Electronic Supplementary Information

Supramolecular design of a bicomponent topochemical reaction between two non-identical molecules

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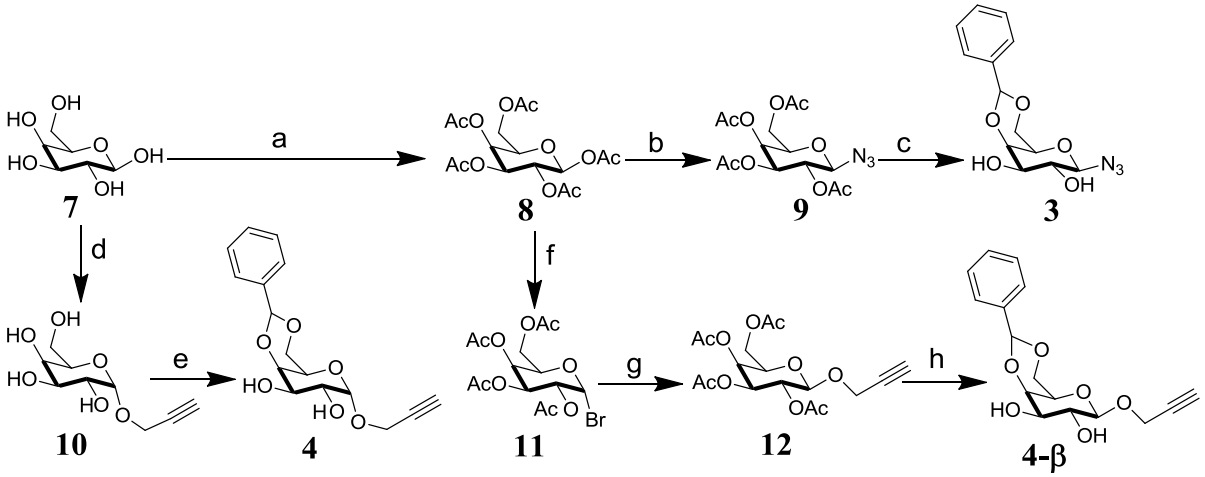
1. Materials and Methods

Chemicals and solvents were purchased from Sigma-Aldrich and were used without further purification. Commercial petrol, diesel and kerosine were purchased from gas outlets and were used without further purification. TLC analyses were carried out using precoated TLC silica gel 60 purchased from Merck. Chromatograms were visualized under UV light and by dipping the plates into either chromic acid staining solution or ceric ammonium sulphate staining solution followed by heating. The column chromatography was carried out using 200-400 mesh silica gel. Melting points were recorded on a Stuart, SMP-30 melting point apparatus. NMR spectra were recorded on an Avance II-500 (Bruker) NMR spectrometer. IR spectra were recorded using IR Prestige-21 (Shimadzu) spectrometer. IR spectra of (i) gel samples were recorded by placing the gel in ATR holder, (ii) the chloroform solution of the gelators were recorded by taking in a NaCl cell and (iii) the xerogel samples were recorded by mixing with KBr and making pellet. Elemental analyses were done on Elementar, vario MICRO cube elemental analyzer. Powder X-ray diffraction spectra were recorded using an X'pert PRO (PANalytics) powder diffractometer. DSC analyses were carried out using DSC Q20 differential scanning calorimeter, at a heating rate of 5 °C/min. TGA analysis were done using Universal V4.7A TA instrument at a heating rate of 3 °C/min. SEM images were recorded using JEOL JSM-5600LV Scanning Electron Microscope.

2. Syntheses of diols 3, 4 and 4-β



Scheme S1. Reagents and conditions: (a) NaOAc, Ac_2O, 60 °C, 12h, 82%. (b) Me_3SiN_3, $SnCl_4$, DCM, rt, Ar, 12h, 83%. (c) i) NaOMe, MeOH, 1 h, rt (ii) $PhCH(OMe)_2$, TsOH, acetonitrile, rt, Ar, 12 h, 64%. (d) Propargyl alcohol, H_2SO_4-silica, 6h, 65 °C, 31%. (e) $PhCH(OMe)_2$, TsOH, acetonitrile, rt, Ar, 12 h, 64%. (f) AcBr, CH_3OH, AcOH, dark, rt, Ar, 10h, 63%. (g) Propargyl

alcohol, $InCl_3$, 4 Å Molecular Sieves, dry DCM, rt, Ar, 12h, 64%. (h) i) NaOMe, MeOH, 1 h, rt; (ii) $PhCH(OMe)_2$, TsOH, acetonitrile, rt, Ar, 12 h, 64%.

Synthesis of 3

Diol **3** was synthesised from D-galactose (**7**) as per Scheme S1 by following the reported procedure.[1] Briefly, D-galactose was peracetylated to β-penta-*O*-acetyl-D-galactopyranoside (**8**), which was converted to β-azide **9**. The acetyl groups were removed by methanolysis and the tetrol thus obtained was reacted with benzaldehyde dimethyl acetal in presence of acid catalyst to afford diol **3**.

Synthesis of 10

A suspension of D-galactose **7** (6.1 g, 33.9 mmol) and H_2SO_4-Silica (240 mg) in propargyl alcohol (9.3 mL, 167 mmol), was stirred at 65 °C under argon atmosphere.[2] Reaction was monitored by TLC. When the reaction was complete (6h), the mixture was directly loaded on a silica gel column and first eluted with DCM to remove the excess propargyl alcohol and then eluted with 10% MeOH in DCM to yield the known tetrol **10** (2.5 g, 31%) as a white solid. ^{1}H NMR (CD_3OD, 500 MHz) δ: 4.93 (d, 1H, *J* = 3.8 Hz), 4.22-4.20 (m, 2H), 3.81 (d, 1H, *J* = 2.9 HZ), 3.74-3.63 (m, 4H), 3.60 (dd, 1H, *J* = 5.5 Hz, *J* = 11 Hz), 2.75 (t, 1H, *J* = 2.5 Hz). ^{1}H NMR of the isolated compound matched the spectral data reported in literature.[3,4]

Synthesis of 4

A solution of tetrol **10** (2.5 g, 11.5 mmol), benzaldehyde dimethyl acetal (8.5 mL, 57.3 mmol) and p-TSA (109 mg, 0.57 mmol) in dry CH_3CN (30 mL) was stirred at room temperature. The reaction was followed by TLC. When the reaction was complete (12 h), it was quenched by adding triethylamine (1 mL). The solvent and excess reagents were removed under reduced pressure using a rotary evaporator. The crude solid thus obtained was chromatographed by using ethyl acetate-petroleum ether mixture (7:3 v/v) as eluent to yield the known[4] diol **4** (2g, 65%) as a white solid. Melting point: 134 °C. Lit.[4] m.p. 128-129 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.44-7.42 (m, 2H), 7.31-7.30 (m, 3H), 5.49 (s, 1H), 5.16 (d, 1H, *J* = 3.5 Hz), 4.26 (d, 2H, *J* = 2.5 Hz), 4.22-4.20 (m, 2H), 4.02 (dd, 1H, *J* = 1.8 Hz, *J* = 12.6 Hz), 3.90 (dd, 1H, *J* = 3.6 Hz, *J* = 10 Hz), 3.85 (dd, 1H, *J* = 3.6 Hz, *J* = 10 Hz), 3.72 (s, 1H), 2.40 (t, 1H, *J* = 2.4 Hz), 2.36 (s, 1H), 2.06 (s, 1H).

Synthesis of 11

To a solution of pentaacetate **8** (5 g, 12.8 mmol) in dry acetic acid (25 mL), acetyl bromide (2.9 mL, 38.5 mmol) and dry MeOH (675µL, 16.7 mmol) were added and the solution was stirred at room temperature in dark until the reaction was complete (10 h).[5] Reaction was quenched by adding saturated sodium bicarbonate solution (100 mL) and then extracted with chloroform (200 mL). The organic layer was separated and the aqueous layer was re-extracted with chloroform (2 times). The combined organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure. Crude solid thus obtained was chromatographed using 30% ethylacetate in petroleum ether as eluent to yield the known bromide **11** (3.32 g, 63%) as a white solid. As the compound **11** was unstable, it was used immediately for the next reaction.

Synthesis of 12

To a solution of **11** (3.2 g, 7.8 mmol) in dry DCM (50 mL), 4 Å molecular sieves (400 mg), propargyl alcohol (450 µL, 7.8 mmol) and $InCl_3$ (760 mg, 3.4 mmol) were added and the mixture was stirred at room temperature.[6] When the reaction was complete (12 h), the reaction mixture was passed through a celite pad and the filtrate was concentrated under reduced pressure. The crude solid thus obtained was chromatographed using 45% ethyl acetate in petroleum ether as eluent to yield the known[7] tetraacetate **12** (1.92 g, 64%) as a white solid. M.p. 56 °C; Lit.[7] m.p. 56 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.42 (d, 1H, *J* = 3.4 Hz), 5.26-5.22 (m, 1H), 5.08 (dd, 1H, *J* = 3.5 Hz, *J* = 10.4 Hz), 4.76 (d, 1H, *J* = 8 Hz), 4.40 (d, 2H, *J* = 2.4 Hz), 4.23-4.11 (m, 2H), 3.95 (t, 1H, *J* = 6.7 Hz), 2.48 (t, 1H, *J* = 2.4 Hz), 2.17 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H).

Synthesis of 4-β

A solution of **12** (1.9 g, 4.9 mmol) in methanol (15 mL) was stirred with sodium methoxide (50 mg) at room temperature. When the reaction was complete (1h), it was quenched by adding Dowex-H^+ ion resin. The mixture was then filtered and the filtrate was concentrated under reduced pressure. The crude material thus obtained was dissolved in dry CH_3CN (20 mL) and to this solution, p-TSA (46.8 mg, 0.25 mmol) and benzaldehyde dimethyl acetal (3.6 mL, 24.6 mmol) were added. The mixture was stirred at room temperature and when the reaction was complete (12 h), it was quenched by adding triethylamine (1 mL). The solvent was removed under reduced pressure and the crude solid thus obtained was chromatographed by using a mixture of ethyl acetate

and petroleum ether (8:2 v/v) as eluent to yield the known[4] diol **4-β** (0.961 g, 64%) as a white solid. Melting point: 172° C; Lit.[4] m.p. 177-178 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.53-7.51 (m, 2H), 7.40-7.37 (m, 3H), 5.59 (s, 1H), 4.58 (d, 1H, *J* = 7.6 Hz), 4.48 (dd, 1H, *J* = 2.5 Hz, *J* = 15.9 Hz), 4.45 (dd, 1H, *J* = 2.5 Hz, *J* = 15.9 Hz), 4.37 (dd, 1H, *J* = 1.6 Hz, *J* = 12.6 Hz), 4.23 (dd, 1H, *J* = 1.1 Hz, *J* = 3.8 Hz), 4.12 (dd, 1H, *J* = 1.9 Hz, *J* = 12.5 Hz), 3.84-3.81 (m, 1H), 3.78-3.74 (m, 1H), 3.56-3.55 (m, 1H), 3.50 (d, 1H, *J* = 3.8 Hz), 2.58 (s, 1H), 2.56 (s, 1H), 2.50 (t, 1H, *J* = 2.4 Hz).

3. Gelation test

10 mg of compound to be tested was dissolved in 250 μL of the solvent in a test tube by heating and the solution was allowed to cool to room temperature. A sample was rated as gel if it is stable to inversion of the test tube.[8] All the three diols (**3**, **4** & **4-β**) were found to be gelators for non-polar solvents (Table S1).

4. Determination of Critical Gelation Concentration (CGC)

10 mg of the gelator was dissolved by heating in 250 μL of the solvent under study in a test tube and gelation test was conducted. If it passes the gelation test, further small measured volume of solvent was added and gelation test was repeated. This process was repeated until the gel failed the gelation test. From the maximum amount of solvent that can be gelated by 10 mg of the gelator, CGC was calculated as wt%. The CGC of **3**, **4** & **4-β** in different solvents are tabulated in Table S1.

5. Determination of Gel Transition Temperature (T_{gel})

The gel of diols **3**, **4** and **4-β** in different solvents were prepared in different test tubes. The test tube was heated gradually in an oil bath and the temperature at which the gel melted to solution was recorded as Tgel.[9] For a proper comparison of the gel stability, T_{gel} of gels of **3**, **4** & **4-β** in different solvents were calculated at 3 wt% and are tabulated in Table S1.

Table S1: CGC and T_{gel} of the gels formed by **3, 4** and **4-β** in different solvents:

Solvent	**3**			**4**			**4-β**		
	Status	CGC in wt%	T_{gel} @ 3 wt%	Status	CGC in wt%	T_{gel} @ 3 wt%	Status	CGC in wt%	T_{gel} @ 3 wt%
Benzene	G	0.83	83	G	0.87	62	TG	0.85	75
Toluene	G	0.50	93	G	1.55	72	TG	1.04	57
o-Xylene	TG	0.40	101	WG	>5	--	TG	1.00	59
p-Xylene	TG	0.30	102	WG	>5	--	TG	0.71	55
Nitrobenzene	S	--	--	S	--	--	--	S	--
Chlorobenzene	G	0.82	75	G	3.00	56	TG	1.31	76
Hexane	P	--	--	P	--	--	--	p	--
Heptane	P	--	--	P	--	--	--	p	--
Kerosene	TG	0.24	101	P	--	--	G	0.92	103
Petrol	TG	0.26	110	P	--	--	G	1.20	101
Diesel	G	0.70	105	P	--	--	G	1.60	103
Sunflower oil	S	--	--	G	2.3	70	G	2.00	91
Hexadecane	G	0.476	80	S	--	--	--	P	--
Pump oil	S	--	--	S	--	--	--	S	--

G-gel, TG-Transparent gel, S-Solution, P-Precipitate, WG-Weak gel.

It is clear from Table S1 that diol **3** is a better gelator among the three gelators. It congealed more number of solvents than the number solvents congealed by diol **4**. Also **3** showed low CGC and higher T_{gel}, indicating the better strength of the gels formed by **3**. Among diols **4** and **4-β**, the latter is a better gelator in terms of the number solvents got congealed, CGC and T_{gel}. This is in agreement with the observation[10] that β-analogs are better gelator than α-analogs.

6. Gelation of benzene by mixtures of 3 and 4 at different molar ratio and comparison of their T_{gel}

As both **3** and **4** are congealing a few common aromatic solvents, we studied the gelation ability of their mixture in benzene at different molar ratio by keeping the overall concentration constant. At a total concentration of 0.1 M, all mixtures of **3** and **4** have congealed benzene. In order to compare their gel strength, the T_{gel} of different mixtures of **3** and **4** were determined. Fig S1 shows the plot of T_{gel} against the mole % of **3** in the mixture of **3** and **4**. It is clear that 1:1 mixture of **3** and **4** forms stronger gel than the other mixtures. Similar enhanced gelation in equimolar mixture of bicomponent gelators have been reported previously.[11]

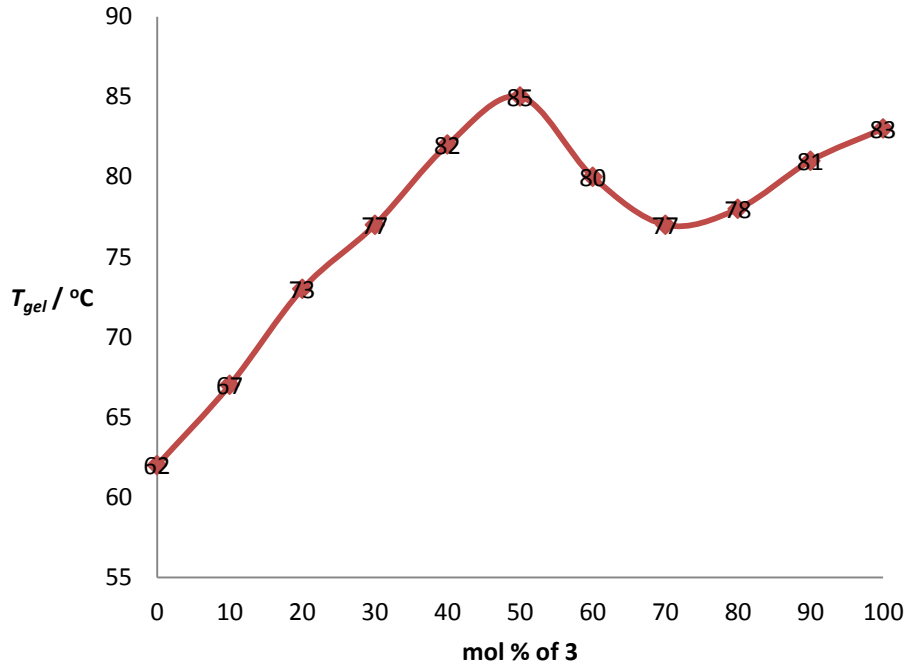


Fig. S1: Variation of T_{gel} with molar ratio of **3** and **4** in their cogels in benzene. The total concentration of the mixture was kept at 0.1 M.

7. Proof for the involvement of hydrogen bonded assembly in gelation

A) From FTIR Spectroscopy: We have compared the IR spectra of diol **3**, diol **4** and their equimolar mixture in their gel sate (benzene gel), xerogel state (obtained by freeze drying their benzene gel) and in solution state in a solvent (chloroform) that can not be congealed by these diols (no self-assembly) (Fig. S2). While the first two will give the IR spectra of their assembled state, the solution spectrum gives the IR of their free monomeric state. The chloroform solutions in all the three cases showed OH stretching as sharp peaks at frequency 3565-3585 cm^{-1} indicative of the presence of free OH. However, in gel states and in xerogel states, OH stretching appeared as broad signals between 3100-3550 cm^{-1} peaking around 3260 and 3390 cm^{-1} suggestive of the involvement of intermolecular hydrogen bonding in their supramolecular assembly and thus in gelation

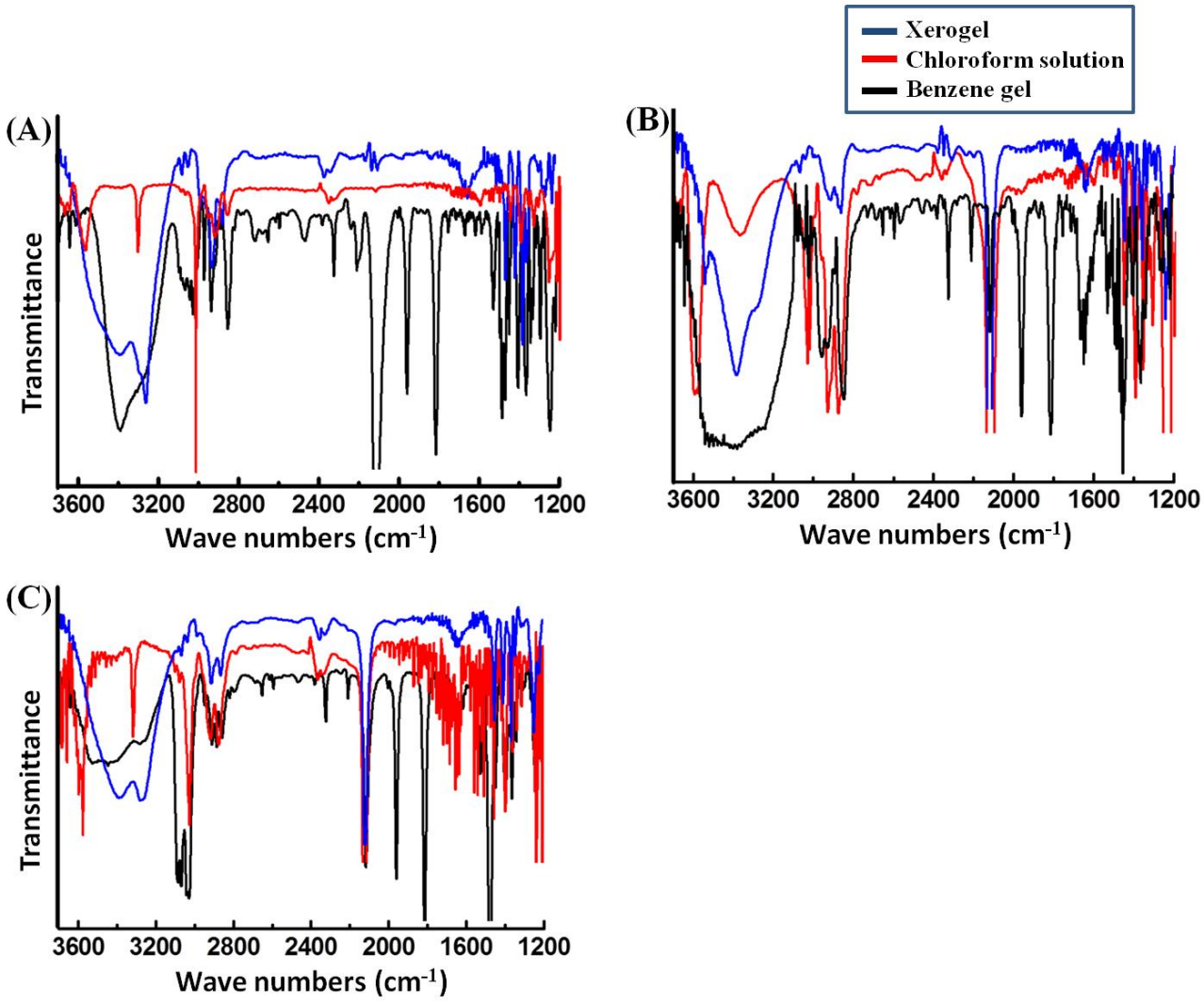


Fig. S2: IR spectra of xerogel (blue), solution in chloroform (red) and benzene gel (black) of **3** (**A**), **4** (**B**) and equimolar mixture of **3** and **4** (**C**).

