Supporting Information

A novel Na^+ coordination mediated supramolecular organogel based on isosteviol: water-assisted self-assembly, *in situ* forming and selective gelation abilities

Tao Zhang,[a] Ya Wu,[a,b] Lihong Gao,[a] Zhongtai Song,[a] Li Zhao[a], Yunxiao Zhang*[a] and Jingchao Tao*[a]

[a] College of Chemistry and Molecular Engineering, Zhengzhou University, 75 Daxue Road, Zhengzhou 450052, P. R. China. Fax: 86-371- 6776 7200; Tel: 86-371- 6776 7200; E-mail: jctao@zzu.edu.cn

[b] School of Pharmacy, Henan College of Traditional Chinese Medicine, Zhengzhou 450008, P. R. China

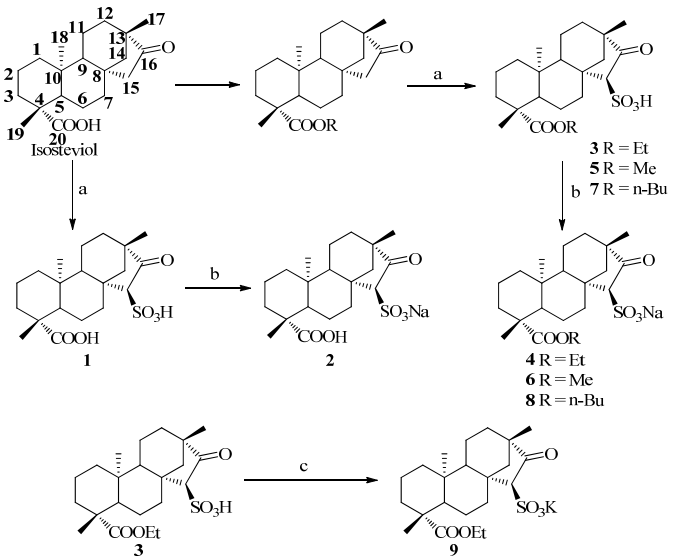
1. General methods

All starting materials were obtained from commercial suppliers and used without further purification unless otherwise noted. ^{1}H NMR and ^{13}C NMR spectra were recorded in a Bruker AVANCE III 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C NMR). Variable temperature ^{1}H NMR of the gel in $CDCl_3$-d was taken from 293K to 331K. ESI-MS was recorded on an Agilent Q-TOF 6540 mass spectrometer in both positive and negative mode. FT-IR spectra were recorded on a Necolet IR380 infrared spectrometer with a KBr disk at room temperature. Atomic force microscopy was carried out on a SPA300HV with a SPI 3800 controller under. The samples was prepared by air-dried the gels on a piece of silicon wafer. Scanning Electron Microscopy (SEM) analysis was performed on a JSM 6700F field emission scanning electron microscope with 10 kV operating voltage. SEM xerogel samples were obtained by air-dried gel on a piece of silicon wafer and coated with a thin layer of platinum of 3–4 nm. Melting points were measured with a X-4 melting point apparatus and are uncorrected. X-ray crystallographic analysis of compound **2** was performed on a Rigaku R-AXIS-IV CCD diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å). Meanwhile, X-ray crystallographic analysis of compound **4** was performed on a Xcalibur, Eos, Gemini CCD diffractometer with Cu-Kα radiation (λ = 1.5418 Å). X-ray diffraction (XRD) measurements were carried out with an X-ray diffractometer (PANalytical, X'Pert PRO) to indentify the xerogel from air-dried chloroform.

2. Synthesis

As reported, isosteviol was obtained by acid hydrolysis of isostevioside,[1, 2] followed by

esterfication with CH_3CH_2Br (CH_3I, n-BuBr) and KOH in DMSO gives esterified compounds respectively.[3]



Scheme S1. Reaction conditions: a) H_2SO_4, Ac_2O, 0□-r.t., 93%; b) NaCl, H_2O, r.t., 95%; c) KCl, H_2O, 95%.

Synthesis of compound 3: To a 100mL round-bottom flask, 2g of concentrated sulfuric acid was placed and cooled on an ice-salt bath. 6mL of acetic anhydride was added slowly through a dropping funnel. 5g of isosteviol ethyl ester was added and stirring was continued until the solid was dissolved. Leave the ice bath warming up to room temperature naturally, large amount of white solid precipitated. The reaction was continued at room temperature for 10 hours and monitored by TLC. 20mL of water was added to the system and the white solid was dissolved after shaking (system A). The aqueous solution was extracted by 3×25mL of ethyl acetate. The crude product was obtained after evaporating the solvent under reduced pressure without drying. Recrystallization of the crude product in ethyl acetate gave 5.6g white crystal. Yield: 92%. Mp: 177.1-177.3 ^{o}C. FT-IR (KBr): 3419, 2987, 2956, 1733, 1714, 1460, 1182, 1156, 1029, 623 cm^{-1}; ^{1}H NMR (400MHz, D_2O, ppm): δ 3.938-3.982 (m, 2H), 3.572 (s, 1H), 2.460-2.495 (d, J = 14 Hz, 1H), 2.183-2.221 (d, J = 11.2, 1H), 1.962-2.019 (m, 2H), 1.693-1.727 (m, 2H), 1.442-1.546 (m, 3H), 1.260 (m, 3H), 1.103-1.138 (m, 6H), 1.054 (m, 3H), 0.993 (m, 1H), 0.863 (m, 4H), 0.769 (m, 1H), 0.617(s, 3H); ^{13}C NMR (100MHz, D_2O): δ 218.148, 178.878, 71.391, 61.137, 57.512, 56.882, 51.332, 48.547, 43.547, 42.602, 39.089, 37.968, 37.623, 35.547, 28.468, 21.382, 19.410, 19.282, 18.858, 13.470, 12.668; HRMS (ESI, m/z) calcd for $C_{22}H_{38}NO_6S$ $[M+NH_4]^+$ 444.2420, $C_{22}H_{35}O_6S$ $[M+Na]^+$ 449.1974 and $C_{22}H_{33}O_6S$ $[M-H]^-$ 425.1998. Found: 444.2424, 449.1972 and 425.1992, respectively.

Synthesis of compound 4: To system A prepared in the former step was added 5mL of saturated brine. The mixed solution was stirred for a few minutes and extracted

with 3×25mL of ethyl acetate. The combined organic layer was evaporated under reduce pressure without drying and the crude product precipitated after about 80% volume of the the solvent was removed. Compound **4** was recrystallized from ethyl acetate to give white needle-like crystals. In addition, this compound can also be obtained through a normal acid-base reaction of **3** with NaOH, Na_2CO_3, $NaHCO_3$, etc. Yield: 95%. Mp: 244-245.3℃. FT-IR (KBr): 3550, 3485, 2989, 2949, 1752, 1742, 1724, 1712, 1460, 1240, 1182, 1046, 628 cm^{-1}; ^1H NMR (400MHz, D_2O, ppm): δ 3.99-4.03 (m, 2H), 3.63 (s, 1H), 2.47-2.51 (d, J = 14Hz, 1H), 2.20-2.23 (d, J = 11.2, 1H), 1.99-2.05 (m, 2H), 1.70-1.77 (m, 2H), 1.48-1.63 (m, 3H), 1.22-1.32 (m, 4H), 1.15-1.18 (m, 5H), 1.10 (m, 3H), 0.95(m, 2H), 0.91(s, 3H), 0.82 (m, 1H), 0.65(s, 3H); ^{13}C NMR (100MHz, D_2O): δ 218.71, 179.55, 71.45, 61.26, 57.36, 56.71, 51.28, 48.22, 43.61, 42.62, 38.98, 37.93, 37.52, 35.46, 28.35, 21.40, 19.40, 19.23, 18.77; HRMS (ESI, m/z) calcd for $C_{22}H_{34}NaO_6S$ $[M+H]^+$ 449.1974, $C_{22}H_{33}Na_2O_6S$ $[M+Na]^+$ 471.1793 and $C_{22}H_{33}O_6S$ $[M-Na]^-$ 425.1998. Found: 449.1975, 471.1796 and 425.1997, respectively.

