



Supporting Information

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**New Twist of Ugi Four-component Reaction:
Synthesis of α -ketoamide via a Molecular Sieves
Promoted Formal Oxidative Coupling of Aliphatic
Aldehyde and Isocyanide**

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General Information

All reagents were obtained from commercial suppliers. Solvents were redistilled if necessary by standard methods. Reactions under inert atmosphere (argon) were performed in oven-dried glassware, sealed with a rubber septum.

Flash chromatography was performed using 40-63 μ m particle sized silica gel (200-400 mesh). Visualization was achieved under a UVP minerallight UVGL-58 lamp.

Melting points were recorded using a Büchi melting point B-540 apparatus and are uncorrected.

IR spectra were recorded on neat samples, unless precised, on a Perkin Elmer Spectrum BX FT-IR System spectrometer and the characteristic IR absorptions bands are reported in cm^{-1} .

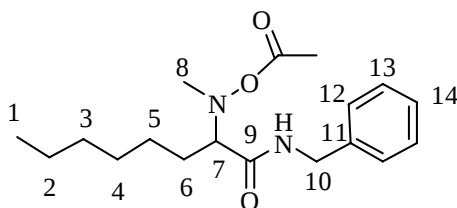
Optical rotations were performed on a Jasco P-1010 polarimeter (589 nm) using a 700- μ L cell with a path length of 1 dm.

Proton NMR (^1H) were recorded at 300 MHz or 500 MHz on a Bruker AC-300 or Bruker AC-500 spectrometer, respectively, using TMS as internal standard. Carbon NMR (^{13}C) spectra were recorded at 75 MHz on a Bruker AC-300 spectrometer.

Chemical shifts (δ) are reported in parts per million (ppm) from tetramethylsilane. NMR experiments were carried out in deuteriochloroform (CDCl_3). The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, dt: doublet of triplet, tt: triplet of triplet, h: heptuplet, m: multiplets, br: broad signal for proton spectra. Coupling constants (J) are reported in Hertz (Hz).

Mass spectra were obtained either from an AEI MS-50 instrument using electron impact ionization (EI) or from an AEI MS-9 using electron spray (ES).

2-[Acetyloxy)(methyl) amino]-*N*-benzyloctanamide **5a**



Heptanal (56 μL , 0.40 mmol, 1 equiv) was added to a solution of *N*-methyl hydroxylamine hydrochloride (37 mg, 0.44 mmol, 1.1 equiv) and NaHCO_3 (66 mg, 0.78 mmol, 2 equiv) in methanol (1.0 mL), and the mixture was stirred for 30 min at room temperature. The benzylisocyanide (50 μL , 0.42 mmol, 1.05 equiv) and acetic acid (200 μL , 9 equiv) were then added, and stirring was continued for 16 h at room temperature. The reaction mixture was then filtrated and the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography (SiO_2 , 40% ethyl acetate in heptane) to afford **5a** (58 mg, 45%) as an oil, **6** (20 mg, 18%) as a white solid and **7** (10 mg, 18%) as a white solid.

$\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_3$ (320.43 $\text{g}\cdot\text{mol}^{-1}$)

Rf : 0.13 (Heptane/ EtOAc 4:1)

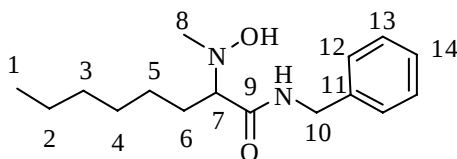
NMR ^1H δ (500 MHz, CDCl_3 , 293K) 7.34–7.18 (6H, m, H_{Ar} , NH), 4.47 (1H, dd, $J_{10,\text{NH}} = 6.5 \text{ Hz}$, $J_{10,10'} = 14.5 \text{ Hz}$, H_{10}), 4.33 (1H, dd, $J_{10',\text{NH}} = 6.0 \text{ Hz}$, $J_{10',10} = 14.5 \text{ Hz}$, $\text{H}_{10'}$), 3.38 (1H, dd, $J_{7,6} = 4.5 \text{ Hz}$, $J_{7,6'} =$

8.0 Hz, H₇), 2.74 (3H, s, H₈), 1.79 (3H, s, COCH₃), 1.77–1.57 (2H, m, H₅), 1.45–1.18 (8H, m, H₂, H₃, H₄, H₅), 0.87 (3H, br t, H₁)
H₆

MS (ESI) (m/z) 321.2 [M+H]⁺

HRMS (ESI) m/z 321.2191 [M+H]⁺, C₁₈H₂₉N₂O₃ requires 321.2178

***N*-benzyl-2-[hydroxy(methyl)amino]octanamide 6**



C₁₆H₂₆N₂O₂ (278.39 g.mol⁻¹)

R_f : 0.23 (Heptane/ EtOAc 5:5)

Melting point : ≈ 69.0–71.0 °C

IR (cm⁻¹) 3277 (N–H), 2923, 2854, 1648 (C=O *ketone*), 1548, 1495, 1453, 1360, 1236

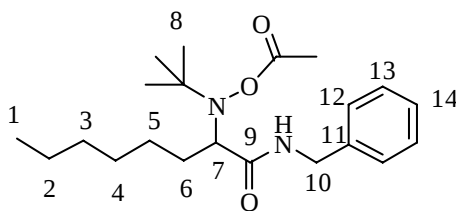
NMR ¹H δ (300 MHz, CDCl₃, 293K) 7.37–7.23 (5H, m, H_{Ar}), 6.74 (1H, br t, NH), 4.48 (2H, d, J = 6.0 Hz), 3.12 (1H, dd, J = 6.0 Hz, 7.8 Hz, H₇), 2.67 (3H, s, H₈), 1.85–1.56 (2H, m, H₆), 1.44–1.14 (8H, m, H₂, H₃, H₄, H₅), 0.87 (3H, br t, H₁)

NMR ¹³C δ (75 MHz, CDCl₃, 293K) 172.4 (C_q, C₉), 138.3 (C_q, C₁₁), 128.7 (2x CH, C₁₂), 127.7 (2x CH, C₁₃), 127.4 (CH, C₁₄), 73.4 (CH, C₇), 45.4 (CH₃, C₈), 43.1 (CH₂, C₁₁), 31.6 (CH₂, C₃), 30.4 (CH₂, C₄), 29.3 (CH₂, C₆), 25.9 (CH₂, C₅), 22.5 (CH₂, C₂), 14.0 (CH₂, C₁)

MS (ESI) (m/z) 301.2 [M+Na]⁺

HRMS (ESI) m/z 301.1886 [M+Na]⁺, C₁₆H₂₆N₂O₂ Na requires 301.1892

2-[Acetyloxy)(*tert*-butyl) amino]-*N*-benzyloctanamide **5b**



Heptanal (56 μL , 0.40 mmol, 1 equiv) was added to a solution of *N*-*tert*-butyl hydroxylamine hydrochloride (55 mg, 0.44 mmol, 1.1 equiv), 4Å molecular sieves (330 mg) and NaHCO_3 (66 mg, 0.78 mmol, 2 equiv) in methanol (0.40 mL), and the mixture was stirred for 30 min at room temperature. The benzylisocyanide (50 μL , 0.42 mmol, 1.05 equiv) and acetic acid (200 μL , 9 equiv) were then added, and stirring was continued for 16 h at room temperature. The reaction mixture was then filtrated and the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography (SiO_2 , 40% ethyl acetate in heptane) to afford **5a** (83 mg, 57%) as an oil.

$\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_3$ (362.50 $\text{g}\cdot\text{mol}^{-1}$)

Rf : 0.14 (Heptane/ EtOAc 4:1)

NMR ^1H δ (500 MHz, CDCl_3 , 293K) 8.93 (1H, br s, NH), 7.46–7.25 (5H, m, H_{Ar}), 4.52 (1H, dd, $J_{10,\text{NH}} = 5.2 \text{ Hz}$, $J_{10,10'} = 14.7 \text{ Hz}$, H_{10}), 4.33 (1H, dd, $J_{10',\text{NH}} = 4.5 \text{ Hz}$, $J_{10',10} = 14.7 \text{ Hz}$, $\text{H}_{10'}$), 3.64 (1H, m, H_7), 2.07 (3H, s, COCH_3), 1.65–1.63 (2H, m, H_5), 1.45–1.21 (8H, m, H_2 , H_3 , H_4 , H_5), 1.09 (9H, s, H_8), 0.87 (3H, br t, H_1)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 174.1 (Cq, C_9), 171.5 (Cq, COCH_3) 138.3 (Cq, C_{11}), 128.4 (2x CH, C_{12}), 127.4 (2x CH, C_{13}), 126.7 (CH, C_{14}), 65.0 (CH, C_7), 60.4 (Cq, *t*-Bu) 43.0 (CH_2 , C_{11}), 31.6 (CH_2 , C_3),

31.4 (CH₂, C₄), 29.5 (CH₂, C₆), 27.9 (CH₂, C₅), 25.3 (CH₃, *t*-Bu),
22.6 (CH₂, C₂), 18.7 (COCH₃), 14.0 (CH₂, C₁)

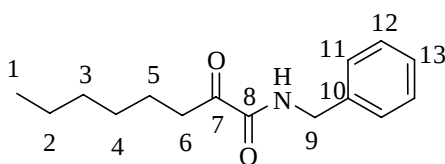
MS (ESI) (m/z) 385.2 [M+Na]⁺

HRMS (ESI) m/z 301.2467 [M+Na]⁺, C₂₁H₃₄N₂O₃ Na requires 385.2462

General procedure for the synthesis of α-ketoamides

Aldehyde (1 equiv.) was added to a solution of *N*-methyl hydroxylamine hydrochloride (1.1 equiv.), NaHCO₃ (2 equiv.) and 4Å molecular sieves (0.75 g/mmol) in dry methanol (1.0 M), and the mixture was stirred for 30 min at room temperature. The isocyanide (1.05 equiv.) and acetic acid (9 equiv.) were then added, and stirring at room temperature until the reaction was judged complete by TLC. The reaction mixture was then filtrated and the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography on silica gel.

N-benzyl-2-oxooctanamide 7^[1]



According to the general procedure, the *N*-benzyl-2-oxooctanamide (**7a**) was obtained from heptanal and benzylisocyanide, as a white solid (65%).

C₁₅H₂₁NO₂ (247.33 g.mol⁻¹)

R_f : 0.42 (Heptane/ EtOAc 4:1)

Melting point : 44.3–46°C

IR (cm⁻¹) 3263 (N-H), 2926, 2867, 1719 (C=O *ketone*), 1668 (C=O *amide*), 1530, 1454, 1363, 1251, 1236, 1130, 1028, 952, 698

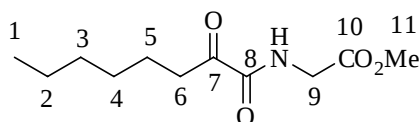
NMR ¹H δ (300 MHz, CDCl₃, 293K) 7.42–7.16 (6H, m, H_{Ar}, NH), 4.47 (2H, d, *J* = 6.1 Hz, H₉), 2.94 (2H, t, *J* = 7.3 Hz, H₆), 1.69–1.53 (2H, m, H₅), 1.40–1.21 (6H, m, H₂, H₃, H₄), 0.88 (3H, br t, *J* = 7.0 Hz, H₁)

NMR ¹³C δ (75 MHz, CDCl₃, 293K) 199.2 (Cq, C₇), 160.0 (Cq, C₈), 137.0 (Cq, C₁₀), 128.8 (2x CH, C₁₁), 127.9 (2x CH, C₁₂), 127.8 (CH, C₁₃), 43.4 (CH₂, C₉), 36.8 (CH₂, C₆), 31.5 (CH₂, C₃), 28.7 (CH₂, C₄), 23.2 (CH₂, C₅), 22.4 (CH₂, C₂), 14.0 (CH₃, C₁)

MS (ESI) (m/z) 270.1 [M+Na]⁺, 302.2 [M+Na+MeOH]⁺

HRMS (ESI) m/z 270.1448 [M+Na]⁺, C₁₅H₂₁NO₂ Na requires 270.1470

Methyl *N*-(2-oxooctanoyl)glycinate



According to the general procedure, the *N*-(2-oxooctanoyl)glycinate (**7b**) was obtained from heptanal and methyl 2-isocyanoacetate, as a white solid (60%).

C₁₁H₁₉NO₄ (229.27 g.mol⁻¹)

R_f : 0.21 (Heptane/ EtOAc 4:1)

Melting point : 40.2–42.7°C

IR (cm⁻¹) 3353 (N-H), 2922, 2852, 1727 (C=O *ketone*), 1671 (C=O *amide*), 1520, 1458, 1443, 1366, 1212, 1139, 983, 962

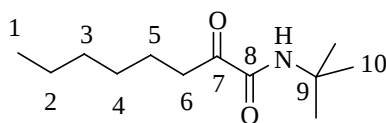
NMR ^1H δ (300 MHz, CDCl_3 , 293K) 7.41 (1H, br s, NH), 4.07 (2H, d, J = 5.7 Hz, H_9), 3.78 (3H, s, H_{11}), 2.90 (2H, t, J = 7.2 Hz, H_6), 1.67–1.51 (2H, m, H_5), 1.40–1.14 (6H, m, H_2 , H_3 , H_4), 0.87 (3H, br t, H_1)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 198.2 (Cq, C_7), 169.3 (Cq, C_{10}), 160.2 (Cq, C_8), 52.5 (CH_2 , C_{11}), 40.9 (CH_2 , C_9), 36.7 (CH_2 , C_6), 31.4 (CH_2 , C_3), 28.7 (CH_2 , C_4), 23.1 (CH_2 , C_5), 22.4 (CH_2 , C_2), 14.0 (CH_3 , C_1)

MS (ESI) (m/z) 252.1 $[\text{M}+\text{Na}]^+$

HRMS (ESI) m/z 252.1203 $[\text{M}+\text{Na}]^+$, $\text{C}_{11}\text{H}_{19}\text{NO}_4\text{Na}$ requires 252.1212

***N*-tert-Butyl-2-oxooctanamide 7c**



According to the general procedure, the *N*-tert-Butyl-2-oxooctanamide (**7c**) was obtained from heptanal and *tert*-butylisocyanide, as an oil (28%).

$\text{C}_{12}\text{H}_{23}\text{NO}_2$ (247.33 g.mol $^{-1}$)

R_f : 0.62 (Heptane/ EtOAc 4:1)

IR (cm $^{-1}$) 3393 (N-H), 2926, 2867, 1719 (C=O *ketone*), 1668 (C=O *amide*), 1530, 1454, 1363, 1251, 1236, 1130, 1028, 952, 698

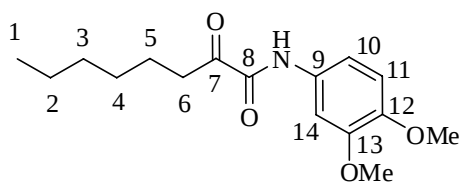
NMR ^1H δ (300 MHz, CDCl_3 , 293K) 6.82 (1H, br s, NH), 2.88 (2H, t, J = 7.2 Hz, H_6), 1.66–1.49 (2H, m, H_5), 1.38 (9H, s, H_{10}), 1.34–1.20 (6H, m, H_2 , H_3 , H_4), 0.87 (3H, br t, J = 7.0 Hz, H_1)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 200.4 (Cq, C₇), 159.4 (Cq, C₈), 51.2 (Cq, C₉), 36.2 (CH_2 , C₆), 31.5 (CH_2 , C₅), 28.7 (CH_2 , C₄), 28.3 (CH_3 , C₁₀), 23.2 (CH_2 , C₃), 22.4 (CH_2 , C₂), 14.0 (CH_3 , C₁)

MS (ESI) (m/z) 214.2 $[\text{M}]^+$

HRMS (ESI) m/z 214.1799 $[\text{M}+\text{H}]^+$, $\text{C}_{12}\text{H}_{24}\text{NO}_2$ requires 214.1807

***N*-(3,4-dimethoxyphenyl)-2-oxooctanamide 7d**



According to the general procedure, the *N*-(3,4-dimethoxyphenyl)-2-oxooctanamide (**7d**) was obtained from heptanal and 4-isocyano-1,2-dimethoxybenzene, as a yellow solid (75%).

$\text{C}_{16}\text{H}_{23}\text{NO}_4$ (293.36 g.mol⁻¹)

R_f : 0.27 (Heptane/ EtOAc 4:1)

Melting point : 109.5– 111.4 °C

IR (cm⁻¹) 3320 (N-H), 2939, 2928, 2868, 1713 (C=O *ketone*), 1662 (C=O *amide*), 1599, 1529, 1513, 1469, 1453, 1446, 1398, 1285, 1229, 1220, 1189, 1141

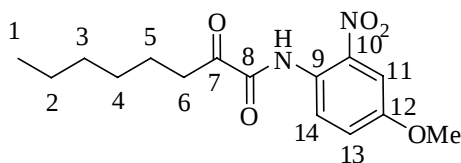
NMR ^1H δ (500 MHz, CDCl_3 , 293K) 8.69 (1H, br s, NH), 7.46 (1H, d, $J_{14-11} = 2.0$ Hz, H₁₄), 7.03 (1H, dd, $J_{11-14} = 2.0$ Hz, $J_{11-10} = 8.5$ Hz, H₁₁), 6.83 (1H, d, $J_{11-13} = 8.5$ Hz, H₁₀), 3.90 (3H, OCH₃) 3.87 (3H, OCH₃), 2.99 (2H, t, $J = 7.5$ Hz, H₆), 1.70–1.61 (2H, m, H₅), 1.40–1.22 (6H, m, H₂, H₃, H₄), 0.88 (3H, br t, $J = 7.0$ Hz, H₁)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 199.6 (Cq, C_7), 157.3 (Cq, C_8), 149.2 (Cq, C_{13}), 146.5 (Cq, C_{12}), 130.0 (Cq, C_9), 111.7 (CH, C_{10}), 111.4 (CH, C_{11}), 104.1 (CH, C_{14}), 56.1 (CH_3 , OCH_3), 55.9 (CH_3 , OCH_3) 36.3 (CH_2 , C_6), 31.5 (CH_2 , C_3), 28.7 (CH_2 , C_4), 23.3 (CH_2 , C_5), 22.4 (CH_2 , C_2), 14.0 (CH_3 , C_1)

MS (ESI) (m/z) 316.2 [$\text{M}+\text{Na}$] $^+$

HRMS (ESI) m/z 316.1534 [$\text{M}+\text{Na}$] $^+$, $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{Na}$ requires 316.1525

***N*-(4-methoxy-2-nitrophenyl)-2-oxooctanamide 7e**



According to the general procedure, the *N*-(4-methoxy-2-nitrophenyl)-2-oxooctanamide (**7e**) was obtained from heptanal and 1-isocyano-4-methoxy-2-nitrobenzene, as a white solid (36%)

$\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_5$ (308.33 $\text{g}\cdot\text{mol}^{-1}$)

R_f : 0.41 (Heptane/ EtOAc 4:1)

Melting point : 68–71°C

IR (cm^{-1}) 3284 (N-H), 2927, 2858, 1717 (C=O *ketone*), 1690 (C=O *amide*), 1578, 1452, 1428, 1345, 1307, 1280, 1248, 1133, 1030, 928, 851, 788, 759