B) From NMR Spectroscopy: We also performed concentration dependent ^{1}H NMR experiments with diols **3** (Fig S3) and **4** (Fig S4) individually and their equimolar mixture (Fig S5) at 298 K in C_6D_6, a gelling solvent. Both the diols showed two distinct signals corresponding to two hydroxyl protons. As the concentration of the gelators increased, signals due to these two OH protons shifted down-field in both the diols. Among diols **3** and **4**, the former showed maximum shift on increasing the concentration suggesting that the intermolecular hydrogen bonding is stronger in diol **3** when dissolved in benzene. This is in agreement with the better gelation ability of diol **3** over diol **4**. Equimolar mixture of **3** and **4** showed all the four OH signals at high dilution. As the concentration increased, all these signals due to OH protons shifted down-field as in the case of individual diols.

Interestingly, for a particular concentration, the magnitude of the shift in equimolar mixture was much more than the shift observed in either of the diols in pure form. This suggests that the intermolecular hydrogen bonding interaction in mixture of diols is much stronger than that in individual diols. This not only explains the increased gelation ability of the mixture but also suggests that there is some kind of cross talks between the two diols in the non-covalent assembly (may be a coassembly involving both the diols) leading to gelation. Thus concentration dependent NMR experiments not only prove the involvement of hydrogen bonding in gelation of diols **3**, **4** and their 1:1 mixture but also provide qualitative explanation for the relative gelation abilities of gelators **3**, **4** and their equimolar mixture.

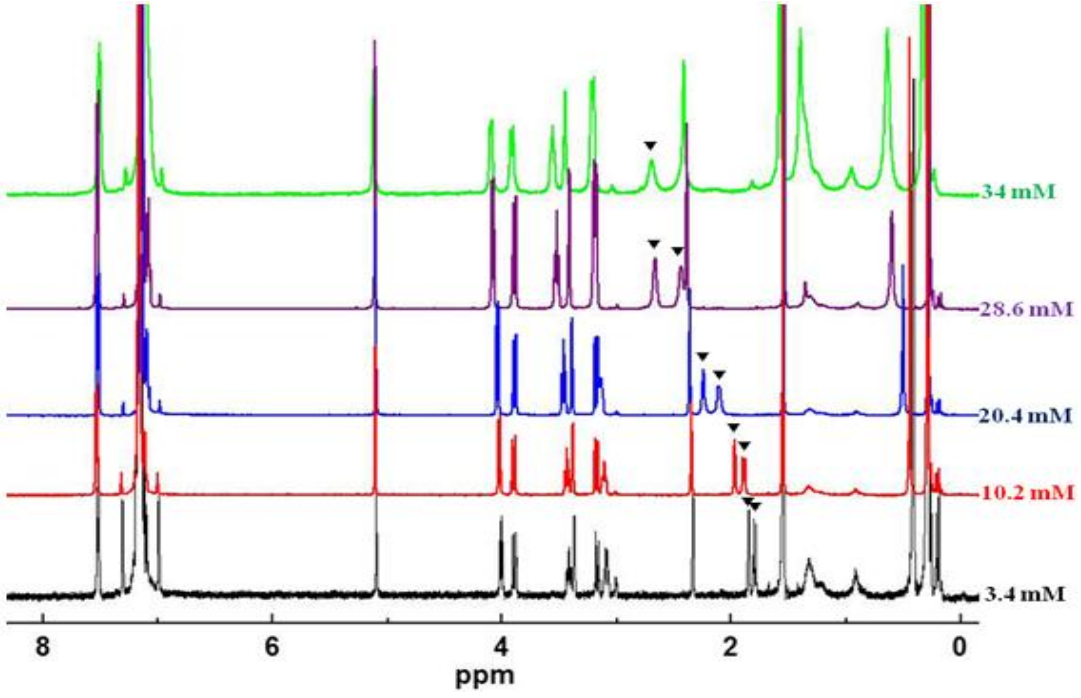


Fig. S3: Concentration dependent ^{1}H NMR of diol **3** in benzene-d6 at 25 °C.

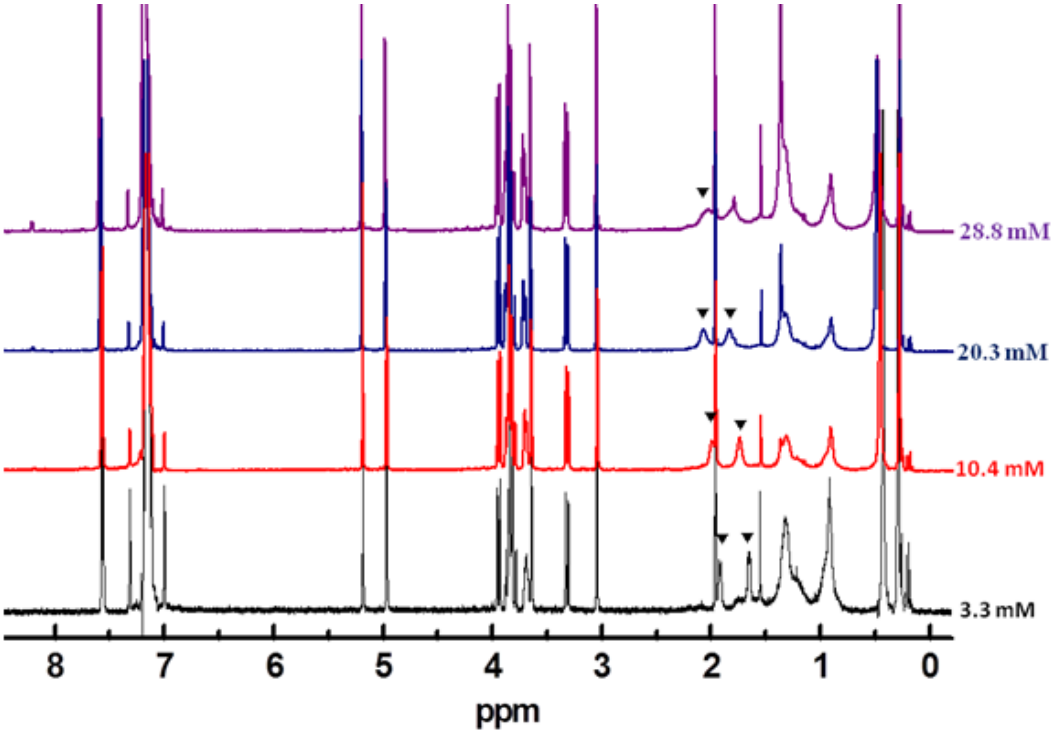


Fig. S4: Concentration dependent ^{1}H NMR of diol **4** in benzene-d6 at 25 °C.

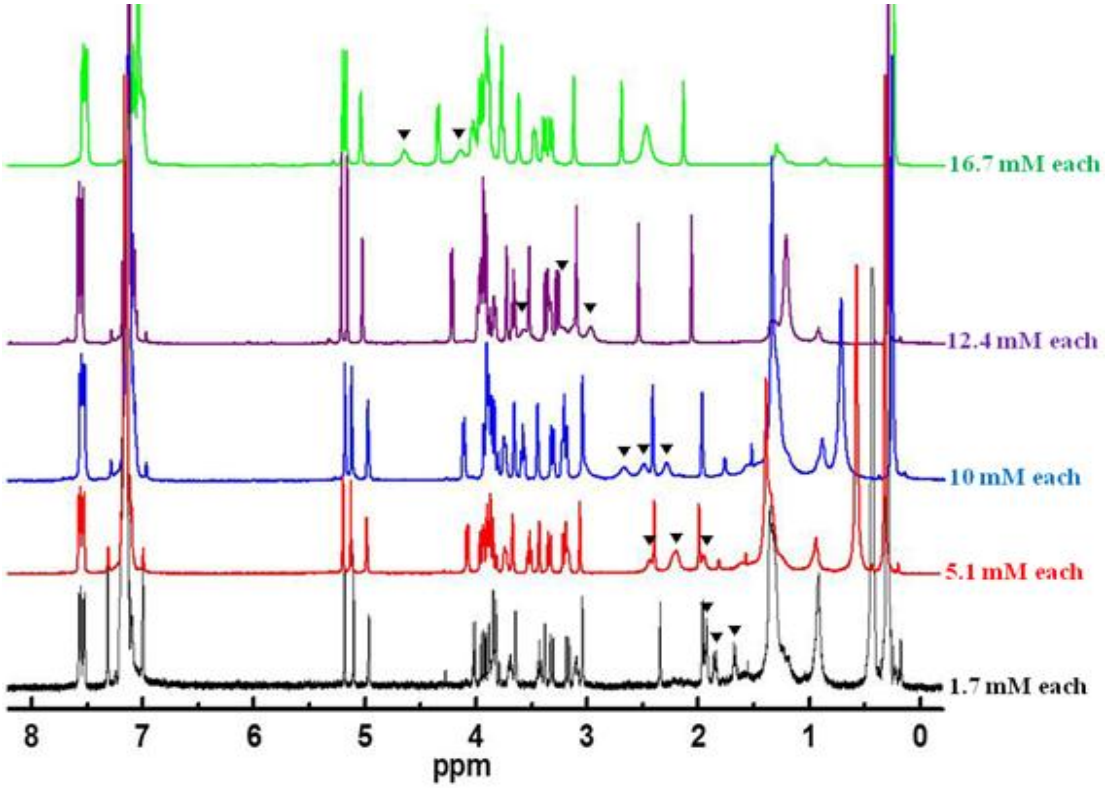


Fig. S5: Concentration dependent ^{1}H NMR of equimolar mixture of diols **3** and **4** in benzene-d6 at 25 °C.

8. Proof for the coassembly of 3 and 4 in their equimolar mixture in benzene

A) From ^{1}H NMR Spectroscopy: Since the concentration dependent ^{1}H NMR of the equimolar mixture suggested a possible coassembly of diols **3** and **4** in benzene, a gelling solvent, we decided to compare the ^{1}H NMR of the equimolar mixture with the overlaid ^{1}H NMR spectra of individual diols in a gelling solvent and in a non-gelling solvent. We have recorded ^{1}H NMR spectra of individual gelators **3**, **4** and their equimolar mixture in benzene-d6 (gelling solvent) and DMSO-d6 (non-gelling solvent) at 298 K. The ^{1}H NMR spectrum of the equimolar mixture in DMSO-d6, coincides with the overlay of ^{1}H NMR spectra of **3** and **4** in DMSO-d6 suggesting that no considerable interaction exists between **3** and **4** in their mixture in a non-gelling solvent (Fig S6). Interestingly, ^{1}H NMR of the equimolar mixture in benzene-d6 is different from the overlay of ^{1}H NMR spectra of individual gelators in benzene-d6 at same concentration (Fig S7). This indicates that in benzene-d6, a gelling solvent, the molecules of **3** and **4** are interacting with each other forming a coassembly during the process of gelation.

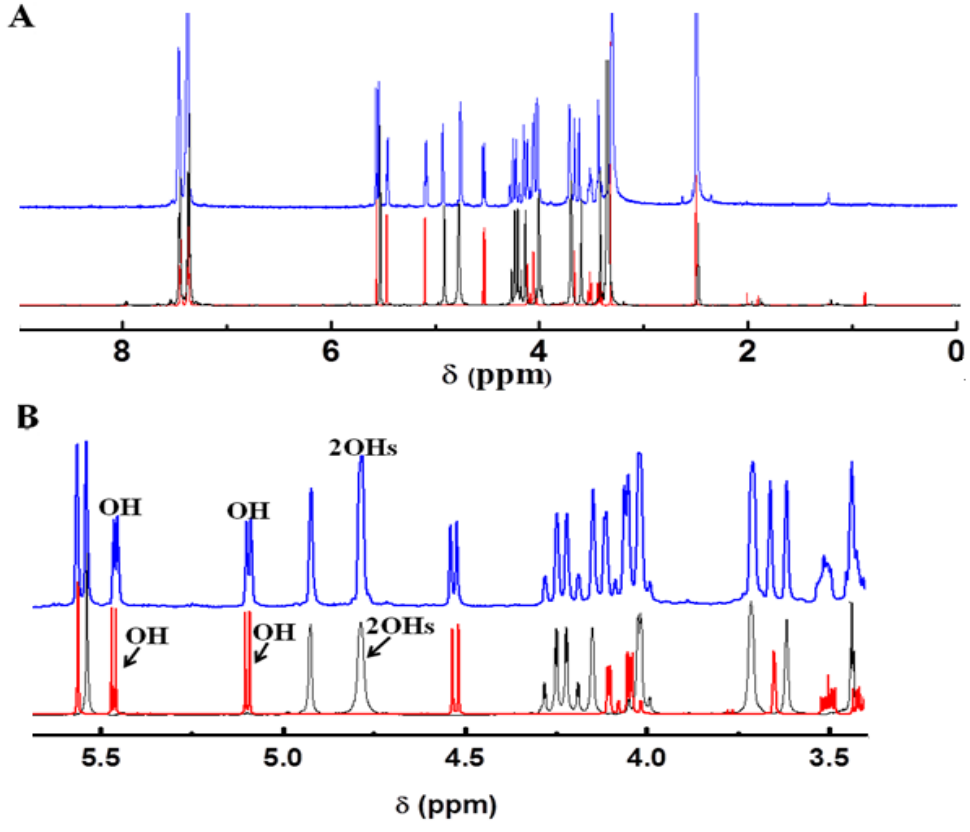


Fig. S6: (**A**) Comparison of ^{1}H NMR spectrum of equimolar mixture of **3** and **4** in DMSO-d6 (blue) with overlaid individual ^{1}H NMR spectra of **3** (red) and **4** (black) in same solvent. (**B**) Zoom showing the resemblance.

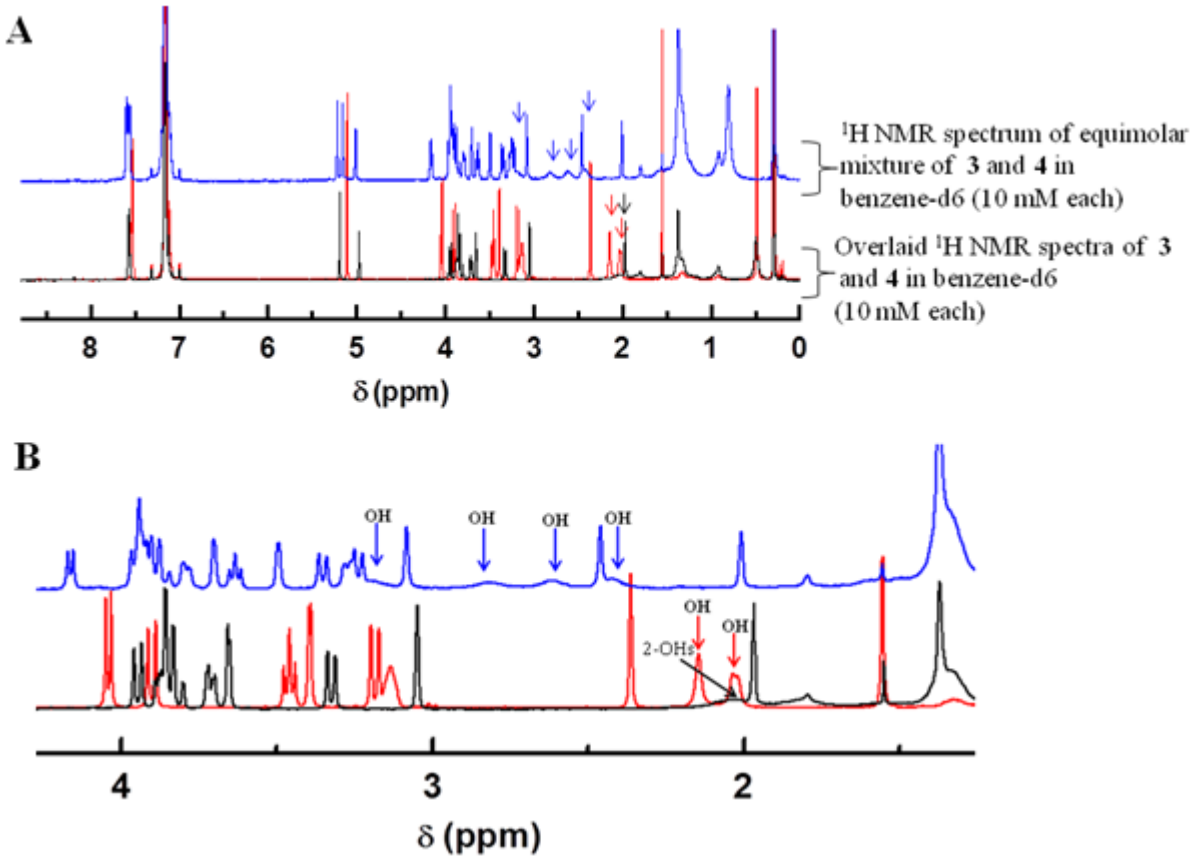


Fig. S7: (**A**) Comparison of ^{1}H NMR spectrum of equimolar mixture of **3** and **4** in benzene-d6 (blue) with overlaid individual ^{1}H NMR spectra of **3** (red) and **4** (black) in same solvent. (**B**) Zoom of spectra showing the mismatch. For these NMR studies, the concentration of each gelator was 10 mM.

B) From NOESY NMR experiment: NOESY spectrum of an equimolar mixture (10 mM each) of gelators **3** and **4** in benzene-d6 at 298 K showed some cross coupling between protons of **3** with protons of **4** (Fig S8). Protons belong to alkyne **4** are labelled as H-x′ in the Fig S8. For instance 2-OH shows cross peaks with both 2′-OH and 3′-OH and 3-OH shows cross peaks with 2′-OH suggesting that these hydroxyl groups are close to each other. This is in support of the coassembly involving intermolecular hydrogen bonding between the molecules of **3** and **4**.

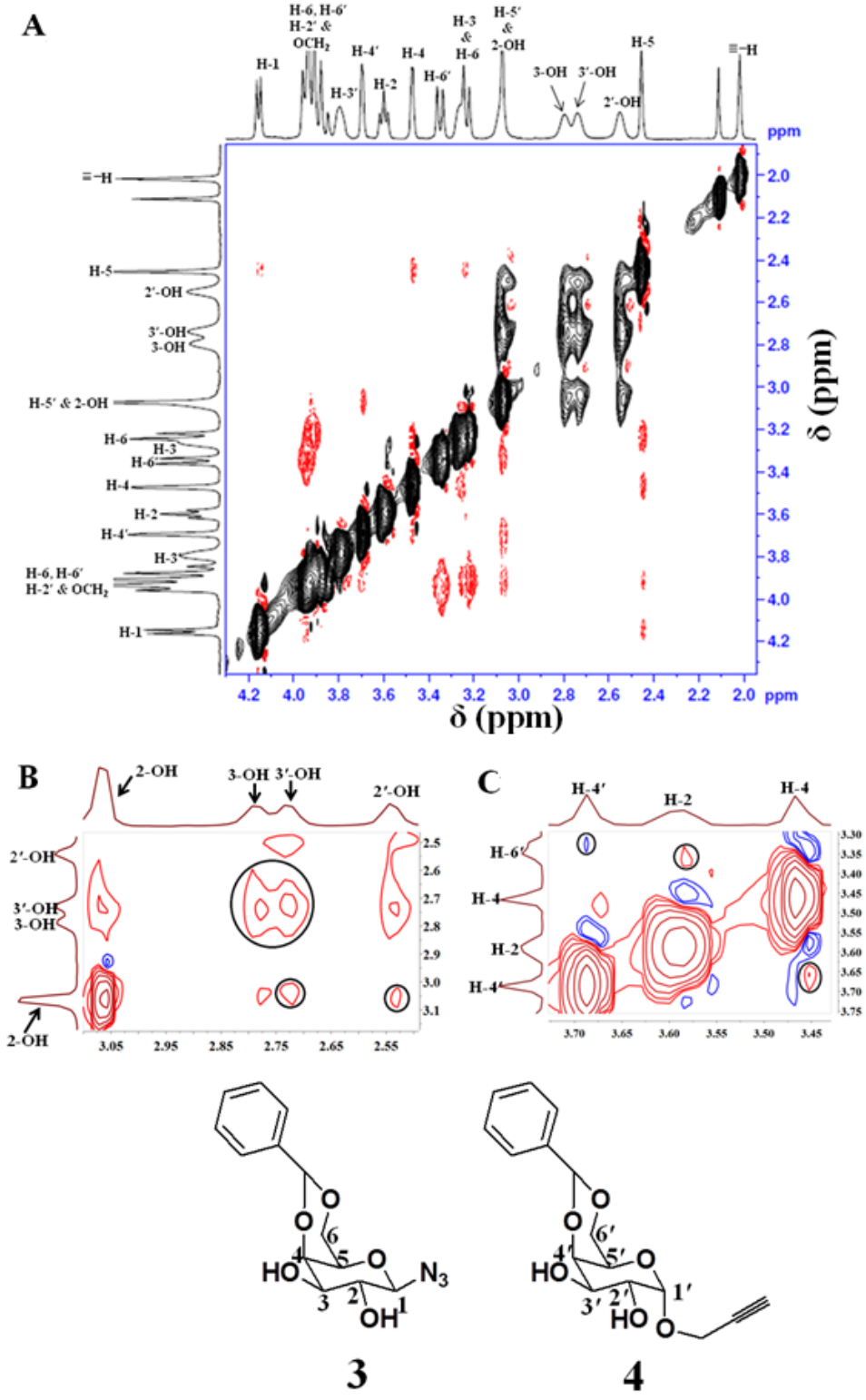


Fig. S8: (**A**) NOESY spectrum of equimolar mixture of **3** and **4** in benzene-d6. (**B**) Cross peak between hydroxyl protons of **3** and **4**. (**C**) Other prominent cross peaks between protons of **3** and **4**.

