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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 perfomed in oven-dried glassware, sealed with a rubber septum.

Flash chromatography was performed using 40-63 ⌠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}.

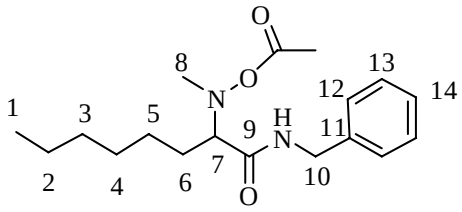
Optical rotations were performed on a Jasco P-1010 polarimeter (589 nm) using a 700-µL cell with a path length of 1 dm.

Proton NMR (^{1}H) 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 deuterochloroform ($CDCl_3$). The following abbrevations 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.

$C_{18}H_{28}N_2O_3$ (320.43 $g.mol^{-1}$)

Rf : 0.13 (Heptane/ EtOAc 4:1)

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

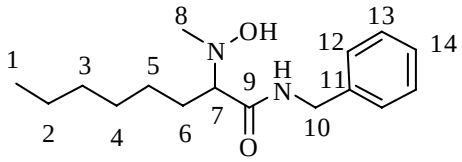
8.0 Hz, H_7), 2.74 (3H, s, H_8), 1.79 (3H, s, COC***H***$_3$), 1.77-1.57 (2H, m, H_5), 1.45-1.18 (8H, m, H_2, H_3, H_4, H_5), 0.87 (3H, br t, H_1)

H6

MS (ESI) (m/z) 321.2 $[M+H]^+$

HRMS (ESI) m/z 321.2191 $[M+H]^+$, $C_{18}H_{29}N_2O_3$ requires 321.2178

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



$C_{16}H_{26}N_2O_2$ (278.39 g.mol^{-1})

Rf : 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

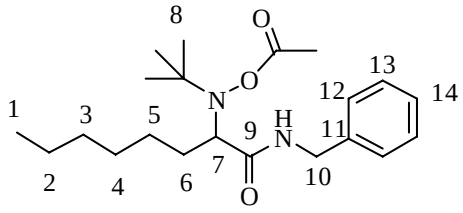
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.37-7.23 (5H, m, H_{Ar}), 6.74 (1H, br t, N***H***), 4.48 (2H, d, J = 6.0 Hz), 3.12 (1H, dd, J = 6.0 Hz, 7.8 Hz, H_7), 2.67 (3H, s, H_8), 1.85-1.56 (2H, m, H_6), 1.44-1.14 (8H, m, H_2, H_3, H_4, H_5), 0.87 (3H, br t, H_1)

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 172.4 (Cq, C_9), 138.3 (Cq, C_{11}), 128.7 (2x ***C***H, C_{12}), 127.7 (2x ***C***H, C_{13}), 127.4 (***C***H, C_{14}), 73.4 (***C***H, C_7), 45.4 (***C***H$_3$, C_8), 43.1 (***C***H$_2$, C_{11}), 31.6 (***C***H$_2$, C_3), 30.4 (***C***H$_2$, C_4), 29.3 (***C***H$_2$, C_6), 25.9 (***C***H$_2$, C_5), 22.5 (***C***H$_2$, C_2), 14.0 (***C***H$_2$, C_1)

MS (ESI) (m/z) 301.2 $[M+Na]^+$

HRMS (ESI) m/z 301.1886 $[M+Na]^+$, $C_{16}H_{26}N_2O_2$ 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.

$C_{21}H_{34}N_2O_3$ (362.50 g.mol^{-1})

Rf : 0.14 (Heptane/ EtOAc 4:1)

NMR ^{1}H δ (500 MHz, $CDCl_3$, 293K) 8.93 (1H, br s, N***H***), 7.46-7.25 (5H, m, H_{Ar},), 4.52 (1H, dd, $J_{10,NH}$ = 5.2 Hz, $J_{10,10'}$ = 14.7 Hz, H_{10}), 4.33 (1H, dd, $J_{10',NH}$ = 4.5 Hz, $J_{10',10}$= 14.7 Hz, $H_{10'}$), 3.64 (1H, m, H_7), 2.07 (3H, s, COC***H***$_3$), 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, ***C***OCH_3) 138.3 (Cq, C_{11}), 128.4 (2x ***C***H, C_{12}), 127.4 (2x ***C***H, C_{13}), 126.7 (***C***H, C_{14}), 65.0 (***C***H, C_7), 60.4 (Cq, ***t***-Bu) 43.0 (***C***H_2, C_{11}), 31.6 (***C***H_2, C_3),

31.4 (***C***H_2, C_4), 29.5 (***C***H_2, C_6), 27.9 (***C***H_2, C_5), 25.3 (***C***H_3, ***t***-Bu), 22.6 (***C***H_2, C_2), 18.7 (CO***C***H_3), 14.0 (***C***H_2, C_1)

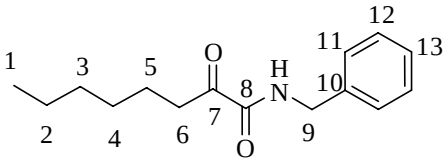
MS (ESI) (m/z) 385.2 $[M+Na]^+$

HRMS (ESI) m/z 301.2467 $[M+Na]^+$, $C_{21}H_{34}N_2O_3$ 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.), $NaHCO_3$ (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%).

$C_{15}H_{21}NO_2$ (247.33 $g.mol^{-1}$)

Rf : 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

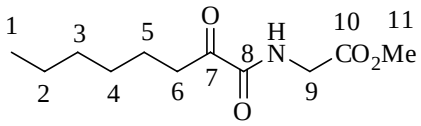
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.42-7.16 (6H, m, H_{Ar}, N*H*), 4.47 (2H, d, ***J*** = 6.1 Hz, H_9), 2.94 (2H, t, ***J*** = 7.3 Hz, H_6), 1.69-1.53 (2H, m, H_5), 1.40-1.21 (6H, m, H_2, H_3, H_4), 0.88 (3H, br t, ***J*** = 7.0 Hz, H_1)

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 199.2 (Cq, C_7), 160.0 (Cq, C_8), 137.0 (Cq, C_{10}), 128.8 (2x ***C***H, C_{11}), 127.9 (2x ***C***H, C_{12}), 127.8 (***C***H, C_{13}), 43.4 (***C***H_2, C_9), 36.8 (***C***H_2, C_6), 31.5 (***C***H_2, C_3), 28.7 (***C***H_2, C_4), 23.2 (***C***H_2, C_5), 22.4 (***C***H_2, C_2), 14.0 (***C***H_3, C_1)

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

HRMS (ESI) m/z 270.1448 $[M+Na]^+$, $C_{15}H_{21}NO_2$ 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%).

$C_{11}H_{19}NO_4$ (229.27 $g.mol^{-1}$)

Rf : 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

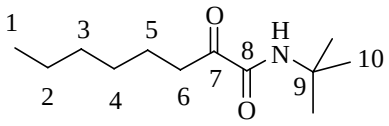
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.41 (1H, br s, N*H*), 4.07 (2H, d, *J* = 5.7 Hz, H_9), 3.78 (3H, s, H_{11}), 2.90 (2H, t, *J* = 7.2 Hz, H_6), 1.67-1.51 (2H, m, H_5), 1.40-1.14 (6H, m, H_2, H_3, H_4), 0.87 (3H, br t, H_1)

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 (*C*H_2, C_{11}), 40.9 (*C*H_2, C_9), 36.7 (*C*H_2, C_6), 31.4 (*C*H_2, C_3), 28.7 (*C*H_2, C_4), 23.1 (*C*H_2, C_5), 22.4 (*C*H_2, C_2), 14.0 (*C*H_3, C_1)

MS (ESI) (m/z) 252.1 $[M+Na]^+$

HRMS (ESI) m/z 252.1203 $[M+Na]^+$, $C_{11}H_{19}NO_4Na$ 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%).

$C_{12}H_{23}NO_2$ (247.33 g.mol^{-1})

Rf : 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

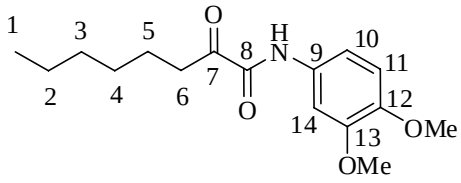
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 6.82 (1H, br s, N*H*), 2.88 (2H, t, *J* = 7.2 Hz, H_6), 1.66-1.49 (2H, m, H_5), 1.38 (9H, s, H_{10}), 1.34-1.20 (6H, m, H_2, H_3, H_4), 0.87 (3H, br t, *J* = 7.0 Hz, H_1)

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 200.4 (Cq, C_7), 159.4 (Cq, C_8), 51.2 (***C***q, C_9), 36.2 (***C***H_2, C_6), 31.5 (***C***H_2, C_5), 28.7 (***C***H_2, C_4), 28.3 (***C***H_3, C_{10}), 23.2 (***C***H_2, C_3), 22.4 (***C***H_2, C_2), 14.0 (***C***H_3, C_1)

MS (ESI) (m/z) 214.2 $[M]^+$

HRMS (ESI) m/z 214.1799 $[M+H]^+$, $C_{12}H_{24}NO_2$ 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%).

$C_{16}H_{23}NO_4$ (293.36 $g.mol^{-1}$)

Rf : 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

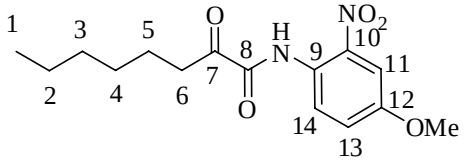
NMR ^1H δ (500 MHz, $CDCl_3$, 293K) 8.69 (1H, br s, N***H***), 7.46 (1H, d, J_{14-11} = 2.0 Hz, H_{14}), 7.03 (1H, dd, J_{11-14} = 2.0 Hz, J_{11-10} = 8.5 Hz, H_{11}), 6.83 (1H, d, J_{11-13} = 8.5 Hz, H_{10}), 3.90 (3H, OC***H***$_3$) 3.87 (3H, OC***H***$_3$), 2.99 (2H, t, ***J*** = 7.5 Hz, H_6), 1.70-1.61 (2H, m, H_5), 1.40-1.22 (6H, m, H_2, H_3, H_4), 0.88 (3H, br t, ***J*** = 7.0 Hz, H_1)

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 (***C***H, C_{10}), 111.4 (***C***H, C_{11}), 104.1 (***C***H, C_{14}), 56.1 (***C***H_3, O***C***H_3), 55.9 (***C***H_3, O***C***H_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$[M+Na]^+$

HRMS (ESI) m/z 316.1534 $[M+Na]^+$, $C_{16}H_{23}NO_4Na$ 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%)

$C_{15}H_{20}N_2O_5$ (308.33 $g.mol^{-1}$)

Rf : 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

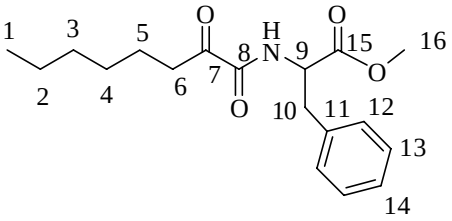
NMR ^1H δ (300 MHz, $CDCl_3$, 293K) 11.45 (1H, br s, N***H***), 8.72 (1H, d, J_{14-13} = 9.3 Hz, H_{14}), 7.73 (1H, d, J_{11-13} = 3.0 Hz, H_{11}), 7.26 (1H, dd, J_{13-11} = 3.0 Hz, J_{13-14} = 9.3 Hz, H_{13}), 3.88 (3H, s, OC***H₃***), 2.99 (2H, t, ***J*** = 7.2 Hz, H_6), 1.73-1.61 (2H, m, H_5), 1.43-1.22 (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, C_7), 158.4 (Cq, C_8), 155.8 (Cq, C_{12}), 137.9 (Cq, C_{10}), 126.6 (Cq, C_9), 123.2 (***C***H, C_{14}), 122.9 (***C***H, C_{13}), 109.3 (***C***H, C_{11}), 55.9 (***C***H_3, O***C***H_3), 36.4 (***C***H_2, C_6), 31.5 (***C***H_2, C_3), 28.7 (***C***H_2, C_4), 23.2 (***C***H_2, C_5), 22.4 (***C***H_2, C_2), 14.0 (***C***H_3, C_1)

MS (ESI) (m/z) 331.1 $[M+Na]^+$

HRMS (ESI) m/z 331.1264 $[M+Na]^+$, $C_{15}H_{20}N_2O_5Na$ 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%)

$C_{18}H_{25}NO_4$ (319.40 g.mol^{-1})

Rf : 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}, N***H***), 4.81 (1H, ddd, $J_{9,10}$ = 6.0 Hz, $J_{9,10'}$ = 6.5 Hz, $J_{9\text{-}NH}$ = 8.5 Hz, H_9), 3.73 (3H, s, H_{16}), 3.17 (1H, dd, $J_{10,9}$ = 6.0 Hz, $J_{10,10'}$ = 14.0 Hz, H_{10}), 3.11 (1H, dd, $J_{10',9}$ = 6.5 Hz, $J_{10',10}$ = 14.0 Hz, $H_{10'}$), 2.91-2.80 (2H,

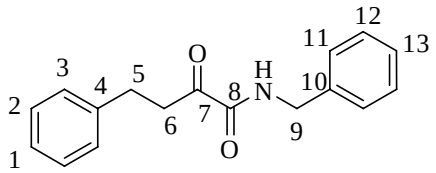
m, H_6), 1.63-1.53 (2H, m, H_5), 1.35-1.20 (6H, m, H_2, H_3, H_4), 0.88 (3H, br t, H_1)

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 198.3 (Cq, C_7), 171.0 (Cq, C_8), 159.6 (Cq, C_{15}), 135.3 (Cq, C_{11}), 129.1 (2x ***C***H, C_{12}), 128.7 (2x ***C***H, C_{13}), 127.3 (***C***H, C_{14}), 53.1 (***C***H, C_9), 52.5 (***C***H_3, C_9), 37.9 (***C***H_2, C_{10}), 36.7 (***C***H_2, C_6), 31.4 (***C***H_2, C_3), 28.7 (***C***H_2, C_4), 23.1 (***C***H_2, C_5), 22.4 (***C***H_2, C_2), 14.0 (***C***H_2, C_1)

MS (ESI) (m/z) 342.2 $[M+Na]^+$

HRMS (ESI) m/z 342.1688 $[M+Na]^+$, $C_{18}H_{25}NO_4Na$ 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%)

$C_{17}H_{17}NO_2$ (267.32 g.mol^{-1})

Melting point : 53.2-54.7°C

Rf : 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

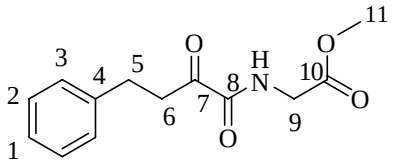
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.44-7.18 (11H, m, H_{Ar}, N***H***), 4.50 (2H, d, ***J*** = 6.3 Hz, H_9), 3.35 (2H, t, ***J*** = 7.5 Hz, H_5), 2.99 (2H, t, ***J*** = 7.5 Hz, H_6)

