Supporting Information:

Isotactic N-Alkyl Acrylamide Oligomers Assume Sheet Structure: Unequivocal Evidence From Crystal Structures

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General Methods. Unless otherwise stated, starting materials were obtained from commercial suppliers and used without further purification. Dry THF and dry MeOH were freshly prepared by distillation over sodium and activated magnesium turnings, respectively. Methylacrylate and methyl acetate were dried over K_2CO_3 and distilled. LDA (lithium diisopropyl amide) was generated *in situ*, by reacting n-butyl lithium with dry diisopropyl amine in THF. All dry reactions were performed under argon atmosphere. Product purification was carried out using 100-200 mesh silica, unless otherwise stated. NMR spectra were recorded in $CDCl_3$ (99.8 D %, Cambridge Isotope), methanol-d_4 (99.8 D %, 0.05 % TMS), D_2O-H_2O (10:90), and DMSO-d_6 (99.8 D %) on AC 200 MHz or MSL-200 MHz or DRX-500 MHz Bruker NMR spectrometers. Electrospray ionization mass spectrometry (ESI-MS) was carried on a Finnigan MAT-1020 mass spectrometer. IR spectra were recorded in $CHCl_3$ or Nujol, from Perkin-Elmer 68515 PC- FTIR spectrometer. Melting points were measured on Buchi 535 melting point apparatus and are uncorrected. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E-Merck silica gel plates.

Single crystal X-ray data were collected on a Brucker SMART APEX CCD diffractometer with graphite-monochromatized (Mo K$\propto$= 0.71073 Å) radiation at room temperature. All data were corrected for Lorentzian, polarization and absorption effects using Bruker's SAINT and SADABS programs. SHELX-97[1] was used for structure solution and full matrix least squares refinement on F^2. Hydrogen atoms were included in the refinement as per the riding model.

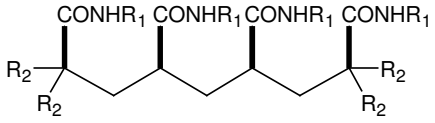
Gelation Test. A weighed amount of the compound in an appropriate solvent (6-8 mM) was placed in a glass vial, which was sealed and heated until the compound was dissolved. The solution was allowed to cool to room temperature and the gel formation was confirmed by the failure of the gel mixture to flow by inverting the glass vial. The thermo reversibility of the gelation was confirmed by repeated heating and cooling.

Scanning Electron Microscopy: Scanning electron micrographs were taken with a LEO 440I microscope equipped with a digital camera. Samples of the xerogels were prepared

by placing the gel on top of a tin plate and, after drying of the solvent they were sputtered with Au.

Synthetic Scheme:

The acrylamide oligomers **1a-e** (figure 1) were synthesized[2] by multi-step synthetic protocols, as described in schemes 1-2.

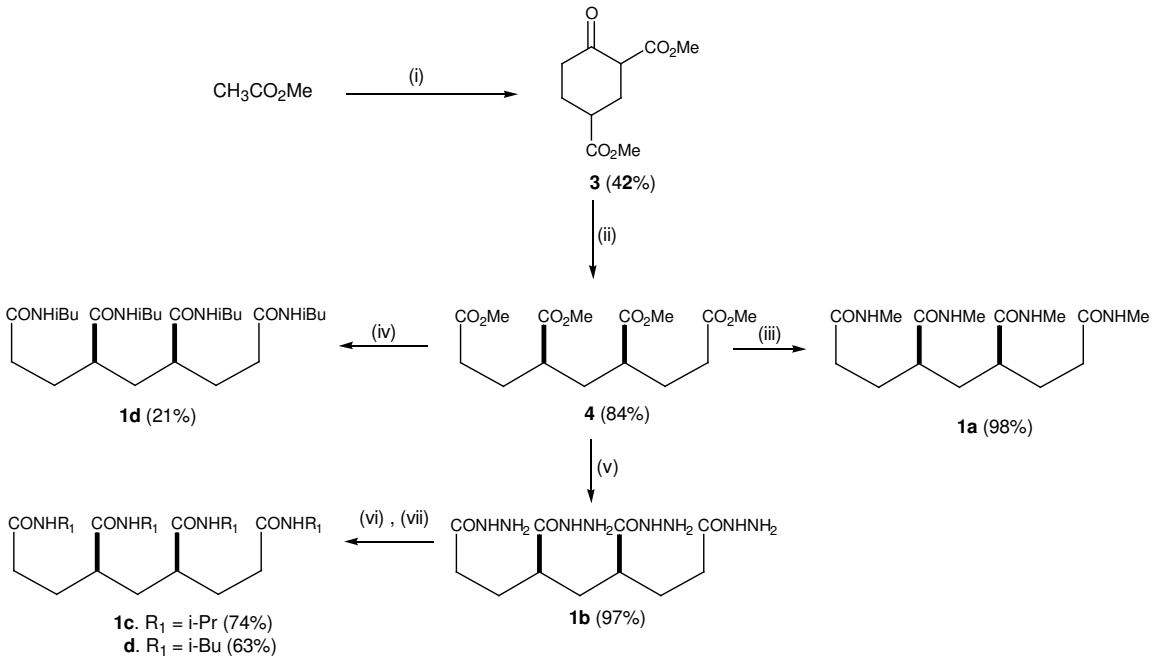


1a. R_1 = Me, R_2 = H
b. R_1 = NH_2, R_2 = H
c. R_1 = iPr, R_2 = H
d. R_1 = iBu, R_2 = H
e. R_1 = R_2 = Me

Figure 1: Various N-acrylamide oligomers **1a-e** synthesized by multi-step synthetic strategies.

Synthesis of 1a-d:

4,6-Bis-methoxycarbonyl-nonanedioic acid dimethyl ester **4**, a key intermediate in the synthesis of the N-acrylamide tetramers **1a-d**, was synthesized by a modified Robinson protocol[3] as follows (scheme 1). The β-keto ester **3**, obtained by the reaction of methyl acetate with methylacrylate in the presence of LDA at -78^0C, was subjected to a one-pot DBU-mediated Michael addition-ring opening reaction sequence by reacting it with methylacrylate in methanol to afford the tetra acrylate ester **4** in good yield. The tetra acrylamide **1a** could be readily obtained in excellent yield by the amidation of the ester **4** with saturated methylamine solution in methanol. Similarly, **1b** was obtained by reacting **4** with excess hydrazine in methanol. The tetra acrylamide oligomers **1c,d** were obtained by following the acyl azide procedure (method A), a strategy extensively used in solution-phase peptide coupling[4]. The tetra acrylamide oligomer **1d** could also be obtained by the reaction of tetra acrylate ester **4** with $AlMe_3$-isobutyl amine complex[5], though the low yield of this strategy discouraged its further application in the synthesis of other oligomers.

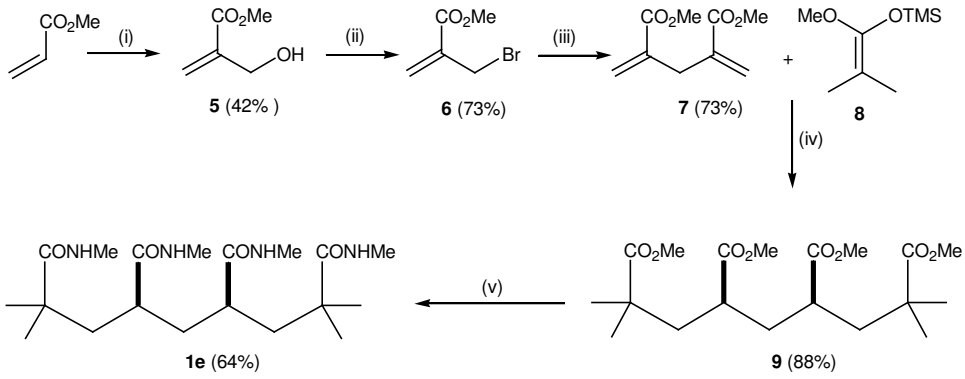


Key: (i) a. LDA, THF, -78°C, b. CH2=CHCO$_2$Me,THF-78°C; (ii) methyl acrylate, MeOH, DBU, 40° C, 36 h; (iii) MeOH, MeNH$_2$, RT, 24h; (iv) a. AlMe$_3$.isobutyl amine complex, Toluene, 90°C, 12h; b. H$^+$ (v) NH$_2$NH$_2$, MeOH, RT, 24h; (vi) NaNO$_2$, AcOH, 5N HCl, DCM; (vii) R$_1$NH$_2$, Et$_3$N, DMAP.

Scheme 1: Synthesis of N-substituted acrylamide tetramers **1a-d.**

Synthesis of 1e:

The tetra acrylamide oligomer **1e** having terminal *gem*-disubstitution was obtained in high yield, following a different strategy using Mukaiyama-Michael addition[6] as a key reaction step (scheme 2). Tetra-*n*-butylammonium bibenzoate (TBABB)-catalyzed bis-conjugate addition of silyl ketene acetal **8**[7] to the α,β-unsaturated bis-olefin[8], obtained in three steps from methyl acrylate, furnished cleanly the terminal *gem*-disubstituted tetra ester **9** in 88% yield. It is noteworthy that use of various Lewis catalysts in the Mukaiyama-Michael addition reaction failed to afford the ester **9**; only intractable



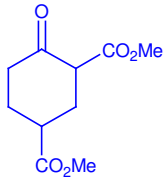
mixture of products could be obtained under such conditions.

Key: (i) CH_2O (37 wt.%), aq. Et_3N, 60°C, 6 h; (ii) 48% HBr, H_2SO_4, DCM, 12 h; (iii) methyl acrylate, DABCO, RT, 7 days; (iv) (a) TBABB (3 mol%), THF, RT, 1h; (b) 1N HCl:THF (1:9); (V) MeOH, $MeNH_2$, Steel bomb / 75°C, 4 days.

Scheme 2: Synthesis of terminal *gem*-disubstituted acrylamide tetramer **1e.**

Experimental Procedures:

4-Oxo-cyclohexane-1,3-dicarboxylic acid dimethyl ester 3[9]:



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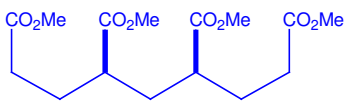
To a flame dried two necked round bottom flask containing dry THF (40 mL), diisopropylamine (7.63 g, 10.57 mL, 75.5 mmol) was added, followed by the drop wise addition of (1.6 M solution in hexane) n-BuLi (5.07 g, 49.46 mL, 79.2 mmol) at 0°C. After stirring for 45 min., the reaction mixture was cooled down to –78° C (acetone-dry ice) and then methyl acetate (5.59 g, 6 mL, 75.5 mmol) was added drop wise. After stirring the reaction mixture for further 45 min. at the same temperature, methylacrylate (13.64 g, 14.27 mL, 158.5 mmol), dissolved in dry THF (10 mL), was added drop wise and the reaction mixture was vigorously stirred for 1 hr. The reaction was quenched by the slow addition of sat. solution of ammonium chloride. The product was isolated by extraction with ethyl acetate (3 x 250 mL). The organic layer was washed with water, followed by brine and dried over an.Na_2SO_4, concentrated and purified by column chromatography (10% pet ether / ethyl acetate, R_f = 0.45) to give 4-oxo-cyclohexane-1,3-dicarboxylic acid dimethyl ester **3** (6.73 g, 42%) as a white crystalline low melting solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ ppm 12.12 (s, 1H), 3.73 (s, 3H), 3.69 (s, 3H), 2.60-2.31 (m, 4H), 2.08-2.01 (m, 2H), 1.87-1.71 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ ppm 174.9, 172.5, 171.0, 96.0, 51.8, 51.4, 38.9, 28.0, 24.7, 24.0; IR ($CHCl_3$) ν (cm^{-1}): 3022, 2952, 2360, 2341, 1733, 1660, 1618, 1442, 1357, 1315, 1280, 1215, 1083, 1054, 1016, 757, 667; ESI Mass: 215.09 (M+1) and 237.07 (M+Na); Anal. Calcd. for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.85; H; 6.89.

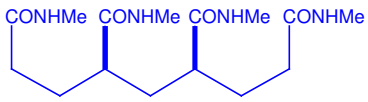
4,6-Bis-methoxycarbonyl-nonanedioic acid dimethyl ester 4[3]:



4

To a flame-dried two necked round bottom flask was added 4-oxo-cyclohexane-1,3-dicarboxylic acid dimethyl ester **3** (1 g, 4.7 mmol) in dry MeOH (15 mL). To this solution, DBU (0.92 g, 0.9 mL, 6.1 mmol) was added at 0°C, followed by the addition of methylacrylate (0.6 g, 0.63 mL, 7.1 mmol). The reaction mixture was stirred at room temperature for 36 hrs. The volatiles were removed on rotavapor under reduced pressure, the reaction mixture was diluted with DCM (20 mL) and 2N HCl was added drop wise at 0°C. The product was isolated by repeated extraction with DCM (3 x 200 mL). The organic layer was sequentially washed with saturated $NaHCO_3$, water, brine and dried over anhydrous Na_2SO_4. Evaporation of DCM under reduced pressure afforded a clear oil which was purified by column chromatography (25% pet ether / ethyl acetate; R_f = 0.35) to provide 4,6-bis-methoxycarbonyl-nonanedioic acid dimethyl ester **4** (1.30 g, 84%) as an oil. ^{1}H NMR ($CDCl_3$ / 500 MHz): δ ppm 3.63-3.66 (m, 12H), 2.43-2.34 (m, 2H), 2.30-2.25 (m, 4H), 2.06-2.00 (m, 1H), 1.87-1.76 (m, 4H), 1.58-1.55 (m, 1H); ^{13}C NMR ($CDCl_3$ / 125 MHz): δ ppm 175.1, 175.0, 173.1, 51.7, 51.6, 51.6, 42.6, 42.4, 34.1, 34.0, 31.4, 27.6, 26.9; IR ($CHCl_3$) ν (cm^{-1}): 3024, 2954, 2954, 2254, 1734, 1437, 1383, 1203, 1166, 1084, 909, 734, 650; ESI Mass: 333.14 (M+1) and 355.10 (M+Na) ; Anal. Calcd. for $C_{15}H_{24}O_8$: C, 54.21; H, 7.28. Found: C, 54.32; H, 7.52.

4,6-Bis-methylcarbamonyl-nonanedioic acid bis-methylamide 1a:

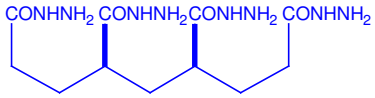


1a

A mixture of 4,6-bis-methoxycarbonyl-nonanedioic acid dimethyl ester **4** (0.50 g, 1.5 mmol) and saturated solution of methylamine[10] in dry methanol (25 mL) in a 100 mL single necked round bottom flask was vigorously stirred for 24 hrs. at room temperature. The white precipitate that formed was filtered off and washed repeatedly with small amounts of chilled methanol and ethyl acetate and dried to furnish analytically pure 4,6-bis-methylcarbamonyl-nonanedioic acid bis-methylamide **1a** [0.480 g, 97%, (R_f = 0.25, 20% methanol / ethyl acetate)], which was further recrystallized from a mixture of water: ethylene glycol (5:1), as colorless needles. mp 243-244°C; ^{1}H NMR [H_20:D_20 (90:10), 500 MHz]: δ ppm 7.99 (b, 1H), 7.83 (b, 1H), 2.74-2.72 (m, 12H), 2.24-2.12 (m, 6H), 1.85-1.72 (m, 5H), 1.63-1.55 (m, 1H); ^{13}C NMR [H_20:D_20, (90:10) 125 MHz]: δ ppm

177.2, 175.7, 43.9, 34.4, 33.0, 27.7, 25.7, 25.6; IR (Nujol) ν (cm^{-1}): 3296, 2945, 2360, 1656, 1641, 1566, 1461, 1377, 1274, 1155, 1053, 1033, 943, 923, 854, 800, 721; ESI Mass: 329.23 (M+1) and 351.20 (M+Na) ; Anal. Calcd. for $C_{15}H_{28}N_4O_4$: C, 54.86; H, 8.59; N, 17.06. Found: C, 54.68; H, 8.72; N, 17.21.

4,6-Bis-aminocarbamonyl-nonanedioic acid bis-hydrazide 1b:

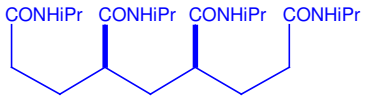


1b

A mixture of 4,6-bis-methoxycarbonyl-nonanedioic acid dimethyl ester **4** (1 g, 3.0 mmol) and (99%) hydrazine monohydrate (1.8 g, 1.75 mL, 36.1 mmol) in dry methanol (20 mL) was vigorously stirred for 24 hrs. at room temperature. The thick white precipitate that formed was filtered and repeatedly washed with small portions of chilled methanol and dried to yield **1b** (0.965 gm, 97%). mp 177-179°C; ^{1}H NMR (DMSO-d_6 / 500 MHz): δ ppm 8.94 (s, 4H), 4.14 (s, 8H), 2.00-1.88 (b, 6H), 1.75-1.30 (m, 6H); ^{13}C NMR (DMSO-d_6 /125 MHz): δ ppm 173.8, 173.7, 171.6, 171.5, 41.7, 41.1, 34.9, 34.8, 31.5, 31.4, 29.1, 28.1; IR (Nujol) ν (cm^{-1}): 3286, 2937, 2725, 2349, 1654, 1622, 1529, 1461, 1377, 1303, 1151, 1053, 983, 721; LC-MS Mass: 333.18 (M+1) and 687.35 (2M+Na); Anal. Calcd. for $C_{11}H_{24}N_8O_4$: C, 39.75; H, 7.28; N, 33.71; Found: C, 39.33; H, 7.45; N, 33.59.

4,6-Bis-isopropylcarbamonyl-nonanedioic acid bis-isopropylamide 1c:

Method A (acyl azide route)[4]:



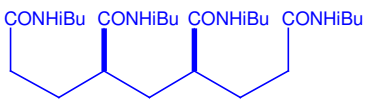
1c

To a stirred mixture of 4,6-bis-aminocarbamonyl-nonanedioic acid bis-hydrazide **1b** (0.50 g, 1.5 mmol), glacial acetic acid (4 mL), 5N HCl (4 mL), and DCM (5 mL) maintained at –5°C (ice-salt mixture) was added a freshly prepared solution of sodium nitrite (1.55 g, 22.6 mmol) in water (3mL) drop wise. After stirring for 20 min. at –5°C, the reaction was quenched by the addition of ice-cold water and extracted with DCM (2 x 10 mL). The organic layer was washed with saturated solution of $NaHCO_3$, followed by water and dried over anhydrous Na_2SO_4 for 5 min. To this mixture, containing the *in situ* generated tetra acyl azide intermediate, was added sequentially triethyl amine (1.82 g, 2.51 mL, 18.1 mmol), DMAP (0.018 g, 0.2 mmol), and isopropyl

amine (0.89 g, 1.28 mL, 15.1 mmol) at 0°C. Once the addition was over, the ice bath was removed and the reaction mixture was allowed to stir vigorously at room temperature for 36 hrs. The volatiles were removed on rotavapor under reduced pressure and the reaction mixture was extracted with ethyl acetate (3 x 200 mL). The organic layer was washed twice with water, brine and dried over anhydrous Na_2SO_4. The organic phase was concentrated and purified by column chromatography (3% Methanol / DCM, R_f = 0.35) to furnish **1c** (0.490 gm, 74 %) as a white solid. mp 269-270°C. ^{1}H NMR (methanol-d_4 / 500 MHz): δ ppm 4.01-3.90 (m, 4H), 2.20-2.06 (m, 6H), 1.78-1.66 (m, 6H), 1.17-1.14 (m, 12H), 1.12 (d, 12H, *J* = 6.85); ^{13}C NMR (methanol-d_4 / 125 MHz): δ ppm 176.4, 176.3, 174.5, 174.3, 45.4, 44.8, 42.5, 42.5, 36.3, 35.6, 34.9, 34.8, 30.9, 29.4, 22.8, 22.8, 22.7, 22.7; IR (Nujol) ν (cm^{-1}): 3298, 2937, 2725, 2360, 2341, 1656, 1631; ESI Mass: 441.36 (M+1) and 463.32 (M+Na) ; Anal. Calcd. for $C_{23}H_{44}N_4O_4$; C, 62.69; H, 10.07; N, 12.72. Found: C, 62.60; H, 9.99; N, 12.60.

4,6-Bis-isobutylcarbamonyl-nonanedioic acid bis-isobutylamide 1d:

Method A (acyl azide route)[4]:

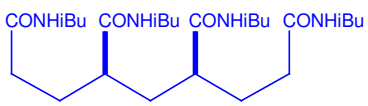


1d

4,6-Bis-isobutylcarbamonyl-nonanedioic acid bis-isobutylamide 1d was made following the similar procedure (method A) described for **1c**. Yield (0.467 g, 63%). mp 195-197 °C; ^{1}H NMR (DMSO-d_6 / 500MHz): δ ppm 7.78-7.70 (m, 4H), 2.92-2.81 (m, 8H), 2.14-2.07 (m, 2H), 1.97 (s, 4H), 1.69-1.51 (m, 9H), 1.41-1.36 (m, 1H), 0.83-0.80 (t, 24 H, *J* =7.9); ^{13}C NMR (DMSO-d_6 / 125 MHz): δ ppm 174.2, 171.8, 171.8, 46.2, 46.1, 46.0, 43.5, 42.8, 34.8, 34.7, 33.3, 33.2, 29.1, 28.2, 28.0, 20.2, 20.2; IR (Nujol) ν (cm^{-1}): 3296, 2937, 2725, 1643, 1522, 1461, 1377, 1249, 1159, 1058, 1047, 968, 937, 721; ESI Mass: 497.41 (M+1) and 519.40 (M+Na) ; Anal. Calcd. for $C_{27}H_{52}N_4O_4$: C, 65.29; H, 10.55; N,11.28. Found: C, 65.31; H, 10.49; N, 11.51.

