Electronic Supplementary Information

Designing a simple organic salt-based supramolecular topical gel capable of displaying *in vivo* self-delivery application

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Table of Content

Materials, methods and synthesis.....2
Physico-chemical data 3-6
^{1}H-NMR and ^{13}C NMR spectra of salts **1-15** 7-21
Gelation experiment, Gelation table, T_{gel} experiment.....22-23,34
TEM studies.....23-24,35
Crystal structures: Crystal parameters, ORTEP plot, Hydrogen bonding parameters 24-31
X-Ray Powder Diffraction pattern of **1, 3, 4, 5** and **8**.....32
MTT assay.....32-33
Rheology.....34
PGE_2 assay, Formulation of topical gel **13**.....35
Check CIF/ PLATON report of **1, 3, 4, 5** and **8**.....36-50

Materials, Methods and Synthesis

Materials

All the chemicals were commercially available and used without further purification. Solvents were of analytical reagent grade and used without further distillation. PGE_2 assay was performed using Prostaglandin E2 EIA Kit – Monoclonal (Cayman Chemicals, Ann Arbor, MI). Hair removing cream Veet (Veet, India) and inflammation inducing agent, imiquimod (Glenmark, India) used in the *in vivo* experiments were purchased from the local market. All the BALB/c male mice were maintained throughout the experiments in the animal house facility of Department of Biological Chemistry, Indian Association for the Cultivation of Science, Kolkata as per guidelines of Institutional Animal Ethics Committee (IAEC).

Methods

The elemental analyses of the salts were carried out using a Perkin–Elmer Precisely, Series-II, CHNO/S Analyser-2400. FT-IR spectra were obtained using instrument FTIR-8300, Shimadzu. NMR spectra (both ^{1}H and ^{13}C) were recorded using 400 MHz and 500 MHz spectrometer (Bruker Ultrasheild Plus-500). TEM images were recorded using a JEOL instrument with 300 mesh copper TEM grid. Rheology studies were carried out using an SDT Q series advanced rheometer AR 2000. MTT and PGE_2 assay were conducted using a multiplate ELISA reader (Varioskan Flash Elisa Reader, Thermo Fisher).

Synthesis of salts

Naproxen β-peptide derivatives were synthesized according to the methods described in our recently reported literature.[1] All the salts were prepared by reacting the corresponding acids and amines in 1:1 molar ratio in methanol at room temperature followed by evaporation of the solvent in a rotary evaporator. The resultant solid was isolated as the salt in near-quantitative yield. FT-IR spectra (KBr) of the salts showed the presence of stretching band of the carboxylate group (COO^-) at ≈ 1650-1533 cm^{-1} and the absence of carbonyl stretching band (C=O) of COOH group at ≈1703-1699 cm^{-1} indicating complete salt formation.

Physico-chemical Data

Salt 1: M.P: 195-196°C. Elemental analysis calculated for $C_{20}H_{27}NO_3$ (%): C, 72.92; H, 8.26; N, 4.25; found: C, 73.06; H, 8.24; N, 3.90. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.71-7.67 (dd, *J* =7, 6.5 Hz, 3H), 7.51-7.49 (d, *J* = 8 Hz,1H), 7.18 (s, 1H), 7.09-7.07 (dd, *J* = 2.5, 2.5 Hz, 1H), 3.89 (s, 3H), 3.74-3.70 (q, *J* = 7 Hz, 1H), 2.93-2.91 (m, 1H), 1.93-1.63 (m, 4H), 1.51-1.50 (d, *J* = 7 Hz, 3H), 1.33-1.23 (m, 4H), 1.18-1.11 (m, 2H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 176.52, 158.70, 140.55, 134.81, 130.54, 130.12, 127.98, 127.59, 126.50, 119.40, 106.61, 55.71, 51.42, 50.14, 32.09, 25.89, 25.36, 19.90 ppm. (Fig. S1). FT-IR (KBr pellet): 1554 (s, salt stretch) cm^{-1}.

Salt 2 : M.P: 153-154°C. Elemental analysis calculated for $C_{26}H_{37}NO_3$ (%): C, 75.87; H, 9.06; N, 3.40; found: C, 75.68; H, 8.66; N, 3.37. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.71-7.68 (dd, *J* =7, 6.5 Hz, 3H), 7.51-7.49 (d, *J* = 8 Hz, 1H), 7.18 (s, 1H), 7.09-7.07 (dd, *J* = 2.5, 2.5 Hz, 1H), 3.89 (s, 3H), 3.74-3.70 (q, *J* = 7 Hz, 1H), 3.15-3.10 (m, 2H), 2.02-2.69 (m, 8H), 1.51-1.49 (d, *J* = 7 Hz, 3H), 1.39-1.27 (m, 8H) , 1.25-1.16 (m, 2H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 183.53, 158.90, 140.43, 134.88, 130.23, 130.07, 128.02, 126.50, 119.44, 106.58, 55.67, 54.37, 50.16, 30.62, 26.12, 25.48, 19.86 ppm. (Fig. S2). FT-IR (KBr pellet): 1533 (s, salt stretch) cm^{-1}.

Salt 3 : M.P: 164-165°C. Elemental analysis calculated for $C_{21}H_{23}NO_3$ (%): C, 74.75; H, 6.87; N, 4.15; found: C, 75.17; H, 6.49; N, 4.04. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.71-7.68 (dd, *J* =7, 6.5 Hz, 2H), 7.67 (s, 1H), 7.50-7.49 (d, *J* = 2.5 Hz, 1H), 7.39 (s, 5H), 7.17 (s, 1H), 7.09-7.07 (dd, *J* =3.0, 2.5 Hz, 1H), 4.01 (s, 2H), 3.89 (s, 3H), 3.75-3.71 (q, *J* = 7 Hz, 1H), 1.51-1.50 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 182.49, 158.83, 139.88, 134.91, 134.81, 130.51, 130.14, 130.02, 129.88, 127.81, 127.75, 126.61, 119.55, 106.59, 101.39, 55.69, 44.79, 44.25, 19.73 ppm. (Fig. S3). FT-IR (KBr pellet): 1548 (s, salt stretch) cm^{-1}.

Salt 4 : M.P: 114-115°C. Elemental analysis calculated for $C_{28}H_{29}NO_3$ (%): C, 78.66; H, 6.84; N, 3.28; found: C, 78.38; H, 6.79; N, 2.91. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.69-7.67 (d, *J* =7, 6.5 Hz, 3H), 7.45-7.43 (d, *J* = 2.5, Hz, 1H), 7.42-7.38 (m, 10H), 7.18-7.17 (d, 1H), 7.09-7.06 (dd, *J* =3, 3 Hz, 1H), 4.08 (s, 4H), 3.88 (s, 3H), 3.79-3.74 (q, *J* = 9 Hz, 1H), 1.51-1.49 (d, *J* = 9 Hz, 3H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 182.14, 158.79, 139.86, 134.90, 134.21, 134.12, 130.76, 130.49, 130.14, 130.01, 127.83, 127.75, 126.63, 119.56, 106.59, 55.70, 52.06, 52.04, 19.69 ppm. (Fig. S4). FT-IR (KBr pellet): 1525 (s, salt stretch) cm^{-1}.

Salt 5 : M.P: 133-134°C. Elemental analysis calculated for $C_{23}H_{32}N_2O_4$ (%): C, 68.97; H, 8.05; N, 6.99; found: C, 68.50; H, 8.10; N, 6.79. ^{1}H NMR (500 MHz, DMSO-d_6, 25°C): δ = 7.97 (s, 1H, N-H), 7.77-7.71 (dd, *J* =7, 6.5 Hz, 2H), 7.69 (s, 1H), 7.43-7.41 (d, *J* = 8 Hz,1H), 7.25 (s, 1H), 7.13-7.11 (dd, *J* = 3, 2.5, Hz, 1H), 3.85 (s, 3H), 3.71-3.67 (q, *J* = 7 Hz, 1H), 3.23-3.12 (m, 2H), 2.77 (m, 1H), 2.12-2.10 (t, *J* = 7 Hz, 2H), 1.83-1.53 (m, 4H), 1.38-1.37 (d, *J* = 7 Hz, 3H) , 1.21-1.13 (m, 4H), 1.08-1.04 (m, 2H), ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 177.07, 176.85, 159.15, 138.22, 135.05, 130.61, 130.46, 128.17, 127.26, 126.76, 119.48, 106.65, 55.74, 51.43, 47.57, 37.88, 31.98, 25.90, 25.34, 25.07,

19.83 ppm. (Fig. S5). FT-IR (KBr pellet): 1649 (s, amide C=O stretch), 1531(s, salt stretch) cm^{-1}.

Salt 6 : M.P: 154-155°C. Elemental analysis calculated for $C_{29}H_{42}N_2O_4$ (%): C, 72.17; H, 8.77; N, 5.80; found: C, 72.43; H, 8.70 ; N, 5.55. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.71-7.69 (d, *J* =7 Hz, 3H), 7.42-7.40 (d, *J* = 8 Hz, 1H), 7.18 (s, 1H), 7.10-7.08 (dd, *J* =7 Hz, 1H), 3.88 (s, 1H), 3.75-3.71 (q, *J* = 7 Hz, 1H), 3.43-3.36 (m, 2H), 3.14-3.09 (m, 2H), 2.32-2.31 (d, *J* = 7 Hz, 2H), 2.04-1.67 (m, 8H), 1.51-1.50 (d, *J* = 7 Hz, 3H). 1.38-1.27 (m, 8H), 1.24-1.14 (m, 4H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 178.60, 175.61, 157.81, 136.88, 133.94, 129.20, 128.99, 126.90, 125.98, 125.50, 118.56, 105.37, 54.49, 53.18, 46.36, 36.99, 36.73, 29.50, 24.94, 24.28, 17.60 ppm. (Fig. S6). FT-IR (KBr pellet): 1641 (s, amide C=O stretch), 1537 (s, salt stretch) cm^{-1}.

Salt 7 : M.P: 113-114°C. Elemental analysis calculated for $C_{24}H_{28}N_2O_4 + H_2O$ (%): C, 67.59; H, 7.09; N, 6.57; found: C, 68.06; H, 6.78; N, 6.43. ^{1}H NMR (500 MHz, DMSO-d_6, 25°C): δ = 8.01 (s, 1H, N-H), 7.77-7.71 (dd, *J* =7, 6.5 Hz, 2H), 7.69 (s, 1H), 7.43-7.41 (d, *J* = 8.5 Hz, 1H), 7.36-7.33 (m, 5H), 7.25 (s, 1H), 7.13-7.11 (d, *J* = 2.5 Hz, 1H), 3.85 (s, 3H), 3.82 (s, 2H), 3.71-3.70 (q, *J* = 7 Hz, 1H), 3.23-3.18 (m, 2H), 2.25-2.24 (t, *J* = 3 Hz, 2H), 1. 38-1.37 (d, *J* = 6 Hz, 3H) ppm. ^{13}C NMR (500 MHz, DMSO-d_6, 25°C): δ = 174.29, 173.87, 157.59, 138.11, 133.72, 129.71, 129.02, 128.86, 128.31, 127.57, 127.18, 127.10, 125.86, 119.11, 106.34, 55.77, 45.59, 44.85, 36.13, 35.65, 19.21 ppm. (Fig. S7). FT-IR (KBr pellet): 1649 (s, amide C=O stretch), 1530 (s, salt stretch) cm^{-1}.

Salt 8 : M.P: 111-112°C. Elemental analysis calculated for $C_{31}H_{34}N_2O_4$ (%): C, 74.67; H, 6.87; N, 5.62; found: C, 74.98; H, 6.62; N, 5.75. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.70-7.68 (d, *J* =7 Hz, 3H), 7.40 (s, 1H), 7.39-7.37 (m, 10H), 7.16-7.15 (d, *J* = 2.5 Hz, 1H), 7.09-7.07 (dd, *J* = 3, 2.5 Hz, 1H), 4.03 (s, 4H), 3.87 (s, 3H), 3.75-3.71 (q, *J* = 7 Hz, 1H), 3.41-3.34 (m, 2H), 2.34-2.31 (t, *J* = 8.5 Hz, 2H), 1.50-1.49 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 177.00, 176.94, 158.73, 138.17, 135.18, 134.06, 130.80, 130.42, 130.25, 130.13, 128.19, 127.25, 126.79, 119.86, 106.66, 55.73, 52.04, 47.54, 37.66, 37.43, 18.84 ppm. (Fig. S8). FT-IR (KBr pellet): 1666 (s, amide C=O stretch), 1533 (s, salt stretch) cm^{-1}.

Salt 9 : M.P: 140-141°C. Elemental analysis calculated for $C_{26}H_{37}N_3O_5 + H_2O$ (%): C, 63.78; H, 8.03; N, 8.58; found: C, 64.15; H, 7.56; N, 8.41. ^{1}H NMR (500 MHz, DMSO-d_6, 25°C): δ = 8.02 (s, 1H, N-H), 7.79 (s, 1H, N-H), 7.76-7.70 (dd, *J* =9, 8.5 Hz,2H), 7.67 (s, 1H), 7.41-7.39 (d, *J* = 8 Hz, 1H), 7.24 (s, 1H), 7.12-7.10 (d, *J* = 9 Hz, 1H), 3.83 (s, 1H), 3.72-3.68 (q, *J* = 7 Hz, 1H), 3.22-3.13 (m, 4H), 2.76 (s, 1H), 2.17-1.64 (m, 4H), 1.54-1.51 (d, *J* = 7 Hz, 3H), 1.37-1.16 (m, 4H), 1.14-1.03 (m, 2H) ppm. ^{13}C NMR (500 MHz, DMSO-d_6, 25°C): δ = 173.96, 170.65, 169.90, 157.57, 138.05, 133.71, 129.69, 128.99, 127.11, 125.83, 119.09, 106.32, 55.76, 49.83, 45.50, 36.32, 36.20, 36.07, 35.91, 31.87, 25.37, 24.54, 19.11 ppm. (Fig. S9).FT-IR (KBr pellet): 1643 (s, amide C=O stretch), 1541 (s, salt stretch) cm^{-1}.

Salt 10 : M.P: 152-153°C. Elemental analysis calculated for $C_{32}H_{47}N_3O_5 + H_2O$ (%): C, 67.22; H, 8.64; N, 7.35; found: C, 67.62; H, 8.38; N, 7.26. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.71-7.69 (dd, *J* =7, 6.5 Hz, 3H), 7.41-7.39 (d, *J* = 8 Hz,1H), 7.19 (s, 1H), 7.11-7.08 (dd, *J* =2.5, 2.5 Hz, 1H), 3.88 (s, 1H), 3.77-3.73 (q, *J* = 7 Hz, 1H), 3.41-3.31 (m, 2H), 3.17-3.12 (m, 2H), 2.32-2.28 (m, 2H), 2.05-2.03 (t, *J* = 7 Hz, 4H), 1.86-1.68 (m, 8H), 1.51-1.50 (d, *J* = 7 Hz, 3H). 1.37-1.28 (m, 8H), 1.23-1.18 (m, 2H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 178.42, 175.99, 172.05, 157.81, 136.77, 133.92, 129.16, 128.95, 126.88, 125.92, 125.48, 118.56, 105.35, 54.46, 53.21, 46.12, 36.89, 36.59, 35.86, 35.32, 29.41, 24.89, 24.23, 17.48 ppm. (Fig. S10). FT-IR (KBr pellet): 1656 (s, amide C=O stretch), 1556 (s, salt stretch) cm^{-1}.

Salt 11 : M.P: 125-126°C. Elemental analysis calculated for $C_{27}H_{33}N_3O_5 + H_2O$ (%): C, 65.17; H, 7.09; N, 8.44; found: C, 64.58; H, 6.36; N, 8.18. ^{1}H NMR (500 MHz, DMSO-d_6, 25°C): δ = 8.01-7.99 (t, 1H, N-H), 7.83-7.81(s, 1H, N-H), 7.76-7.70 (dd, *J* =7, 6.5 Hz,1H), 7.67 (s, 1H), 7.41-7.40 (d, *J* =8.5 Hz 1H), 7.37-7.30 (m, 5H), 7.25 (s, 1H), 7.12-7.10 (d, *J* =9 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 2H), 3.71-3.67 (q, *J* = 7 Hz, 1H), 3.22-3.15 (m, 4H), 2.22-2.15 (m, 4H), 1.37-1.36 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (500 MHz, DMSO-d_6, 25°C): δ = 174.27, 173.95, 170.73, 157.56, 138.04, 133.70, 129.68, 128.99, 128.89, 128.49, 127.79, 127.14, 127.10, 125.82, 119.09, 106.30, 55.74, 45.50, 44.47, 36.03, 35.90, 35.85, 35.70, 19.09 ppm. (Fig. S11). FT-IR (KBr pellet): 1641 (s, amide C=O stretch), 1552 (s, salt stretch) cm^{-1}.

Salt 12 : M.P: 184-185°C. Elemental analysis calculated for $C_{34}H_{39}N_3O_5 + H_2O$ (%): C, 69.48; H, 7.03; N, 7.15; found: C, 69.23; H, 6.66; N, 7.26. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.70-7.67 (dd, *J* =4.5, 3 Hz, 3H), 7.44-7.43 (d, *J* =6.5, Hz 1H), 7.40-7.39 (m, 10H), 7.17 (s, 1H), 7.09-7.07 (dd, *J* = 2.5, 2 Hz, 1H), 4.11 (s, 4H), 3.86 (s, 3H), 3.75-3.71 (q, *J* = 7 Hz, 1H), 3.39-3.36 (t, *J* =7.5 Hz, 4H), 2.31-2.28 (t, *J* = 7 Hz, 4H), 1.49-1.48 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 176.08, 176.04, 172.16, 157.84, 136.79, 133.95, 132.89, 129.53, 129.17, 128.97, 128.91, 128.87, 126.92, 125.94, 125.52, 118.61, 111.66, 105.39, 54.49, 51.03, 46.17, 36.22, 36.04, 35.84, 35.33, 17.50 ppm. (Fig. S12). FT-IR (KBr pellet): 1643 (s, amide C=O stretch), 1552 (s, salt stretch) cm^{-1}.

Salt 13 : M.P: 126-127°C. Elemental analysis calculated for $C_{17}H_{23}NO_5$+H_2O(%): C, 60.16; H, 7.42; N, 4.13; found: C, 59.93; H, 7.32; N, 3.86. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.68-7.66 (dd, *J* =7, 6.5 Hz, 2H), 7.65 (s, 1H), 7.48-7.47 (d, *J* = 2.5 Hz, 1H), 7.15 (s, 1H), 7.06-7.05 (d, *J* = 6.5 Hz, 1H), 3.87 (s, 3H), 3.71-3.67 (m, 4H), 3.60-3.57 (q, *J* = 7 Hz, 1H), 3.14-3.13 (d, *J* = 2.5, 1H), 1.49-1.47 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 183.90, 158.70, 140.27, 134.79, 130.46, 130.11, 127.87, 127.67, 126.50, 119.48, 106.56, 60.41, 55.89, 55.68, 55.48, 19.87 ppm. (Fig. S13). FT-IR (KBr pellet): 3168 (brs., O-H stretch), 1558 (s, salt stretch) cm^{-1}.

Salt 14 : M.P: 122-123°C. Elemental analysis calculated for $C_{20}H_{28}N_2O_6$+H_2O(%): C, 58.52; H, 7.37; N, 6.82; found: C, 58.40; H, 6.94; N, 6.44. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.71-7.69 (d, *J* =7, 6.5 Hz,2H), 7.68 (s, 1H), 7.41-7.40 (d, *J* = 2.5 Hz, 1H), 7.18 (s, 1H), 7.18 (s, 1H), 7.10-7.08 (dd, *J* =7, 6.5 Hz, 1H), 3.88 (s, 3H), 3.75-3.70 (m,

4H), 3.63-3.60 (q, *J* = 7 Hz, 1H), 3.43-3.36 (m, 2H), 3.20-3.16 (m, 1H), 2.34-2.31 (m, 2H), 1.51-1.50 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 180.56, 177.08, 159.10, 138.17, 135.22, 130.49, 130.26, 128.17, 127.23, 126.77, 119.81, 106.66, 60.74, 56.00, 55.75, 47.63, 37.80, 18.84 ppm. (Fig. S14). FT-IR (KBr pellet): 3251 (brs., O-H stretch), 1645 (s., amide C=O stretch), 1546 (s, salt stretch) cm^{-1}.