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 ***C***H, C_{Ar}), 128.3 (2x ***C***H, C_{Ar}), 127.8 (3x ***C***H, C_{Ar}), 126.2 (***C***H, C_{Ar}), 43.4 (***C***H_2, C_9), 38.4 (***C***H_2, C_6), 29.1 (***C***H_2, C_5)

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

HRMS (ESI) m/z 290.1154 $[M+Na]^+$, $C_{17}H_{17}NO_2Na$ 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%)

$C_{13}H_{15}NO_4$ (249.10 $g.mol^{-1}$)

Rf : 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

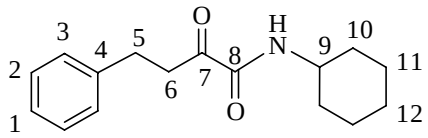
NMR ^1H δ (500 MHz, $CDCl_3$, 293K) 7.41 (1H, s, NH), 7.25-7.01 (5H, m, H_{Ar}), 3.98 (2H, d, ***J*** = 6.0 Hz, H_9), 3.67 (3H, s, H_{11}), 3.18 (2H, br t, ***J*** = 7.5 Hz, H_6), 2.85 (2H, br t, ***J*** = 7.5 Hz, H_5)

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 ***C***H, C_{Ar}), 128.4 (2x ***C***H, C_{Ar}), 126.3 (***C***H, C_1), 52.5 (***C***H_3, C_{11}), 40.9 (***C***H_2, C_9), 38.4 (***C***H_2, C_6), 29.0 (***C***H_2, C_5)

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

HRMS (ESI) m/z 272.0909 $[M+Na]^+$, $C_{13}H_{15}NO_4Na$ 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%)

$C_{16}H_{21}NO_2$ (259.34 $g.mol^{-1}$)

Rf : 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

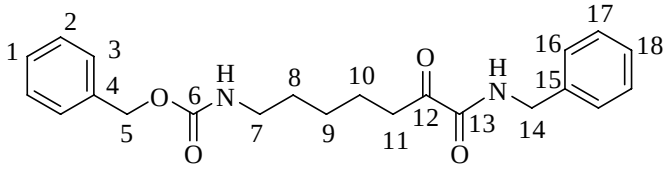
NMR ^1H δ (500 MHz, $CDCl_3$, 293K) 7.29-7.04 (5H, m, H_{Ar}), 6.88-6.64 (1H, m, N*H*), 3.71-3.53 (1H, m, H_9), 3.19 (2H, t, ***J*** = 7.5 Hz, H_6), 2.85 (2H, t, ***J*** = 7.5 Hz, H_5), 1.88-1.02 (10H, m, H_{10}, H_{11}, H_{12})

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 198.6 (Cq, C_7), 158.9 (Cq, C_8), 140.4 (Cq, C_4), 128.4 (CH, C_{Ar}), 128.3 (2x ***C***H, C_{Ar}), 126.1 (2x ***C***H, C_{Ar}), 48.2 (***C***H, C_9), 38.2 (***C***H_2, C_6), 32.6 (2x ***C***H_2, C10), 29.1 (***C***H_2, C_5), 25.3 (***C***H_2, C_{11}), 24.6(2x ***C***H_2, C_{12})

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

HRMS (ESI) m/z 282.1462 [M+Na], $C_{16}H_{21}NO_2Na$ 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 benzylisocyanide, as a white solid (68%)

$C_{22}H_{26}N_2O_4$ (382.45 g.mol^{-1})

Rf : 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

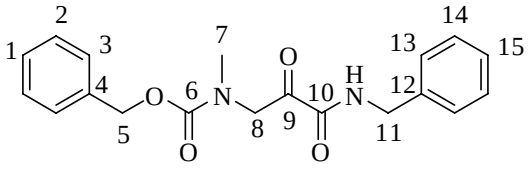
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.40-7.19 (11H, m, H_{Ar}, N***H amide***), 5.09 (2H, s, H_5), 4.76 (1H, br s, N***H carbamate***), 4.46 (2H, d, ***J*** = 6.0 Hz, H_{14}) 3.19 (2H, m, H_7), 2.95 (2H, t, ***J*** = 7.2 Hz, H_{11}), 1.70-1.21 (6H, m, H_8, H_9, H_{10})

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 198.8 (Cq, C_{12}), 159.9 (Cq, C_{13}), 156.3 (Cq, C_6), 136.9 (Cq, C_{15}), 136.6 (Cq, C_4), 128.8 (2x ***C***H, C_{Ar}), 128.5 (2x ***C***H, C_{Ar}), 128.1 (3x ***C***H, C_{Ar}), 127.9 (3x ***C***H, C_{Ar}), 66.6 (***C***H_2, C_5), 43.4 (***C***H_2, C_{14}), 40.8 (***C***H_2, C_7), 36.6 (***C***H_2, C_{11}), 29.7 (***C***H_2, C_8), 26.1 (***C***H_2, C_9), 22.8 (***C***H_2, C_{10})

MS (ESI) (m/z) 405.2 $[M+Na]^+$

HRMS (ESI) m/z 405.1788 $[M+Na]^+$, $C_{22}H_{26}N_2O_4$ 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 benzylisocyanide, as an oil (46%)

$C_{19}H_{20}N_2O_4$ (340.37 g.mol^{-1})

Rf : 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 ^{1}H δ (300 MHz, $CDCl_3$, 293K) Rotamer A: 7.48-7.22 (10H, m, H_{Ar}), 7.16 (1H, br s, N***H***), 5.15 (2H, s, H_5), 4.77-4.71 (2H, m, H_{11}), 4.54-4.40 (2H, m, H_8), 2.97 (3H, s, H_7)

Rotamer B: 7.48-7.22 (10H, m, H_{Ar}), 7.13 (1H, br s, N***H***), 5.08 (2H, s, H_5), 4.77-4.71 (2H, m, H_{11}), 4.54-4.40 (2H, m, H_8), 2.97 (3H, s, H_7)

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) Rotamer A: 193.6 (Cq, C_9), 159.4 (Cq, C_{10}), 156.7 (Cq, C_6), 136.7 (Cq, C_{12}), 136.5 (Cq, C_4), 128.9 (2x ***C***H, C_{Ar}), 128.5 (2x ***C***H, C_{Ar}), 128.0 (2x ***C***H, C_{Ar}), 127.9 (4x ***C***H, C_{Ar}), 127.8 (2x ***C***H, C_{Ar}), 67.6 (***C***H_2, C_5), 55.4 (***C***H_2, C_{11}), 43.3 (***C***H_2, C_8), 36.0 (***C***H_3, C_7)

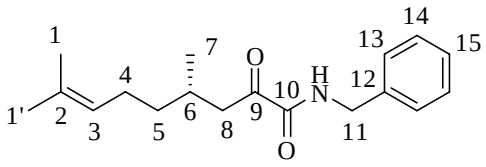
Rotamer B: 193.4 (Cq, C_9), 159.2 (Cq, C_{10}), 156.0 (Cq, C_6), 136.6 (Cq, C_{12}), 136.4 (Cq, C_4), 128.9 (2x ***C***H, C_{Ar}), 128.4 (2x ***C***H, C_{Ar}),

128.0 (2x ***C***H, C_{Ar}), 127.9 (2x ***C***H, C_{Ar}), 127.7 (2x ***C***H, C_{Ar}), 67.4 (***C***H_2, C_5), 54.9 (***C***H_2, C_{11}), 43.3 (***C***H_2, C_8), 35.5 (***C***H_3, C_7)

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

HRMS (ESI) m/z 363.1314 $[M+Na]^+$, $C_{19}H_{20}N_2O_4$ Na requires 363.1321

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



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

$C_{18}H_{25}NO_2$ (287.40 g.mol^{-1})

Rf : 0.48 (Heptane/ EtOAc 4:1)

$[\alpha]_D$: -4.1 °, c = 2.0, $CHCl_3$

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 ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.46-7.22 (6H, m, H_{Ar}, N*H*), 5.05-5.20 (1H, m, H_3), 4.49 (2H, d, ***J*** **=** 6.0 Hz, H_{11}), 2.95 (1H, dd, $J_{8\text{-}6}$ = 5.7 Hz, $J_{8\text{-}8'}$ = 17.1 Hz, H_8), 2.82 (1H, dd, $J_{8'\text{-}6}$ = 8.1 Hz, $J_{8'\text{-}8}$ = 17.1 Hz, $H_{8'}$), 2.19-1.93 (3H, m, H_5, H_6), 1.70 (3H, s, H_1), 1.62 (3H, s, $H_{1'}$), 1.45-1.22 (2H, m, H_4), 0.95 (3H, d, $J_{7\text{-}6}$ = 6.6 Hz, H_7)

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 198.9 (Cq, C_9), 160.1 (Cq, C_{10}), 137.0 (Cq, C_{12}), 131.6 (Cq, C_2), 128.8 (2x ***C***H, C_{13}), 127.9 (3x ***C***H, C_{14}, C_{15}), 124.2 (***C***H, C_3), 43.7 (***C***H_2, C_8), 43.4 (***C***H_2, C_{11}), 37.0 (***C***H_2,

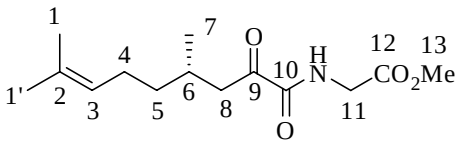
C_5), 28.8 (***C***H_2, C_6), 25.7 (***C***H_3, $C_{1'}$), 25.5 (***C***H_2, C_4), 19.8 (***C***H_3, C_7), 18.0 (***C***H_3, C_1)

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

HRMS (ESI) m/z 310.1785 $[M+Na]^+$, $C_{18}H_{25}NO_2$ 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%)

$C_{14}H_{23}NO_4$ (269.34 $g.mol^{-1}$)

Rf : 0.23 (Heptane/ EtOAc 4:1)

$[\alpha]_D$: -8.1°, c = 2.0, $CHCl_3$

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

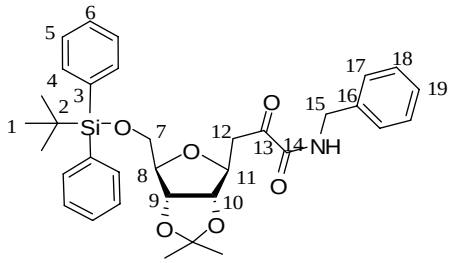
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.40 (1H, br s, N***H***), 5.06 (1H, br t, ***J*** = 6.9 Hz, H_3), 4.07 (2H, d, ***J*** = 5.7 Hz, H_{11}), 3.77 (3H, s, H_{13}), 2.89 (1H, dd, J_{8-6} = 5.4 Hz, $J_{8-8'}$ = 17.1 Hz, H_8), 2.75 (1H, dd, $J_{8'-6}$ = 8.1 Hz, $J_{8'-8}$ = 17.1 Hz, $H_{8'}$), 2.13-1.84 (3H, m, H_5, H_6), 1.66 (3H, s, H_1), 1.58 (3H, s, $H_{1'}$), 1.44-1.14 (2H, m, H_4), 0.92 (3H, d, J_{7-6} = 6.9 Hz, H_7)

NMR ^{13}C δ (75 MHz, $CDCl_3$, 293K) 197.9 (Cq, C_9), 169.2 (Cq, C_{10}), 160.3 (Cq, C_{12}), 131.6 (Cq, C_2), 124.1 (***C***H, C_3), 52.5 (***C***H_3, C_{13}), 43.6 (***C***H_3, C_8), 40.9 (***C***H_2, C_{11}), 36.9 (***C***H_2, C_4), 28.7 (***C***H, C_6), 25.6 (***C***H_3, C_1), 25.4 (***C***H_3, C_5), 19.7 (***C***H_2, C_7), 17.6 (***C***H_3, $C_{1'}$)

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

HRMS (ESI) m/z 292.1527 $[M+Na]^+$, $C_{14}H_{23}NO_4$ Na requires 292.1525

***N*-benzyl-3-((3α*S*,4*S*,6R,6α*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-((3αS,4S,6R,6αR)-6-((tert-butyldiphenylsilyloxy)methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)acetaldehyde and benzylisocyanide, as an oil (68%)

$C_{34}H_{41}NO_6Si$ (587.78 $g.mol^{-1}$)

Rf : 0.40 (Heptane/ EtOAc 4:1)

$[\alpha]_D$: -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

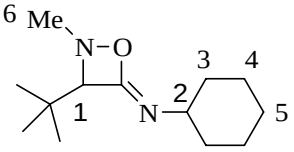
NMR ^{1}H δ (300 MHz, $CDCl_3$, 293K) 7.74-7.62 (4H, m, H_4), 7.49-7.31 (12H, m, H_{Ar}), 4.75 (1H, dd, $J_{9,10}$ = 3.0 Hz, $J_{9,8}$= 6.0 Hz, H_9), 4.54-4.35 (4H, m, H_{10}, H_{11}, H_{15}), 4.15-4.04 (1H, m, H_8), 3.75 (2H, d, $J_{7,8}$= 3.9 Hz, H_7), 3.34-3.26 (2H, m, H_{12}), 1.55 (3H, s, $C(CH_3)_2$), 1.35 (3H, s, $C(CH_3)_2$), 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 $C_{4'}$), 133.2 (Cq, C_3), 133.1 (Cq, $C_{3'}$), 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 $[M+Na]^+$, 642.2 $[M+Na+MeOH]^+$

HRMS (ESI) m/z 610.2590 $[M+Na]^+$, $C_{34}H_{41}NO_6$ SiNa requires 610.2601

***N*-(3-tert-butyl-2-methyl-1,2-oxazetidin-4-ylidene)cyclohexanamine 15**

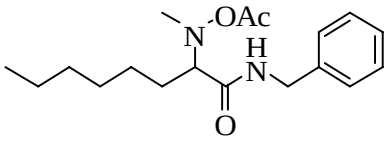


A mixture of cyclohexylisocyanide (270 μL, 2.17 mmol) and triethylamide (300 μL, 2.17 mmol) in dry dichloromethane (2 mL) is added to solution of *N*-(2,2-dimethylpropylidene)methanamine oxide (310 mg, 2.17 mmol) and $BF_3.OEt_2$ (260 μL, 2.06 mmol) in dry dichloromethane (4 mL) at -40°C. The reaction mixture was stirred for 5 mim and quenched with saturated solution of $NaHCO_3$ (15 mL)

