Supporting Information

Transferring a concept from medicinal chemistry into soft matter: Replacing an amide with a triazole for modifying gelation properties

Contents List

1. Material characterization

1.1. Compound characterization:

a) Thin layer chromatography (TLC) analyses were performed using fluorescent-indicating plates (aluminum sheets precoated with silica gel 60 F_{254}, thickness 0.2 mm, Merck), and visualization achieved by UV light (λ_{max} = 254 nm) and staining with phosphomolybdic acid and/or iodine.

b) Nuclear magnetic resonance (NMR) spectra were recorded at 25 ºC on Bruker Avance-300 instrument. Chemical shifts are denoted in δ (ppm) relative to residual solvent peaks. Coupling constants, *J*, are given in Hertz. The following standard abbreviations are used for characterization of ^{1}H-NMR signals: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets. Estimated error of reported values: 0.01 ppm (δ, ^{1}H-NMR), 0.1 ppm (δ, ^{13}C-NMR), 0.1 Hz (*J*, coupling constant).

c) Low resolution mass spectroscopy was carried out on a Varian MAT 311A.

d) Elemental analysis was performed on a Heraeus Mikro-Rapid analyzer.

e) UV-vis spectroscopy was performed using a Varian Cary 50 UV spectrophotometer and quartz-glass cuvettes of 0.5 cm thickness.

1.2. Characterization of gel-based materials:

a) Critical gelation concentration (*CGC*) values were estimated by continuously adding aliquots of solvent (0.02-0.1 mL) into vials containing the formamidine compound and performing a typical heating-cooling or ultrasonication enhanced protocol for gel-formation until no gelation was observed. The starting point for *CGC* determinations was 200 mg/mL.

b) Thermal *gel*-to-*sol* transition temperature (T_{gel}) values were determined using a custom made set-up (the sealed vial was placed in a mold of an alumina block which was heated up using an electric heating plate equipped with a temperature control couple at 1 °C/ 5 min, values obtained have been crosschecked with data from literature known compounds). The hereby obtained values have been verified by the inverse flow method[1] (the sealed vial containing the gel-material was hung horizontally into an oil bath, which was heated up at 1 ºC/ 5 min) and DSC measurements. Herein, the temperature at which the gel started to break was defined as T_{gel}. Each measurement was made at least by duplicate and the average value reported. T_{gel} values were found almost unaltered within a difference of 1-2 ºC after several heating-cooling cycles. Also verification on the independence of the position inside the apparatus has been carried out.

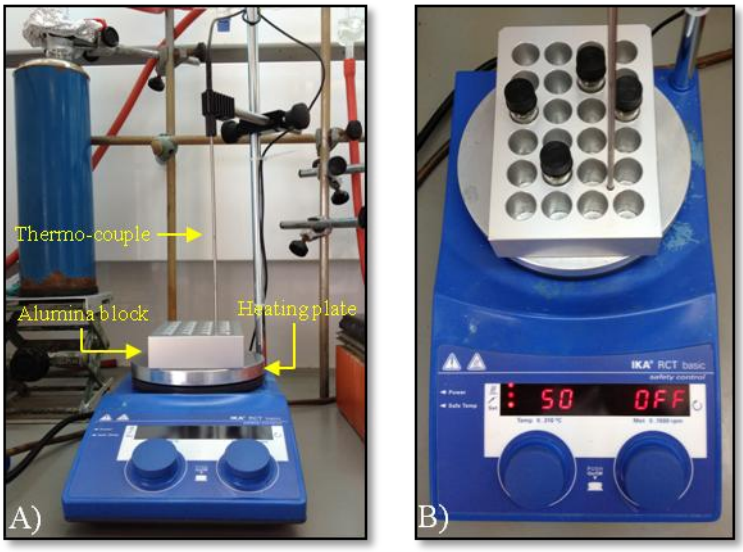


Fig. S1 Custom made set-up for T_{gel}-determinations. A) Front view showing the composition between electric heating plate, alumina block and digital thermo-couple. B) Top view of the set-up during experimentation containing vials (4 cm length x 1 cm diameter) with gel-materials. It is important to mention that the alumina block was constructed especially for one type of vials which fit smoothly inside the molds to ensure a good transmission of the heat-flow.

c) Fourier transform infrared (FT-IR) spectra were recorded at room temperature using an Excalibur FTS 3000 FT-IR spectrometer (Biorad) equipped with a single reflection ATR (attenuated total reflection) accessory (Golden Gate, Diamond).

d) Differential scanning calorimetry (DSC) measurements were performed on a Mettler Toledo Differential Scanning Calorimeter using a DSC 30 measuring cell. The DSC thermograms were obtained under dynamic argon atmosphere (gas flow rate = 25 mL min^{-1}) at a heating rate of 10 ºC min^{-1}. Samples were placed in closed aluminum pans (Mettler Toledo). An empty sample holder was used as reference and the runs were performed by heating the samples from 25 to 90 ºC. The values were reported as the average of two independent measurements.

e) Field Emission Scanning Electron Microscopy (FESEM) images of xerogels were obtained with a Zeiss Merlin, Field Emission Scanning Electron Microscope operated at an accelerating voltage of 10 kV. Scanning Electron Microscope (SEM) was performed using a JEOL JSM 6400 scanning electron microscope equipped with a digital camera and operating at 15 kV. For visualization, samples were prepared by the freeze-drying (FD) method: An Eppendorf tube containing the corresponding gel-material (100–200 µL) was frozen in liquid nitrogen or dry ice/acetone and the solvent immediately evaporated under reduced pressure (0.6 mmHg) for 2 days at RT. A fibrous solid was obtained, which was placed on top of a tin plate and shielded by Pt (40 mA during 30-60 s (film thickness = 5-10 nm).

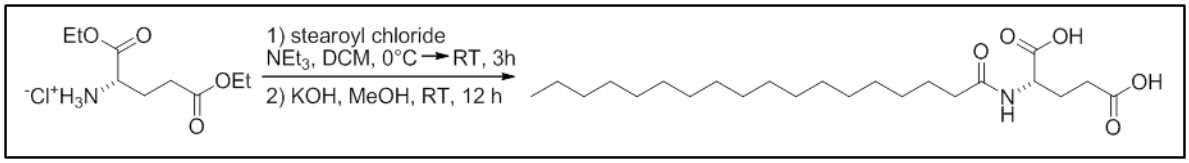
f) Oscillatory rheology was performed with an AR 2000 Advanced rheometer (TA Instruments) equipped with a Julabo C cooling system. A 1000 µm gap setting and a torque setting of 40,000 dynes/cm^2 at 25 ºC were used for the measurements in a plain-plate (20 mm, stainless steel). The data were found to be highly reproducible for independent batches. The following experiments were

carried out for each sample, using 2 mL total gel volume: a) Dynamic strain sweep (DSS): variation of G' and G'' with strain (from 0.01 to 100%); b) dynamic frequency sweep (DFS): variation of G' and G'' with frequency (from 0.1 to 10 Hz at 0.1% strain); c) dynamic time sweep (DTS): variation of G' and G'' with time keeping the strain and frequency values constant and within the linear viscoelastic regime (strain = 0.1% strain; frequency = 1 Hz). Mechanical inertial effects of the measuring head was accounted by the software package to accurate evaluate the thixotropic nature of the materials through loop tests. For this, fixed rest time after sample loading and pre-shearing to equilibrium at different shear rates were routinely made in order to minimize prehistory effects. Loop-tests involved the following steps: (1) Application of a low stress phase for 10 min at 0.1% oscillatory strain and 1Hz frequency as defined by DTS experiments (gel state, $G' > G''$), (2) increase of the shear strain rate until 100% strain and 1 Hz frequency for 5 min to ensure gel-to-sol transition ($G' < G''$) and minimize inertial effects, and (3) relaxation for 30 min at the same conditions as for step (1) (recovered gel state, $G' > G''$). Steps (2) and (3) were repeated once to show the reversible thixotropic nature of the gel-materials.

g) Controlled release of vancomycin: A weighted amount of the corresponding gelator (50 mg; minimum amount of gelator to obtain stable gels for both compounds), vancomycin (2 mg) and water (1 mL) were placed in a screw-capped glass vial and gently heated until all solid materials were completely dissolved. The obtained isotropic solution was then spontaneously cooled to RT resulting in gel-formation with physically incorporated vancomycin. Obtained gel-materials were overlaid with phosphate buffer saline (PBS, 1 mL, pH = 7.4) 12 h after their formation, which was considered as the starting point for the experiments. At selected points of time aliquots (100 µL) were removed and stored at -20 °C and the release buffer was completely replaced with fresh PBS to maintain infinite sink conditions. Drug concentration in the aliquots was determined at the end of the experiments using UV-spectroscopy after calibration using the maximum absorbance of vancomycin in aqueous media at 280 nm. Samples have been diluted with PBS to a total volume of 1 mL and subsequently centrifuged (EBA 12 Hettich Zentrifugen) at 4000 rpm for 10 min before measurements. It was verified that degraded gel-materials exhibited a minimum absorbance in the region of drug detection.