4,6-Bis-isobutylcarbamonyl-nonanedioic acid bis-isobutylamide 1d:

Method B ($AlMe_3$ route)[5]:

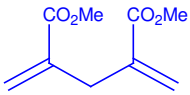


1d

To a flame dried two necked RB fitted with reflux condenser was added dry toluene (5 mL) and 2M toluene solution of trimethylaluminum (0.347 g, 2.4 mL, 4.8 mmol). To this was then added isobutyl amine (0.44 g, 0.59 mL, 6.0 mmol) at 0°C drop wise and the reaction mixture was allowed to stir for 10 min at 0°C under argon and then warmed to room temperature. After 1 hr, this reaction mixture was again cooled to 0°C and 4,6-bis-methoxycarbonyl-nonanedioic acid dimethyl ester **4** (0.20 g, 0.6 mmol) dissolved in dry toluene (5 mL) was added to the above reaction mixture over a period of 10 min. Once the addition over, the reaction mixture was heated to 90°C for 12 hrs. The reaction was quenched by the addition of water (4 mL) drop wise at 0°C and stirred for 30 min. Then the reaction mixture was diluted with (50 mL) ethyl acetate and 1N HCl was added drop wise and stirred for another 10-20 min. The product was isolated by extraction with ethyl acetate (3 x 75 mL). The organic layer was sequentially washed with saturated solution of $NaHCO_3$, water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (5% methanol / DCM) to afford 4,6-bis-isobutylcarbamonyl-nonanedioic acid bis-isobutylamide **1d** (0.062 g, 21%) as a white solid, whose authenticity was confirmed by comparing with a sample obtained by **method A**.

2,4-Dimethoxycabonylpenta-1,4-diene 7[8]:

(i)[8a] To a round bottom flask fitted with a reflux condenser, 37wt.% formaldehyde (10 g, 24.79 mL, 333.0 mmol), methylacrylate (57.33 g, 59.96 mL, 666.0 mmol), and triethyl amine (40.43 g, 55.69 mL, 399.6 mmol) and water (10 mL) were added. The reaction mixture was stirred at 60°C for the period of 6 hrs. The reaction was quenched with the addition of ice-cold water and the volatiles were removed under reduced pressure. The residue was extracted with ethyl acetate (3 x 100 mL), washed sequentially with brine, water, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to furnish the crude Baylis-Hillman adduct 2-hydroxymethyl-acrylic acid methyl ester **5** (5.71 g, 42 %, R_f = 0.35, 30% pet ether / ethyl acetate), which was used without further purification for the next step.



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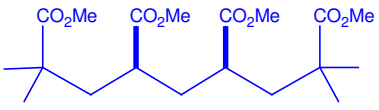
(ii)[8b] The crude Baylis-Hillman adduct **5** (3.7 g, 31.9 mmol) was taken in a 100 mL RB containing DCM (35mL). To the above solution, at 0°C, was added drop wise 48 % HBr (12 mL, 3.24 mL / g of Baylis-Hillman adduct **5**) with constant stirring. After 5 min, conc.H_2SO_4 (11 mL, 2.97 mL / g of Baylis-Hillman adduct **5**) was added at 0°C drop wise and the reaction mixture was stirred for another 10 min at the same temperature, after which stirring was allowed to continue over night at room temperature. The reaction was quenched with the addition of ice-cold water and extracted with DCM (4 x 200 mL). The organic layer was washed successively with brine and chilled water, dried over anhydrous Na_2SO_4, and concentrated to give crude 2-bromomethyl-acrylic acid methyl ester **6** (4.195 g , 73 %, R_f = 0.6 , 5% pet ether / ethyl acetate), as a thick liquid, which was used without further purification for the next step.

(iii)[8c] The crude 2-bromomethyl-acrylic acid methyl ester **6** (4.195 g, 23.4 mmol) was taken in a 100 mL RB containing excess methylacrylate (30mL). To the above well-stirred solution, DABCO (5.78 g, 51.5 mmol) was added and the reaction mixture was then allowed to stand at room temperature for 7 days. The reaction mixture was diluted with diethyl ether (100 mL) and washed successively with 2N HCl and water. The product was isolated by extracting with diethyl ether (3 x 150 mL). The organic layer was successively washed with saturated solution of $NaHCO_3$, water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The product was purified by column chromatography (5% pet ether / ethyl acetate, R_f = 0.45) to provide 2,4-dimethoxycabonylpenta-1,4-diene **7** (3.125 g, 73 %). ^{1}H NMR ($CDCl_3$ / 200 MHz): δ ppm 6.27 (s, 2H), 5.61 (s, 2H), 3.76 (s, 6H), 3.34 (s, 2H); ^{13}C NMR ($CDCl_3$ / 50 MHz): δ ppm 166.9, 137.6, 126.8, 51.8, 33.7; IR ($CHCl_3$) ν (cm^{-1}): 3024, 2952, 2358, 2341, 1720, 1629, 1438, 1307, 1276, 1215, 1141, 99, 952, 815, 756; ESI Mass: 185.10 (M+1) .

4,6-Bis-methoxycarbonyl-2,2,8,8-tetramethyl-nonanedioic acid dimethyl ester 9:

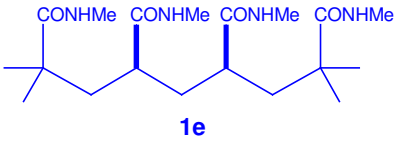


9

To a flame dried 25 mL two-necked round bottom flask, TBABB (0.007 g, 0.02 mmol) was taken, and dissolved in dry THF (3mL). [(1-Methoxy-2-methyl-1-propenyl)oxy)]trimethylsilane **8** (0.284 g, 0.33 mL, 1.6 mmol) dissolved in dry THF (5 mL) was added drop wise to the above solution. After stirring the reaction mixture for 10

min., a solution of 2,4-dimethoxycabonylpenta-1,4-diene **7** (0.10 g, 0.5 mmol) in dry THF (3 mL) was added in one lot to the above reaction mixture at room temperature and stirring was allowed to continue for 1 hr. After quenching the reaction by the addition of 1N HCl:THF (1:9) solution at 0°C, the volatiles were removed under reduced pressure and the product was isolated by extraction with DCM (3 x 50 mL). The organic layer was washed successively with saturated solution of $NaHCO_3$, water, brine, dried over anhydrous Na_2SO_4 and concentrated. Purification by column chromatography (15% pet ether / acetone, R_f= 0.35) afforded 4,6-bis-methoxycarbonyl-2,2,8,8-tetramethyl-nonanedioic acid dimethyl ester **9** (0.184 g, 88 %) as a viscous liquid. ^{1}H NMR ($CDCl_3$ / 200 MHz): 3.67-3.60 (m, 12H), 2.40-2.26 (m, 2H), 2.12-1.88 (m, 2H), 1.72-1.48 (m, 4H), 1.17 (s, 6H), 1.14 (s, 6H); ^{13}C NMR ($CDCl_3$ / 50 MHz): δ ppm 177.5, 175.9, 51.7, 51.6, 51.5, 43.2, 42.3, 41.8, 40.0, 39.9, 38.3, 26.3, 26.2; IR ($CHCl_3$) ν (cm^{-1}): 3024, 2952, 2844, 2360, 2343, 1735, 1475, 1448, 1390, 1369, 1303, 1259, 1195, 1168, 1139, 1039, 979, 829, 756, 667; ESI Mass: 389.21 (M+1) and 799.39 (2M+Na); Anal. Calcd. For $C_{19}H_{32}O_8$: C, 58.75; H, 8.30; Found: C, 58.85; H, 8.23.

4,6-Bis-methylcabamoyl-2,2,8,8-Tetramethylcarbamoyl-nonanedioic acid bis-methylamide 1e:



1e

In a two necked 25 mL round bottom flask containing dry methanol (10 mL), 4,6-bis-methoxycarbonyl-2,2,8,8-tetramethyl-nonanedioic acid dimethyl ester **9** (0.20 g, 0.5 mmol) was added. After maintaining the solution at 0°C, methylamine was slowly bubbled into it for 1 hr. The above reaction mixture was transferred into a 25 mL test tube, and the test tube was kept in a steel bomb. The steel bomb was heated in an oven maintained at 75°C, for 4 days. Evaporation of the volatiles under reduced pressure afforded a white residue, which was crystallized from acetonitrile to give analytically pure 4,6-bis-methylcabamoyl-2,2,8,8-Tetramethylcarbamoyl-nonanedioic acid bis-methylamide **1e** as white solid (0.127 g, 64 %), R_f = 0.35, 20% methanol / ethyl acetate). mp 206-207°c; ^{1}H NMR [D_2O: H_2O (10: 90) / 500MHz): δ ppm 7.92 (b, 2H), 7.57 (b, 2H), 2.79-2.73 (m, 12H), 2.22-2.13 (m, 2H), 1.97-1.88 (m, 2H), 1.78-1.69 (m, 1H), 1.68-1.61 (m, 2H), 1.51-1.42 (m, 1H), 1.18 (s, 6H), 1.16 (s, 6H); ^{13}C NMR (H_20:D_20, 90:10,

125 MHz): δ ppm 180.4, 177.8, 42.1, 41.4, 41.0, 37.9, 26.2, 25.9, 24.8, 24.4; IR (Nujol) ν (cm^{-1}): 3355, 3259, 3099, 2952, 1656, 1577, 1529, 1502, 1404, 1377, 1315, 1244, 1215, 1164, 1045, 1006, 966, 721; ESI Mass: 385.34 (M+1) and 407.32 (M+Na) ; Anal. Calcd. for $C_{19}H_{36}N_4O_4$: C, 59.35; H, 9.44; N, 14.57. Found: C, 59.76; H, 9.35; N, 14.58.

References:

1. G. M. Sheldrick, SHELX-97 program for crystal structure solution and refinement, University of Göttingen, Germany, (1997)

2. Detailed experimental procedures would be published elsewhere.

3. Openshaw, H. T. & Robinson, R. Strychnine and brucine. XLV. Synthetical experiments. 3. *J. Chem. Soc.*, 912-18 (1946)

4. Bodanszky, M. & Bodanszky, A. *The practice of peptide synthesis*-2nd Edition; Berlin, Springer-Verlag Publishers, (1984).

5. Amide-bond formation has been realized by the reaction of esters with $AlMe_3$-amine complexes. For related references, see: (a) Sidler, D. R., Lovelace, T. C., McNamara, J. M. & Reider, P. J. Aluminum-Amine Complexes for the Conversion of Carboxylic Esters to Amides. Application to the Synthesis of LTD4 Antagonist MK-0679. *J. Org. Chem.*, **59**, 1231-1233 (1994). (b) Lee, S. H., Matsushita, H.; Clapham, B. & Janda, K. D. The direct conversion of carbamates to ureas using aluminum amides. *Tetrahedron*, **60**, 3439-3443 (2004).

6. (a) Gorobets, E. V., Miftakhov, M. S. & Valeev, F. A. Tandem transformations initiated and determined by the Michael reaction. *Russ. Chem. Rev.* **69**, 1001-1019 (2000). (b) Zhi-Liang, S., Shun-Jun, J. & Teck-Peng, L. An environmentally friendly procedure for Mukaiyama aldol and Mukaiyama-Michael reactions using a catalytic amount of DBU under solvent- and metal-free conditions. *Tetrahedron Letters*, **46**, 507-508 (2005).

7. Tetra-*n*-butylammonium bibenzoate (TBABB), a 2:1 complex of benzoic acid and tetra-*n*-butylammonium hydroxide, which functions as a weak Lewis base, has been shown to be an efficient catalyst for Mukaiyama-Michael additions. See: Gnaneshwar, R., Wadgaonkar, P. P. & Sivaram, Swaminathan. The Mukaiyama-Michael addition of a α,α-dimethyl substituted silyl ketene acetal to α,β-unsaturated ketones using tetra-n-

butylammonium bibenzoate as a nucleophilic catalyst. *Tetrahedron Letters*, **44**, 6047-6049 (2003).

8. (a) Basavaiah, D., Krishnamacharyulu, M. & Rao, A. J. The aqueous trimethylamine-mediated Baylis-Hillman reaction. *Synth. commun*.**, 30**, 2061-2069 (2000). (b) Buchholz, R. & Hoffmann, H. M. R. *Helv. Chim. Acta*., **74**, 1213 (1991). (c) Basavaiah, D., Sharada, D. S., Baran, N. K. & Reddy, R. M. The Baylis-Hillman Reaction: One-Pot Facile Synthesis of 2,4-Functionalized 1,4-Pentadienes. *J. Org. Chem*. **67**, 7135-7137 (2002).

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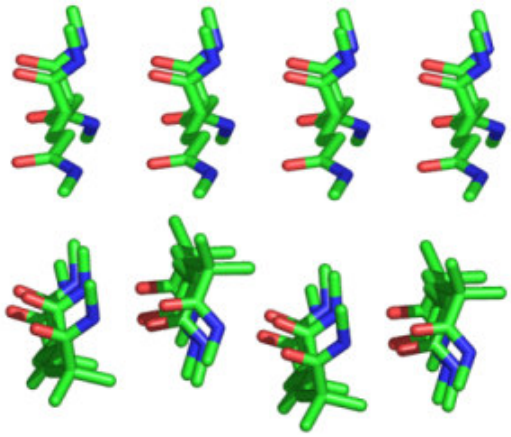
10. (a) An aqueous solution of methylamine (40 wt.%) was heated at 60°C and the evolving methylamine gas, dried by passing through a KOH trap, was bubbled into a methanolic solution of the respective ester compounds at 0°C for 1 hr. Alternatively, the evolving methylamine gas was bubbled into a round bottom flask containing dry methanol and this solution was preserved and used in the amidation reactions. (b) For a related reference, see: Dietrich, E. & Lubell, W. D. Efficient Synthesis of Enantiopure Pyrrolizidine Amino Acid, *J. Org. Chem*., **68**, 6988-6996 (2003).

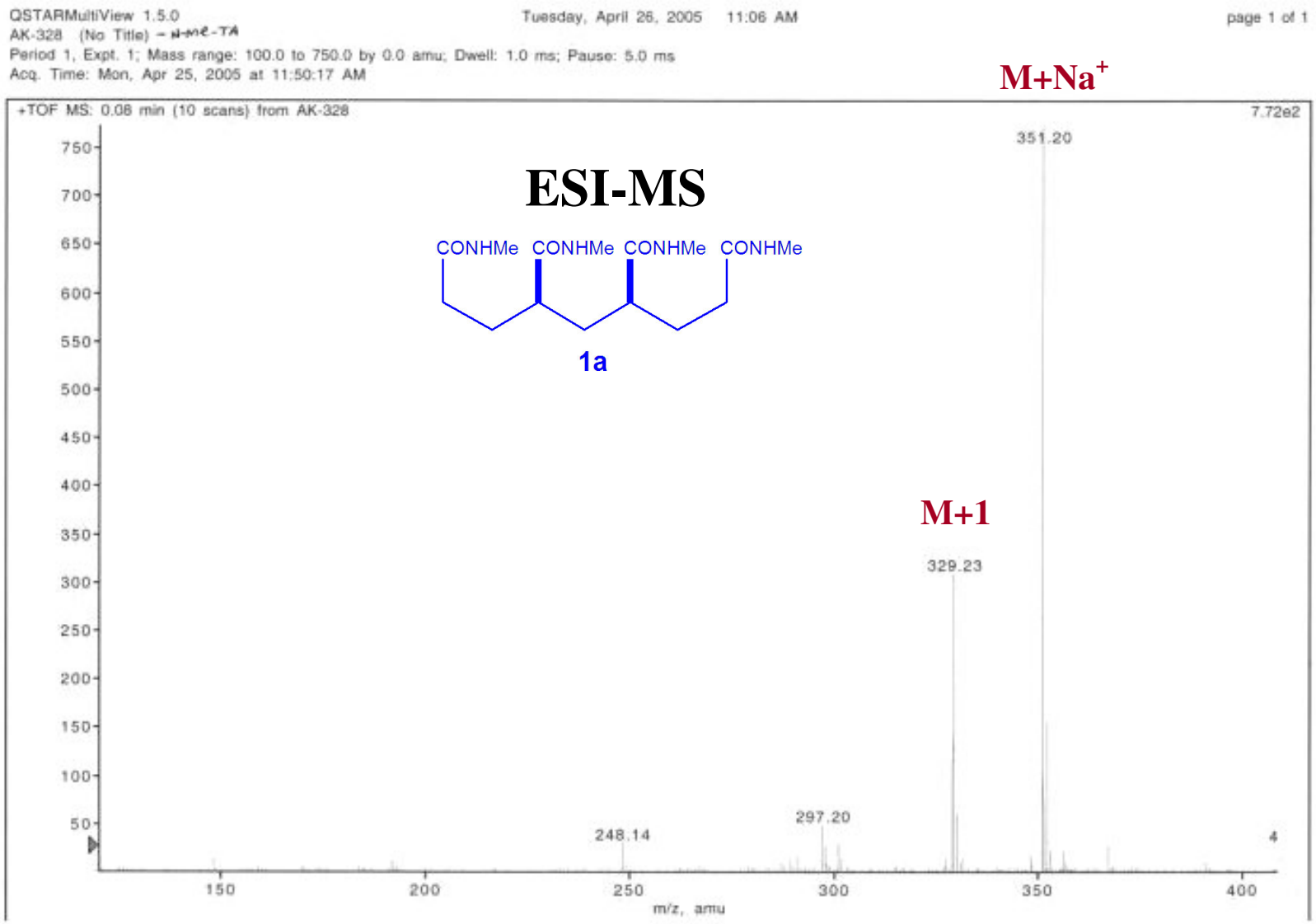
11. W. L. DeLano, *The PyMOL Molecular Graphics System*; http://www.pymol.org. (2004).

Crystal data for 1a ($C_{15}H_{28}N_4O_4$): M = 328.41, Crystal dimensions 0.80 x 0.22 x 0.14 mm^3, triclinic, space group P-1, a = 4.8971(8), b = 7.7453(13), c = 23.813(4) Å, α = 85.109(3), β = 88.701(3), γ = 76.425(3)°; V = 874.8(3) $Å^3$; Z = 2; ρ_{calcd} = 1.247 gcm^{-3}, μ (Mo-K_α) = 0.091 mm^{-1}, $F(000)$ = 356, $2\theta_{max}$ = 50.00°, 7633 reflections collected, 3046 unique, 2636 observed ($I > 2\sigma(I)$) reflections, 212 refined parameters, R value 0.0485, $wR2$ = 0.1302 (all data R = 0.0555, $wR2$ = 0.1355), S = 1.088, minimum and maximum transmission 0.9305 and 0.9871 respectively, maximum and minimum residual electron densities +0.358 and –0.250 e $Å^{-3}$.

Crystal data for 1e ($C_{19}H36N_4O_4$): M = 384.52, Crystal dimensions 0.95 x 0.11 x 0.08 mm^3, orthorhombic, space group P $P2_12_12_1$, a = 9.676(3), b = 12.826(4), c = 17.434(6) Å, V = 2163.6(13) $Å^3$; Z = 4, ρ_{calcd} = 1.180 gcm^{-3}, μ (Mo-Kα) = 0.083 mm^{-1}, *F(000)* = 840, $2\theta_{max}$ = 50.00°, 10757 reflections collected, 3801 unique, 2231 observed ($I > 2\sigma(I)$) reflections, 252 refined parameters, R value 0.0574, $wR2$ = 0.1070 (all data R = 0.1227, $wR2$ = 0.1240), S = 0.961, minimum and maximum transmission 0.9252 and 0.9938 respectively, maximum and minimum residual electron densities +0.184 and –0.178 e $Å^{-3}$.



