Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting Information

Gelation properties of self-assembling *N*-acyl modified cytidine derivatives

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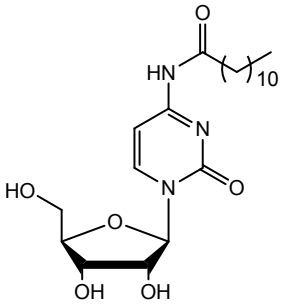
S1: Methods and Analysis for compounds 2-5



N-lauroyl cytidine, 2

To a solution of 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT, 20 mmol, 3.50 g) in anhydrous CH_2Cl_2 (60 mL) at 0 °C, *N*-methylmorpholine (NMM, 27.2 mmol, 2.75 g) was added with continuous stirring until a white suspension had formed. The mixture was then left to stir for 1 h. Lauric acid (20 mmol) was added directly into the mixture as a solution in anhydrous DMF (20 mL) and stirred for a further hour. A solution of cytidine (20 mmol, 4.86 g) in anhydrous DMF (20 mL) was made up at 0 °C. The cold triazine solution was added drop wise to the cooled cytidine solution over 30 mins, before heating to 50 °C and stirring for 14 - 24 h. The cooled solution was filtered *in vacuo* before adding water and triturating to remove excess CDMT, NMM and cytidine. This was followed by trituration with CH_2Cl_2 to remove any excess fatty acid. The products were purified using flash silica column chromatography, eluting at 5 - 7 % methanol in CH_2Cl_2.

2 ^{1}H NMR (DMSO-d_6, 400 MHz) δ 0.85 (t, J = 6.7 Hz, 3H, C$\underline{H}_3$), 1.24 (s, 18H, CH_2-($\underline{CH}_2)_{\underline{10}}$-$CH_3$), 1.53 (m. 2H, C=O-$CH_2$- C$\underline{H}_2$), 2.38 (t, J = 7.5 Hz, 2H, C= -CH_2), 3.56 - 3.61 (m, 1H, C$\underline{H}_2$-OH), 3.71 – 3.76 (m, 1H, C$\underline{H}_2$-OH), 3.89 – 3.90 (m, 1H, C$\underline{H}$-CH_2-OH), 3.93 – 3.98 (m, 2H, 2(C$\underline{H}$-OH)), 5.03 (d, J = 5.6 Hz, 1H, N-CH--CH-CH-O$\underline{H}$), 5.15 (t, J = 4.9 Hz, 1H, CH_2-O$\underline{H}$), 5.46 (d, J = 4.8 Hz, 1H, N-CH-CH-O$\underline{H}$), 7.20 (d, J = 7.5 Hz, 1H, N-C$\underline{H}$-CH-C), 8.41 (d, J = 7.7 Hz, 1H, N-CH-C$\underline{H}$-C), 10.82 (s, 1H, NH).^{13}C NMR (DMSO-d_6, 100 MHz) δ 13.93, 22.09, 24.42, 28.42, 28.68, 28.84, 28.95, 29.00, 31.27, 36.33, 59.91, 68.65, 74.51, 84.19, 90.14, 95.21, 145.32, 154.67, 162.31, 173.93. HRMS calculated for $C_{23}H_{40}N_3O_6^+$ 426.2599 $(M+H)^+$; found 426.1556. Analytical RP-HPLC t_R = 18.5 min, Yield: 46.0 %, 99.4 % purity.