2. Synthesis and characterization of compounds

2.1. General synthetic approach towards C_{18}-Glu [2]

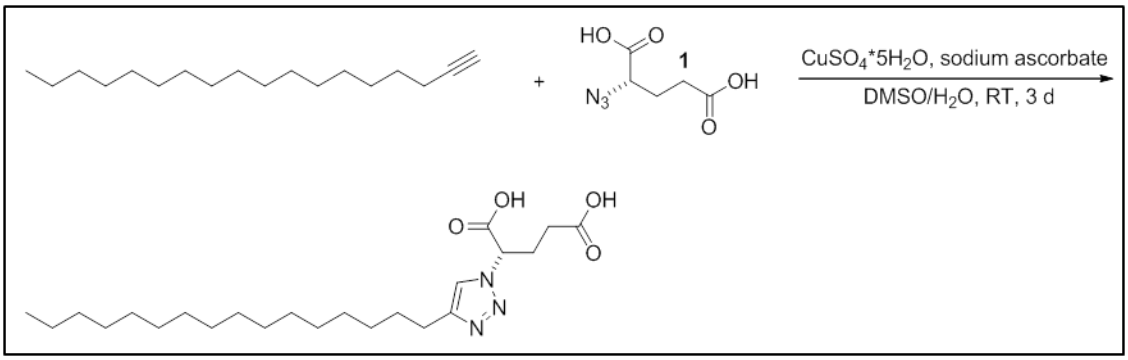


*(S)-2-Stearamidopentanedioic acid (**C_{18}-Glu**)*

To a stirred solution of (*L*)-glutamic acid diethyl ester hydrochloride (1.72 g, 7.2 mmol) and NEt_3 (2.17 g, 3.0 mL, 21.5 mmol) in dry DCM (150 mL) at 0 °C, stearoyl chloride (2.39 g, 7.9 mmol) in dry DCM (20

mL) was added slowly over a period of 1h. The mixture was allowed to warm to RT and stirred for additional 3h when water (50 mL) was added. The organic layer was separated, washed with water (3 x 50 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The obtained residue was dissolved in a 1:1 mixture of MeOH/water (150 mL) when KOH (1.21 g, 21.5 mmol) was added and the suspension was stirred for 12 h at RT. The MeOH was removed under reduced pressure and the aqueous phase was acidified with 2M HCl to pH = 2. The formed precipitate was filtered off, thoroughly washed with water, dried and recrystallized from acetone to obtain the title compound as white solid in high yield (2.40 g, 5.8 mmol, 81%). ^{1}H-NMR (400 MHz, DMSO-d^6) δ (ppm) = 7.95 (d, *J* = 7.8 Hz, 1H), 4.19 – 4.14 (m, 1H), 2.24 (t, *J* = 7.6 Hz, 2H), 2.08 (td, *J* = 7.1, 1.5 Hz, 2H), 1.89 (td, *J* = 13.4, 7.5 Hz, 1H), 1.81 – 1.67 (m, 1H), 1.48 – 1.41 (m, 2H), 1.23 (s, 28H), 0.85 (t, *J* = 6.8 Hz, 3H); ^{13}C-NMR (101 MHz, DMSO-d^6) δ (ppm) = 173.73, 173.73, 173.39, 173.39, 172.08, 172.08, 51.11, 51.11, 34.99, 34.99, 31.20, 31.20, 30.32, 30.32, 28.95, 28.95, 28.91, 28.91, 28.89, 28.89, 28.73, 28.73, 28.61, 28.61, 28.51, 28.51, 26.56, 26.56, 25.15, 25.15, 21.99, 21.99, 13.82, 13.82; FT-IR (ATR) ν_{max} (cm^{-1}) = 3309, 2937, 2914, 2848, 1730, 1714, 1701, 1651, 1624, 1543; MS (ESI): *m/z* = 414.3 [MH]$^+$, 436.3 [M+Na]$^+$, 827.6 [2M+H]$^+$, 849.6 [2M+Na]$^+$; Elemental analysis calculated for $C_{23}H_{43}NO_5$: C, 66.79; H, 10.48; N, 3.39; found: C, 66.87; H, 10.45; N, 3.25.

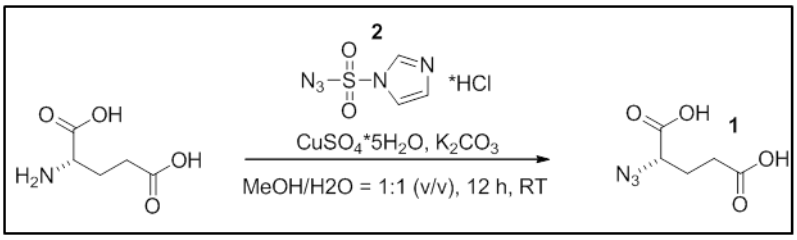
2.2. General synthetic approach towards Click-Glu



*(S)-2-(4-Hexadecyl-1H-1,2,3-triazol-4-yl)pentanedioic acid (**Click-Glu**)*

To a stirred solution of octadec-1-yne (0.61 g, 2.40 mmol) and compound **1** (0.42 g, 2.40 mmol) in a 1:2 (v/v) mixture of DMSO/H_2O (2.5 mL) at RT were added 1M stock-solutions of $CuSO_4 \times 5H_2O$ (0.23 mL, 0.24 mmol) and sodium ascorbate (0.92 mL, 0.96 mmol). Due to a clear increase of viscosity after a short period of time the total solvent volume was increased to 10 mL. After 3 d of stirring the solvent mixture was removed by lyophilization, the obtained residue was redissolved in a 1:1 (v/v) mixture of EtOAc/THF (50 mL) and washed with brine containing 0.1 M EDTA*Na_2 (2 x 50 mL), pure brine (2 x 25 mL) and water (3 x 25 mL) in order to remove inorganic impurities having a high affinity towards the product. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained residue was recrystallized from acetone to obtain the title compound as a white solid in high yield (0.89 g, 2.09 mmol, 87 %). ^{1}H-NMR (400 MHz, DMSO-d^6) δ (ppm) = 7.94 (s, 1H), 5.35 (dd, *J* = 10.2, 5.2 Hz, 1H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.47 – 2.35 (m, 1H), 2.37 – 2.23 (m, 1H), 2.20 – 1.99 (m, 2H), 1.59 (bs, 2H), 1.26 (s, 26H), 0.85 (t, *J* = 6.8 Hz, 3H).; ^{13}C-NMR (101 MHz, DMSO-d^6) δ (ppm) = 173.04, 169.96, 146.83, 121.57, 61.04, 31.19, 29.63, 28.94, 28.87, 28.77, 28.67, 28.60, 28.49, 26.46, 24.93, 21.99, 13.83; FT-IR (ATR) ν_{max} (cm^{-1}) = 3155, 2960, 2916, 2848, 1749, 1699, 1556; MS (ESI): *m/z* = 424.3 [MH]$^+$, 847.6 [2M+H]$^+$; Elemental analysis calculated for $C_{23}H_{41}N_3O_5$: C, 65.22; H, 9.76; N, 9.92; found: C, 65.35; H, 9.70; N, 10.08.

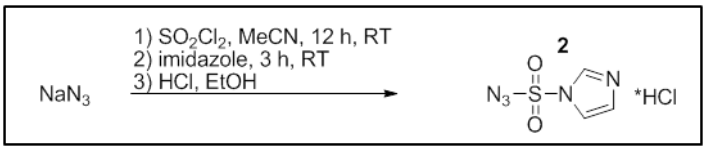
2.3. General synthetic approach towards precursor molecules 1 [3]



*(S)-2-Azidopentanedioic acid (**1**)*

Compound **2** (3.77 g, 18.0 mmol) was added to a solution of *L*-glutamic acid (2.21 g, 15.0 mmol), $CuSO_4 \times 5H_2O$ (0.04 g, 0.15 mmol) and K_2CO_3 (7.67 g, 55.5 mmol) in MeOH/H_2O (1:1 (v/v), 150 mL). The resulting mixture was stirred for 12 h when most of the MeOH was removed using a rotary evaporator. The aqueous solution was acidified with concentrated HCl to pH = 2 and extracted with EtOAc (3×50 mL). The combined organic phases were dried over Na_2SO_4, filtered and evaporated to a total volume of ca. 5 mL. The obtained concentrated solution was subjected to column chromatography using EtOAc as eluent to afford the desired compound as colorless oil in moderate yield (1.75 g, 10.1 mmol, 67 %). The compound was not evaporated to complete dryness due to a potential explosive nature of azide-containing compounds. Hence the product still contained ca. 15 % of EtOAc as determined by NMR-spectroscopy. ^{1}H-NMR (300 MHz, DMSO-d^6) δ (ppm) = 4.14 (dd, *J* = 8.7, 4.9 Hz, 1H), 2.38 – 2.25 (m, 2H), 2.07 – 1.92 (m, 1H), 1.89 – 1.71 (m, 1H); ^{13}C-NMR (75 MHz, DMSO-d^6) δ (ppm) = 173.36, 171.43, 60.48, 29.80, 26.09.