Side view of the H-bonded self-assembled network, in the crystal structures, of **1a** (top) and **1e** (bottom) showing arrangement of the individual strands. All hydrogens have been deleted for clarity. Color: C green, H gray, N blue, and O red.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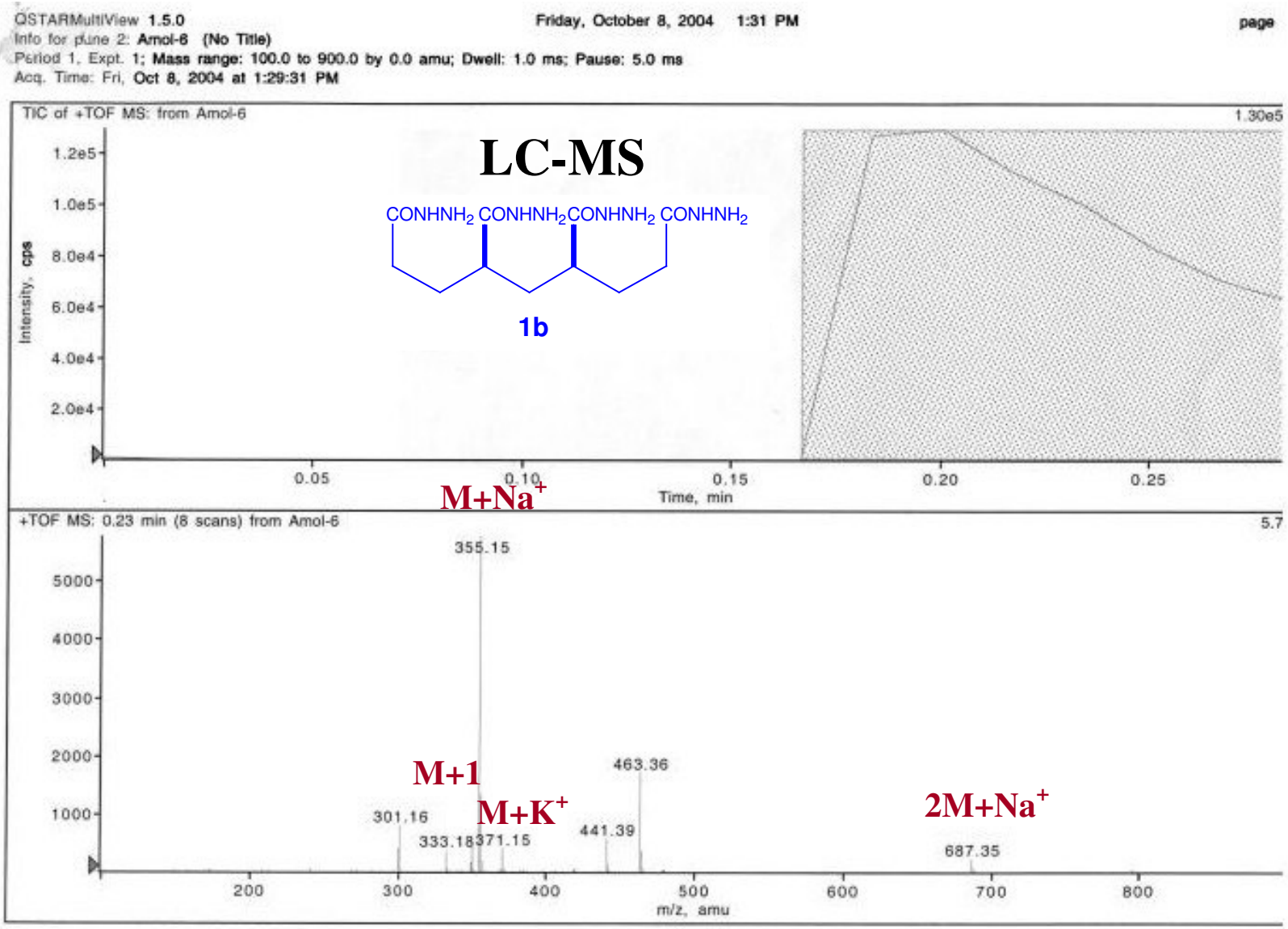
248.14
m/z, amu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1b
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8.0e4
6.0e4
4.0e4
2.0e4
0.05
0.10
0.15
0.20
0.25
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5000
4000
3000
2000
1000
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M+K+
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400
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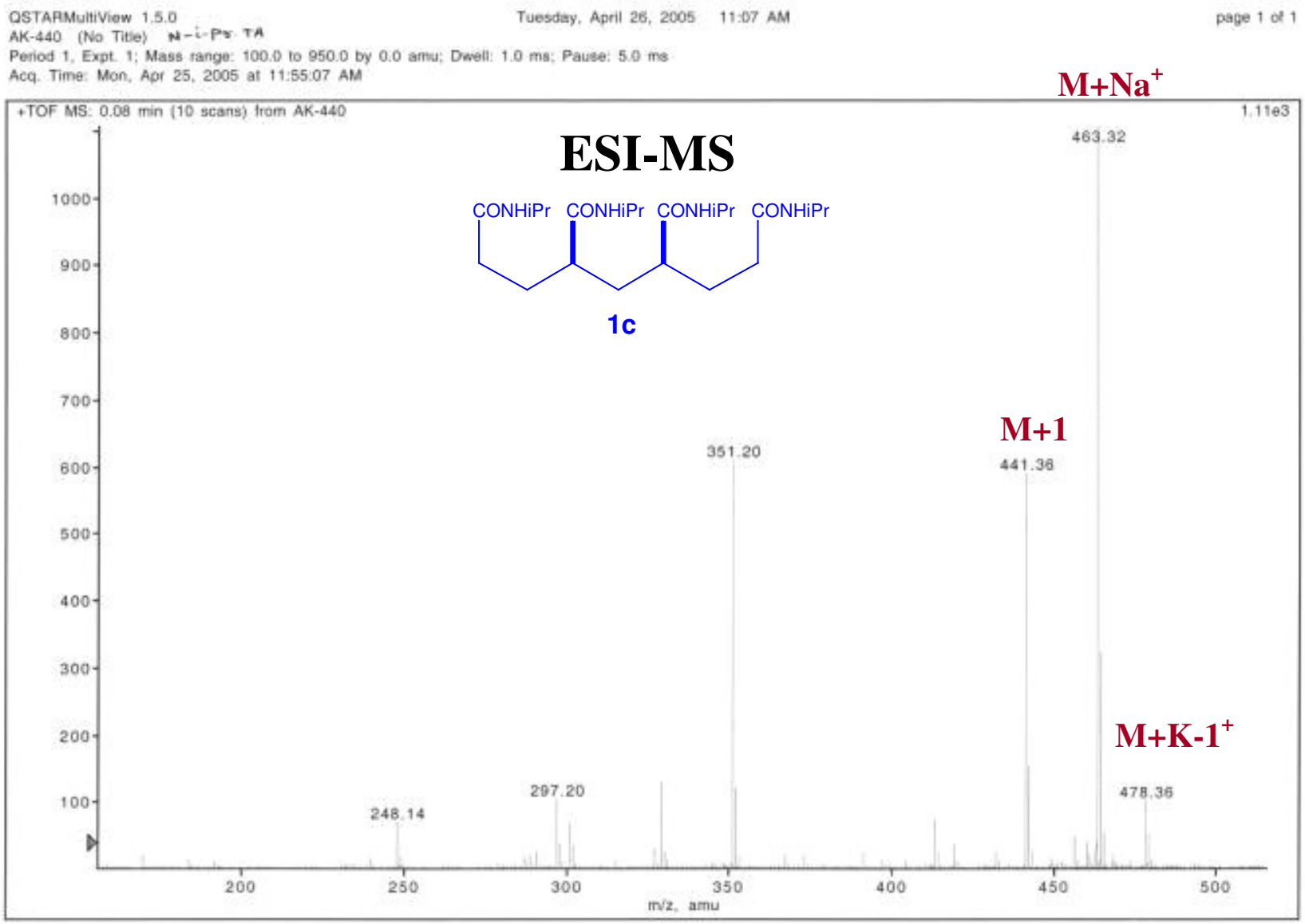
700
800
m/z, amu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page 1 of 1
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1c
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M+1
441.36
351.20
M+K-1+
478.36
297.20
248.14
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800
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600
500
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200
100
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250
300
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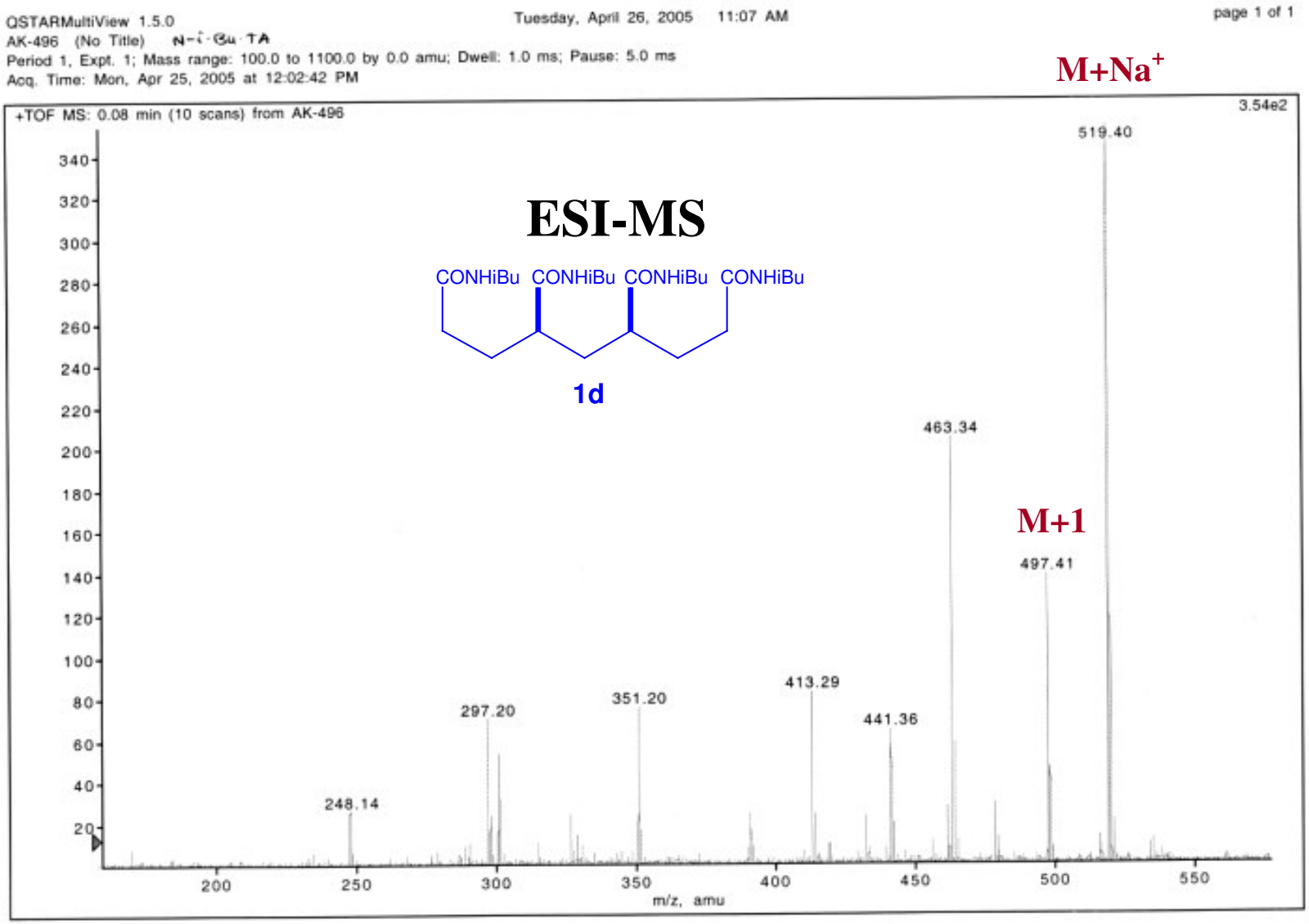
500
m/z, amu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page 1 of 1
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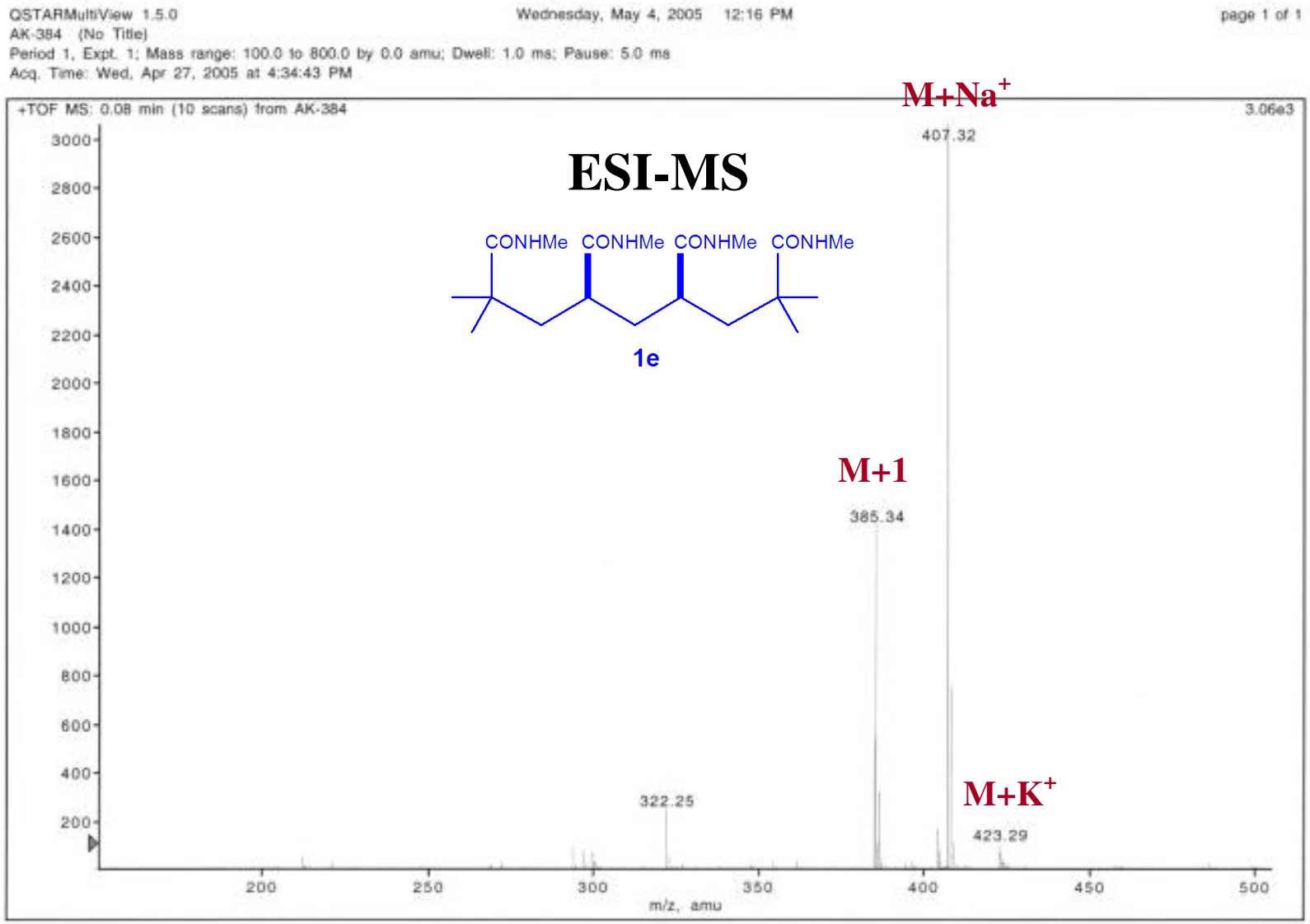
248.14
m/z, amu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M+1
385.34
M+K+
423.29
322.25
m/z, amu

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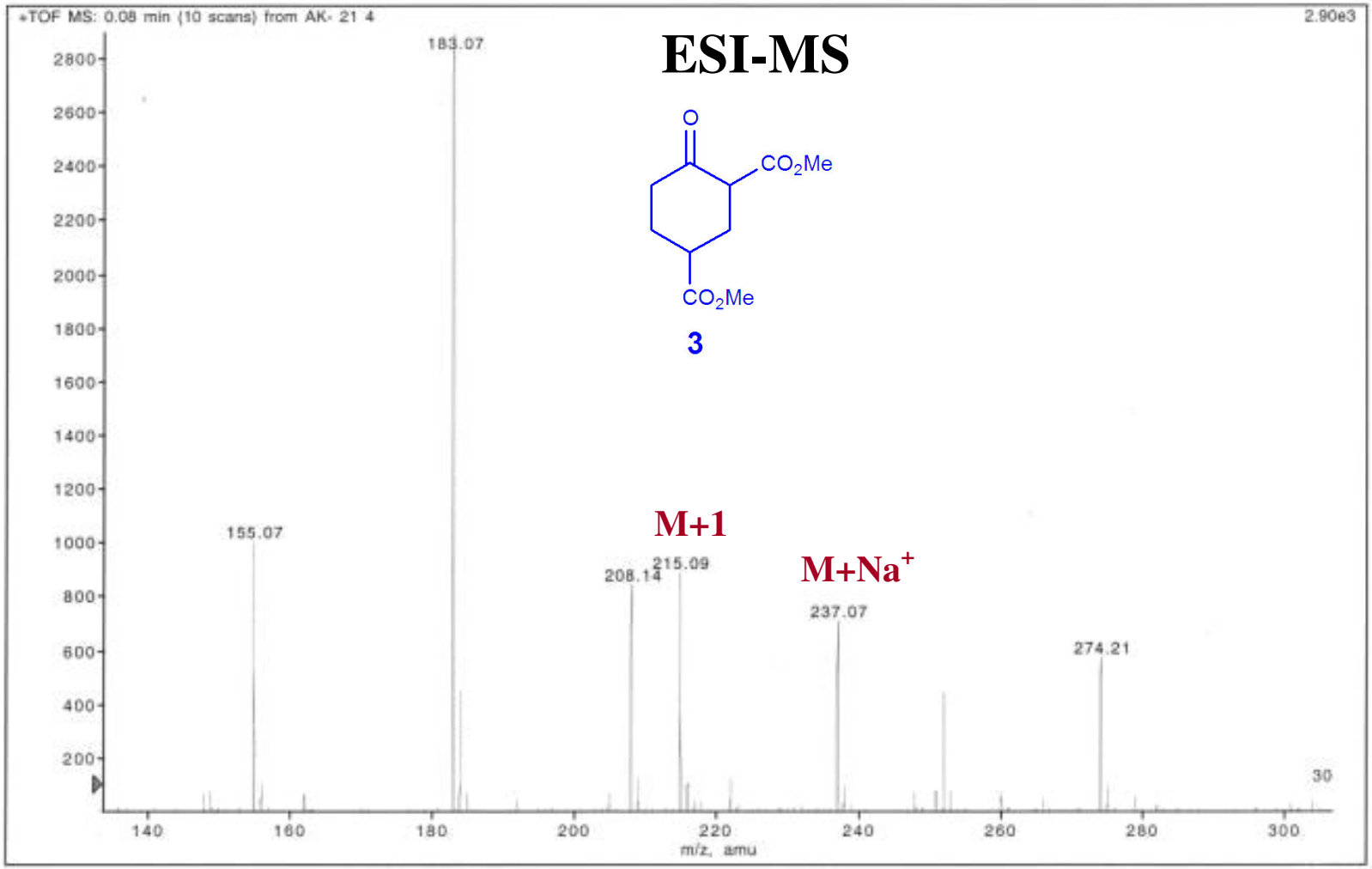