Synthesis of compounds 1, 5 and 7: These compounds were prepared from isosteviol esters with the similar procedure for synthesis of **3**. Compound **1**: Yield: 93%. Mp: 207.6-207.8 ℃. FT-IR (KBr): 3410, 2957, 2876, 1720, 1668, 1462, 1242, 1183, 1030, 623 cm^{-1}; ^1H NMR (400MHz, D_2O, ppm): δ 3.61 (s, 1H), 2.41-2.44 (d, *J* = 14, 1H), 2.16-2.19 (d, J = 11.2, 1H), 1.92-1.97 (m, 2H), 1.69-1.73 (m, 2H), 1.54-1.60 (m, 2H), 1.44-1.47 (m, 1H), 1.29-1.33 (m, 2H), 1.12-1.22 (m, 4H), 1.08 (s, 3H), 0.94 (m, 2H), 0.86 (s, 3H), 0.78 (m, 1H), 0.68 (s, 3H); ^{13}C NMR (100MHz, D_2O): δ 218.63, 181.96, 71.44, 57.40, 56.58, 51.25, 48.21, 43.33, 42.61, 39.03, 37.98, 37.53, 35.43, 28.45, 21.31, 19.38, 19.18, 18.76, 12.49; HRMS (ESI, m/z) calcd for $C_{20}H_{34}NO_6S$ $[M+NH_4]^+$ 416.2107, $C_{20}H_{30}NaO_6S$ $[M+Na]^+$ 421.1661 and $C_{20}H_{29}O_6S$ $[M-H]^-$ 397.1685. Found: 416.2110, 421.1662 and 397.1694, respectively. Compound **5:** Yield : 90%. Mp: 193-195 °C. FT-IR (KBr): 3448, 2945, 2886, 1722, 1461, 1399, 1239, 1040, 754, 621 cm^{-1}; ^1H NMR (400MHz, DMSO, ppm): 3.54 (s, 3H), 3.29-3.30 (d, *J* = 4, 1H), 2.75-2.78 (q, 1H), 2.37-2.41 (q, 1H), 2.00-2.09 (m, 2H), 1.73-1.76 (m, 1H), 1.55-1.65 (m, 3H), 1.26-1.37 (m, 3H), 1.08-1.18 (m, 6H), 0.94-1.05 (m, 3H), 0.83-0.90 (m, 4H), 0.62 (s,3H); ^{13}C NMR (100MHz, DMSO): δ 213.65, 176.88, 71.65, 57.21, 56.47, 51.01, 50.90, 46.72, 43.08, 42.26, 38.67, 37.79, 37.62, 37.39, 35.42, 28.42, 21.45, 20.11, 19.02, 18.55, 12.54; HRMS (ESI, m/z) calcd for $C_{21}H_{32}NaO_6S$ $[M+Na]^+$ 435.1812. Found: 435.1816. Compound **7:** Yield: 92%. Mp: 233-239 °C. FT-IR (KBr): 3576, 3459, 2957, 2872, 1731, 1713, 1658, 1624, 1461, 1240, 1197, 1044, 626 cm^{-1}; ^1H NMR (400MHz, DMSO, ppm): 3.89-3.99 (m, 2H), 3.30 (s, 1H), 2.77-2.81 (d, *J* = 16, 1H), 2.39-2.42 (q, 1H), 2.12-2.15 (q, 1H), 2.00-2.03 (d, *J* = 12, 1H), 1.70-1.80 (m, 1H), 1.55-1.59 (m, 5H), 1.35-1.38 (m, 5H), 1.08-1.17 (m, 6H),

0.99-1.03 (m, 2H), 0.87-0.91 (t, 7H), 0.65 (s, 3H); ^{13}C NMR (100MHz, DMSO): δ 214.85, 176.41, 71.53, 63.36, 57.15, 56.52, 50.94, 46.77, 43.12, 42.23, 38.71, 37.76, 37.69, 37.38, 35.41, 29.91, 28.56, 21.43, 20.08, 19.05, 18.87, 18.57, 13.54, 12.72; HRMS (ESI, m/z) calcd for $C_{24}H_{38}NaO_6S$ $[M+Na]^+$ 477.2281 and C24H39O6S $[M+H]^+$ 455.2462. Found: 477.2282 and 455.2458.

Synthesis of compounds 2, 6 and 8: Prepared and purified following the similar procedure as that of **4**. Compound **2**: Yield: 93%. Mp: >250 ^{o}C. FT-IR (KBr): 3460, 2948, 2846, 1930, 1456, 1240, 1195, 1172, 1043, 1035, 631; ^{1}H NMR (400MHz, D_2O, ppm): δ 3.67 (s, 1H), 2.43-2.47 (d, J = 14, 1H), 2.19-2.22 (d, J = 11.6, 1H), 2.00(m, 2H), 1.71-1.77 (m, 2H), 1.57-1.67 (m, 2H), 1.48 (m, 1H), 1.17-1.42 (m, 6H), 1.12 (s, 3H), 0.97-1.06 (m, 2H), 0.90 (s, 3H), 0.83 (m, 1H), 0.72(s, 3H); ^{13}C NMR (100MHz, D_2O): δ 219.02, 182.32, 71.44, 57.40, 56.58, 51.25, 48.21, 43.33, 42.61, 39.03, 37.98, 37.53, 35.43, 28.45, 21.31, 19.38, 19.18, 18.76, 12.47; HRMS (ESI, m/z) calcd for $C_{20}H_{30}NaO_6S$ $[M+H]^+$ 421.1661, $C_{20}H_{29}Na_2O_6S$ $[M+Na]^+$ 443.1480 and $C_{20}H_{29}O_6S$ $[M-Na]^-$ 397.1685. Found: 421.1658, 443.1483 and 397.1693, respectively. Compound **6**: Yield: 91%. Mp: >250 ^{o}C. FT-IR (KBr): 3471, 2951, 2842, 1724, 1459, 1399, 1242, 1202, 1114, 1044, 979,631 cm^{-1}; ^{1}H NMR (400MHz, DMSO, ppm): 3.54 (s, 3H), 3.32 (s, 1H), 2.78-2.81(d, J = 12, 1H), 2.39-2.42(d, J = 12, 1H), 2.00-2.08 (m, 2H), 1.73-1.76 (m, 1H), 1.55-1.64 (t, 3H), 1.33-1.39 (m, 3H), 1.18 (s, 1H), 1.12 (s, 4H), 0.98-1.01 (m, 4H), 0.86 (m, 4H), 0.62 (s, 3H); ^{13}C NMR (100MHz, DMSO): δ 215.89, 176.90, 71.63, 57.18, 56.48, 50.98, 46.89, 43.10, 42.20, 38.73, 37.72, 37.60, 37.43, 35.35, 28.41, 21.48, 20.09, 19.04, 18.56, 12.60; HRMS (ESI, m/z) calcd for $C_{21}H_{31}Na_2O_6S$ $[M+Na]^+$ 457.1631. Found: 457.1636. Compound **8**: Yield: 92%. Mp: 224-226 ^{o}C. FT-IR (KBr): 3472, 2957, 2847, 1733, 1719, 1640, 1461, 1239, 1190, 1151, 1041, 626 cm^{-1}; ^{1}H NMR (400MHz, DMSO, ppm): 3.87-3.97 (m, 2H), 3.34 (s, 1H), 2.78-2.81 (d, J = 12, 1H), 2.38-2.41 (d, J = 12, 1H), 2.09-2.19 (q, 1H), 2.00-2.03 (d, J = 12, 1H), 1.70-1.81 (m, 1H), 1.53-1.64 (m, 5H), 1.30-1.40 (m, 5H), 1.07-1.69 (m, 6H), 0.93-1.02 (m, 3H), 0.87-0.90 (t, 8H), 0.65 (s, 3H); ^{13}C NMR (100MHz, DMSO): δ 215.89, 176.41, 71.59, 63.37, 57.14, 56.51, 51.00, 46.87, 43.11, 42.19, 38.73, 37.70, 37.67, 37.40, 5.38, 29.91, 28.54, 21.44, 20.08, 19.03, 18.88, 18.57, 13.55, 12.71; HRMS (ESI, m/z) calcd for $C_{24}H_{37}Na_2O_6S$ $[M+Na]^+$ 499.2101. Found: 499.2101.

Synthesis of compound 9: Prepared by treatment of **3** with KCl aqueous solution, compound **9** was obtained as a white solid. It was collected by filtration, then washed with water and dried. Yield: 90%. Mp: >250 ^{o}C. FT-IR (KBr): 3467, 2953, 1713, 1458, 1396, 1185, 1114, 1040, 629 cm^{-1}; ^{1}H NMR (400MHz, DMSO, ppm): 3.96-4.02 (m, 2H), 3.33 (s, 1H), 2.79-2.82 (d, J = 12, 1H), 2.39-2.42 (m, J = 12, 1H), 2.11-2.20 (q, 1H), 1.99-2.02 (m, J = 12, 1H), 1.71-1.81 (m, 1H), 1.55-1.63 (m, 3H), 1.28-1.36

(m, 3H), 1.17-1.20 (t, 3H), 1.08-1.13 (m, 5H), 0.95-1.05 (m, 4H), 0.852-0.88 (m, 4H), 0.67 (s, 3H); ^{13}C NMR (100MHz, DMSO): δ 214.88, 176.47, 71.76, 59.55, 57.28, 56.61, 51.09, 46.79, 43.10, 42.30, 38.79, 37.87, 37.81, 37.49, 35.55, 28.54, 21.62, 21.11, 20.12, 19.13, 18.63, 13.93.

3. Gel tests

3.1 *In situ* gel formation:

Method 1: Added suitable amount of compound **3** to the two-phase mixture of halohydrocarbon solvent and brine, then kept the mixture standing at room temperature. Gel formation was determined by inversed tube method (Figure 1). In more polar halohydrocarbon solvents the gel formation took place at room temperature in less than 30 minutes. For less polar solvents, the gelation needed a longer time at room temperature. The gel could also form *via* a heating-cooling process due to the poor solubility of gelator **4** in less polar solvents.