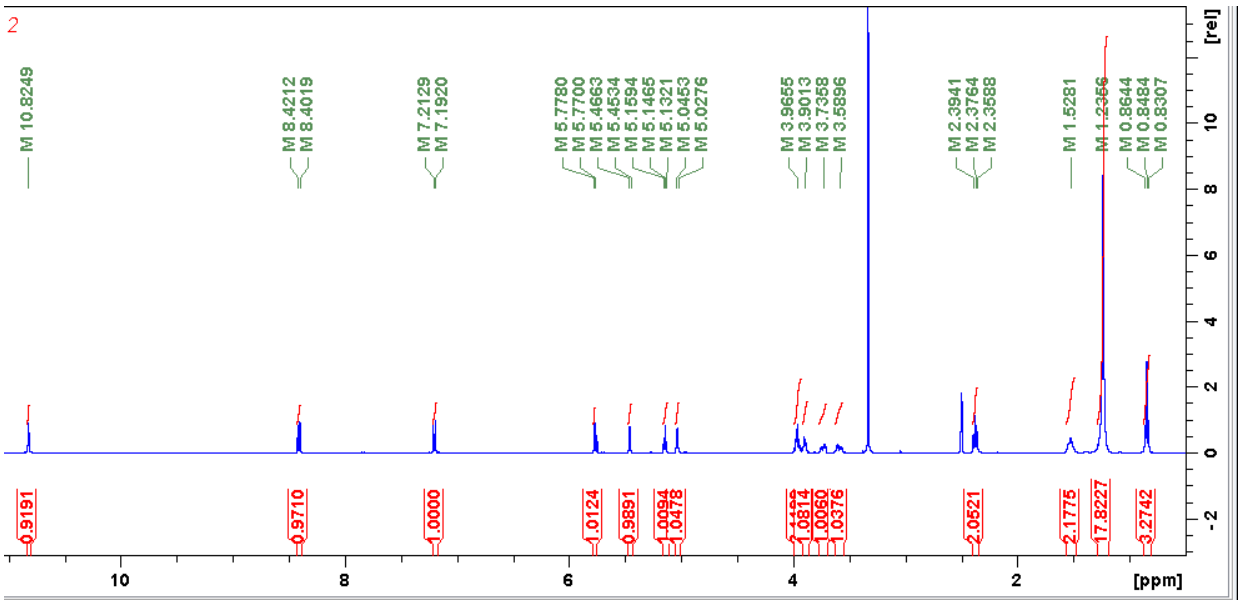


Figure S1.1: ^{1}H NMR Spectrum of 2

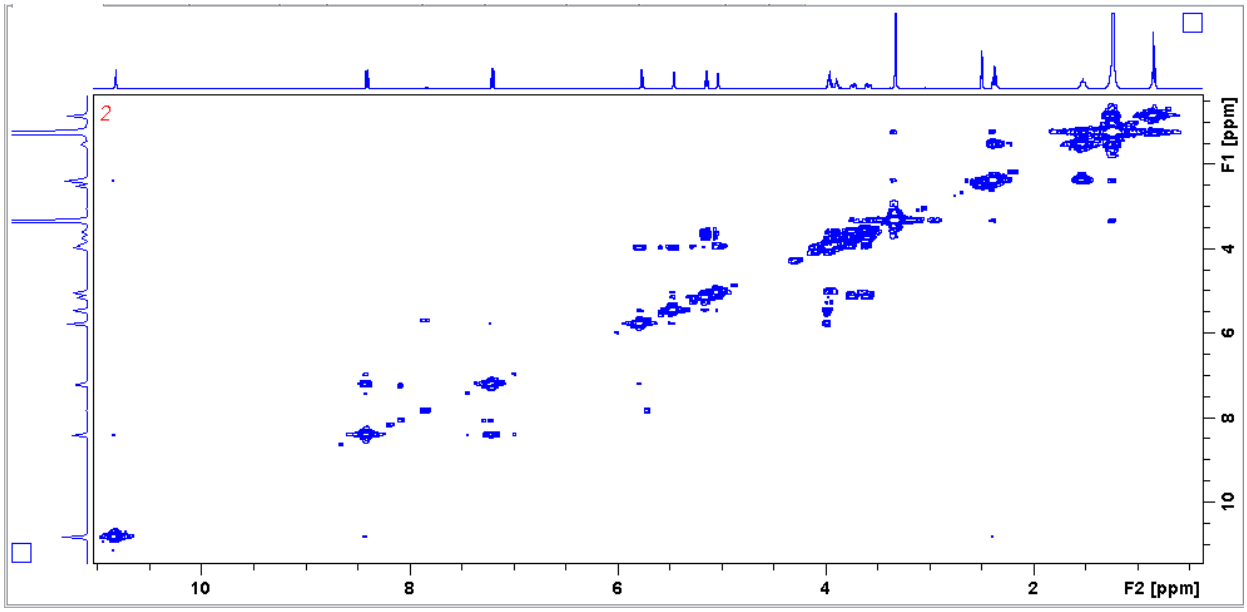


Figure S1.2: 2D COSY Spectrum of compound 2