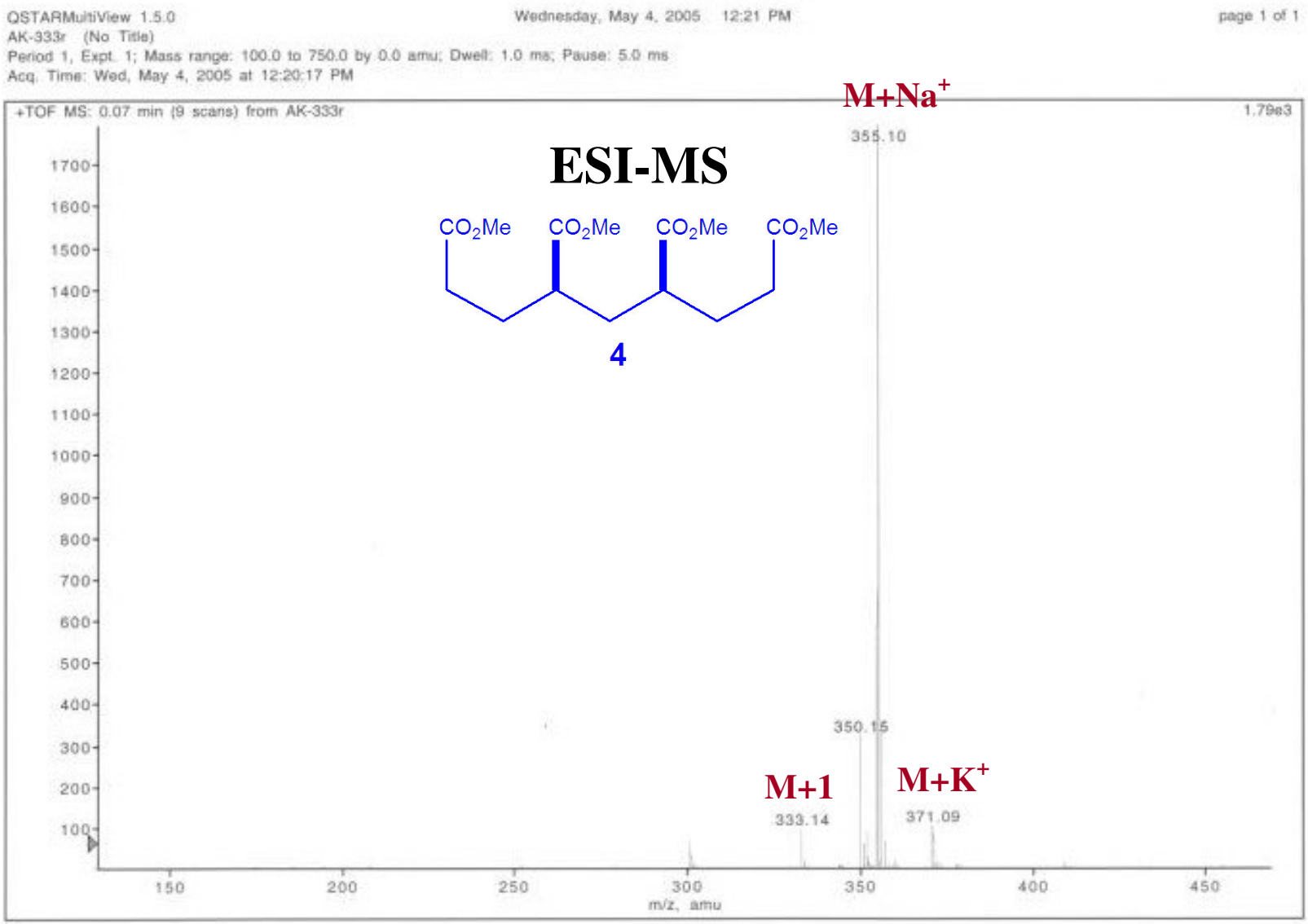
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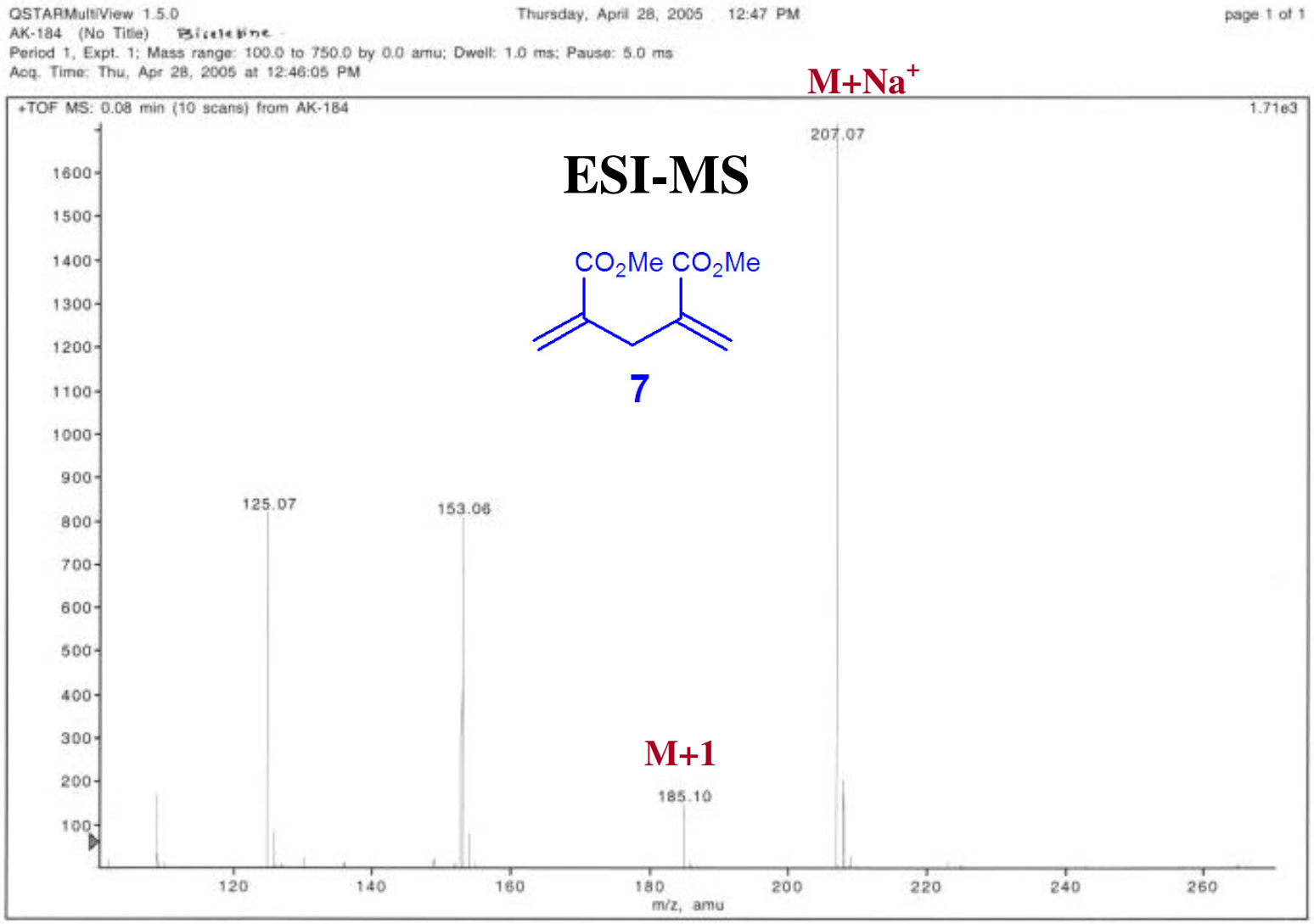
m/z, amu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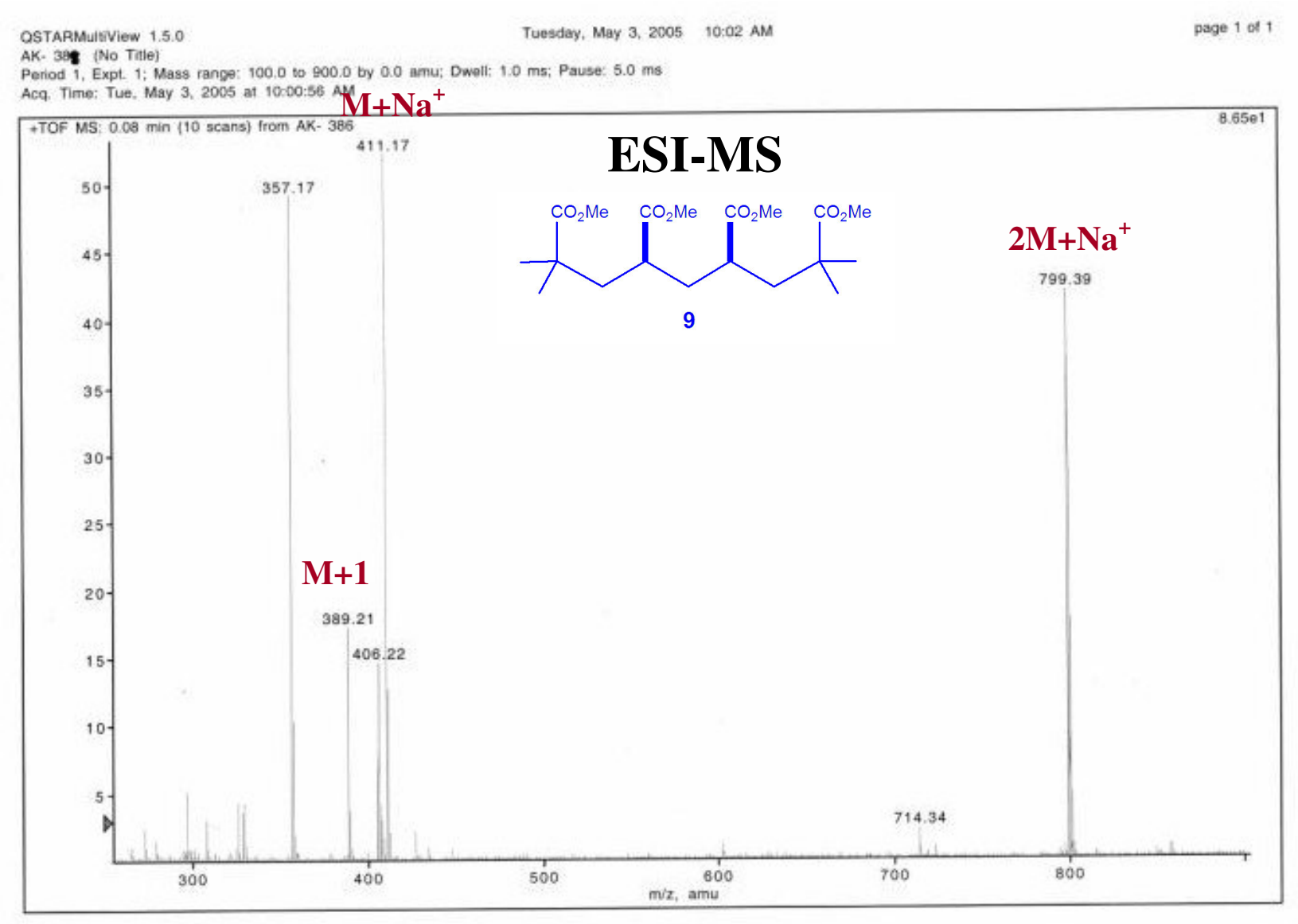
185.10
m/z, amu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M+1
389.21
406.22
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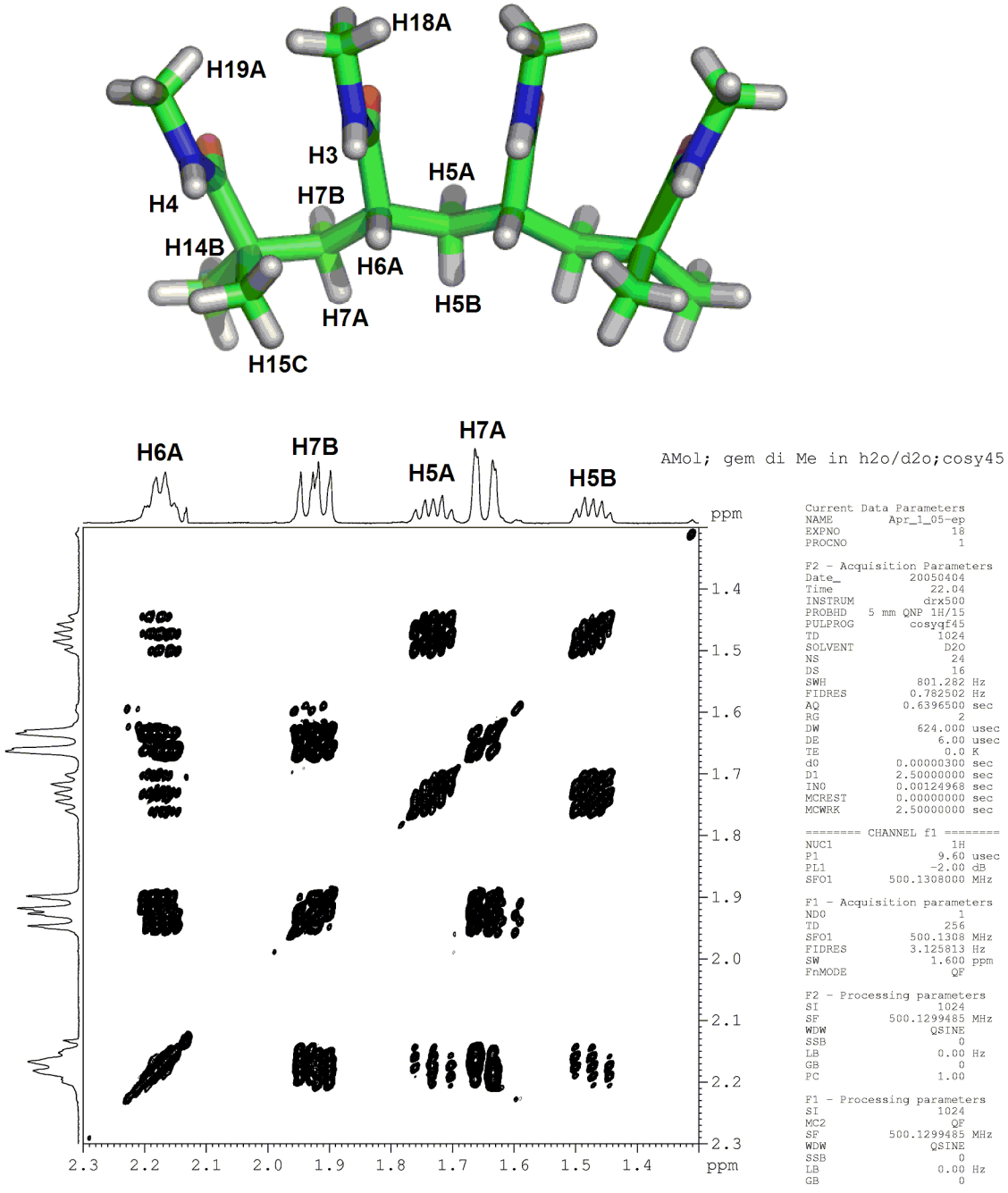
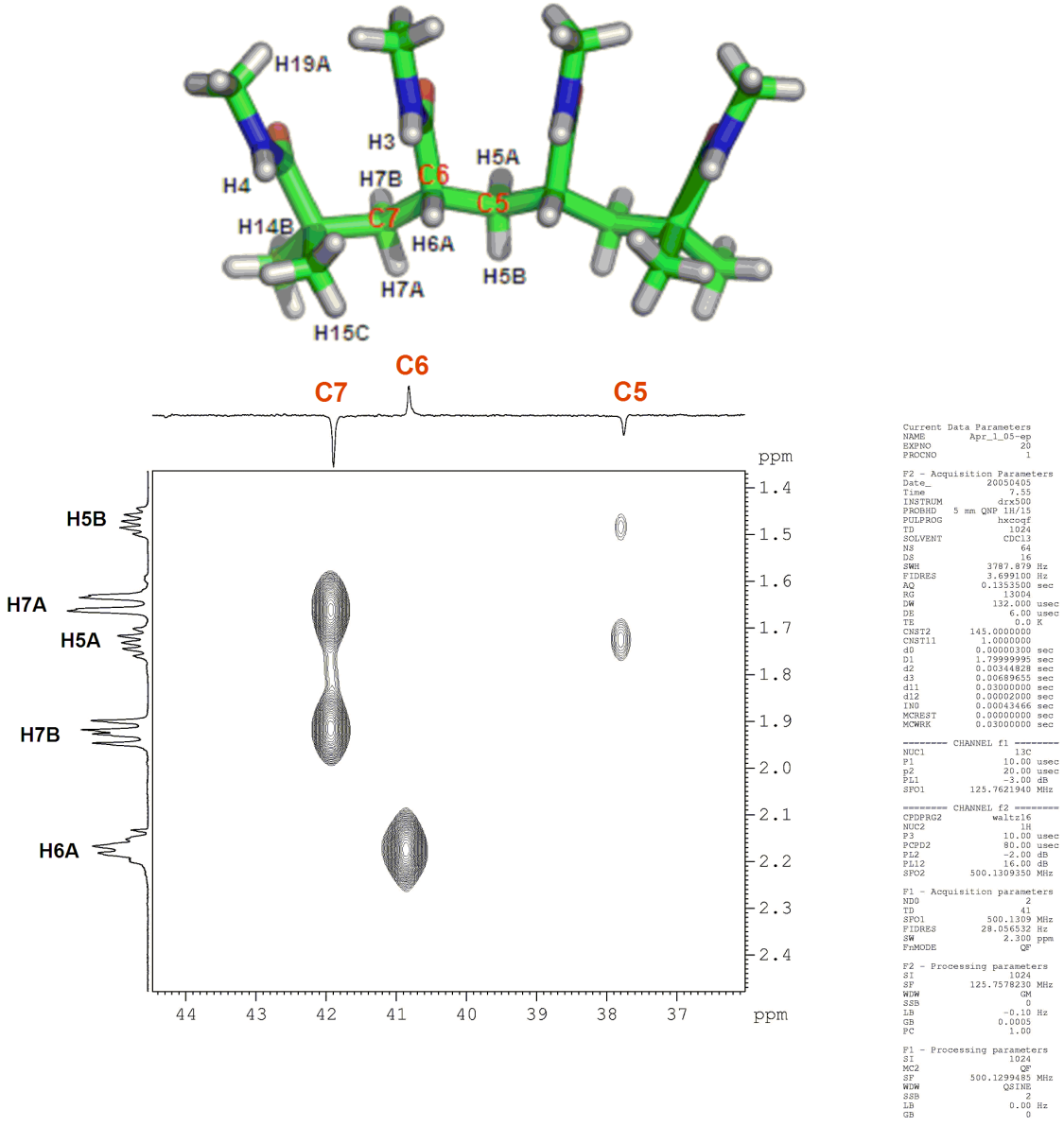
m/z, amu



Partial 2D COSY-45 spectrum of **1e** [500 MHz, H_2O:D_2O (90:10)]. Single Crystal X-ray structure of **1e** with selected labeled atoms is at the top (color: C green, H gray, N blue, O red).

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TD                 1024
SOLVENT            CDCl3
NS                   64
DS                   16
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RG                 13004
DW              132.000 usec
DE                6.00 usec
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MCWRK       0.03000000 sec

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NUC1               13C
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p2               20.00 usec
PL1              -3.00 dB
SFO1        125.7621940 MHz

======== CHANNEL f2 ========
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NUC2                1H
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PCPD2            80.00 usec
PL2              -2.00 dB
PL12             16.00 dB
SFO2        500.1309350 MHz

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TD                  41
SFO1          500.1309 MHz
FIDRES       28.056532 Hz
SW             2.300 ppm
FnMODE              QF

F2 - Processing parameters
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SF          125.7578230 MHz
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SSB                  0
LB               -0.10 Hz
GB                0.0005
PC                1.00

F1 - Processing parameters
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SSB                  2
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GB                   0
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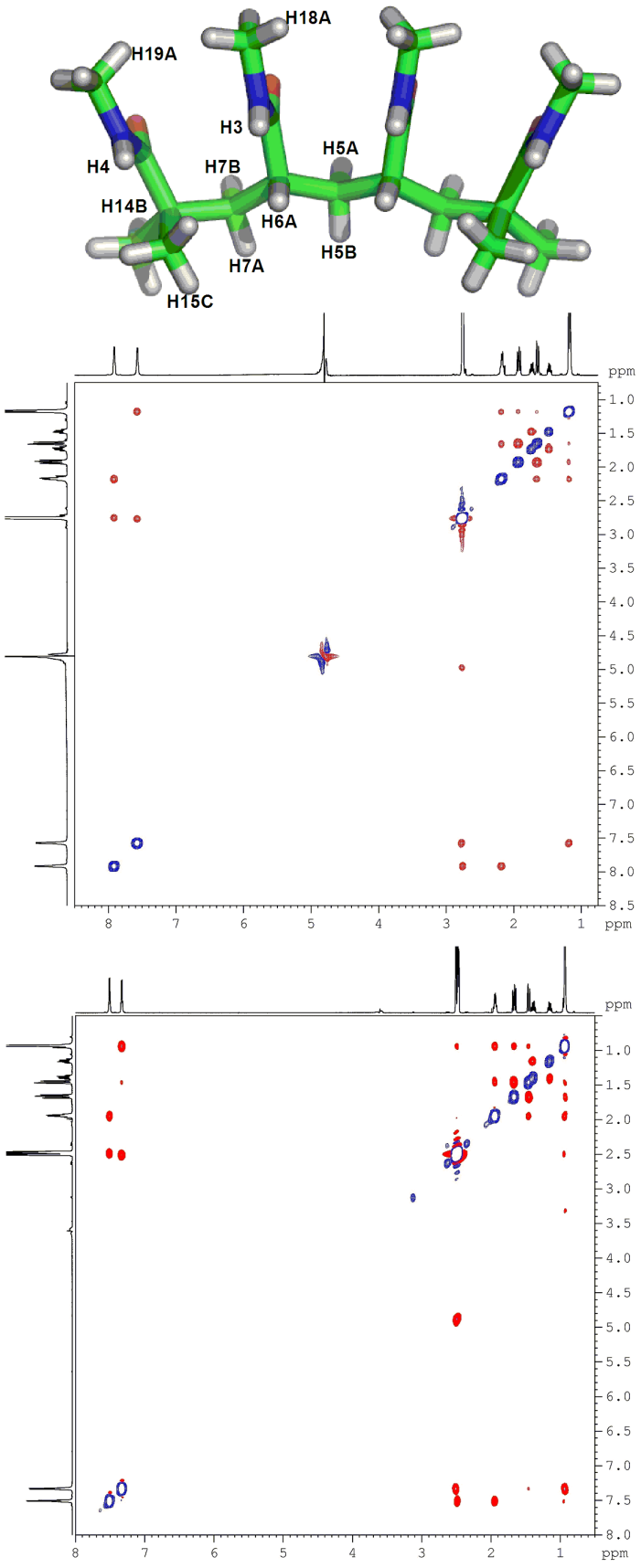
Partial 2D HETCOR spectrum of **1e** [500 MHz (^{1}H), 125 MHz (^{13}C), H_2O:D_2O (90:10)]. Single Crystal X-ray structure of **1e** with selected labeled atoms is at the top (color: C green, H gray, N blue, O red).

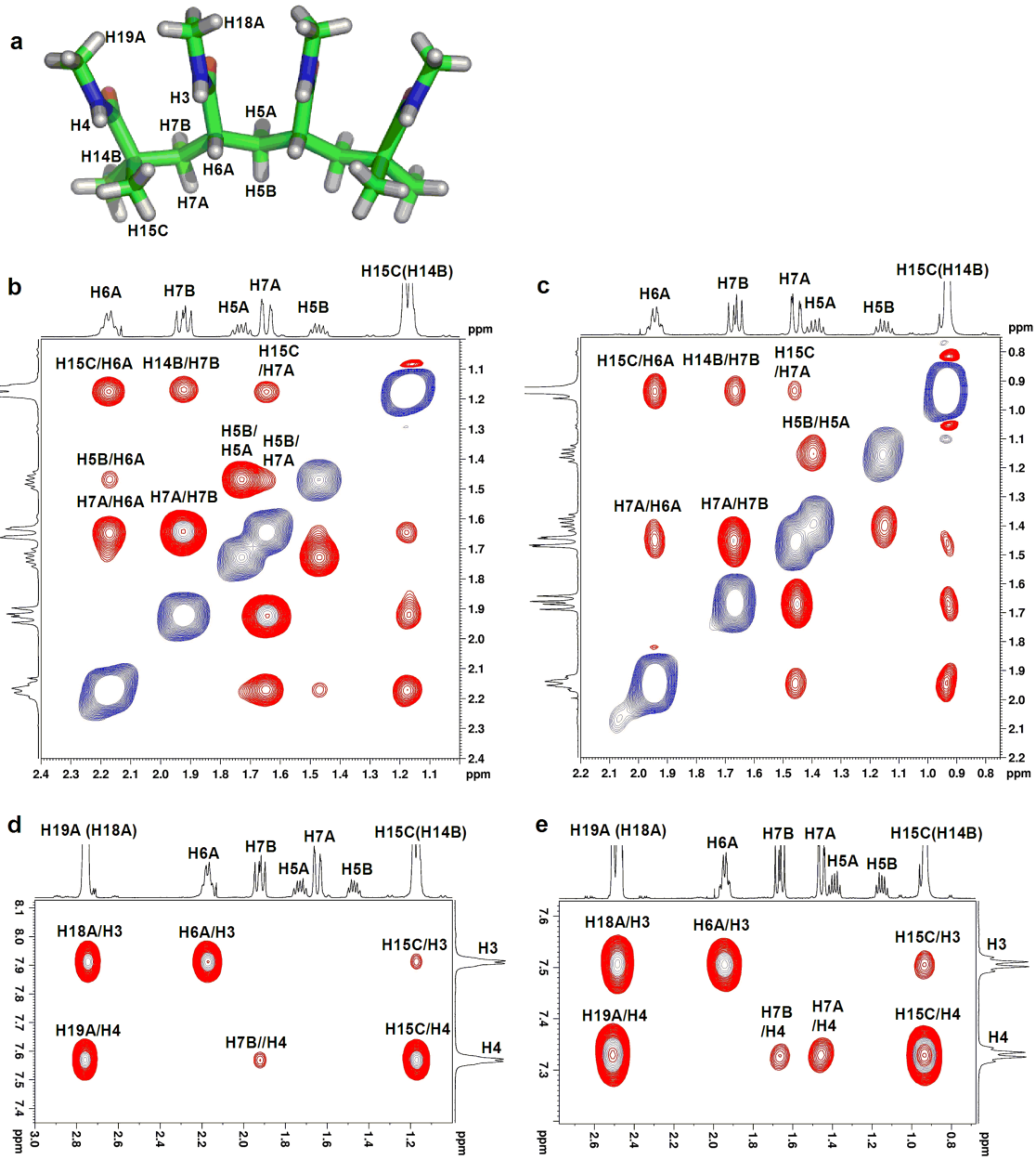


2D NOESY spectrum of **1e** [500 MHz, H_2O:D_2O (90:10)]. For detailed signal assignments, see on page 27.