Method 2: Dissolved compound **3** in halohydrocarbon solvent and mixed the solution with brine.

3.2 Gelation ability: A suspension of **3** in a given solvent (1 ml) was heated around the boiling point until a clear solution appeared. The solution was standing for about 20 minutes at room temperature. Then gel formation was determined by inversed tube method (Figure S1). The gelation of various solvents by **4** was summarized in Table S1. For *in situ* gel formation, addition of other common metal ions or change pH value of the brine, or mixed the gel formation process was also observed after addition of **3** to the mixture without any observed change, but the fibrous network was breakdown when the gel system was contacted with ethanol, methanol or DMSO (Table S1).

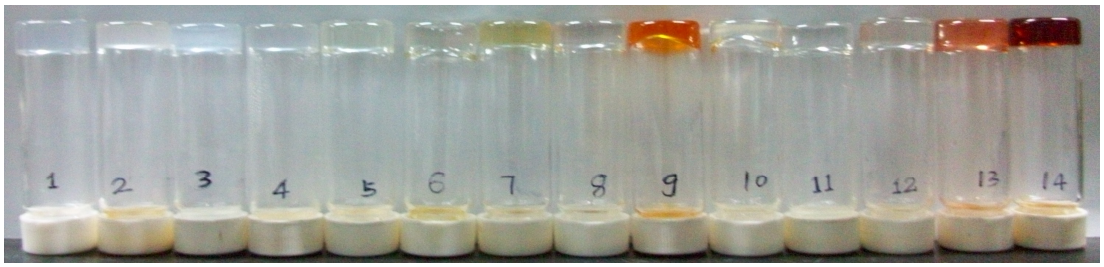


Figure S1. Gels of compound **2**. Solvents for gelation: chloroform, dichloromethane, trichloroethylene, chloropropylene oxide, 1,1,2,2-tetrachloroethane, chlorobenzene, bromoethane, fluorobenzene, bromoform, bromobenzene, 1,2-dibromoethane, 1,2-dichloroethane, iodobenzene and iodomethane from 1 to 14.

Table S1. Influence of pH, metal ions and solvents on *in situ* gel formation of chloroform/brine mixture

pH, metal ions and solvents [a]	observable changes
HCl (pH = 2)	N
NaOH (pH = 12)	N
$MgSO_4$	N
$CuSO_4$	N
$ZnCl_2$	N
$MnSO_4$	N
$Co(AcO)_2$	N
HgBr	N
$NiSO_4$	N
$BaCl_2$	N
LiCl	N
$PbCl_2$	N
methanol	Y
ethanol	Y
DMSO	Y
acetic acid	Y

a) additive to the chloroform/brine mixture. N = No changes were observed. Y = gel formation not occurred.

4. Crystallographically parameters

Crystallographically parameters of **2** and **4** were summarized in Table S2.

Table S2. Crystallographically parameters

	Compound **2**	Compound **4**
Formula	C22H39NaO9S	C44H70Na2O14S2
Fw	502.58	933.10
temp/K	291(2)	293(2)
cryst syst	monoclinic	orthorhombic
space group	P2(1)	P 21 21 21
a (Å)	12.847(3)	7.35356(14)
b (Å)	7.4420(15)	22.3698(4)
c (Å)	13.875(3)	28.0780(6)
α/deg	90.00	90.00
β/deg	106.04(3)	90.00
γ/deg	90.00	90.00
V (Å^3)	1274.9(4)	4618.77(16)
Z	2	4
D_c (mg·m^{-3})	1.309	1.342
μ/(mm^{-1})	0.191	1.773
F (000)	540	2000.0
rflns collected	4605	17225
unique rflns	4522	8245
R(int)	0.0509	0.0280
GOF on F^2	1.071	1.001
R_1[a] (I>2sigmaI)	0.0482	0.0601
wR_2 [a]	0.1092	0.1604

