Electronic Supplementary Material (ESI) for ChemComm.

Carbon Isotope Labeling of Carbamates by Late-Stage [^{11}C], [^{13}C] and [^{14}C] Carbon Dioxide Incorporation

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Table of contents

1. General information

***Reactants and solvents**:*

Unless otherwise noted, all reactions were carried out in oven-dried glassware
Commercially available chemicals were purchased from from ABCR, Acros Organics, Sigma-Aldrich, Alfa Aesar, Combi-Blocks, Carbolution, Fluorochem, and TCI Europe and used as received unless otherwise stated. The following solvents were dried by distillation over the drying agents indicated in parentheses: THF (Sodium), Dichloromethane (CaH_2). Additional anhydrous solvents were purchased from Acros Organics, SigmaAldrich, Alfa Aesar and stored over molecular sieves under an argon atmosphere.

***Purifications**:*

Flash chromatography were performed on silica gel (Merck Kieselgel 60, grading 40-63 μm) or using automate Puriflash XS 520 Plus with pre-packed column RediSep® Rf (grading 35-70 μm).
Chiral HPLC chromatograms were recorded using a JASCO SFC apparatus with CHIRALCEL IA chiral column (250 mm × 4.6 mm x 5 μm), mobile phase : CO_2/iPrOH:10/90 , flow rate 1.0 $ml.min^{-1}$ at 25 °C, UV detection (300 nm).

Analysis:

Reactions were monitored by TLC carried out on silica 0,25 mm (60 F254, Merck) using UV light as visualizing agent. For staining, the TLC plates were dipped into a solution basic aqueous permanganate (1 g $KMnO_4$, 6 g K_2CO_3 and 0.1 g KOH in 100 mL H_2O) and developed with a heat gun.

Nuclear Magnetic Resonance (NMR) Spectroscopy: ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) were measured on a Brucker Avance 400 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from residual solvents peaks and coupling constants are reported as Hertz (Hz). Splitting patterns are designated as singlet (s), broad singlet (br. s), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m).

Electrospray mass spectra were obtained using an ESI-Quadripole autopurify, Waters (pump: 2545, mass: ZQ2000) mass Spectrometer.
LC-MS spectra were recorded on a Waters Acquity UPLC® equipped PDA eλ Detector and SQ Detector 2, mobile phase A: H_2O + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid.

High-resolution mass spectra (HRMS) were performed on a Bruker maXis mass spectrometer by the "Fédération de Recherche" ICOA/CBM (FR2708) platform (University of Orléans).

Infrared spectra (IR) were obtained on a Perkin Elmer UATR TWO FTIR spectrophotometer and are reported as wavelength numbers (cm^{-1}).
Melting points (Mp) were obtained on a BÜCHI Melting Point B-545 and are reported in °C.

Carbon-14 radiolabeling:

Carbon-14 reagents and compounds were handled by experimentalist uniquely trained in working with radioactive materials and operating in specialized laboratories.

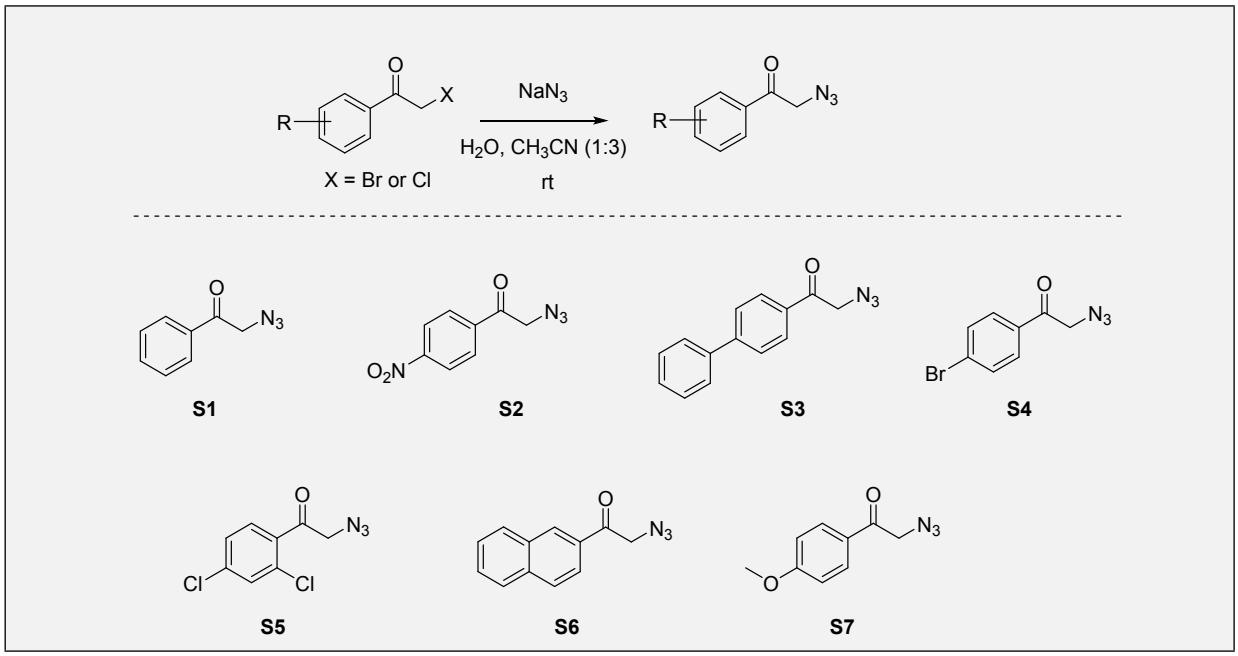
Carbon-14 radioactivity was measured either with a PerkinElmer Ultra Gold liquid scintillation cocktail or with a PerkinElmer 3110TR liquid scintillation analyzer.

RadioHPLC and HPLC-UV analyses were conducted with a Waters Alliance 2695 connected to a MS detector Waters ZQ 2000 and a Scintillation Analyzer Berthold 514 (column Xbridge BEH C18 100x4.6 mm, 3.5 µm). Alternatively, they were also conducted on a Waters Acquity UPLC® equipped PDA eλ Detector and SQ Detector 2, mobile phase A: H_2O + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid and a Scintillation Analyzer Berthold 509 (Xbridge BEH C18 50x2.1, 1.7).

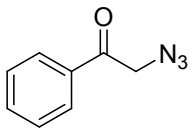
When using $^{14}CO_2$: $^{14}CO_2$ (2.172 GBq mmol-1) was generated using a $^{14}CO_2$ manifold system (RC Tritec AG). Mass spectra (ESI) for the calculation of molar activities (A_m) were obtained using a Waters Micromass ZQ spectrometer. Radiochemical purities were determined by Thin Layer Chromatography on TLC silica gel 60F254 glass plates (Merck) using a RITA scanner (Raytest) for the radioactive detection.

2. Materials and methods

2.1. Procedures for the preparation of α-azido-ketones



2-azido-1-phenylethan-1-one **(S1)**

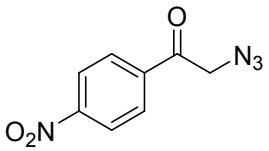


$C_8H_7N_3O$
MW: 161.10 g.mol^{-1}
Yield: 86%
Yellowish oil

To a solution of 2-chloro-1-phenylethan-1-one (1.00 g, 6.47 mmol) at room temperature in a mixture of 3.0 mL H_2O and 9.0 mL of CH_3CN was added sodium azide (650 mg, 10.0 mmol). After adding a catalytic amount of KI (56 mg, 0.33 mmol), the reaction mixture was stirred at room temperature for 2 hours. After addition of 50 mL of EtOAc, the organic phase was washed twice with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-phenylethan-1-one **S1** as a yellowish solid (900 mg, 86%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.63 (m, 1H), 7.51 (m, 2H), 4.57 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 134.2, 134.0, 128.9 (2C), 127.8 (2C), 54.7.
IR (cm^{-1}) 3050, 2912, 2102, 1621, 1591, 1432, 1351, 1251, 1223, 901, 873, 771, 749, 663, 453.
LCMS (ESI) ***m/z*** $C_8H_7N_3O$ $[M+H]^+$ 162.1.

***2-azido-1-(4-nitrophenyl)ethan-1-one* (S2)**

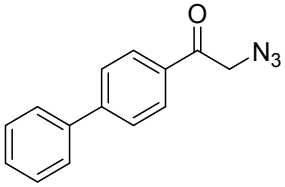


$C_8H_6N_4O_3$
MW: 206.16 g.mol^{-1}
Yield: 49%
Yellowish solid

To a solution of 2-bromo-1-(4-nitrophenyl)ethan-1-one (1.00 g, 4.10 mmol) at room temperature in a mixture of 2.0 mL H_2O and 6.0 mL of CH_3CN was added sodium azide (400 mg, 6.14 mmol). The reaction mixture was stirred at room temperature for 2 hours. After addition of 50 mL of EtOAc, the organic phase was washed twice with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(4-nitrophenyl)ethan-1-one **S2** as a yellowish solid (410 mg, 49%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.9 Hz, 2H), 8.08 (d, J = 8.9 Hz, 2H), 4.62 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 150.9, 138.8, 129.2 (2C), 124.3 (2C), 55.3.
IR (cm^{-1}) 2895, 2150, 2107, 1704, 1601, 1521, 1342, 1209, 1005, 914, 852, 748, 689, 640, 552, 501.
LCMS (ESI) ***m/z*** $C_8H_6N_4O_3$ $[M+H-N_2]^+$ 179.3.

***1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-one* (S3)**

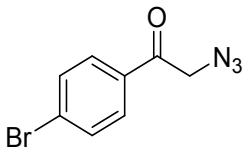


$C_{14}H_{11}N_3O$
MW: 237.26 g.mol^{-1}
Yield: 99%
Yellowish solid

To a solution of 1-([1,1'-biphenyl]-4-yl)-2-bromoethan-1-one (1.10 g, 4.0 mmol) at room temperature in a mixture of 2.0 mL H_2O, 2.0 mL of THF and 6.0 mL of CH_3CN was added sodium azide (390 mg, 6.0 mmol). The reaction mixture was stirred at room temperature for 2 hours. After addition of 50 mL of EtOAc, the organic phase was washed twice with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-one **S3** as a yellowish solid (937 mg, 99%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 8.5 Hz, 2H), 7.62 (m, 2H), 7.44 (m, 2H), 7.41 (m, 1H), 4.57 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 146.8, 139.5, 133.1, 129.1 (2C), 128.62, 128.59 (2C), 127.6 (2C), 127.3 (2C), 54.9.
IR (cm^{-1}) 3030, 2909, 2137, 2097, 1682, 1601, 1403, 1344, 1220, 1192, 1000, 908, 831, 759, 723, 695, 670, 571.
LCMS (ESI) ***m/z*** $C_{14}H_{11}N_3O$ $[M+H]^+$ 238.3.

***2-azido-1-(4-bromophenyl)ethan-1-one* (S4)**

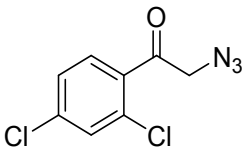


$C_8H_6BrN_3O$
MW: 240.06 g.mol^{-1}
Yield: 89%
Yellowish solid

To a solution of 2-bromo-1-(4-bromo)ethan-1-one (1.11 g, 4.0 mmol) at room temperature in a mixture of 2.0 mL H_2O and 6.0 mL of CH_3CN was added sodium azide (400 mg, 6.14 mmol). The reaction mixture was stirred at room temperature for 30 min. After addition of 50 mL of EtOAc, the organic phase was washed twice with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(4-bromophenyl)ethan-1-one **S4** as a yellowish solid (854 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.7 Hz, 2H), 7.63 (d, J = 8.7 Hz, 2H), 4.52 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 133.2, 132.4 (2C), 129.6, 129.5 (2C), 54.9.
IR (cm^{-1}) 3368, 2905, 2102, 1692, 1586, 1398, 1292, 1216, 1071, 1000, 908, 719, 645, 552, 496.
LCMS (ESI) ***m/z*** $C_8H_6{}^{79}BrN_3O$ $[M+H]^+$ 240.0, $C_8H_6{}^{81}BrN_3O$ $[M+H]^+$ 242.1.

***2-azido-1-(2,4-dichlorophenyl)ethan-1-one* (S5)**

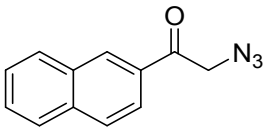


$C_8H_5Cl_2N_3O$
MW: 230.05 g.mol^{-1}
Yield: 75%
Yellow solid

To a solution of 2-chloro-1-(2,4-dichlorophenyl)ethan-1-one (894 mg, 4.0 mmol) at room temperature in a mixture of 2.0 mL H_2O, 2.0 mL of THF and 6.0 mL of CH_3CN was added sodium azide (390 mg, 6.0 mmol). After adding a catalytic amount of KI (34.0 mg, 0.20 mmol), the reaction mixture was stirred at room temperature for 9 hours. After addition of 50 mL of EtOAc, the organic phase was washed twice with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(2,4-dichlorophenyl)ethan-1-one **S5** as a yellow solid (687 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H), 7.34 (dd, J = 8.4, 2.0 Hz, 1H), 4.49 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 139.0, 134.1, 132.8, 131.2, 130.8, 127.8, 57.9.
IR (cm^{-1}) 3090, 2099, 1693, 1581, 1374, 1274, 1255, 1204, 1106, 1064, 995, 911, 826, 780, 576.
LCMS (ESI) ***m/z*** $C_8H_5{}^{35}Cl_2N_3O$ $[M+H-N_2]^+$ 202.1, $C_8H_5{}^{35}Cl^{37}ClN_3O$ $[M+H-N_2]^+$ 204.2, $C_8H_5{}^{37}Cl_2N_3O$ $[M+H-N_2]^+$ 206.0.

***2-azido-1-(naphthalen-2-yl)ethan-1-one* (S6)**

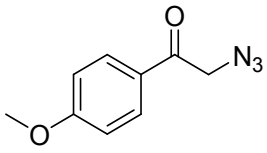


$C_{12}H_9N_3O$
MW: 211.22 g.mol^{-1}
Yield: 96%
Yellowish solid

To a solution of 2-bromo-1-(naphthalen-2-yl)ethan-1-one (996 mg, 4.0 mmol) at in a mixture of 2 mL H_2O, 2 mL of THF and 6 mL of CH_3CN was added sodium azide (390 mg, 6.0 mmol). The reaction mixture was stirred at room temperature for 2 hours. After addition of 50 mL of EtOAc, the organic phase was washed twice with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(naphthalen-2-yl)ethan-1-one **S6** as a yellowish solid (854 mg, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.95 – 7.92 (m, 2H), 7.90 – 7.86 (m, 2H), 7.63 (ddd, J = 8.2, 6.9, 1.4 Hz, 1H), 7.57 (ddd, J = 8.1, 7.0, 1.3 Hz, 1H), 4.66 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 136.0, 132.4, 131.7, 129.8, 129.7, 129.1, 129.0, 128.0, 127.2, 123.3, 55.0.
IR (cm^{-1}) 3060, 2983, 2902, 2089, 1675, 1595, 1419, 1354, 1255, 1210, 909, 857, 772, 736, 664, 471.
LCMS (ESI) ***m/z*** $C_{12}H_9N_3O$ $[M+H]^+$ 212.2.

***2-azido-1-(4-methoxyphenyl)ethan-1-one* (S7)**

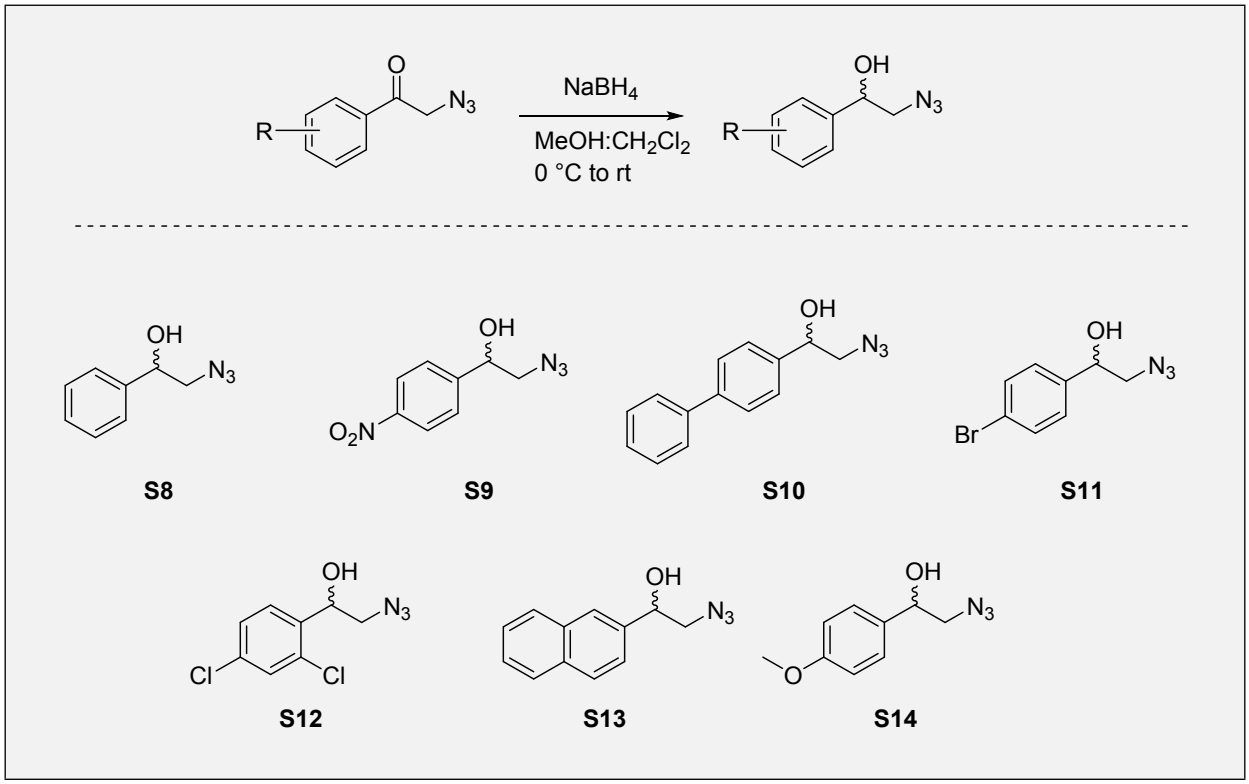


$C_9H_9N_3O_2$
MW: 191.19 g.mol^{-1}
Yield: 98%
Yellowish solid

To a solution of 2-bromo-1-(4-methoxyphenyl)ethan-1-one (917 mg, 4.10 mmol) at room temperature in a mixture of 2.0 mL H_2O and 6.0 mL of CH_3CN was added sodium azide (400 mg, 6.14 mmol). The reaction mixture was stirred at room temperature for 1 hour. After addition of 50 mL of EtOAc, the organic phase was washed twice with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(4-methoxyphenyl)ethan-1-one **S7** as a yellowish solid (747 mg, 98%).

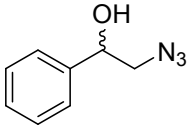
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.9 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 4.49 (s, 2H), 3.86 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 164.3, 130.3 (2C), 127.4, 114.2 (2C), 55.6, 54.6.
IR (cm^{-1}) 2902, 2842, 2120, 1862, 1597, 1515, 1267, 1235, 1174, 1021, 944, 823, 771, 627, 597, 566.
LCMS (ESI) ***m/z*** $C_9H_9N_3O_2$ $[M+H]^+$ 192.2.

2.2. General procedure for the reduction of α-azidoketone to α-azidoalcohols



To a solution of 1.00 mmol of α-azidoketone in 7.0 mL of dry MeOH and 3.0 mL of dry CH_2Cl_2 at 0 °C was added 1.00 mmol of $NaBH_4$. The resulting mixture was then stirred at room temperature under argon for 30 min. After the reaction was completed, the reaction was stopped by adding 10 mL of a saturated solution of $NaHCO_3$ and the phases were separated. The aqueous phase was extracted twice with 10.0 mL of CH_2Cl_2, the organic layers were combined, dried over $MgSO_4$ and evaporated to dryness. The crude mixture was then purified by Flash Chromatography on SiO_2 gel using the opportune eluent.

2-azido-1-phenylethan-1-ol **(S8)**



$C_8H_9N_3O$
MW: 163.18 g.mol^{-1}
Yield: 90%
Colorless oil

2-azido-1-phenylethan-1-ol **S8** was prepared accordingly to the general procedure.The reaction was conducted using 161 mg of 2-azido-1-phenylethan-1-one **(S1)** as starting material. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-phenylethan-1-ol **S8** as a colorless oil (146 mg, 90%).

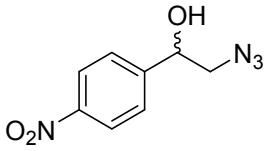
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 5H), 4.84 (dd, J = 8.0, 4.0 Hz, 1H), 3.42 (m, 2H), 2.74 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 128.7 (2C), 128.4, 126.0 (2C), 73.4, 58.0.

IR (cm^{-1}) 3404, 2103, 1493, 1453, 1299, 1261, 1063, 881, 758, 700, 617.

LCMS (ESI) ***m/z*** $C_8H_9N_3O$ $[M-H+HCO_2H]^-$ 208.1.

2-azido-1-(4-nitrophenyl)ethan-1-ol **(S9)**



$C_8H_8N_4O_3$
MW: 208.18 $g.mol^{-1}$
Yield: 89%
Yellow solid

2-azido-1-(4-nitrophenyl)ethan-1-ol **S9** was prepared accordingly to the general procedure. The reaction was conducted using 205 mg of 2-azido-1-(4-nitrophenyl)ethan-1-one **(S2)** as starting material. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(4-nitrophenyl)ethan-1-ol **S9** as a yellow solid (184 mg, 89%).

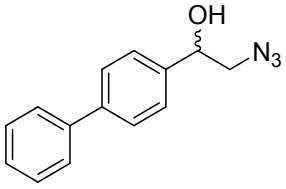
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.8 Hz, 2H), 4.99 (dd, J = 7.4, 4.1 Hz, 1H), 3.54 – 3.43 (m, 2H), 3.05 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 147.7, 126.9 (2C), 123.9 (2C), 72.5, 57.8.

IR (cm^{-1}) 3417, 2923, 2098, 1603, 1514, 1343, 1300, 1256, 1076, 851, 820, 750, 700, 519.

LCMS (ESI) ***m/z*** $C_8H_8N_4O_3$ $[M-H+HCO_2H]^-$ 253.3.

1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-ol **(S10)**



$C_{14}H_{13}N_3O$
MW: 239.28 $g.mol^{-1}$
Yield: 71%
White solid

1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-ol **S10** was prepared accordingly to the general procedure. The reaction was conducted using 237 mg of 1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-one **(S3)** as starting material. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-ol **S10** as a white solid (169 mg, 71%).

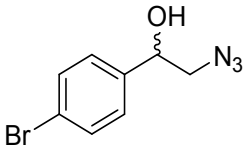
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (m, 4H), 7.47 (m, 4H), 7.38 (m, 1H), 4.92 (dd, J = 7.9, 4.4 Hz, 1H), 3.58 – 3.42 (m, 2H), 2.71 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 140.6, 139.6, 128.9 (2C), 127.6, 127.5 (2C), 127.2 (2C), 126.5 (2C), 73.3, 58.1.

IR (cm^{-1}) 3401, 3029, 2096, 1485, 1405, 1266, 1073, 1007, 837, 763, 732, 695.

LCMS (ESI) ***m/z*** $C_{14}H_{13}N_3O$ $[M\text{-}H+HCO_2H]^-$ 284.3.

2-azido-1-(4-bromophenyl)ethan-1-ol **(S11)**



$C_8H_8BrN_3O$
MW: 242.08 $g.mol^{-1}$
Yield: 98%
White solid

2-azido-1-(4-bromophenyl)ethan-1-ol **S11** was prepared accordingly to the general procedure. The reaction was conducted using 239 mg of 2-azido-1-(4-bromophenyl)ethan-1-one **(S4)** as starting material. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(4-bromophenyl)ethan-1-ol **S11** as a white solid (237 mg, 98%).

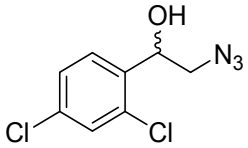
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.6 Hz, 2H), 7.22 (d, J = 8.6 Hz, 2H), 4.79 (dd, J = 7.5, 4.1 Hz, 1H), 3.46 – 3.35 (m, 2H), 2.89 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 131.8 (2C), 127.70 (2C), 122.2, 72.8, 57.9.

IR (cm^{-1}) 3398, 2919, 2097, 1487, 1299, 1259, 1070, 1009, 819, 523.

LCMS (ESI) ***m/z*** $C_8H_8{}^{79}BrN_3O$ $[M\text{-}H+HCO_2H]^-$ 286.2, $C_8H_8{}^{81}BrN_3O$ $[M\text{-}H+HCO_2H]^-$ 288.2.

2-azido-1-(2,4-dichlorophenyl)ethan-1-ol **(S12)**



$C_8H_7Cl_2N_3O$
MW: 232.06 $g.mol^{-1}$
Yield: 84%
Yellowish solid

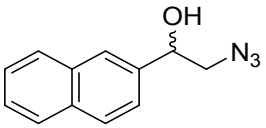
2-azido-1-(2,4-dichlorophenyl)ethan-1-ol **S12** was prepared accordingly to the general procedure. The reaction was conducted using 232 mg of 2-azido-1-(2,4-dichlorophenyl)ethan-1-one **(S5)** as starting material. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(2,4-dichlorophenyl)ethan-1-ol **S12** as a yellowish solid (194 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 2.1 Hz, 1H), 7.29 (dd, J = 8.4, 2.1 Hz, 1H), 5.22 (dd, J = 8.0, 2.8 Hz, 1H), 3.54 (dd, J = 12.7, 3.0 Hz, 1H), 3.32 (dd, J = 12.7, 8.0 Hz, 1H), 2.95 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 134.5, 132.3, 129.3, 128.5, 127.7, 69.8, 56.2.

IR (cm^{-1}) 3401, 2923, 2098, 1590, 1468, 1381, 1295, 1267, 1081, 1045, 820, 765, 563, 549, 480.
LCMS (ESI) ***m/z*** $C_8H_7{}^{35}Cl_2N_3O$ $[M-H+HCO_2H]^-$ 276.2, $C_8H_7{}^{35}Cl^{37}ClN_3O$ $[M-H+HCO_2H]^-$ 278.2, $C_8H_7{}^{37}Cl_2N_3O$ $[M-H+HCO_2H]^-$ 280.2.

2-azido-1-(naphthalen-2-yl)ethan-1-ol **(S13)**

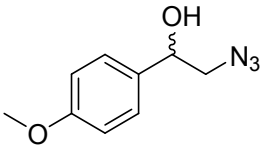


$C_{12}H_{11}N_3O$
MW: 213.24 $g.mol^{-1}$
Yield: 97%
White solid

2-azido-1-(naphthalen-2-yl)ethan-1-ol **S13** was prepared accordingly to the general procedure. The reaction was conducted using 211 mg of 2-azido-1-(naphthalen-2-yl)ethan-1-one **(S6)** as starting material. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-1-(naphthalen-2-yl)ethan-1-ol **S13** as a white solid (208 mg, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.80 (m, 4H), 7.55 – 7.49 (m, 2H), 7.42 (dd, J = 8.5, 1.7 Hz, 1H), 4.98 (dd, J = 8.0, 3.9 Hz, 1H), 3.50 (m, 2H), 2.94 (brs, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 133.3, 133.2, 128.6, 128.1, 127.8, 126.5, 126.3, 125.0, 123.7, 73.5, 57.9.
IR (cm^{-1}) 3391, 3055, 2095, 1436, 1270, 1257, 1073, 897, 857, 817, 745, 475.
LCMS (ESI) ***m/z*** $C_{12}H_{11}N_3O$ $[M-H+HCO_2H]^-$ 258.3.

2-azido-1-(4-methoxyphenyl)ethan-1-ol **(S14)**



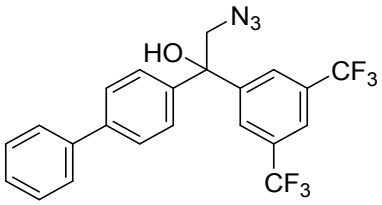
$C_9H_{11}N_3O_2$
MW: 193.21 $g.mol^{-1}$
Yield: 95%
Colorless oil

2-azido-1-(4-methoxyphenyl)ethan-1-ol **S14** was prepared accordingly to the general procedure. The reaction was conducted using 191 mg of 2-azido-1-(4-methoxyphenyl)ethan-1-one **(S7)** as starting material. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 8:2) to afford the 2-azido-1-(4-methoxyphenyl)ethan-1-ol **S14** as a colorless oil (184 mg, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 4.77 (dd, J = 8.2, 4.0 Hz, 1H), 3.78 (s, 3H), 3.39 (ddd, J = 16.5, 12.6, 6.1 Hz, 2H), 2.79 (brs, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 132.9, 127.3 (2C), 114.1 (2C), 73.0, 58.0, 55.3.
IR (cm^{-1}) 3416, 2933, 2094, 1611, 1512, 1462, 1242, 1173, 1029, 829, 540.
LCMS (ESI) ***m/z*** $C_9H_{11}N_3O_2$ $[M-H+HCO_2H]^-$ 238.2.

2.3. Synthesis of tertiary alcohol

1-([1,1'-biphenyl]-4-yl)-2-azido-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol (S15)



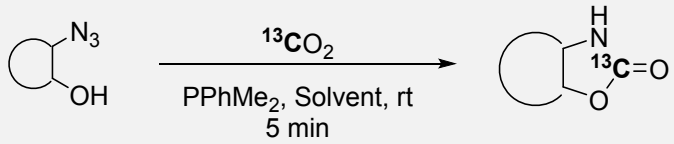
$C_{22}H_{15}F_6N_3O$
MW: 451.37 g.mol^{-1}
Yield: 39%
White solid

To a 0.5 M THF solution of (3,5-bis(trifluoromethyl)phenyl)magnesium bromide (3.00 mL, 1.5 mmol) at 0 °C, 1-methoxy-2-(2-methoxyethoxy)ethane (0.22 mL, 1.5 mmol) was added followed by tetrabutylammonium chloride (28.0 mg, 0.1 mmol). After stirring for 30 minutes at 0 °C, a solution of ketone (**X**) (237 mg, 1.0 mmol) in THF (1.0 mL) was slowly added and the resulting mixture was stirred at 0 °C for 3 additional hours. After completion, the reaction was quenched with NH_4Cl and extracted with EtOAc (3x20 mL). The combined organic phases were dried over $MgSO_4$, filtrated and evaporated under reduce pressure. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 95:5) to afford the 1-([1,1'-biphenyl]-4-yl)-2-azido-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol **S15** as a white solid (175 mg, 39%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 2H), 7.82 (s, 1H), 7.65 – 7.56 (m, 4H), 7.48 – 7.42 (m, 4H), 7.39 – 7.34 (m, 1H), 4.16 (d, J = 12.7 Hz, 1H), 4.04 (d, J = 12.7 Hz, 1H), 3.12 (brs, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 141.6, 141.1, 140.2, 131.9 (q, $J_{C\text{-}F}$ = 32.7 Hz, 2C), 129.0 (2C), 127.9, 127.8 (2C), 127.3 (2C), 126.7 – 126.5 (m, 4C), 123.4 (q, $J_{C\text{-}F}$ = 268 Hz, 2C), 122.0 – 121.9 (m), 77.7, 60.1.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7 (s).
IR (cm^{-1}) 2107, 1377, 1277, 1168, 1132, 900, 844, 768, 749, 734, 698, 682.
LCMS (ESI) ***m/z*** $C_{22}H_{15}F_6N_3O$ $[M+H-H_2O]^+$ 434.3.

2.4. Synthesis of [^{13}C]labeled aliphatic cyclic carbamates

General Staudinger-aza-Wittig procedure for the synthesis of [^{13}C]cyclic carbamates



Into 1.0 mL vial, $PPhMe_2$ (1.00 equiv.) was added to a solution of hydroxy-azide derivative (1.00 equiv.) in the appropriate solvent (0.70 mL). The mixture was transferred into a Wilmad® low pressure/*vacuum* NMR tube that was further frozen in to N_2 bath. At this point then 1.00 to 1.20 equiv. of gaseous $^{13}CO_2$ are added using Tritec® (figure 1). The mixture was maintained at room temperature for 5 to 10 minutes then the unreacted $^{13}CO_2$ was removed by opening the NMR tube and the solvent was evaporated. The crude products were purified by Flash Chromatography on SiO_2 gel, affording corresponding [^{13}C]labeled carbamates.

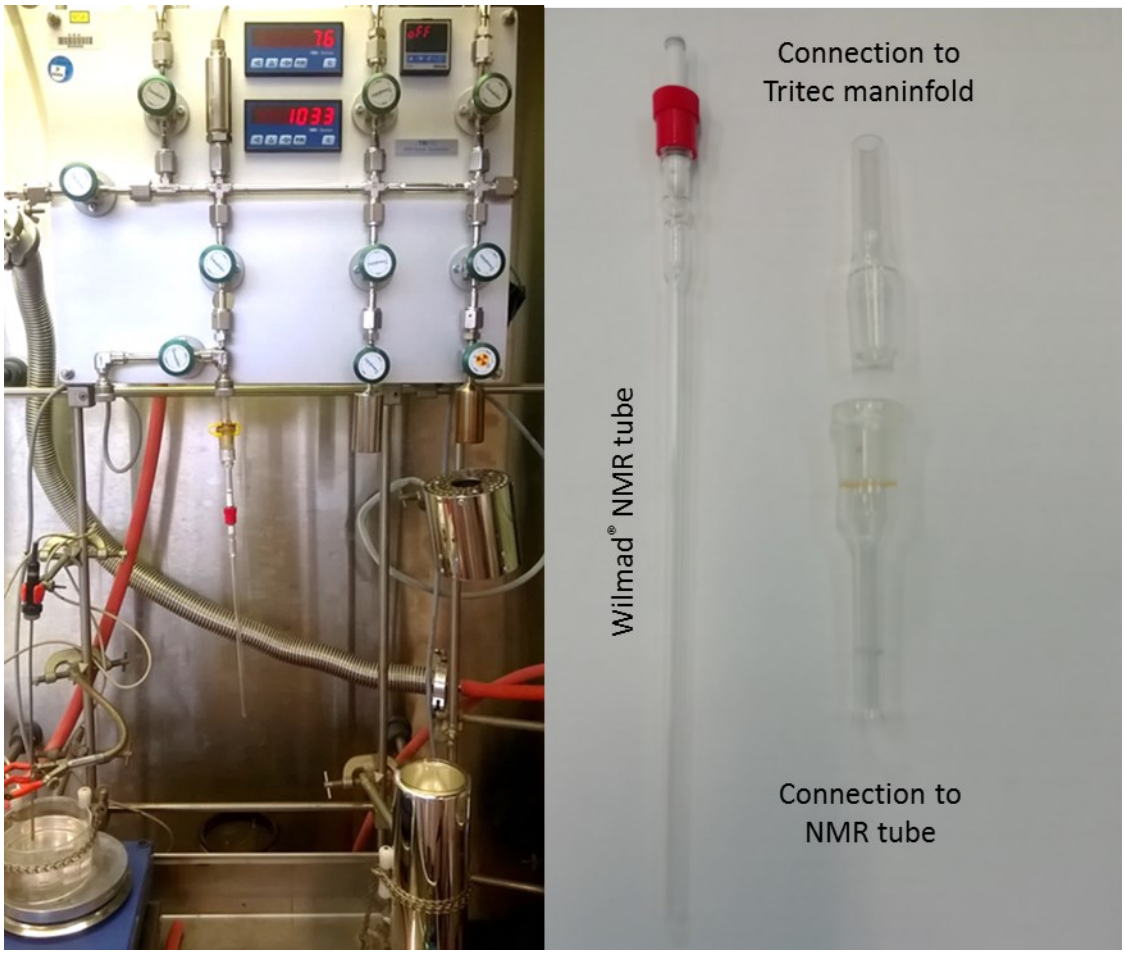
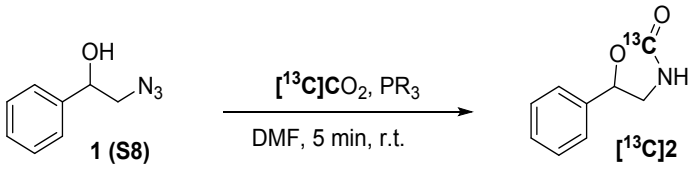


Figure S1: RC Tritec® manifold system utilized to charge labeled CO_2 into the reactions.

2.4.a. Optimization of the Staudinger Aza-Wittig reaction

The optimization of the reaction conditions was performed according to the general procedure reported above.



Entry	*Eq. CO_2*	*Phosphine*	*Yield (%)*
1	1	**a**	63
2	1	**b**	46
3	1	**c**	62
4	1	**e**	0
5	1	**f**	0
6	1	**d**	84
7	0.5	**d**	70

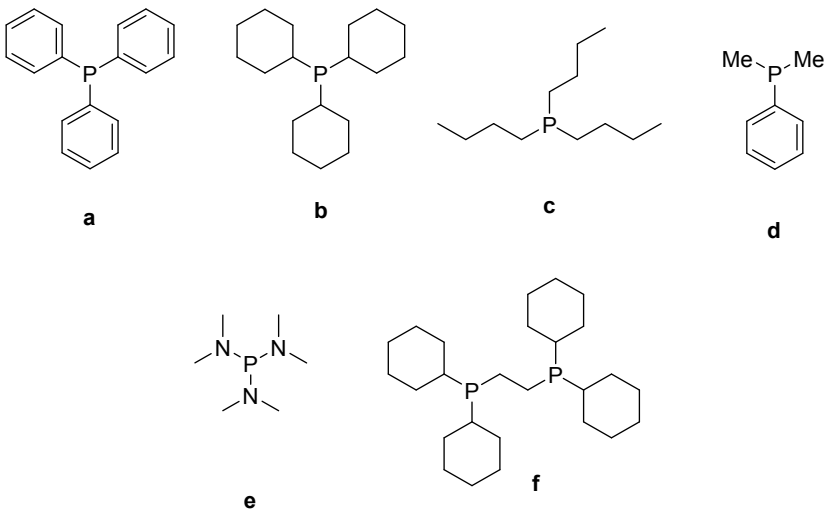


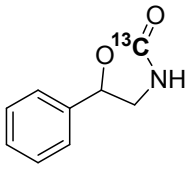
***Table S1**: Phosphine screening.*

Entry	*Solvent*	*T °C*	*Conversion (isolated yield%)*
1	DMF-d_7	25	88 (84)
2	DMSO-d_6	25	61
3	CH_3CN-d_3	25	76
4	THF-d_8	25	52
5	DMF-d_7	65	82
6	DMSO-d_6	65	37
7	CH_3CN-d_3	65	60
8	THF-d_8	65	48

Table S2*: Solvent and temperature screening.*

2.5. Synthesis of ^{13}C-labeled aliphatic carbamates

[^{13}C] 5-phenyloxazolidine-2-one **([^{13}C]2)**

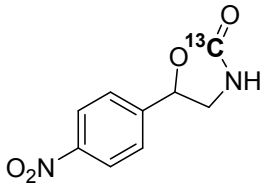


$C_8{}^{13}CH_9NO_2$
MW: 164.17 g.mol^{-1}
Yield: 84%
White solid

The [^{13}C]-5-phenyloxazolidin-2-one **[^{13}C]2** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-phenylethan-1-ol **1/(S8)** (16.3 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2 /MeOH 99:1) affording the ^{13}C-labeled 5-phenyloxazolidin-2-one **[^{13}C]2** as a white solid (13.7 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.35 (m, 5H), 5.88 (brs, 1H), 5.63 (ddt, J = 16.4, 8.6, 1.6 Hz, 1H), 3.99 (ddt, J = 16.3, 3.8, 0.4 Hz, 1H), 3.57 – 3.53 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1 (^{13}C labeled), 138.5, 129.1, 129.0 (2C), 125.8 (2C), 78.0, 48.5 (d, J = 3.5 Hz).
IR (cm^{-1}) 3287, 2925, 1704, 1225, 1075, 966, 926, 700.
Melting point: 87-88 °C.
LCMS (ESI) ***m/z*** $C_8{}^{13}CH_9NO_2$ $[M+H]^+$ 165.2.

[^{13}C] 5-(4-nitrophenyl)oxazolidin-2-one **([^{13}C]3)**



$C_8{}^{13}CH_8N_2O_4$
MW: 209.17 g.mol^{-1}
Yield: 81%
Yellow solid

The [^{13}C] 5-(4-nitrophenyl)oxazolidin-2-one [^{13}C]**3** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-(4-nitrophenyl)ethan-1-ol **S9** (20.8 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 5-(4-nitrophenyl)oxazolidin-2-one [^{13}C]**3** as a yellow solid (17.0 mg, 81%).

^{1}H NMR (400 MHz, MeOD-d_4) δ 8.28 (d, J = 8.8, 2H), 7.65 (d, J = 8.4, 2H), 5.81 (ddd, J = 9.0, 7.2, 2.1 Hz, 1H), 4.08 (td, J = 9.0, 3.6 Hz, 1H), 3.47 (ddd, J = 9.2, 5.6, 2.0 Hz, 1H).

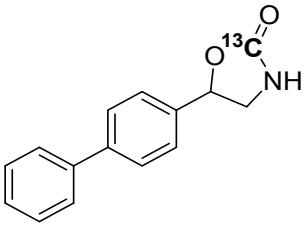
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 161.6 (^{13}C labeled), 149.4, 147.9 (d, J = 1.4 Hz), 127.8 (2C), 125.0 (2C), 77.9 (d, J = 1.2 Hz), 48.9 (Under solvent peak).

IR (cm^{-1}) 3285, 1708, 1607, 1519, 1346, 1222, 1076, 968, 855.

Melting point : 119-120 °C.

LCMS (ESI) ***m/z*** $C_8{}^{13}CH_8N_2O_4$ $[M+H]^+$ 210.2.

[^{13}C] 5-([1,1'-biphenyl]-4-yl)oxazolidin-2-one **([^{13}C]4)**



$C_{14}{}^{13}CH_{13}NO_2$
MW: 240.27 g.mol^{-1}
Yield: 67%
Yellow solid

The [^{13}C] 5-([1,1'-biphenyl]-4-yl)oxazolidin-2-one **[**^{13}C]**4** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-ol **S10** (23.9 mg, 0.100 mmol) and $^{13}CO_2$ (0.105 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 5-([1,1'-biphenyl]-4-yl)oxazolidin-2-one **[**^{13}C]**4** as a yellow solid (16.2 mg, 67%).

^{1}H NMR (400 MHz, MeOD-*d*$_4$) δ 7.69 (d, J = 8.4, Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.1 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.35 (m, 1H), 5.71 (t, J = 16, 8.8 Hz, 1H), 4.01 (td, J = 8.9, 3.7 Hz, 1H), 3.52 (ddd, J = 9.9, 7.5, 2.7 Hz, 1H).

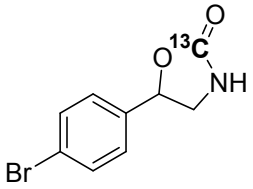
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 162.2 (^{13}C labeled), 143.0, 141.7, 139.5 (d, J = 1.4 Hz), 129.9 (2C), 128.6, 128.5 (2C), 128.0 (2C), 127.4 (2C), 79.2, 48.7 (Under solvent peak).

IR (cm^{-1}) 3263, 2923, 1677, 1488, 1395, 1233, 1078, 841, 765, 696.

Melting point : 186-187 °C.

LCMS (ESI) ***m/z*** $C_{14}{}^{13}CH_{13}NO_2$ $[M+H]^+$ 241.3.

[^{13}C] 5-(4-bromophenyl)oxazolidin-2-one **([^{13}C]5)**



$C_8{}^{13}CH_8BrNO_2$
MW: 243.06 g.mol^{-1}
Yield: 62%
White solid

The [^{13}C] 5-(4-bromophenyl)oxazolidin-2-one **[**^{13}C]**5** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-(4-bromophenyl)ethan-1-ol **S11** (24.2 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography

on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 5-(4-bromophenyl)oxazolidin-2-one **[**^{13}C**]5** as a white solid (15.2 mg, 62%).

^{1}H NMR (400 MHz, MeOD-*d*$_4$) δ 7.58 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 5.70 – 5.56 (m, 1H), 3.99 (td, J = 8.9, 3.7 Hz, 1H), 3.44 (ddd, J = 8.9, 7.3, 3.7 Hz, 1H).

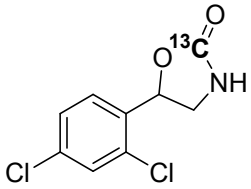
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 161.9 (^{13}C labeled), 139.9 (d, J = 1.5 Hz), 133.1 (2C), 128.8 (2C), 123.6, 78.6, 49.1 (d, J = 3.6 Hz).

IR (cm^{-1}) 3236, 2406, 1703, 1667, 1486, 1400, 1270, 1175, 1074, 983, 841, 727.

Melting point : 157-158 °C.

LCMS (ESI) *m/z* $C_8{}^{13}CH_8{}^{79}BrNO_2$ $[M+H]^+$ 243.1, $C_8{}^{13}CH_8{}^{81}BrNO_2$ $[M+H]^+$ 245.1.

[^{13}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one **([**^{13}C**]6)**



$C_8{}^{13}CH_7Cl_2NO_2$
MW: 233.05 g.mol^{-1}
Yield: 89%
Yellow solid

The [^{13}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one **[**^{13}C**]6** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-(2,4-dichlorophenyl)ethan-1-ol **S12** (23.2 mg, 0.100 mmol) and $^{13}CO_2$ (0.110 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 5-(2,4-dichlorophenyl)oxazolidin-2-one **[**^{13}C**]6** as a yellow solid (20.9 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.4 Hz, 1H), 7.41 (d, J = 2.0 Hz, 1H), 7.32 (dd, J = 8.4, 2.0 Hz, 1H), 6.20 (brs, 1H), 5.87 (ddd, J = 8.9, 6.7, 2.3 Hz, 1H), 4.16 (td, J = 8.9, 2.3 Hz, 1H), 3.39 (ddd, J = 8.8, 6.6, 2.4 Hz, 1H).

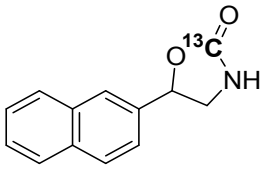
^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5 (^{13}C labeled), 135.6, 135.2, 131.8, 129.7, 127.9, 127.3, 74.6, 47.4 (d, J = 3.5 Hz).

IR (cm^{-1}) 3283, 1713, 1591, 1473, 1336, 1226, 1080, 1034, 968, 819, 740.

Melting point : 134-135 °C.

LCMS (ESI) *m/z* $C_8{}^{13}CH_7{}^{35}Cl_2NO_2$ $[M+H]^+$ 233.2, $C_8{}^{13}CH_7{}^{35}Cl^{37}ClNO_2$ $[M+H]^+$ 235.2, $C_8{}^{13}CH_7{}^{37}Cl_2NO_2$ $[M+H]^+$ 237.1.

***[^{13}C] 5-(naphthalen-2-yl)oxazolidin-2-one* ([^{13}C]7)**

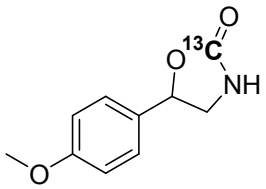


$C_{12}{}^{13}CH_{11}NO_2$
MW: 214.23 g.mol^{-1}
Yield: 50%
Yellow solid

The [^{13}C] 5-(naphthalen-2-yl)oxazolidin-2-one **[**^{13}C]**7** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol,), 2-azido-1-(naphthalen-2-yl)ethan-1-ol **S13** (21.3 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 5-(naphthalen-2-yl)oxazolidin-2-one **[**^{13}C]**7** as a yellow solid (10.7 mg, 50%).

^{1}H NMR (400 MHz, MeOD-d_4) δ 7.93 (d, J = 8.5 Hz, 1H), 7.91 – 7.86 (m, 3H), 7.54 – 7.49 (m, 3H), 5.87 – 5.78 (m, 1H), 4.06 (td, J = 9.0, 3.7 Hz, 1H), 3.58 (ddd, J = 9.0, 7.4, 2.8 Hz, 1H).
^{13}C NMR (100 MHz, MeOD-d_4) δ 162.2 (^{13}C labeled), 137.8, 134.9, 134.6, 130.0, 129.1, 128.8, 127.6, 127.6, 126.2, 124.1, 79.5, 54.8.
IR (cm^{-1}) 3270, 2924, 1705, 1227, 1079, 950, 823, 745.
Melting point : 169-170 °C.
LCMS (ESI) ***m/z*** $C_{12}{}^{13}CH_{11}NO_2$ $[M+H]^+$ 215.2.

***[^{13}C] 5-(4-methoxyphenyl)oxazolidin-2-one* ([^{13}C]8)**



$C_9{}^{13}CH_{11}NO_3$
MW: 194.19 g.mol^{-1}
Yield: 80%
White solid

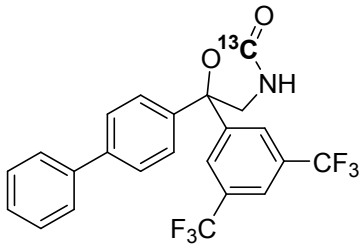
The [^{13}C] 5-(4-methoxyphenyl)oxazolidin-2-one **[**^{13}C]**8** was prepared accordingly to the general procedure, using $PPhMe_2$ (14.5 µL,0.100 mmol), 2-azido-1-(4-methoxyphenyl)ethan-1-ol **S14** (19.3 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 5-(4-methoxyphenyl)oxazolidin-2-one **[**^{13}C]**8** as a white solid (15.7 mg, 80%).

^{1}H NMR (400 MHz, MeOD-d_4) δ 7.34 (d, J = 8.4, 2H), 6.96 (d, J = 8.8, 2H), 5.65 – 5.51 (m, 1H), 3.92 (td, J = 9.0, 3.9 Hz, 1H), 3.80 (s, 3H), 3.49 (ddd, J = 9.0, 7.7, 2.6 Hz, 1H).
^{13}C NMR (100 MHz, MeOD-d_4) δ 162.2 (^{13}C labeled), 161.7, 132.2 (d, J = 1.6 Hz), 128.6 (2C), 115.2 (2C), 79.5, 55.8, 48.8 (Under solvent peak).
IR (cm^{-1}) 3250, 2967, 1706, 1672, 1611, 1518, 1296, 1251, 1181, 1029, 835.

Melting point : 103-104 °C.

LCMS (ESI) ***m/z*** $C_9{}^{13}CH_{11}NO_3$ $[M+H]^+$ 195.3.

[^{13}C] 5-([1,1'-biphenyl]-4-yl)-5-(3,5-bis(trifluoromethyl)phenyl)oxazolidin-2-one ([^{13}C]**9***)***



$C_{22}{}^{13}CH_{15}F_6NO_2$
MW: 452.36 g.mol^{-1}
Yield: 87%
White solid

The [^{13}C] 5-([1,1'-biphenyl]-4-yl)-5-(3,5-bis(trifluoromethyl)phenyl)oxazolidin-2-one **[**^{13}C]**9** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 1-([1,1'-biphenyl]-4-yl)-2-azido-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol **(S15)** (45.1 mg, 0.100 mmol) and $^{13}CO_2$ (0.113 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) affording the ^{13}C-labeled 5-([1,1'-biphenyl]-4-yl)-5-(3,5-bis(trifluoromethyl) phenyl)oxazolidin-2-one **[**^{13}C]**9** as a white solid (39.5 mg, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (br. s, 2H), 7.87 (br. s, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 8.4, Hz, 2H), 7.49 – 7.43 (m, 4H), 7.39-7.35 (m, 1H), 5.61 (br d, J = 4.3 Hz, 1H), 4.37 (dd, J = 8.9, 3.3 Hz, 1H), 4.21 (dd, J = 8.9, 3.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0 (^{13}C labeled), 145.4 (d, J = 1.3 Hz), 142.2, 140.0, 139.6 (d, J = 1.0 Hz), 132.5 (q, $J_{C\text{-}F}$ = 33.7 Hz, 2C), 129.1 (2C), 128.0, 128.0 (2C), 127.3 (2C), 125.9 (2C), 125.8 (m, 2C), 124.5 (q, $J_{C\text{-}F}$ = 271 Hz, 2C), 122.6 (m), 85.6 (d, J = 1.2 Hz), 53.3 (d, J = 3.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7 (s).

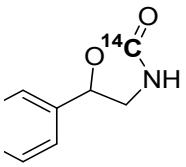
IR (cm^{-1}) 1718, 1377, 1278, 1237, 1173, 1134, 845, 740, 682.

Melting point: 205-206 °C.

LCMS (ESI) ***m/z*** $C_{22}{}^{13}CH_{15}F_6NO_2$ $[M+H]^+$ 453.5.

2.6. Synthesis of ^{14}C-labeled aliphatic carbamates

[^{14}C] 5-phenyloxazolidine-2-one **([^{14}C]2)**

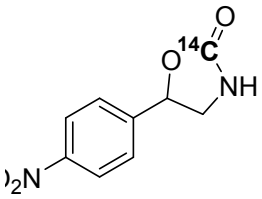


$C_8{}^{14}CH_9NO_2$
MW: 165.17 g.mol^{-1}
RCYield: 71%
White solid

The [^{14}C] 5-phenyloxazolidine-2-one **[^{14}C]2** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-phenylethan-1-ol **1(S8)** (16.3 mg, 0.100 mmol) and $^{14}CO_2$ (0.093 mmol, 215.06 MBq) in DMF-d_7. The reaction was heated at 70 °C for 5 minutes. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent EtOAc/Heptane 30:70) affording the ^{14}C-labeled 5-phenyloxazolidine-2-one **[^{14}C]2** as a white solid (144.67 MBq, 71%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}
Molar activity (MS (ESI)): 2.098 GBq mmol^{-1}
TLC (silicagel 60F254, EtOAc/Heptane (30/70)) Rf=0.42. Radiochemical purity: ≥99%.

[^{14}C] 5-(4-nitrophenyl)oxazolidin-2-one **([^{14}C]3)**

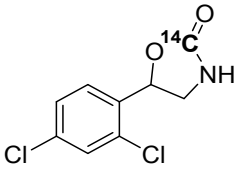


$C_8{}^{14}CH_8N_2O_4$
MW: 210.17 g.mol^{-1}
RCYield: 73%
Yellow solid

The [^{14}C] 5-(4-nitrophenyl)oxazolidin-2-one **[^{14}C]3** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-(4-nitrophenyl)ethan-1-ol **S9** (20.8 mg, 0.100 mmol) and $^{14}CO_2$ (0.100 mmol, 231.25 MBq) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent EtOAc/Heptane 90:10) affording the ^{14}C-labeled 5-(4-nitrophenyl)oxazolidin-2-one **[^{14}C]3** as a yellow solid (154.66 MBq, 73%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}
Molar activity (MS (ESI)): 2.113 GBq mmol^{-1}
TLC (silicagel 60F254, EtOAc/Heptane (90/10)) Rf=0.25. Radiochemical purity: ≥99%.

***[^{14}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one* ([^{14}C]6)**



$C_8{}^{14}CH_7Cl_2NO_2$
MW: 234.05 g.mol^{-1}
RCYield: 75%
Yellow solid

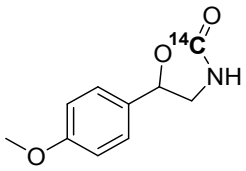
The [^{14}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one **[**^{14}C]**6** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-(2,4-dichlorophenyl)ethan-1-ol **S12** (23.2 mg, 0.100 mmol) and $^{14}CO_2$ (0.067 mmol, 154.93 MBq) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent EtOAc/Heptane 40:60) affording the ^{14}C-labeled 5-(2,4-dichlorophenyl)oxazolidin-2-one **[**^{14}C]**6** as a yellow solid (109.67 MBq, 75%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}

Molar activity (MS (ESI)): 2.10 GBq mmol^{-1}

TLC (silicagel 60F254, EtOAc/Heptane (40/60)) Rf=0.42. Radiochemical purity: ≥99 %.

***[^{14}C] 5-(4-methoxyphenyl)oxazolidin-2-one* ([^{14}C]8)**



$C_9{}^{14}CH_{11}NO_3$
MW: 195.19 g.mol^{-1}
RCYield: 55 %
White solid

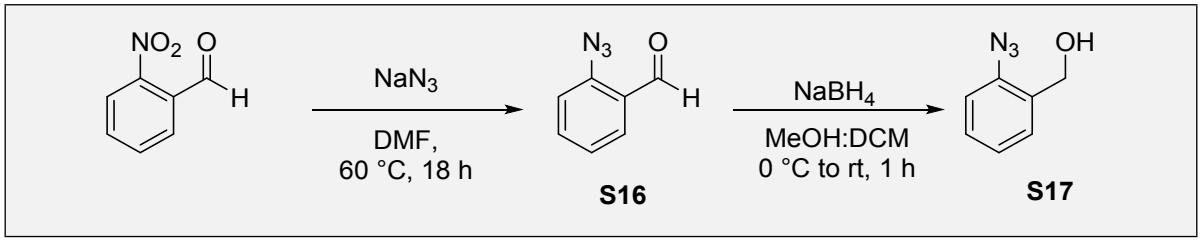
The [^{14}C] 5-(4-methoxyphenyl)oxazolidin-2-one **[**^{14}C]**8** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-1-(4-methoxyphenyl)ethan-1-ol **S14** (19.3 mg 0.100 mmol,) and $^{14}CO_2$ (0.082 mmol, 189.62 MBq) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent EtOAc/Heptane 70:30) affording the ^{14}C-labeled 5-(4-methoxyphenyl)oxazolidin-2-one **[**^{14}C]**8** as a white solid (102.49 MBq, 55 %).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}

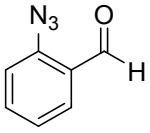
Molar activity (MS (ESI)): 2.045 GBq mmol^{-1}

TLC (silicagel 60F254, EtOAc/Heptane (70/30)) Rf=0.25. Radiochemical purity: ≥99 %.

2.7. Preparation of the (2-azidophenyl)metanol



2-azidobenzaldehyde (S16)

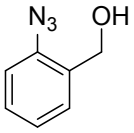


$C_7H_5N_3O$
MW: 147.04 g.mol^{-1}
Yield: 88%
Yellowish solid

To a solution of 2-nitrobenzaldehyde (1.0 g, 6.66 mmol) in 20 mL of DMF was added sodium azide (870 mg, 13.4 mmol). The resulting mixture was then stirred at 60 °C for 18 hours. After the reaction was completed, the mixture was diluted in 100 mL of EtOAc and then washed twice with brine. The organic layer was dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azidobenzaldehyde **S16** as a yellowish solid (849 mg, 88%). The spectral data matched that reported literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (d, J = 0.7 Hz, 1H), 7.90 (dd, J = 7.8, 1.5 Hz, 1H), 7.64 (ddd, J = 8.1, 7.8, 1.5 Hz, 1H), 7.32 – 7.23 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 186.6, 143.0, 135.5, 129.0, 127.0, 125.0, 119.1.
IR (cm^{-1}) 2120, 2095, 1686, 1591, 1475, 1454, 1391, 1289, 1271, 1194, 832, 763, 693, 621, 532, 462.
LCMS (ESI) ***m/z*** $C_7H_5N_3O$ $[M+H]^+$ 148.2.

(2-azidophenyl)metanol (S17)



$C_7H_7N_3O$
MW: 149.06 g.mol^{-1}
Yield: 89%
Colorless oil

To a solution of 2-azidobenzaldehyde **S16** (147 mg, 1.0 mmol) in 6.0 mL of dry MeOH and 4.0 mL of dry DCM at 0 °C was added $NaBH_4$ (37.8 mg, 1.0 mmol). The resulting mixture was then stirred at 0 °C for 15 minutes then 30 additional minutes at room temperature under argon. After the reaction was completed, the reaction was stopped by adding 10 mL of a saturated solution of $NaHCO_3$ and the phases were separated. The aqueous phase was extracted twice with 10 mL of CH_2Cl_2, the organic layers were

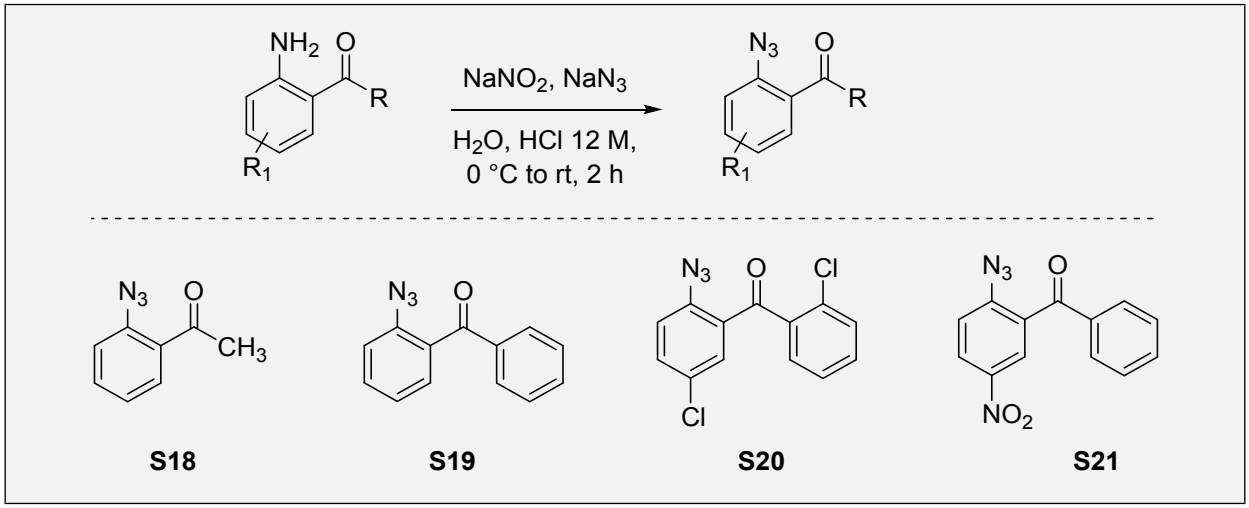
[1] Stokes, B. J.; Vogel, C. V.; Urnezis, L. K.; Pan, M.; Driver, T. G. *Org. Lett*. **2010**, *12*, 2884-87.

combined, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the (2-azidophenyl)methanol **S17** as a colorless oil (131 mg, 89%). The spectral data matched that reported literature.[2]

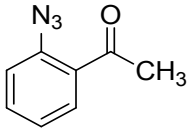
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 2H), 7.13 (m, 2H), 4.60 (s, 2H), 2.47 (br. s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 131.9, 129.2, 129.1, 125.0, 118.1, 61.5.
IR (cm^{-1}) 3269, 3168, 2127, 1581, 1483, 1449, 1272, 1093, 1037, 988, 749, 672, 533.
LCMS (ESI) ***m/z*** $C_7H_7N_3O$ $[M+H-N_2]^+$ 122.2.

[2] Demko, Z. P.; Sharpless, K. B. *Org. Lett.* **2001,** *3*, 4091-4094.

2.7. Preparation of 1-(2-azidophenyl) derivatives (by means of the Sandmeyer reaction)



1-(2-azidophenyl)ethan-1-one **(S18)**



$C_8H_7N_3O$
MW: 161.16 g.mol^{-1}
Yield: 92%
yellowish oil

To a solution of 1-(2-aminophenyl)ethan-1-one (405 mg, 3.00 mmol) in 10 mL of deionized water at 0 °C was added HCl 12N (750 µL, 9.0 mmol) and the reaction was kept at 0 °C. A solution of $NaNO_2$ (207 mg, 3.00 mmol) in 1.0 mL of water was slowly added and the resulting mixture was stirred at 0 °C for 15 min after what sodium azide (207 mg, 3.60 mmol) was added by portion. The reacting mixture was then allowed to warm to room temperature and kept under stirring for 2 hours. The aqueous phase was extracted twice with 20 mL EtOAc. The organic layers were combined then washed with brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 95:5) to afford the 1-(2-azidophenyl)ethan-1-one **S18** as a yellowish oil (443 mg, 92%). The spectral data matched that reported literature.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, J = 7.8, 1.6 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.20 – 7.13 (m, 2H), 2.59 (s, 3H).

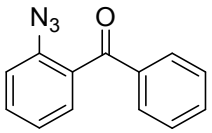
^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 138.7, 133.0, 131.0, 130.4, 124.8, 119.7, 31.1.

IR (cm^{-1}) 2120, 2090, 1678, 1593, 1444, 1357, 1291, 1277, 1241, 756, 595.

LCMS (ESI) ***m/z*** $C_8H_7N_3O$ $[M+H]^+$ 162.2.

[3] Smith, C. J.; Smith, C. D.; Nikbin, N.; Ley, S. V.; Baxendale, I. R. *Org. Biomol. Chem.* **2011,** *9*, 1927-1937.

***(2-azidophenyl)(phenyl)methanone* (S19)**

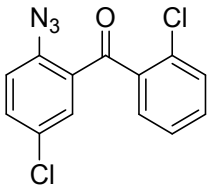


$C_{13}H_9N_3O$
MW: 223.24 g.mol^{-1}
Yield: 71%
Yellow oil

To a solution of (2-aminophenyl)(phenyl)methanone (183 mg, 0.93 mmol) in 3.0 mL of deionized water at 0 °C was added HCl 12N (232 µL, 2.79 mmol) and the reaction was kept at 0 °C. A solution of $NaNO_2$ (64 mg, 0.93 mmol) in 500 µL of water was slowly added and the resulting mixture was stirred at 0 °C for 15 min after what sodium azide (78 mg, 1.20 mmol) was added by portion. The reacting mixture was then allowed to warm to room temperature and kept under stirring for 2 hours. The aqueous phase was extracted twice with 15 mL EtOAc. The organic layers were combined then washed with brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the (2-azidophenyl)(phenyl)methanone **S19** as a yellow oil (168 mg, 71%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (m, 2H), 7.58 (m, 1H), 7.53 (m, 1H), 7.45 (m, 2H), 7.39 (m, 1H), 7.24 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 138.2, 137.1, 133.5, 131.7, 131.3, 130.0 (2C), 129.8, 128.5 (2C), 124.7, 118.9.
IR (cm^{-1}) 2116, 2090, 1662, 1595, 1578, 1481, 1443, 1285, 1257, 1151, 925, 746, 700, 658, 631, 530.
LCMS (ESI) ***m/z*** $C_{13}H_9N_3O$ $[M+H]^+$ 224.2.

***(2-azido-5-chlorophenyl)(2-chlorophenyl)methanone* (S20)**



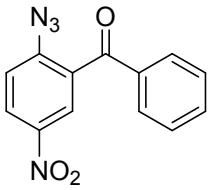
$C_{13}H_7Cl_2N_3O$
MW: 292.12 g.mol^{-1}
Yield: 46%
Beige solid

To a solution of (2-amino-5-chlorophenyl)(2-chlorophenyl)methanone (532 mg, 2.00 mmol) in 7.0 mL of deionized water at 0 °C was added HCl 12N (500 µL, 6.00 mmol) and the reaction was kept at 0 °C. A solution of $NaNO_2$ (138 mg, 2.00 mmol) in 1.0 mL of water was slowly added and the resulting mixture was stirred at 0 °C for 30 min after what sodium azide (156 mg, 2.4 mmol) was added by portion. The reacting mixture was then allowed to warm to room temperature and kept under stirring for 4 hours. The aqueous phase was extracted twice with 20 mL EtOAc. The organic layers were combined then washed with brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by

Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1 to 8:2) to afford the (2-azido-5-chlorophenyl)(2-chlorophenyl)methanone **S20** as a beige solid (267 mg, 46%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.38 (m, 5H), 7.35 (m, 1H), 7.14 (d, J = 7.9 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 138.2, 138.0, 133.2, 132.5, 132.1, 131.8, 131.0, 130.51, 130.50, 130.4, 127.0, 120.8.
IR (cm^{-1}) 2129, 2100, 2057, 1663, 1587, 1469, 1395, 1294, 1263, 1243, 1165, 1113, 960, 816, 746.
LCMS (ESI) ***m/z*** $C_{13}H_7{}^{35}Cl_2N_3O$ $[M+H-N_2]^+$ 264.2, $C_{13}H_7{}^{35}Cl^{37}ClN_3O$ $[M+H-N_2]^+$ 266.1, $C_{13}H_7{}^{37}Cl_2N_3O$ $[M+H-N_2]^+$ 268.2.

(2-azido-5-nitrophenyl)(phenyl)methanone **(S21)**

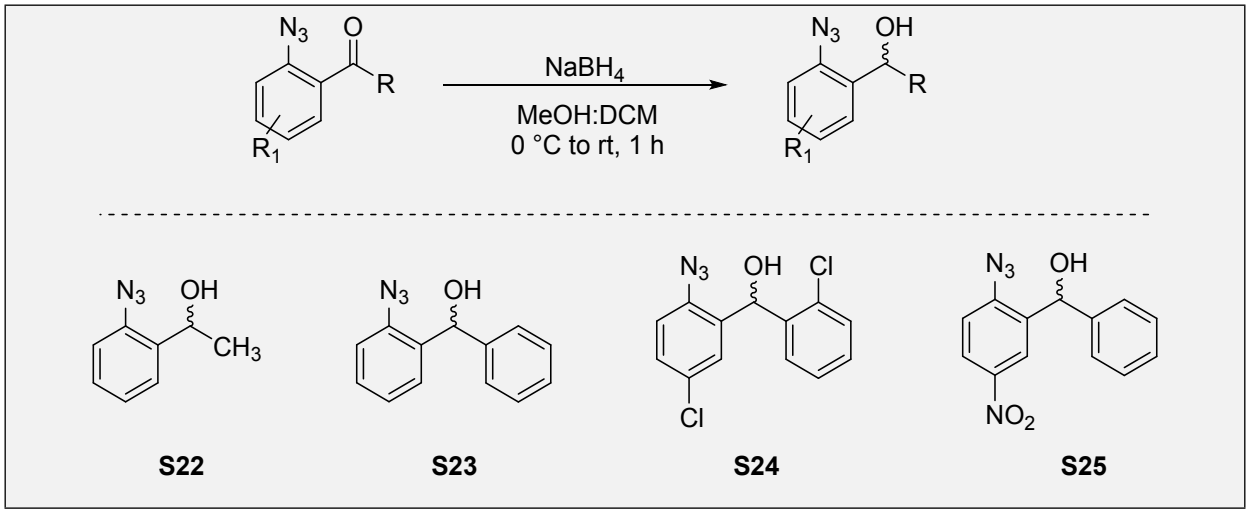


$C_{13}H_8N_4O_3$
MW: 268.23 g.mol^{-1}
Yield: 72%
Yellow solid

To a solution of (2-amino-5-nitrophenyl)(phenyl)methanone (484 mg, 2.00 mmol) in 7.0 mL of deionized water at 0 °C was added HCl 12N (500 µL, 6.00 mmol) and the reaction was kept at 0 °C. A solution of $NaNO_2$ (138 mg, 2.00 mmol) in 1.0 mL of water was slowly added and the resulting mixture was stirred at 0 °C for 30 min after what sodium azide (156 mg, 2.40 mmol) was added by portion. The reacting mixture was then allowed to warm to room temperature and kept under stirring for 4 hours. The aqueous phase was extracted twice with 20 mL EtOAc. The organic layers were combined then washed with brine, dry over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the (2-azido-5-nitrophenyl)(phenyl)methanone **S21** as a yellow solid (388 mg, 72%).

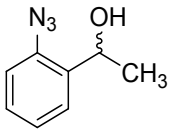
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, J = 8.9, 2.6 Hz, 1H), 8.27 (d, J = 2.6 Hz, 1H), 7.79 – 7.75 (m, 2H), 7.67 – 7.62 (m, 1H), 7.53 – 7.47 (m, 2H), 7.40 (d, J = 8.9 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 144.8, 144.2, 136.0, 134.4, 131.9, 130.1 (2C), 129.0 (2C), 126.7, 125.4, 119.6.
IR (cm^{-1}) 2124, 1667, 1580, 1521, 1477, 1342, 1291, 1273, 1150, 1076, 867, 799, 744, 687, 639.
LCMS (ESI) ***m/z*** $C_{13}H_8N_4O_3$ $[M+H]^+$ 269.0.

2.8. General procedure for the preparation of 1-(2-azidophenyl)alcohols



To a solution of the corresponding azido derivative (**S18-S21**) (1.00 equiv.) in the appropriate amount of CH_2Cl_2 and MeOH at 0 °C, was added $NaBH_4$ (1.00 equiv). The resulting mixture was then stirred at room temperature under argon for 1 hour. After the reaction was completed, the appropriate amount of a saturated solution of $NaHCO_3$ was added and the phases separated. The aqueous phase was extracted twice with CH_2Cl_2 and the organic phases were combined, dried over $MgSO_4$ and evaporated under *vacuum*. The crude mixture was purified by Flash Chromatography on SiO_2 gel within the appropriate conditions, to afford the corresponding product of reduction (**57-60**).

1-(2-azidophenyl)ethan-1-ol **(S22)**



$C_8H_9N_3O$
MW: 163.18 g.mol^{-1}
Yield: 95%
Yellowish oil

1-(2-azidophenyl)ethan-1-ol **S22** was prepared accordingly to the general procedure. To a solution of 1-(2-azidophenyl)ethan-1-one **S18** (235 mg, 1.46 mmol) in 10 mL of dry MeOH and 4 mL of dry CH_2Cl_2 at 0 °C was added $NaBH_4$ (55 mg, 1.46 mmol). At the end of the reaction, 20 mL of a saturated solution of $NaHCO_3$ were added and the resulting phases were separated. The aqueous phase was extracted twice with 10 mL of CH_2Cl_2 and the organic phases combined, dried over $MgSO_4$ and evaporated. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 1-(2-azidophenyl)ethan-1-ol **S22** as a yellowish oil (227 mg, 95%). The spectral data matched that reported literature.[4]

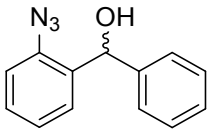
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 7.7, 1.5 Hz, 1H), 7.30 (td, J = 7.7, 1.6 Hz, 1H), 7.17 – 7.09 (m, 2H), 5.04 (q, J = 6.5 Hz, 1H), 2.78 (brs, 1H), 1.43 (d, J = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 136.4, 128.4, 126.5, 125.1, 118.0, 65.7, 23.7.

IR (cm^{-1}) 3339, 2124, 2101, 1581, 1485, 1447, 1293, 1275, 1113, 1071, 1008, 898, 749, 670.

LCMS (ESI) ***m/z*** $C_8H_9N_3O$ $[M+H]^+$ 164.2.

(2-azidophenyl)(phenyl)methanol **(S23)**



$C_{13}H_{11}N_3O$
MW: 225.25 $g.mol^{-1}$
Yield: 98%
Yellow solid

(2-azidophenyl)(phenyl)methanol **S23** was prepared accordingly to the general procedure. To a solution of (2-azidophenyl)(phenyl)methanone **S19** (150 mg, 0.59 mmol) in 4.5 mL of dry MeOH and 1.5 mL of dry CH_2Cl_2 at 0 °C was added $NaBH_4$ (18.5 mg, 0.59 mmol). After the end of the reaction, 10 mL of a saturated solution of $NaHCO_3$ were added and the phases were separated. The aqueous phase was extracted twice with 10 mL of CH_2Cl_2 and the organic phases combined, dried over $MgSO_4$ and evaporated. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1 to 8:2) to afford the (2-azidophenyl)(phenyl)methanol **S23** as a yellow solid (149 mg, 98%). The spectral data matched that reported literature.[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, J = 7.7, 1.5 Hz, 1H), 7.42 – 7.26 (m, 6H), 7.20 – 7.13 (m, 2H), 6.02 (s, 1H), 2.90 (brs, 1H).

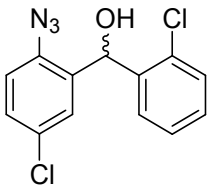
^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 137.0, 134.8, 128.8, 128.4 (2C), 128.0, 127.6, 126.7 (2C), 125.1, 118.2, 71.5.

IR (cm^{-1}) 3351, 2119, 2089, 1582, 1485, 1449, 1291, 1182, 1015, 749, 696.

LCMS (ESI) ***m/z*** $C_{13}H_{11}N_3O$ $[M+H-N_2]^+$ 198.2.

[4] Stopka, T.; Niggemann, M. *Chem. Commun.* **2016,** *52*, 5761-5764.

***(2-azido-5-chlorophenyl)(2-chlorophenyl)methanol* (S24)**

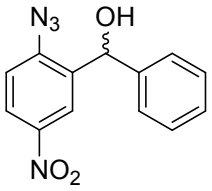


$C_{13}H_9Cl_2N_3O$
MW: 294.14 g.mol^{-1}
Yield: 94%
Brown solid

(2-azido-5-chlorophenyl)(2-chlorophenyl)methanol **S24** was prepared accordingly to the general procedure. To a solution of (2-azido-5-chlorophenyl)(2-chlorophenyl)methanone **S20** (225 mg, 0.77 mmol) in 6.0 mL of dry MeOH and 2.0 mL of dry CH_2Cl_2 at 0 °C was added $NaBH_4$ (29.1 mg, 0.77 mmol). At the end of the reaction, 10 mL of a saturated solution of $NaHCO_3$ and the phases were separated. The aqueous phase was extracted twice with 10 mL of CH_2Cl_2 and the organic phases combined, dried over $MgSO_4$ and evaporated. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1 to 8:2) to afford the (2-azido-5-chlorophenyl)(2-chlorophenyl)methanol **S24** as a brown solid (212 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 2H), 7.29 – 7.22 (m, 3H), 7.19 (d, J = 2.4 Hz, 1H), 7.04 (d, J = 8.5 Hz, 1H), 6.25 (s, 1H), 2.84 (br. s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 136.4, 134.8, 133.1, 130.5, 129.8, 129.3, 129.1, 128.4, 128.3, 127.2, 119.4, 67.7.
IR (cm^{-1}) 3272, 2122, 2092, 1475, 1441, 1407, 1112, 1021, 905, 810, 755.
LCMS (ESI) ***m/z*** $C_{13}H_9{}^{35}Cl_2N_3O$ [M-H+HCOOH]$^-$ 338.2, $C_{13}H_9{}^{35}Cl^{37}ClN_3O$ [M-H+HCOOH]$^-$ 340.0, $C_{13}H_9{}^{37}Cl_2N_3O$ [M-H+HCOOH]$^-$ 342.0.

***(2-azido-5-nitrophenyl)(phenyl)methanol* (S25)**



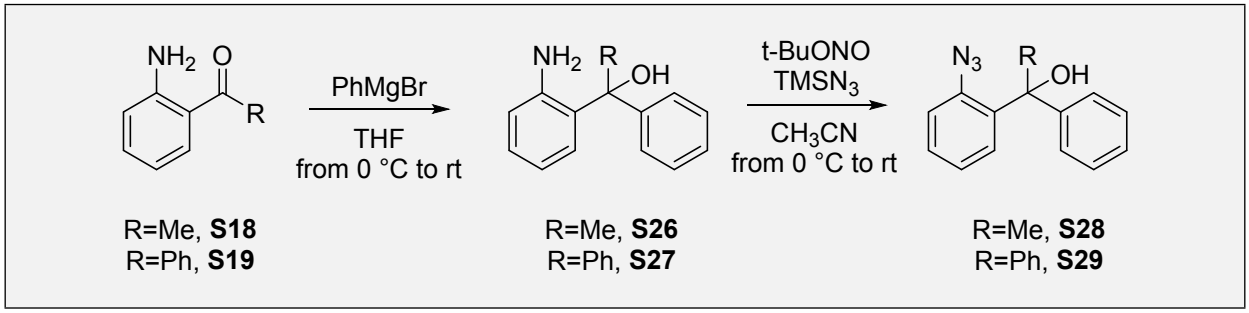
$C_{13}H_{10}N_4O_3$
MW: 270.25 g.mol^{-1}
Yield: 89%
Yellow solid

(2-azido-5-nitrophenyl)(phenyl)methanol **S25** was prepared accordingly to the general procedure. To a solution of (2-azido-5-nitrophenyl)(phenyl)methanone **S21** (269 mg, 1.00 mmol) in 7.0 mL of dry MeOH and 3.00 mL of dry CH_2Cl_2 at 0 °C was added $NaBH_4$ (37.8 mg, 1.0 0mmol). The resulting mixture was then stirred at room temperature under argon for 1 hour. At the end of the reaction, 10 mL of a saturated solution of $NaHCO_3$ and the phases were separated. The aqueous phase was extracted twice with 10 mL of CH_2Cl_2 and the organic phases were combined, dried over $MgSO_4$ and evaporated.

The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1 to 8:2) to afford the (2-azido-5-nitrophenyl)(phenyl)methanol **S25** as a yellow solid (241 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 2.6 Hz, 1H), 8.12 (dd, J = 8.8, 2.7 Hz, 1H), 7.35 – 7.22 (m, 5H), 7.16 (d, J = 8.8 Hz, 1H), 5.95 (s, 1H), 2.91 (brs, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 143.4, 141.7, 136.1, 128.8 (2C), 128.3, 126.8 (2C), 124.1, 123.2, 118.6, 70.8.
IR (cm^{-1}) 3395, 2121, 1091, 1585, 1518, 1480, 1340, 1084, 1034, 1021, 829, 913, 699.
LCMS (ESI) ***m/z*** $C_{13}H_{10}N_4O_3$ $[M-H+HCO_2H]^-$ 315.

