6, 77.8, 79.8 (C-3', C-3, C-4, C-5, C-2", C-3", C-4", C-5"), 69.7 (CH_2O), 71.6 (C-2), 84.2 (C-4'), 85.2 (C-1'), 86.9 (C-1), 103.8 (C-1"), 109.1 (C-5 thymine), 122.5, 124.6 (CH triazole), 135.1 (C-6 thymine), 142.7, 144.3 (C-4 triazole), 150.3, 162.3 (C=O thymine).

HRMS (ESI): (M+Na) Calcd. 1645.6840, Found 1645.6846.

1,12-bis{((1-(*N*3-[(1-(β-D-lactopyranosyl)-1*H*-1,2,3-triazol-4-yl)methyl]thymidin-5'-yl)-1*H*-1,2,3-triazol-4-yl)methyl)amino)carbamoyl}dodecane (6-Lac)



6-Lac

Chemical Formula: $C_{70}H_{106}N_{20}O_{30}$
Molecular Weight: 1707,73

Compound **4** (120 mg, 0.18 mmol) and 1,1'-(dodecane-1,12-diyl)bis(3-[propargyl]urea)[3]

(36 mg, 0.1 mmol, 0.55 equiv) were dissolved in 6 mL of ^{t}BuOH/H_2O (1:1). Bromotris(triphenylphosphine)copper(I) (19 mg, 0.02 mmol, 0.1 equiv) and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (11 mg, 0.02 mmol, 0.1 equiv) were successively added and the mixture was heated at 75 °C for 15 hours. After cooling to room temperature, solvents were removed under reduced pressure and the resulting green solid was purified by flash chromatography on silica gel eluting with CH_2Cl_2/MeOH/H_2O (50:40:8 to 50:40:10) to provide the title compound as a white solid (88 mg, 58 %).

Rf: 0.50 (CH_2Cl_2/MeOH/H_2O 50:40:10)

^{1}H NMR (300 MHz, DMSO-*d6*) δ (ppm): 1.16-1.26 (m, 16H, CH_2), 1.26-1.41 (m, 4H, CH_2), 1.88 (s, 6H, CH_3 thymine), 2.07-2.30 (m, 4H, H-2'), 2.89-3.00 (m, 4H, C**H**$_2$NHC=O), 3.31-3.66 (m, 20H, H-3, H-4, H-5, H-6a, H-2", H-3", H-4", H-5", H-6"), 3.71-3.90 (m, 4H, H-2, H-6b), 4.04-4.13 (m, 2H, H-4'), 4.16-4.31 (m, 8H, H-3', H-1", NH_{urea}C**H**$_2$ triazole), 4.26-4.33 (m, 2H, H-3'), 4.44-4.49 (m, 4H, OCH_2 triazole), 4.54-4.77 (m, 10H, H-5', OH), 4.82-4.91 (m, 4H, OH), 4.98-5.11 (m, 4H, NCH_2 triazole), 5.14 (d, *J*= 4.4 Hz, 2H, OH), 5.50-5.63 (m, 6H, H-1, OH), 5.98 (apparent t, *J*= 5.5, 5.8 Hz, 2H, NH), 6.22 (apparent t, *J*= 6.6, 7.0 Hz, 2H, H-1'), 6.29 (t, *J*= 5.6 Hz, 2H, NH), 7.50 (s, 2H, H-6 thymine), 7.89 (s, 2H, CH triazole), 8.13 (s, 2H, CH triazole).

^{13}C NMR (125 MHz, DMSO-*d6*) δ (ppm): 12.7 (CH_3 thymine), 26.5, 28.9, 29.1, 30.0 (CH_2), 35.0 ($NH_{urea}CH_2$ triazole), 36.1 (NCH_2 triazole), 38.1 (C-2'), 51.1 (C-5'), 60.0, 60.4 (C-6, C-6"), 68.1, 70.6, 70.7, 73.3, 75.2, 75.6, 77.8, 79.7 (C-3', C-3, C-4, C-5, C-2", C-3", C-4", C-5"), 71.6 (C-2), 84.3 (C-4'), 85.2 (C-1'), 86.9 (C-1), 103.8 (C-1"), 109.1 (C-5 thymine), 122.5, 123.2 (CH triazole), 135.1 (C-6 thymine), 142.7, 146.2 (C-4 triazole), 150.3, 157.9 (C=O thymine), 162.3 (C=O urea).

HRMS (ESI): (M+H) Calcd. 1707.7462, Found 1707.7485.