5. Spectra of all new compounds and the gels

5.1 NMR spectra:

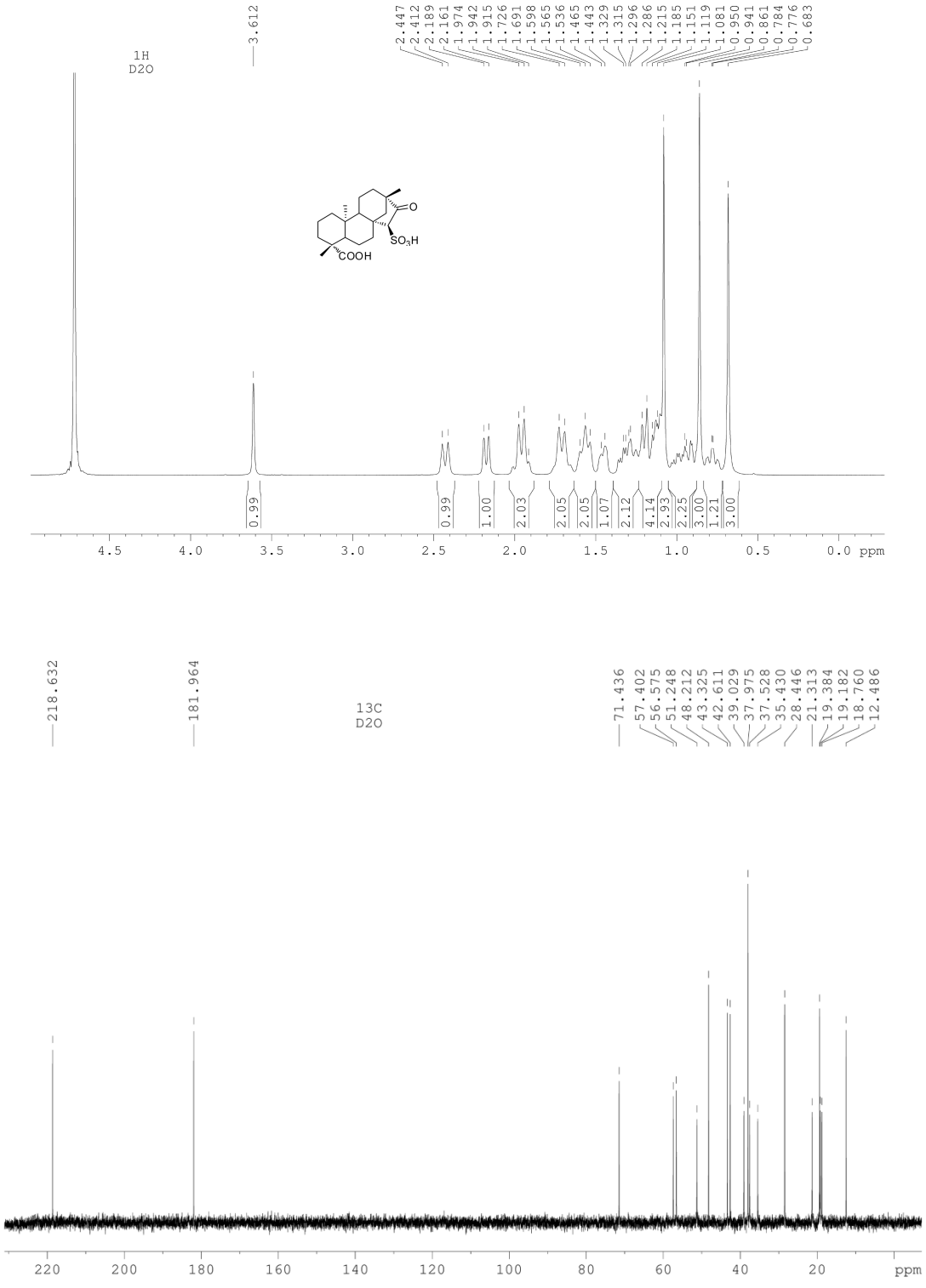


Figure S2. ^{1}H and ^{13}C NMR of **1**

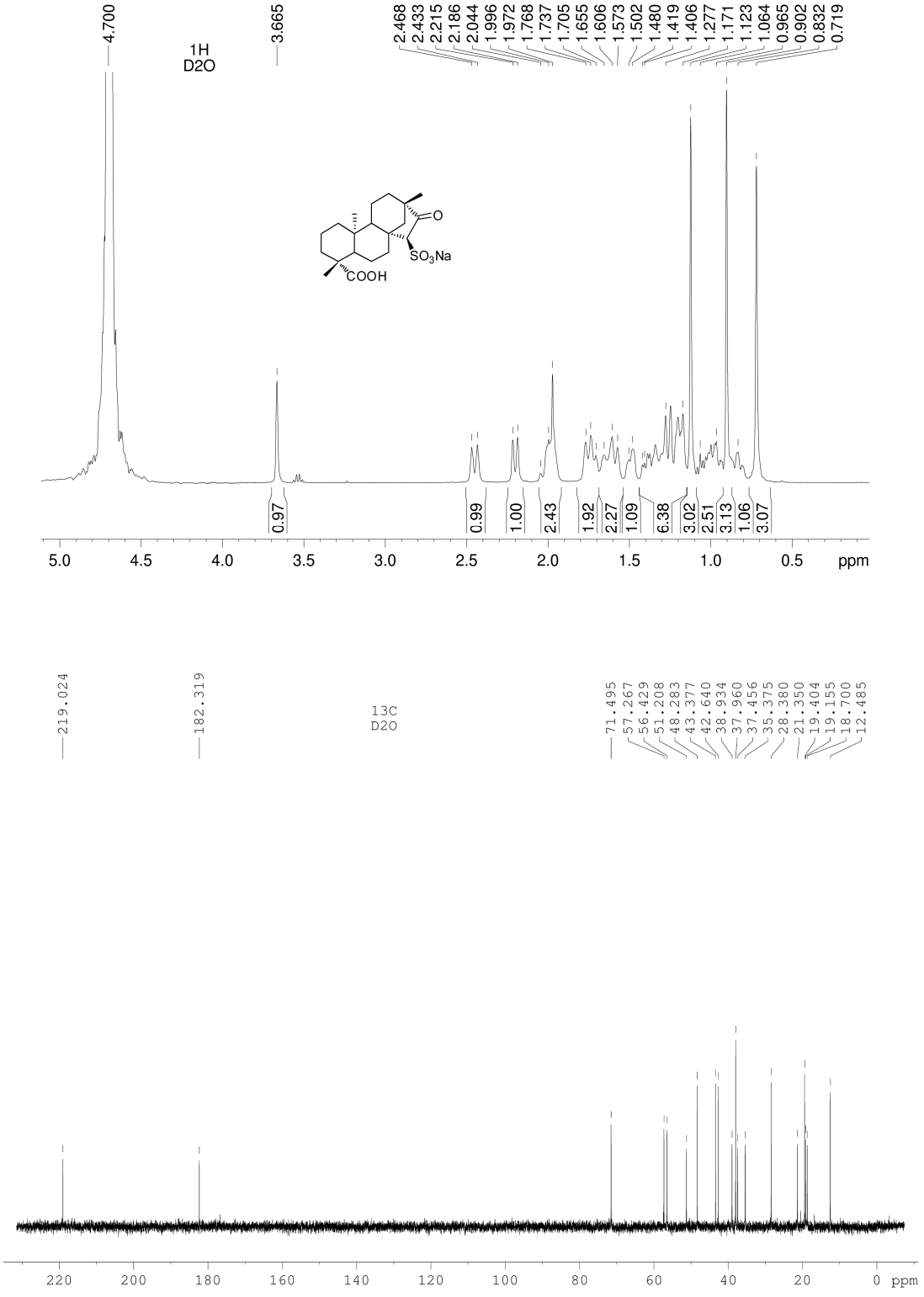


Figure S3. ^{1}H and ^{13}C NMR of **2**

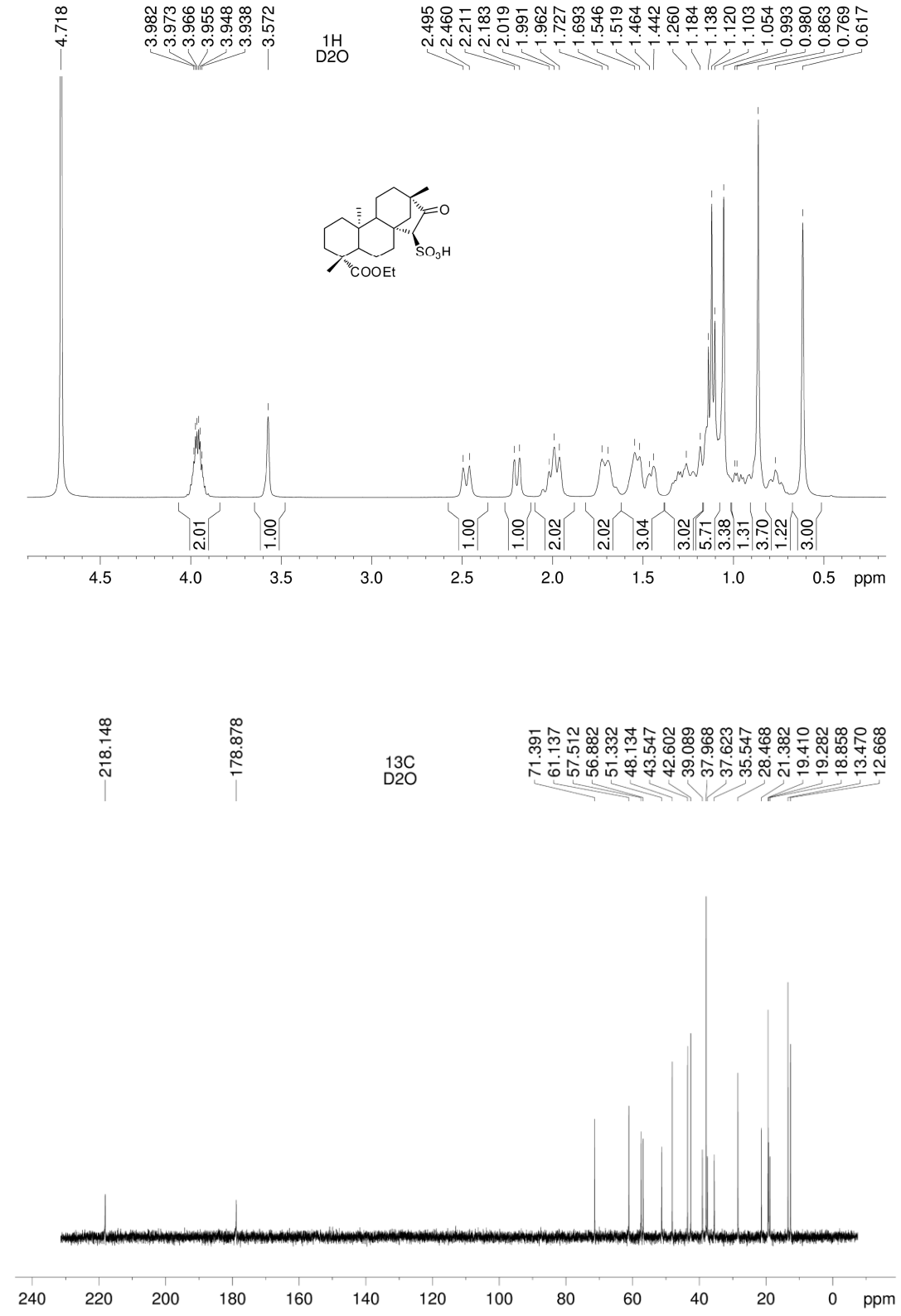