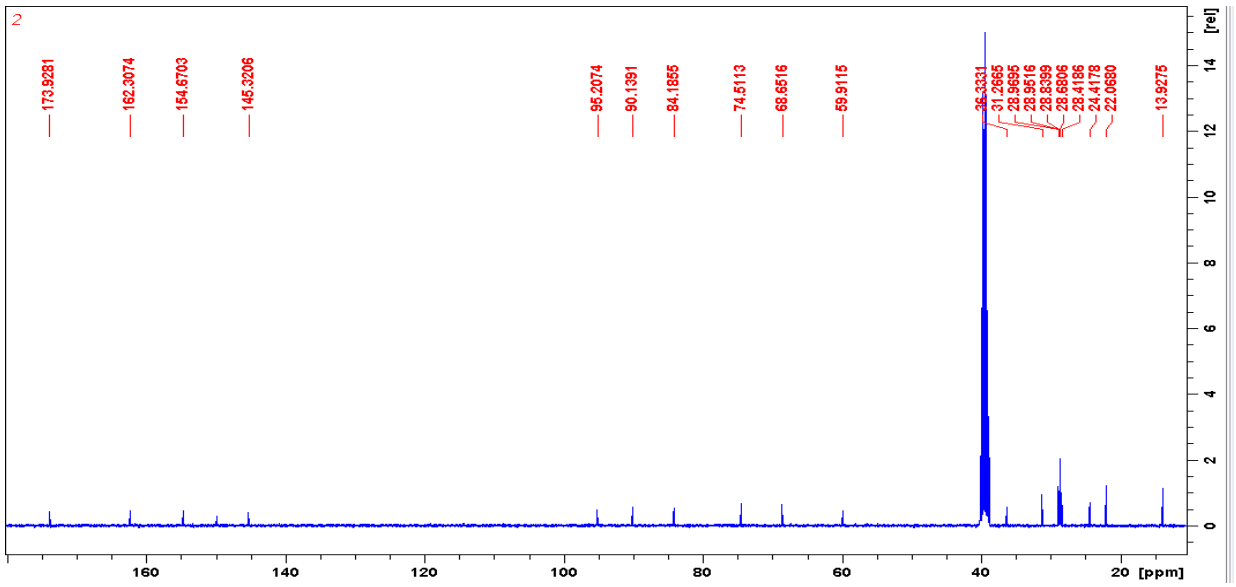


Figure S1.3: ^{13}C NMR spectrum of 2

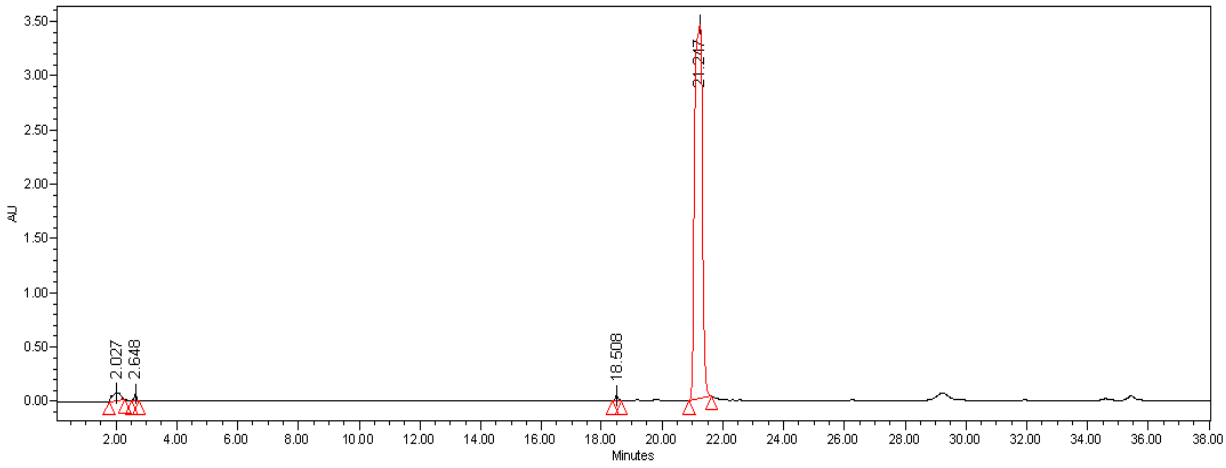
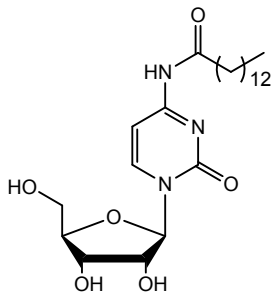