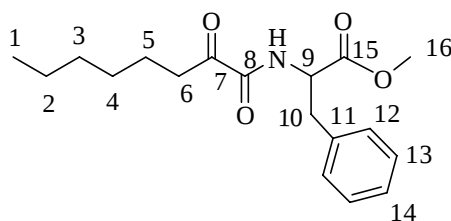
NMR ^1H δ (300 MHz, CDCl_3 , 293K) 11.45 (1H, br s, NH), 8.72 (1H, d, $J_{14-13} = 9.3$ Hz, H_{14}), 7.73 (1H, d, $J_{11-13} = 3.0$ Hz, H_{11}), 7.26 (1H, dd, $J_{13-11} = 3.0$ Hz, $J_{13-14} = 9.3$ Hz, H_{13}), 3.88 (3H, s, OCH_3), 2.99 (2H, t, $J = 7.2$ Hz, H_6), 1.73–1.61 (2H, m, H_5), 1.43–1.22 (6H, m, H_2 , H_3 , H_4), 0.89 (3H, t, $J = 6.6$ Hz, H_1)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 198.1 (Cq, C₇), 158.4 (Cq, C₈), 155.8 (Cq, C₁₂), 137.9 (Cq, C₁₀), 126.6 (Cq, C₉), 123.2 (CH, C₁₄), 122.9 (CH, C₁₃), 109.3 (CH, C₁₁), 55.9 (CH₃, OCH₃), 36.4 (CH₂, C₆), 31.5 (CH₂, C₃), 28.7 (CH₂, C₄), 23.2 (CH₂, C₅), 22.4 (CH₂, C₂), 14.0 (CH₃, C₁)

MS (ESI) (m/z) 331.1 [M+Na]⁺

HRMS (ESI) m/z 331.1264 [M+Na]⁺, C₁₅H₂₀N₂O₅Na requires 331.1270

2-(2-Oxo-octanoylamino)-3-phenyl propionic acid methyl ester **7f**



According to the general procedure, the 2-(2-Oxo-octanoylamino)-3-phenyl propionic acid methyl ester (**7f**) was obtained from heptanal and methyl 2-isocyano-3-phenylpropanoate, as an oil (44%)

C₁₈H₂₅NO₄ (319.40 g.mol⁻¹)

R_f : 0.58 (Heptane/ EtOAc 7:3)

IR (cm⁻¹) 3335 (N-H), 2953, 2928, 2857, 2333, 1737 (C=O *ketone*), 1731 (C=O *ester*), 1681 (C=O *amide*), 1603, 1515, 1497, 1455, 1435, 1359, 1266, 1213, 1201, 1176, 1134

NMR ^1H δ (500 MHz, CDCl_3 , 293K) 7.38–7.08 (6H, 2m, H_{Ar}, NH), 4.81 (1H, ddd, $J_{9,10} = 6.0$ Hz, $J_{9,10'} = 6.5$ Hz, $J_{9-NH} = 8.5$ Hz, H₉), 3.73 (3H, s, H₁₆), 3.17 (1H, dd, $J_{10,9} = 6.0$ Hz, $J_{10,10'} = 14.0$ Hz, H₁₀), 3.11 (1H, dd, $J_{10',9} = 6.5$ Hz, $J_{10',10} = 14.0$ Hz, H_{10'}), 2.91–2.80 (2H,

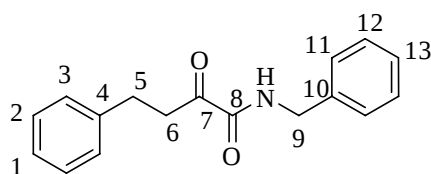
m, H₆), 1.63–1.53 (2H, m, H₅), 1.35–1.20 (6H, m, H₂, H₃, H₄), 0.88 (3H, br t, H₁)

NMR ¹³C δ (75 MHz, CDCl₃, 293K) 198.3 (Cq, C₇), 171.0 (Cq, C₈), 159.6 (Cq, C₁₅), 135.3 (Cq, C₁₁), 129.1 (2x CH, C₁₂), 128.7 (2x CH, C₁₃), 127.3 (CH, C₁₄), 53.1 (CH, C₉), 52.5 (CH₃, C₉), 37.9 (CH₂, C₁₀), 36.7 (CH₂, C₆), 31.4 (CH₂, C₃), 28.7 (CH₂, C₄), 23.1 (CH₂, C₅), 22.4 (CH₂, C₂), 14.0 (CH₂, C₁)

MS (ESI) (m/z) 342.2 [M+Na]⁺

HRMS (ESI) m/z 342.1688 [M+Na]⁺, C₁₈H₂₅NO₄Na requires 342.1681

***N*-benzyl-2-oxo-4-phenylbutanamide 7g^[2]**



According to the general procedure, the *N*-benzyl-2-oxo-4-phenylbutanamide (**7g**) was obtained from phenylpropionaldehyde and benzylisocyanide, as a white solid (70%)

C₁₇H₁₇NO₂ (267.32 g.mol⁻¹)

Melting point : 53.2–54.7°C

R_f : 0.30 (Heptane/ EtOAc 4:1)

IR (cm⁻¹) 3329 (N-H), 3025, 1718 (C=O *ketone*), 1662 (C=O *amide*), 1526, 1496, 1369, 1118, 1076, 1029, 962, 743

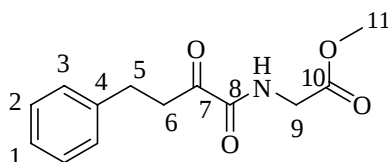
NMR ¹H δ (300 MHz, CDCl₃, 293K) 7.44–7.18 (11H, m, H_{Ar}, NH), 4.50 (2H, d, *J* = 6.3 Hz, H₉), 3.35 (2H, t, *J* = 7.5 Hz, H₅), 2.99 (2H, t, *J* = 7.5 Hz, H₆)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 198.1 (Cq, C_7), 159.8 (Cq, C_8), 140.3 (Cq, C_{10} or C_4), 136.9 (Cq, C_4 or C_{10}), 128.8 (2x CH, C_{Ar}), 128.5 (2x CH, C_{Ar}), 128.3 (2x CH, C_{Ar}), 127.8 (3x CH, C_{Ar}), 126.2 (CH, C_{Ar}), 43.4 (CH_2 , C_9), 38.4 (CH_2 , C_6), 29.1 (CH_2 , C_5)

MS (ESI) (m/z) 290.1 $[\text{M}+\text{Na}]^+$, 322.1 $[\text{M}+\text{Na}+\text{MeOH}]^+$

HRMS (ESI) m/z 290.1154 $[\text{M}+\text{Na}]^+$, $\text{C}_{17}\text{H}_{17}\text{NO}_2\text{Na}$ requires 290.1157

Methyl *N*-(2-oxo-4-phenylbutanoyl)glycinate **7h**



According to the general procedure, the Methyl *N*-(2-oxo-4-phenylbutanoyl)glycinate (**7h**) was obtained from phenylpropionaldehyde and methyl 2-isocyanoacetate, as an oil (61%)

$\text{C}_{13}\text{H}_{15}\text{NO}_4$ (249.10 $\text{g}\cdot\text{mol}^{-1}$)

R_f : 0.22 (Heptane/ EtOAc 7:3)

IR (cm^{-1}) 3356 (N-H), 1952, 1748 (C=O *ketone*), 1722 (C=O *ester*), 1681 (C=O *amide*), 1523, 1435, 1365, 1209, 1182, 1135

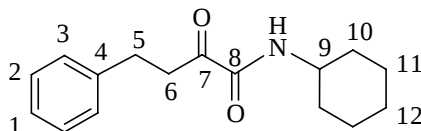
NMR ^1H δ (500 MHz, CDCl_3 , 293K) 7.41 (1H, s, NH), 7.25-7.01 (5H, m, H_{Ar}), 3.98 (2H, d, J = 6.0 Hz, H_9), 3.67 (3H, s, H_{11}), 3.18 (2H, br t, J = 7.5 Hz, H_6), 2.85 (2H, br t, J = 7.5 Hz, H_5)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 197.2 (Cq, C_7), 169.3 (Cq, C_{10}), 160.2 (Cq, C_8), 140.3 (Cq, C_4), 128.5 (2x CH, C_{Ar}), 128.4 (2x CH, C_{Ar}), 126.3 (CH, C_1), 52.5 (CH_3 , C_{11}), 40.9 (CH_2 , C_9), 38.4 (CH_2 , C_6), 29.0 (CH_2 , C_5)

MS (ESI) (m/z) 272.1 [M+Na]⁺, 304.1 [M+Na+MeOH]⁺

HRMS (ESI) m/z 272.0909 [M+Na]⁺, C₁₃H₁₅NO₄Na requires 272.0899

***N*-(4-methoxy-2-nitrophenyl)-2-oxo-4-phenylbutanamide 7i**^[2]



According to the general procedure, the Methyl *N*-(4-methoxy-2-nitrophenyl)-2-oxo-4-phenylbutanamide (**7i**) was obtained from phenylpropionaldehyde and cyclohexylisocyanide, as a white solid (53%)

C₁₆H₂₁NO₂ (259.34 g.mol⁻¹)

R_f : 0.45 (Heptane/ EtOAc 4:1)

Melting point : 85.2–86.1 °C

IR (cm⁻¹) 3305 (N-H), 2934, 2852, 1720 (C=O *ketone*), 1656, 1646 (C=O *amide*), 1530, 1496, 1450, 1394, 1374, 1150, 1119, 744, 725, 658, 696

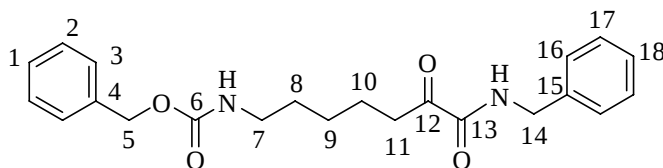
NMR ¹H δ (500 MHz, CDCl₃, 293K) 7.29–7.04 (5H, m, H_{Ar}), 6.88–6.64 (1H, m, NH), 3.71–3.53 (1H, m, H₉), 3.19 (2H, t, *J* = 7.5 Hz, H₆), 2.85 (2H, t, *J* = 7.5 Hz, H₅), 1.88–1.02 (10H, m, H₁₀, H₁₁, H₁₂)

NMR ¹³C δ (75 MHz, CDCl₃, 293K) 198.6 (Cq, C₇), 158.9 (Cq, C₈), 140.4 (Cq, C₄), 128.4 (CH, C_{Ar}), 128.3 (2x CH, C_{Ar}), 126.1 (2x CH, C_{Ar}), 48.2 (CH, C₉), 38.2 (CH₂, C₆), 32.6 (2x CH₂, C₁₀), 29.1 (CH₂, C₅), 25.3 (CH₂, C₁₁), 24.6 (2x CH₂, C₁₂)

MS (ESI) (m/z) 282.1 [M+Na]

HRMS (ESI) m/z 282.1462 [M+Na], C₁₆H₂₁NO₂Na requires 282.1470

Benzyl-7-(benzylamino)-6,7-dioxoheptylcarbamate **7j**



According to the general procedure, the Benzyl-7-(benzylamino)-6,7-dioxoheptylcarbamate (**7j**) was obtained from benzyl 6-oxohexylcarbamate and benzylnisocyanide, as a white solid (68%)

C₂₂H₂₆N₂O₄ (382.45 g.mol⁻¹)

R_f : 0.68 (Heptane/EtOAc 2:3)

Melting point : 100.4–102.8 °C

IR (cm⁻¹) 3350 (N-H), 3301 (N-H), 2943, 1725 (C=O *ketone*), 1684 (C=O *amide*), 1658 (C=O, carbamate), 1524, 1481, 1453, 1381, 1360, 1244, 1139, 1099

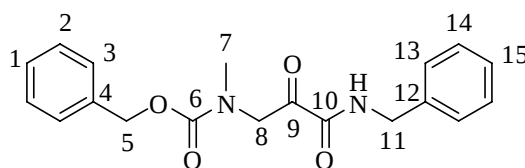
NMR ¹H δ (300 MHz, CDCl₃, 293K) 7.40–7.19 (11H, m, H_{Ar}, NH *amide*), 5.09 (2H, s, H₅), 4.76 (1H, br s, NH *carbamate*), 4.46 (2H, d, J = 6.0 Hz, H₁₄) 3.19 (2H, m, H₇), 2.95 (2H, t, J = 7.2 Hz, H₁₁), 1.70–1.21 (6H, m, H₈, H₉, H₁₀)

NMR ¹³C δ (75 MHz, CDCl₃, 293K) 198.8 (Cq, C₁₂), 159.9 (Cq, C₁₃), 156.3 (Cq, C₆), 136.9 (Cq, C₁₅), 136.6 (Cq, C₄), 128.8 (2x CH, C_{Ar}), 128.5 (2x CH, C_{Ar}), 128.1 (3x CH, C_{Ar}), 127.9 (3x CH, C_{Ar}), 66.6 (CH₂, C₅), 43.4 (CH₂, C₁₄), 40.8 (CH₂, C₇), 36.6 (CH₂, C₁₁), 29.7 (CH₂, C₈), 26.1 (CH₂, C₉), 22.8 (CH₂, C₁₀)

MS (ESI) (m/z) 405.2 [M+Na]⁺

HRMS (ESI) m/z 405.1788 [M+Na]⁺, C₂₂H₂₆N₂O₄ Na requires 405.1790

Benzyl[2-(benzylamino)-2-oxoethyl]methylcarbamate 7k



According to the general procedure, the Benzyl[2-(benzylamino)-2-oxoethyl]methylcarbamate (**7k**) was obtained from benzyl 2-oxoethylcarbamate and benzylnisocyanide, as an oil (46%)

C₁₉H₂₀N₂O₄ (340.37 g.mol⁻¹)

R_f : 0.68 (Heptane/ EtOAc 2:3)

IR (cm⁻¹) 3315 (N-H), 2929, 2359, 1736 (C=O *ketone*), 1673 (C=O *amide*), 1524, 1453, 1401, 1215, 1143

NMR ¹H δ (300 MHz, CDCl₃, 293K) Rotamer A: 7.48-7.22 (10H, m, H_{Ar}), 7.16 (1H, br s, NH), 5.15 (2H, s, H₅), 4.77-4.71 (2H, m, H₁₁), 4.54-4.40 (2H, m, H₈), 2.97 (3H, s, H₇)

Rotamer B: 7.48-7.22 (10H, m, H_{Ar}), 7.13 (1H, br s, NH), 5.08 (2H, s, H₅), 4.77-4.71 (2H, m, H₁₁), 4.54-4.40 (2H, m, H₈), 2.97 (3H, s, H₇)

NMR ¹³C δ (75 MHz, CDCl₃, 293K) Rotamer A: 193.6 (Cq, C₉), 159.4 (Cq, C₁₀), 156.7 (Cq, C₆), 136.7 (Cq, C₁₂), 136.5 (Cq, C₄), 128.9 (2x CH, C_{Ar}), 128.5 (2x CH, C_{Ar}), 128.0 (2x CH, C_{Ar}), 127.9 (4x CH, C_{Ar}), 127.8 (2x CH, C_{Ar}), 67.6 (CH₂, C₅), 55.4 (CH₂, C₁₁), 43.3 (CH₂, C₈), 36.0 (CH₃, C₇)

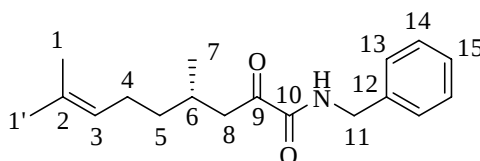
Rotamer B: 193.4 (Cq, C₉), 159.2 (Cq, C₁₀), 156.0 (Cq, C₆), 136.6 (Cq, C₁₂), 136.4 (Cq, C₄), 128.9 (2x CH, C_{Ar}), 128.4 (2x CH, C_{Ar}),

128.0 (2x CH, C_{Ar}), 127.9 (2x CH, C_{Ar}), 127.7 (2x CH, C_{Ar}), 67.4 (CH₂, C₅), 54.9 (CH₂, C₁₁), 43.3 (CH₂, C₈), 35.5 (CH₃, C₇)

MS (ESI) (m/z) 363.1 [M+Na]⁺, 395.1 [M+Na+MeOH]⁺

HRMS (ESI) m/z 363.1314 [M+Na]⁺, C₁₉H₂₀N₂O₄ Na requires 363.1321

(S)-N-Benzyl-4,8-dimethyl-2-oxonon-7-enamide 71



According to the general procedure, the (S)-N-Benzyl-4,8-dimethyl-2-oxonon-7-enamide (**71**) was obtained from (S)-citronellal and benzylisocyanide, as an oil (49%)

C₁₈H₂₅NO₂ (287.40 g.mol⁻¹)

R_f : 0.48 (Heptane/ EtOAc 4:1)

[α]_D : -4.1 °, c = 2.0, CHCl₃

IR (cm⁻¹) 3331 (N-H), 2960, 2952, 2852, 2339, 1715 (C=O *ketone*), 1667 (C=O *amide*), 1519, 1496, 1454, 1376, 1359, 1256, 1115

NMR ¹H δ (300 MHz, CDCl₃, 293K) 7.46–7.22 (6H, m, H_{Ar}, NH), 5.05–5.20 (1H, m, H₃), 4.49 (2H, d, J = 6.0 Hz, H₁₁), 2.95 (1H, dd, J₈₋₆ = 5.7 Hz, J_{8-8'} = 17.1 Hz, H₈), 2.82 (1H, dd, J_{8'-6} = 8.1 Hz, J_{8'-8} = 17.1 Hz, H_{8'}), 2.19–1.93 (3H, m, H₅, H₆), 1.70 (3H, s, H₁), 1.62 (3H, s, H_{1'}), 1.45–1.22 (2H, m, H₄), 0.95 (3H, d, J₇₋₆ = 6.6 Hz, H₇)

NMR ¹³C δ (75 MHz, CDCl₃, 293K) 198.9 (C_q, C₉), 160.1 (C_q, C₁₀), 137.0 (C_q, C₁₂), 131.6 (C_q, C₂), 128.8 (2x CH, C₁₃), 127.9 (3x CH, C₁₄, C₁₅), 124.2 (CH, C₃), 43.7 (CH₂, C₈), 43.4 (CH₂, C₁₁), 37.0 (CH₂,

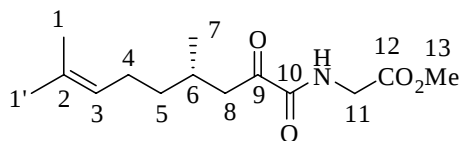
C₅), 28.8 (CH₂, C₆), 25.7 (CH₃, C_{1'}), 25.5 (CH₂, C₄), 19.8 (CH₃, C₇), 18.0 (CH₃, C₁)

MS (ESI) (m/z) 310.2 [M+Na]⁺, 342.2 [M+Na+MeOH]⁺

HRMS (ESI) m/z 310.1785 [M+Na]⁺, C₁₈H₂₅NO₂ Na requires 310.1783

(S)-4,8-dimethyl-2-oxonon-7-enoylamino] acetic acid methyl ester

7m



According to the general procedure, the (S)-4,8-dimethyl-2-oxonon-7-enoylamino] acetic acid methyl ester (**7m**) was obtained from (S)-citronellal and methyl 2-isocyanoacetate, as an oil (47%)

C₁₄H₂₃NO₄ (269.34 g.mol⁻¹)

R_f : 0.23 (Heptane/ EtOAc 4:1)

[α]_D : -8.1°, c = 2.0, CHCl₃

IR (cm⁻¹) 3376 (N-H), 2956, 2918, 2340, 1753 (C=O *ester*), 1720 (C=O *ketone*), 1681 (C=O *amide*), 1524, 1519, 1454, 1438, 1366, 1207, 1179, 1135