Figure S4. ^{1}H and ^{13}C NMR of **3**

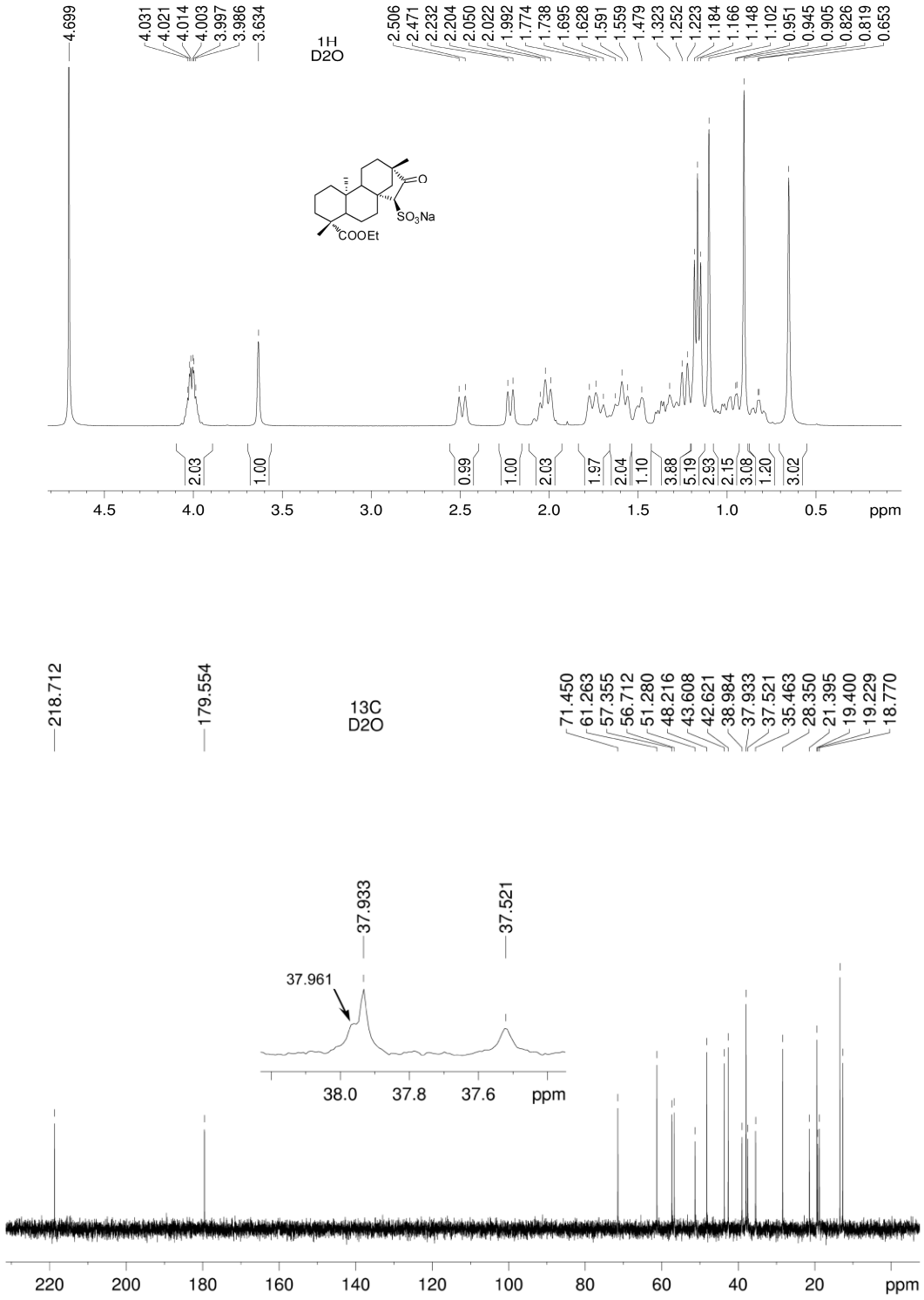


Figure S5. ^{1}H and ^{13}C NMR of **4**

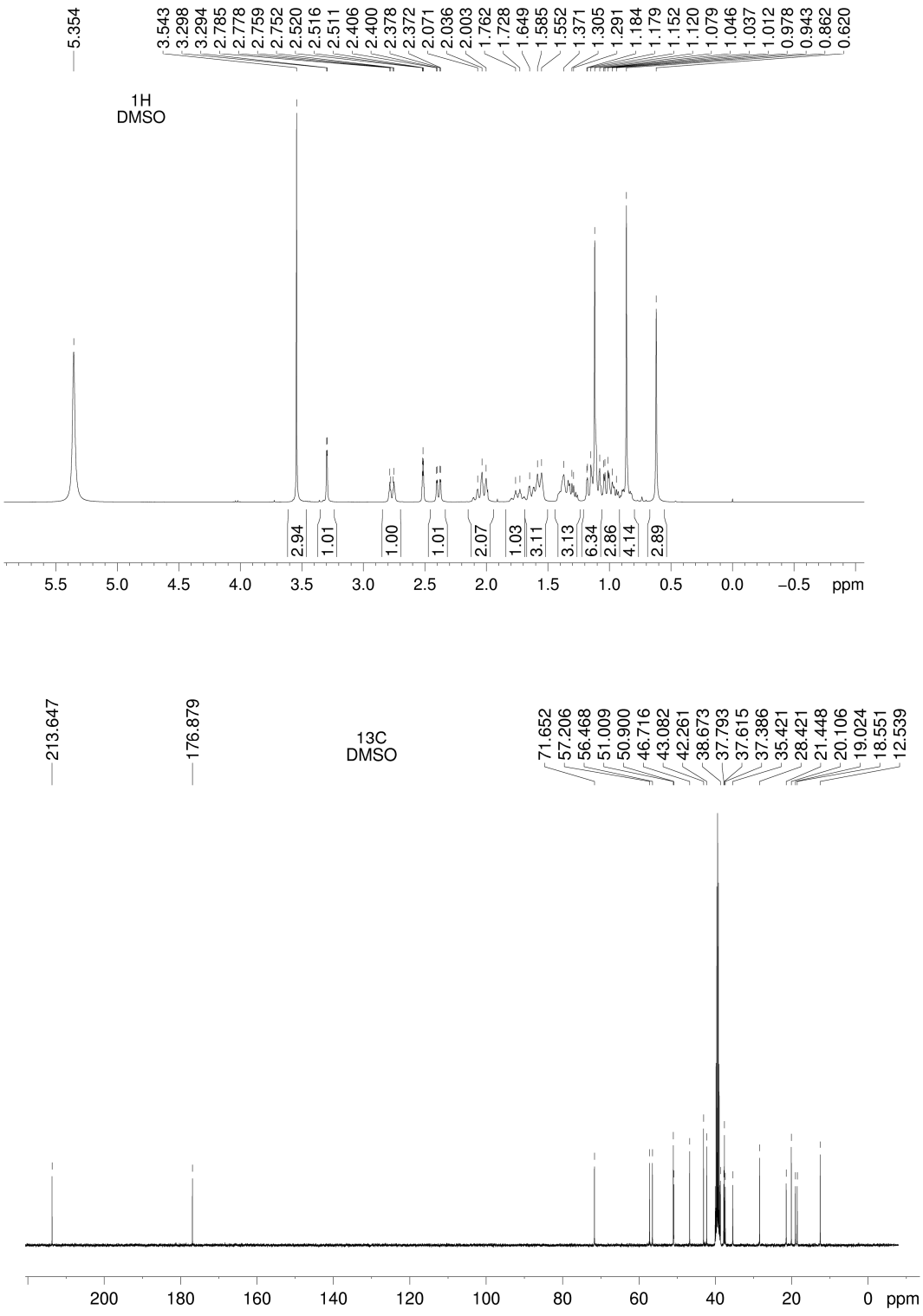


Figure S6. ^{1}H and ^{13}C NMR of **5.**

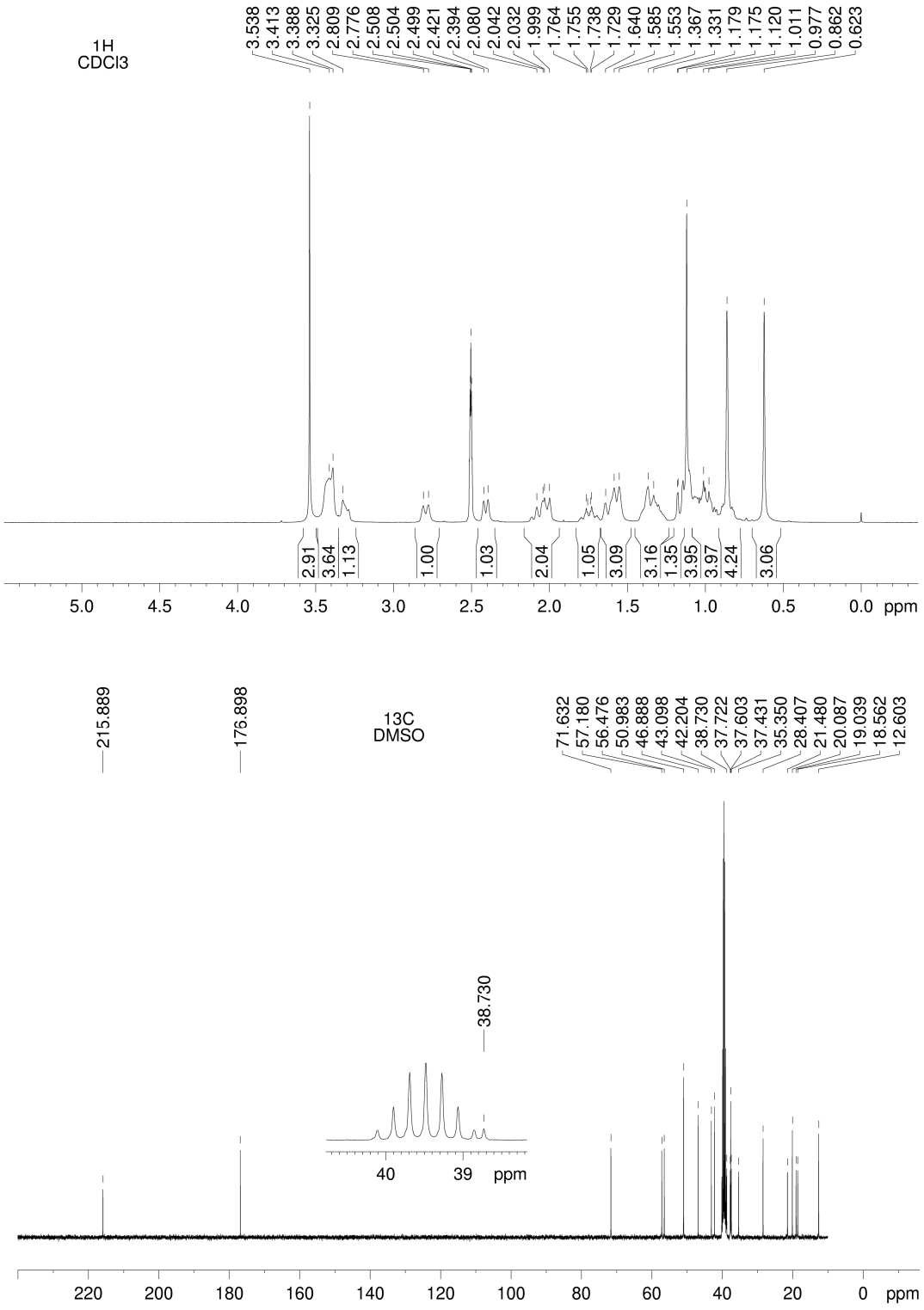


Figure S7. ^{1}H and ^{13}C NMR of **6**.