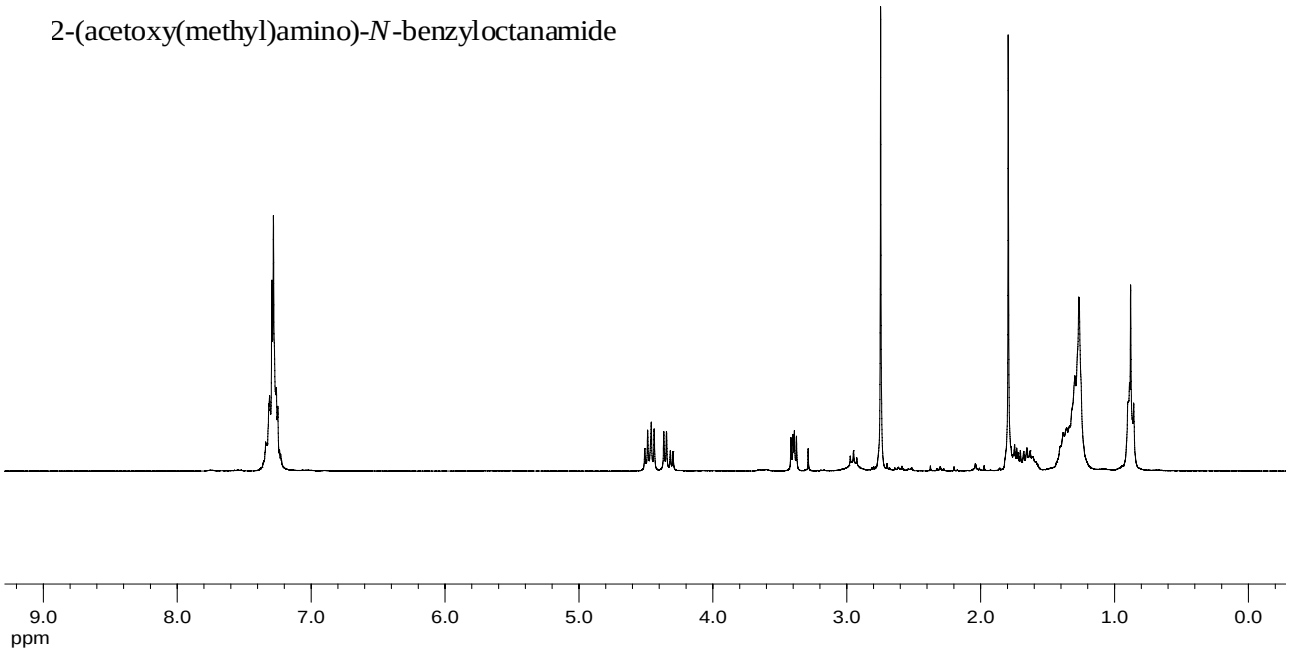
and extracted with dichloromethane. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford **15** (296 mg, 61%) as an oil.

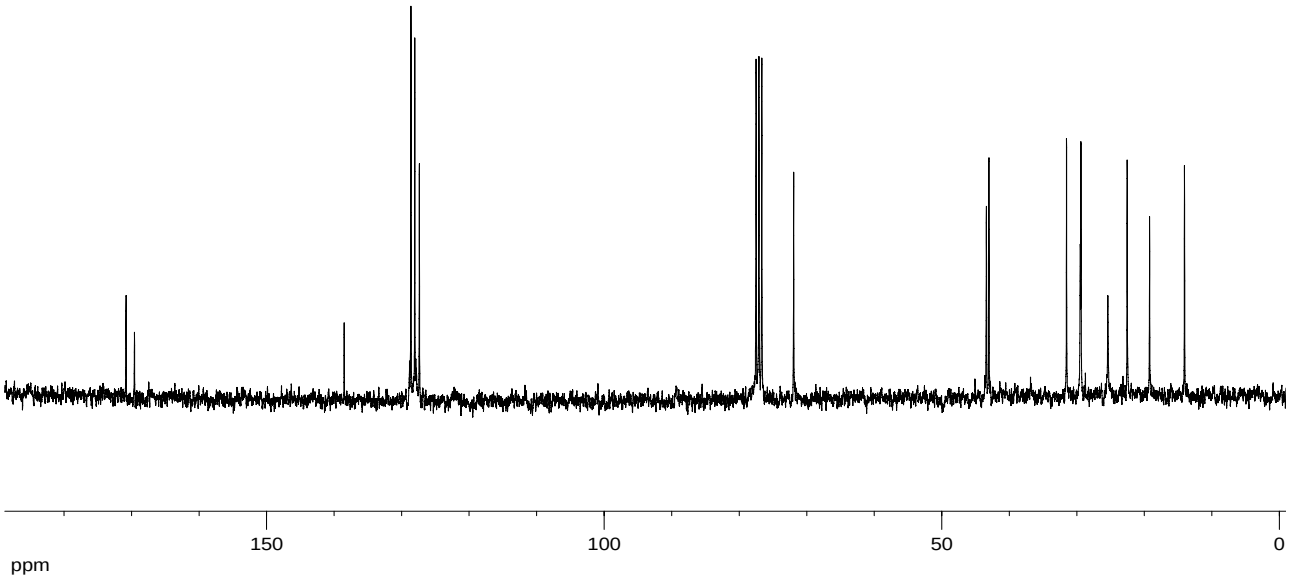
$C_{13}H_{24}N_2O$ (224.34 $g.mol^{-1}$)

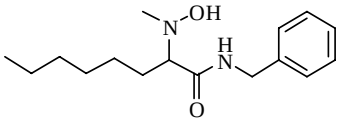
NMR ^1H δ (300 MHz, $CDCl_3$, 293K) 3.62 (1H, s, H_1), 3.42-3.30 (1H, m, H_2), 2.91 (3H, s, H_6), 1.85-1.04 (10H, m, H_3, H_4 and H_5), 0.96 (9H, s, $C(CH_3)_3$)



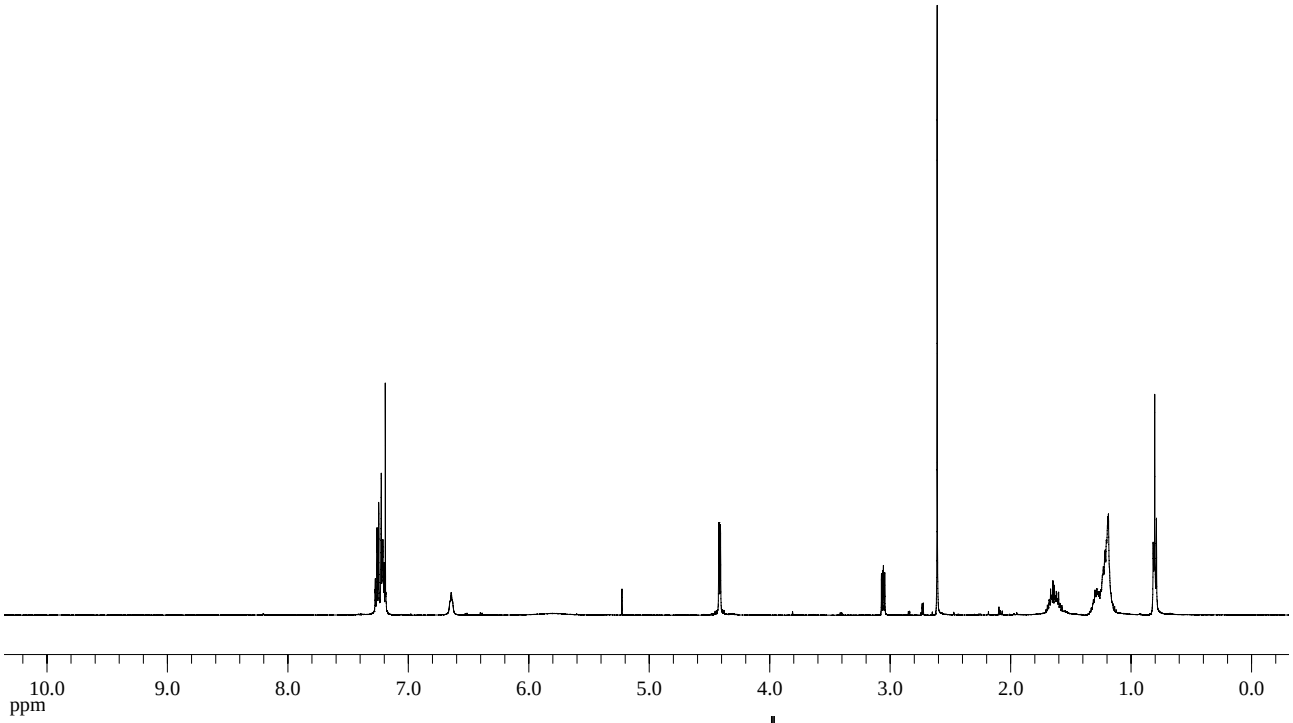
2-(acetoxy(methyl)amino)-*N*-benzyloctanamide

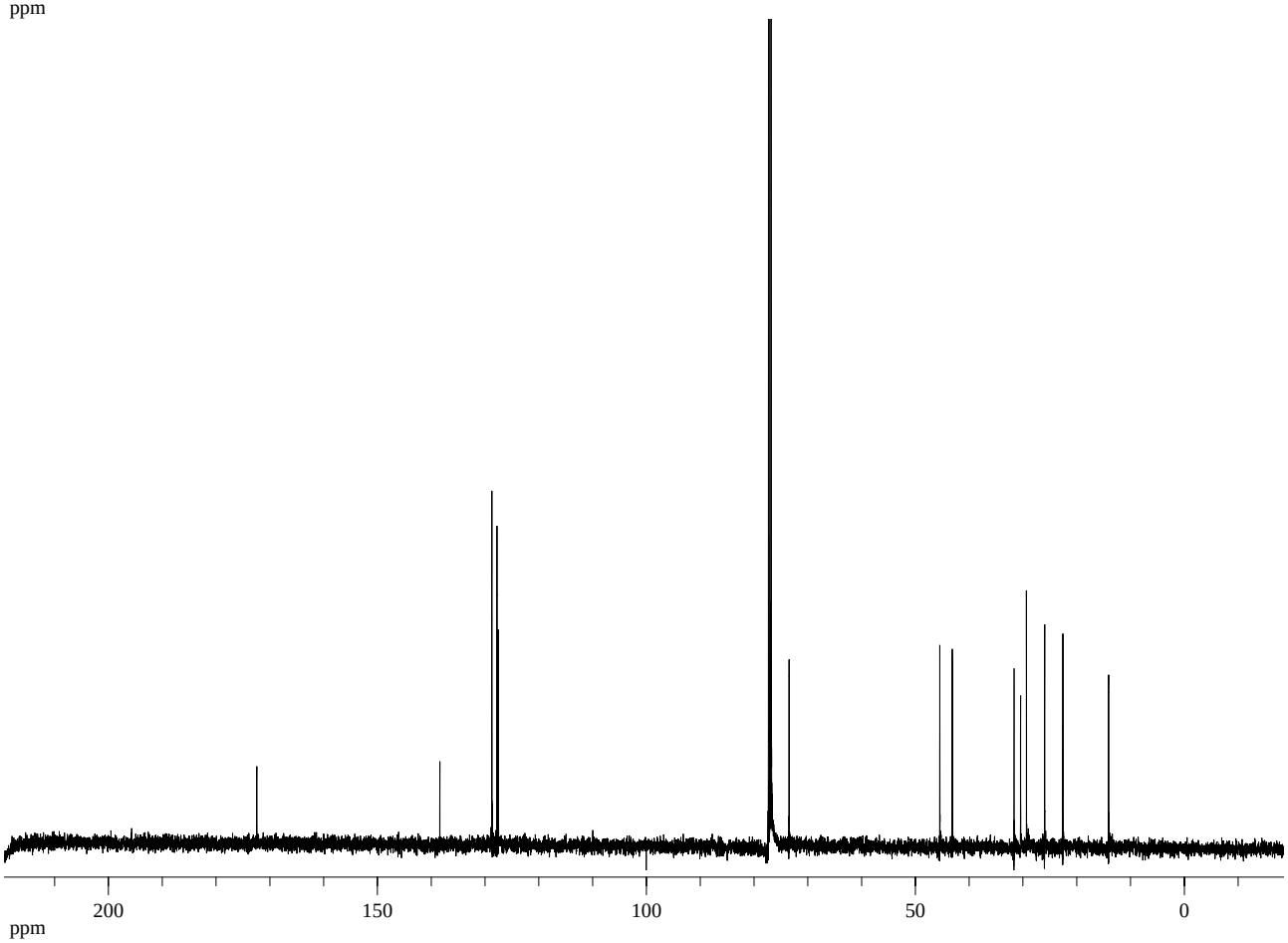


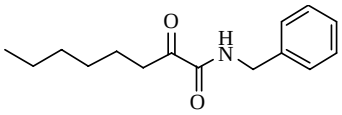




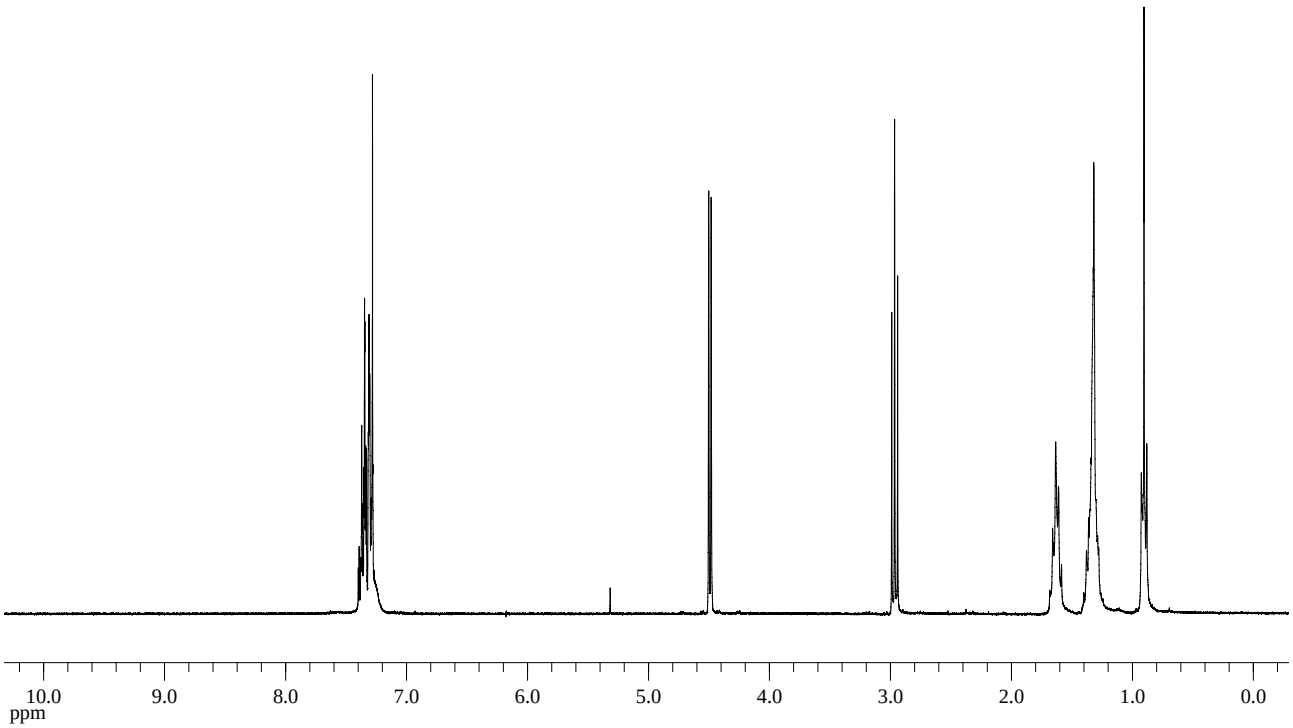
N-benzyl-2-[hydroxy(methyl)amino]octanamide