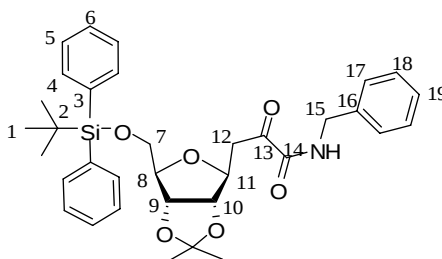
NMR ¹H δ (300 MHz, CDCl₃, 293K) 7.40 (1H, br s, NH), 5.06 (1H, br t, J = 6.9 Hz, H₃), 4.07 (2H, d, J = 5.7 Hz, H₁₁), 3.77 (3H, s, H₁₃), 2.89 (1H, dd, J₈₋₆ = 5.4 Hz, J_{8-8'} = 17.1 Hz, H₈), 2.75 (1H, dd, J_{8'-6} = 8.1 Hz, J_{8'-8} = 17.1 Hz, H_{8'}), 2.13-1.84 (3H, m, H₅, H₆), 1.66 (3H, s, H₁), 1.58 (3H, s, H_{1'}), 1.44-1.14 (2H, m, H₄), 0.92 (3H, d, J₇₋₆ = 6.9 Hz, H₇)

NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 197.9 (C_q , C_9), 169.2 (C_q , C_{10}), 160.3 (C_q , C_{12}), 131.6 (C_q , C_2), 124.1 (CH , C_3), 52.5 (CH_3 , C_{13}), 43.6 (CH_3 , C_8), 40.9 (CH_2 , C_{11}), 36.9 (CH_2 , C_4), 28.7 (CH , C_6), 25.6 (CH_3 , C_1), 25.4 (CH_3 , C_5), 19.7 (CH_2 , C_7), 17.6 (CH_3 , $\text{C}_{1'}$)

MS (ESI) (m/z) 292.1 $[\text{M}+\text{Na}]^+$, 324.2 $[\text{M}+\text{Na}+\text{MeOH}]^+$

HRMS (ESI) m/z 292.1527 $[\text{M}+\text{Na}]^+$, $\text{C}_{14}\text{H}_{23}\text{NO}_4 \text{ Na}$ requires 292.1525

***N*-benzyl-3-((3 α S,4S,6R,6 α R)-6-((*tert*-butyldiphenylsilyloxy)methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-2-oxopropanamide 7n**



According to the general procedure, the (*S*)-*N*-Benzyl-4,8-dimethyl-2-oxonon-7-enamide (**7n**) was obtained from 2-((3 α S,4S,6R,6 α R)-6-((*tert*-butyldiphenylsilyloxy)methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)acetaldehyde and benzylnisocyanide, as an oil (68%)

$\text{C}_{34}\text{H}_{41}\text{NO}_6\text{Si}$ (587.78 $\text{g}\cdot\text{mol}^{-1}$)

R_f : 0.40 (Heptane/ EtOAc 4:1)

$[\alpha]_\text{D}$: -2.9 °, $c = 0.90$, CHCl_3

IR (cm^{-1}) 3335 (N-H), 2929, 2856, 1722 (C=O *ketone*), 1682 (C=O *amide*), 1520, 1471, 1455, 1427, 1381, 1372, 1258, 1210, 1111, 1075

NMR ^1H δ (300 MHz, CDCl_3 , 293K) 7.74–7.62 (4H, m, H_4), 7.49–7.31 (12H, m, H_{Ar}), 4.75 (1H, dd, $J_{9,10} = 3.0$ Hz, $J_{9,8} = 6.0$ Hz, H_9), 4.54–4.35 (4H, m, H_{10} , H_{11} , H_{15}), 4.15–4.04 (1H, m, H_8), 3.75 (2H, d, $J_{7,8} = 3.9$ Hz, H_7), 3.34–3.26 (2H, m, H_{12}), 1.55 (3H, s, $\text{C}(\text{CH}_3)_2$), 1.35 (3H, s, $\text{C}(\text{CH}_3)_2$), 1.06 (9H, s, H_1)

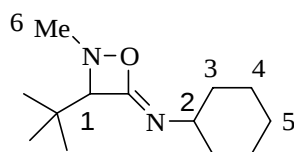
NMR ^{13}C δ (75 MHz, CDCl_3 , 293K) 196.1 (Cq, C_{13}), 159.6 (Cq, C_{14}), 136.8 (Cq, C_{16}), 135.6 (4x CH, C_4 and $\text{C}_{4'}$), 133.2 (Cq, C_3), 133.1 (Cq, $\text{C}_{3'}$), 129.7 (2x CH, C_{Ar}), 128.8 (2x CH, C_{Ar}), 127.8 (3x CH, C_{Ar}), 127.7 (4x CH, C_{Ar}), 114.2 (Cq, CMe_2), 84.6 (CH, C_{10}), 84.5 (CH, C_8), 81.8 (CH, C_9), 80.0 (CH, C_{11}), 64.0 (CH_2 , C_7), 43.4 (CH_2 , C_{15}), 41.0 (CH_2 , C_{12}), 27.5 (CH_3 , CMe_2), 26.8 (CH_3 , C_1), 25.6 (CH_3 , CMe_2), 19.2 (Cq, C_2)

MS (ESI) (m/z) 610.2 $[\text{M}+\text{Na}]^+$, 642.2 $[\text{M}+\text{Na}+\text{MeOH}]^+$

HRMS (ESI) m/z 610.2590 $[\text{M}+\text{Na}]^+$, $\text{C}_{34}\text{H}_{41}\text{NO}_6$ SiNa requires 610.2601

***N*-(3-tert-butyl-2-methyl-1,2-oxazetidin-4-ylidene)cyclohexanamine**

15

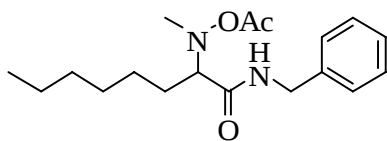


A mixture of cyclohexylisocyanide (270 μL , 2.17 mmol) and triethylamide (300 μL , 2.17 mmol) in dry dichloromethane (2 mL) is added to solution of *N*-(2,2-dimethylpropylidene)methanamine oxide (310 mg, 2.17 mmol) and $\text{BF}_3 \cdot \text{OEt}_2$ (260 μL , 2.06 mmol) in dry dichloromethane (4 mL) at -40°C . The reaction mixture was stirred for 5 min and quenched with saturated solution of NaHCO_3 (15 mL)

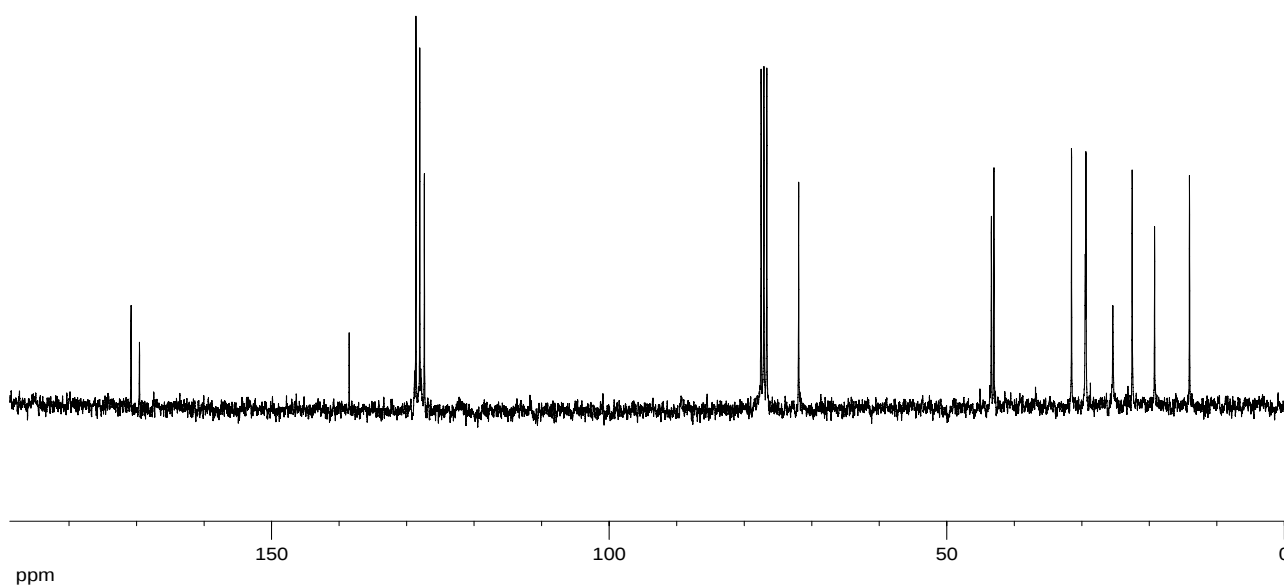
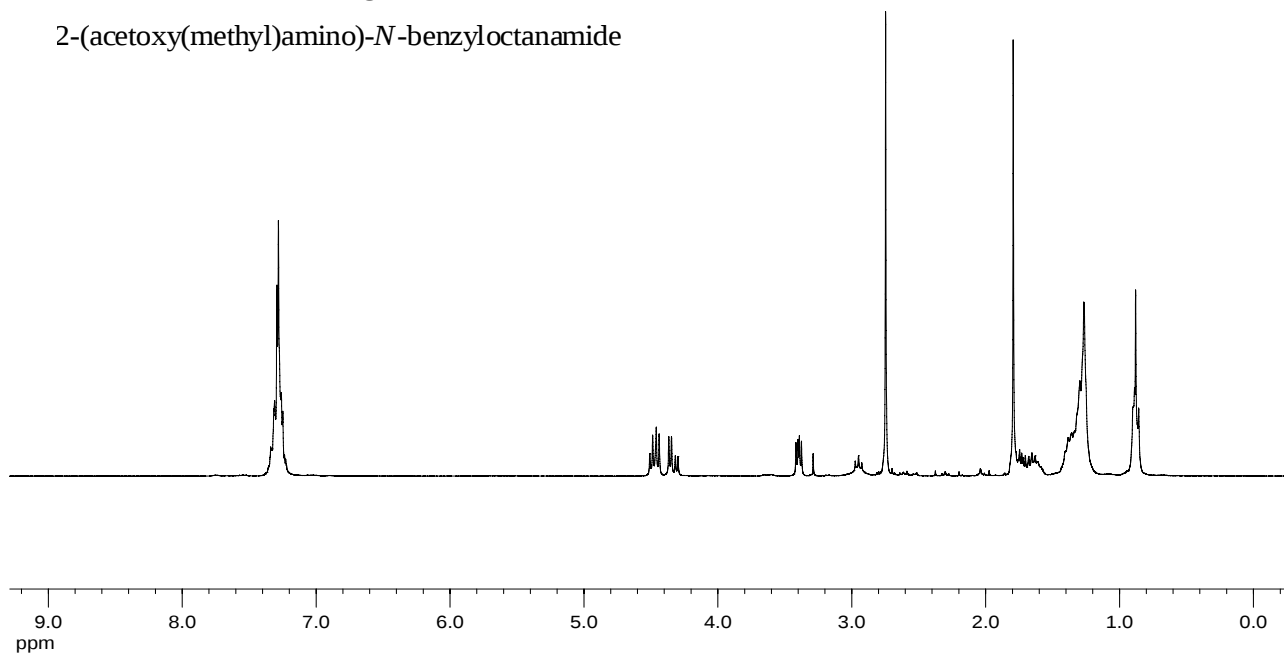
and extracted with dichloromethane. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford **15** (296 mg, 61%) as an oil.

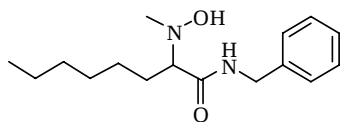
C₁₃H₂₄N₂O (224.34 g.mol⁻¹)

NMR ¹H δ (300 MHz, CDCl₃, 293K) 3.62 (1H, s, H₁), 3.42-3.30 (1H, m, H₂), 2.91 (3H, s, H₆), 1.85-1.04 (10H, m, H₃, H₄ and H₅), 0.96 (9H, s, C(CH₃)₃)

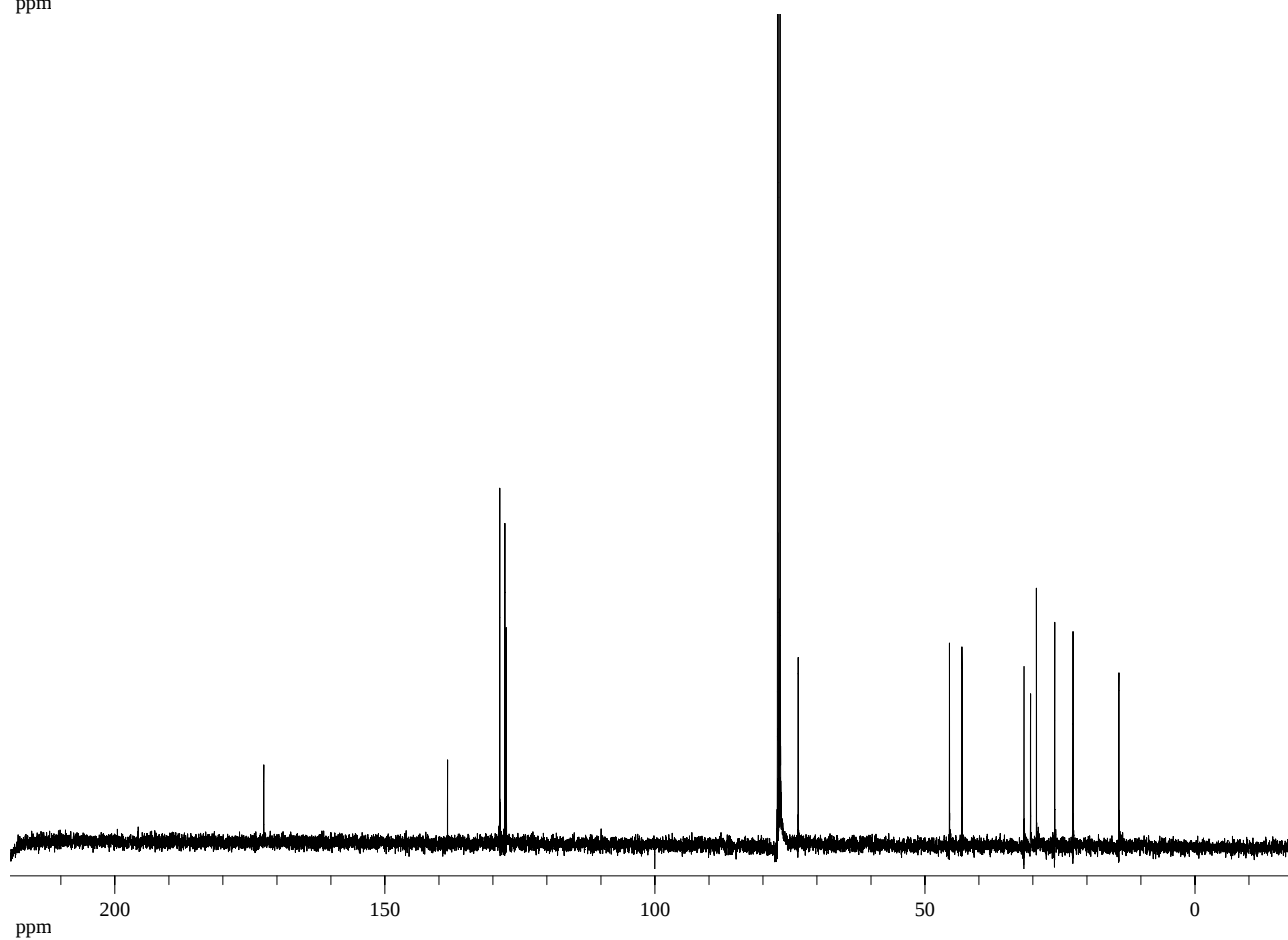
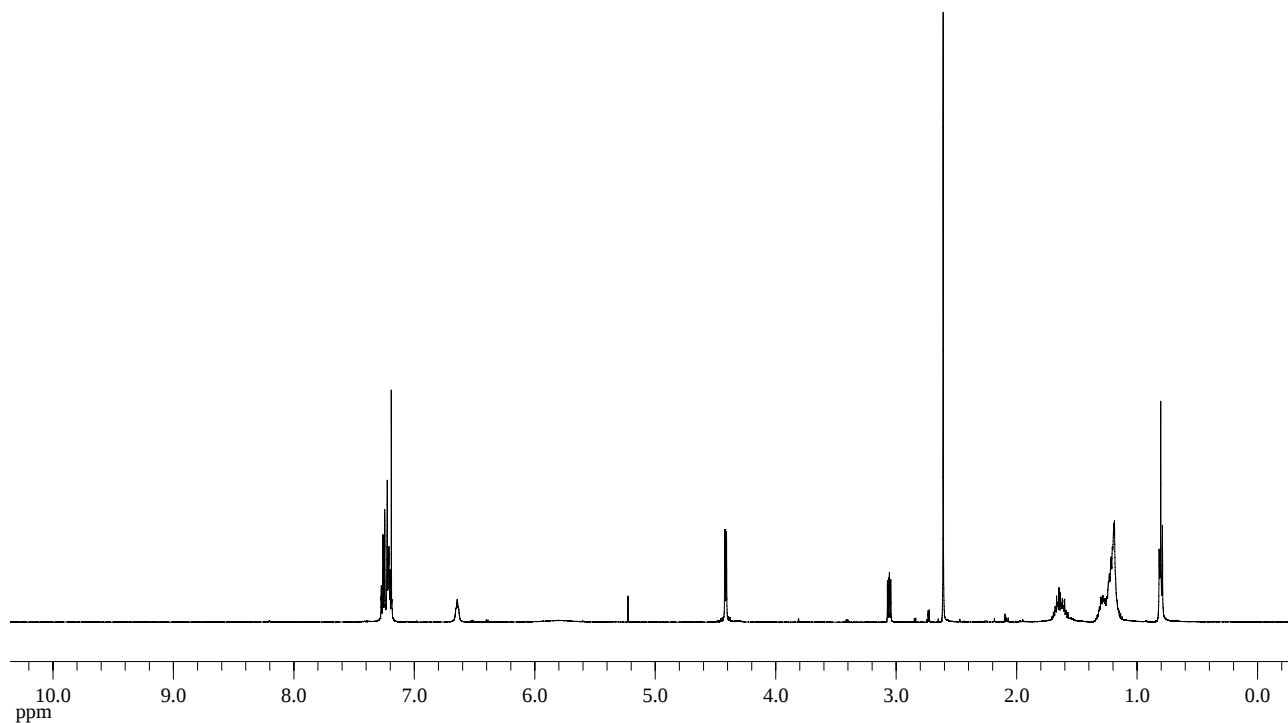


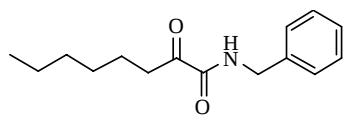
2-(acetoxy(methyl)amino)-*N*-benzyloctanamide