2.9. Preparation of trisubstituted alcohols

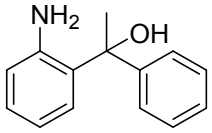


R=Me, **S18**
R=Ph, **S19**

R=Me, **S26**
R=Ph, **S27**

R=Me, **S28**
R=Ph, **S29**

1-(2-aminophenyl)-1-phenylethan-1-ol (S26)



$C_{14}H_{15}NO$
MW: 213.28 g.mol^{-1}
Yield: 90%
Beige solid

To a solution of 1-(2-aminophenyl)ethan-1-one **S18** (121 µL, 1 mmol) in THF (2 mL) a 1M THF solution of phenylmagnesium bromide was added (2 mL, 2 mmol) at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 2 hours. The reaction was quenched with NH_4Cl and extracted with EtOAc (3x10 mL). The combined organic phases were dried over $MgSO_4$, filtrated and evaporated under reduce pressure. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 1-(2-aminophenyl)-1-phenylethan-1-ol (**S26)** as an beige solid (194 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 3H), 7.35 – 7.29 (m, 2H), 7.28 – 7.23 (m, 1H), 7.16 (td, J = 7.6, 1.2 Hz, 1H), 6.89 (td, J = 7.6, 1.2 Hz, 1H), 6.66 (dd, J = 7.6, 1.2 Hz, 1H), 3.75 (br. s, 3H), 1.89 (s, 3H).

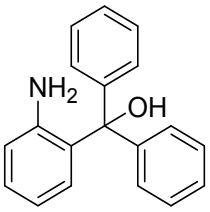
^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 144.2, 132.3, 128.8, 128.4 (2C), 127.0, 126.7, 125.2 (2C), 119.1, 118.8, 76.7, 31.6.

IR (cm^{-1}) 1613, 1492, 1453, 1064, 1047, 1027, 920, 908, 765, 748, 701, 625.

Melting point: 86-87 °C.

LCMS (ESI) ***m/z*** $C_{14}H_{15}NO$ $[M+H]^+$ 214.3.

1-(2-aminophenyl)-1-phenylethan-1-ol (S27)

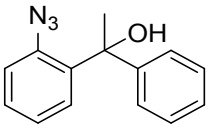


$C_{19}H_{17}NO$
MW: 275.35 g.mol^{-1}
Yield: 89%
Brown solid

To a solution of (2-aminophenyl)(phenyl)methanone **S19** (394.5 mg, 2 mmol) in THF (4 mL) a 1M THF solution of phenylmagnesium bromide was added (4 mL, 4 mmol) at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 2 hours. The reaction was then quenched with NH_4Cl and extracted with EtOAc (3x20 mL). The combined organic phases were dried over $MgSO_4$, filtrated and evaporated under reduce pressure. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the (2-aminophenyl)diphenylmethanol (**S27)** as an brown solid (493.8 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 10H), 7.14 (td, J = 7.7, 1.4 Hz, 1H), 6.83 – 6.78 (m, 1H), 6.73 (t, J = 7.7 Hz, 1H), 6.50 (dd, J = 7.7, 1.4 Hz, 1H), 3.80 (br. s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8 (2C), 144.1, 133.4, 130.0, 128.8, 128.2 (4C), 127.9 (4C), 127.5 (2C), 119.3, 119.2, 86.5.
IR (cm^{-1}) 1614, 1489, 1446, 1308, 1159, 1002, 905, 752, 733, 699, 637.
Melting point : 123-124 °C.
LCMS (ESI) ***m/z*** $C_{19}H_{17}NO$ $[M+H-H_2O]^+$ 258.2.

1-(2-azidophenyl)-1-phenylethan-1-ol (S28)



$C_{14}H_{13}N_3O$
MW: 239.28 g.mol^{-1}
Yield: 90%
Orange solid

To a solution of 1-(2-aminophenyl)-1-phenylethan-1-ol (**S26)** (107 mg, 0.5 mmol) in CH_3CN (2.5 mL) was added at *t*-BuONO (238 µL, 2 mmol) followed by $TMSN_3$ (200 µL, 1.5 mmol) at 0 °C. The resulting mixture was stirred 1 hour at room temperature. The solvent was then removed under reduce pressure and the crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 95:5) to afford the 1-(2-azidophenyl)-1-phenylethan-1-ol (**S28)** as an orange solid (108.1 mg, 90%).

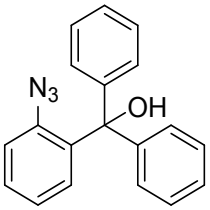
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 7.8, 1.5 Hz, 1H), 7.39 (td, J = 7.8, 1.5 Hz, 1H), 7.32 – 7.27 (m, 4H), 7.25 – 7.20 (m, 2H), 7.16 (dd, J = 7.8, 1.5 Hz, 1H), 4.17 (s, 1H), 1.88 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 137.7, 137.2, 129.0, 128.1 (2C), 127.9, 126.8, 125.2 (2C), 124.9, 119.3, 76.3, 30.5.

IR (cm^{-1}) 2125, 1578, 1482, 1446, 1375, 1347, 1280, 1102, 1035, 753, 699, 658.

LCMS (ESI) ***m/z*** $C_{14}H_{13}N_3O$ $[M+H-H_2O]^+$ 222.2.

(2-azidophenyl)diphenylmethanol (S29)



$C_{19}H_{15}N_3O$
MW: 301.35 $g.mol^{-1}$
Yield: 97%
Orange solid

To a solution of (2-aminophenyl)diphenylmethanol (**S27)** (138 mg, 0.5 mmol) in CH_3CN (2.5 mL) was added at 0 °C *t*-BuONO (238 µL, 2 mmol) followed by $TMSN_3$ (200 µL, 1.5 mmol). The resulting mixture was stirred 1 hour at room temperature. The solvent was then removed under reduce pressure and the crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 95:5) to afford the (2-azidophenyl)diphenylmethanol **S29** as an orange solid (147 mg, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 7H), 7.22 – 7.18 (m, 5H), 6.99 (td, J = 7.7, 1.2 Hz, 1H), 6.60 (dd, J = 7.8, 1.5 Hz, 1H), 4.96 (s, 1H).

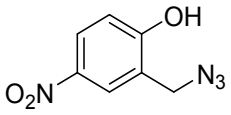
^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2 (2C), 137.9, 137.8, 131.1, 129.2, 128.0 (4C), 128.0 (4C), 127.4 (2C), 124.5, 119.1, 82.1.

IR (cm^{-1}) 2123, 2087, 1578, 1479, 1446, 1246, 1046, 905, 753, 699, 662.

LCMS (ESI) ***m/z*** $C_{19}H_{15}N_3O$ $[M+H-N_2]^+$ 274.4.

2.9. Preparation of hydroxy-azides analogues (S30)

2-(azidomethyl)-4-nitrophenol **(S30)**

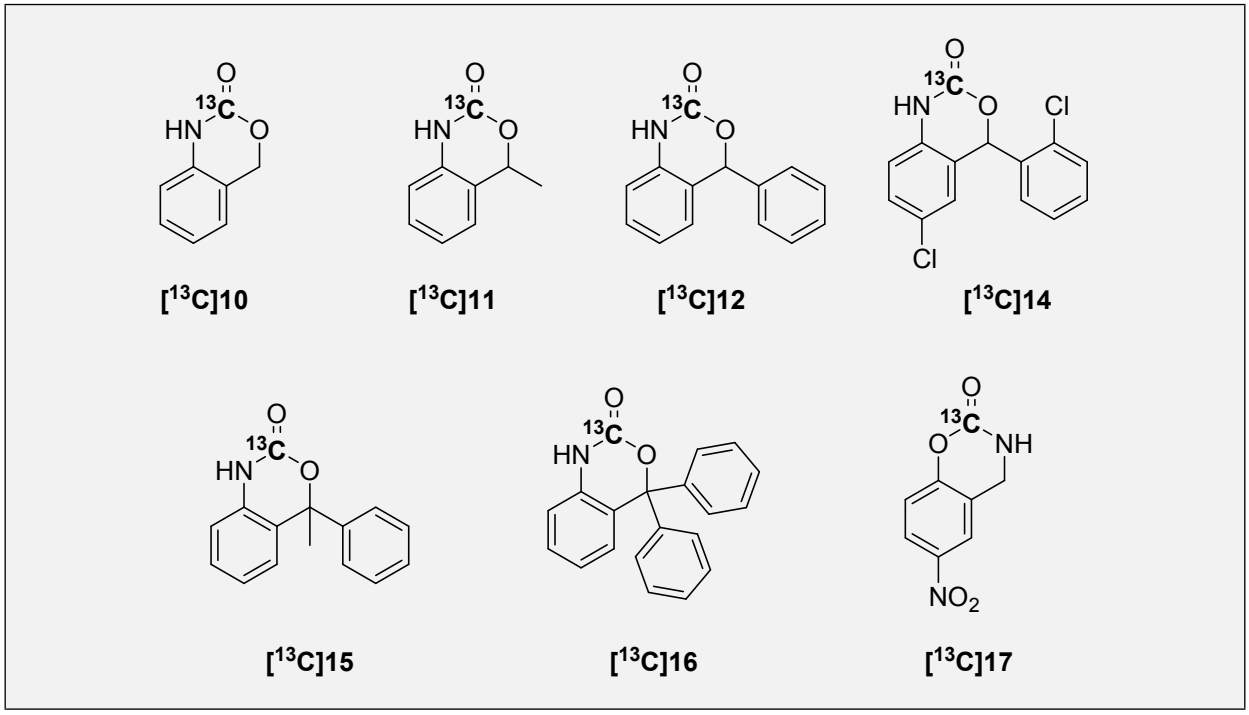


$C_7H_6N_4O_3$
MW: 194.04 g.mol^{-1}
Yield: 98%
Yellowish solid

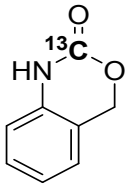
Sodium azide (195 mg, 3.0 mmol) was added to a solution of 2-(bromomethyl)-4-nitrophenol (464 mg, 2.00 mmol) in H_2O and CH_3CN (1.0 mL and 3.0 mL) maintained at 0 °C. The resulting mixture was then stirred at room temperature under argon for 3 hours. At reaction complete, the mixture was diluted in 50 mL of EtOAc and washed twice with brine. The organic phase was then dried over $MgSO_4$ and evaporated under *vacuum*. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1 to 8:2) to afford the 2-(azidomethyl)-4-nitrophenol **S30** as a yellowish solid (378 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (m, 2H), 6.96 (m, 1H), 6.91 (s, 1H), 4.52 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 141.5, 126.1, 125.9, 122.9, 116.5, 50.6.
IR (cm^{-1}) 3351, 2105, 1594, 1522, 1494, 1335, 1282, 1229, 1087, 937, 832, 751.
LCMS (ESI) ***m/z*** $C_7H_6N_4O_3$ $[M-H]^-$ 193.2.

2.10. Synthesis of ^{13}C-labeled 6-membered ring cyclic carbamate derivatives



[^{13}C] 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{13}C]10)**



$C_7{}^{13}CH_7NO_2$
MW: 150.14 g.mol^{-1}
Yield: 67%
White solid

The [^{13}C] 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]10** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), (2-azidophenyl)methanol **S17** (14.9 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]10** as a white solid (10.1 mg, 67%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (brs, 1H), 7.26 (dd, J = 15.2, 1.2 Hz, 1H), 7.12 – 7.08 (m, 1H), 7.05 (td, J = 7.4, 0.9 Hz, 1H), 6.87 (d, J = 7.9 Hz, 1H), 5.33 (d, J = 4.3 Hz, 2H).

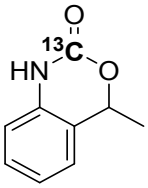
^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8 (^{13}C labeled), 135.7, 129.4, 124.3, 123.5, 118.0 (d, J = 3.6 Hz), 114.3, 68.8 (d, J = 2.4 Hz).

IR (cm^{-1}) 3221, 1671, 1602, 1499, 1408, 1284, 1259, 1213, 1063, 745.

Melting point : 124-125 °C

LCMS (ESI) ***m/z*** $C_7{}^{13}CH_7NO_2$ $[M+H]^+$ 151.2.

***[^{13}C] 4-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{13}C]11)**

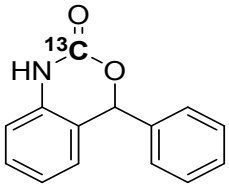


$C_8{}^{13}CH_9NO_2$
MW: 164.17 g.mol^{-1}
Yield: 87%
White solid

The [^{13}C] 4-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]11** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 1-(2-azidophenyl)ethan-1-ol **S22** (16.3 mg, 0.100 mmol) and $^{13}CO_2$ (0.110 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 4-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]11** as a white solid (14.4 mg, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (br. s, 1H), 7.25 (ddd, J = 7.6, 1., 0.8 Hz, 1H), 7.11 – 7.03 (m, 2H), 6.89 (br. d, J = 7.6 Hz, 1H), 5.52 (qd, J = 6.6, 3.7 Hz, 1H), 1.71 (d, J = 6.6 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4 (^{13}C labeled), 135.0, 129.2, 123.8, 123.5, 122.7 (d, J = 3.2 Hz), 114.6 (d, J = 3.5 Hz), 76.1 (d, J = 2.4 Hz), 20.5 (d, J = 2.0 Hz).
IR (cm^{-1}) 3231, 1671, 1598, 1500, 1432, 1377, 1252, 1068, 1039, 753, 679.
Melting point: 111-112 °C.
LCMS (ESI) ***m/z*** $C_8{}^{13}CH_9NO_2$ $[M+H]^+$ 165.2.

***[^{13}C] 4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{13}C]12)**



$C_{13}{}^{13}CH_{11}NO_2$
MW: 226.24 g.mol^{-1}
Yield: 88%
Orange solid

The [^{13}C] 4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]12** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), (2-azidophenyl)(phenyl)methanol **S23** (22.5 mg 0.100 mmol) and $^{13}CO_2$ (0.110 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]12** as a orange solid (20.1 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (br. s, 1H), 7.44 – 7.33 (m, 5H), 7.27 (dd, J = 7.8, 1.2 Hz, 1H), 7.02 (dd, J = 7.4, 1.2 Hz, 1H), 6.95 (br. d, J = 7.9 Hz, 1H), 6.85 (br. d, J = 7.6 Hz, 1H), 6.39 (d, J = 4.0 Hz, 1H).

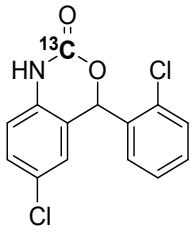
^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4 (^{13}C labeled), 137.6, 135.4, 129.6, 129.3, 128.9 (2C), 127.9 (2C), 125.9, 123.5, 121.0, 114.6 (d, J = 3.6 Hz), 81.4 (d, J = 2.3 Hz).

IR (cm^{-1}) 3233, 3064, 1673, 1599, 1494, 1371, 1341, 1248, 1025, 753, 697.

Melting point : 187-188 °C.

LCMS (ESI) ***m/z*** $C_{13}{}^{13}CH_{11}NO_2$ $[M+H]^+$ 227.3.

[^{13}C] 6-chloro-4-(2-chlorophenyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{13}C]14)**



$C_{13}{}^{13}CH_9Cl_2NO_2$
MW: 295.12 g.mol^{-1}
Yield: 80%
Yellow solid

The [^{13}C] 6-chloro-4-(2-chlorophenyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]14** was prepared accordingto the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), (2-azido-5-chlorophenyl)(2-chlorophenyl)methanol **S24** (29.4 mg, 0.100 mmol) and $^{13}CO_2$ (0.110 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 6-chloro-4-(2-chlorophenyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]14** as a yellow solid (23.6 mg, 80%).

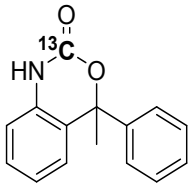
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.56 (s, 1H), 7.61 (dd, J = 8.0, 1.3 Hz, 1H), 7.49 (td, J = 7.7, 1.7 Hz, 1H), 7.42 (dd, J = 7.6, 1.3 Hz, 1H), 7.40– 7.37 (m, 1H), 7.23 (dd, J = 7.7, 1.7 Hz, 1H), 7.00 (dd, J = 8.0, 1.3 Hz, 1H), 6.83 (br. d, J = 3.4 Hz, 1H), 6.80 (dd, J = 2.3, 0.4 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 150.0 (^{13}C labeled), 135.3 (m), 134.7 (m), 133.0, 131.2, 130.3, 129.8, 129.4, 127.9, 126.3, 124.8, 121.4 (m), 115.9 (m), 76.4 (m).

IR (cm^{-1}) 3235, 1681, 1594, 1494, 1331, 1246, 1033, 755.

LCMS (ESI) ***m/z*** $C_{13}{}^{13}CH_9{}^{35}Cl_2NO_2$ $[M+H]^+$ 295.2, $C_{13}{}^{13}CH_9{}^{35}Cl^{37}ClNO_2$ $[M+H]^+$ 297.2, $C_{13}{}^{13}CH_9{}^{37}Cl_2NO_2$ $[M+H]^+$ 299.1.

[^{13}C] 4-methyl-4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{13}C]15)**

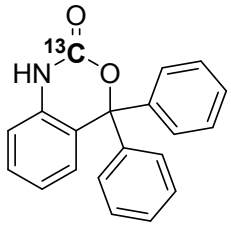


$C_{14}{}^{13}CH_{13}NO_2$
MW: 240.27 g.mol^{-1}
Yield: 35%
Brown solid

The [^{13}C] 4-methyl-4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]15** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 1-(2-azidophenyl)-1-phenylethan-1-ol **S28** (24.9 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The mixture was then heated at 150 °C for 15 minutes before the unreacted CO_2 was released. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 5:5) affording the ^{13}C-labeled-4-methyl-4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]15** as a brown solid (8.5 mg, 35%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (br. s, 1H), 7.33 – 7.26 (m, 7H), 7.14 (td, J = 7.6, 1.1 Hz, 1H), 6.87 (dd, J = 7.6, 1.1 Hz, 1H), 2.05 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2 (^{13}C labeled), 143.2, 134.9, 129.5, 128.6 (2C), 128.3, 125.5 (2C), 125.4 (d, J = 2.8 Hz), 125.3, 123.4, 114.9 (d, J = 3.5 Hz), 85.4 (d, J = 2.4 Hz), 28.3.
IR (cm^{-1}) 1677, 1599, 1493, 1444, 1327, 1276, 1259, 1059, 1006, 756, 744, 725, 701, 628.
LCMS (ESI) ***m/z*** $C_{14}{}^{13}CH_{13}NO_2$ $[M+H]^+$ 241.3.

[^{13}C] 4,4-diphenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{13}C]16*)***



$C_{19}{}^{13}CH_{15}NO_2$
MW: 302.34 g.mol^{-1}
Yield: 28%
Brown solid

The [^{13}C] 4,4-diphenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]16** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), (2-azidophenyl)diphenylmethanol **S29** (30.1 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The mixture was then heated at 150 °C for 30 minutes before the unreacted CO_2 was released and heated for 1 hour and 30 minutes more. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 95:5 to 80:20) affording the ^{13}C-labeled 4,4-diphenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **[^{13}C]16** as a brown solid (8.6 mg, 28%).

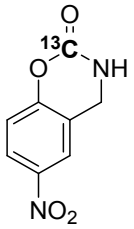
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 7.43 – 7.38 (m, 6H), 7.34 (td, *J* = 7.8, 1.3 Hz, 1H), 7.12 – 7.07 (m, 4H), 7.02 (td, *J* = 7.6, 1.0 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.61 (dd, *J* = 7.7, 1.1 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 150.64 (^{13}C labeled), 141.46 (d, *J* = 1.6 Hz), 135.9, 135.8, 129.5, 128.5 (2C), 128.3 (4C), 127.5 (4C), 127.0, 124.7 (m), 122.3, 114.5 (m), 88.0.

IR (cm^{-1}) 1677, 1596, 1492, 1448, 1320, 1258, 1014, 754, 698.

LCMS (ESI) ***m/z*** $C_{19}{}^{13}CH_{15}NO_2$ $[M+H]^+$ 303.4.

[^{13}C] 6-nitro-3,4-dihydro-2H-benzo[e][1,3]oxazin-2-one **([^{13}C]17)**



$C_7{}^{13}CH_6N_2O_4$
MW: 194.19 g.mol^{-1}
Yield: 74%
Yellow solid

The [^{13}C] 6-nitro-3,4-dihydro-2H-benzo[e][1,3]oxazin-2-one **[^{13}C]17** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-(azidomethyl)-4-nitrophenol **S30** (19.3 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 6-nitro-3,4-dihydro-2H-benzo[e][1,3]oxazin-2-one **[^{13}C]17** as a yellow solid (14.4 mg, 74%).

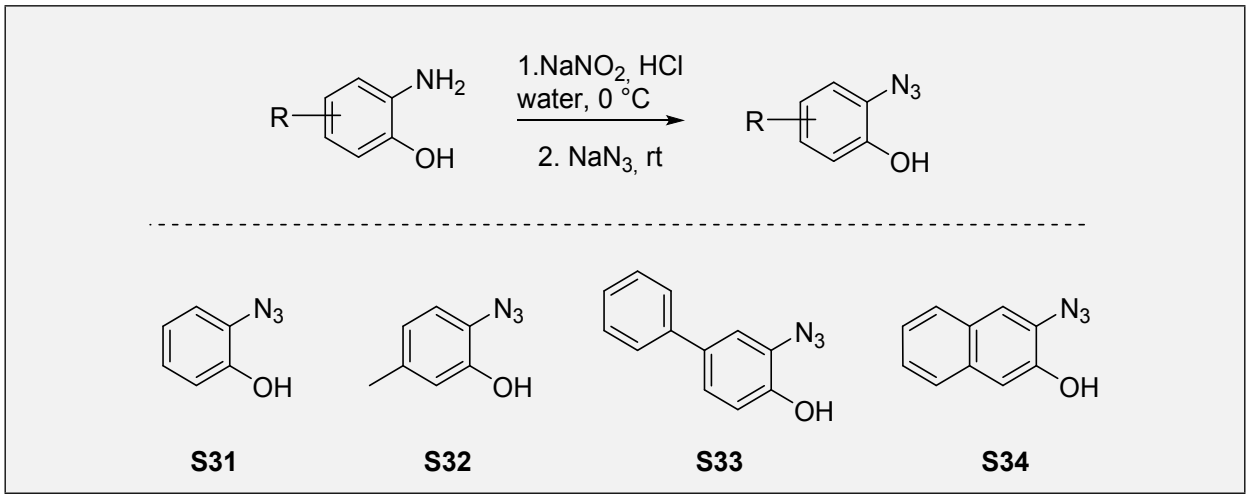
^{1}H NMR (400 MHz, DMSO-d_6) *δ* 8.25 (d, *J* = 2.8 Hz, 2H), 8.16 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.26 (d, *J* = 9.0 Hz, 1H), 4.51 (br. s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) *δ* 159.0, 157.0, 148.8 (^{13}C labeled), 143.3, 124.5, 122.6, 117.1 (d, *J* = 3.2 Hz), 40.9.

IR (cm^{-1}) 2924, 2853, 1708, 1588, 1522, 1335, 1288, 1245, 1092.

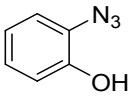
LCMS (ESI) ***m/z*** $C_7{}^{13}CH_6N_2O_4$ $[M-H]^-$ 194.2.

2.11. General procedure for the preparation of the aromatic azido derivatives *via* Sandmeyer reaction



To a solution of aminophenol (3.00 mmol) in 10 mL of deionized water at 0 °C was added HCl 12N (833 µL, 10.0 mmol) and the reaction was kept at 0 °C. A solution of $NaNO_2$ (207 mg, 3.00 mmol) in 1 mL of water was slowly added and the resulting mixture was stirred at 0 °C for 15 minutes after what sodium azide (234 mg, 3.60 mmol) was added by portion. The reacting mixture was then allowed to warm to room temperature and kept under stirring for 2 hours. The aqueous phase was extracted twice with 20 mL of EtOAc. The organic layers were combined then washed with 30 mL of brine, dry over $MgSO_4$ and evaporated to dryness. Purification by Flash Chromatography on SiO_2 gel using adapted eluent afforded the desired ortho-azido-phenols.

2-azidophenol **(S31)**



$C_6H_5N_3O$
MW: 135.13 g.mol^{-1}
Yield: 74%
Orange solid

2-azidophenol **S31** was prepared accordingly to the general procedure. The reaction has been conducted using 327 mg of *o*-aminophenol and the crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1 to 8:2) to afford the 2-azido-phenol **S31** as an orange solid (300 mg, 74%). The spectral data matched that reported literature.[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 – 7.05 (m, 2H), 6.98 – 6.92 (m, 2H), 5.42 (s, 1H).

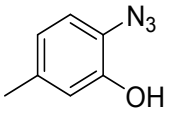
^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 126.2, 126.0, 121.3, 118.4, 116.1.

IR (cm^{-1}) 3414, 2117, 1089, 1591, 1492, 1349, 1292, 1245, 1205, 742, 649.

[5] Ngai, M. H.; Yang, P.-Y.; Liu, K.; Shen, Y.; Wenk, M. R.; Yao, S. Q.; Lear, M. J. *Chem. Commun.* **2010,** *46*, 8335-8337.

LCMS (ESI) ***m/z*** $C_6H_5N_3O$ [M-H]$^-$ 134.2.

2-azido-5-methylphenol **(S32)**

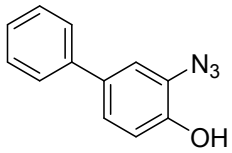


$C_7H_7N_3O$
MW: 149.15 g.mol^{-1}
Yield: 75%
Brown solid

2-azido-5-methylphenol **S32** was prepared accordingly to the general procedure. The reaction has been conducted using 369 mg of 2-amino-5-methylphenol and the crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-5-methylphenol **S32** as a brown solid (337 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (d, J = 8.4 Hz, 1H), 6.76 (m, 2H), 5.34 (br. s, 1H), 2.30 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 136.4, 123.2, 121.9, 118.1, 116.7, 21.1.
IR (cm^{-1}) 3375, 2914, 2139, 2093, 1584, 1502, 1313, 1256, 1159, 9444, 696, 793, 633, 520.
LCMS (ESI) ***m/z*** $C_7H_7N_3O$ [M-H]$^-$ 148.0.

3-azido-[1,1'-biphenyl]-4-ol **(S33)**



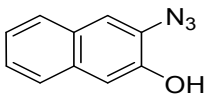
$C_{12}H_9N_3O$
MW: 211.22 g.mol^{-1}
Yield: 68%
Brown solid

3-azido-[1,1'-biphenyl]-4-ol **S33** was prepared accordingly to the general procedure. The reaction has been conducted using 617 mg of 3-amino-[1,1'-biphenyl]-4-ol and the crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 3-azido-[1,1'-biphenyl]-4-ol **S33** as a brown solid (428 mg, 68%). The spectral data matched that reported literature.[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.52 (m, 2H), 7.48 – 7.42 (m, 2H), 7.38 – 7.32 (m, 1H), 7.31 – 7.27 (m, 2H), 7.04 – 6.99 (m, 1H), 5.40 (br. s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 140.2, 134.9, 129.0 (2C), 127.3, 126.9 (2C), 126.3, 125.0, 116.9, 116.4.
IR (cm^{-1}) 3401, 2139, 2103, 1593, 1523, 1491, 1455, 1410, 1317, 1254, 1214, 1151, 823, 810, 756, 683.
LCMS (ESI) ***m/z*** $C_{12}H_9N_3O$ [M-H]$^-$ 210.2.

[6] Novak, M.; Glover, S. A. *J. Am. Chem. Soc.* **2004,** *126*, 7748-7749.

***3-azidonaphthalen-2-ol* (S34)**

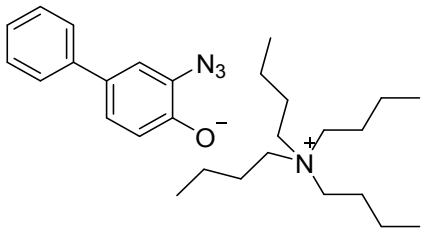


$C_{10}H_7N_3O$
MW: 185.19 g.mol^{-1}
Yield: 81%
Beige solid

3-azidonaphthalen-2-ol **S34** was prepared accordingly to the general procedure. The reaction has been conducted using (318 mg, 2.0 mmol) of 3-aminonaphthalen-2-ol and a proportional amount of other reagents. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 3-azidonaphthalen-2-ol **S34** as a beige solid (299 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (t, J = 7.9 Hz, 2H), 7.47 (s, 1H), 7.43-7.33 (m, 2H), 7.28 (s, 1H), 5.57 (br. s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 132.3, 128.9, 128.0, 126.7, 126.6, 126.1, 124.6, 115.9, 110.9.
IR (cm^{-1}) 3400, 2109, 1599, 1522, 1446, 1399, 1362, 1286, 1144, 1069, 863, 740, 617, 476.
LCMS (ESI) ***m/z*** $C_{10}H_7N_3O$ $[M-H]^-$ 184.1.

***tetrabutylammonium 3-azido-[1,1'-biphenyl]-4-olate* (S35)**

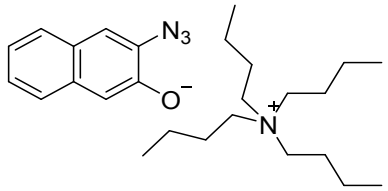


$C_{28}H_{44}N_4O$
MW: 452.69 g.mol^{-1}
Yield: >99%
Brown oil

Compound **S33** (21.1 mg, 0.100 mmol) was dissolved in H_2O at room temperature, then terbutylammonium hydroxide 30·H_2O (120 mg, 0.150 mmol) was added and the mixture stirred vigorously for 3 hours. Extraction occurred with twice CH_2Cl_2. The unified organic phases were than dried over $MgSO_4$ and evaporated under vacuum to afford tetrabutylammonium 3-azido-[1,1'-biphenyl]-4-olate **S35** (46 mg, >99%) as sticky brown oil quantitatively, which was used without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.46 (m, 2H), 7.37 – 7.30 (m, 2H), 7.23 – 7.12 (m, 2H), 7.06 (d, J = 2.4 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 3.24 (dd, J = 10.0, 7.0 Hz, 8H), 1.63 – 1.53 (m, 8H), 1.44 – 1.34 (m, 8H), 1.00 – 0.93 (m, 12H).

***tetrabutylammonium 3-azidonaphthalen-2-olate* (S36)**



$C_{29}H_{46}N_4O$
MW: 426.65 g.mol^{-1}
Yield: >99%
Brown oil

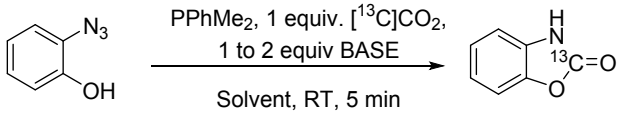
Compound **S34** (18.5 mg, 0.100 mmol) was dissolved in H_2O at room temperature, then terbutylammonium hydroxide 30·H_2O (120 mg, 0.150 mmol) was added and the mixture stirred vigorously for 3 hours. Extraction occurred with twice CH_2Cl_2. The unified organic phases were than dried over $MgSO_4$ and evaporated under vacuum to afford tetrabutylammonium 3-azidonaphthalen-2-olate **S36** (43 mg, >99%) as sticky brown oil quantitatively, which was used without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.55 (m, 2H), 7.51 (s, 1H), 7.32 (s, 1H), 7.28 (dd, J = 6.9, 1.3 Hz, 1H), 7.22 – 7.18 (m, 1H), 3.29 (dd, J = 10.1, 7.0 Hz, 8H), 1.66 – 1.55 (m, 8H), 1.40 (dd, J = 14.8, 7.4 Hz, 8H), 0.97 (t, J = 7.3 Hz, 12H).

2.12. Synthesis of ^{13}C-labeled aromatic cyclic carbamates

2.12.1 Optimisation

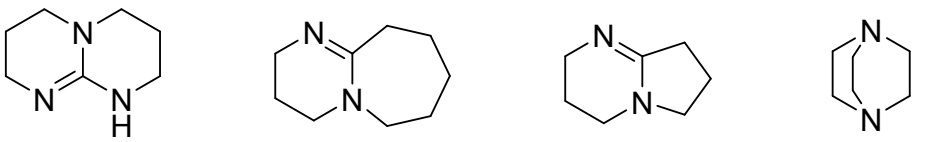
A)



S31 **[^{13}C]18**

Entry	*Base*	*Equiv. of base*	*Solvent*	*Conversion (isolated yield%)*
1	-	-	DMF-d_7	(64)
2	DABCO	1	CH_3CN-d_3	0
3	DBN	1	CH_3CN-d_3	0
4	DBU	1	CH_3CN-d_3	0
5	TBD	1	CH_3CN-d_3	0
6	DMAP	2	CH_3CN-d_3	71
7	NaOtBu	2	CH_3CN-d_3	23
8	Proton Sponge	2	CH_3CN-d_3	59
9	TEA	2	CH_3CN-d_3	81
10	DIPEA	2	CH_3CN-d_3	90 (85)
11	DIPEA	2	DMF-d_7	(83)

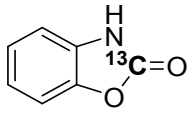
B)



TBD **DBU** **DBN** **DABCO**

***Table S3**: **A)** Screening of bases; **B)** Different amine, amidine and guanidine bases used.*

***[^{13}C] benzo[d]oxazol-2(3H)-one* ([^{13}C]18)**

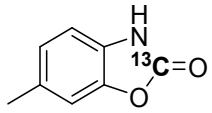


$C_6{}^{13}CH_5NO_2$
MW: 136.11 g.mol^{-1}
Yield: 85%
White solid

The [^{13}C] benzo[d]oxazol-2(3H)-one **[**^{13}C]**18** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol,), 2-azidophenol **S31** (13.5 mg, 0.100 mmol,), $^{13}CO_2$ (0.100 mmol) and DIPEA (26 µL, 0.2 mmol) in CD_3CN. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 70:30) affording the [^{13}C] benzo[d]oxazol-2(3H)-one **[**^{13}C]**18** as a white solid (11.6 mg, 85%).

^{1}H NMR (400 MHz, MeOD-*d*$_4$) δ 7.22 – 7.18 (m, 1H), 7.15 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.11 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.09 – 7.06 (m, 1H).
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 157.2 (^{13}C labeled), 125.1 (2C), 123.4 (2C), 110.8 (d, *J* = 4.8 Hz), 110.6 (d, *J* = 4.0 Hz).
IR (cm^{-1}) 2926, 1714, 1593, 1482, 1252, 1142, 1008, 934, 742, 697.
LCMS (ESI) ***m/z*** $C_6{}^{13}CH_5NO_2$ $[M+H]^+$ 137.2.

***[^{13}C] 5-methylbenzo[d]oxazol-2(3H)-one* ([^{13}C]19)**

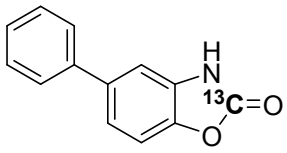


$C_7{}^{13}CH_7NO_2$
MW: 150.14 g.mol^{-1}
Yield: 78%
Brown solid

The [^{13}C] 5-methylbenzo[d]oxazol-2(3H)-one **[**^{13}C]**19** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol,), 2-azido-5-methylphenol **S32** (14.9 mg, 0.100 mmol,) $^{13}CO_2$ (0.100 mmol) and DIPEA (26 µL, 0.200 mmol) in CD_3CN. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 70:30) affording the [^{13}C]5-methylbenzo[d]oxazol-2(3H)-one **[**^{13}C]**19** as a brown solid (11.7 mg, 78%).

^{1}H NMR (400 MHz, MeOD-*d*$_4$) δ 7.03 (br. s, 1H), 6.99 – 6.92 (m, 2H), 2.36 (s, 3H).
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 157.4 (^{13}C labeled), 145.5 (d, *J* = 1.9 Hz), 133.7, 129.1 (d, *J* = 4.6 Hz), 125.4, 111.2 (d, *J* = 3.9 Hz), 110.4 (d, *J* = 4.7 Hz), 21.3.
IR (cm^{-1}) 3229, 1731, 1690, 1498, 1290, 1265, 928, 816, 707.
Melting point: 135-136 °C.
LCMS (ESI) ***m/z*** $C_7{}^{13}CH_7NO_2$ $[M+H]^+$ 151.2.

***[^{13}C] 5-phenylbenzo[d]oxazol-2(3H)-one* ([^{13}C]20)**

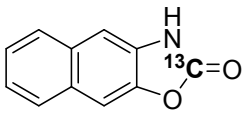


$C_{12}{}^{13}CH_9NO_2$
MW: 212.21 g.mol^{-1}
Yield: 37%
Yellow solid

The [^{13}C] 5-phenylbenzo[d]oxazol-2(3H)-one **[**^{13}C]**20** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol,), tetrabutylammonium 3-azido-[1,1'-biphenyl]-4-olate **S35**[7] (46 mg, 0.100 mmol,) and $^{13}CO_2$ (0.100 mmol) in CD_3CN. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 70/30) affording the [^{13}C]5-phenylbenzo[d]oxazol-2(3H)-one **[**^{13}C]**20** as a yellow solid (7.8 mg, 37%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (br. s, 1H), 7.57 – 7.51 (m, 2H), 7.48 – 7.42 (m, 2H), 7.39-7.37 (m, 1H), 7.34 (dd, J = 8.3, 1.8 Hz, 1H), 7.30 (br. d, J = 1.5 Hz, 1H), 7.28 (br. s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7 (^{13}C labeled), 143.5 (d, J = 1.6 Hz), 140.6, 138.3, 129.9 (d, J = 4.8 Hz), 129.1 (2C), 127.7, 127.4 (2C), 122.1, 110.5 (d, J = 4.0 Hz), 108.8 (d, J = 4.7 Hz).
IR (cm^{-1}) 3218, 1716, 1480, 1469, 1257, 940, 760, 697.
Melting point: 150-151 °C.
LCMS (ESI) ***m/z*** $C_{12}{}^{13}CH_9NO_2$ $[M+H]^+$ 213.2.

***[^{13}C] naphtho[2,3-d]oxazol-2(3H)-one* ([^{13}C]21)**



$C_{10}{}^{13}CH_7NO_2$
MW: 186.17 g.mol^{-1}
Yield: 45%
Pale yellow solid

The [^{13}C] naphtho[2,3-d]oxazol-2(3H)-one [^{13}C]**21** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), tetrabutylammonium 3-azidonaphthalen-2-olate **S36**[8] (43 mg, 0.100 mmol) and $^{13}CO_2$ (0.110 mmol) in CD_3CN. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 70/30) affording the [^{13}C] naphtho[2,3-d]oxazol-2(3H)-one [^{13}C]**21** as a white solid (8.4 mg, 45%).

^{1}H NMR (400 MHz, MeOD-*d*$_4$) δ 7.82 (ddd, J = 9.4, 7.1, 2.6 Hz, 2H), 7.58 (brs, 1H), 7.45 – 7.36 (m, 3H).
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 157.2 (^{13}C labeled), 145.4, 132.5, 131.8, 131.4, 128.9, 128.2, 126.3, 125.7, 106.7 (d, J = 4.1 Hz), 106.5 (d, J = 5.0 Hz).

[7] When **[^{13}C]20** was prepared from phenol **S33** using DIPEA (2 equiv.), a lower yield was obtained.
[8] When **[^{13}C]21** was prepared from phenol **S34** using DIPEA (2 equiv.), a lower yield was obtained.

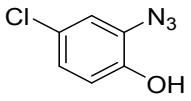
IR (cm^{-1}) 3282, 2445, 1737, 1703, 1470, 1272, 1254, 949, 858.

Melting point : 192-193 °C.

LCMS (ESI) ***m/z*** $C_{10}{}^{13}CH_7NO_2$ $[M+H]^+$ 187.2.

2.13. Synthesis of drug precursors

***2-azido-4-chlorophenol* (S37)**



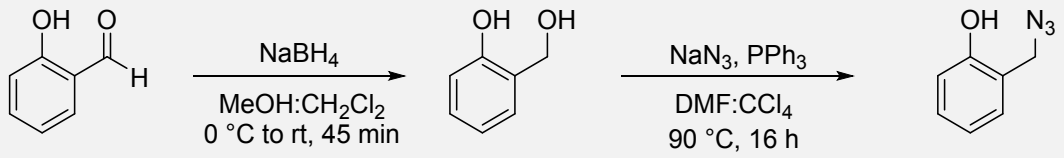
$C_6H_4ClN_3O$
MW: 169.57 g.mol^{-1}
Yield: 99%
Orange solid

2-azido-4-chlorophenol **S37** was prepared accordingly to the general procedure. The reaction has been conducted using 431 mg of 2-amino-4-chlorophenol and the crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-azido-4-chlorophenol **S37** as an orange solid (507 mg, 99%). The spectral data matched that reported literature.[9]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, J = 2.3 Hz, 1H), 7.01 (dd, J = 8.6, 2.3 Hz, 1H), 6.85 (d, J = 8.6 Hz, 1H), 5.35 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 127.1, 126.1, 125.8, 118.4, 117.0.
IR (cm^{-1}) 3333, 2117, 1601, 1491, 1416, 1352, 1291, 1267, 1233, 1213, 1147, 1105, 888, 851, 647, 569.
LCMS (ESI) ***m/z*** $C_6H_4{}^{35}ClN_3O$ $[M+H]^-$ 168.1, $C_6H_4{}^{37}ClN_3O$ $[M+H]^-$ 170.1.
HRMS (ESI) ***m/z*** calcd for $C_6H_4ClN_3O$ $[M+H]^+$ 167.9970; found: 167.9966.

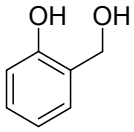
[9] Ren, L.; Jiao, N. *Chem. Commun.* **2014,** *50*, 3706-3709.

***Synthesis of caroxazone precursor* (S40)**



S38 **S39** **S40**

***2-(hydroxymethyl)phenol* (S39)**

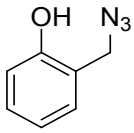


$C_7H_8O_2$
MW: 124.14 g.mol^{-1}
Yield: 93%
White solid

2-(hydroxymethyl)phenol **S39** was synthetized following the general procedure of section **2.2** of this experimental part**.** To a solution of 2-hydroxybenzaldehyde **S38** (122 mg, 1.00 mmol) in 6.0 mL of dry MeOH and 4.0 mL of dry CH_2Cl_2 at 0 °C was added $NaBH_4$ (37.8 mg, 1.0 mmol). The resulting mixture was then stirred at 0 °C for 15 min then 30 additional minutes at room temperature, under argon. At the end of the reaction, 10 mL of a saturated solution of $NaHCO_3$ were added and the phases separated. The aqueous phase was extracted twice with 10 mL of CH_2Cl_2 and the organic phases were combined, dried over $MgSO_4$ and evaporated to afford the 2-(hydroxymethyl)phenol **S39** (116 mg, 93%) as a white solid. The crude mixture was used for the subsequent step without any further purification. Analytical data were consistent with the reported literature.[10]

^{1}H NMR (400 MHz, MeOD-*d*$_4$) δ 7.29 – 7.22 (m, 1H), 7.08 (td, J = 8.0, 1.7 Hz, 1H), 6.80 (td, J = 7.4, 1.0 Hz, 1H), 6.76 (dd, J = 8.0, 1.0 Hz, 1H), 4.65 (s, 2H).
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 156.2, 129.4, 129.3, 128.5, 120.4, 115.8, 61.1.

***2-(azidomethyl)phenol* (S40)**



$C_7H_7N_3O$
MW: 149.15 g.mol^{-1}
Yield: 50%
Orange oil

A stirring mixture of 2-(hydroxymethyl)phenol **S39** (97.0 mg, 0.78 mmol), sodium azide (101.5 mg, 1.56 mmol) and triphenylphosphine (205.0 mg, 0.78 mmol) in CCl_4 and DMF (0.5 and 2.0 mL) was heated to 90 °C over 16 hours. At reaction complete, the mixture was cooled down at room temperature and partitioned between EtOAc and water. The aqueous phase was extracted twice with 10 mL of EtOAc

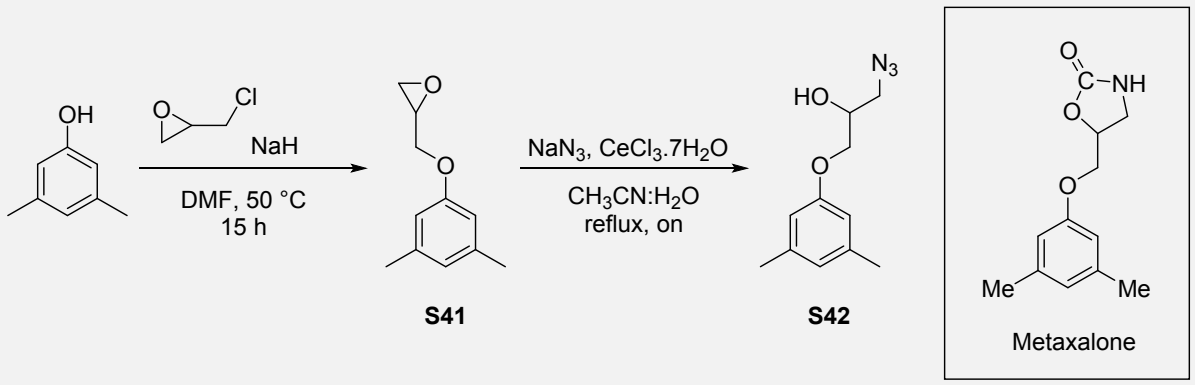
[10] Li, H.-J.; Wu, Y.-Y.; Wu, Q.-X.; Wang, R.; Dai, C.-Y.; Shen, Z.-L.; Xie, C.-L.; Wu, Y.-C. *Org. Biomol. Chem.* **2014,** *12*, 3100-3107.

and the organic phases were combined, dried over $MgSO_4$ and evaporated under *vacuum*. The crude was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 8:2) to afford the 2-(azidomethyl)phenol **S40** as an orange oil (59.3 mg, 50%). Analytical data were consistent with the reported literature.[11]

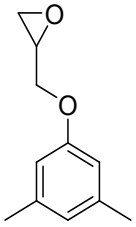
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, J = 8.0, 1.5 Hz, 1H), 7.19 (dd, J = 7.8, 1.5 Hz, 1H), 6.92 (td, J = 7.5, 0.9 Hz, 1H), 6.84 (dd, J = 8.0, 0.9 Hz, 1H), 5.51 (br. s, 1H), 4.40 (s, 2H).
LCMS (ESI) ***m/z*** $C_7H_7N_3O$ $[M-H]^-$ 148.1.

[11] ZhangJames, Q., Takacs, M., *Org. Lett.,* **2008**, *10*, 545-548.

Synthesis of Metaxalone precursor



***2-((3,5-dimethylphenoxy)methyl)oxirane* (S41)**

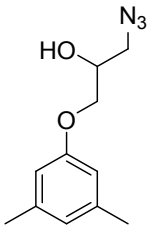


$C_{11}H_{14}O_2$
MW: 178.23 g.mol^{-1}
Yield: 72%
Colorless oil

To a solution of 3,5-dimethylphenol (300 mg, 2.50 mmol) in DMF (7.5 mL) was added at 0 °C NaH (147 mg, 3.70 mmol). The resulting solution was stirred for 1 hour at 0 °C before the addition of epichloridrine (290 µL, 3.70 mmol). The mixture was then heated at 50 °C for 15 hours. After being cooled to room temperature, diethyl ether and water were added and the phases were separated. The aqueous layer was extracted twice with 50 mL of Et_2O. The combined organic phases were dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford the 2-((3,5-dimethylphenoxy)methyl)oxirane **S41** as a colorless oil (314 mg, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62 (s, 1H), 6.56 (s, 2H), 4.17 (dd, J = 11.0, 3.3 Hz, 1H), 3.95 (dd, J = 11.0, 5.5 Hz, 1H), 3.37 – 3.31 (m, 1H), 2.92 – 2.88 (m, 1H), 2.75 (dd, J = 5.0, 2.7 Hz, 1H), 2.31 – 2.25 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 139.4 (2C), 123.1, 112.5 (2C), 68.7, 50.3, 44.9, 21.6 (2C).
IR (cm^{-1}) 1613, 1595, 1472, 1454, 1321, 1296, 1172, 1153, 1067, 907, 830, 688.
LCMS (ESI) ***m/z*** $C_{11}H_{14}O_2$ $[M+H]^+$ 179.2.

***1-azido-3-(3,5-dimethylphenoxy)propan-2-ol* (S42)**

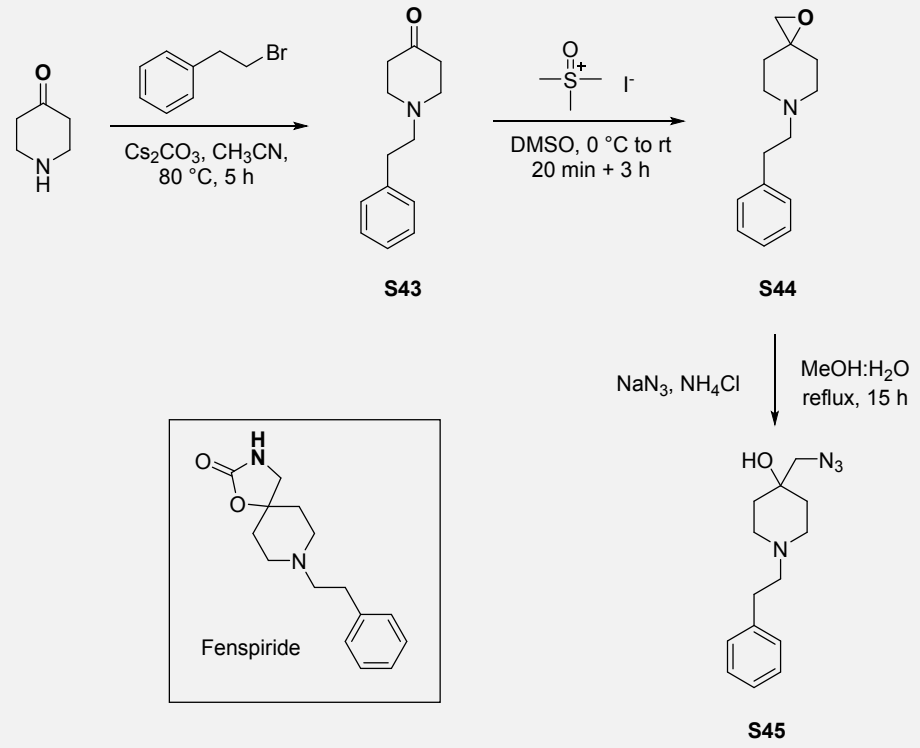


$C_{11}H_{14}N_3O_2$
MW: 221.26 g.mol^{-1}
Yield: 70%
Colorless oil

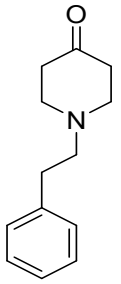
To a solution of 2-((3,5-dimethylphenoxy)methyl)oxirane **S41** (100 mg, 0.56 mmol) in CH_3CN/H_2O (15 mL, 9:1) was added successively $CeCl_3.7H_2O$ (63 mg, 0.17 mmol) and sodium azide (109 mg, 1.68 mmol) and the resulting mixture was heated to reflux for overnight. After cooling down the reactional mixture was treated with water and the aqueous layer was washed with EtOAc (3 x 20 mL). The combined organic phases were dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 7:3) to afford the 1-azido-3-(3,5-dimethylphenoxy)propan-2-ol **S42** (87 mg, 70%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (d, J = 0.6 Hz, 1H), 6.55 (s, 2H), 4.18 – 4.13 (m, 1H), 4.02 – 3.96 (m, 2H), 3.57 – 3.45 (m, 2H), 2.29 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 139.5 (2C), 123.4, 112.4 (2C), 69.5, 69.0, 53.5, 21.6 (2C).
IR (cm^{-1}) 2099, 1613, 1594, 1457, 1321, 1295, 1170, 1157, 1100, 1071, 829, 687.
LCMS (ESI) ***m/z*** $C_{11}H_{15}N_3O_2$ $[M+H]^+$ 222.3.
HRMS (ESI) ***m/z*** calcd for $C_{11}H_{15}N_3O_2$ $[M+H]^+$ 222.1237; found: 222.1235.

Synthesis of the Fenspiride precursor



1-phenethylpiperidin-4-one **(S43)**



$C_{13}H_{17}NO$
MW: 203.29 g.mol^{-1}
Yield: 65%
Light yellow oil

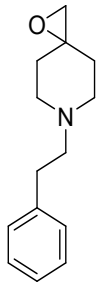
Commercial 4-piperidone monohydrate hydrochloride (1.0 g, 6.50 mmol) was dissolved in CH_3CN (18 mL). The colorless solution was treated sequentially with cesium carbonate (4.6 g, 14.1 mmol) and (2-bromoethyl)benzene (0.88 mL, 6.40 mmol) at room temperature. The resulting suspension was vigorously stirred and refluxed at 80 °C, for 5 hours. After 5 hours, the CH_3CN was evaporated and the crude mixture was extracted 3 times with CH_2Cl_2, dried over $MgSO_4$ and concentrated under *vacuum* to provide a yellow oil. The oily mixture was purified by Flash Chromatography on SiO_2 gel, after neutralization with 1% Et_3N (eluent EtOAc/Hexanes 1:1 to 7:3 with 1% Et_3N) to give 1-phenethylpiperidin-4-one **S43** as a light yellow oil (853 mg, 65%). The experimental data are consistent with the reported procedure.[12]

[12] Valdez, C.A., Leif, R.N., Mayer, B.P. *PLoS One*, **2014**, *9*, e108250/1-e108250/8;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.25 –7.21 (m, 3H), 2.86 – 2.81 (m, 6H), 2.75 – 2.70 (m, 2H), 2.48 (t, *J* = 6.2 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 209.2, 140.1, 128.8 (2C), 128.6 (2C), 126.3, 59.4, 53.12 (2C), 41.3 (2C), 34.2.

6-phenethyl-1-oxa-6-azaspiro[2.5]octane **(S44)**



$C_{14}H_{19}NO$
MW: 217.31 g.mol^{-1}
Yield: 58%
Colorless oil

This compound was prepared by adapting a described procedure.[13] To a 25-mL flask equipped with a magnetic stirrer was added sodium hydride 60% in mineral oil (52.0 mg, 2.18 mmol). The flask was repeatedly evacuated and recharged with argon then cooled down to 0 °C. Next, a solution of trimethyloxosulfonium iodide (478 mg, 2.18 mmol) in DMSO (3.0 mL) was added and the mixture was stirred for 20 minutes at room temperature. A solution of 1-phenethylpiperidin-4-one **S43** (340 mg, 1.60 mmol) in DMSO (1.2 mL) was then added at once. After stirring 1 hour at 0 °C and for other 2 hours at room temperature, DMSO was evaporated. The resulting white solid was dissolved in a mixture of EtOAc/Heptane (75:25) and extracted twice from water, dried over $MgSO_4$ and evaporated under *vacuum* to give a pale yellow oil, A purification occurred on Flash Chromatography on SiO_2 gel after neutralization with 1% Et_3N (eluent Heptane/EOAc 6:4 with 1% Et_3N) affording 6-phenethyl-1-oxa-6-azaspiro[2.5]octane **S44** as colorless oil (209.6 mg, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.18 (m, 5H), 2.83 (dd, *J* = 16.0, 4 Hz, 2H), 2.74 – 2.60 (m, 8H), 1.93 – 1.86 (m, 2H), 1.61 – 1.55 (m, 2H).

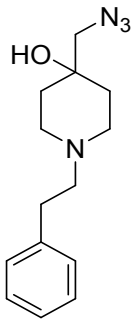
^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 128.7 (2C), 128.4 (2C), 126.1, 60.5, 57.4, 53.7, 52.0 (2C), 33.9, 33.0 (2C).

IR (cm^{-1}): 2948, 2920, 2801, 1093, 920, 748, 699.

LCMS (ESI) ***m/z*** $C_{14}H_{19}NO$ $[M+H]^+$ 218.4.

[13] Davis, R., Kluge, A.F., Maddox, M.L., Sparacino, M.L., *J. Org. Chem.*, **1983**, *48*, 255-259.

***4-(azidomethyl)-1-phenethylpiperidin-4-ol* (S45)**

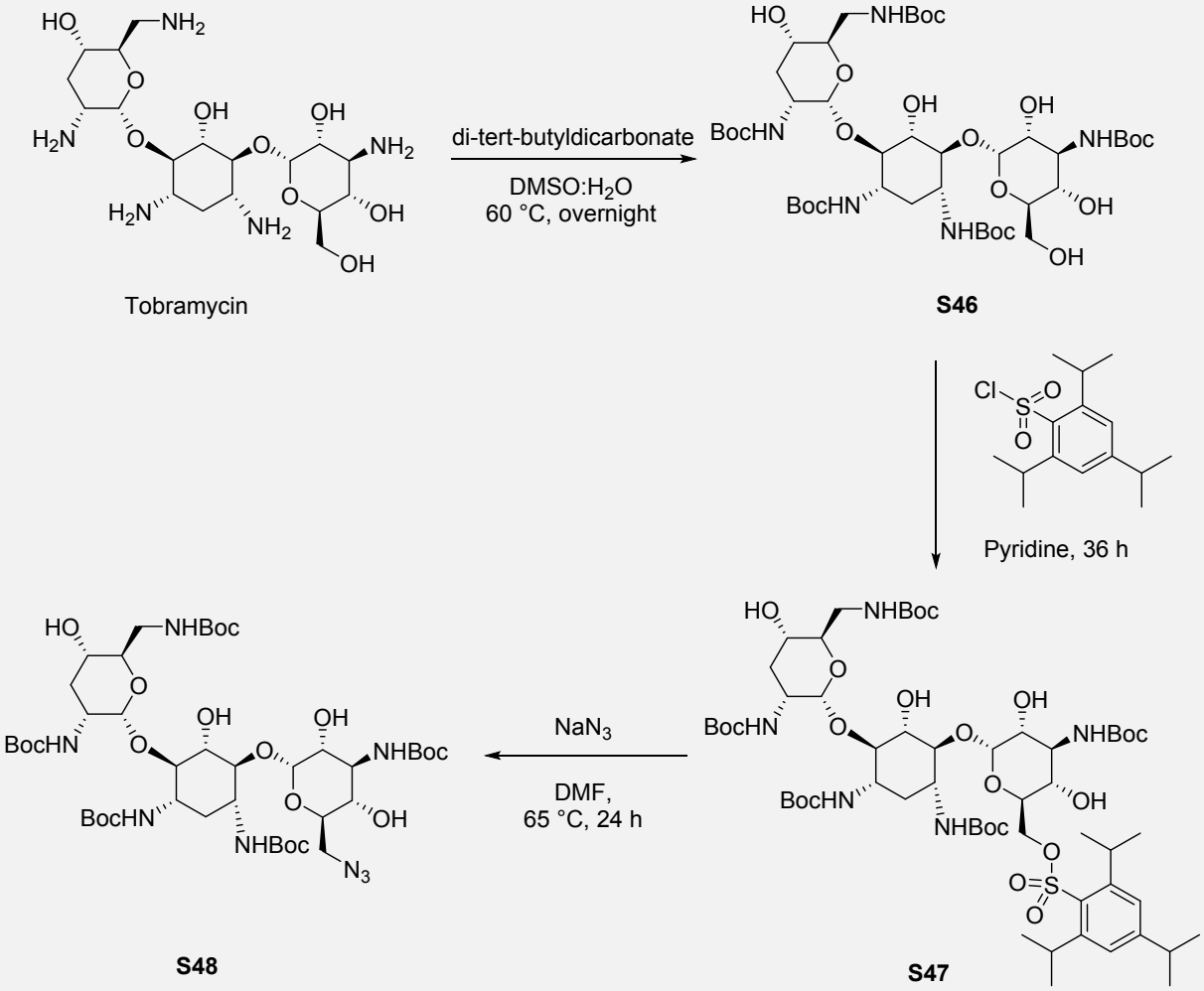


$C_{14}H_{20}N_4O$
MW: 260.34 g.mol^{-1}
Yield: 61%
Brown oil

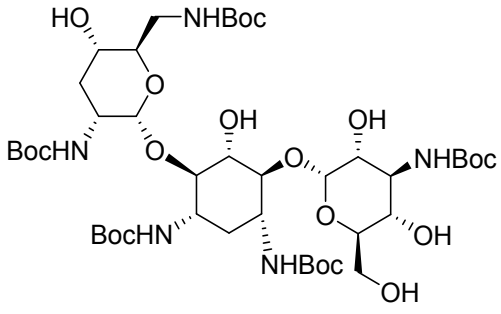
A solution of 6-phenethyl-1-oxa-6-azaspiro[2.5]octane **S44** (80 mg, 0.360 mmol) in MeOH (2 mL) and H_2O (0.4 ml) was treated with sodium azide (119 mg, 1.80 mmol) and ammonium chloride (39.3 mg, 0.74 mmol). The mixture was heated to reflux over 15 hours. The crude product was then extracted from water with CH_2Cl_2 and the organic phase dried over $MgSO_4$. The resulting crude solution was filtered and evaporated to afford 4-(azidomethyl)-1-phenethylpiperidin-4-ol **S45** as sticky brown oil (57.7 mg, 61%), which was used without further purifications.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.22 – 7.18 (m, 3H), 3.32 (s, 2H), 2.88 – 2.80 (m, 4H), 2.69 – 2.65 (m, 2H), 2.54 – 2.42 (m, 2H), 1.78 – 1.65 (m, 5H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 129.1 (2C), 128.9 (2C), 126.6, 70.1, 62.1, 60.9, 49.4 (2C), 35.0 (2C), 34.1.
IR (cm^{-1}) 3336, 2929, 2099, 1603, 1496, 1453, 1288, 1124, 1089, 975, 750, 700.
LCMS (ESI) ***m/z*** $C_{14}H_{20}N_4O$ $[M+H]^+$ 261.5.
HRMS (ESI) ***m/z*** calcd for $C_{14}H_{20}N_4O$ $[M+H]^+$ 261.1710; found: 261.1710.

Synthesis of precursor S48



***di-tert-butyl ((1S,3R,4S,5S,6R)-4-(((2S,3R,4S,5S,6R)-4-((tert-butoxycarbonyl)amino)-3,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-6-(((2R,3R,5S,6R)-3-((tert-butoxycarbonyl)amino)-6-(((tert-butoxycarbonyl)amino)methyl)-5-hydroxytetrahydro-2H-pyran-2-yl)oxy)-5-hydroxycyclohexane-1,3-diyl)dicarbamate* (S46)**



$C_{43}H_{77}N_5O_{19}$
MW: 968.11 g.mol^{-1}
Yield: 81%
White solid

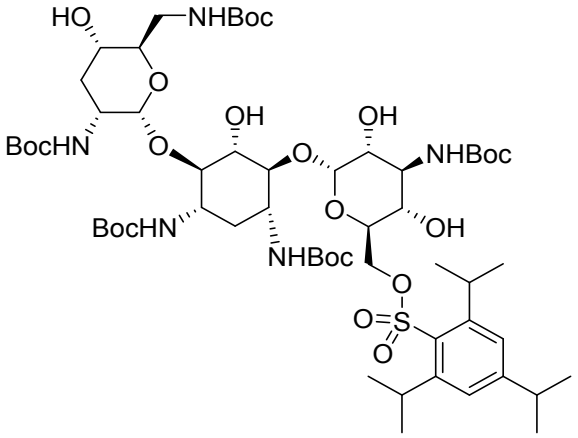
Boc-Tobramycine **S46** was obtained according to a reported procedure.[14] A solution of tobramycin (935 mg, 2.00 mmol) in 28 mL aqueous DMSO (DMSO/water, 6/1) was treated with di-*tert*-butyldicarbonate

[14] K. Michael, H. Wang, Y. Tor, *Bioorg. Med. Chem.* **1999**, *7*, 1361–1371.

(2.62 g, 12.0 mmol). The solution was heated at 60 °C overnight, then cooled to room temperature. A solution of 30% aqueous ammonia (5 mL) was added dropwise to the mixture. The precipitated solid was filtered, washed with H_2O and dried in a dessicator. The desired product was obtained as a white solid (1.58 g, 81%). The spectroscopic data are in agreement with the reported one.[14]

^{1}H NMR (400 MHz, MeOD-*d_4*) δ 5.11 (s, 1H), 5.07 (s, 1H), 3.94 (m, 1H), 3.80 (m, 1H), 3.71 (m, 2H), 3.61 (m, 3H), 3.56 – 3.33 (m, 10H), 2.11 (m, 1H), 2.00 (m, 1H), 1.50 – 1.42 (m, 45H).
LCMS (ESI) ***m/z*** $C_{43}H_{77}N_5O_{19}$ $[M+H]^+$ 969.

((2R,3S,4S,5R,6S)-6-(((1S,2S,3R,4S,6R)-4,6-bis((tert-butoxycarbonyl)amino)-3-(((2R,3R,5S,6R)-3-((tert-butoxycarbonyl)amino)-6-(((tert-butoxycarbonyl)amino)methyl)-5-hydroxytetrahydro-2H-pyran-2-yl)oxy)-2-hydroxycyclohexyl)oxy)-4-((tert-butoxycarbonyl)amino)-3,5-dihydroxytetrahydro-2H-pyran-2-yl)methyl 2,4,6-triisopropylbenzenesulfonate **(S47)**

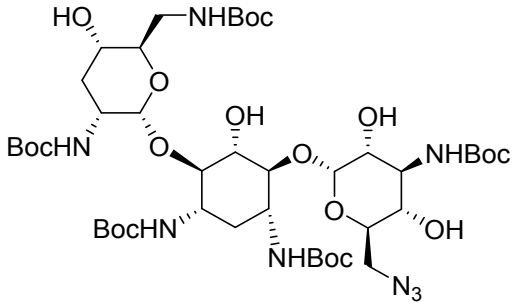


$C_{58}H_{99}N_5O_{21}S$
MW: 1234.50 g.mol^{-1}
Yield: 72%
White solid

A solution of the previously reported Boc-Tobramycine **S46** (267 mg, 0.30 mmol) in pyridine (5 mL) was treated with 2,4,6-triisopropylbenzenesulfonyl chloride (636 mg, 2.1 mmol). The reaction mixture was stirred at room temperature for 36 hours. It was neutralized by adding hydrochloric acid (1.0 N), and partitioned between H_2O and EtOAc. The aqueous layer was isolated and extracted with ethyl acetate. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated under *vacuum*. Flash Chromatography on SiO_2 gel (eluent, CH_2Cl_2/MeOH, from 99:1 to 96:4) afforded the desired product **S47** as a white solid (267 mg, 72%). The spectroscopic data are in agreement with those reported in the literature.[14]

^{1}H NMR (400 MHz, MeOD-*d_4*) δ 7.27 (s, 2H), 5.05 (m, 2H), 4.40 (m, 1H), 4.26 (m, 1H), 4.15 (m, 3H), 3.72 (m, 1H), 3.64 – 3.35 (m, 12H), 2.94 (sept., J = 6.8 Hz, 1H), 2.12 – 1.94 (m, 2H), 1.65 (m, 2H), 1.45 (m, 27H), 1.40 (m, 18H), 1.26 (m, 18H).
LCMS (ESI) ***m/z*** $C_{58}H_{99}N_5O_{21}S$ $[M+H]^+$ 1235.

di-tert-butyl ((1S,3R,4S,5S,6R)-4-(((2R,3R,4S,5S,6R)-6-(azidomethyl)-4-((tert-butoxycarbonyl)amino)-3,5-dihydroxytetrahydro-2H-pyran-2-yl)oxy)-6-(((2R,3R,5S,6R)-3-((tert-butoxycarbonyl)amino)-6-(((tert-butoxycarbonyl)amino)methyl)-5-hydroxytetrahydro-2H-pyran-2-yl)oxy)-5-hydroxycyclohexane-1,3-diyl)dicarbamate **(S48)**



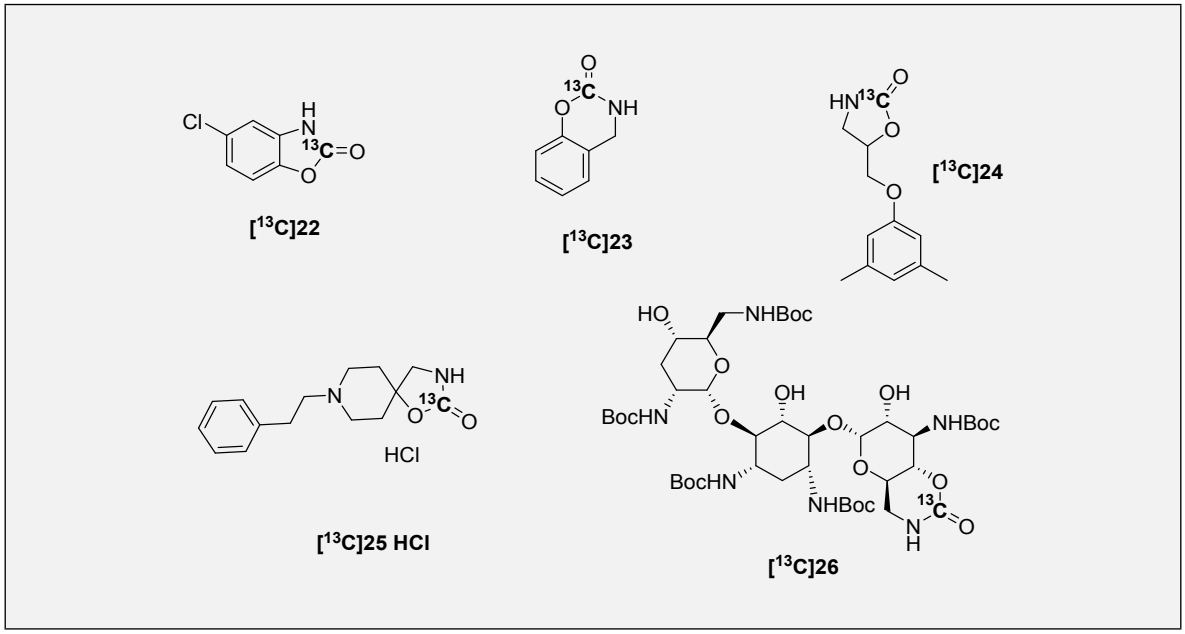
$C_{43}H_{76}N_8O_{18}$
MW: 993.12 g.mol^{-1}
Yield: 84%
White solid

Compound **S48** was obtained according to a reported procedure.[15] To a solution of **S47** (247 mg, 0.20 mmol) in DMF (2.5 mL), sodium azide (104 mg, 1.60 mmol) was added. The yellow solution was heated to 65 °C and stirred over 24 hours. The solvent was removed under reduced pressure and the resulting solid was dissolved in CH_2Cl_2 and washed with water. The organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was isolated by Flash Chromatography on SiO_2 gel (eluent, CH_2Cl_2/MeOH, from 97:3 to 95:5) as a white solid (167 mg, 84%). The spectroscopic data are in agreement with those reported in the literature.[15]

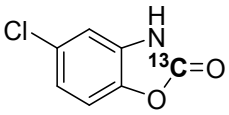
^{1}H NMR (400 MHz, MeOD-*d_4*) δ 5.11 (s, 1H), 5.08 (s, 1H), 4.14 (m, 1H), 3.70 (m, 1H), 3.65 – 3.33 (m, 14H), 2.11 (m, 1H), 2.01 (m, 1H), 1.70 – 1.54 (m, 2H), 1.50 – 1.42 (m, 45H).
LCMS (ESI) ***m/z*** $C_{43}H_{76}N_8O_{18}$ $[M+H]^+$ 994.
HRMS (ESI) ***m/z*** calcd for $C_{43}H_{76}N_8O_{18}$ $[M+H]^+$ 993.5350; found: 993.5347.

[15] R. J. Fair, L. S. McCoy, M. E. Hensler, B. Aguilar, V. Nizet, Y. Tor, *Chem. Med. Chem.,* **2014**, *9*, 2164–2171.

2.14. Synthesis of ^{13}C-labeled drug derivatives



[^{13}C]Chloroxazone ([^{13}C]**22**)

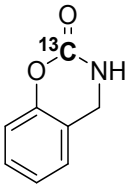


$C_6{}^{13}CH_4ClNO_2$
MW: 170.56 g.mol^{-1}
Yield: 53%
Yellow solid

The ^{13}C-labeled Chloroxazone [^{13}C]**22** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-4-chlorophenol **S37** (16.9 mg, 0.100 mmol,), DIPEA (26 µL, 0.200 mmol) and $^{13}CO_2$ (0.100 mmol) in CD_3CN. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 70:30) affording the ^{13}C-labeled Chloroxazone [^{13}C]**22** as a yellow solid (9.0 mg, 53%).

^{1}H NMR (400 MHz, MeOD-*d_4*) δ 7.19 – 7.16 (m, 1H), 7.12 – 7.07 (m, 2H).
^{13}C NMR (100 MHz, MeOD-*d_4*) δ 156.8, 144.0 (d, J = 1.8 Hz), 132.9 (d, J = 4.8 Hz), 130.3, 123.1, 111.7 (d, J = 3.9 Hz), 111.1 (d, J = 5.0 Hz).
IR (cm^{-1}) 3189, 1726, 1611, 1478, 1258, 960, 922, 844, 802, 704.
Melting point : 184-185 °C.
LCMS (ESI) *m/z* $C_6{}^{13}CH_4{}^{35}ClNO_2$ $[M+H]^+$ 169.1, $C_6{}^{13}CH_4{}^{37}ClNO_2$ $[M+H]^+$ 171.1.

***[^{13}C] Caroxazone precursor* ([^{13}C]23)**

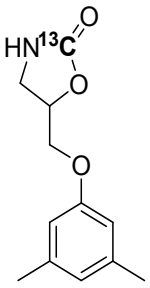


$C_7{}^{13}CH_7NO_2$
MW: 150.14 g.mol^{-1}
Yield: 57%
White solid

The ^{13}C-labeled Caroxazone precursor **[^{13}C]23** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-(azidomethyl)phenol **S40** (14.9 mg, 0.10 mmol) and $^{13}CO_2$ (0.109 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 5:5) affording the ^{13}C-labeled Caroxazone precursor **[^{13}C]23** as a white solid (8.5 mg, 57%).

^{1}H NMR (400 MHz, MeOD-d_4) δ 7.28 (ddt, J = 16.8, 6.4, 0.8 Hz, 1H), 7.20 (d, J = 6.4 Hz, 1H), 7.14 (td, J = 7.5, 1.2 Hz, 1H), 6.99 (dd, J = 8.2, 0.8 Hz, 1H), 4.48 (br. d, J = 3.6 Hz, 2H).
^{13}C NMR (100 MHz, MeOD-d_4) δ 153.8 (^{13}C labeled), 151.1, 129.8, 127.2, 125.7, 118.8 (d, J = 4.6 Hz), 117.1 (d, J = 3.1 Hz), 42.7.
IR (cm^{-1}) 1665, 1618, 1593, 1480, 1459, 1431, 1268, 1235, 1186, 745, 726.
Melting point : 188-189 °C.
LCMS (ESI) *m/z* $C_7{}^{13}CH_7NO_2$ $[M+H]^+$ 151.1.

***[^{13}C]Metaxalone* [^{13}C]24**



$C_{11}{}^{13}CH_{15}NO_3$
MW: 222.25 g.mol^{-1}
Yield: 72%
White solid

The ^{13}C-labeled Metaxalone was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 1-azido-3-(3,5-dimethylphenoxy)propan-2-ol **S42** (22.1 mg, 0.100 mmol) and $^{13}CO_2$ (0.100 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 50:50) affording the ^{13}C-labeled Metaxalone **[^{13}C]24** as a white solid (16.0 mg, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (br. s, 1H), 6.54 (br. s, 2H), 5.63 (br. s, 1H), 4.95 (dtd, J = 11.5, 5.9, 2.9 Hz, 1H), 4.16 – 4.08 (m, 2H), 3.76 (td, J = 8.7, 2.9 Hz, 1H), 3.66 – 3.53 (m, 1H), 2.29 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8 (^{13}C labeled), 158.3, 139.5 (2C), 123.5, 112.5 (2C), 74.4, 68.0, 42.9 (d, J = 3.7 Hz), 21.5 (2C).

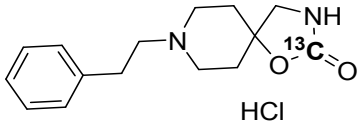
IR (cm^{-1}) 2918, 1698, 1593, 1321, 1295, 1227, 1172, 1157, 1078, 963, 830.

Melting point : 123-124 °C.

LCMS (ESI) ***m/z*** $C_{11}{}^{13}CH_{15}NO_3$ $[M+H]^+$ 223.3.

HRMS (ESI) ***m/z*** calcd for $C_{11}{}^{13}CH_{15}NO_3$ $[M+H]^+$ 223.1158; found: 223.1156.

[^{13}C]Fenspiride hydrochloride ([^{13}C]**25 HCl**)



$C_{14}{}^{13}CH_{21}ClN_2O_2$
MW: 297.79 g.mol^{-1}
Yield: 91%
Beige solid

The ^{13}C-labeled Fenspiride hydrochloride **[**^{13}C]**25 HCl** was prepared according to the general procedure, using $PPhMe_2$ (10.6 µL, 0.075 mmol,), 4-(azidomethyl)-1-phenethylpiperidin-4-ol **S45** (19.5 mg, 0.075 mmol) and $^{13}CO_2$ (0.075 mmol) in DMF-d_7. After solvent evaporation, the crude product was redissolved in EtOAc and treated with 4N HCl in dioxane (37.0 µL) for 30 minutes at room temperature, to give a white precipitate which was filtered, washed with Et_2O and dried, providing ^{13}C-labeled Fenspiride hydrochloride **[**^{13}C]**25 HCl** as a beige solid (20.3 mg, 91%).

Spectroscopic data are in agreement to the reported literature.[16]

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.77 (br. s, 1H), 7.74 (br. s, 1H), 7.55 – 7.47 (m, 1H), 7.35 – 7.29 (m, 3H), 5.61 (br. s, 1H), 3.79 – 3.76 (m, 1H), 3.67 – 3.63 (m, 1H), 3.57 (br. s, 1H), 3.48 (br. s, 1H), 3.27 – 3.20 (m, 4H), 2.75 (br. s, 1H), 2.14 (br. s, 1H); 1.80-1.77 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4 (^{13}C labeled), 135.8, 129.3 (2C), 128.8 (2C), 127.6, 77.4, 58.8, 50.8, 49.1 (2C), 32.9 (2C), 30.4.

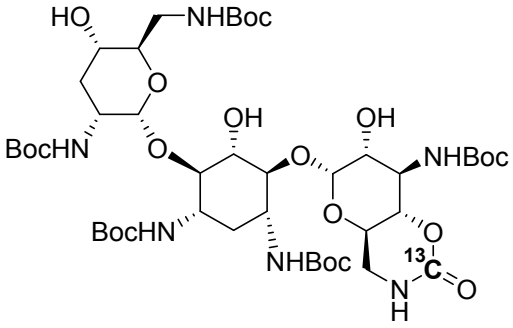
IR (cm^{-1}) 1703, 1437, 1248, 1152, 1117, 1080, 973, 936, 866, 747, 731, 699.

LCMS (ESI) ***m/z*** $C_{14}{}^{13}CH_{20}N_2O_2$ $[M+H]^+$ 262.3.

HRMS (ESI) ***m/z*** calcd for $C_{14}{}^{13}CH_{20}N_2O_2$ $[M+H]^+$ 262.1631; found: 262.1629.

[16] Loh,,Y.Y., Nagao, K., Hoover,, A.J., Hesk, D., Rivera, N.R., Colletti,, S.L., Davies, I.W., David W. C. MacMillan, D.W.C., *Science,* **2017**, *358*, 1182–1187.

***[^{13}C]-5-Boc-Tobramycine carbamate derivative* ([^{13}C]26)**

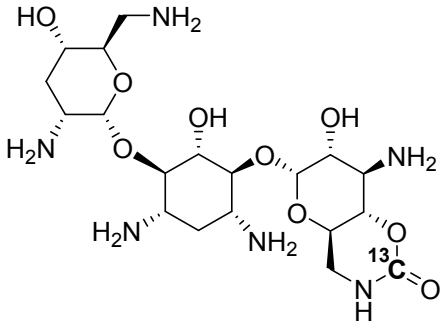


$C_{43}{}^{13}CH_{76}N_6O_{19}$
MW: 994.11 g.mol^{-1}
Yield: 64%
White solid

The 5-Boc-Tobramycine carbamate **[**^{13}C]**26** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol,), compound **S48** as precursor (99.3 mg, 0.100 mmol,) and $^{13}CO_2$ (0.120 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 98:2 to 95:5) affording the ^{13}C- labeled 5-Boc-Tobramycine carbamate **[**^{13}C]**26** as a white solid (63.7 mg, 64%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.37 (s, 1H), 6.99 (s, 1H), 6.76 (br. d, J = 8.6 Hz, 1H), 6.60 (br. s, 1H), 6.54 (br. d, J = 6.8 Hz, 1H), 6.46 (br. s, 1H), 5.13 (s, 1H), 5.09 (s, 1H), 4.92 – 4.84 (m, 2H) 4.34 – 4.23 (m, 2H), 3.76 – 3.60 (m, 2H), 3.55 – 3.35 (m, 8H), 3.30 – 3.15 (m, 4H), 2.93 (t, J = 9.8 Hz, 1H), 1.91 – 1.75 (m, 2H), 1.56 – 1.45 (m, 1H), 1.42 – 1.27 (m, 45H).
IR (cm^{-1}) 1679, 1519, 1392, 1366, 1274, 1247, 1163, 1084, 1043, 1003, 865, 556.
LCMS (ESI) ***m/z*** $C_{43}{}^{13}CH_{76}N_6O_{19}$ $[M+H]^+$ 994.4.
HRMS (ESI) ***m/z*** calcd for $C_{43}{}^{13}CH_{76}N_6O_{19}$ $[M+H]^+$ 994.5271; found: 994.5267.