Salt 15 : M.P: 115-116°C. Elemental analysis calculated for $C_{23}H_{33}N_3O_7$+H_2O(%): C, 57.37; H, 7.33; N, 8.73; found: C, 56.83; H, 6.89; N, 8.47. ^{1}H NMR (500 MHz, MeOD, 25°C): δ = 7.71-7.70 (d, *J* =7, 6.5 Hz, 2H), 7.68 (s, 1H), 7.41-7.39 (d, *J* = 2.5 Hz, 1H), 7.19 (s, 1H), 7.10-7.09 (d, *J* =7, 6.5 Hz, 1H), 3.88 (s, 3H), 3.77-3.72 (q, *J* = 7 Hz, 1H), 3.71-3.69 (m, 4H), 3.62-3.59 (m, 2H), 3.41-3.39 (m, 2H), 3.17-3.15 (t, *J* = 6 Hz, 1H), 2.33-2.28 (m, 4H), 1.51-1.49 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (500 MHz, MeOD, 25°C): δ = 176.02, 172.32, 172.12, 157.80, 136.75, 133.91, 129.15, 128.93, 126.88, 125.90, 125.47, 118.55, 105.36, 59.74, 54.66, 54.45, 46.14, 36.75, 36.52, 35.84, 35.30, 17.46 ppm. (Fig. S15). FT-IR (KBr pellet): 3299 (brs.,O-H stretch), 1643 (s., amide C=O stretch), 1538 (s, salt stretch) cm^{-1}.

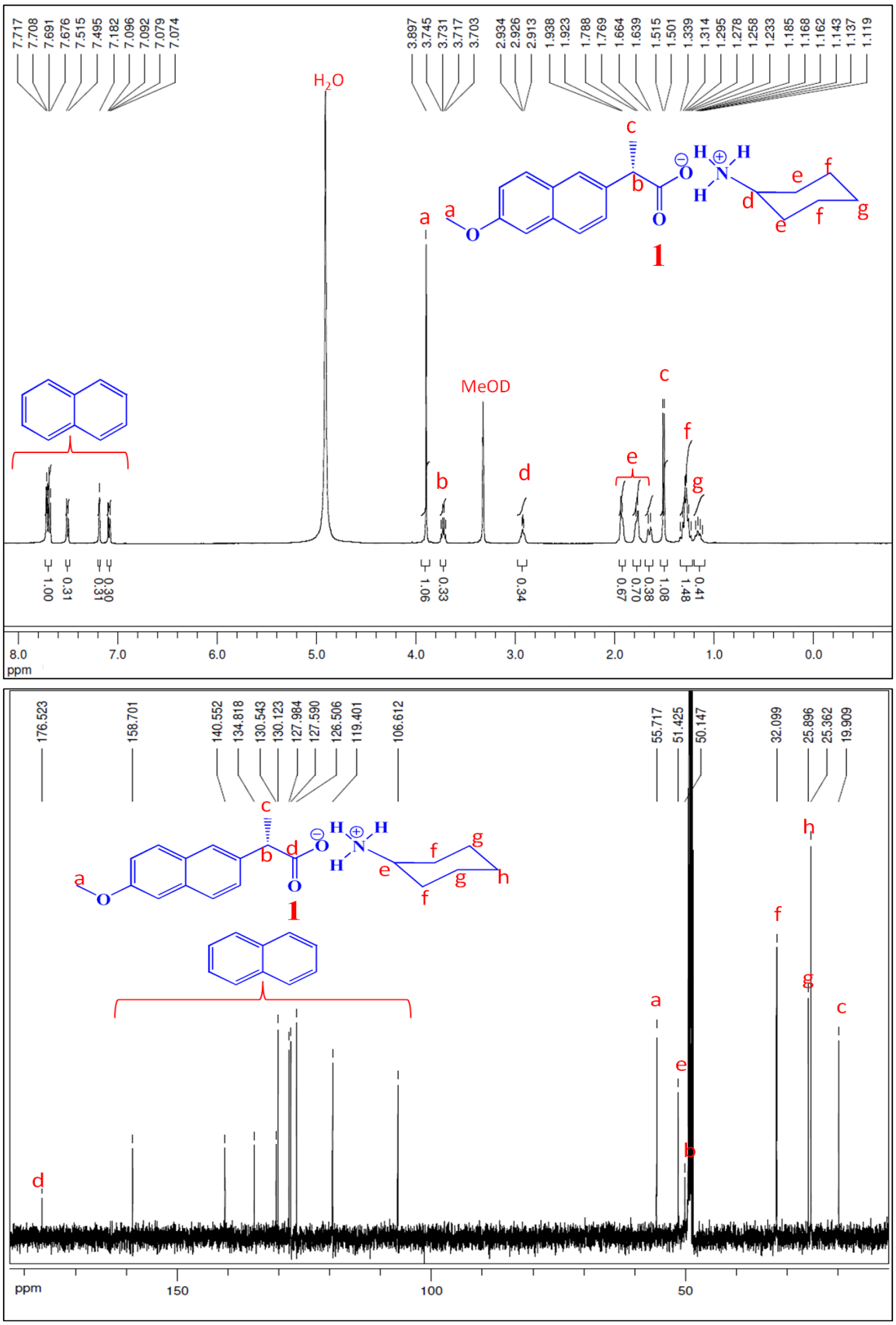


Fig. S1: ^{1}H NMR and ^{13}C-NMR spectra of **1** in MeOD.

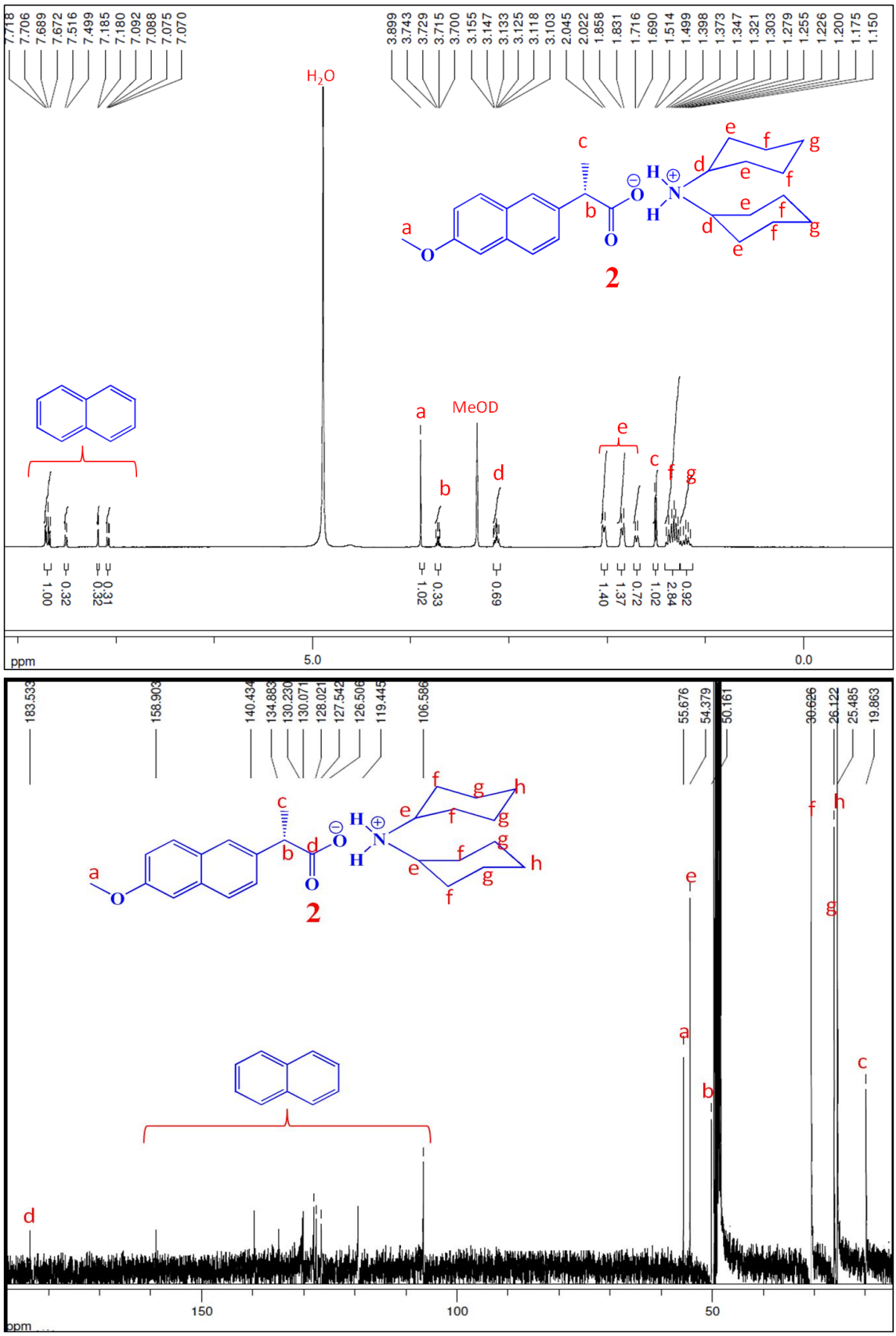


Fig. S2: ^{1}H NMR and ^{13}C-NMR spectra of **2** in MeOD.

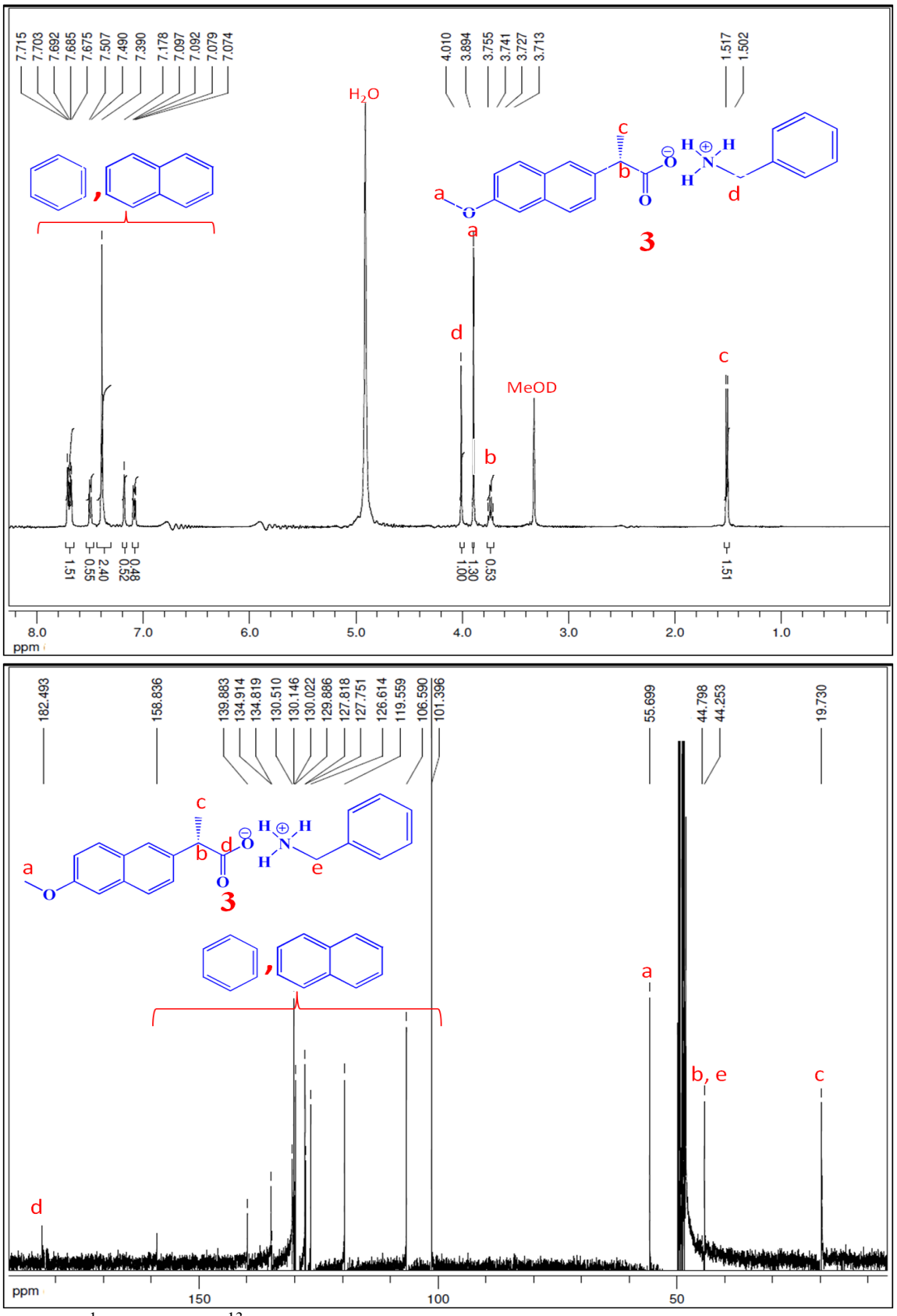


Fig. S3: ^{1}H NMR and ^{13}C-NMR spectra of **3** in MeOD.

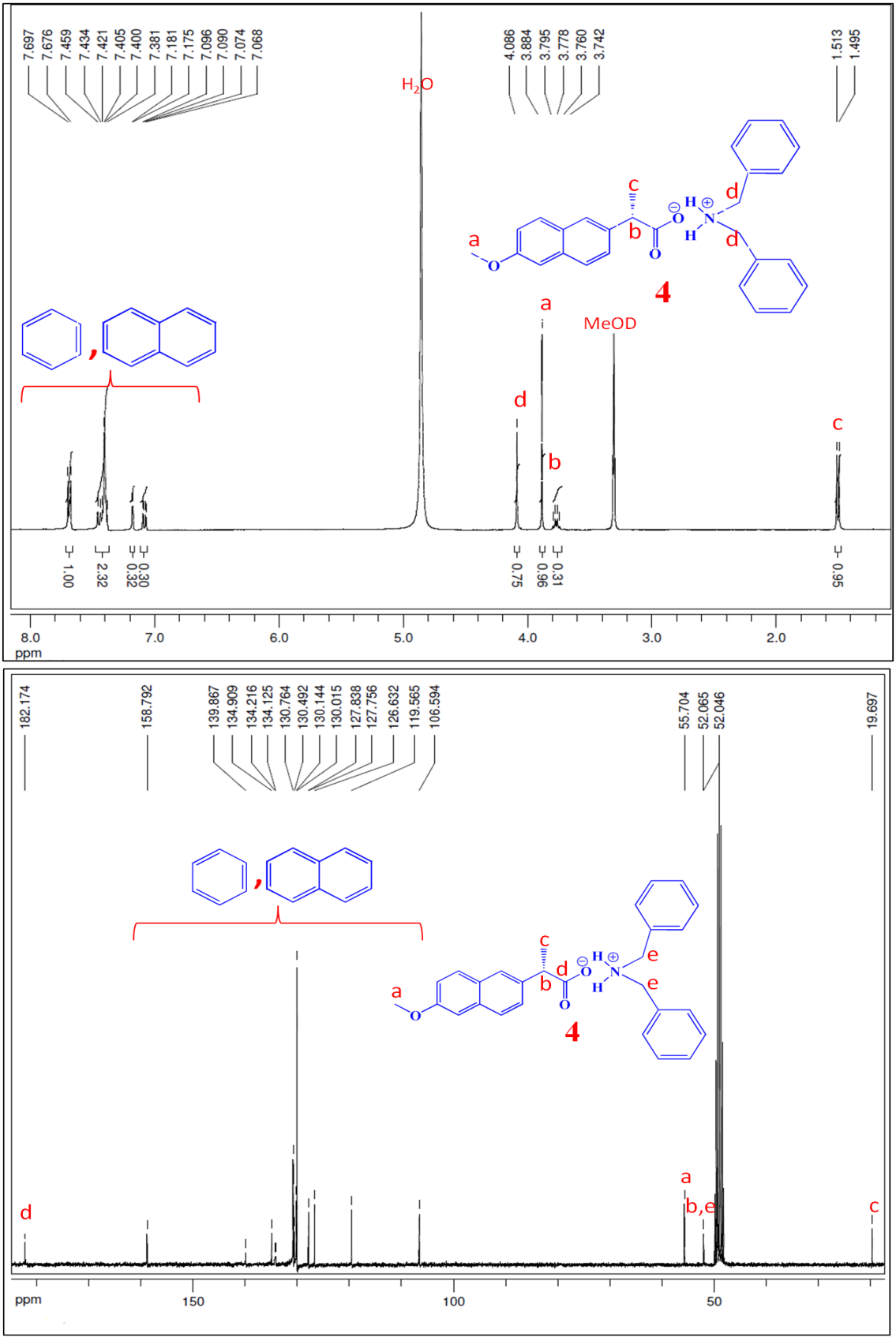


Fig. S4: ^{1}H NMR and ^{13}C-NMR spectra of **4** in MeOD.

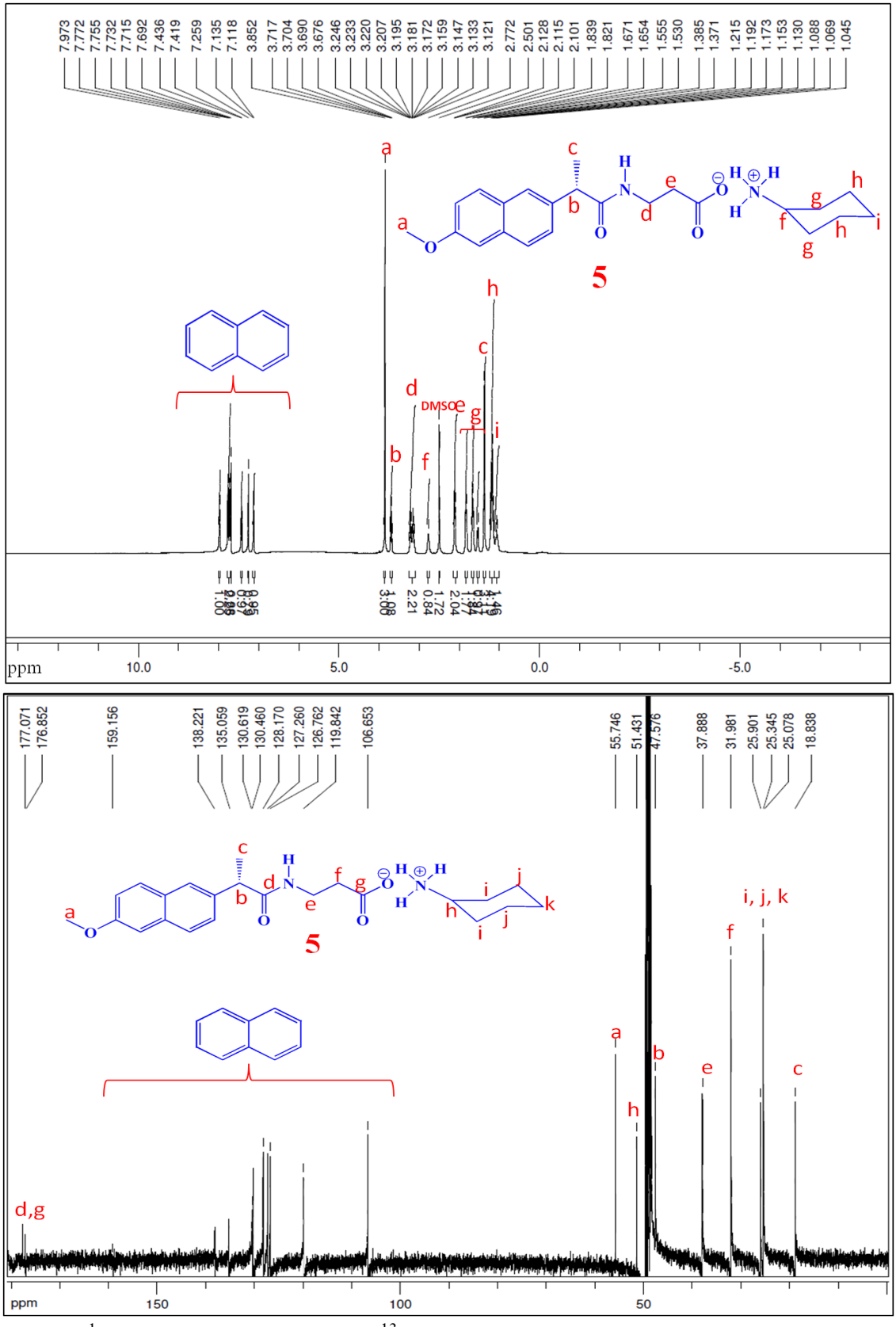


Fig. S5: ^{1}H NMR (in DMSO-d_6) and ^{13}C-NMR spectra of **5** (in MeOD).