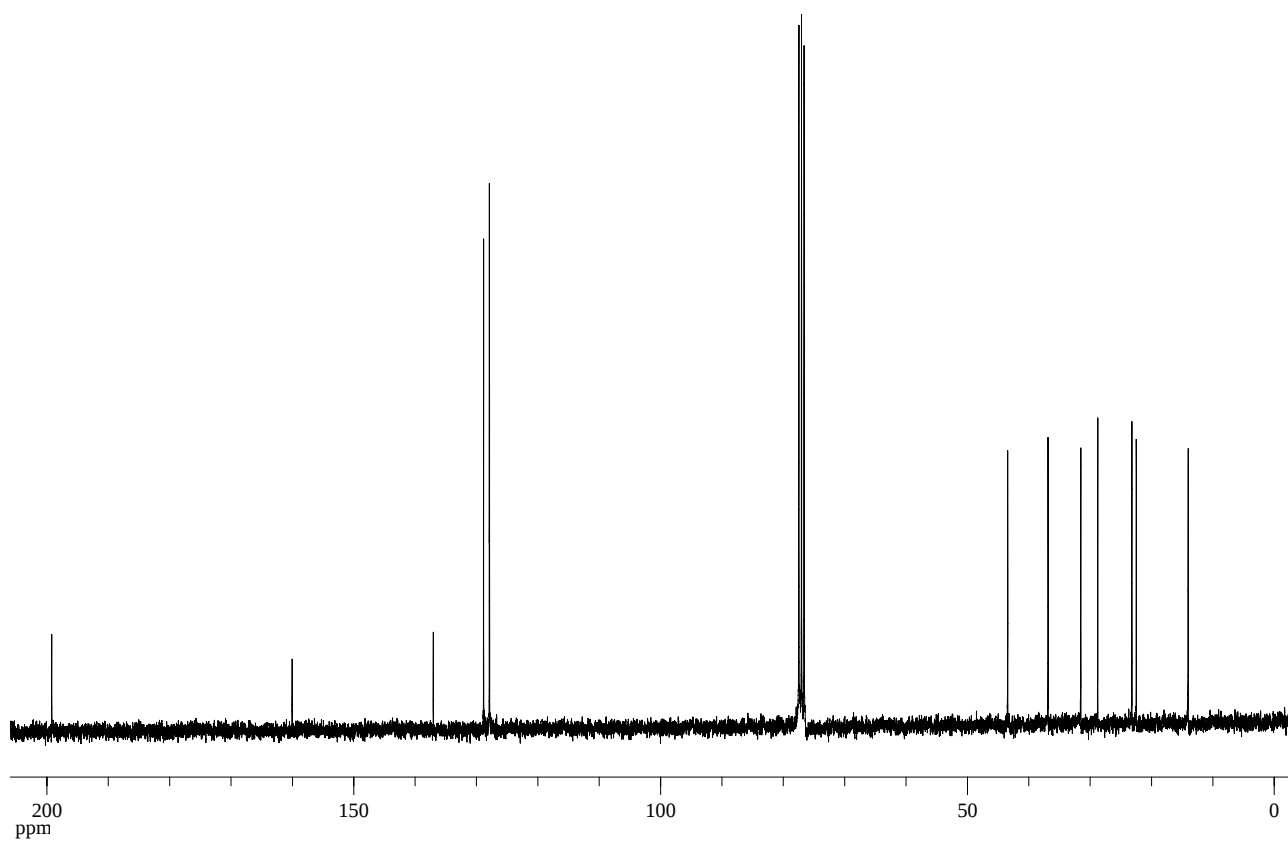
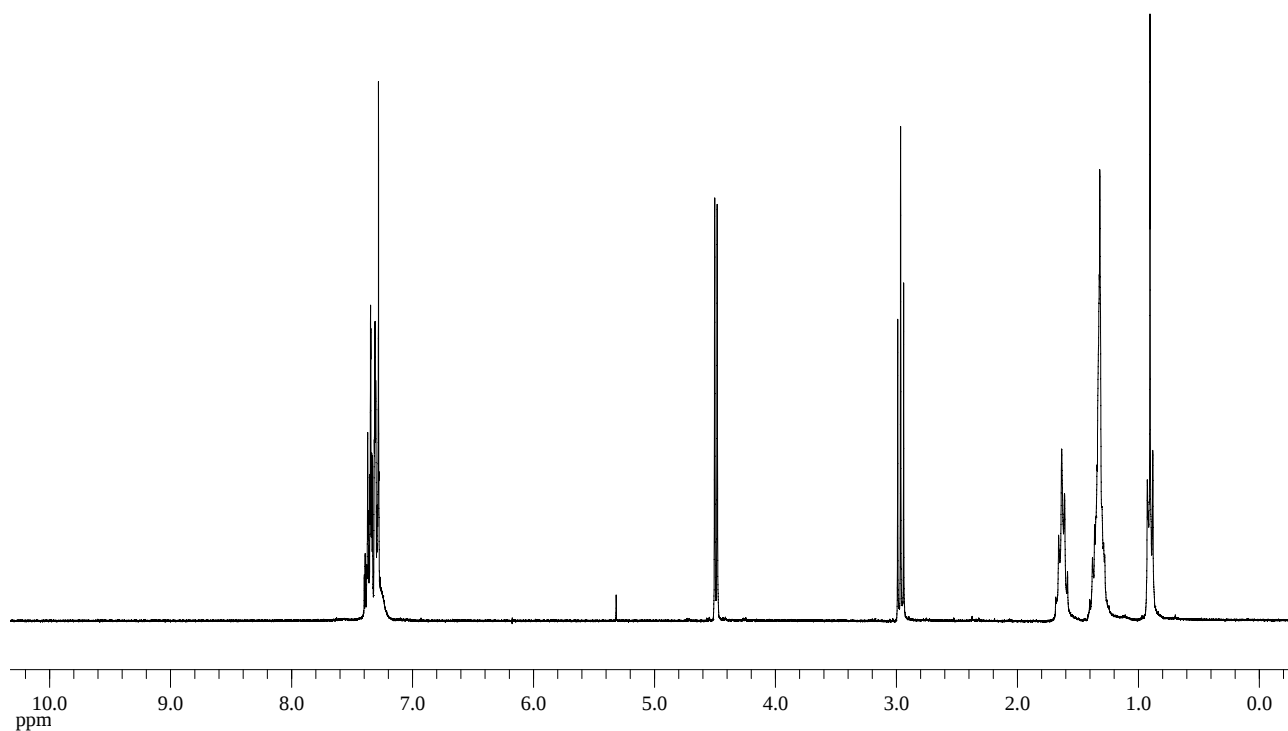


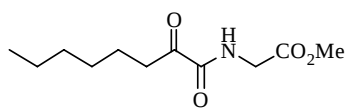
N-benzyl-2-[hydroxy(methyl)amino]octanamide



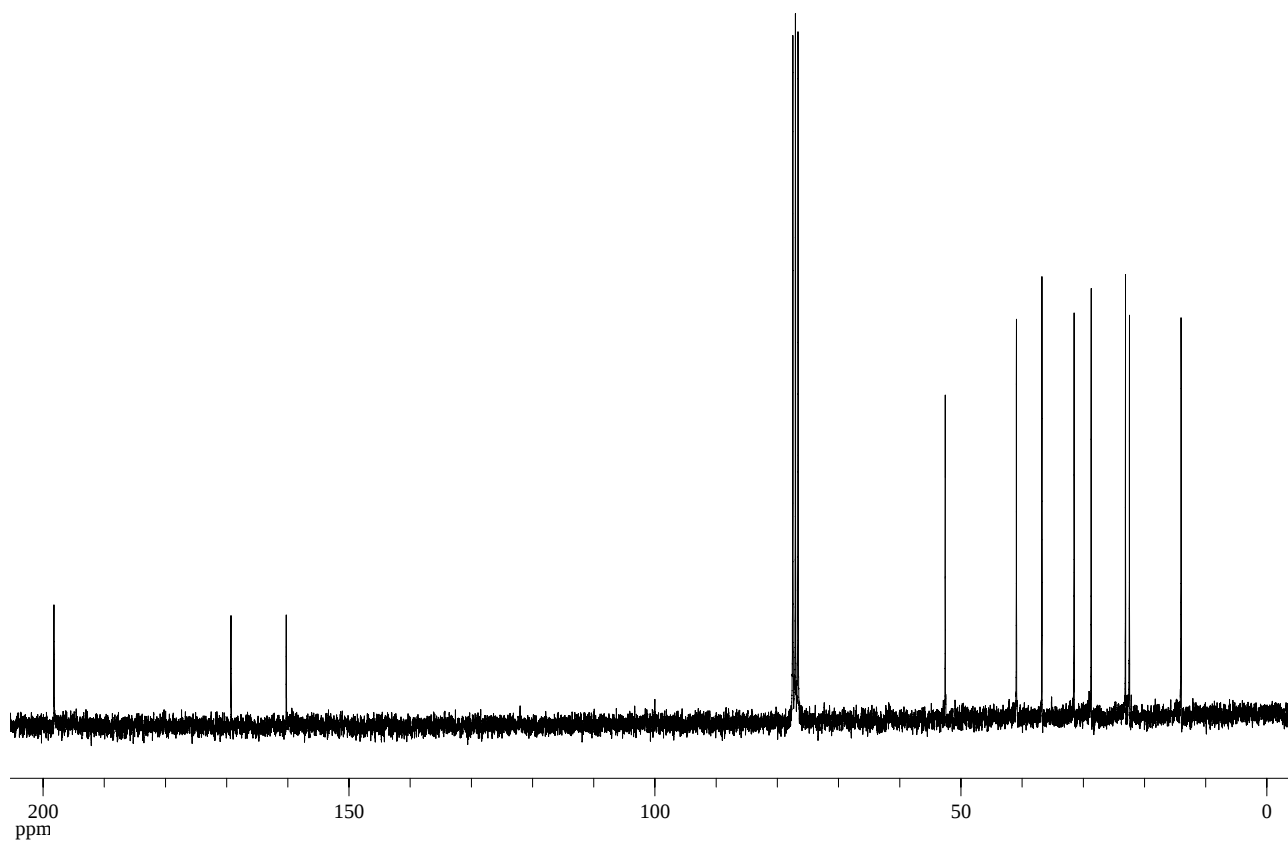
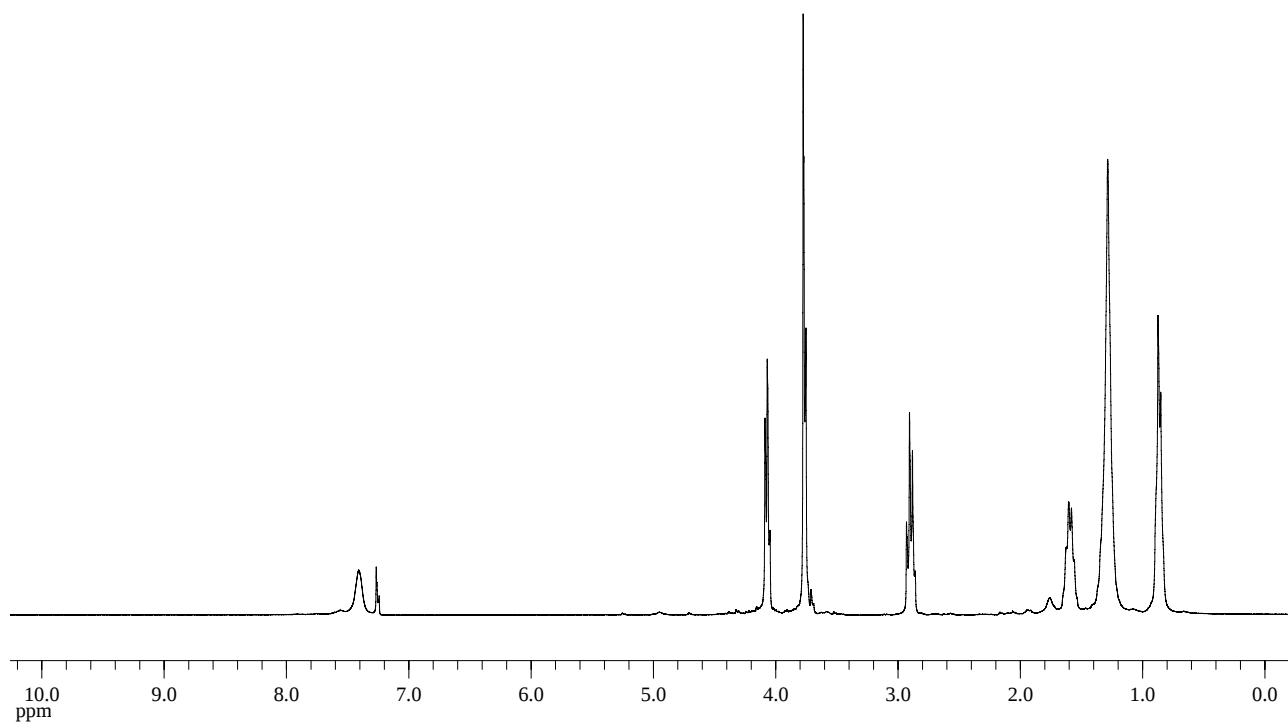


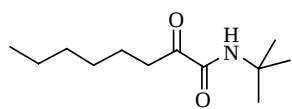
N-Benzyl-2-oxooctanamide



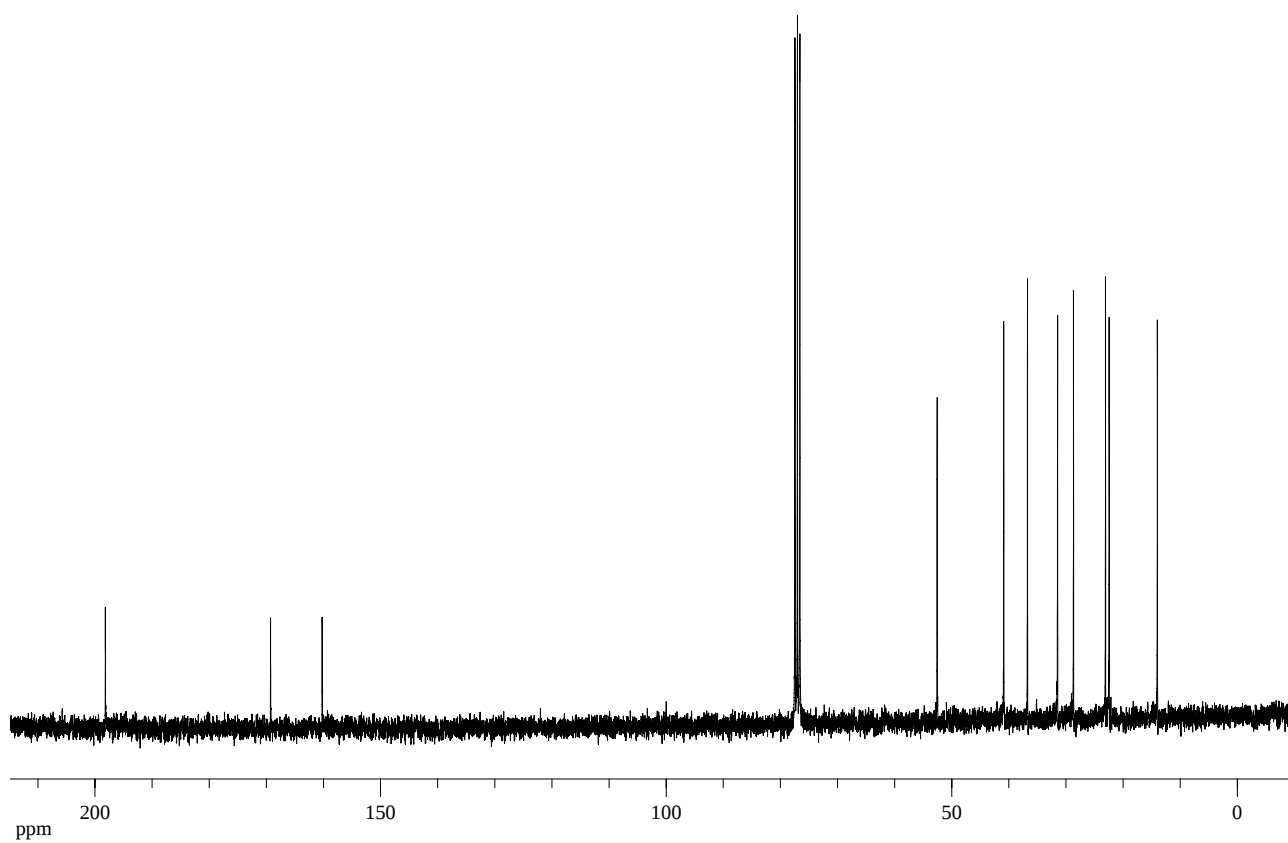
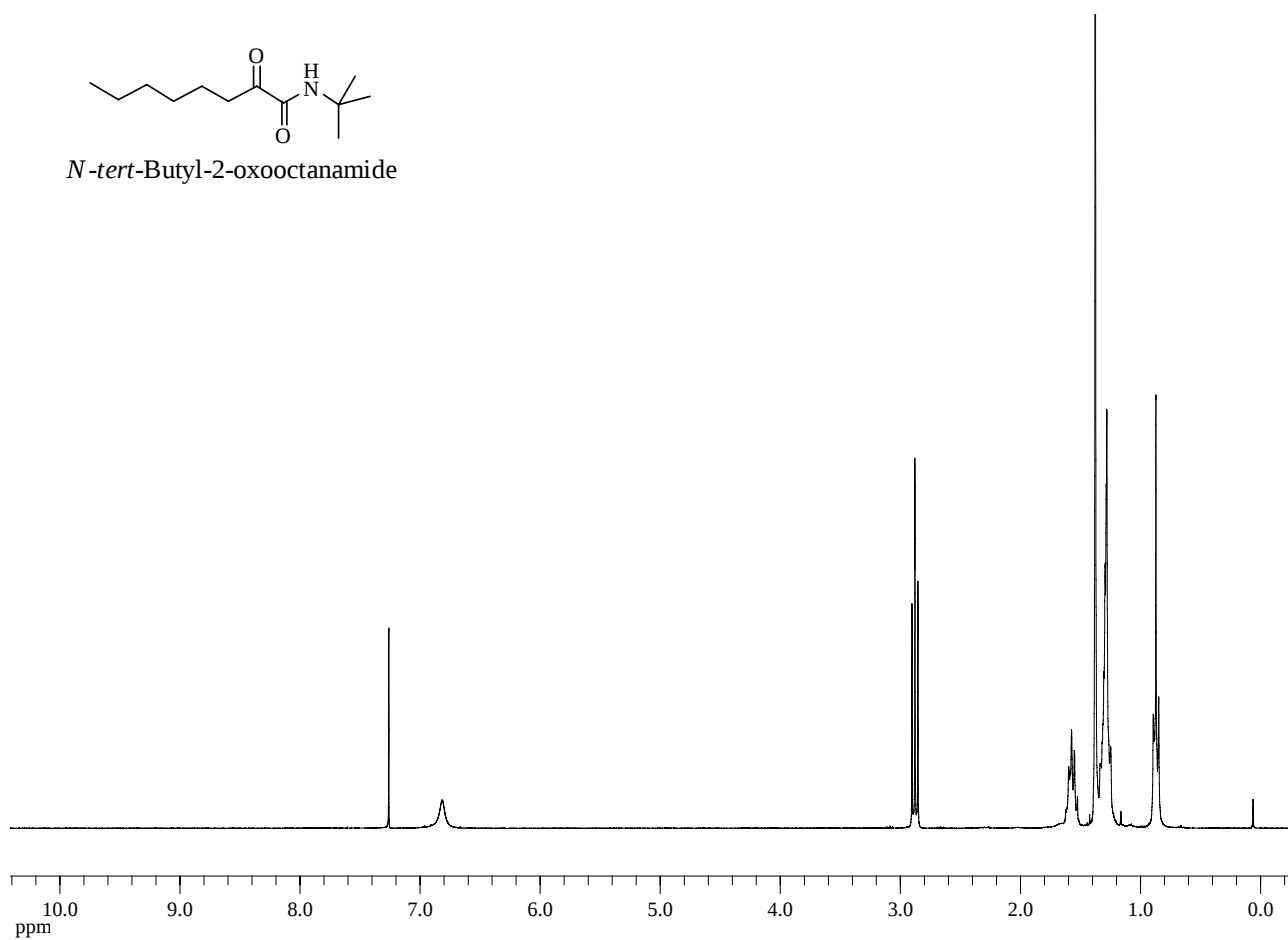