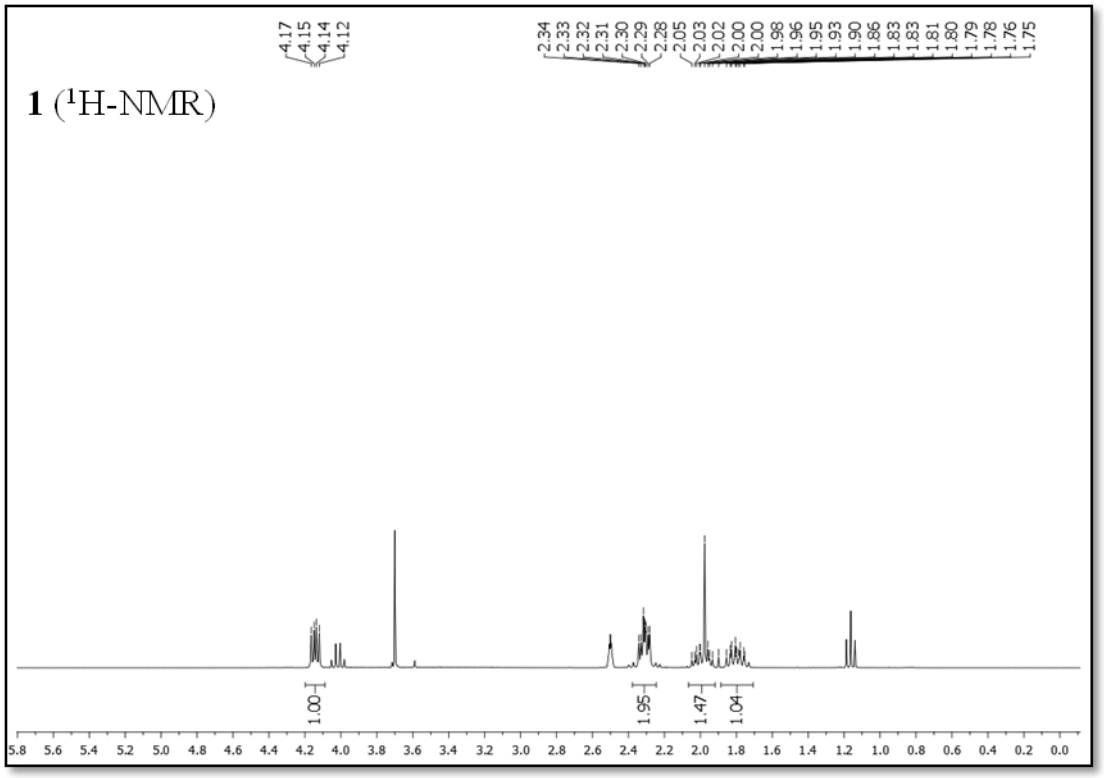
2.4. General synthetic approach towards precursor molecules 2 [3]