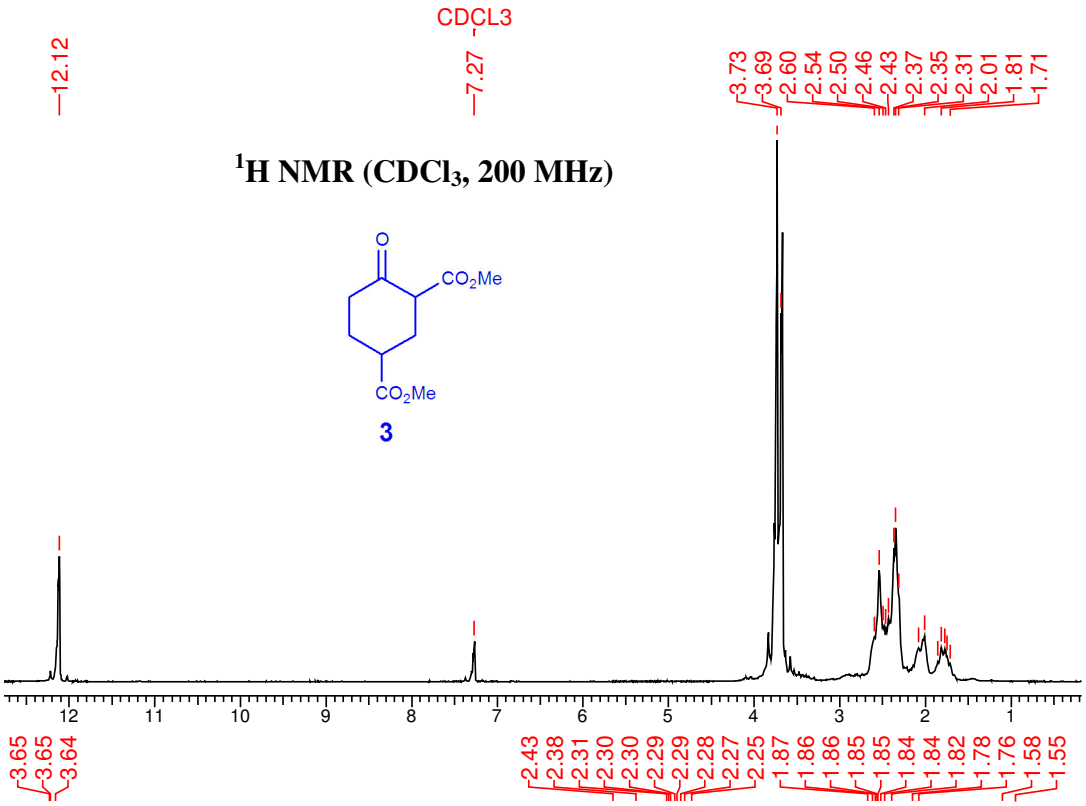
Note: Residual water signal was suppressed, by pre-saturation technique.

2D NOESY spectrum of **1e** [500 MHz, DMSO-d_6). For detailed signal assignments, see on page 27.

Note: Residual water signal was suppressed, by pre-saturation technique.

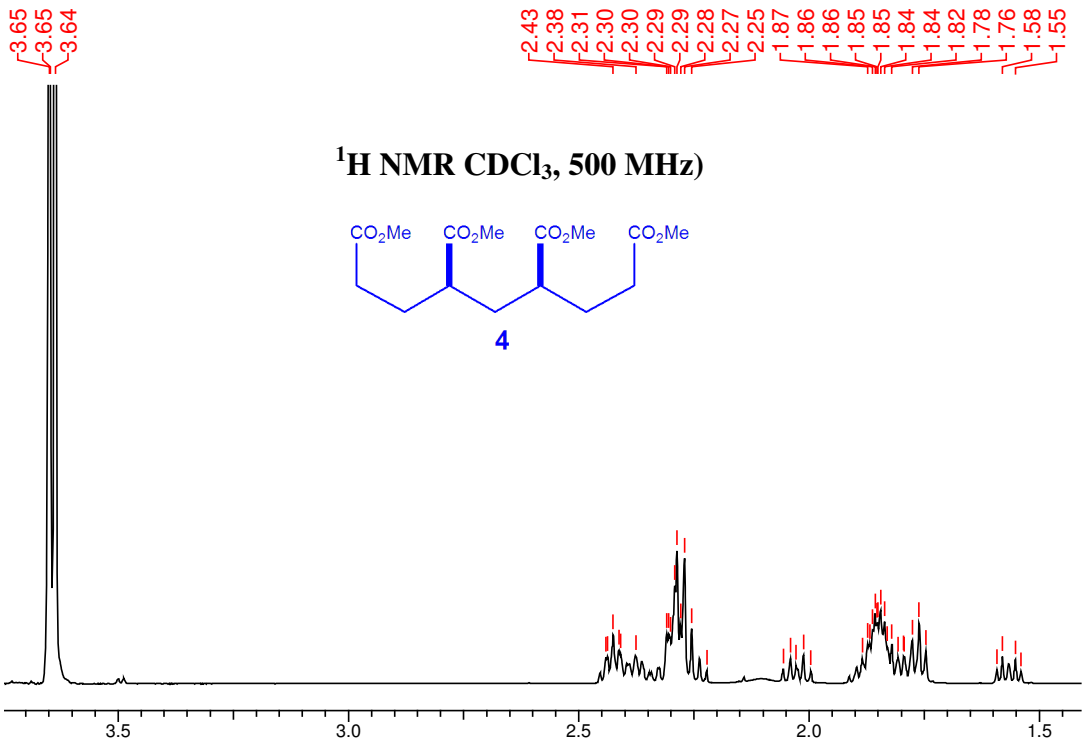


Expanded 2D NOESY spectra (500 MHz) of **1e** in H_2O:D_2O (90:10) and DMSO-d_6. For the ease of spectral interpretation and comparison, the single crystal X-ray structure of **1e** with selected labeled atoms is also shown (color: C green, H gray, N blue, O red). **a**, PyMol-rendered[11] single crystal X-ray structure. **b**, Expanded 2D NOESY spectrum (1.0 – 2.4 ppm) of **1e** in H_2O:D_2O (90:10). **c**, Expanded 2D NOESY spectrum (0.75 – 2.2 ppm) of **1e** in DMSO-d_6. **d**, Expanded 2D NOESY spectrum (NH / backbone protons) of **1e** in H_2O:D_2O (90:10). **e**, Expanded 2D NOESY spectrum (NH / backbone protons) of **1e** in DMSO-d_6.



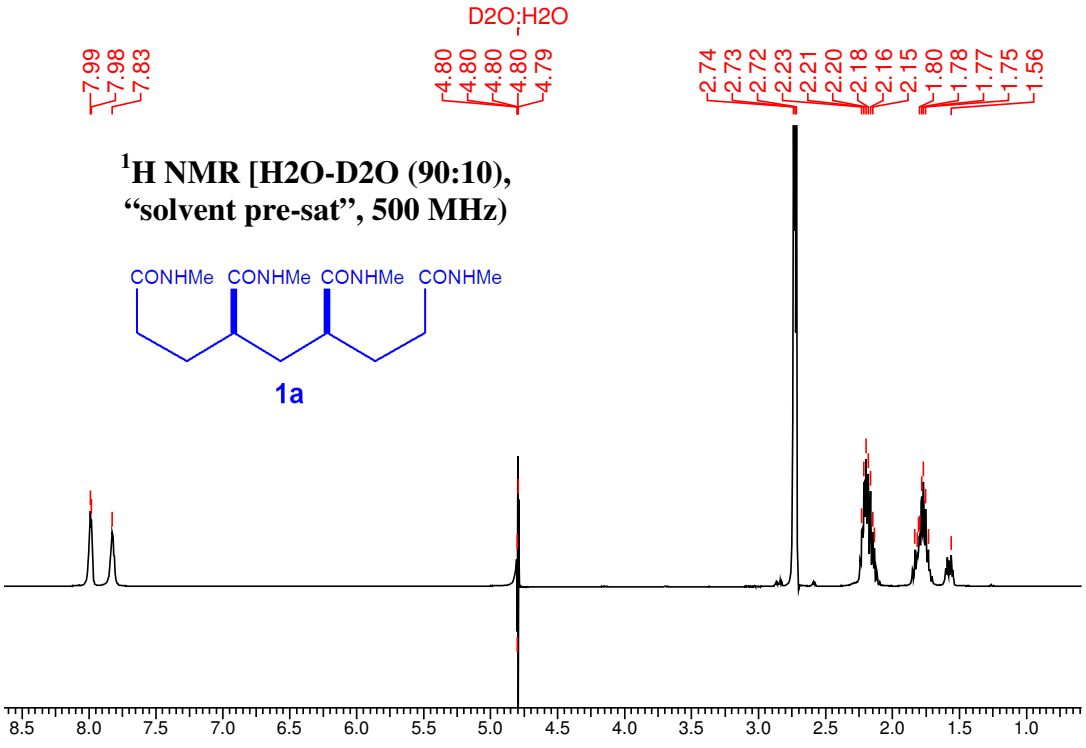
^{1}H NMR ($CDCl_3$, 200 MHz)

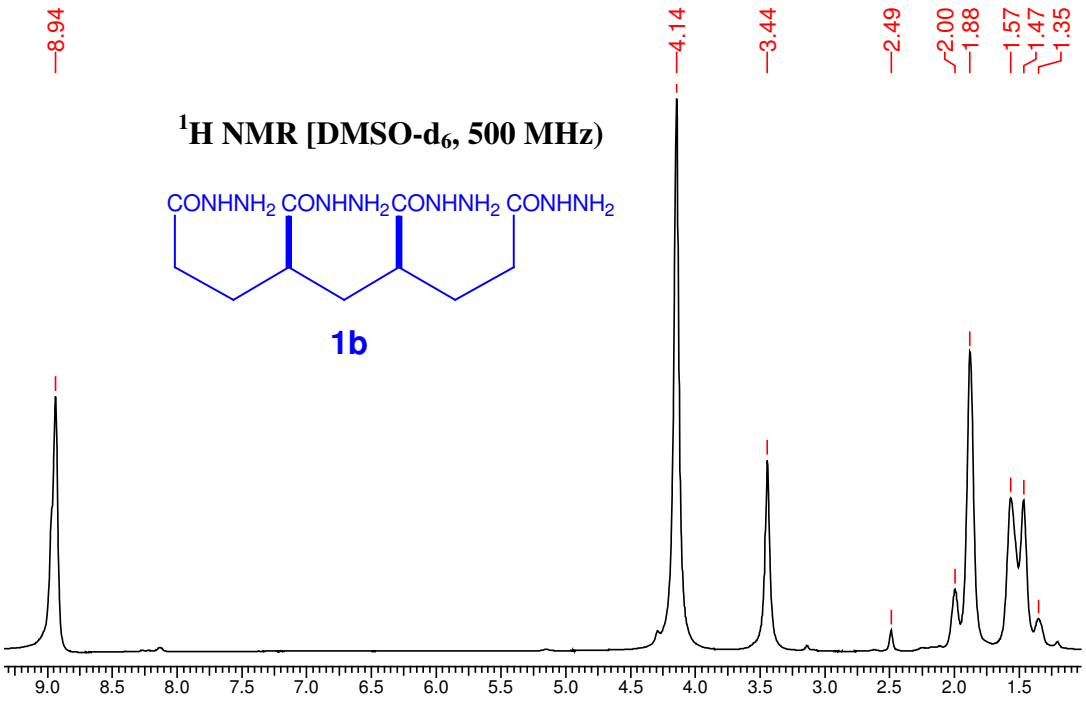
3

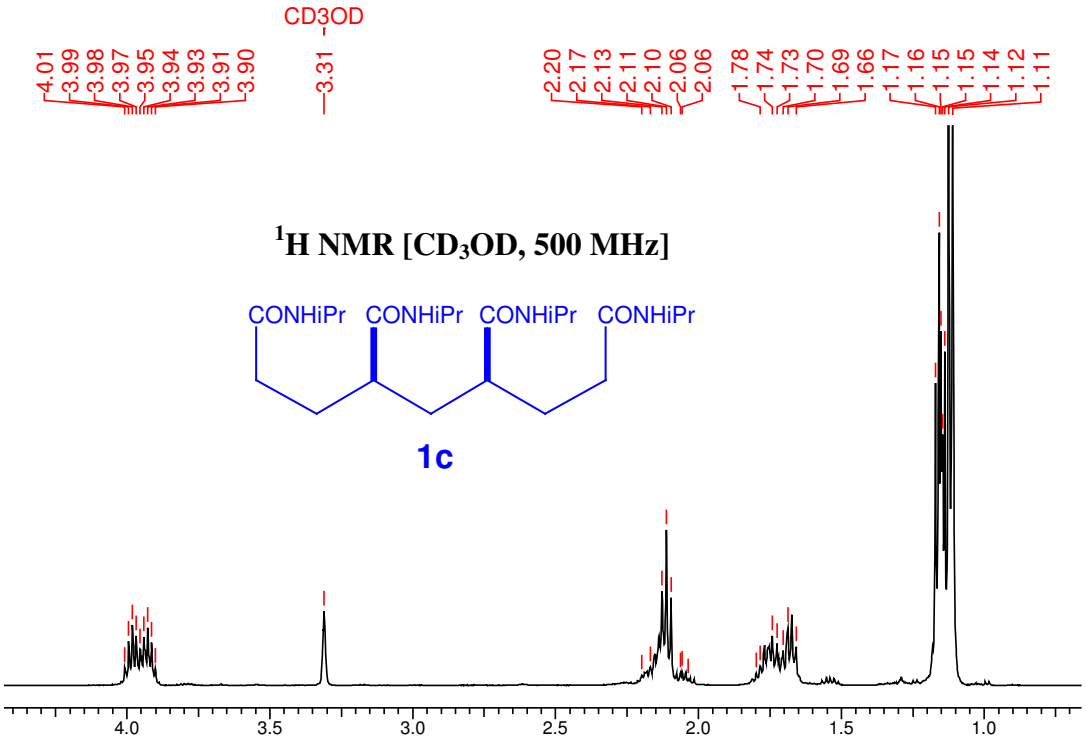


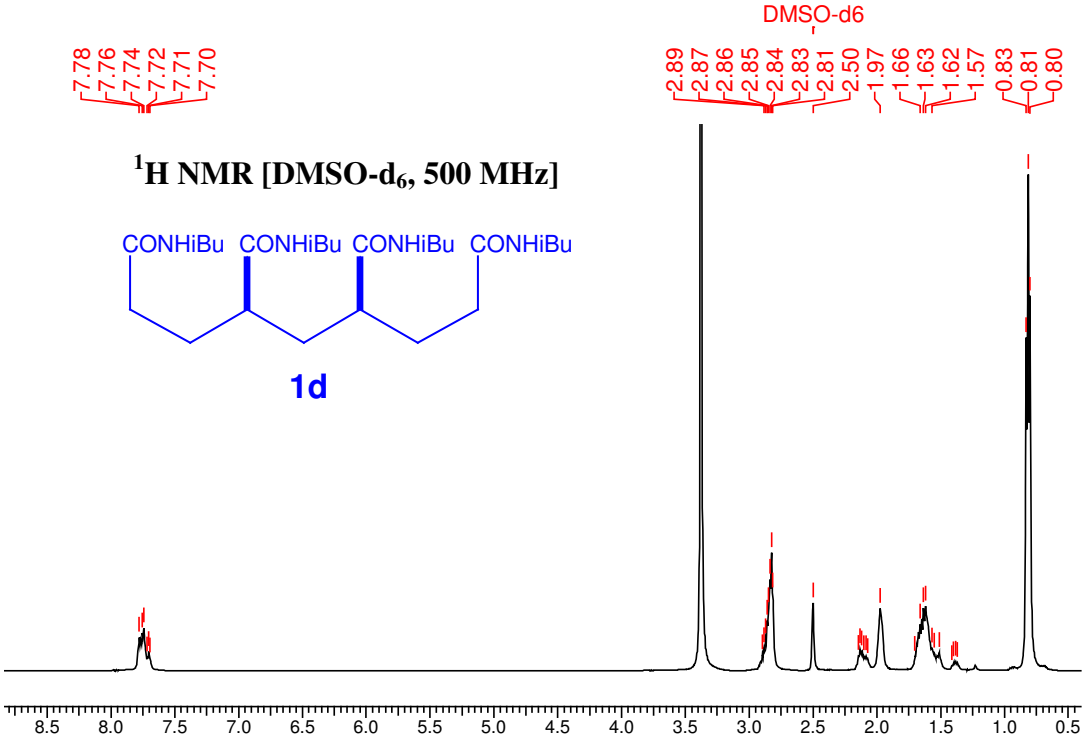
^{1}H NMR $CDCl_3$, 500 MHz)

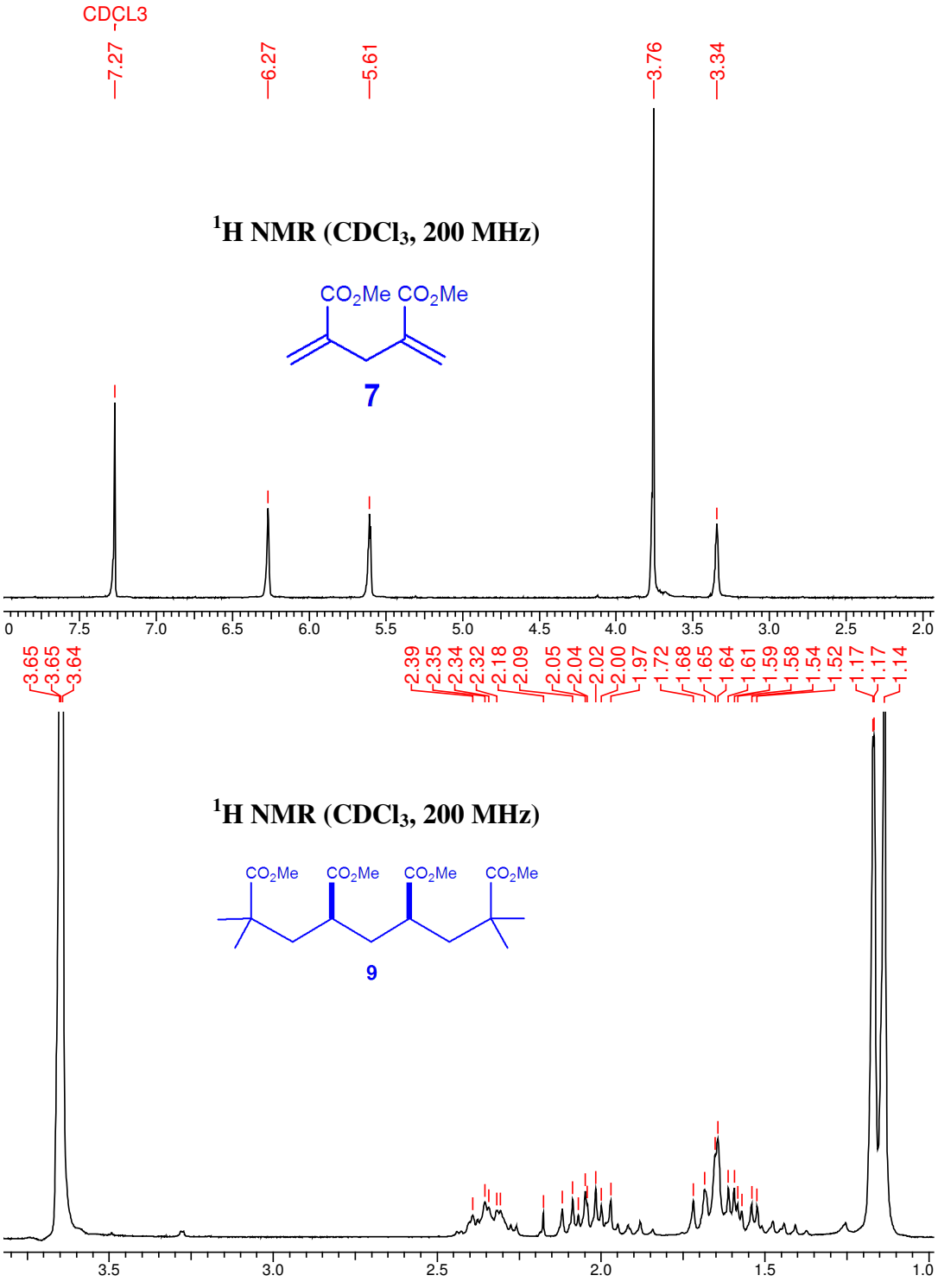
4

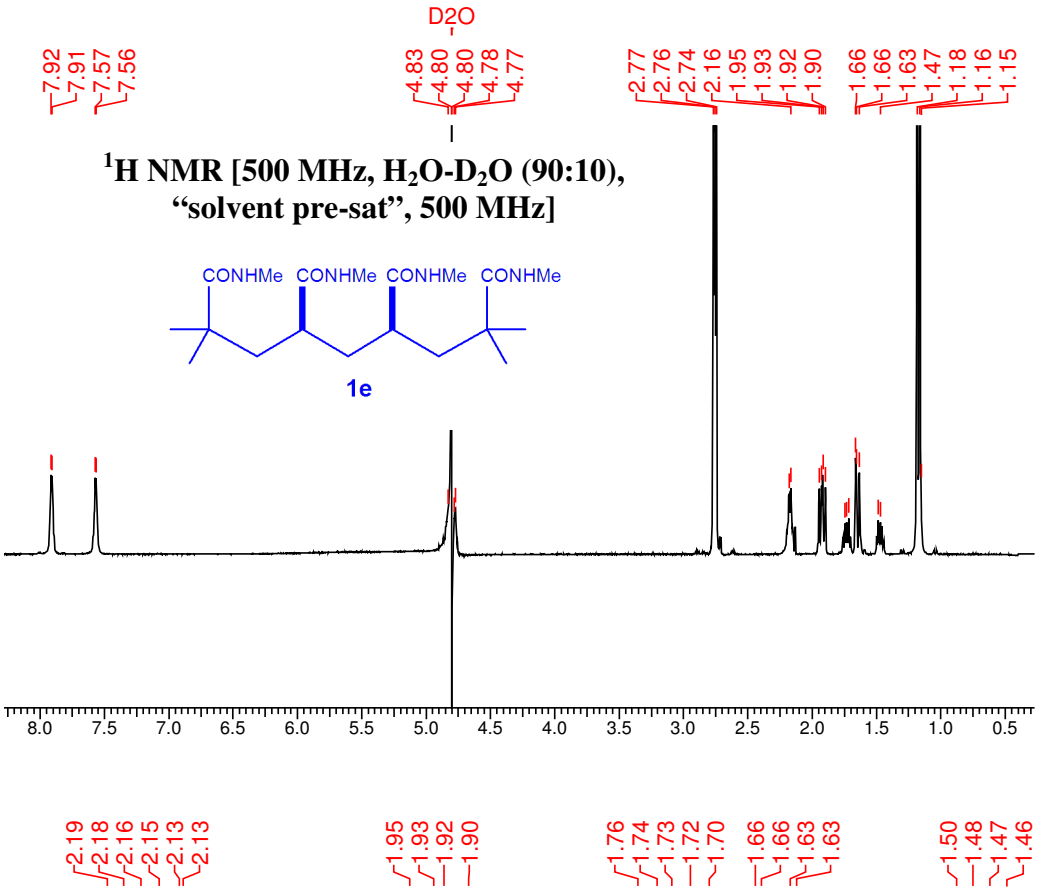

D2O;H2O
7.99
7.98
7.83
4.80
4.80
4.80
4.80
4.79
2.74
2.73
2.72
2.23
2.21
2.20
2.18
2.16
2.15
1.80
1.78
1.77
1.75
1.56
1H NMR [H2O-D2O (90:10), "solvent pre-sat", 500 MHz)
CONHMe CONHMe CONHMe CONHMe
1a
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0