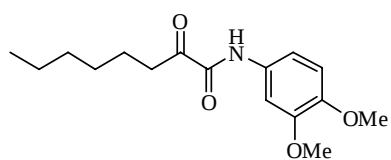
Methyl *N*-(2-oxooctanoyl)glycinate



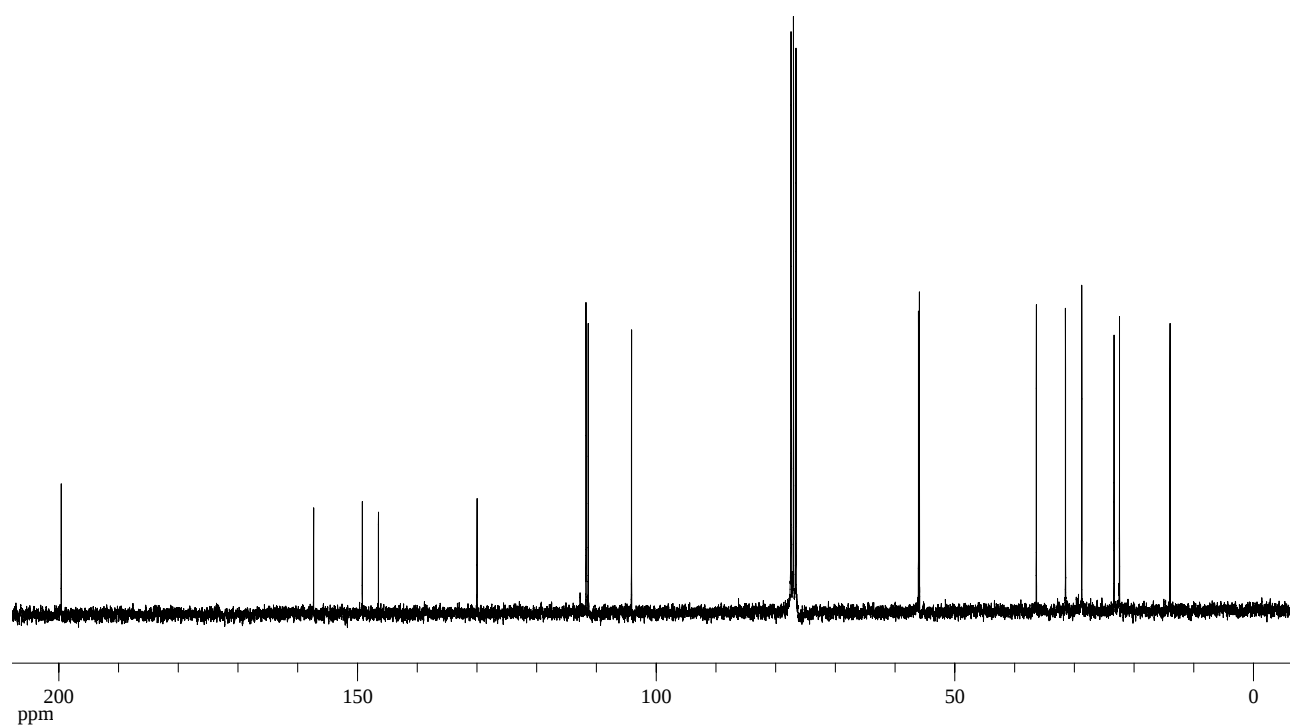
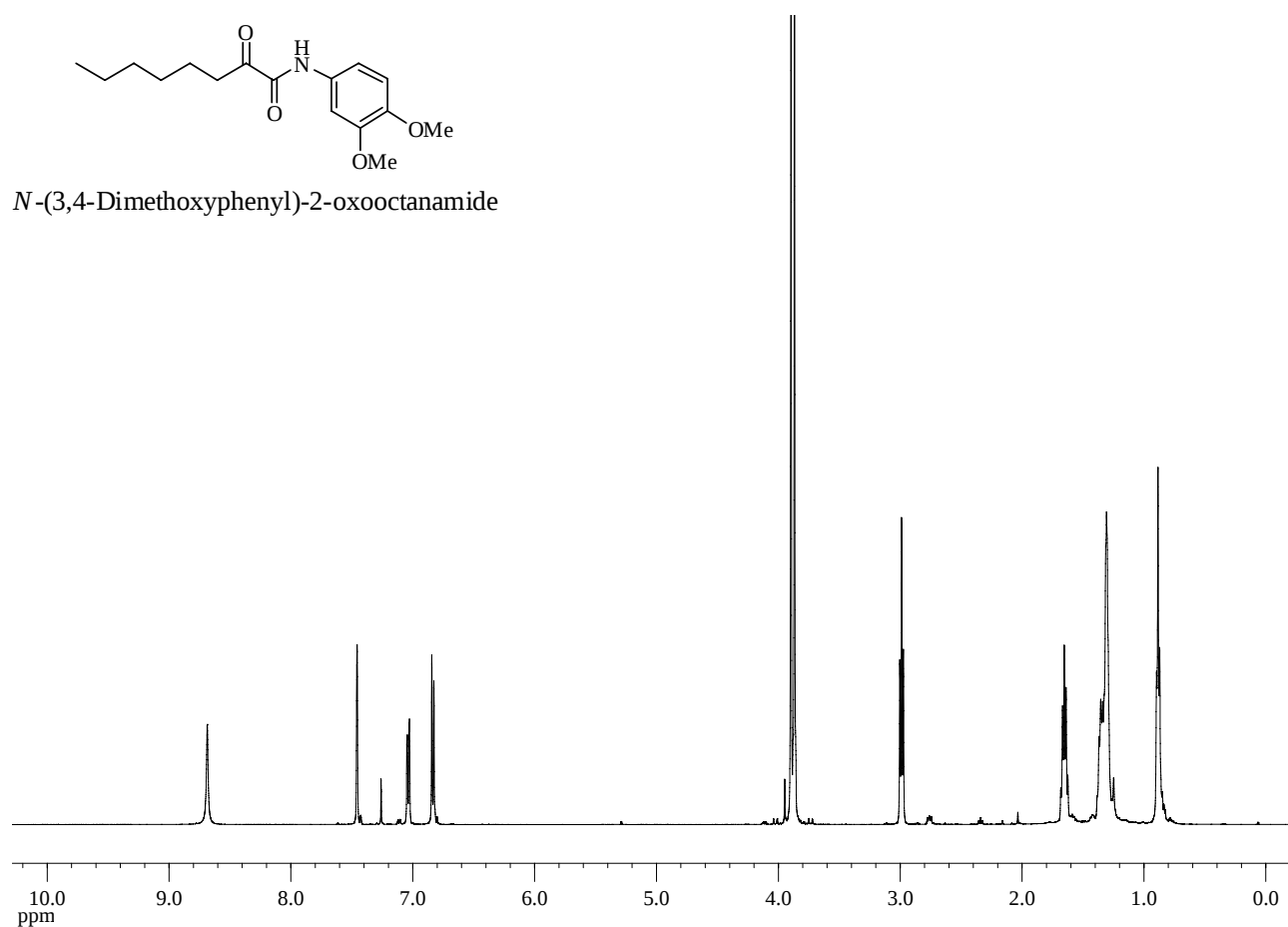


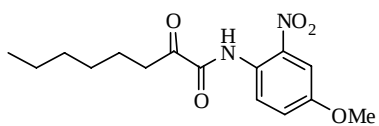
N-*tert*-Butyl-2-oxooctanamide



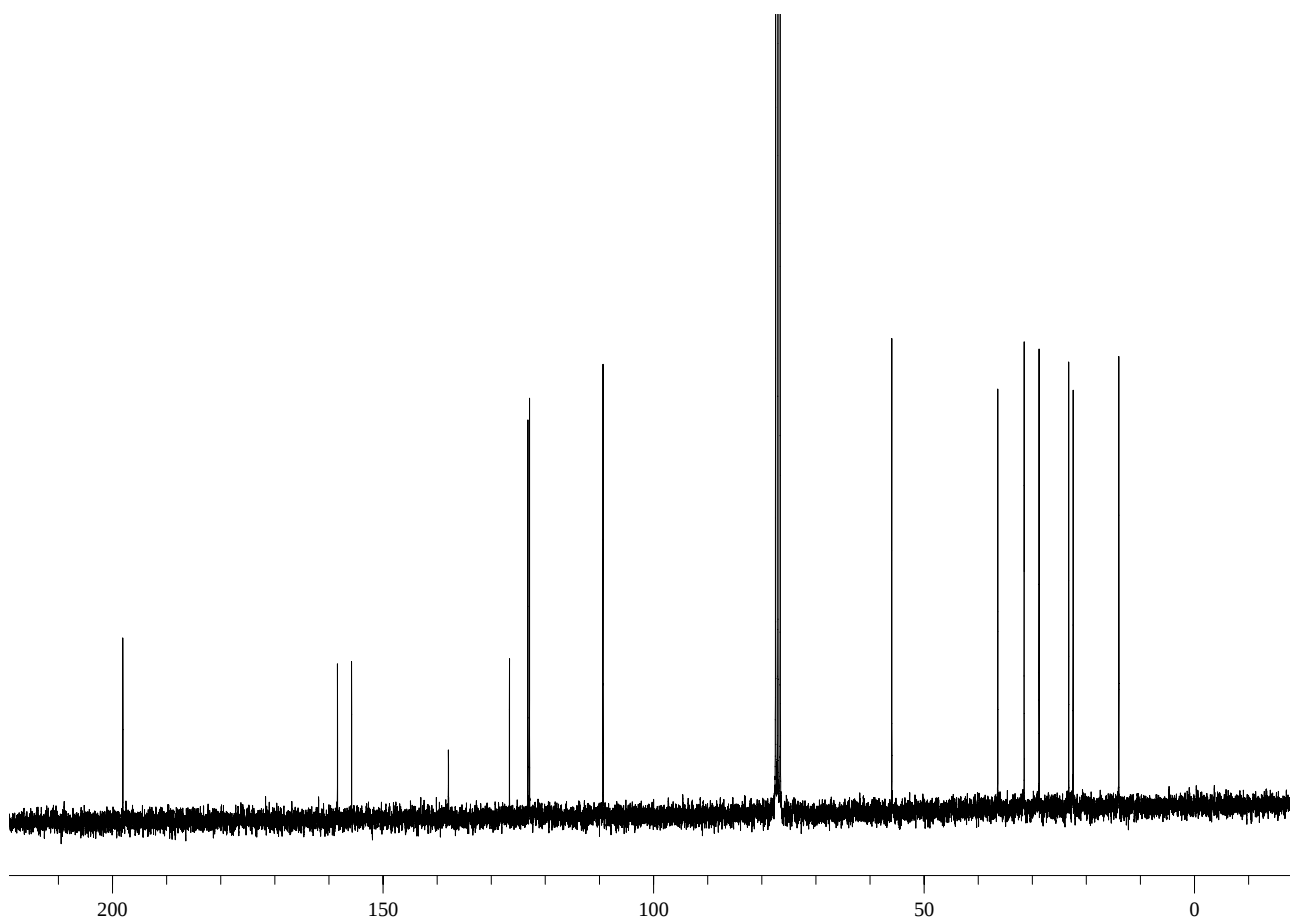
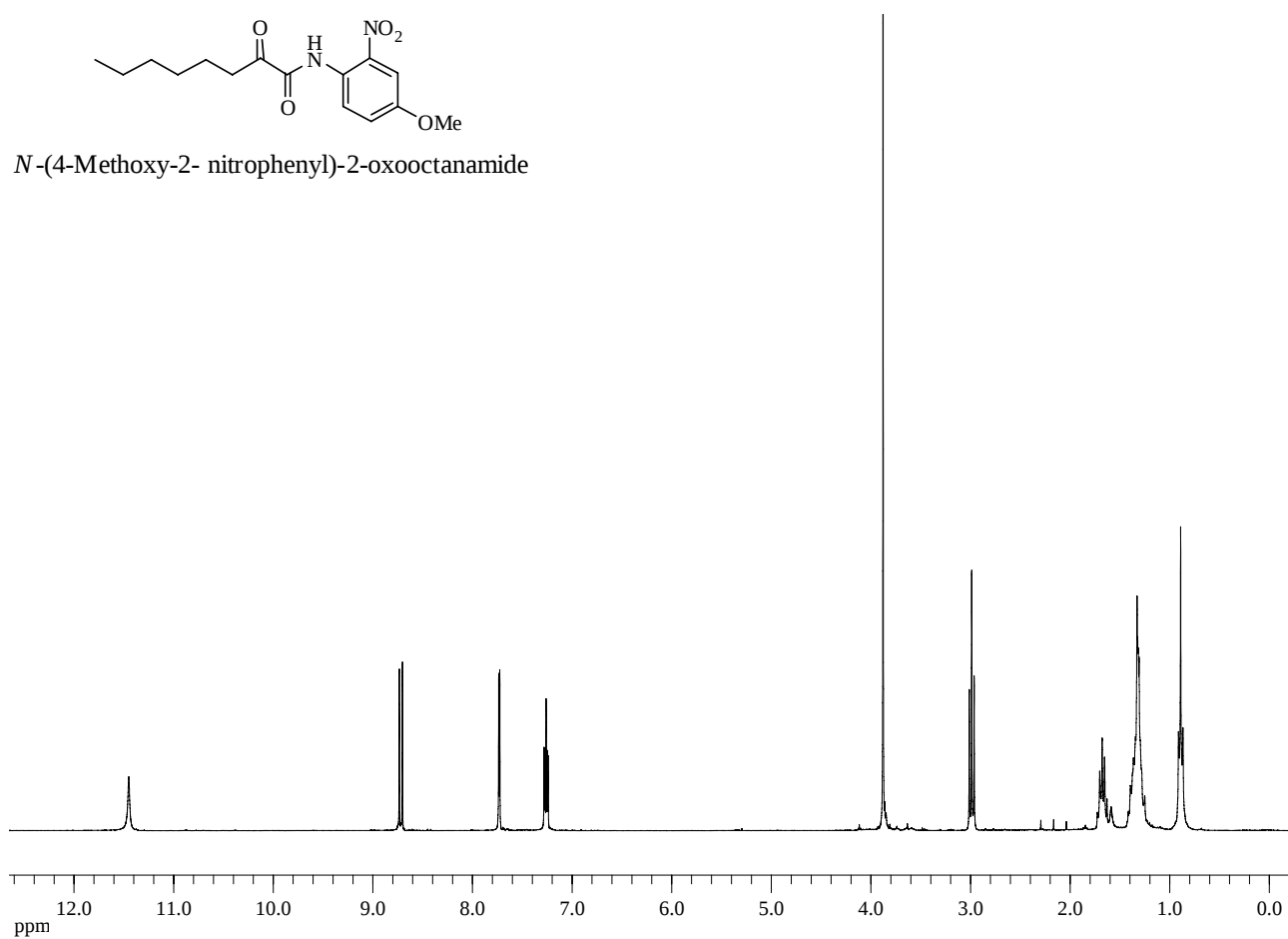


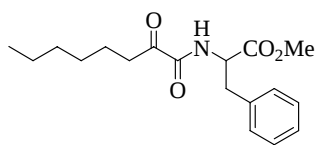
N-(3,4-Dimethoxyphenyl)-2-oxooctanamide



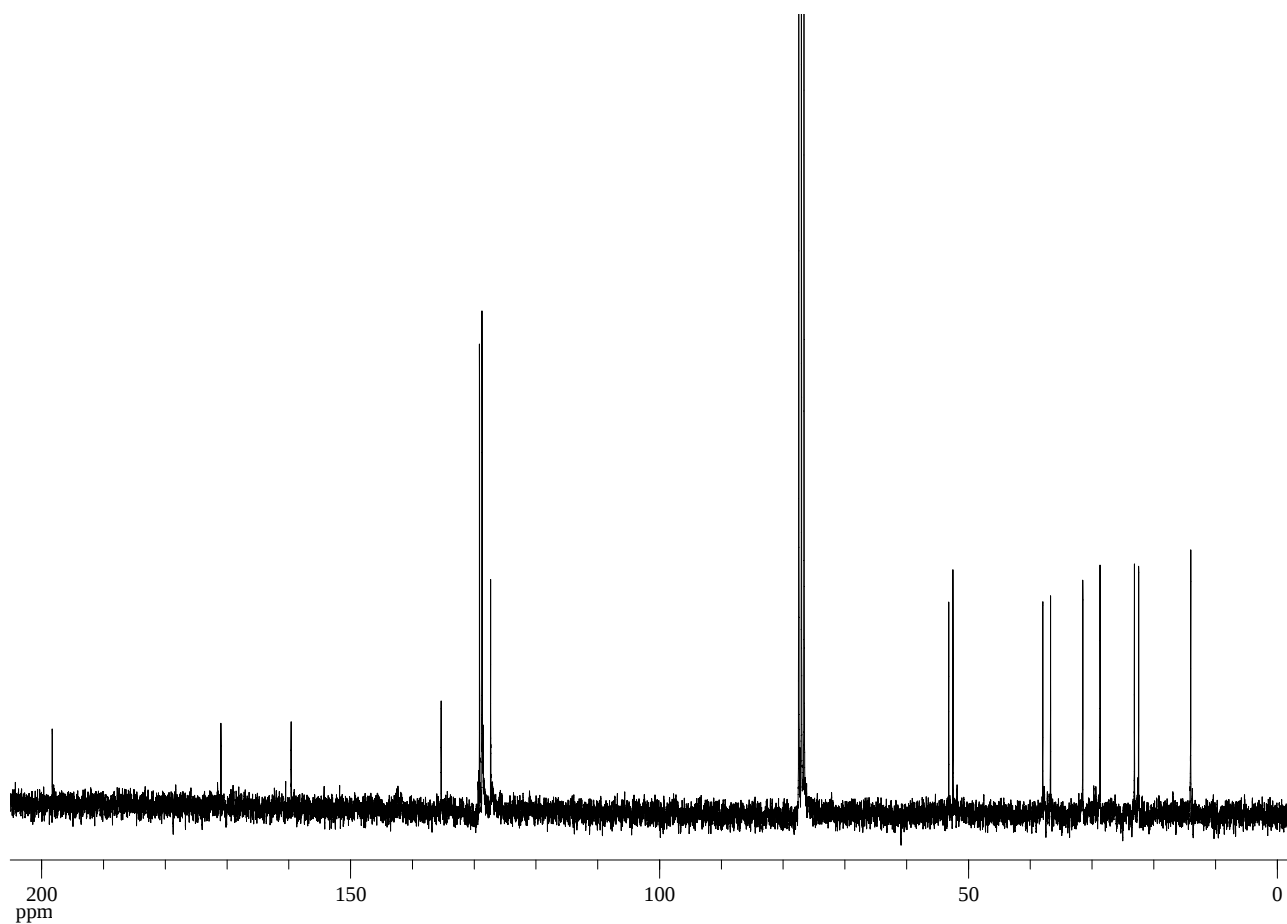
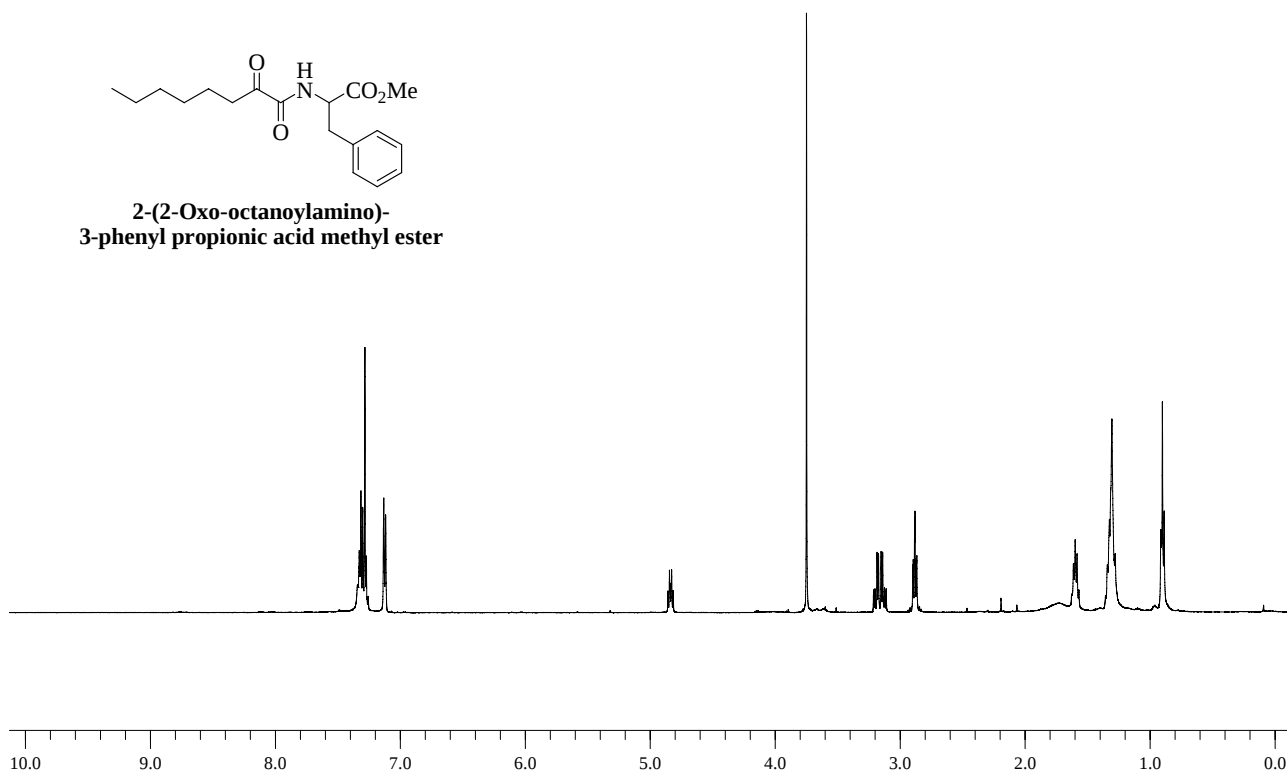