C) From Thermo Gravimetric Analysis (TGA): Thermogravimetric analysis of xerogels of **3**, **4** and their equimolar mixture were conducted using Universal V4.7A TA instrument. Small amount of xerogel was placed in alumina holder inside the furnace of TGA instrument and heated till the material was decomposed. While the xerogel of azide **3** decomposed at 157 °C and alkyne **4** decomposed at 213 °C, the xerogel of their equimolar mixture was stable up to 258 °C (Fig S9). This suggests that the equimolar mixture is much more stable than the individual components. This is supportive of a coassembly between the two components.

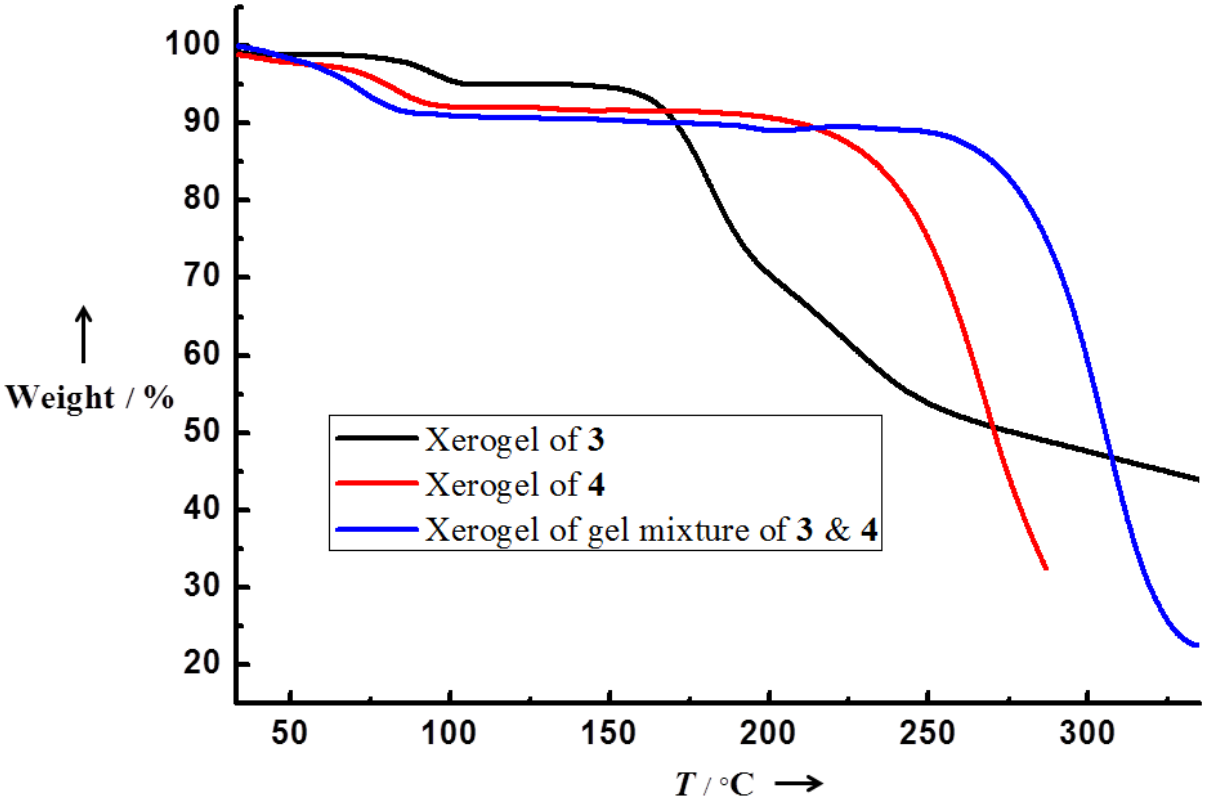


Fig. S9: TGA profiles of xerogels of gelators **3**, **4** and their equimolar mixture.

D) From Powder XRD experiments: We have prepared xerogels of **3**, **4** and their equimolar mixture by freeze drying their 2 wt% benzene gel. Also, we prepared a physically mixed xerogels of **3** and **4** in 1:1 ratio. The PXRD experiments of all these samples were done in a slow and continuous scan rate mode using Cu as anode material ($K_{\alpha 1}$ = 1.540598Å). The PXRD pattern of the physical mixture (red) matched with the overlay of PXRD spectra of **3** (black) and **4** (blue) as expected (Fig S10). However, the PXRD spectrum of the xerogel of equimolar mixture (green) was

different from the overlay of PXRD spectra of **3** and **4** or their physical mixture. This provides strong evidence for the formation of a new phase through the coassembly of **3** and **4** in the gel of their equimolar mixture.

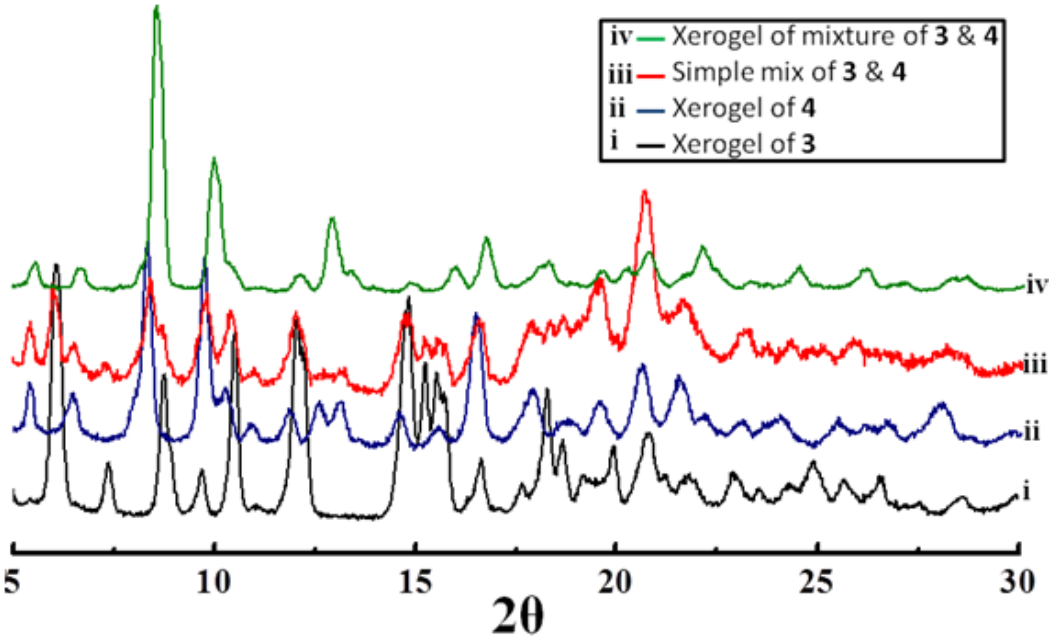


Fig. S10: PXRD spectra of xerogel of **3** (**i**), xerogel of **4** (**ii**), physical mixture of xerogels of **3** & **4** (**iii**) and xerogel of equimolar mixture of **3** & **4** (**iv**).

9. Morphological studies of xerogels of 3, 4 and their equimolar mixture using Scanning Electron Microscopy (SEM)

The xerogels were made by freeze drying the gels in benzene. A small amount of xerogel was placed on carbon-tape pasted on a copper disc and then the sample was sputter coated with gold using JEOL Fine coat Ion sputter JFC-1100 and directly imaged under the scanning electron microscope. The xerogels of **3** and **4** showed elongated fibrous or rod-like structures whereas the xerogel of equimolar mixture of **3** and **4** showed cross linked fibers with multiple fusion nodes (Fig S11). This morphological difference explains the increased stability of the gels formed by equimolar mixture of **3** and **4**.

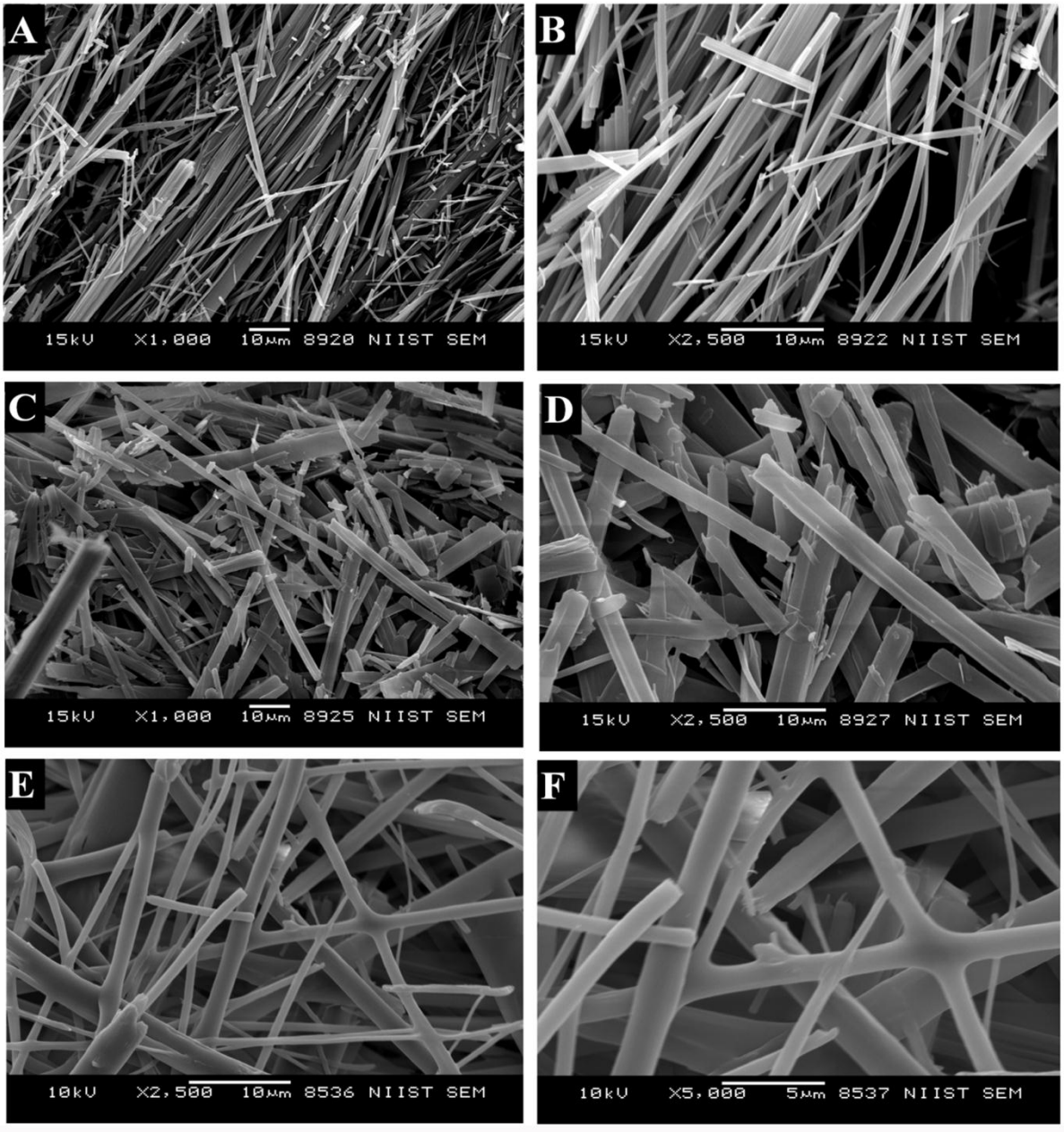
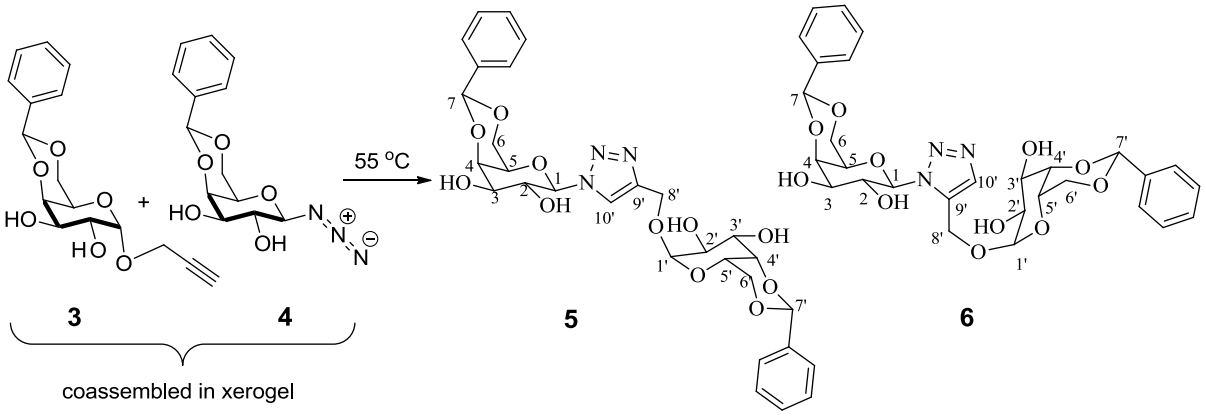


Fig. S11: SEM images of xerogel of: (**A**) & (**B**) **3** made from 0.83 wt % benzene gel; (**C**) & (**D**) **4** made from 0.87 wt % benzene gel; (**E**) & (**F**) equimolar mixture of **3** and **4** made from 1 wt % benzene gel

10. Topochemical Huisgen reaction between 3 and 4 in xerogel state



73 mg (0.25 mmol) of **3** and 76 mg (0.25 mmol) of **4** were dissolved in 7.5 mL of benzene by heating and the resultant solution was cooled to room temperature to obtain 2 wt% gel. The equimolar co-gel thus obtained was freeze dried (without disturbing the gel) in a freeze-drier under high vaccum to get the xerogel. In order to check the topochemical Huisgen reaction in this coassembly, the xerogel of equimolar mixture of **3** and **4** was kept at room temperature for several days. Trace amount of products could be identified (judged from ^{1}H NMR spectrum) after one week. However, the reaction was too slow to be probed systematically. Though the azide-alkyne cycloaddition has a high thermodynamic drive ($\Delta G^{o} \approx$ -61 kcal mol^{-1}), the high activation barrier ($\Delta G \approx$ +26 kcal mol^{-1}) might prevent/slow-down the spontaneous reaction unless the azide and alkyne are trapped in a transition-state like arrangement.[12] One way to overcome this barrier and to facilitate faster reaction is by increasing the temperature. Hence the xerogel was was kept in an oil bath maintained at 55 °C. The progress of the reaction was monitored by TLC. Once the reaction is almost complete (about one week, after which no further change in product/starting material is observed), the products were purified by flash column chromatography using 10% methanol in chloroform as the eluent to obtain **5** (R_F = 0.25, white solid, 53 mg, 35.6%) and **6** (R_F = 0.36, white solid, 54 mg, 36.2%). In addition, 34 mg of the left over starting materials was isolated as a 1:1 mixture of **3** & **4** (not separated).

The structure of each isomer was unambiguously established by using different NMR techniques such as ^{1}H NMR, ^{13}C NMR, DEPT, COSY, HMQC and HMBC. The high polar isomer (R_F = 0.25) showed a singlet at δ 8.30 ppm corresponding to a single triazolyl proton and the low polar isomer (R_F = 0.36) showed the triazolyl proton at δ 7.83 ppm. The high polar isomer, showed HMBC correlation between C-10′ and H-1. However, no correlation was seen between H-1 and C-9′. On

the other hand, the HMBC spectrum of low polar isomer, showed cross peak between C-9′ and H-1but not between C-10′ and H-1 or between C-1 and H-10′. These correlations confirm that the high polar isomer is 1,4-isomer **5** and the low polar isomer is 1,5-isomer **6**. Both compounds **5** and **6** or their mixture could not congeal any of the common polar or non-polar solvents.

Data of 1,4-isomer **5**: m.p. 166-167°C**;** ^{1}H NMR (DMSO-d6, 500 MHz) δ: 8.30 (s, 1H, H-10′), 7.53 (d, 2H, *J* = 6.5 Hz, Ar-*H*), 7.48-7.47 (m, 2H, Ar-*H*), 7.43-7.37 (m, 6H, Ar-*H*), 5.66 (d, 1H, *J* = 9.2 Hz, H-1), 5.63 (s, 1H), 5.55 (s, 1H), 5.38 (d, 1H, *J* = 5.9 Hz, OH-2), 5.27 (d, 1H, *J* = 5.9 Hz, OH), 4.98 (d, 1H, *J* = 3.2 Hz, H-1′), 4.77 (d, 1H, *J* = 12.2 Hz, H-8′), 4.71 (t, 2H, *J* = 6 Hz, OHs), 4.62 (d, 1H, *J* = 12.2 Hz, H-8′), 4.26 (d, 1H, *J* = 3.2 Hz), 4.19-4.14 (m, 2H, H-2), 4.11-4.03 (m, 4H), 3.91 (s, 1H), 3.79-3.69 (m, 3H, H-3, H-2′ & H-3′), 3.68 (s, 1H). ^{13}C NMR (DMSO-d6, 125 MHz) δ: 144.05 (C-9′), 138.76, 138.56, 128.65, 128.51, 127.92, 127.83, 126.38, 126.26 (aromatic carbons), 122.77 (C-10′), 100.03, 99.78, 99.45 (C-1′), 87.69 (C-1), 76.50, 75.89, 72.34, 68.74, 68.64, 68.58, 68.23, 68.15, 67.88, 62.85, 60.65 (C-8′). Anal. Calcd for $C_{29}H_{33}N_3O_{11,}$ $[M+H]^+$, 600.2144; HRMS calcd for $C_{29}H_{33}N_3O_{11,}$ $[M+H]^+$, 600.2115. Elemental analysis calculated for $C_{29}H_{33}N_3O_{11}$, C = 58.09, H = 5.55, N = 7.01; Found C = 58.13, H = 5.37, N = 6.91.

Data for 1,5-isomer **6**: m.p. 161-162°C; ^{1}H NMR (DMSO-d6, 500 MHz) δ: 7.83 (s, 1H, H-10′), 7.53-7.51 (m, 2H, Ar-*H*), 7.48-7.47 (m, 2H, Ar-*H*), 7.43-7.37 (m, 6H, Ar-*H*), 5.73 (d, 1H, *J* = 9.2 Hz, H-1), 5.64 (s, 1H), 5.56 (s, 1H), 5.28 (d, 1H, *J* = 6.1 Hz, OH-2), 5.24 (d, 1H, *J* = 5.9 Hz, OH), 4.98 (d, 1H, *J* = 13.7 Hz, H-8′), 4.89 (m, 3H, H-1′, OHs), 4.83 (d, 1H, *J* = 11.1 Hz, H-8′), 4.33-4.28 (m, 1H, H-2), 4.26 (d, 1H, *J* = 2.9 Hz), 4.16 (d, 1H, *J* = 2.9 Hz), 4.12-4.06 (m, 2H), 3.99-3.93 (m, 2H), 3.91 (s, 1H), 3.81-3.71 (m, 3H, H-3, H-2′ & H-3′), 3.59 (s, 1H). ^{13}C NMR (DMSO-d6, 125 MHz) δ: 138.65, 138.54, 134.65 (C-9′), 133.55 (C-10′), 128.78, 128.58, 128.00, 127.88, 126.37, 126.25, 100.11, 99.70, 99.13 (C-1′), 87.10 (C-1), 76.38, 75.96, 68.47, 68.42, 68.24, 67.97, 67.85, 67.65, 63.06, 57.70 (C-8′). Anal. Calcd for $C_{29}H_{33}N_3O_{11,}$ $[M+H]^+$, 600.2144; HRMS calcd for $C_{29}H_{33}N_3O_{11,}$ $[M+H]^+$, 600.2115. Elemental analysis calculated for $C_{29}H_{33}N_3O_{11}$, C = 58.09, H = 5.55, N = 7.01; Found C = 58.11, H = 5.69, N = 7.04.

11. The textural characterization of the xerogel after the reaction

A) By SEM: Xerogel of an equimolar mixture of **3** and **4** after the reaction (55 ºC, 7 days) was analyzed using SEM. It was found that the fibrous texture was retained even after the reaction (Fig

S12) suggesting that there is no phase change during the reaction, which is in support ofthe topochemical nature of the reaction. Though the junction nodes are not seen in the SEM after the reaction, smaller fibers are seen. Probably, the longer fibers with junction nodes are fragmented into smaller fibers, due to the fragile nature of the fibril after reaction because of the lack of strong interaction between the products in the fibers (in contrast to the one dimensional hydrogen bonded assembly of gelators **3** and **4** in the fibril before reaction). The fact that the products, **5** & **6**, don't form gels supports this line of thought (that means they cant form/stabilize one dimensional hydrogen bonded assembly).

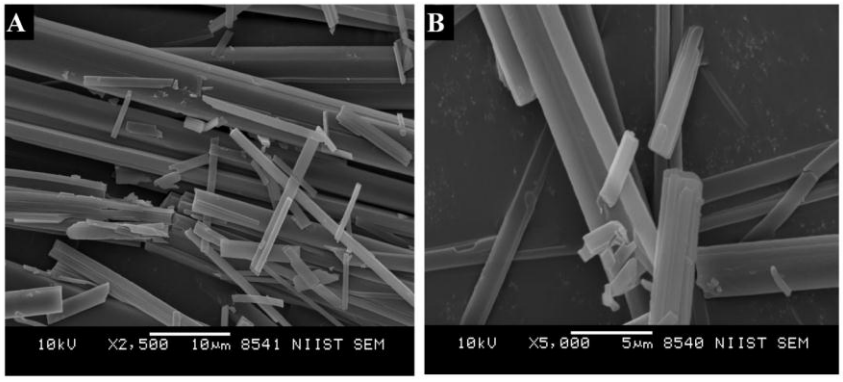


Fig. S12: SEM image of the xerogel of an equimolar mixture of **3** and **4** after topochemical reaction at 55 ºC for 7 days.