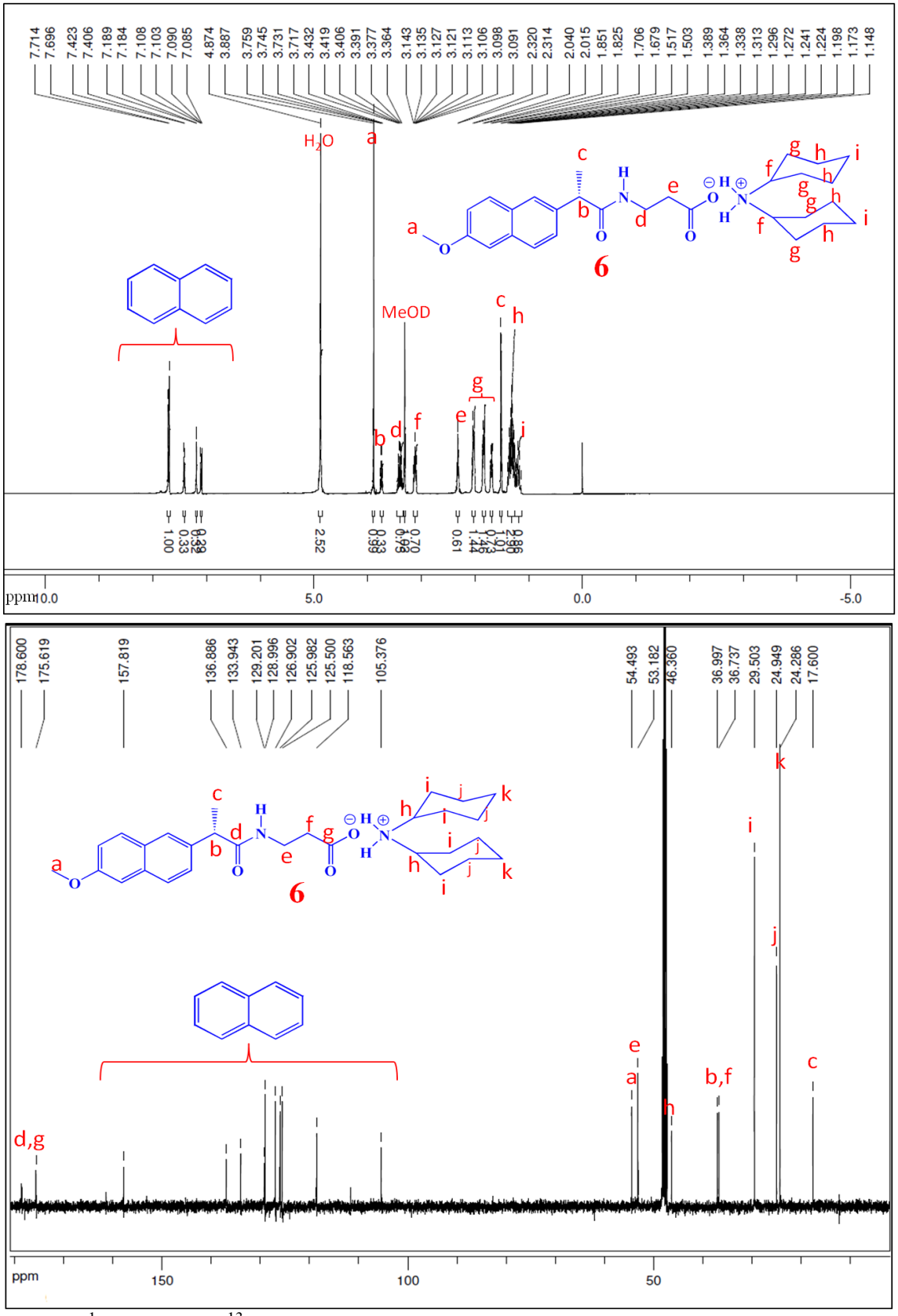


Fig. S6: ^{1}H NMR and ^{13}C-NMR spectra of **6** in MeOD.

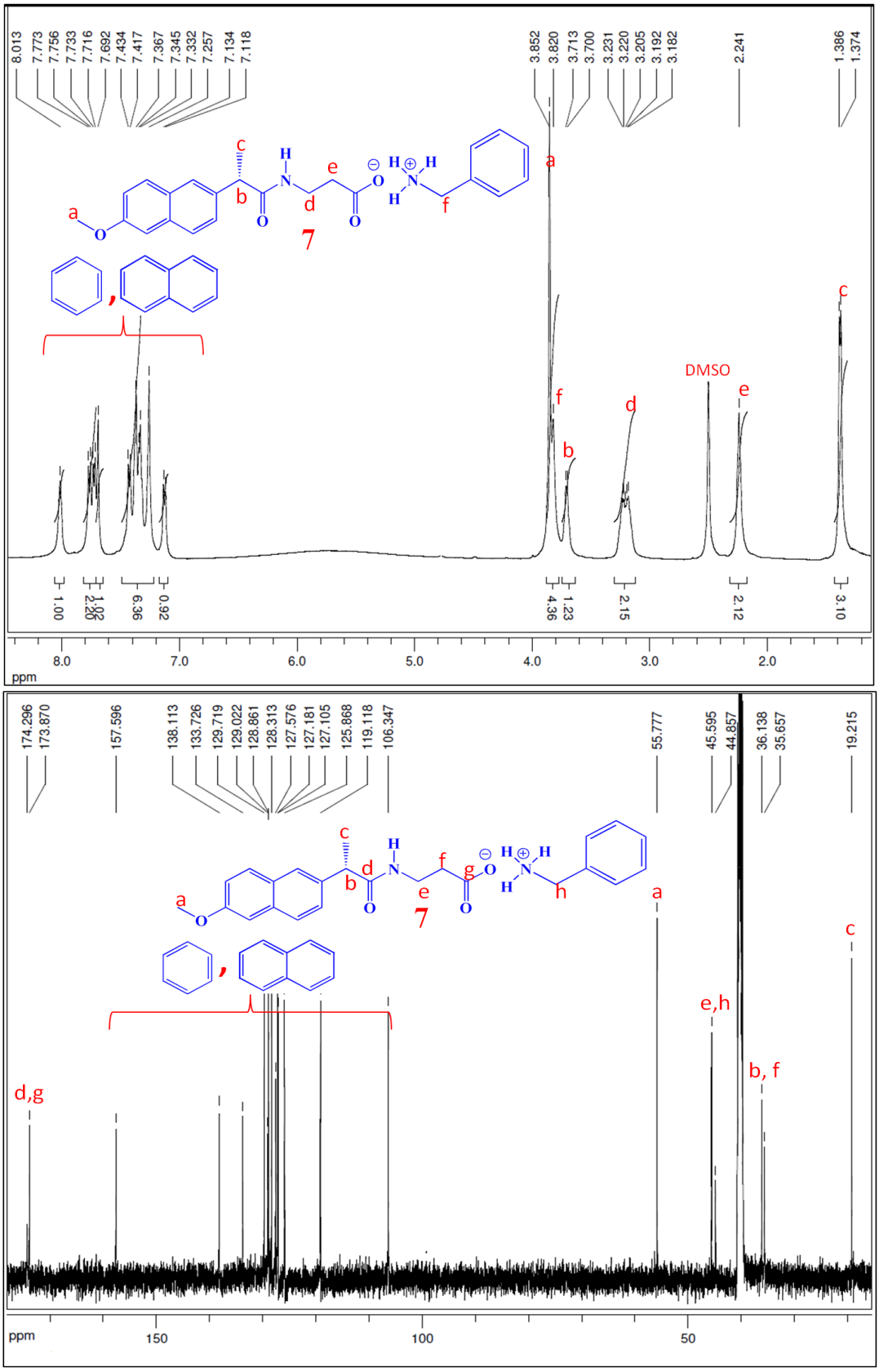


Fig. S7: ^{1}H NMR and ^{13}C-NMR spectra of **7** in DMSO-d_6.

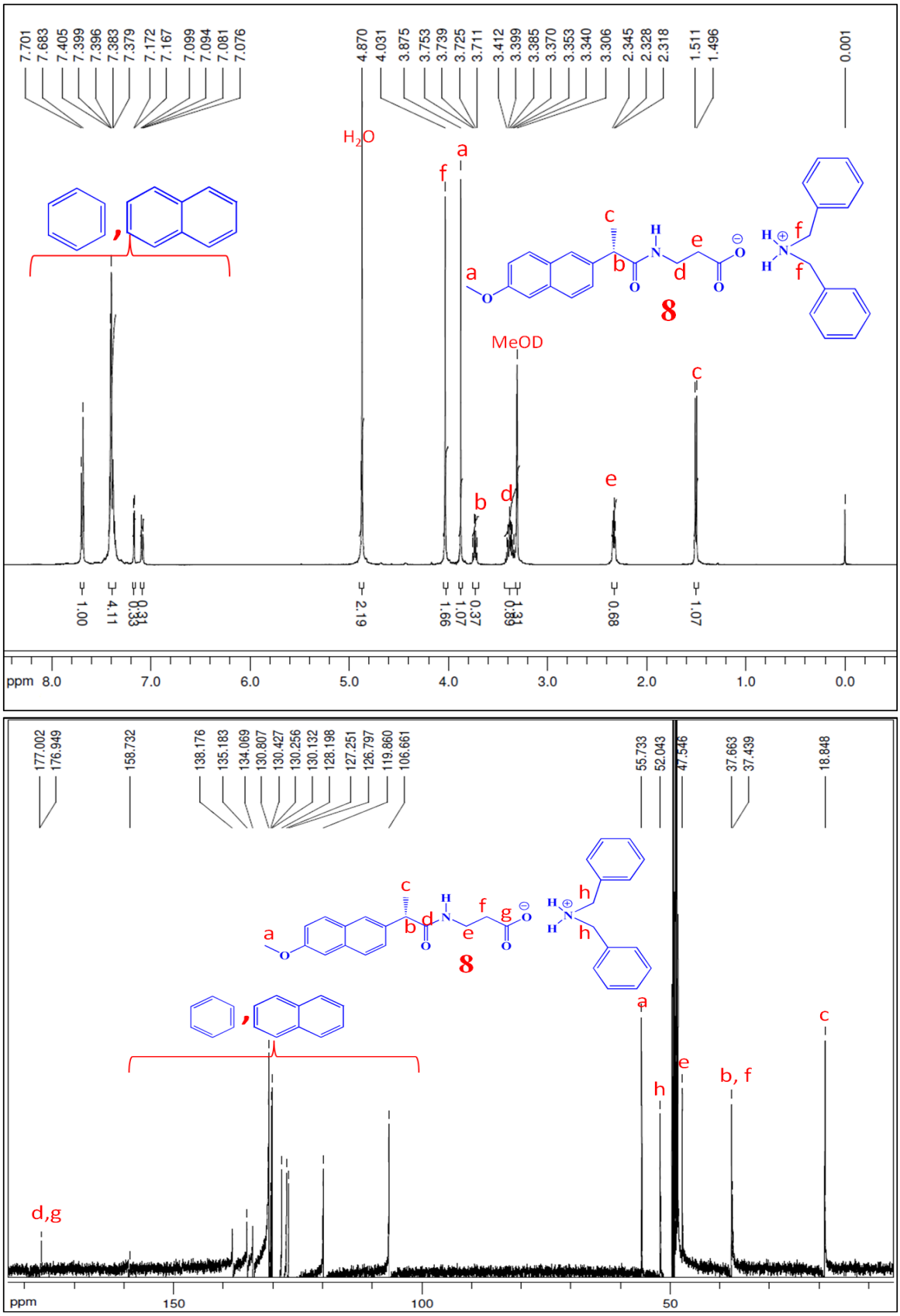


Fig. S8: ^{1}H NMR and ^{13}C-NMR spectra of **8** in MeOD.

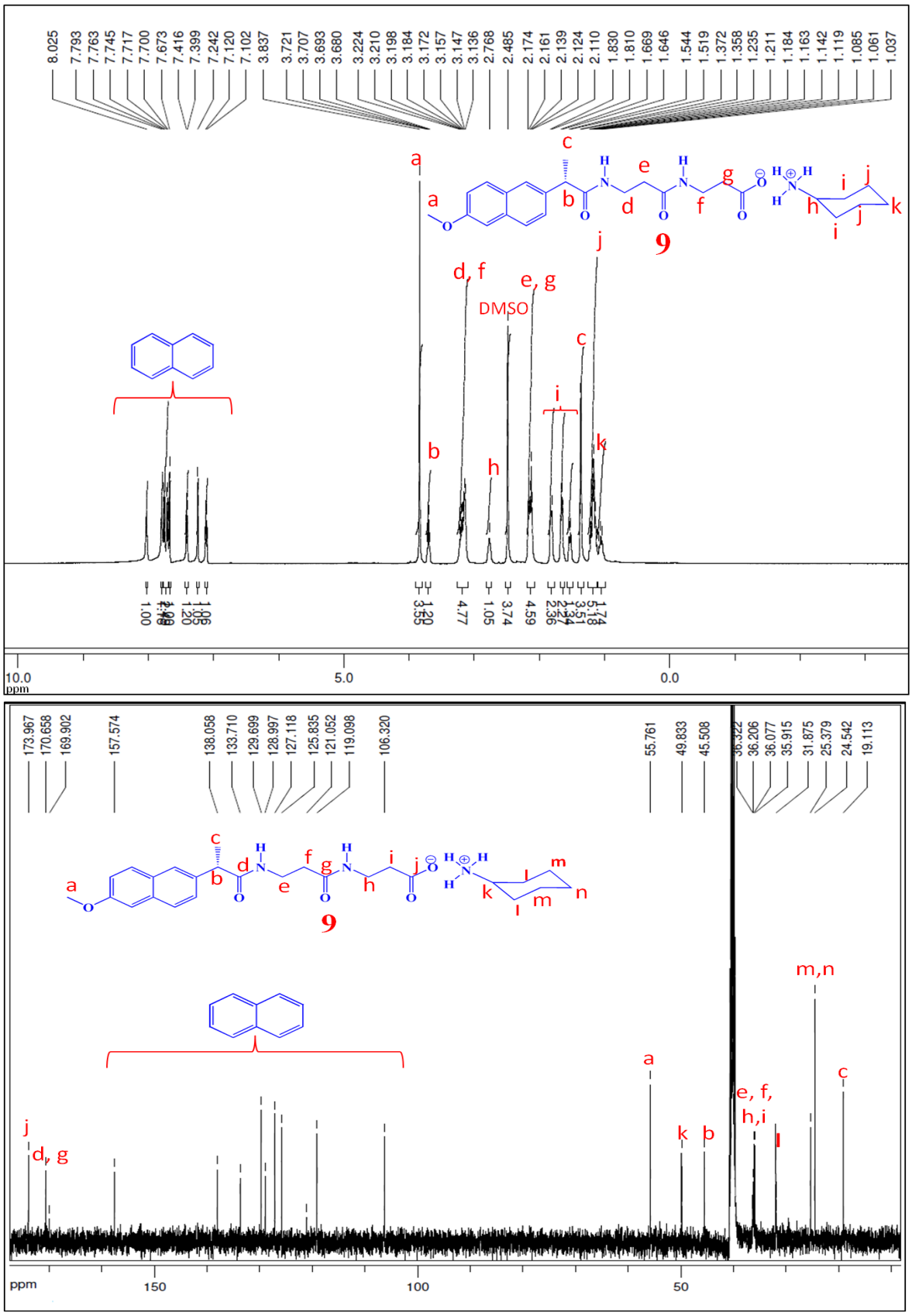


Fig. S9: ^{1}H NMR and ^{13}C-NMR spectra of **9** in DMSO-d_6.

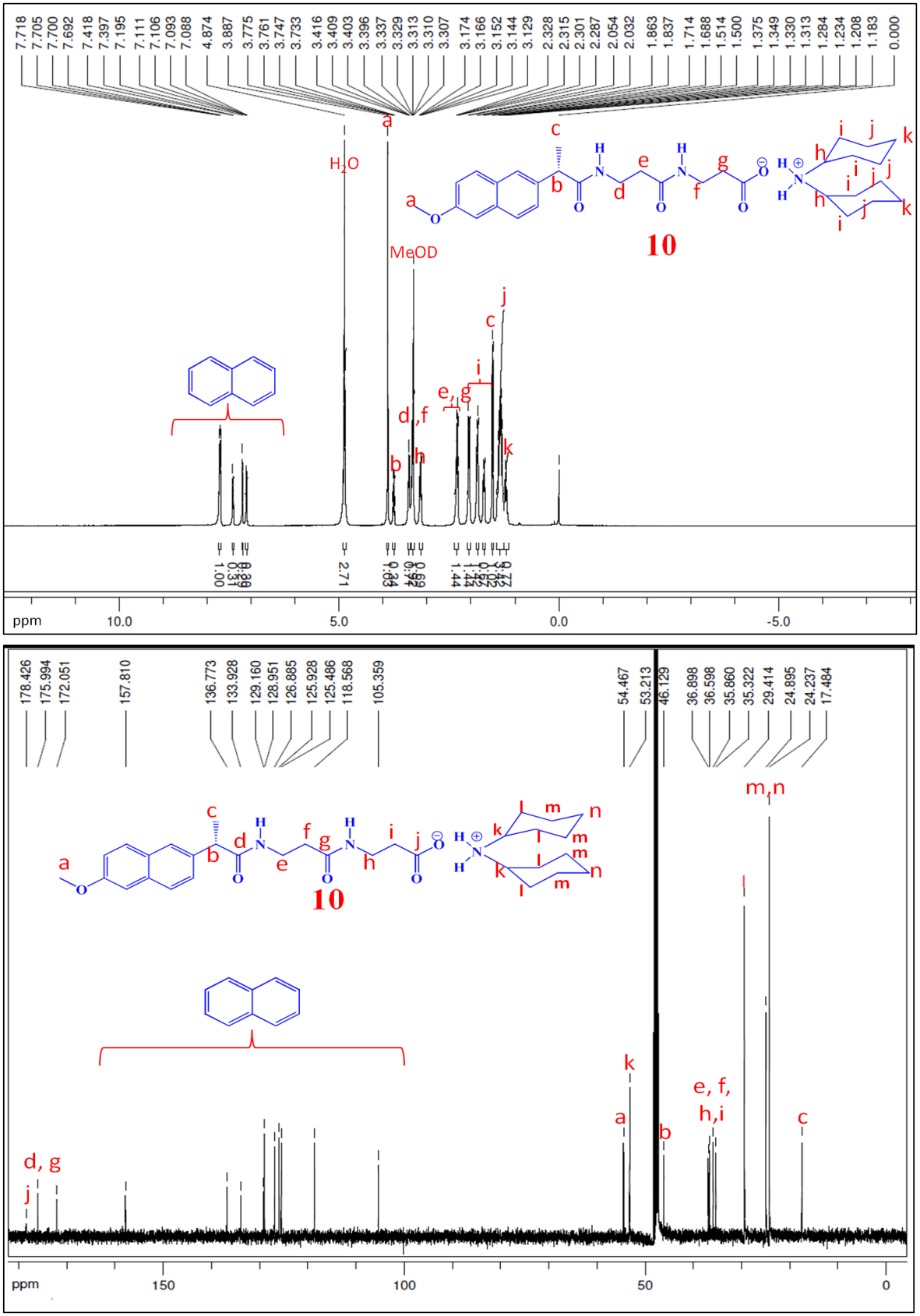


Fig. S10: ^{1}H NMR and ^{13}C-NMR spectra of **10** in MeOD.