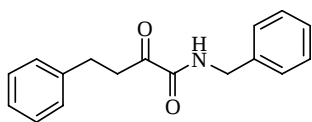
N-(4-Methoxy-2- nitrophenyl)-2-oxooctanamide



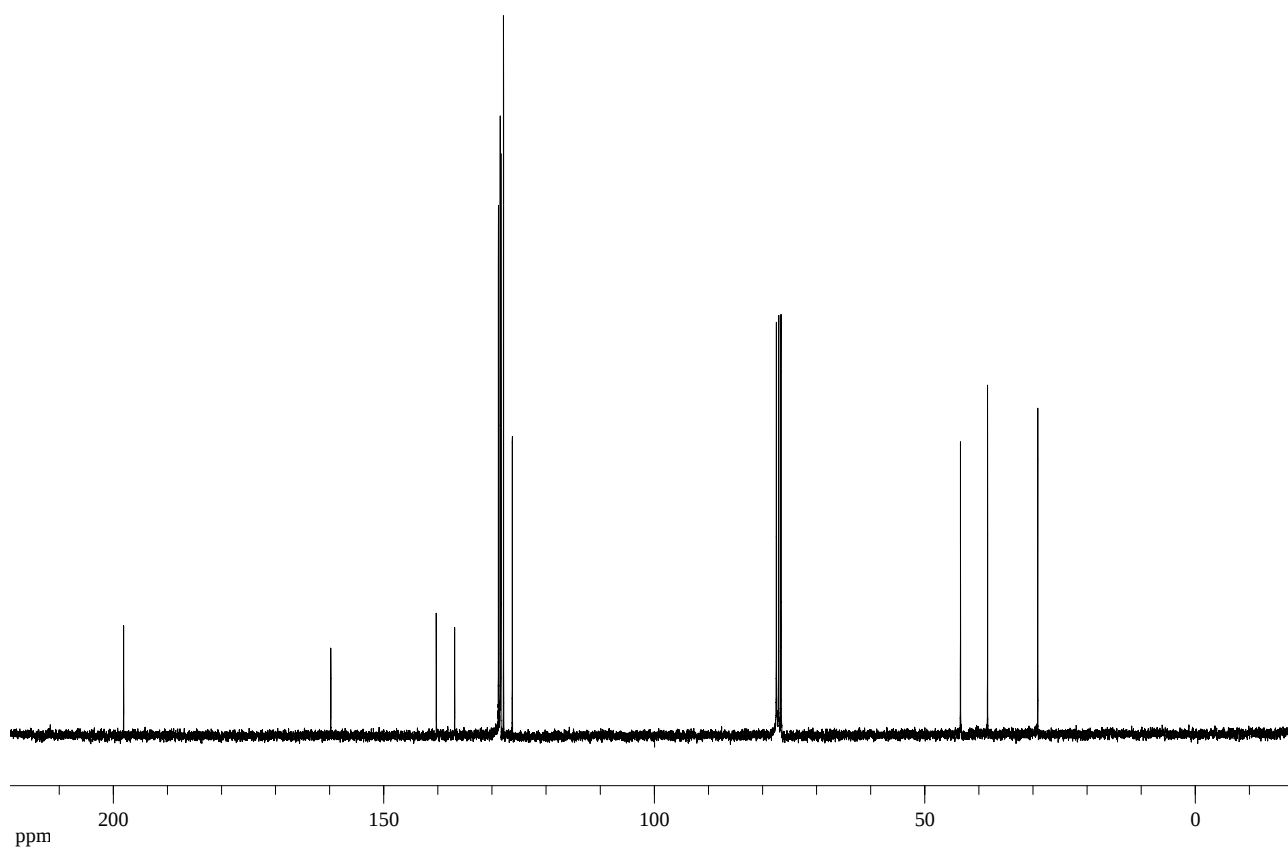
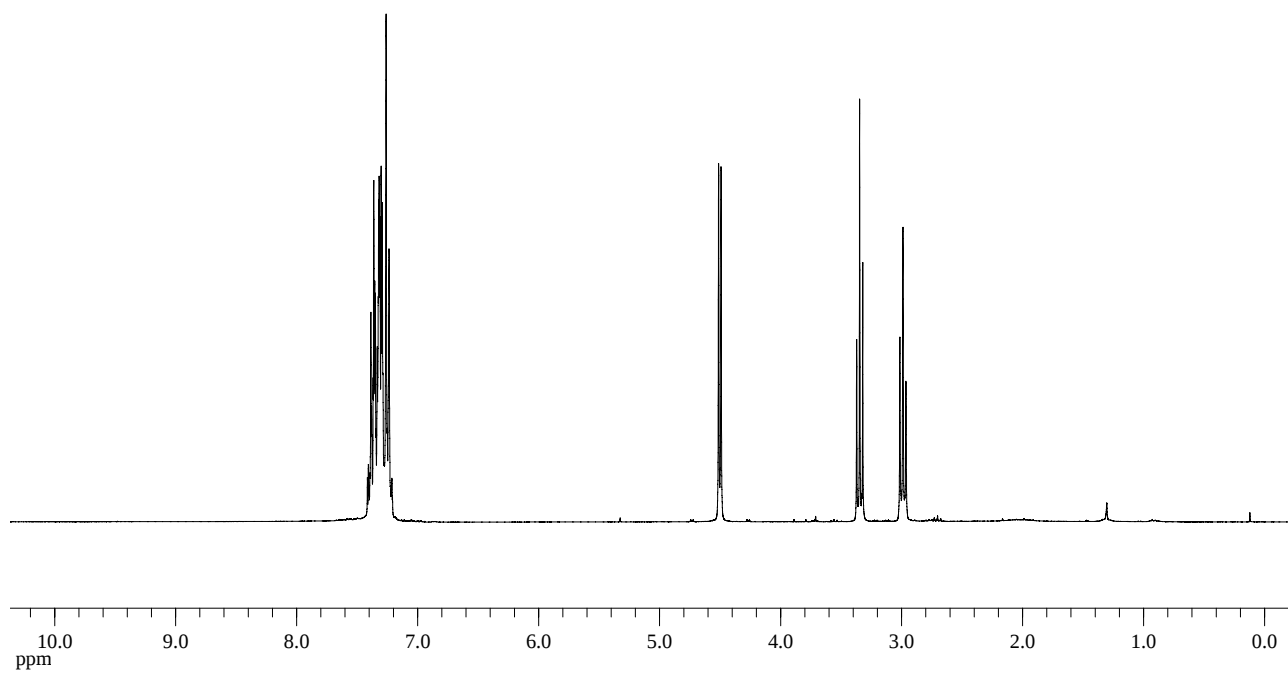


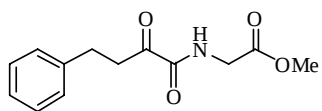
**2-(2-Oxo-octanoylamino)-
3-phenyl propionic acid methyl ester**



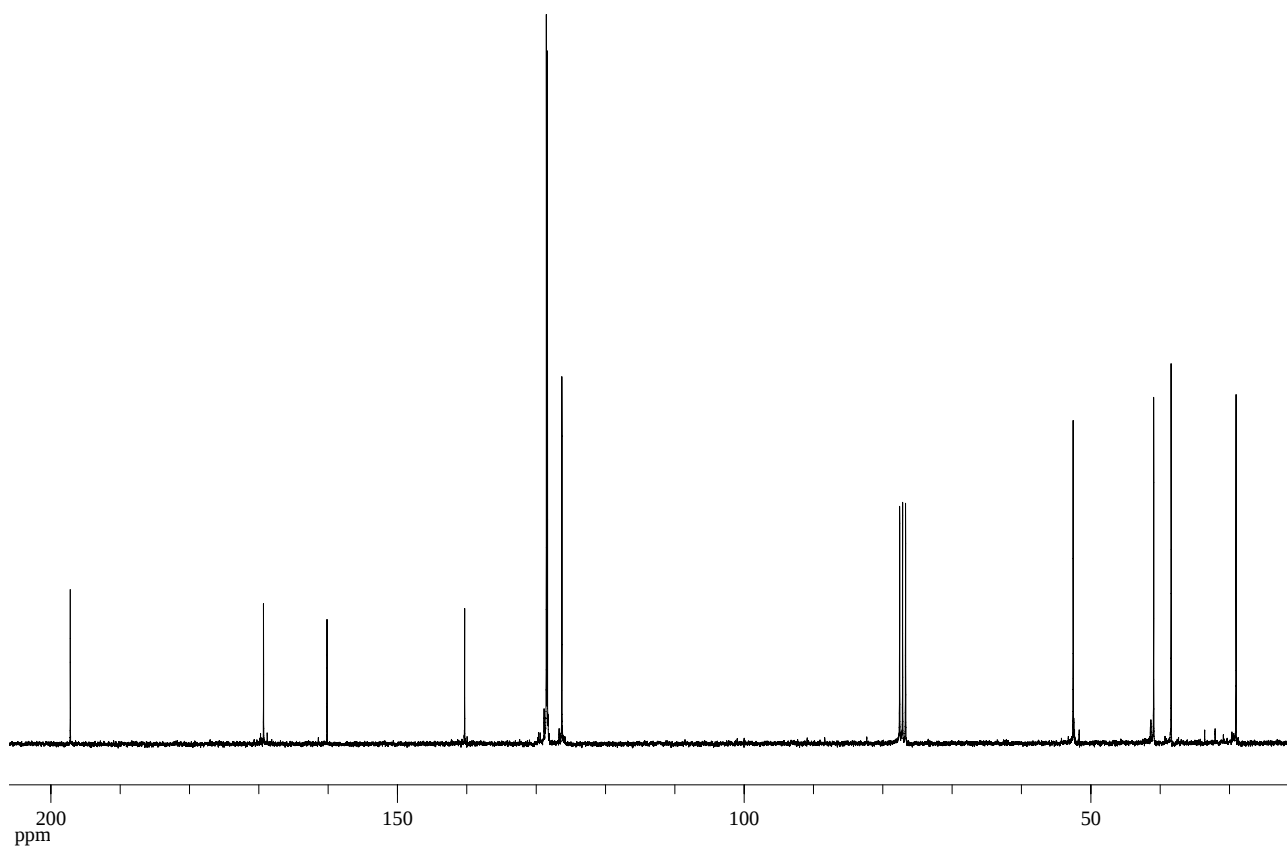
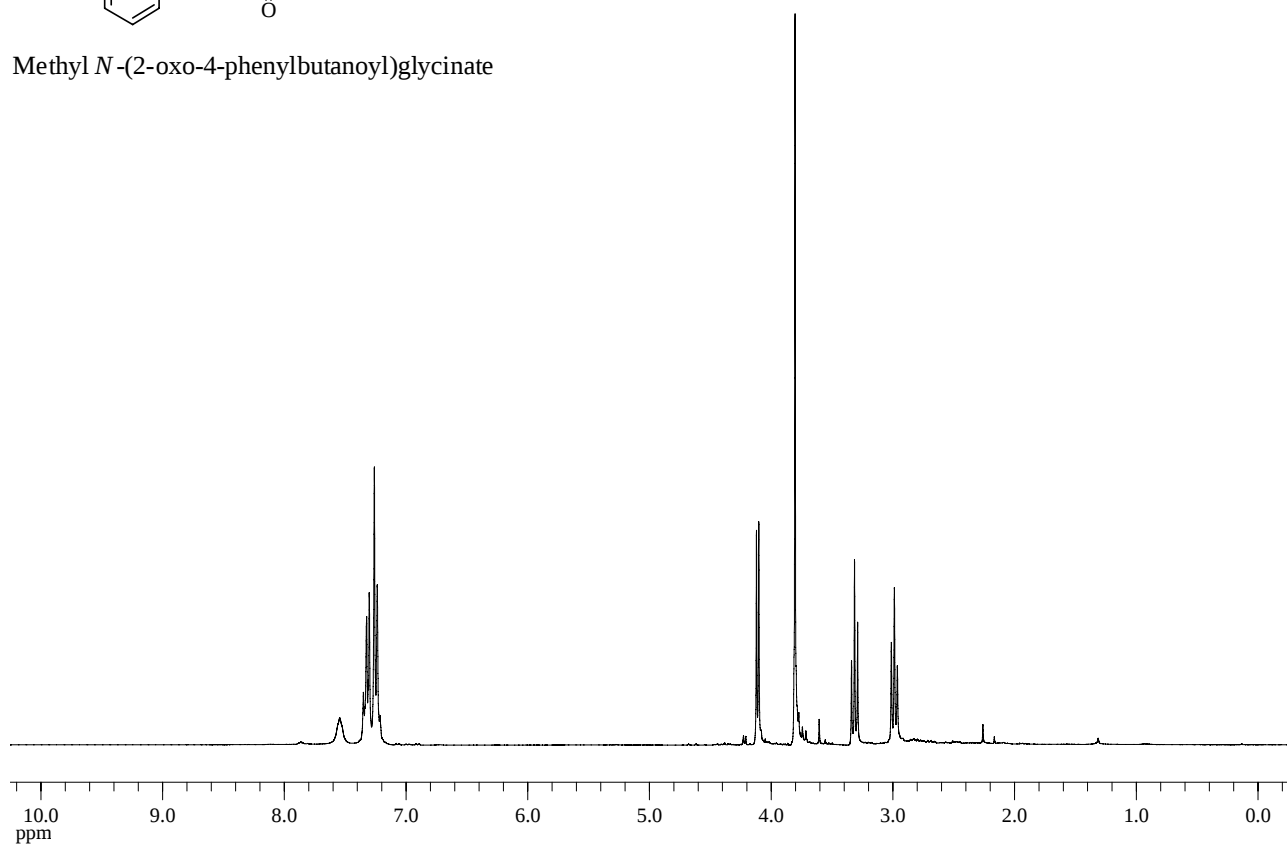


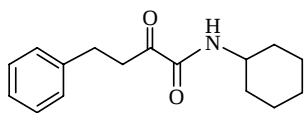
N-Benzyl-2-oxo-4-phenylbutanamide



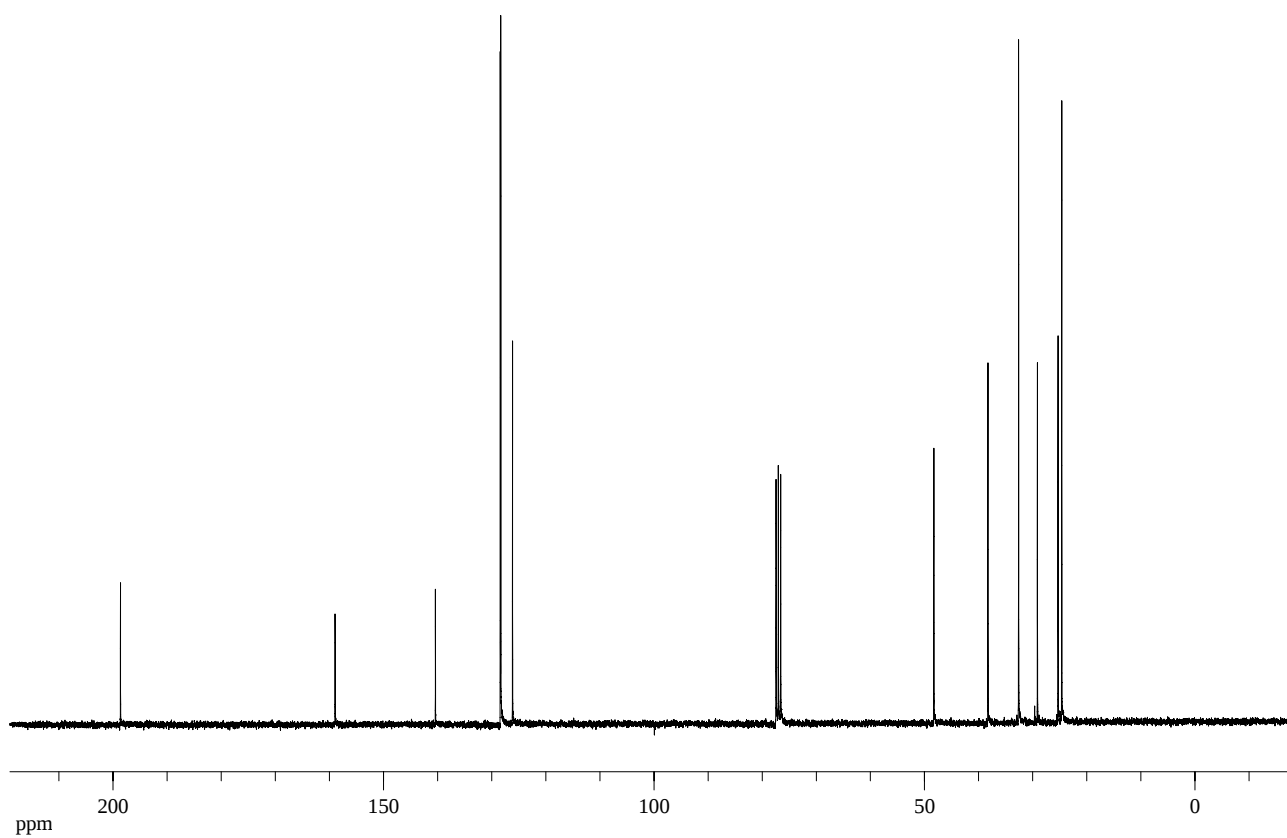
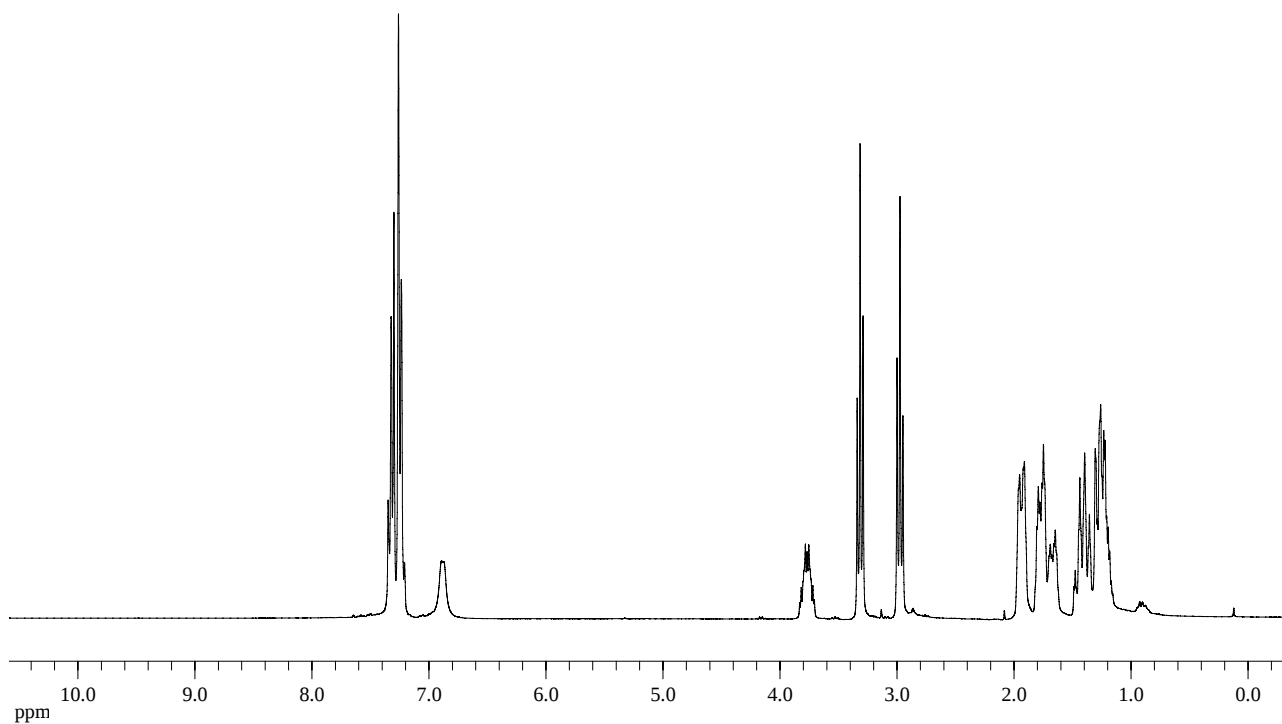