NMR spectra of 5-Lac and 6-Lac

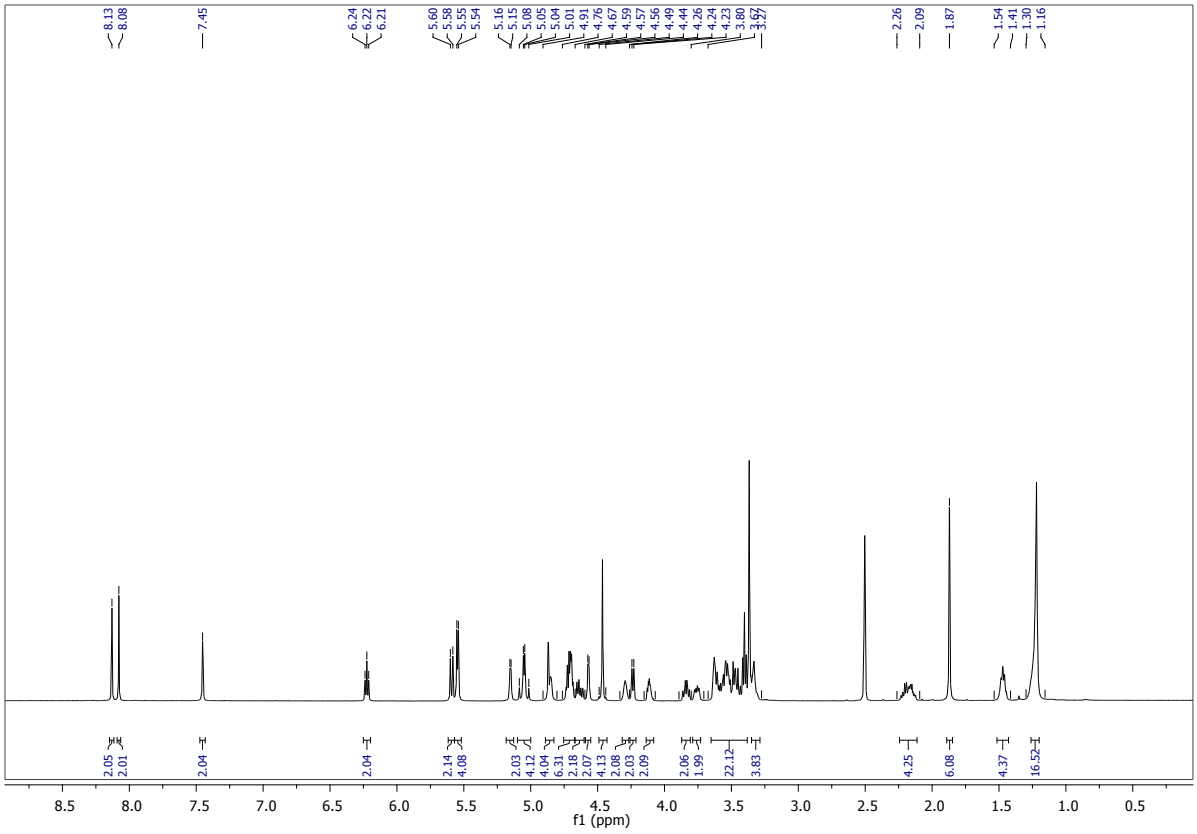


Figure SI2: ^{1}H NMR spectrum of bolaamphiphile **5-Lac** (DMSO-*d6*, 500 MHz).

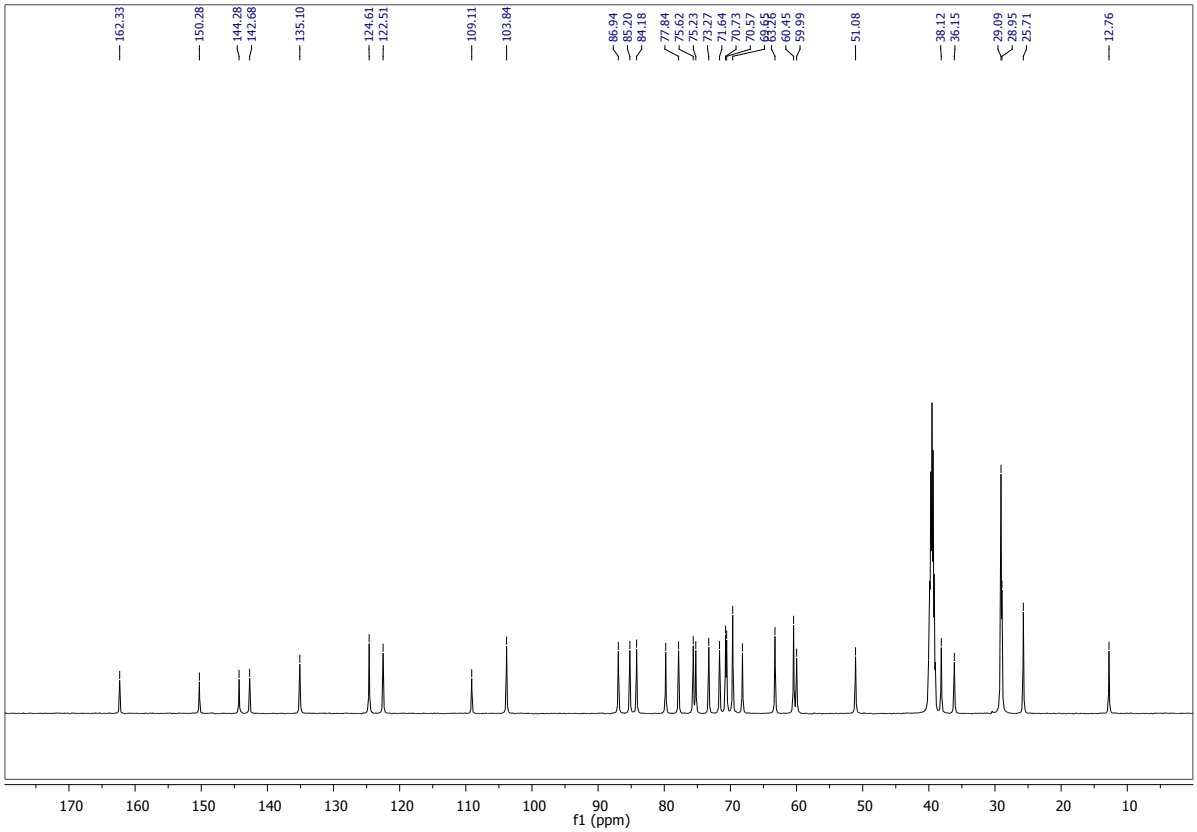


Figure SI3: ^{13}C NMR spectrum of bolaamphiphile **5-Lac** (DMSO-*d6*, 500 MHz).