DMSO-d6
8.94
4.14
3.44
2.49
2.00
1.88
1.57
1.47
1.35
1H NMR [DMSO-d6, 500 MHz)
CONHNH2 CONHNH2 CONHNH2 CONHNH2
1b
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5


CD3OD
4.01
3.99
3.98
3.97
3.95
3.94
3.93
3.91
3.90
3.31
2.20
2.17
2.13
2.11
2.10
2.06
2.06
1.78
1.74
1.73
1.70
1.69
1.66
1.17
1.16
1.15
1.15
1.14
1.12
1.11
1H NMR [CD3OD, 500 MHz]
CONHiPr
CONHiPr
CONHiPr
CONHiPr
1c
4.0
3.5
3.0
2.5
2.0
1.5
1.0


DMSO-d6
7.78
7.76
7.74
7.72
7.71
7.70
2.89
2.87
2.86
2.85
2.84
2.83
2.81
2.50
1.97
1.66
1.63
1.62
1.57
0.83
0.81
0.80
1H NMR [DMSO-d6, 500 MHz]
CONHiBu
CONHiBu
CONHiBu
CONHiBu
1d
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

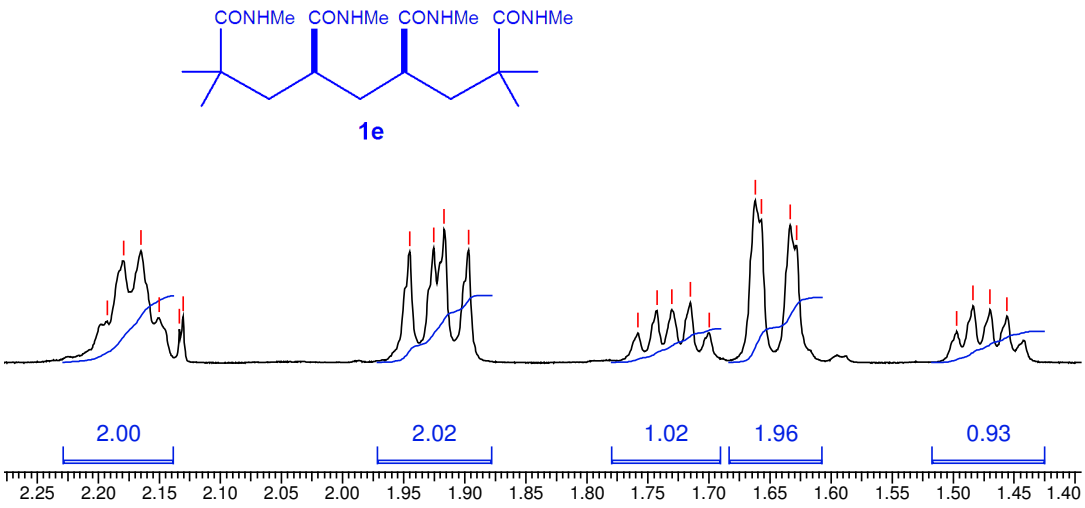

CDCL3
7.27
6.27
5.61
3.76
3.34
^{1}H NMR ($CDCl_3$, 200 MHz)
CO_2Me CO_2Me
7
3.65
3.65
3.64
2.39
2.35
2.34
2.32
2.18
2.09
2.05
2.04
2.02
2.00
1.97
1.72
1.68
1.65
1.64
1.61
1.59
1.58
1.54
1.52
1.17
1.17
1.14
^{1}H NMR ($CDCl_3$, 200 MHz)
CO_2Me CO_2Me CO_2Me CO_2Me
9

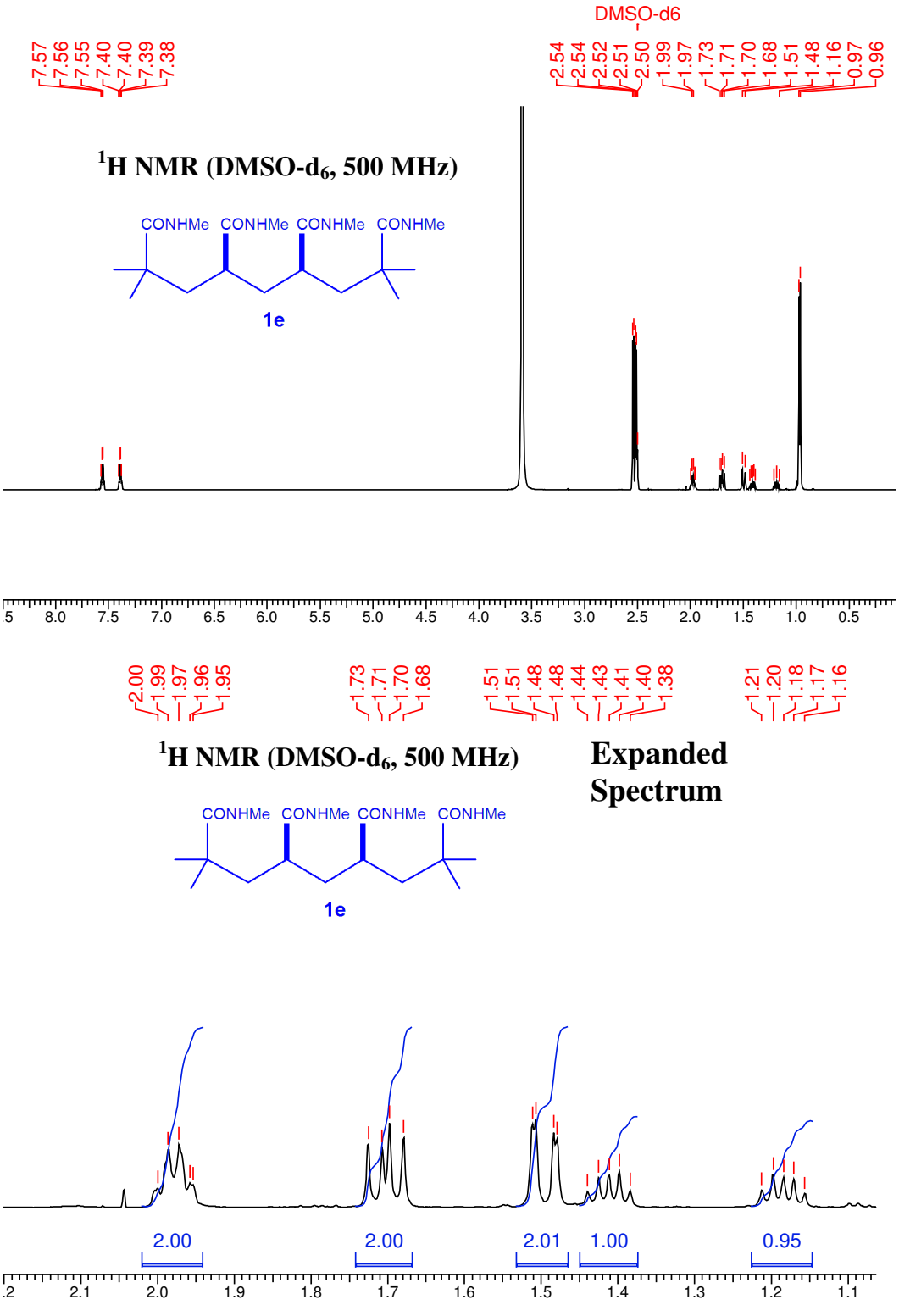


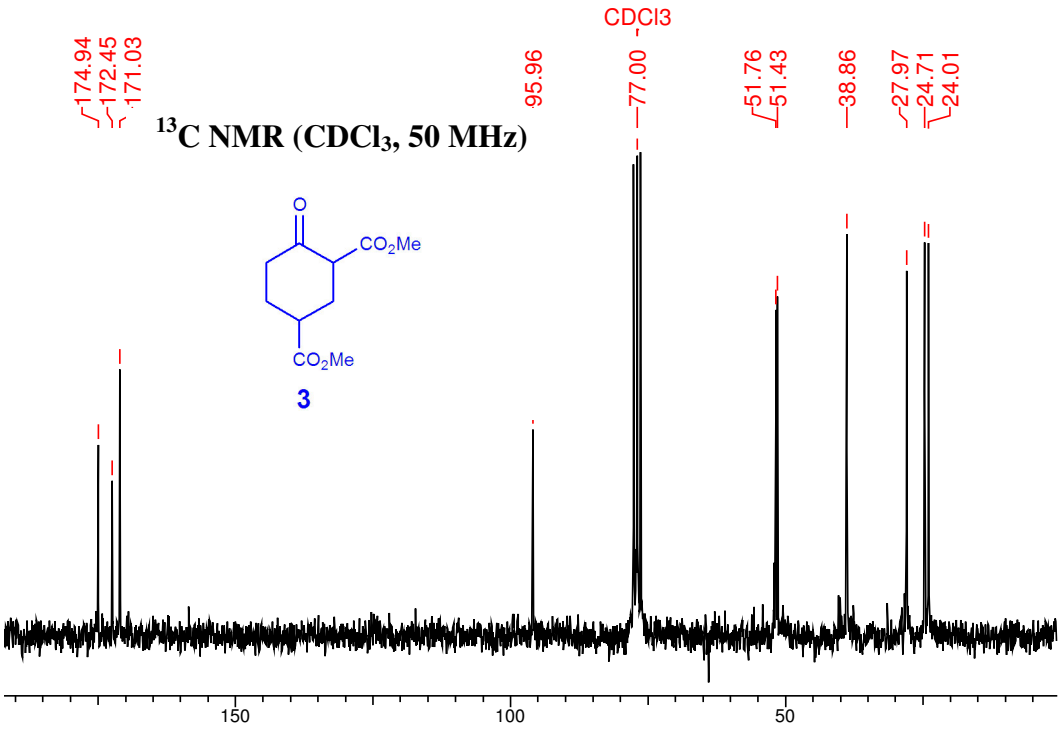
^{1}H NMR [500 MHz, H_2O-D_2O (90:10), "solvent pre-sat", 500 MHz]

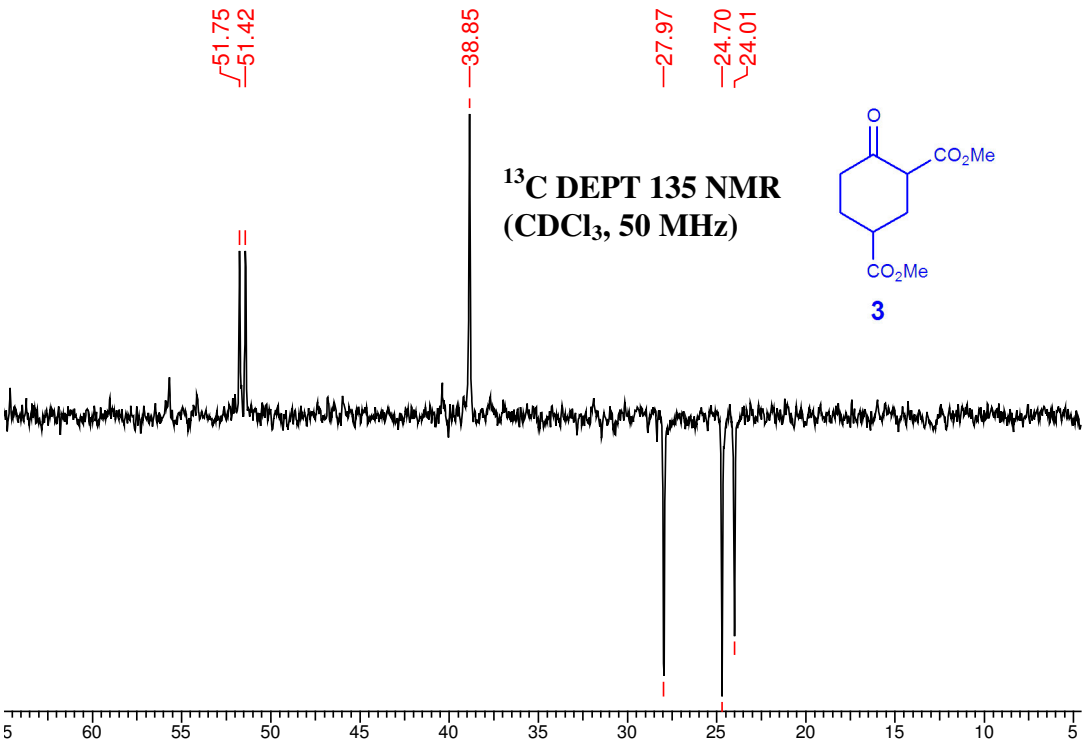
^{1}H NMR [500 MHz, H_2O-D_2O (90:10)]

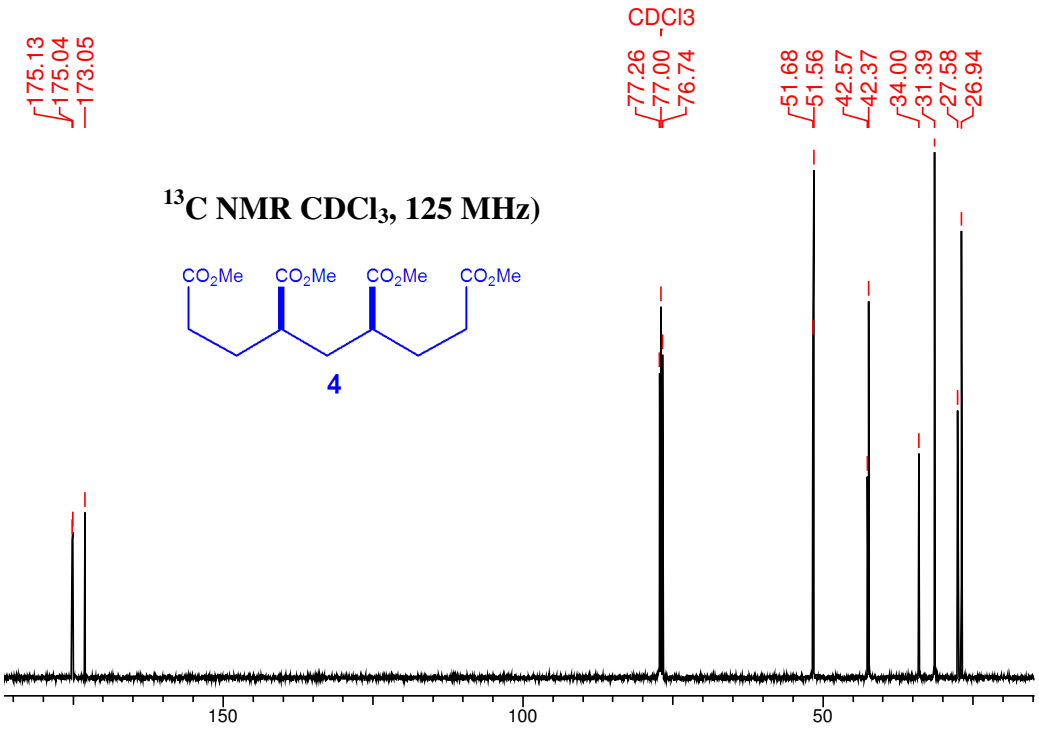
Expanded Spectrum




DMSO-d6
7.57
7.56
7.55
7.40
7.40
7.39
7.38
2.54
2.54
2.52
2.51
2.50
1.99
1.97
1.73
1.71
1.70
1.68
1.51
1.48
1.16
0.97
0.96
1H NMR (DMSO-d6, 500 MHz)
CONHMe CONHMe CONHMe CONHMe
1e
2.00
1.99
1.97
1.96
1.95
1.73
1.71
1.70
1.68
1.51
1.51
1.48
1.48
1.44
1.43
1.41
1.40
1.38
1.21
1.20
1.18
1.17
1.16
1H NMR (DMSO-d6, 500 MHz)
Expanded Spectrum
CONHMe CONHMe CONHMe CONHMe
1e
2.00
2.00
2.01
1.00
0.95

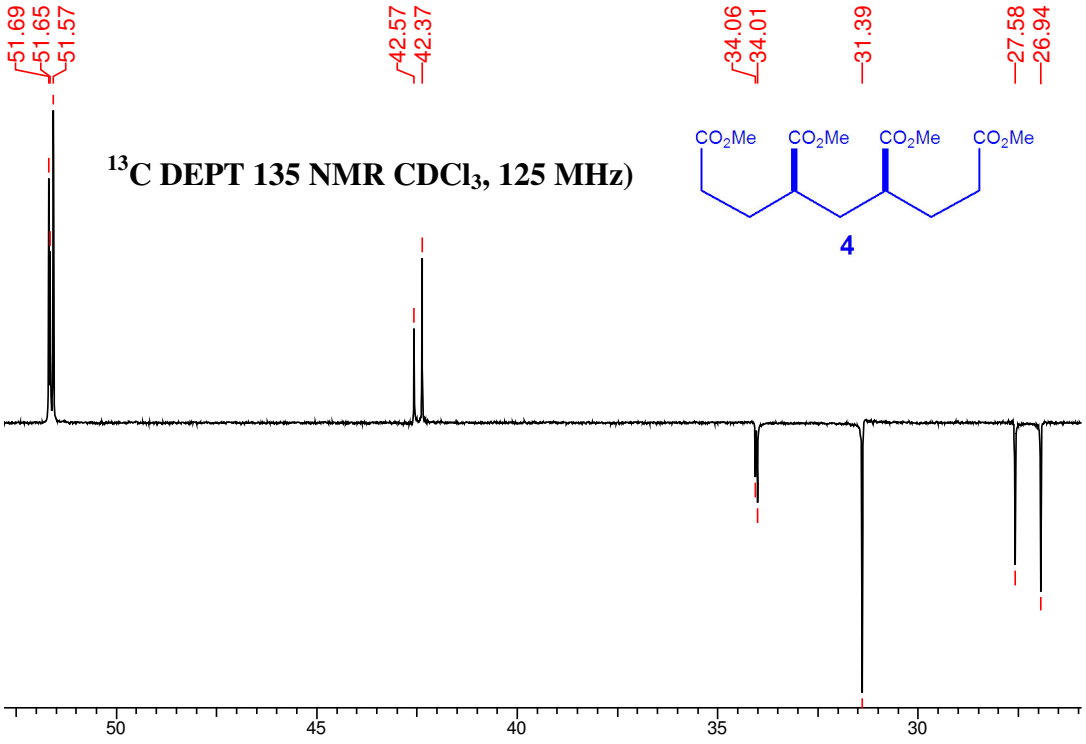

CDCl3
174.94
172.45
171.03
95.96
77.00
51.76
51.43
38.86
27.97
24.71
24.01
^{13}C NMR (CDCl$_3$, 50 MHz)
CO$_2$Me
CO$_2$Me
3
150
100
50


51.75
51.42
38.85
27.97
24.70
24.01
^{13}C DEPT 135 NMR
(CDCl$_3$, 50 MHz)
CO$_2$Me
CO$_2$Me
3
5
60
55
50
45
40
35
30
25
20
15
10
5