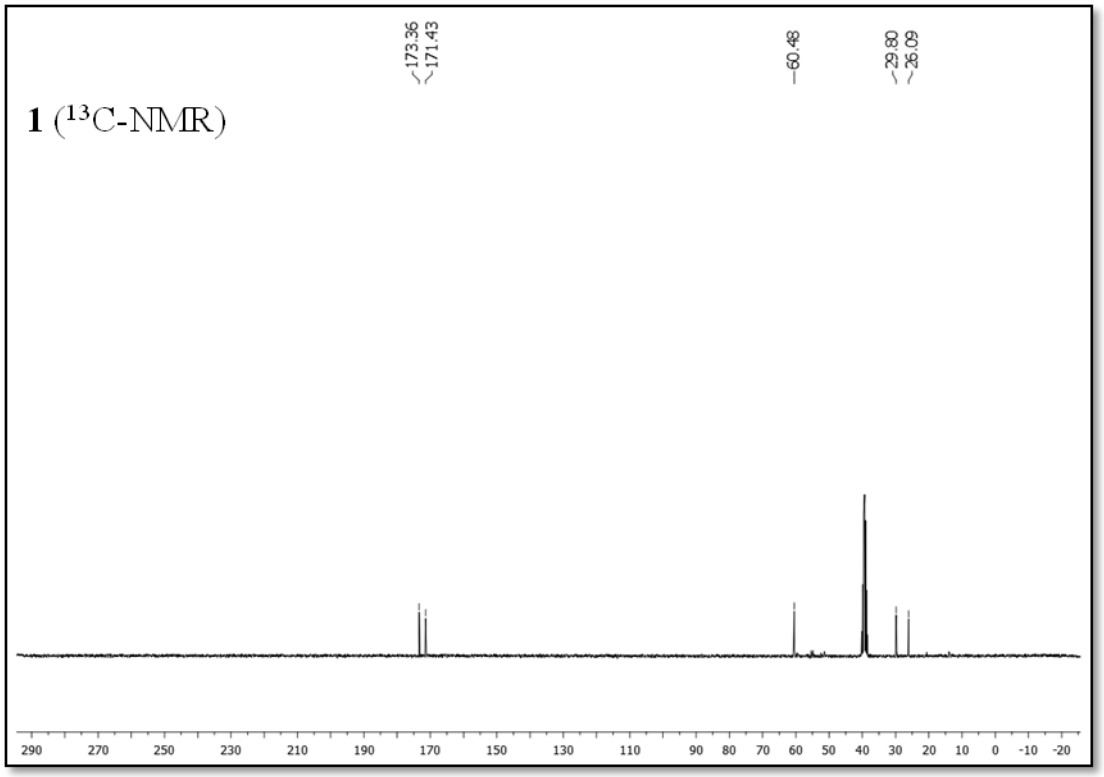


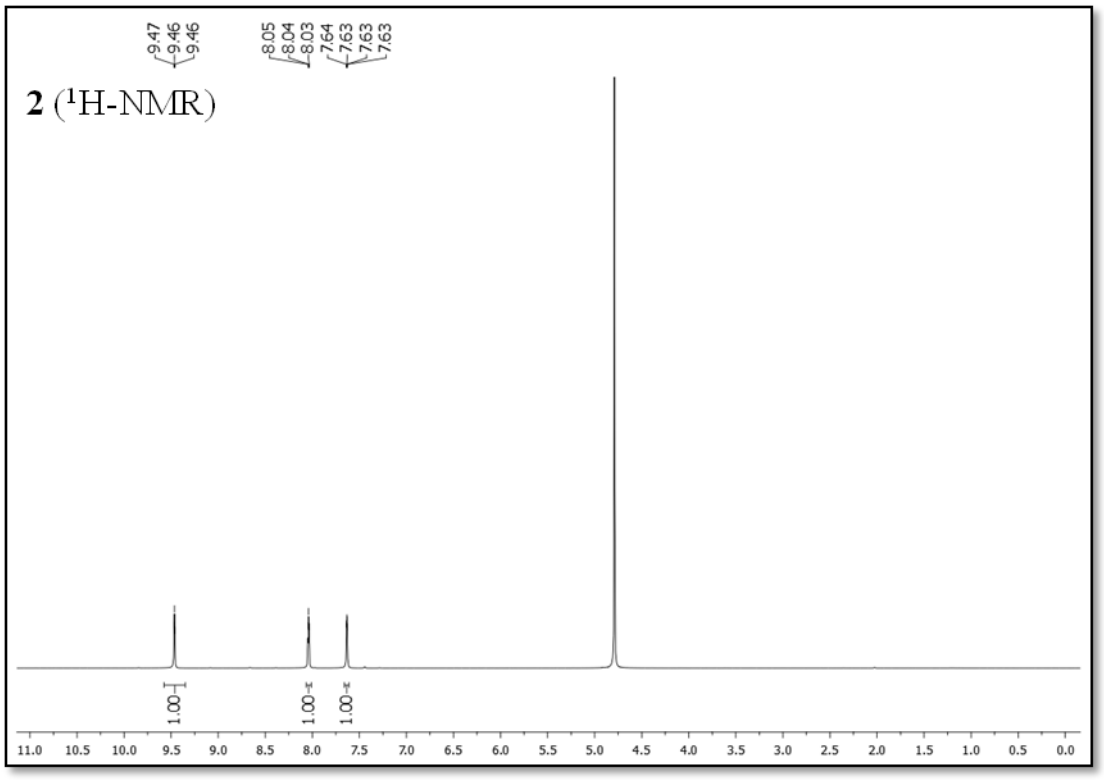
*1H-Imidazole-1-sulfonyl azide (**2**)*

Sulfuryl chloride (8.1 mL, 100 mmol) was added drop-wise to a suspension of NaN_3 (7.5 g, 100 mmol) in MeCN (100 mL) over a period of 30 min at 0 °C. After stirring 12 h at RT imidazole (13.0 g, 190 mmol) was added portion-wise to the ice-cold mixture and the slurry was stirred for additional 3 h at RT. The mixture was diluted with EtOAc (200 mL), washed with H_2O (3×100 mL) and sat. $NaHCO_3$ (3×100 mL), dried over Na_2SO_4 and filtered. A solution of HCl in EtOH (obtained by the drop-wise addition of AcCl (10.7 mL, 150 mmol) to dry EtOH (40 mL) at 0 °C) was added drop-wise to the filtrate while stirring at 0 °C. After chilling for 1h in an ice-bath the resulting precipitate was filtered of, thoroughly washed with cold EtOAc and dried in vacuum to afford the desired compound as white crystalline solid in moderate yield (12.1 g, 57.8 mmol, 58 %). ^{1}H-NMR (300 MHz, D_2O) δ (ppm) = 9.46 (t, *J* = 1.3 Hz, 1H), 8.13 – 7.95 (m, 1H), 7.63 (dd, *J* = 2.0, 1.3 Hz, 1H).