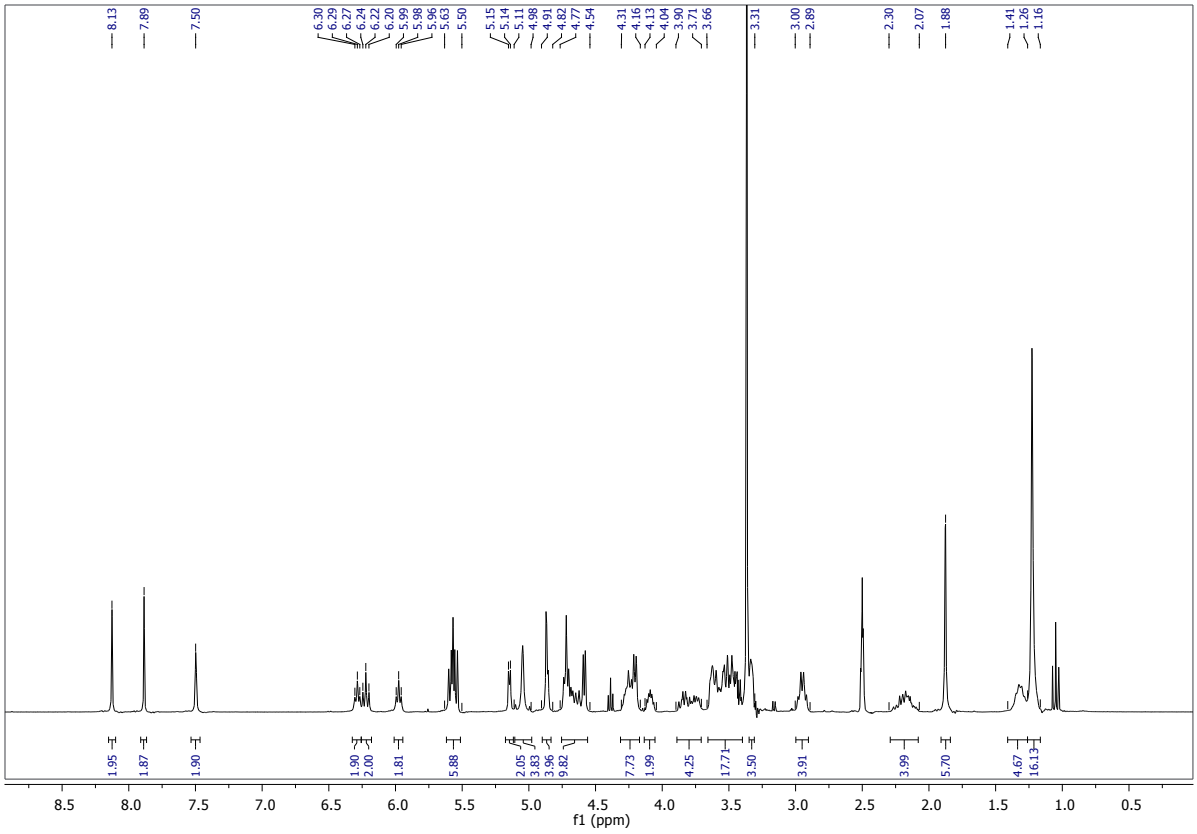


Figure SI4: ^{1}H NMR spectrum of bolaamphiphile **6-Lac** (DMSO-*d6*, 300 MHz).