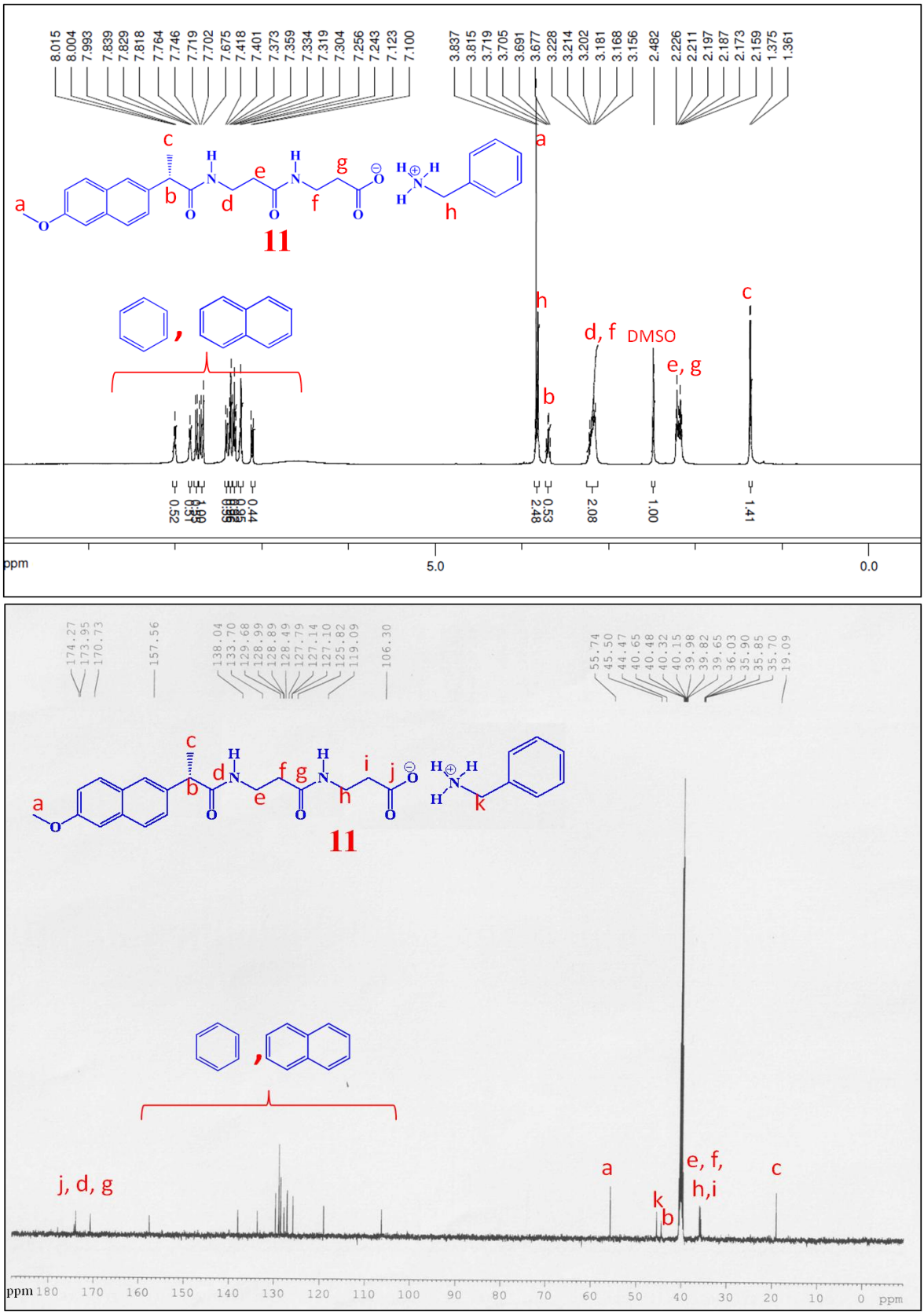


Fig. S11: ^{1}H-NMR and ^{13}C-NMR spectra of **11** in DMSO-d_6.

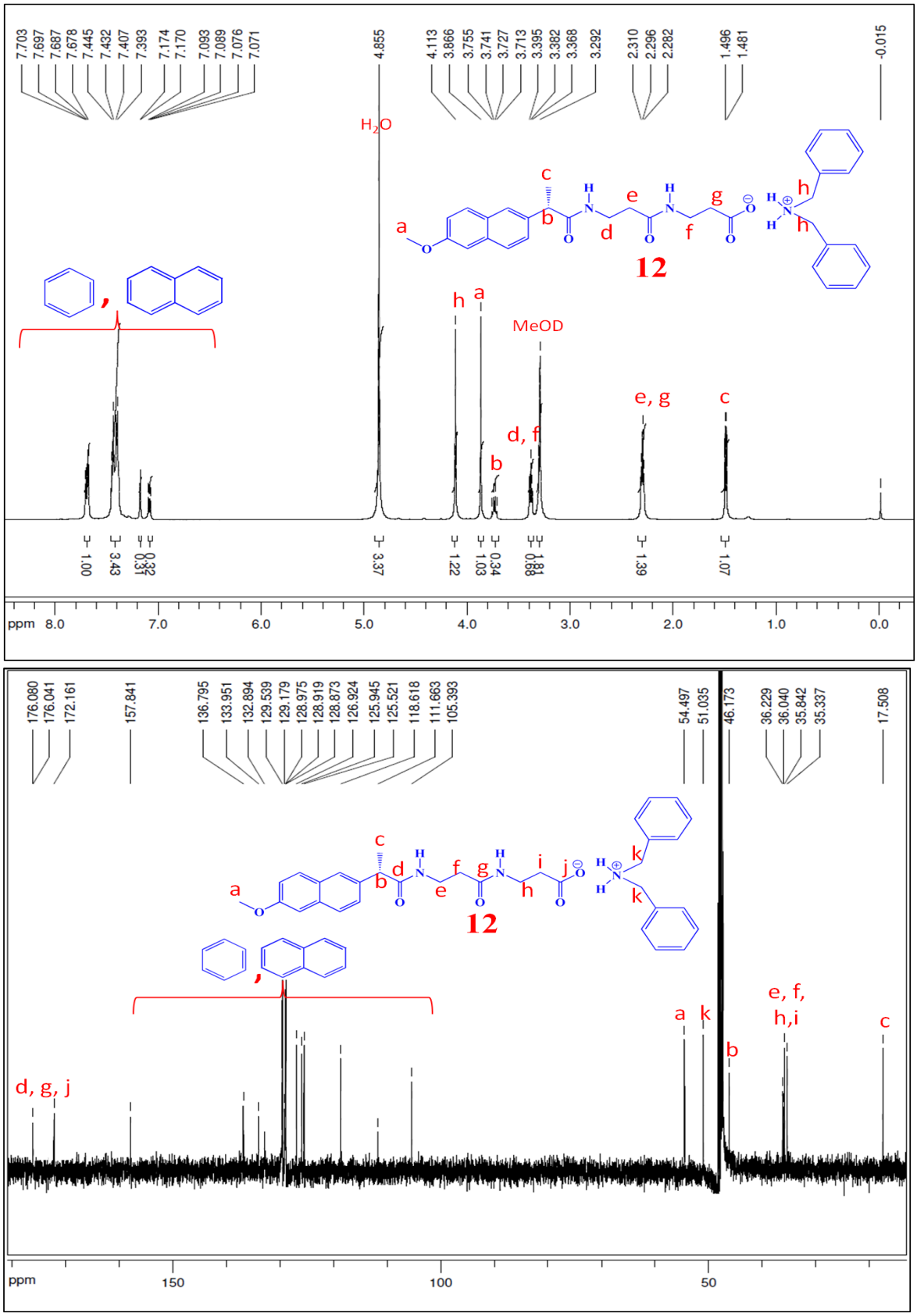


Fig. S12: ^{1}H NMR and ^{13}C-NMR spectra of **12** in MeOD.

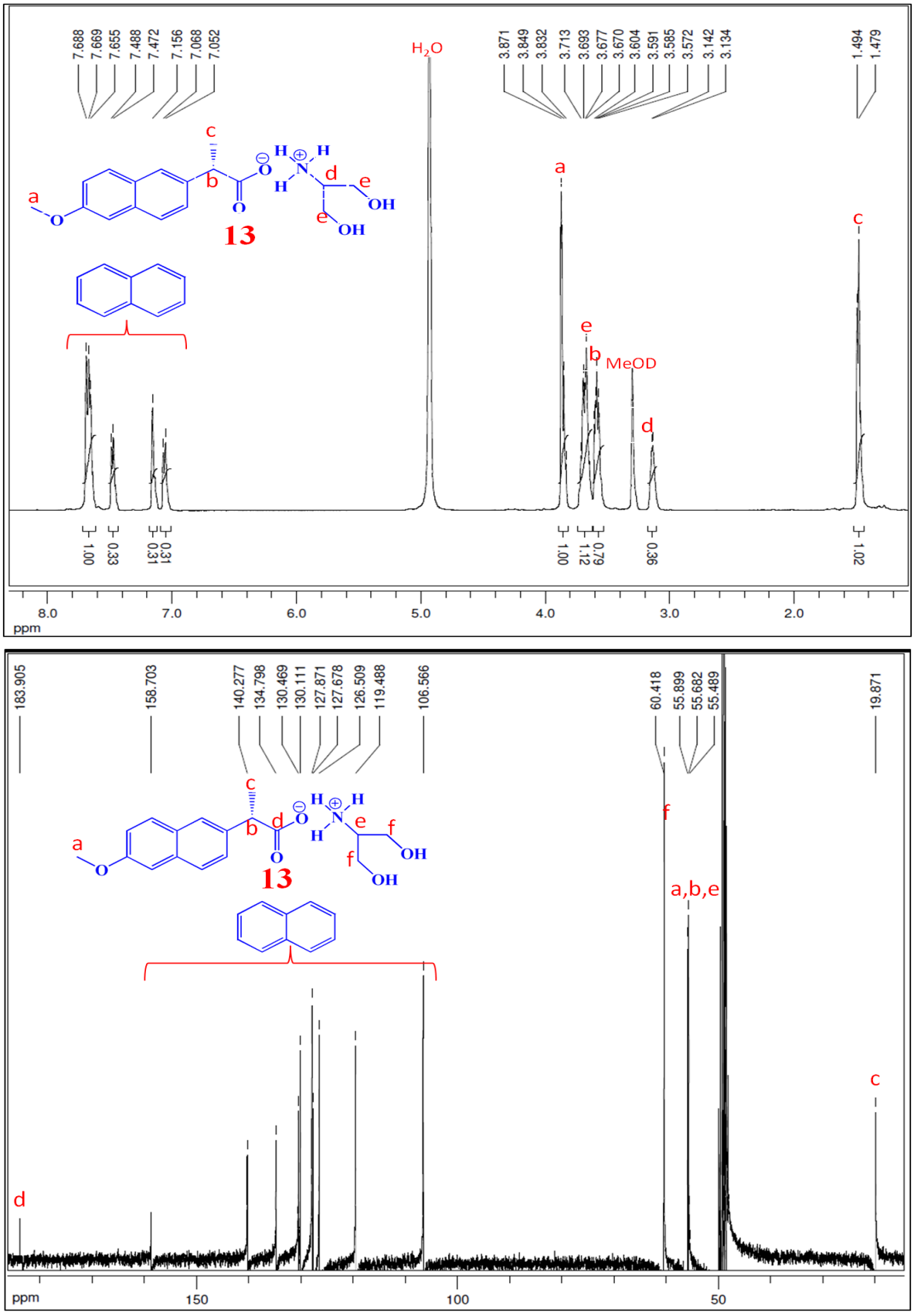


Fig. S13: ^{1}H NMR and ^{13}C-NMR spectra of **13** in MeOD.

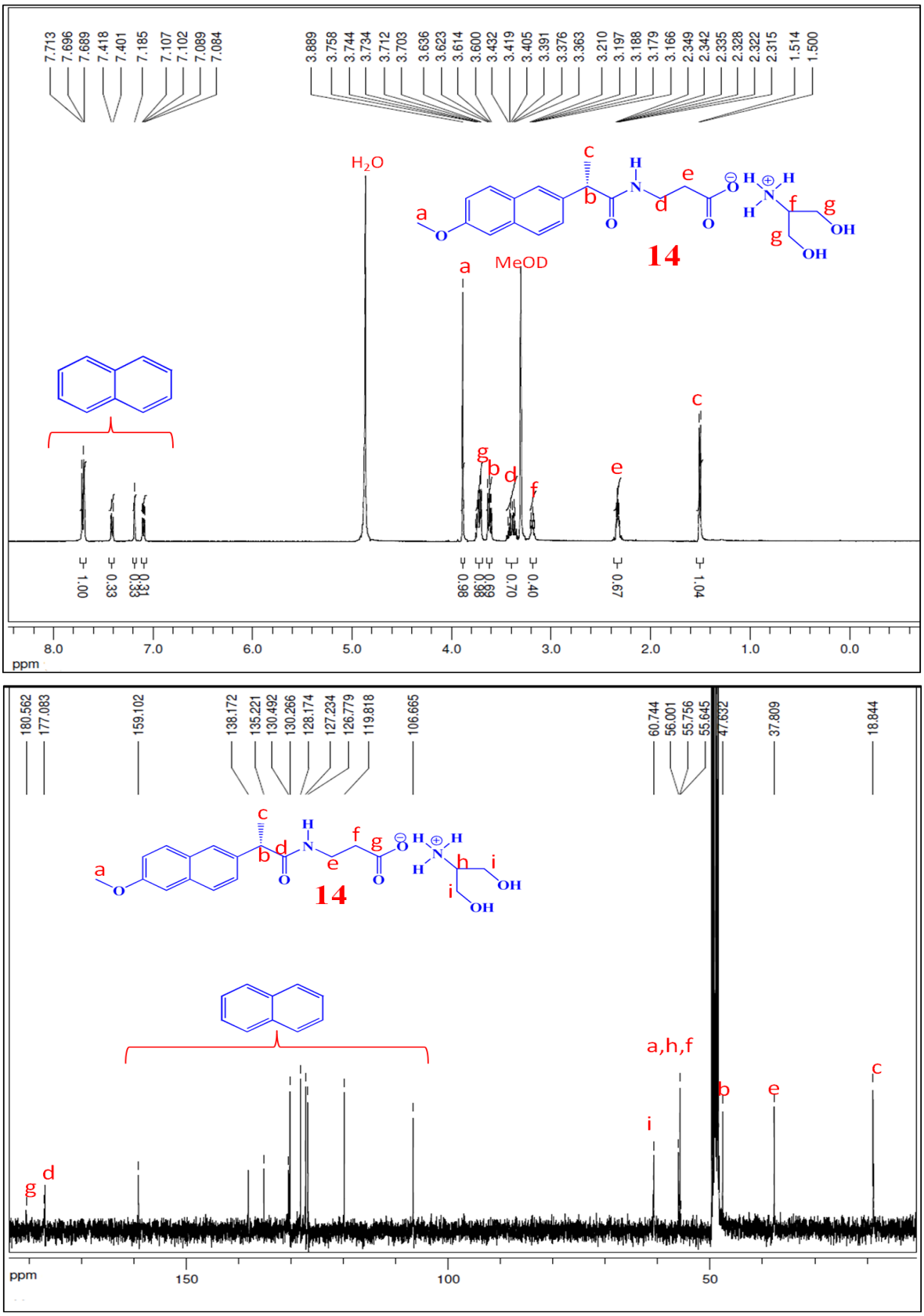


Fig. S14: ^{1}H NMR and ^{13}C-NMR spectra of **14** in MeOD.

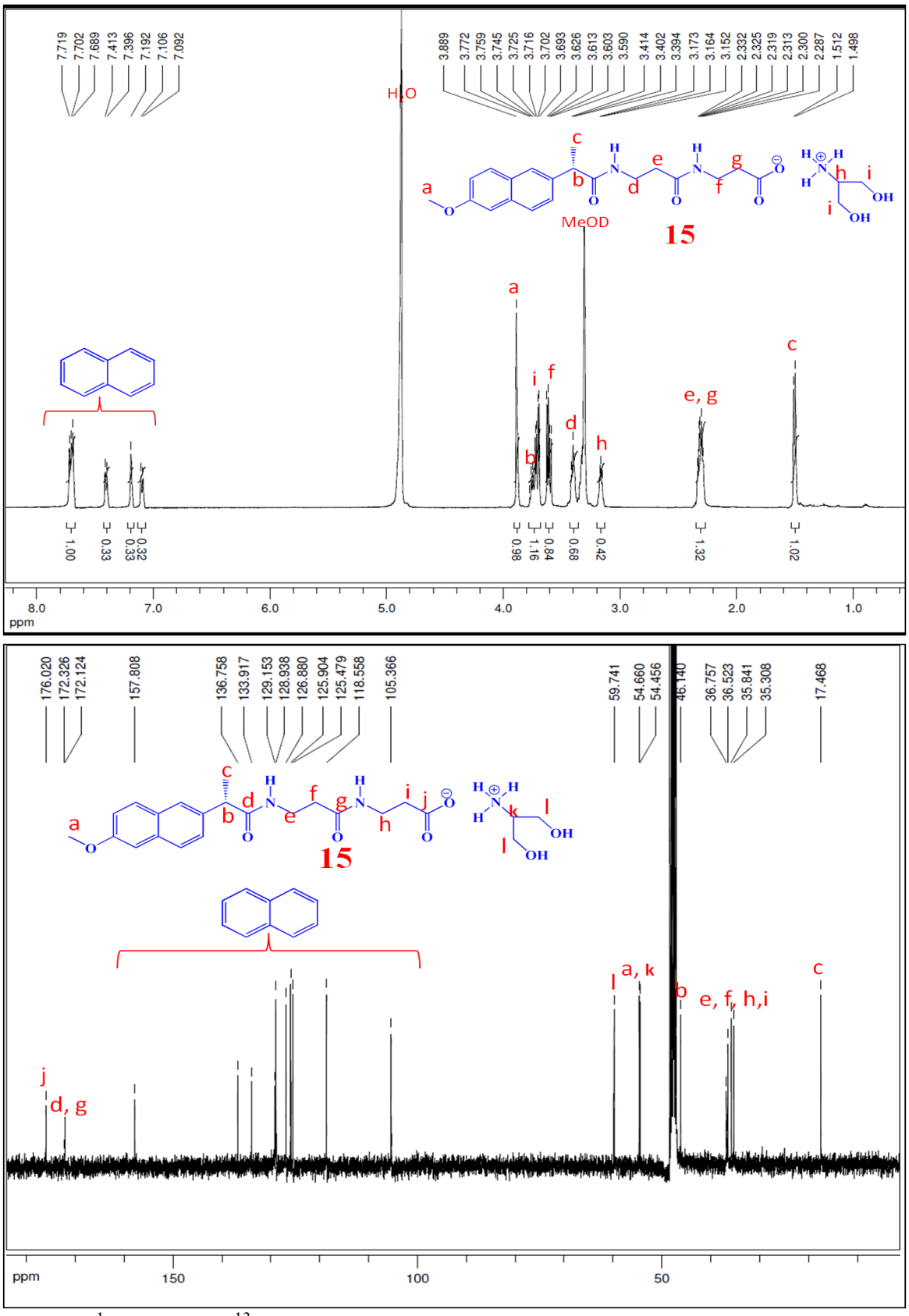


Fig. S15: ^{1}H NMR and ^{13}C-NMR spectra of **15** in MeOD.