Figure S1.4: RP-HPLC of 2



N-myrostoyl cytidine, 3

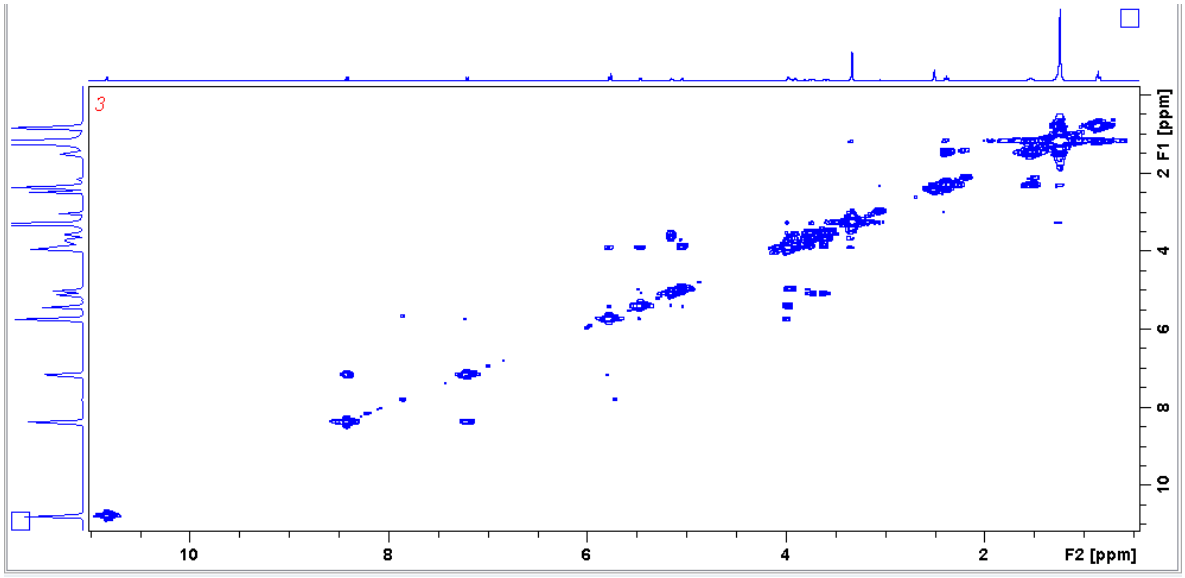


Figure S1.5: ^{1}H NMR Spectrum of 3

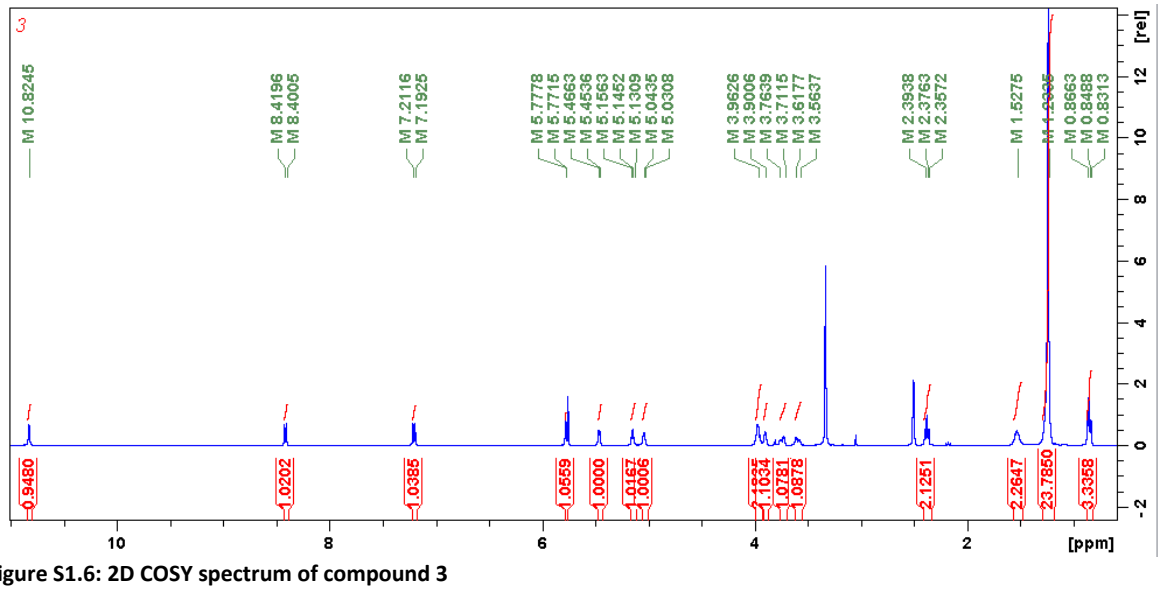


Figure S1.6: 2D COSY spectrum of compound 3

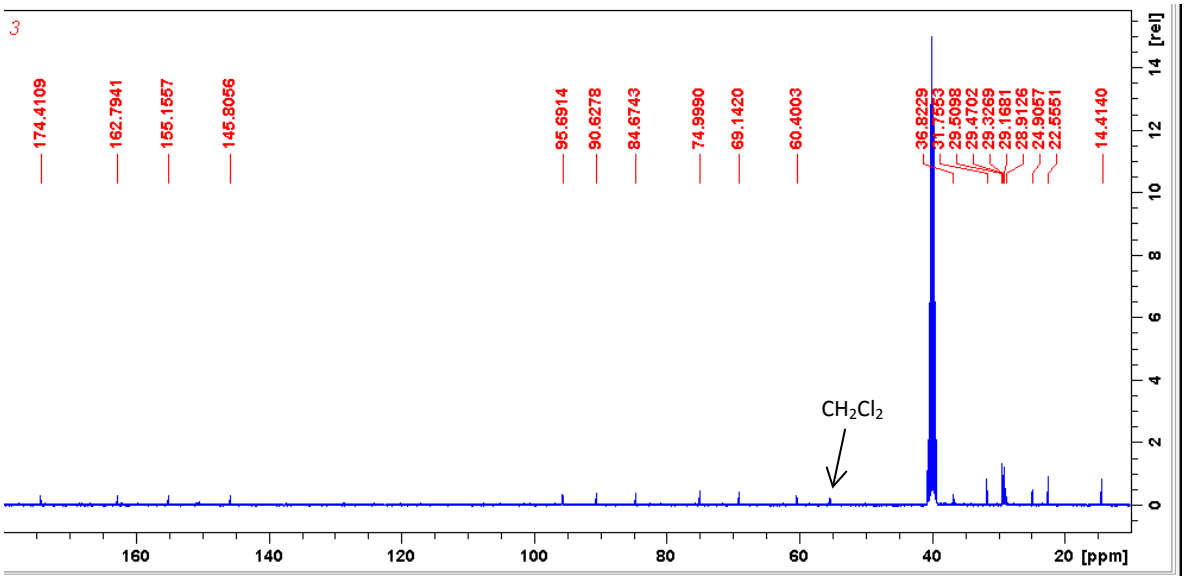


Figure S1.7: ^{13}C NMR spectrum of compound 3

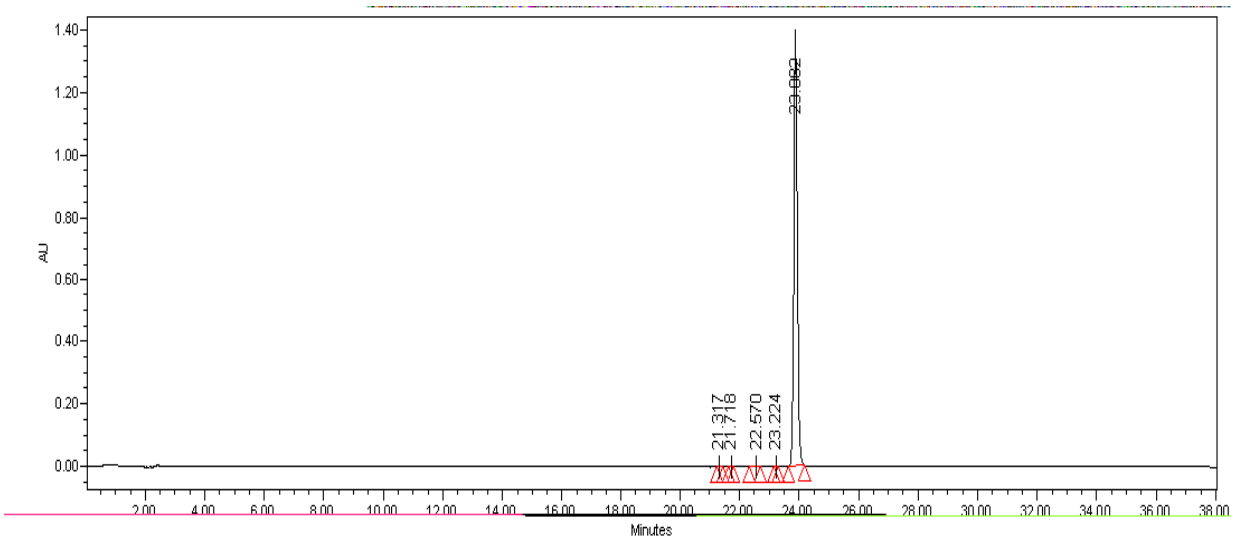
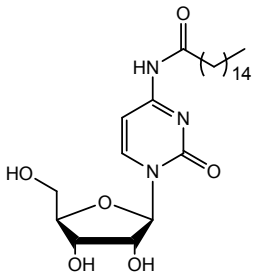