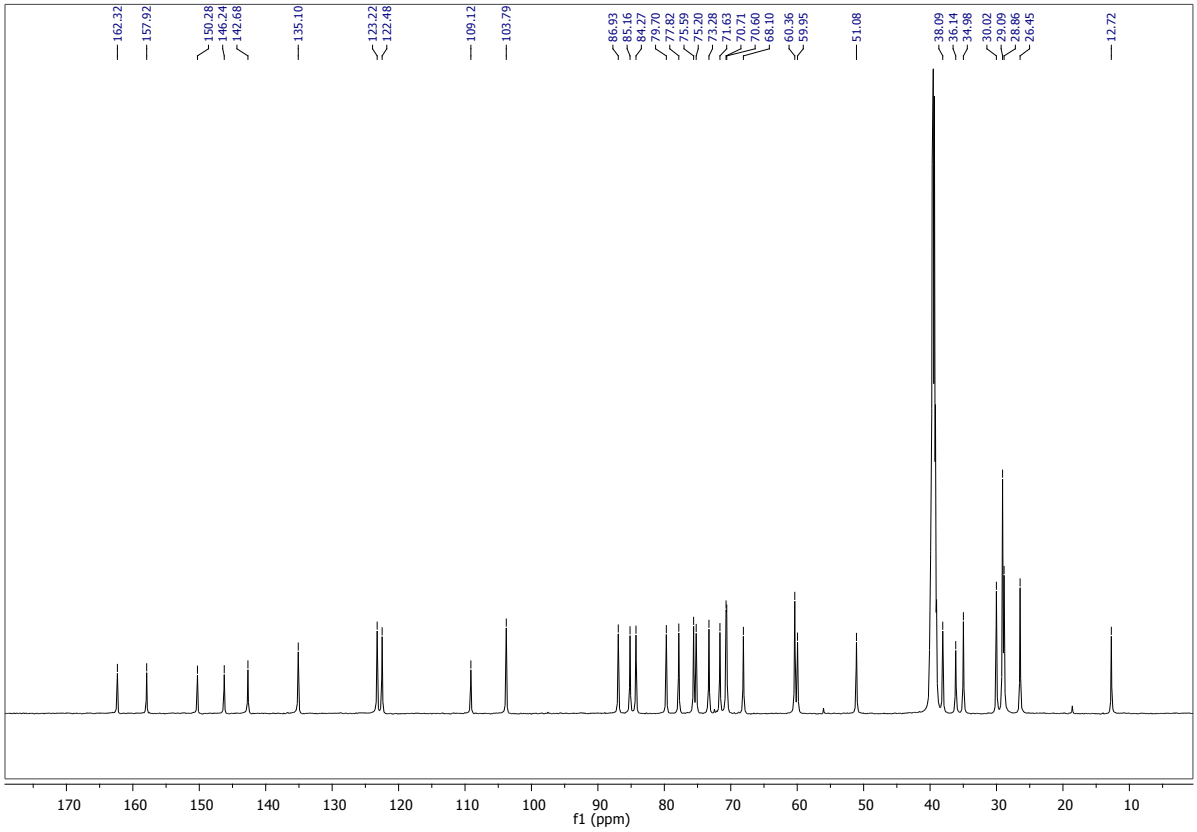


Figure SI5: ^{13}C NMR spectrum of bolaamphiphile **6-Lac** (DMSO-*d6*, 500 MHz).

Physico-chemical studies

Incubation assays

Lactose based bolaamphiphiles **5-Lac** and **6-Lac** at 4 % (w/v) and 1 % (w/v) respectively were incubated in plastic vials with solutions containing the adequate quantity of ß-galactosidase from *Aspergillus Oryzae* (12.1 units.mg^{-1}) in PBS 1X (Sigma-Aldrich, France). Samples were then acidified with an hydrochloric acid solution (20 µL, 0.005 M in MilliQ water) to reach pH 4.60 and stirred at 50 °C, 800 rpm for 15 hours using a Thermomixer compact (Eppendorf, Hauppauge, NY, USA). Optimal conditions of pH and temperature were determined from Park et al. [4].

Table SI6: Physico-chemical properties of **5-Glc** and **6-Glc** based hydrogels[3] (11.55 mM).

	G' (kPa)	**Gelation kinetic**	**CGC (% (w/v))**
5-Glc	30	Few hours	0.5
6-Glc	12	5 minutes	0.1

^{1}H Nuclear magnetic resonance experiments

Following the incubation step, samples were lyophilized for 5 hours and dissolved in DMSO-*d6* (Eurisotop, Saarbrücken, Germany). The amount of cleavage was assessed by the difference of H triazole peaks integration. Signals at 8.105 ppm and 8.128 ppm can be attributed to 5-H triazole linked to glucose (**5-Glc**, **6-Glc**) and lactose (**5-Lac, 6-Lac**) respectively. Experiments were repeated at least three times for each sample. Standard deviations were calculated from at least three samples and used to determine the estimated error.