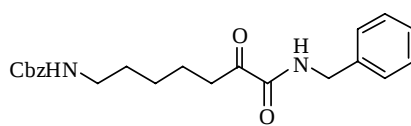
Methyl *N*-(2-oxo-4-phenylbutanoyl)glycinate



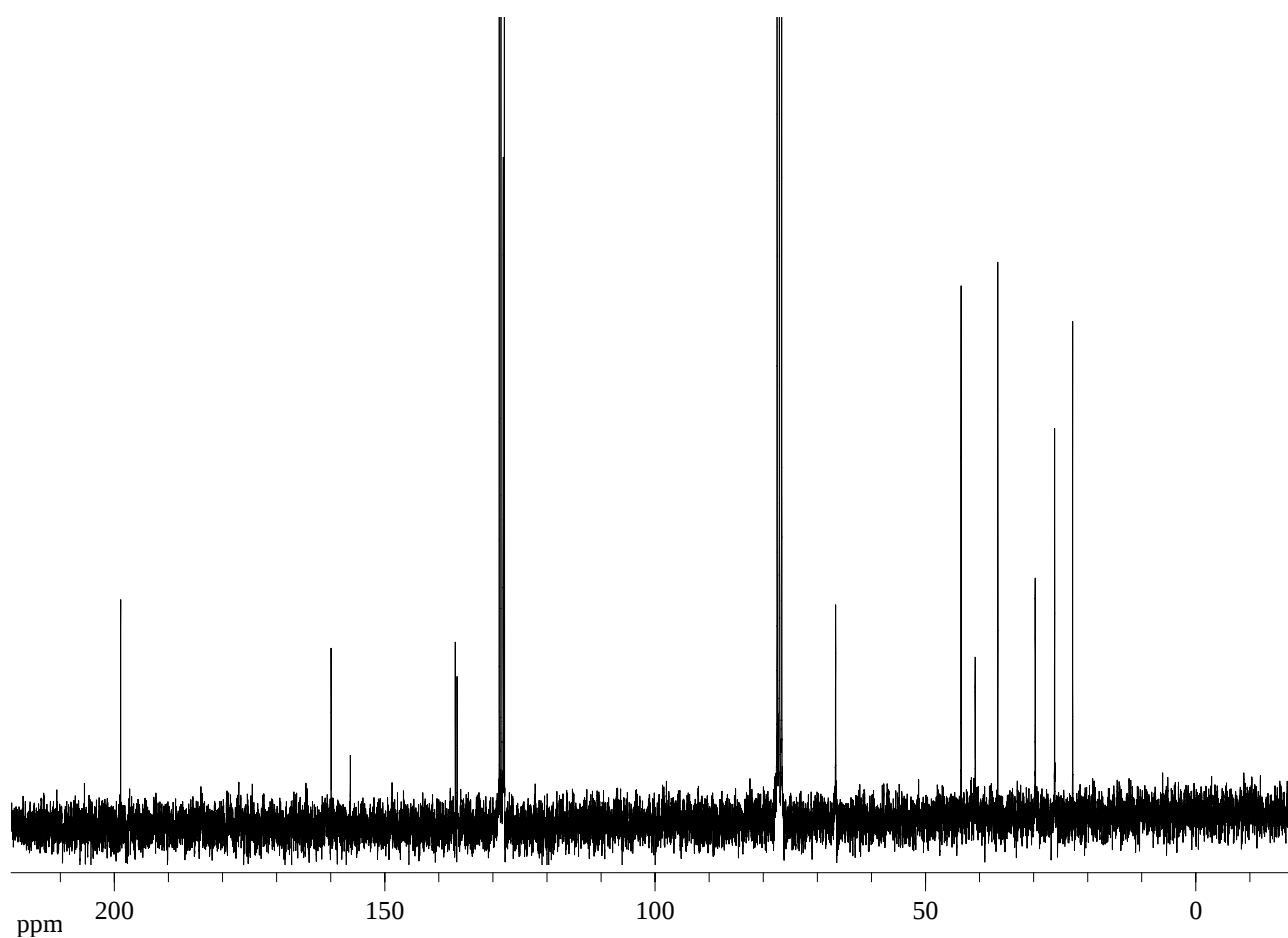
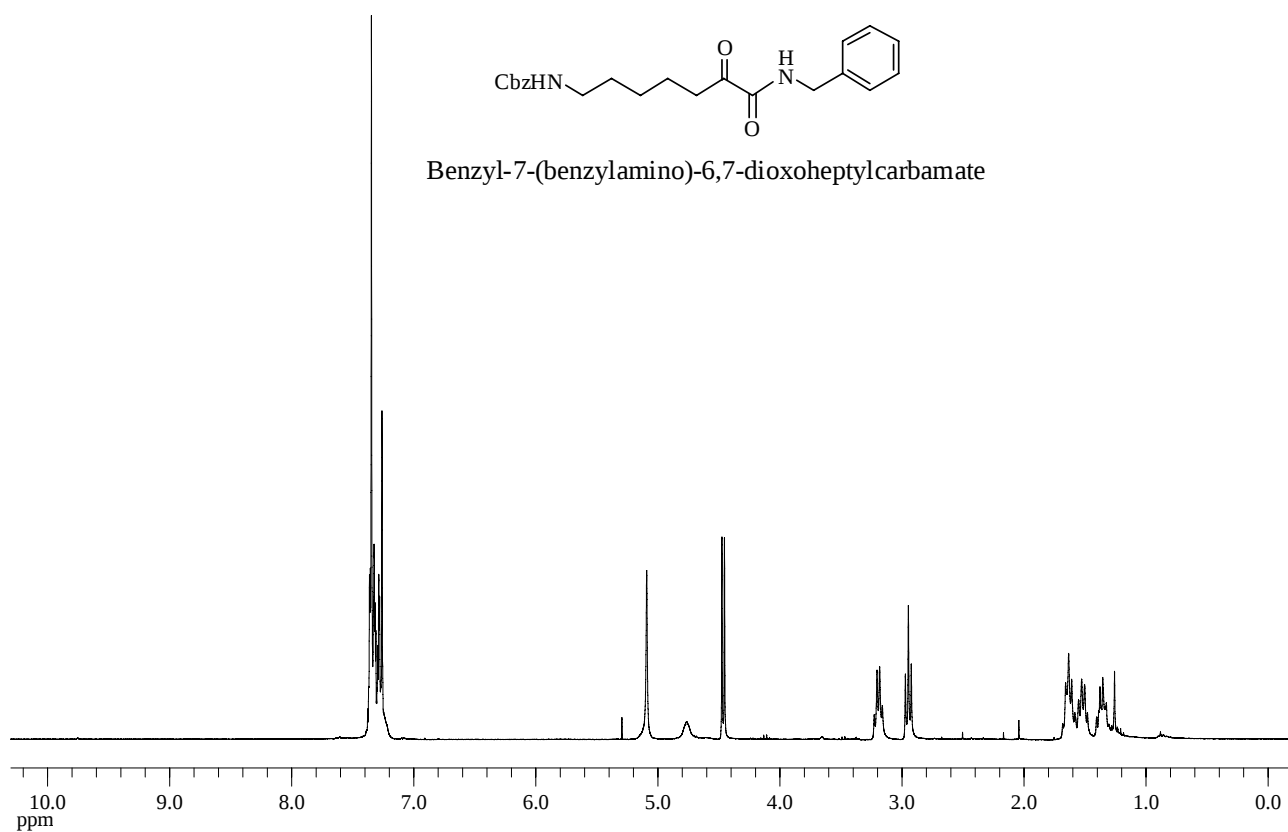


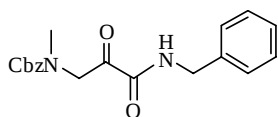
N-(4-Methoxy-2-nitrophenyl)-2-oxo-4-phenylbutanamide



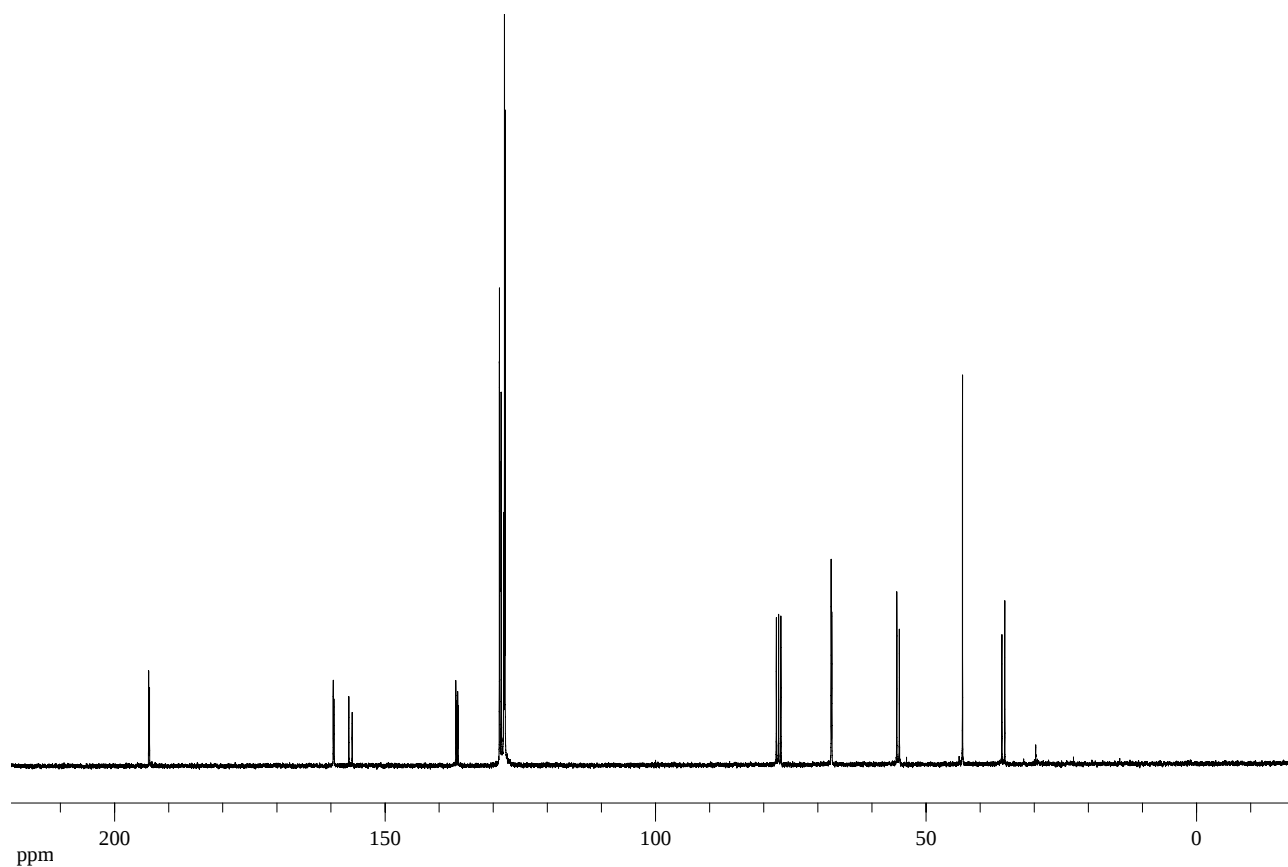
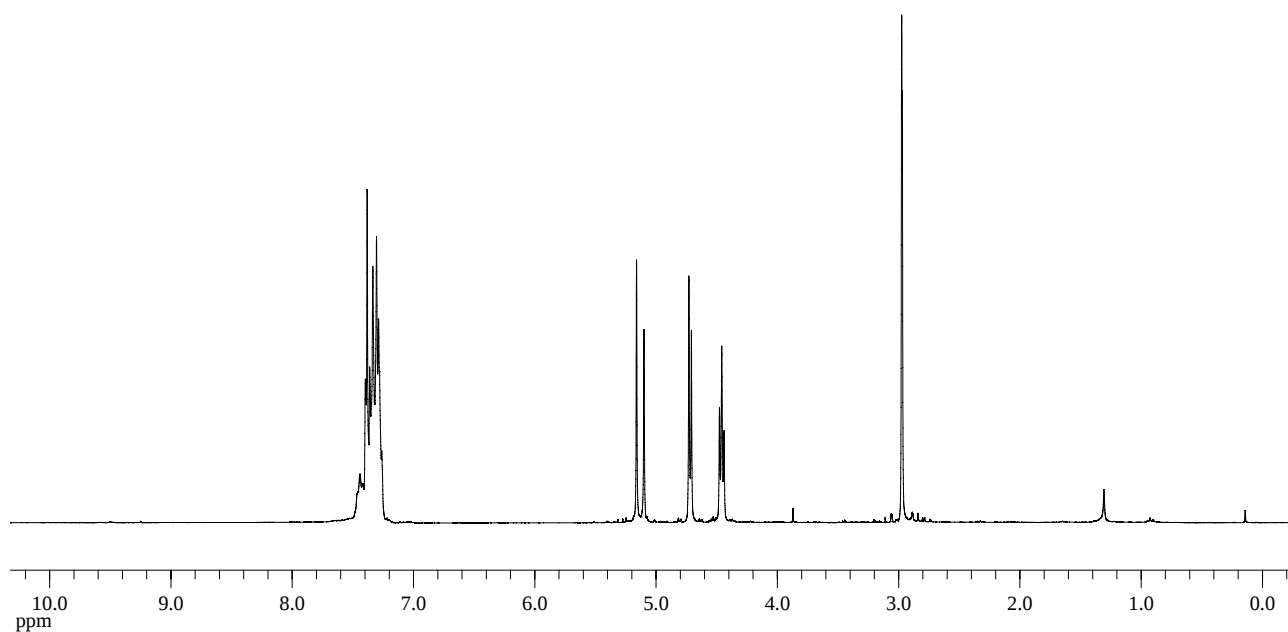


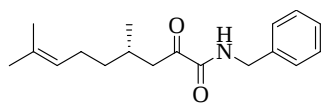
Benzyl-7-(benzylamino)-6,7-dioxoheptylcarbamate



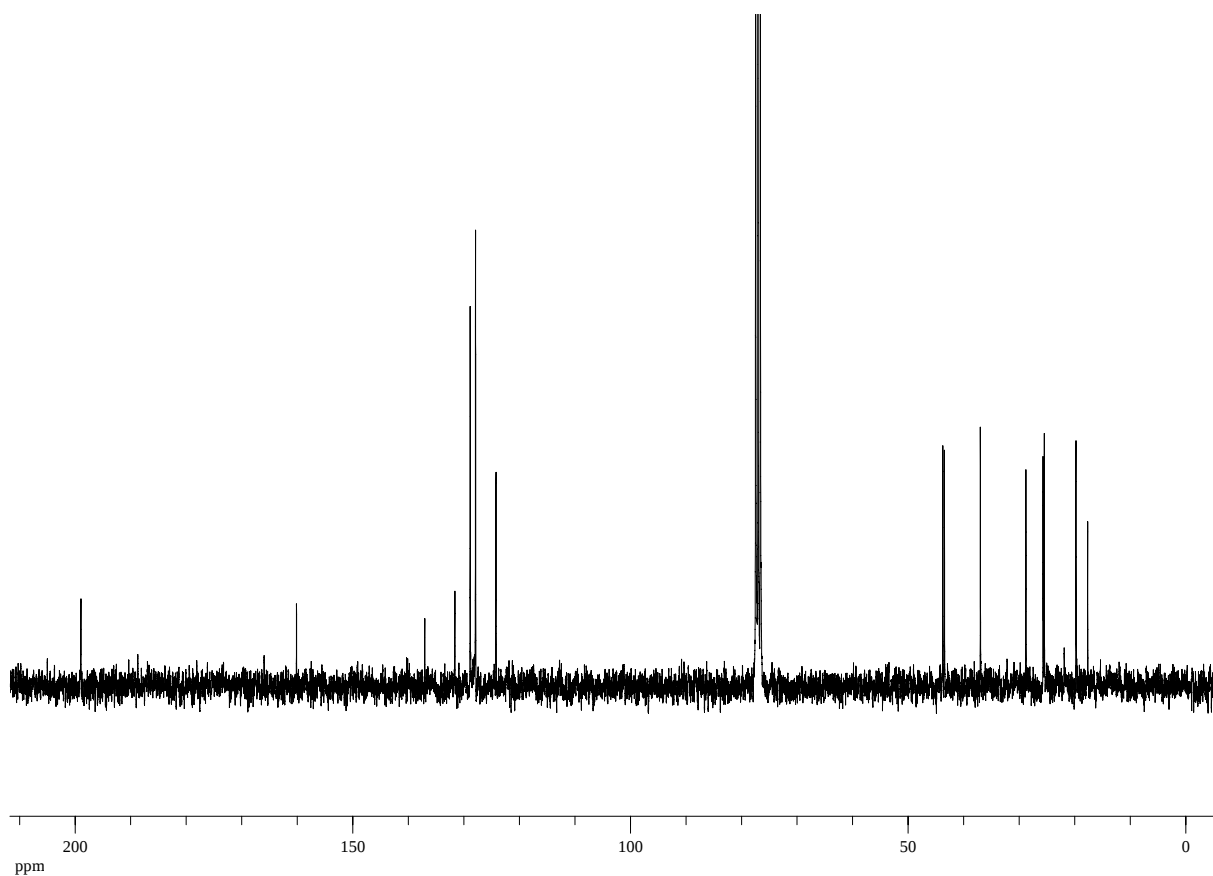
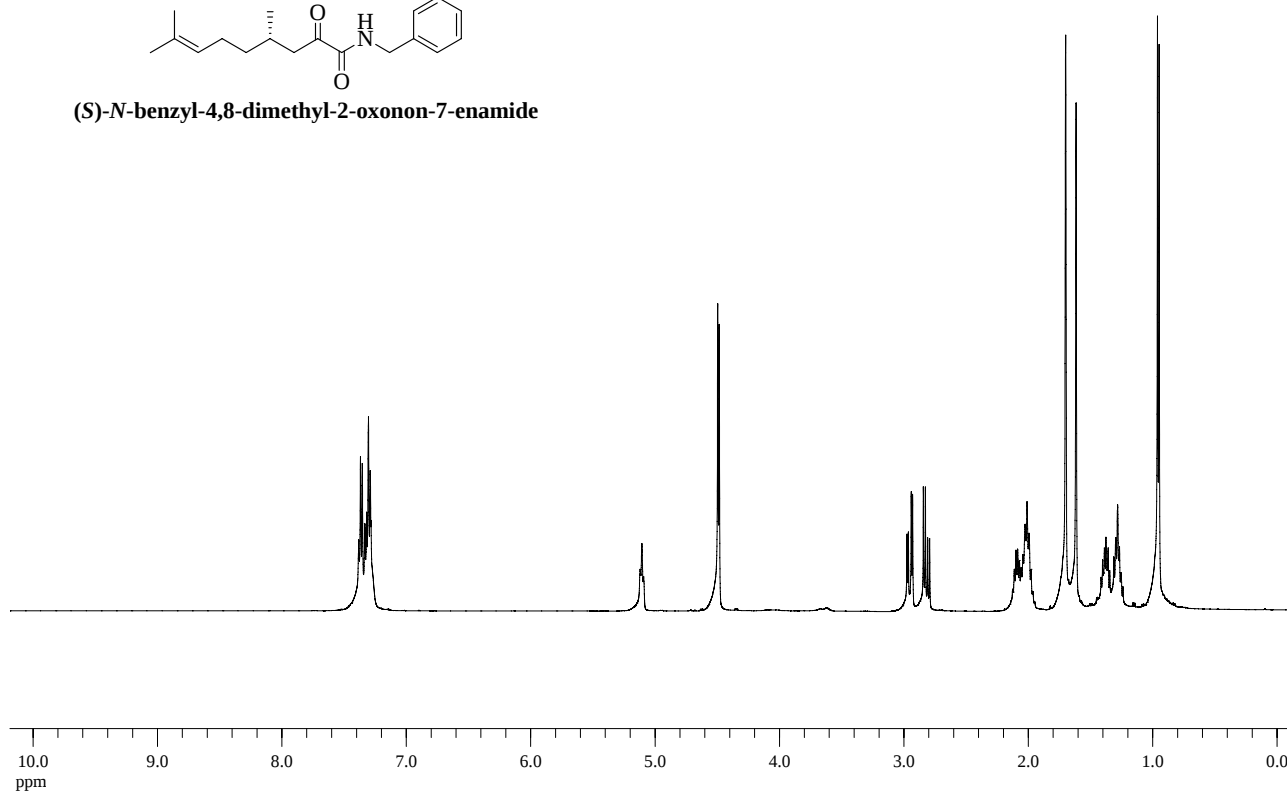