Figure S1.8: RP-HPLC of 3.



N-palmitoyl cytidine, 4

To a solution of 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT, 20 mmol, 3.50 g) in anhydrous CH_2Cl_2 (60 mL) at 0 °C, *N*-methylmorpholine (NMM, 27.2 mmol, 2.75 g) was added with continuous stirring until a white suspension had formed. The mixture was then left to stir for 1 h. Palmitic acid (20 mmol) was added directly into the mixture as a solution in anhydrous DMF (20 mL) and stirred for a further hour. A solution of cytidine (20 mmol, 4.86 g) in anhydrous DMF (20 mL) was made up at 0 °C. The cold triazine solution was added drop wise to the cooled cytidine solution over 30 mins, before heating to 50 °C and stirring for 14 - 24 h. The cooled solution was filtered *in vacuo* before adding water and triturating to remove excess CDMT, NMM and cytidine. This was followed by trituration with CH_2Cl_2 to remove any excess fatty acid. The products were purified using flash silica column chromatography, eluting at 5 - 7 % methanol in CH_2Cl_2.

4 ^{1}H NMR (DMSO-d_6, 400 MHz) δ 0.85 (t, J = 7.03 Hz, 3H, C$\underline{H}_3$), 1.24 (s, 22H, CH_2-($\underline{CH}_2)_{10}$-CH_3), 1.53 (m. 2H, C=O-CH_2- C$\underline{H}_2$), 2.37 (t, J = 8.04 Hz, 2H, C=O-C$\underline{H}_2$), 3.56 - 3.61 (m, 1H, C$\underline{H}_2$-OH), 3.71 – 3.76 (m, 1H, C$\underline{H}_2$-OH), 3.88 – 3.91 (m, 1H, C$\underline{H}$-CH_2-OH), 3.93 – 3.99 (m, 2H, 2(C$\underline{H}$-OH)), 5.04 (d, J = 5.53 Hz, 1H, N-CH--CH-CH-O$\underline{H}$), 5.15 (t, J = 4.52 Hz, 1H, CH_2-O$\underline{H}$), 5.46 (d, J = 4.52 Hz, 1H, N-CH-CH-O$\underline{H}$), 7.20 (d, J = 7.54 Hz, 1H, N-C$\underline{H}$-CH-C), 8.41 (d, J = 7.54 Hz, 1H, N-CH-C$\underline{H}$-C), 10.83 (s, 1H, NH).^{13}C NMR (DMSO-d_6, 100 MHz) δ 13.90, 22.06, 24.40, 28.43, 28.68, 28.86, 29.01, 31.26, 36.32, 59.88, 68.62, 74.51, 84.17, 90.14, 95.18, 145.29, 154.65, 162.29, 173.88 HRMS calculated for $C_{25}H_{44}N_3O_6^+$ 482.3225 $(M+H)^+$; found 482.3046. Analytical RP-HPLC t_R = 26.4 min, Yield: 44.2 % 99.2 % purity.