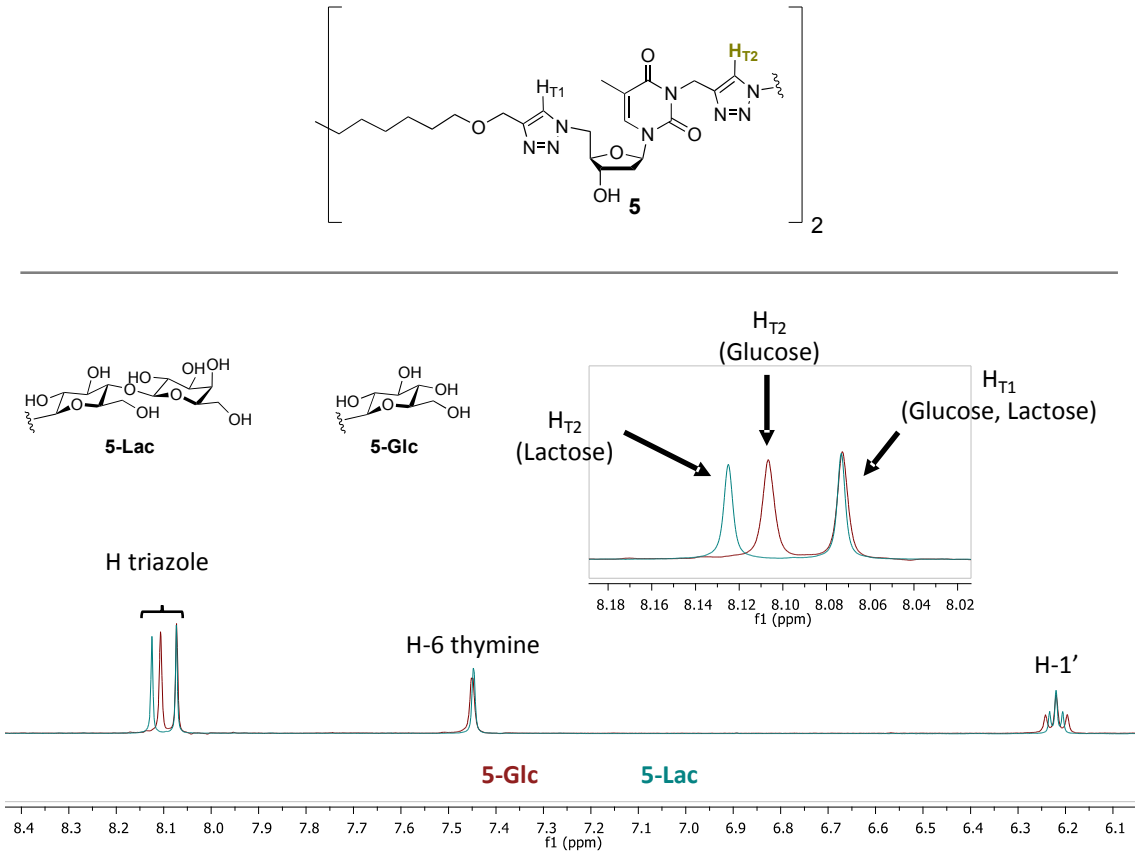


Figure SI7: ^{1}H NMR spectra of ether lactose **5-Lac** (green) and glucose **5-Glc** (red) based bolaamphiphiles.

Gelation abilities

Ether based bolaamphiphiles **5-Lac** and **5-Glc**

Following the incubation step, a solution of **5-Lac** (4 % (w/v)) containing 3.1 U or 2.5 U of ß-galactosidase was heated for 15 minutes at 65 °C and stirred at 800 rpm using a Thermomixer compact (Eppendorf, Hauppauge, NY, USA). The sample was then cooled down to room temperature. Formation of a heterogeneous hydrogel was observed after 7 days with 2.5 U of enzyme. Two heating cycles (65 °C, 800 rpm, 15 minutes) and sonication (room temperature, 10 minutes) using an ultrasound bath FB 11205 (37 kHz, Fischer Scientific, Strasbourg, France) were necessary to give an homogeneous hydrogel.

Bolaamphiphile **5-Glc** (3.2 % (w/v)) was diluted with the required amount of PBS 1X to obtain the same molar concentration than **5-Lac** based hydrogel after total cleavage. The hydrogel was formed as previously described (heating at 65 °C, 15 minutes, 800 rpm combined with sonication at room temperature, 10 minutes using an ultrasound bath FB 11205).

Urea based bolaamphiphiles **6-Lac** and **6-Glc**

Following the incubation step, a solution of **6-Lac** (1 % (w/v)) containing 6 U of ß-galactosidase was heated for 15 minutes at 85 °C and stirred at 800 rpm using a Thermomixer compact (Eppendorf, Hauppauge, NY, USA). The sample was then cooled down to room temperature to give a homogeneous hydrogel within 5 minutes.

Bolaamphiphile **6-Glc** (0.8 % (w/v)) was diluted with the required amount of PBS 1X to obtain the same molar concentration than **6-Lac** based hydrogel after total cleavage. Hydrogel was formed as previously described (heating at 85 °C, 15 minutes, 800 rpm before cooling down to room temperature).

Gel macroscopic behavior was assessed when no flow could be observed once the test tube was turned upside-down.

Transmission Electron Microscopy (TEM)

TEM images were acquired using a Hitachi H750 coupled to an ORIUS SC1000 11MPX (GATAN). All samples were put on a carbon-coated grid (Delta Microscopies, France) for 3 min then washed with distilled water for 1 min (to remove PBS) before drying at room temperature.

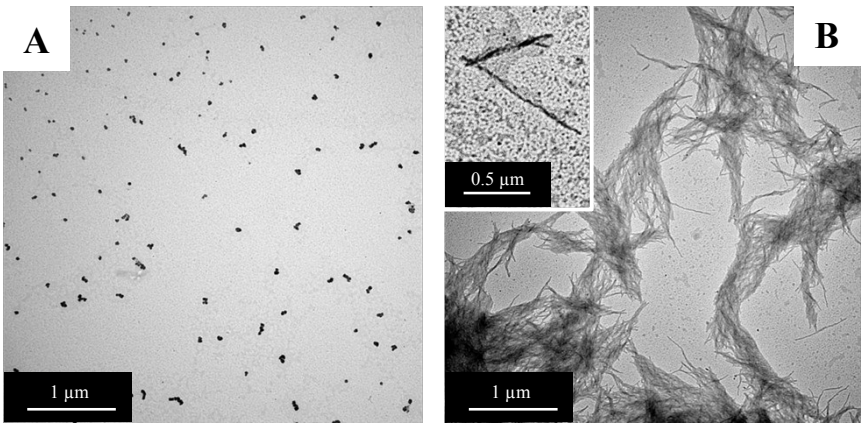


Figure SI8: TEM images of precursors A - **5-Lac** and B - **6-Lac** in solution in PBS (4 % (w/v) and 1 % (w/v) respectively). Inset shows a zoom of helicoidal nanofibers. Scale bars: 0.5 µm, 1 µm.