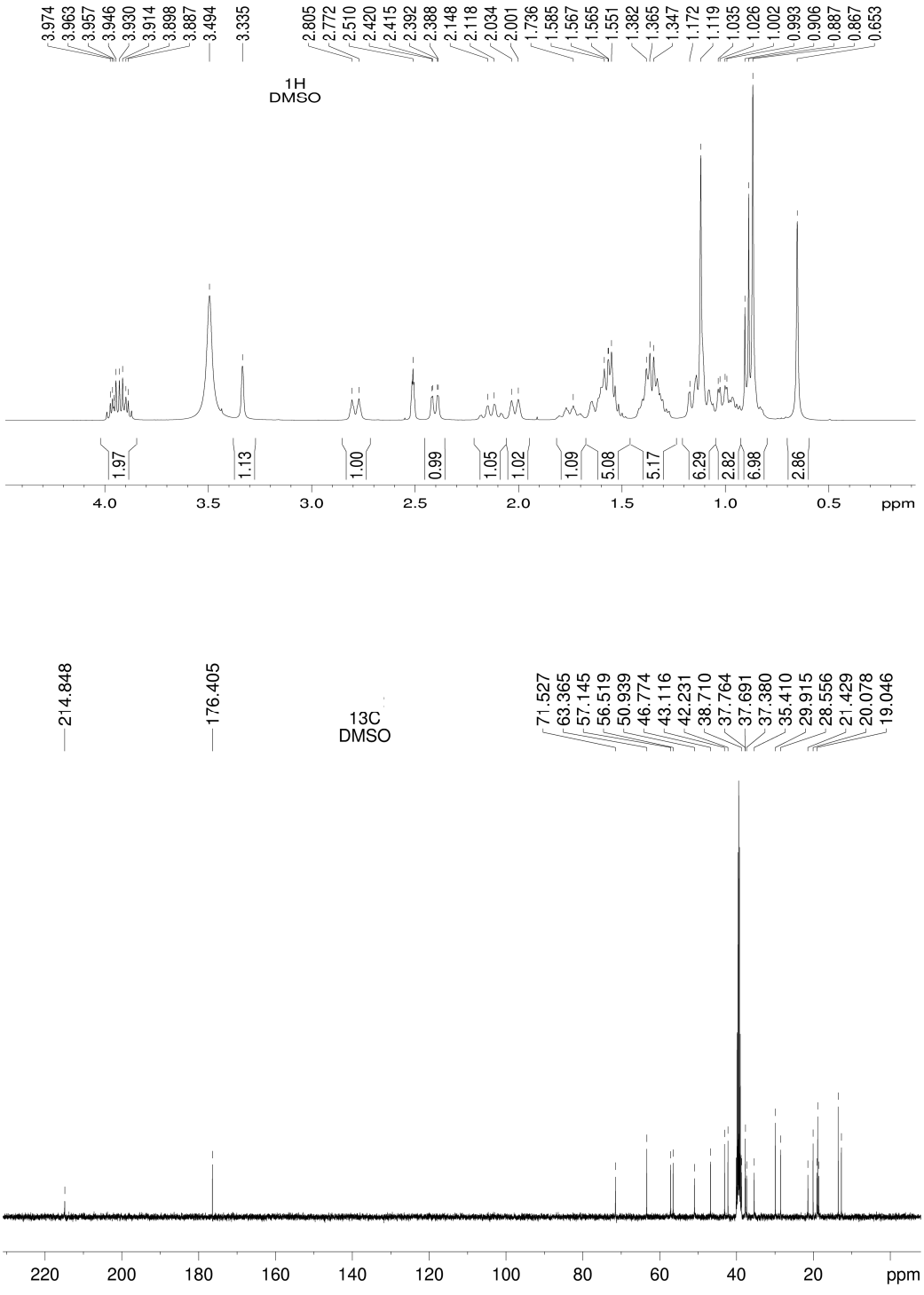


Figure S8. ^{1}H and ^{13}C NMR of **7**.

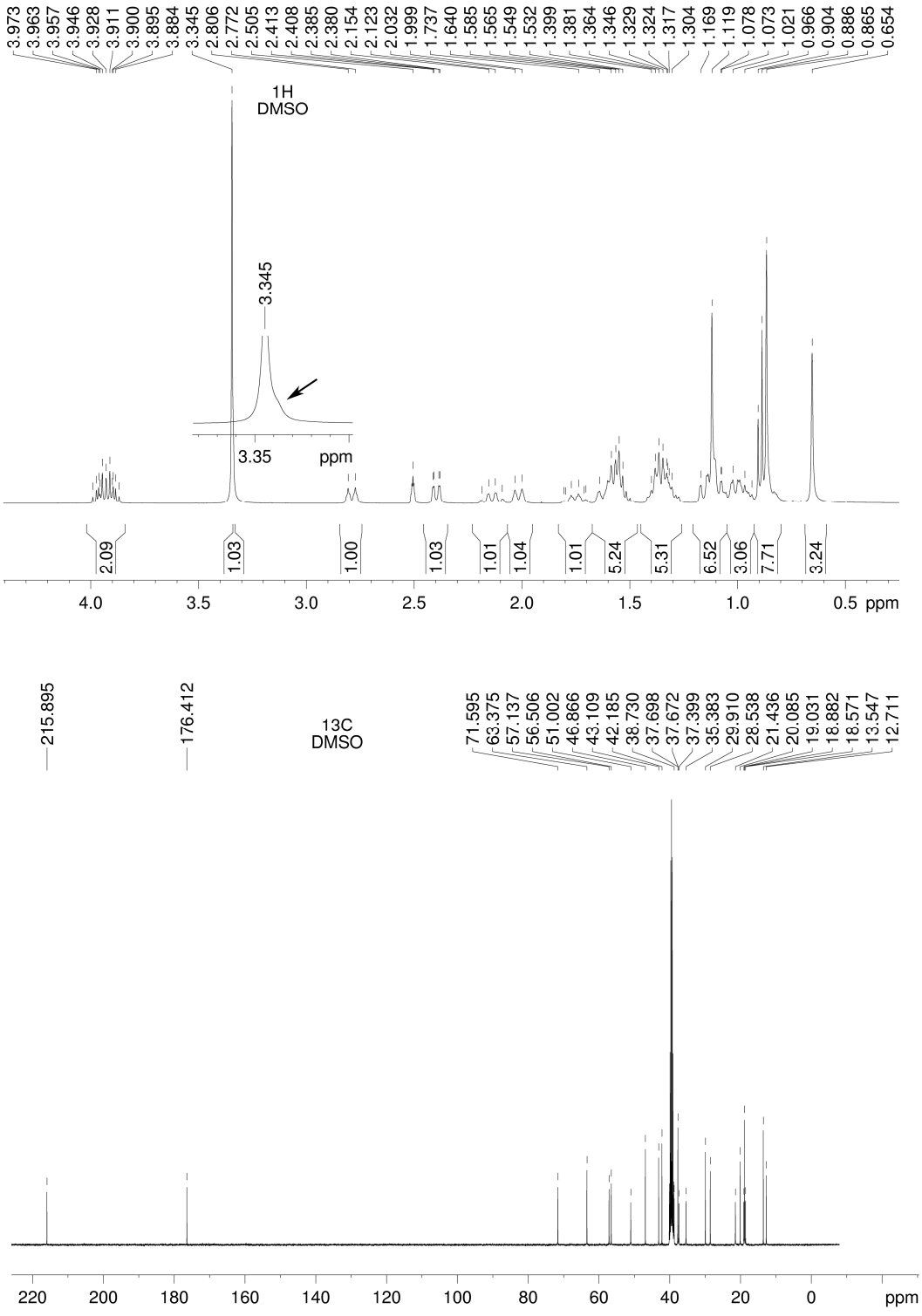


Figure S9. ^{1}H and ^{13}C NMR of **8**.