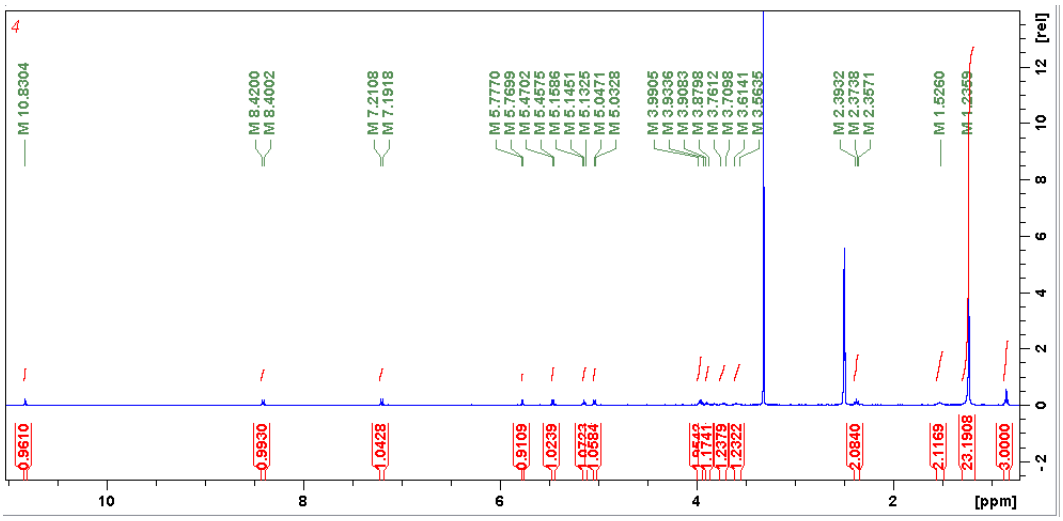


Figure S1.9: ^{1}H NMR Spectrum of 4

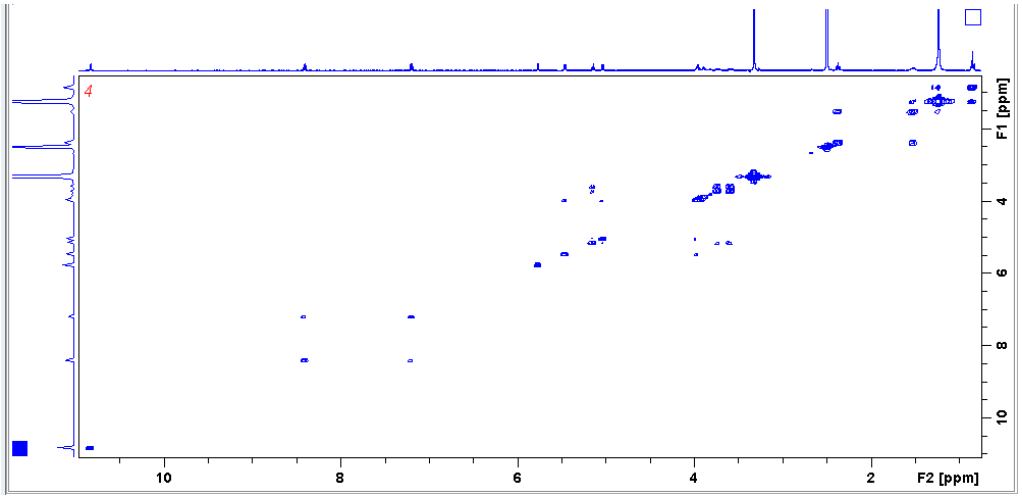


Figure S1.10: 2D COSY Spectrum of 4

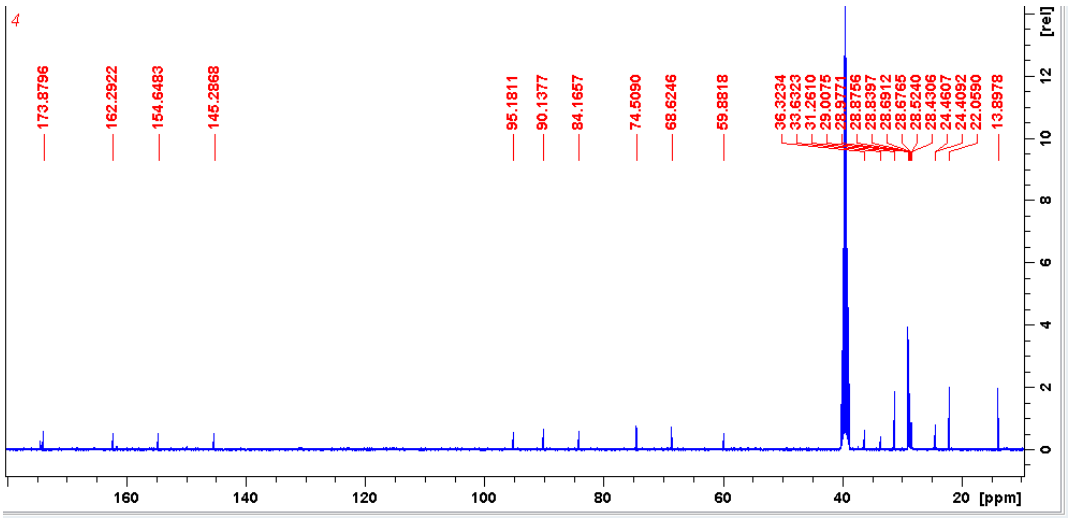


Figure S1.11: ^{13}C NMR spectrum of 4

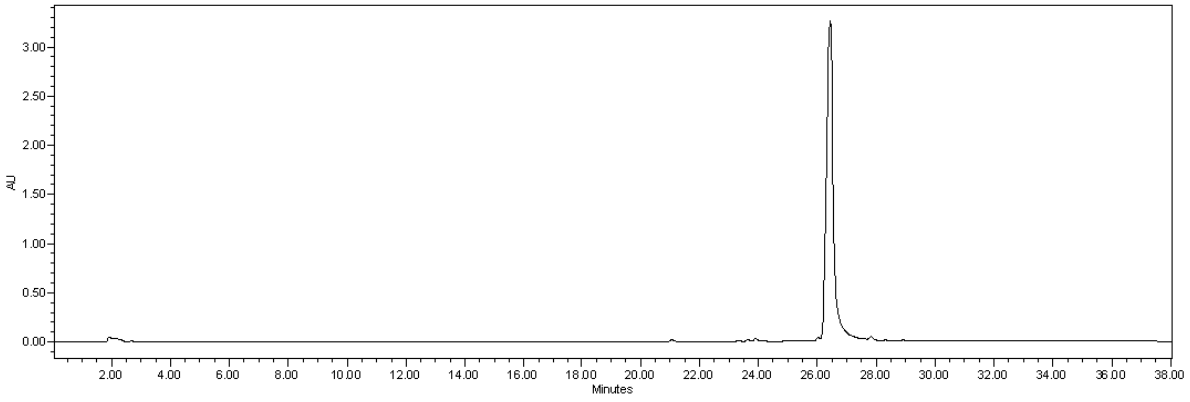
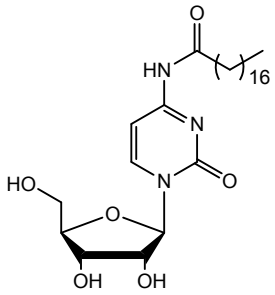