2.5. Spectroscopic characterization of synthesized compounds



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8.03
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7.63
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7.63
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1.00
1.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
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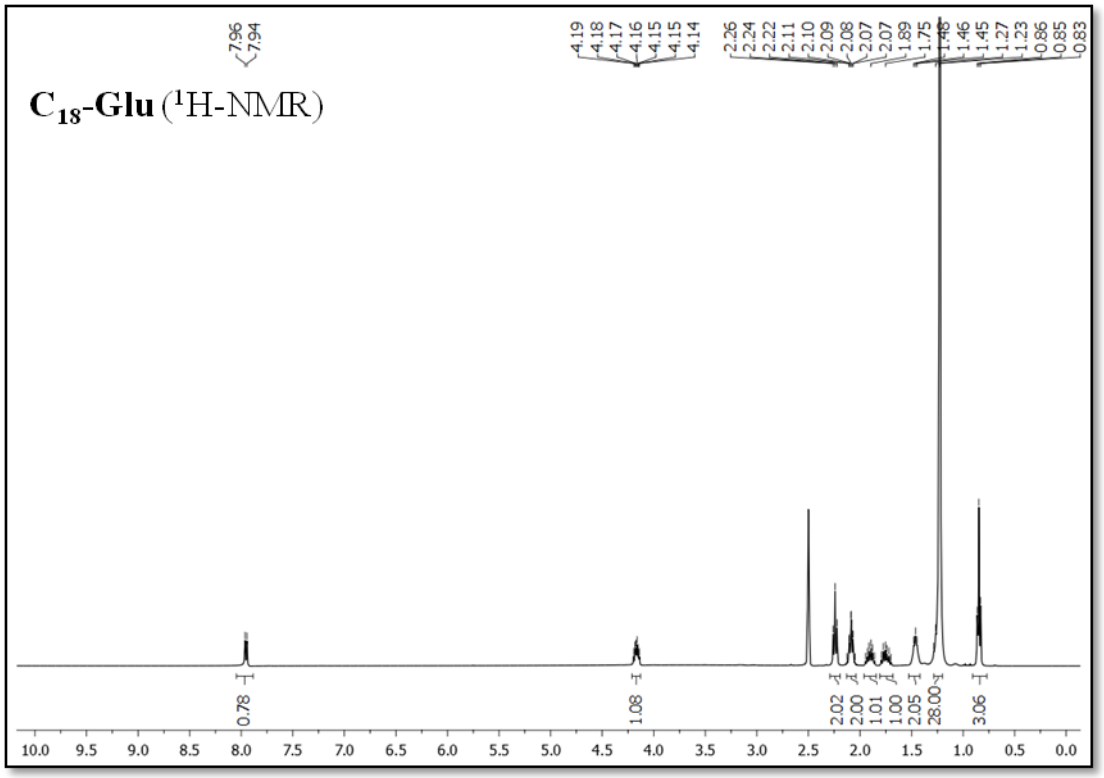
C18-Glu (1H-NMR)
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2.22
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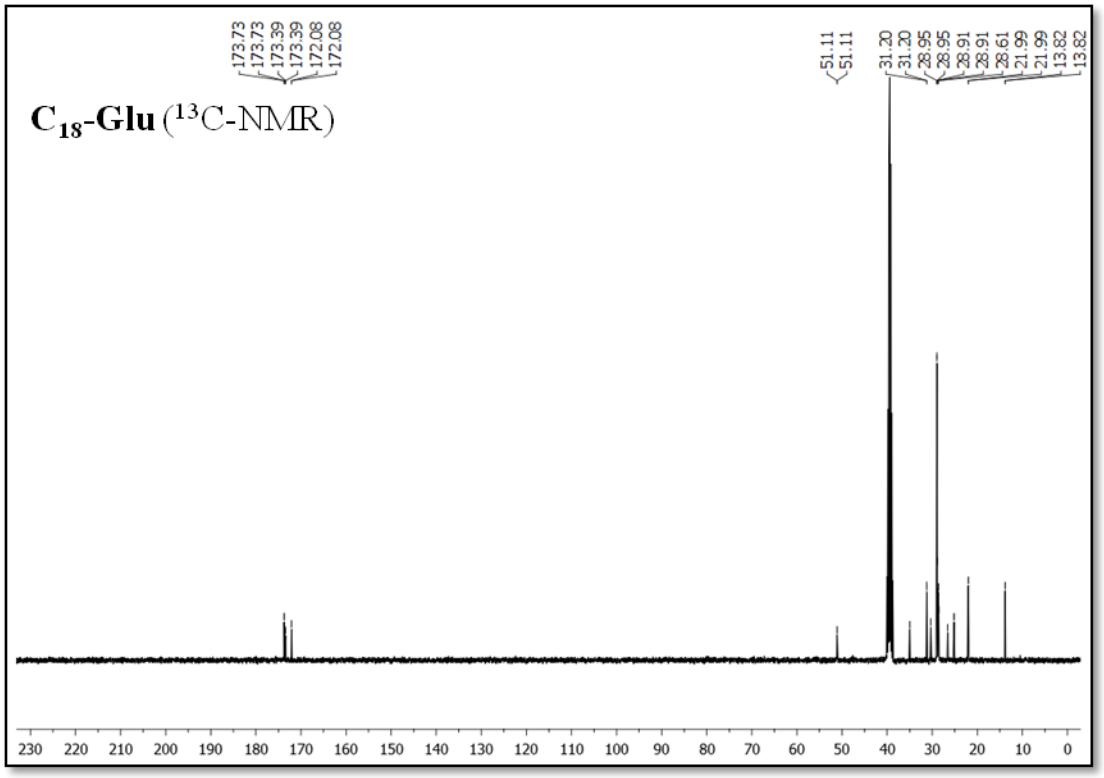
2.09
2.08
2.07
2.07
1.89
1.75
1.48
1.46
1.45
1.27
1.23
0.86
0.85
0.83
0.78
1.08
2.02
2.00
1.01
1.00
2.05
28.00
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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13.82
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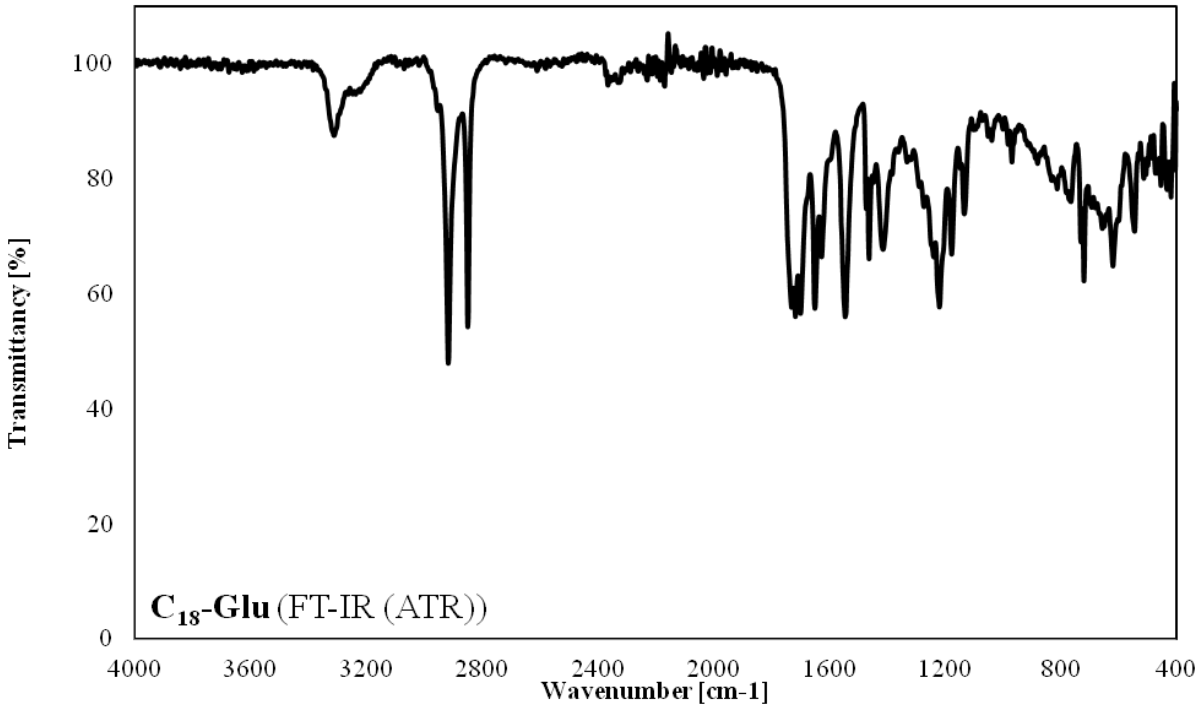
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60
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20
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4000
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3200
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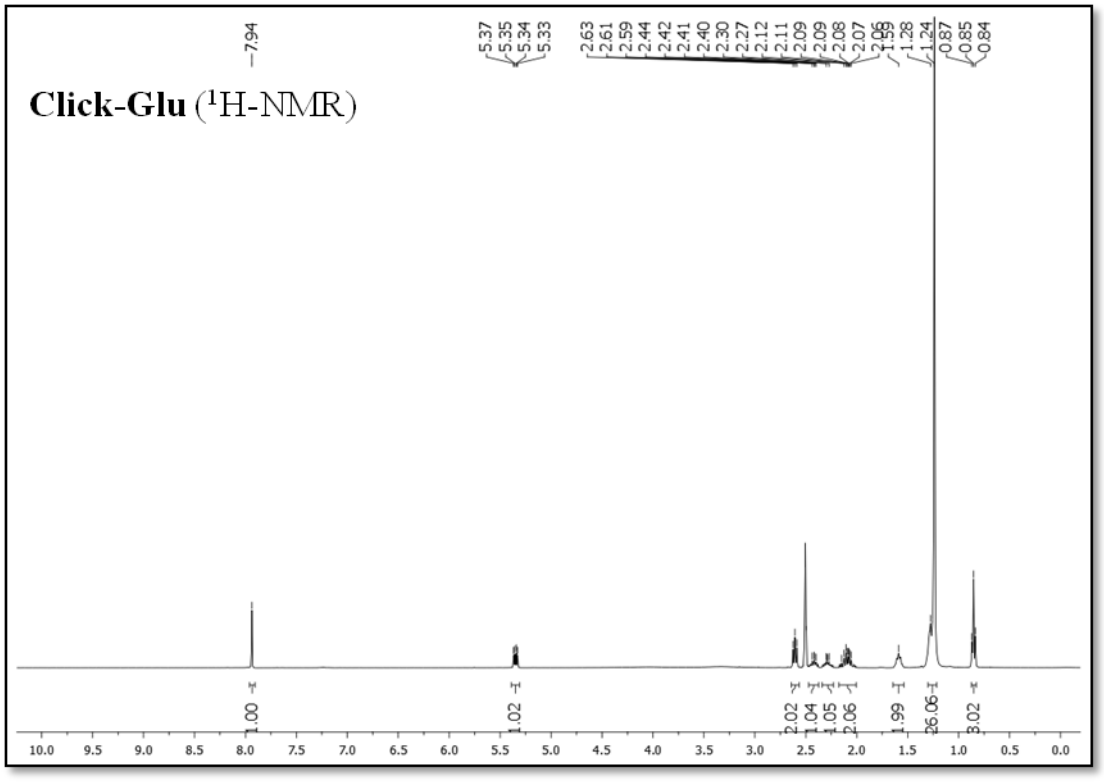
1600
1200
800
400
Wavenumber [cm-1]
C18-Glu (FT-IR (ATR))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2.30
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2.08
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1.28
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1.00
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10.0
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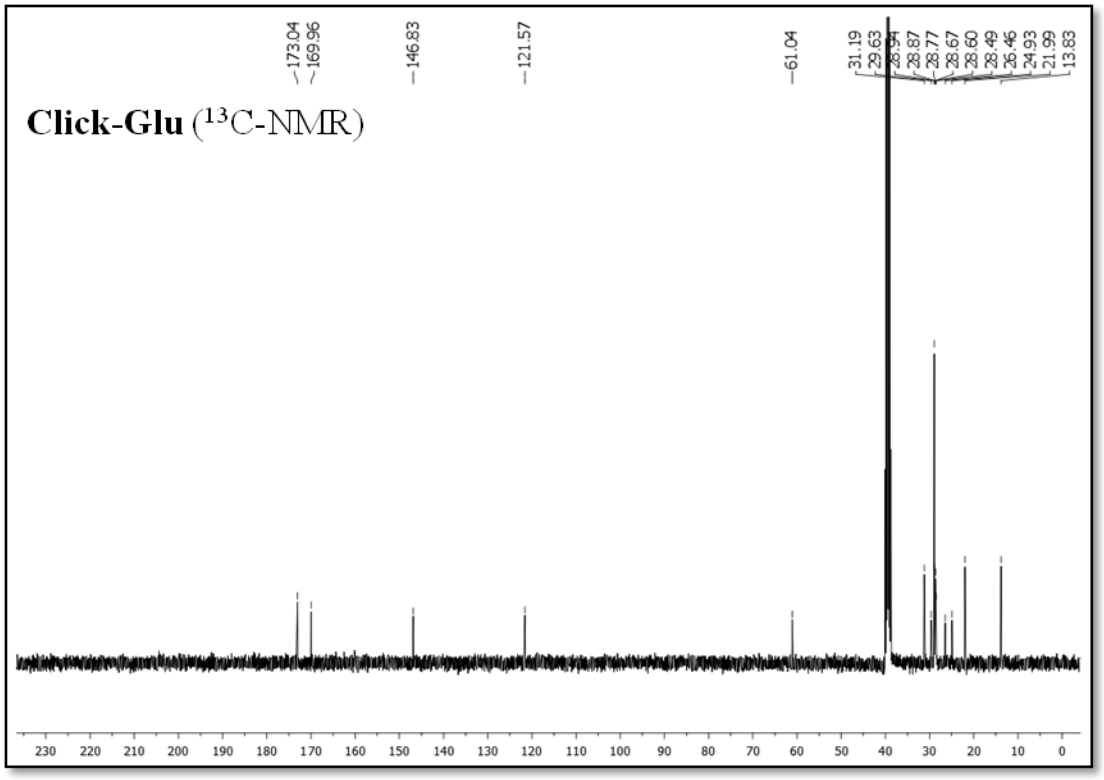
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13.83
Click-Glu (13C-NMR)
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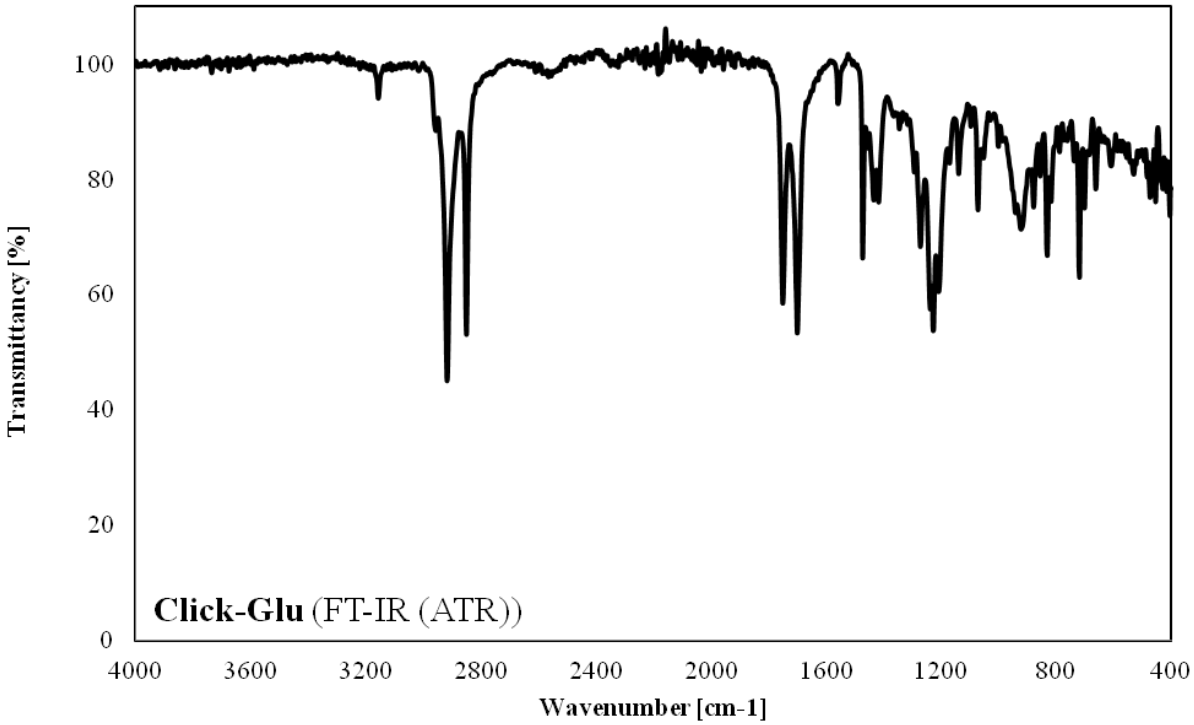
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Wavenumber [cm-1]