Gelation Experiment

To prepare gel, we first dissolved 20 mg of the salt in 0.5 mL gelling solvent by heating around 60-70°C and the hot clear solution was then allowed to cool to room temperature to afford stable gel within a few minutes. Gel formation was confirmed by test tube inversion method.

Scanning with 10 different solvents revealed that majority of the salts displayed good to moderate gelling ability with the solvents chlorobenzene, bromobenzene and methylsalicylate. Since methylsalicylate (MS) is present in many commercially available NSAID based topical gels/spray etc., we concentrated our studies with the methylsalicylate gels. Salts **1, 3, 8, 11** and **12** were found to be capable of forming gels with MS having minimum gelator concentration (MGC) in the range of 0.6-4.0 wt % with excellent thermal stability (gel-sol dissociation temperature i.e. T_{gel} = 84-121°C) (Table S1-S2). T_{gel} *vs* gelator concentration ([gelator]) plot of the MS gels revealed that various supramolecular interactions were responsible for gelation as indicated from the steady increase of T_{gel} with the increase in [gelator] (Fig. S16).

Table S1: Gelation data of the salts **1-12**[a].

Solvents	**Salt 1**	**Salt 2**	**Salt 3**	**Salt 4**	**Salt 5**	**Salt 6**	**Salt 7**	**Salt 8**	**Salt 9**	**Salt 10**	**Salt 11**	**Salt 12**
Ethanol	S	S	S	S	S	S	S	S	S	S	S	S
Ethylinglycol	S	S	S	S	S	S	S	S	S	S	S	S
Water	P	P	P	P	P	P	P	P	P	P	P	P
Cholorobenzene	*G/1.5*	*S*	*G/2*	S	P	WG	P	*G/1.5*	P	WG	*G/4*	*G/3*
Bromobenzene	*G/2*	S	*G/4*	S	P	P	P	*G/1.5*	P	WG	*G/4*	*G/4*
Methylsalycilate	*G/3*	S	*G/2*	S	P	WG	P	*G/2*	S	WG	*G/2.5*	*G/0.6*
Toluene	S	P	P	S	P	P	P	WG	P	P	P	P
o-Xylene	S	P	P	S	P	P	P	WG	P	P	P	WG
DMF	S	S	S	S	S	S	S	S	S	S	S	S
DMSO	S	S	S	S	S	S	S	S	S	S	S	S

[a]G = Gel; S = Solution; P = Precipitate; WG=Weak Gel. The numerical values indicate the minimum gelator concentration (MGC) in Wt % (w/v); the italic type is used to highlight gels.

T_{gel} Experiment

T_{gel} of the gels was measured by the dropping ball method at various gelator concentrations. In this experiment, a glass ball of weighing 216.40 mg was placed on a 0.5 mL gel (at their respective minimum gelator concentration, MGC), taken in a test tube (15x100 mm).The test tube was then immersed in an oil bath placed on a magnetic stirrer to ensure uniform heating. The temperature was noted when the ball touched the bottom of the test tube.

Table S2: T_{gel} of methylsalicylate gel of **1, 3, 8, 11** and **12**[a].

Methylsalicylate (B.P)	Salt	**1**	**3**	**8**	**11**	**12**
220-224 °C	T_{gel} °C	120-121	84-85	76-77	105-106	120-121

[a]To determine T_{gel} in each case 0.5 mL methylsalicylate gel with respective MGC was used.

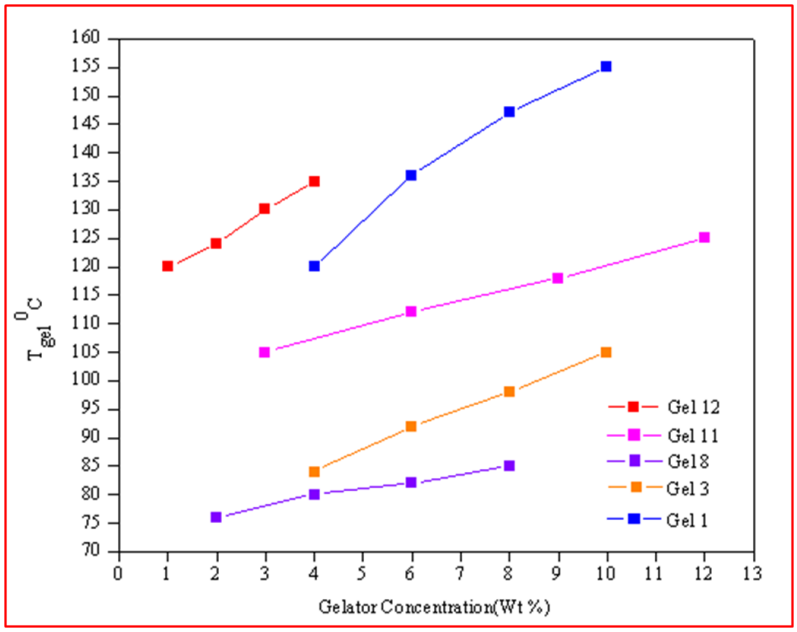


Fig. S16: T_{gel} vs [gelator] plots for the methylsalicylate gels of **1, 3, 8, 11** and **12**.

Tranmission Electron Microscopy (TEM)

To study the morphology of the SAFINs, we carried out HR-TEM of MS xerogel samples of **1, 3, 8, 11** and **12**. While the xerogels of **1** and **3** showed tape type of morphology (width = 0.27 ± 0.09 and 0.55 ± 0.12 μm for **1** and **3** respectively), the corresponding MS xerogels of **8, 11-12** displayed nanofibers (width = 20 ± 7, 12 ± 5, 13 ± 3 nm for **8, 11** and **12**, respectively). It is intriguing to note that the gelators **1** and **3** were directly derived from Np whereas **8, 11-12** were synthetic modification of Np with β-amino acid/peptide. Thus, introducing additional hydrogen bonding functionalities (amide/peptide) while going from **1, 3** to **8, 11-12** seemed to have profound effect on the morphology of the SAFINs and the appearance of the gels (tape to nanofiber and opaque to translucent, respectively) (Fig. S17).

TEM Sample Preparation

Dilute (0.1 wt %) solution of the corresponding gelator was drop cast on a carbon-coated Cu (300 mesh) TEM grid for each sample**.** The grid was dried under vacuum at room temperature for one day and used for recording TEM images using an accelerating voltage of 200 kV without staining.

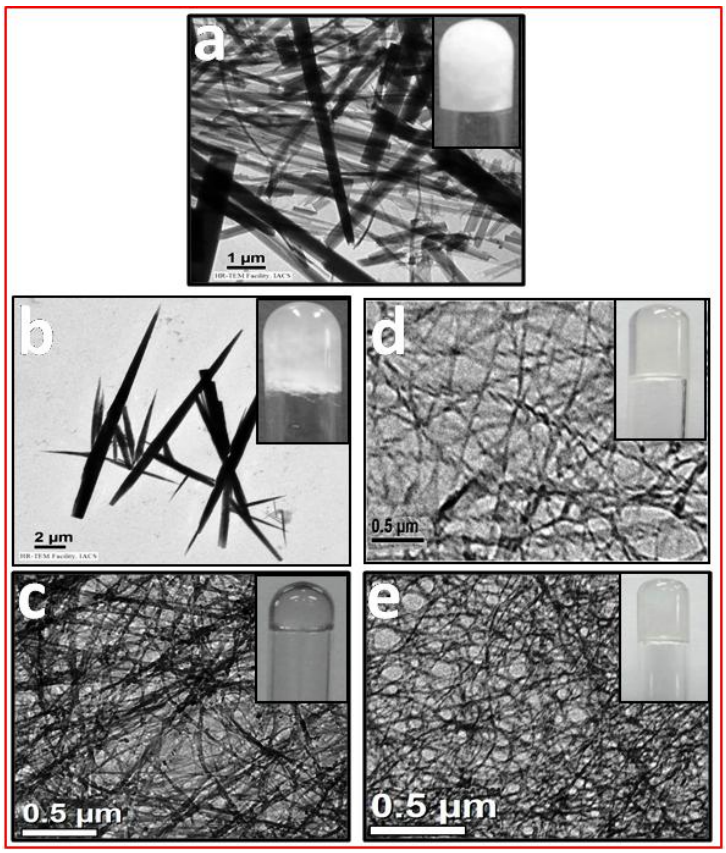


Fig. S17: TEM images of methylsalicylate gels of (a) **1;** (b) **3**; (c) **8**; (d) **11** and (e) **12** (inset: optical images of the corresponding methylsalicylate gel).

Single Crystal X-ray Diffraction

X-ray quality single crystal of the salt **1, 3, 4, 5** and **8** were grown at room temperature via slow evaporation method from suitable solvent systems. Salt **1, 3** and **8** were crystallized from methanol. While **1** and **3** crystalised in the noncentrosymmetric monoclinic space group $P2_1$, **4** crystalised in the noncentrosymmetric orthorhombic space group $P2_12_12_1$. Salt **5** and **8** were crystallized from methylsalicylate during gellation test in the noncentrosymmetric monoclinic space group $P2_1$ and C2 respectively.

Data were collected using MoK_α (λ = 0.7107 Å) radiation on a BRUKER APEX II diffractometer equipped with CCD area detector. Data collection, data reduction, structure solution/refinement were carried out using the software package of SMART APEX-II. All structures were solved by direct method and refined in a routine manner. Nonhydrogen atoms were treated anisotropically. All the hydrogen atoms were geometrically fixed. CCDC No. 944131, 947071, 947072, 947177 and 955413 for **1**, **3**, **4**, **5** and **8** respectively contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

Supramolecular synthons

To gain further insights such as the supramolecular synthons present in these salts, we undertook single crystal X-ray diffraction (SXRD) studies. Crystallization attempts

resulted in X-ray quality single crystals of **1, 3, 8** (gelators) and **4, 5** (nongelators) (Table S3-S9). While 1D PAM synthon 'W' was present in **1**, **3** and **5**, the SAM salt **4** showed typical 1D SAM synthon. Presence of amide moiety in **5** attracted water molecules occluded in the crystal lattice sustained by hydrogen bonding interactions with the carboxylate and amide functionality. In the SAM salt **8**, the terminal $-CH_2COO^-$ moiety was found to be disordered. In this structure, the N-H…O hydrogen bonding (2.800-2.832Å) involving the amide functionality lead to the formation of 1D HBN wherein the cationic moieties were bridging the anionic moieties sustained by N-H…O interactions (2.681-2.850Å) (Fig. S18).

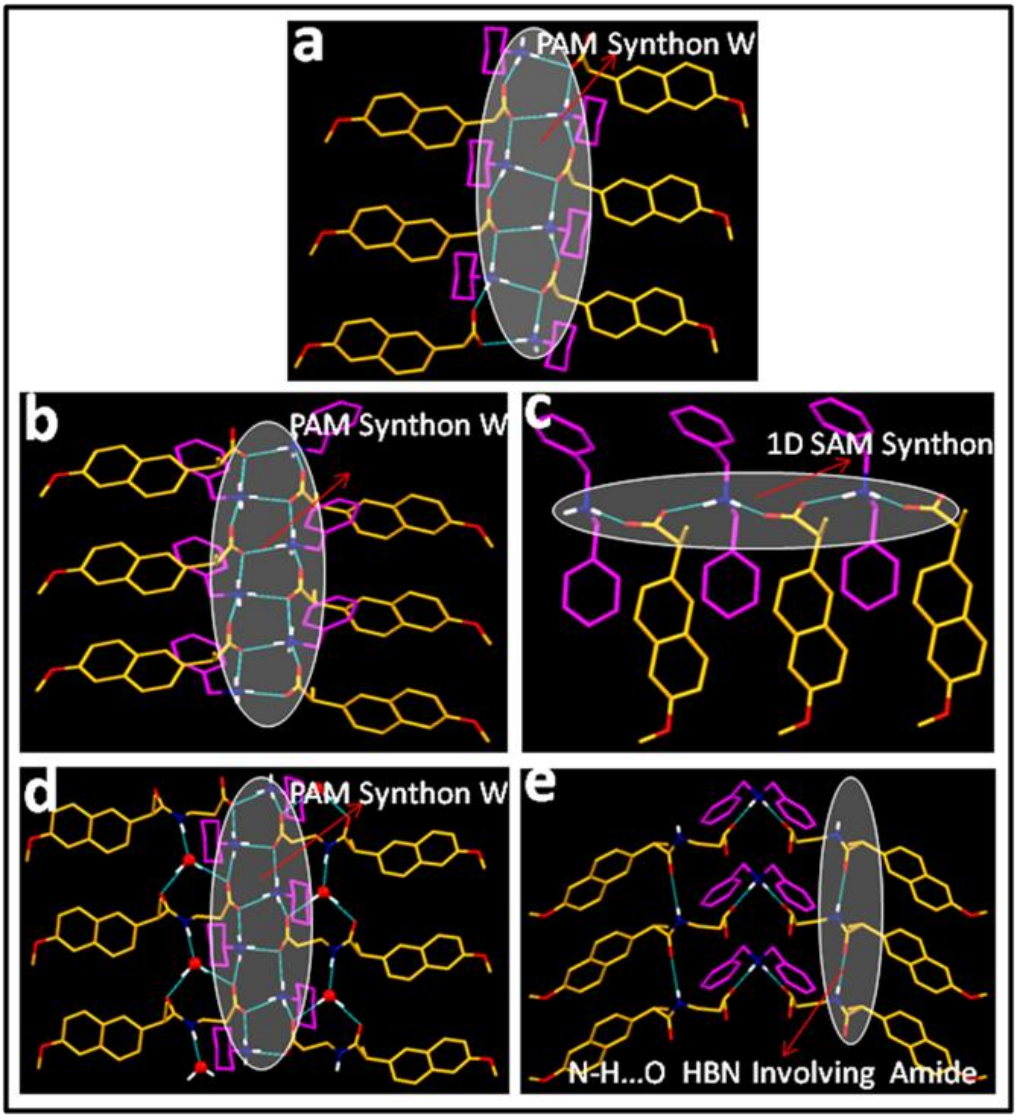
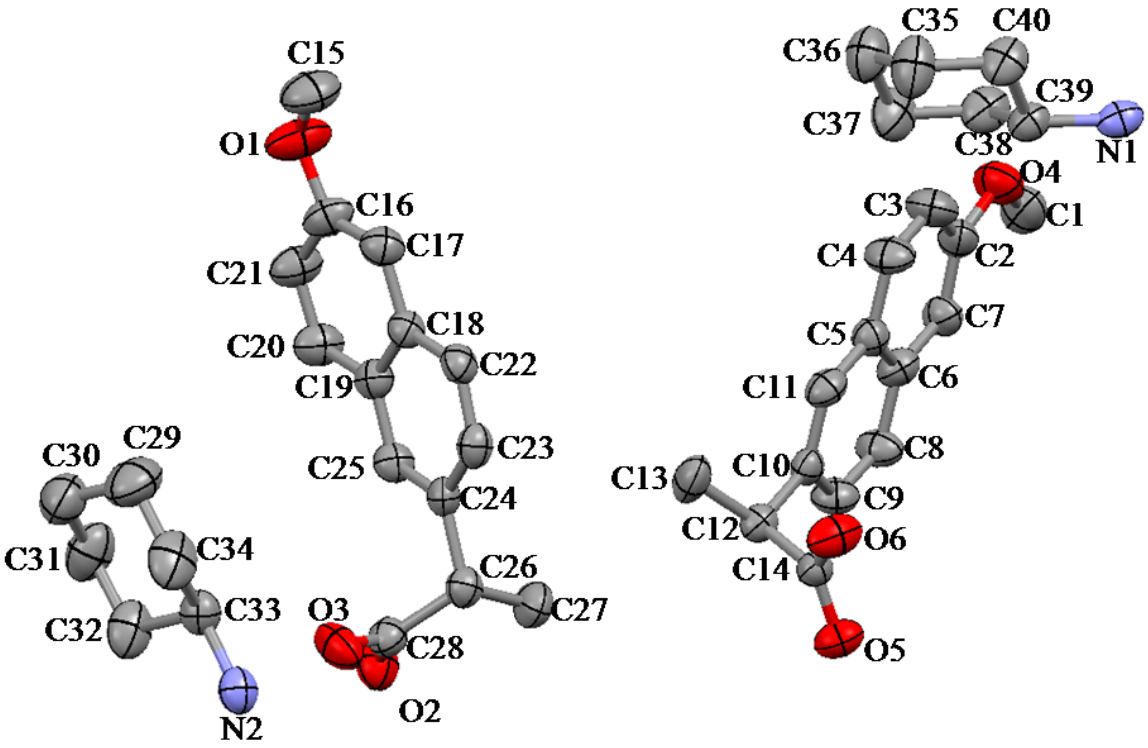


Fig. S18: Typical PAM synthon 'W' in gelator salts a) **1;** b) **3;** c) Typical 1D SAM synthon in nongelator salt **4;** d) water mediated tape like 1D HBN in nongelator salt **5** displaying PAM synthon 'W' and e) N-H…O mediated 1D-HBN in gelator salt **8** (In the SAM salt **8**, the terminal $-CH_2COO^-$ moiety was found to be disordered; the disordered atoms are hidden for better clarity).

Table S3: Crystallographic parameters for **1**, **3**, **4**, **5** and **8**.