***[^{13}C] Tobramycine carbamate derivative (*[^{13}C]**S49**)**



$C_{18}{}^{13}CH_{36}N_6O_9$
MW: 493.52 g.mol^{-1}
Yield: 63%
Yellow solid

A solution of **[**^{13}C]**26** (20.1 mg, 0.02 mmol) in a mixture of MeOH and concentrated HCl (4 mL, 6:4) was stirred for 2 hours at room temperature. The solvent was evaporated under reduced pressure and the

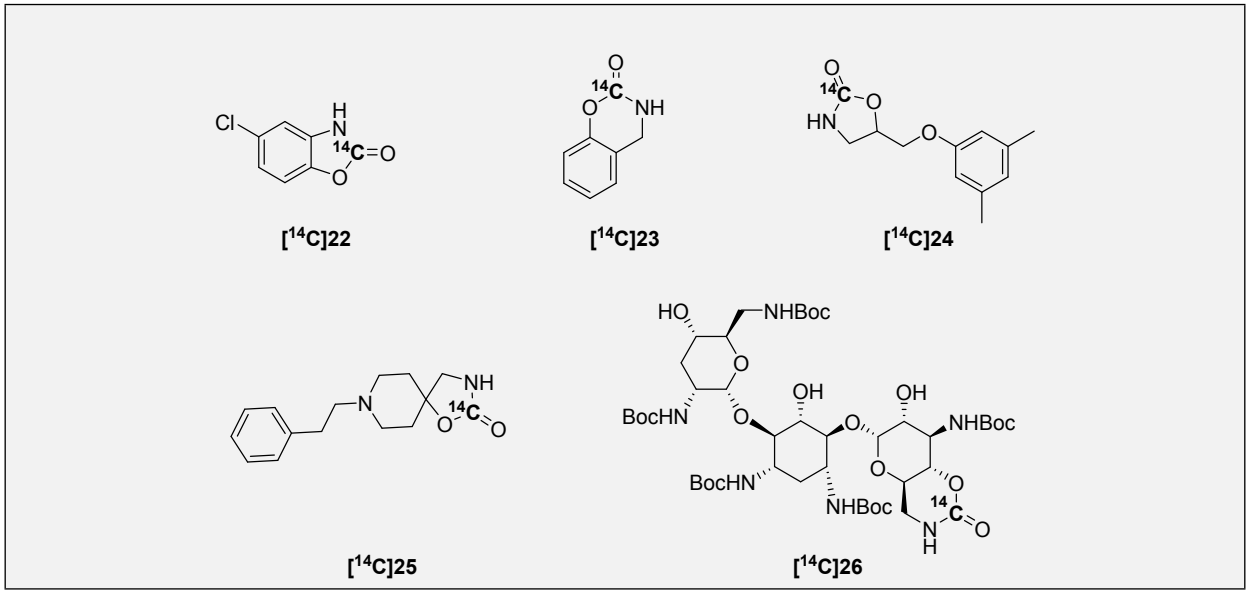
crude product was purified by preparative HPLC to afford the [^{13}C] Tobramycine carbamate **[**^{13}C]**S49** as a yellow solid (6.3 mg, 63%).

^{1}H NMR (400 MHz, D_2O+DMSO-d_6) δ 5.62 (d, J = 3.5 Hz, 1H), 5.00 (d, J = 3.5 Hz, 1H), 4.25 – 4.12 (m, 2H), 3.92 – 3.84 (m, 2H), 3.78 – 3.71 (m, 1H), 3.70 – 3.60 (m, 3H), 3.59 – 3.33 (m, 5H), 3.25 (dd, J = 13.6, 3.5 Hz, 1H), 3.17 – 3.04 (m, 2H), 2.38 (dt, J = 12.2, 4.1 Hz, 1H), 2.11 (dt, J = 12.2, 4.1 Hz, 1H), 1.93 – 1.75 (m, 2H).

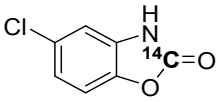
^{13}C NMR (100 MHz, D_2O+DMSO-d_6) δ 155.9 (^{13}C labeled), 102.7, 95.5, 85.3, 78.6, 75.6, 75.2, 71.9, 69.4, 66.0, 63.2 (d, J = 3.4 Hz), 53.4, 51.3, 49.9, 49.3, 43.6, 41.4, 30.8, 29.3.

LCMS (ESI) ***m/z*** $C_{18}{}^{13}CH_{36}N_6O_9$ $[M+H]^+$ 494.5.

2.15. Synthesis of ^{14}C-labeled drug derivatives



[^{14}C] Chloroxazone (*[^{14}C]**22**)



$C_6{}^{14}CH_4ClNO_2$
MW: 171.56 g.mol^{-1}
RCYield: 39%
White solid

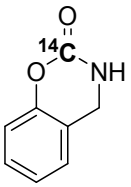
^{14}C-labeled Chloroxazone **[**^{14}C**]22** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 2-azido-4-chlorophenol **S37** (16.9 mg, 0.100 mmol), $^{14}CO_2$ (0.083 mmol, 191.93 MBq) and DIPEA (26 µL, 0.200 mmol) in CD_3CN. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent EtOAc/Heptane 30:70) affording the [^{14}C] Chloroxazone **[**^{14}C**]22** as white solid (70.855 MBq, 39%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}

Molar activity (MS (ESI)): 2.000 GBq mmol^{-1}

TLC (silicagel 60F254, EtOAc/Heptane (50/50)) Rf=0.26. Radiochemical purity: ≥99%.

[^{14}C] Caroxazone precursor ([^{14}C]23)

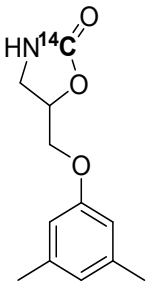


$C_7{}^{14}CH_7NO_2$
MW: 151.14 g.mol^{-1}
RCYield: 30%
White solid

^{14}C-labeled Caroxazone precursor **[^{14}C]23** was prepared according to the general procedure, using $PPhMe_2$ (14.4 µL, 0.100 mmol,), 2-(azidomethyl)phenol **S40** (14.9 mg, 0.100 mmol) and $^{14}CO_2$ (0.085 mmol, 196.56 MBq) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 95:5) affording the ^{14}C-labeled Caroxazone precursor **[^{14}C]23** as white solid (55.463 MBq, 30%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}
Molar activity (MS (ESI)): 2.002 GBq mmol^{-1}
TLC (silicagel 60F254, CH_2Cl_2/MeOH (95/5)) Rf=0.38. Radiochemical purity: ≥99%.

[^{14}C] Metaxalone ([^{14}C]24)

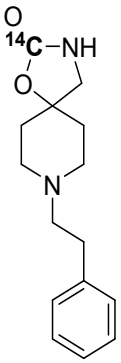


$C_{11}{}^{14}CH_{15}NO_3$
MW: 223.25 g.mol^{-1}
RCYield: 59%
White solid

^{14}C-labeled Metaxalone **[^{14}C]24** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 1-azido-3-(3,5-dimethylphenoxy)propan-2-ol **S42** (22.1 mg, 0.100 mmol) and $^{14}CO_2$ (0.086 mmol, 198.87 MBq) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent EtOAc/Heptane 50:50) affording the ^{14}C-labeled Metaxalone **[^{14}C]22** as white solid (111.037 MBq, 59%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}
Molar activity (MS (ESI)): 2.041 GBq mmol^{-1}
TLC (silicagel 60F254, EtOAc/Heptane (50/50)) Rf=0.26. Radiochemical purity: ≥99%.

[^{14}C] Fenspiride **([^{14}C]25)**

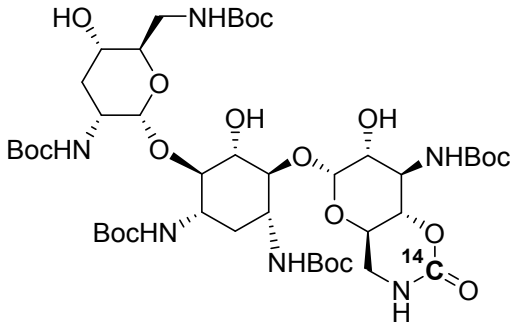


$C_{14}{}^{14}CH_{20}N_2O_2$
MW: 262.33 g.mol^{-1}
RCYield: 45%
Yellow solid

^{14}C-labeled Fenspiride **[^{14}C]25** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), 4-(azidomethyl)-1-phenethylpiperidin-4-ol **S45** (26 mg, 0.100 mmol) and $^{14}CO_2$ (0.092 mmol, 212.75 MBq) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 95:5) affording the ^{14}C-labeled Fenspiride **[^{14}C]25** as yellow solid (90.354 MBq, 45%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}
Molar activity (MS (ESI)): 1.729 GBq mmol^{-1}
TLC (silicagel 60F254, CH_2Cl_2/MeOH (95/5)) Rf=0.23. Radiochemical purity: ≥99%.

[^{14}C]-5-Boc-Tobramycine carbamate derivative **([^{14}C]26)**



$C_{43}{}^{14}CH_{76}N_6O_{19}$
MW: 995.11 g.mol^{-1}
RCYield: 35%
White solid

^{14}C-labeled 5-Boc-Tobramycine carbamate derivative **[^{14}C]26** was prepared according to the general procedure, using $PPhMe_2$ (9.93 µL, 0.069 mmol), di-tert-butyl ((1R,3S,4R,5R,6S)-4-(((2R,3R,4S,5S,6R)-6-(azidomethyl)-4-((tert-butoxycarbonyl)amino)-3,5-dihydroxytetrahydro-2H-pyran-2-yl)oxy)-6-(((2R,3R,5S,6R)-3-((tert-butoxycarbonyl)amino)-6-(((tert-butoxycarbonyl)amino)methyl)-5-hydroxytetrahydro-2H-pyran-2-yl)oxy)-5-hydroxycyclohexane-1,3-diyl)dicarbamate **S48** (69 mg, 0.069 mmol) and $^{14}CO_2$ (0.064 mmol, 148.0 MBq) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 95:5) affording the ^{14}C-labeled 5-Boc-Tobramycine carbamate **[^{14}C]26** as white solid (48.544 MBq, 35%).

$^{14}CO_2$ Molar activity: 2.172 GBq $mmol^{-1}$

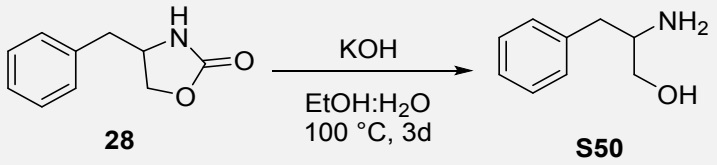
Molar activity (MS (ESI)): 1.955 GBq $mmol^{-1}$

TLC (silicagel 60F254, DCM/MeOH (95/5)) Rf=0.27. Radiochemical purity: ≥99%.

2.16. Disconnection/reconnection strategy to label carbamates

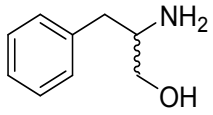
2.16.1 Labeling of carbamate (28)

Cleavage procedure on 4-benzyloxazolidin-2-one (28)



28 **S50**

2-Amino-3-phenyl-1-propanol **(S50)**



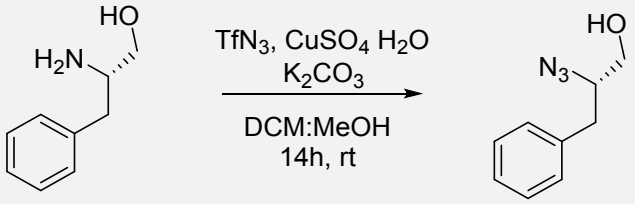
$C_9H_{13}NO$
MW: 151.21 g.mol^{-1}
Yield: 80%
White solid

To a stirred suspension of (S)-4-benzyloxazolidin-2-one (35.4 mg, 0.20 mmol) in EtOH:H_2O (0.8 and 0.2 mL), KOH (34 mg, 0.60 mmol) was added at once. The reaction was stirred over 3 days at 100 °C then the mixture of solvents was partially evaporated. The crude product was extracted twice with CH_2Cl_2 (2 x 10 mL) and the combined organic phases were dried over $MgSO_4$, filtered and evaporated to provide 2-amino-3-phenyl-1-propanol **S50** as white solid (24.7 mg, 80%) without any further purification. Analytical data were consistent with the commercially available reference.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.14 (m, 5H), 3.64 (dd, J = 10.7, 3.8 Hz, 1H), 3.39 (dd, J = 10.7, 7.2 Hz, 1H), 3.16 – 3.07 (m, 1H), 2.79 (dd, J = 13.4, 5.2 Hz, 1H), 2.52 (dd, J = 13.4, 8.7 Hz, 1H), 1.95 (s, 3H).

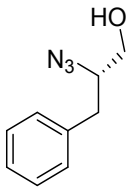
LCMS (ESI) ***m/z*** $C_9H_{13}NO$ $[M+H]^+$ 152.1.

***Synthesis of 2-azido-3-phenylpropan-1-ol* (29)**



S50 **29**

***2-azido-3-phenylpropan-1-ol* (29)**



$C_9H_{11}N_3O$
MW: 177.21 g.mol^{-1}
Yield: 64%
White solid

Preparation of trifluoromethanesulfonyl azide (TfN_3): [17]

ATTENTION: TfN_3 is a potentially explosive reagent; it must be prepared and handled with extreme care, using adequate protection and an additional shield for safety.

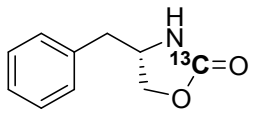
To a solution of sodium azide (130 mg, 2.00 mmol) in CH_2Cl_2:H_2O (1.5 mL, 2:1) at 0 °C was added the trifluoromethanesulfonic anhydride (84 µL, 0.5 mmol). The mixture was then stirred at 0 °C for 2 hours before being quenched by using a saturated solution of $NaHCO_3$. The aqueous phase was extracted twice with 2 mL of CH_2Cl_2 to give a crude solution of trifluoromethanesulfonyl azide (0.5 mmol, 5 mL) which was directly used for the next step to avoid degradation.

To a suspension of commercially available (R)-2-amino-3-phenylpropan-1-ol (37.8 mg, 0.25 mmol) in H_2O was added $CuSO_4 \cdot H_2O$ (2.0 mg, 0.005 mmol). The reaction was the basified to pH 9 using K_2CO_3 before addition of MeOH (0.7 mL) and a freshly prepared solution of trifluoromethanesulfonyl azide (5 mL, 0.08M in CH_2Cl_2). The mixture was stirred for 14 hours before being quenched by addition of water and CH_2Cl_2. The aqueous phase then acidified to pH = 2 using a solution of HCl was extracted by CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 9:1) to afford (R)-2-azido-3-phenylpropan-1-ol **29** as a white solid (28.6 mg, 64%). Analytical data were consistent with the reported literature.[18]

[17] a) Cavender, C. J.; Shiner, V. J., Trifluoromethanesulfonyl azide. Its reaction with alkyl amines to form alkyl azides. *J. Org. Chem.* **1972,** *37*, 3567-3569. b) Yan, R.-B.; Yang, F.; Wu, Y.; Zhang, L.-H.; Ye, X.-S., An efficient and improved procedure for preparation of triflyl azide and application in catalytic diazotransfer reaction. *Tetrahedron Lett.* **2005,** *46*, 8993-8995.
[18] Dey, S., Sudalai, A., *Tetrahedron:Asymmetry,* **2015**, *26*, 67–72; Jensen, J.F., Worm-Leonhard, K., Meldal, M., *Eur. J. Org. Chem*., **2008**, 3785–3797; Fan, Q.-H.; Ni, N.-T.; Li, Q.; Zhang, L.-H.; Ye, X.-S. *Org. Lett.* **2006,** *8*, 1007-1009.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 2H), 7.29 – 7.26 (m, 1H), 7.26 – 7.22 (m, 2H), 3.78 – 3.68 (m, 2H), 3.61 – 3.50 (m, 1H), 2.93 – 2.81 (m, 2H).
IR (cm^{-1}) 3367, 2106, 1496, 1455, 1343, 1260, 1080, 1032, 747, 700, 551.

[^{13}C] 4-benzyloxazolidin-2-one-2 ([^{13}C]28)

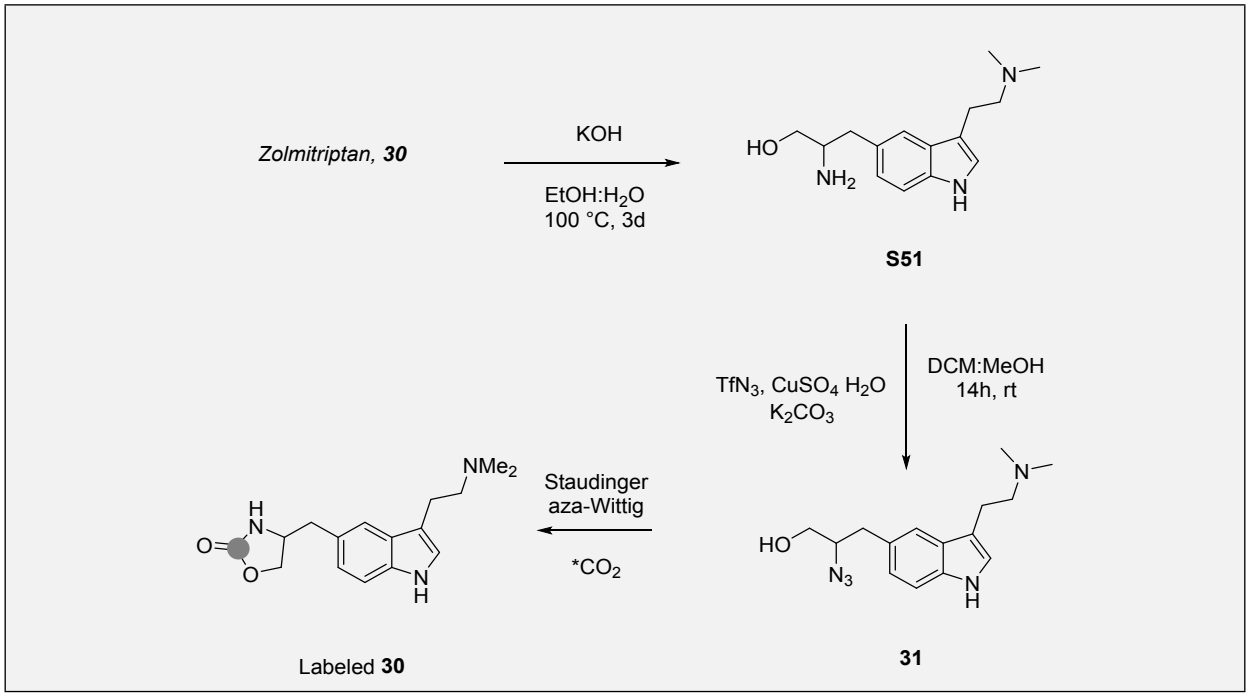


$C_9{}^{13}CH_{11}NO_2$
MW: 178.20 $g.mol^{-1}$
Yield: 65%
White solid

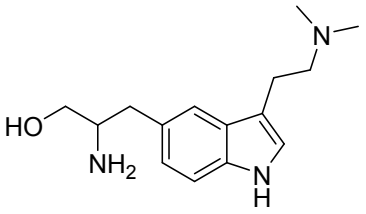
The ^{13}C-labeled 4-benzyloxazolidin-2-one-2 **[^{13}C]28** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.100 mmol), (R)-2-azido-3-phenylpropan-1-ol **29** (17.7 mg, 0.100 mmol) and $^{13}CO_2$ (0.108 mmol) in DMF-d_7. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent CH_2Cl_2/MeOH 99:1) affording the ^{13}C-labeled 4-benzyloxazolidin-2-one-2 **[^{13}C]28** as a white solid (11.6 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 2H), 7.30-7.28 (m, 1H), 7.18 (d, J = 6.8 Hz, 2H), 5.54 (br. s, 1H), 4.46 (td, J = 8.6, 2.6 Hz, 1H), 4.18-4.13 (m 1H), 4.11-4.07 (m, 1H), 2.88 (d, J = 6.8 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (^{13}C labeled), 136.1, 129.2 (2C), 129.1 (2C), 127.4, 69.8, 53.9 (d, J = 4.3 Hz), 41.6.
IR (cm^{-1}) 1694, 1454, 1395, 1223, 1095, 1023, 935, 745, 701.
LCMS (ESI) *m/z* $C_9{}^{13}CH_{11}NO_2$ $[M+H]^+$ 179.1.

2.16.2 Labeling of Zolmitriptan (30)



2-amino-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol (S51)

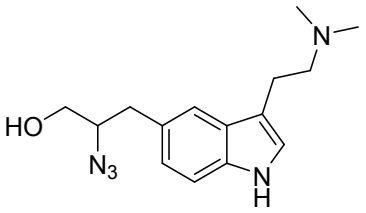


$C_{15}H_{23}N_3O$
MW: 261.37 g.mol^{-1}
Yield: quantitative
Pale yellow solid

To a solution of commercially available Zolmitriptan (57.5 mg, 0.2 mmol, 1 eq) in a mixture EtOH :H_2O (2 mL, 4:1), was added KOH (112 mg, 2 mmol, 10 eq) and the resulting mixture was refluxed for 3 days. The reacting mixture was then cooled down to room temperature, and the solvent was evaporated to give the 2-amino-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol **S51**, which was used in the subsequent step without further purification.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.67 (s, 1H), 7.27 (s, 1H), 7.22 (d, J = 8.2 Hz, 1H), 7.08 (d, J = 1.9 Hz, 1H), 6.89 (dd, J = 8.2, 1.9 Hz, 1H), 3.47 – 3.40 (m, 1H), 3.33 –.3.28 (m, 1H), 2.93 – 2.82 (m, 1H), 2.82 – 2.67 (m, 3H), 2.48 – 2.41 (m, 2H), 2.20 (s, 6H).
LCMS (ESI) ***m/z*** $C_{15}H_{23}N_3O$ $[M+H]^+$ 262.3.

2-azido-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol (31)

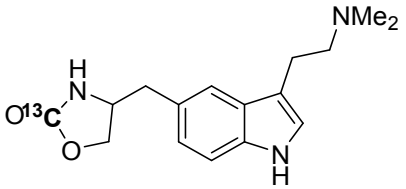


$C_{15}H_{21}N_5O$
MW: 287.37 g.mol^{-1}
Yield: 46% over 2 steps
Orange oil

To a suspension of 2-amino-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol **S51** in water (1 mL) (considered 0.2 mmol from the previous step) was added $CuSO_4 \cdot H_2O$ (1.5 mg, 0.01 mmol). The mixture was then basified to pH 9 using K_2CO_3 before addition of MeOH (0.8 mL) and a freshly prepared solution of trifluoromethanesulfonyl azide (5 mL, 0.08M in CH_2Cl_2), adapting a reported procedure.[19] The mixture was stirred for 14 hours before being quenched by addition of water and CH_2Cl_2. The aqueous phase was then acidified to pH = 6 using a solution of NH_4Cl and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated. The crude mixture was purified by Flash Chromatography on SiO_2 gel (eluent DCM/MeOH 95:5 to 85:15) to afford 2-azido-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol **31** as a orange oil (27.0 mg, 46% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.45 (s, 1H), 7.28 (d, J = 8.3 Hz, 1H), 7.04 (dd, J = 8.3, 1.4 Hz, 1H), 7.00 (d, J = 1.4 Hz, 1H), 3.77 – 3.70 (m, 2H), 3.62 – 3.54 (m, 1H), 3.00 – 2.90 (m, 4H), 2.72 – 2.63 (m, 2H), 2.37 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 127.9, 127.9, 123.4, 122.2, 119.3, 114.0, 111.4, 66.0, 64.4, 60.3, 45.5 (2C), 37.3, 23.7.
IR (cm^{-1}) 3251, 2922, 2857, 2825, 2781, 2102, 1464, 1348, 1259, 1097, 1039, 796.
LCMS (ESI) ***m/z*** $C_{15}H_{21}N_5O$ $[M+H]^+$ 288.3.

[^{13}C] Zolmitriptan (*[^{13}C]**30**)



$C_{15}{}^{13}CH_{21}N_3O_2$
MW: 288.36 g.mol^{-1}
Yield: 16%
White solid

The ^{13}C-labeled Zolmitriptan **[**^{13}C]**30** was prepared according to the general procedure, using $PPhMe_2$ (14.2 µL, 0.097 mmol), 2-azido-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol (27.9 mg, 0.097 mmol,) and $^{13}CO_2$ (0.099 mmol) in DMF-d_7 and the reaction was heated at 70 °C for 15 minutes

[19] Jensen, J.F., Worm-Leonhard, K., Meldal, M., *Eur. J. Org. Chem*., **2008**, 3785–3797.

before the unreacted $^{13}CO_2$ was released. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent DCM/MeOH 95:5 to 80:20) affording the ^{13}C-labeled Zolmitriptan **[**^{13}C**]30** as white solid (4.7 mg, 16%).

^{1}H NMR (400 MHz, MeOD-*d*$_4$) δ 7.42 (d, *J* = 0.9 Hz, 1H), 7.30 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.07 (s, 1H), 6.99 (dd, *J* = 8.3, 1.6 Hz, 1H), 4.41 – 4.32 (m, 1H), 4.23 – 4.16 (m, 2H), 3.01 – 2.88 (m, 4H), 2.79 – 2.74 (m, 2H), 2.43 (s, 6H).

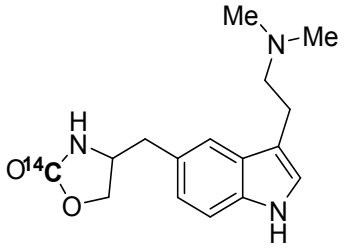
^{13}C NMR (100 MHz, MeOD-*d*$_4$) δ 162.3 (^{13}C labeled), 137.4, 128.9, 127.4, 124.0, 123.9, 119.8, 112.7, 112.5, 70.7, 60.9, 55.4 (d, *J* = 4.1 Hz), 45.0 (2C), 42.1, 23.7.

IR (cm^{-1}) 3251, 2921, 2851, 1698, 1463, 1394, 1232, 1098, 1023, 930, 804, 728.

LCMS (ESI) ***m/z*** $C_{15}{}^{13}CH_{21}N_3O_2$ $[M+H]^+$ 289.2.

HRMS (ESI) ***m/z*** calcd for $C_{15}{}^{13}CH_{21}N_3O_2$ $[M+H]^+$ 289.1740; found: 289.1738.

[^{14}C] Zolmitriptan (*[^{14}C]**30**)



$C_{15}{}^{14}CH_{21}N_3O_2$
MW: 289.16 g.mol^{-1}
RCY: 8%
White solid

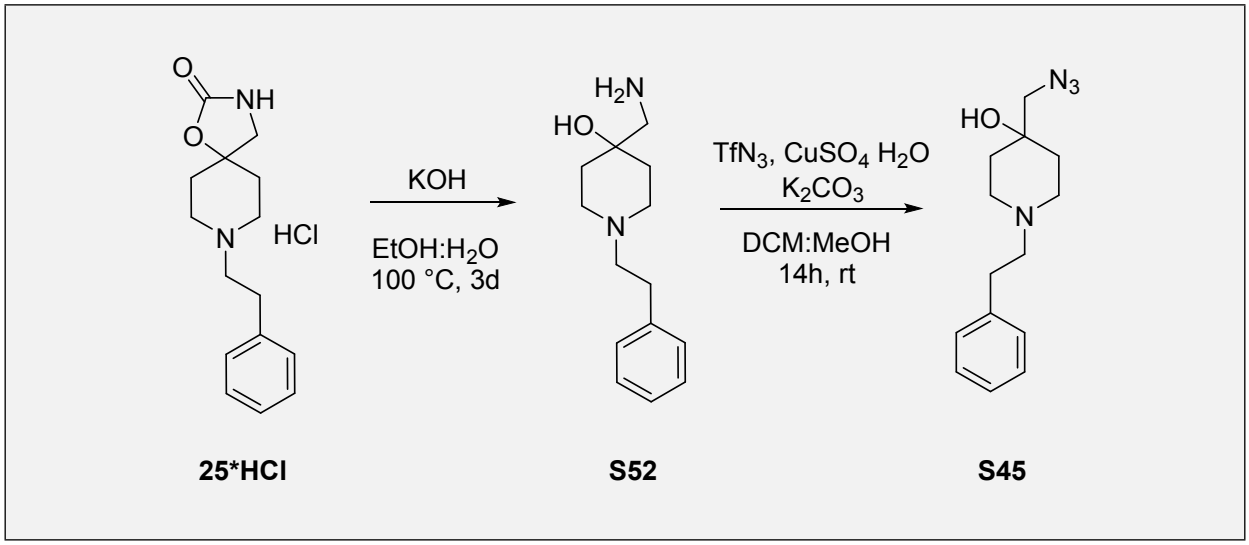
^{14}C-labeled Zolmitriptan **[**^{14}C**]30** was prepared according to the general procedure, using $PPhMe_2$ (13.5 µL, 0.094 mmol), 2-azido-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol **(31)** (27.0 mg, 0.094 mmol) and $^{14}CO_2$ (0.079 mmol) in DMF-*d*$_7$. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent DCM/MeOH/Et_3N 95:5:1% to 8:2:1%) affording the ^{14}C-labeled Zolmitriptan **[**^{14}C**]30** as white solid (14.393 MBq, 8%).

$^{14}CO_2$ Molar activity: 2.172 GBq mmol^{-1}

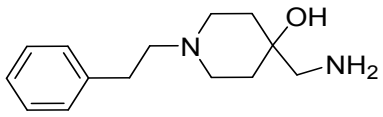
Molar activity (MS (ESI)): 2.035 GBq mmol^{-1}

TLC (silicagel 60F254, DCM/MeOH/Et_3N (8:2:1%)) Rf=0.41. Radiochemical purity: ≥99 %.

2.16.3 Labeling of Fenspiride (25)



4-(aminomethyl)-1-phenethylpiperidin-4-ol **(S52)**

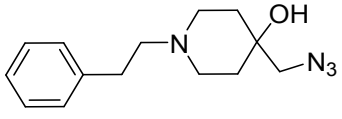


$C_{14}H_{22}N_2O$
MW: 234.34 g.mol^{-1}
Yield: not calculated

To a solution of Fenspiride hydrochloride **25 HCl** (118.7 mg, 0.4 mmol) in a mixture EtOH:H_2O (4 mL, 3:1), was added KOH (224 mg, 4.00 mmol). The resulting mixture was refluxed for 3 days and then cooled down to room temperature. The solvent was further evaporated to give the 4-(aminomethyl)-1-phenethylpiperidin-4-ol **S52,** which was used in the subsequent step without further purification.

^{1}H NMR (400 MHz, MeOD-*d_4*) δ 7.37 – 7.31 (m, 4H), 7.29 – 7.23 (m, 1H), 3.60 – 3.50 (m, 2H), 3.41 – 3.33 (m, 4H) 3.17 – 3.10 (m, 2H), 3.05 (s, 2H), 2.10 – 1.93 (m, 4H).
LCMS (ESI) ***m/z*** $C_{14}H_{22}N_2O$ $[M+H]^+$ 235.2.

4-(azidomethyl)-1-phenethylpiperidin-4-ol **(S45)**



$C_{14}H_{20}N_4O$
MW: 260.34 g.mol^{-1}
Yield: 82% over 2 steps
Brown oil

To a suspension of 4-(aminomethyl)-1-phenethylpiperidin-4-ol **S52** in water (considered 0.4 mmol from the previous step, 2 mL) was added $CuSO_4 \cdot H_2O$ (3.0 mg, 0.02 mmol). The mixture was then basified to pH 9 using K_2CO_3 before addition of MeOH (1.2 mL) and a freshly prepared solution of

trifluoromethanesulfonyl azide (10 mL, 0.08M in CH_2Cl_2), adapting a reported procedure.[20] The mixture was stirred for 14 hours before being quenched by addition of water and CH_2Cl_2. The aqueous phase was then acidified to pH = 6 using a solution of NH_4Cl and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated to give the 4-(azidomethyl)-1-phenethylpiperidin-4-ol **S45** as a brown oil (86 mg, 82% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.22 – 7.18 (m, 3H), 3.32 (s, 2H), 2.88 – 2.80 (m, 4H), 2.69 – 2.65 (m, 2H), 2.54 – 2.42 (m, 2H), 1.78 – 1.65 (m, 5H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 129.1 (2C), 128.9 (2C), 126.6, 70.1, 62.1, 60.9, 49.4 (2C), 35.0 (2C), 34.1.
IR (cm^{-1}) 3336, 2929, 2099, 1603, 1496, 1453, 1288, 1124, 1089, 975, 750, 700.
LCMS (ESI) ***m/z*** $C_{14}H_{20}N_4O$ $[M+H]^+$ 261.5.
HRMS (ESI) ***m/z*** calcd for $C_{14}H_{20}N_4O$ $[M+H]^+$ 261.1710; found: 261.1710.

For the conversion of **S45** into the corresponding ^{13}C, ^{14}C and ^{11}C-labeled fenspiride **25** see the corresponding sections in this document.

[20] Jensen, J.F., Worm-Leonhard, K., Meldal, M., *Eur. J. Org. Chem*., **2008**, 3785–3797.

2.3. Synthesis of ^{11}C-labeled aliphatic cyclic carbamates

2.3.1 General procedure for ^{11}C radiolabeling

Automated radiosynthesis with carbon-11 was performed using a MeI_{plus} research synthesizer (Synthra GmbH, Germany) with modifications to undergo direct bubbling of $[^{11}C]CO_2$ into the reaction vessel (Figure S2, see supporting information). No carrier-added $[^{11}C]CO_2$ (3.5-18 GBq) was produced via the $^{14}N(p, \alpha)^{11}C$ nuclear reaction by irradiation of a $[^{14}N]N_2$ target containing 0.15-0.5% of O_2 on a cyclone 18/9 cyclotron (IBA, Belgium) and trapped at -180 °C. $[^{11}C]CO_2$ was released at 50 °C under a stream of helium (8 mL/min) to bubble for 10 s into the reaction vessel containing a solution of the precursor (1 mg) and dimethylphenyl phosphine (15 µL) in anhydrous DMF (300 µL) at -50 °C. The mixture was heated at 70 °C for 5 min and hydrolyzed with glacial acetic acid (100 µL) followed by a mixture of CH_3CN/H_2O (1 mL, 50/50 v/v).

Quality control is performed by HPLC using a 717_{plus} Autosampler system equipped with a 1525 binary pump and a 2996 photodiode array detector (Waters, USA) and a Flowstar LB 513 (Berthold, France) gamma detector. The system was monitored with the Empower 3 software (Waters, USA). HPLC was realized on a reverse phase analytical Symmetry C18 50 x 3.9 mm, 5 µm column (Waters, USA) using a mixture of H_2O/CH_3CN/PicB7® (proportions depending on the compound, 2 mL/min) as eluent. UV detection was performed at the maximum absorbance of the compound. Identification of the peak was assessed by comparing the retention time of carbon-11 labeled compounds with the retention time of their non-radioactive reference (t_R^{ref}). For acceptance, the retention time must be within the t_R^{ref} ± 10% range. Radiochemical purity (RCP) was calculated as the ratio of the area under the curve (AUC) of the peak over the sum of the AUCs of all other peaks on gamma chromatograms. Radiochemical purity is the mean value of three consecutive runs. The radiochemical yield (RCY) of the labeling reaction was calculated as the ratio of the decay-corrected activity at the end of the synthesis (A_{EOS}), measured in an ionization chamber (Capintec®, Berthold, France) over the starting activity of $[^{11}C]CO_2$ (A_{CO2}) measured by the calibrated detector of the synthesizer. This ratio was corrected for the radiochemical purity following the equation: RCY = (A_{EOS} / A_{CO2}) x RCP. Molar activity was calculated as the ratio of the activity of the collected peak of the radioactive product measured in an ionization chamber (Capintec®, Berthold, France) over the molar quantity of the compound determined using calibration curves. Molar activity was calculated as the mean value of three consecutive runs.

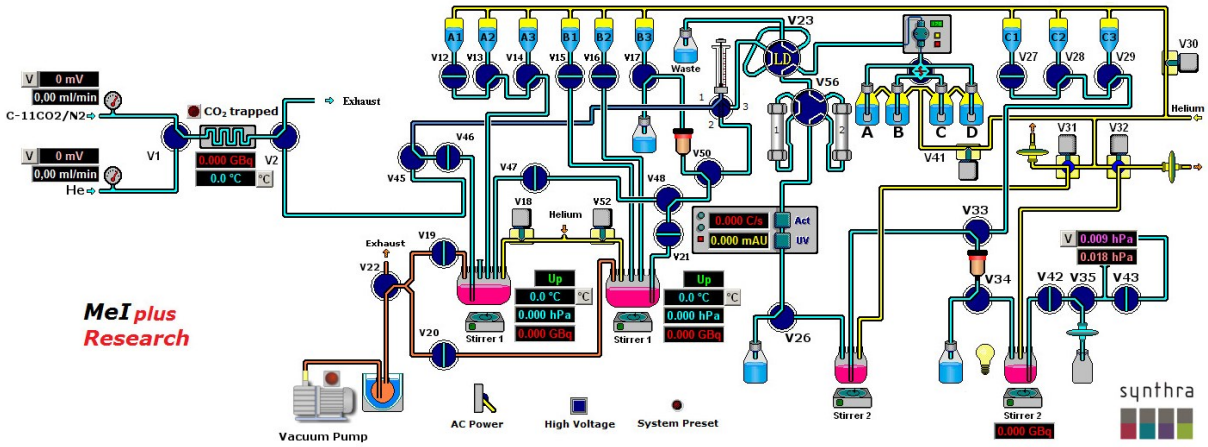
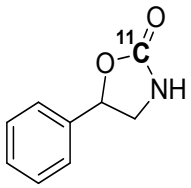


Figure S2. Modified MeI_{plus} Research module for direct CO_2 labeling.

2.3.2 Synthesis of ^{11}C-labeled 5-membered ring carbamate derivatives

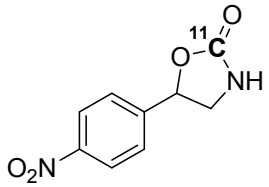
[^{11}C] 5-phenyloxazolidin-2-one **([^{11}C]2)**



$C_8{}^{11}CH_9NO_2$
RCYield: 76%

Compound **[^{11}C]2** (3.1 GBq) was synthesized from compound **1(S8)** according to the general procedure within 15 minutes in 76% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 55/45/0.2 v/v/v, 2 mL/min, λ = 261 nm).

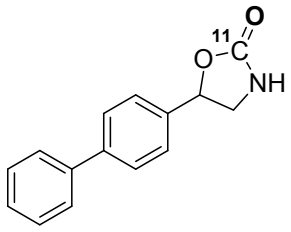
[^{11}C] 5-(4-nitrophenyl)oxazolidin-2-one **([^{11}C]3)**



$C_8{}^{11}CH_8N_2O_2$
RCYield: 80%

Compound **[^{11}C]3** (3.1 GBq) was synthesized from compound **S9** according to the general procedure within 15 minutes in 80% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 80/20/0.2 v/v/v, 2 mL/min, λ = 269 nm).

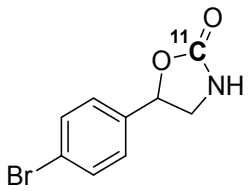
[^{11}C] 5-([1,1'-biphenyl]-4-yl)oxazolidin-2-one **([^{11}C]4)**



$C_{14}{}^{11}CH_{13}NO_2$
RCYield: 77%

Compound **[^{11}C]4** (2.8 GBq) was synthesized from compound **S10** according to the general procedure within 15 minutes in 77% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 65/35/0.2 v/v/v, 2 mL/min, λ = 253nm).

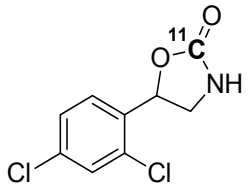
***[^{11}C] 5-(4-bromophenyl)oxazolidin-2-one* ([^{11}C]5)**



$C_8{}^{11}C\ H_8BrNO_2$
RCYield: 74%

Compound **[^{11}C]5** (2.8 GBq) was synthesized from compound **S11** according to the general procedure within 15 minutes in 74% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 70/30/0.2 v/v/v, 2 mL/min, λ = 223 nm).

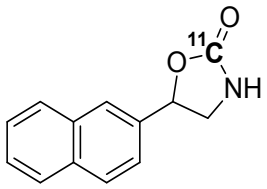
***[^{11}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one* ([^{11}C]6)**



$C_8{}^{11}CH_7Cl_2NO_2$
RCYield: 79%

Compound **[^{11}C]6** (3.3 GBq) was synthesized from compound **S12** according to the general procedure within 15 minutes in 79% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 55/45/0.2 v/v/v, 2 mL/min, λ = 242nm).

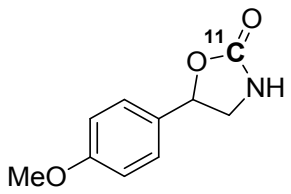
***[^{11}C] 5-(naphthalen-2-yl)oxazolidin-2-one* ([^{11}C]7)**



$C_{12}{}^{11}CH_{11}NO_2$
RCYield: 68%

Compound **[^{11}C]7** (2.5 GBq) was synthesized from compound **S13** according to the general procedure within 15 minutes in 68% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 70/30/0.2 v/v/v, 2 mL/min, λ = 222 nm).

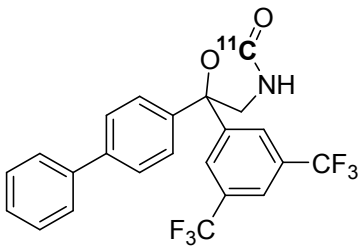
***[^{11}C] 5-(4-methoxyphenyl)oxazolidin-2-one* ([^{11}C]8)**



$C_9{}^{11}CH_{11}NO_3$
RCYield: 83%

Compound **[^{11}C]8** (3.0 GBq) was synthesized from compound **S14** according to the general procedure within 15 minutes in 83% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 82/18/0.2 v/v/v, 2 mL/min, λ = 227 nm).

[^{11}C] 5-([1,1'-biphenyl]-4-yl)-5-(3,5-bis(trifluoromethyl)phenyl)oxazolidin-2-one (*[^{11}C]*9)

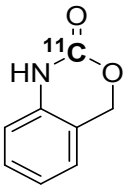


$C_{22}{}^{11}CH_{15}F_6NO_2$
RCYield: 82%

Compound **[^{11}C] 9** (3.4 GBq) was synthesized from compound **S15** according to the general procedure within 15 minutes in 82% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 35/65/0.2 v/v/v, 2 mL/min, λ = 242 nm).

2.3.1 Synthesis of ^{11}C-labeled 6-membered ring carbamate derivatives

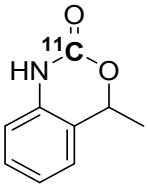
[^{11}C] 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{11}C]10)**



$C_7{}^{11}CH_7NO_2$
RCYield: 57%

Compound **[^{11}C]10** (2.1 GBq) was synthesized from compound S**17** according to the general procedure within 15 minutes in 57% RCC and 97% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 90/10/0.2 v/v/v, 2 mL/min, λ = 240 nm).

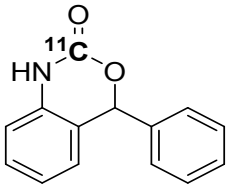
[^{11}C] 4-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{11}C]11)**



$C_8{}^{11}CH_9NO_2$
RCYield: 62%

Compound **[^{11}C]11** (2.5 GBq) was synthesized from compound **S22** according to the general procedure within 15 minutes in 62% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 90/10/0.2 v/v/v, 2 mL/min, λ = 275 nm).

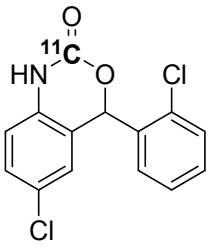
[^{11}C] 4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{11}C]12)**



$C_{13}{}^{11}CH_{11}NO_2$
RCYield: 50%

Compound **[^{11}C]12** (1.9 GBq) was synthesized from compound **S23** according to the general procedure within 15 minutes in 50% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 85/15/0.2 v/v/v, 2 mL/min, λ = 242 nm).

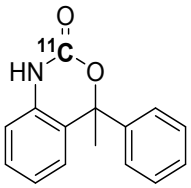
***[^{11}C] 6-chloro-4-phenyl-1H-benzo[d][1,3]oxazin-2(4H)-one* ([^{11}C]14)**



$C_{13}{}^{11}CH_{10}Cl_2NO_2$
RCYield: 24%

Compound **[^{11}C]14** (0.9 GBq) was synthesized from compound **S24** according to the general procedure within 15 minutes in 24% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 65/35/0.2 v/v/v, 2 mL/min, λ = 222 nm).

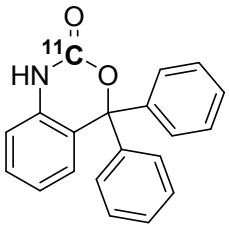
***[^{11}C] 4-methyl-4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{11}C]15)**



$C_{14}{}^{11}CH_{13}NO_2$
RCYield: 18%

Compound **[^{11}C]15** (0.5 GBq) was synthesized from compound **S28** according to the general procedure within 15 minutes in 18% RCC and 75% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 75/35/0.2 v/v/v, 2 mL/min, λ = 240 nm).

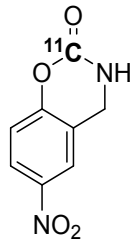
[^{11}C] 4,4-diphenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{11}C]16*)



$C_{19}{}^{11}CH_{15}NO_2$
RCYield: 12%

Compound **[^{11}C]16** (0.3 GBq) was synthesized from compound **S29** according to the general procedure within 15 minutes in 12% RCC and 75% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 45/55/0.2 v/v/v, 2 mL/min, λ = 242 nm).

***[^{11}C] 6-nitro-3,4-dihydro-2H-benzo[e][1,3]oxazin-2-one* ([^{11}C]17)**

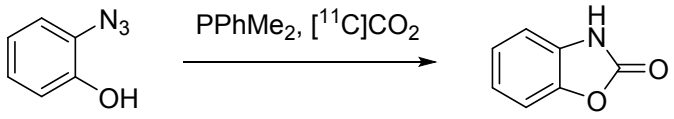


$C_7{}^{11}CH_6N_2O_4$
RCYield: 72%

Compound **[^{11}C]17** (2.8 GBq) was synthesized from compound **S30** according to the general procedure within 15 minutes in 72% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 85/15/0.2 v/v/v, 2 mL/min, λ = 287 nm).

2.3.4 Synthesis of ^{11}C-labeled aromatic cyclic carbamates

For the ^{11}C-radiolabeling of carbamate 18, radiochemical conditions were optimized according to Table S4.

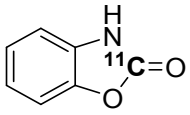


[^{11}C]18

Entry	Temp. (° C)	Time	Solvant	Additif	RCC	RCP
1	25	5 min	DMF	None	32%	100%
2	70	5 min	DMF	None	59%	100%
3	110	5 min	DMF	None	55%	100%
4	25	5 min	DMF	DIPEA (1.5 eq)	37%	100%
5	70	5 min	DMF	DIPEA (1.5 eq)	57%	100%
6	25	5 min	DMF	DBU (2 eq)	7%	n.d.
7	25	5 min	DMF	NaOH (2 eq)	10%	n.d.

Table S4 : Procedure : On Synthra. Irrad 5 min. Quench 200 µL AcOH then 1mL CH_3CN/H_2O/TFA (50/50/0.1).

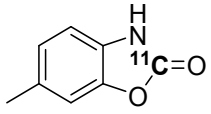
***[^{11}C] benzo[d]oxazol-2(3H)-one* ([^{11}C]18)**



$C_6{}^{11}CH_5NO_2$
RCYield: 59%

Compound [^{11}C]**18** (2.1 GBq) was synthesized from compound **S31** according to the general procedure within 15 minutes in 59% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 90/10/0.2 v/v/v, 2 mL/min, λ = 270 nm).

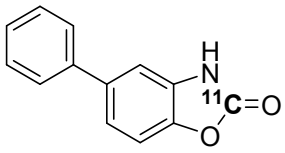
***[^{11}C] 5-methylbenzo[d]oxazol-2(3H)-one* ([^{11}C]19)**



$C_7{}^{11}CH_7NO_2$
RCYield: 48%

Compound [^{11}C]**19** (1.8 GBq) was synthesized from compound **S32** according to the general procedure within 15 minutes in 48% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 80/20/0.2 v/v/v, 2 mL/min, λ = 270 nm).

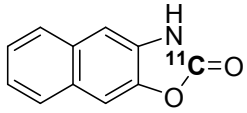
***[^{11}C] 5-phenylbenzo[d]oxazol-2(3H)-one* ([^{11}C]20)**



$C_{12}{}^{11}CH_9NO_2$
RCYield: 53%

Compound [^{11}C]**20** (2.0 GBq) was synthesized from compound **S33** according to the general procedure within 15 minutes in 53% RCC and 96% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 70/30/0.2 v/v/v, 2 mL/min, λ = 270 nm).

***[^{11}C] naphtho[2,3-d]oxazol-2(3H)-one* ([^{11}C]21)**

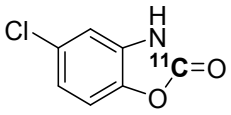


$C_{10}{}^{11}CH_7NO_2$
RCYield: 19%

Compound [^{11}C]**21** (0.7 GBq) was synthesized from compound **S34** according to the general procedure within 15 minutes in 19% RCC and 100% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 75/25/0.2 v/v/v, 2 mL/min, λ = 236 nm).

2.3.5 Synthesis of ^{11}C-labeled drug derivatives

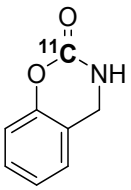
***[^{11}C]Chloroxazone* ([^{11}C]22)**



$C_6{}^{11}CH_4ClNO_2$
RCYield: 37 ± 2%

The crude product was synthesized from compound **S37** following the general procedure. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of H_2O/CH_3CN/TFA (60/40/0.1 v/v/v, 5 mL/min) as eluent with gamma and UV (λ = 280 nm) detection. The collected peak (t_R = 10.3-11.5 min) of [^{11}C]chlorzoxazone [^{11}C]**22** was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]chlorzoxazone [^{11}C]**22** (2.8 ± 0.3 GBq) was obtained within 30 min from end of beam in 37 ± 2% RCY and 85 ± 4 GBq/µmol molar activity (n = 2). Quality control was performed following the general procedure (H_2O/CH_3CN/PicB7® 75/25/0.2 v/v/v, 2 mL/min, λ = 280 nm).

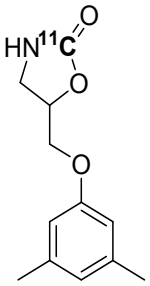
***[^{11}C]*Caroxazone precursor ([^{11}C]23)**



$C_7{}^{11}CH_7NO_2$
RCYield: 25 ± 5%

The crude product was synthesized from compound **40** following the general procedure. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of H_2O/CH_3CN/TFA (75/25/0.1 v/v/v, 5 mL/min) as eluent with gamma and UV (λ = 240 nm) detection. The collected peak (t_R = 8.5-12.5 min) of the [^{11}C]caroxazone precursor **[**^{11}C]**23** was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]caroxazone precursor **[**^{11}C]**23** (0.9 ± 0.1 GBq) was obtained within 30 min from end of beam in 25 ± 5% RCY and 75 ± 10 GBq/µmol molar activity (n = 2). Quality control was performed following the general procedure (H_2O/CH_3CN/PicB7® 90/10/0.2 v/v/v, 2 mL/min, λ = 240 nm).

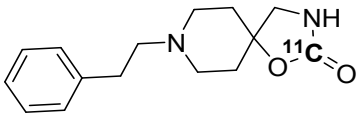
***[^{11}C]Metaxalone* ([^{11}C]24)**



$C_{11}{}^{11}CH_{15}NO_3$
RCYield: 44 ± 3%

The crude product was synthesized from compound **S42** following the general procedure. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of H_2O/CH_3CN/TFA (50/50/0.1 v/v/v, 5 mL/min) as eluent with gamma and UV (λ = 279 nm) detection. The collected peak (t_R = 10.8-11.8 min) of [^{11}C]Metaxalone **[**^{11}C]**24** was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]Metaxalone **[**^{11}C]**24** (2.1 ± 0.4 GBq) was obtained within 35 min from end of beam in 44 ± 3% RCY and 78 ± 3 GBq/µmol molar activity (n = 2). Quality control was performed following the general procedure (H_2O/CH_3CN/PicB7® 70/30/0.2 v/v/v, 2 mL/min, λ = 279 nm).

***[^{11}C]Fenspiride* ([^{11}C]25)**

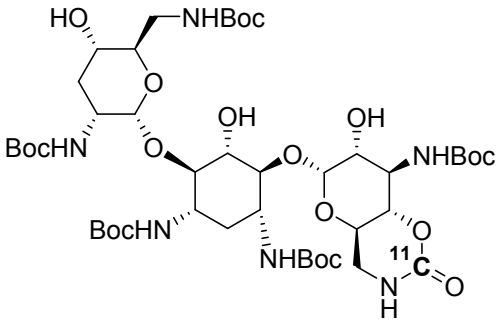


$C_{14}{}^{11}CH_{20}N_2O_2$
RCYield: 23 ± 3%

The crude product was synthesized from compound **S45** following the general procedure. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of NaH_2PO_{4aq} (2.76 g/L)/CH_3OH (60/40 v/v, 5 mL/min) as eluent with gamma and UV (λ = 210 nm) detection. The collected peak (t_R = 8.0-10.0 min) of [^{11}C]Fenspiride **[**^{11}C]**25** was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]Fenspiride **[**^{11}C]**25** (0.8 ± 0.2 GBq) was obtained within 30 min from end of beam in 23 ± 3% RCY and 81 ± 8 GBq/µmol molar activity (n = 3). Quality control was performed following the general procedure using a Zorbax® SB-C18 4.6 x 250

mm, 3.5 µm column (Agilent, USA) with aqueous NaH_2PO_4 (2.76 g/L, pH 3)/CH_3OH 50/50 v/v as eluent at 1 mL/min and UV detection at λ = 210 nm.

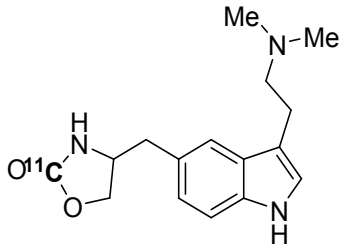
[^{11}C]-5-Boc-Tobramycine carbamate derivative **([^{11}C]26)**



$C_{43}{}^{11}CH_{76}N_6O_{19}$
RCYield: 68 ± 2%

The crude product was synthesized from compound **S48** following the general procedure. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of H_2O/CH_3CN/TFA (40/60/0.1 v/v/v, 5 mL/min) as eluent with gamma detection. The collected peak (t_R = 32.7-33.3 min) of the [^{11}C]tobramycine derivative **[**^{11}C]**26** was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]tobramycine derivative **[**^{11}C]**26** (1.1 ± 0.2 GBq) was obtained within 55 min from end of beam in 68 ± 2% RCY (n = 2). Giving the absence of UV absorption of this molecule, the quality control was performed using ultra performance liquid chromatography-mass spectroscopy. Chromatography was realized on a Ultimate 3000 (Thermo Scientific, USA) device equipped with an Acquity BEH 2.1 x 50 mm, 1.7 µm column (Waters, USA). A gradient of water with 0.1% of formic acid and acetonitrile with 0.1% of formic acid (3% of CH_3CN/HCHO for 2 minutes, then rising to 100% during 7 minutes then decreasing to 3% during 1 minute then keeping 3% for 2 minutes) at a flowrate of 0.3 mL/min was applied. Mass spectroscopy was performed with a Linear Trap Quadripole Orbitrap Velos (Thermo Scientific, USA) equipped with an electron spray ionization (ESI) chamber. Spectrum was recorded between 100 and 1000 m/z.

[^{11}C]Zolmitriptan ([^{11}C]30)



$C_{15}{}^{11}CH_{21}N_3O_2$
RCYield: 25 ± 2%

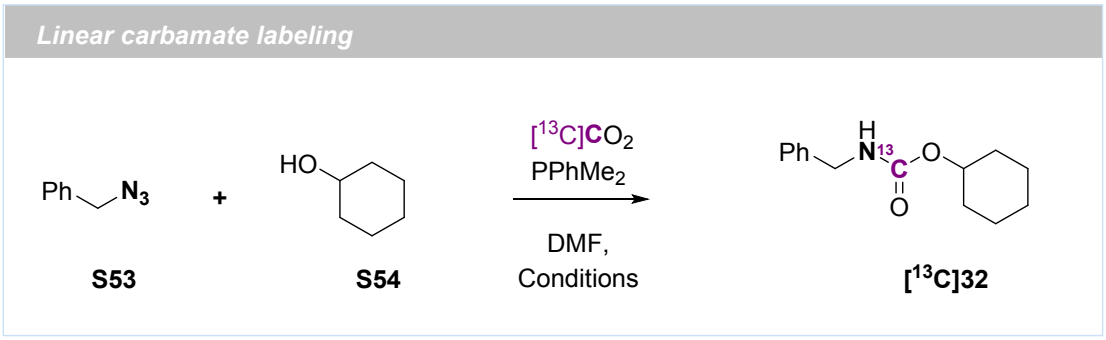
The crude product was synthesized from compound **31** following the general procedure. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of $H_2O/CH_3CN/Et_3N$ (55/45/0.1 v/v/v, 5 mL/min) as eluent with gamma and UV (λ = 283 nm) detection. The collected peak (t_R = 10.5-12.0 min) of [^{11}C]Zolmitriptan **[**^{11}C]**30** was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]Zolmitriptan **[**^{11}C]**30** (1.0 ± 0.2 GBq) was obtained within 35 min from end of beam in 25 ± 2% RCY and 74 ± 6 GBq/µmol molar activity (n = 2). Quality control was performed following the general procedure using a Zorbax® SB-C18 4.6 x 250 mm, 3.5 µm column (Agilent, USA) with aqueous $H_2O/CH_3CN/Et_3N$ 55/45/0.1 v/v/v as eluent at 1 mL/min and UV detection at λ = 283 nm.

3. Preliminary optimization on model linear carbamate (32)

3.1 Synthesis of ^{13}C-labeled linear carbamate [^{13}C]32

General procedure :

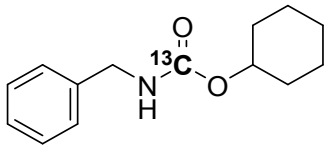
In a oven-dried vial (2mL), to a solution of (azidomethyl)benzene (0.1 mmol) **S53** in DMF-d_7 (0.7 mL, previously dried on molecular sieve) was added $PPhMe_2$ (0.1 mmol) and when indicated, the additive (0.2 mmol). The mixture was transfer to a Young NMR tube, sealed and freezed in liquid N_2. Next, [^{13}C]CO_2 (0.1 to 0.3 mmol) was added *via* the Tritec manifold. The mixture was then allowed to warm up to room temperature for 30 minutes. Cyclohexanol **S54**(0.1 to 1 mmol, previously dried on molecular sieve) was then added and the mixture heated at 150 °C for 5 to 30 minutes. The crude was then purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 7:3) affording the ^{13}C-labeled cyclohexyl benzylcarbamate **[^{13}C]32.**



Entry	S54 equiv.	CO_2 equiv.	Additive	Conditions[a]	Yield[b]
1[c]	5	1	-	5 min at 150 °C	29%
2	5	1	DMAP	5 min at 150 °C	54%
3	5	2	DMAP	15 min at 150 °C	53%
4	5	2	-	5 min at 150 °C	57%
5	5	3	-	15 min at 150 °C	64%
6	10	2	-	30 min at 150 °C	56%
7	10	2	DMAP	15 min at 150 °C	53%

Table S5: Carbon-13 labeling of carbamate 32. [a] After the 30 minutes at room temperature [b] Isolated Yield, [c] Addition of **S54** before [^{13}C]CO_2

***[^{13}C]cyclohexyl benzylcarbamate* ([^{13}C]32)**



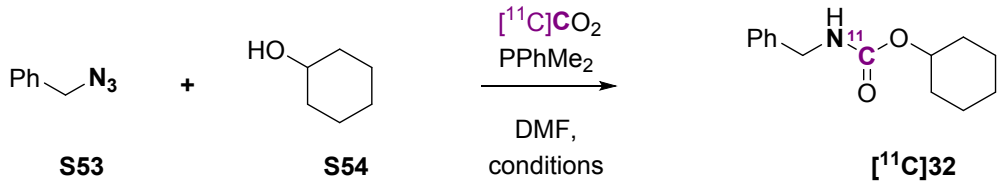
$C_{13}{}^{13}CH_{19}NO_2$
MW: 234.3 g.mol^{-1}
Yield: 64%
White solid

The ^{13}C-labeled cyclohexyl benzylcarbamate **[^{13}C]32** was prepared according to the general procedure, using $PPhMe_2$ (14.5 µL, 0.10 mmol), (azidomethyl)benzene **S53** (13.3 mg, 0.10 mmol) and $^{13}CO_2$ (0.30 mmol) in DMF-d_7. After 30 minutes at room temperature, cyclohexanol **S54** (0.30 mL, 0.50 mmol) was added and the mixture was heated to 150 °C for 5 minutes. The crude product was purified by Flash Chromatography on SiO_2 gel (eluent Heptane/EtOAc 7:3) affording the ^{13}C-labeled cyclohexyl benzylcarbamate **[^{13}C]32** as a white solid (15.0 mg, 64%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H), 5.01 – 4.83 (m, 1H), 4.76 – 4.60 (m, 1H), 4.43 – 4.26 (m, 2H), 1.96 – 1.80 (m, 2H), 1.77 – 1.62 (m, 2H), 1.60 – 1.46 (m, 1H), 1.44 – 1.29 (m, 5H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4 (^{13}C labeled), 138.9, 128.8 (2C), 127.7, 127.6 (2C), 74.4, 45.1, 32.2 (2C), 25.5, 24.0 (2C).
LCMS (ESI) *m/z* $C_{13}{}^{13}CH_{19}NO_2$ $[M+H]^+$ 235.3.

3.2 Synthesis of ^{11}C-labeled linear carbamate [^{11}C]32

Linear carbamate labeling



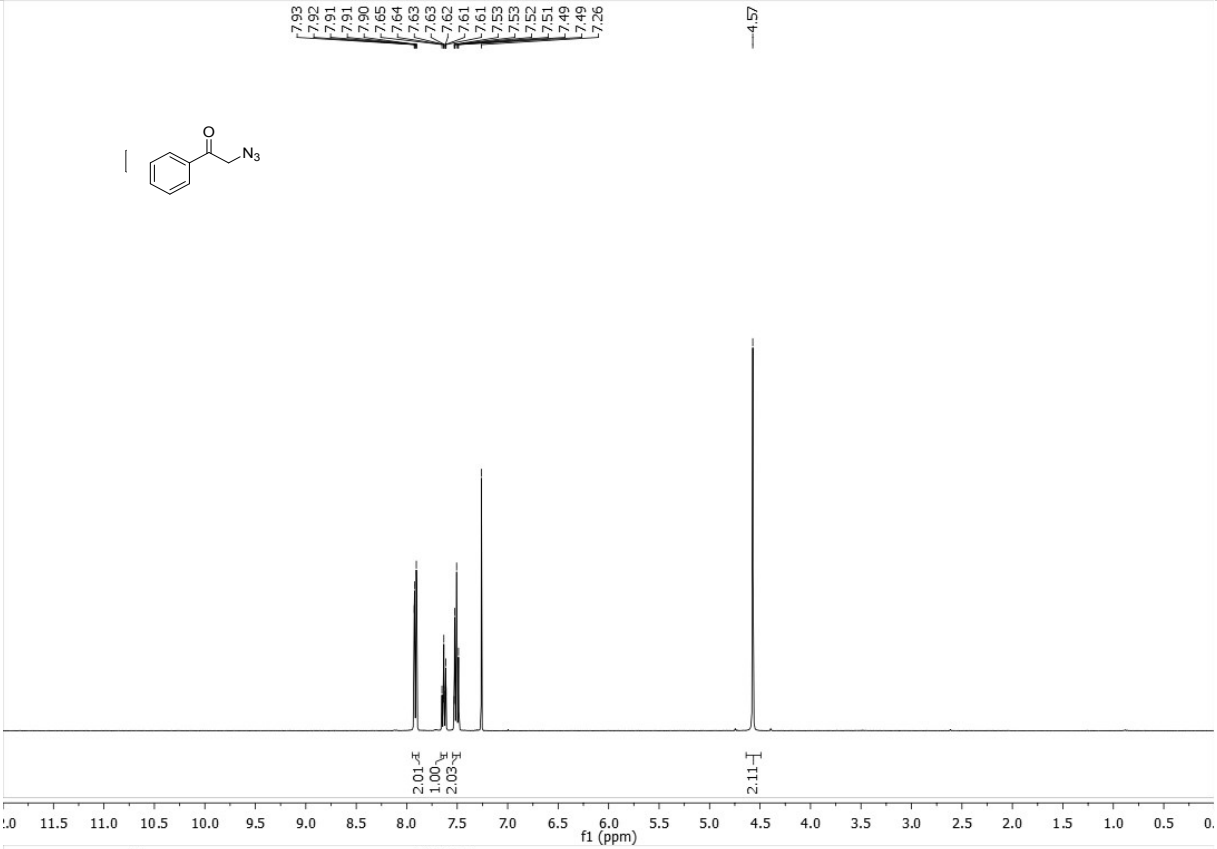
S53 **S54** **[^{11}C]32**

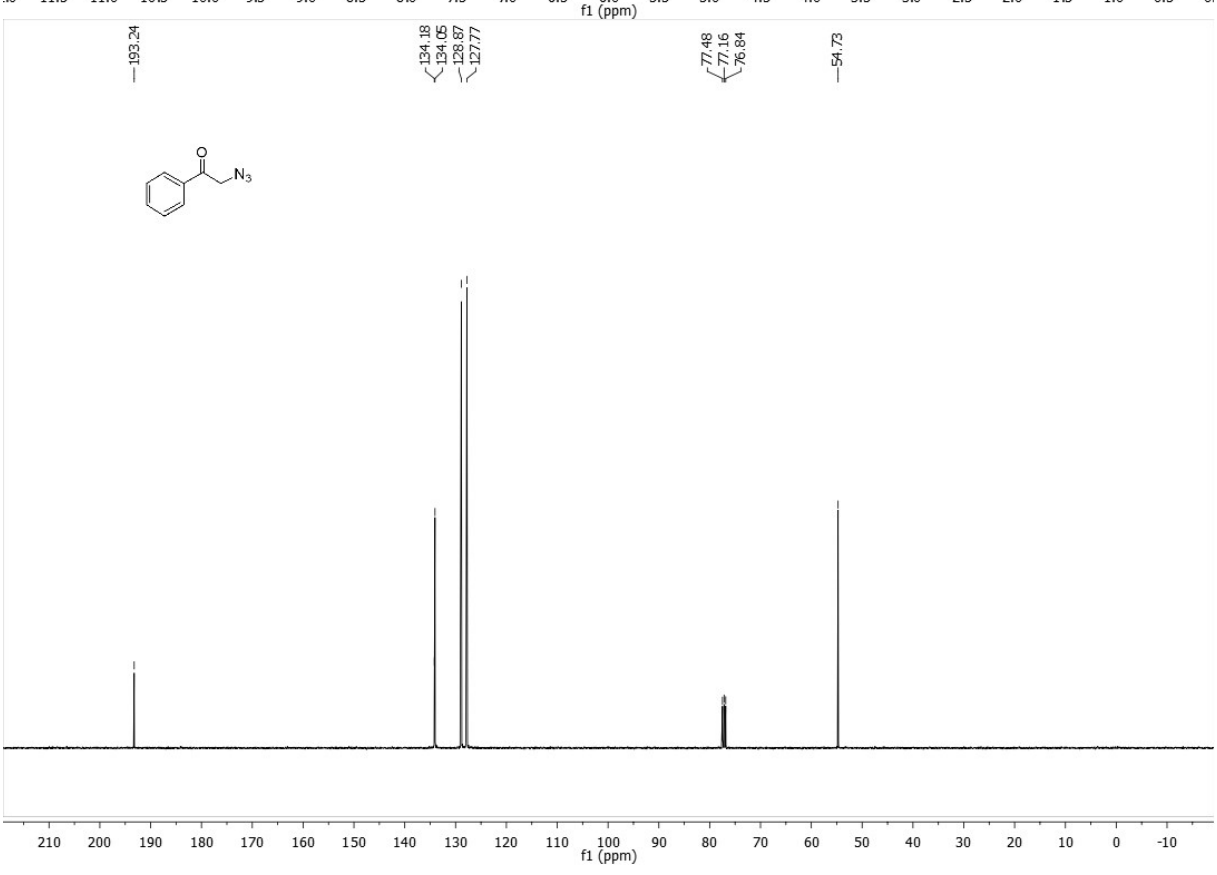
S53	S54	Conditions	Results	RCC
1 mg	5 mg	2 steps : 1) **S53**, DMF rt 5 min 2) **S54**, DMF, 150 °C, 10 min	2 radioactive side products only	0%
200 µg	150 µL	1 step : **S53** in DMF/**S54** 1/1 v/v (300 µL) ; 150 °C, 5 min	5 radioactive products formed including **[^{11}C]32**	2%
20µg	150 µL	1 step : **S53** in DMF/**S54** 1/1 v/v (300 µL) ; 150 °C, 5 min	Only **[^{11}C]32** formed together with unreacted [^{11}C]CO_2	4%
3 * 20 µg	150µL	1 step : **S53** (added in three times every 3 min) in DMF/**S54** 1/1 v/v (200 µL) ; 80 °C, 10 min	**[^{11}C]32** with secondary products	2%

Table S6: Carbon-11 labeling of carbamate **32**.