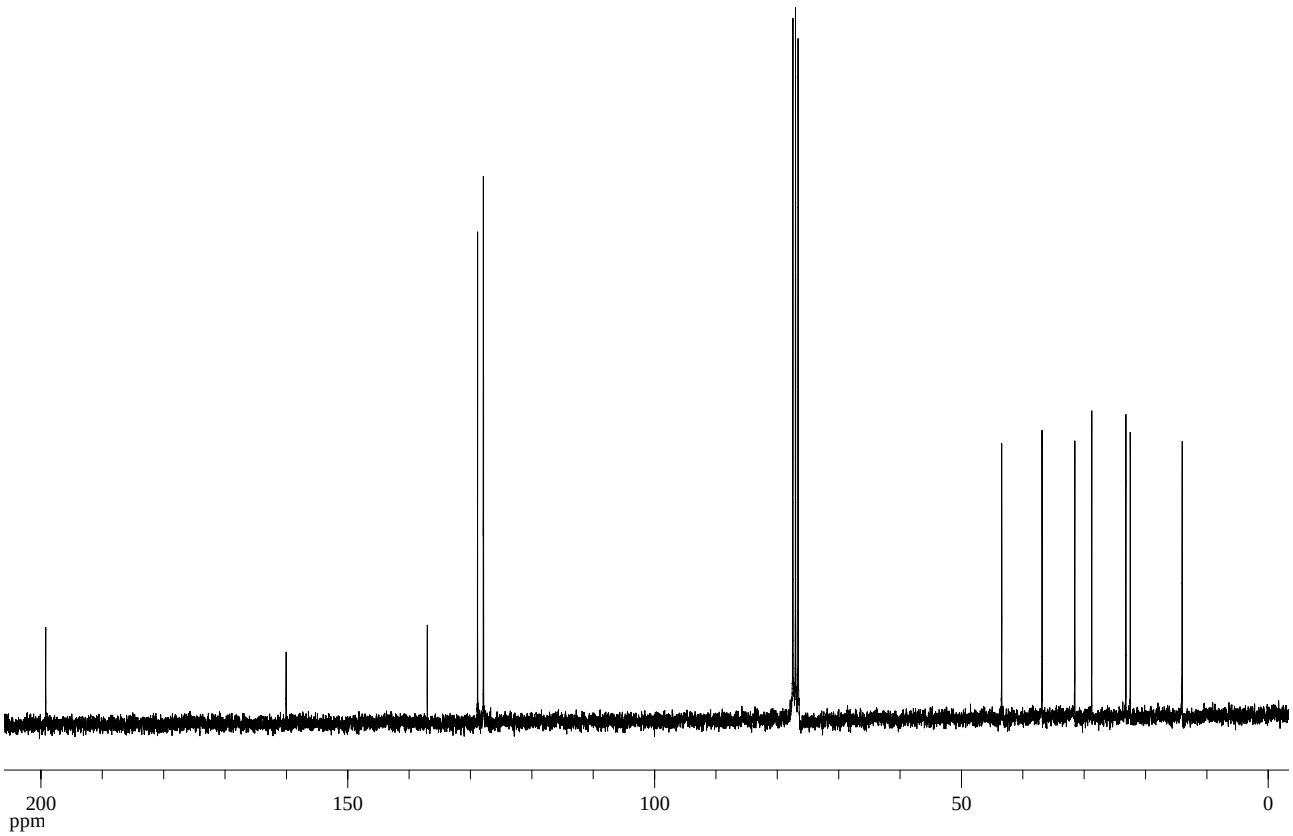


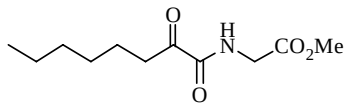




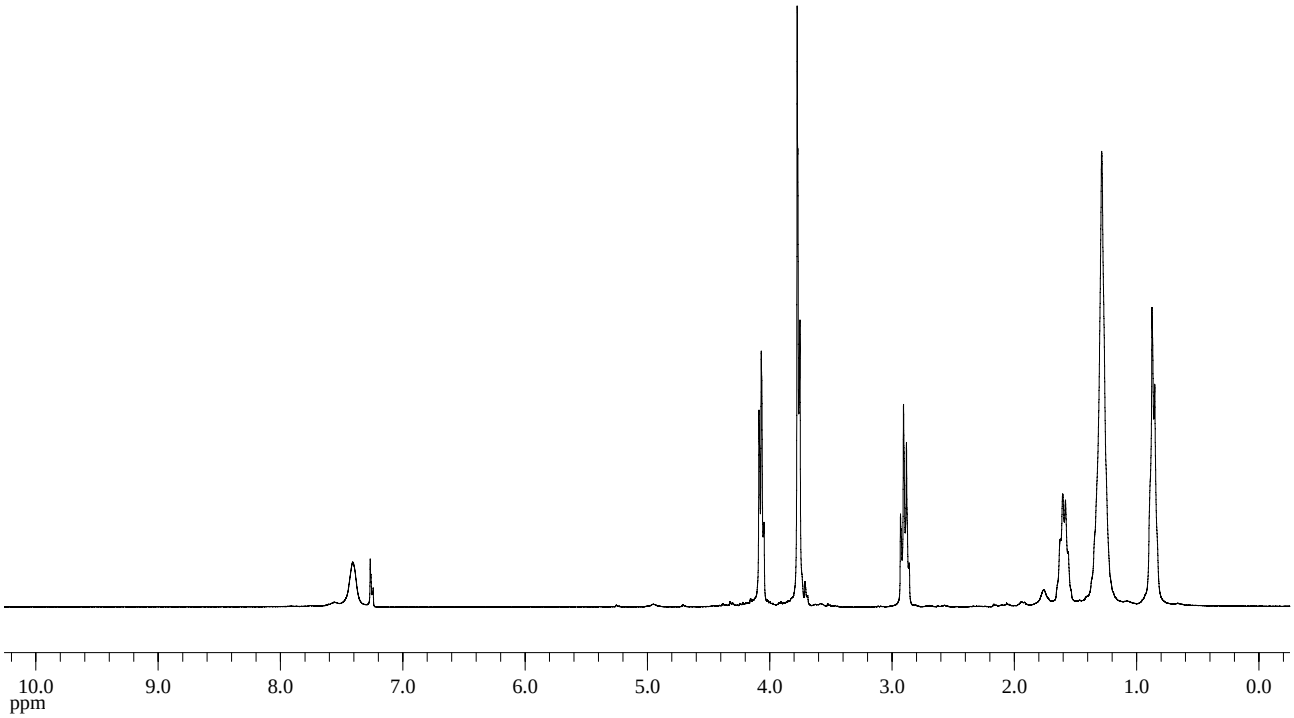
N-Benzyl-2-oxooctanamide

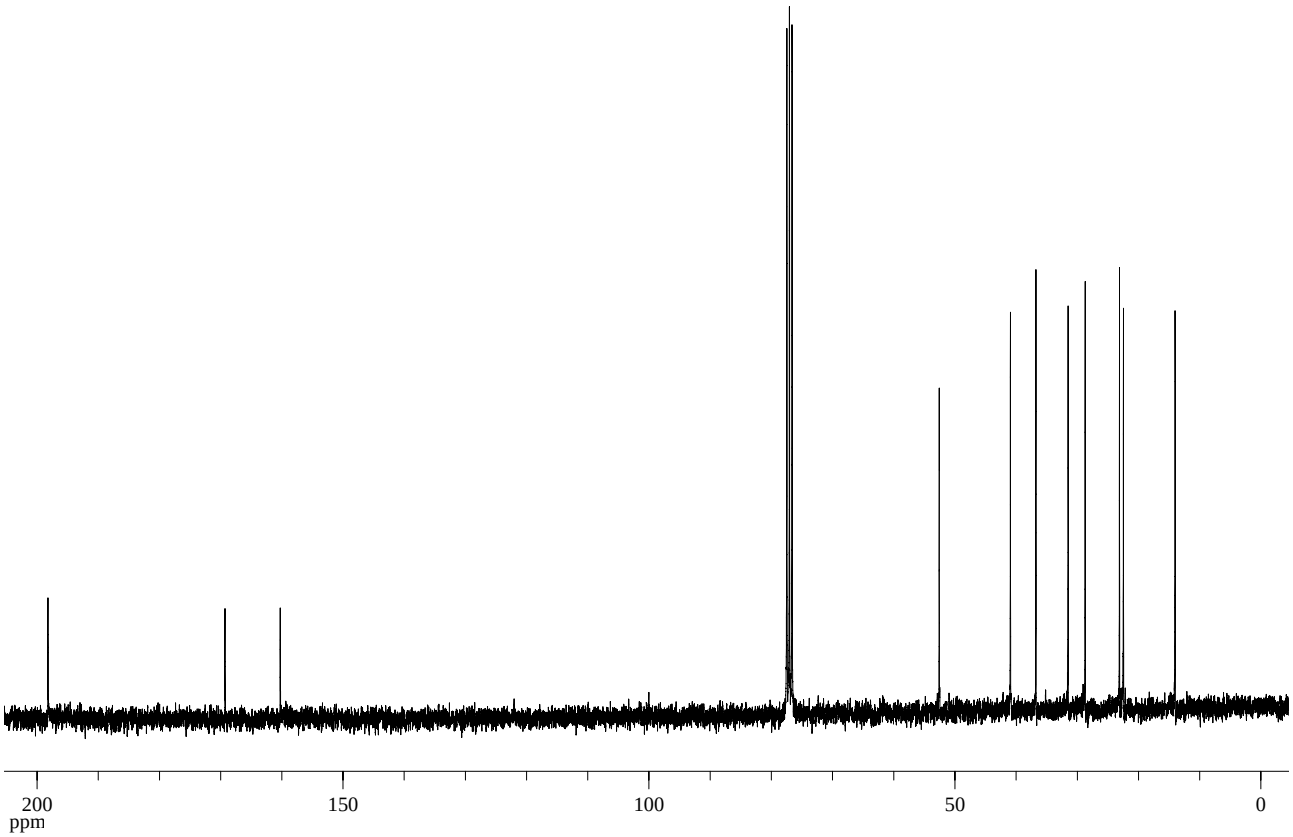


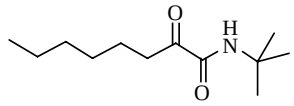




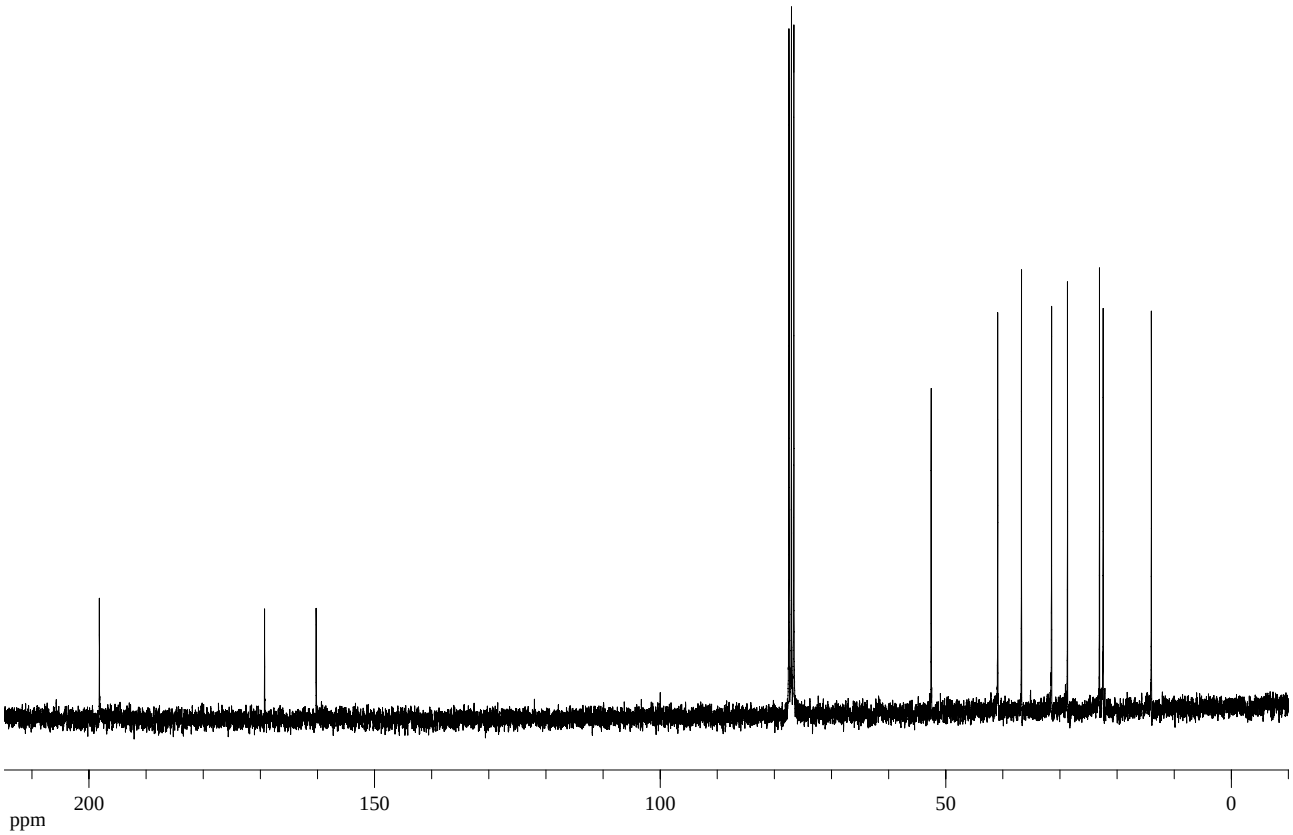
Methyl *N*-(2-oxooctanoyl)glycinate

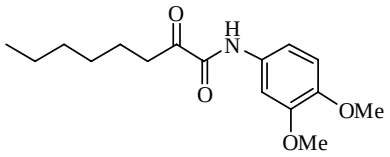