B) By Powder XRD: A bulk of the xerogel of an equimolar mixture of **3** and **4** was kept at 55 ºC. At different time period small fractions were withdrawn and analyzed using PXRD. A comparison of the PXRD profiles of the xerogel obtained at different time revealed that the crystalline nature is maintained during the reaction with gradual disappearnace of some of the peaks in the starting xerogel (Fig S13). For instance, the peak at $2\theta = 8^{o}$ diasppaeared gradually during the course of the reaction and other peaks shifted slightly. The conserved crystalline nature during the reaction is another strong evidence for the topochemical control in the reaction.

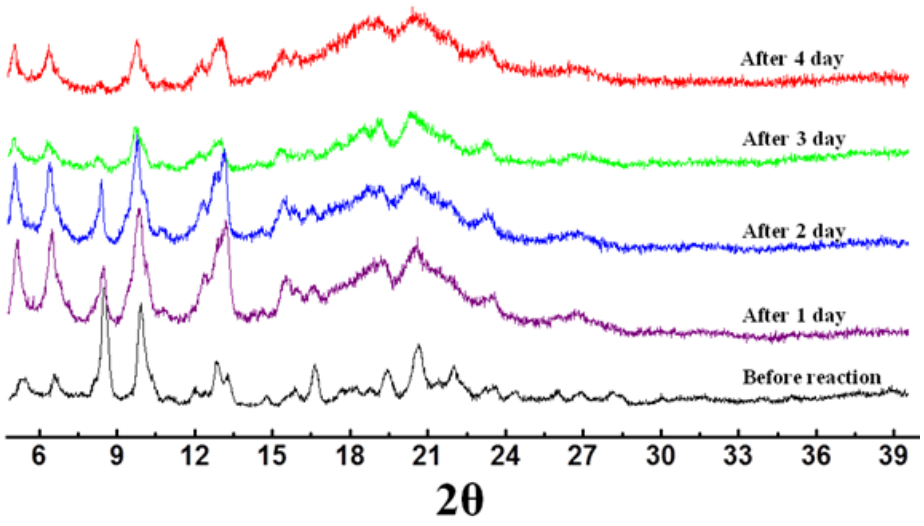


Fig. S13: PXRD spectra at different time shows that the reaction is a crystal-to-crystal transformation (topochemical reaction).

12. Kinetic study of the topochemical reaction using NMR spectroscopy

A bulk amount of xerogel of the equimolar mixture of **3** and **4** was made as described previously and was a kept in an oil bath maintained at constant temperature of 55 ºC. A small fraction was withdrawn from this bulk at different time and recorded its ^{1}H NMR spectrum after dissolving in DMSO-d6. This was continued till no more change in the ratio of product to the reactants was observed. At each point of time, the ratio of two products **5** and **6** was 1:1 (Fig S14). The triazolyl proton peaks at δ 8.29 and 7.83 due to two isomeric products were distinct and well separated from other peaks. Similarly, the anomeric proton of the diol **3**, one of the reactants, appeared at δ 4.55 is also clear and separated from other signals in the mixture of reactants and products. As the reaction proceeds, the relative integration of this anomeric proton will decrease and that of both the triazolyl protons will increase. Since each one mol of **3** will react with one mol of **4** to give half a mole each of both the products **5** and **6**, the fraction of reaction at any point of time was calculated by dividing sum of integration of peaks at δ 8.29 and 7.83 (proportional to the amount of product formed) with sum of integrations of peaks at δ 8.29, 7.83 and 4.55 (proportional to the initial amount of starting material) in the ^{1}H NMR spectrum at that time.

$$\%\ \text{of reaction} = \frac{100 \times (\text{area of peak at } \delta\ 8.29 + \text{area of peak at } \delta\ 7.83)}{(\text{area of peak at } \delta\ 8.29 + \text{area of peak at } \delta\ 7.83 + \text{area of peak at } \delta\ 4.55)}$$

Plot of % of reaction against time (Fig S15) revealed that this topochemical reaction follows a sigmoidal kinetics.

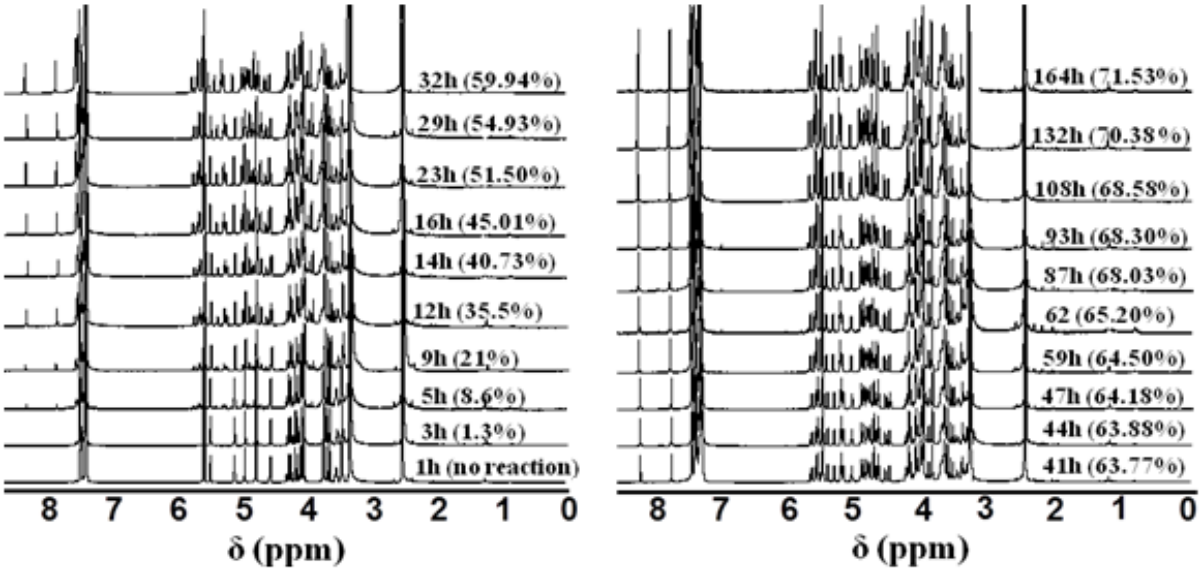


Fig. S14: Kinetics of the Huisgen reaction in the xerogel at 55 °C followed by ^{1}H NMR.

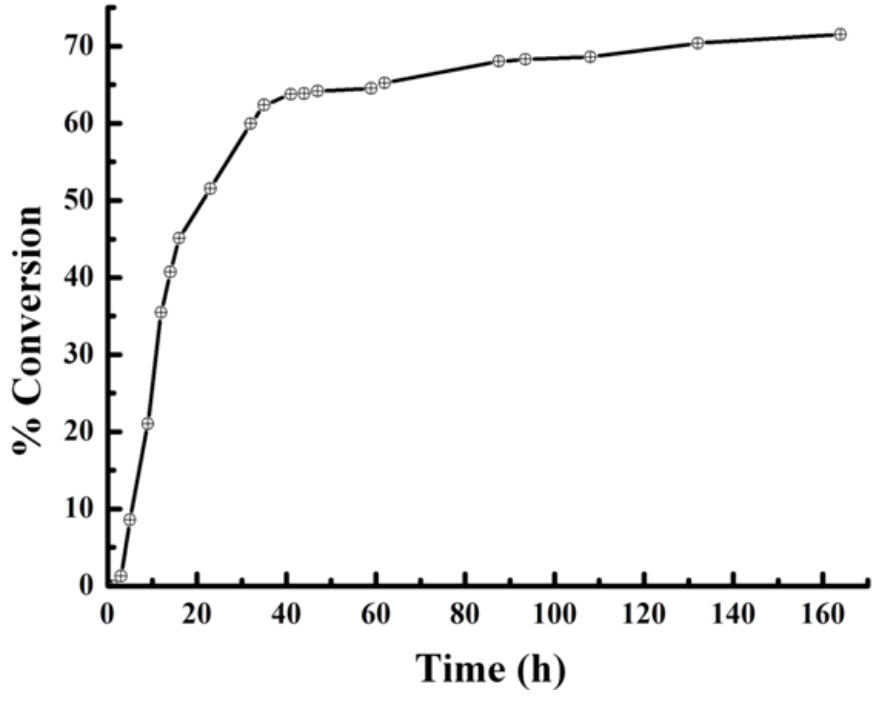


Fig. S15. Progress of reaction with time.

13. A) Probable arrangements of 3 and 4 in their coassembly leading to gelation

Based on (i) Shinkai's well studied prediction that 1D hydrogen bonding is required for gelation; (ii) the fact that hydrogen bond based organogelators adopt similar molecular packing in their crystals and in their gel fibers (iii) the reported crystal structures (Fig S16) of gelators methyl-4,6-*O*-benzylidyne-α-D-glucopyranoside (**1α**; CCDC-141743) and methyl-4,6-*O*-benzylidyne-β-D-glucopyranoside (**1β**; CCDC-149830) which are structurally similar to gelators **3** and **4** and (iv) the fact that equimolar mixture of **3** and **4** are better gelators than the individual components, we expected the coassembly of **3** and **4** to adopt hydrogen bonded assembly similar to **1α** and **1β** (One dimensional hydrogen bonding with zig-zag arrangement).

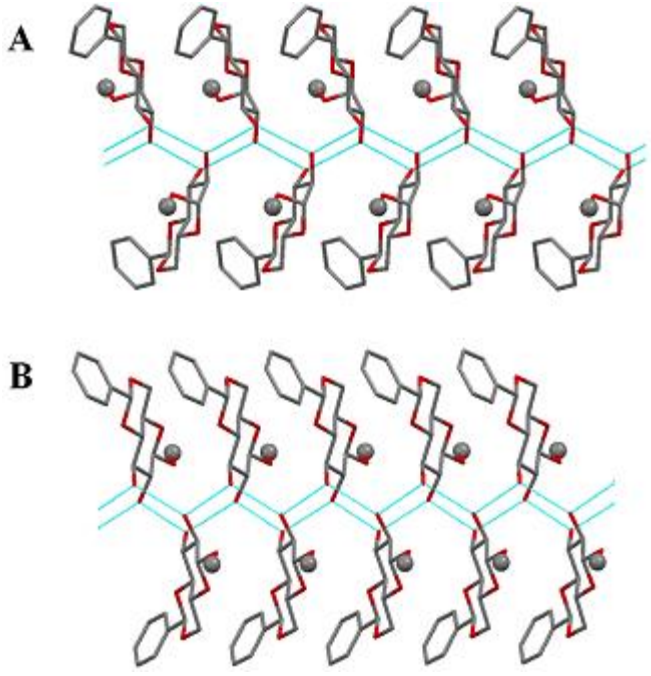


Fig. S16: Zig-zag arrangements of (**A**) Methyl-4,6-*O*-benzylidyne-α-D-glucopyranoside (CCDC-141743), (**B**) Methyl-4,6-*O*-benzylidyne-β-D-glucopyranoside (CCDC 149830).

In an equimolar mixture of **3** and **4**, several packing arrangements are possible for their coassembly into 1D hydrogen bonded assembly and are shown in Fig S17. Fig S17A shows the self sorted assembly where in both diol **3** and diol **4** self assemble separately. This possibility is ruled out based on better gelation of the equimolar mixture and different PXRD profile of its xerogel than

that of **3** or **4**. Fig S17B shows a coassembly with regular arrangement of **3** and **4** in the zig-zag hydrogen bonded assembly. But this arrangement does not explain the topochemical reaction between **3** and **4** in the fiber. Fig S17C represents another regular arrangement. This arrangement of **3** and **4** very well explains the feasibility of a topochemical reaction between azide and alkyne in **3** and **4** respectively. Also, the improved gelation ability of the equimolar mixture can be explained by invoking attractive force of interaction such as CH...π, π...π, CH...N interactions between azide and alkyne. Though minor defect in the regular assembly Fig S17C cannot be ruled out, the random arrangement (Fig S17D) is unable to explain the formation of 1:1 ratio of isomers in high (72%) yield.

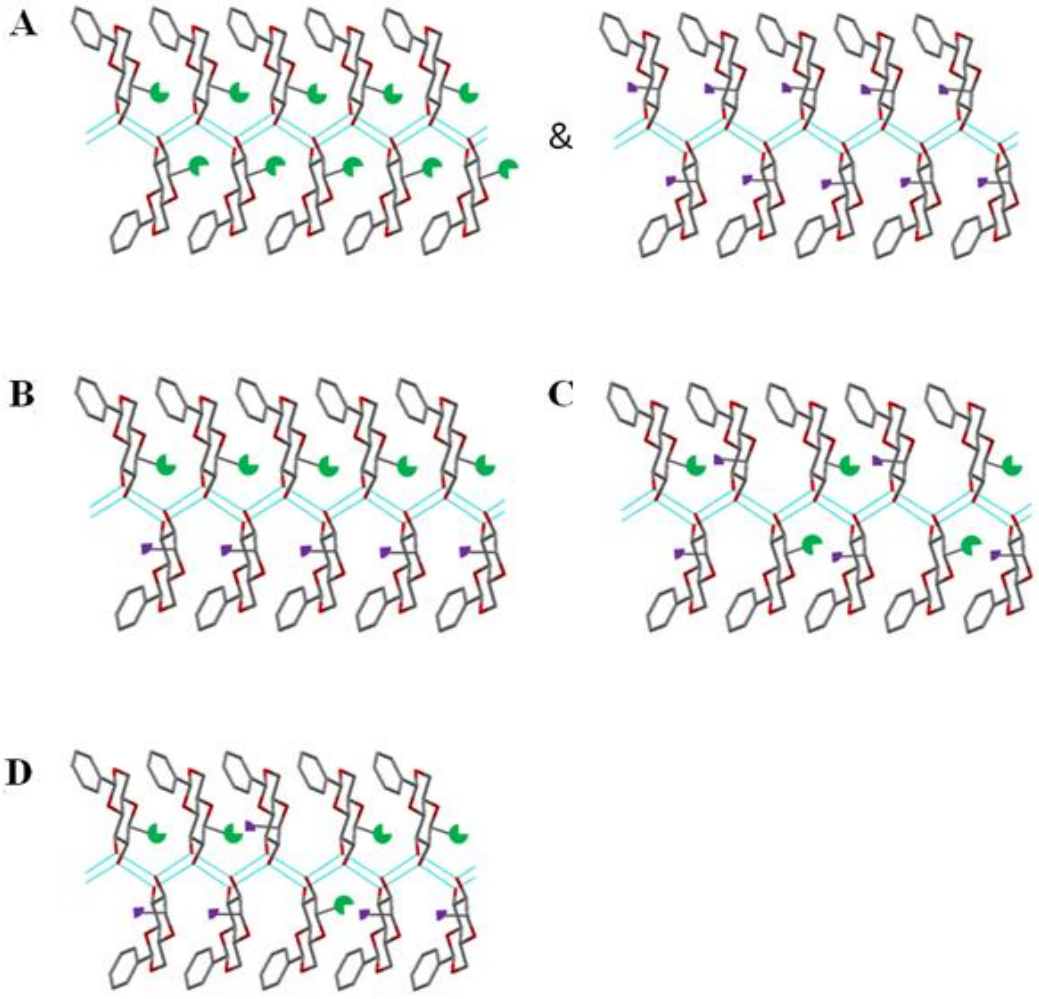


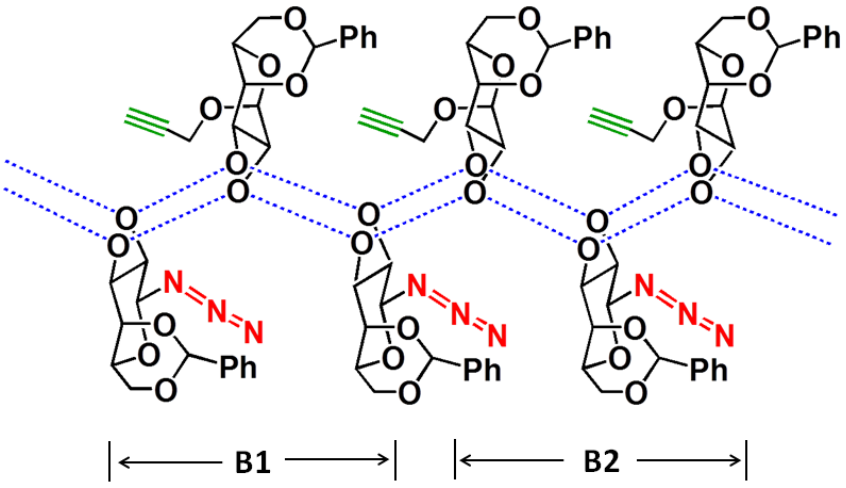
Fig. S17: Possible arrangements of **3** and **4** in coassembly.

B) DFT Calculations

The stability of the two possible coassembled arrangements B and C were comapred computationally. The geometries of these arrangements were optimized at B3LYP[13-17]/6-31G[18, 19]

level of theory using Guassian09[20] package. For convenience, we have chosen two different units (one unit containing two molecules of azide **3** & one molecule of alkyne **4** and the other unit consisting of one molecule of azide **3** & two molecules of alkyne **4**) of three consecutive molecules from each of these arrangements B and C. B1 and B2 are the two different units chosen from arrangement B and C1 and C2 are two units of arrangement C (Fig. S18).

Arrangement B



Arrangement C

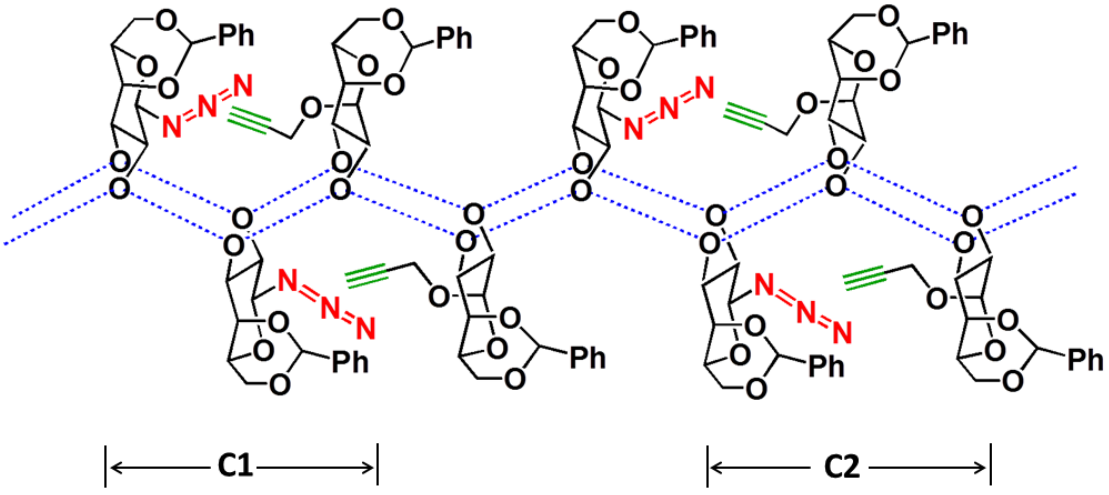


Fig. S18: Possible arrangements of **3** and **4** in coassembly

In order to understand the relative stabilities of arrangements B and C, the energies of identical units were compared. Thus B1 was compared with C1 (both containing two molecules of **3** & one molecule of **4**) and B2 was compared with C2 (both containing two molecules of **4** & one molecule of **3**). The final geometries and relative energies of optimized units are shown in Fig. S19 and Fig. S20. It was found that energy of **C2** is lower than that of **B2**. While C1 also gave an

optimized geometry similar to that of C2, we could not locate a minimum for the unit **B1** even after several days suggesting that this arrangement is very unstable. This could be due to the repulsion between two azide motifs. Thus the arrangement C, which favors the topochemical reaction, is more stable than the arrangement B.

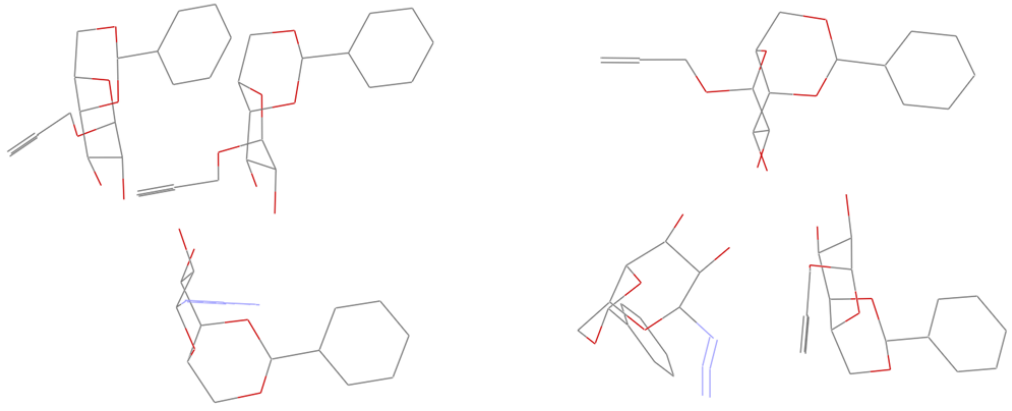


Fig. S19: Optimized structures and relative energies of units **B2** and **C2**. Hydrogen atoms are omitted for clarity.

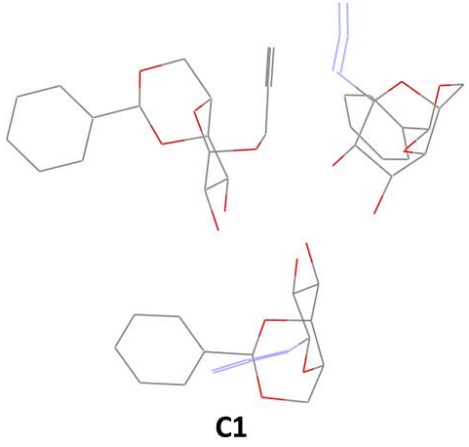


Fig. S20: Optimized structure of unit **C1.** Hydrogen atoms are omitted for clarity.