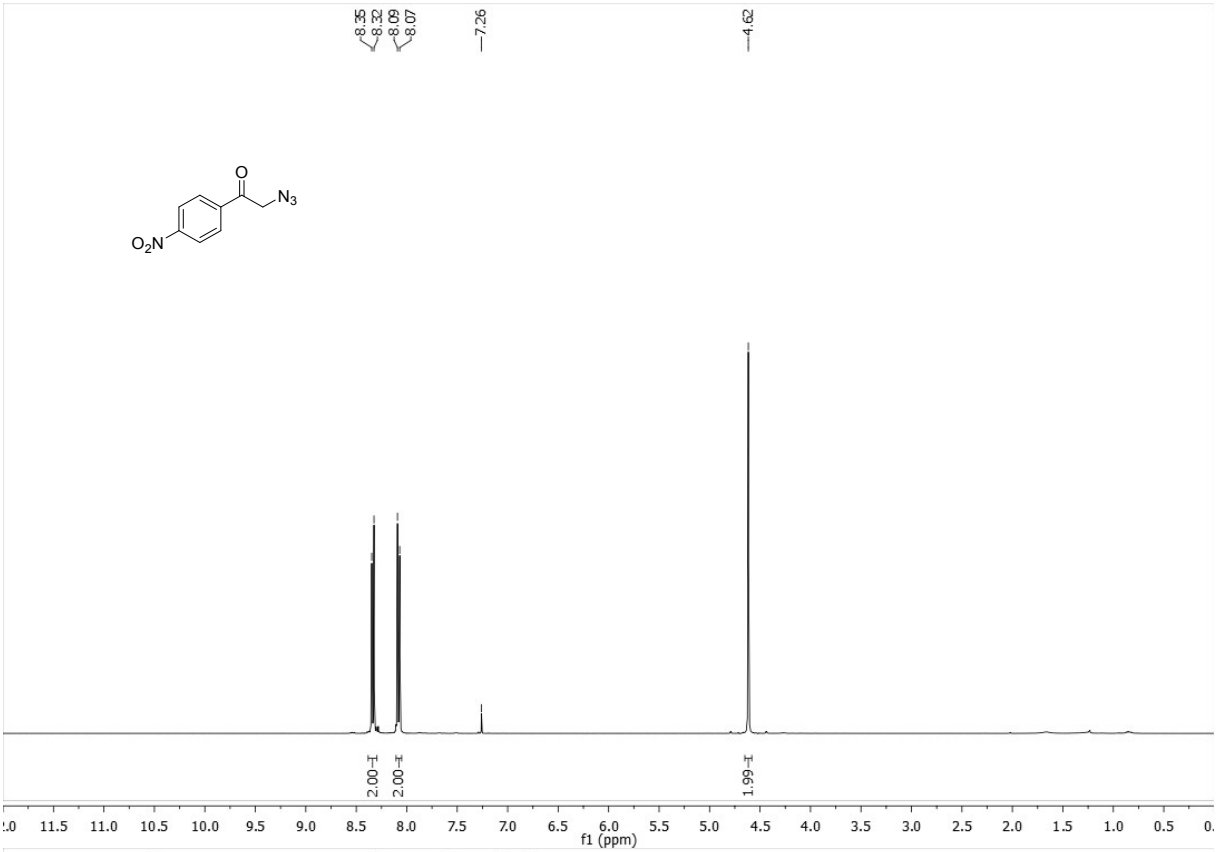
4. NMR Spectra

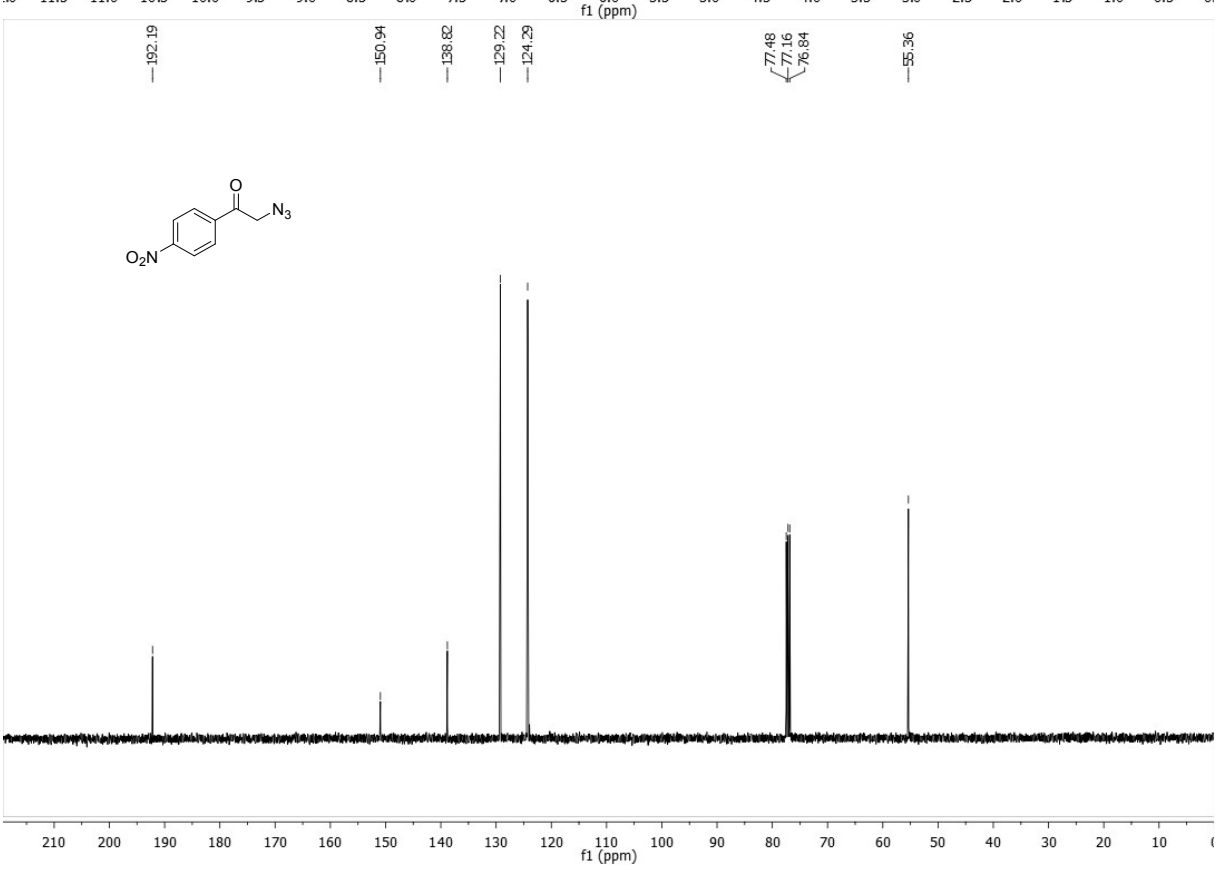
2-azido-1-phenylethan-1-one **(S1)**



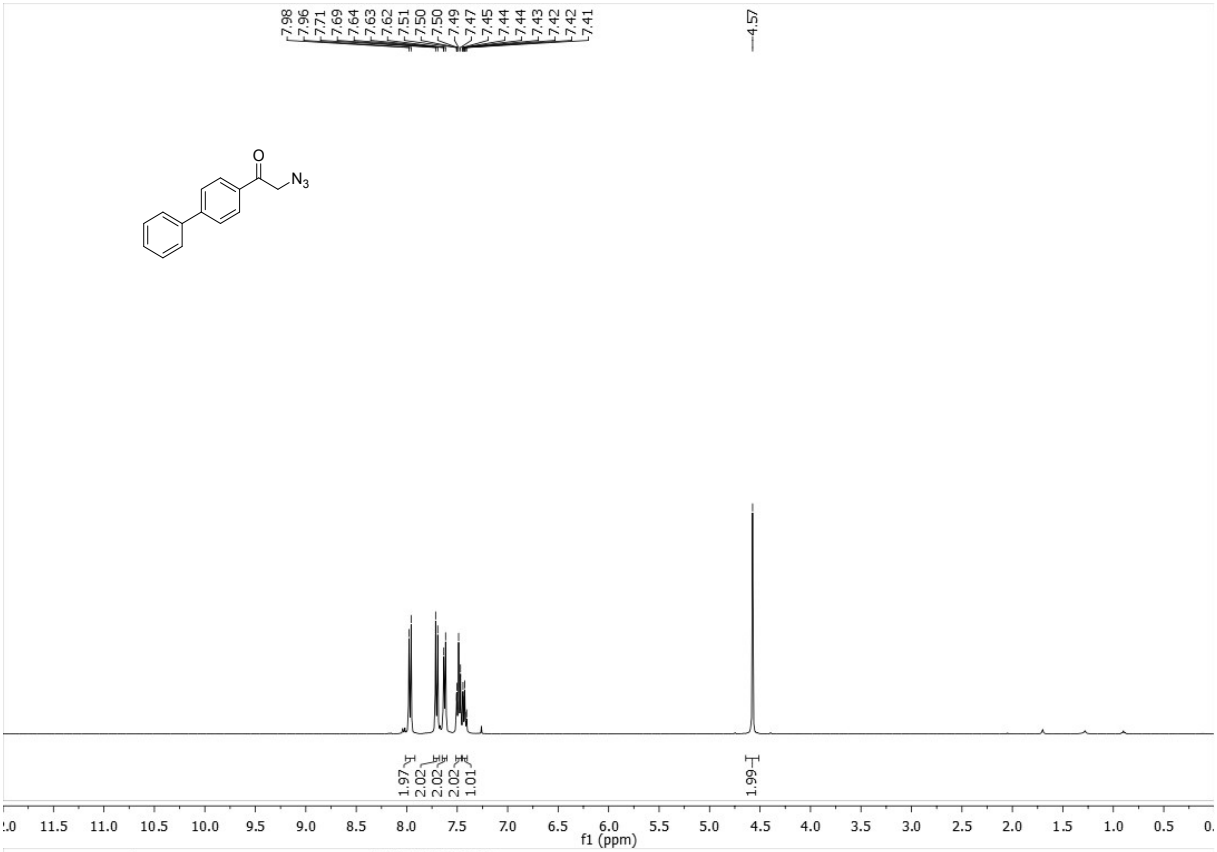


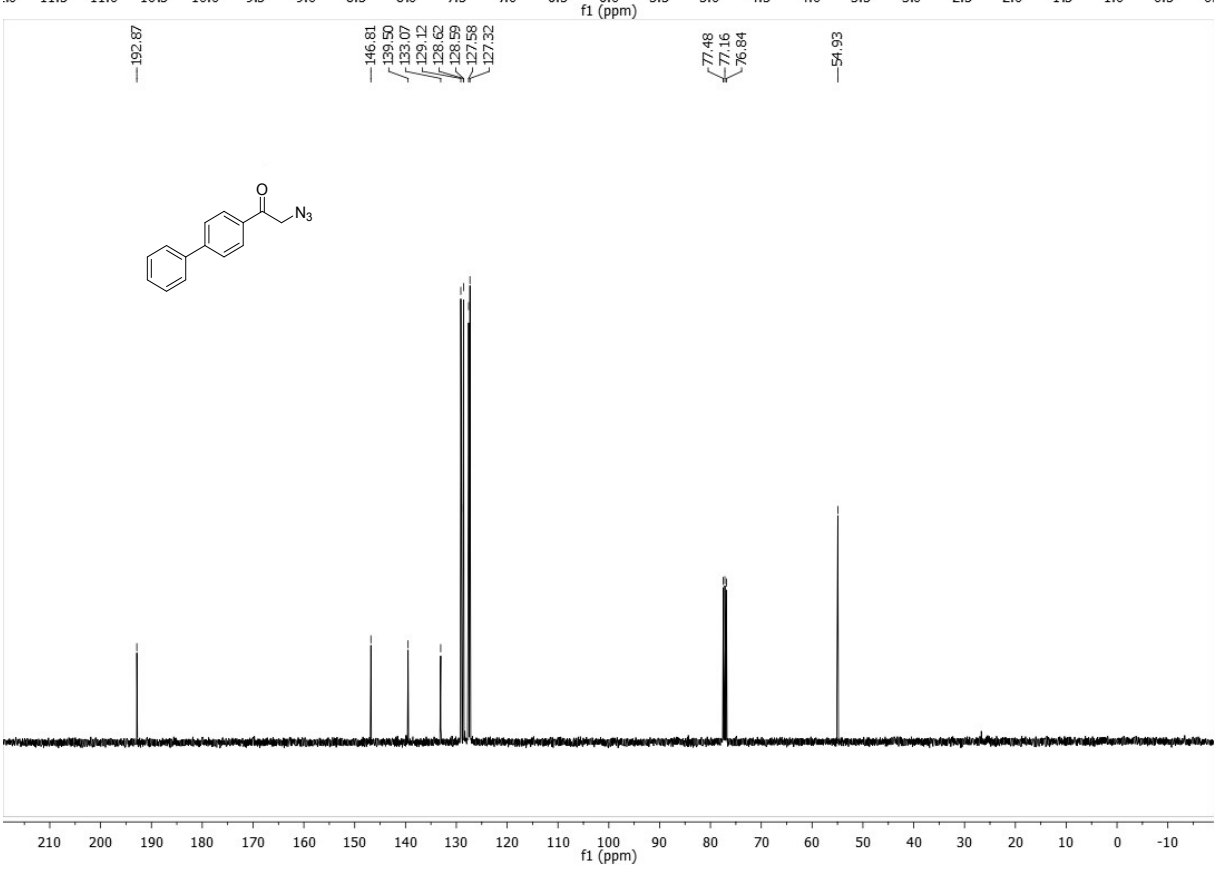
2-azido-1-(4-nitrophenyl)ethan-1-one (S2)



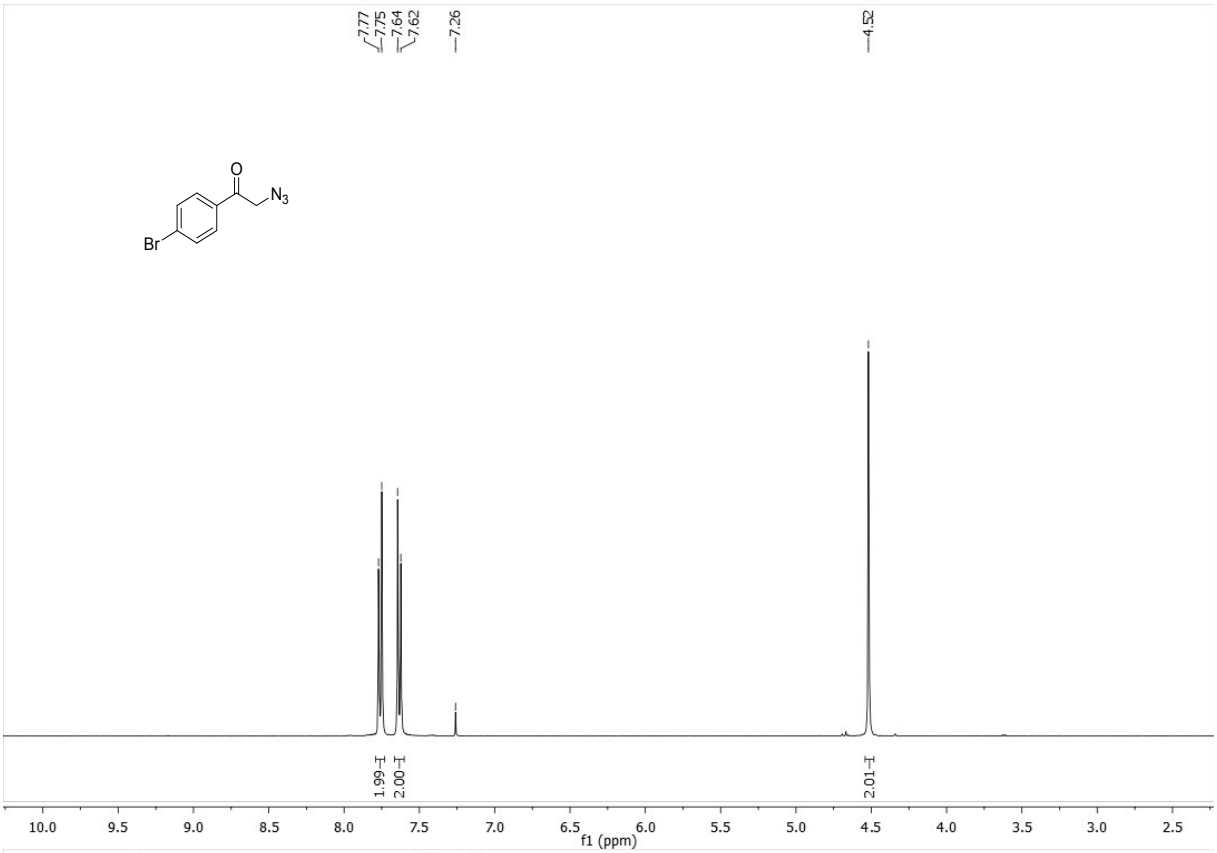


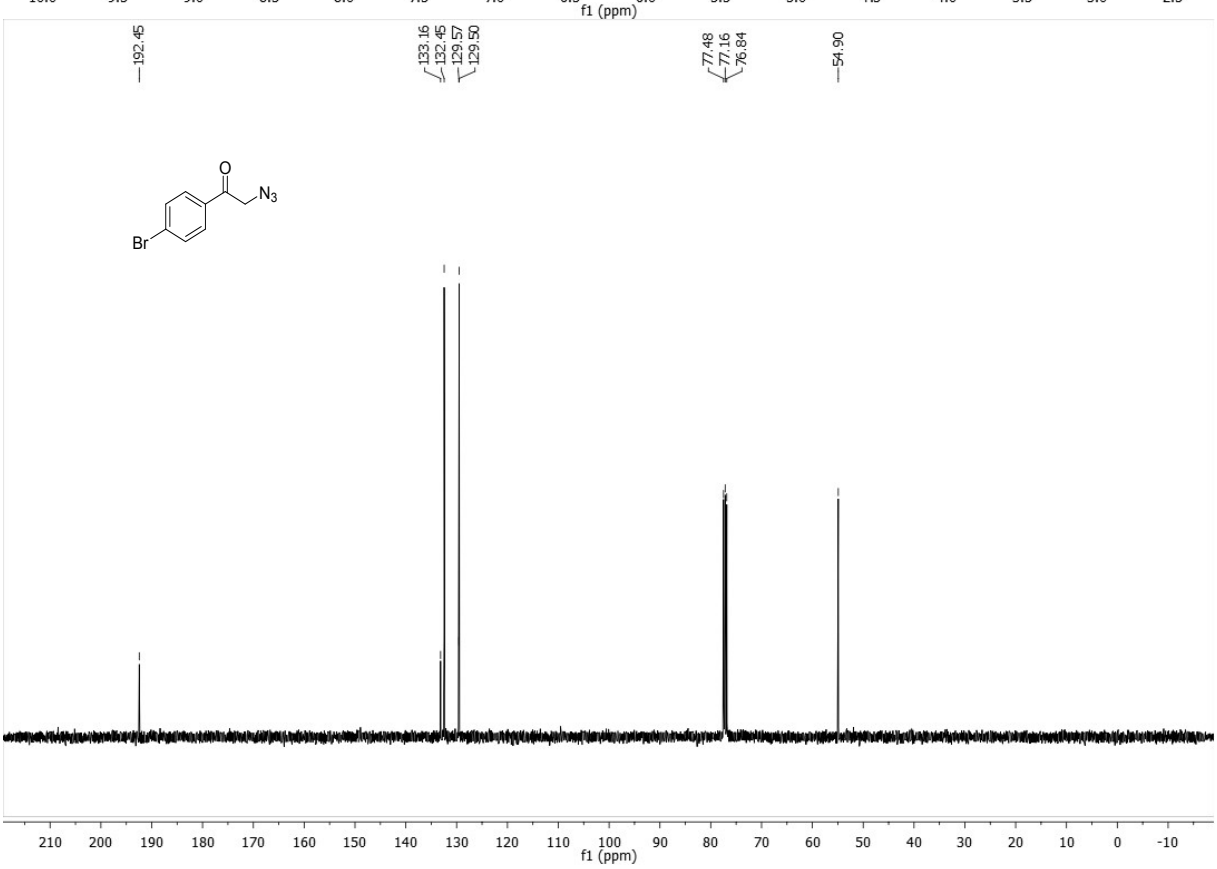
1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-one (S3)



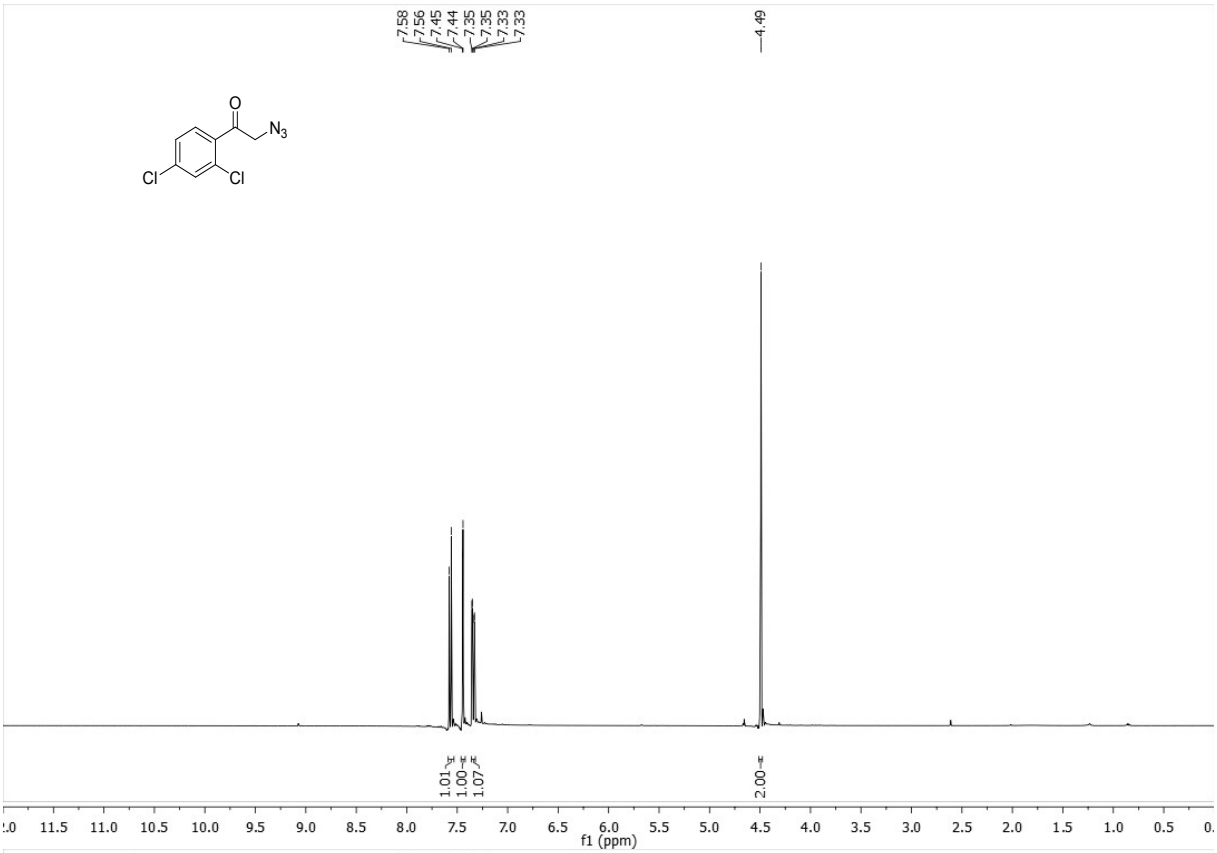


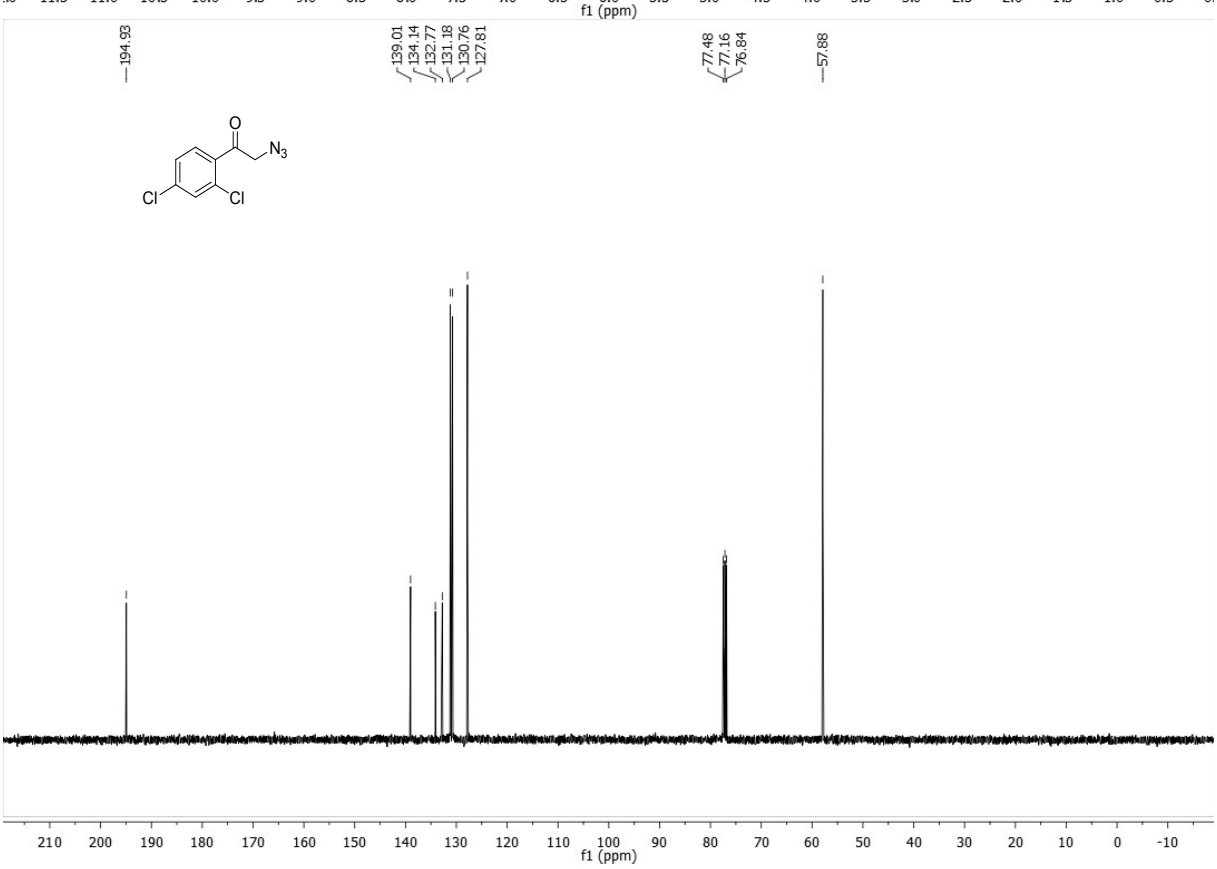
***2-azido-1-(4-bromophenyl)ethan-1-one* (S4)**



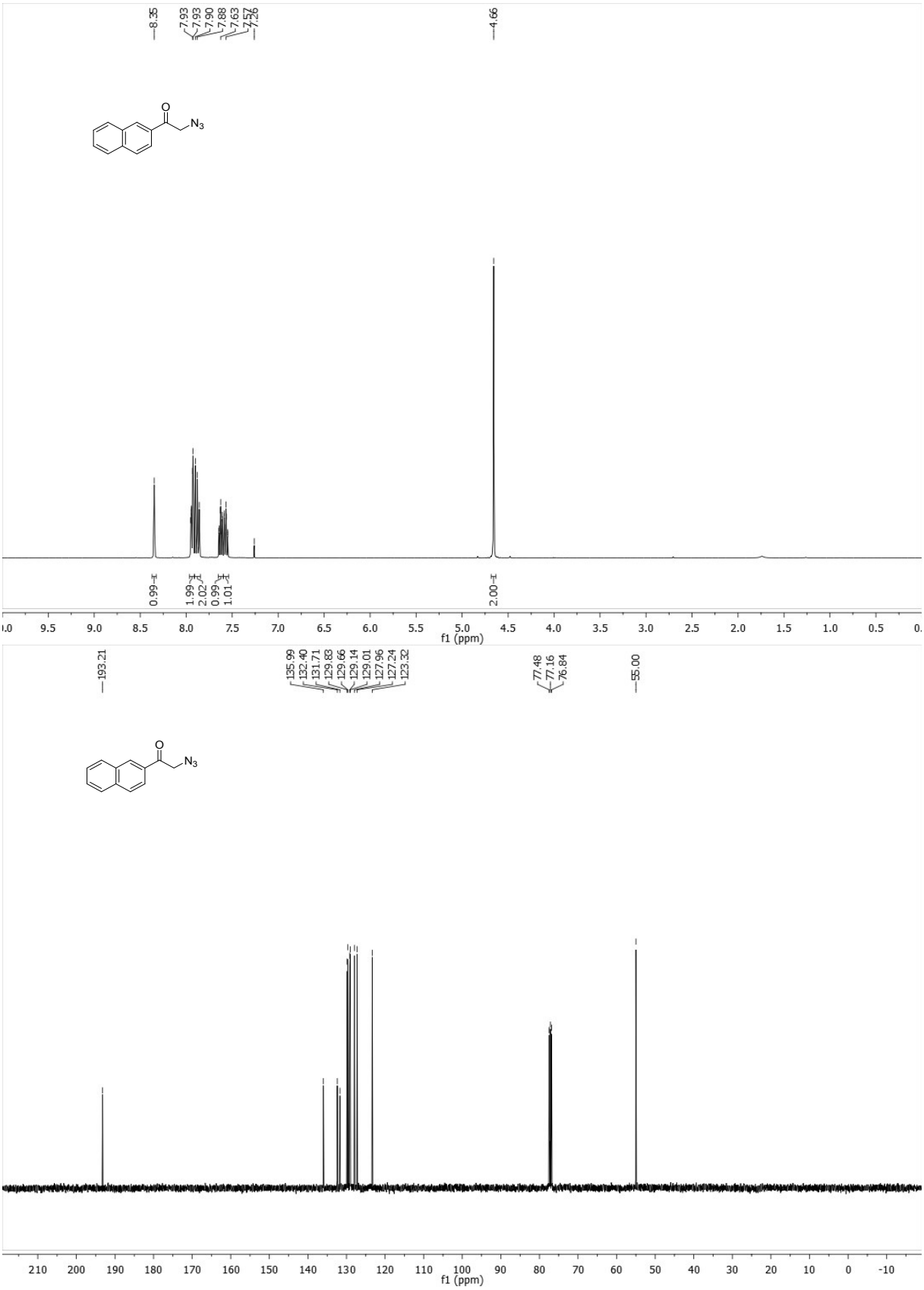


***2-azido-1-(2,4-dichlorophenyl)ethan-1-one* (S5)**

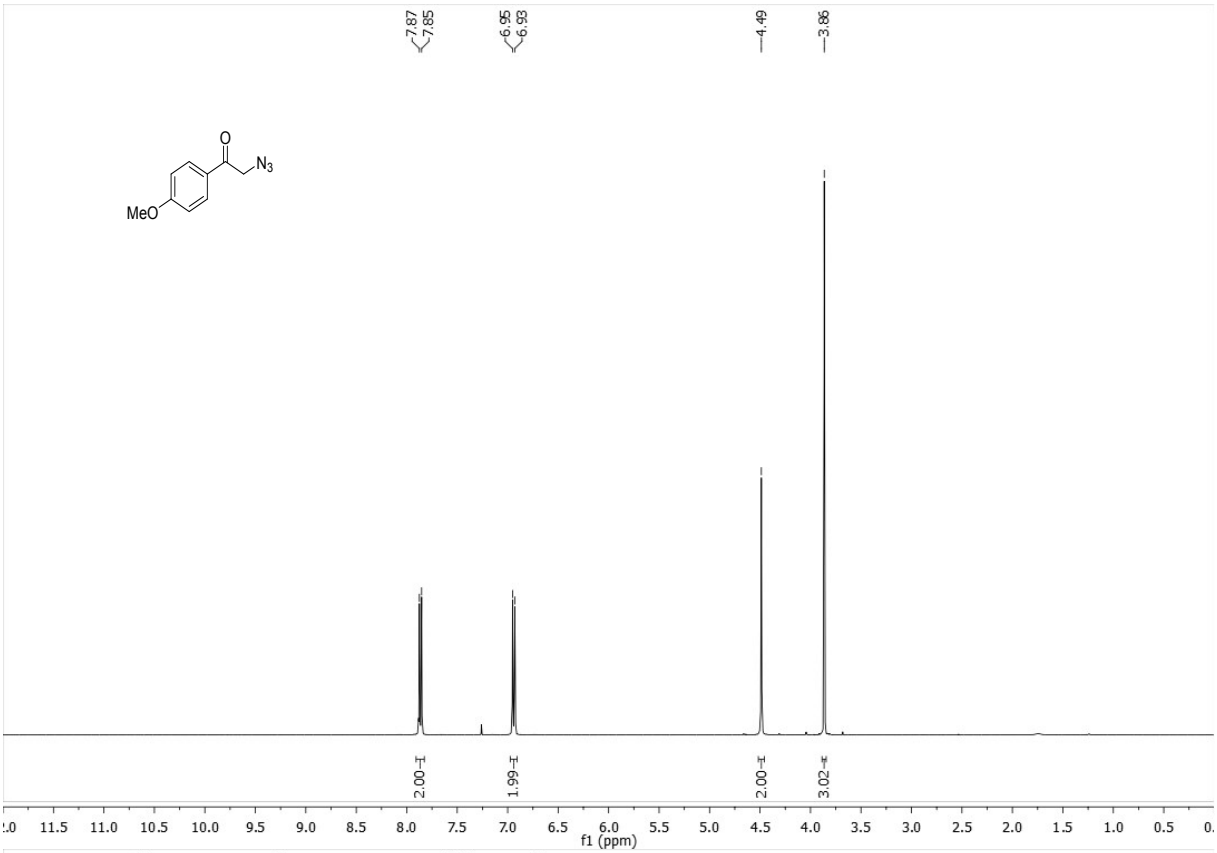


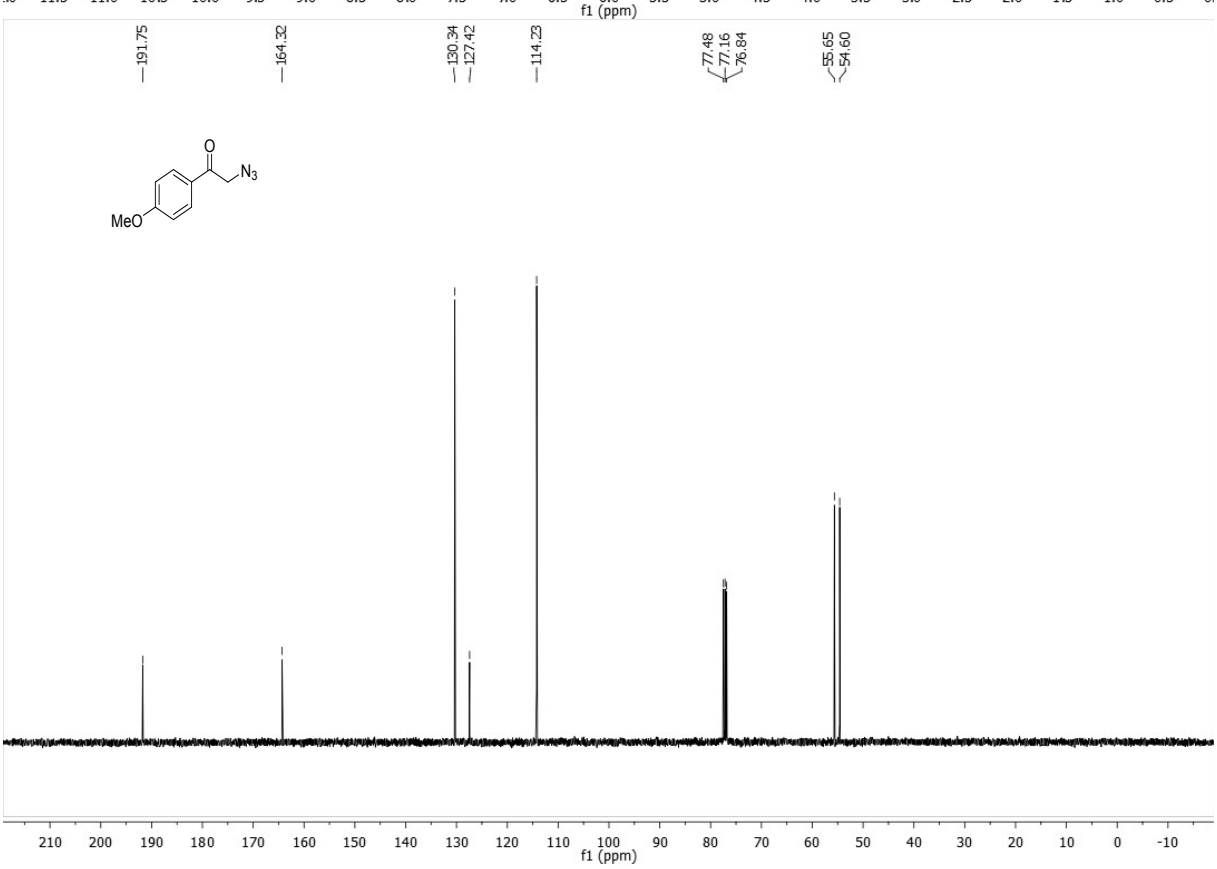


***2-azido-1-(naphthalen-2-yl)ethan-1-one* (S6)**

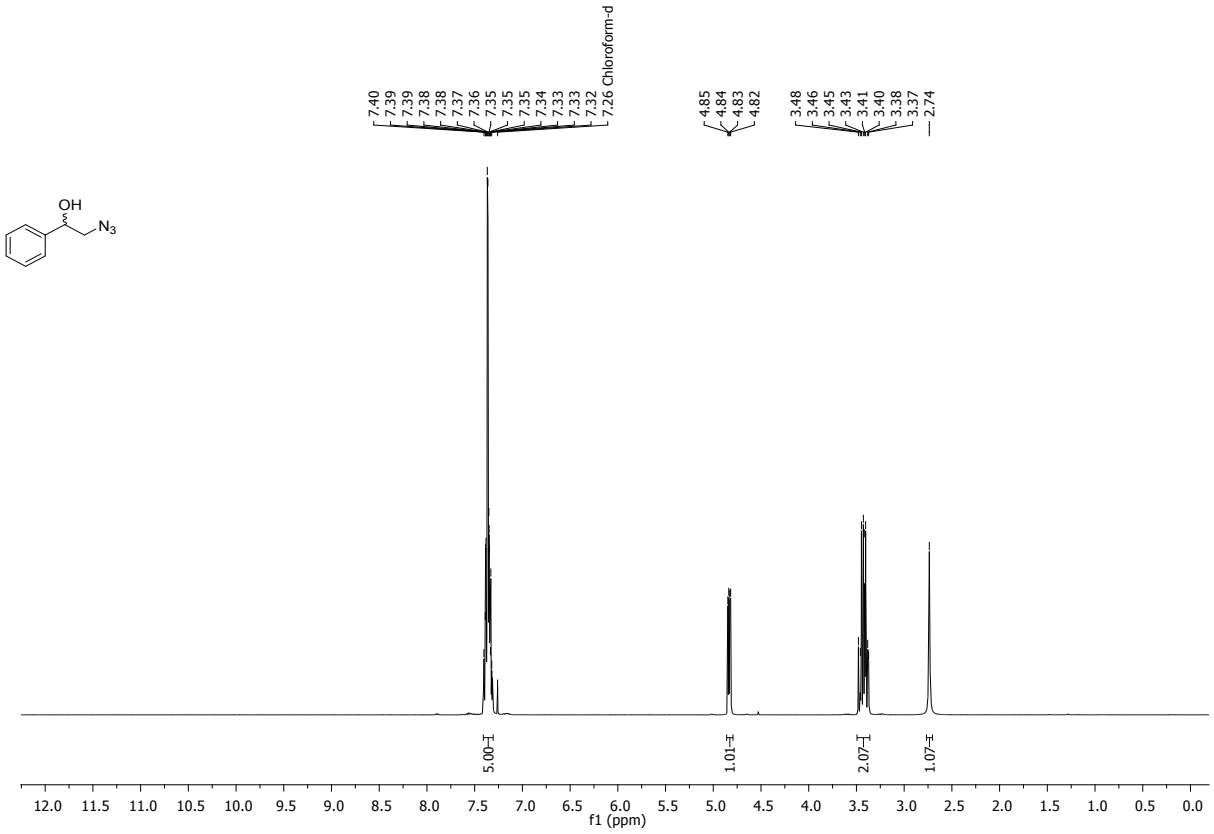


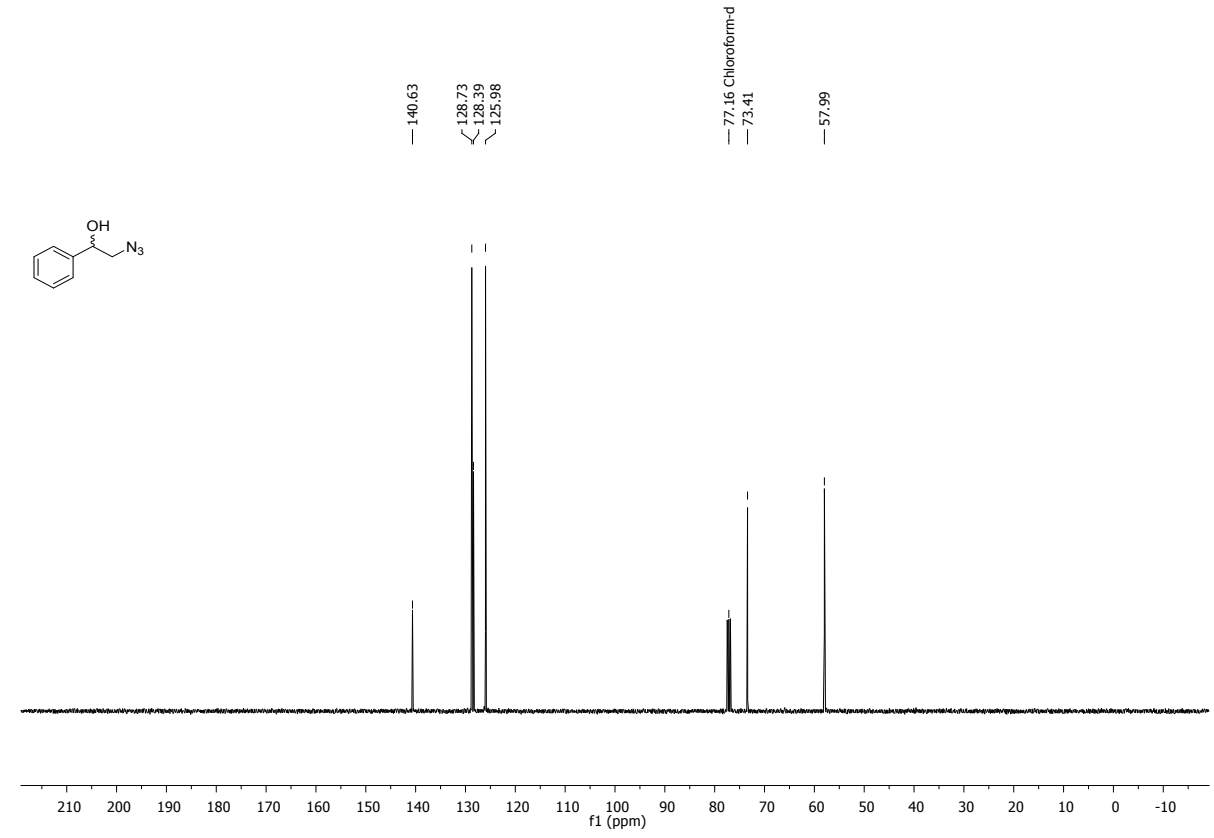
***2-azido-1-(4-methoxyphenyl)ethan-1-one* (S7)**



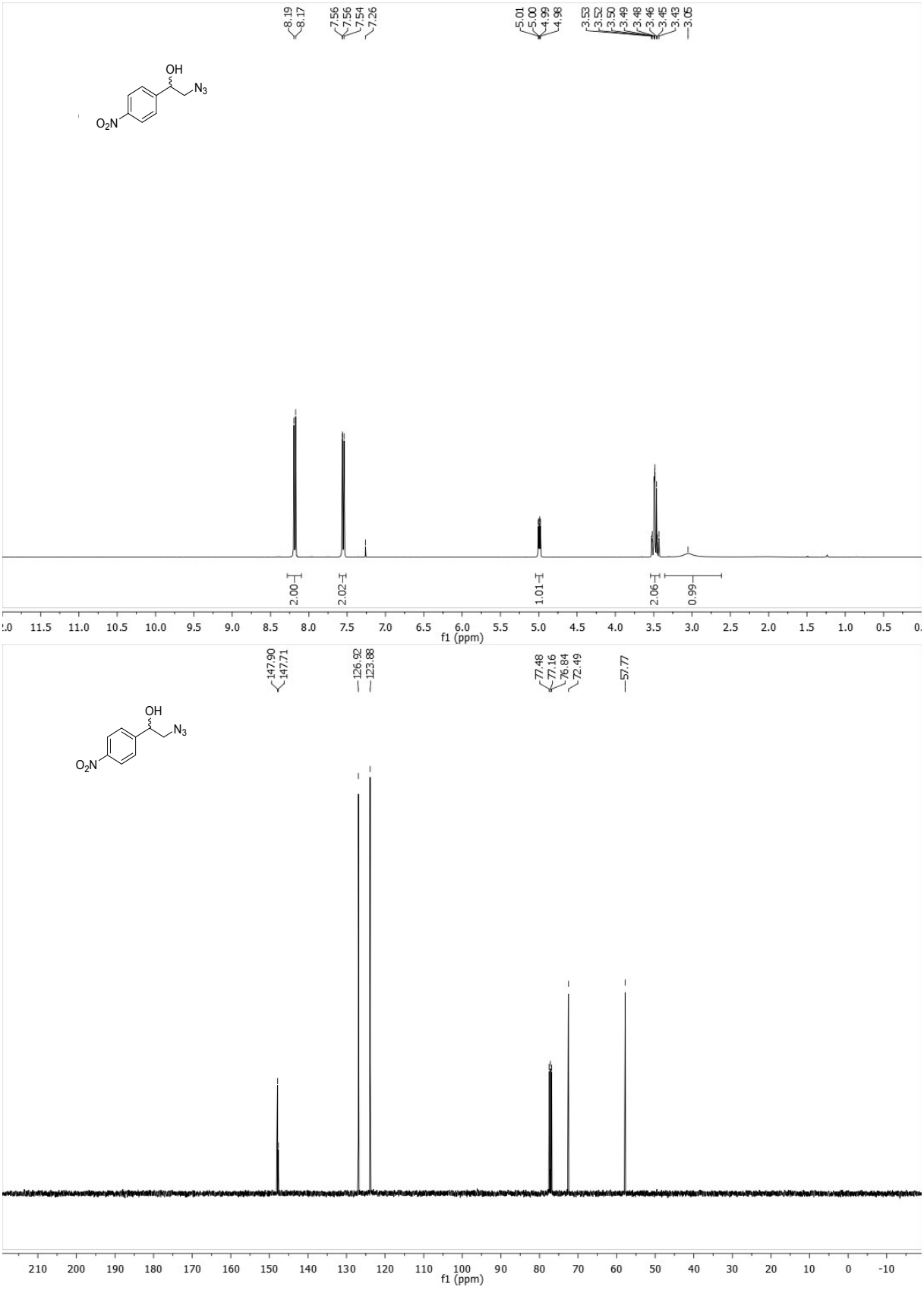


2-azido-1-phenylethan-1-ol (S8)

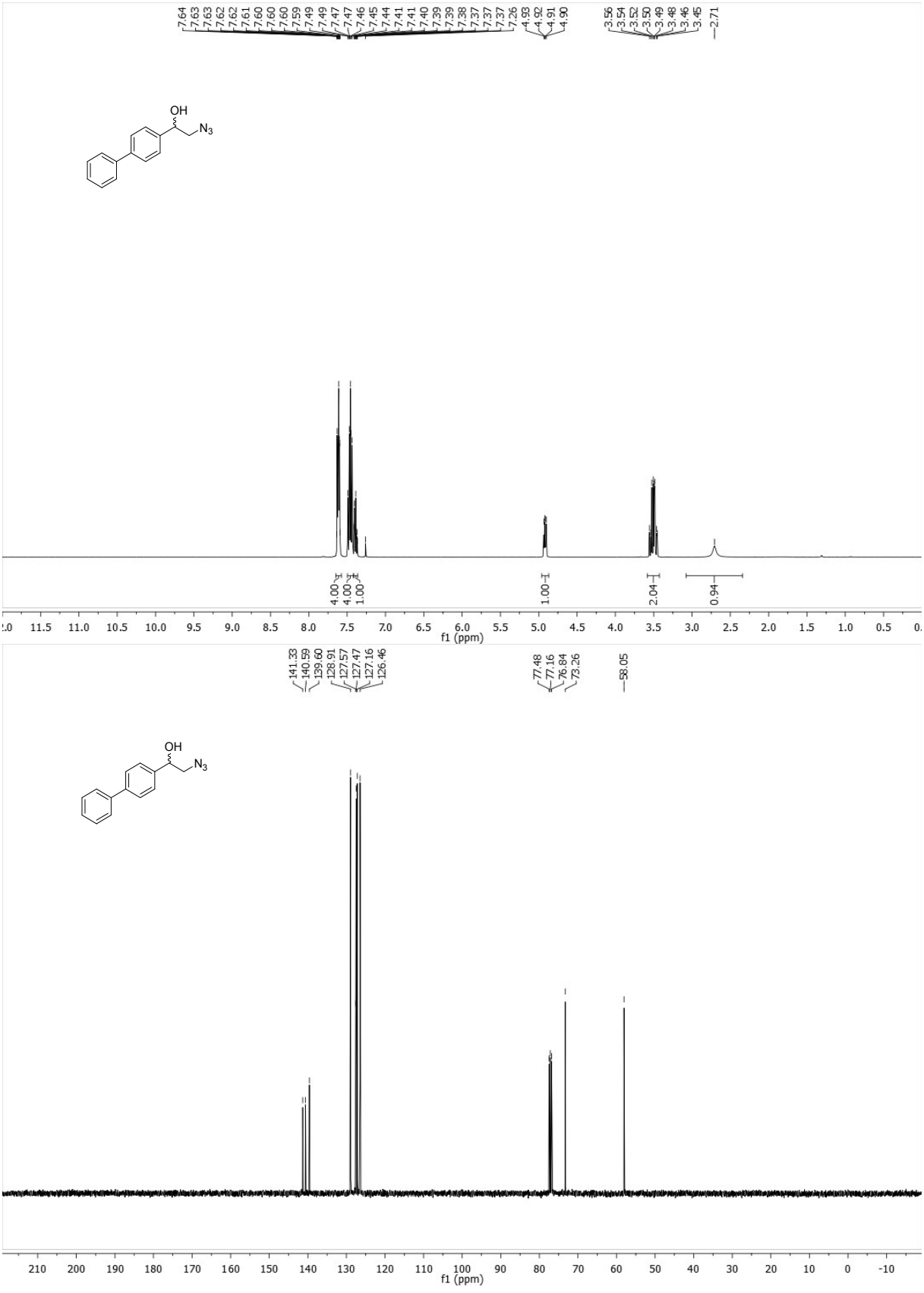




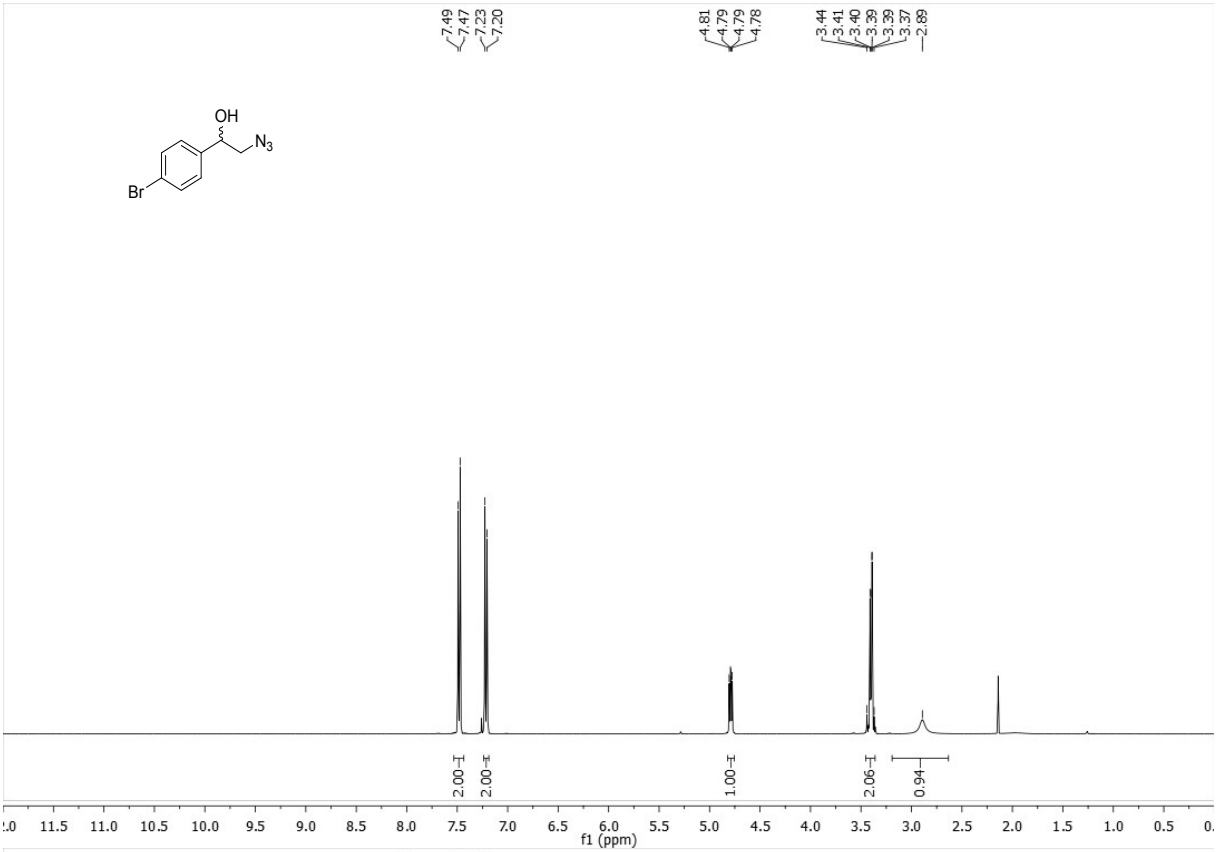
***2-azido-1-(4-nitrophenyl)ethan-1-ol* (S9)**

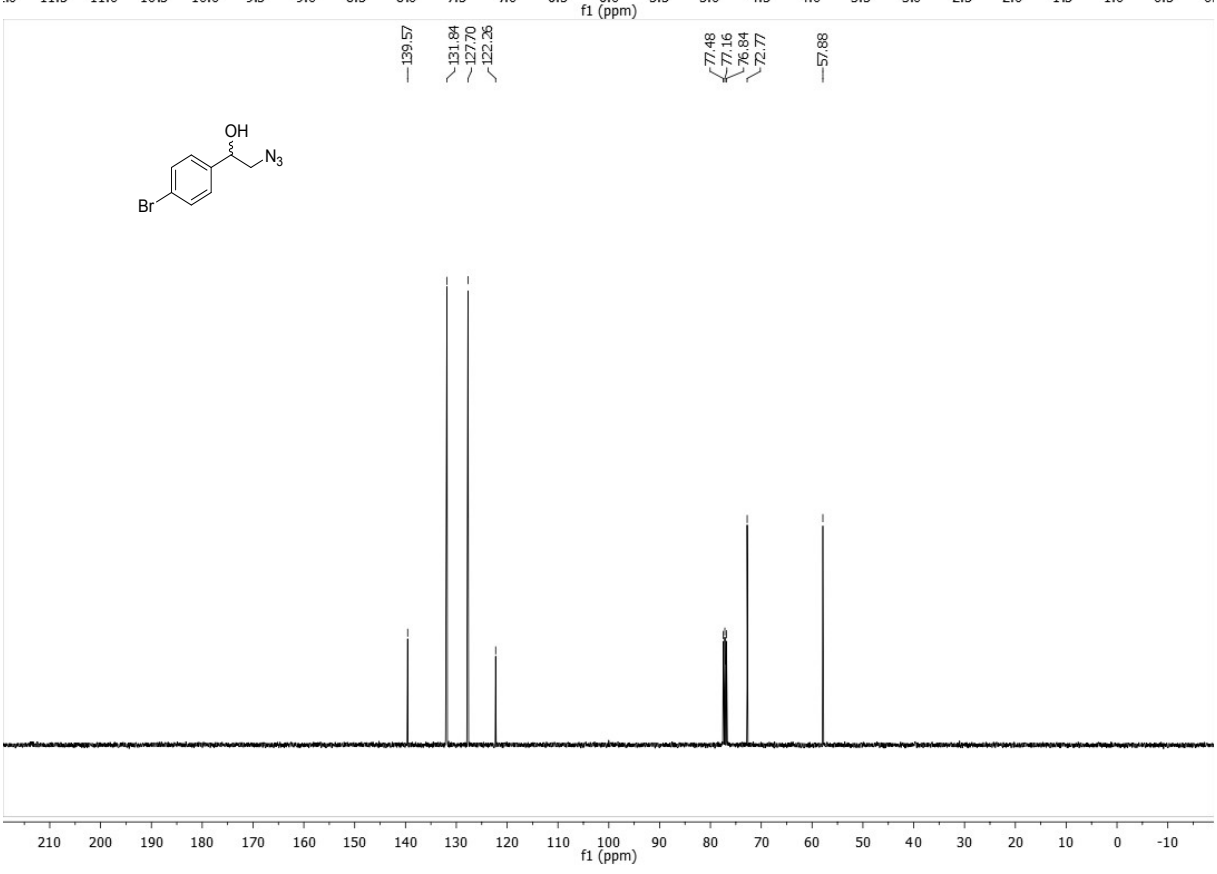


1-([1,1'-biphenyl]-4-yl)-2-azidoethan-1-ol (S10)

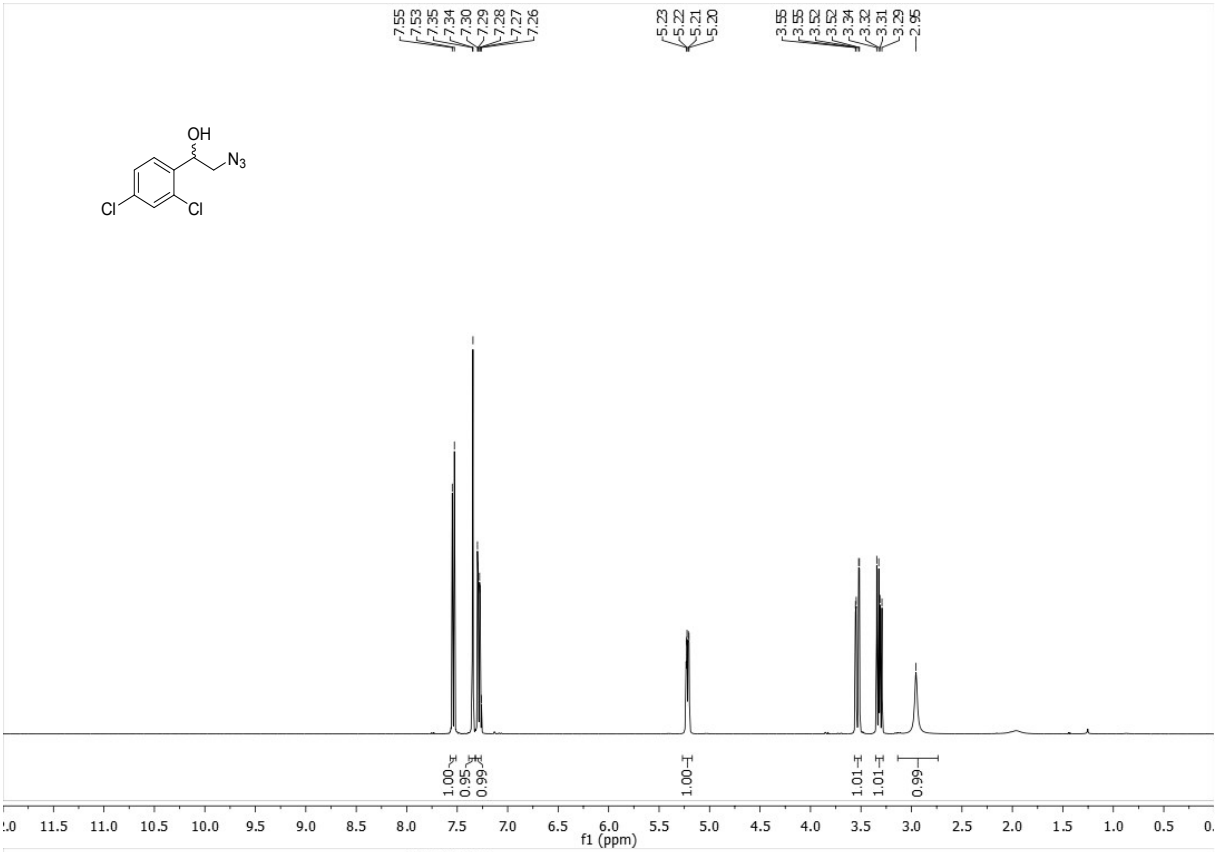


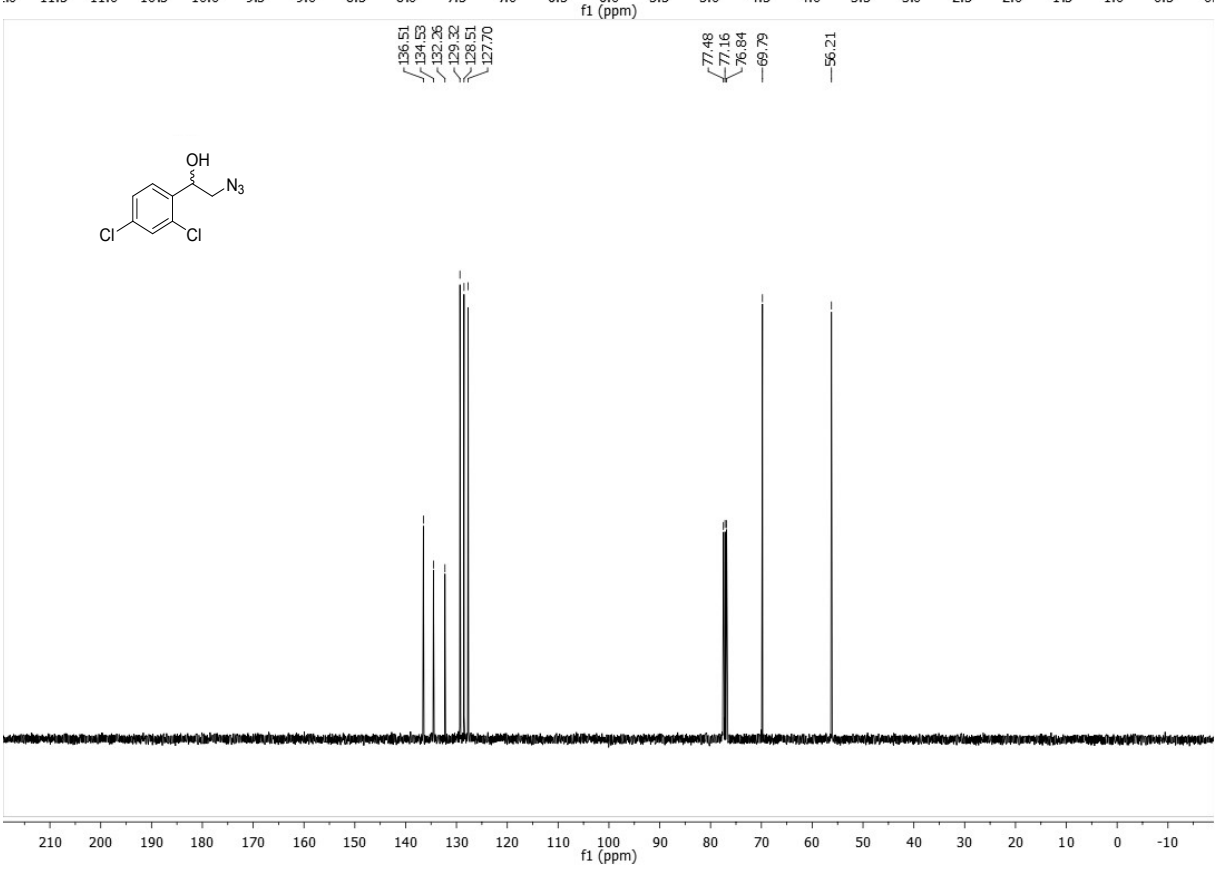
2-azido-1-(4-bromophenyl)ethan-1-ol **(S11)**



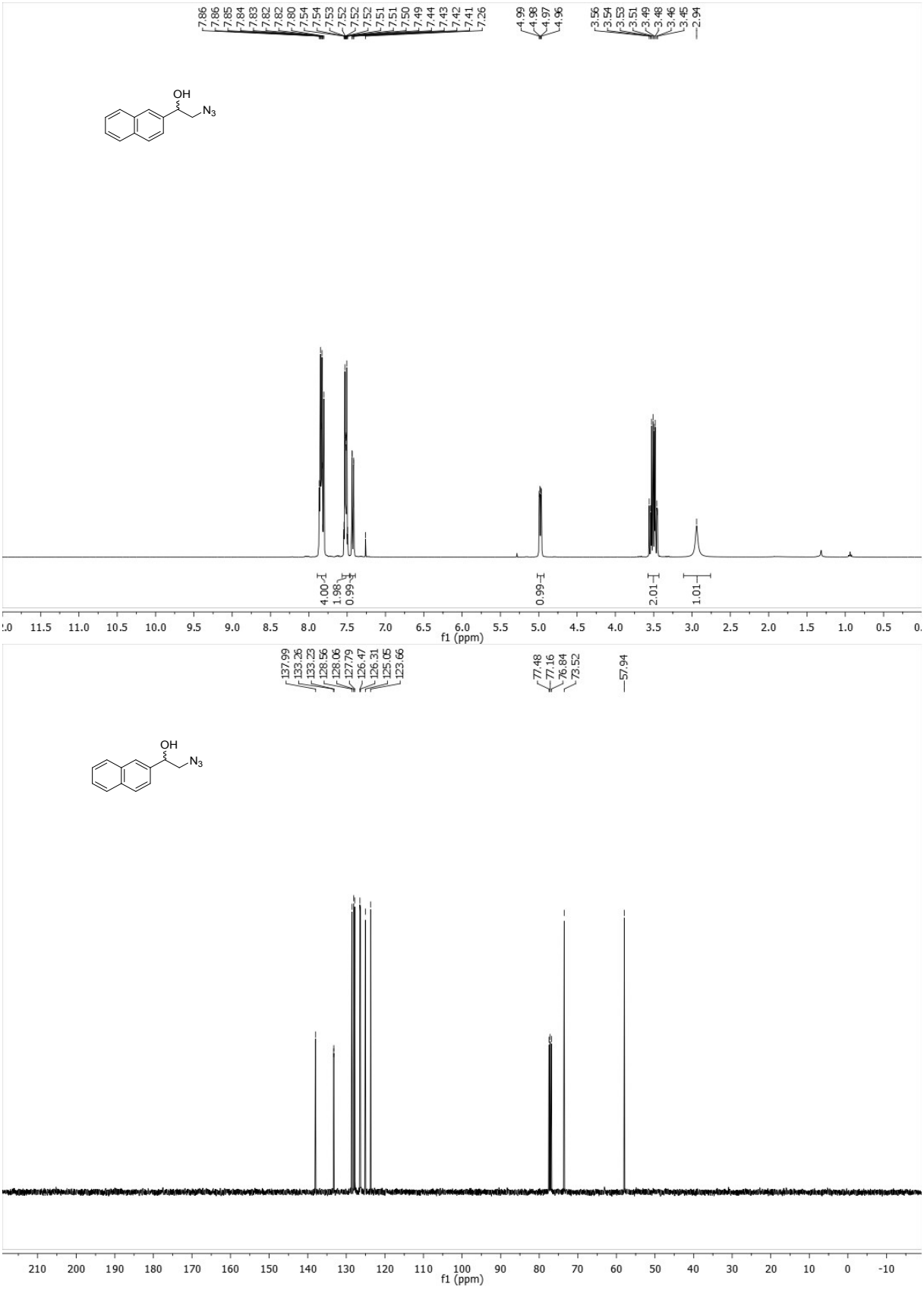


***2-azido-1-(2,4-dichlorophenyl)ethan-1-ol* (S12)**

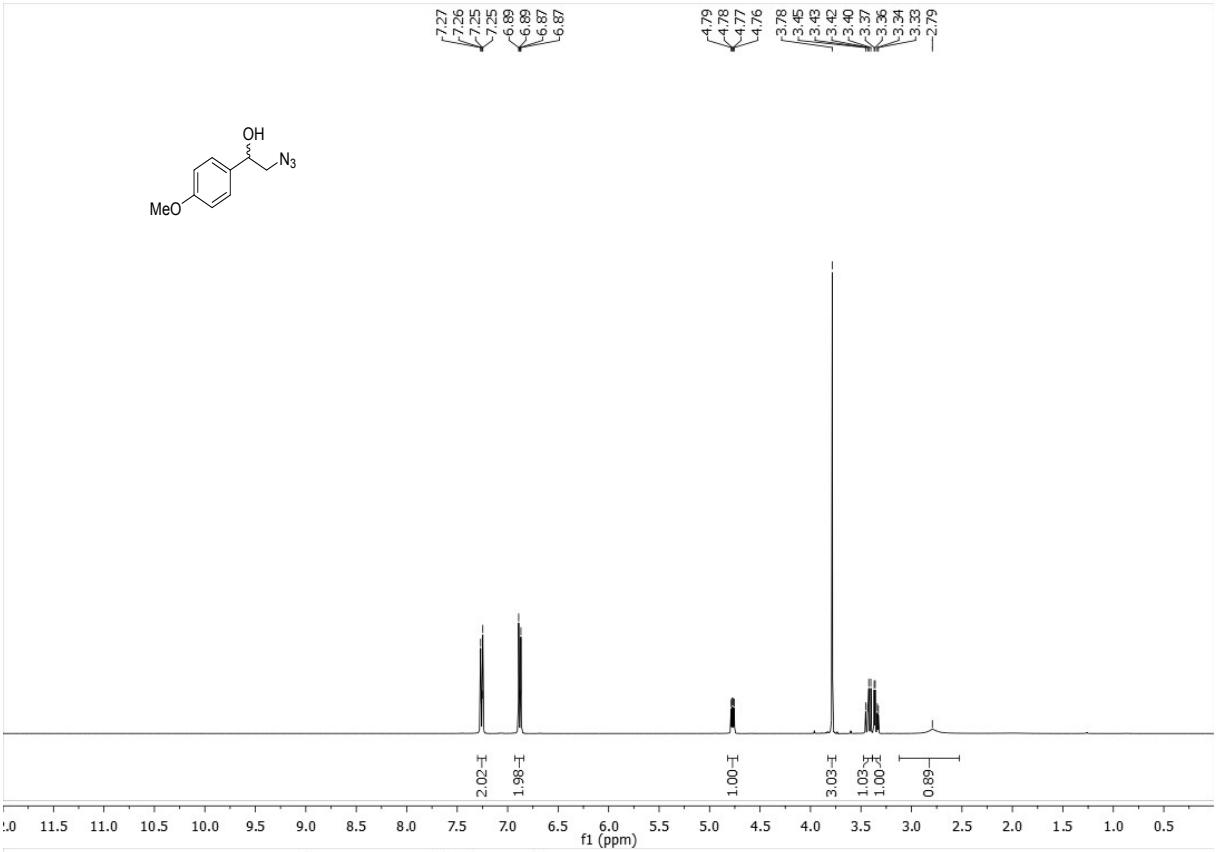


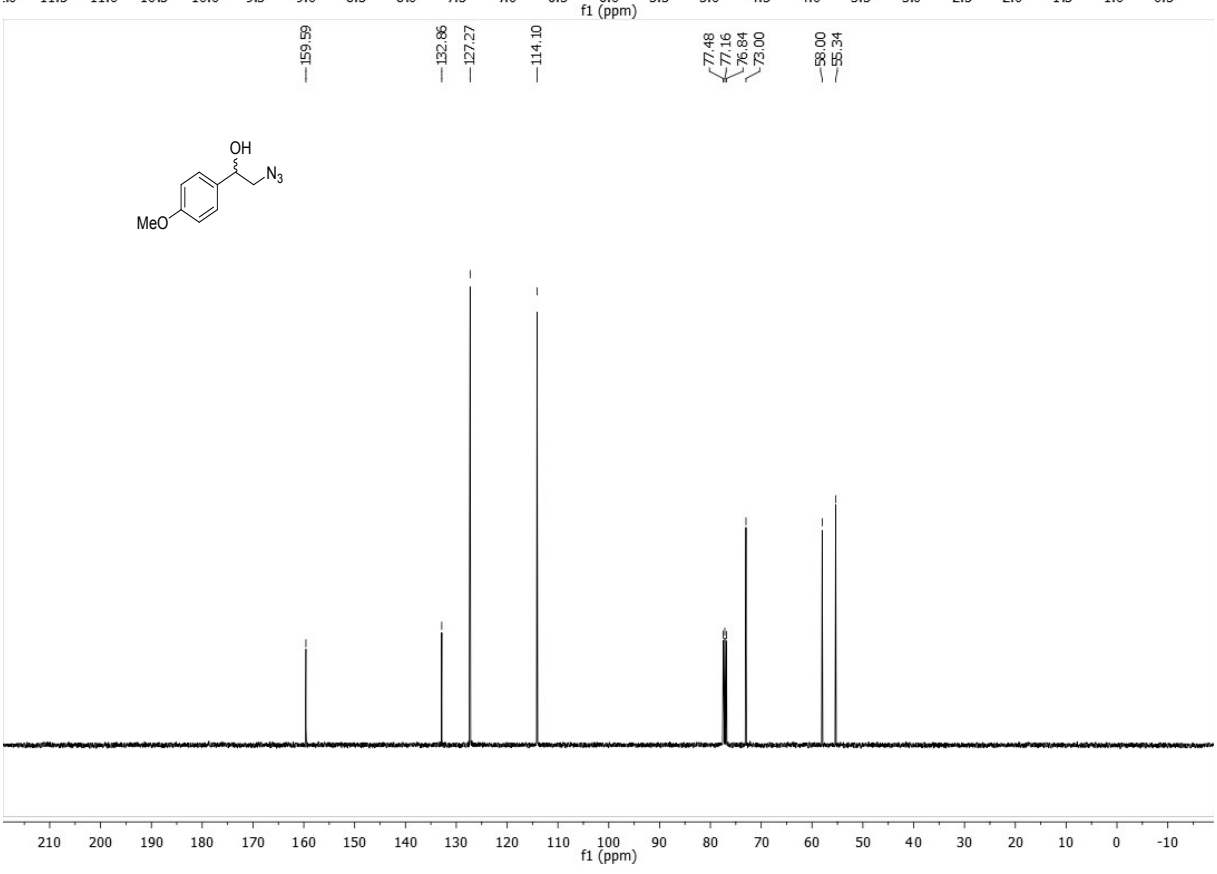


2-azido-1-(naphthalen-2-yl)ethan-1-ol (S13)

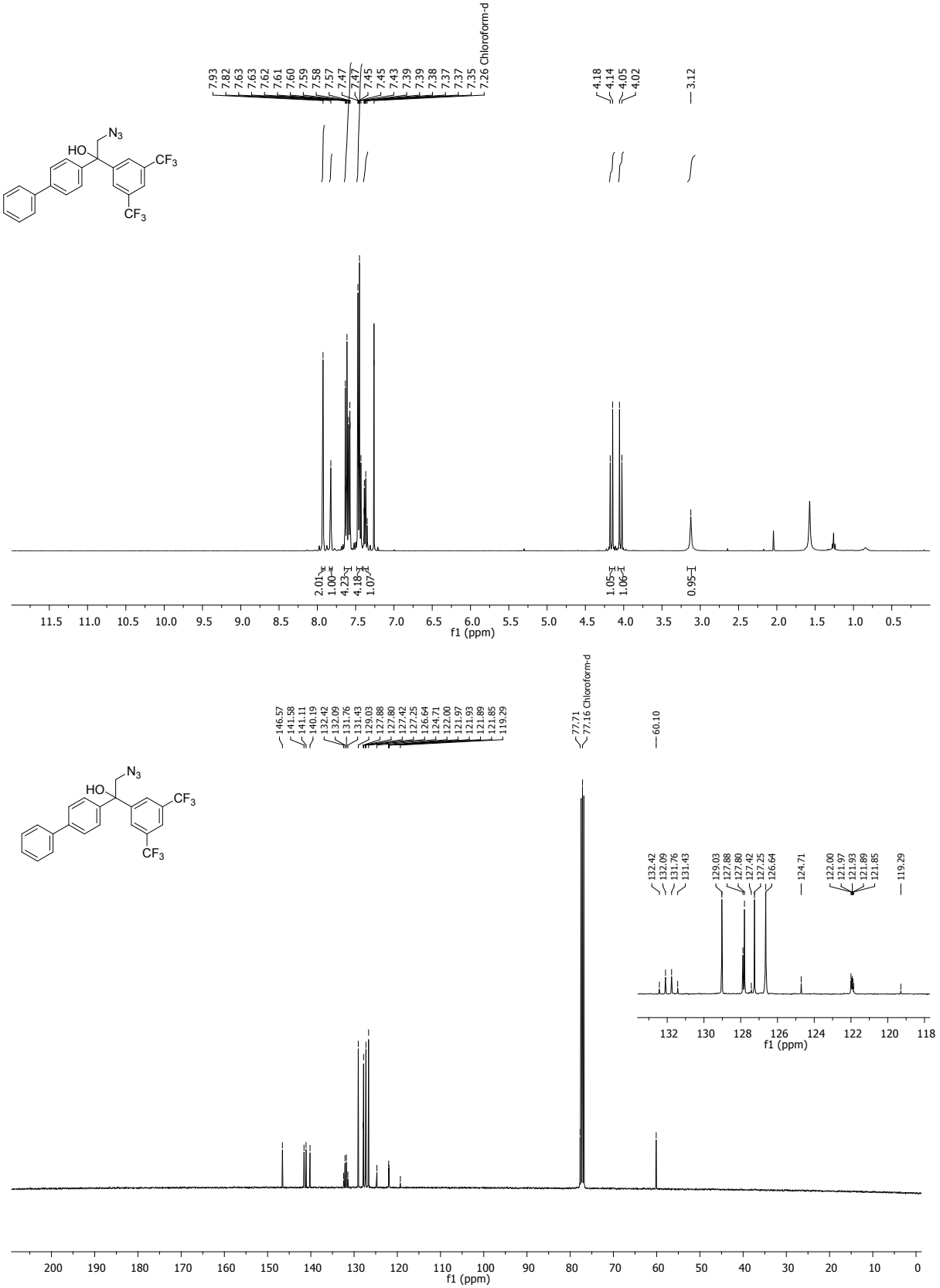


2-azido-1-(4-methoxyphenyl)ethan-1-ol **(S14)**





1-([1,1'-biphenyl]-4-yl)-2-azido-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol (S15)



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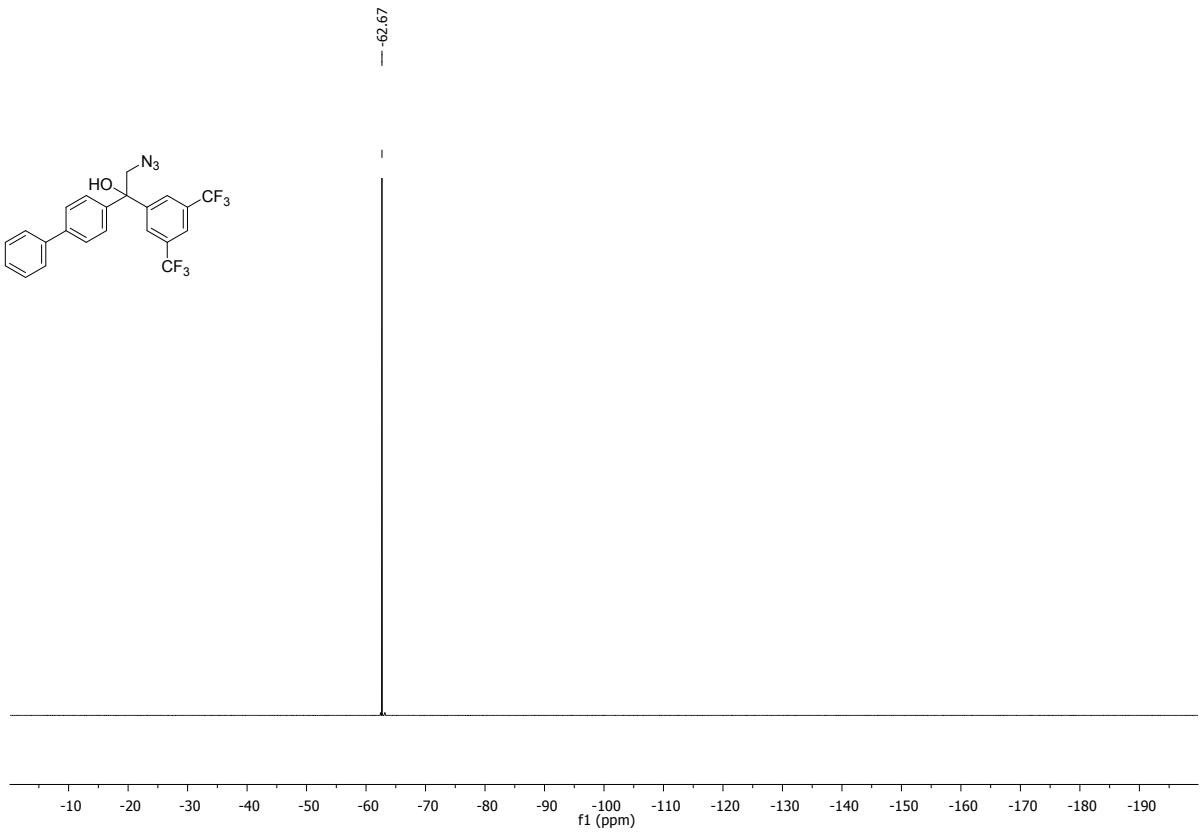
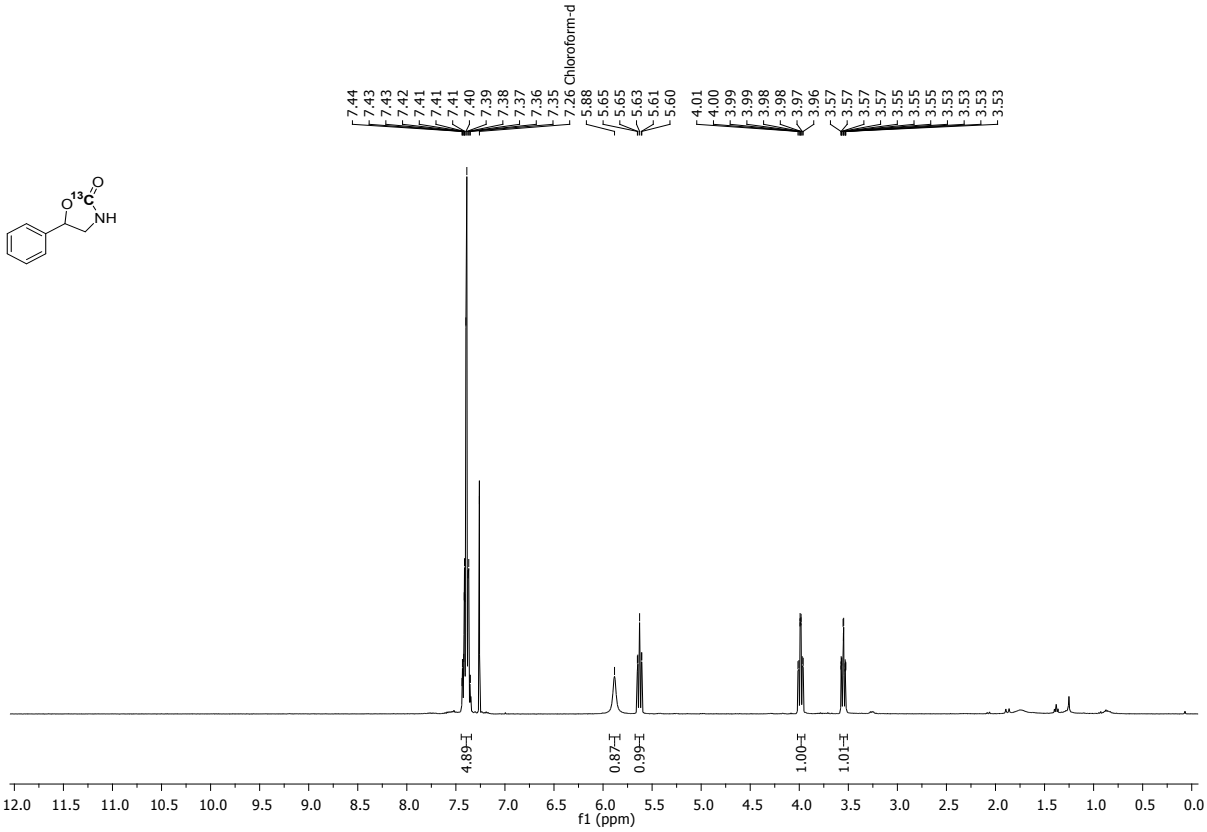
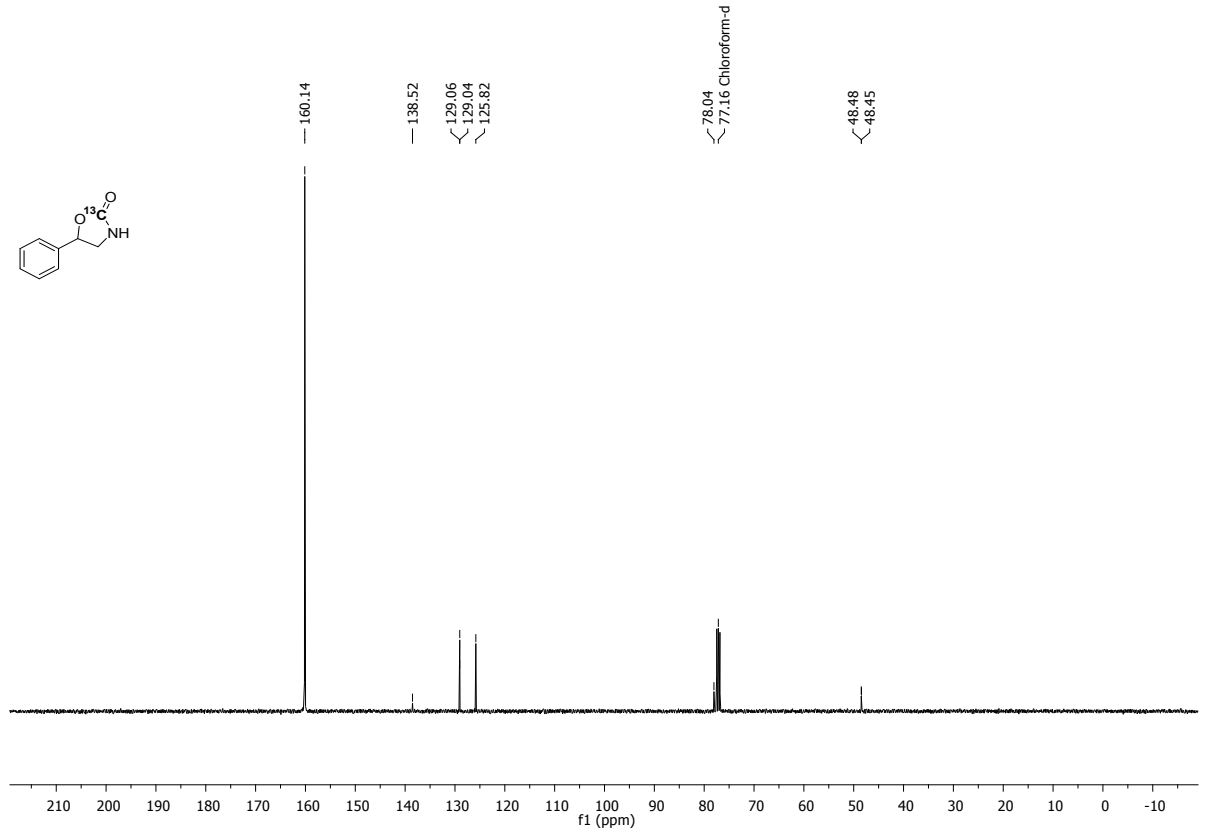
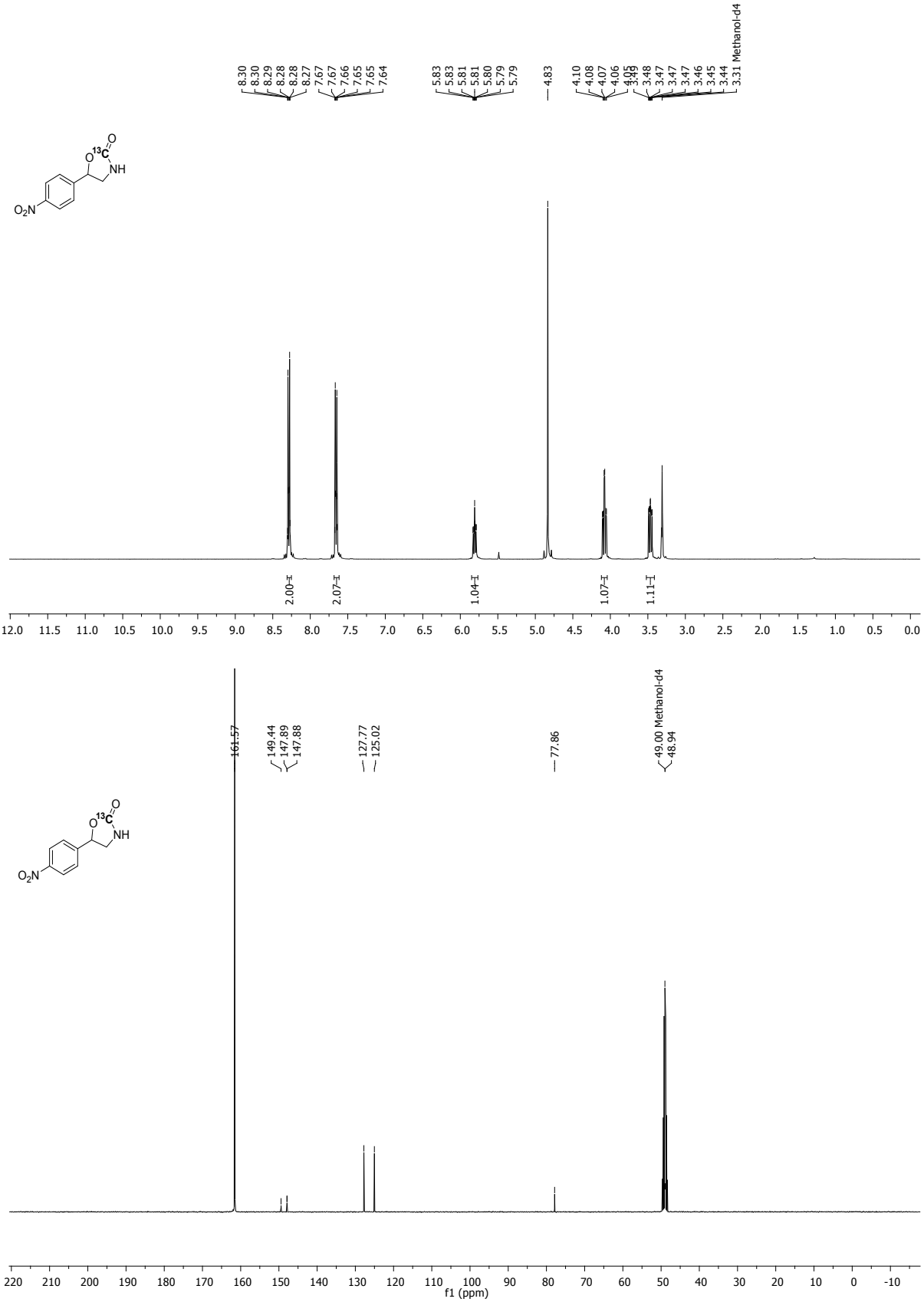

-62.67
N3
HO
CF3
CF3
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

[^{13}C] 5-phenyloxazolidine-2-one ([^{13}C]**2**)