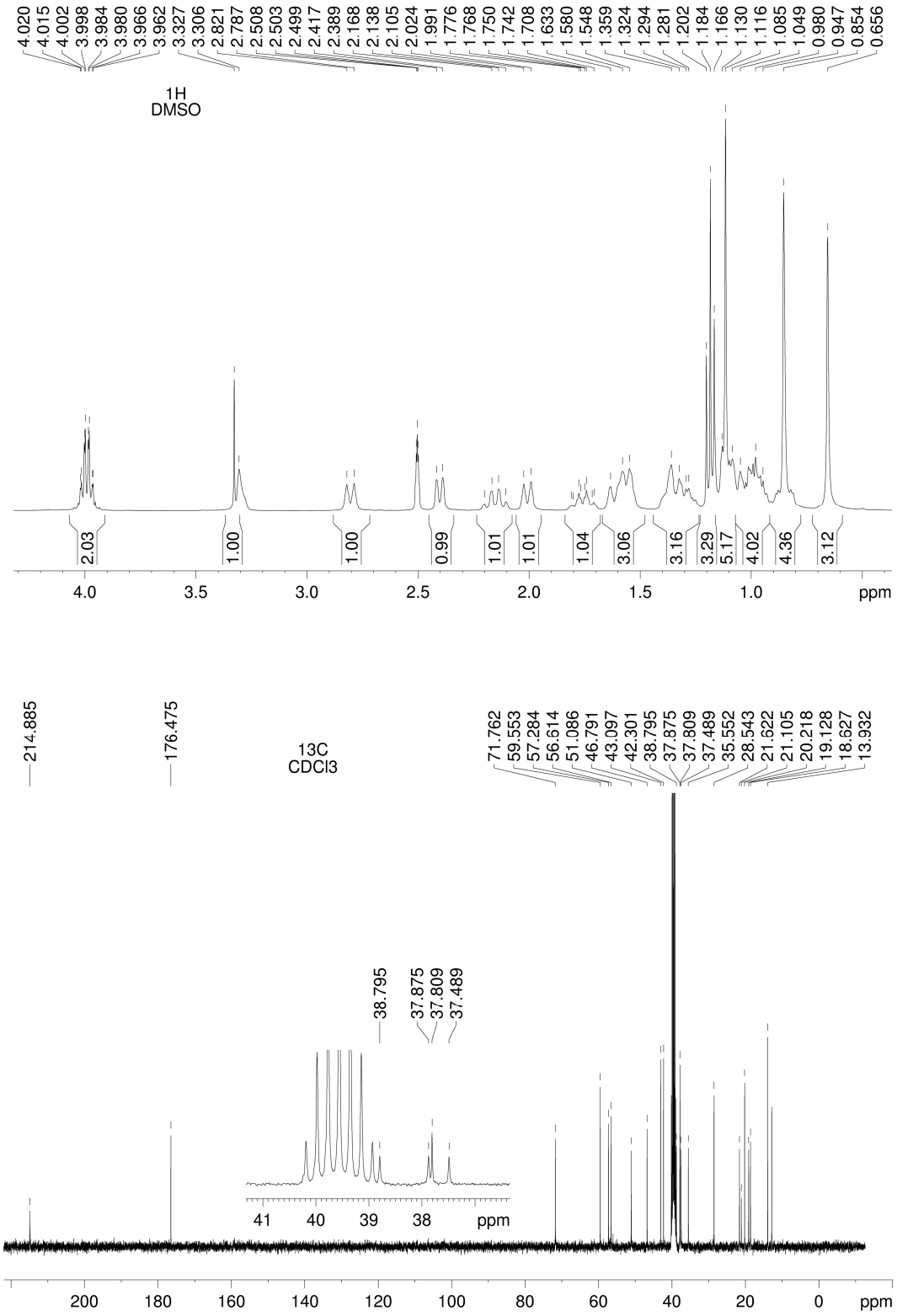


Figure S10. ^{1}H and ^{13}C NMR of **9**.

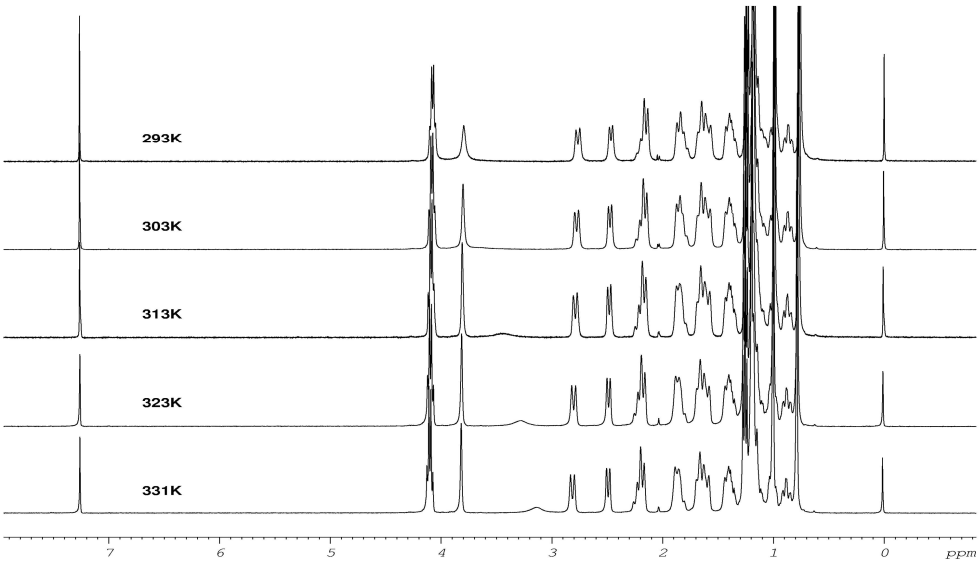


Figure S11. Variable temperature ^{1}H NMR of the gel in $CDCl_3$-d

5.2 FT-IR spectra

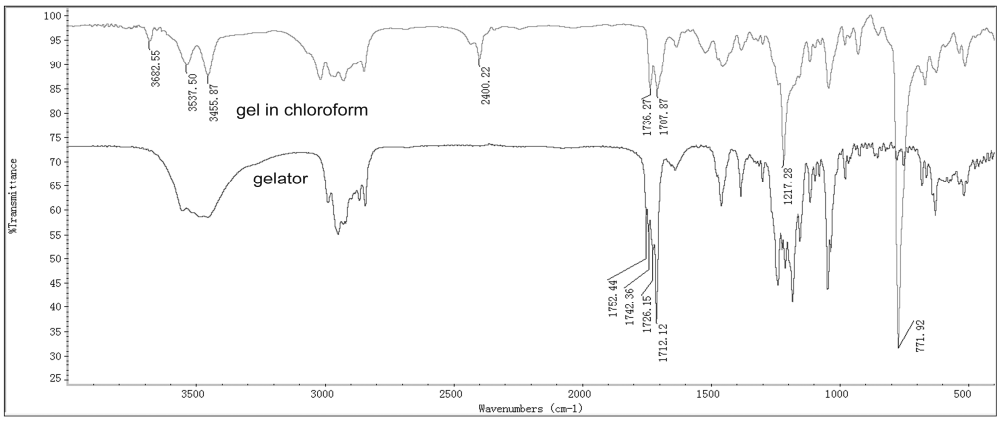


Figure S12. FT-IR of **4** and the gel in chloroform. The peaks at 771, 1217, 2400, 3682 cm^{-1} are absorptions of chloroform.

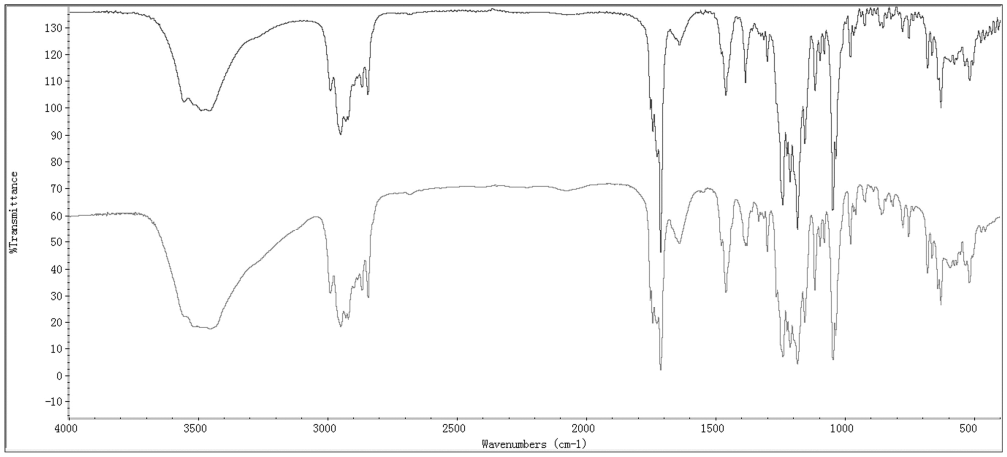


Figure S13. FT-IR of **4** and the xerogel from air-dried chloroform.