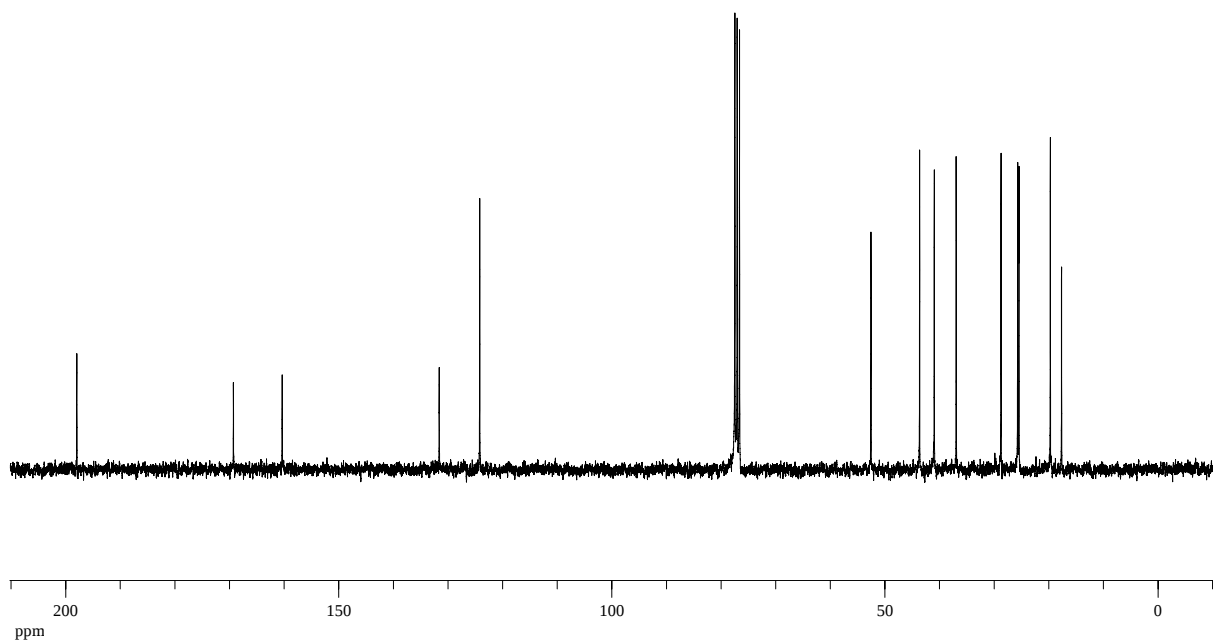
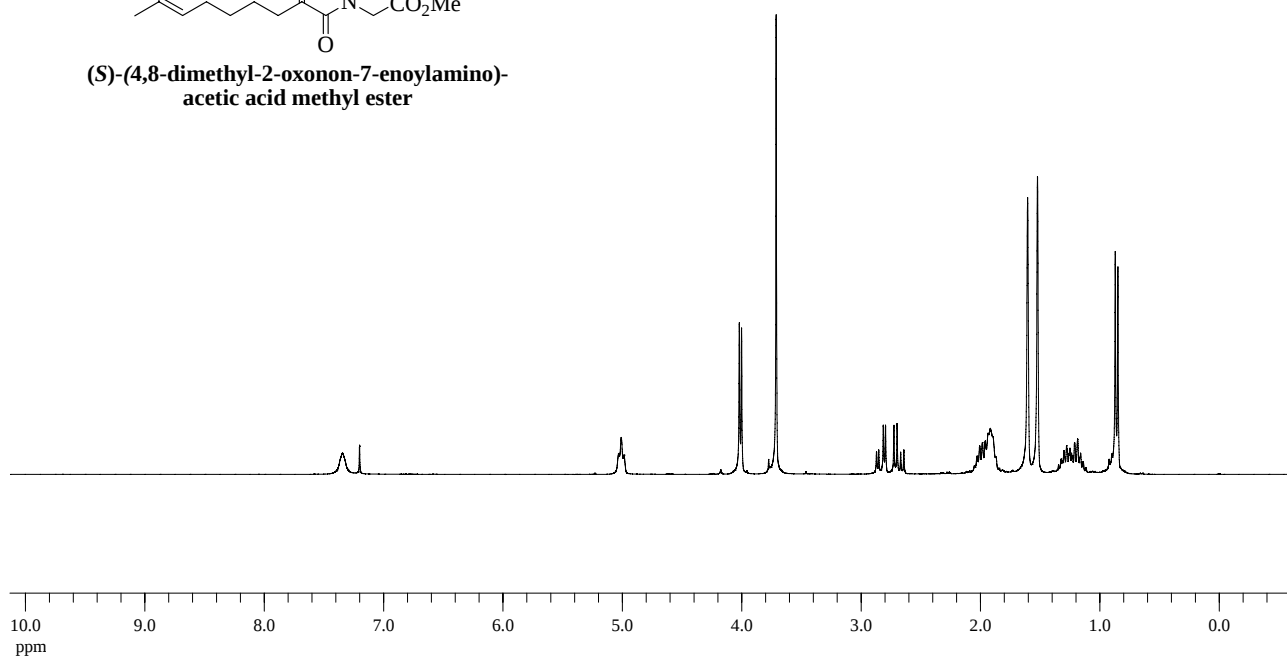
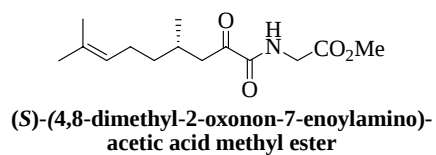
Benzyl[2-(benzylamino)-2-oxoethyl]methylcarbamate

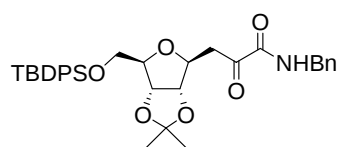




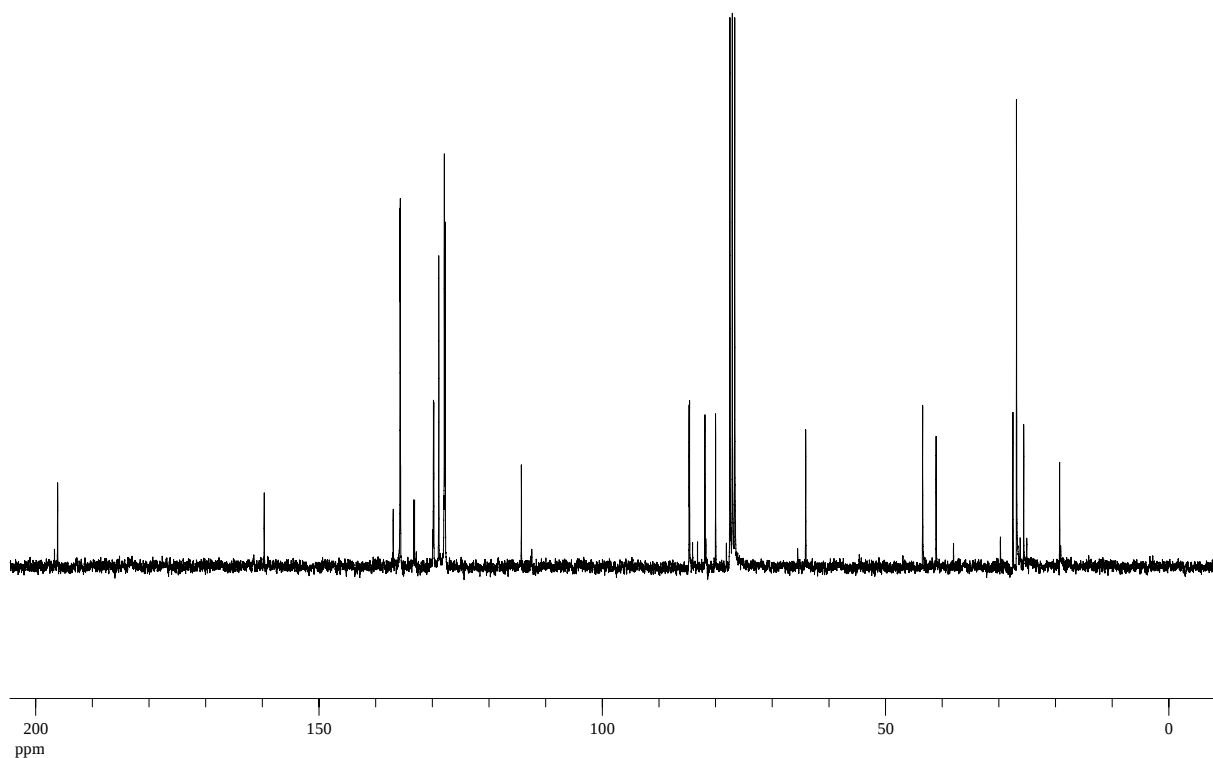
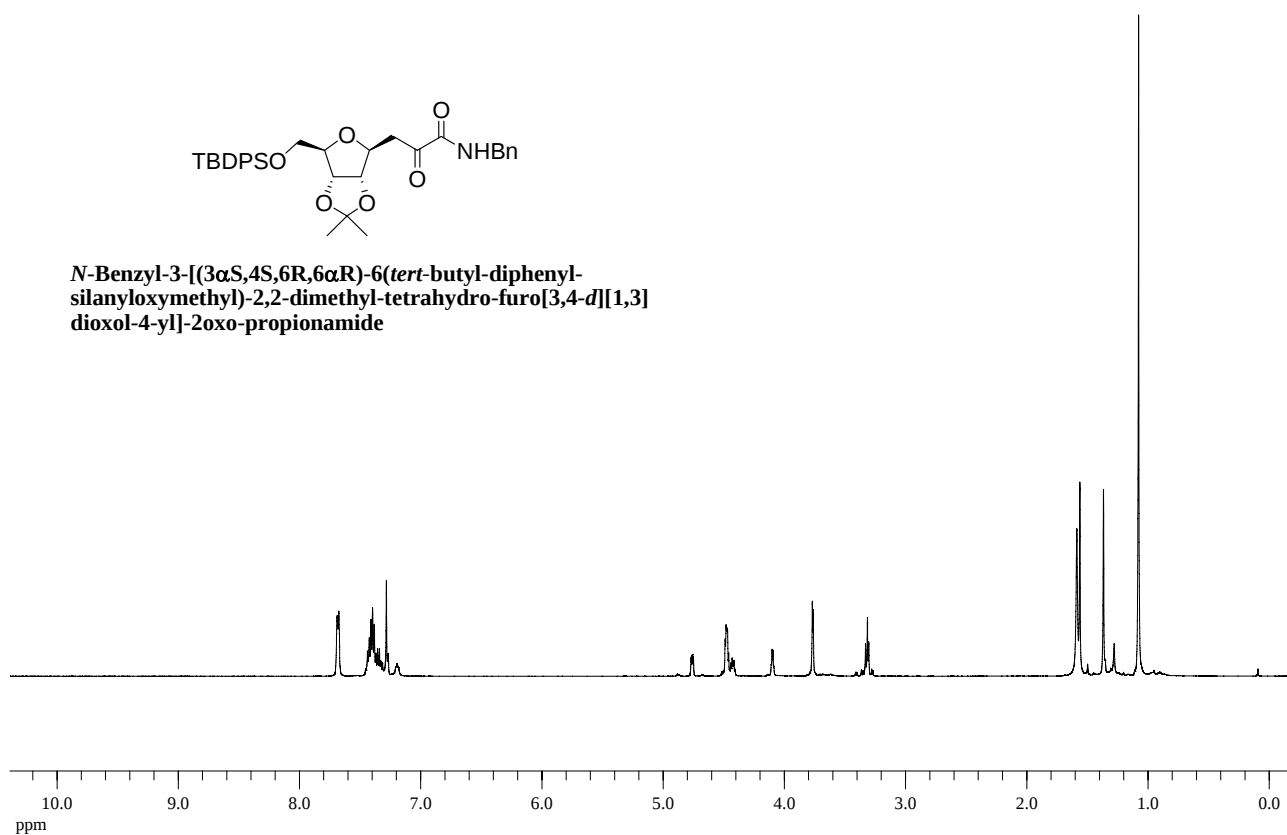
(S)-N-benzyl-4,8-dimethyl-2-oxonon-7-enamide

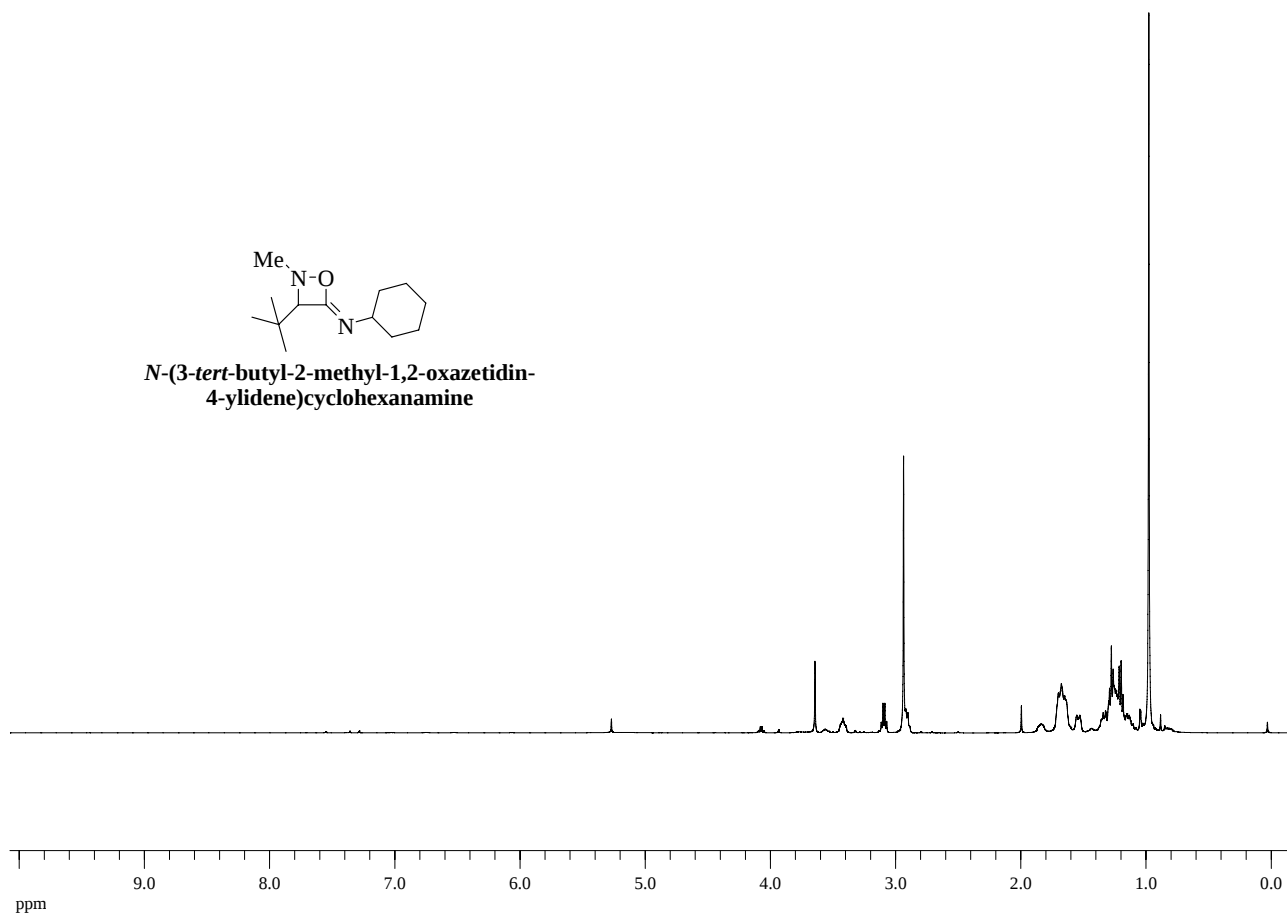
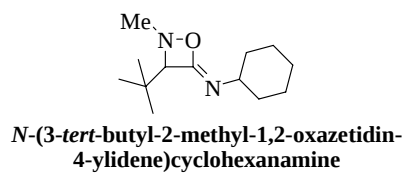






***N*-Benzyl-3-[(3 α S,4S,6R,6 α R)-6(*tert*-butyl-diphenyl-silyloxy)methyl]-2,2-dimethyl-tetrahydro-furo[3,4-*d*][1,3]dioxol-4-yl]-2-oxo-propionamide**





[1] M. -K. Wong, C.-W. Yu, W.-H. Yuen, D. Yang, *J. Org. Chem.* **2001**, *66*, 3606-3609.

[2] J. J. Deshpande, V. Seema, *Tetrahedron Lett*, **2003**, *44*, 8873-8876.