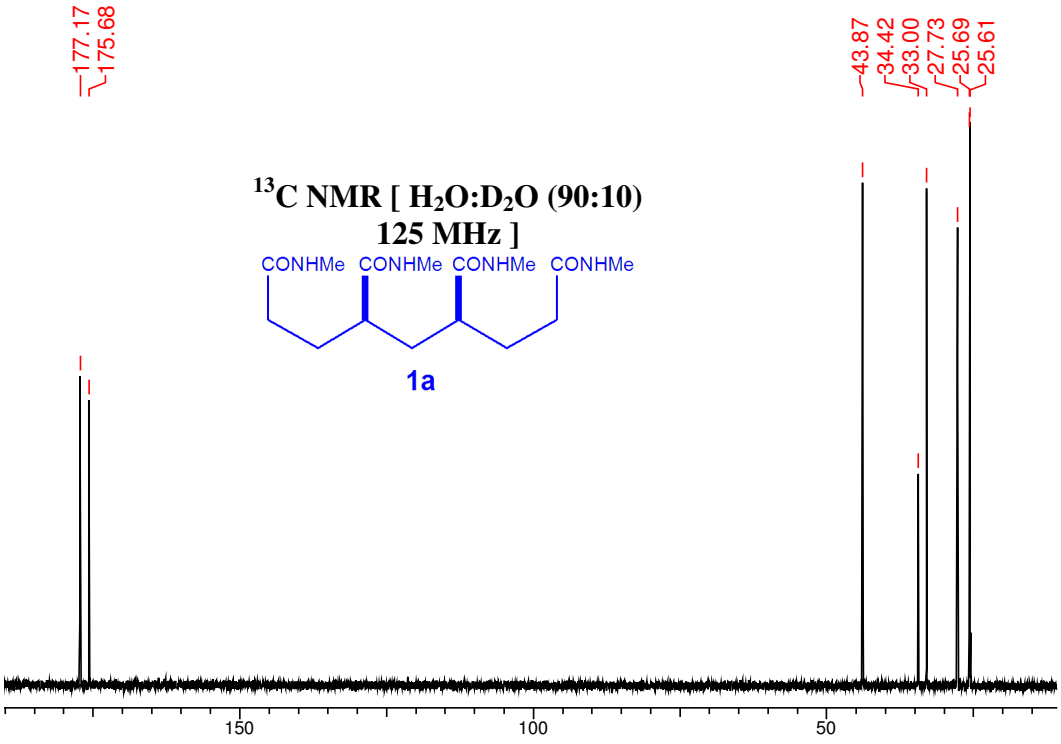
^{13}C NMR $CDCl_3$, 125 MHz)

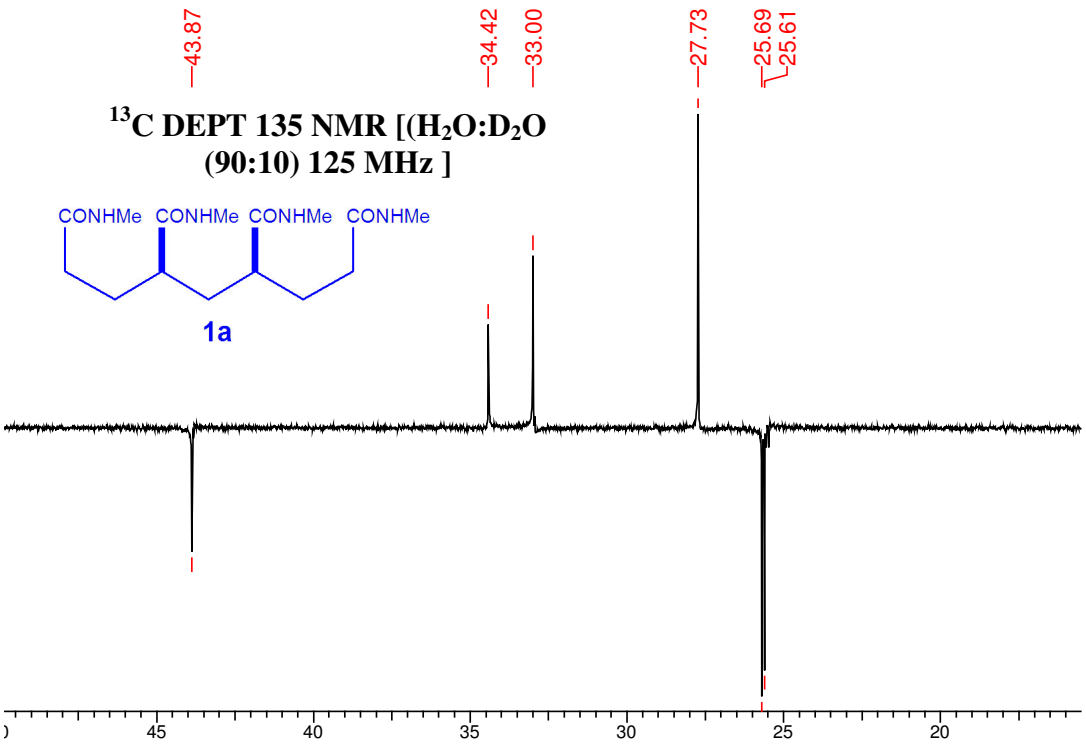
4

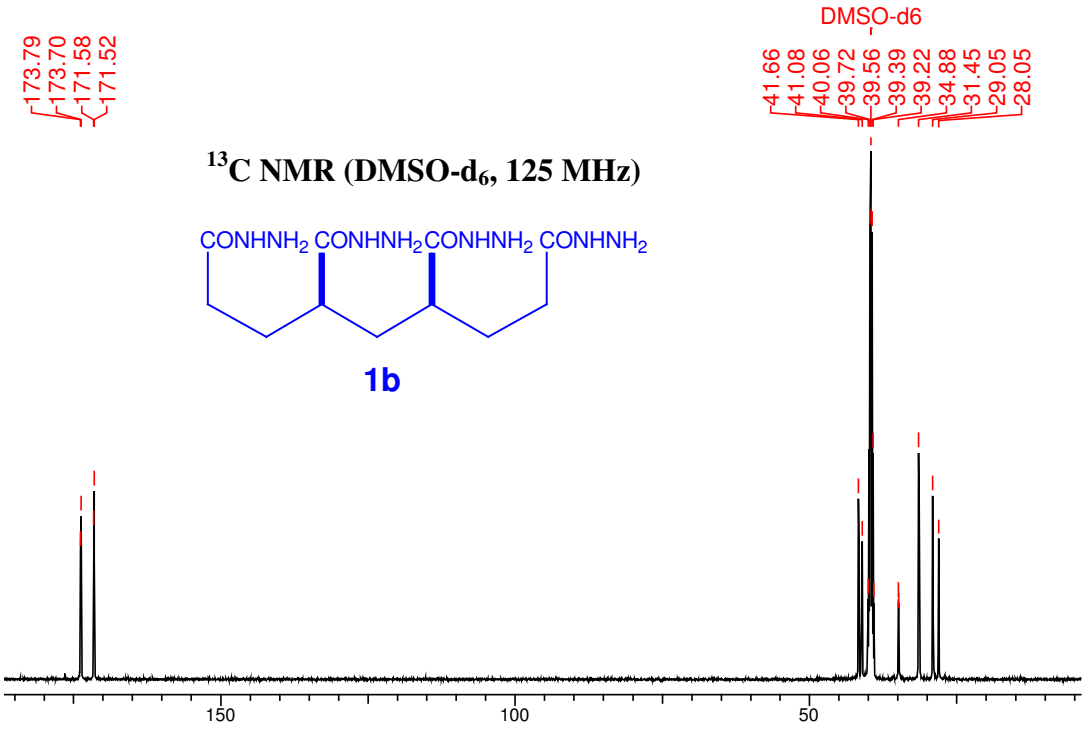


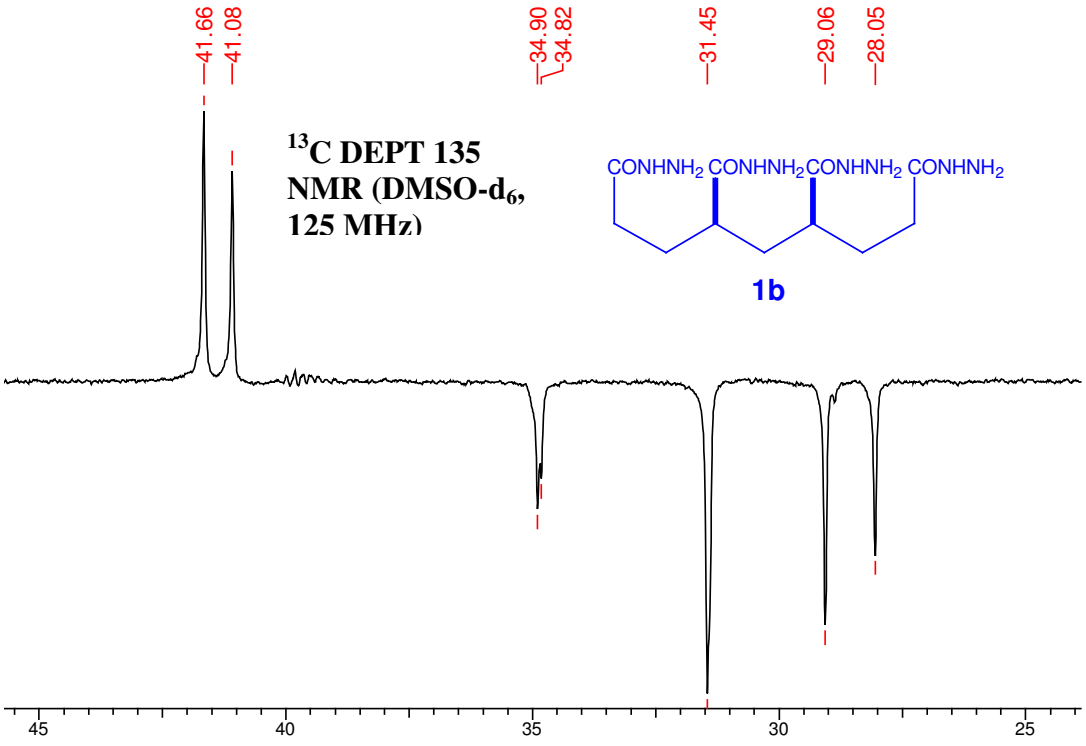
^{13}C DEPT 135 NMR $CDCl_3$, 125 MHz)

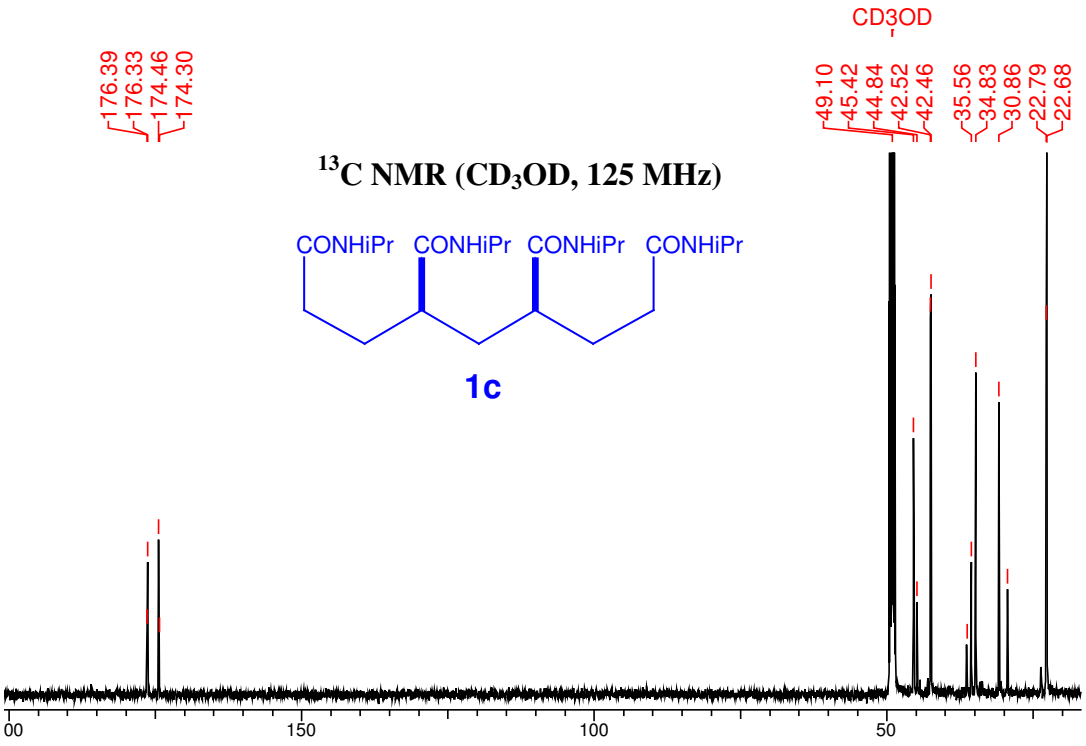
4

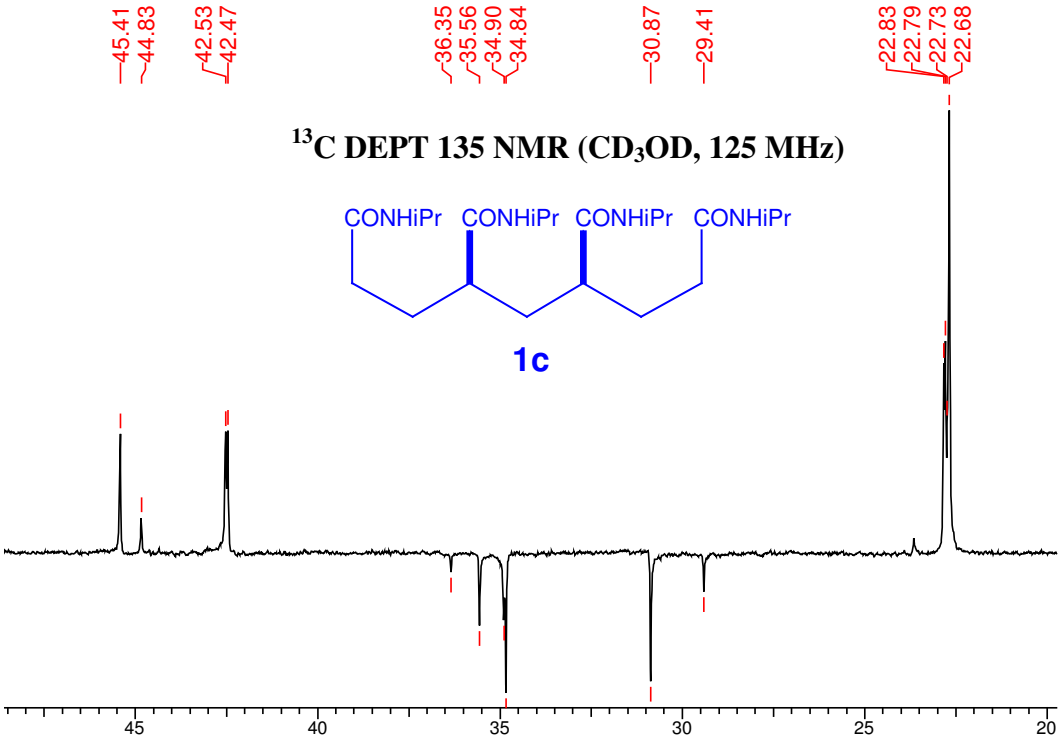

177.17
175.68
43.87
34.42
33.00
27.73
25.69
25.61
13C NMR [H2O:D2O (90:10)
125 MHz]
CONHMe CONHMe CONHMe CONHMe
1a
150
100
50

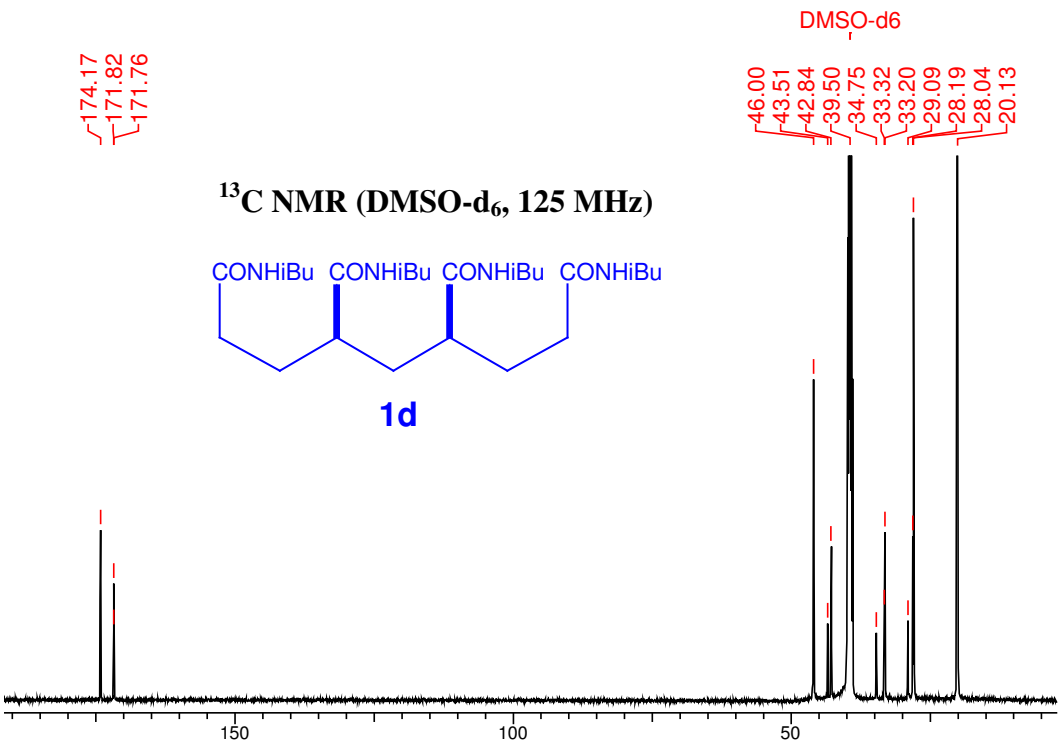

43.87
34.42
33.00
27.73
25.69
25.61
13C DEPT 135 NMR [(H2O:D2O
(90:10) 125 MHz]
CONHMe CONHMe CONHMe CONHMe
1a
45
40
35
30
25
20

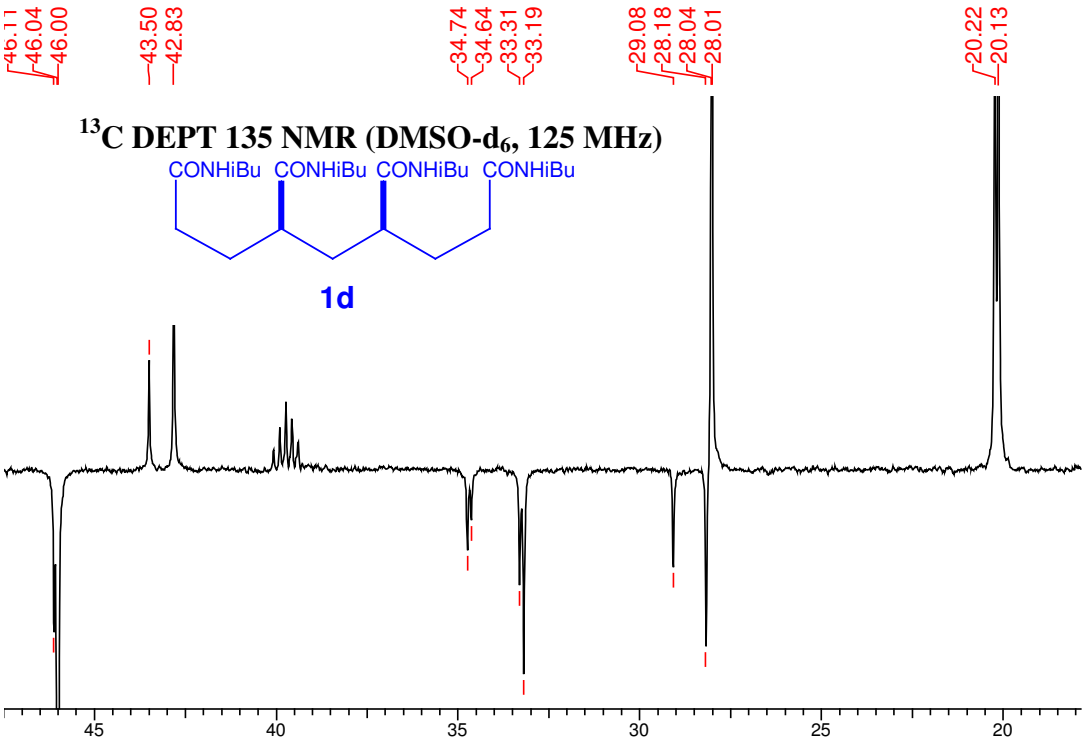

DMSO-d6
173.79
173.70
171.58
171.52
41.66
41.08
40.06
39.72
39.56
39.39
39.22
34.88
31.45
29.05
28.05
13C NMR (DMSO-d6, 125 MHz)
CONHNH2 CONHNH2 CONHNH2 CONHNH2
1b
150
100
50

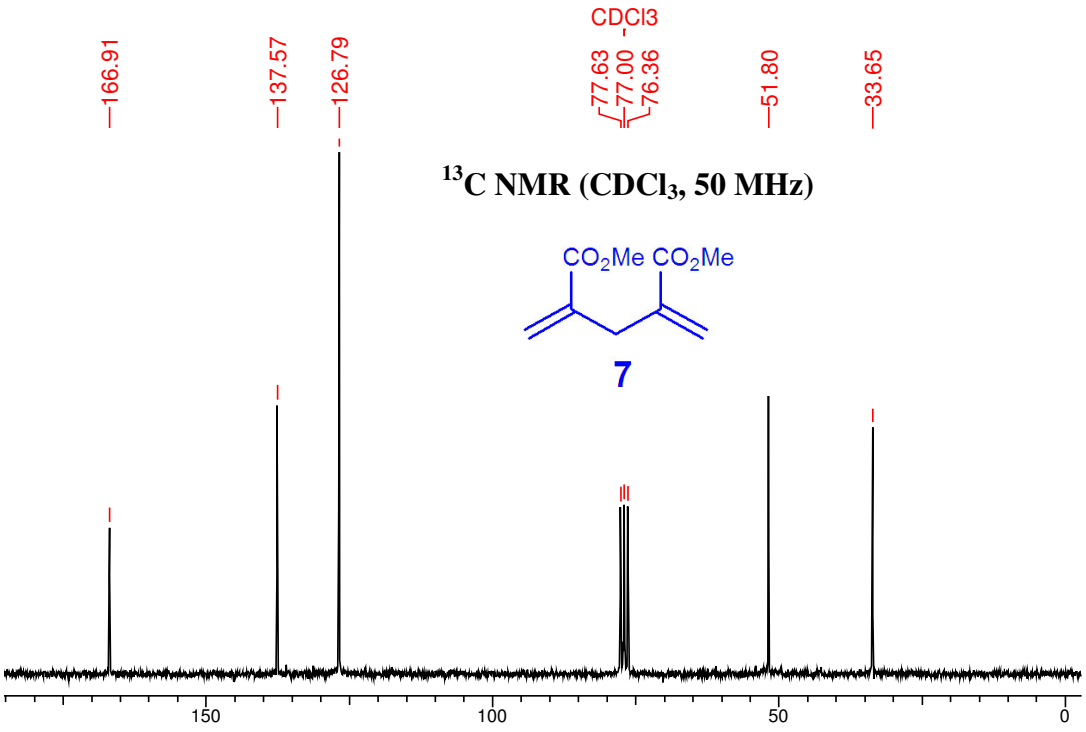

41.66
41.08
34.90
34.82
31.45
29.06
28.05
13C DEPT 135
NMR (DMSO-d6,
125 MHz)
CONHNH2 CONHNH2 CONHNH2 CONHNH2
1b
45
40
35
30
25