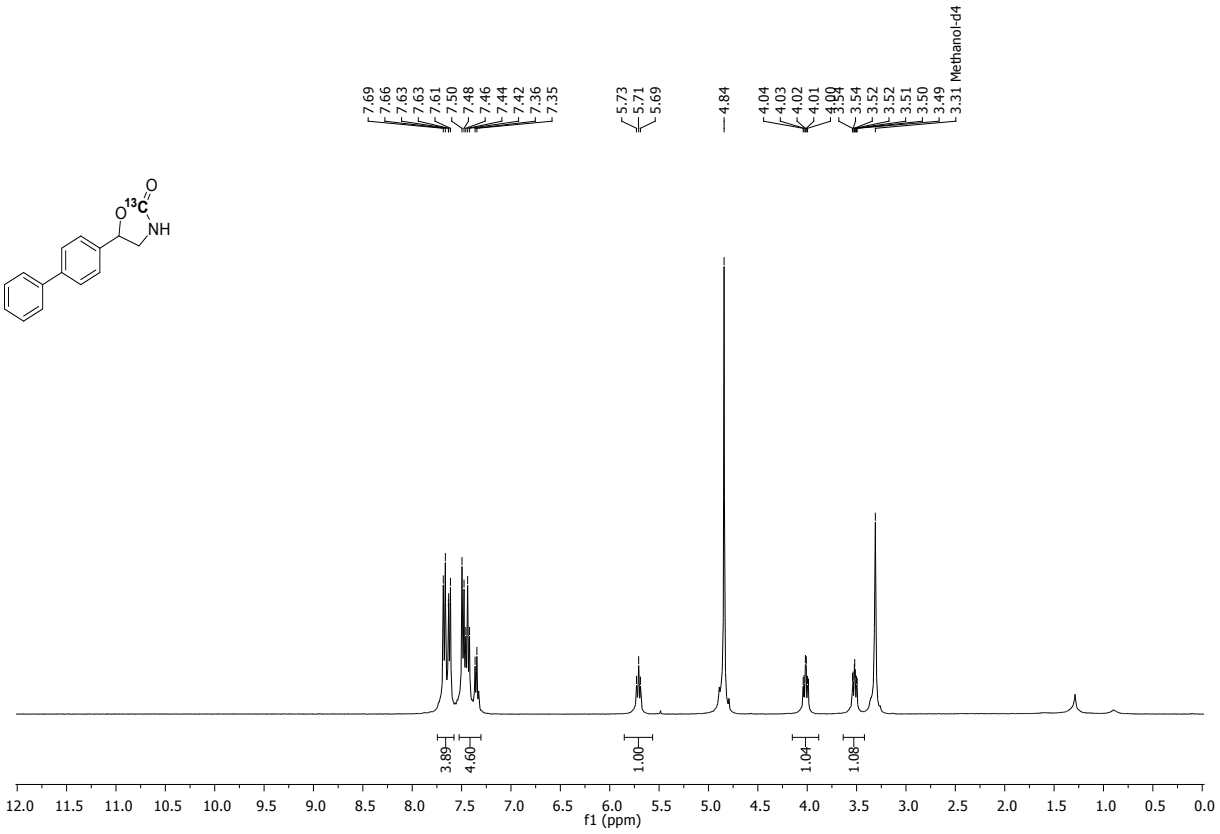


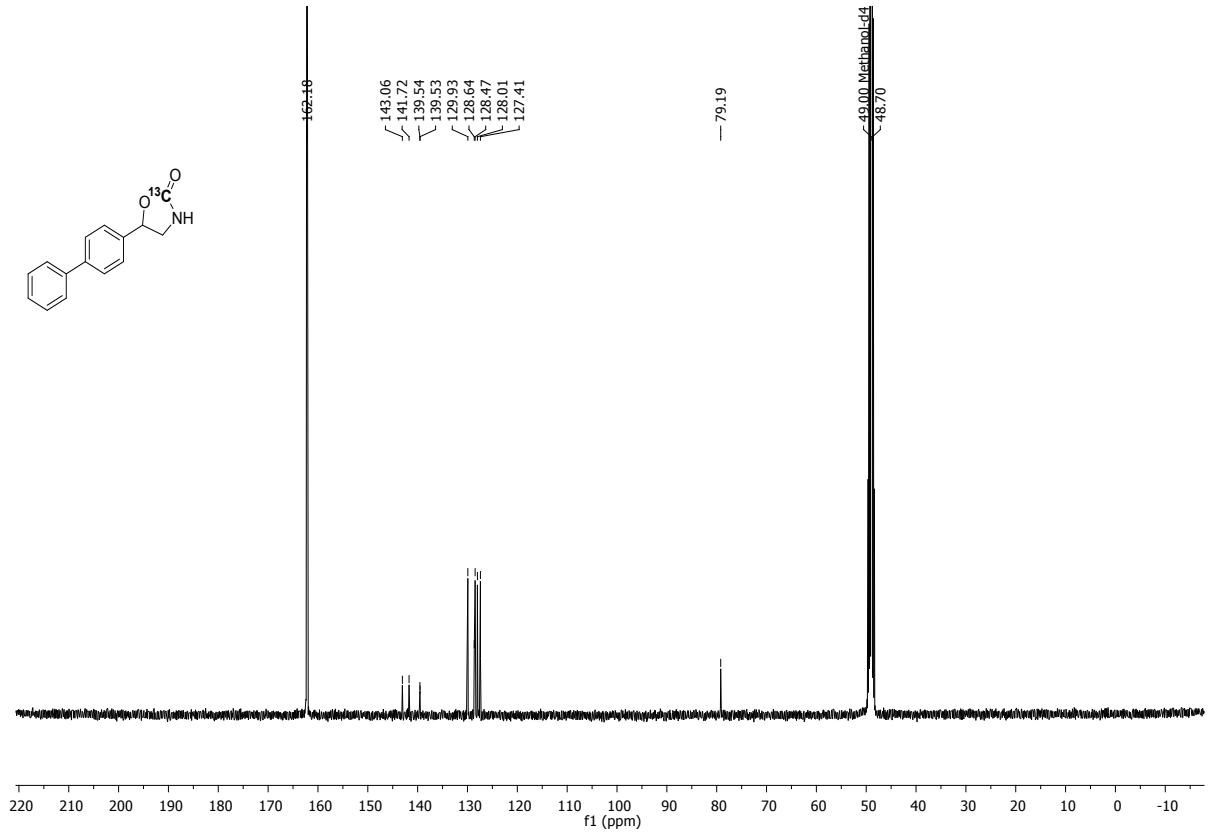


[^{13}C] 5-(4-nitrophenyl)oxazolidin-2-one ([^{13}C]**3**)

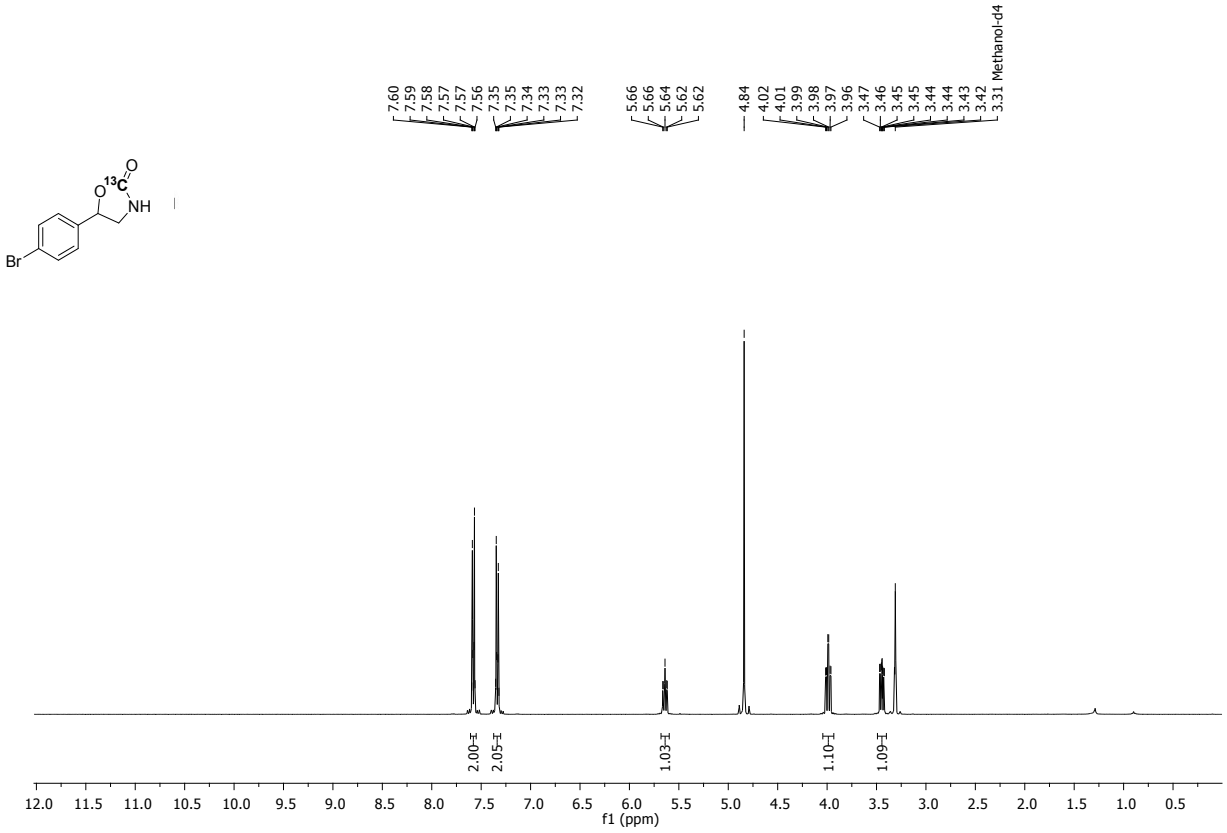


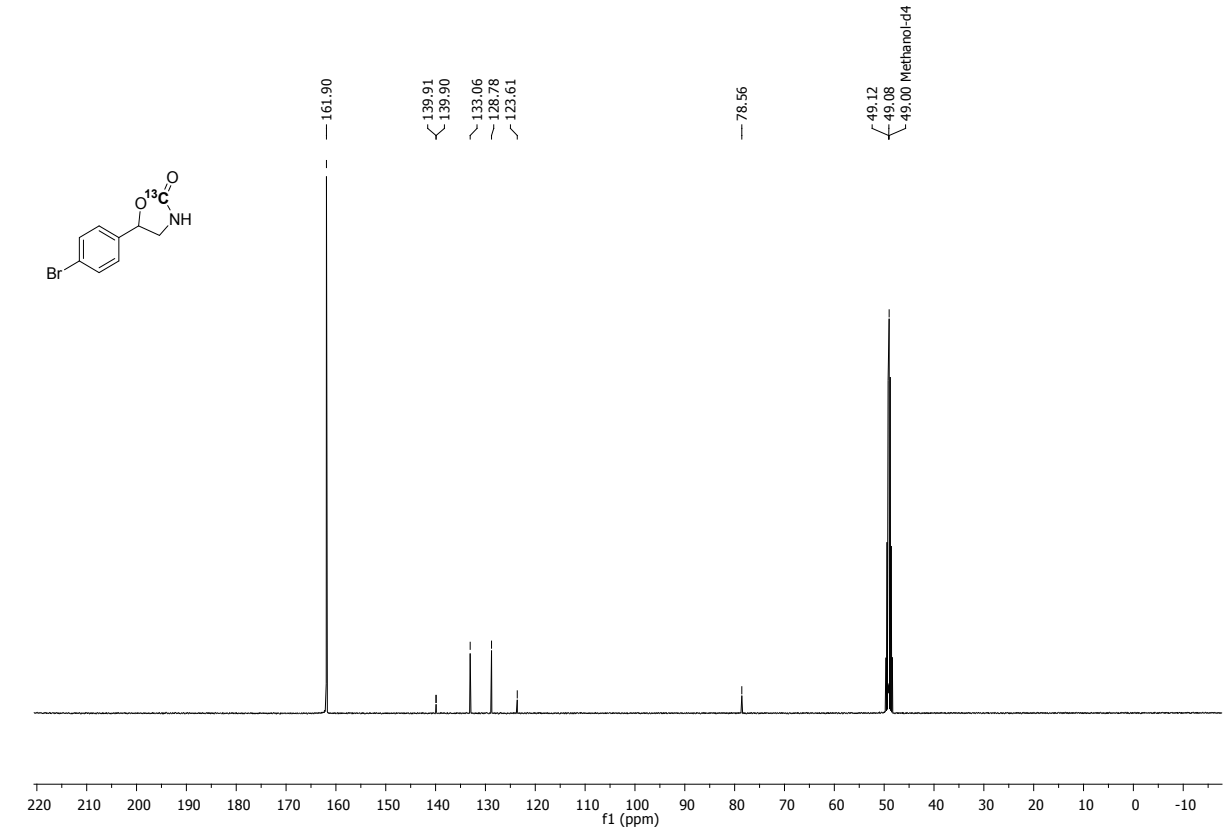
[^{13}C] 5-([1,1'-biphenyl]-4-yl)oxazolidin-2-one ([^{13}C]**4**)



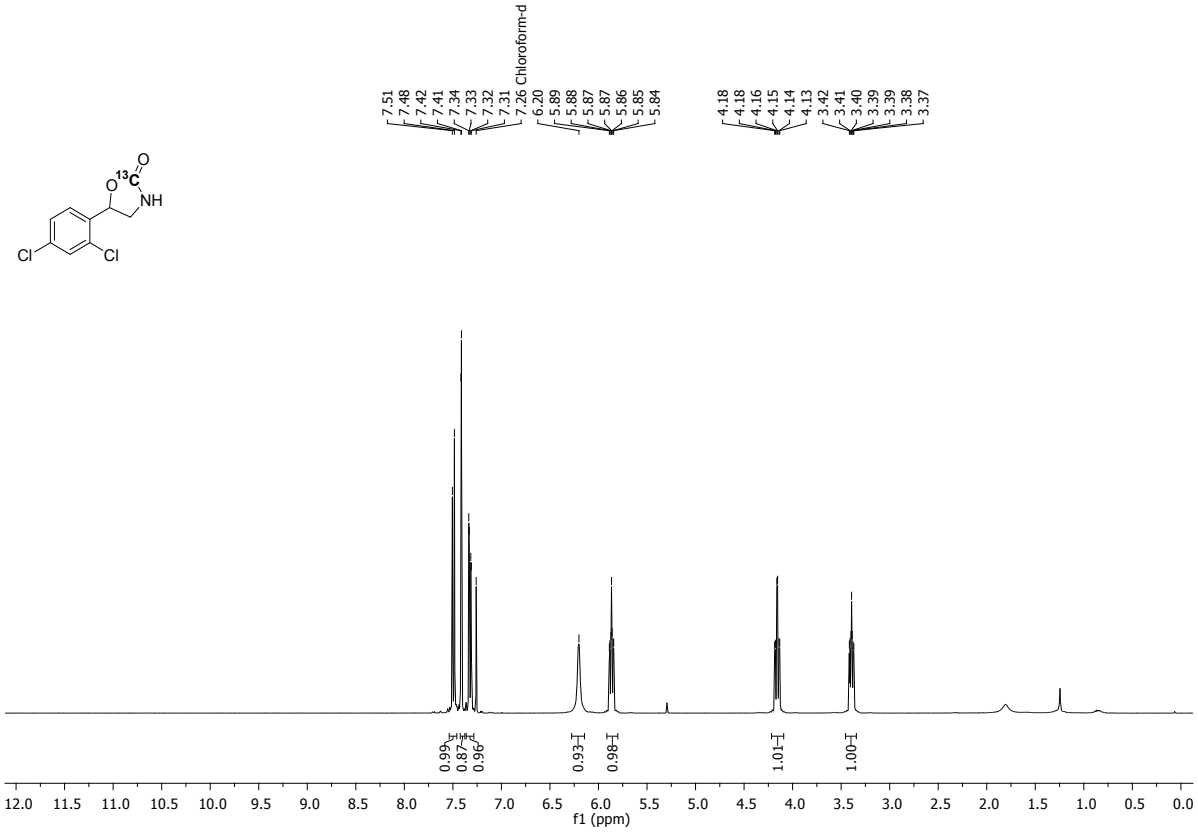


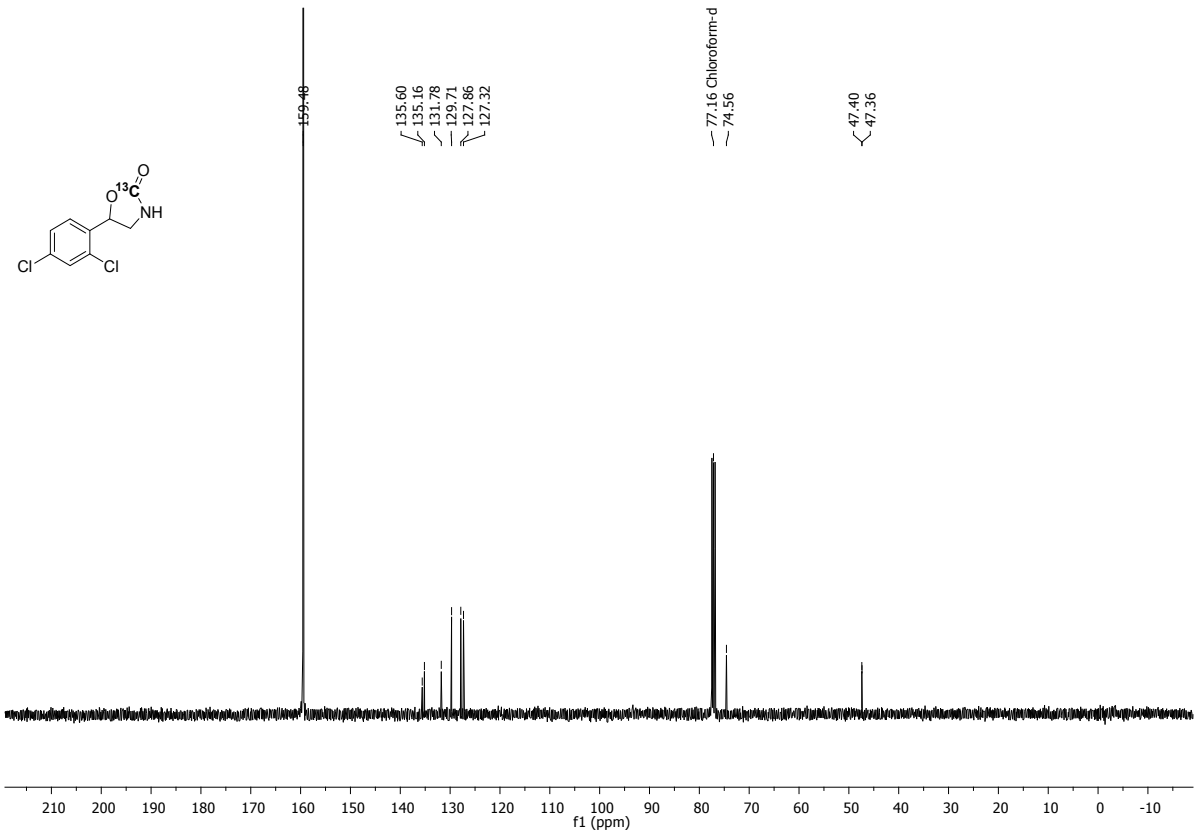
[^{13}C] 5-(4-bromophenyl)oxazolidin-2-one ([^{13}C]**5**)



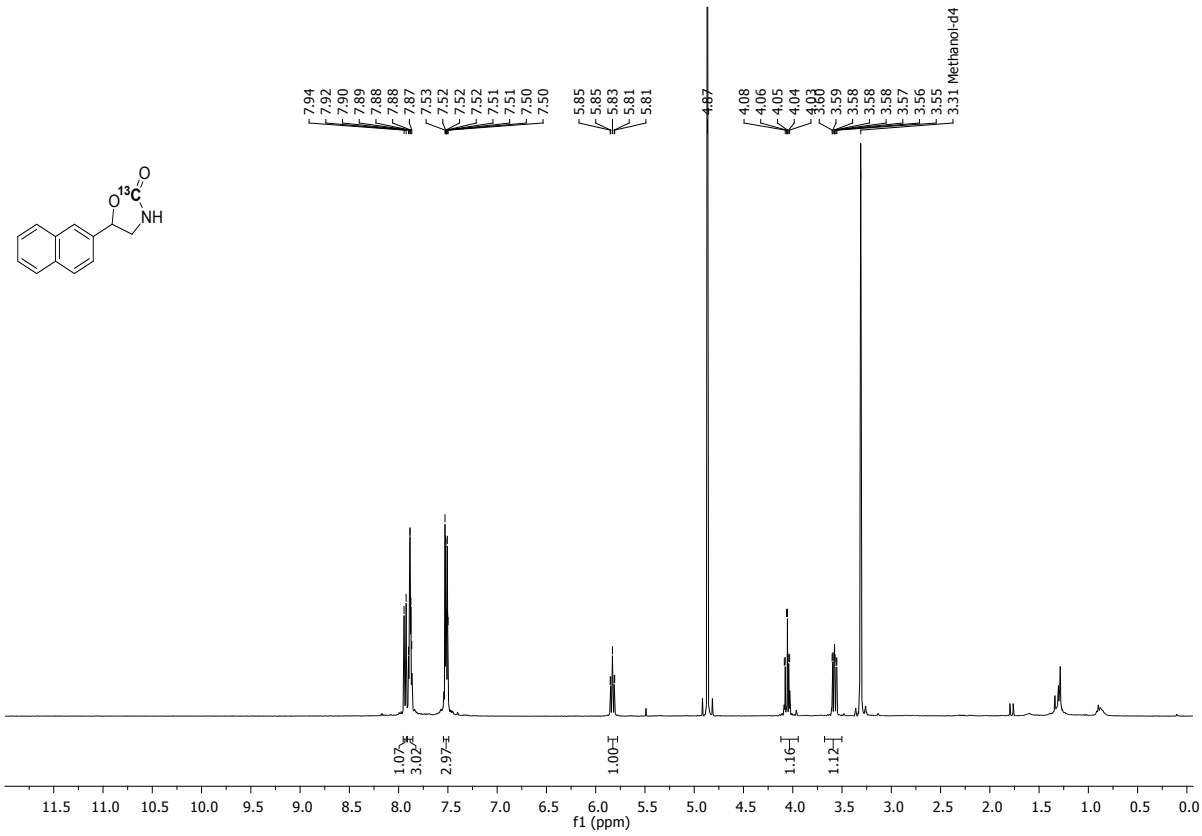


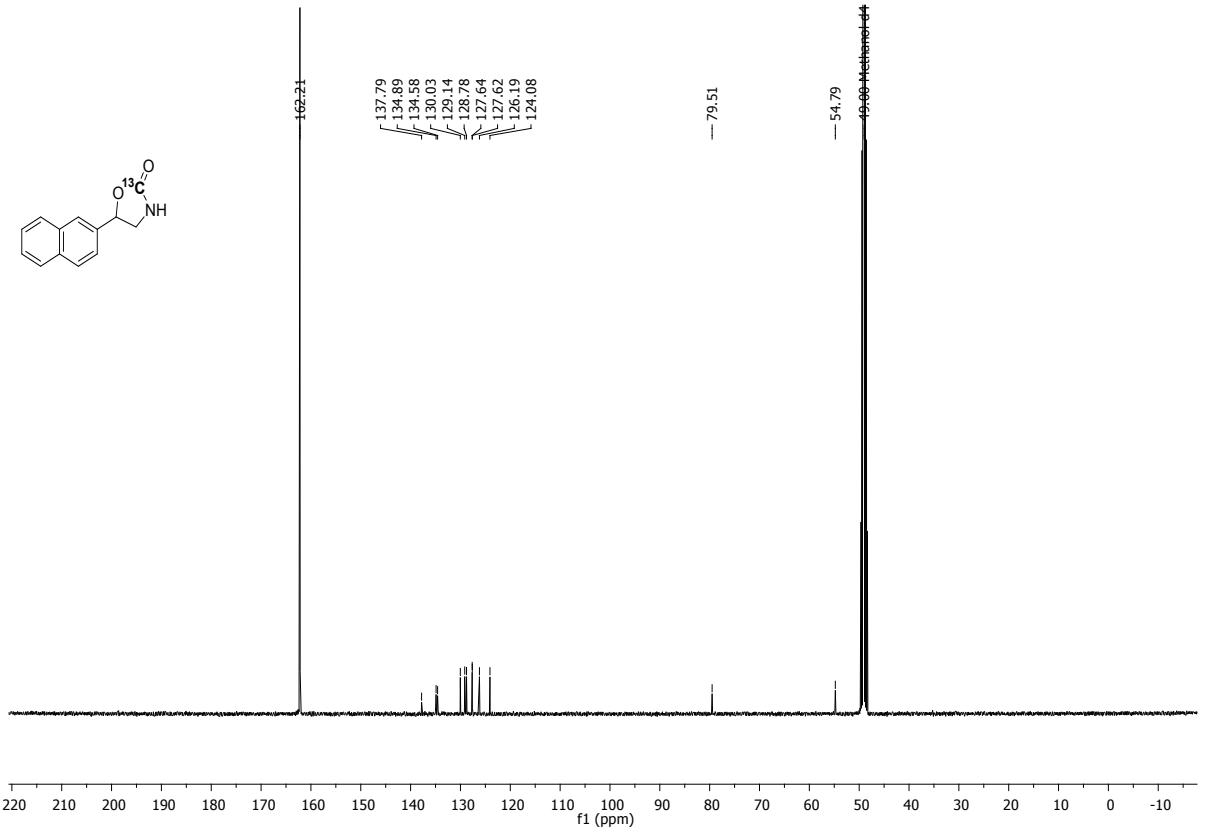
[^{13}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one ([^{13}C]**6**)



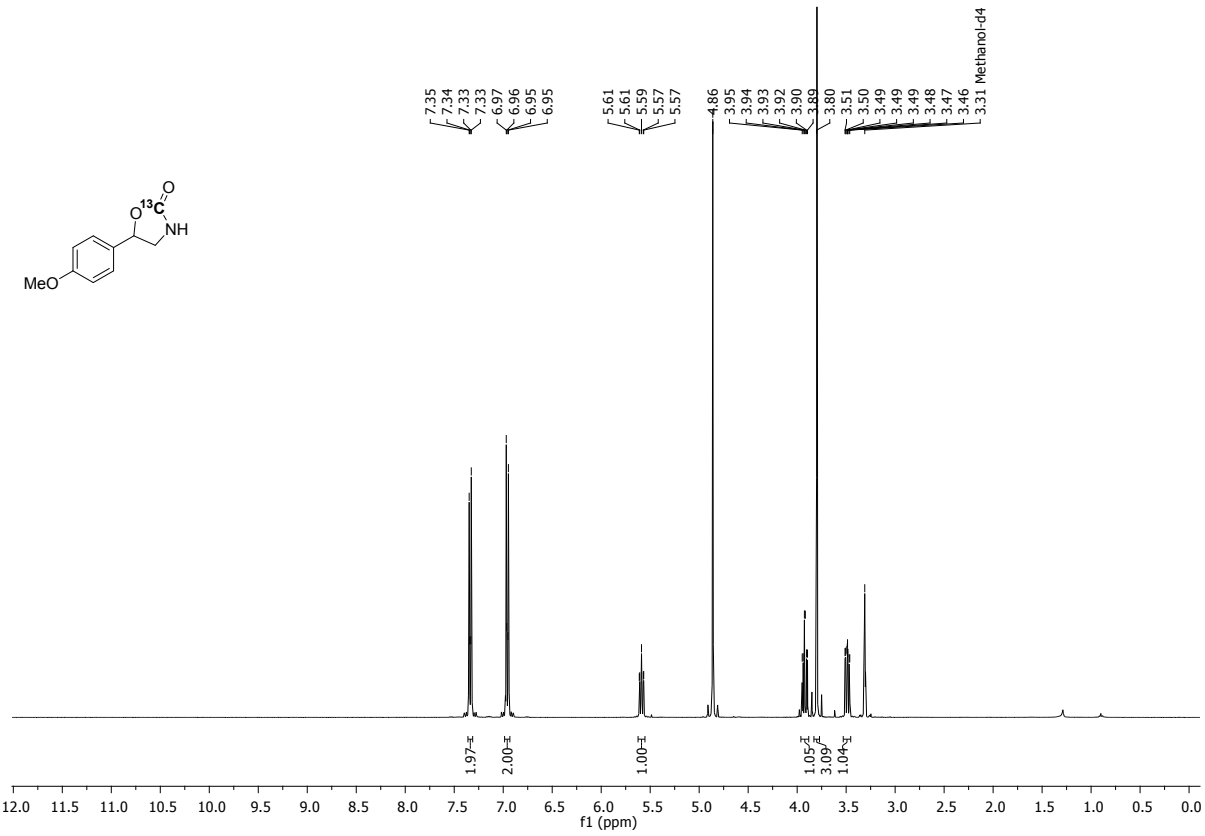


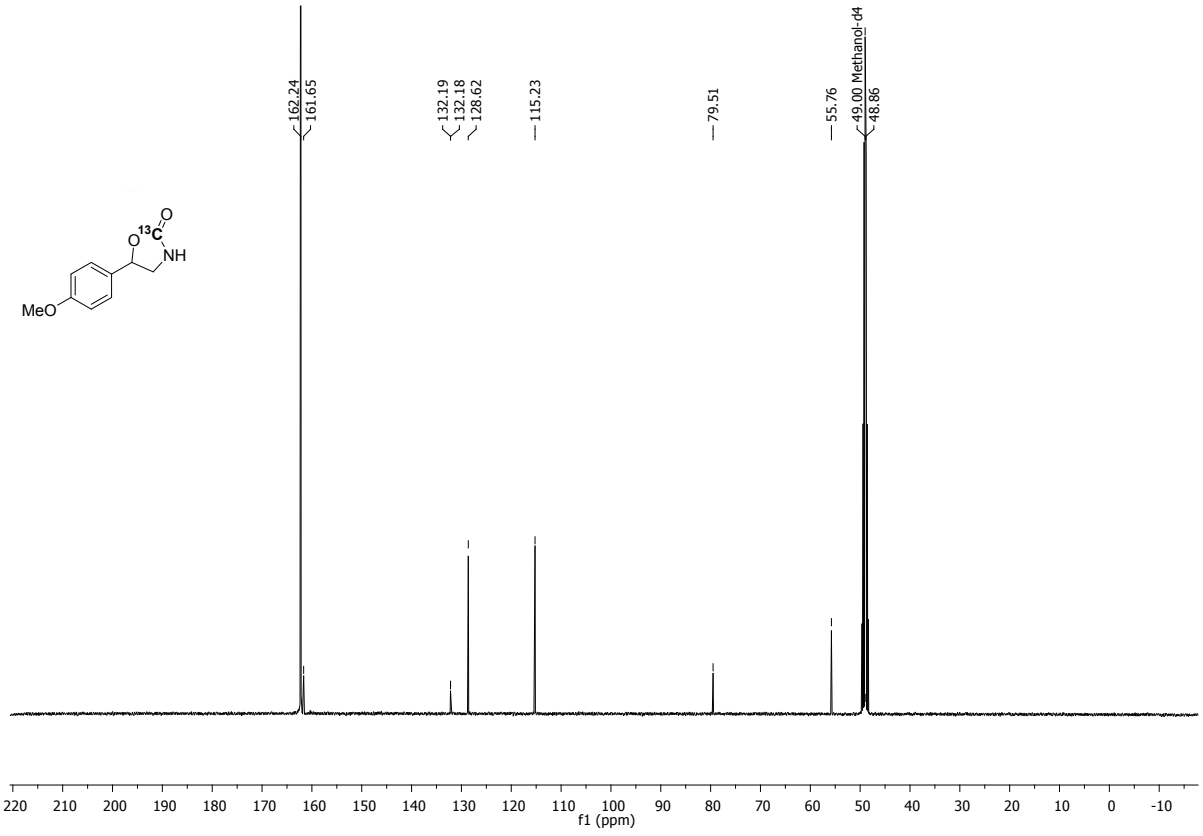
[^{13}C] 5-(naphthalen-2-yl)oxazolidin-2-one ([^{13}C]**7**)



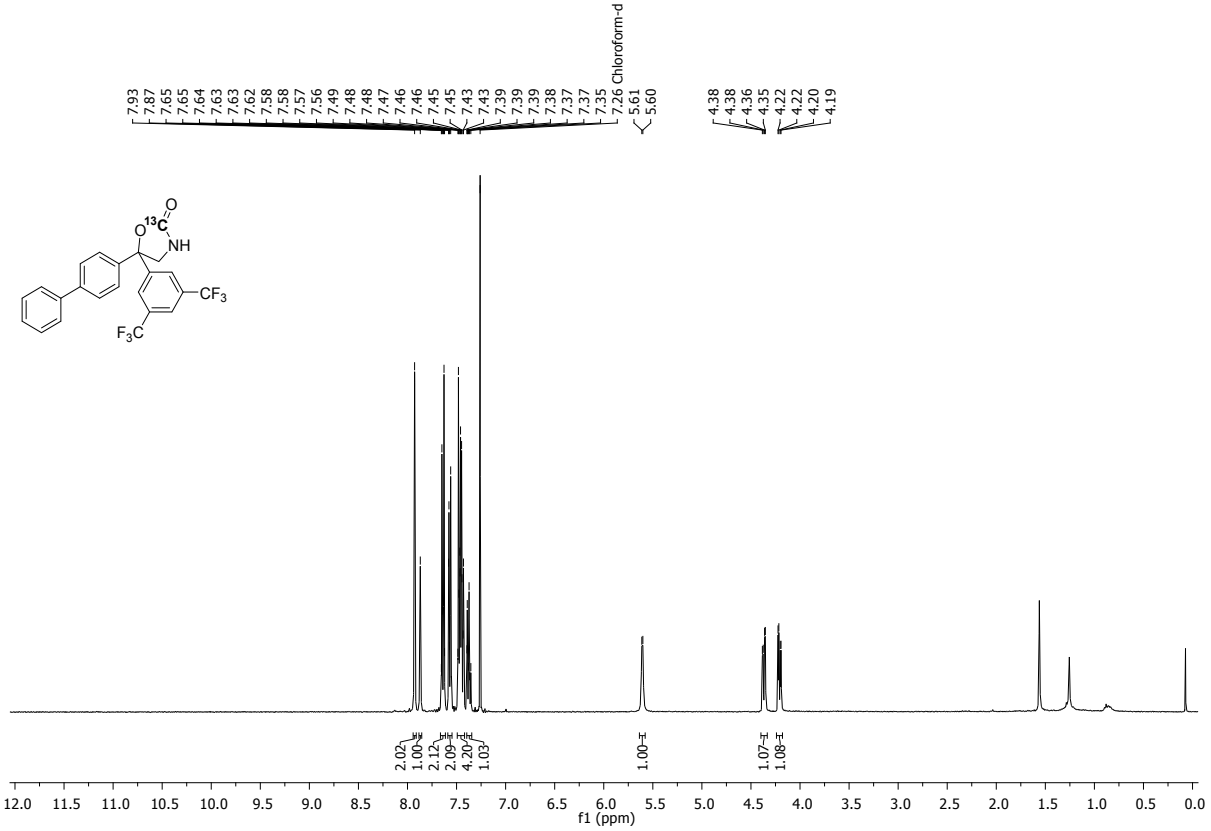


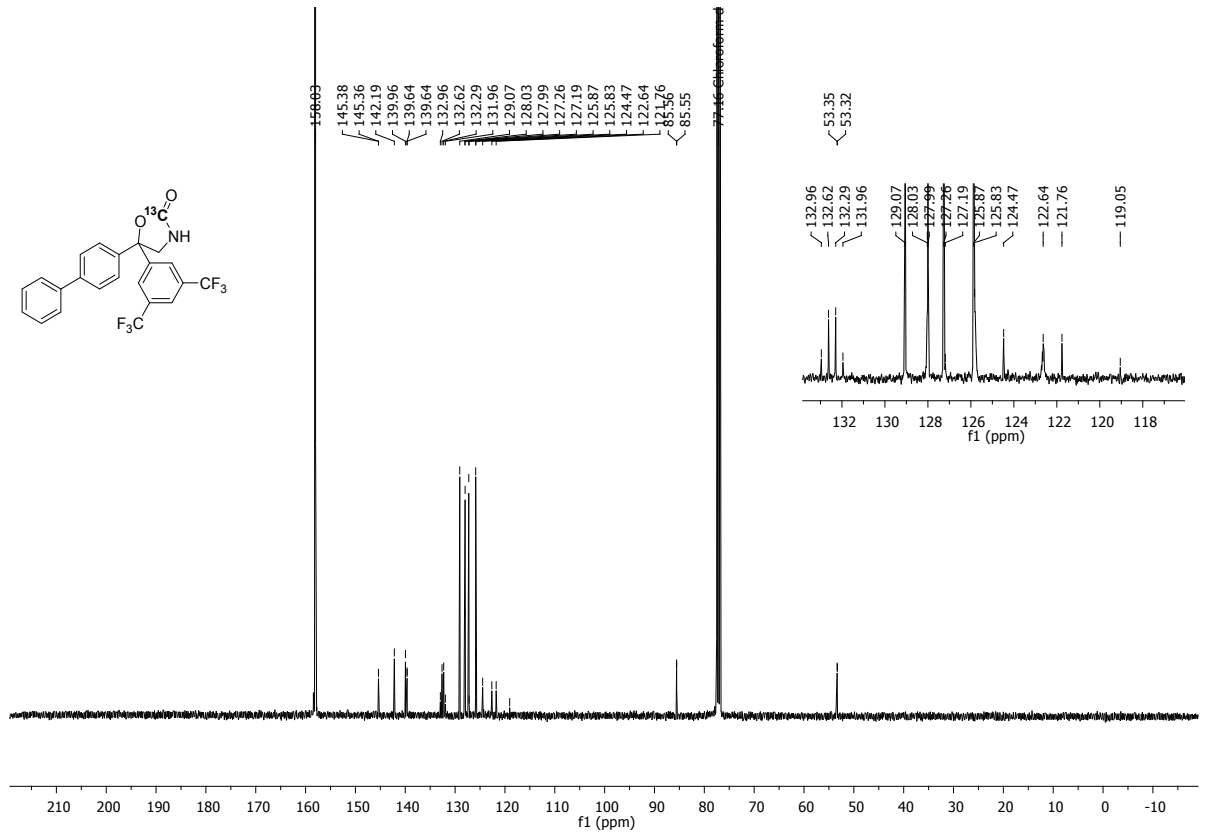
***[^{13}C] 5-(4-methoxyphenyl)oxazolidin-2-one* ([^{13}C]8)**

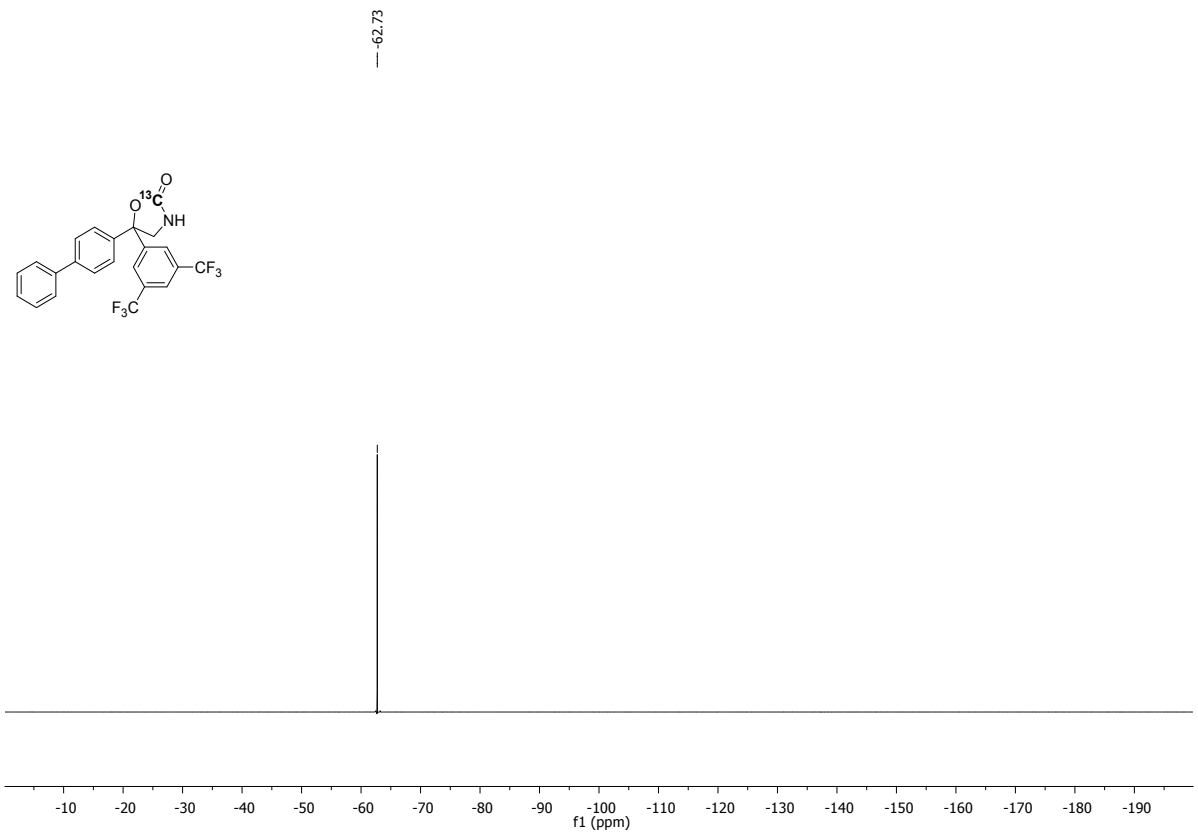




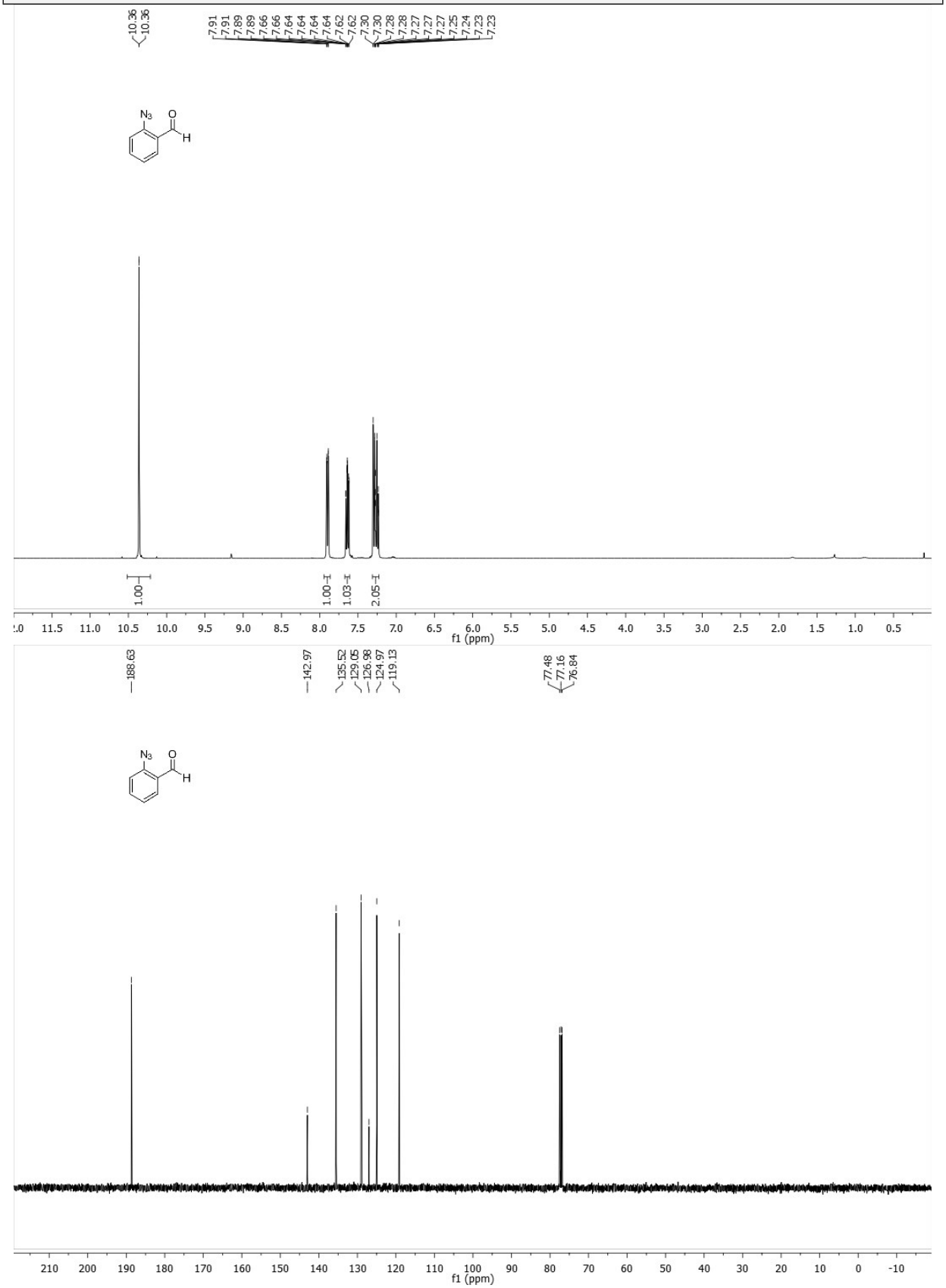
[^{13}C] 5-([1,1'-biphenyl]-4-yl)-5-(3,5-bis(trifluoromethyl)phenyl)oxazolidin-2-one ([^{13}C]9)



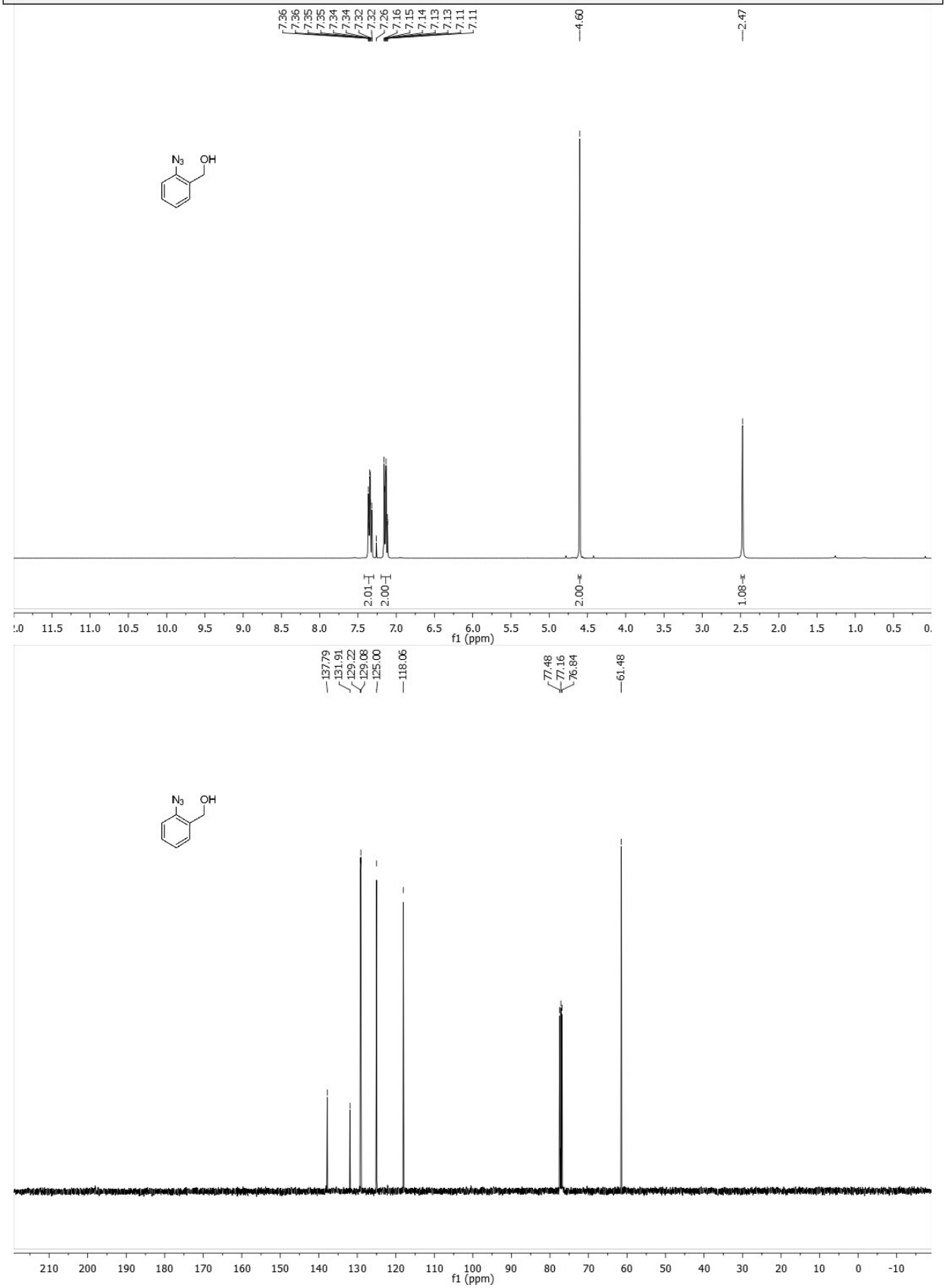



-62.73
O
13C
O
NH
CF3
F3C
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

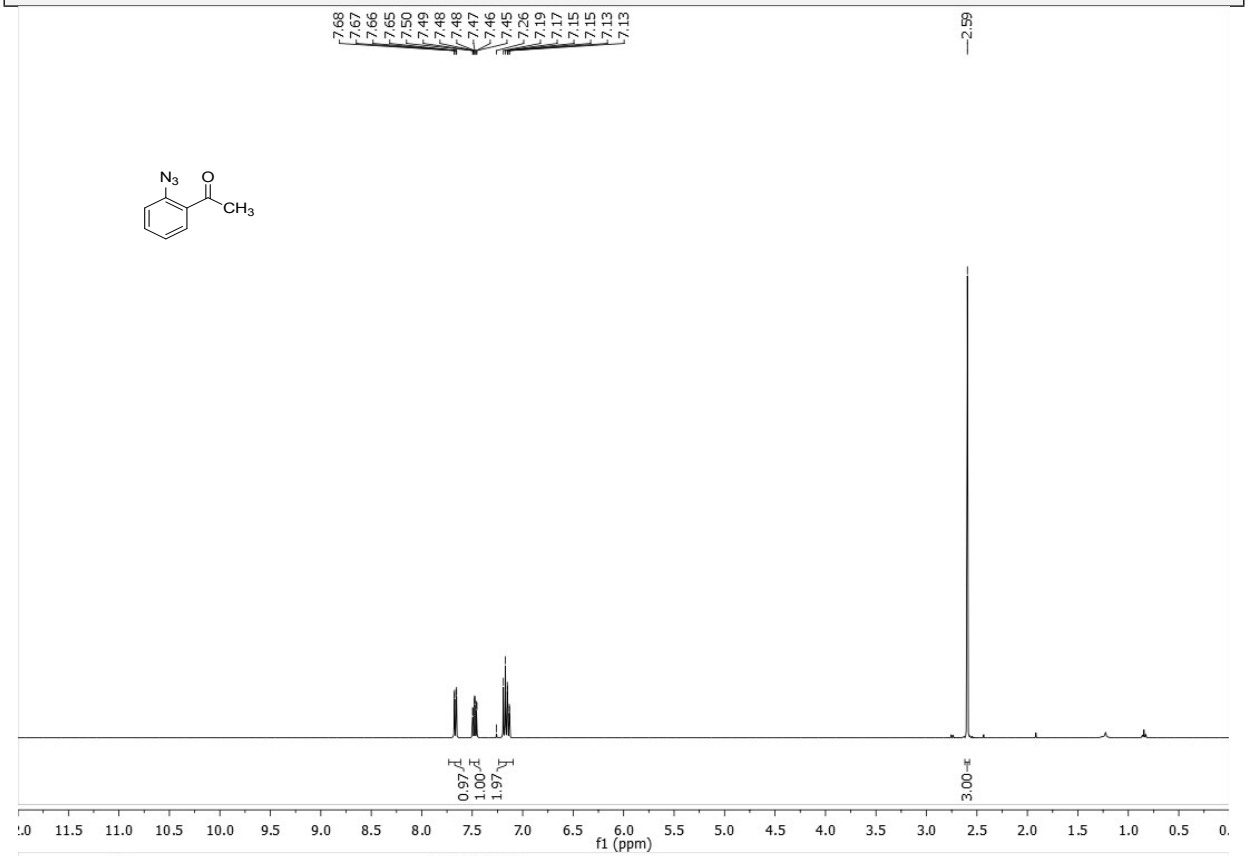
2-azidobenzaldehyde (S16)

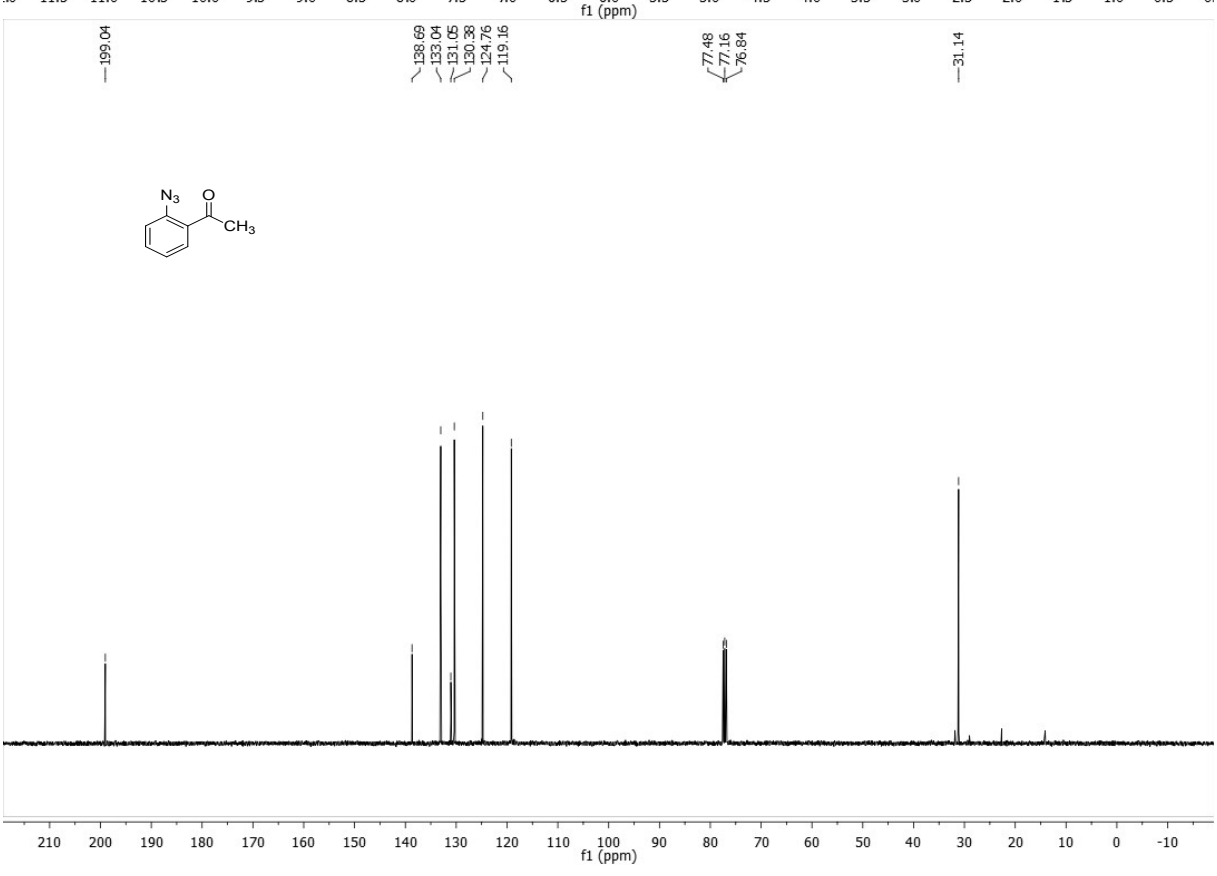


(2-azidophenyl)metanol (S17)

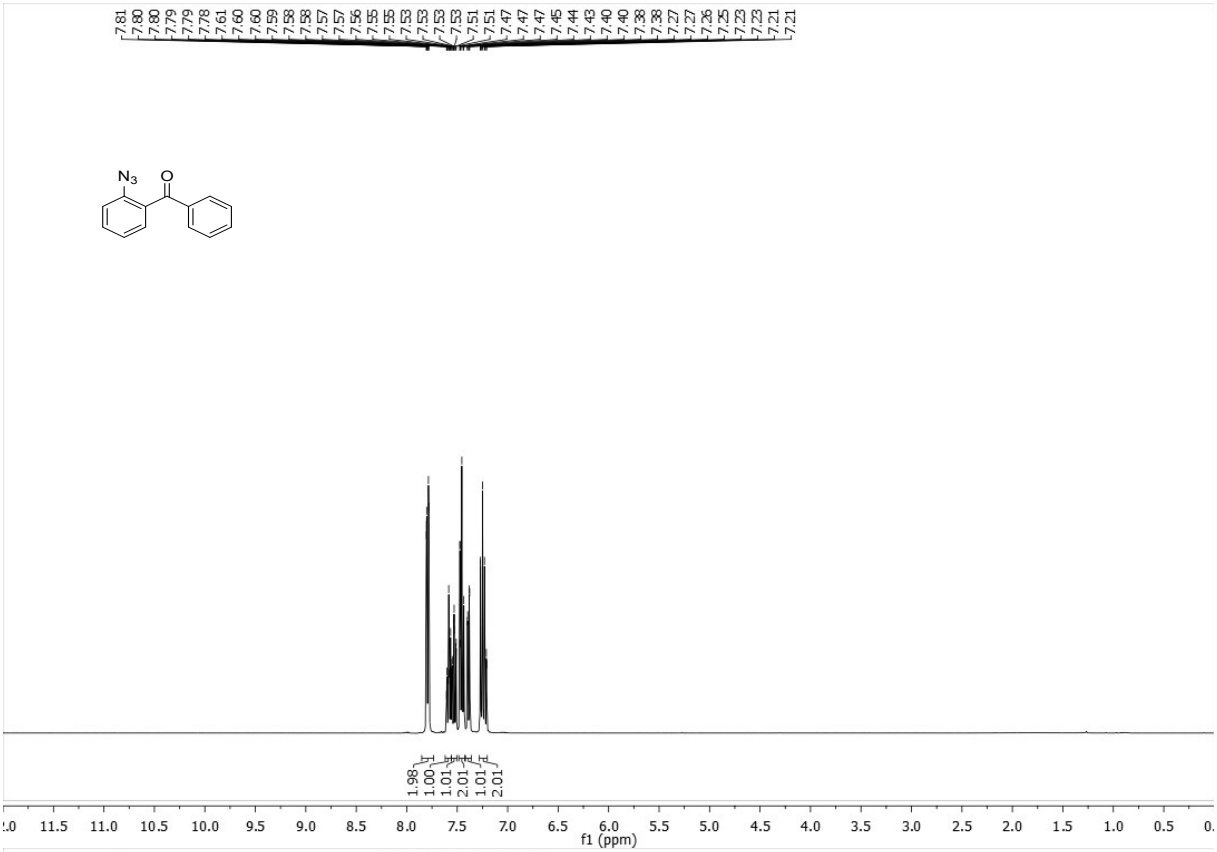


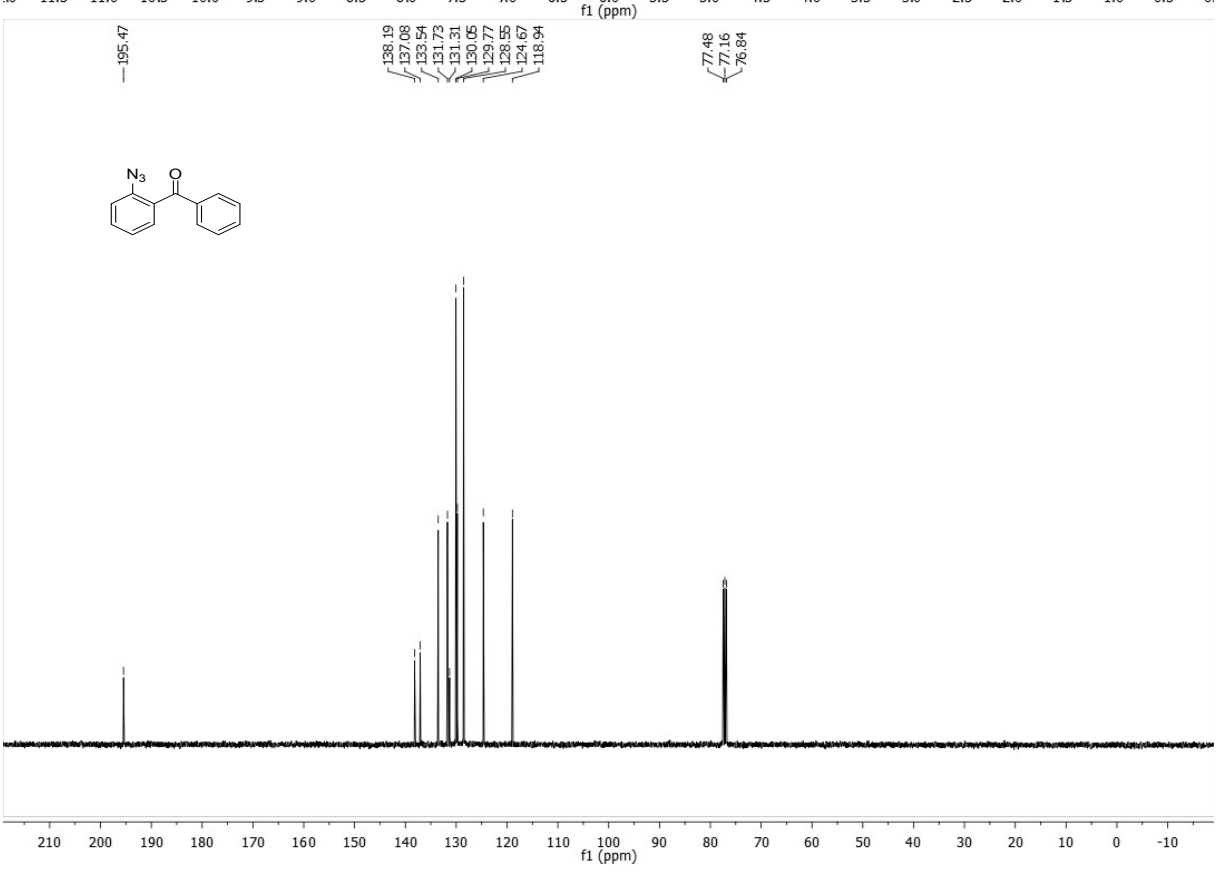
1-(2-azidophenyl)ethan-1-one (S18)



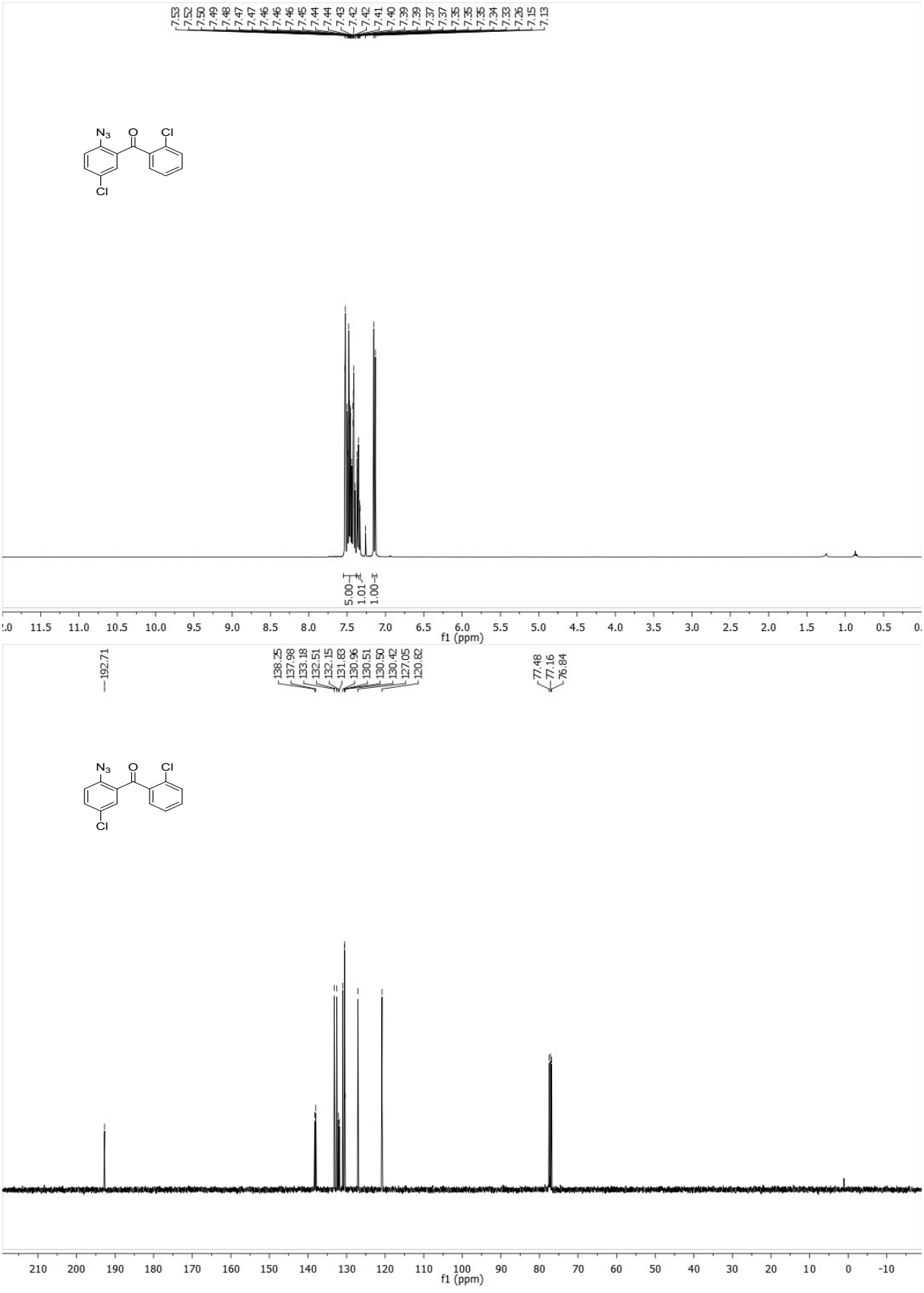


(2-azidophenyl)(phenyl)methanone (S19)

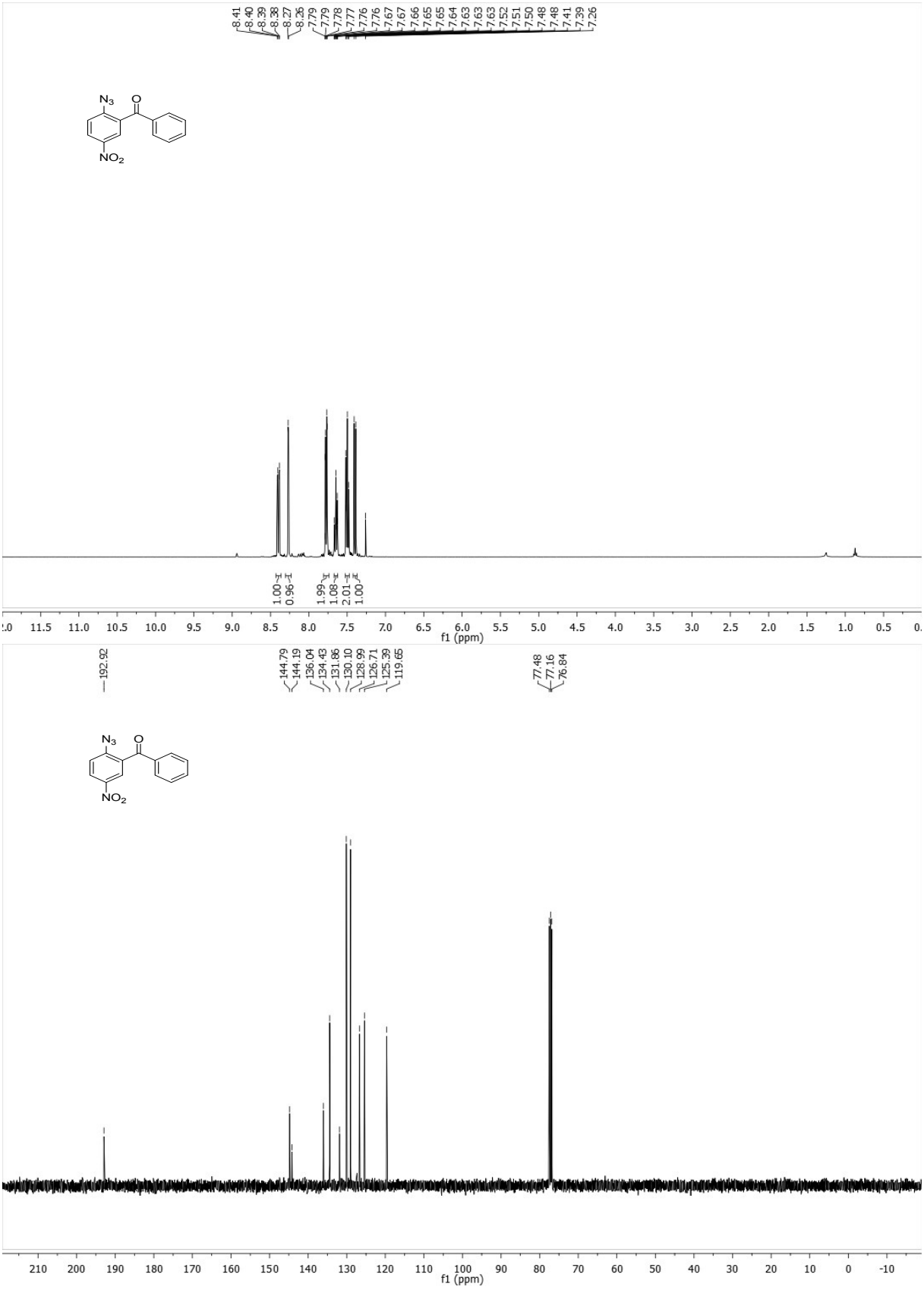




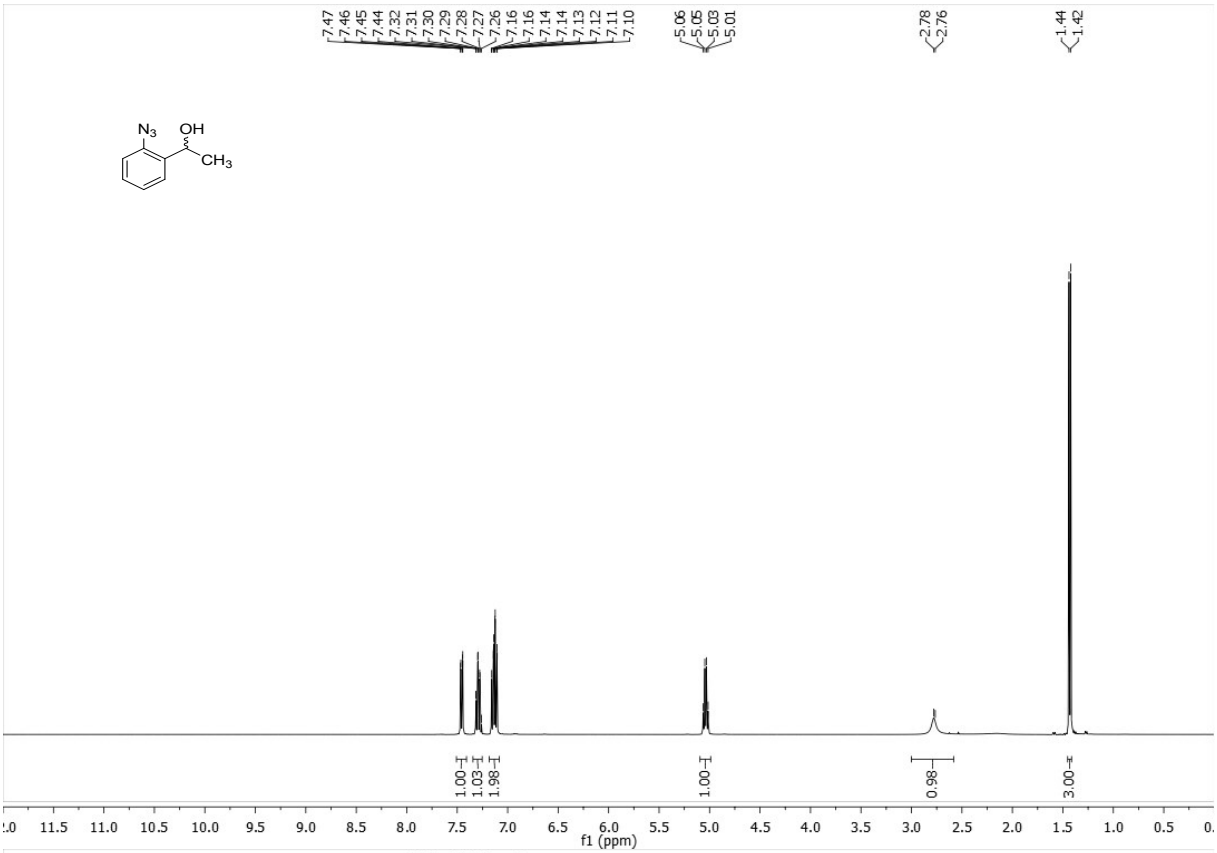
***(2-azido-5-chlorophenyl)(2-chlorophenyl)methanone* (S20)**

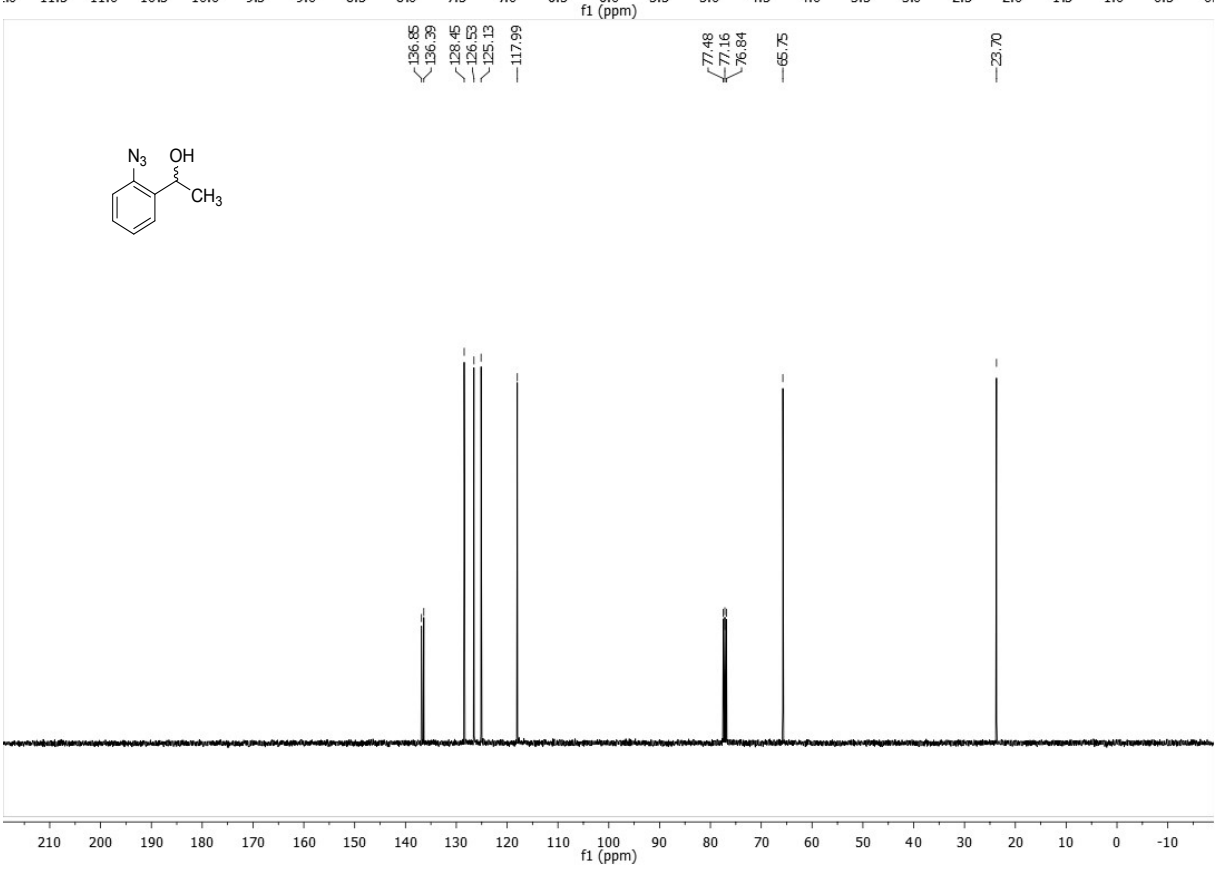


***(2-azido-5-nitrophenyl)(phenyl)methanone* (S21)**

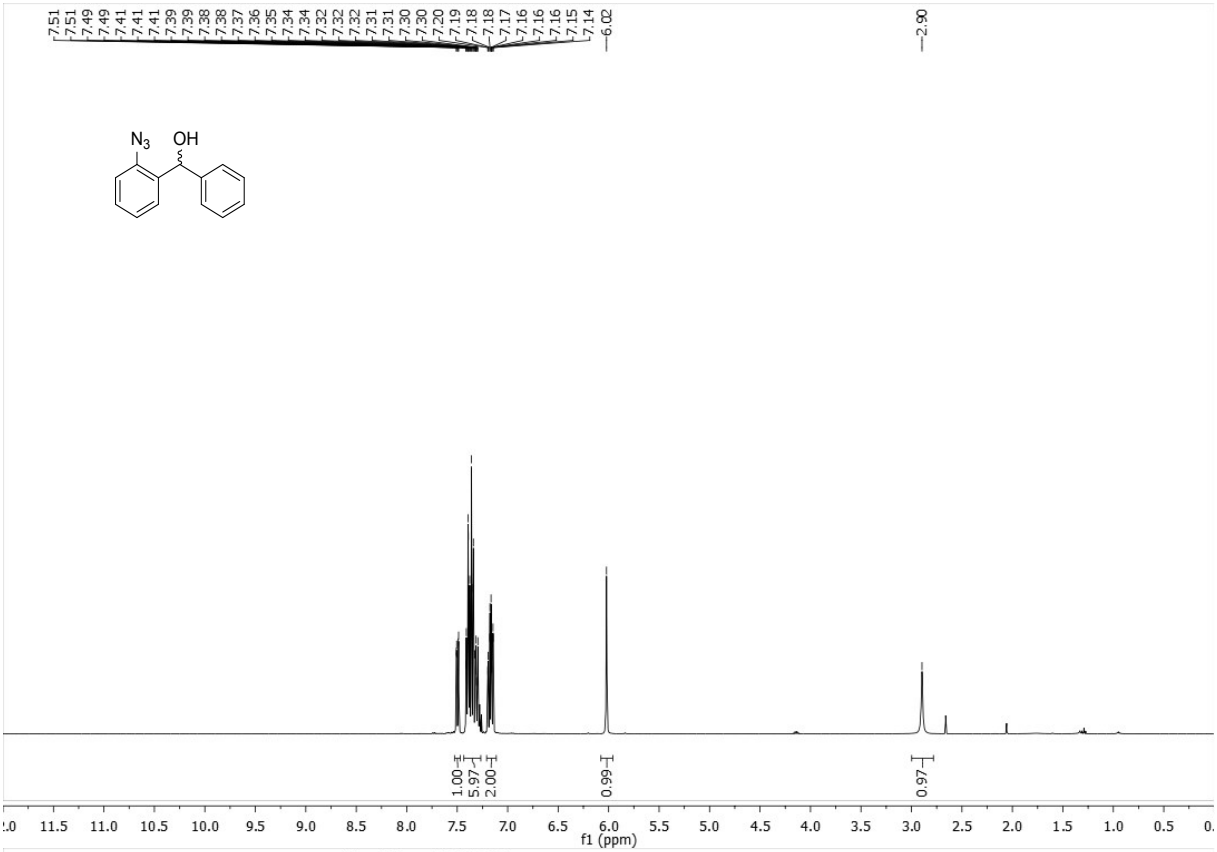


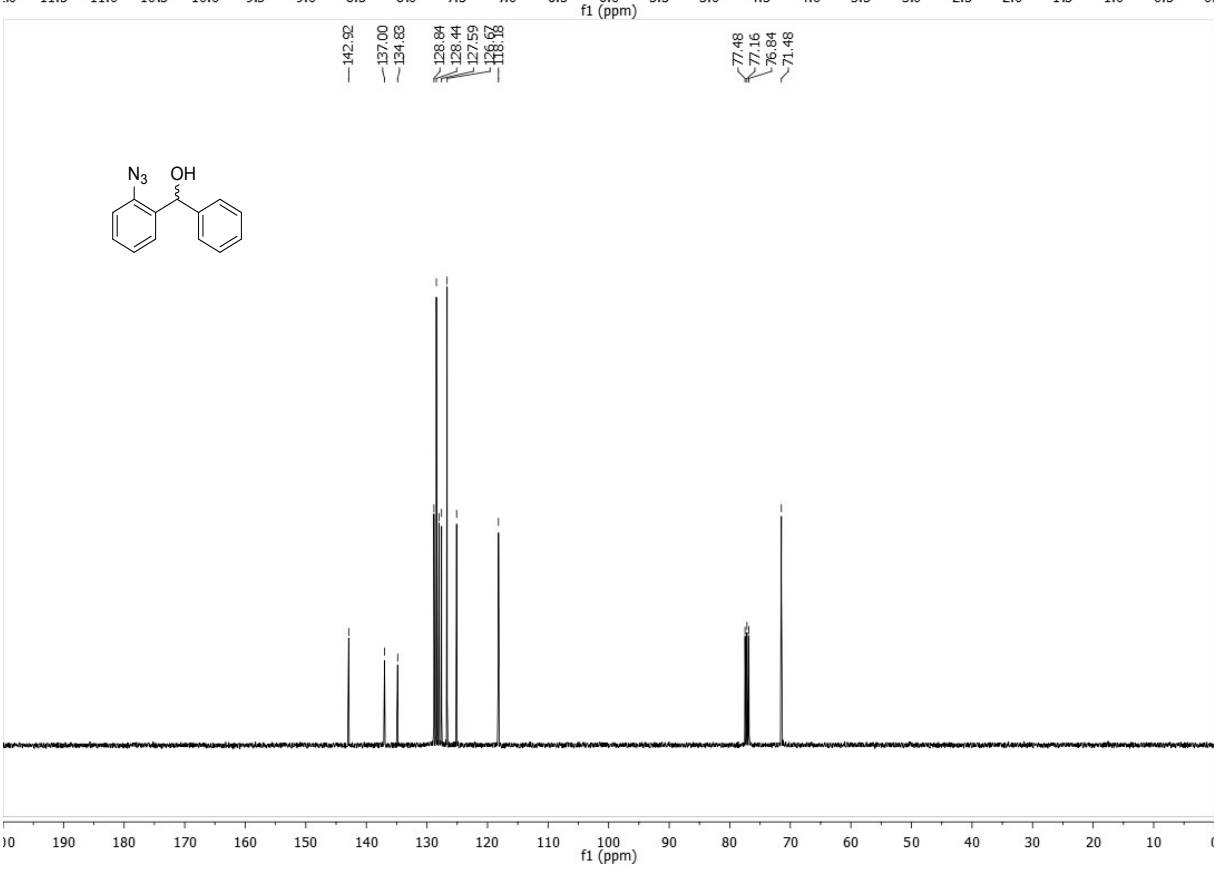
1-(2-azidophenyl)ethan-1-ol (S22)