14. Probable mechanism for the topochemical reaction

We have recently shown that alkyne and azide arranged in a transition state like arrangement in the crystal undergoes spontaneous topochemical Huisgen reaction.[21] The inability of the xerogel to undergo the topochemical reaction to a considerable extent suggests that the azide and alkyne are not arranged in a TS-like arrangement. The formation of both the isomers (1,4- and 1,5-) in 1:1 ratio suggests that azide and alkyne are arranged in a way that it can attain both the possible

transition states with equal probability. It has been known that the activation barriers for the reaction leading to the formation of both 1,4-triazole and 1,5-traizole (in a model system) is very close, 25.7 kcal/mol and 26.0 kcal/mol respectively.[12] It is reasonable to think that azide and alkyne are arranged in perpendicular orientation. On heating, the flexible propargyl group can orient to both the possible transition states with equal probability (Fig S21). This explains the formation of products **5** and **6** in 1:1 ratio. However, the simultaneous existence of two packing patterns in the organogel fibers, each one favoring the formation of one of the two products cannot be ruled out.

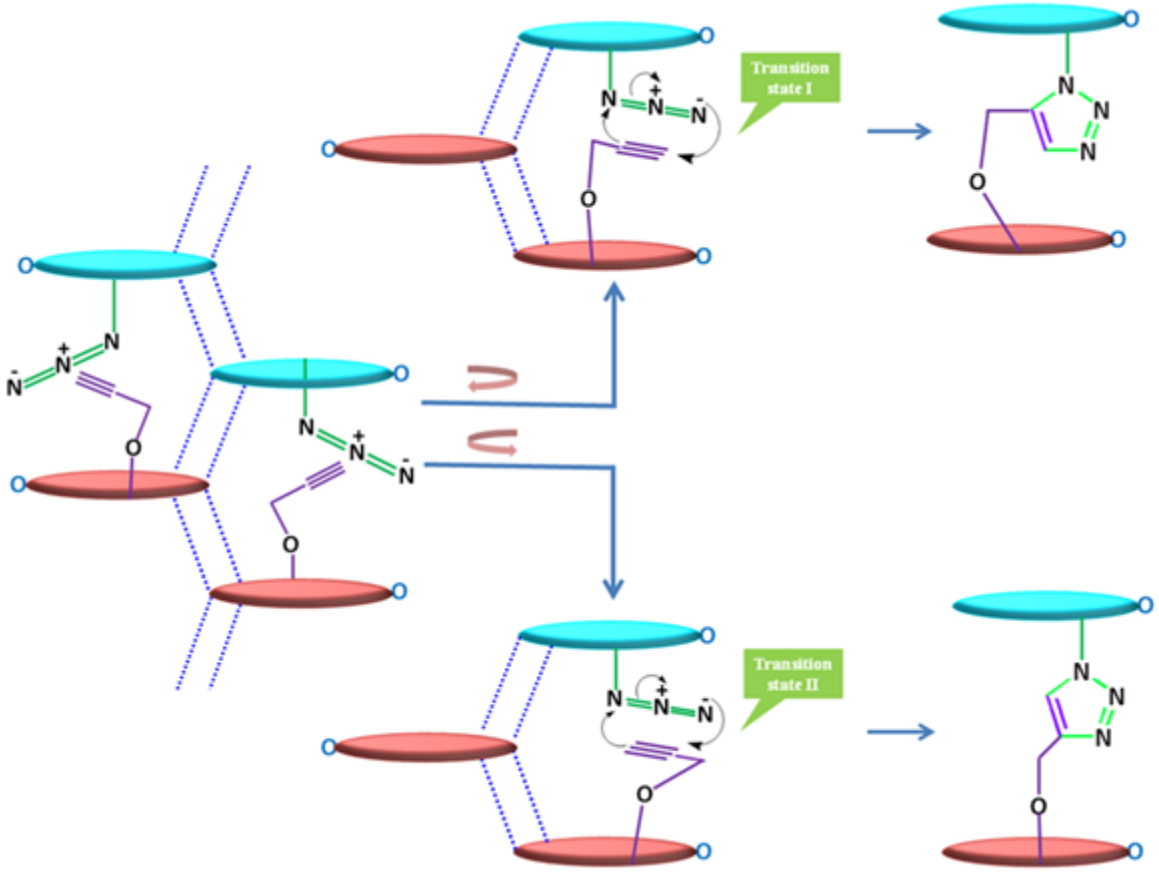


Fig. S21: Probable mechanism for the topochemical reaction between **3** and **4** in their coassembly explaining the formation of 1,4-isomer **5** and 1,5-isomer **6** in 1:1 ratio.

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15. Other control experiments to prove the topochemical nature of the reaction

A) Reaction between 3 and 4 in the organogel of their equimolar mixture: We have prepared a 2 wt% gel in benzene from equimolar mixture of **3** and **4**. The gel was kept at room temperature for 7 days. Evaporation of the benzene followed by ^{1}H NMR in DMSO-d6 revealed the formation of negligibly small amount of products. The reaction was too slow to investigate in a systematic

manner (Fig S23). Even at 50°C, the reaction did not improve in terms of yield. We presume that the dynamic nature of the assembly (especially under thermal conditions) in the gel state may be preventing it from the reaction. Also, since the products (**5** and **6**) of the reaction are non-gelators, the self assembly might get disrupted locally.

B) Reaction between 3 and 4 in the xerogel of their equimolar mixture at rt: A xerogel of equimolar mixture of **3** and **4** was kept at room temperature for several days. ^{1}H NMR of a small fraction of this after 10 days showed the presence of negligibly small amount of triazoles. This reaction was also too slow to investigate in a systematic manner (Fig S24).

C) Reaction between 3 and 4 in the xerogel of their equimolar mixture at 120 °C: A xerogel of equimolar mixture of **3** and **4** was kept in a preheated oil bath at 120 °C for 10 minutes. The xerogel melted immediately. ^{1}H NMR of a small fraction of this melt revealed that 20% of the reaction was complete in 10 minutes. But the relative ratio of the products **5** and **6** was 2.5:1. This suggest that when the reaction happened in the melt (not topochemically controlled), the relative ratio of product is not 1:1 but the reaction proceeded with a clear selectivity for the sterically less crowded 1,4-isomer **5** as expected (Fig S25).

D) No Reaction between 3 and 4 in a mixture of their xerogels at 55 °C: Xerogels of diols **3** and **4** were prepared separately. A 1:1 physical mixture of them was made by mixing thoroughly 19.8 mg of xerogel of azide **3** (0.068 mmol) and 20.8 mg of xerogel of alkyne **4** (0.068 mmol) using a spatula. This mixture was kept at 55 °C for several days. There was no reaction even after 7 days (judged by ^{1}H NMR) (Fig S26).

E) Effect of anomeric stereochemistry: No Reaction between 3 and 4-β in xerogel of their equimolar mixture at 55 °C: In order to investigate the role of anomeric stereochemistry, in this topochemical reaction, we have prepared the β-anomer of **4**, **4-β**. Diol **4-β** formed a two component 1:1 gelator system with **3** suggestive of similar mode of H-bonded coassembly as in the mixture of **3** and **4**. In order to test whether topochemical reaction between **3** and **4-β** is feasible in their xerogels, 21 mg (0,072 mmol) of **3** and 22 mg (0.072 mmol) of **4-β** were dissolved in benzene (2.15 mL) by heating and the clear solution was allowed to cool to room temperature to obtain 2 wt% gel in benzene. This gel was freeze dried to obtain its xerogel. The xerogel was kept at 55 °C. There was no reaction even after 10 days. Also, increase of temperature to 60 °C did not make any difference. Despite the fact that equimolar mixture of **3** and **4-β** make good co-gel, the inability of their xerogel to undergo Huisgen reaction support the proposed mode of assembly. As both the

reacting motifs are disposed in β-anomeric orientation, they will orient in the same direction in their coassembly (Fig S22) and hence they can not react topochemically (Fig S27) as the reacting motifs will not proximally placed in such assembly.

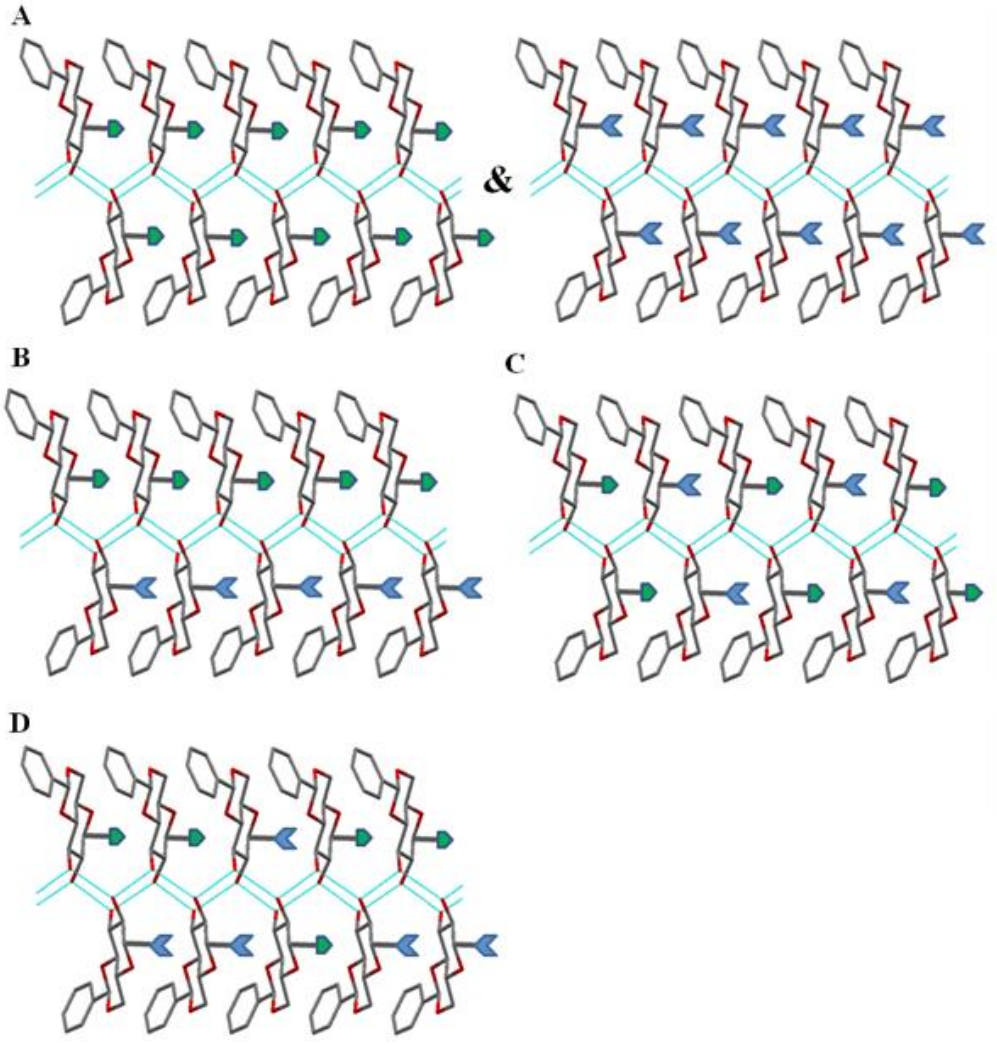

Fig. S22: Possible mode of coassembly between **3** and **4-β**. As the azide and alkyne groups are not proximal to each other, topochemical reaction is not possible.

Spectral details of control experiments

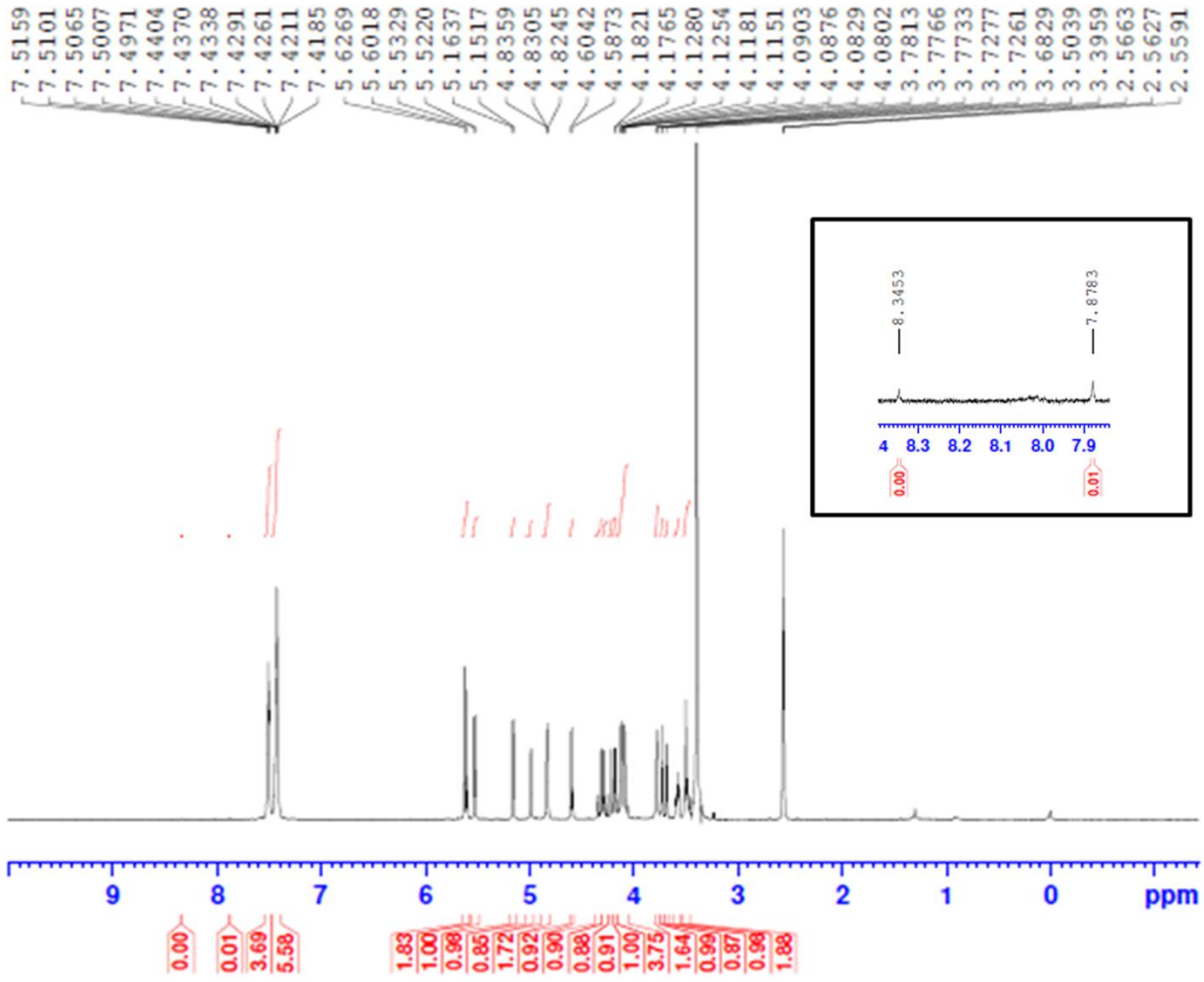

Fig. S23: ^{1}H NMR spectrum of reaction mass of **3** and **4** in organogel of their equimolar mixture at room temperature after 7 days.

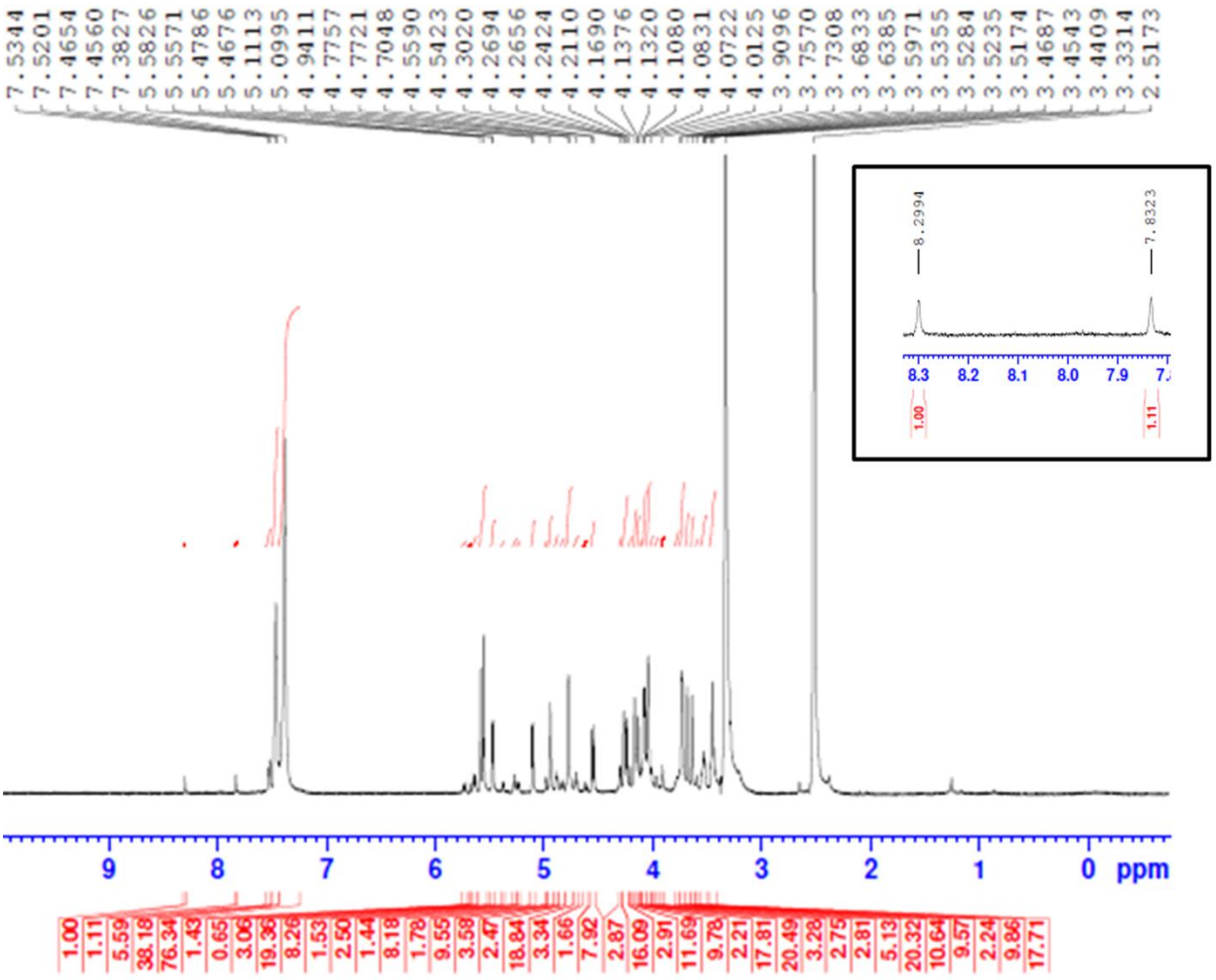

Fig. S24: ^{1}H NMR spectrum of reaction mass of **3** and **4** in the xerogel of their equimolar mixture at room temperature after 10 days.

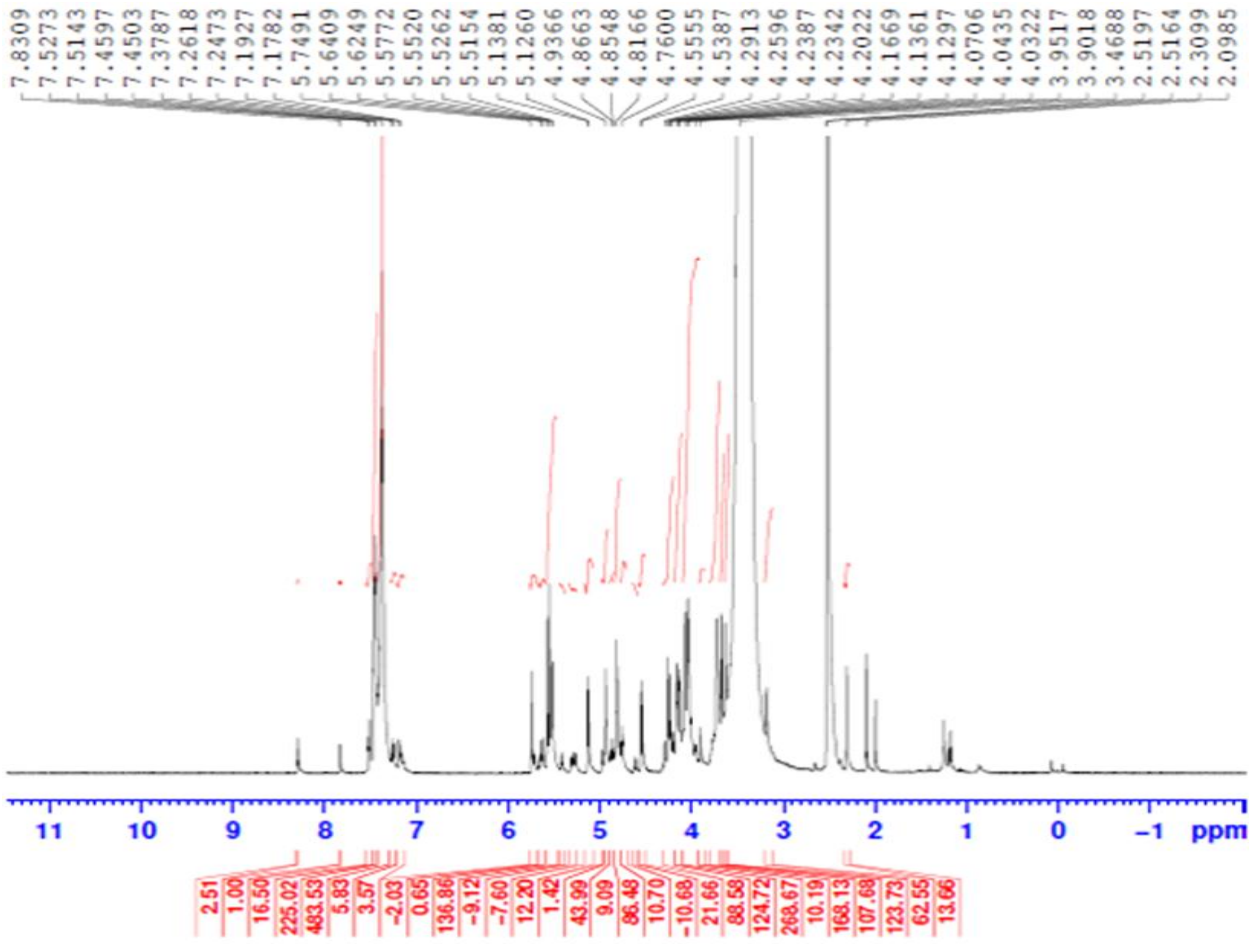

Fig. S25: ^{1}H NMR spectrum of reaction mass of **3** and **4** in the xerogel of their equimolar mixture at 120 °C.