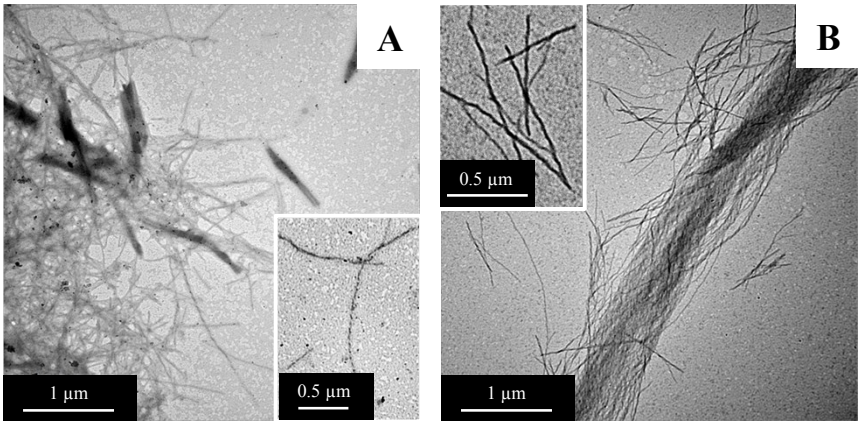


Figure SI9: TEM images of A - **5-Lac** and B - **6-Lac** solutions after enzyme catalysis (4 % (w/v) and 1 % (w/v) respectively). Insets show a zoom of helicoidal nanofibers. Scale bars: 0.5 µm, 1 µm.

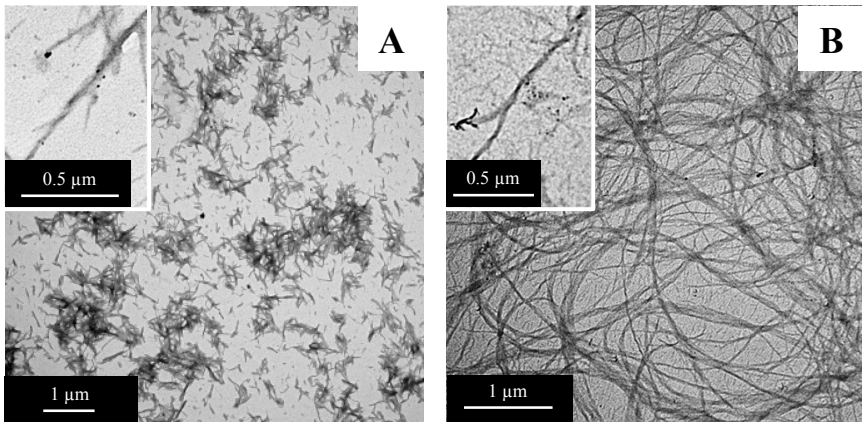


Figure SI10: TEM images of A - **5-Lac** and B - **6-Lac** hydrogels from enzyme catalysis after the heating step (4 % (w/v) and 1 % (w/v) respectively). Insets show a zoom of helicoidal nanofibers. Scale bars: 0.5 µm, 1 µm.

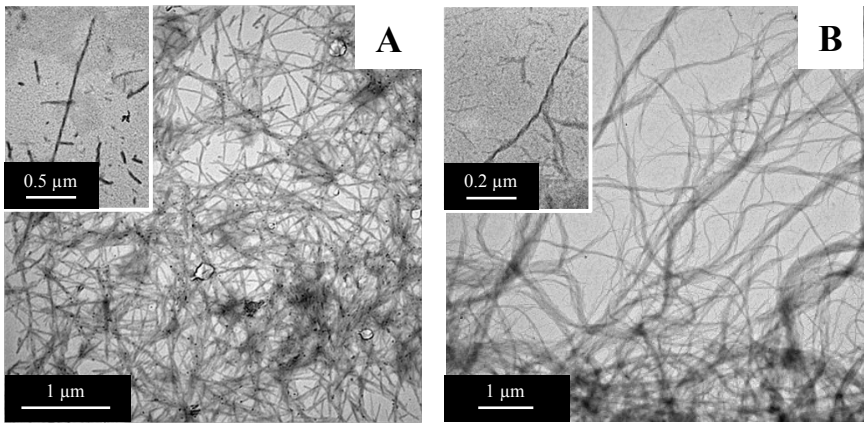


Figure SI11: TEM images of A - **5-Glc** and B - **6-Glc** hydrogels (3.2 % (w/v) and 0.8 % (w/v) respectively). Insets show a zoom of helicoidal nanofibers. Scale bars: 0.2 µm, 0.5 µm, 1 µm.

Table SI12: Diameter and pitch of helicoidal nanofibers from **5-Lac**, **5-Glu**, **6-Lac**, and **6-Glu** hydrogels.