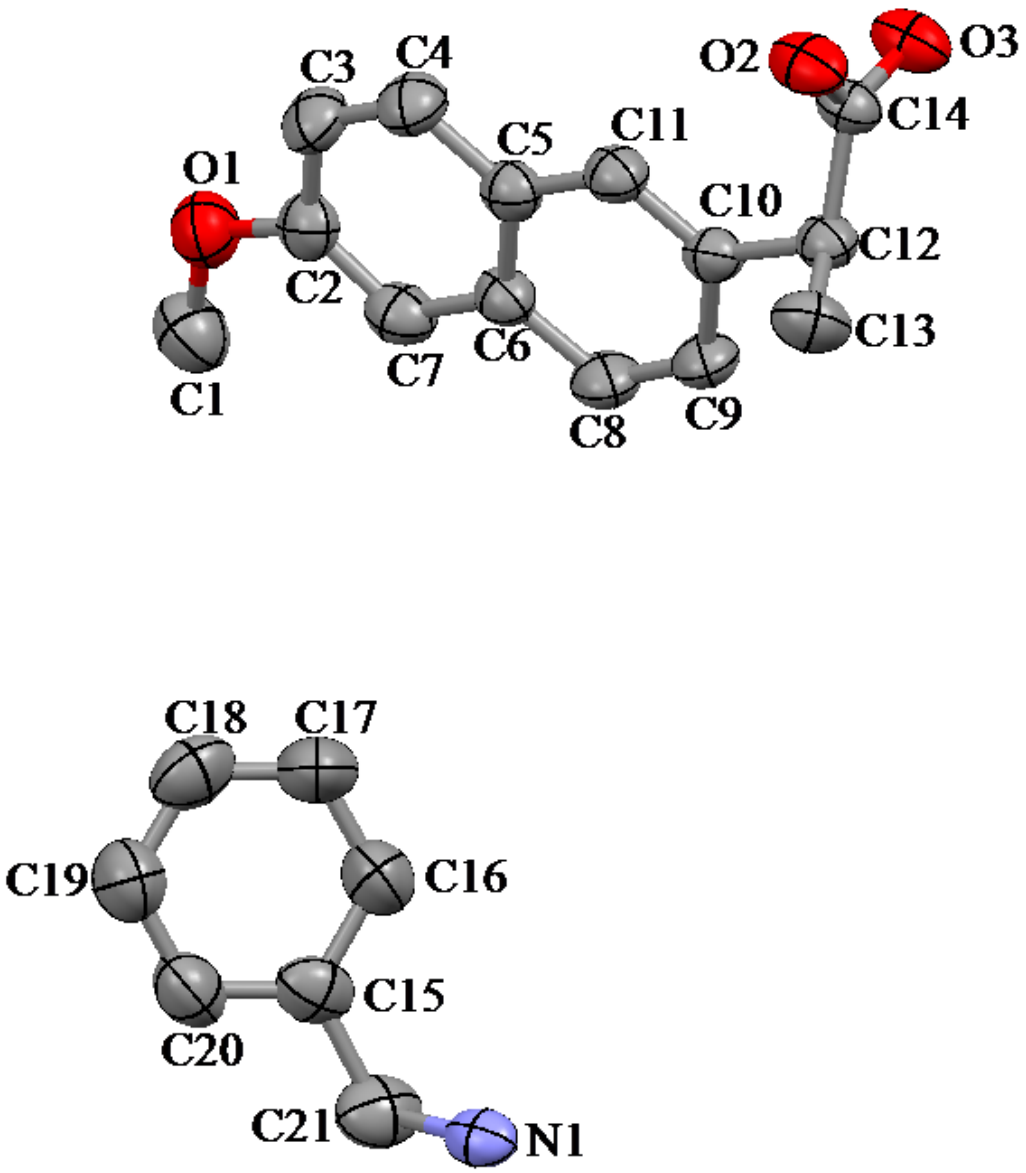
Crystal Parameters	**1**	**3**	**4**	**5**	**8**
CCDC Number	944131	947071	947072	947177	955413
Empirical formula	C_{20} H_{27} N O_3	C_{21} H_{23} N O_3	C_{28} H_{29} N O_3	C_{23} H_{34} N_2 O_5	C_{48} H_{48} N_3 O_8
Formula weight	329.43	337.40	427.52	418.52	794.89
Crystal size/mm	0.45x0.08x0.05	0.55x0.11x0.04	0.95x0.06x0.02	0.50x0.26x0.08	0.45x0.12x0.05
Crystal system	Monoclinic	Monoclinic	Orthorhombic	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1$	P_{212121}	$P2_1$	$C2$
a /Å	15.9309(14)	11.632(4)	5.7688(14)	9.3305(11)	23.570(4)
b/Å	6.3941(6)	5.9372(19)	8.478(2)	6.4425(8)	4.8479(8)
c /Å	18.8138(16)	13.377(4)	48.065(12)	19.573(2)	18.554(3)
$\alpha/^0$	90.00	90.00	90.00	90.00	90.00
$\beta/^0$	107.606(3)	90.327(5)	90.00	99.120(3)	90.115(9)
$\gamma/^0$	90.00	90.00	90.00	90.00	90.00
Volume/$Å^3$	1826.7(3)	923.8(5)	2350.6(10)	1161.7(2)	2120.1(6)
Z	4	2	4	2	2
F(000)	712	360	912	452	842
μ MoKα /mm^1 Mo *K*α radiation,	0.080 λ = 0.71073 Å	0.081 λ = 0.71073 Å	0.078 λ = 0.71073 Å	0.084 λ = 0.71073 Å	0.085 λ = 0.71073 Å
Temperature/ K	296(2)	296(2)	296(2)	296(2)	296(2)
R_{int}	0.1153	0.0693	0.0663	0.0384	0.0423
Range of h, k, l	-20/21, -8/8, -24/24	-14/14, -7/7, -16/16	-5/7, -10/8, -54/39	-9/9, -6/6, -19/19	-29/30, -6/5, -24/24
θmin/max/°	1.14/28.35	1.52/27.36	0.85/27.05	1.05/20.76	1.50/28.20
Reflections collected/unique/observed [I>2σ(I)]	25915/ 8305/ 3233	7466/ 3685/ 1546	7900/ 2648/ 1358	7339/2288/ 1984	14773/4381/ 2624
Data/restraint/ parameters	8305/1/439	3685/1/229	2648/0/291	2288/1/286	4381/1/277
Goodness of fit on F^2	0.957	0.836	1.015	0.816	1.14
Final R indices [I>2σ(I)]	$R_{1=}$ 0.0664 wR_2= 0.1413	$R_{1=}$ 0.0558 wR_2= 0.1260	$R_{1=}$ 0.0632 wR_2= 0.1512	$R_{1=}$ 0.0400 wR_2= 0.1071	$R_{1=}$0.0571 wR_2=0.1533
R indices (all data)	$R_{1=}$ 0.2234 wR_2= 0.2305	$R_{1=}$ 0.1908 wR_2= 0.2198	$R_{1=}$ 0.1564 wR_2= 0.2094	$R_{1=}$ 0.0489 wR_2= 0.1167	$R_{1=}$ 0.1171 wR_2=0.2047



ORTEP Plot of **1** (50% probability)

Table S4: Hydrogen bonding parameter of **1**.

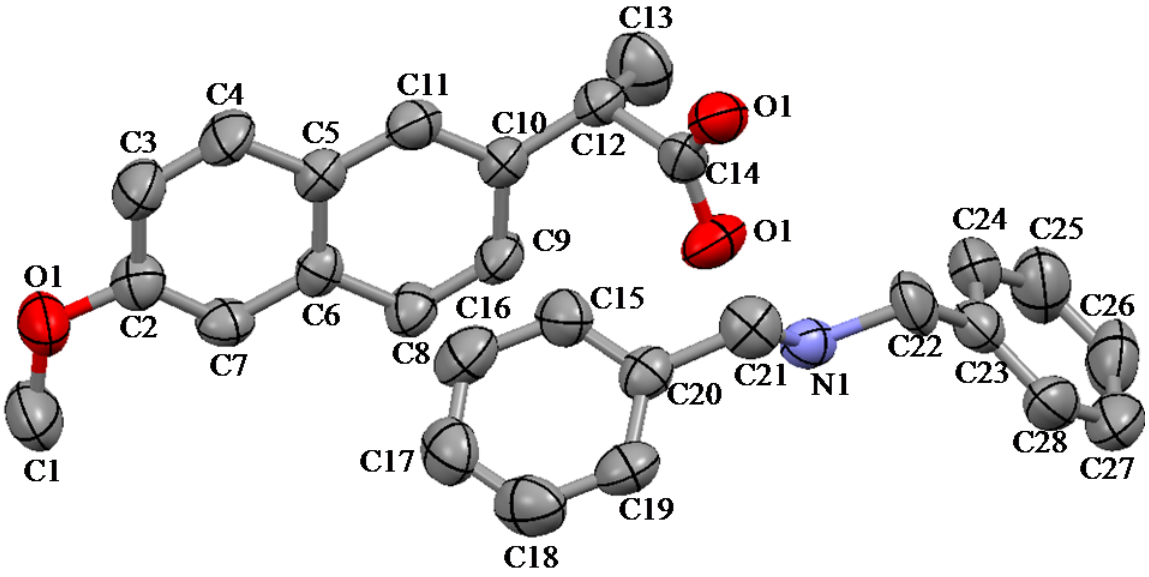
D–H•••A	D–H (Å)	H•••A (Å)	D•••A (Å)	D–H•••A (º)	Symmetry operator
N(1)–H(1D)•••O(5)	0.89	1.91	2.791(5)	170	−*x*+1, *y*+1/2, −*z*+2
N(1)–H(1E) •••O(5)	0.89	1.93	2.823(5)	175	*x*−1, *y*+1, *z*
N(1)–H(IF) •••O(6)	0.89	1.84	2.728(5)	178	−*x*+1, *y*+3/2, −*z*+2
N(2)–H(2A)•••O(3)	0.89	1.87	2.749(6)	172	−*x*+2, *y*+1/2, −*z*+1
N(2)–H(2B) •••O(2)	0.89	1.90	2.785(6)	173	*x*, *y*, *z*
N(2)–H(2C) •••O(3)	0.89	1.91	2.782(6)	168	*x*, *y*+1, *z*



ORTEP Plot of **3** (50% probability)

Table S5: Hydrogen-bond parameters of **3**.

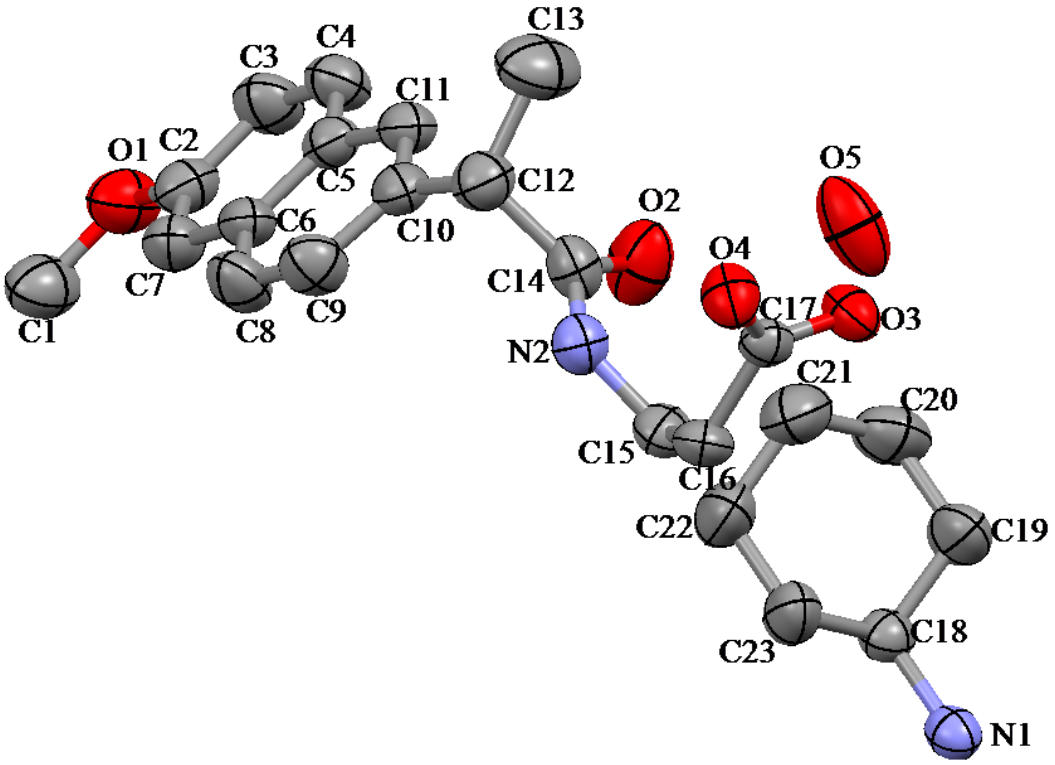
D–H•••A	D–H (Å)	H•••A (Å)	D•••A (Å)	D–H•••A (º)	Symmetry operator
N(1)–H(1F) •••O(3)	0.89	1.83	2.714(6)	170	*x*, *y*, *z*−1
N(1)–H(1E) •••O(2)	0.89	1.87	2.723(6)	161	*x*, *y*+1, *z*−1
N(1)–H(ID) •••O(3)	0.89	1.96	2.850(5)	175	−*x*+1, *y*+1/2, −*z*+1



ORTEP Plot of **4** (50% probability)

Table S6: Hydrogen-bond parameters of **4**.

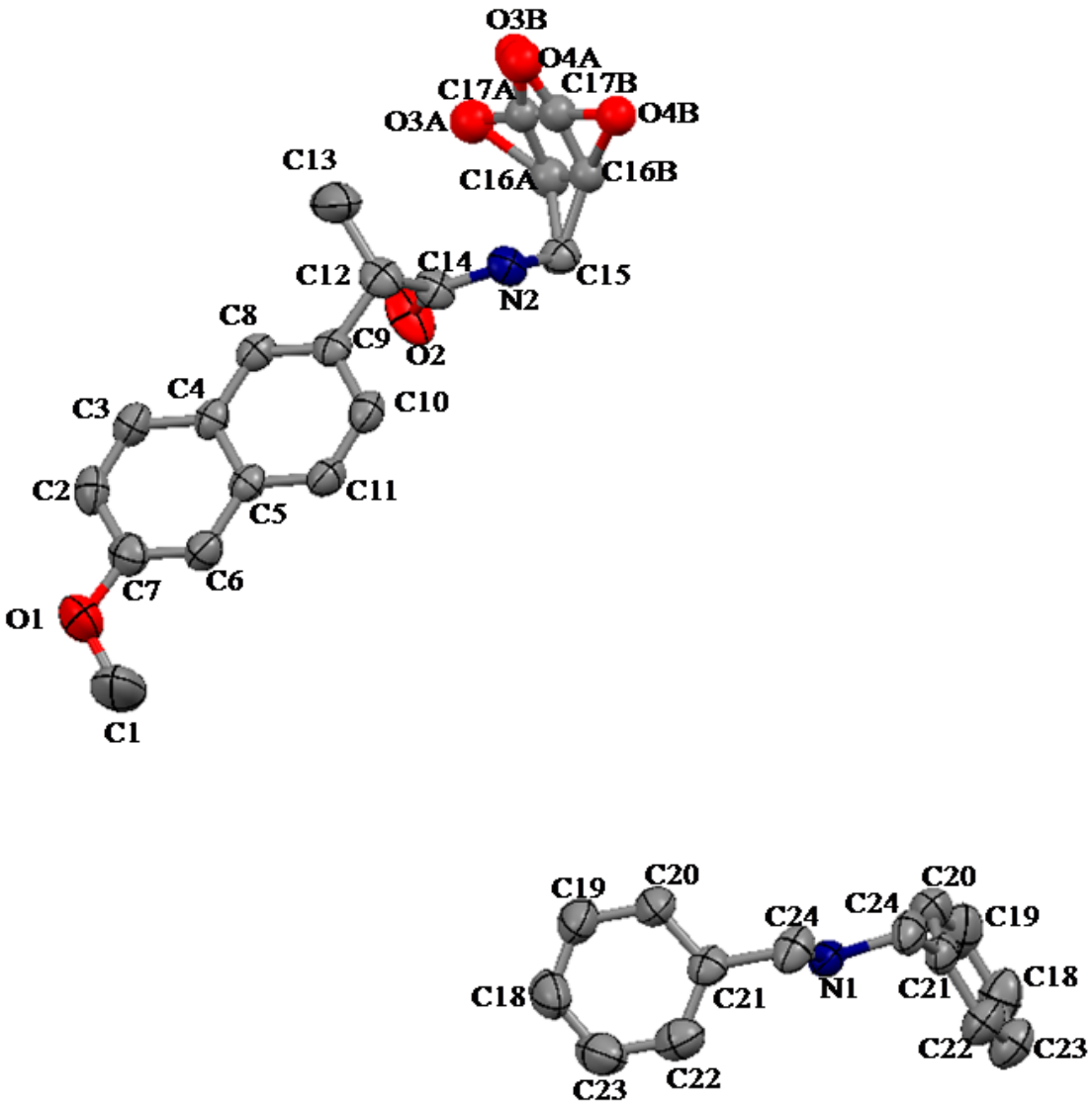
D–H•••A	D–H (Å)	H•••A (Å)	D•••A (Å)	D–H•••A (º)	Symmetry operator
N(1)–H(1E) •••O(3)	0.90	1.84	2.739(8)	177	*x*, *y*, z
N(1)–H(ID) •••O(2)	0.90	1.78	2.682(8)	174	*x*+1, *y*, *z*



ORTEP Plot of **5** (50% probability)

Table S7: Hydrogen-bond parameters of **5**.

D–H•••A	D–H (Å)	H•••A (Å)	D•••A (Å)	D–H•••A (º)	Symmetry operator
O(5)–H(26) •••O(2)	1.07(6)	1.67(7)	2.726(5)	167(5)	x, y, z
N(2)–H(25) •••O(5)	1.01(4)	1.81(4)	2.800(5)	165(3)	*x*, *y*+1, *z*
N(1)–H(1F) •••O(3)	0.89	1.91	2.799(4)	173	*x*−1, *y*, *z*
N(1)–H(1E) •••O(4)	0.89	1.92	2.803(4)	169	*x*−1, *y*−1, *z*
N(1)–H(ID) •••O(4)	0.89	1.91	2.789(3)	169	−*x*+1, *y*−1/2, −*z*+2



ORTEP Plot of **8** (50% probability)

Table S8: Hydrogen-bond parameters of **8.**

D–H•••A	D–H (Å)	H•••A (Å)	D•••A (Å)	D–H•••A (º)	Symmetry operator
N(2)–H(1)•••O(2)	0.68(5)	2.15(5)	2.832(4)	176(5)	*x*, *y*−1, *z*
N(1)–H(1E) •••O(4A)	0.90	1.94	2.814(6)	163	−*x*, *y*+1, −*z*+
N(1)–H(1E) •••O(3B)	0.90	1.87	2.772(6)	177	−*x*, *y*+1, −*z*+
N(1)–H(1D)•••O(4A)	0.90	1.94	2.814(6)	163	*x*, *y*+1, *z*+1
N(1)–H(1D) •••O(3B)	0.90	1.87	2.772(6)	177	*x*, *y+1*, *z+1*

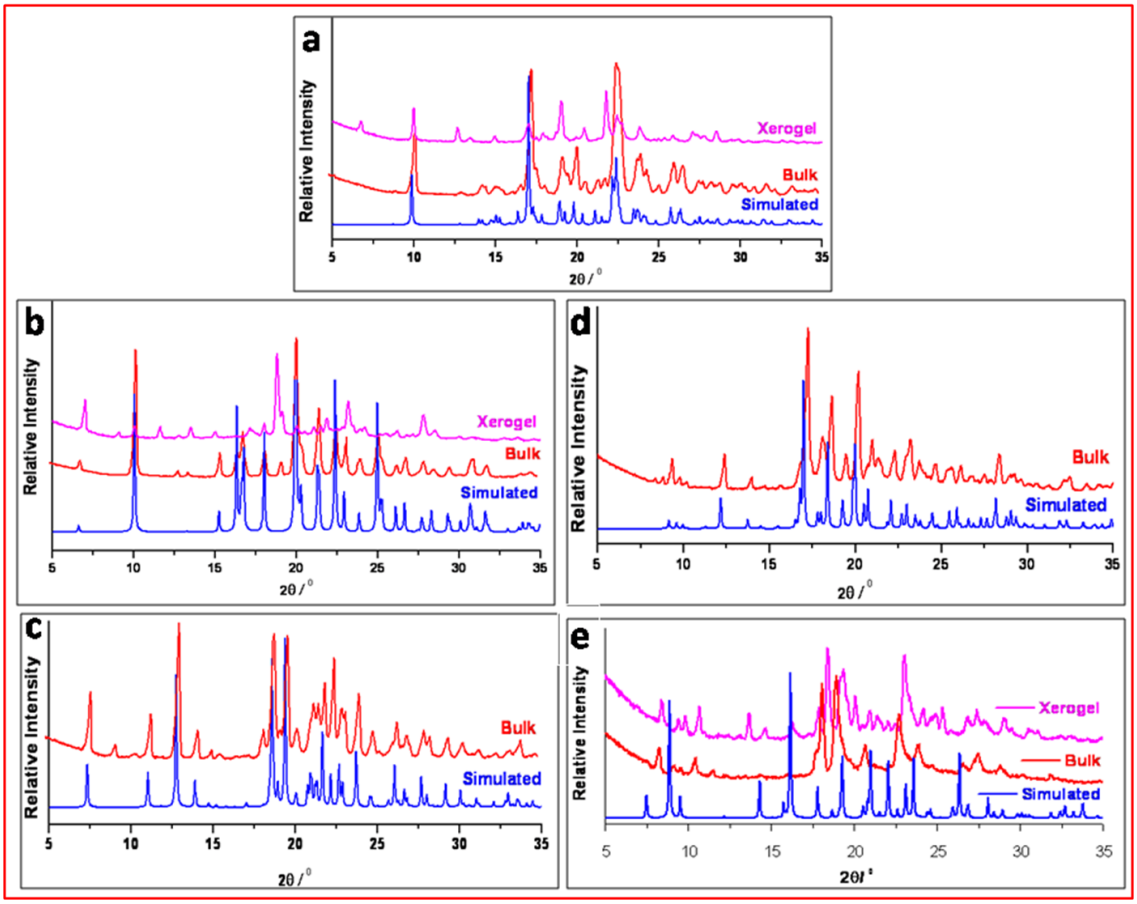


Fig. S19: X-ray powder diffraction pattern of a) **1**; b) **3**; c) **4;** d) **5** and e) **8.**

MTT Assay

The cytotoxicity of the gelator salts was evaluated in RAW 264.7 cells using standard MTT (3-(4, 5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay.[2] The mouse macrophage RAW 264.7 cells were purchased from American Type Culture Collection (ATCC) and maintained following their guidelines. The cells were grown in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% Fetal Bovine Serum (FBS), 1% penicillin and streptomycin in a humidified incubator at 37° C and 5% CO_2. The cells were seeded in 96-well plates at a density of 1×10^4 cells/well for 24 h. After 24 h of seeding, the cells were treated with various concentrations (upto 2 mM) of the salts or DMEM alone for 24, 48 and 72 hrs. in humidified incubator at 37˚C and 5% CO_2. Then, the culture medium was replaced with 100 µg of MTT per well and kept for 4 h at 37˚C. To dissolve the formazan produced by mitochondrial reductase from live cells, DMSO (100 µL/ well) was added and incubated for 30 minutes at room temperature. The color intensity of the formazan solution, which is positively correlated to the cell viability, was measured using a multiplate ELISA reader at 570 nm (Varioskan Flash Elisa Reader, Thermo Fisher). The percentage of live cells in salt-treated sample was calculated considering DMEM-treated sample as 100% (Figure S20 and Figure S21).