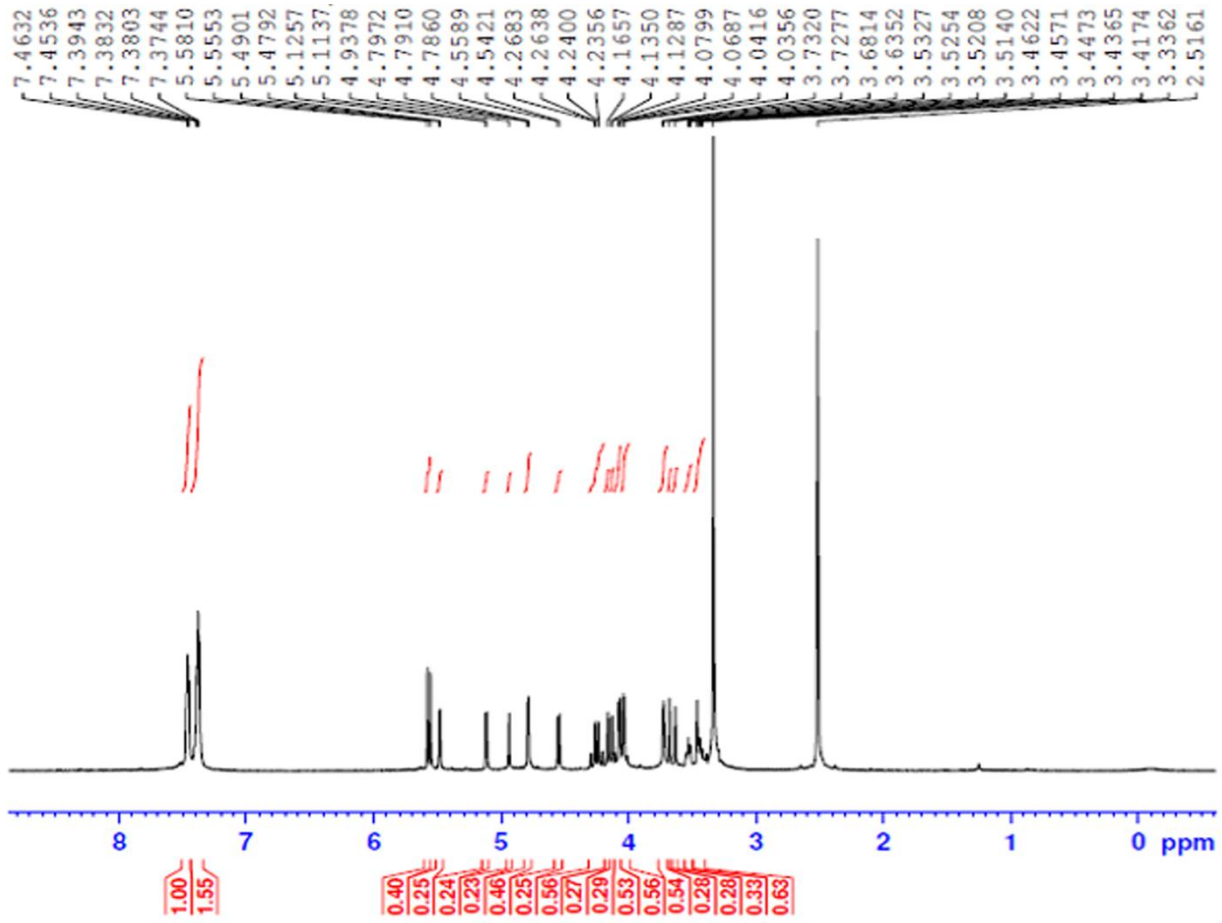

Fig. S26: ^{1}H NMR spectrum of reaction mass of **3** and **4** in a mixture of their xerogels at 55 °C after 7 days.

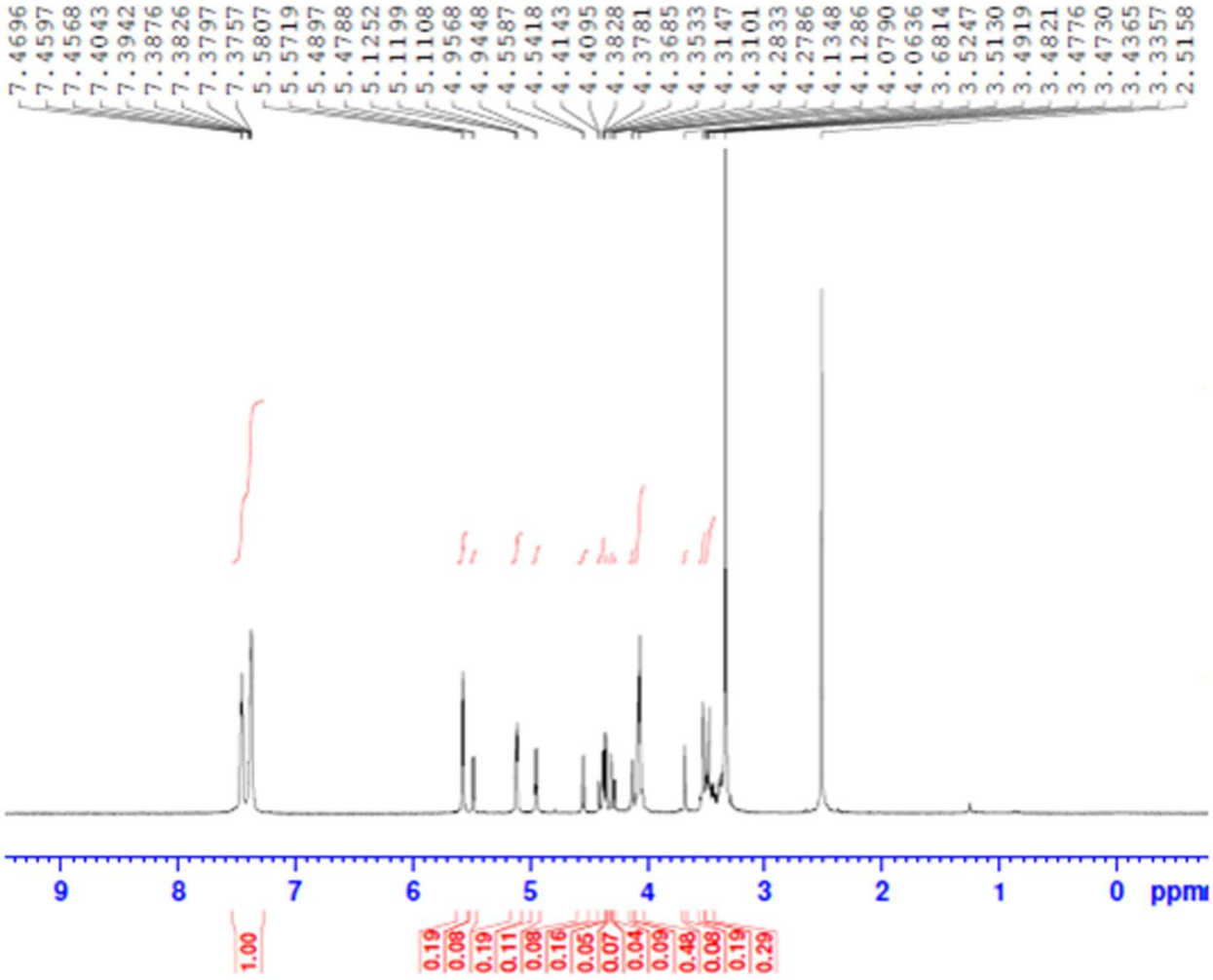

Fig. S27: ^{1}H NMR spectrum of reaction mass of **3** and **4-β** in the xerogel of their equimolar mixture at 55 °C after 10 days.

Spectral details of Compounds 5 and 6

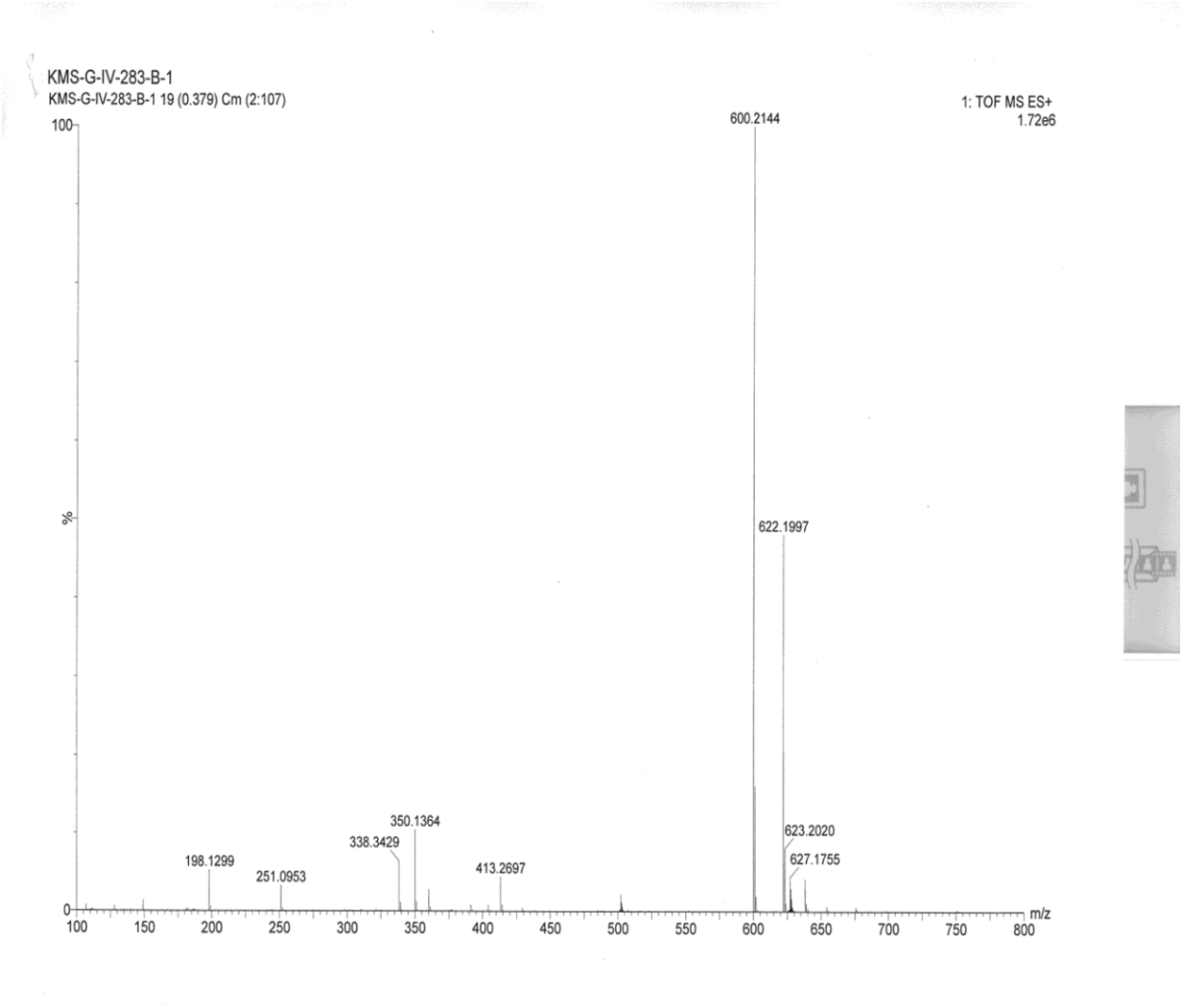

Fig. S28: HRMS spectrum of **5**.

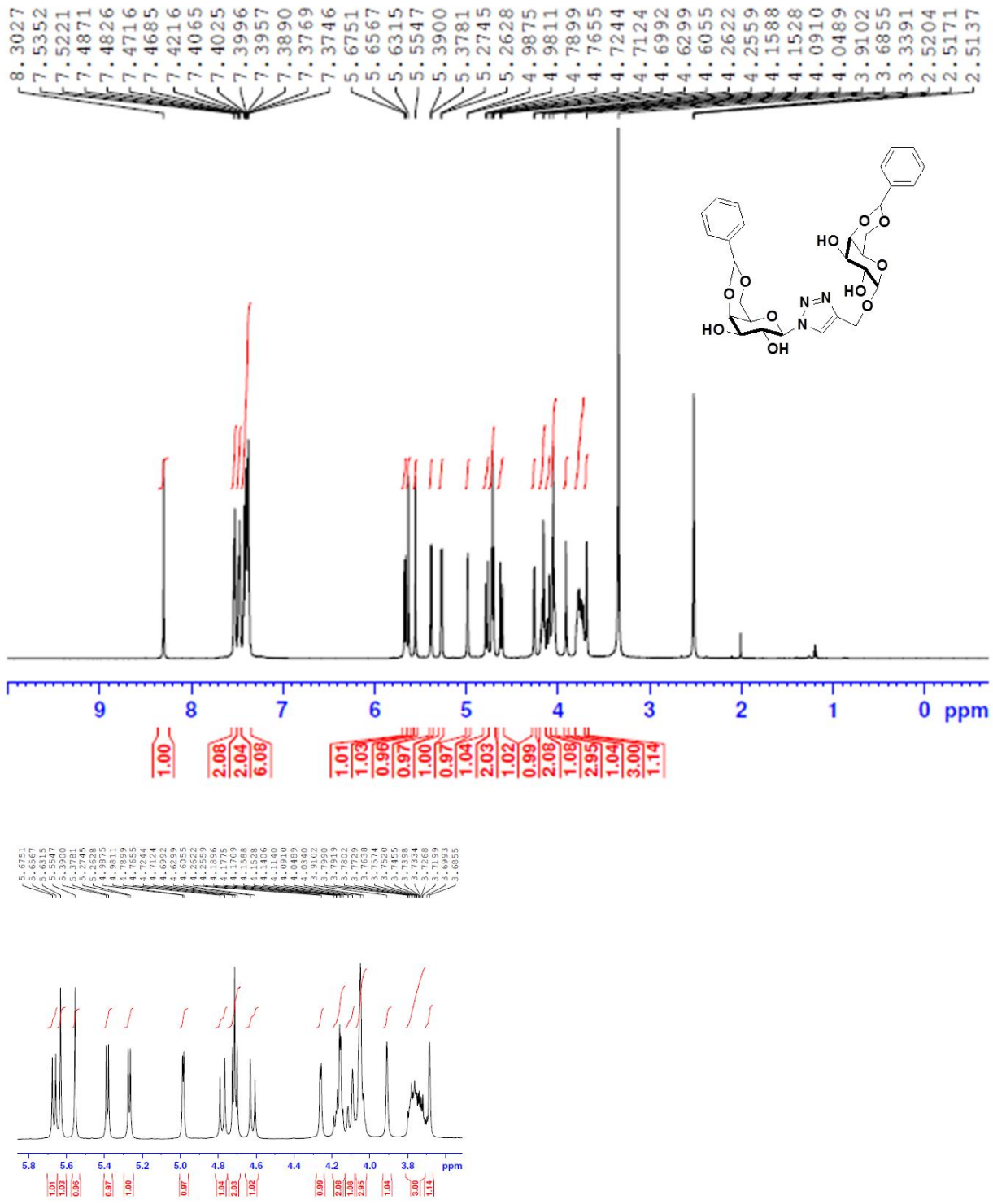

Fig. S29: ^{1}H NMR spectrum of **5** in DMSO-d6 (500 MHz).

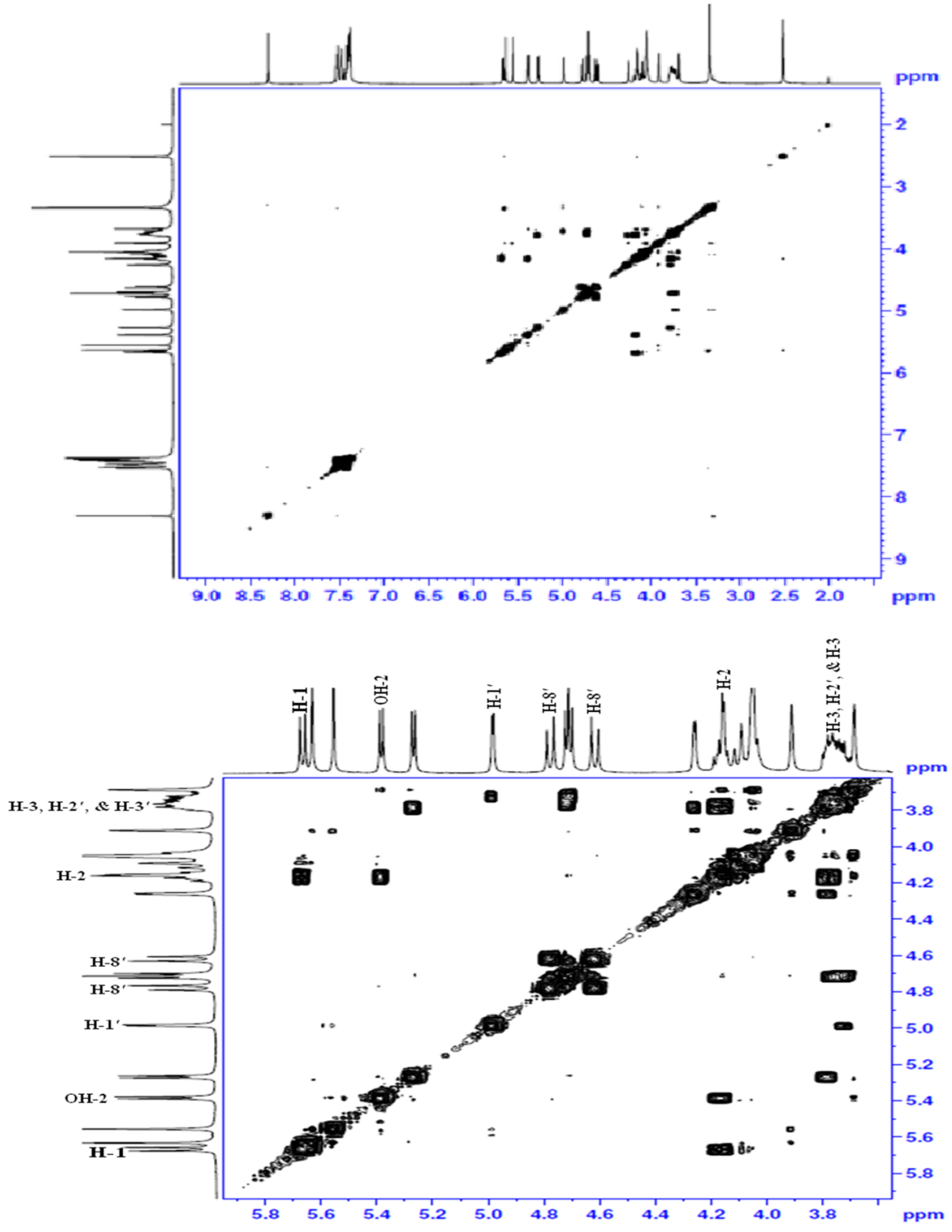

Fig. S30: COSY spectrum of **5** in DMSO-d6 (500 MHz).