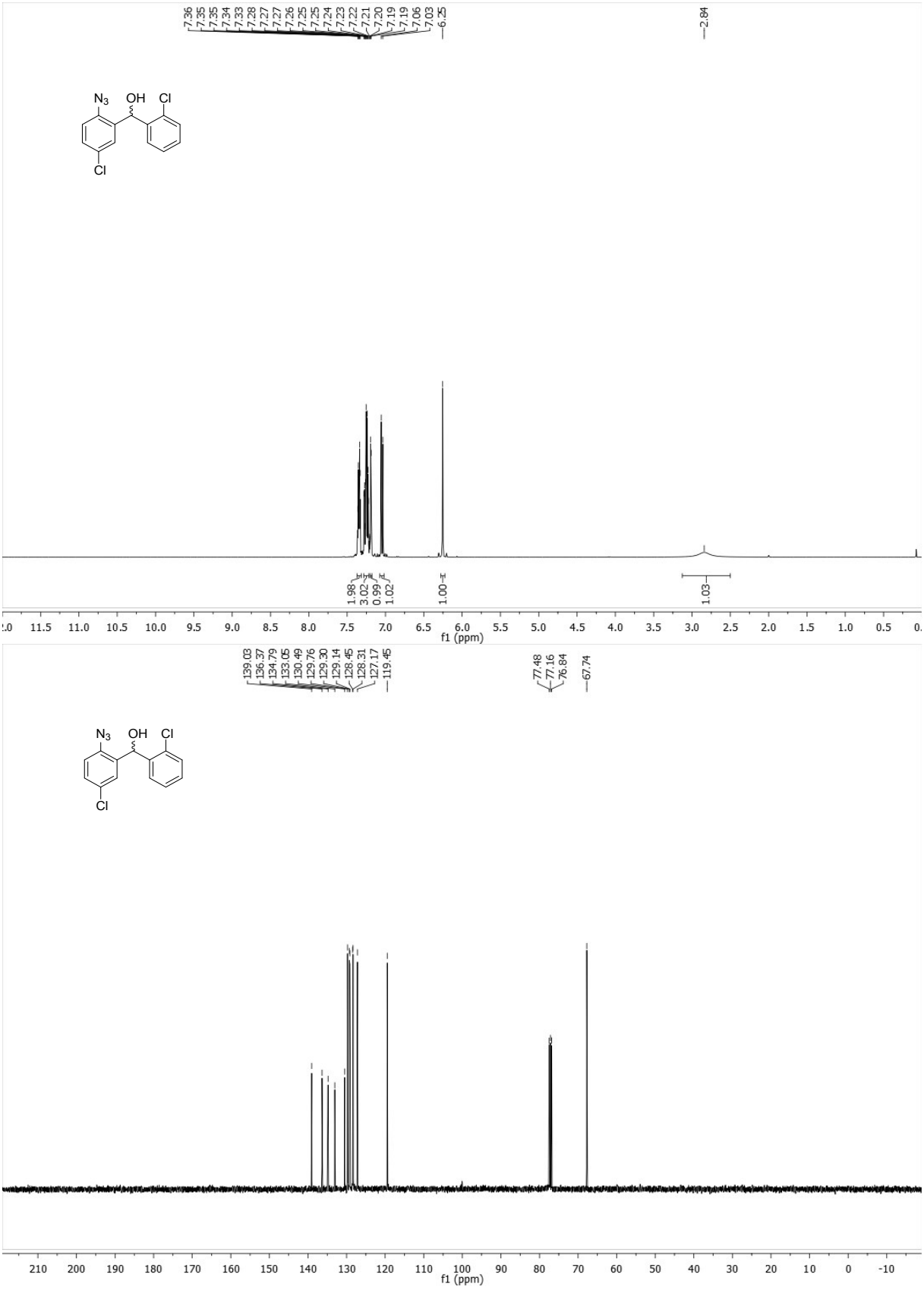


***(2-azidophenyl)(phenyl)methanol* (S23)**

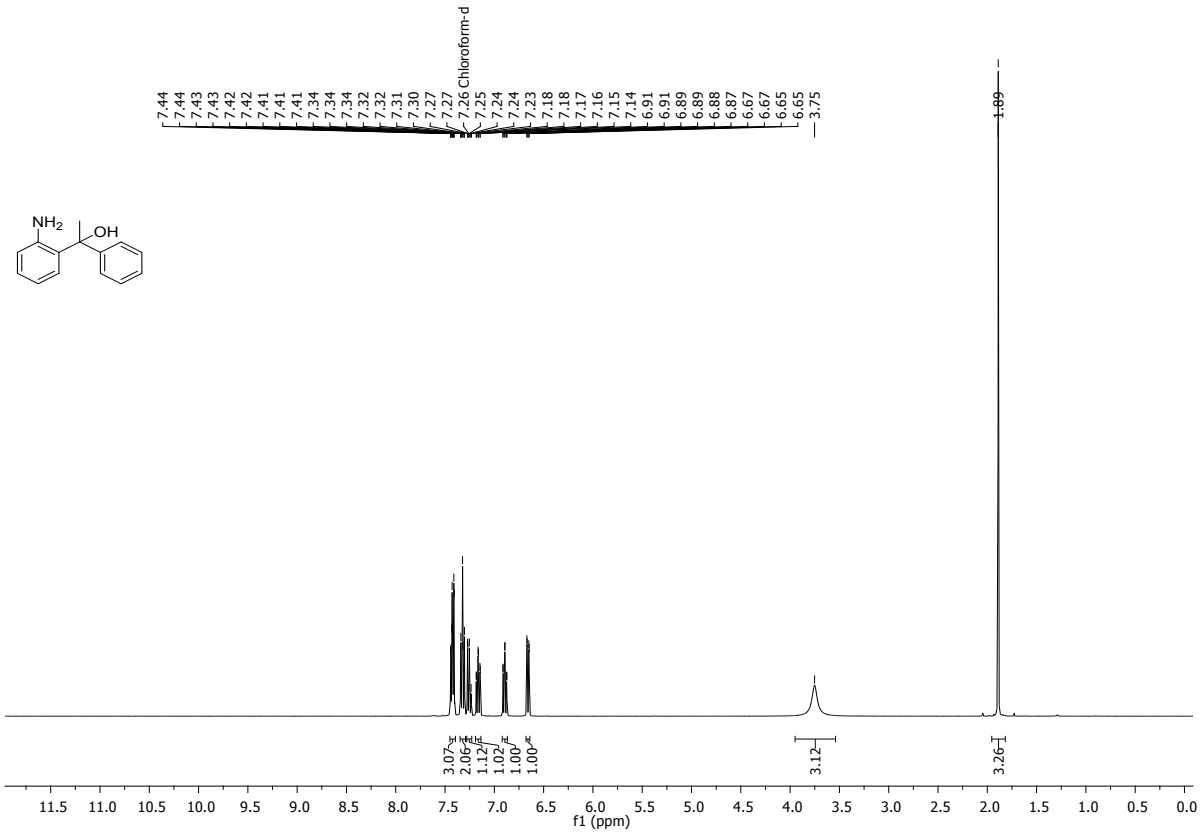


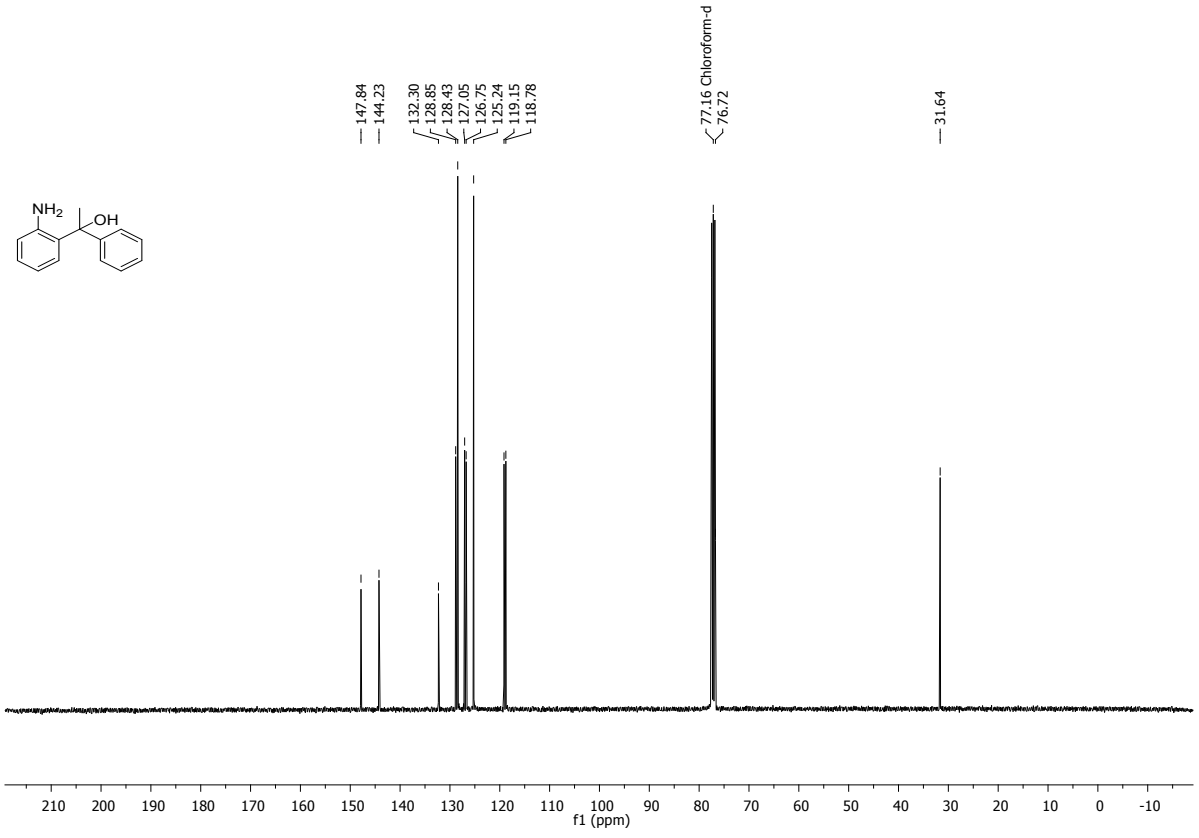


***(2-azido-5-chlorophenyl)(2-chlorophenyl)methanol* (S24)**

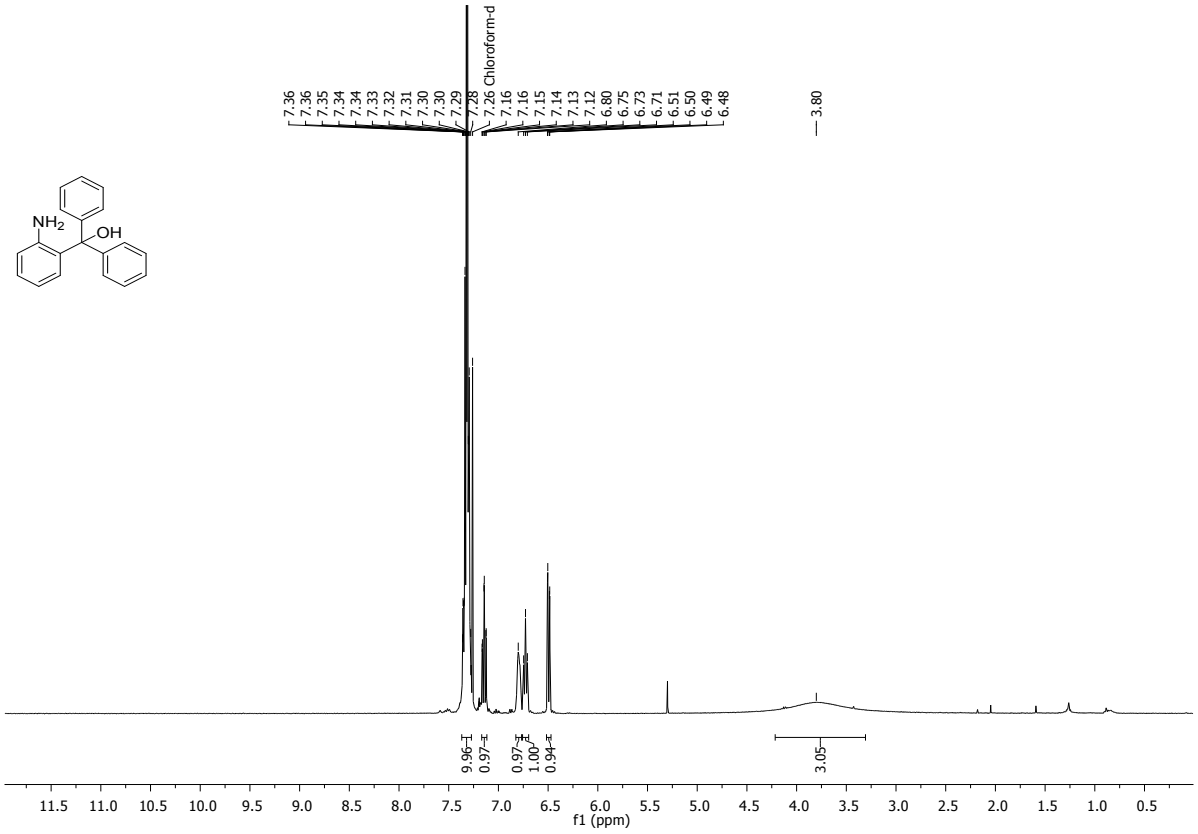


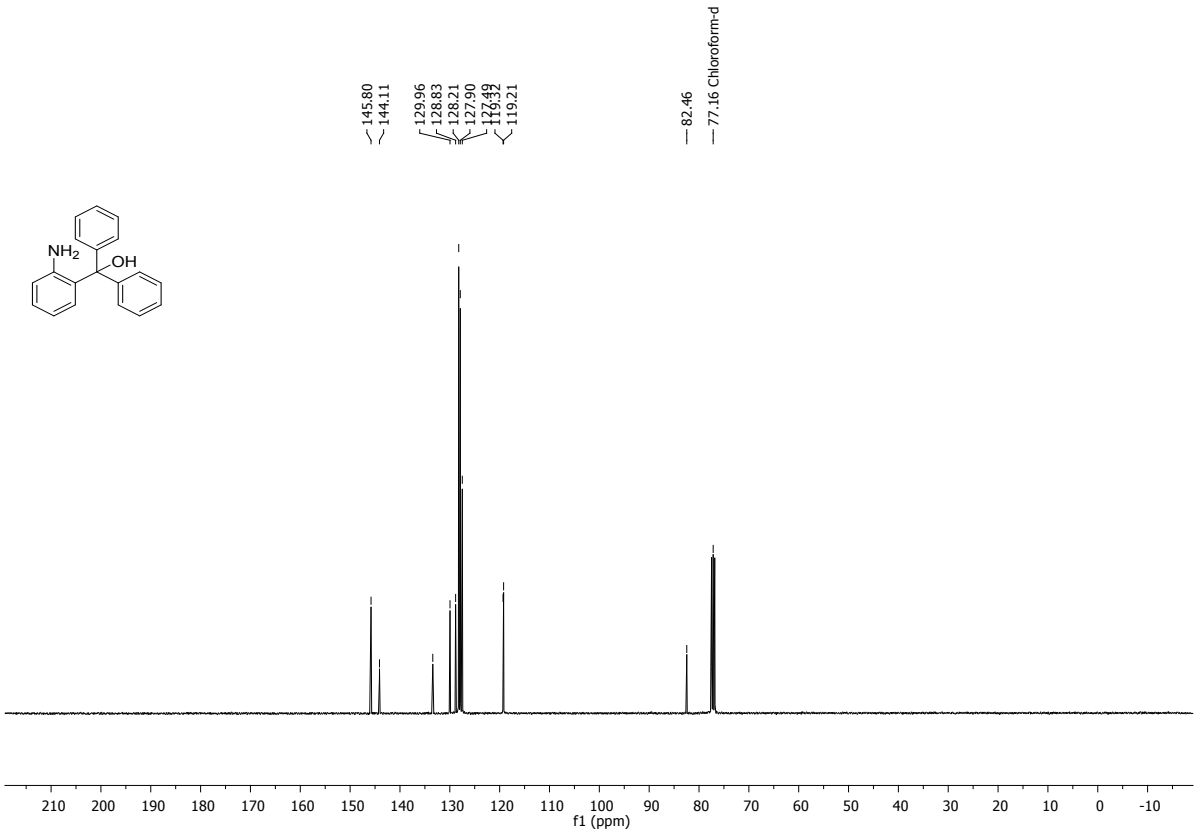
1-(2-aminophenyl)-1-phenylethan-1-ol (S26)



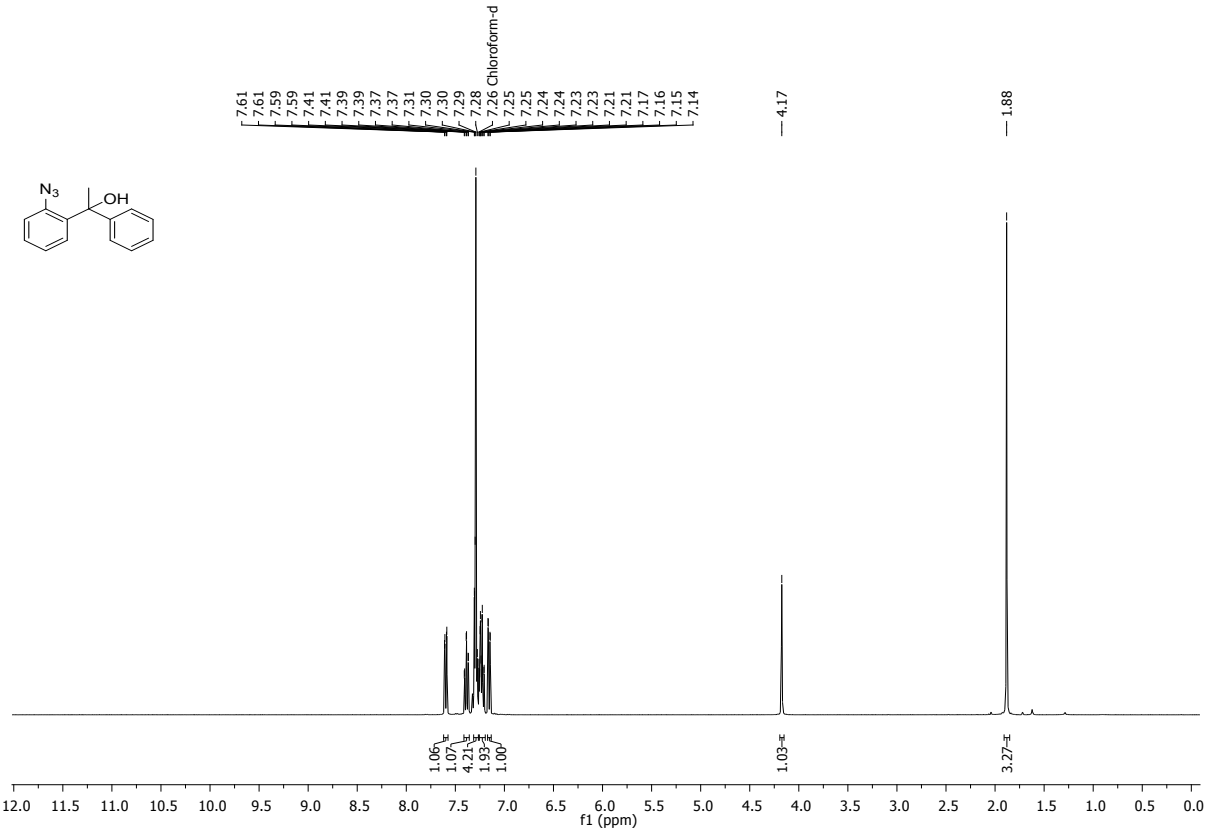


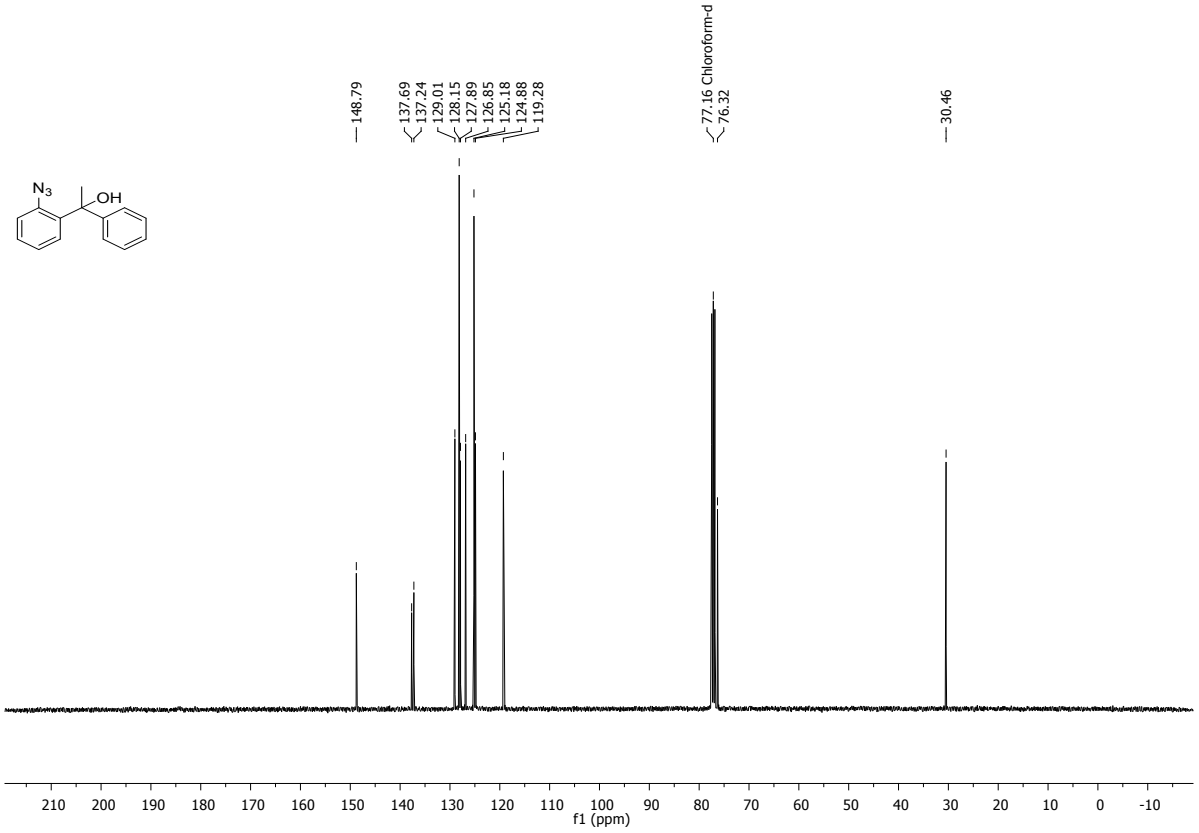
1-(2-aminophenyl)-1-phenylethan-1-ol (S27)



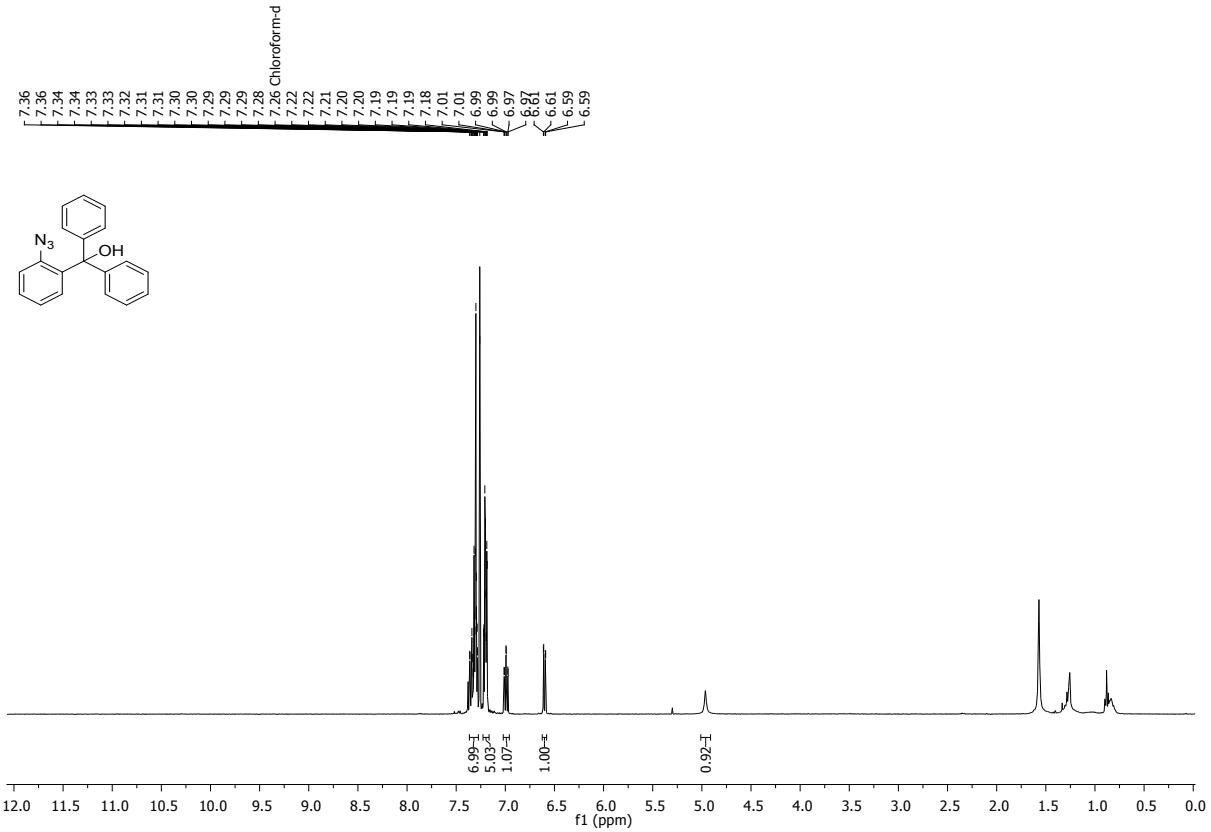


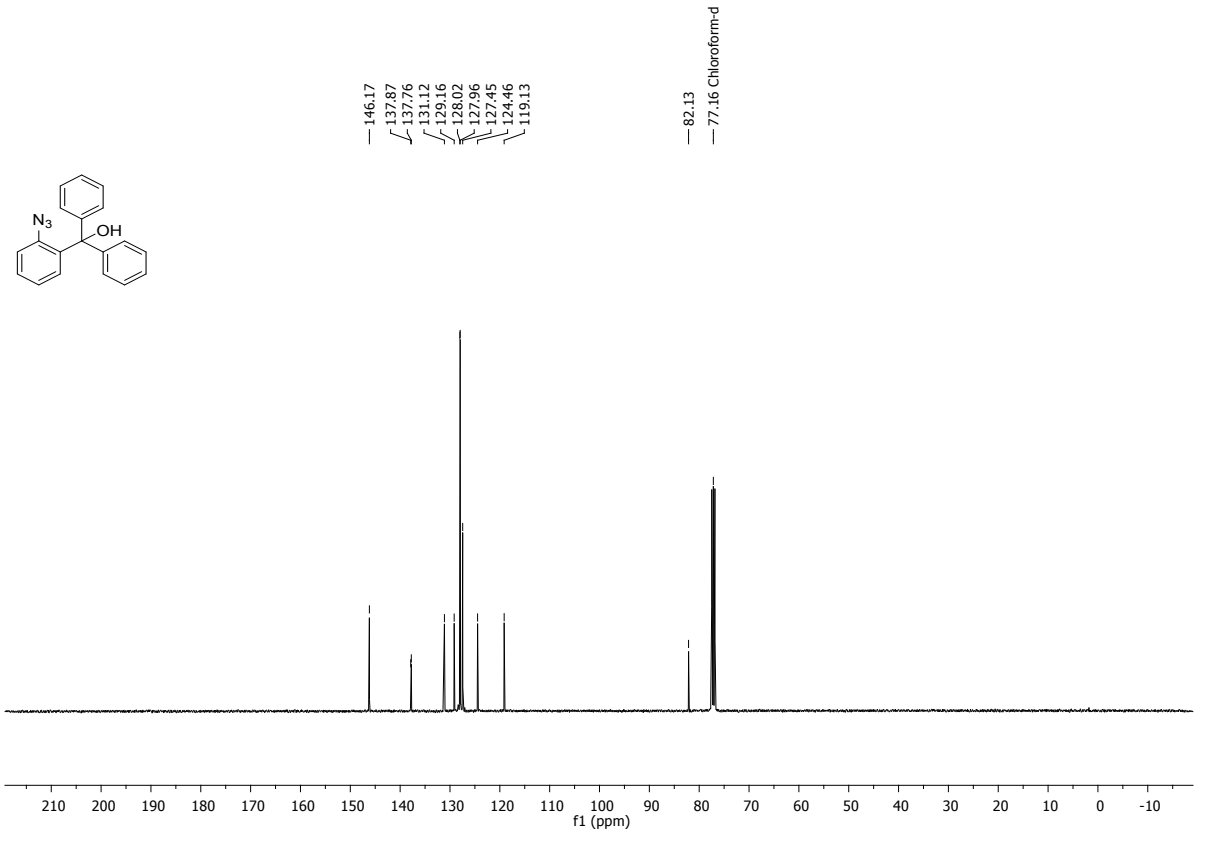
1-(2-azidophenyl)-1-phenylethan-1-ol (S28)



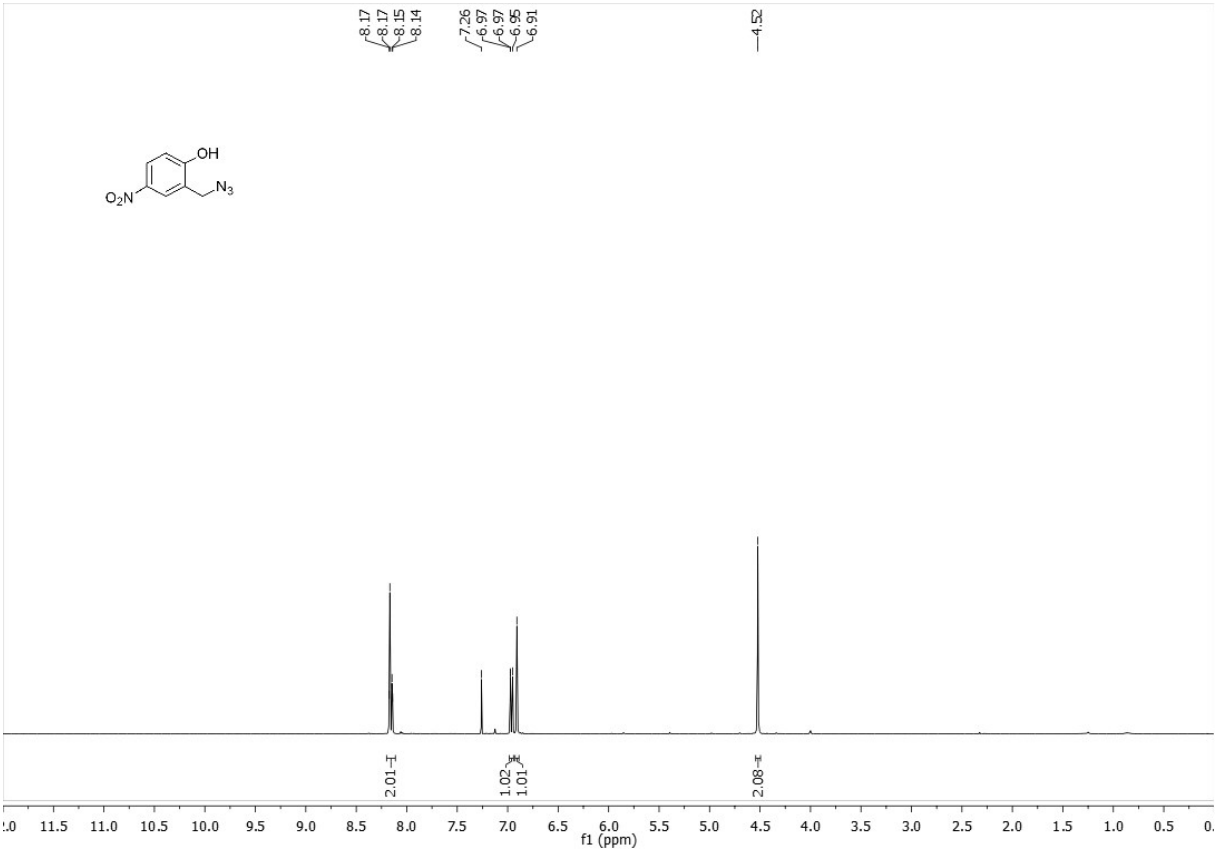


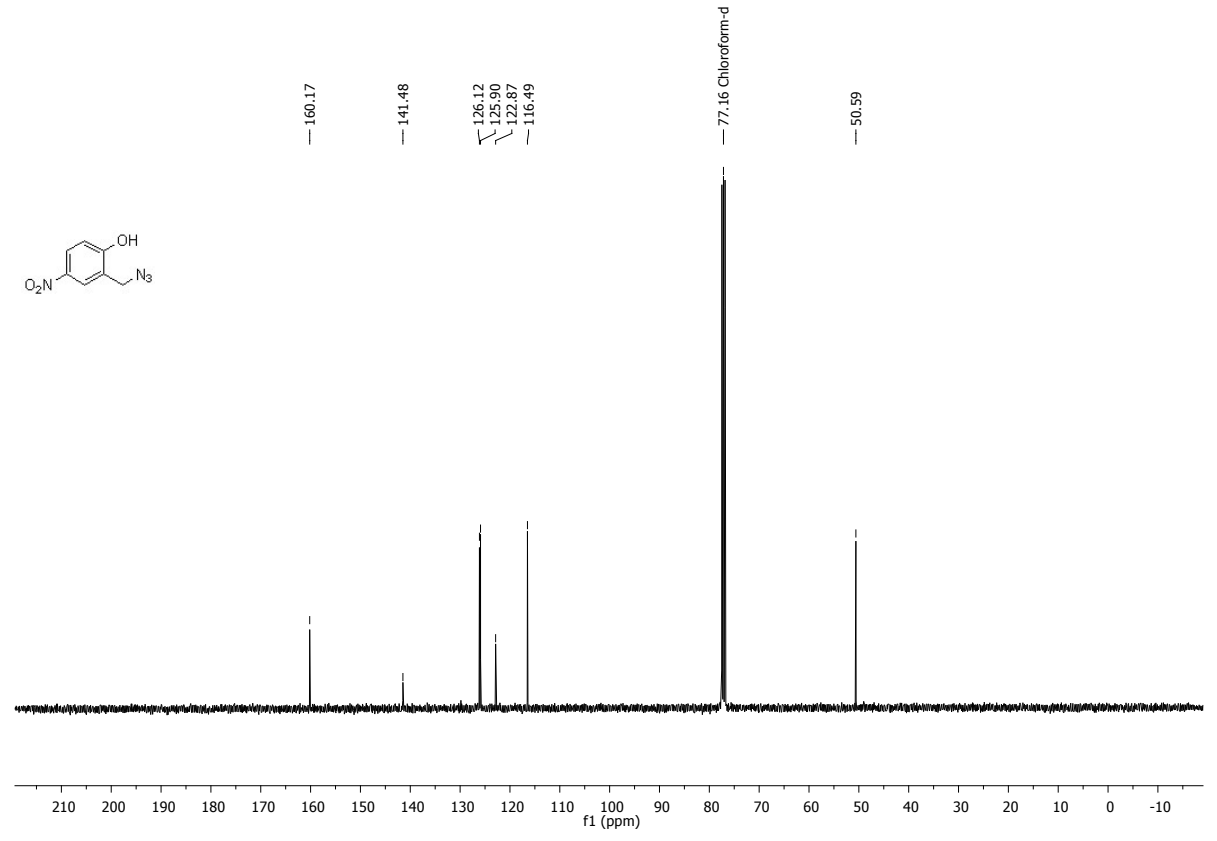
(2-azidophenyl)diphenylmethanol (S29)



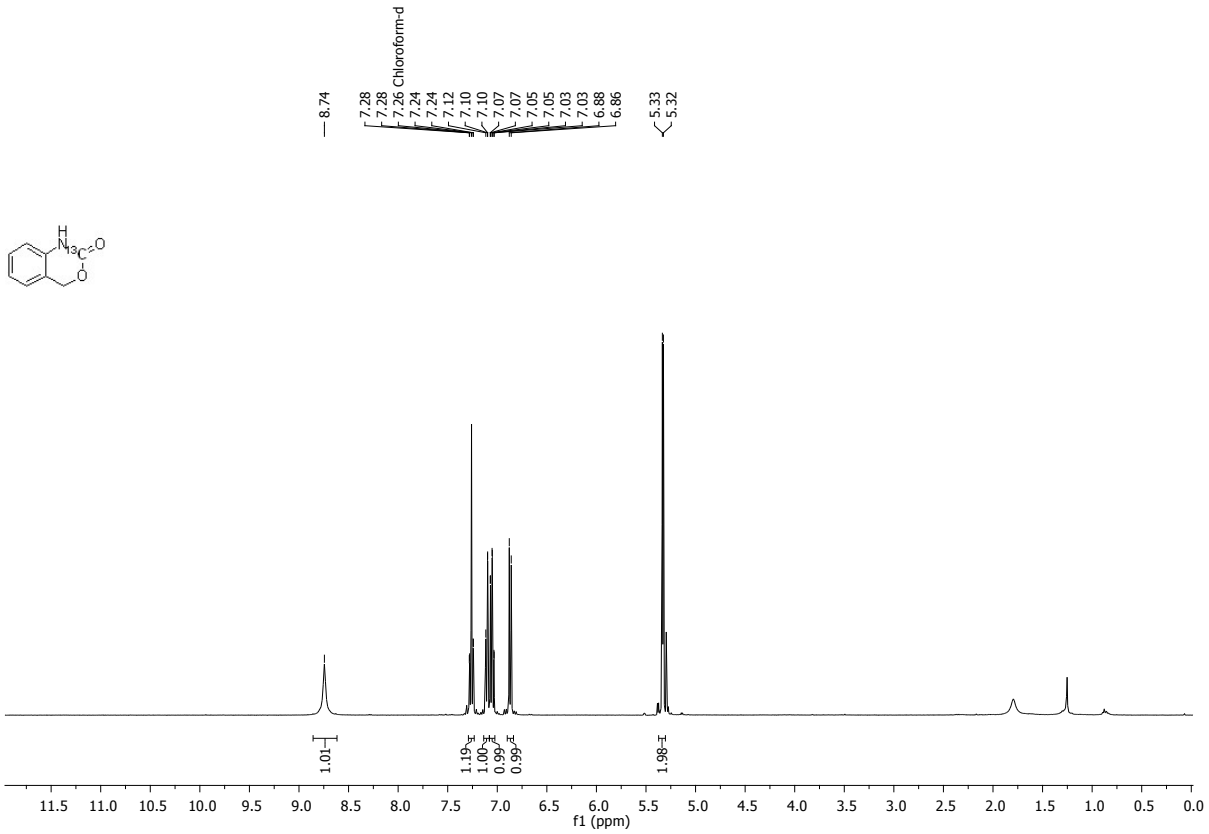


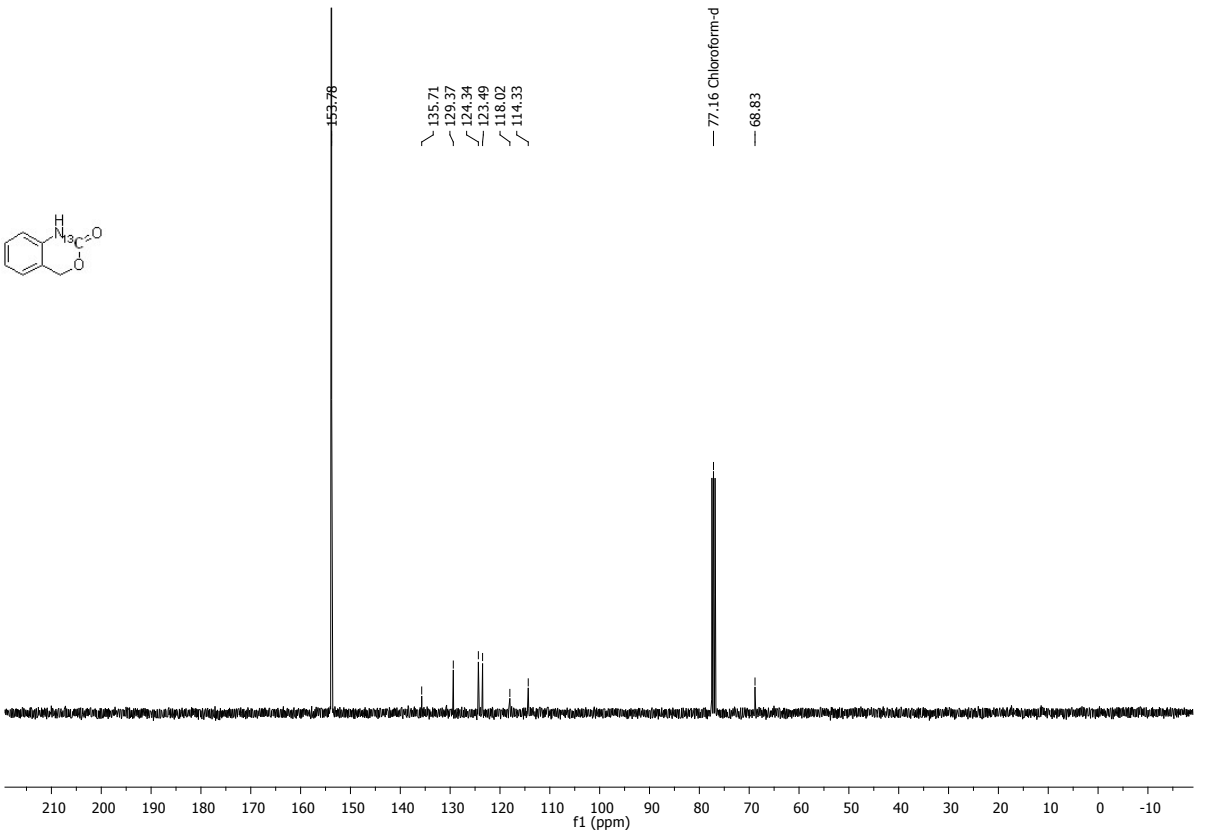
2-(azidomethyl)-4-nitrophenol (S30)



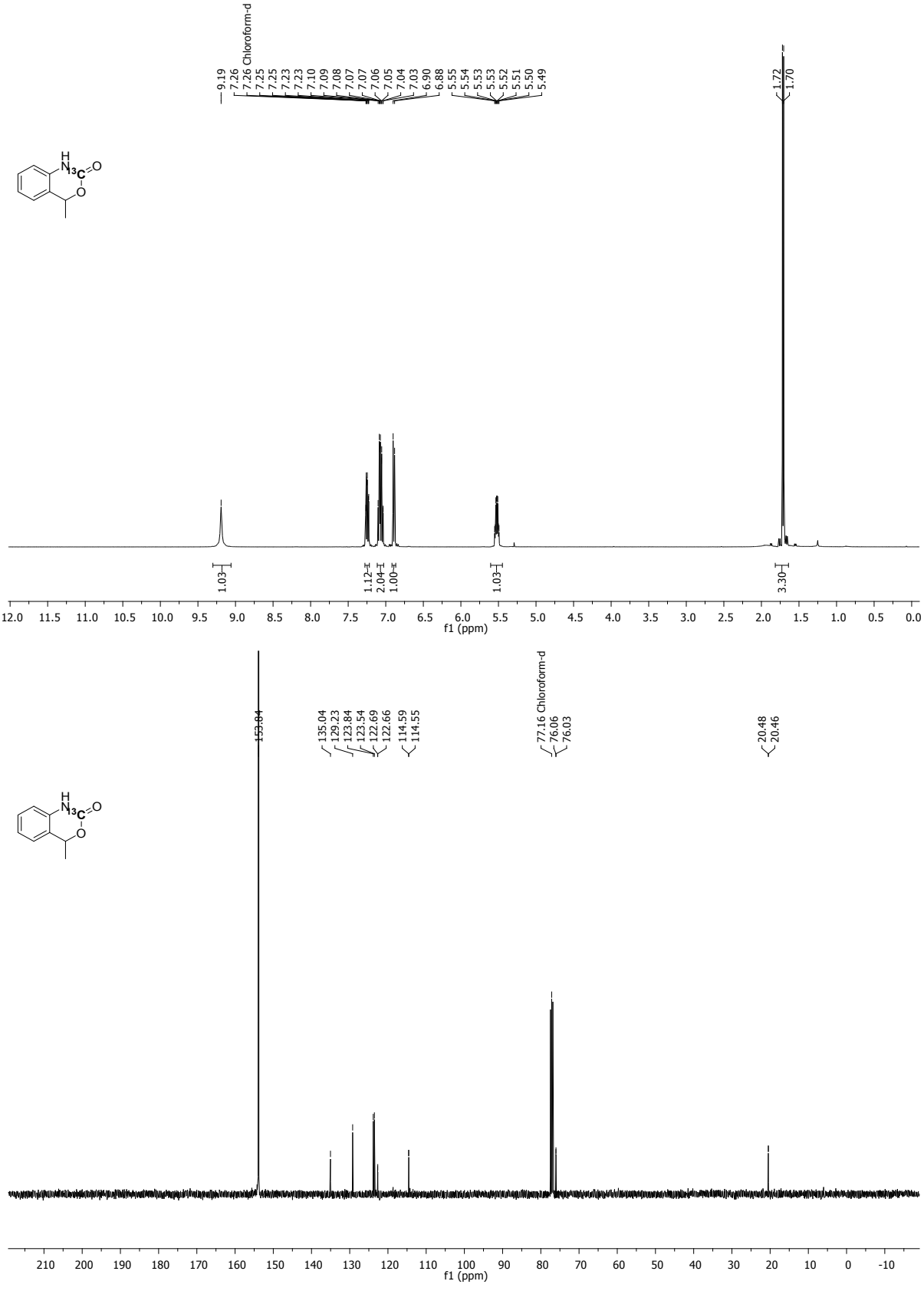


[^{13}C] 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one ([^{13}C]10)

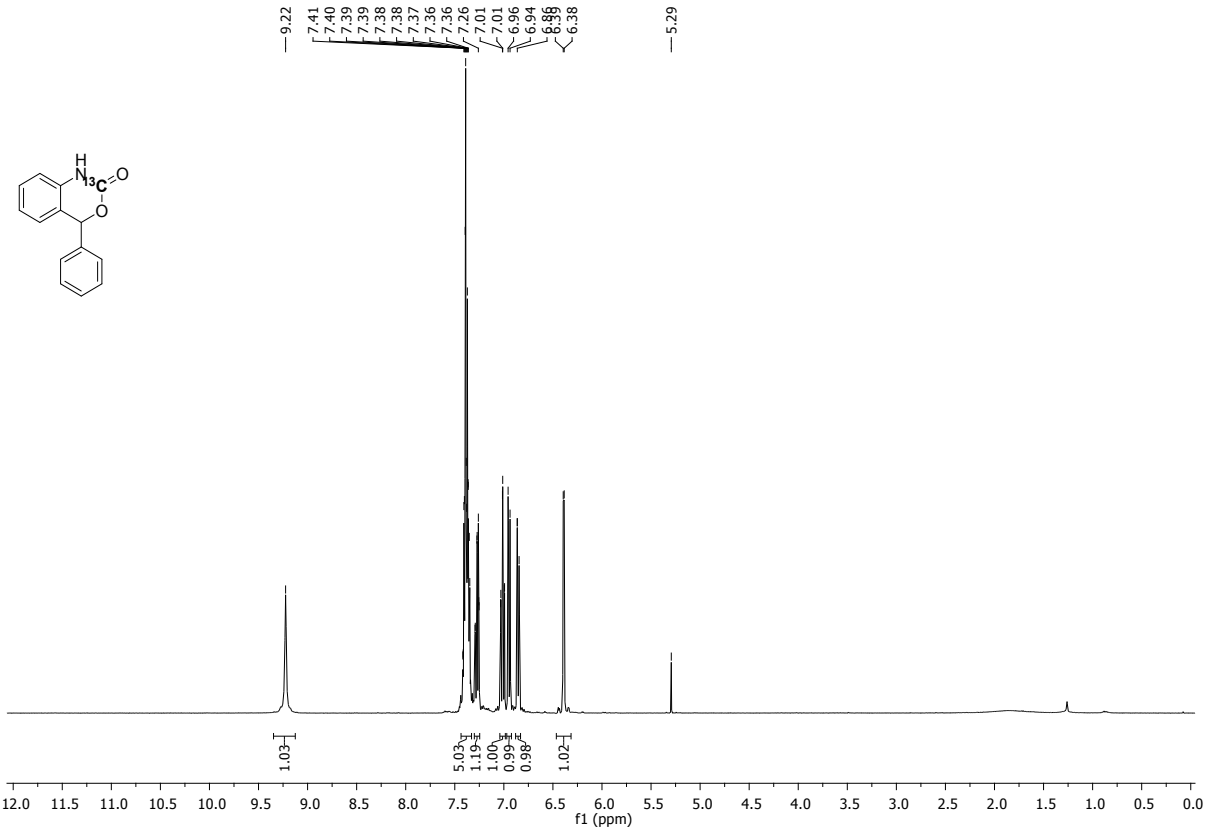


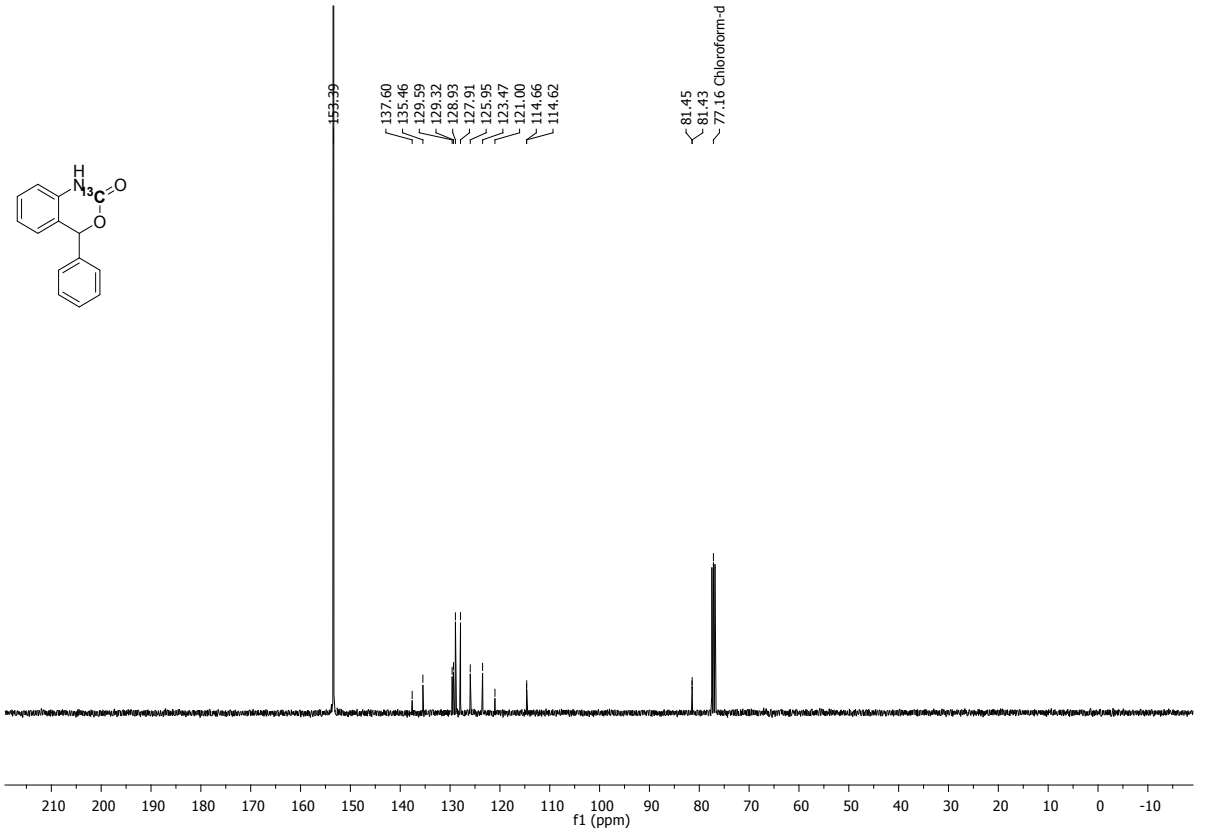


***[^{13}C] 4-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{13}C]11)**

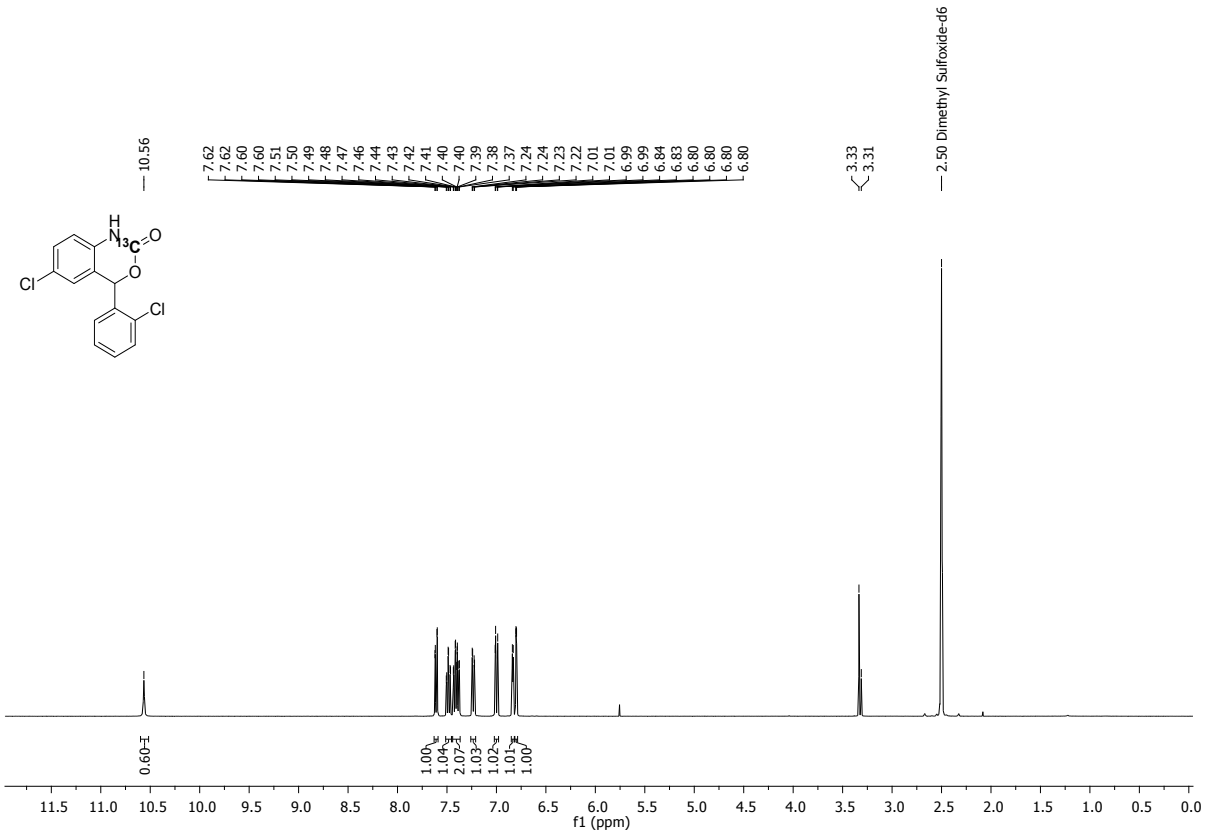


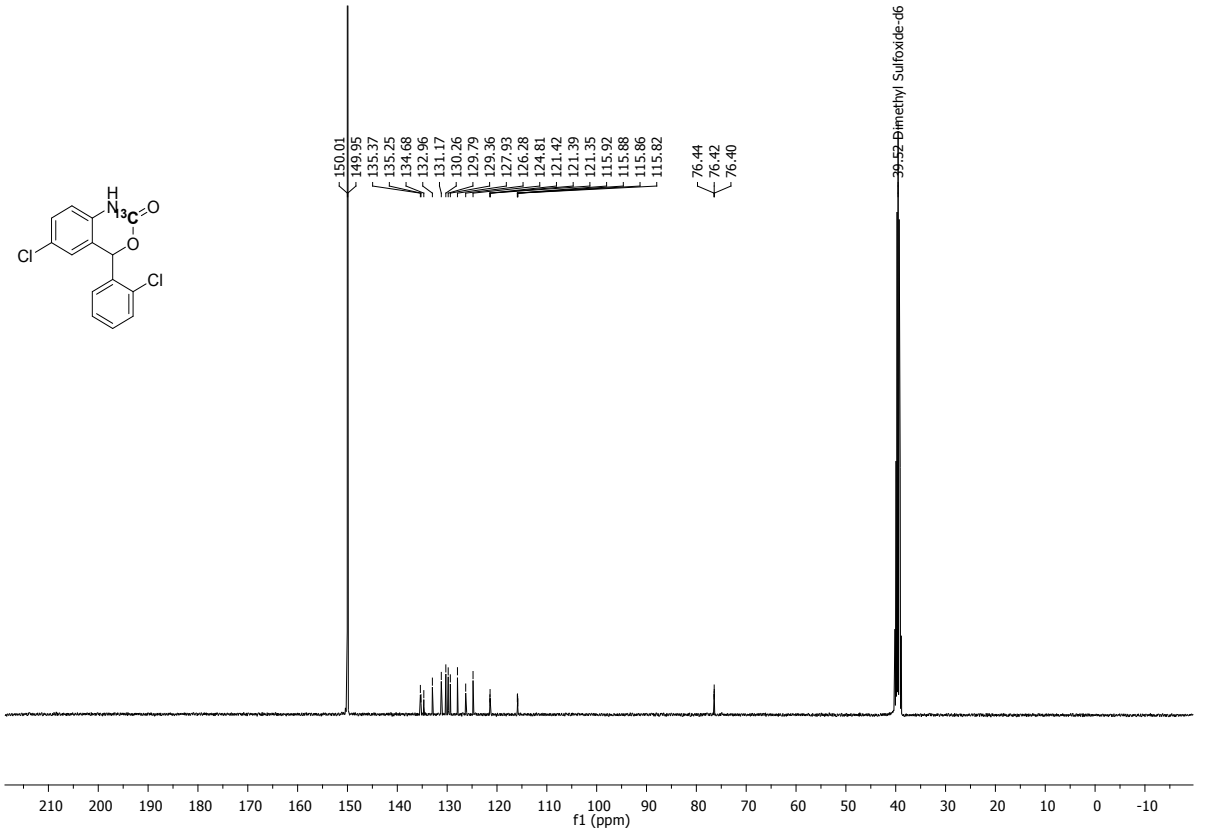
[^{13}C] 4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{13}C]12)**



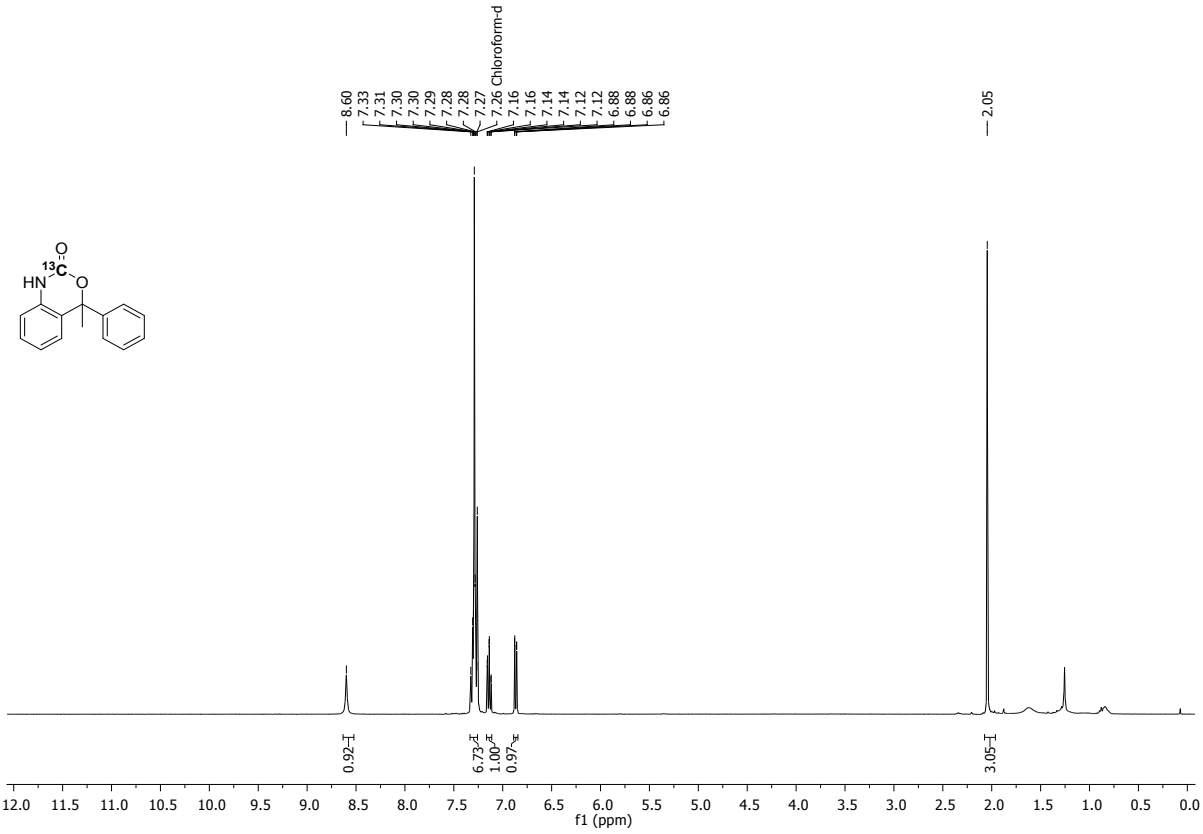


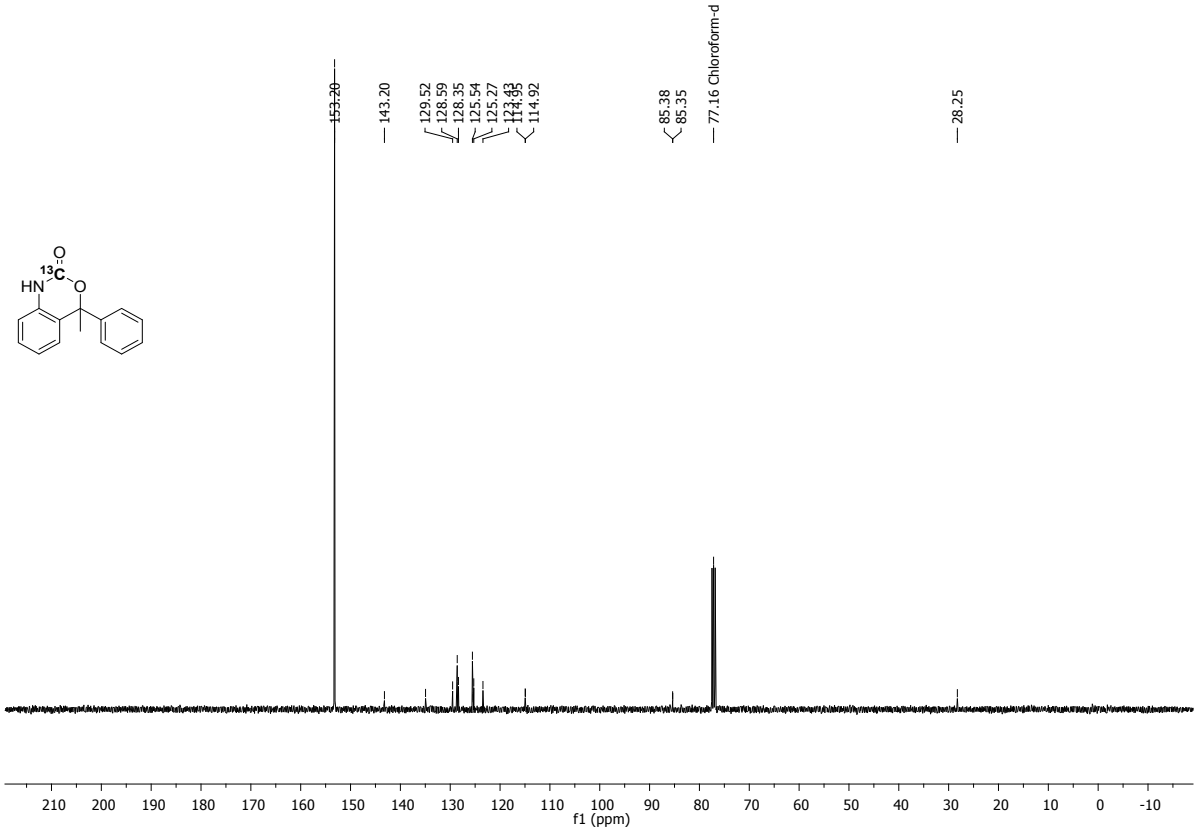
[^{13}C] 6-chloro-4-(2-chlorophenyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{13}C]14)**



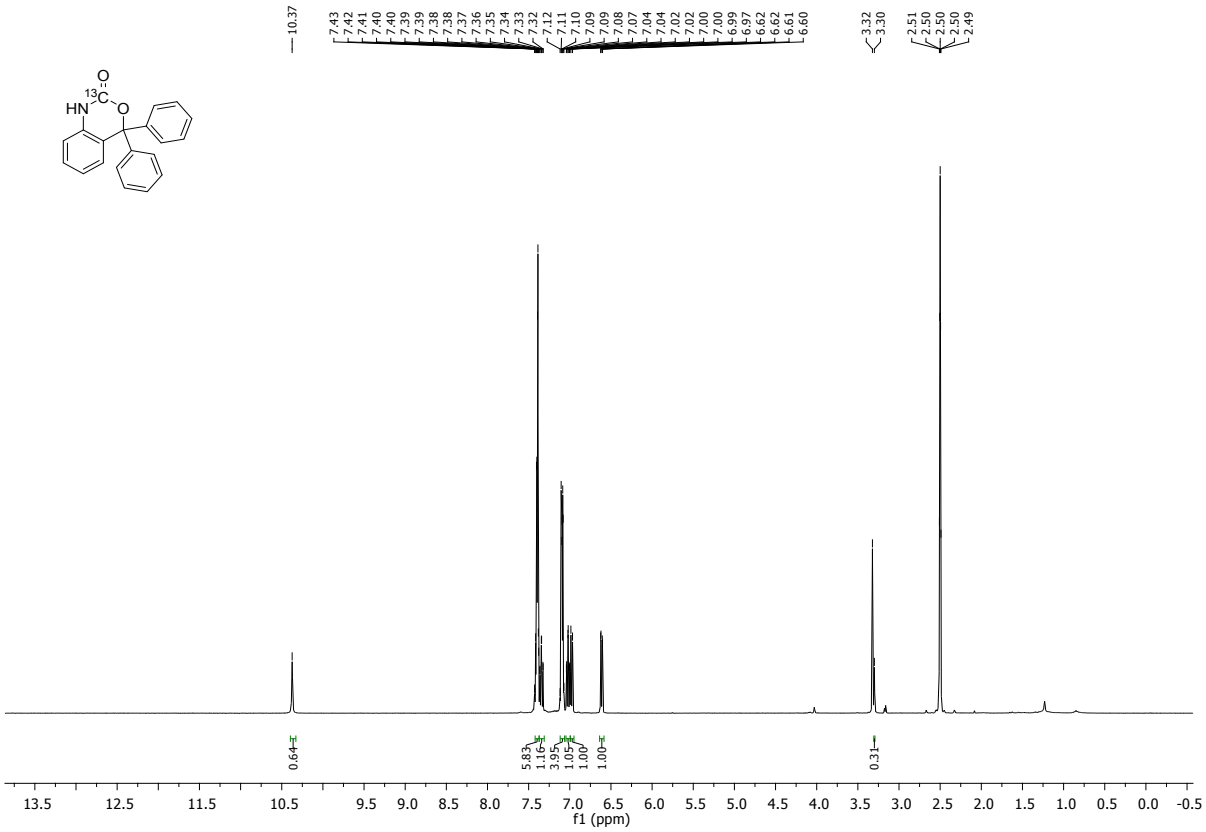


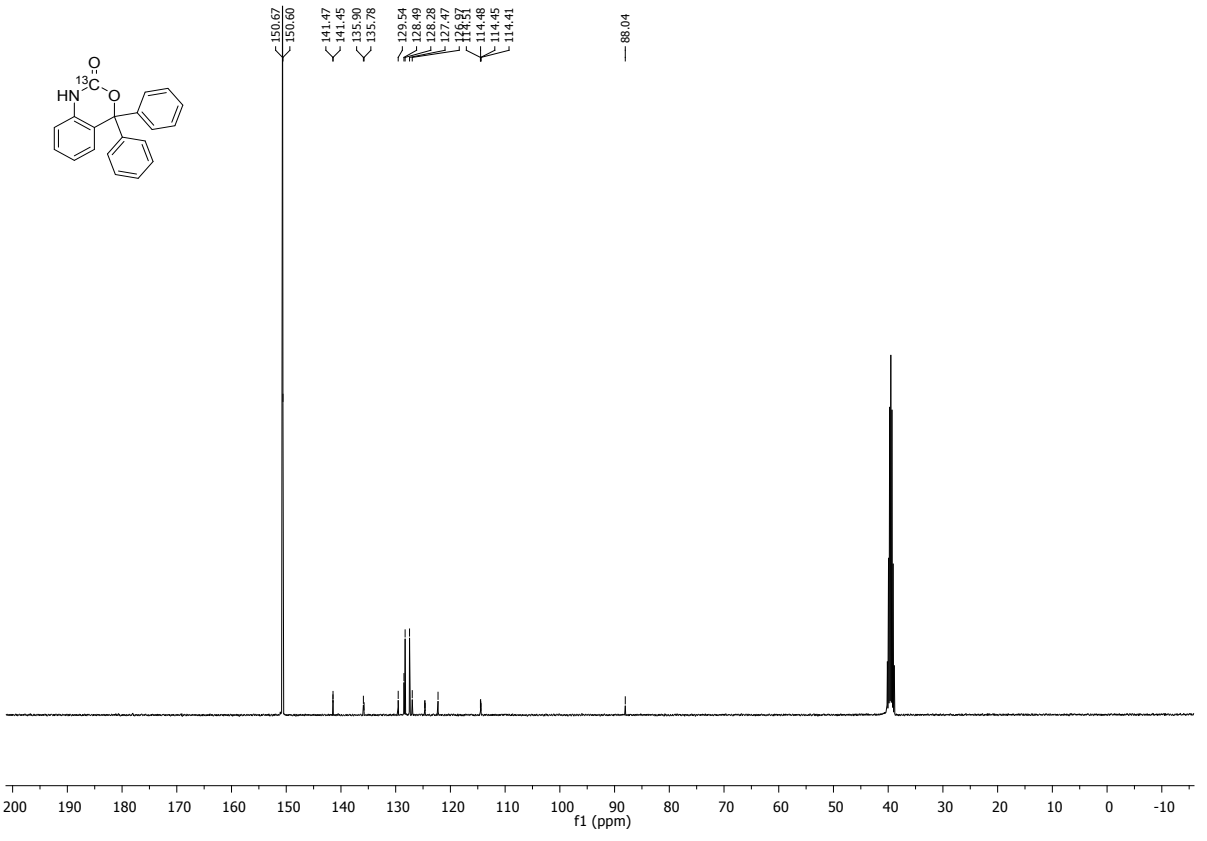
***[^{13}C] 4-methyl-4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{13}C]15)**



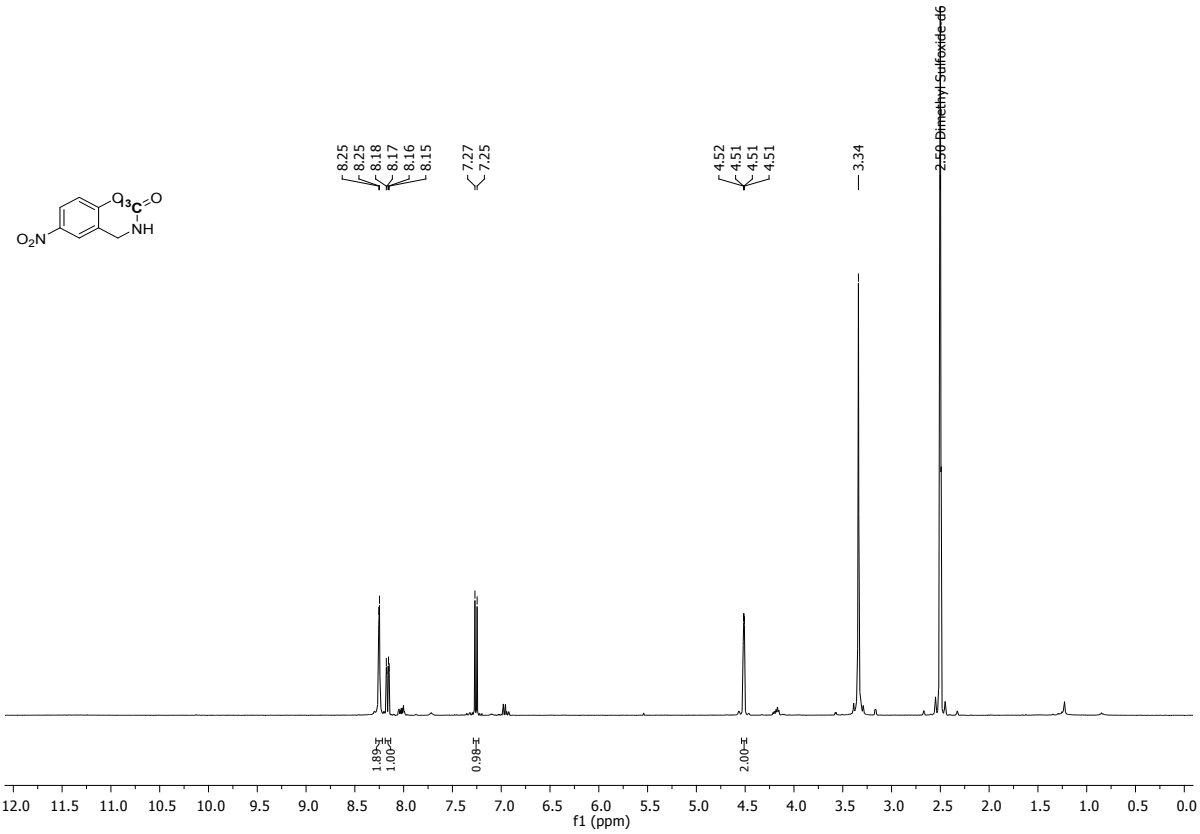


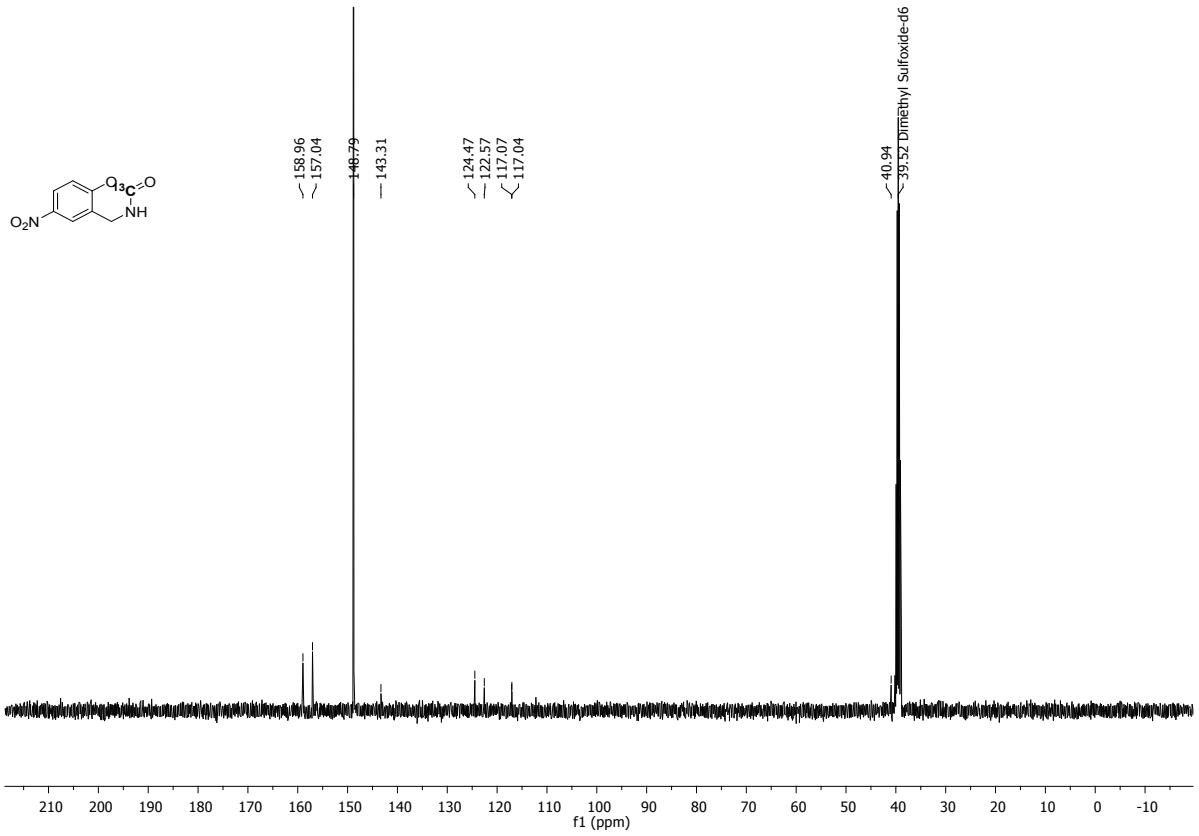
[^{13}C] 4-methyl-4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one ([^{13}C]16)