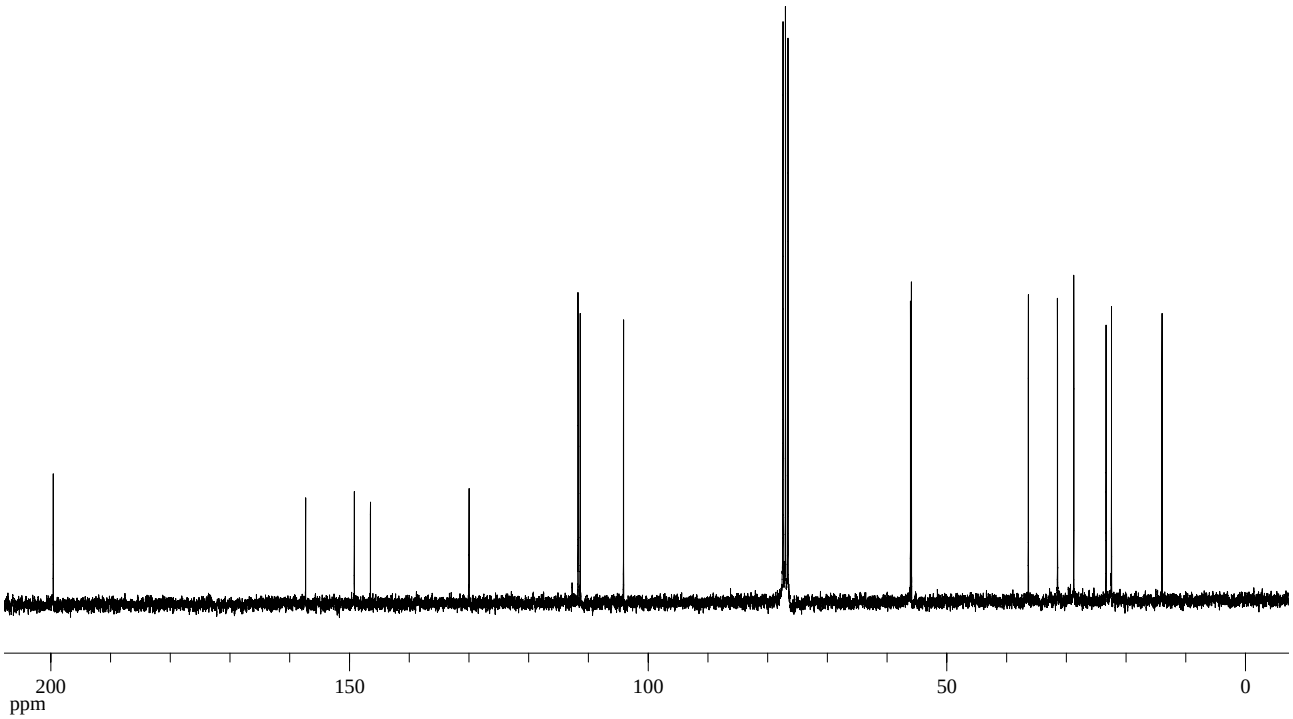


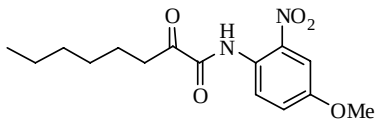
N-*tert*-Butyl-2-oxooctanamide



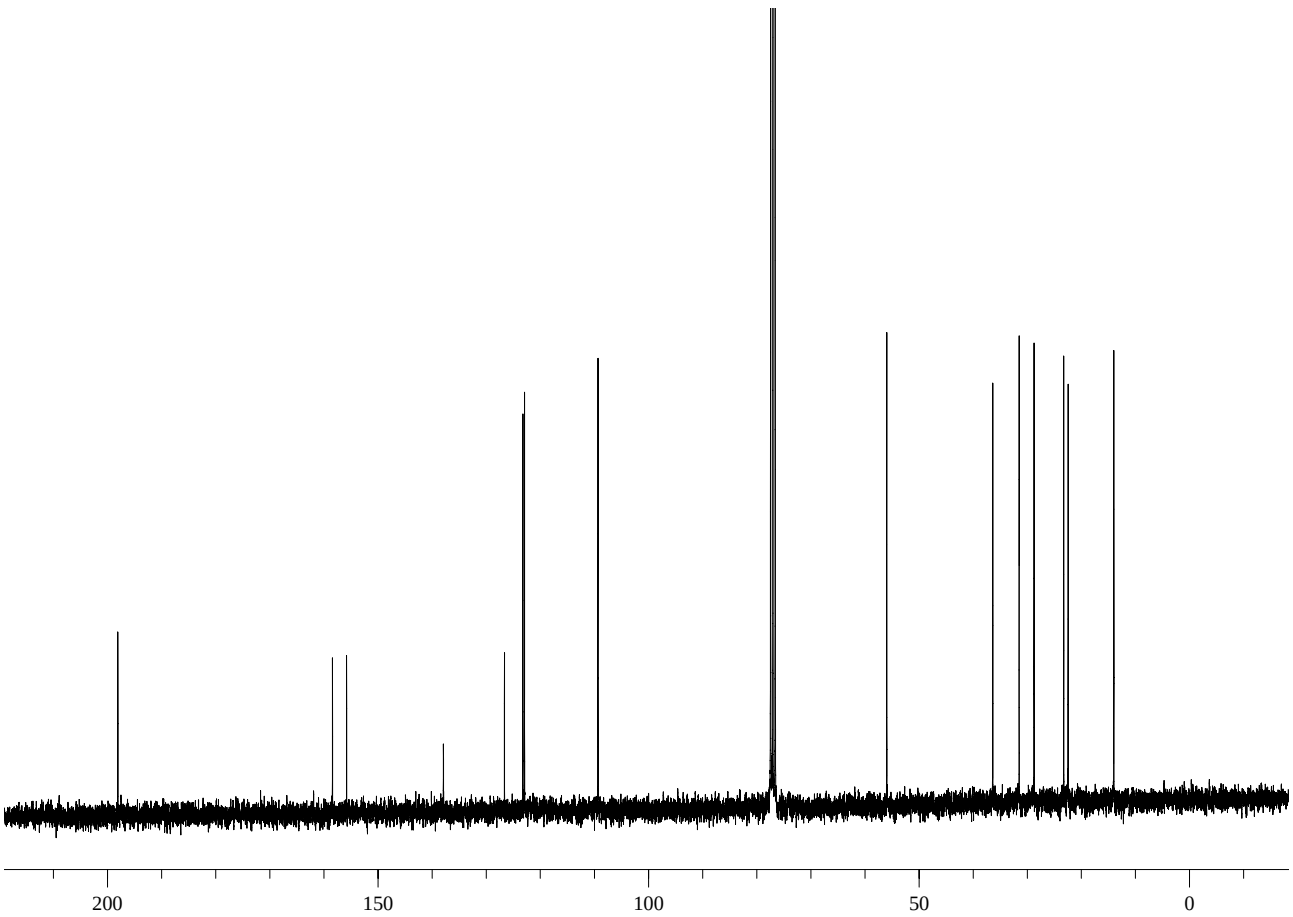


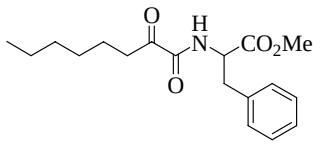
N-(3,4-Dimethoxyphenyl)-2-oxooctanamide



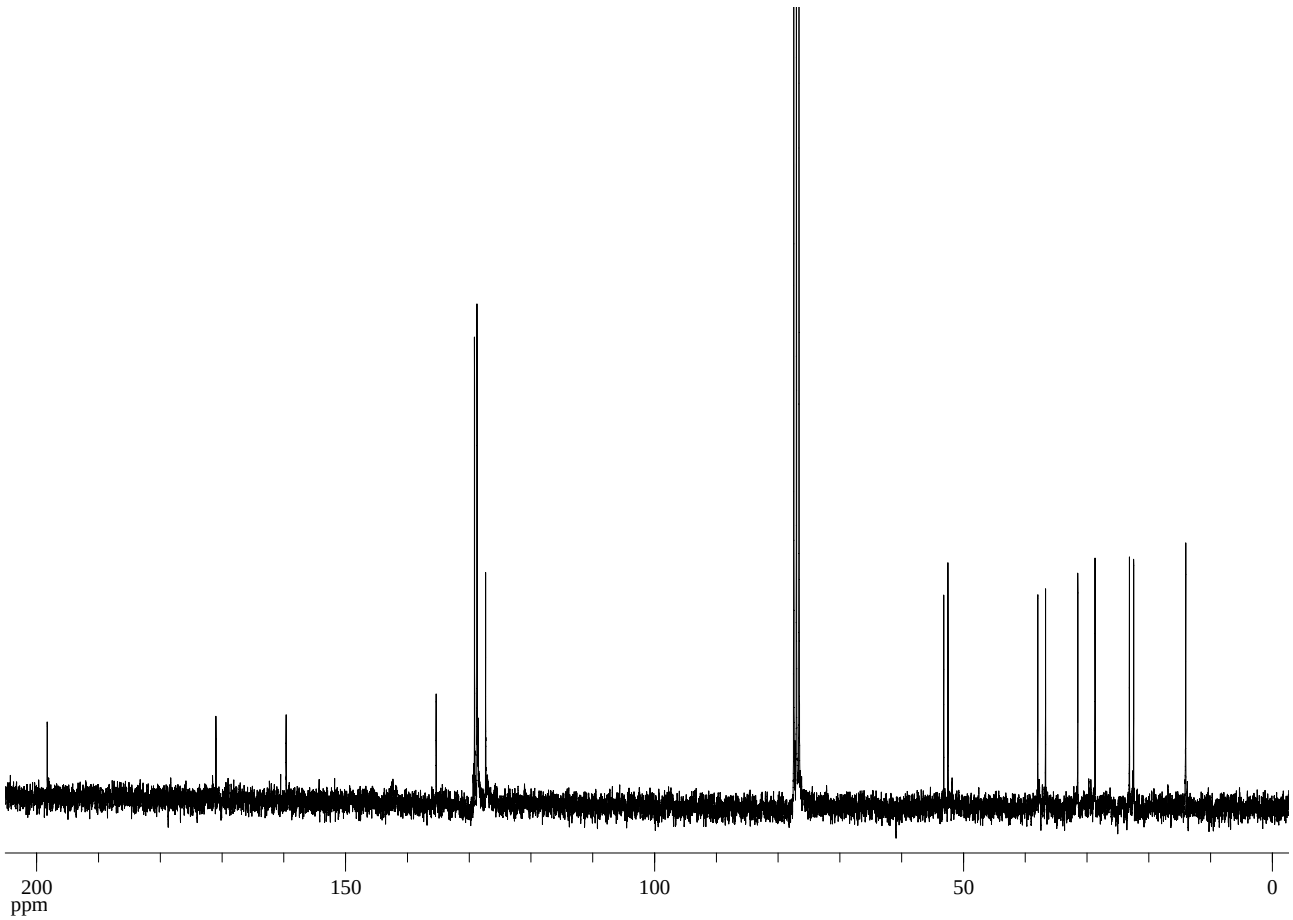


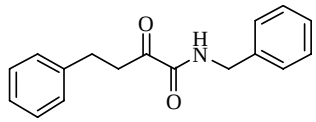
N-(4-Methoxy-2- nitrophenyl)-2-oxooctanamide