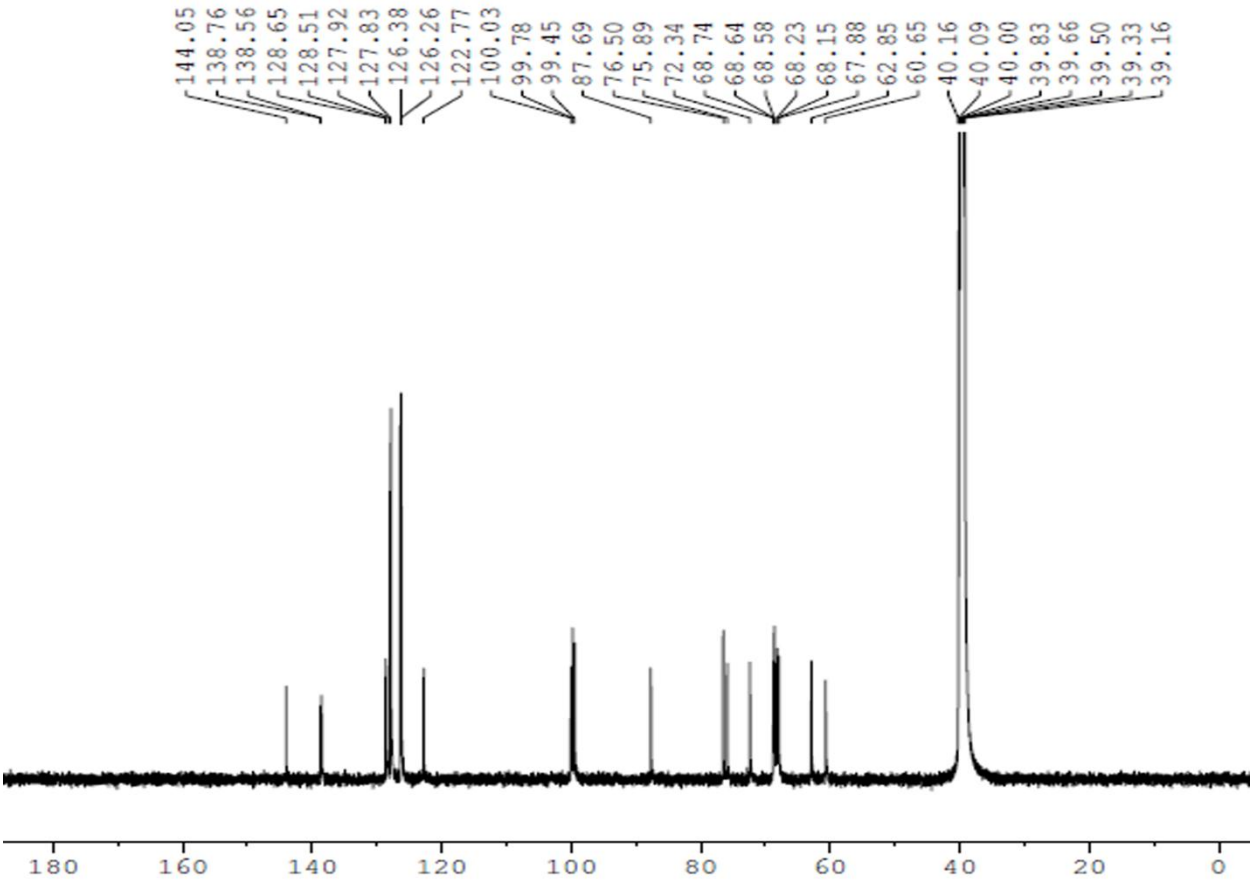

Fig. S31: ^{13}C spectrum of **5** in DMSO-d6 (500 MHz).

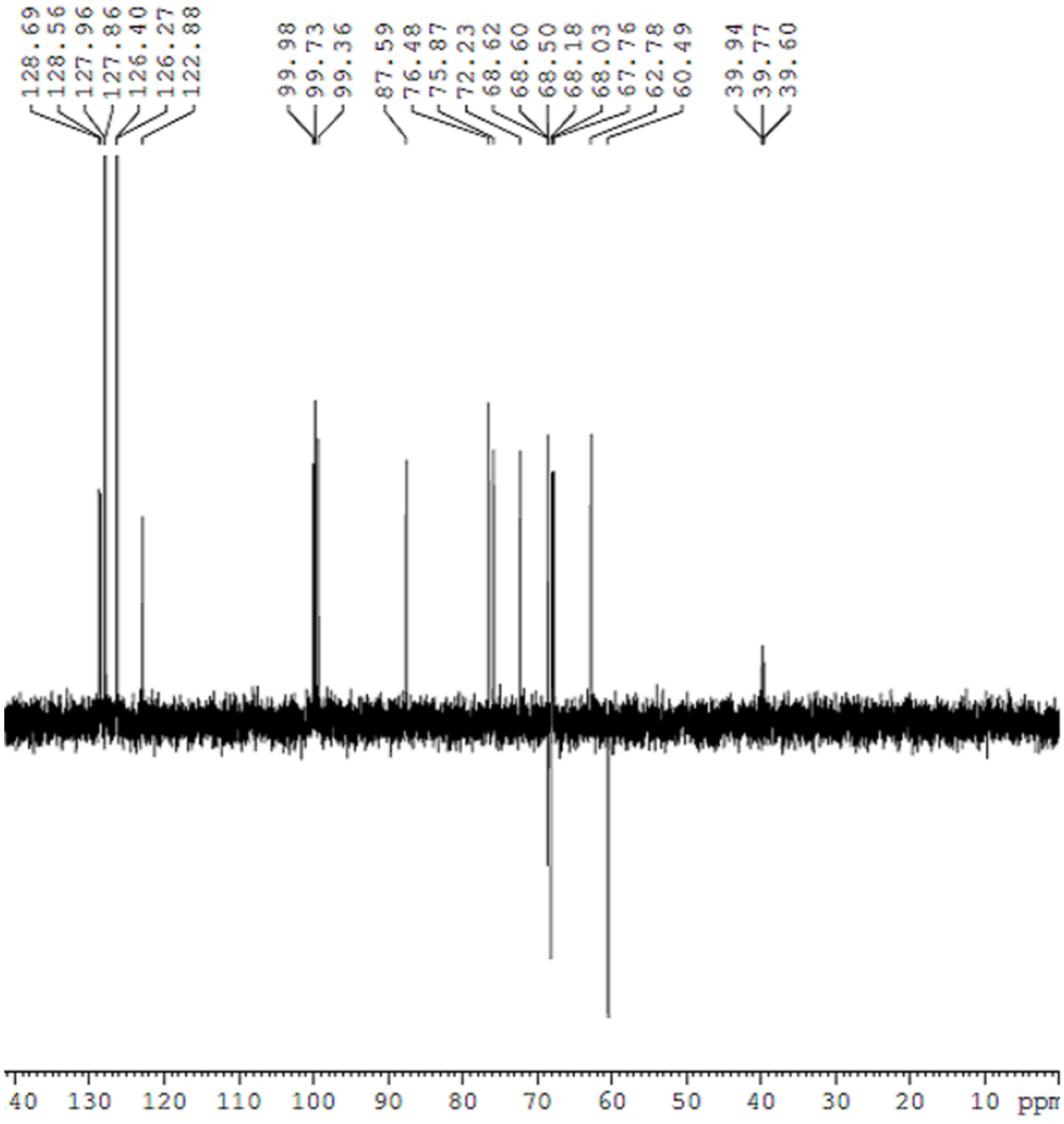

Fig. S32: DEPT spectrum of **5** in DMSO-d6 (500 MHz).

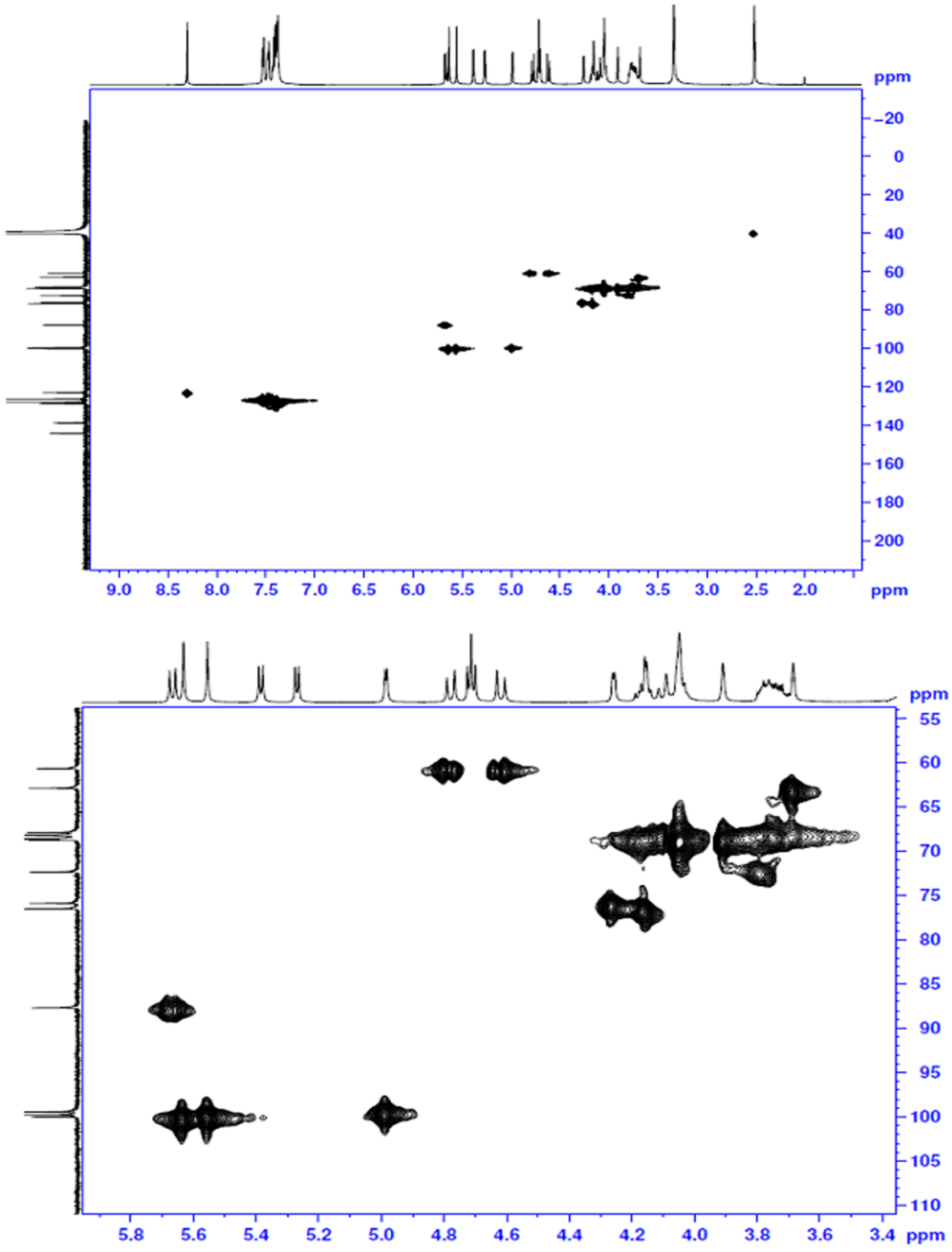

Fig. S33: HMQC spectrum of **5** in DMSO-d6 (500 MHz).

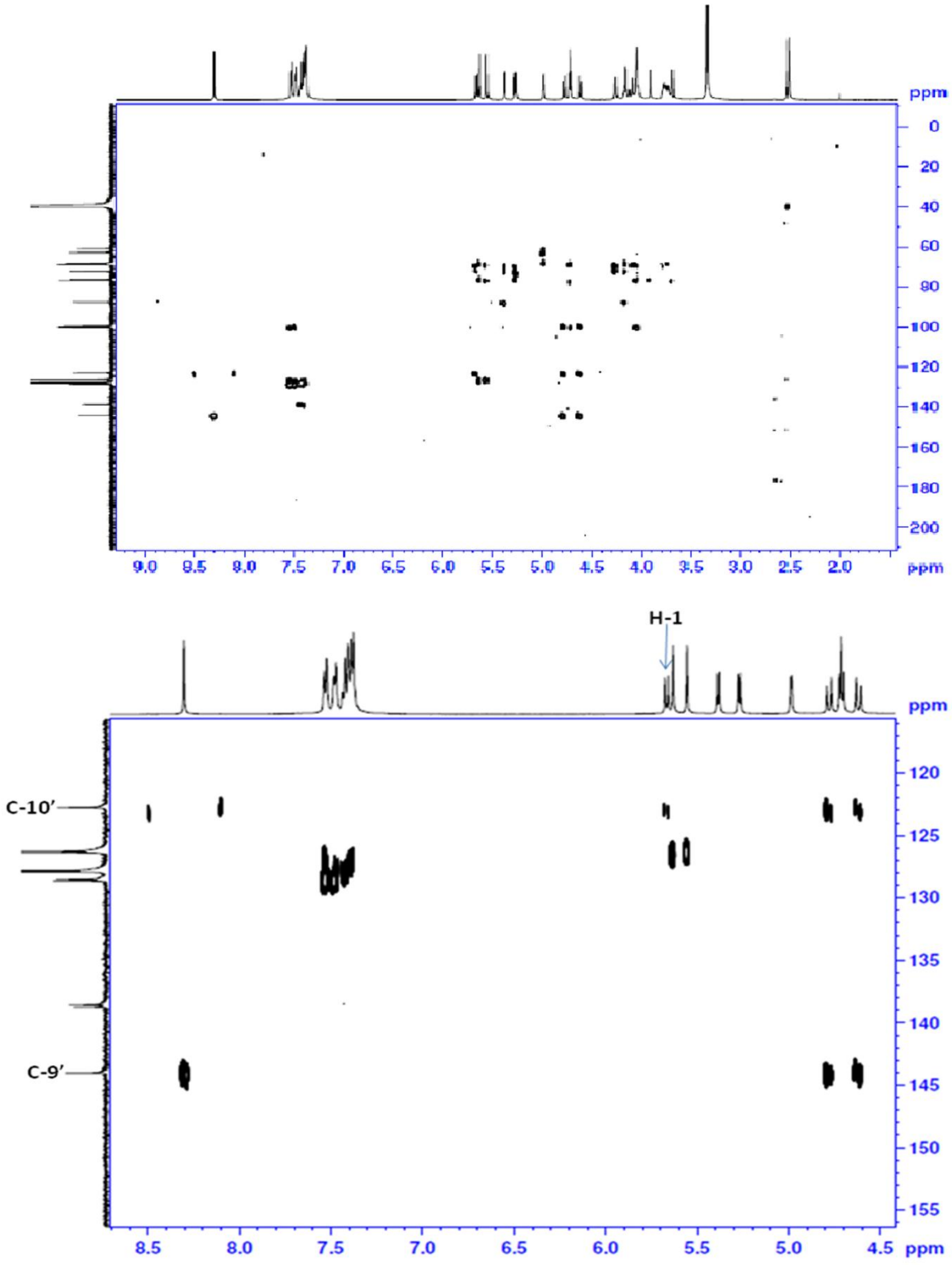

Fig. S34: HMBC spectrum of **5** in DMSO-d6. C-10′ shows cross peaks with H-1. C- 9′ does not show cross peaks with H-1.

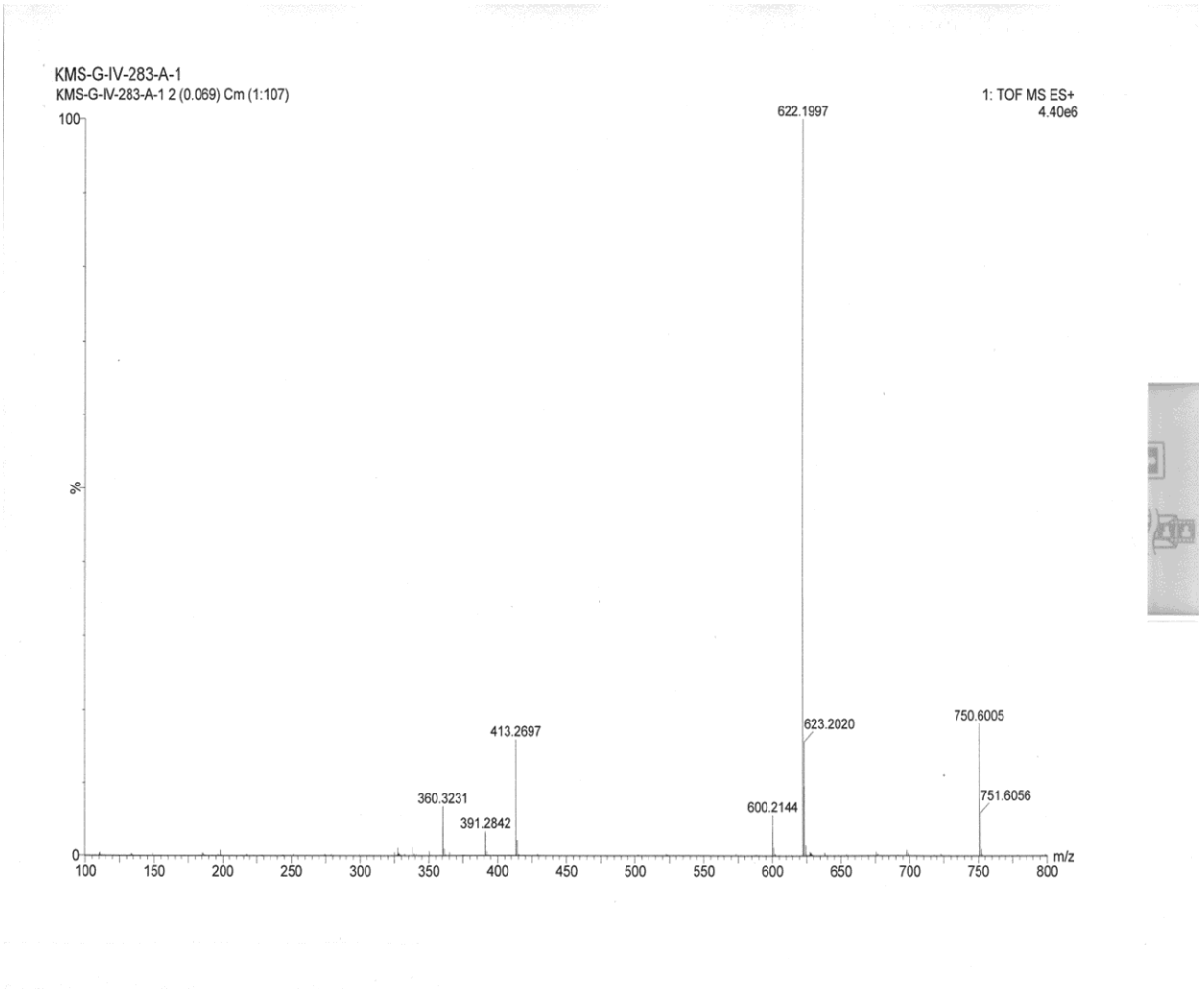

Fig. S35: HRMS Spectrum of **6**

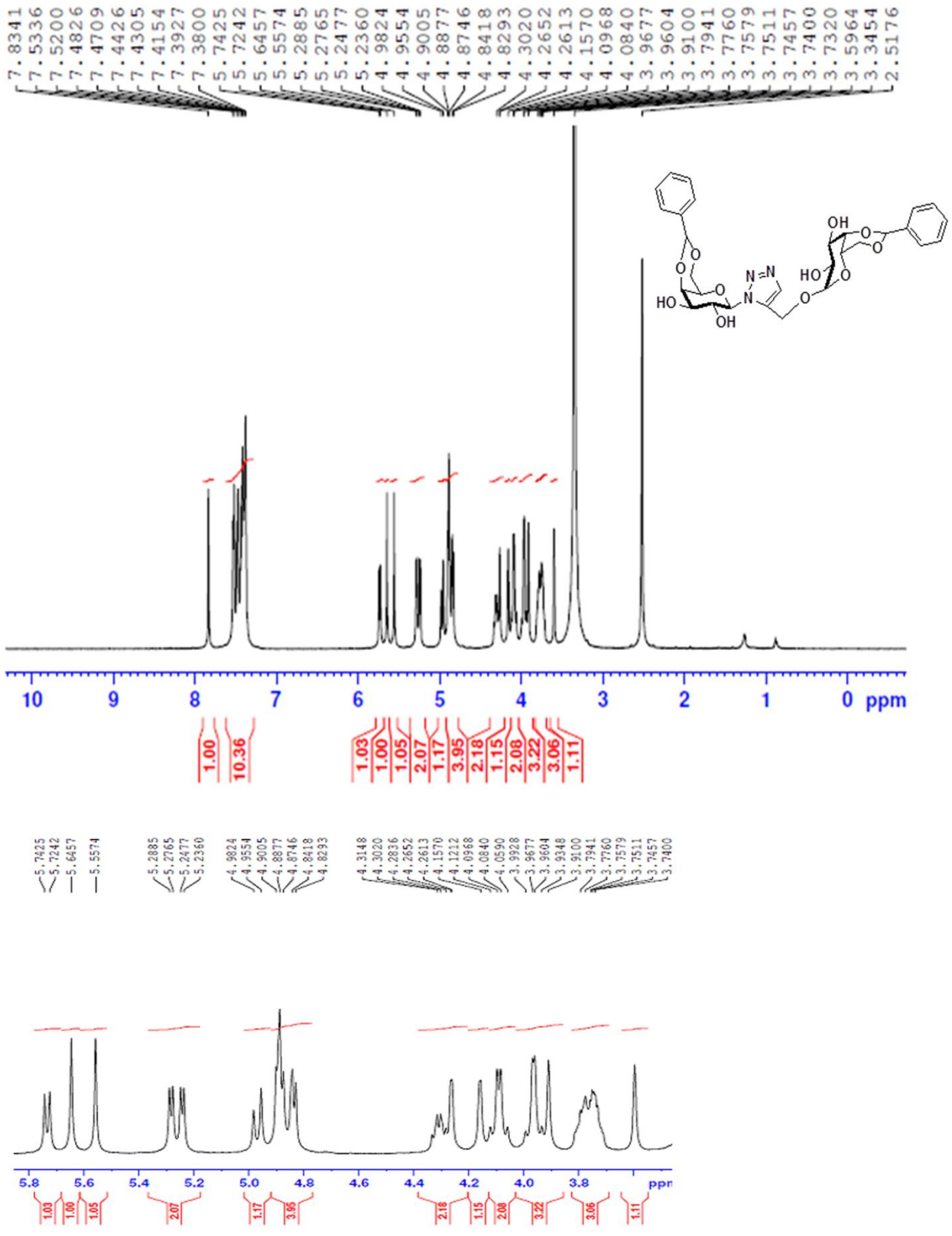

Fig. S36: ^{1}H NMR spectrum of **6** in DMSO-d6 (500 MHz).