3. Additional data on gelation behavior of the gelator-compounds

3.1. Graphical data on gelation properties of compounds C_{18}-Glu and Click-Glu

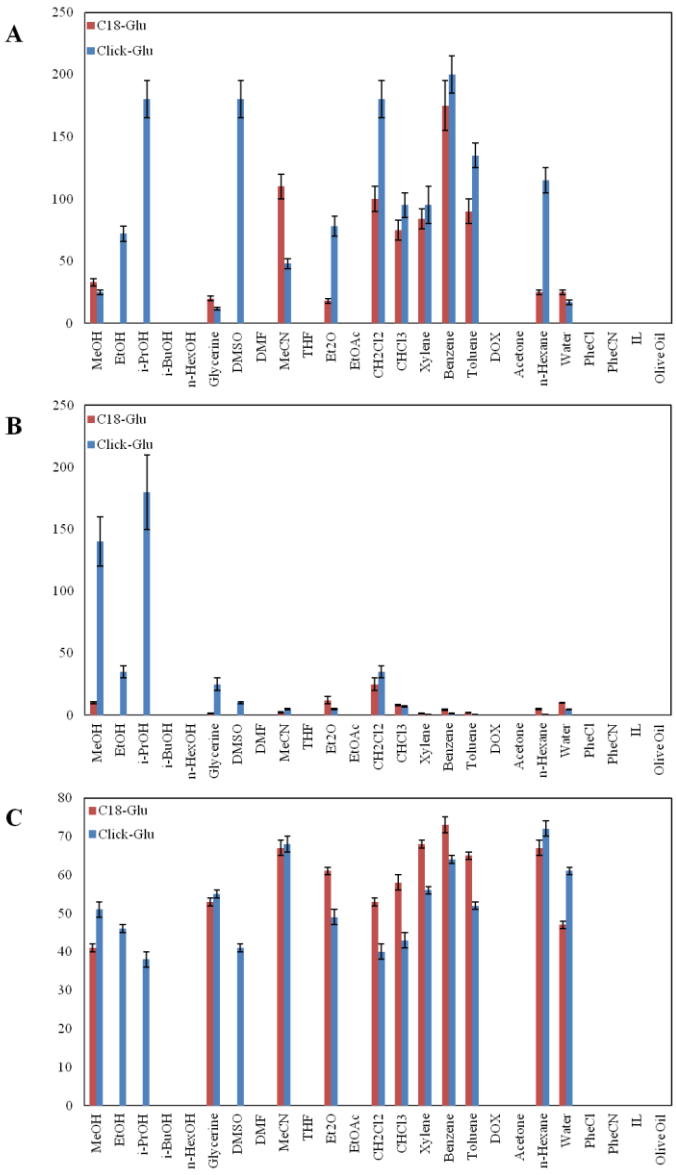

Fig. S2 Bar graphs indicating differences in gelation properties of **C_{18}-Glu** and **Click-Glu**. **A** *CGC*-values; **B** Gelation-time; **C** T_{gel}-values. Data obtained from **Tab. S1**.

3.2. Tabular data on gelation behavior of compounds C_{18}-Glu and Click-Glu

Tab. S1 Comparison of gelation ability and typical gel-properties of **C_{18}-Glu** and **Click-Glu** in aqueous environment and various organic media. [a)]

Solvent	C_{18}-Glu				Click-Glu			
	CGC [mg/mL]	Gel-Time [min]	T_{gel} [°C]	Appearance	*CGC* [mg/mL]	Gel-Time [min]	T_{gel} [°C]	Appearance
MeOH	33 (3)	10 (1)	41 (1)	OG	25 (2)	140 (20)	51 (2)	OG
EtOH	> 200	-	-	PG	72 (6)	35 (5)	46 (1)	OG
i-PrOH	> 200	-	-	PG	180 (15)	180 (30)	38 (2)	SG/OG
2-BuOH	> 200	-	-	PG	> 200	-	-	PG
1-Hexanol	> 200	-	-	P	> 200	-	-	PG
Glycerin	20 (2)	1.5 (0.3)	53 (1)	TLG	12 (1)	25 (5)	55 (1)	TLG
DMSO	> 200	-	-	P	180 (15)	10 (1)	41 (1)	OG
DMF	> 200	-	-	P	> 200	-	-	P
MeCN	110 (10)	2 (0.5)	67 (2)	OG	48 (4)	5 (0.5)	68 (2)	OG
THF	> 200	-	-	CS	> 200	-	-	CS
Et_2O	18 (2)	12 (3)	61 (1)	OG	78 (8)	5 (0.5)	49 (2)	OG
EtOAc	> 200	-	-	P	> 200	-	-	P
CH_2Cl_2	100 (10)	25 (5)	53 (1)	OG	180 (15)	35 (5)	40 (2)	OG
$CHCl_3$	75 (8)	8 (0.5)	58 (2)	OG	100 (10)	7 (0.5)	43 (2)	OG
Xylenes	84 (8)	1.5 (0.3)	68 (1)	OG	95 (15)	0.5 (0.1)	56 (1)	OG
Benzene	175 (20)	4.5 (0.5)	73 (2)	OG	200 (15)	1.5 (0.3)	64 (1)	OG
Toluene	90 (10)	2 (0.3)	65 (1)	OG	135 (10)	0.5 (0.1)	52 (1)	OG
DOX	> 200	-	-	CS	> 200	-	-	CS
Acetone	> 200	-	-	P	> 200	-	-	P
n-Hexane	25 (2)	5 (0.5)	67 (2)	OG	115 (10)	0.5 (0.1)	72 (2)	OG
H_2O	25 (2)	10 (0.5)	47 (1)	OG	17 (2)	4.5 (0.3)	61 (1)	OG
PheCl	> 200	-	-	PG	> 200	-	-	PG
PheCN	> 200	-	-	PG	> 200	-	-	PG
IL	0.1-20	-	-	I	0.1-20	-	-	I
Olive oil	0.1-20	-	-	I	0.1-20	-	-	I
Silicon oil	0.1-20	-	-	I	0.1-20	-	-	I

[a)] Values in brackets indicate experimental errors from at least two randomized experiments. Abbreviations: CS = clear solution resulting after heating a mixture of the compound and the corresponding solvent; DOX = 1,4-dioxane; I = insolubility of the compound in the corresponding solvent; IL = 1-butyl-3-methylimidazolium hexafluorophosphate (BMIM·PF_6; room temperature ionic liquid); OG = opaque gel; P = precipitation of the compound from isotropic solutions of compound and corresponding solvent (usually after 4-36 h); PG = partial gel (phase separation between gel and sol after time); PheCl = chlorobenzene; PheCN = benzonitrile; SG = soft gel (gravitational flow of the material after inversion of the test tube within 2 h); TLG = translucient gel.