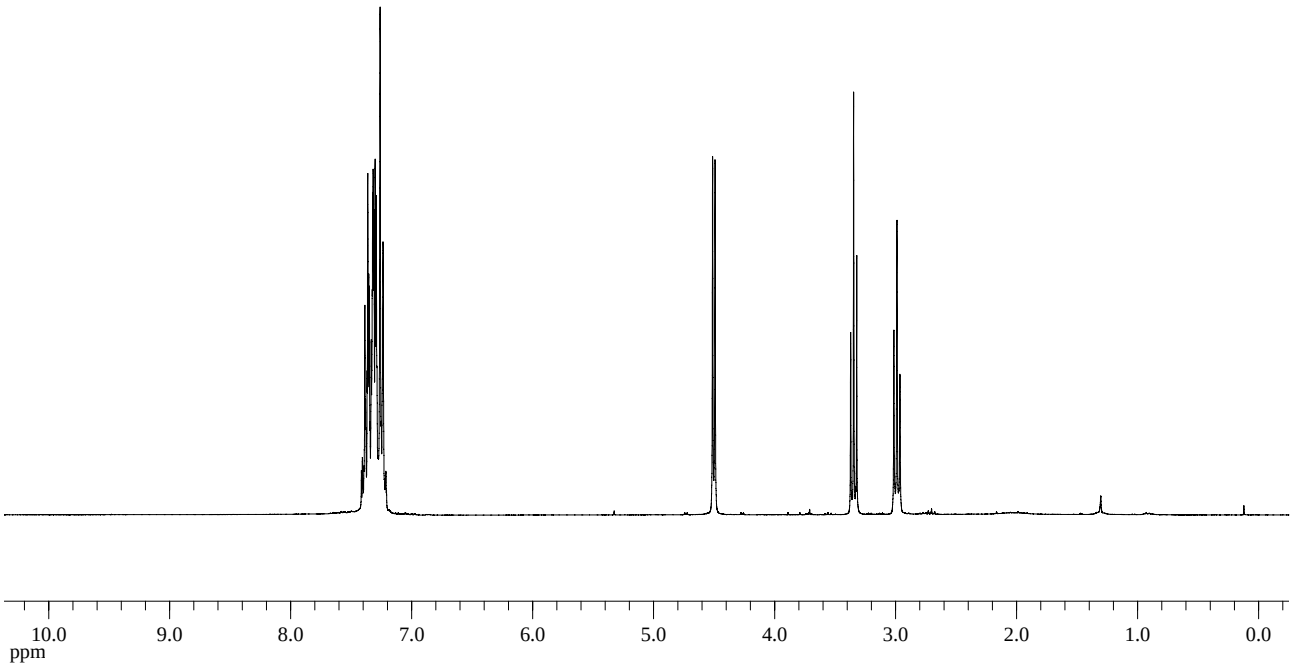


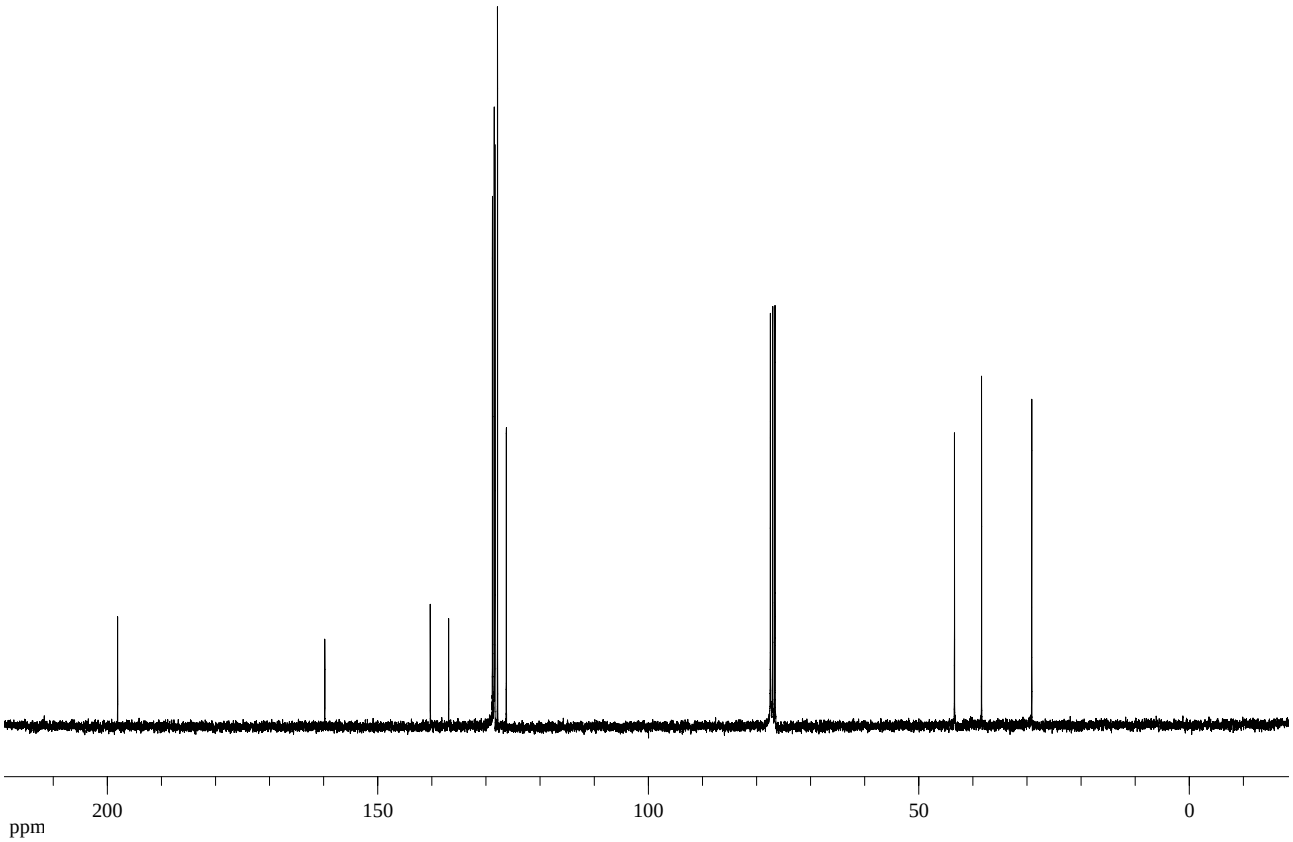
2-(2-Oxo-octanoylamino)-
3-phenyl propionic acid methyl ester

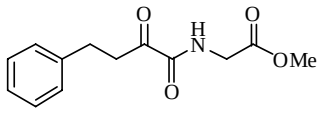




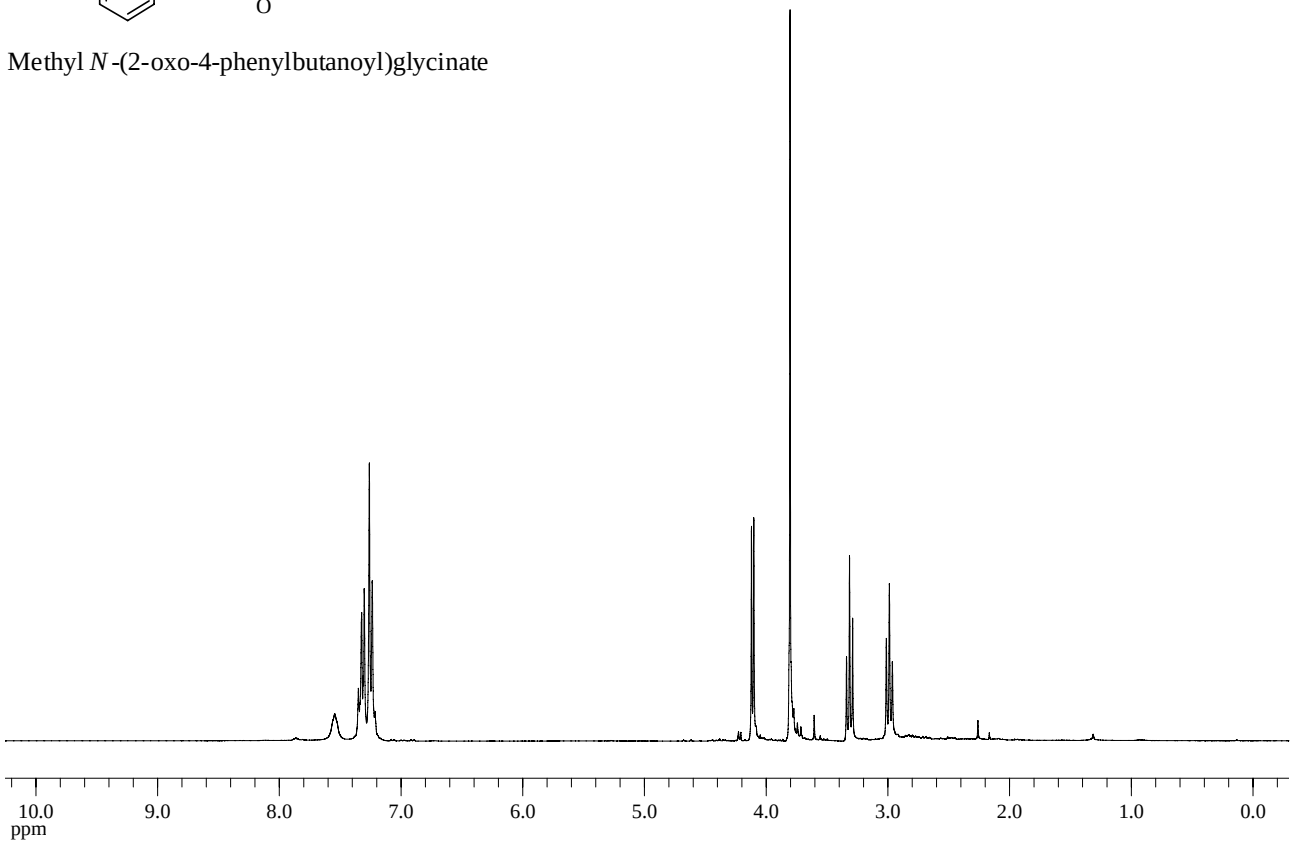
N-Benzyl-2-oxo-4-phenylbutanamide

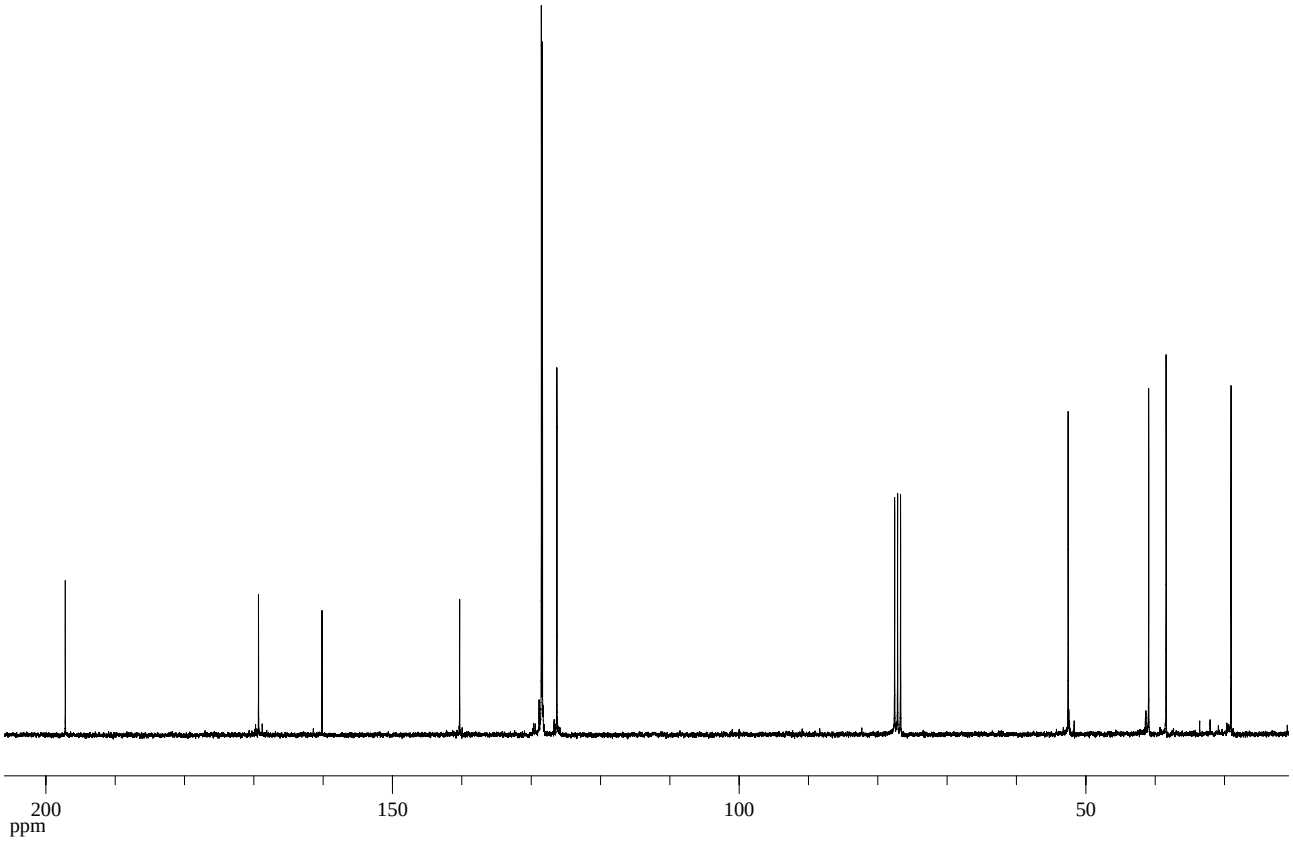


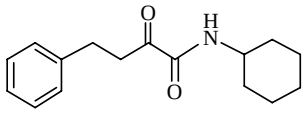




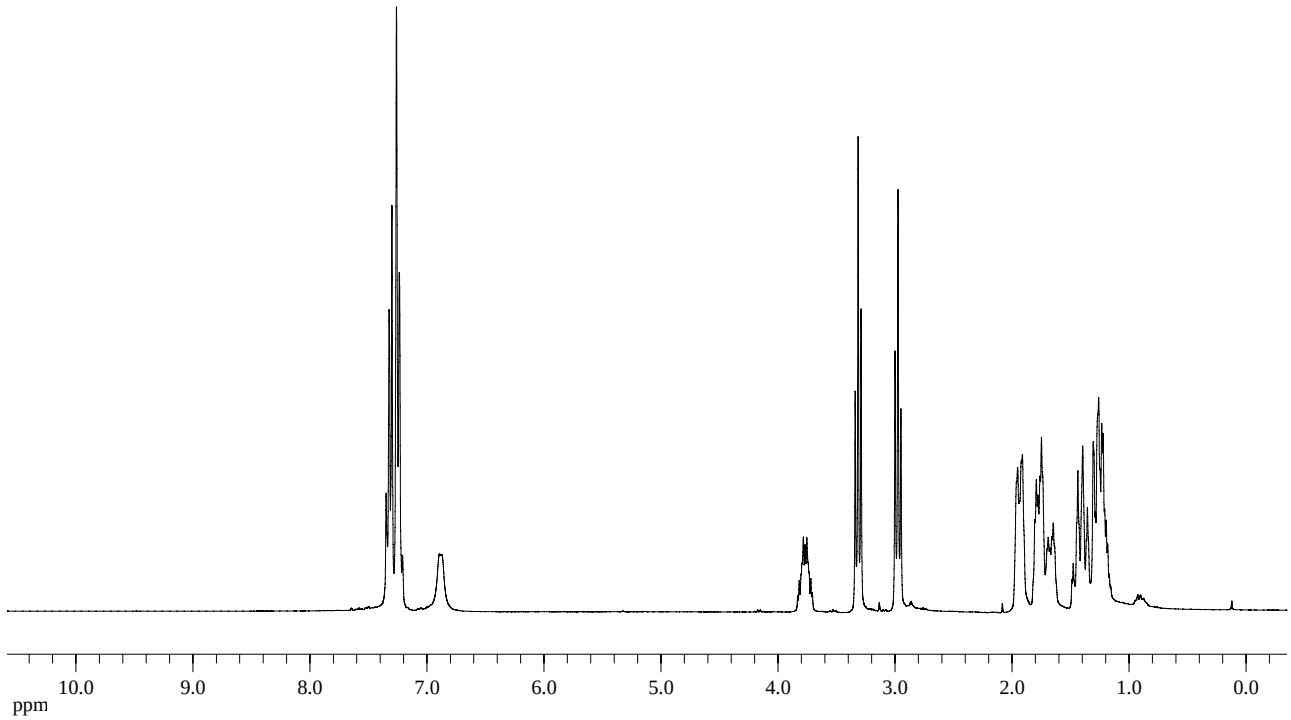
Methyl *N*-(2-oxo-4-phenylbutanoyl)glycinate