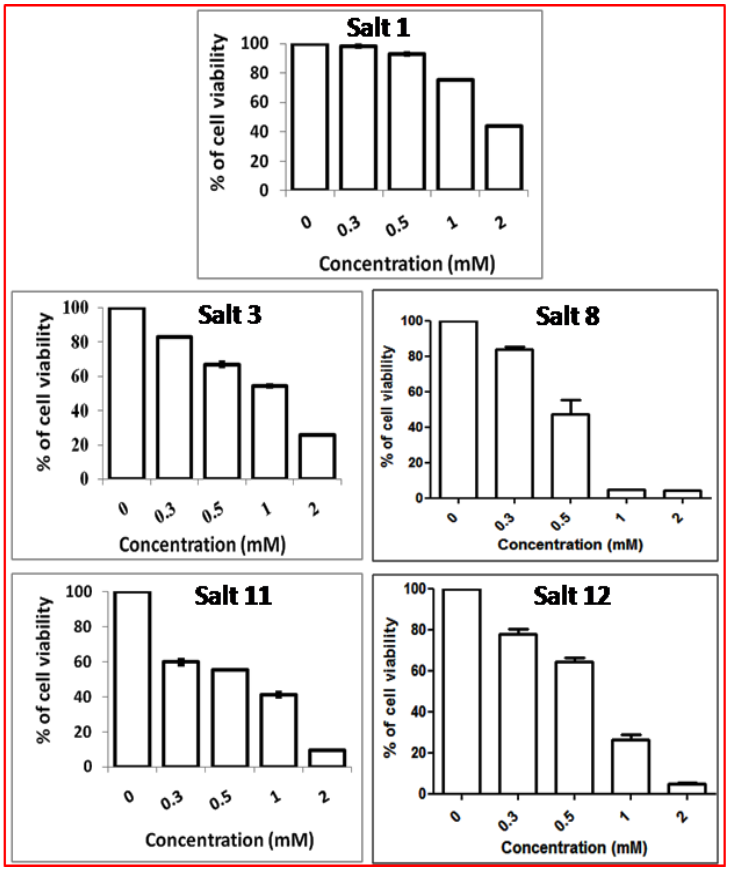


Fig. S20: MTT assay of gelator salts**1**, **3**, **8, 11** and **12** in RAW 264.7 cell line for 24 hrs. at 37˚C.

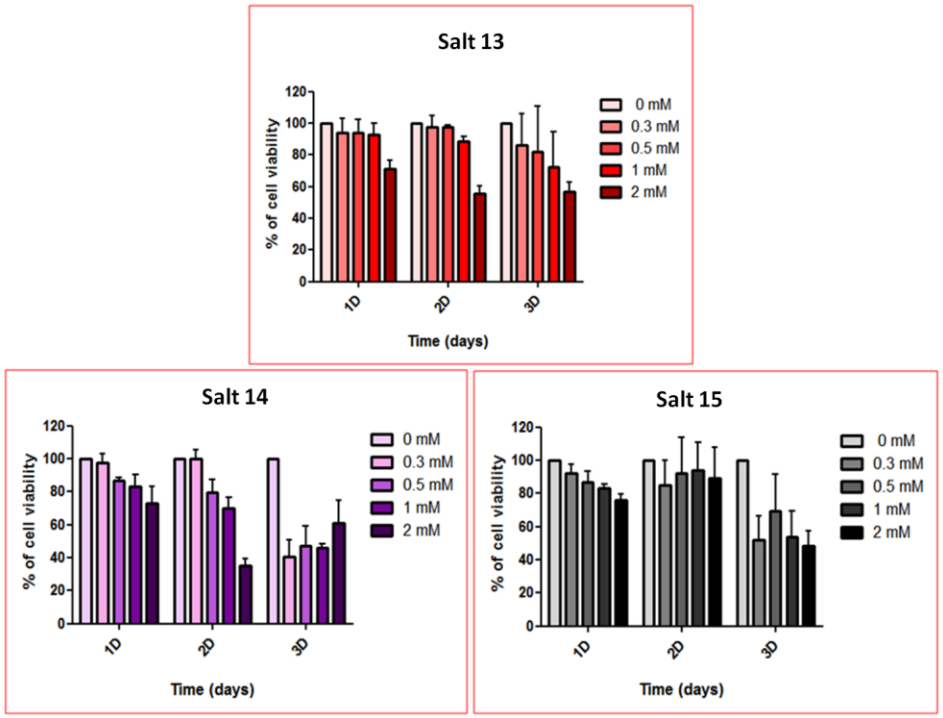


Fig. S21: MTT assay of salt **13, 14** and **15** in RAW 264.7 cell line for 24, 48 and 72 hrs. at 37˚C**.** Here 1D, 2D and 3D stand for 1, 2 and 3 days respectively.

MTT assay of the serinol salts 13-15: MTT assay of the serinol salts **13-15** was carried out in RAW 264.7 cell line upto 3 days at 37°C. The increase in cell viability for **14** may be due to the proliferation of the cells at longer time and the development of resistivity of the cells toward the salt **14** at higher concentration and longer time (Fig. S21).

Table S10: Gelation data of the salts **13-15**[a].

Salts	Gelling Solvent (Methylsalicylate)	T_{gel} (^{0}C)
13	Gel (MGC=4.0 wt %)	87-88
14	Gel (MGC=2.0 wt %)	86-87
15	Gel (MGC=2.0 wt %)	90-91

[a]MGC- minimum gelator concentration of the corresponding MS gel, T_{gel}-Gel dissociation temperature at the respective MGC.

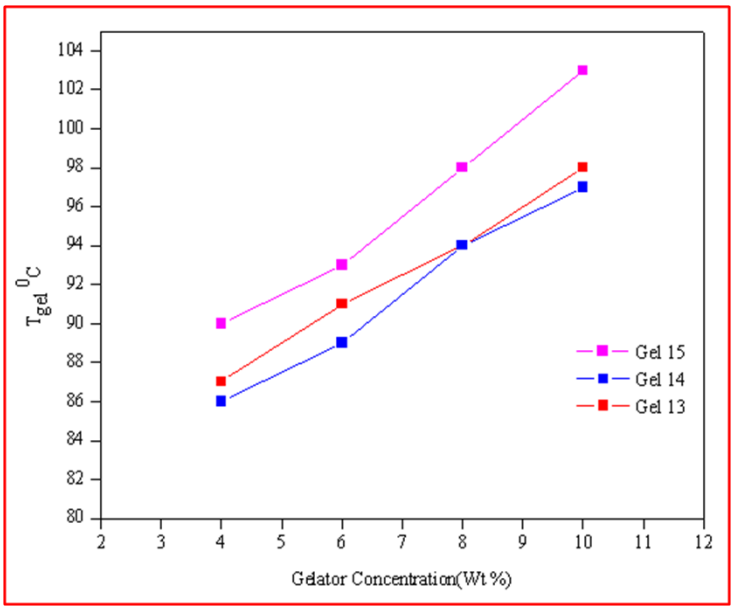


Fig. S22: T_{gel} vs [gelator] plots for the methylsalicylategels of **13, 14** and **15.**

Rheology Studies

Rheology studies were carried out using an SDT Q series advanced rheometer AR 2000. 8 wt % methylsalicylate gel of **13** and 4 wt% methylsalicylate gel of **14** and **15** were taken in this experiment.

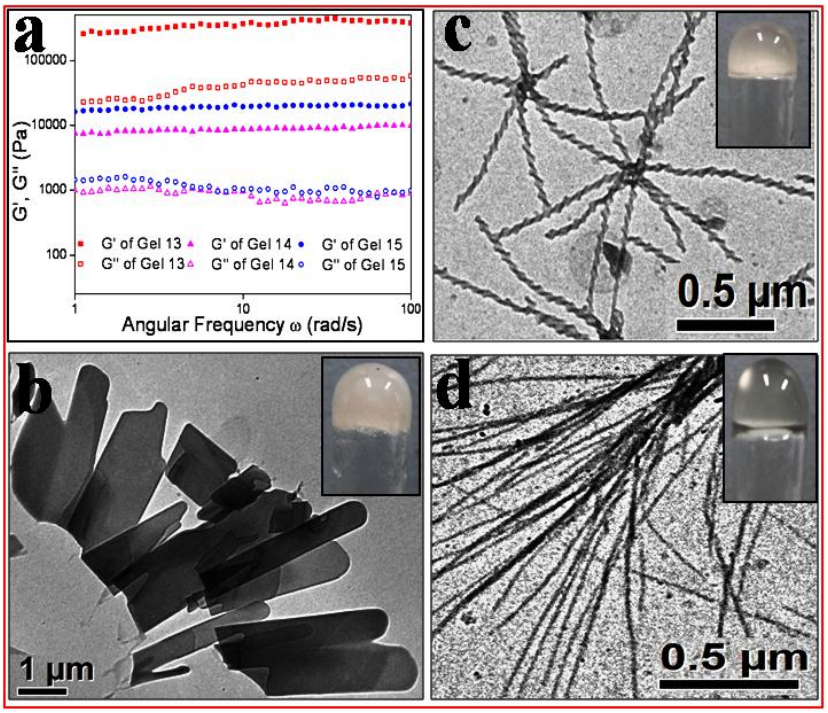


Fig. S23: Rheology and microscopy of the serinol salts**;** a) Rheological response of methylsalicylate gel of **13, 14** and **15**; TEM images of methylsalicylate gel of b) **13**; c) **14** and d) **15** (inset: optical images of the corresponding methylsalicylate gel).

PGE_2 Assay

Production of PGE_2 was estimated according to a published protocol[3] using 6-well plate and RAW 264.7 cell line. Approximately $1x10^6$ cells/well were seeded in 6-well plate (4 wells using 6-well plate) for 24 hrs. One of the wells was treated with 2 mL of DMEM only as control experiment, the rest three wells were treated with 1 μg/mL lipopolysaccharide (LPS) and 100 ng/mL interferon-gamma (IFN-γ); out of these LPS/IFN-γ treated wells, two wells were treated with 0.3 mM naproxen sodium (Ns) and salt **13** respectively in such a way that the total media (DMEM) volume in each well was 2 mL and all the wells were further incubated for 24 h. The culture media was diluted to 1:100 or 1:500 for measuring PGE_2 using Prostaglandin E2 EIA Kit – Monoclonal (Cayman Chemicals, Ann Arbor, MI). This experiment was done in triplicate.

Formulation of topical gel 13

100 mg salt **13** (5 % w/v) and 100 mg menthol (5 % w/v) were dissolved in 2.0 mL methylsalicylate by heating and the hot clear solution was then allowed to cool to room temperature. After few minutes gel formation was observed (Figure S24).

Fig. S24: Optical image of 5% menthol containing topical gel of **13.**

Check CIF/ PLATON Report of 1

checkCIF/PLATON report

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: jm0199j

```
Bond precision:  C-C = 0.0081 A          Wavelength=0.71073

Cell:           a=15.9309(14)    b=6.3941(6)        c=18.8138(16)
                alpha=90         beta=107.606(3)    gamma=90
Temperature:    296 K

                Calculated                Reported
Volume          1826.7(3)                 1826.7(3)
Space group     P 21                      P21
Hall group      P 2yb                     P 2yb
Moiety formula  C14 H13 O3, C6 H14 N      C14 H13 O3,C6 H14 N
Sum formula     C20 H27 N O3              C20 H27 N O3
Mr              329.43                    329.43
Dx,g cm-3       1.198                     1.198
Z               4                         4
Mu (mm-1)       0.080                     0.080
F000            712.0                     712.0
F000'           712.32
h,k,lmax        21,8,25                   21,8,24
Nref            9158[ 4982]               8305
Tmin,Tmax       0.992,0.996               0.965,0.996
Tmin'           0.965

Correction method= MULTI SCAN

Data completeness= 1.67/0.91      Theta(max)= 28.350

R(reflections)= 0.0664( 3233)     wR2(reflections)= 0.2305( 8305)

S = 0.957                 Npar= 439
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT026_ALERT_3_B Ratio Observed / Unique Reflections too Low .... 39 %

Alert level C

PLAT029_ALERT_3_C _diffrn_measured_fraction_theta_full Low 0.968
PLAT234_ALERT_4_C Large Hirshfeld Difference C29 -- C34 .. 0.17 Ang.
PLAT244_ALERT_4_C Low 'Solvent' Ueq as Compared to Neighbors of C33
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.0081 Ang.
PLAT751_ALERT_4_C Bond Calc 0.00000, Rep 0.000(11) ..... Senseless su
O2 -O2 1.555 1.555 # 100

Alert level G

PLAT005_ALERT_5_G No _iucr_refine_instructions_details in the CIF ? Do !
PLAT007_ALERT_5_G Note: Number of Unrefined Donor-H Atoms 6
PLAT042_ALERT_1_G Calc. and Reported MoietyFormula Strings Differ ? Check
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 100
O2 -C28 -O2 1.555 1.555 1.555 0.00 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 179
O2 -O2 -C28 1.555 1.555 1.555 0.00 Deg.
PLAT791_ALERT_4_G Note: The Model has Chirality at C12 (Verify) S
PLAT791_ALERT_4_G Note: The Model has Chirality at C26 (Verify) S

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
5 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
7 **ALERT level G** = General information/check it is not something unexpected

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
0 ALERT type 2 Indicator that the structure model may be wrong or deficient
3 ALERT type 3 Indicator that the structure quality may be low
7 ALERT type 4 Improvement, methodology, query or suggestion
2 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

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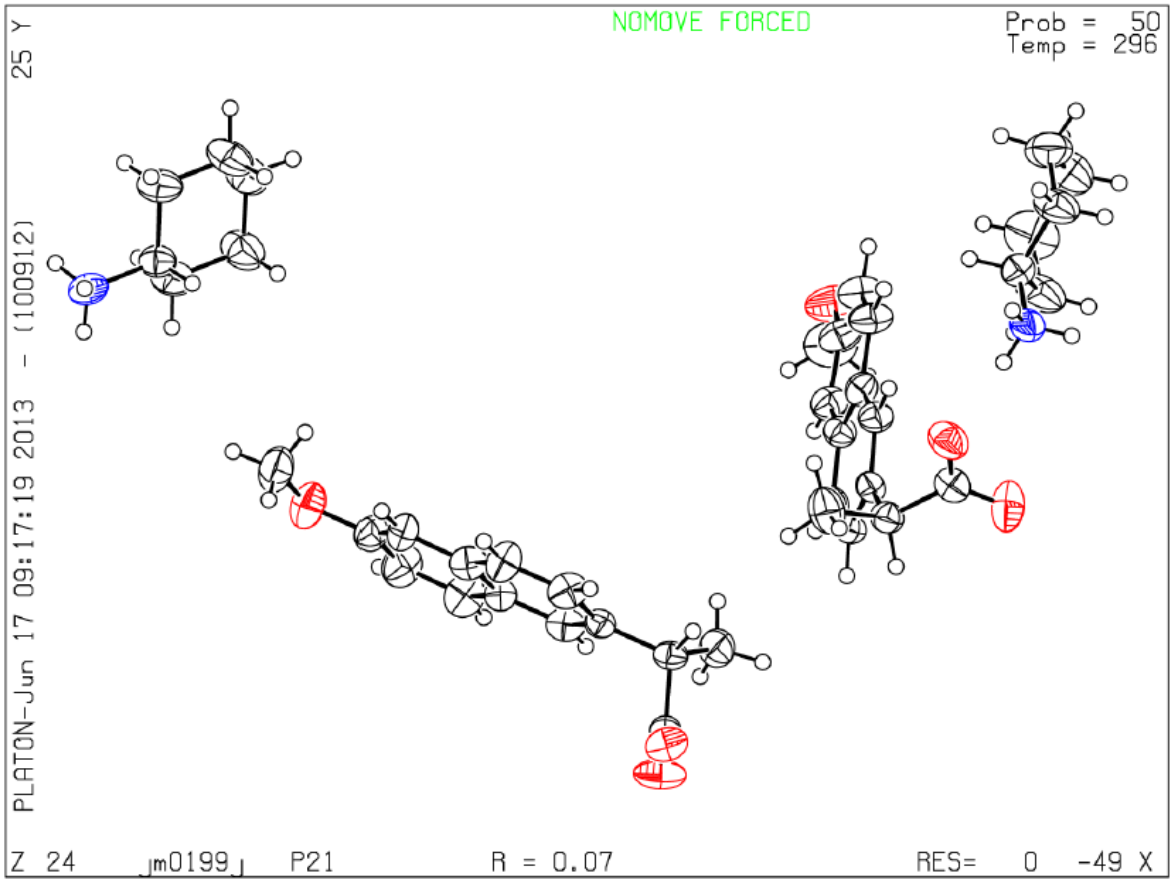
Datablock jm0199j - ellipsoid plot



Check CIF/ PLATON report of 3

checkCIF/PLATON report

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: jmnpbs

```
Bond precision:  C-C = 0.0091 A          Wavelength=0.71073

Cell:            a=11.632(4)     b=5.9372(19)        c=13.377(4)
                 alpha=90        beta=90.327(5)      gamma=90
Temperature:     296 K
```

	Calculated	Reported
Volume	923.8(5)	923.8(5)
Space group	P 21	P21
Hall group	P 2yb	P 2yb
Moiety formula	C14 H13 O3, C7 H10 N	C14 H13 O3, C7 H10 N
Sum formula	C21 H23 N O3	C21 H23 N O3
Mr	337.40	337.40
Dx,g cm-3	1.213	1.213
Z	2	2
Mu (mm-1)	0.081	0.081
F000	360.0	360.0
F000'	360.16	
h,k,lmax	15,7,17	14,7,16
Nref	4200[2303]	3685
Tmin,Tmax	0.989,0.997	0.957,0.997
Tmin'	0.956	

```
Correction method= MULTI-SCAN

Data completeness= 1.60/0.88      Theta(max)= 27.360

R(reflections)= 0.0558( 1546)     wR2(reflections)= 0.2198( 3685)

S = 0.836                  Npar= 229
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
PLAT026_ALERT_3_C Ratio Observed / Unique Reflections too Low ....         42 %
PLAT243_ALERT_4_C High  'Solvent' Ueq as Compared to Neighbors of         C21
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ...............     0.0091 Ang.
```

Alert level G