3.3. Tabular data for crosschecking the accuracy of the costume made set-up to determine T_{gel}-values

Tab. S2 Evaluation of the accuracy of T_{gel}-values determined using the costume made set-up as described in **Fig. S1**. [a)]

Entry	Compound	Solvent	Conc. [mg/mL]	T_{gel} [°C]		
				IFM [1]	DBM [4 d)]	CM
1	**C_{18}-Glu**	H_2O	25	49 (1)	49 (2)	47 (1)
2	**C_{18}-Glu**	$CHCl_3$	75	58 (1)	56 (1)	58 (2)
3	**C_{18}-Glu**	Et_2O	18	57 (2)	63 (1)	61 (1)
4	**C_{18}-Glu** [b)]	MeCN	110	66 (2)	64 (1)	67 (2)
5	**C_{18}-Glu**	Toluene	90	63 (1)	63 (1)	65 (1)
6	**Click-Glu** [b)]	H_2O	17	62 (1)	58 (2)	61 (1)
7	**Click-Glu**	$CHCl_3$	100	42 (1)	39 (2)	43 (2)
8	**Click-Glu**	Et_2O	78	49 (2)	48 (1)	49 (2)
9	**Click-Glu** [b)]	MeCN	48	67 (1)	62 (2)	68 (2)
10	**Click-Glu**	Toluene	135	52 (2)	51 (1)	52 (1)
11	**A4** [c)]	*i*-PrOH	19	54 (1)	56 (1)	51 (1)
12	**A4** [c)]	Toluene	20	40 (2)	36 (2)	40 (1)
13	**A4** [c)]	EtOH	70	51 (1)	51 (1)	53 (2)

[a)] Abbreviations: IFM = Inverse flow method; DBM = dropping ball method; CM = costume made set-up. Values in brackets indicate errors from at least two randomized experiments. b) The system has been investigated by DSC and T_{gel}-values were correlated with the first endothermic transition as indicated in **Fig. S3**. [c)] For comparative purposes literature-known compound A4 [5] in *i*-PrOH (19 mg/mL, T_{gel} = 52 °C determined by IFM and verified by correlation to the first transition in modulated DSC (56±1 °C)), toluene (20 mg/mL, T_{gel} = 37 °C determined by IFM) and EtOH (70 mg/mL, T_{gel} = 52 °C determined by IFM) was also investigated. [d)] Balls used for the determinations: 0.1±0.02 mm diameter, 0.105±0.010 g weight.

3.4. Differential scanning calorimetry

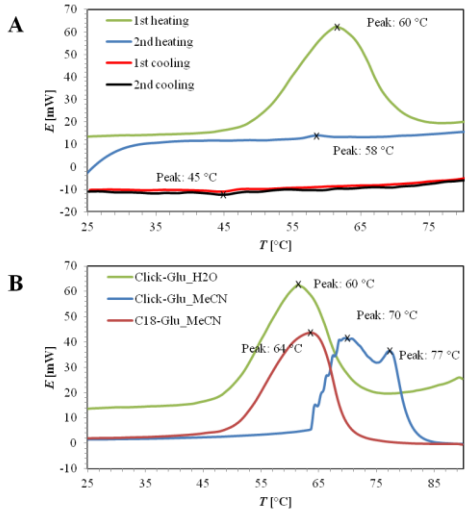

Fig. S3 A) Representative DSC spectrum of the gel made of **Click-Glu** in H_2O (17 mg/mL). *Gel*-to-*sol* transition temperature (endothermic effect) was estimated in ca. 59 ± 1 °C in two different cycles (first-order transition), which was in good agreement with the value obtained using IFM (T_{gel} = 62 ± 1 °C) and the costume made set-up (T_{gel} = 61 ± 1 °C). In the other hand, *sol*-to-*gel* transition temperature (exothermic effect) was estimated in ca. 46 °C due to thermal cycling hysteresis. B) Representative heating curves obtained by DSC of different gel-materials for T_{gel}-determinations at concentrations as indicated in **Tab. S2**. The observation of second order transition in gels from **Click-Glu** in MeCN (48 mg/mL) could be an indication for cluster-formation of fibre-assemblies. In general the obtained values are in good agreement with experiments carried out in **Tab. S2**.

3.5. Additional remarks on stimuli-responsive nature

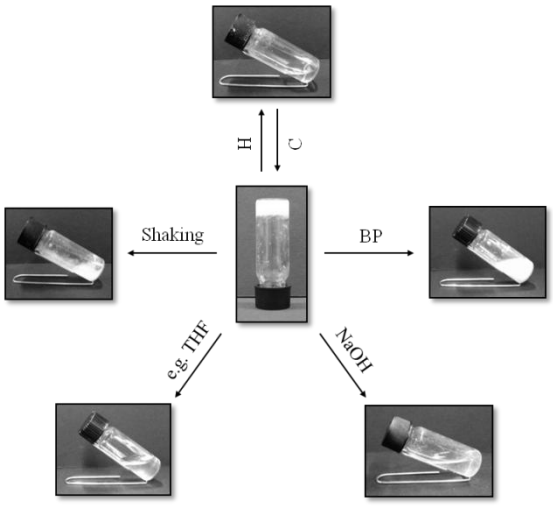

Fig. S4 Representative diagram showing the preparation of multi-stimuli responsive gels derived from **C_{18}-Glu** in water (25 mg/mL). Abbreviations: C = cooling; H = heating; BP = borate buffer (pH = 9.2). Systems based on $CHCl_3$ as solvent behave approximately the same (only differences in the time-scale of response can be observed).

3.6. Additional electron microscopy

Several serious differences can be observed from electron microscopy imaging for the two gelator compounds in the same solvents at comparable concentrations. This finding may be a result from different patterns of interactions between the gelator-molecules and gelator-solvent interactions. Depending on the nature of the linker (amide or triazole) and the solvent polarity formation of various nanostructures from sheet- and disc-like over dense wrinkles and draperies or networks consisting of twisted fibres (single fibres are visible from e.g. **C_{18}-Glu** in MeCN (100 mg/mL) with diameters of ca. 35-75 nm (view **Fig. S5 F**)) can be observed. As main driving-forces for gelation in both cases H-bonding is predominating accompanied by hydrophobic van der Waals interactions. In **Click-Glu** additional π-π-stacking and additional physico-chemical properties of the triazole in comparison to the amide-moiety might be responsible for the changes in the nanostructures.