5.3 X-ray powder diffraction patterns of the xerogel and gelator 4.

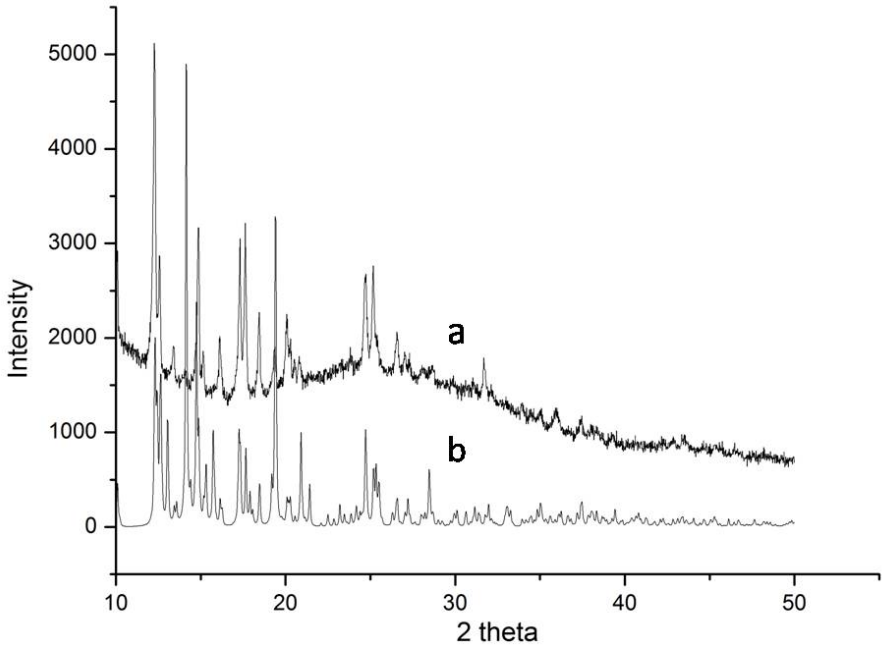


Figure S14. a) X-ray powder diffraction patterns of xerogel. b) powder diffractogram of the crystal of gelator **4.**

5.4 H-bonds and weak interactions in molecular packing

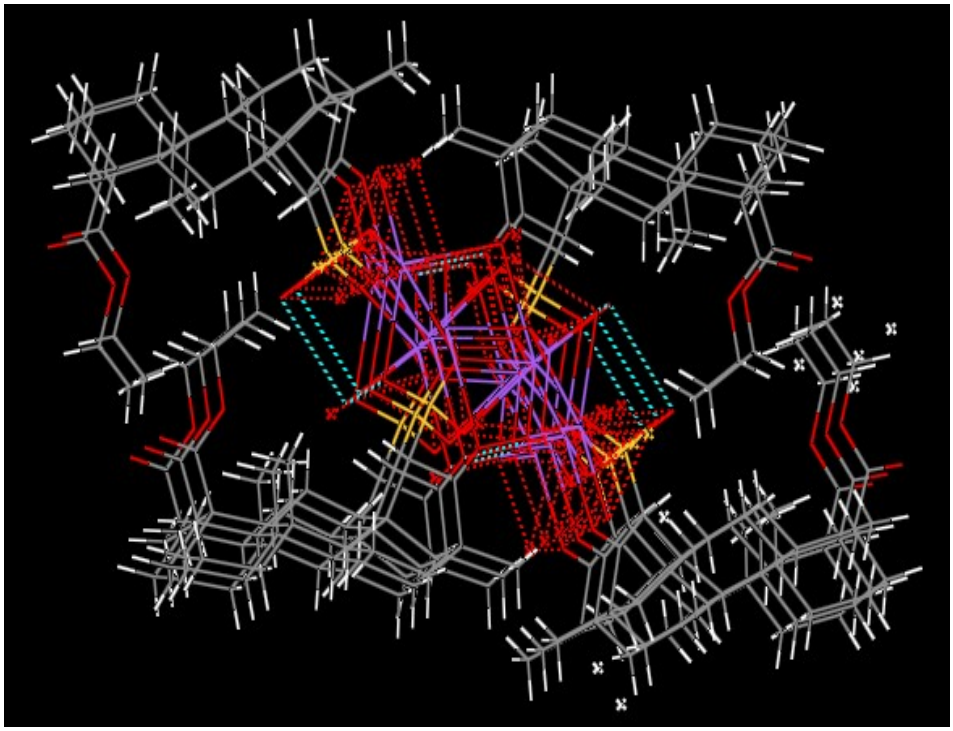


Figure S15. H-bonds in the crystalline structure.

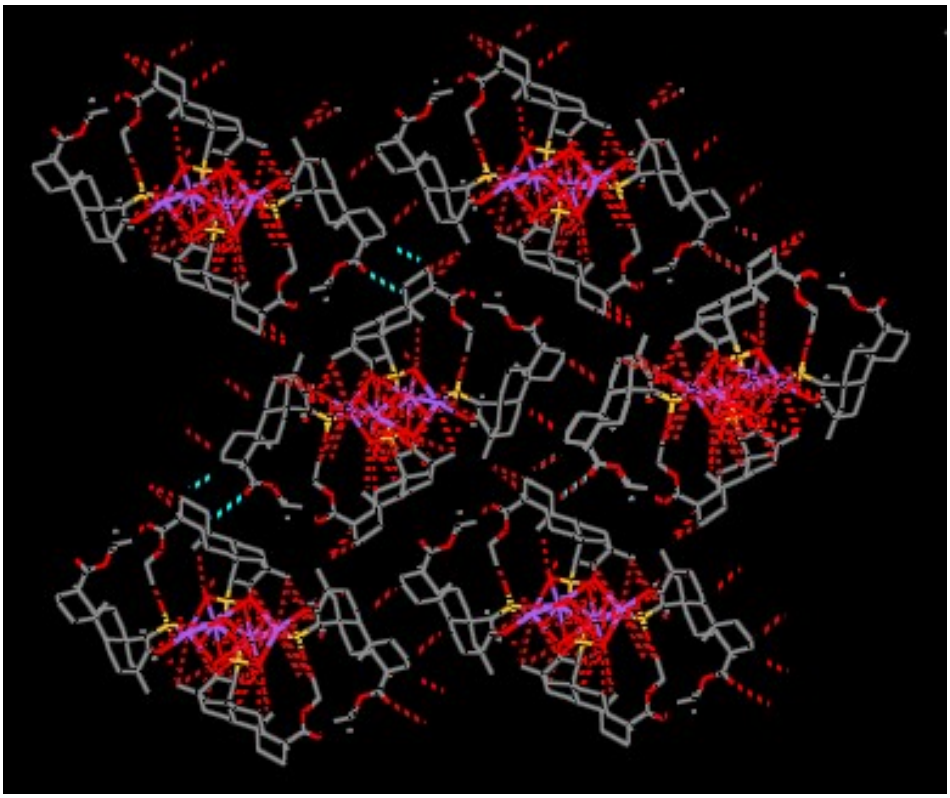


Figure S16. Weak interactions between the 1-D structure.

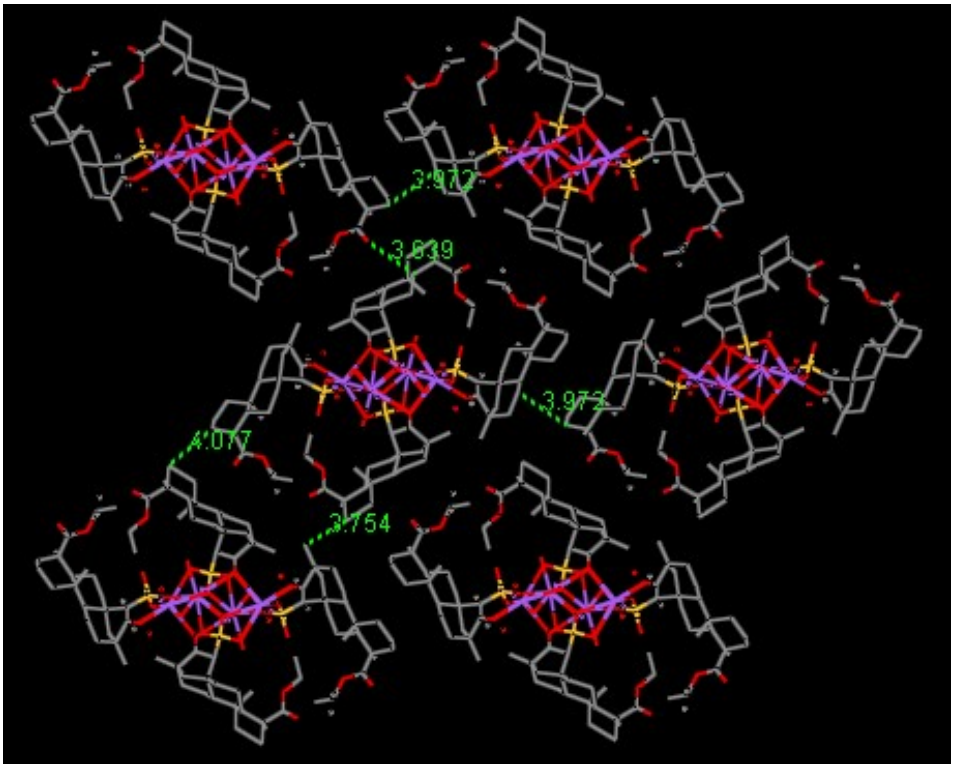


Figure S17. Distances between the nearest carbons in the neighbouring 1-D structures.

References:

S1. A. D. Kinghorn, D. D. Soejarto, N. P. D. Nanayakkara, C. M. Compadre, H. C. Makapugay, J. M. Hovanec-Brown, P. J. Medon and S. K. Kamath, *J. Nat. Prod.*, 1984, **47**, 439;

S2. M. S. Melis, *J. Nat. Prod.*, 1992, **55**, 688.

S3. X. F. Liu, X. Huang and H. S. Xu, *Wuhandaxue Xuebao* (*Ziran Kexueban*) 1994, **2**, 74.