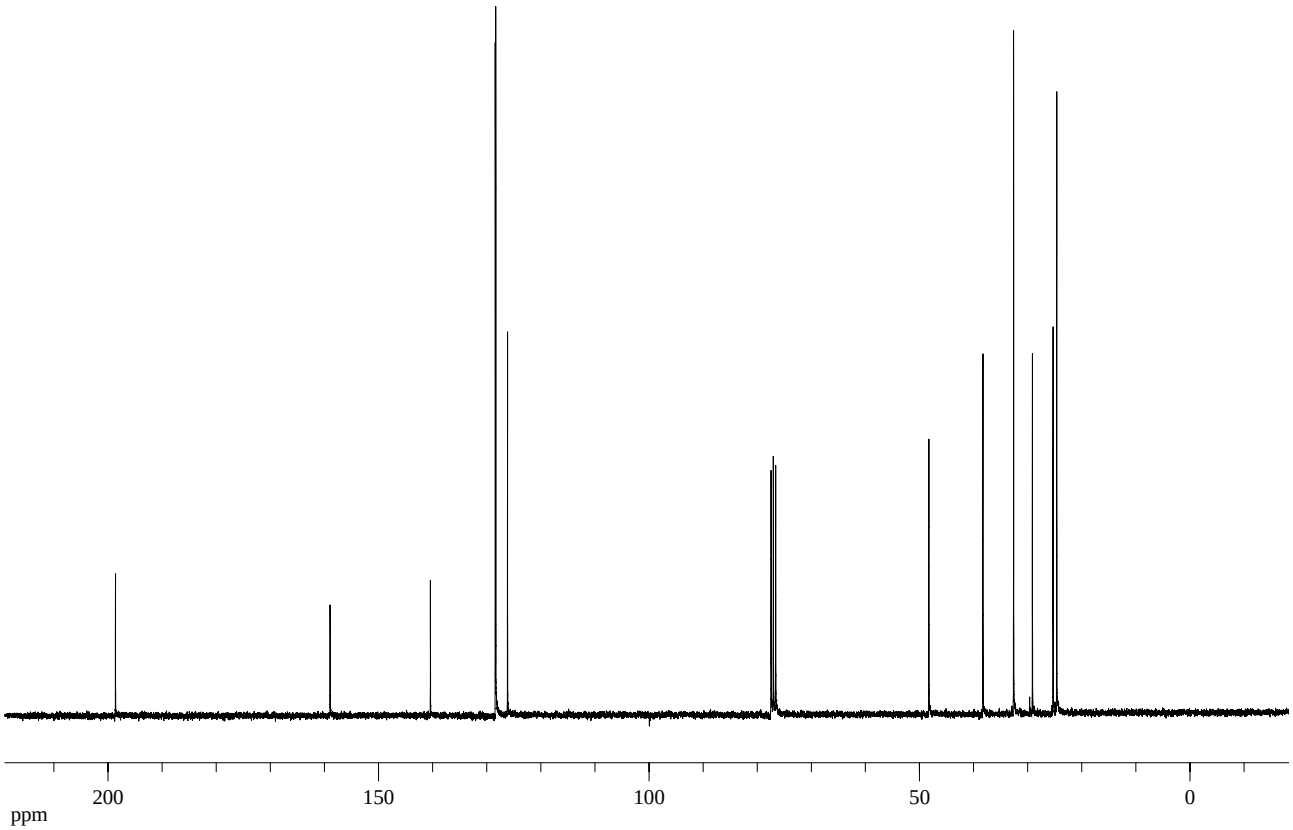


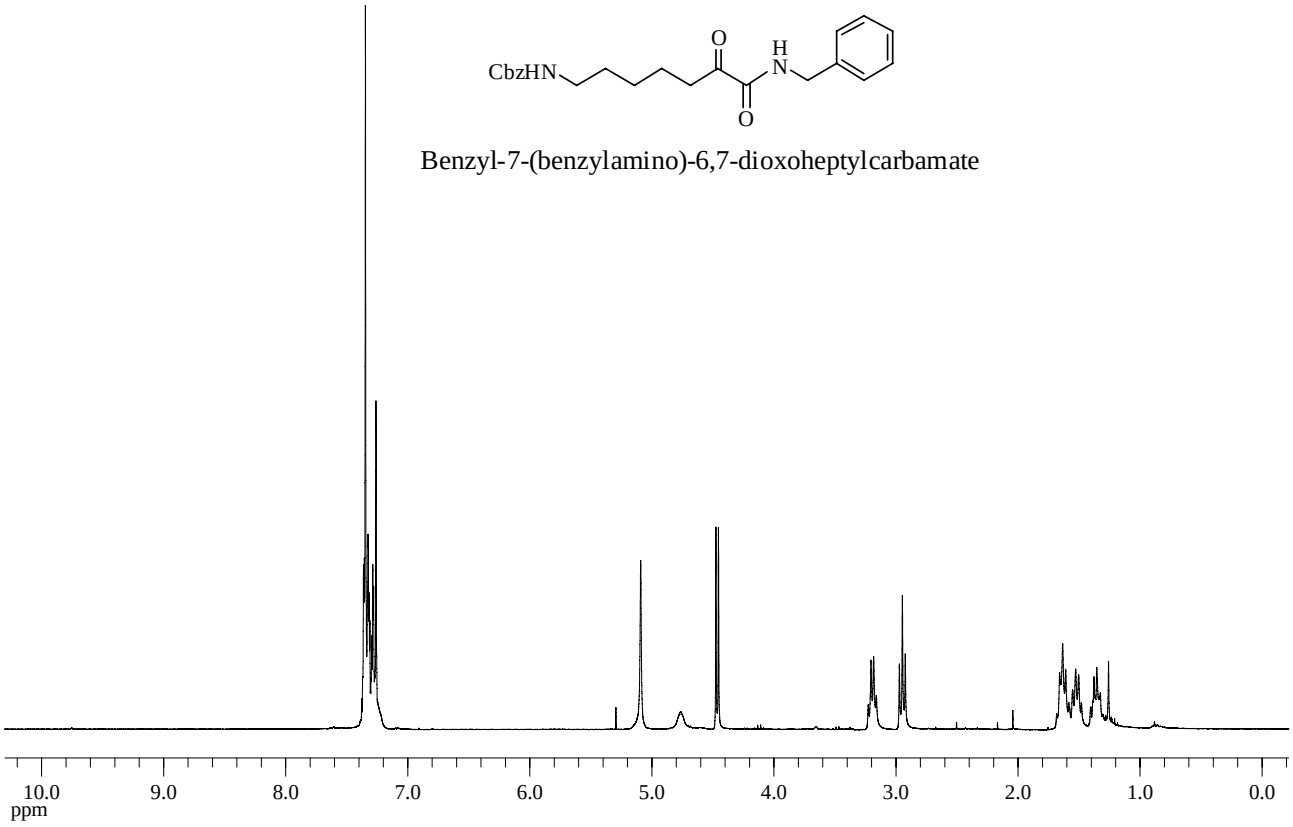




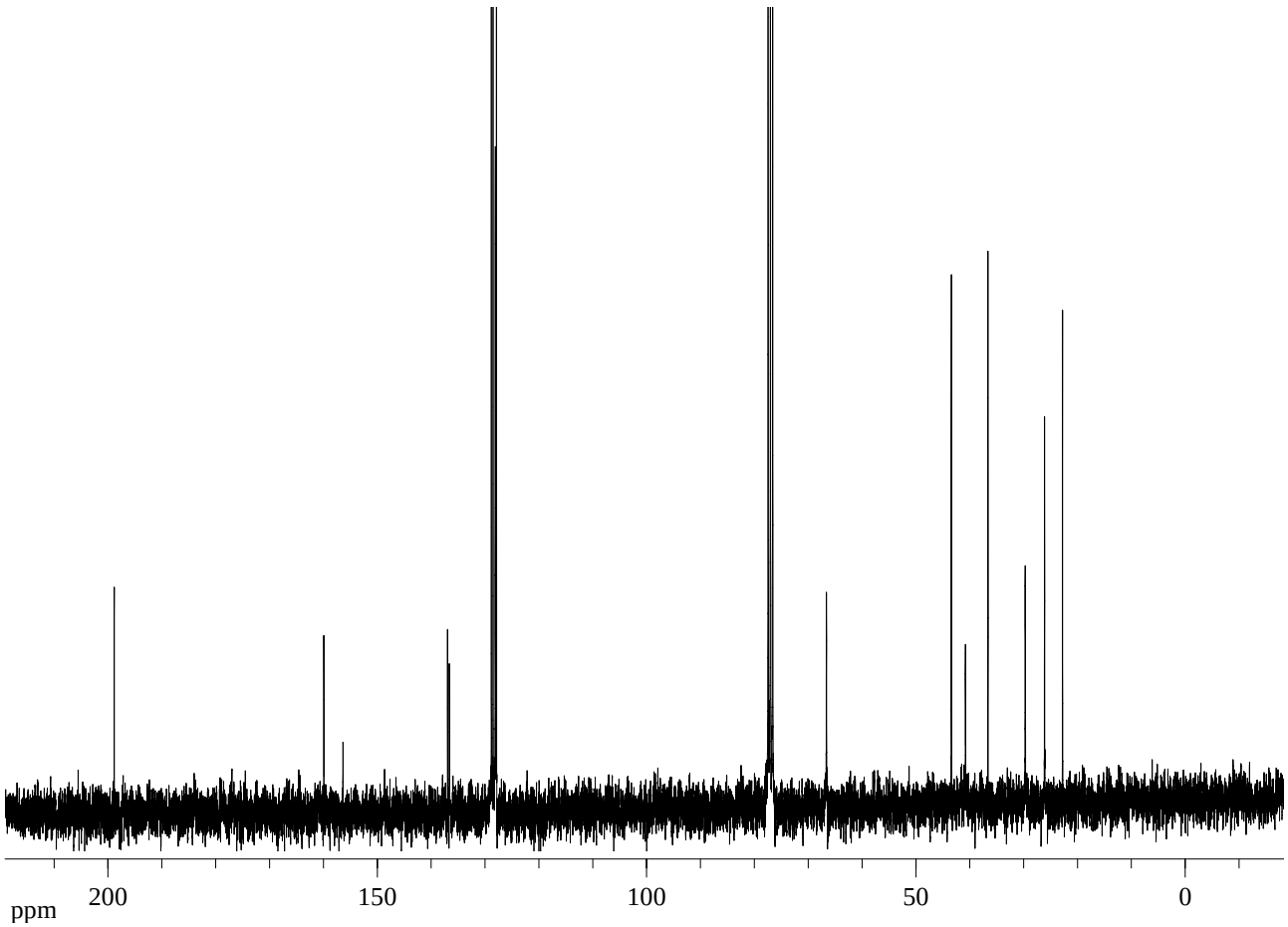
N-(4-Methoxy-2-nitrophenyl)-2-oxo-4-phenylbutanamide

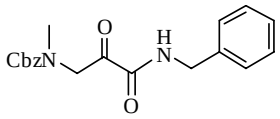




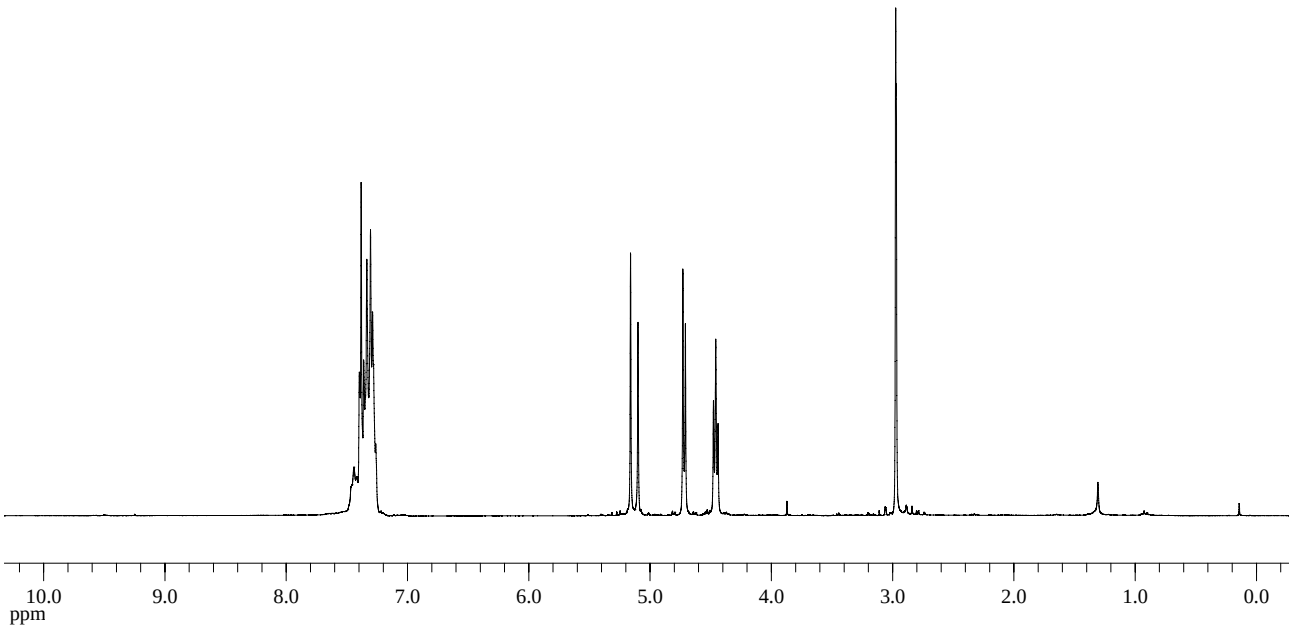


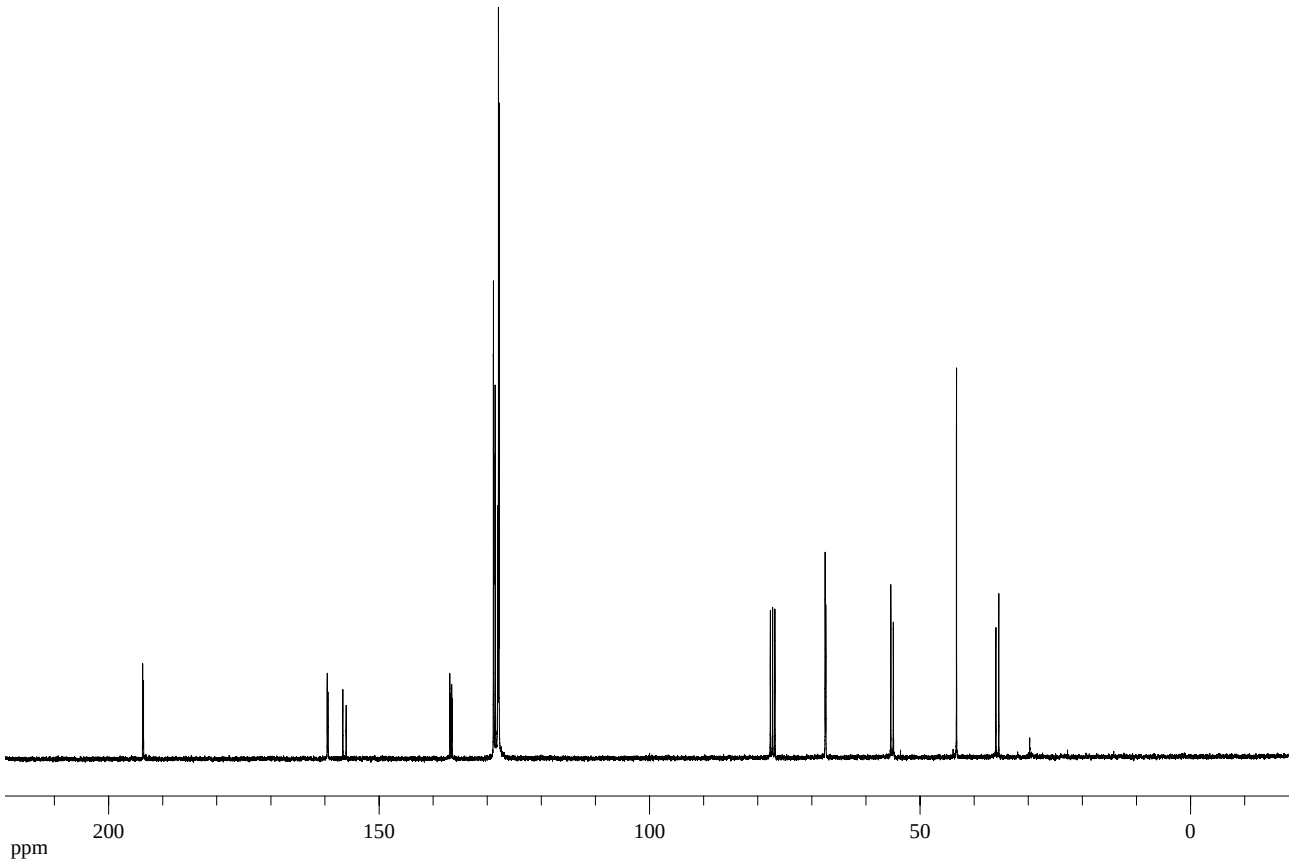
Benzyl-7-(benzylamino)-6,7-dioxoheptylcarbamate