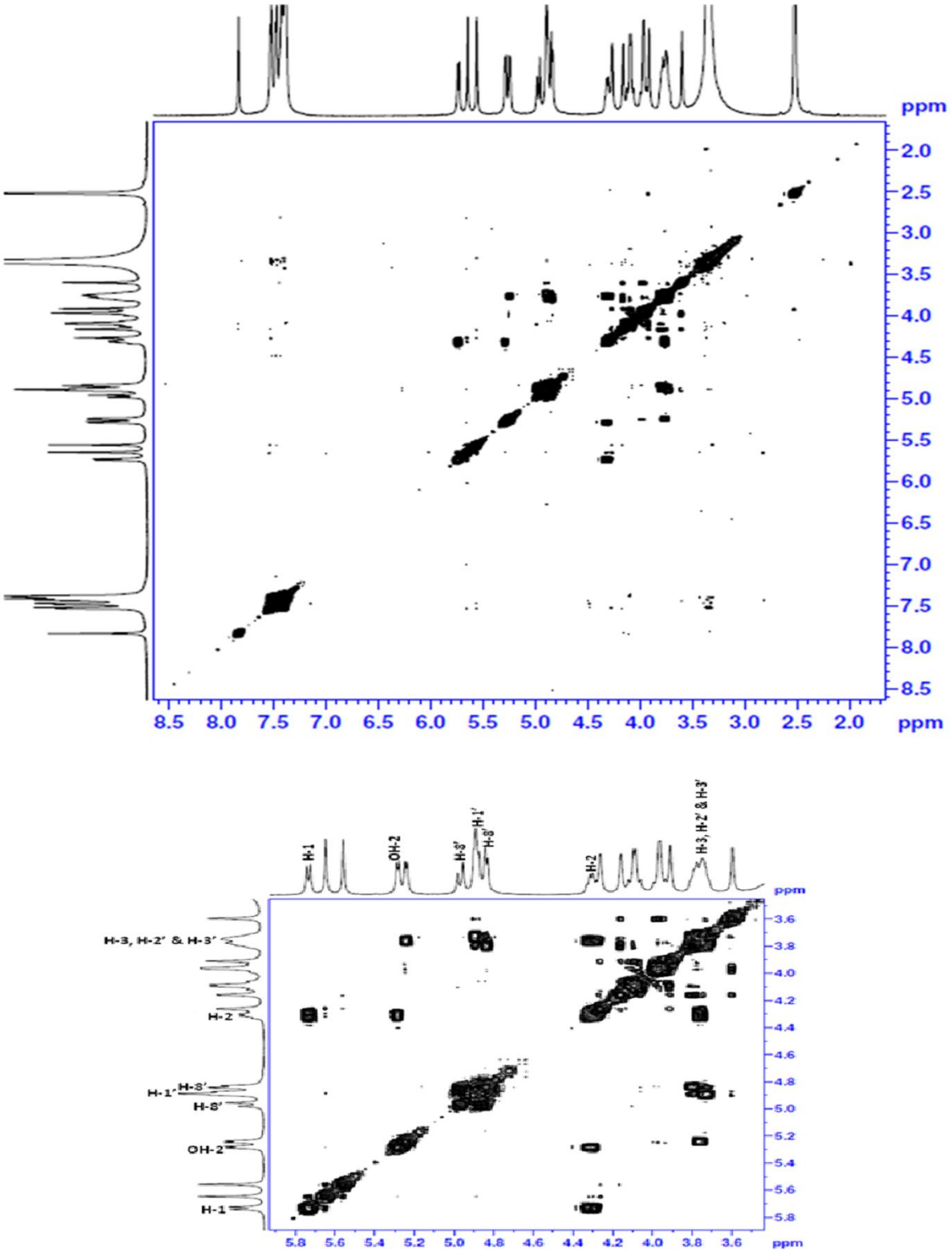

Fig. S37: COSY spectrum of compound **6** in DMSO-d6 (500 MHz).

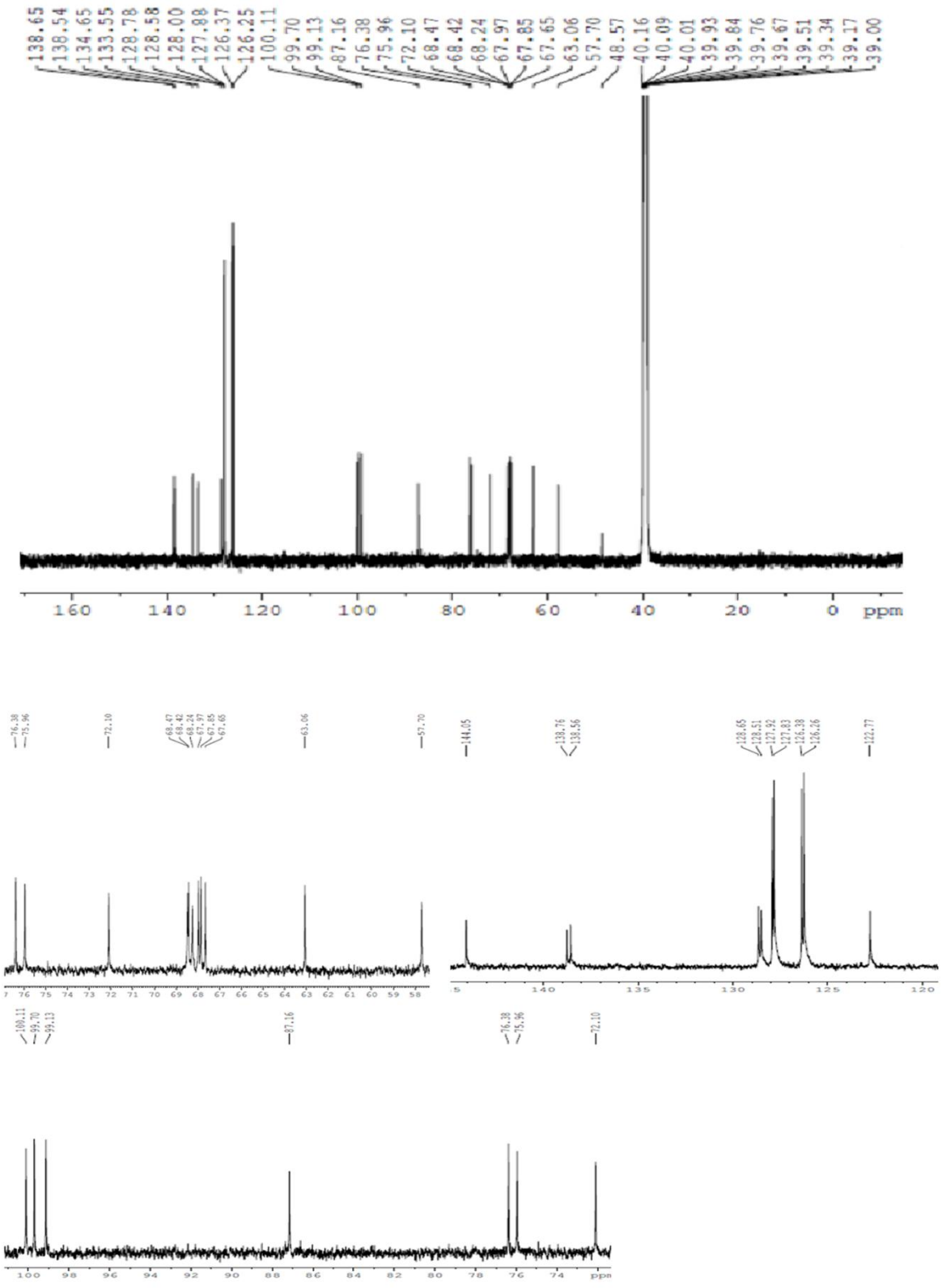

Fig. S38: ^{13}C spectrum of compound **6** in DMSO-d6 (500 MHz).

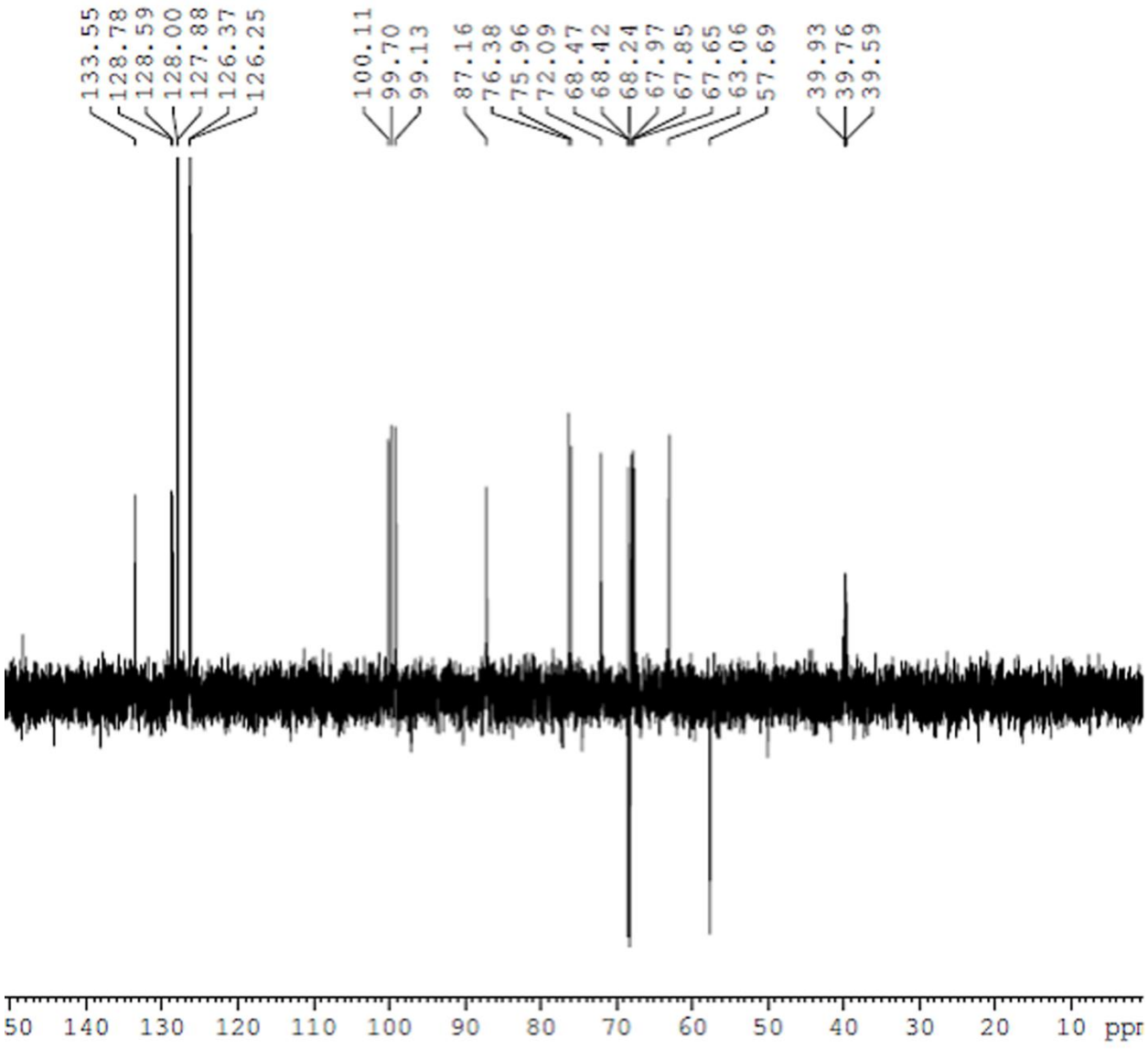

Fig. S39: DEPT spectrum of compound **6** in DMSO-d6 (500 MHz).

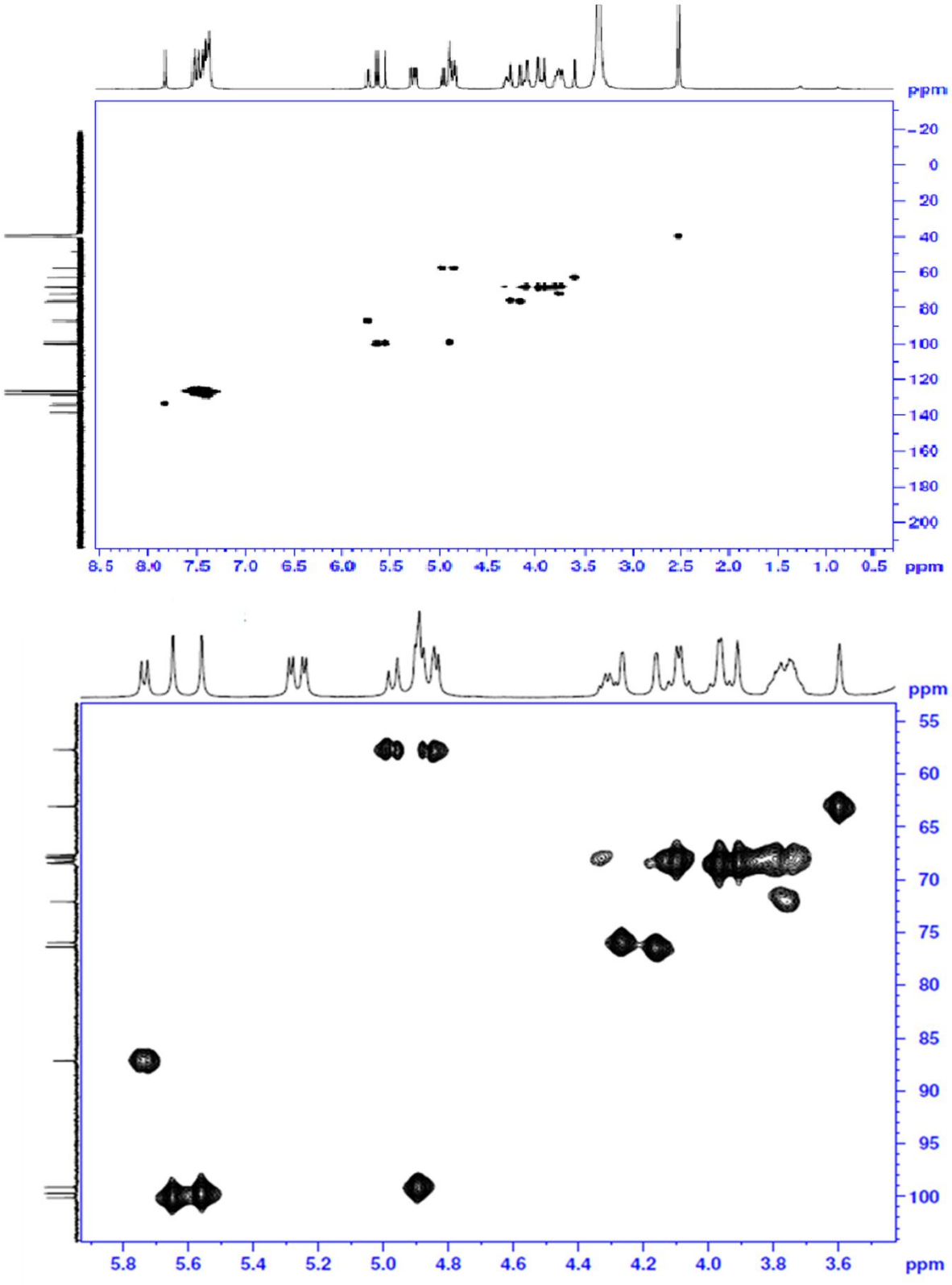

Fig. S40: HMQC spectrum of compound **6** in DMSO-d6 (500 MHz).

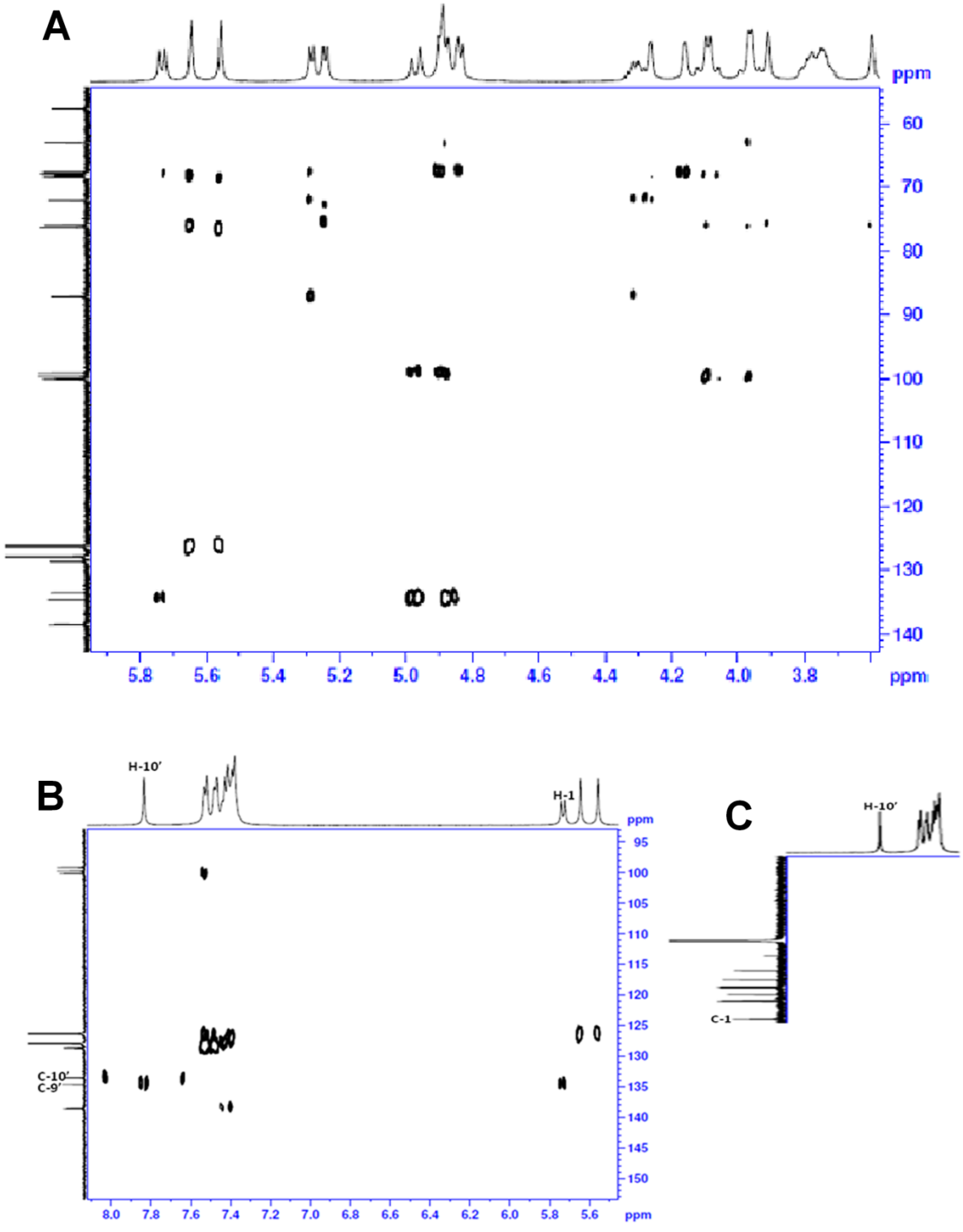

Fig. S41: (**A**) HMBC spectrum of **6** in DMSO-d6. (**B**) C-10′ does not show cross peaks with H-1. C- 9′ shows cross peaks with H-1. (**C**) C-1 does not show cross peaks with H-10′.

16. References

(1) J. Ohlsson and U. J. Nilsson, *Tetrahedron Lett*., 2003, **44**, 2785.

(2) B. Roy and B. Mukhopadhyay, *Tetrahedron Lett*., 2007, **48**, 3783.

(3) P. Simerska, M. Kuzma, D. Monti, S. Riva, M. Mackova and V. Kren, *J. Mol. Catal. B: Enzym*., 2006, **39**, 128.

(4) A. S. Rowan, N. I. Nicely, N. Cochrane, W. A. Wlassoff, A. Claiborne and C. J. Hamilton, *Org. Biomol. Chem.*, 2009, **7**, 4029.

(5) M. Hunsen, D. A. Long, C. R. D'Ardenne and A. L. Smith, *Carbohydr. Res.*, 2005, **340**, 2670.

(6) R. Ghosh, A. Chakraborty, D.K. Maiti and S. B. Swaraj, *Indian J. Chem. Sect B*., 2002, **41**, 583.

(7) H. B. Mereyala and S. R. Gurrala, *Carbohydr. Res*., 1998, **307**, 351.

(8) K. M. Sureshan, K.Yamaguchi, Y. Sei and Y. Watanabe, *Eur. J. Org. Chem*., 2004, 4703.

(9) F. M. Menger and K. L. Caran, *J. Am. Chem. Soc*., 2000, **122**, 11679.

(10) O. Gronwald and S. Shinkai, *Chem. Eur. J*., 2001, **7**, 4329.

(11) A. Friggeri, O. Gronwald, K. J. C. van Bommel, S. Shinkai and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 2002, **124**, 10754.

(12) F. Himo, T. Lovell, R. Hilgraf, V. V. Rostovtsev, L. Noodleman, K. B. Sharpless and V. V. Fokin, *J. Am. Chem. Soc*., 2005, **127**, 210.

(13) A. D. Becke, *Phy. Rev. A.*, 1988, **38**, 3098.

(14) A. D. Becke, *J. Chem. Phys*, 1993, **98**, 5648.

(15) C. Lee, W. Yang and R. G. Parr, *Phy. Rev. B.*, 1988, **37**, 785.

(16) P. J. Stephens, F. J. Devlin, C. F. Chabalowski and M. J. Frisch, *J. Phys.Chem*, 1994, **98**, 11623.

(17) S. H. Vosko, L. Wilk and M. Nusair, *Can. J. Phy.*, 1980, **58**, 1200.

(18) R. Ditchfield, W. J. Hehre and J. A. Pople, *J. Chem. Phys*, 1971, **54**, 724.

(19) W. J. Hehre, R. Ditchfield and J. A. Pople, *J. Chem. Phys*, 1972, **56**, 2257.

(20) Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T.

Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G.

(21) A. Pathigoolla, R. G. Gonnade and K. M. Sureshan, *Angew. Chem. Int. Ed.*, 2012, **51**, 4362.