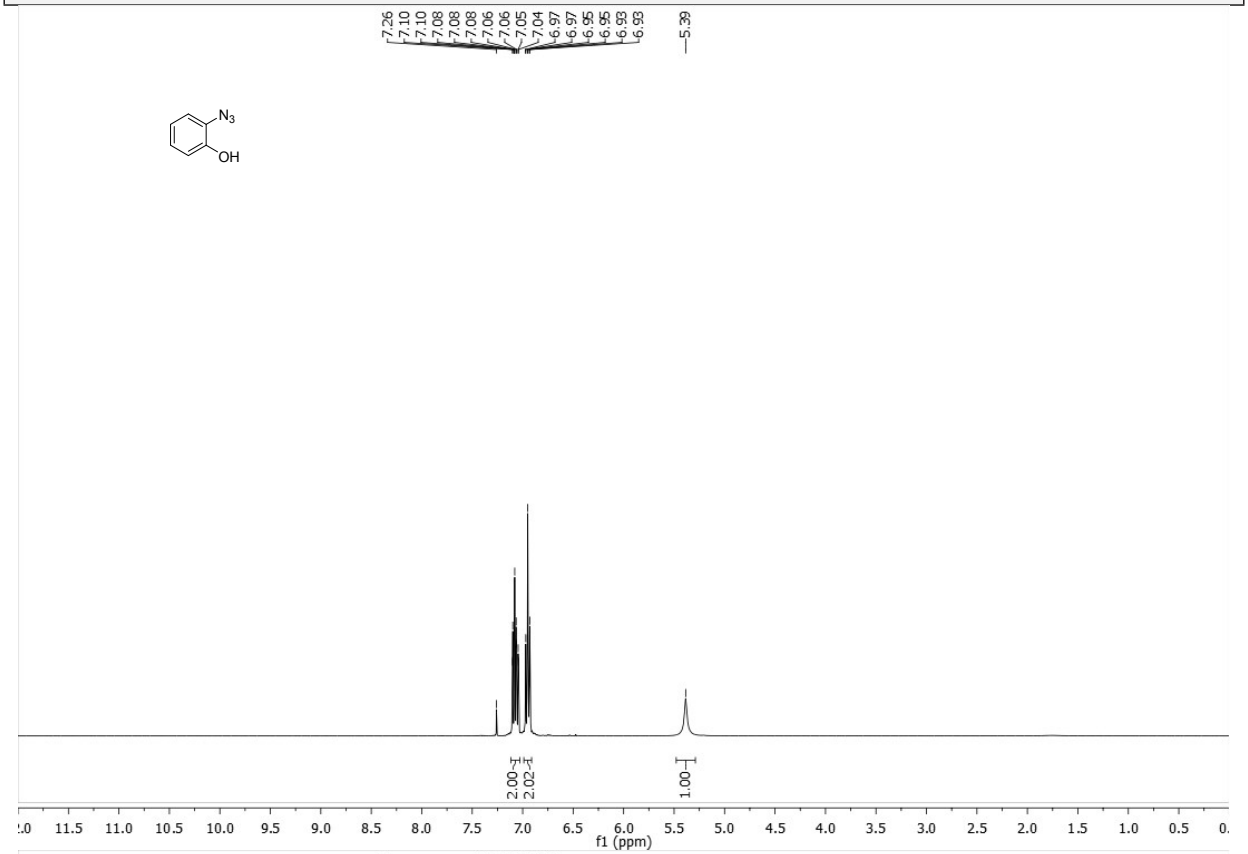


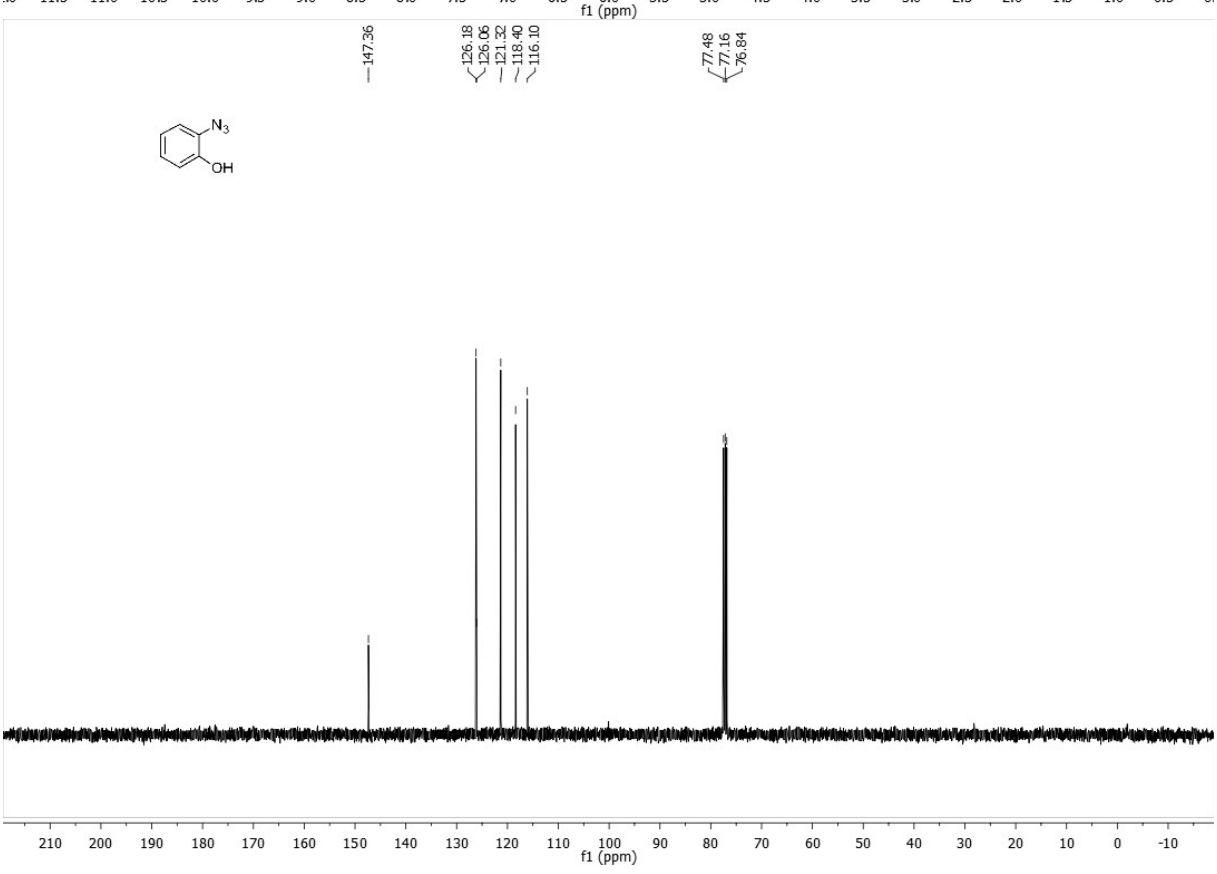
[^{13}C] 6-nitro-3,4-dihydro-2H-benzo[e][1,3]oxazin-2-one **([^{13}C]17)**



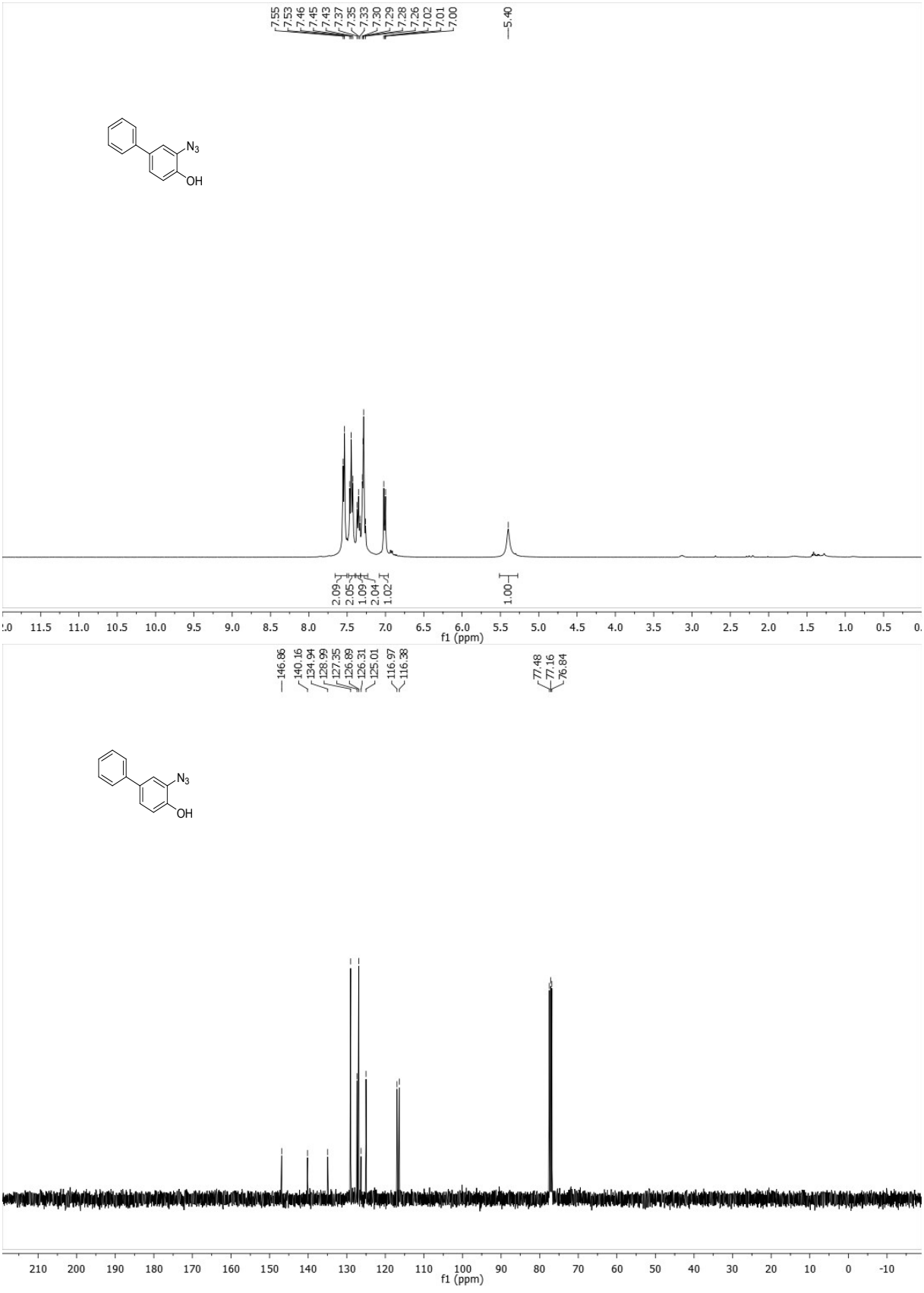


2-azidophenol (S31)

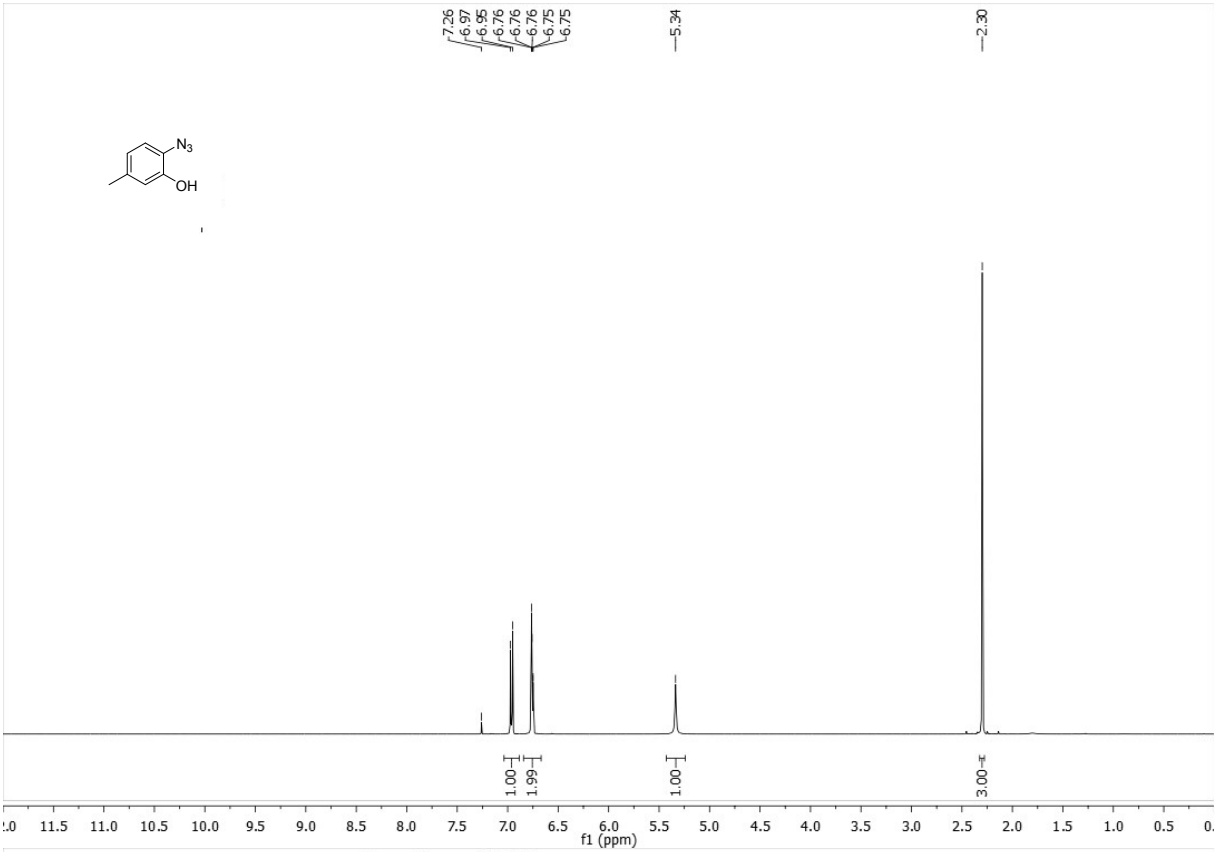


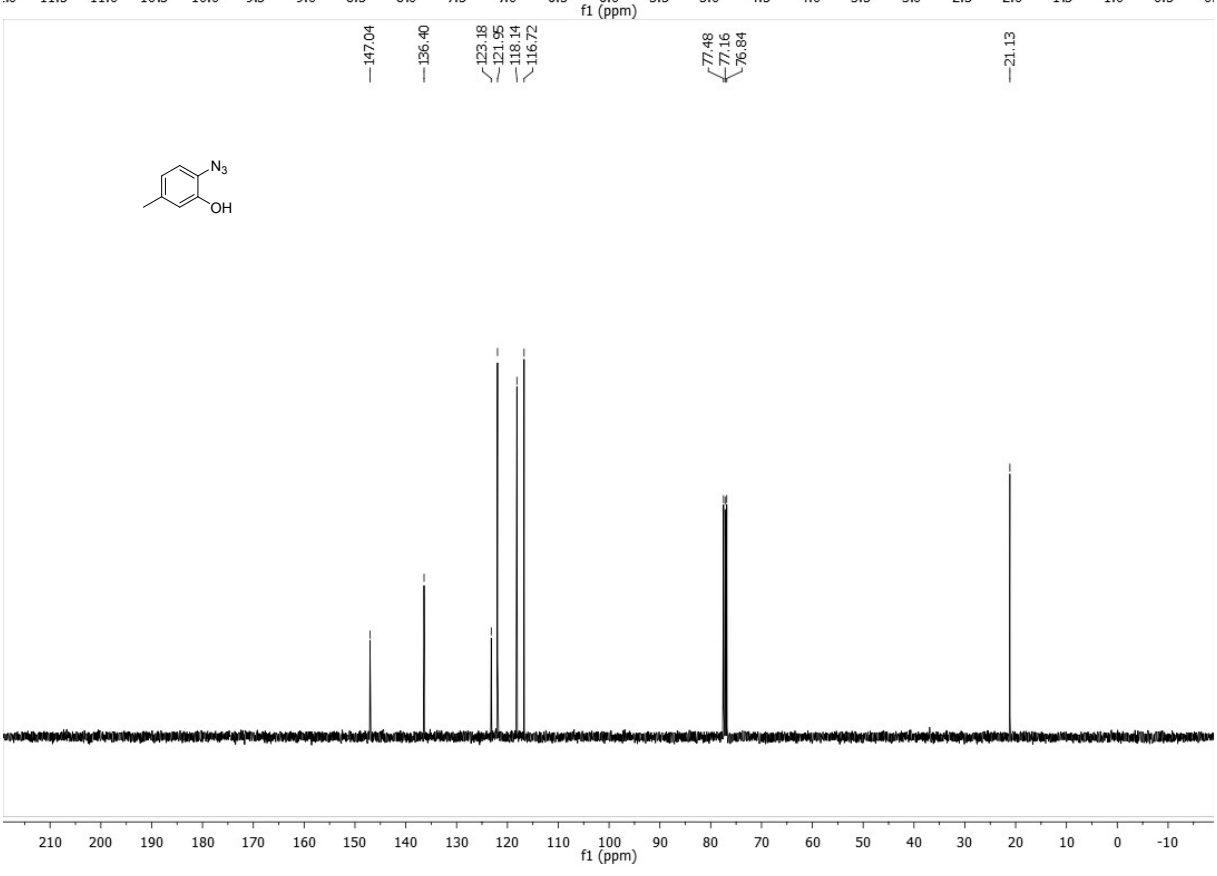


3-azido-[1,1'-biphenyl]-4-ol **(S33)**

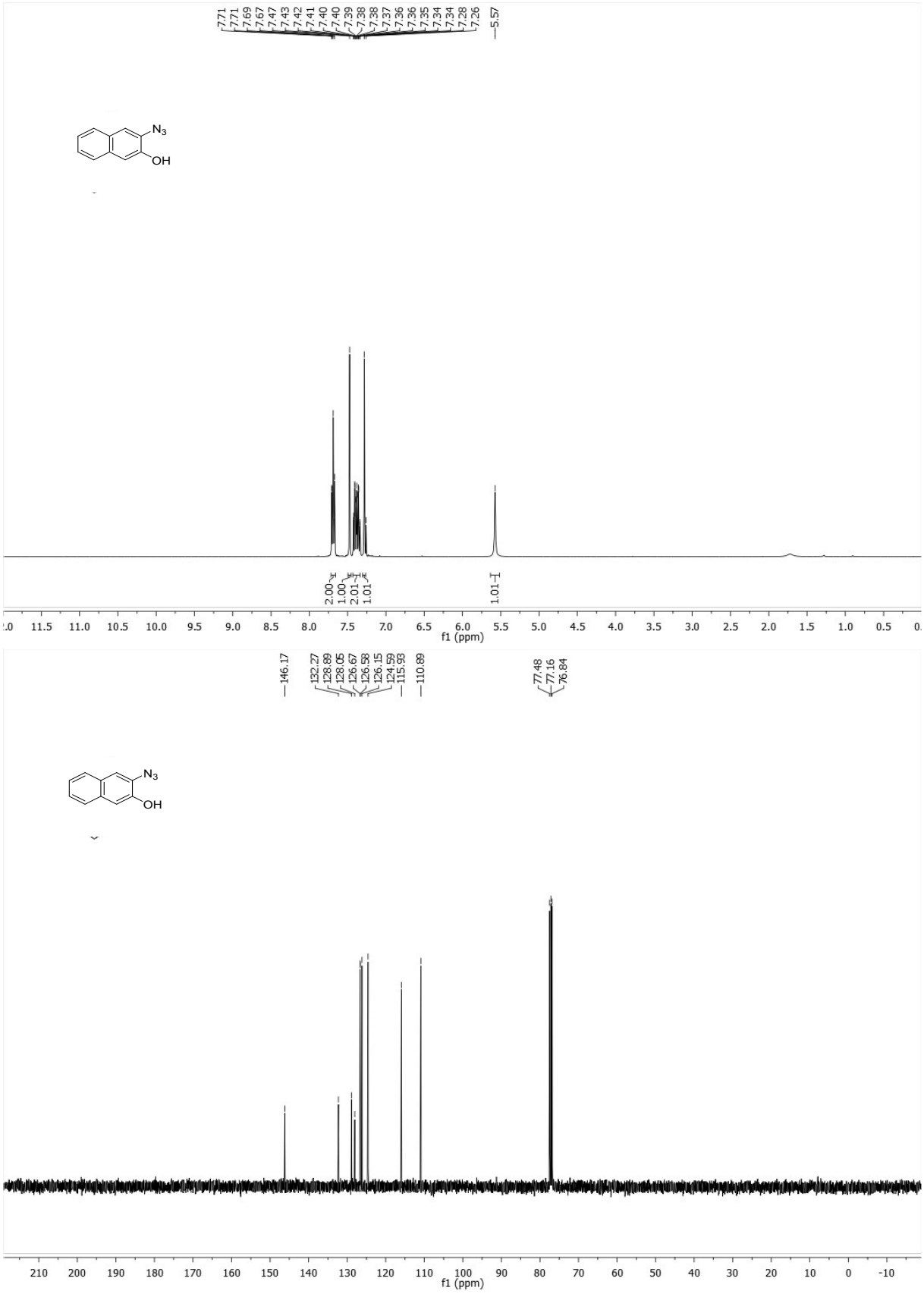


2-azido-5-methylphenol (S32)

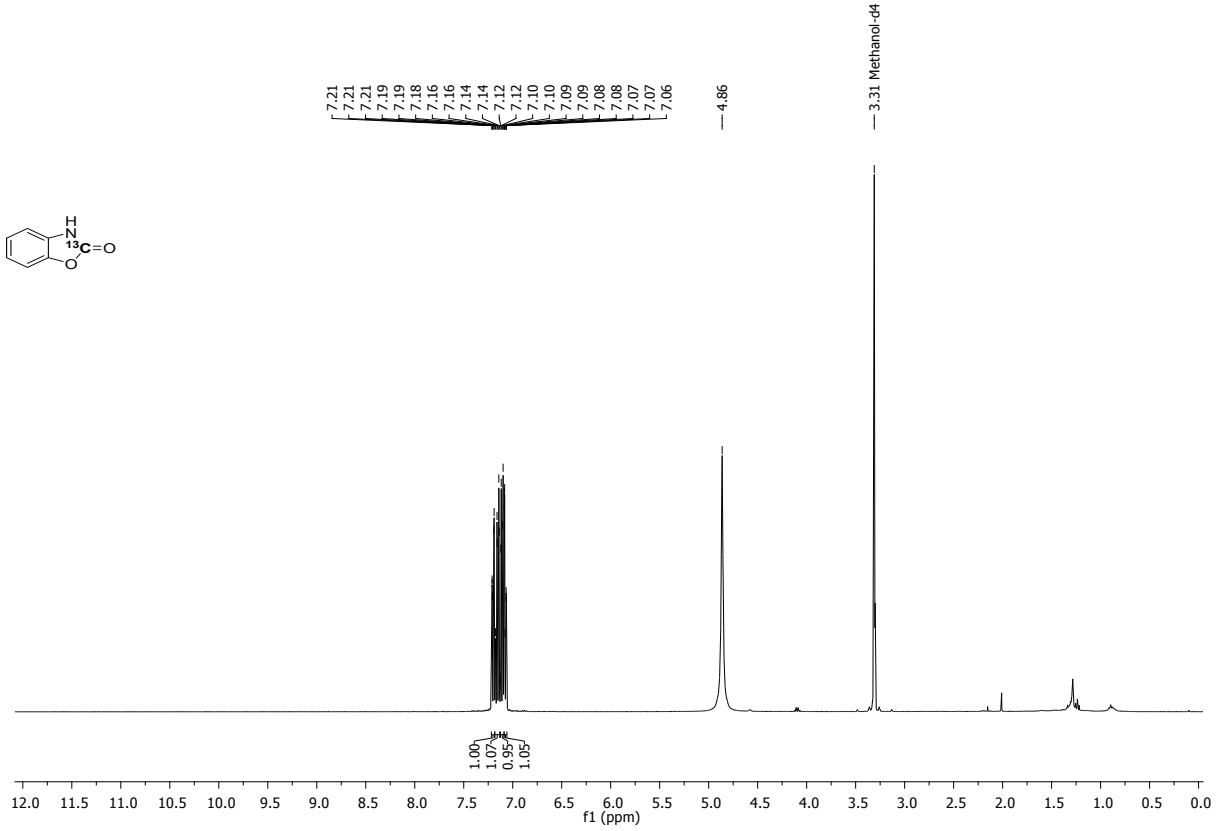


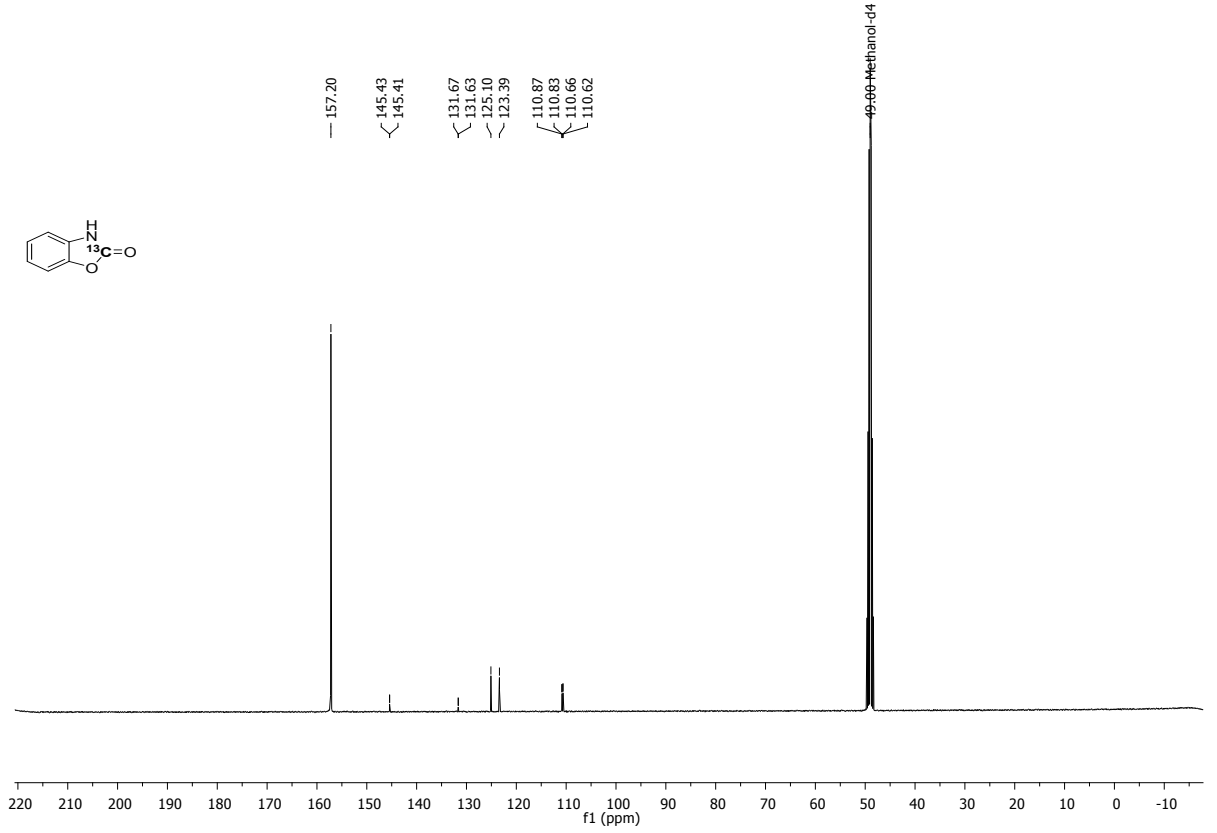


***3-azidonaphthalen-2-ol* (S34)**

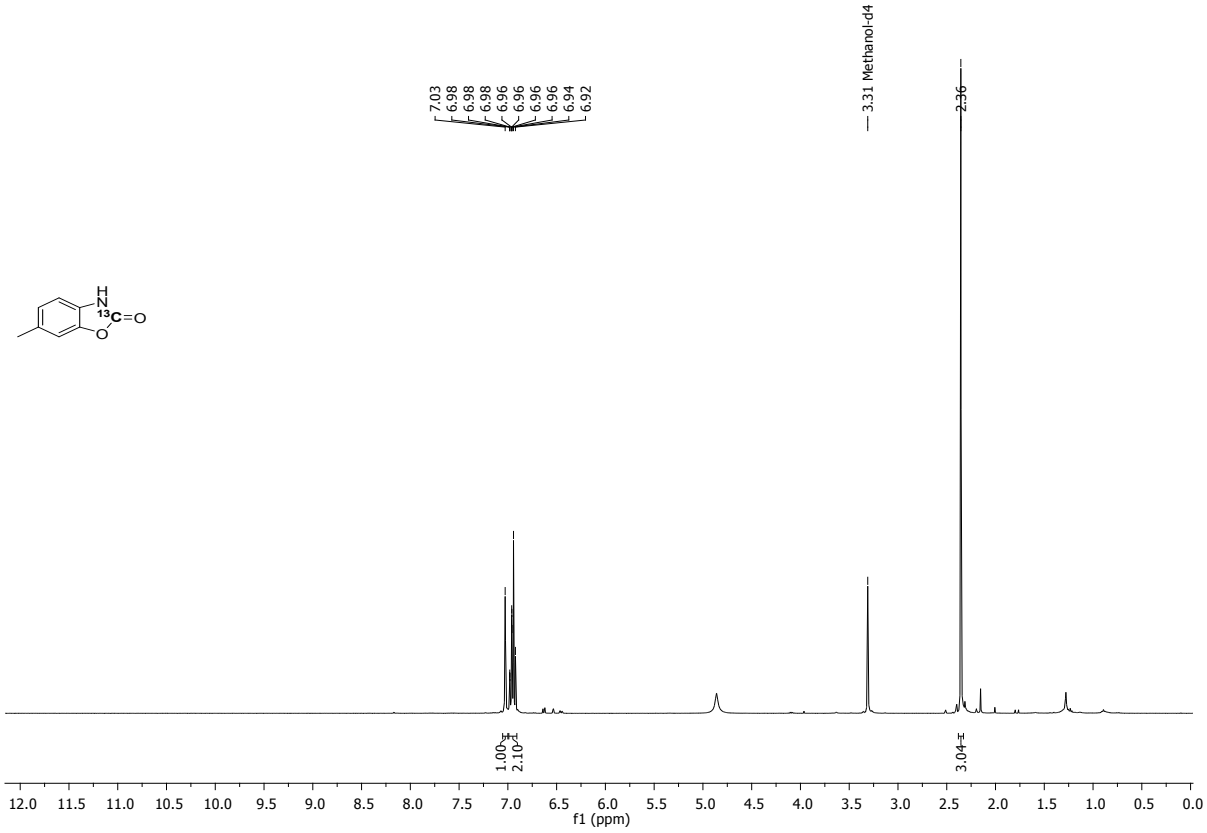


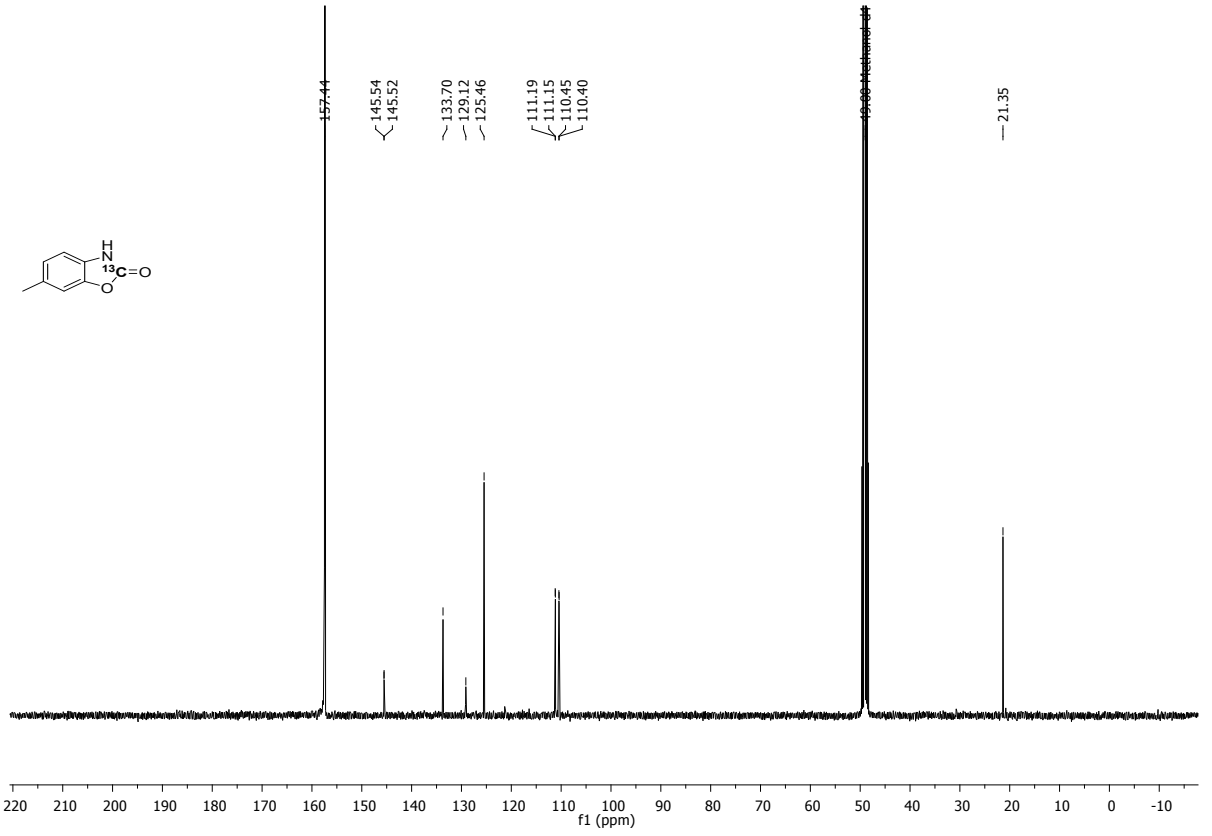
[^{13}C] benzo[d]oxazol-2(3H)-one ([^{13}C]**18**)



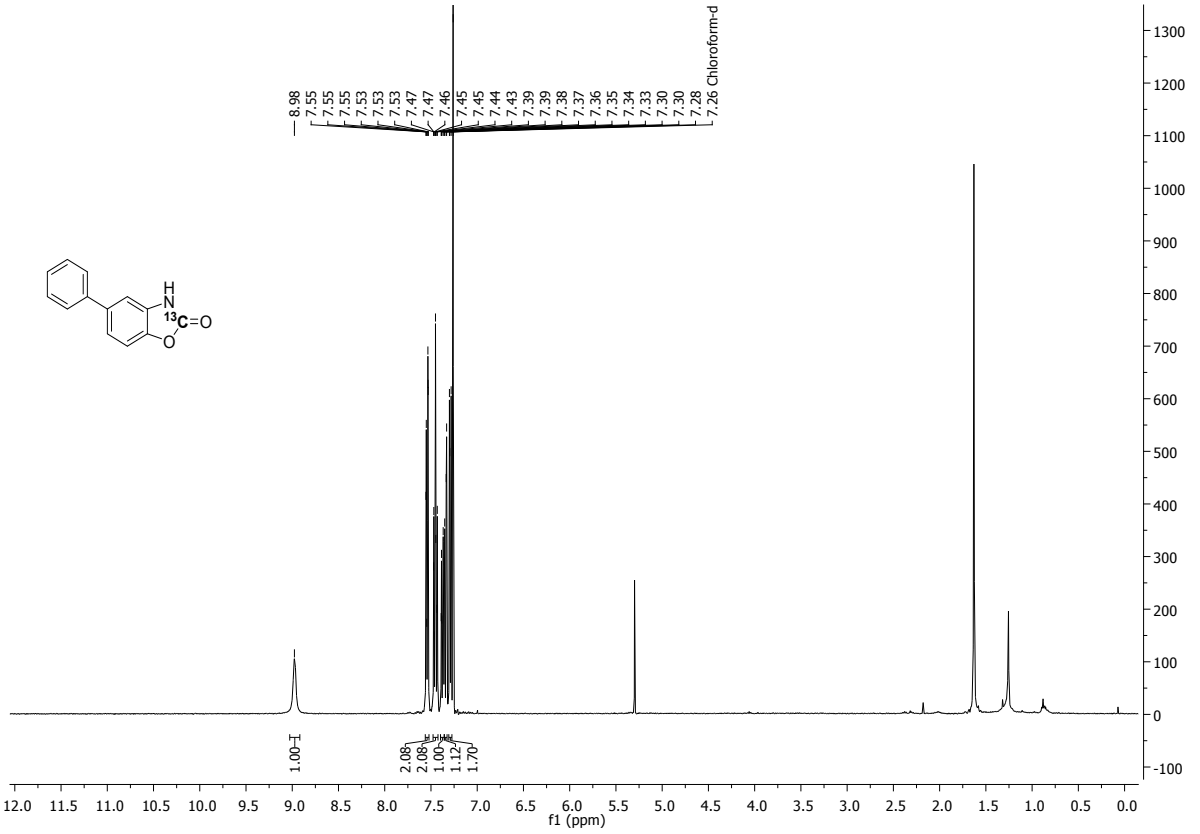


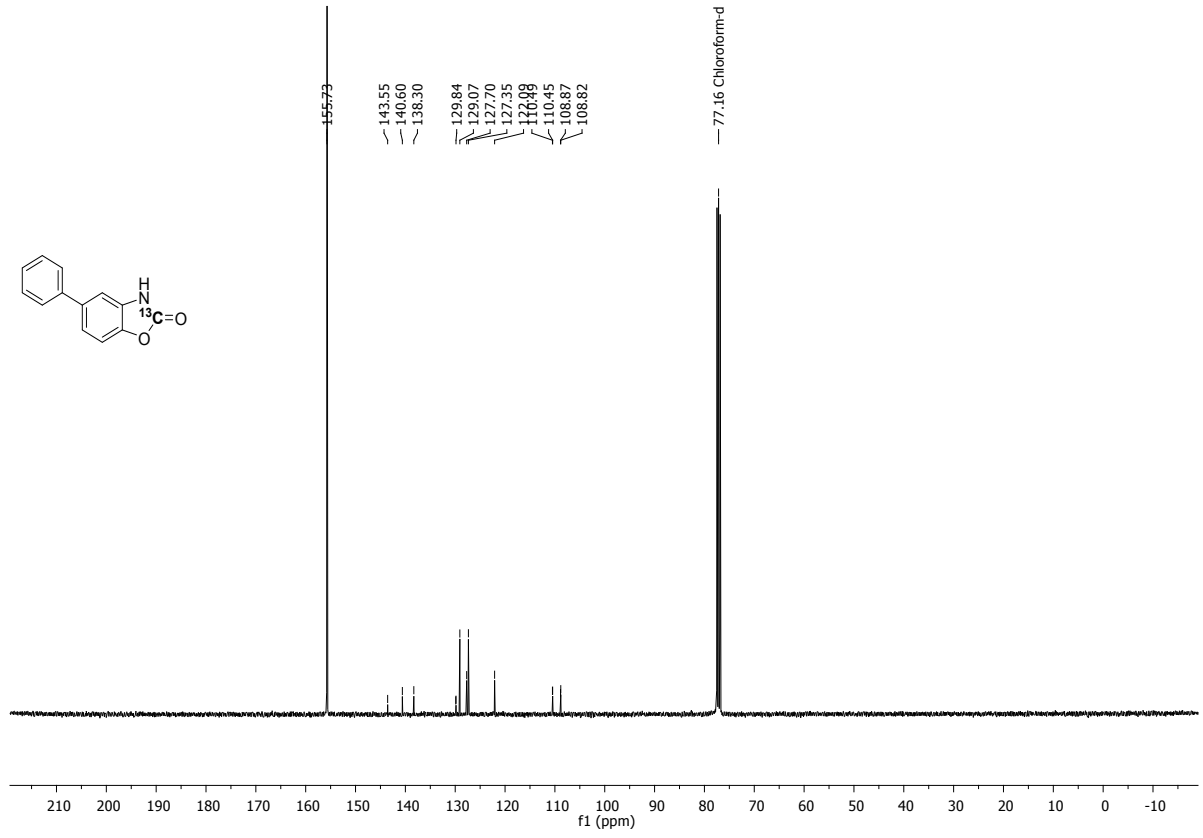
[^{13}C] 4-methylbenzo[d]oxazol-2(3H)-one ([^{13}C]**19**)



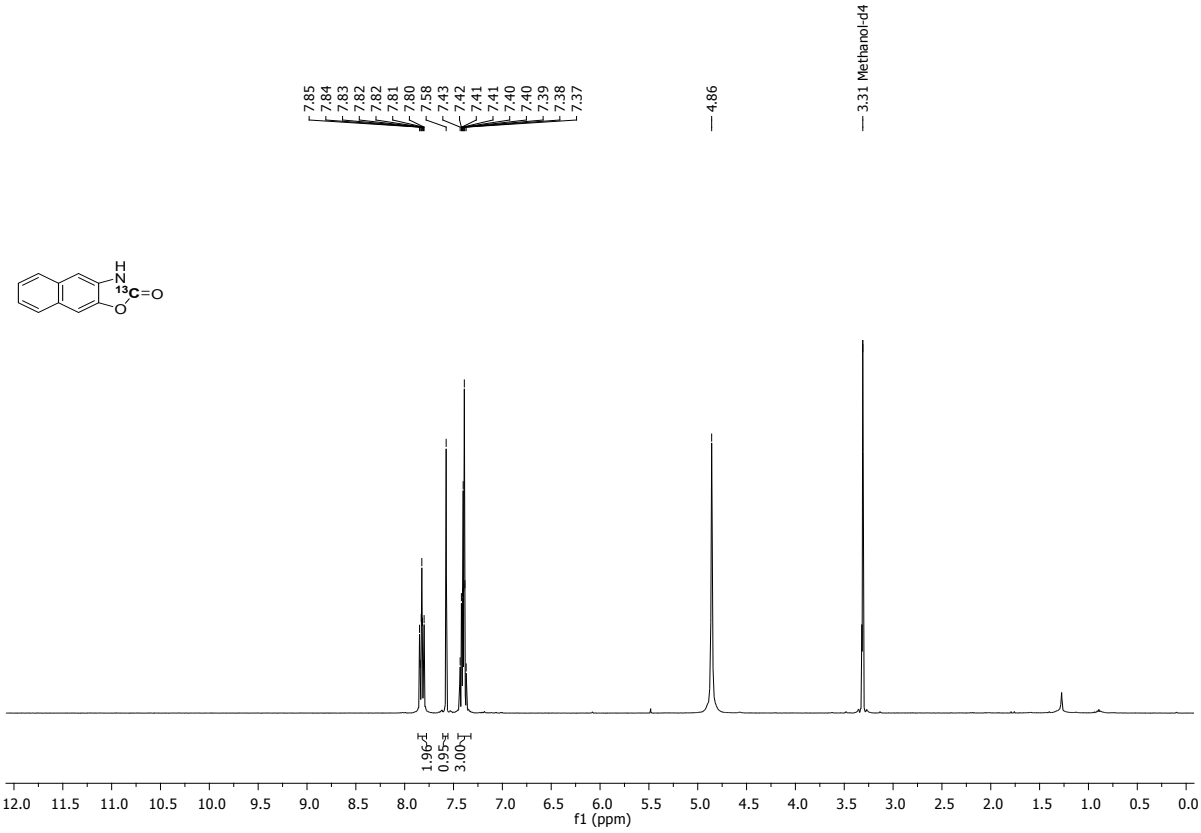


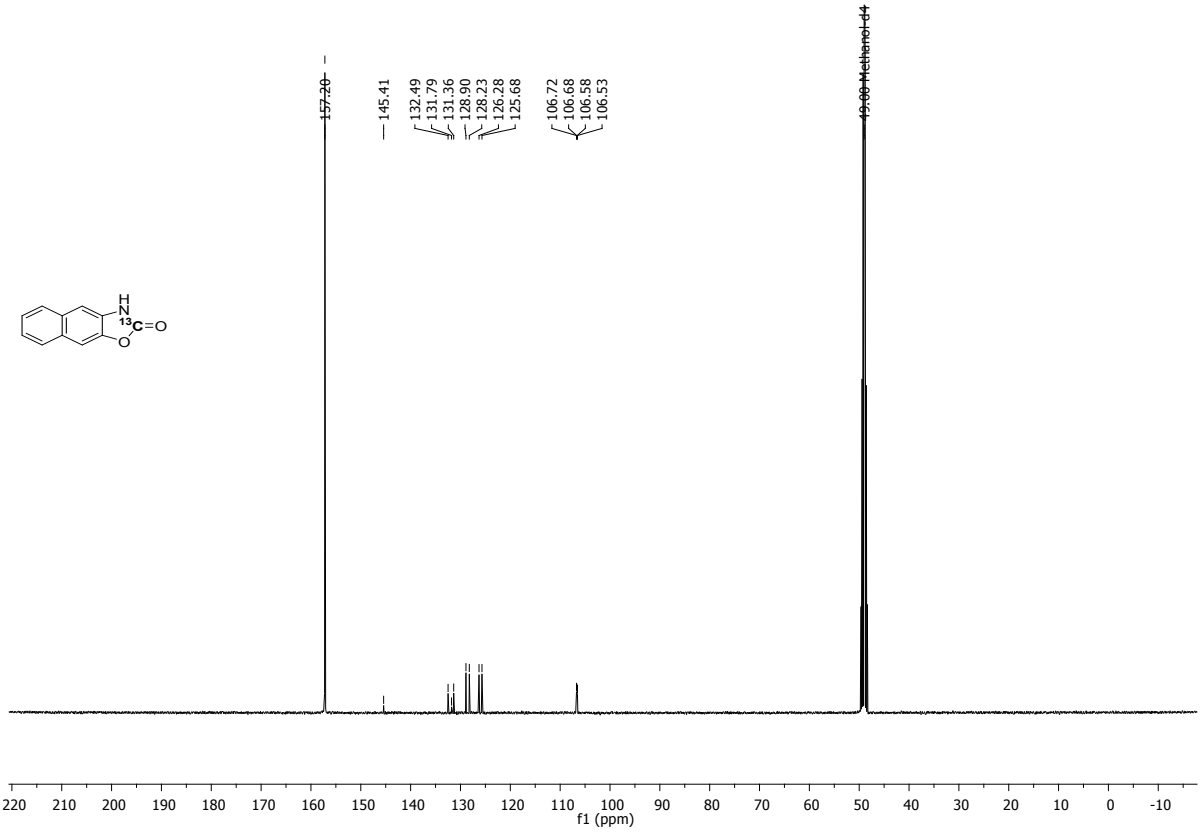
[^{13}C] 5-phenylbenzo[d]oxazol-2(3H)-one ([^{13}C]**20**)



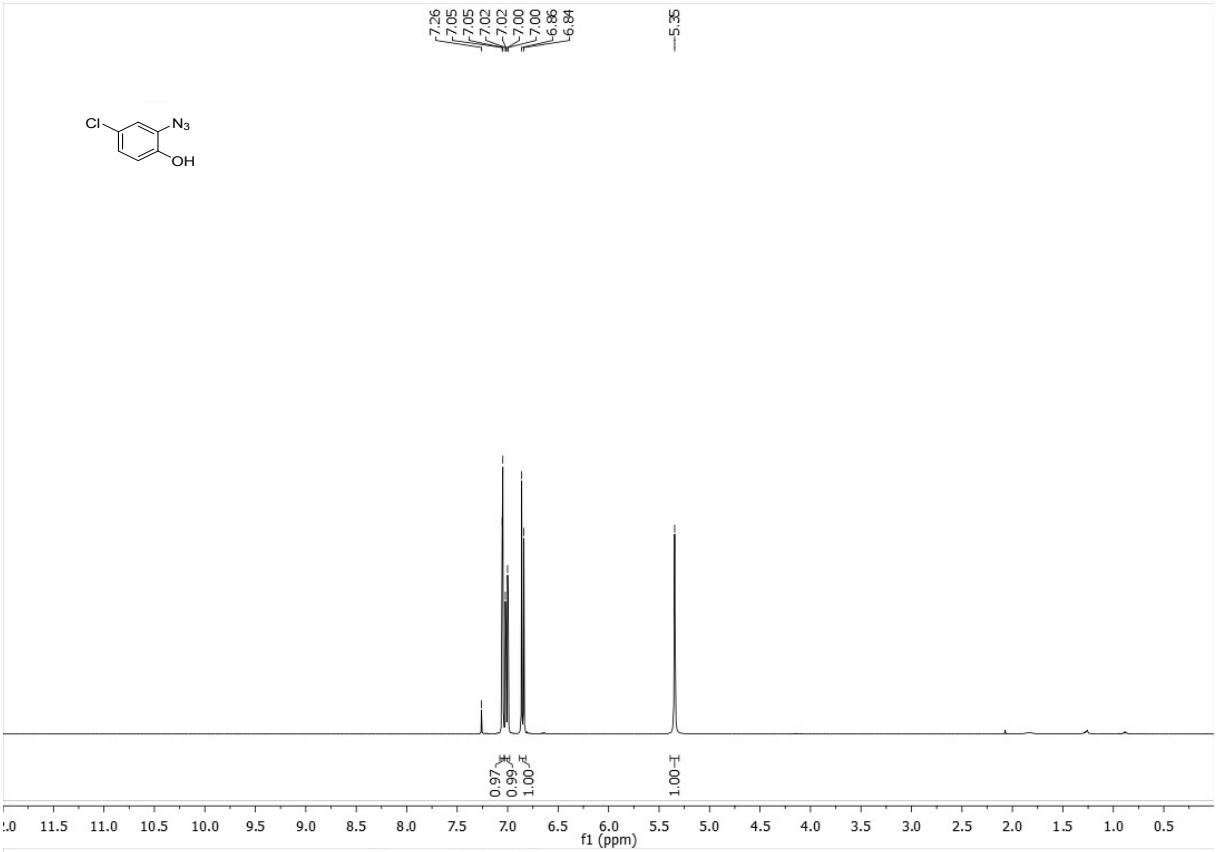


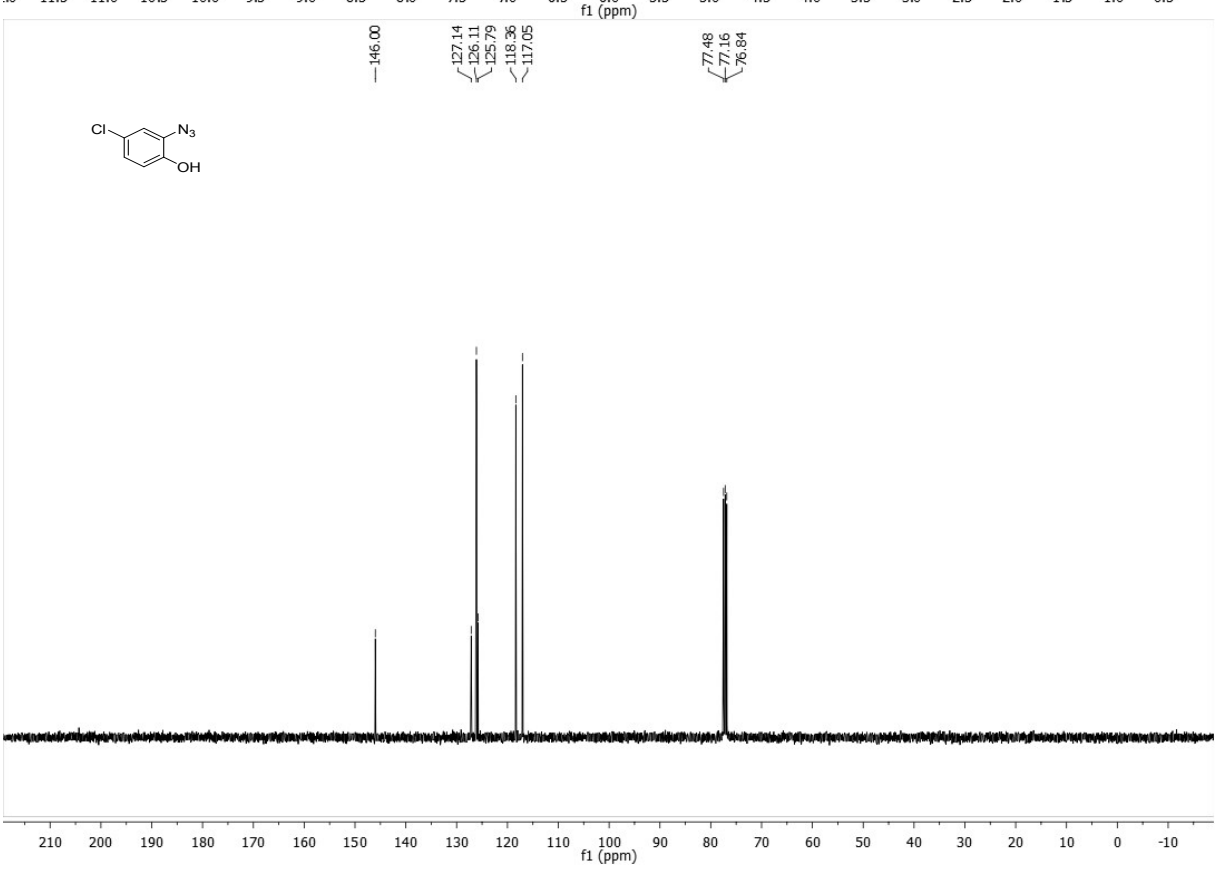
[^{13}C] naphtho[2,3-d]oxazol-2(3H)-one ([^{13}C]**21**)



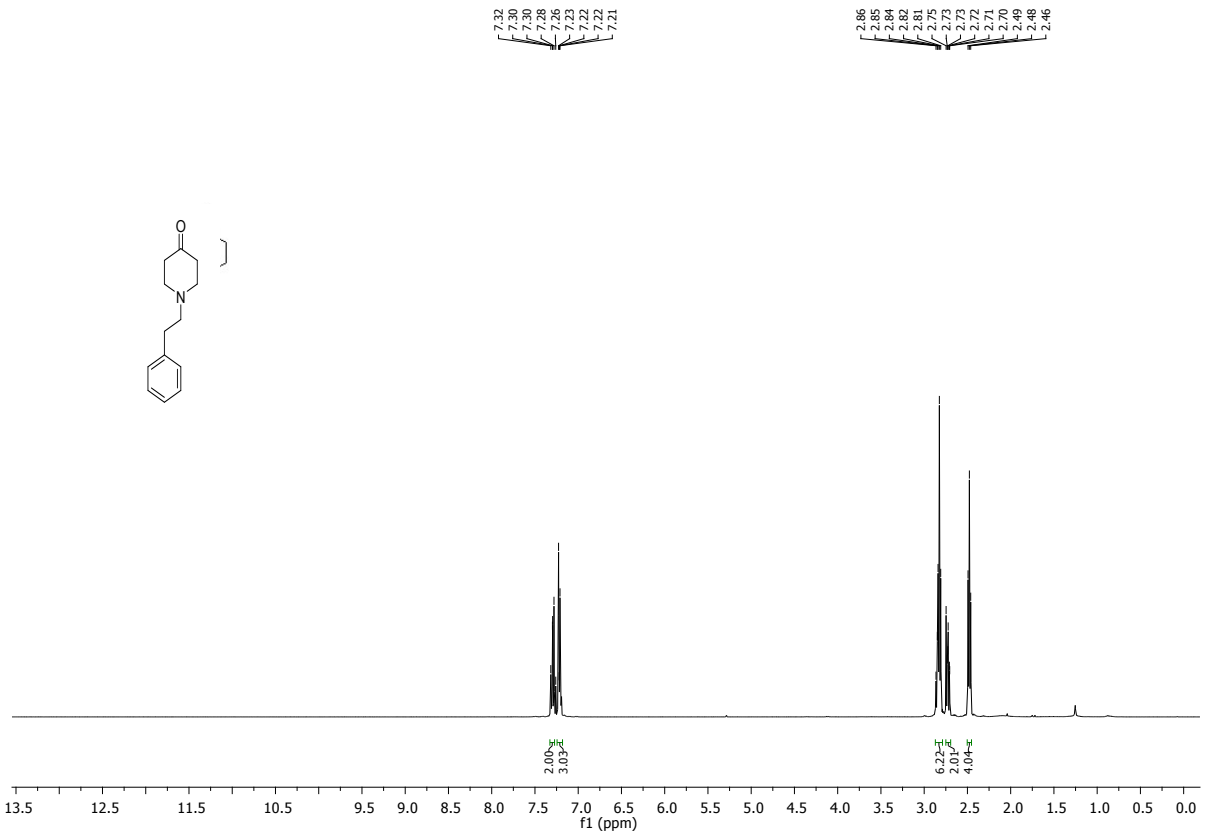


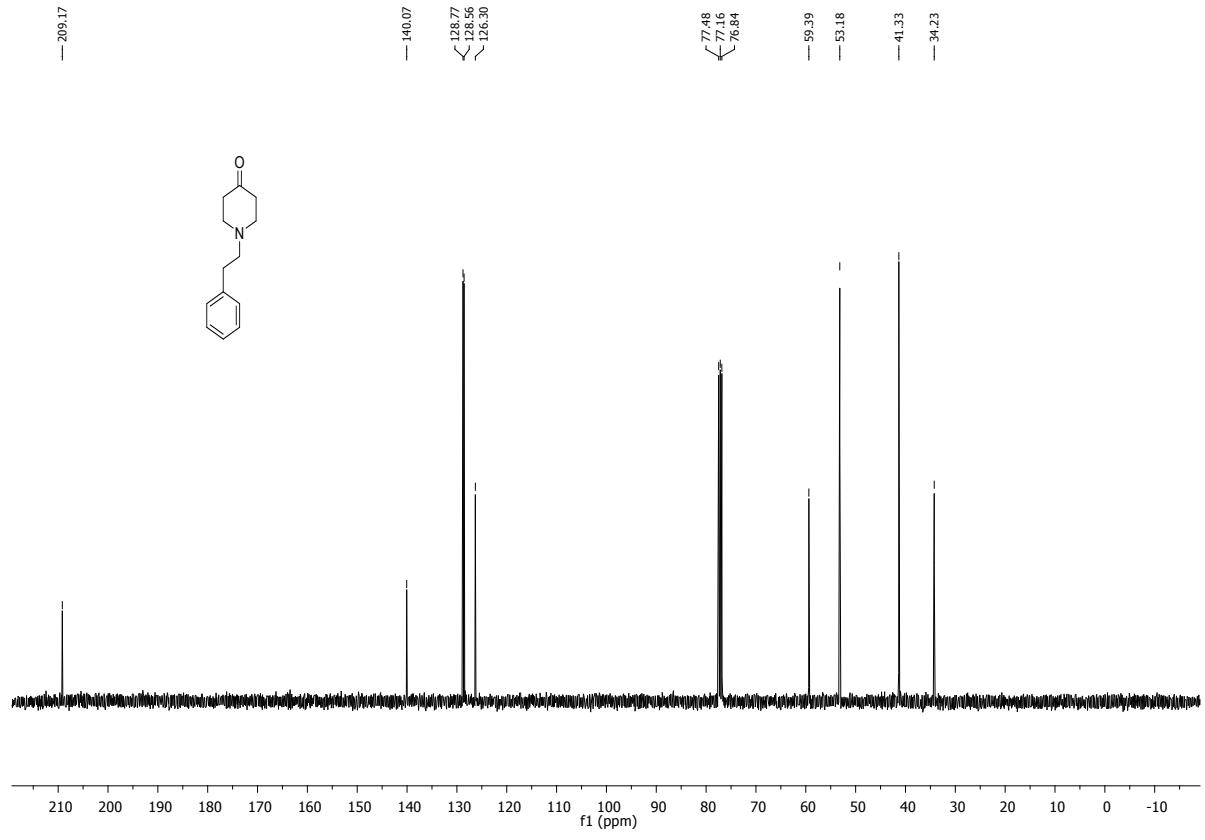
2-azido-4-chlorophenol (S37)



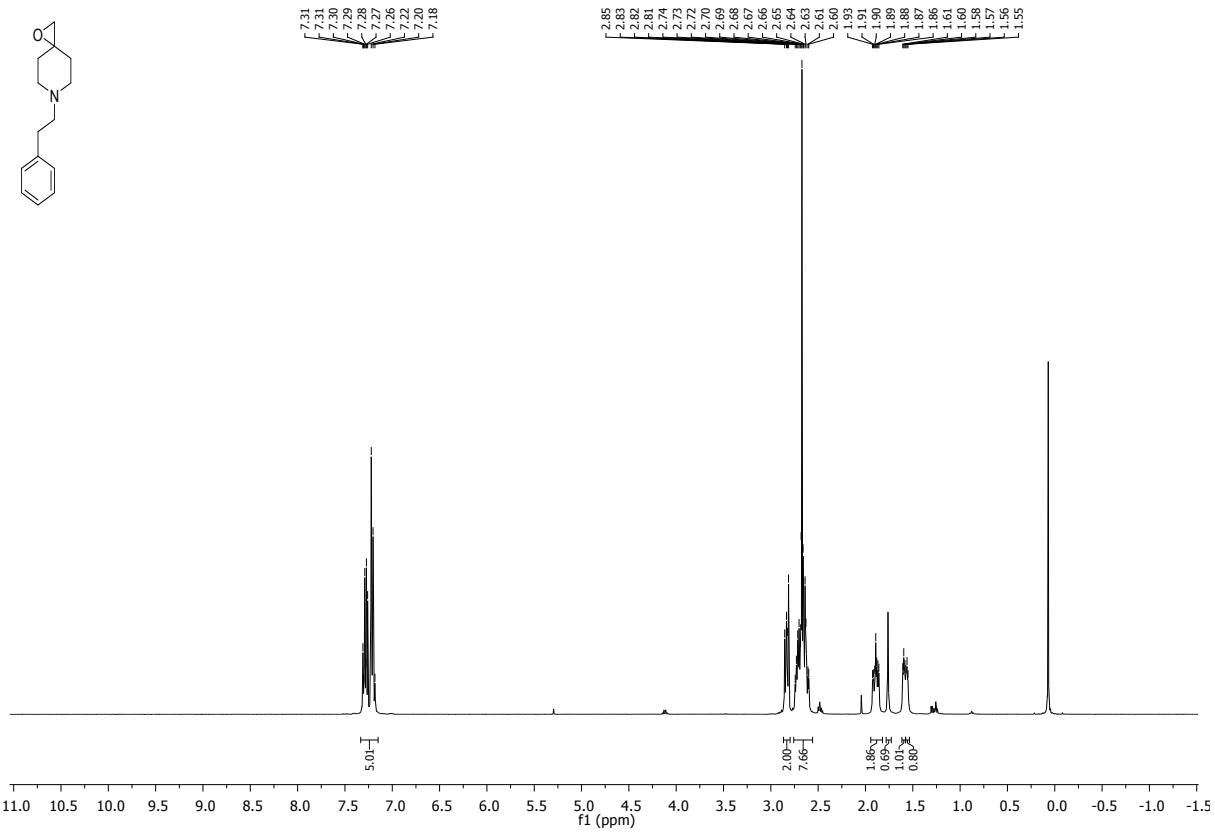


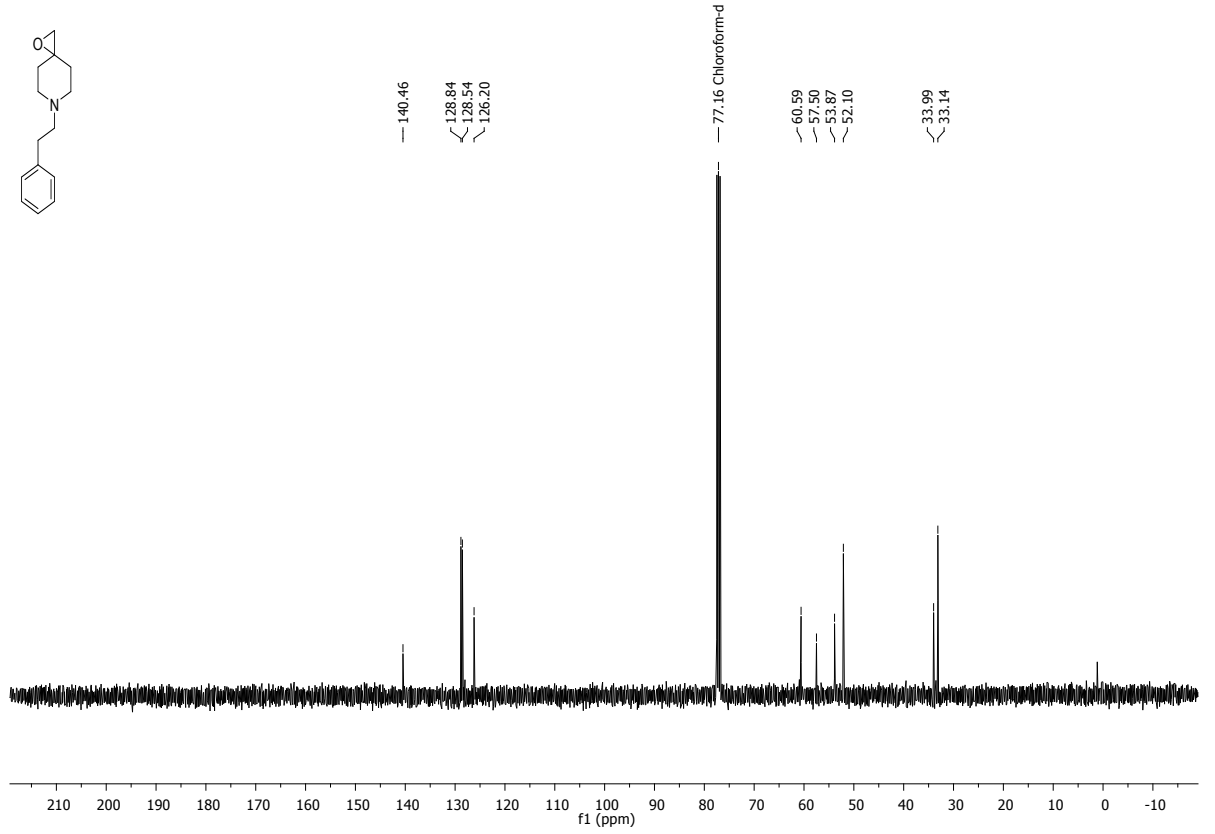
1-phenethylpiperidin-4-one (S43)



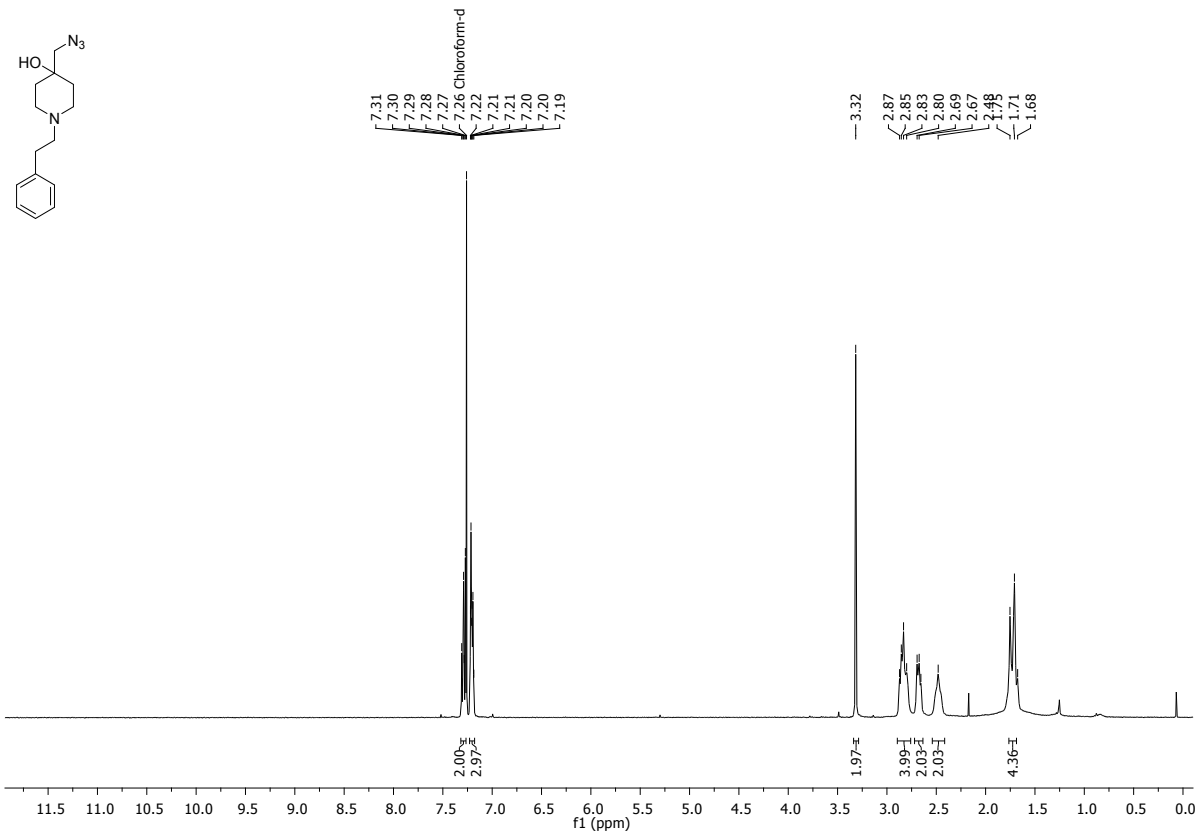


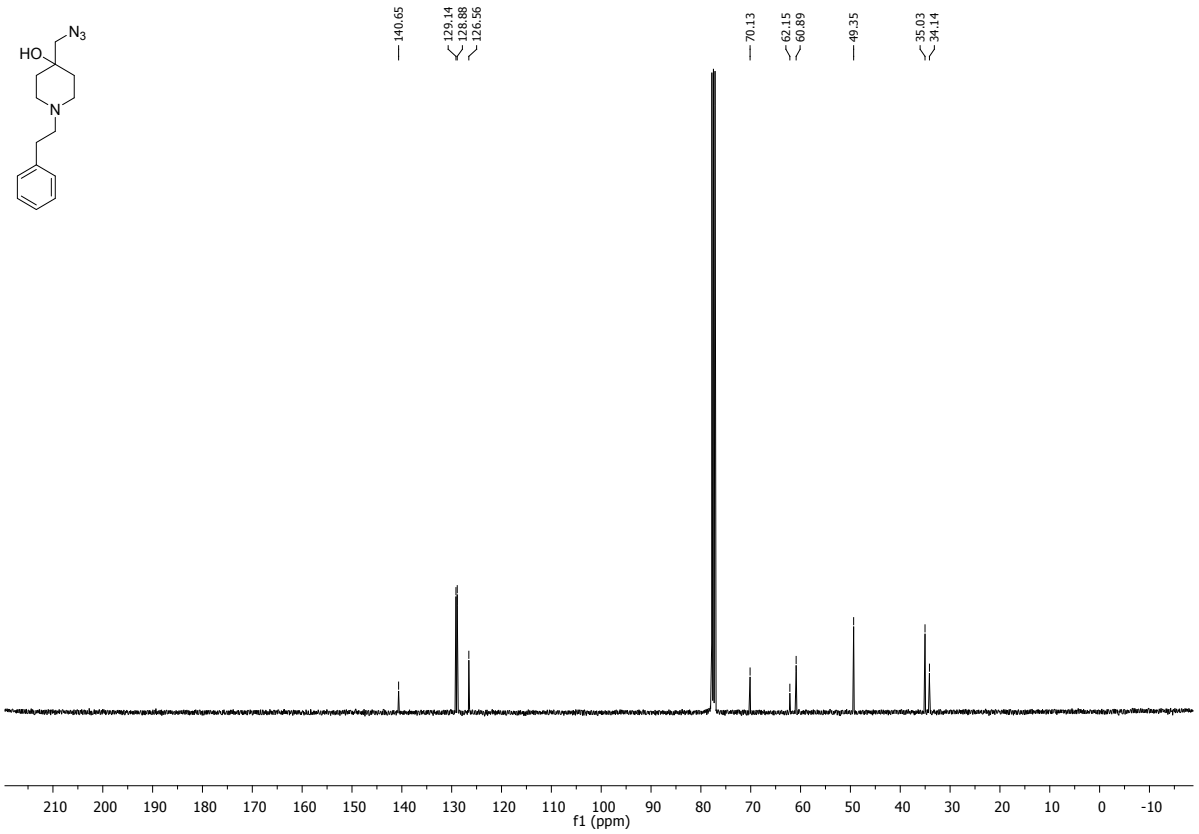
6-phenethyl-1-oxa-6-azaspiro[2.5]octane (S44)



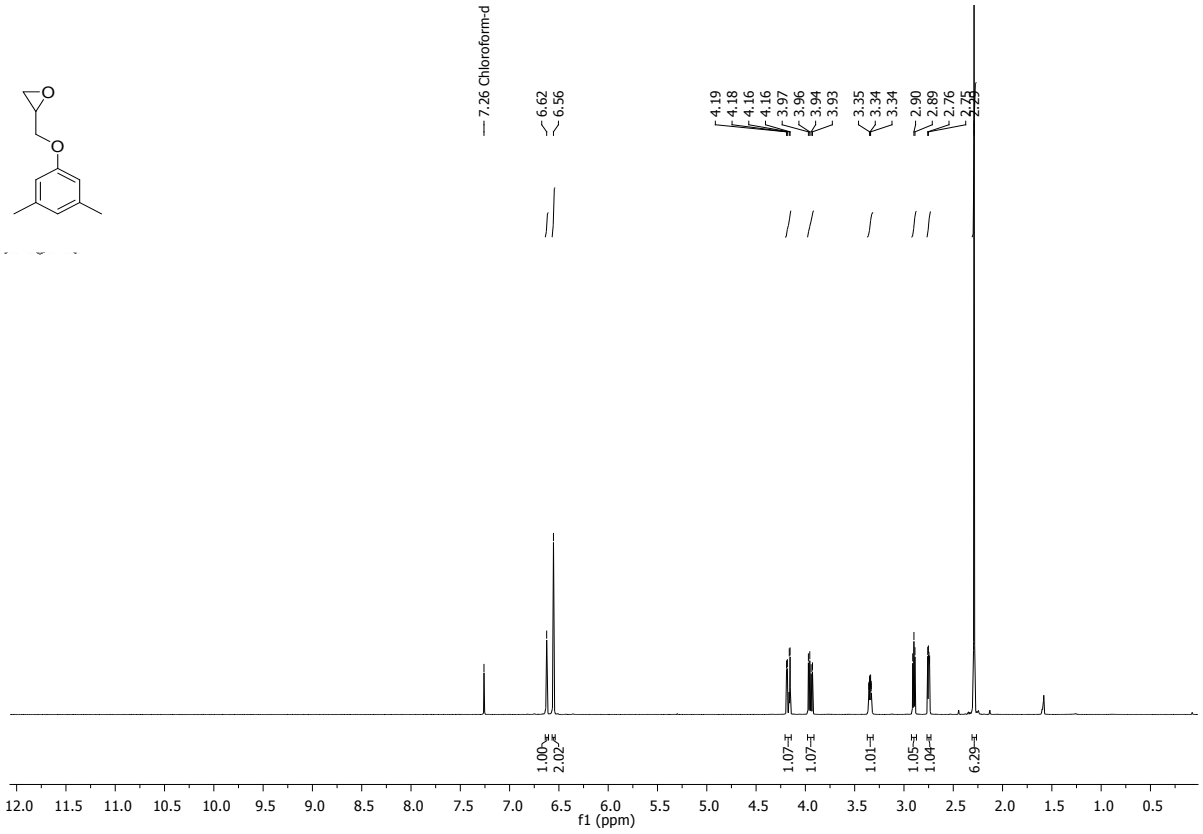


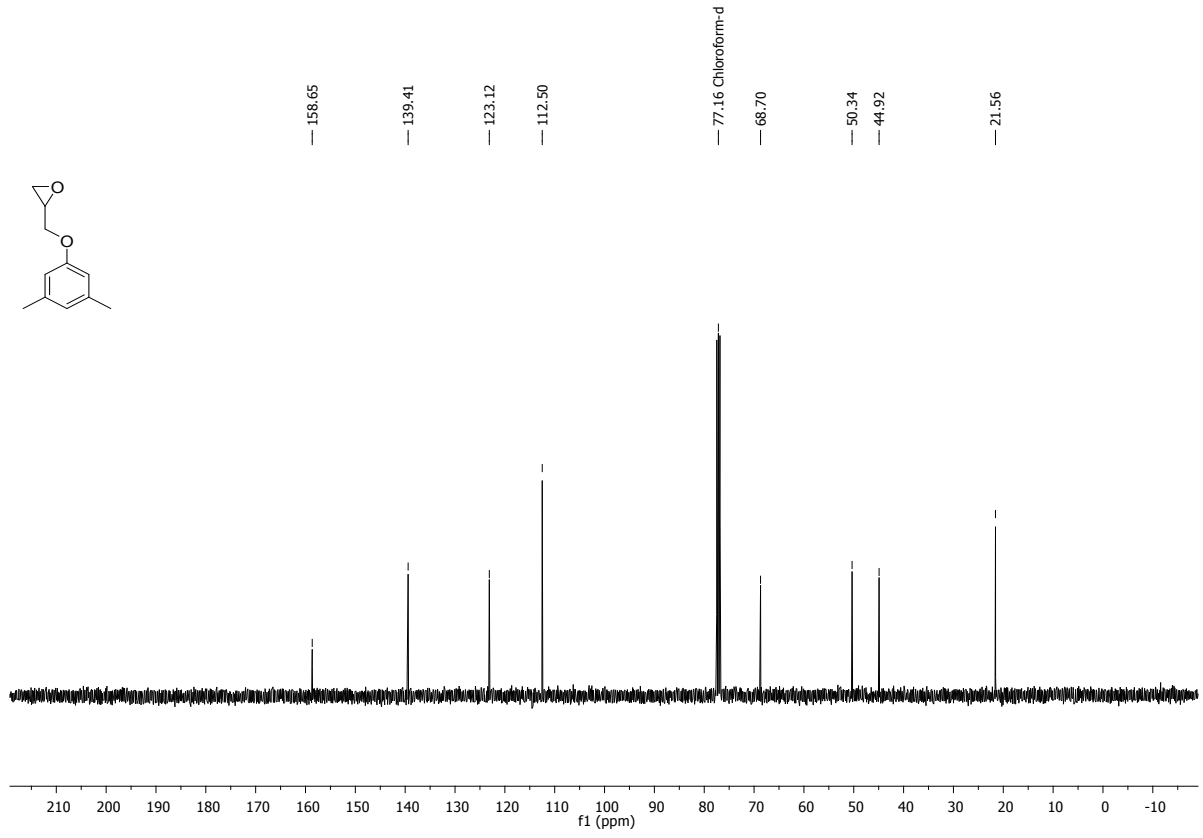
4-(azidomethyl)-1-phenethylpiperidin-4-ol (S45)



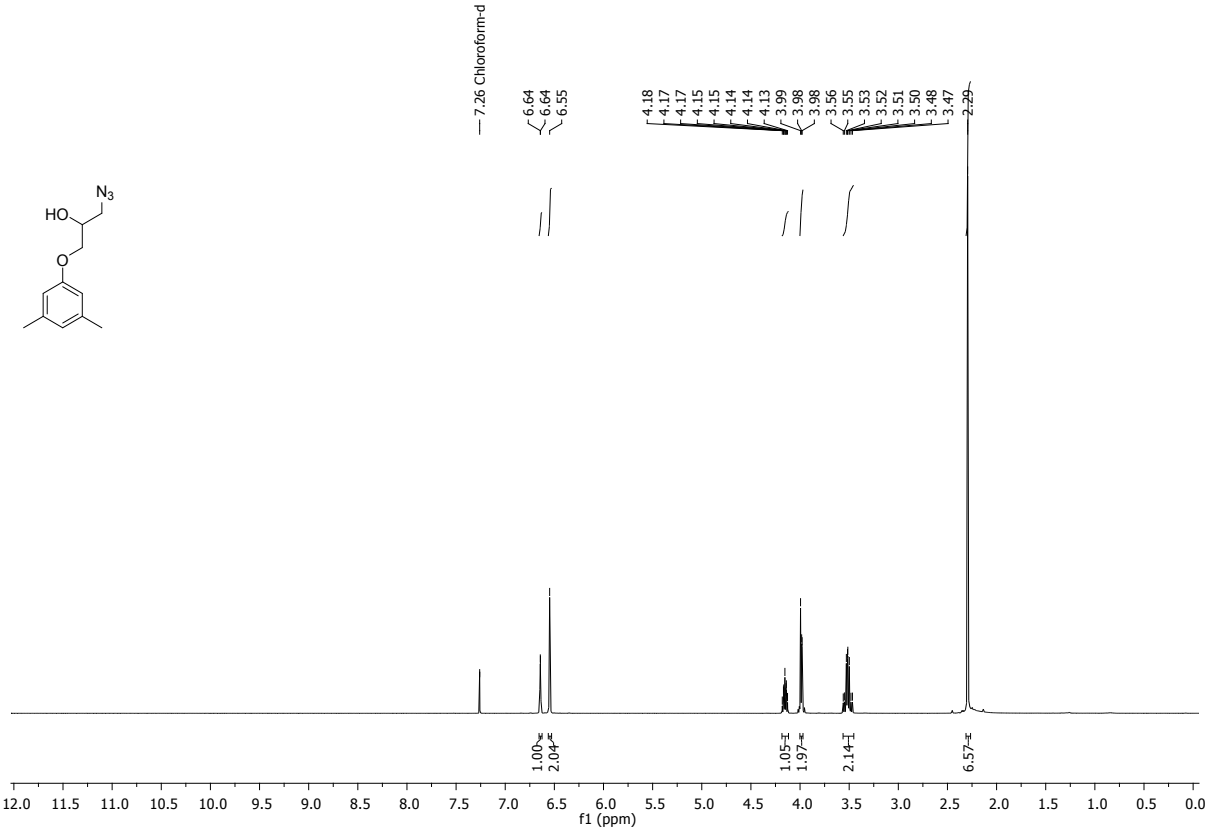


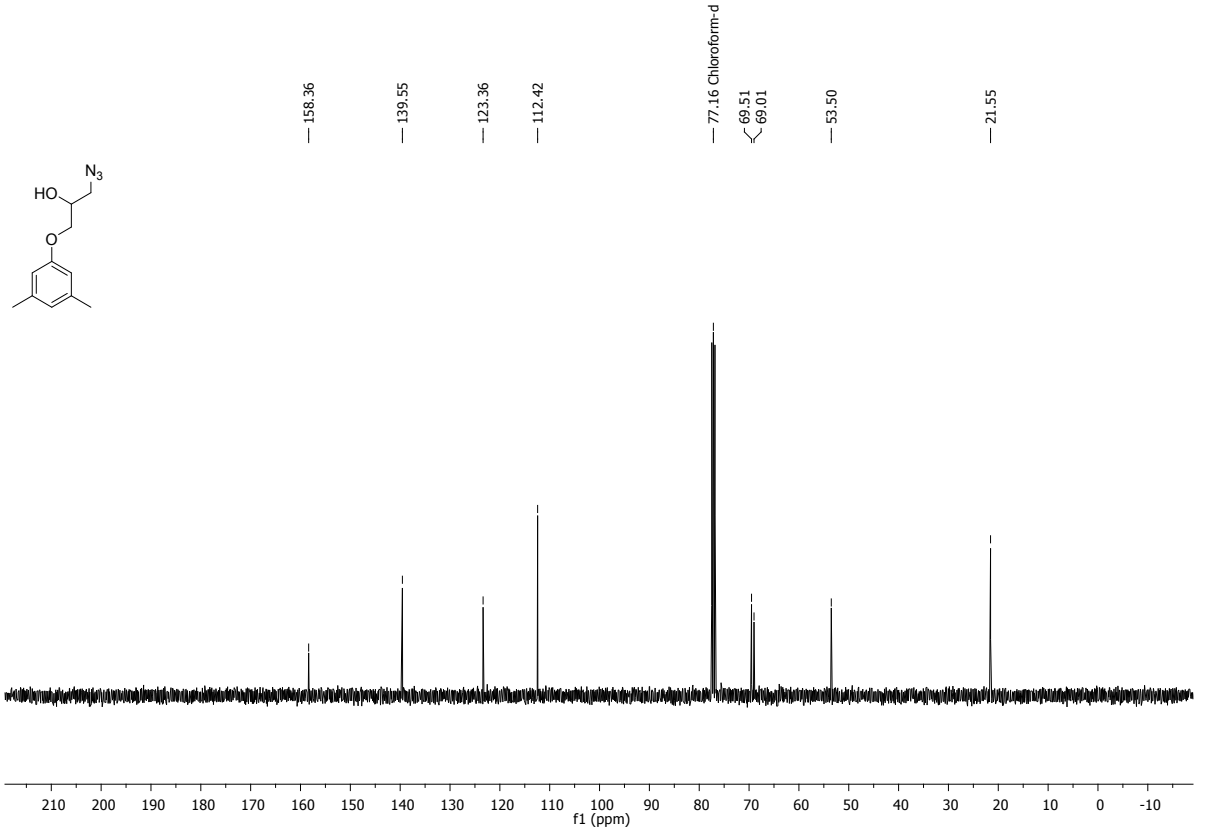
2-((3,5-dimethylphenoxy)methyl)oxirane (S41)