	5-Lac	**5-Glu**	**6-Lac**	**6-Glu**
Diameter (nm)	33.7 ± 13.6	21.6 ± 3.7	14.6 ± 2.7	18.9 ± 3.2
Pitch (nm)	219.0 ± 43.1	157.8 ± 33.9	66.0 ± 14.4	99.8 ± 23.9

Student test

5-Lac/**5-Glu**: $p < 0.001$ (diameter), $p = 0.03$ (pitch)

6-Lac/**6-Glu**: $p < 0.001$ (diameter), $p = 0.03$ (pitch)

Rheology

Rheological experiments were conducted on a Malvern Kinexus® Pro+ rheometer (Malvern Instruments Ltd., Orsay, France) equipped with a Peltier temperature control system on the lower plate. Experiments were performed at 25 ± 0.01 °C with an upper steel cone geometry (diameter: 20 mm, angle: 2°, gap: 0.029 mm). A solvent trap was added to prevent solvent evaporation and to control temperature. Gel samples were placed under gel state with a spatula on the lower geometry and submitted to sinusoidal oscillations after a 45 minutes rest. Linear viscoelastic region (LVR), in which G' and G" displayed no dependence towards the applied strain, was measured by an amplitude strain sweep experiment (strain: 0.1 to 100 %, constant frequency: 1 Hz). Further experiments were conducted within the LVR as frequency sweep (frequency: 0.10 to 10 Hz, constant strain: 0.05 % for **5-Lac**/**5-Glc**, 0.1 % for **6-Lac**, 0.5 % for **6-Glc**) and gel-sol transition temperature assays (temperature: 25 to 90 °C, ramp: 2 °C/min, constant frequency: 1 Hz, constant strain: 0.05 % for **5-Lac**/**5-Glc**, constant stress: 1 Pa for **6-Lac**/**6-Glc**). Transition temperatures were recorded when G' became inferior to G". Thixotropic experiments were performed at a fixed frequency of 1 Hz and 3 steps: 1) low strain (0.05 % for **5-Lac**/**5-Glc**, 0.1 % for **6-Lac**, 0.5 % for **6-Glc**, within LVR) for 5 min; 2) high strain (50 % for **5-Lac**/**5-Glc**, 100 % for **6-Lac**/**6-Glc**, outside LVR) for 2 min; 3) low strain (identical to 1), within LVR) for 60 min. All experiments were repeated three times or more for each sample. Standard deviations were calculated from three samples or more and used to determine the estimated error.

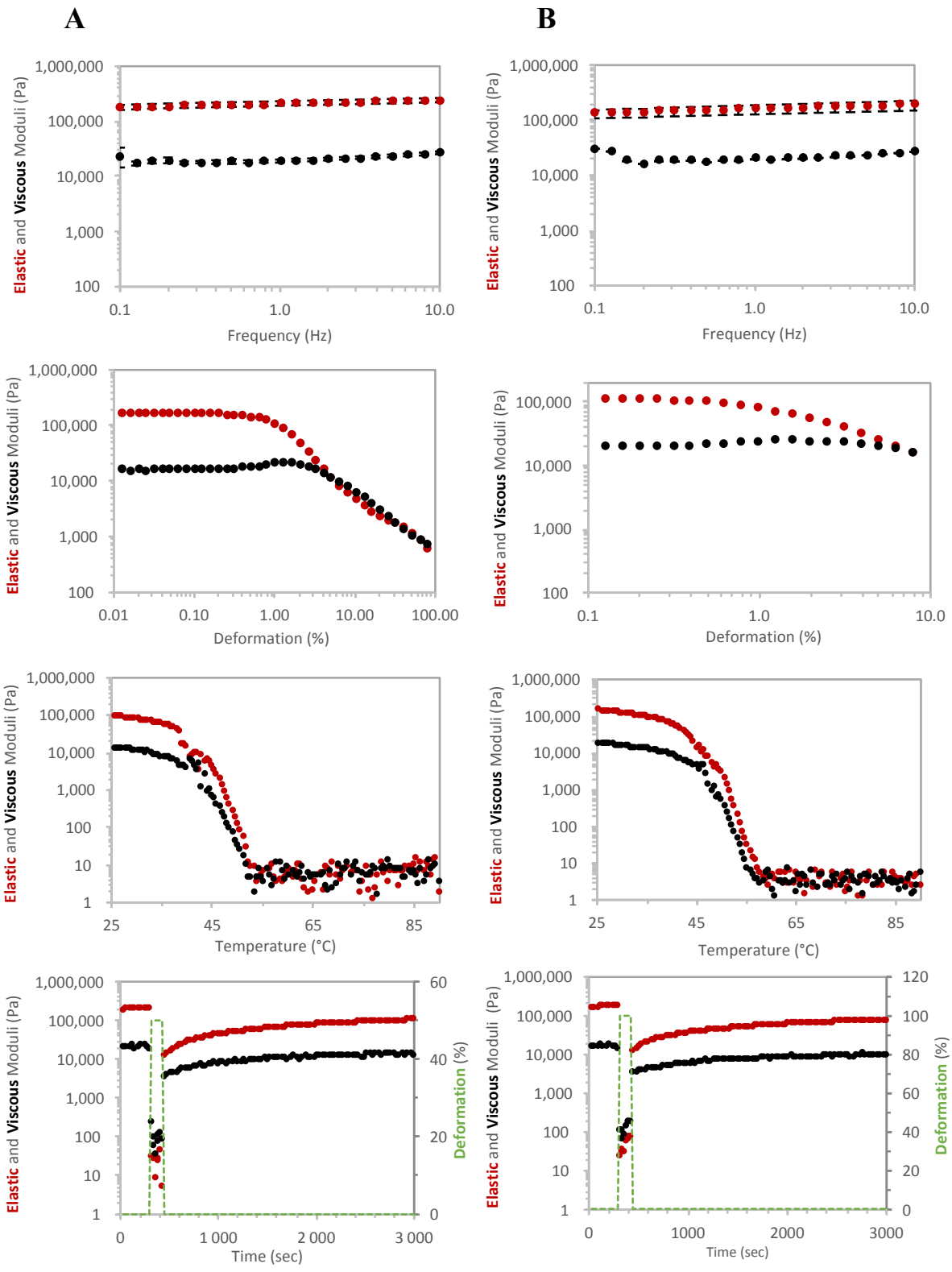


Figure SI13: Frequency sweep, amplitude strain sweep, gel-sol transition and thixotropic experiments of A - **5-Glc** hydrogel (3.2 % (w/v)) and B - **5-Lac** hydrogel (4 % (w/v)).