```
PLAT005_ALERT_5_G No _iucr_refine_instructions_details  in the CIF          ? Do !
PLAT007_ALERT_5_G Note: Number of Unrefined Donor-H Atoms ........          3
PLAT791_ALERT_4_G Note: The Model has Chirality at C12    (Verify)          S
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   3 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   3 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   0 ALERT type 2 Indicator that the structure model may be wrong or deficient
   2 ALERT type 3 Indicator that the structure quality may be low
   2 ALERT type 4 Improvement, methodology, query or suggestion
   2 ALERT type 5 Informative message, check
```

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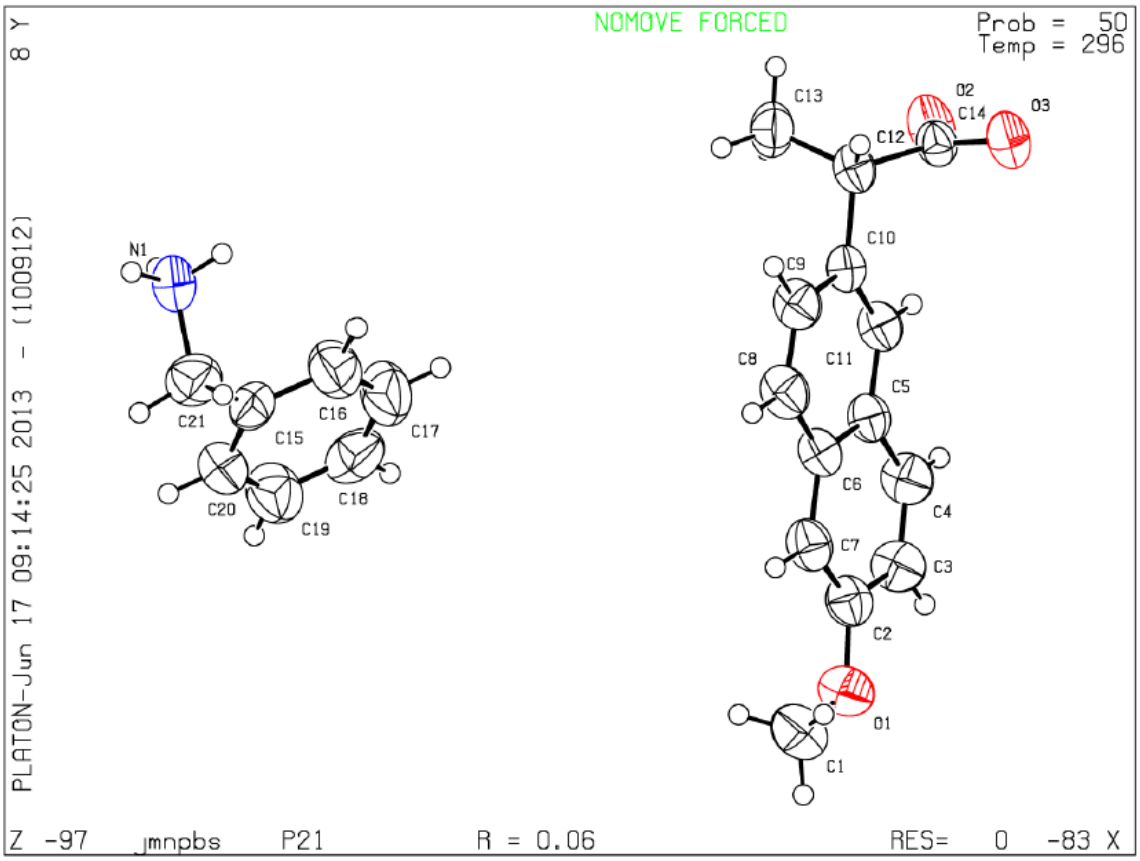
PLATON version of 01/06/2013; check.def file version of 24/05/2013

Datablock jmnpbs - ellipsoid plot



Check CIF/ PLATON report of 4

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: jm0198j_0m

Bond precision: C-C = 0.0126 A Wavelength=0.71073

Cell: a=5.7688(14) b=8.478(2) c=48.065(12)
alpha=90 beta=90 gamma=90
Temperature: 296 K

	Calculated	Reported
Volume	2350.8(10)	2350.6(10)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C14 H13 O3, C14 H16 N	C14 H13 O3, C14 H16 N
Sum formula	C28 H29 N O3	C28 H29 N O3
Mr	427.52	427.52
Dx,g cm-3	1.208	1.208
Z	4	4
Mu (mm-1)	0.078	0.078
F000	912.0	912.0
F000'	912.40	
h,k,lmax	7,10,61	7,10,54
Nref	5151[3027]	2648
Tmin,Tmax	0.994,0.998	0.930,0.998
Tmin'	0.929	

Correction method= MULTI-SCAN

Data completeness= 0.87/0.51 Theta(max)= 27.050

R(reflections)= 0.0632(1358) wR2(reflections)= 0.2094(2648)

S = 1.015 Npar= 291

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level A

PLAT029_ALERT_3_A _diffrn_measured_fraction_theta_full Low 0.728

Author Response: The crystal was poorly diffracting at higher Bragg angles. The situation did not improve even after recrystallisation and fresh data collection.

Alert level B

PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds ..... 0.0126 Ang.

Author Response: The crystal was poorly diffracting at higher Bragg angles. The situation did not improve even after recrystallisation and fresh data collection.

Alert level C

PLAT234_ALERT_4_C Large Hirshfeld Difference N1 -- C22 .. 0.16 Ang.
PLAT234_ALERT_4_C Large Hirshfeld Difference C15 -- C16 .. 0.17 Ang.
PLAT234_ALERT_4_C Large Hirshfeld Difference C15 -- C20 .. 0.16 Ang.
PLAT234_ALERT_4_C Large Hirshfeld Difference C22 -- C23 .. 0.18 Ang.
PLAT751_ALERT_4_C Bond Calc 0.00000, Rep 0.000(19) ..... Senseless su
O3 -O3 1.555 1.555 # 65

Alert level G

PLAT005_ALERT_5_G No _iucr_refine_instructions_details in the CIF ? Do !
PLAT007_ALERT_5_G Note: Number of Unrefined Donor-H Atoms 2
PLAT063_ALERT_4_G Crystal Size Likely too Large for Beam Size .... 0.95 mm
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 51
O3 -C14 -O3 1.555 1.555 1.555 0.00 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 110
O3 -O3 -C14 1.555 1.555 1.555 0.00 Deg.
PLAT791_ALERT_4_G Note: The Model has Chirality at C12 (Verify) S
PLAT952_ALERT_5_G Reported and Calculated Lmax Values Differ by .. 7

---

1 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
5 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
7 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
0 ALERT type 2 Indicator that the structure model may be wrong or deficient
2 ALERT type 3 Indicator that the structure quality may be low
9 ALERT type 4 Improvement, methodology, query or suggestion
3 ALERT type 5 Informative message, check

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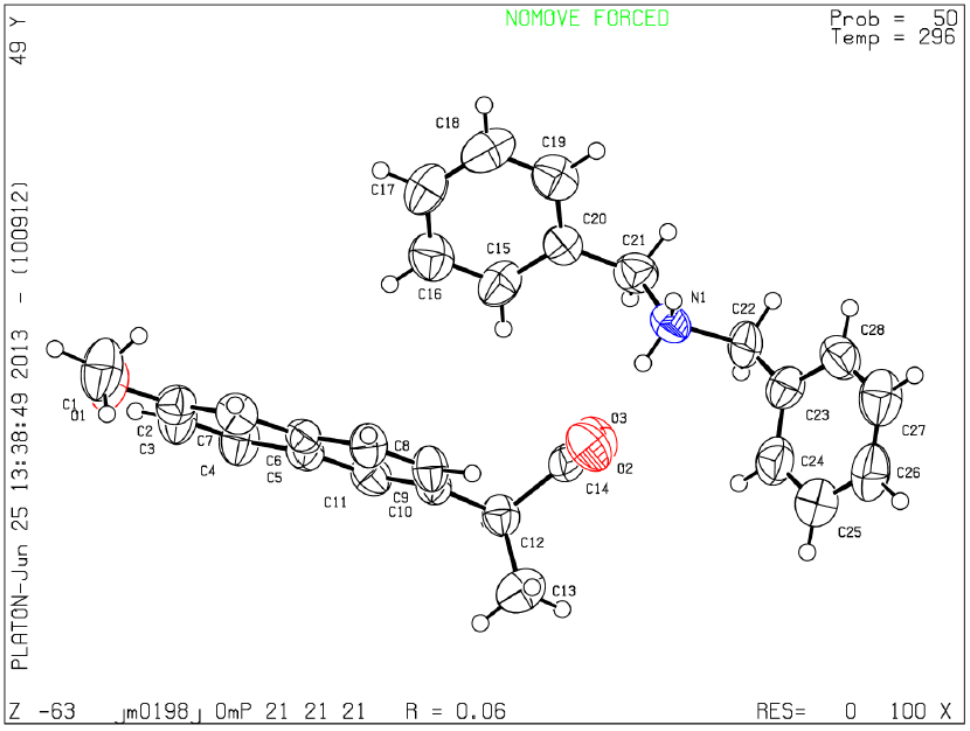
Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 01/06/2013; check.def file version of 24/05/2013

Datablock jm0198j_0m - ellipsoid plot



Check CIF/ PLATON report of 5

checkCIF/PLATON report

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: jm117_0m

```
Bond precision:  C-C = 0.0058 A          Wavelength=0.71073

Cell:            a=9.3305(11)     b=6.4425(8)        c=19.573(2)
                 alpha=90         beta=99.120(3)     gamma=90
Temperature:     293 K
```

	Calculated	Reported
Volume	1161.7(2)	1161.7(2)
Space group	P 21	P21
Hall group	P 2yb	P 2yb
Moiety formula	C17 H18 N O4, C6 H14 N, H2 O	C17 H18 N O4, C6 H14 N, H2 O
Sum formula	C23 H34 N2 O5	C23 H34 N2 O5
Mr	418.52	418.52
Dx,g cm-3	1.196	1.196
Z	2	2
Mu (mm-1)	0.084	0.084
F000	452.0	452.0
F000'	452.21	
h,k,lmax	9,6,19	9,6,19
Nref	2429[1356]	2288
Tmin,Tmax	0.974,0.993	0.959,0.993
Tmin'	0.959	

```
Correction method= MULTI-SCAN

Data completeness= 1.69/0.94      Theta(max)= 20.760

R(reflections)= 0.0400( 1984)     wR2(reflections)= 0.1167( 2288)

S = 0.816                 Npar= 286
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level A

THETM01_ALERT_3_A The value of sine(theta_max)/wavelength is less than 0.550
Calculated sin(theta_max)/wavelength = 0.4987

Author Response: The crystal was poorly diffracting at higher Bragg angles. The situation did not improve even after recrystallisation and fresh data collection.

Alert level B

PLAT089_ALERT_3_B Poor Data / Parameter Ratio (Zmax < 18) 4.74

Author Response: The crystal was poorly diffracting at higher Bragg angles. The situation did not improve even after recrystallisation and fresh data collection.

Alert level C

PLAT244_ALERT_4_C Low 'Solvent' Ueq as Compared to Neighbors of C18
PLAT245_ALERT_2_C U(iso) H27 Smaller than U(eq) O5 by ... 0.017 AngSq
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.0058 Ang.
PLAT353_ALERT_3_C Long N-H (N0.87,N1.01A) N2 - H25 ... 1.01 Ang.
PLAT355_ALERT_3_C Long O-H (X0.82,N0.98A) O5 - H26 ... 1.07 Ang.
PLAT751_ALERT_4_C Bond Calc 0.00000, Rep 0.000(9) ..... Senseless su
O2 -O2 1.555 1.555 # 64

Alert level G

PLAT005_ALERT_5_G No _iucr_refine_instructions_details in the CIF ? Do !
PLAT007_ALERT_5_G Note: Number of Unrefined Donor-H Atoms 3
PLAT199_ALERT_1_G Check the Reported _cell_measurement_temperature 293 K
PLAT200_ALERT_1_G Check the Reported _diffrn_ambient_temperature 293 K
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 49
O2 -C14 -O2 1.555 1.555 1.555 0.00 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 116
O2 -O2 -C14 1.555 1.555 1.555 0.00 Deg.
PLAT791_ALERT_4_G Note: The Model has Chirality at C12 (Verify) S

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1 **ALERT level A** = Most likely a serious problem - resolve or explain
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1 ALERT type 2 Indicator that the structure model may be wrong or deficient
5 ALERT type 3 Indicator that the structure quality may be low
5 ALERT type 4 Improvement, methodology, query or suggestion
2 ALERT type 5 Informative message, check

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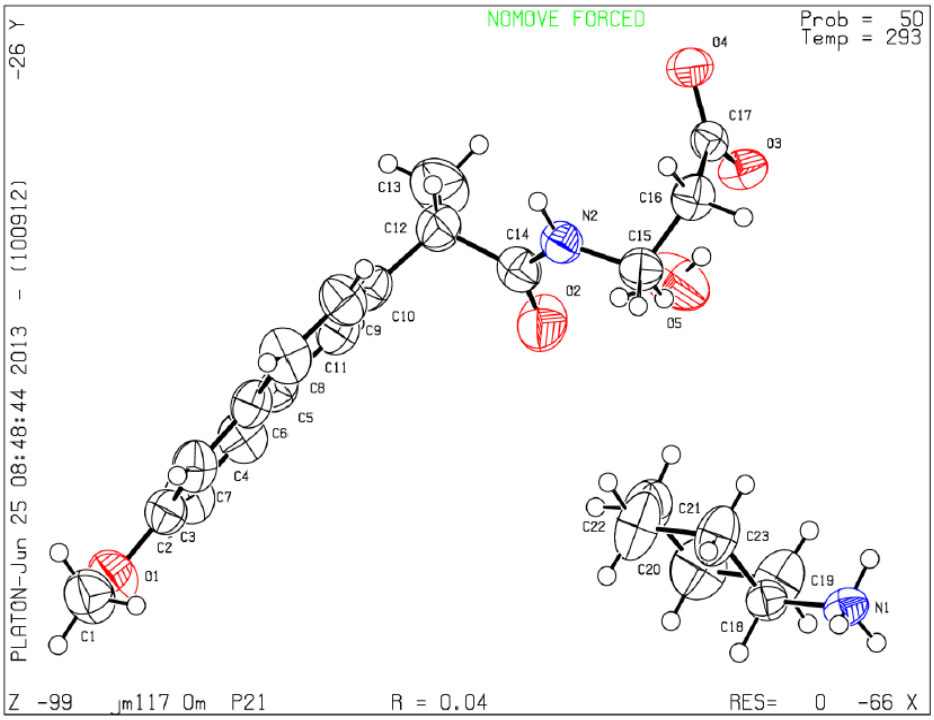
PLATON version of 01/06/2013; check.def file version of 24/05/2013

Datablock jm117_0m - ellipsoid plot



Check CIF/ PLATON report of 8

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: jm01102r

Bond precision: C-C = 0.0055 A Wavelength=0.71073

Cell: a=23.570(4) b=4.8479(8) c=18.554(3)
alpha=90 beta=90.115(9) gamma=90
Temperature: 296 K

	Calculated	Reported
Volume	2120.1(6)	2120.0(6)
Space group	C 2	C2
Hall group	C 2y	C2y
Moiety formula	2(C16 H16 N O2), C14 H16 N, 1.02(O2), 2(C), 1.96(O)	2(C16 H16 N O2), C14 H16 N, 1.02(O2), 2(C), 1.96(O)
Sum formula	C48 H48 N3 O8	C48 H48 N3 O8
Mr	794.89	794.89
Dx,g cm-3	1.245	1.245
Z	2	2
Mu (mm-1)	0.085	0.085
F000	842.0	842.0
F000'	842.40	
h,k,lmax	30,6,24	30,6,24
Nref	5236[2922]	4381
Tmin,Tmax	0.988,0.996	0.930,0.985
Tmin'	0.962	

Correction method= MULTI-SCAN

Data completeness= 1.50/0.84 Theta(max)= 28.200

R(reflections)= 0.0571(2624) wR2(reflections)= 0.2047(4381)

S = 1.144 Npar= 277

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT201_ALERT_2_B Isotropic non-H Atoms in Main Residue(s) 1

Author Response: The non-hydrogen atoms C16, C17, O3 and O4 were refined with isotropic displacement parameters only in the main residue because of minor disorder \ modelling.

Alert level C

PLAT029_ALERT_3_C _diffrn_measured_fraction_theta_full Low 0.979
PLAT202_ALERT_3_C Isotropic non-H Atoms in Anion/Solvent 3
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.0055 Ang.
PLAT350_ALERT_3_C Short C-H (X0.96,N1.08A) C15 - H3A ... 0.82 Ang.
PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N2 - H1 ... 0.69 Ang.

Alert level G

PLAT005_ALERT_5_G No _iucr_refine_instructions_details in the CIF ? Do !
PLAT007_ALERT_5_G Note: Number of Unrefined Donor-H Atoms 2
PLAT301_ALERT_3_G Note: Main Residue Disorder ..... 3 %
PLAT302_ALERT_4_G Note: Anion/Solvent Disorder ..... 100 %
PLAT311_ALERT_2_G Isolated Disordered Oxygen Atom (No H's ?) O3A
PLAT311_ALERT_2_G Isolated Disordered Oxygen Atom (No H's ?) O4B
PLAT764_ALERT_4_G Overcomplete CIF Bond List Detected (Rep/Expd) . 1.48 Ratio
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 27
C16B -C15 -C16A 1.555 1.555 1.555 37.30 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 30
C17A -C16A -C17B 1.555 1.555 1.555 27.60 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 45
C17B -C16B -C17A 1.555 1.555 1.555 25.00 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 52
O4A -C17B -O3B 1.555 1.555 1.555 25.80 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 60
C16B -C17B -C16A 1.555 1.555 1.555 41.60 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 63
C17A -C17B -O3A 1.555 1.555 1.555 12.60 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 71
O3B -C17A -O4A 1.555 1.555 1.555 26.80 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 83
C16A -C17A -C16B 1.555 1.555 1.555 38.80 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 97
C17A -O3A -C17B 1.555 1.555 1.555 6.80 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 101
C17A -O3B -C17B 1.555 1.555 1.555 32.50 Deg.
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle in CIF .... # 104
C17B -O4A -C17A 1.555 1.555 1.555 32.30 Deg.
PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd. # 6
O
PLAT791_ALERT_4_G Note: The Model has Chirality at C12 (Verify) S

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0 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully

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 5 ALERT level C = Check. Ensure it is not caused by an omission or oversight
20 ALERT level G = General information/check it is not something unexpected

 0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
 3 ALERT type 2 Indicator that the structure model may be wrong or deficient
 6 ALERT type 3 Indicator that the structure quality may be low
15 ALERT type 4 Improvement, methodology, query or suggestion
 2 ALERT type 5 Informative message, check
```

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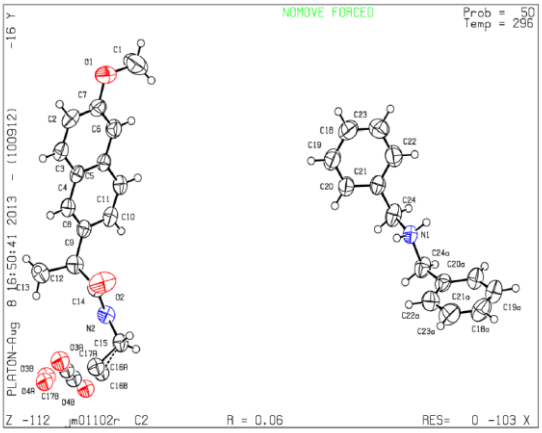

REFERENCES

(1) J. Majumder, M. R. Das, J. Deb, S. S. Jana and P. Dastidar, *Langmuir* 2013, **29**, 10254.
(2) Q-S. Wang, Y. Xiang, Y-L. Cui, K-M. Lin and X-F. Zhang, *PLoS ONE* 2012, **7**, e34122.
(3) E. Heiss, C. Herhaus, K. Klimo, B. Bartsch and C. Gerha¨user, *J. Biol. Chem*. 2001, **276**, 32008.