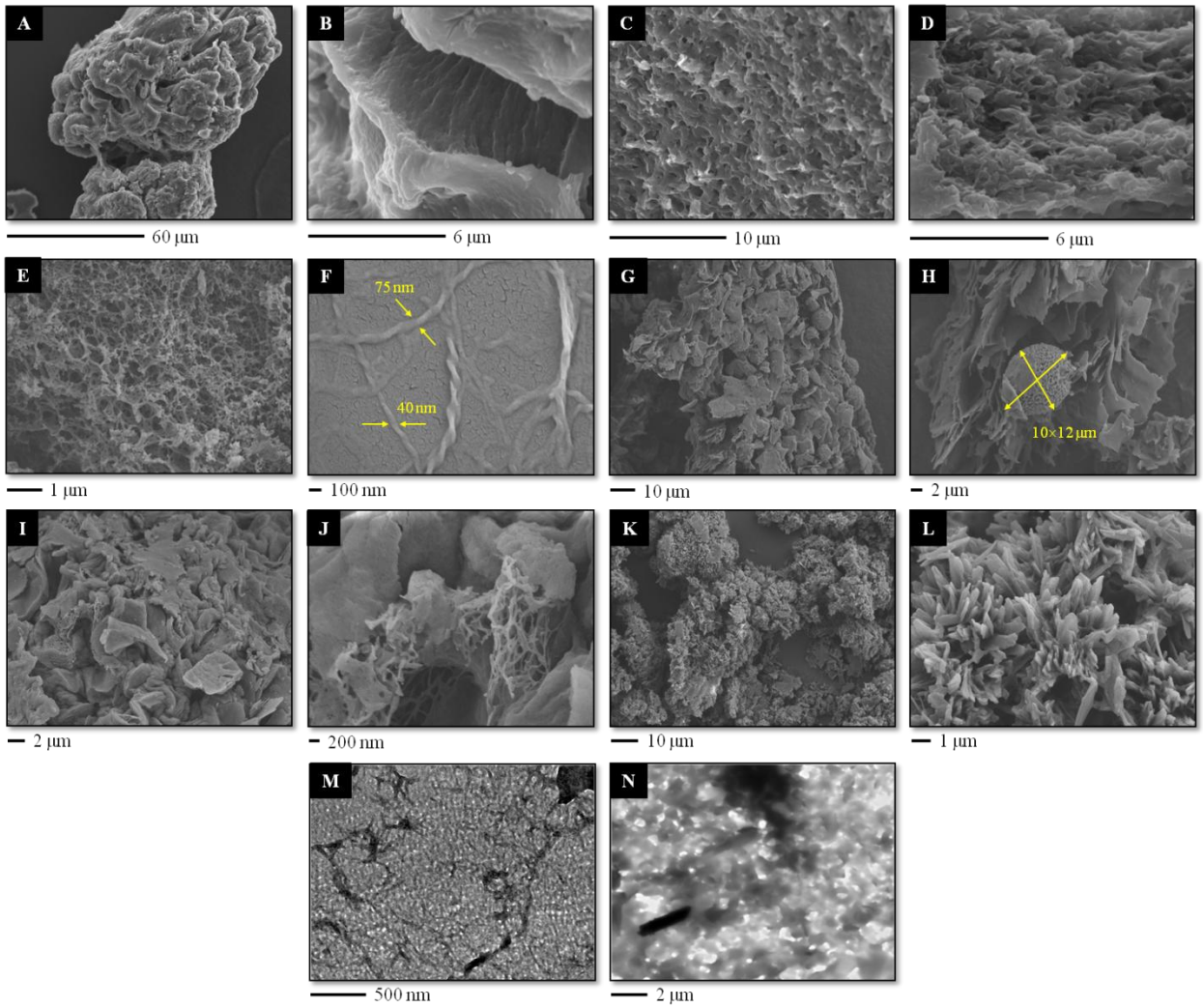

Fig. S5 SEM (**A-D**), FESEM (**E-L**) and TEM (**M-N**) images of cryogels prepared by the freeze-drying method of materials derived from **C_{18}-Glu** and **Click-Glu** at comparable concentrations. **A, B, M**: **C_{18}-Glu** in toluene (135 mg/mL); **C, D, N**: **Click-Glu** in toluene (135 mg/mL); **E, F**: **C_{18}-Glu** in MeCN (110 mg/mL); **G, H**: **Click-Glu** in MeCN (100 mg/mL); **I, J**: **C_{18}-Glu** in Et_2O (78 mg/mL); **K, L**: **Click-Glu** in Et_2O (78 mg/mL).

4. Gas-adsorption

Low pressure gas-adsorption measurements (up to 1 bar) were performed on a Quantachrome Quadrasorb automatic volumetric instrument at 77 K using N_2-gas. Xerogels of the compounds were obtained from hydrogels (25 mg/mL) by the freeze-drying method. Both materials are able to reversible uptake N_2 indicating pore-sizes of bigger than the kinetic diameter of N_2 (3.6 Å). Materials derived from **C_{18}-Glu** can uptake up to 35.7 mmol/g (207.2 cm^3/g at 77 K) N_2, whereas materials based on **Click-Glu** can uptake 6.2 mmol/g (36.0 cm^3/g at 77 K) at 1 bar pressure, which is in good agreement with the determined surface areas of 53.4 and 22.6 m^2/g respectively. Gas-adsorption and desorption plots are illustrated in **Fig. S6**.

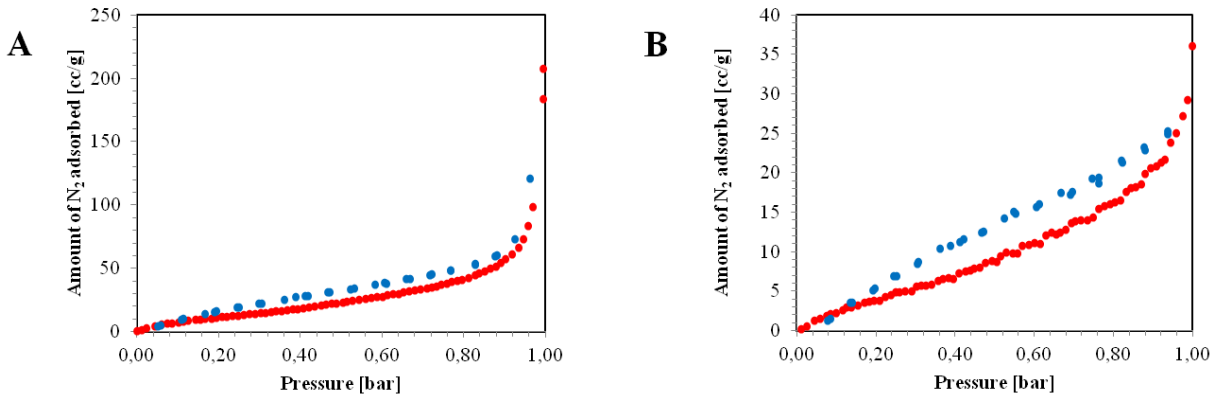

Fig. S6 N_2-adsorption isotherms below 1.0 bar for xerogels derived from hydrogels of **C_{18}-Glu** (**A**) and **Click-Glu** (**B**) with comparable concentrations (25 mg/mL). Red and blue circles represent adsorption and desorption respectively.

5. Calibration curve of vancomycin-release

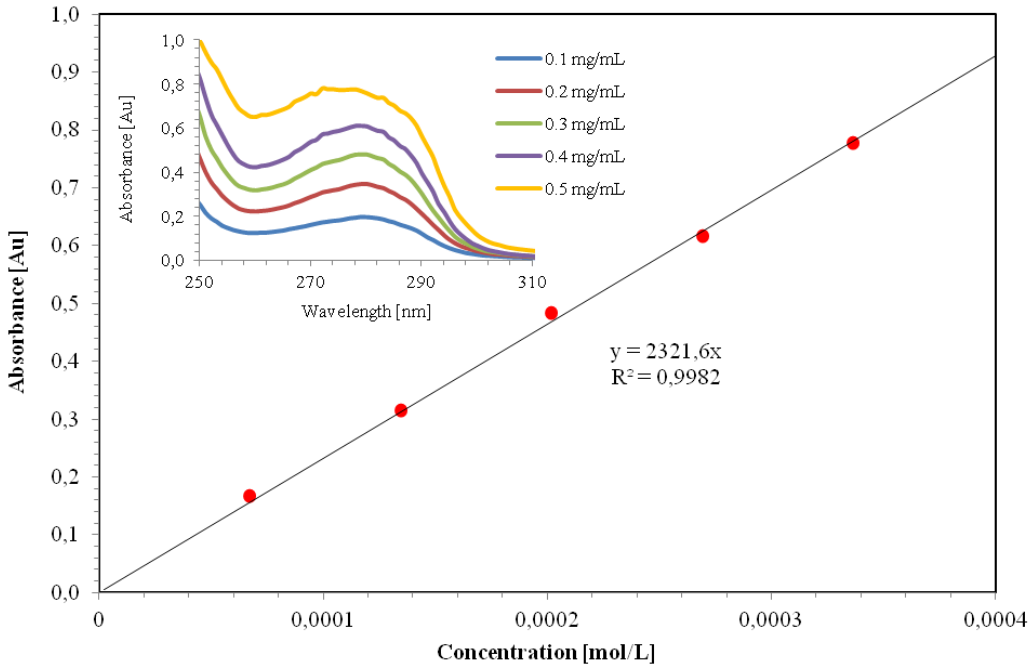

Fig. S7 Vancomycin-release calibration curve in the presence of PBS. The absorbances of PBS and degraded gel-materials at a maximum concentration of 25 mg/mL have proven to be negligible at the maximum absorbance of vancomycin at 280 nm.

6. References

1 J. E. Eldrige, J. D. Ferry, *J. Phys. Chem*., 1954, **58**, 992-995.
2 P. Gao, C. Zhan, L. Liu, Y. Zhou and M. Liu, *Chem. Commun.*, 2004, **10**, 1174-1175.
3 E. D. Goddard-Borger and R. V. Stick, *Org. Lett*., 2007, **9**, 3797-3800.
4 A. Takahashi, M. Sakai, and T. Kato, *Polym. J.*, 1980, **12**, 335-341.
5 P. Fatás, J. Bachl, S. Oehm, A. I. Jiménez, C. Cativiela and D. D. Díaz, *Chem. Eur. J.*, 2013, **19**, 8861-8874.