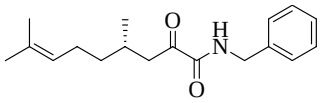




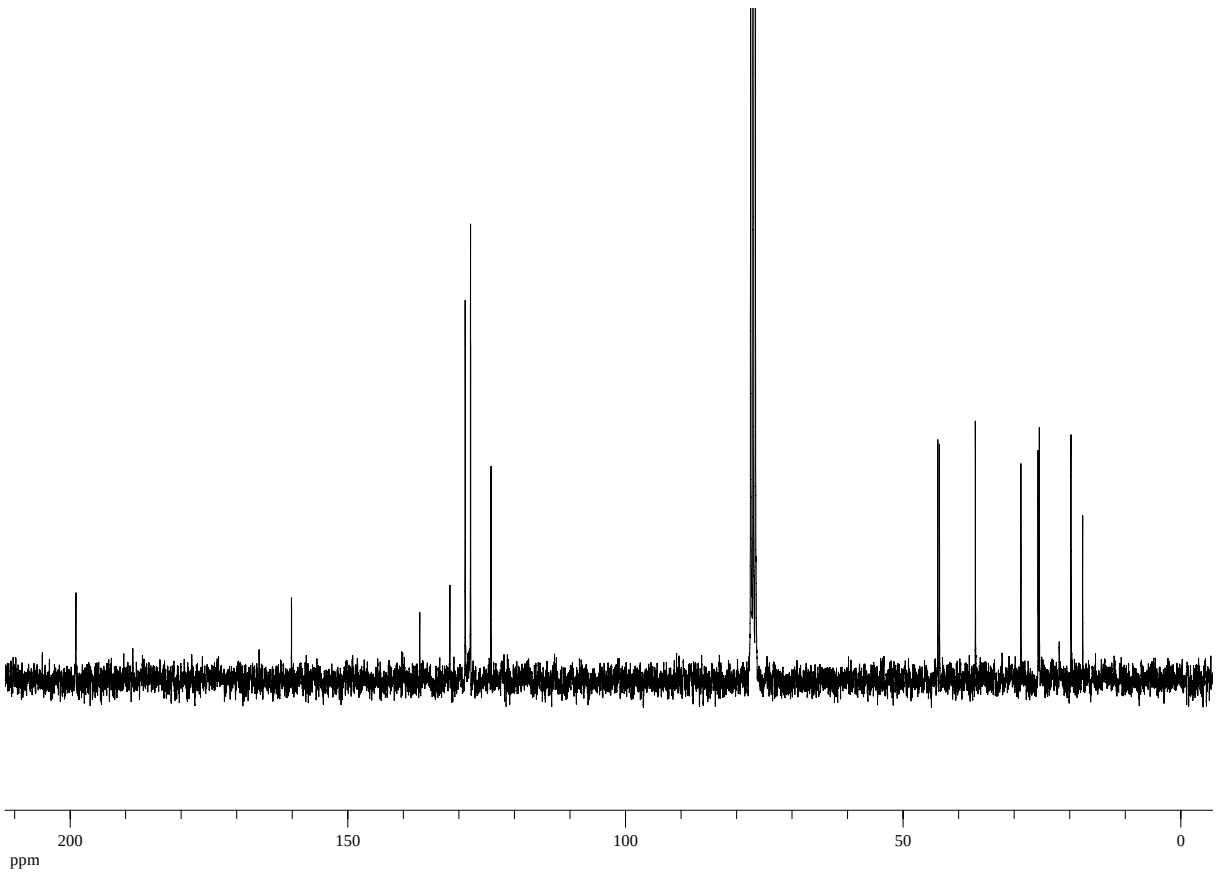
Benzyl[2-(benzylamino)-2-oxoethyl]methylcarbamate

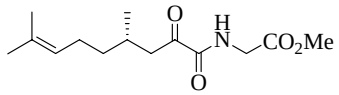




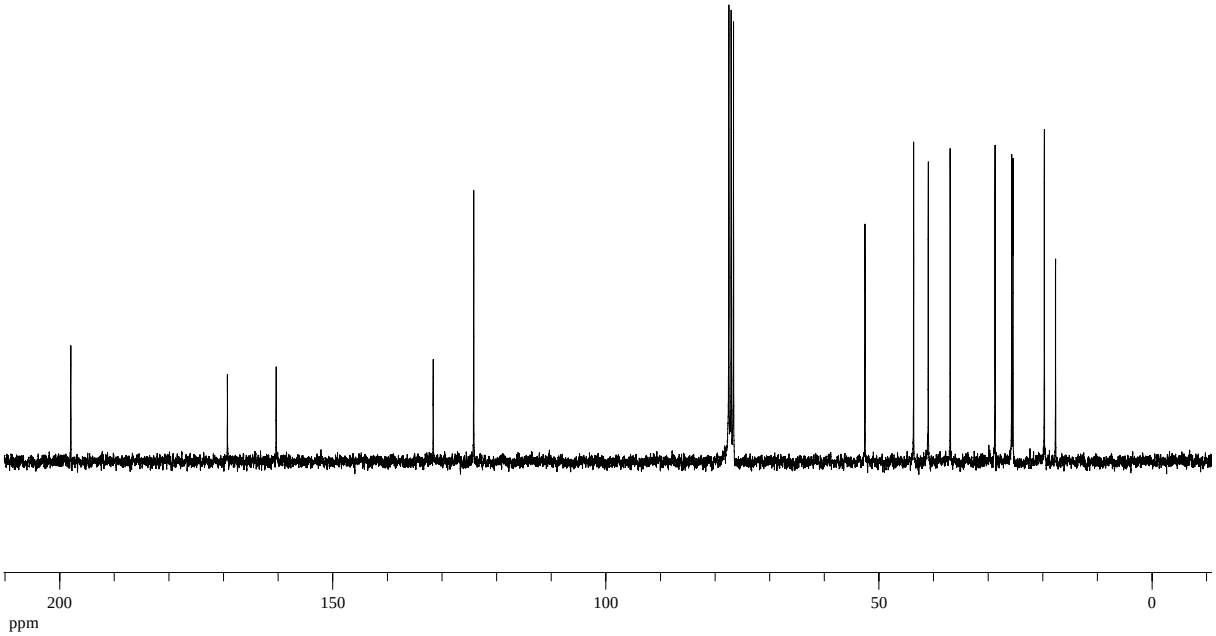


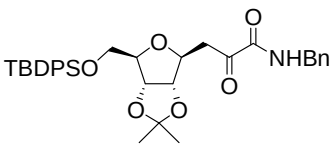
(*S*)-*N*-benzyl-4,8-dimethyl-2-oxonon-7-enamide



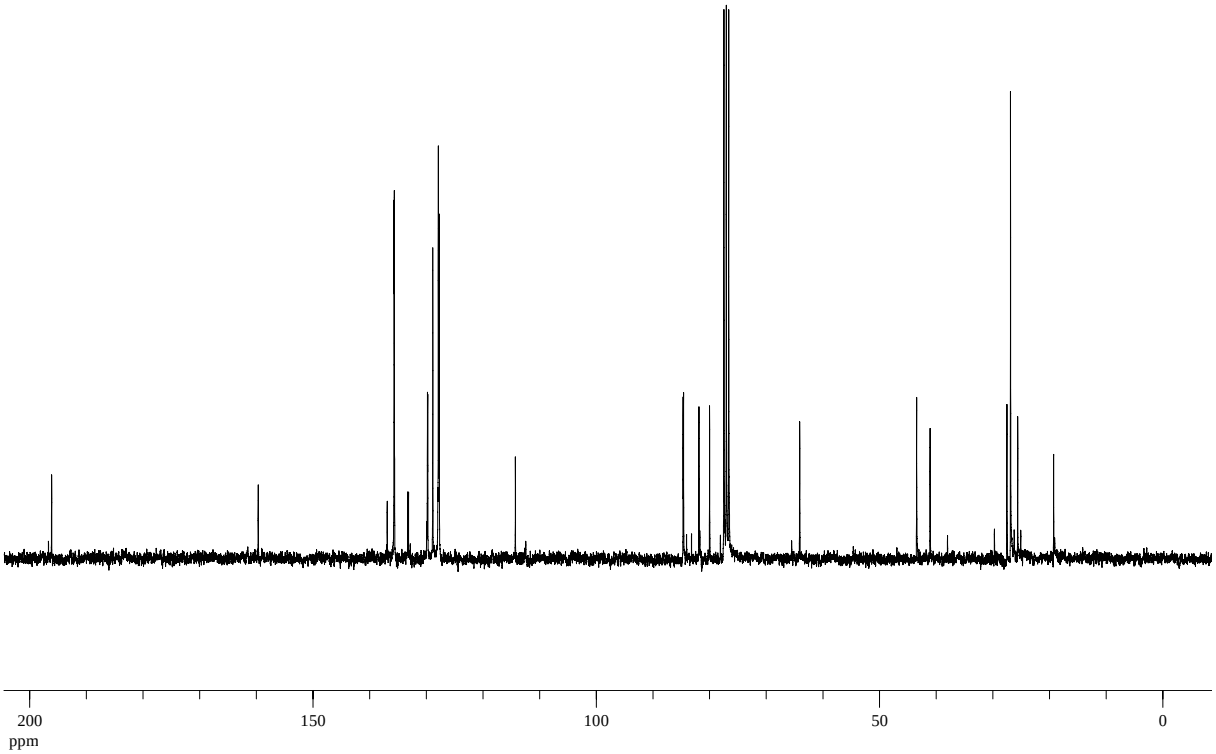


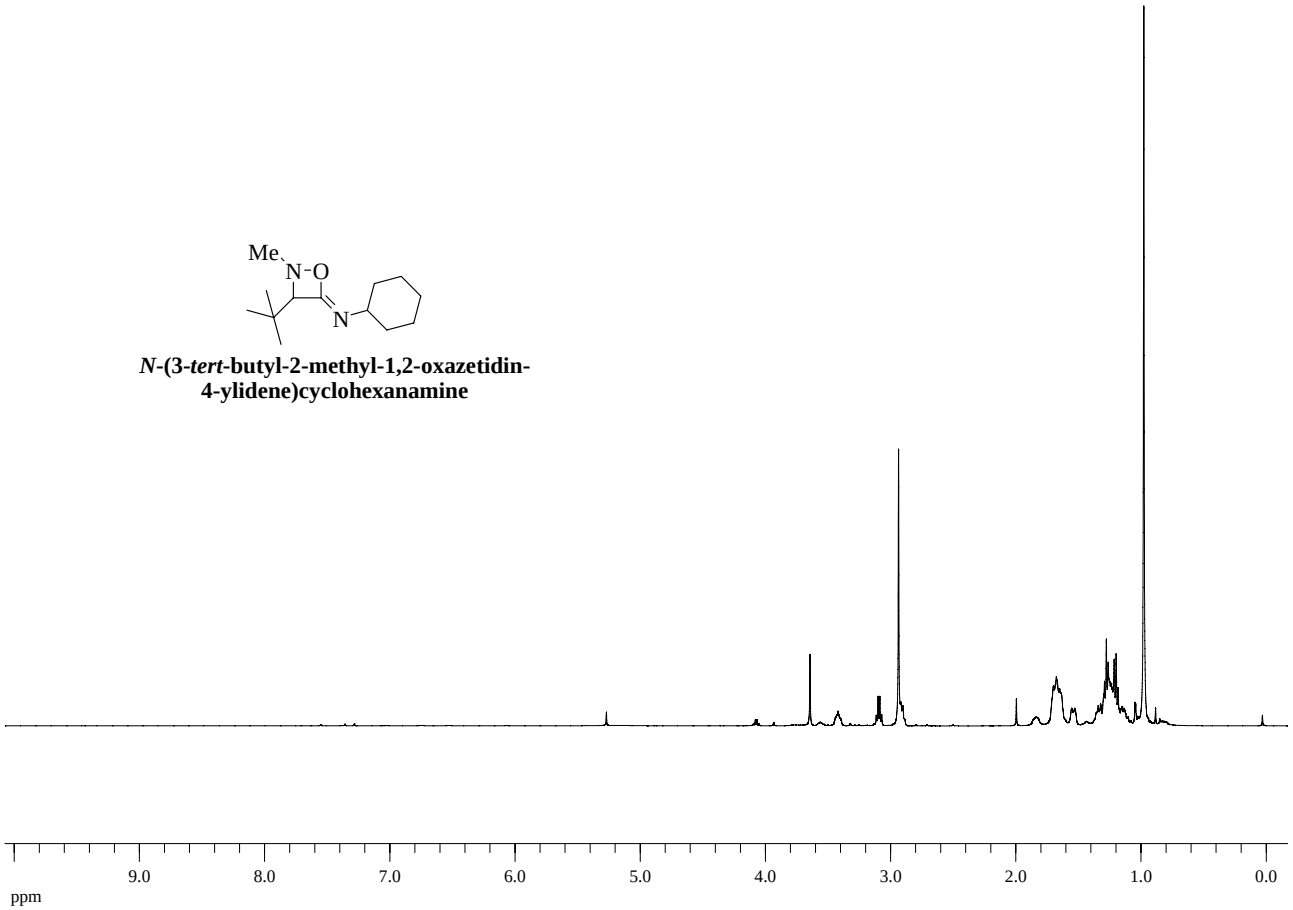
(*S*)-(4,8-dimethyl-2-oxonon-7-enoylamino)-acetic acid methyl ester





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





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

[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.