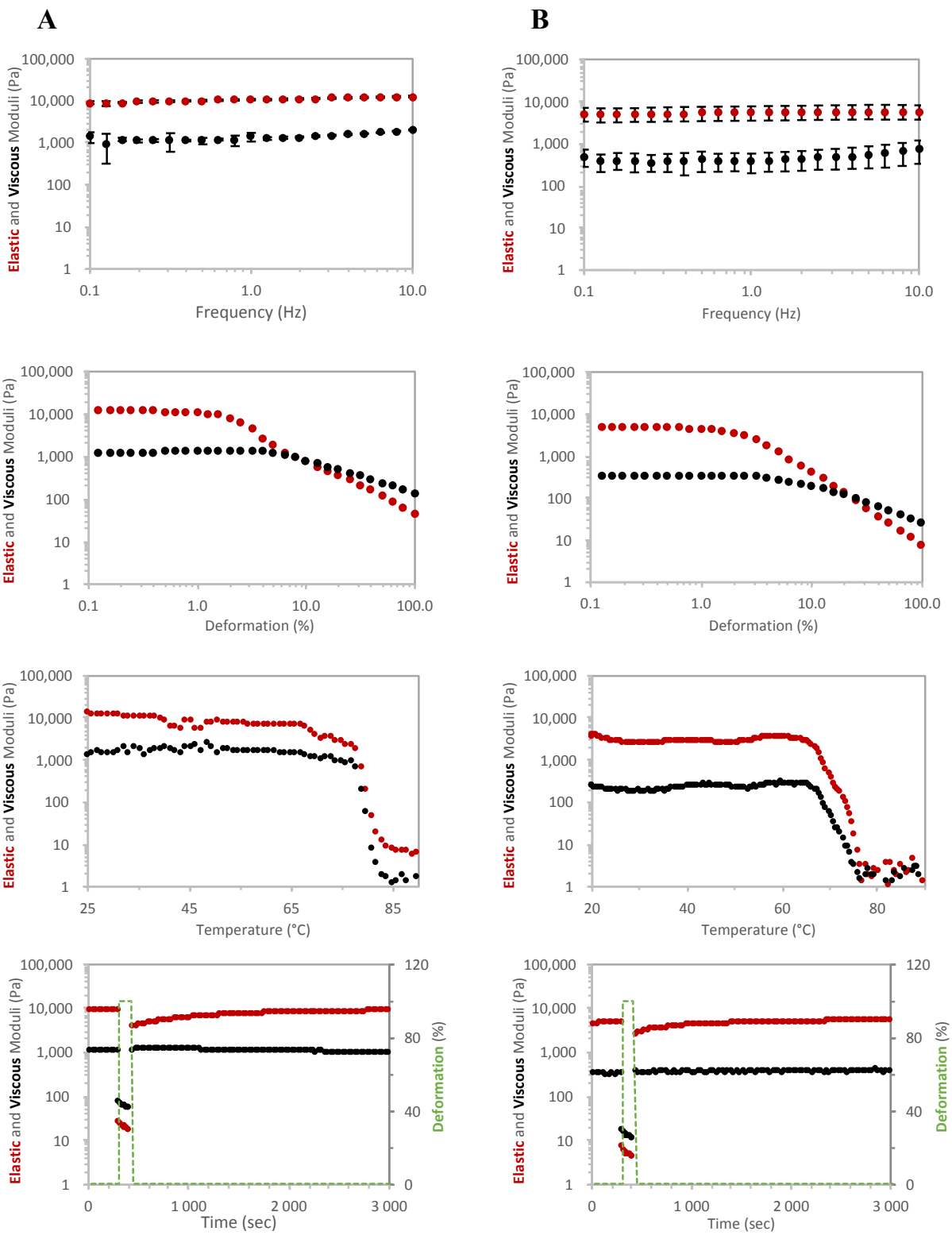


Figure SI14: Frequency sweep, amplitude strain sweep, gel-sol transition and thixotropic experiments of A - **6-Glc** hydrogel (0.8 % (w/v)) and B - **6-Lac** hydrogel (1 % (w/v)).

Table SI15: Rheological properties of **5-Lac**, **5-Glc**, **6-Lac** and **6-Glc** based hydrogels

	LVR (%)	**G' (kPa)**	**G'' (kPa)**	**T_{GelSol} (°C)**
		Ether based hydrogels		
5-Lac	0.14 ± 0.03	156.9 ± 29.6	19.4 ± 5.9	58.8
5-Glc	0.29 ± 0.03	212.2 ± 20.5	19.0 ± 1.2	54.0
		Urea based hydrogels		
6-Lac	0.71 ± 0.08	5.6 ± 2.1	0.4 ± 0.2	78.8
6-Glc	1.29 ± 0.29	10.2 ± 1.2	1.1 ± 0.2	81.7

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