CD3OD
176.39
176.33
174.46
174.30
49.10
45.42
44.84
42.52
42.46
35.56
34.83
30.86
22.79
22.68
13C NMR (CD3OD, 125 MHz)
CONHiPr CONHiPr CONHiPr CONHiPr
1c
00
150
100
50


45.41
44.83
42.53
42.47
36.35
35.56
34.90
34.84
30.87
29.41
22.83
22.79
22.73
22.68
13C DEPT 135 NMR (CD3OD, 125 MHz)
CONHiPr CONHiPr CONHiPr CONHiPr
1c
45
40
35
30
25
20

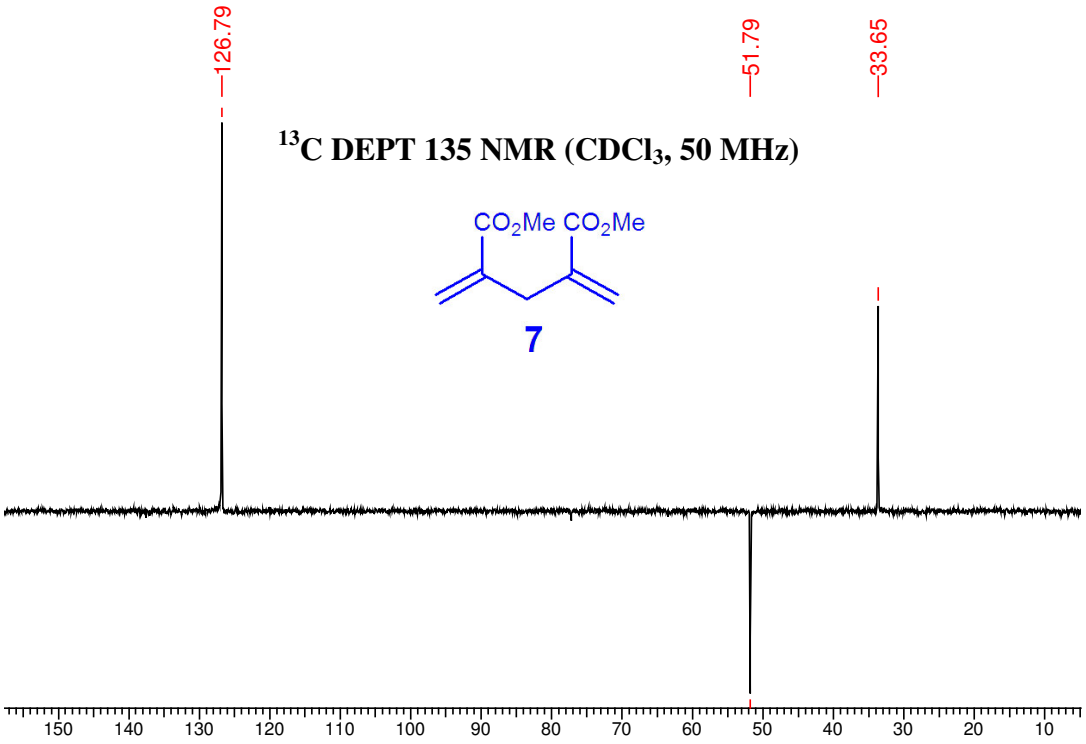

DMSO-d6
174.17
171.82
171.76
46.00
43.51
42.84
39.50
34.75
33.32
33.20
29.09
28.19
28.04
20.13
13C NMR (DMSO-d6, 125 MHz)
CONHiBu CONHiBu CONHiBu CONHiBu
1d
150
100
50


46.11
46.04
46.00
43.50
42.83
34.74
34.64
33.31
33.19
29.08
28.18
28.04
28.01
20.22
20.13
13C DEPT 135 NMR (DMSO-d6, 125 MHz)
CONHiBu CONHiBu CONHiBu CONHiBu
1d
45
40
35
30
25
20



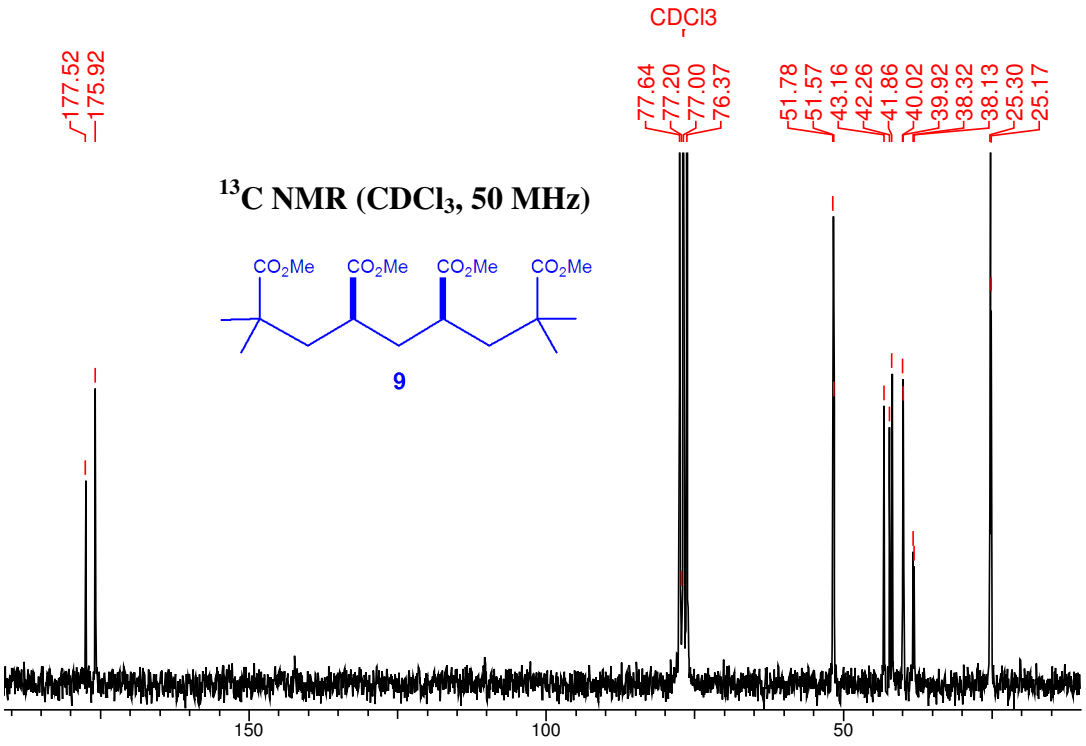
^{13}C NMR ($CDCl_3$, 50 MHz)

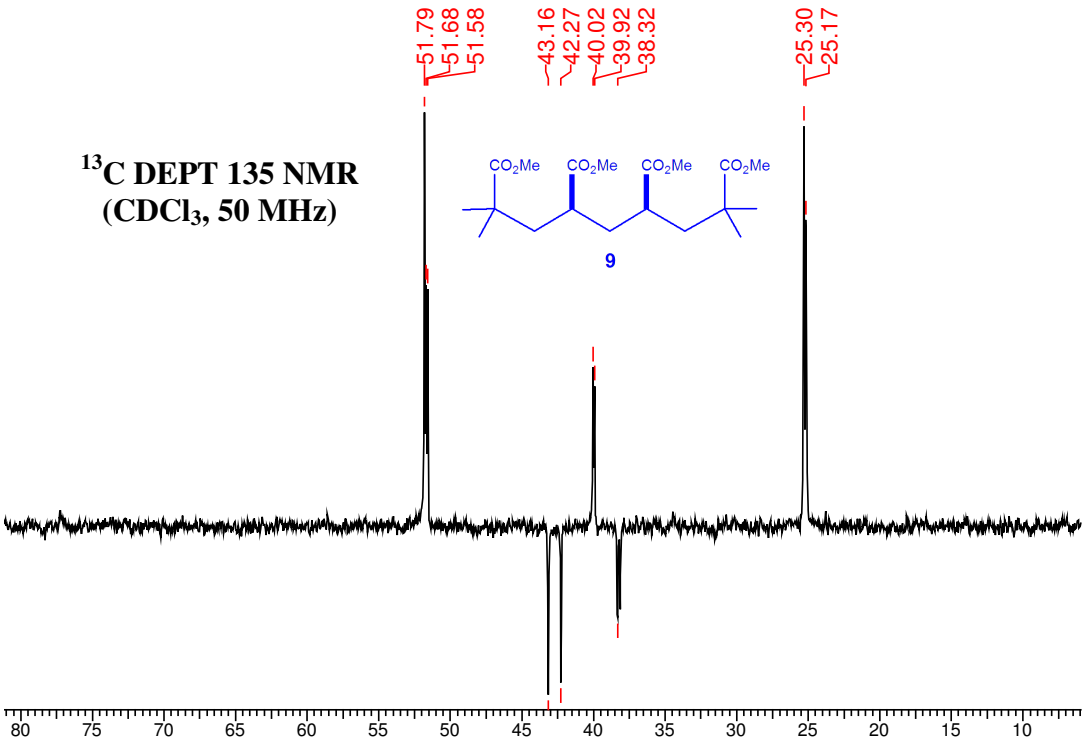
7

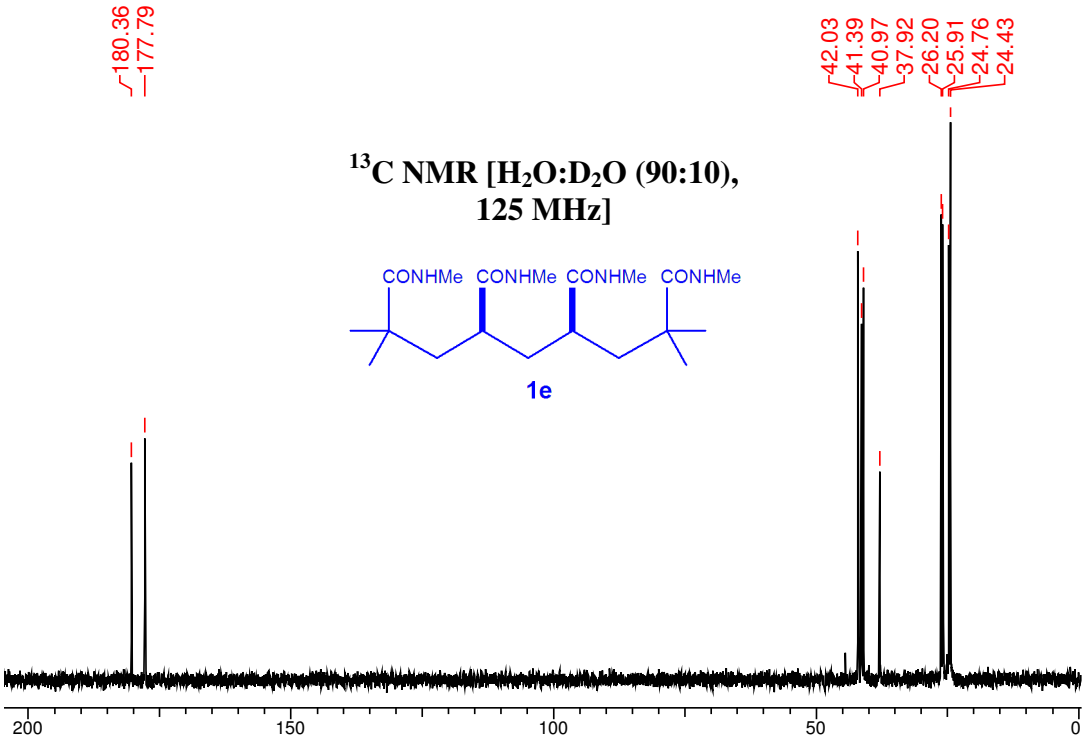


^{13}C DEPT 135 NMR ($CDCl_3$, 50 MHz)

7

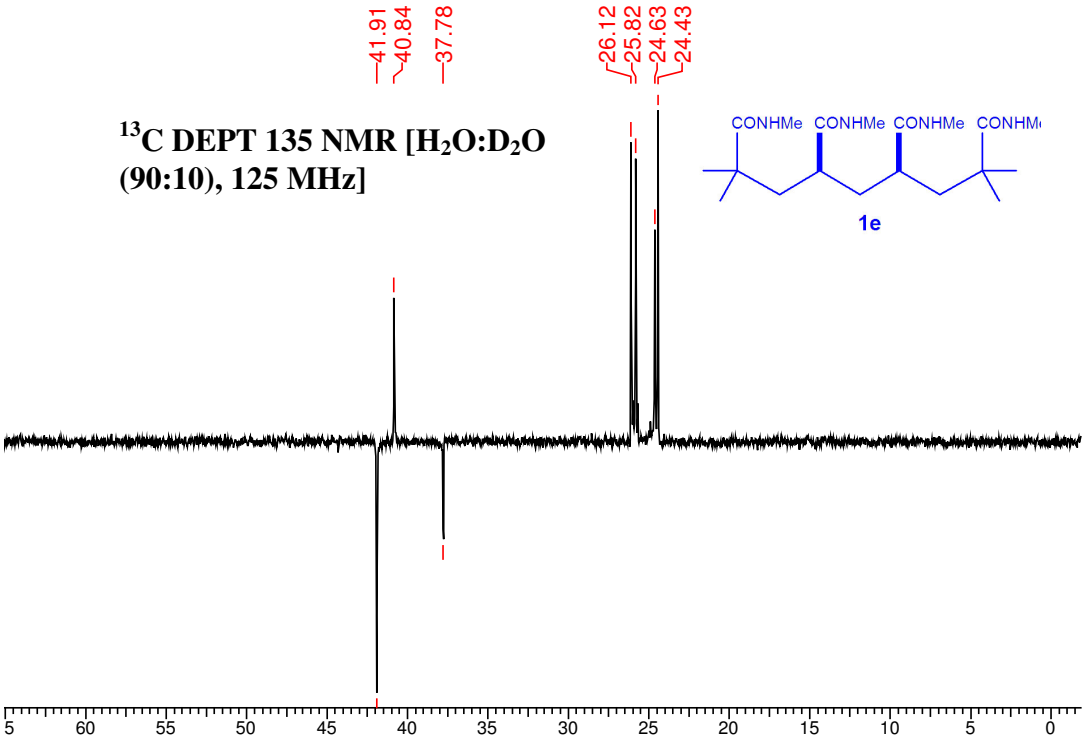

CDCl3
177.52
175.92
77.64
77.20
77.00
76.37
51.78
51.57
43.16
42.26
41.86
40.02
39.92
38.32
38.13
25.30
25.17
^{13}C NMR (CDCl$_3$, 50 MHz)
CO$_2$Me CO$_2$Me CO$_2$Me CO$_2$Me
9
150
100
50


51.79
51.68
51.58
43.16
42.27
40.02
39.92
38.32
25.30
25.17
^{13}C DEPT 135 NMR
(CDCl$_3$, 50 MHz)
CO$_2$Me CO$_2$Me CO$_2$Me CO$_2$Me
9
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10



^{13}C NMR [H_2O:D_2O (90:10), 125 MHz]

1e



^{13}C DEPT 135 NMR [H_2O:D_2O (90:10), 125 MHz]

1e

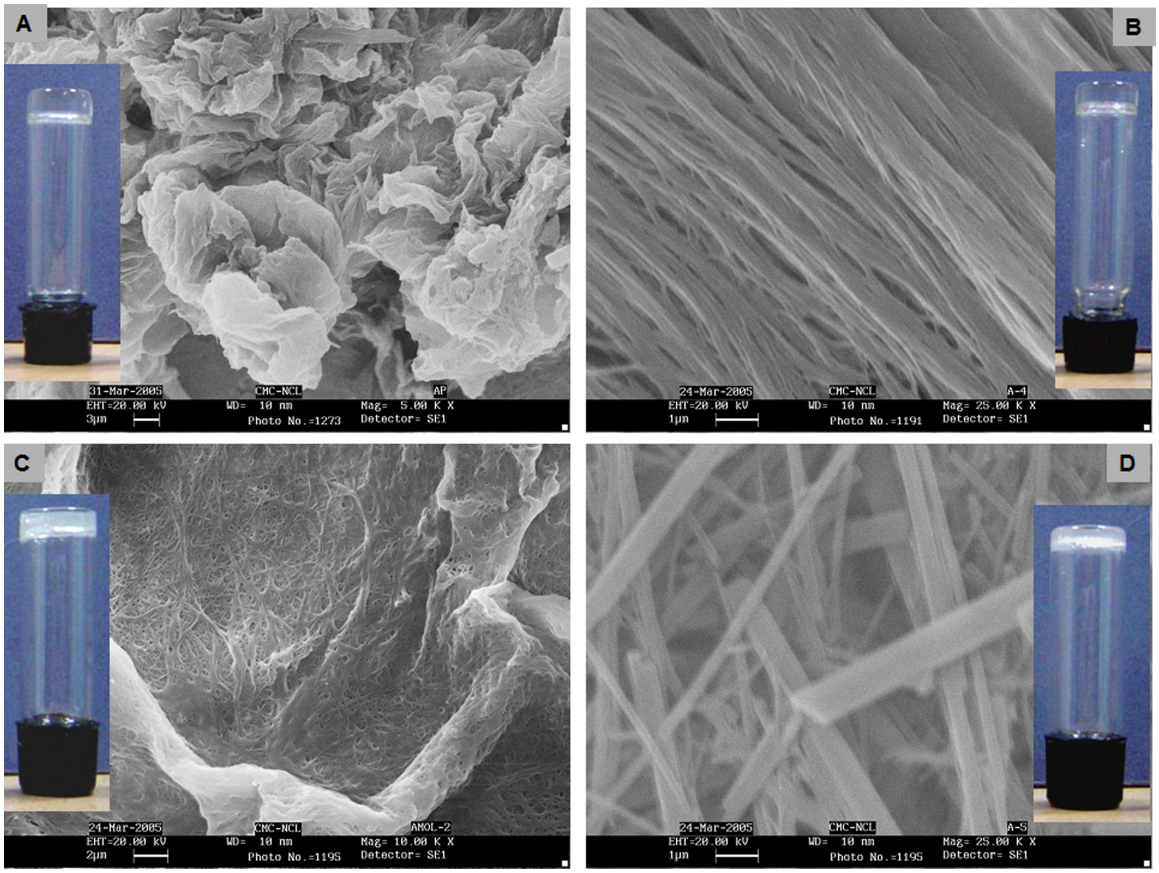
Table 1: Gelation Properties of the acrylamide oligomers 1a-e[a]

Compound	DMSO	MeOH	MeOH:H_2O	o-Tolunitrile
1a	PG	S	S	I
1b	S	I	S	I
1c	PG	S	P	CG Tgs: 54-55°C CGC: 0.3 %
1d	OG Tgs: 53°C CGC: 3.5%	S	WG Tgs: 59°C CGC: 3 %	CG Tgs: 65°C CGC: 0.4 %
1e	S	S	S	OG Tgs: 108°C CGC: 2 %

a. PG- partial gel, S- soluble, I- insoluble, P- precipitation, CG- clear gel, OG- opaque gel, WG- white gel.
Tgs: The *gel to sol*. melting temperature in °C
CGC: Critical Gel Concentration in wt.%.

Acrylamide oligomers **1c-e** gelated polar organic solvents, such as dimethyl sulfoxide, o-toluonitrile, and aqueous methanol. Their gelation ability was examined by adopting the "stable-to-inversion of container" method (F. M. Menger, K. L. Caran, *J. Am. Chem. Soc.* 2000, **122**, 11679). Among the various gelators, **1c** and **1d** having hydrophobic isopropyl and isobutyl groups, respectively, gelled o-toluonitrile at relatively low concentrations (<0.5 wt-%) forming clear gels. All gels were stable for several months and showed

excellent thermo reversibility, a key feature of low-molecular-mass organogelators (X. Huang, P. Terech, S. R. Raghavan, R. G. Weiss, R. G, *J. Am. Chem. Soc*. 2005, **127**, 4336). The superstructures built up with **1c-e** in various organic solvents were examined by scanning electron microscopy (SEM) of the xerogels (*vide infra*). The SEM images of the acrylamide oligomers **1c-e** with different amide substituents show different textures. In the case of the N-isopropyl substituted oligomer **1c** that gelated *o*-toluonitrile, the presence of a clearly distinct domain of aggregate can be observed (figure **A**). Whereas **1d** showed, in both o-toluonitrile and DMSO, interconnected fibrillar networks (figure **B, C**), a lamellar structure (figure **D**) was evident for **1e** in o-toluonitrile.



Scanning Electron Micrograph (SEM) images of dried xerogels of (**A**) **1c** in o-toluonitrile (scale bar 3 µm, magnification 5.00k), (**B**) **1d** in o-toluonitrile (scale bar 1 µm, magnification 25.00k), (**C**) **1d** in dimethyl sulphoxide (scale bar 2 µm, magnification 10.00k), and (**D**) **1e** in o-toluonitrile (scale bar 1 µm, magnification 25.00k). The corresponding gels ("inverted vials") are in the insets.