Figure S1.12: RP-HPLC of 4



N-steroyl cytidine, 5

To a solution of 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT, 20 mmol, 3.50 g) in anhydrous CH_2Cl_2 (60 mL) at 0 °C, *N*-methylmorpholine (NMM, 27.2 mmol, 2.75 g) was added with continuous stirring until a white suspension had formed. The mixture was then left to stir for 1 h. Stearic acid (20 mmol) was added directly into the mixture as a solution in anhydrous DMF (20 mL) and stirred for a further hour. A solution of cytidine (20 mmol, 4.86 g) in anhydrous DMF (20 mL) was made up at 0 °C. The cold triazine solution was added drop wise to the cooled cytidine solution over 30 mins, before heating to 50 °C and stirring for 14 - 24 h. The cooled solution was filtered *in vacuo* before adding water and triturating to remove excess CDMT, NMM and cytidine. This was followed by trituration with CH_2Cl_2 to remove any excess fatty acid. The products were purified using flash silica column chromatography, eluting at 5 - 7 % methanol in CH_2Cl_2.

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n.b. purity of cpd **5** determined by NMR.

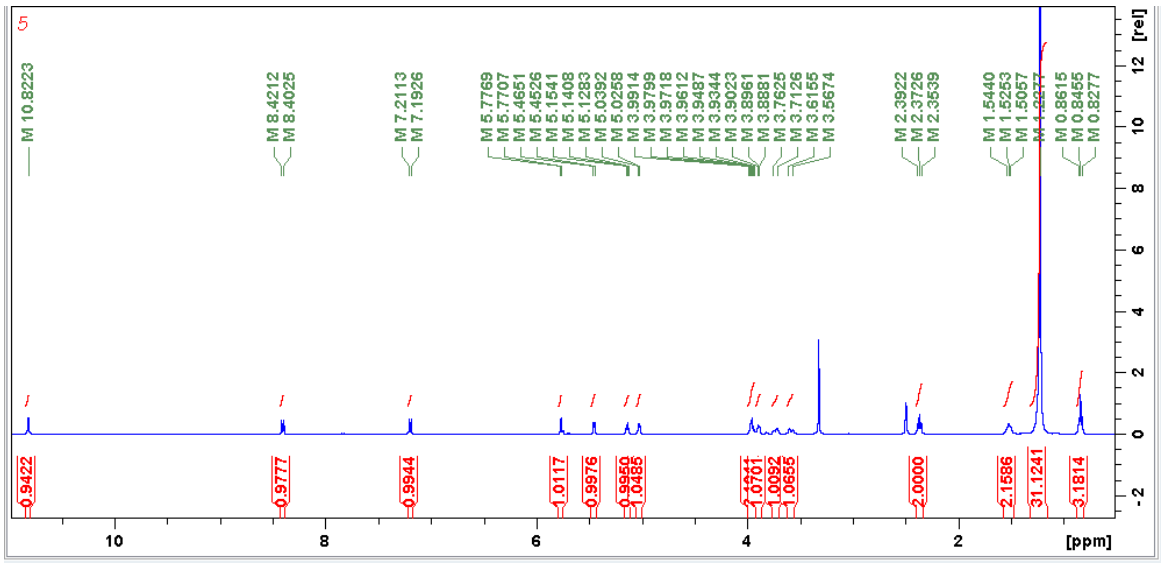


Figure S1.13: ^{1}H NMR Spectrum of 5

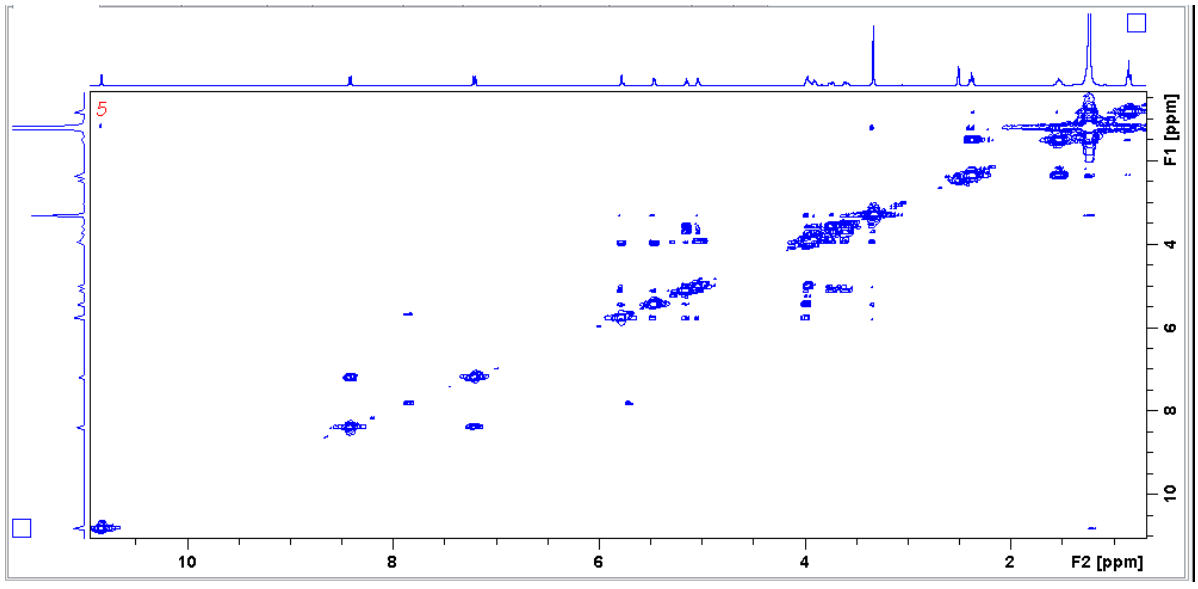


Figure S1.14: 2D COSY Spectrum of 5

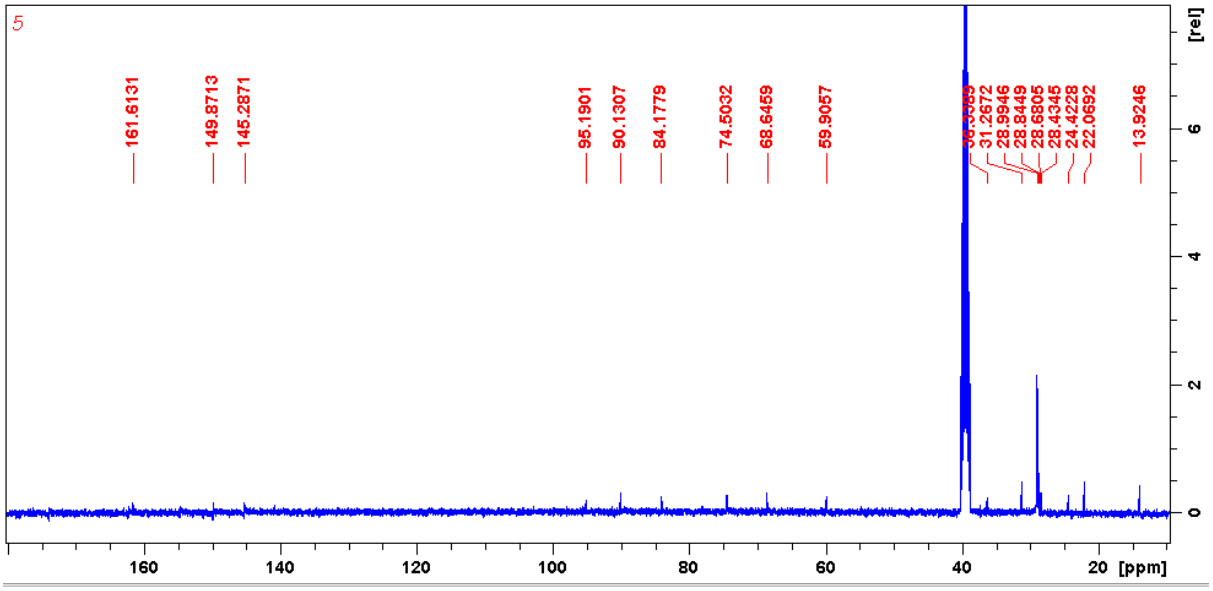


Figure S1.15: ^{13}C NMR spectrum of 5

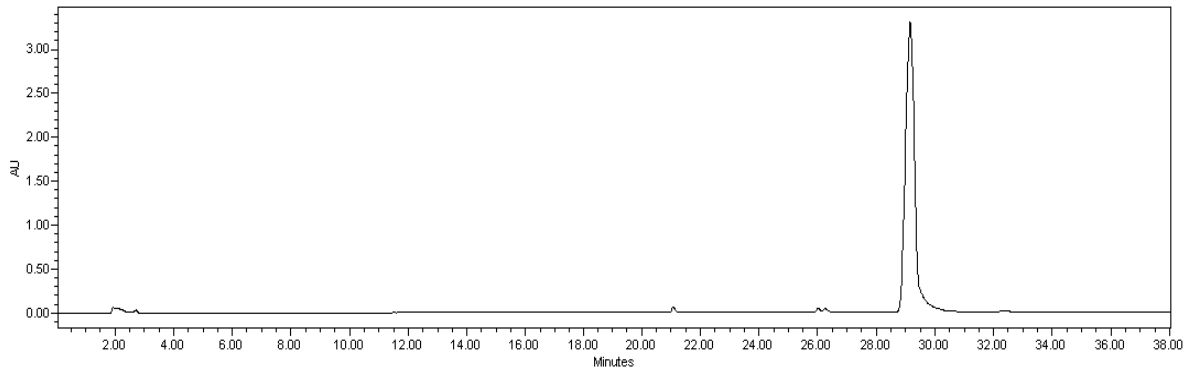
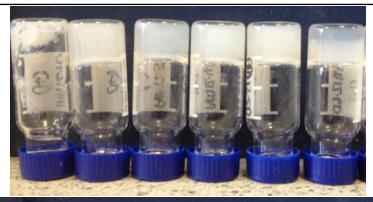


Figure S1.16: RP-HPLC of 5

S2 Vial inversion table of gelators 2-5, when P: Precipitate, WG: Weak Gel, G: Gel, S: Solution.

Conjugate	DMSO	Ethanol
2		
3		
4		
5