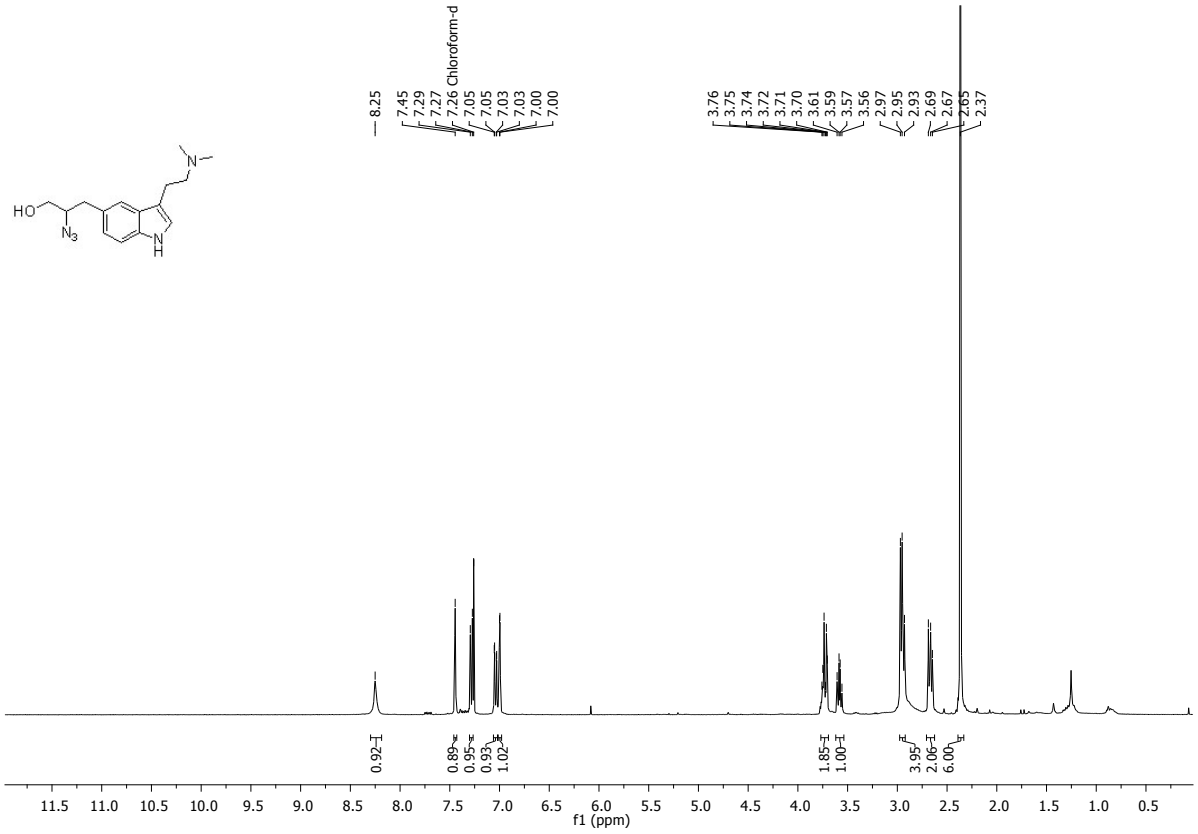


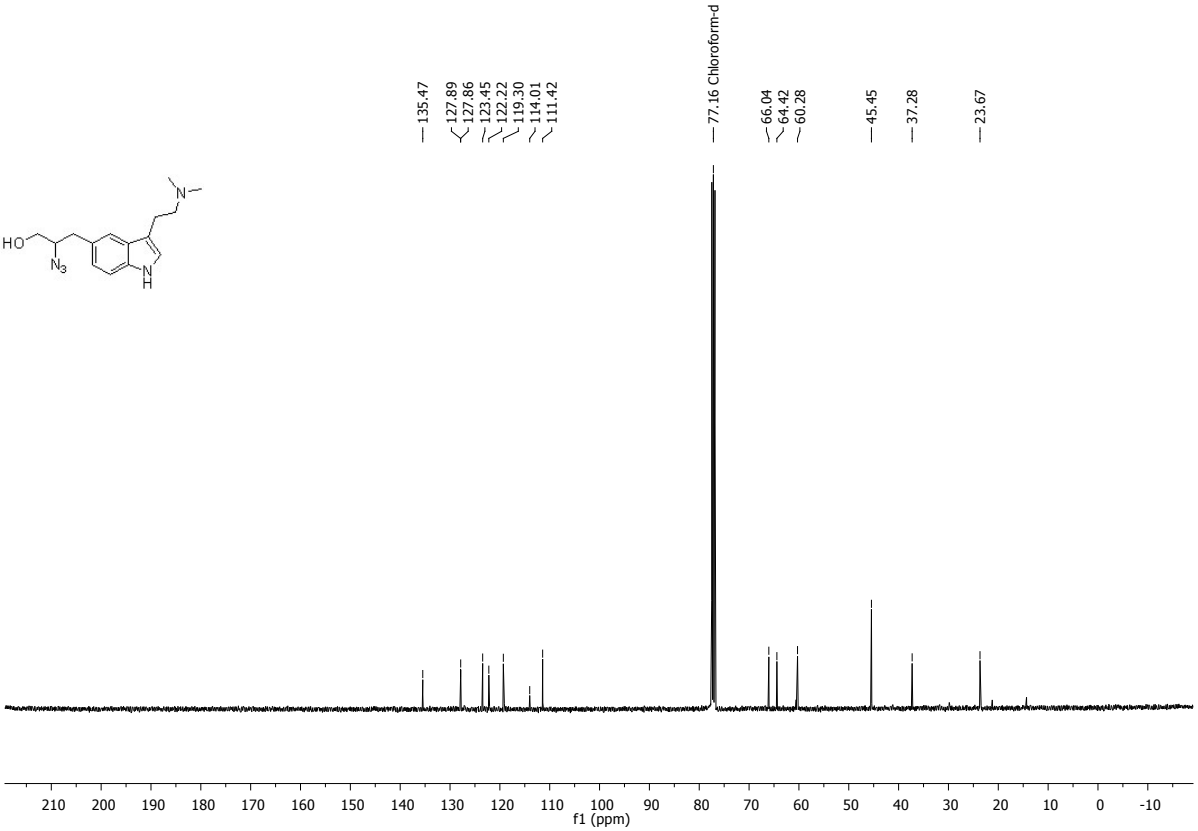
***1-azido-3-(3,5-dimethylphenoxy)propan-2-ol* (S42)**



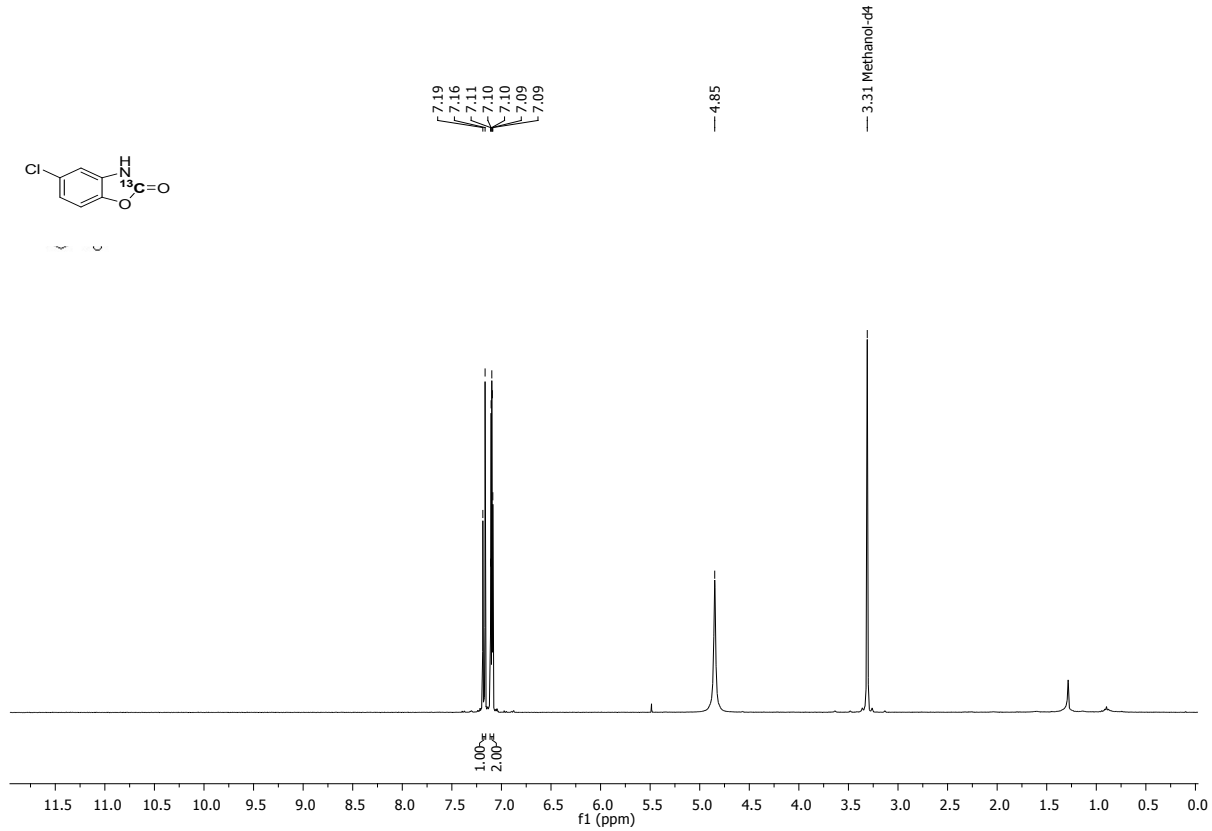


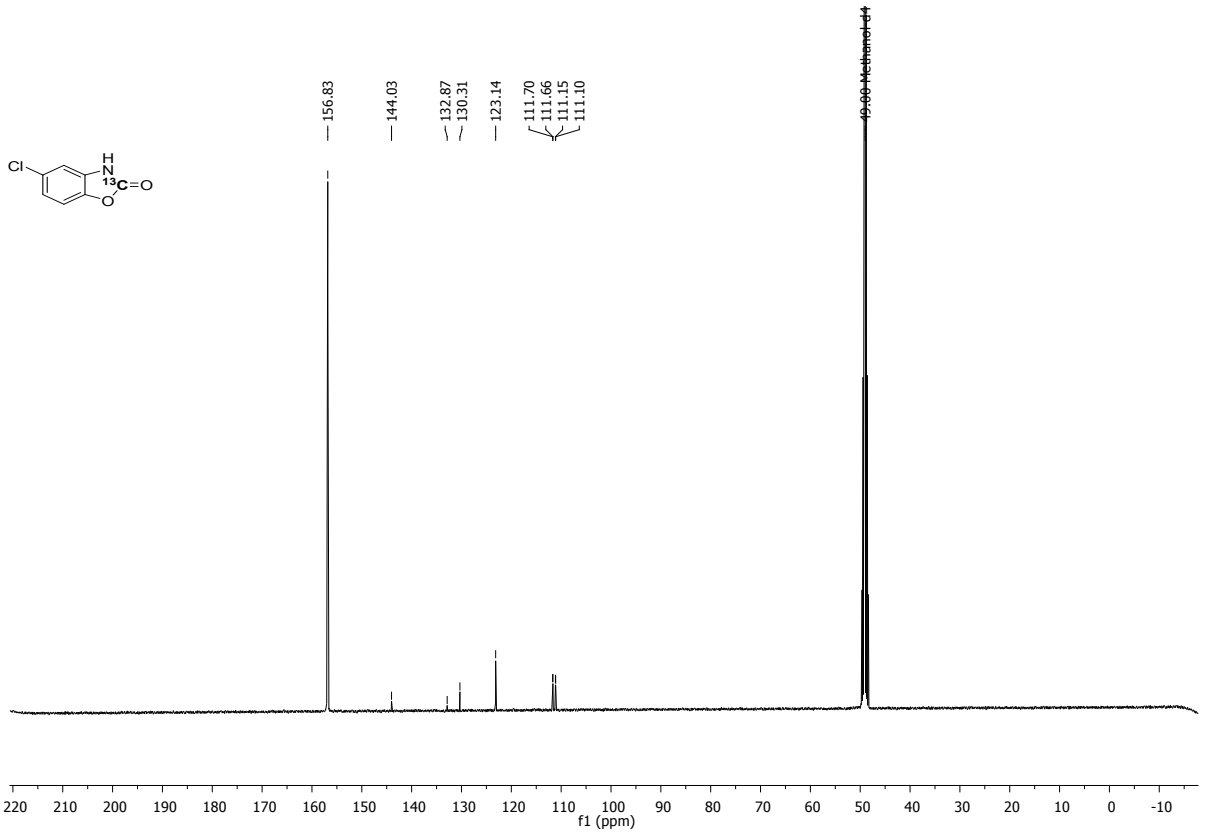
2-azido-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)propan-1-ol (S51)



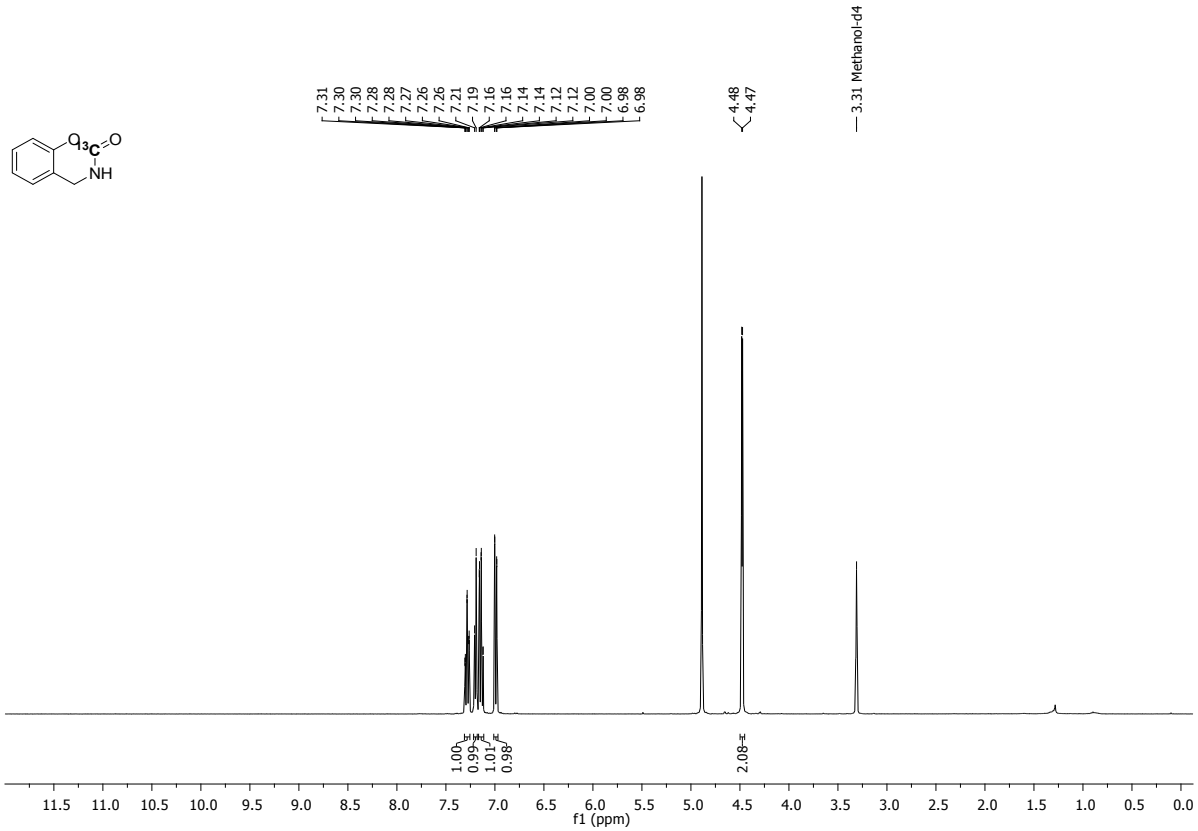


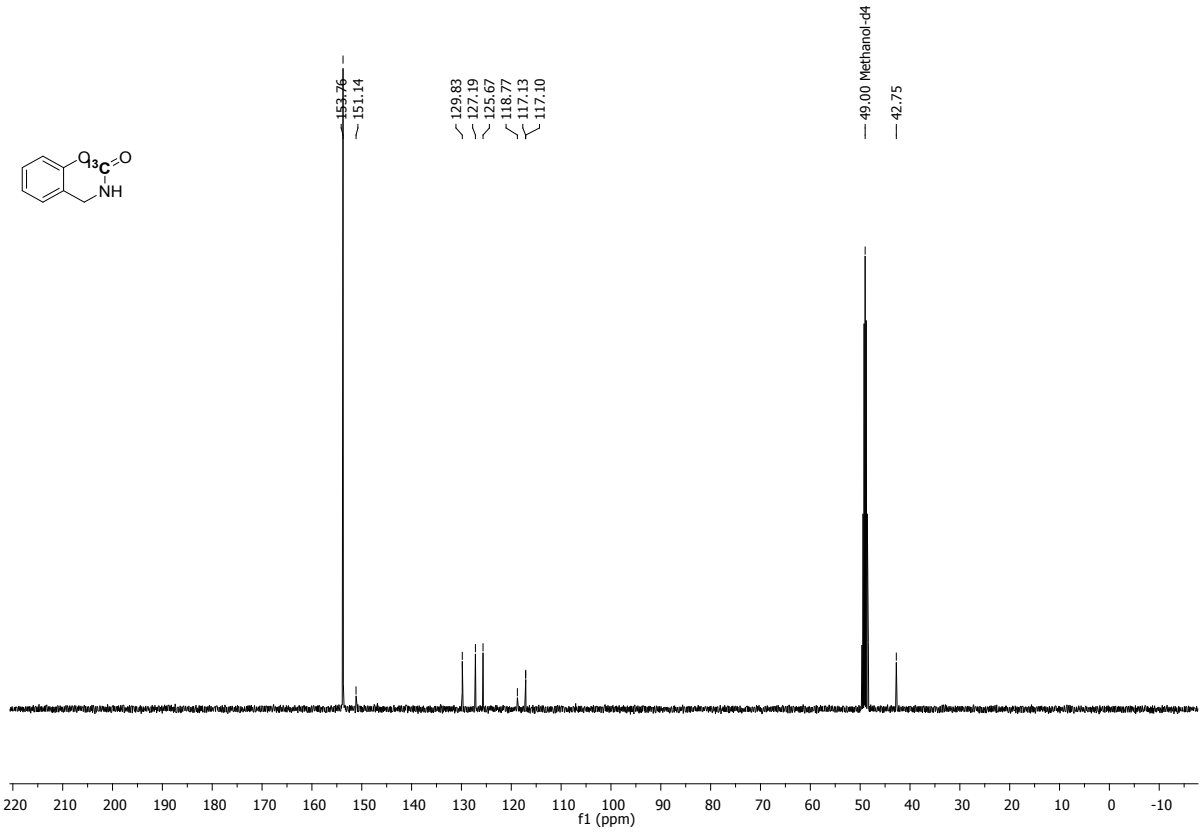
[^{13}C]Chloroxazone ([^{13}C]22)



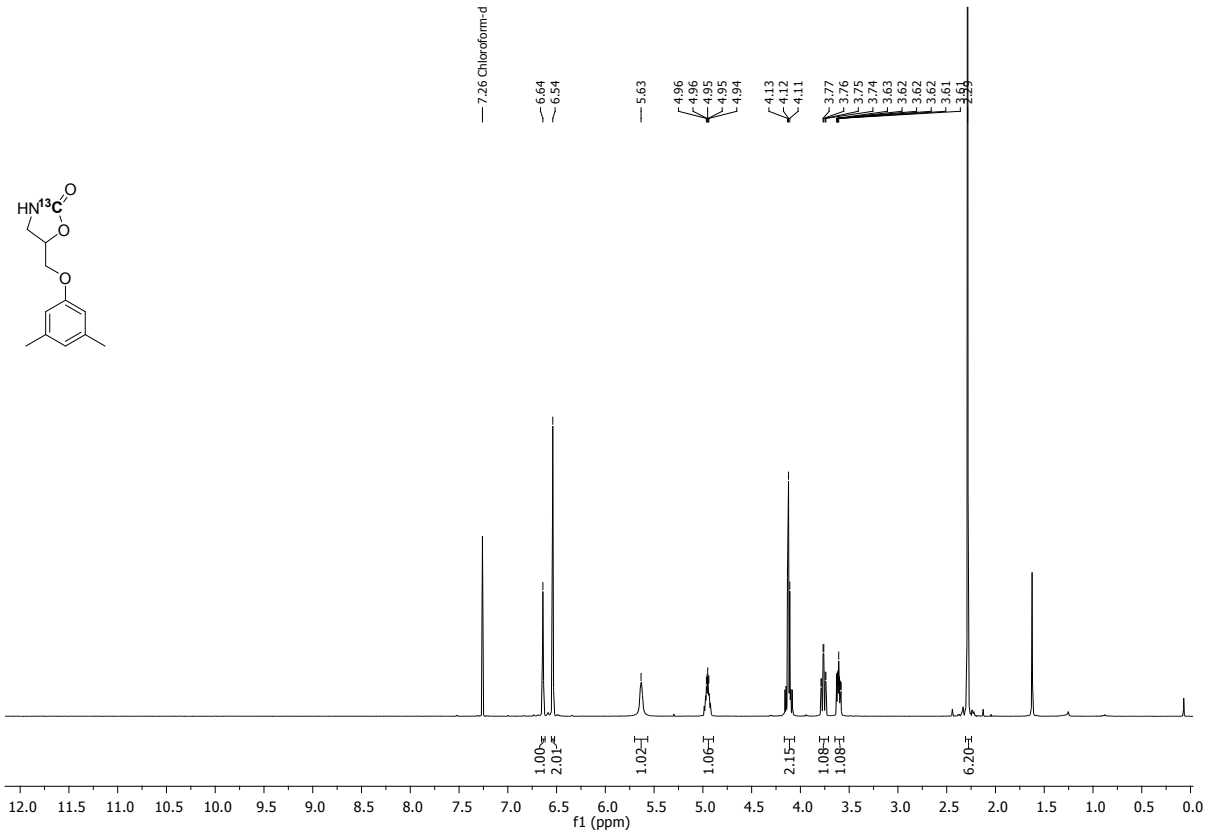


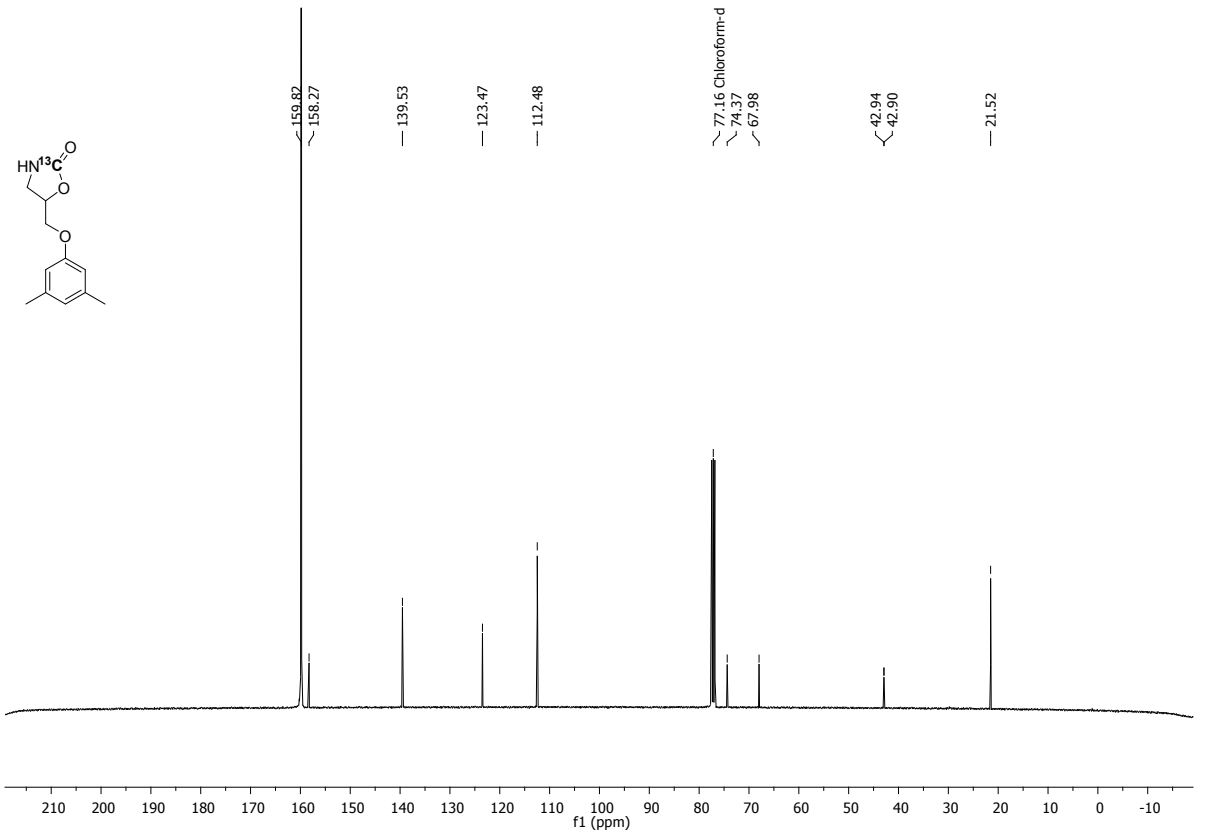
[^{13}C] Caroxazone precursor ([^{13}C]**23**)



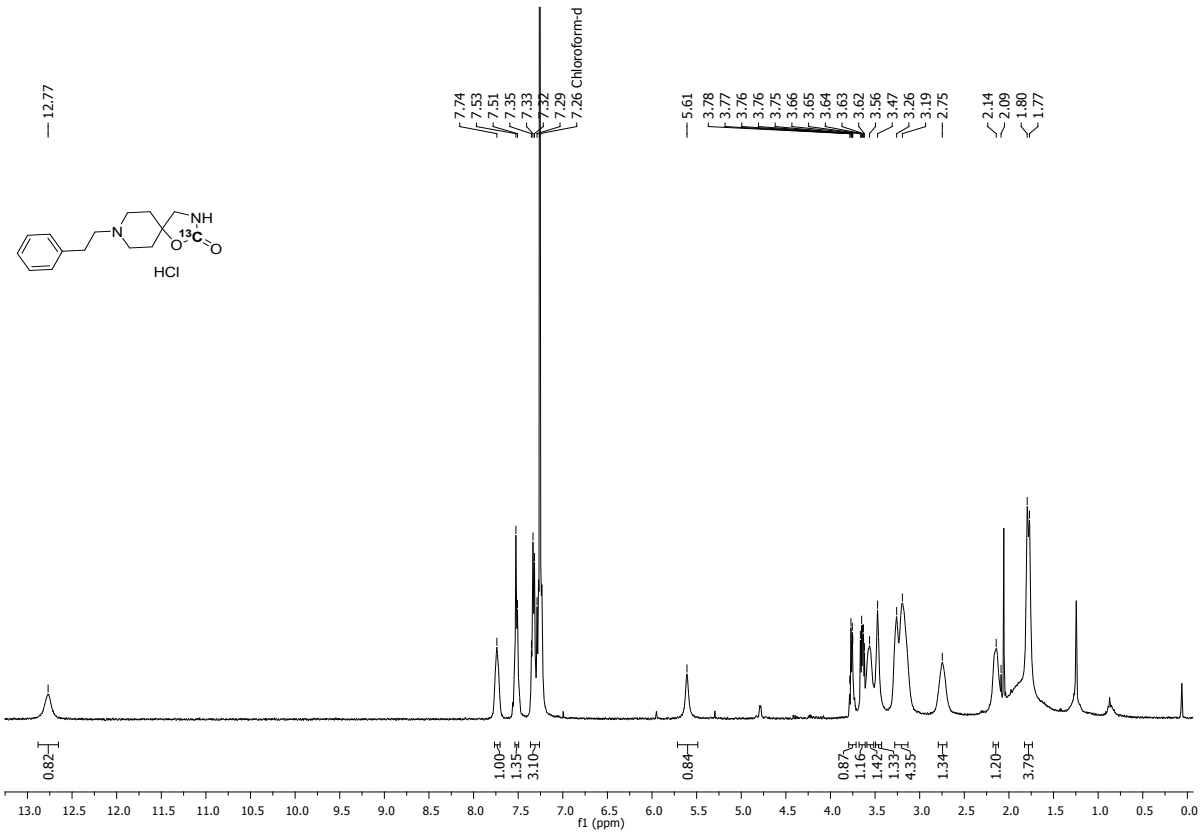


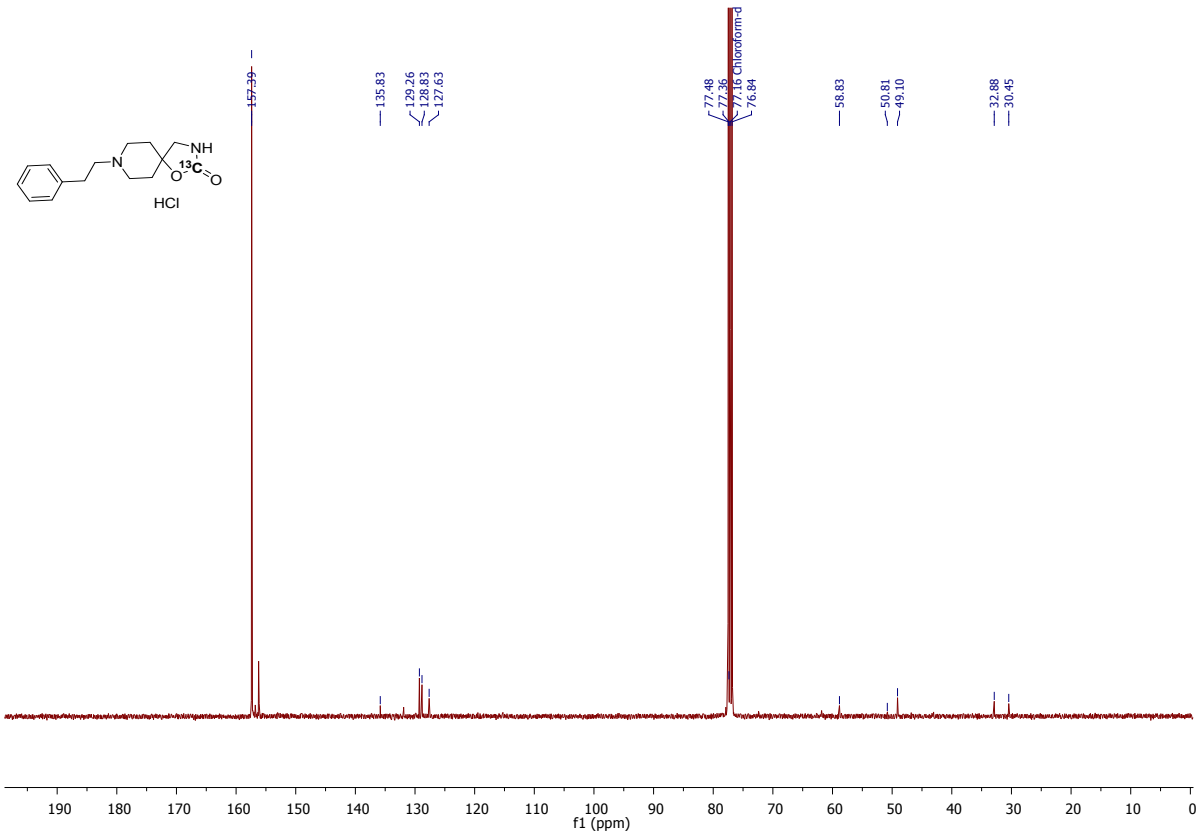
[^{13}C]Metaxalone [^{13}C]24



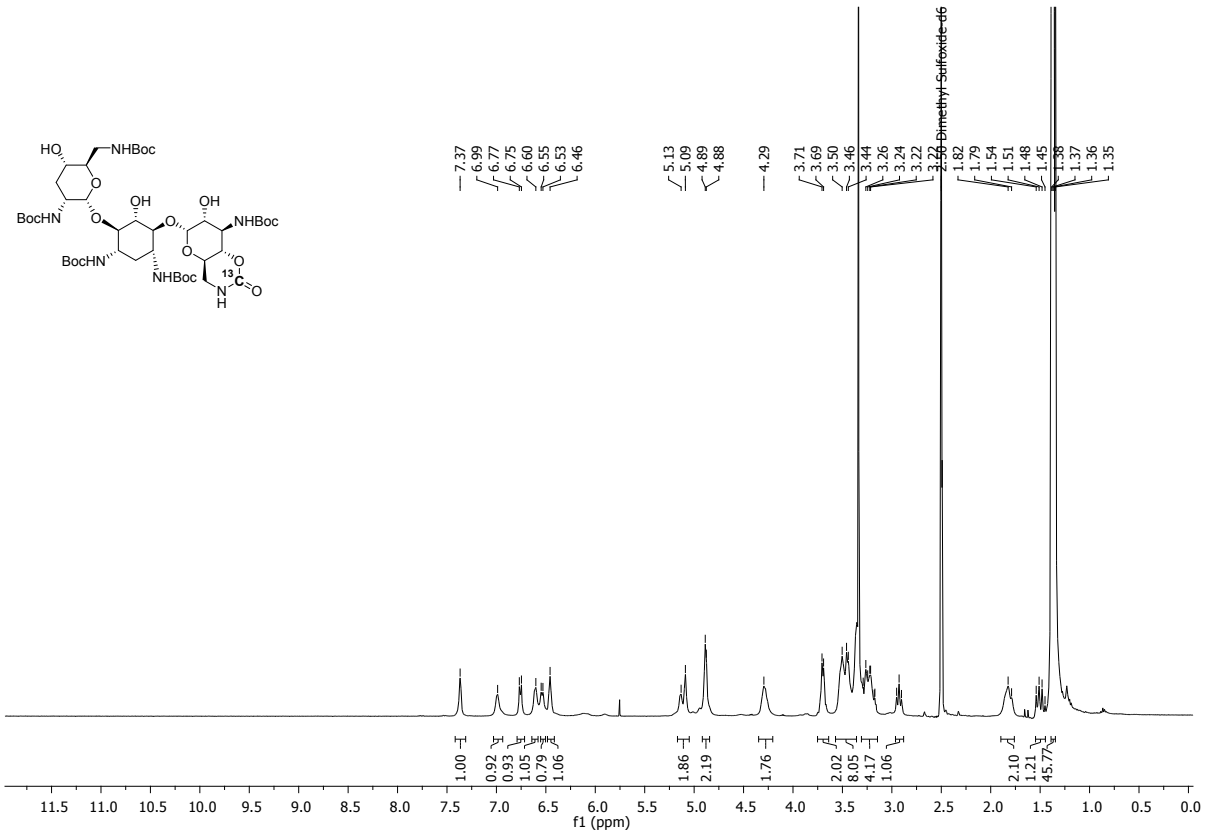


[^{13}C]Fenspiride hydrochloride ([^{13}C]25 HCl)

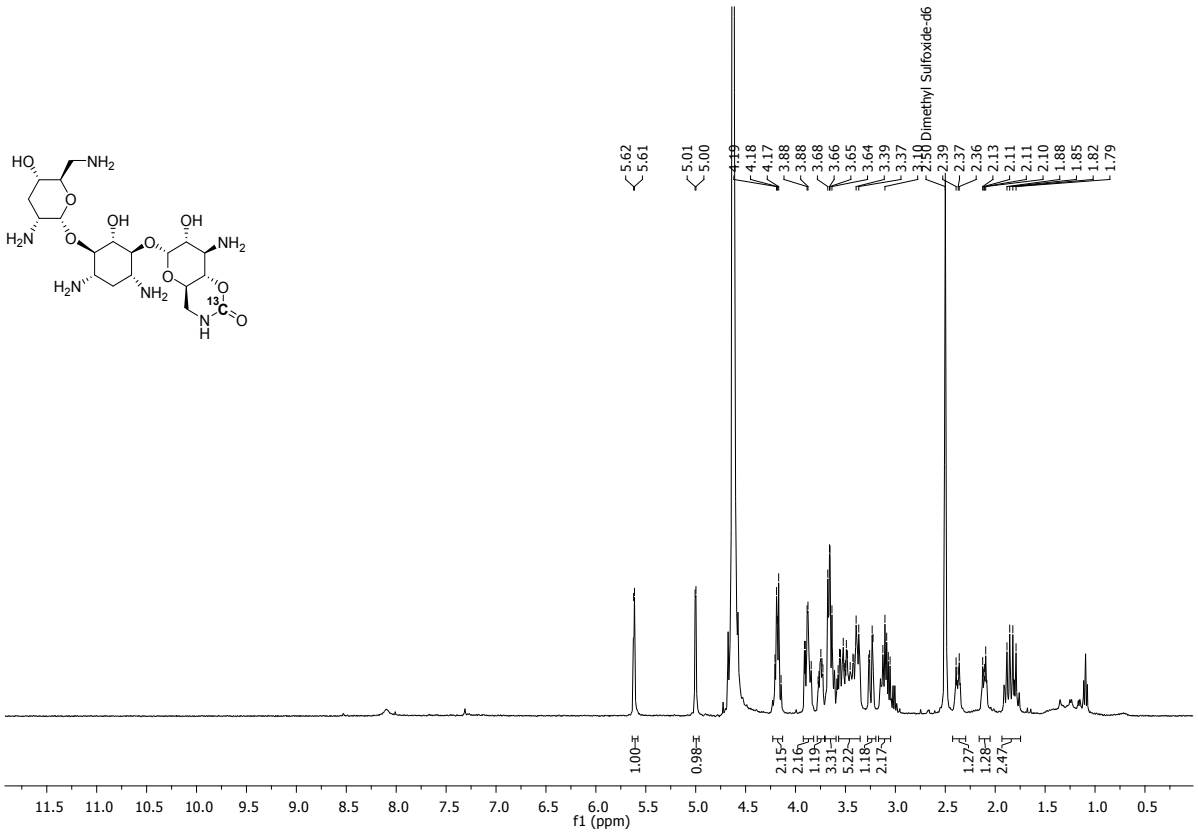


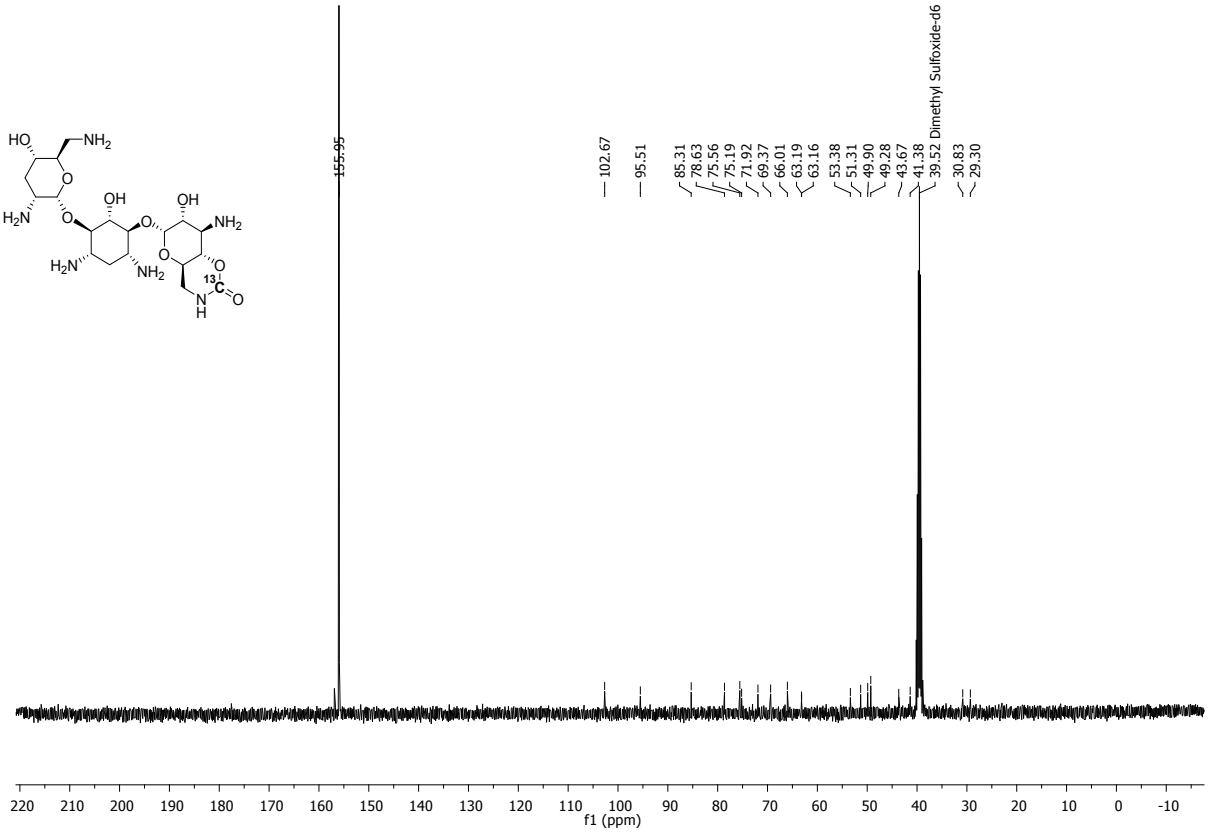


[^{13}C]-5-Boc-Tobramycine carbamate derivative ([^{13}C]**26**)

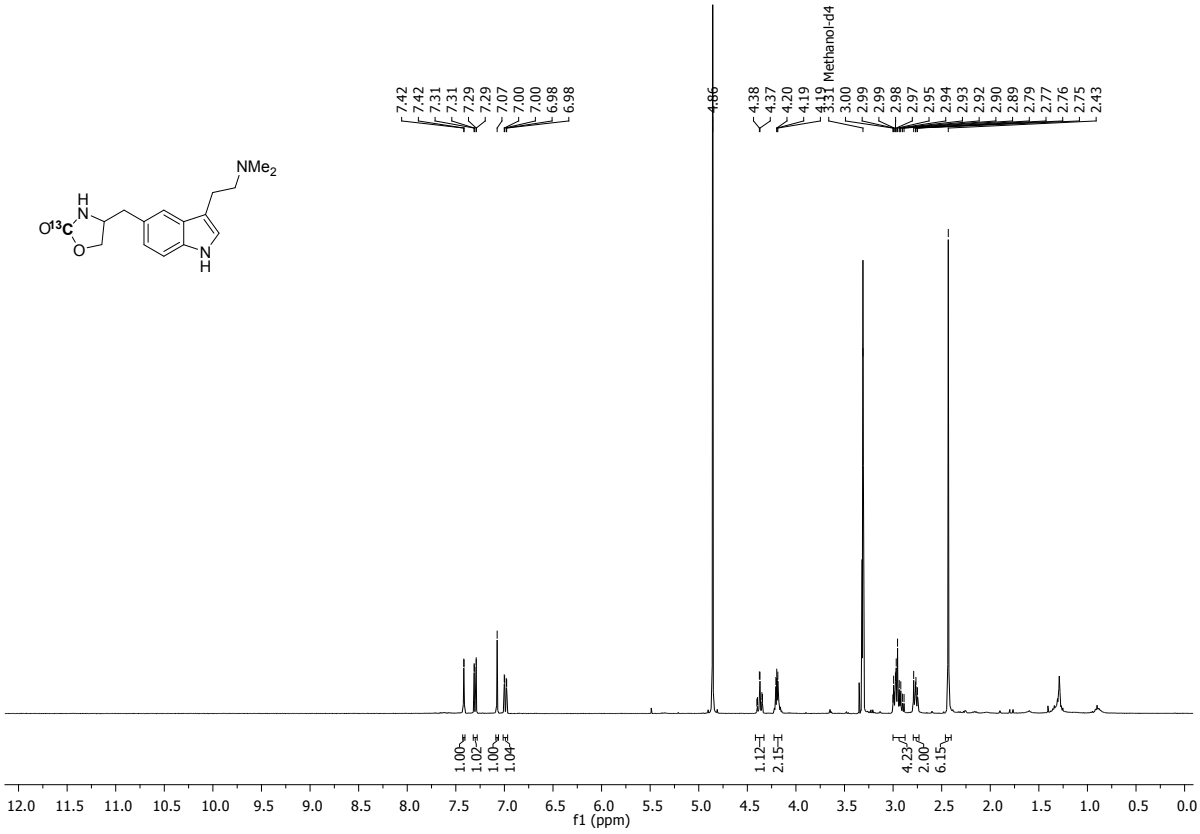


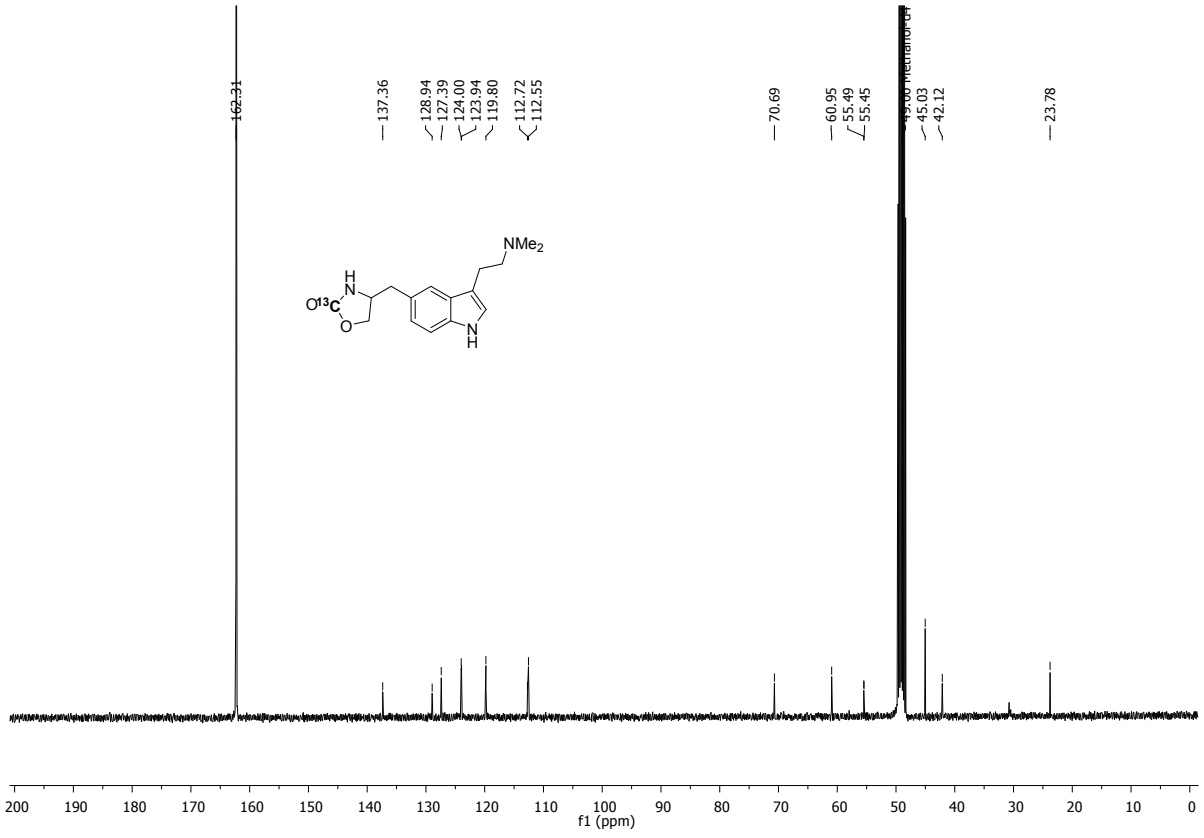
[^{13}C] Tobramycine carbamate derivative ([^{13}C]**S49***)*



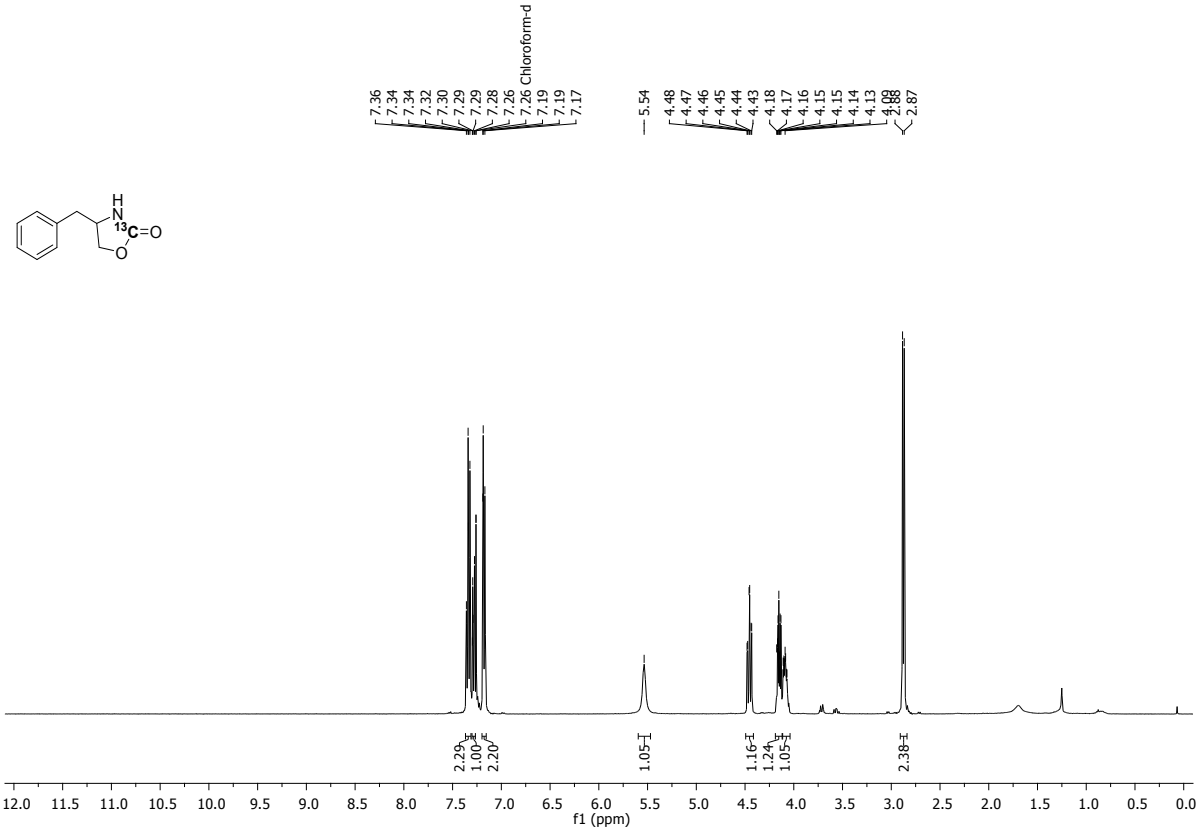


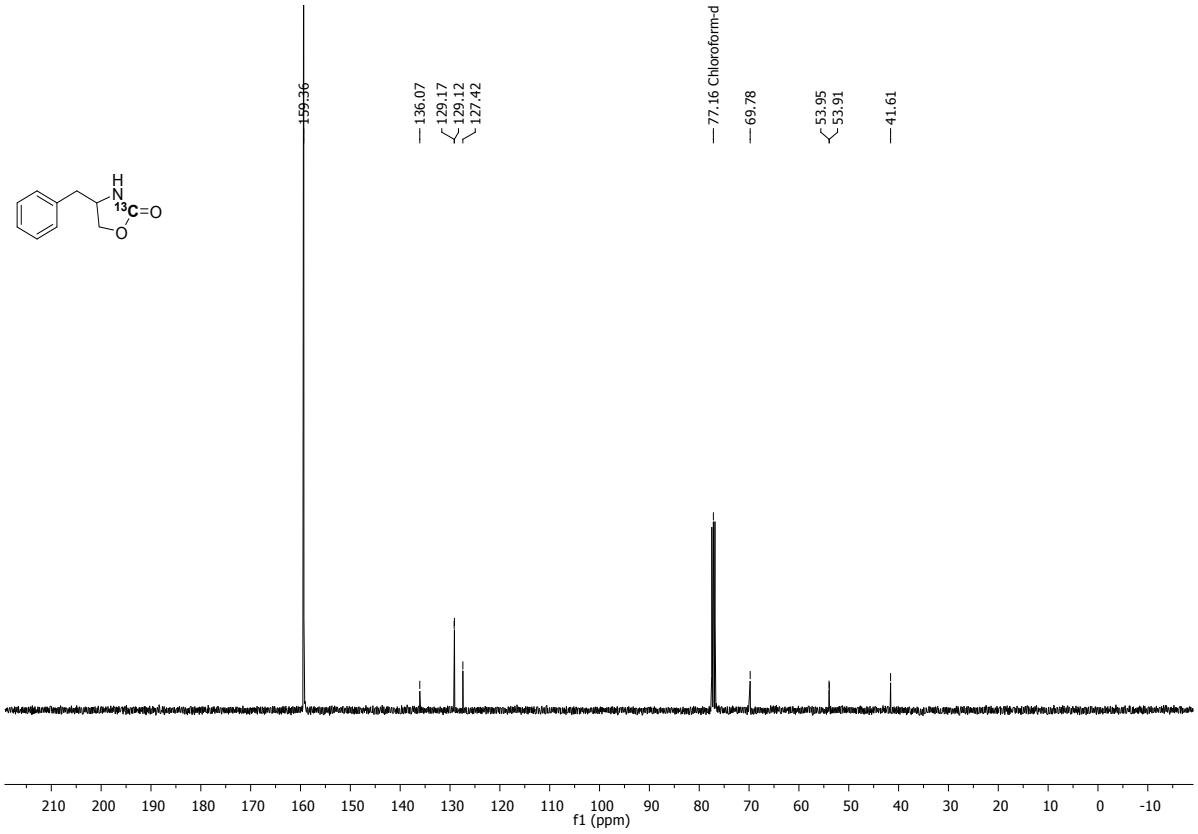
[^{13}C] Zolmitriptan ([^{13}C]30)



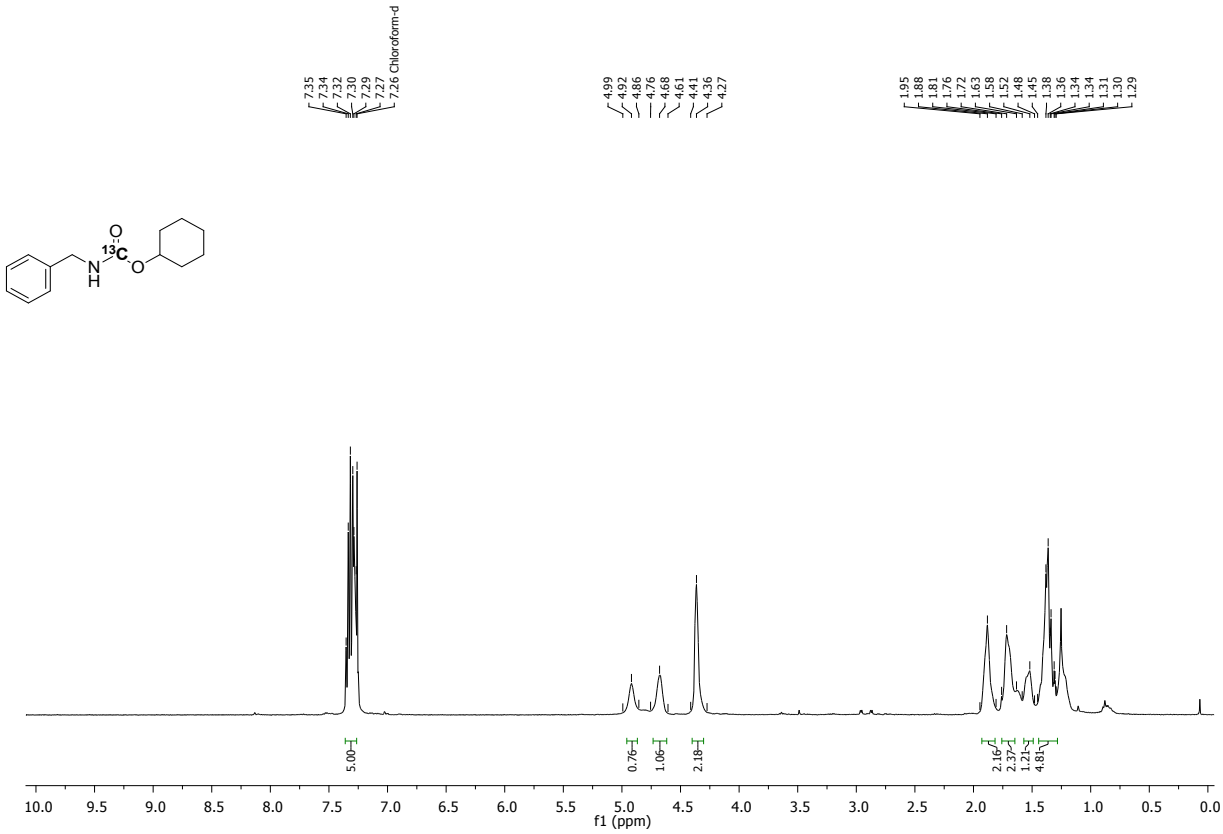


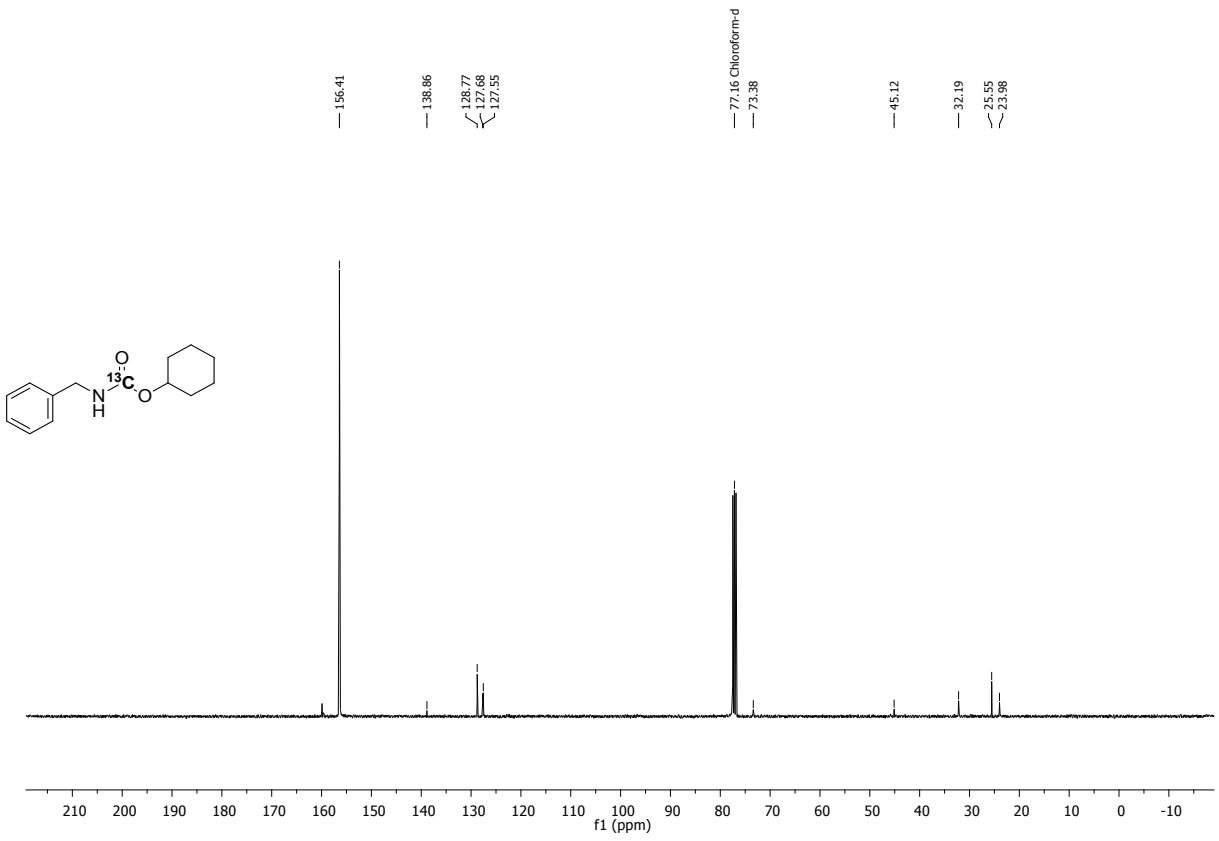
[^{13}C] 4-benzyloxazolidin-2-one-2 ([^{13}C]28)





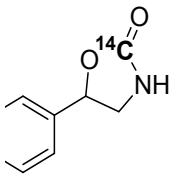
[13C] cyclohexyl benzylcarbamate ([^{13}C]**32**)



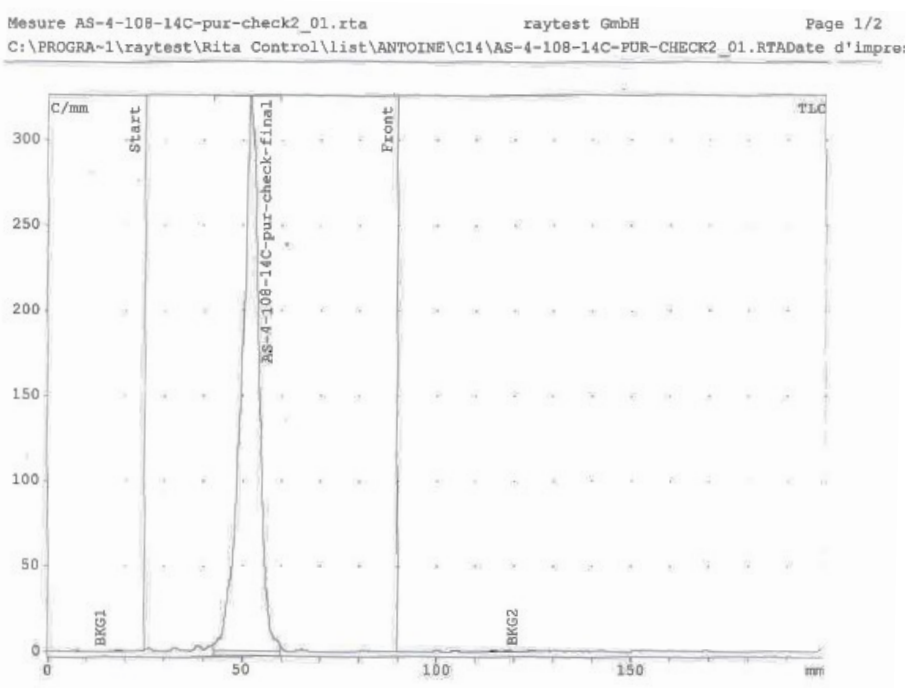

156.41
138.86
128.77
127.68
127.55
77.16 Chloroform-d
73.38
45.12
32.19
25.55
23.98
O
13C
N
H
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

5. Radio-TLC of ^{14}C-labeled compounds

[^{14}C] 5-phenyloxazolidine-2-one ([^{14}C]2)



$C_8{}^{14}CH_9NO_2$
MW: 165.17 g.mol^{-1}
RCYield: 71 %



Description de l'échantillon

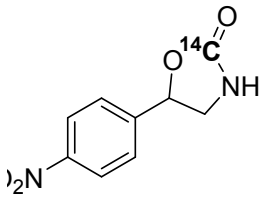
Etude:	ANTOINE		
Mesure:	AS-4-108-14C-pur-check2_01.rta, commencé:		13/11/2018 17:
Méthode:	C14		
Origine:	25 mm	Front 90 mm	
Meas. time:	0,3 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		

AS-4-108-14c-pur-check2
silicagel 20F254
70AcOEt/30Hept
14C
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

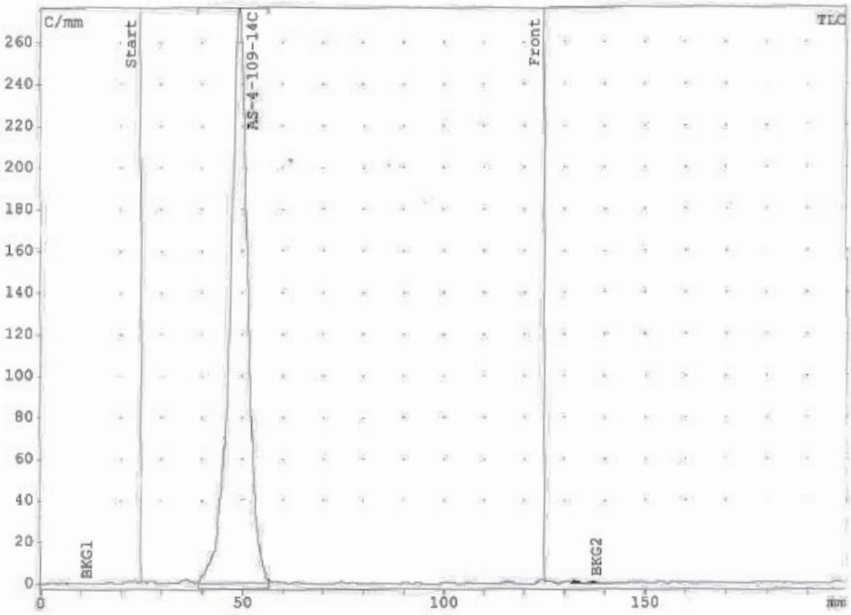
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS-4-108-14C-pu	0,418	DD	1704,372	100,00
Sum in ROI			1704,372	
Aire totale			1720,944	
Aire RF			1717,396	
BKG1			0,1515	
BKG2			0,1544	
Remainder RF			13,02	0,76
Remainder (Tot)			16,57	0,96

[^{14}C] 5-(4-nitrophenyl)oxazolidin-2-one ([^{14}C]3)



$C_8{}^{14}CH_8N_2O_4$
MW: 210.17 g.mol^{-1}
Yield: 73 %

Mesure AS-4-109-14C-Pur_02.rta raytest GmbH Page 1/2
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS-4-109-14C-PUR_02.RTADate d'impression : 09.



Description de l'échantillon

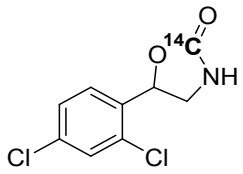
Etude:	ANTOINE		
Mesure:	AS-4-109-14C-Pur_02.rta, commencé:		09/11/2018 11:22
Méthode:	C14		
Origine:	25 mm	Front 125 mm	
Meas. time:	0,3 min	Résolution: 0,4 mm	
Tray number:	1,0	Position de scan:	215,0 mm
Haute tension:	1620,0 V		

AS-4-109-14C-Pur
Silicagel Merck 60F254
Heptane 10 AcOEt 90
14C
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

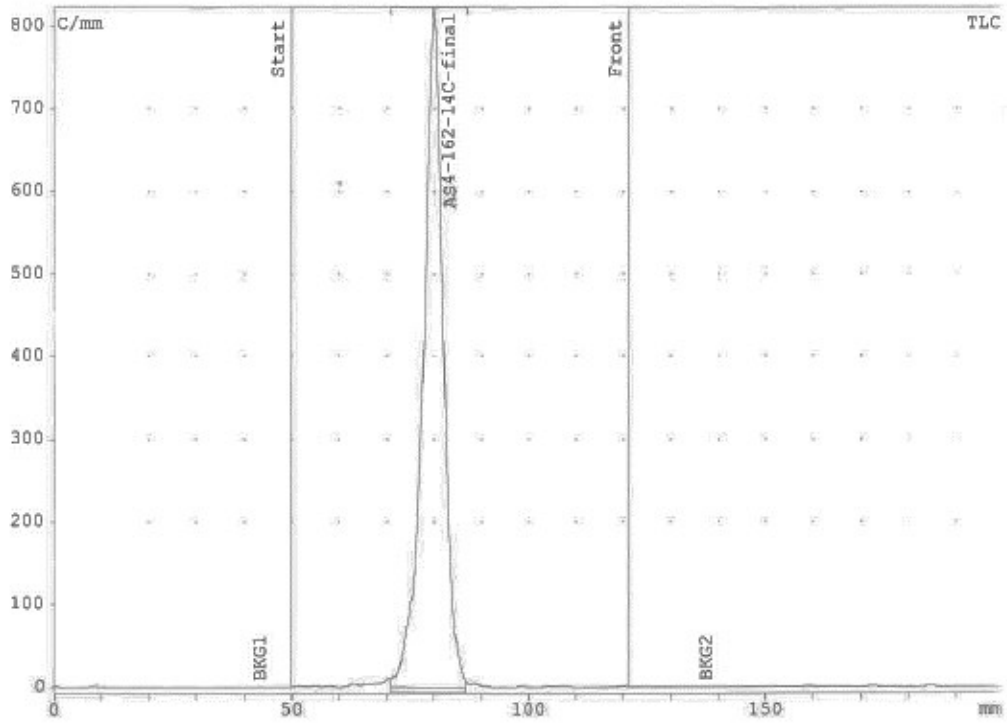
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS-4-109-14C	0,245	DD	1408,933	100,00
Sum in ROI			1408,933	
Aire totale			1393,727	
Aire RF			1391,485	
BKG2			0,4132	
2 ROIs BKG			0,2273	
Remainder RF			-17,45	-1,25

[^{14}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one ([^{14}C]6)



$C_8{}^{14}CH_7Cl_2NO_2$
MW: 234.05 g.mol^{-1}
RCYield: 75 %

Mesure AS4-162-14C-final_01.rta raytest GmbH Page 1/1
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS4-162-14C-FINAL_01.RTADate d'impression :



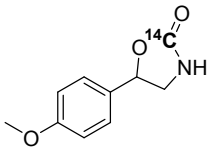
Description de l'échantillon

Etude:	ANTOINE		
Mesure:	AS4-162-14C-final_01.rta, commencé:	19/04/2019	17:39
Méthode:	C14		
Origine:	50 mm	Front 121 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		
Détecteur de radioactivité: raytest RITA			
Autre Square flow cell #0			
Cell volume 0 ul			

Intégration TLC

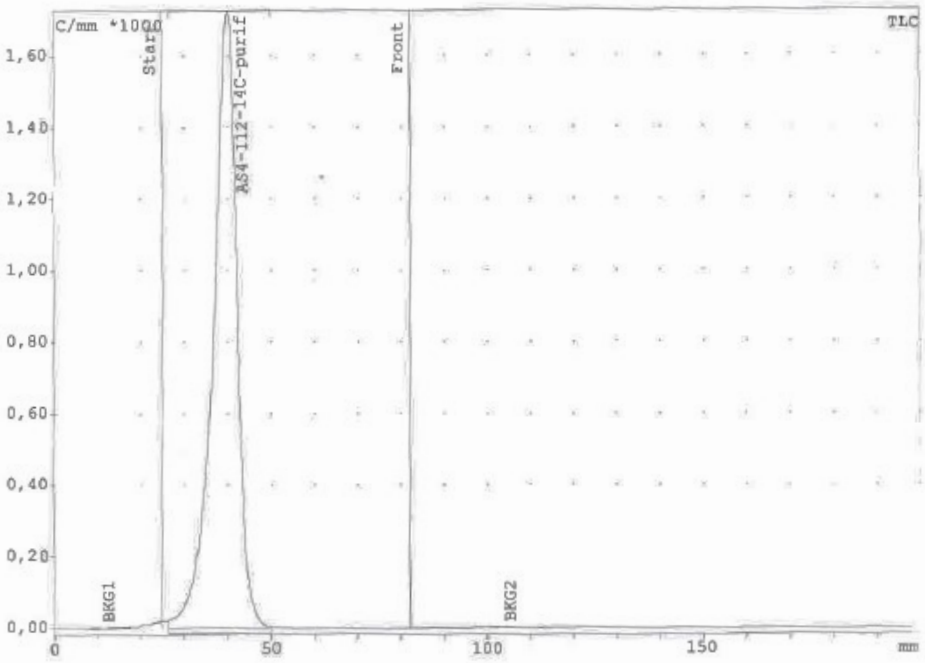
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS4-162-14C-fin	0,423	DD	4020,000	100,00
Sum in ROI			4020,000	
Aire totale			4077,000	
Aire RF			4070,000	
2 ROIs BKG			0,0000	

[^{14}C] 5-(4-methoxyphenyl)oxazolidin-2-one ([^{14}C]8)



$C_9{}^{14}CH_{11}NO_3$
MW: 195.19 g.mol^{-1}
RCYield: 55 %

Mesure AS-4-112-14C-purif-tubes2-10_03.rta raytest GmbH Page 1/1
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS-4-112-14C-PURIF-TUBES2-10_03.RTADate d'imp



Description de l'échantillon

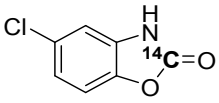
Etude:	ANTOINE		
Mesure:	AS-4-112-14C-purif-tubes2-10_03.rta, commencé:		22/11/2018 16:
Méthode:	C14		
Origine:	25 mm	Front 82 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Tray number:	2,0	Position de scan:	220,0 mm
Haute tension:	1620,0 V		

AS-4-112-14C-purif-tube2-10 silicagel merck 60F254 7/3 AE/Hept
04
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

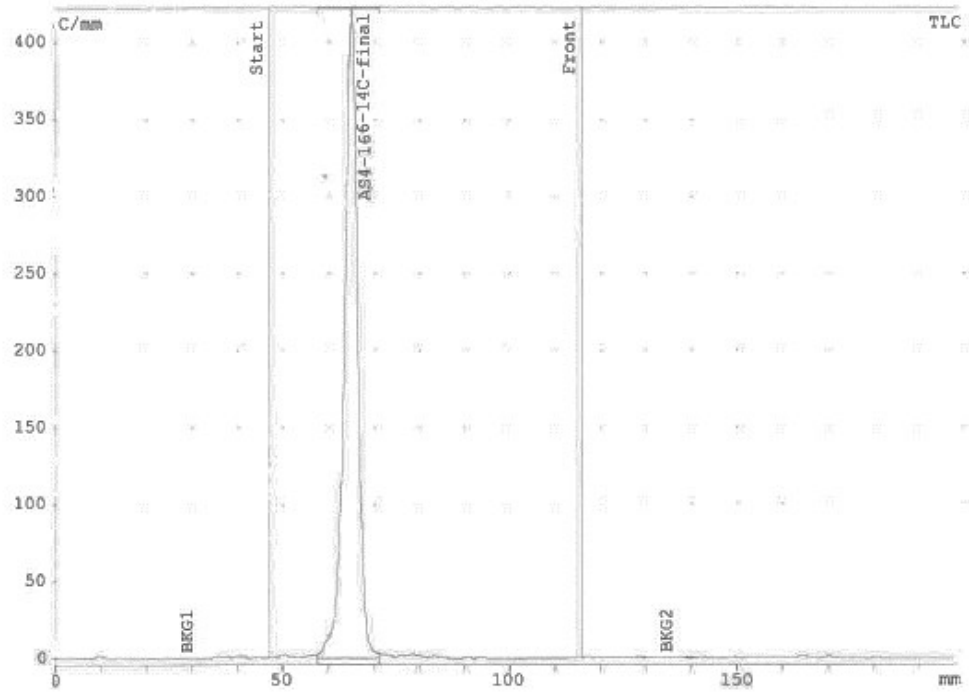
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS4-112-14C-pur	0,263	DD	10955,19	100,00
Sum in ROI			10955,19	
Aire totale			11069,99	
Aire RF			11002,10	
BKG1			1,469	
BKG2			0,273	
Remainder RF			46,91	0,43
Remainder (Tot)			114,80	1,04

[^{14}C] Chloroxazone ([^{14}C]22)



$C_6{}^{14}CH_4ClNO_2$
MW: 171.56 g.mol^{-1}
Radioactive Yield: 39 %

Mesure AS4-166-14C-tlc final_02.rta raytest GmbH Page 1/1
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS4-166-14C-TLC FINAL_02.RTADate d'impression



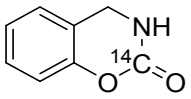
Description de l'échantillon

Etude:	ANTOINE		
Mesure:	AS4-166-14C-tlc final_02.rta, commencé:		04/06/2019 17:
Méthode:	C14		
Origine:	47 mm	Front 116 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Tray number:	1,0	Position de scan:	215,0 mm
Haute tension:	1620,0 V		
Détecteur de radioactivité: raytest RITA			
Autre Square flow cell #0			
Cell volume 0 ul			

Intégration TLC

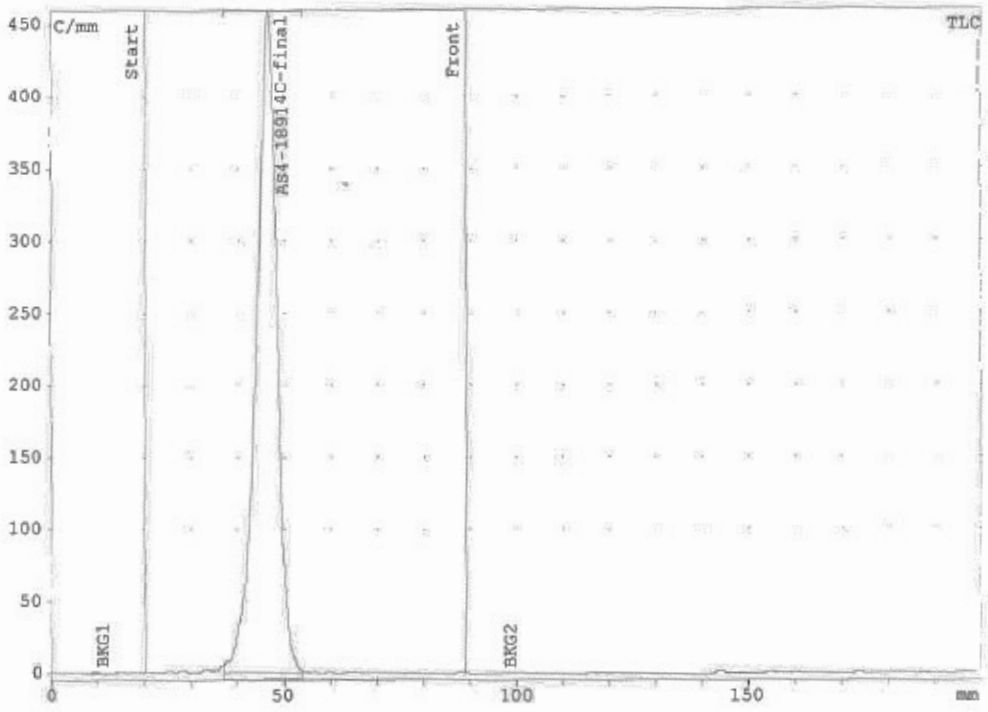
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS4-166-14C-fin	0,261	DD	1422,233	100,00
Sum in ROI			1422,233	
Aire totale			1455,938	
Aire RF			1448,063	
BKG2			0,1705	
2 ROIs BKG			0,0974	
Remainder RF			25,83	1,78
Remainder (Tot)			33,70	2,31

[^{14}C] Caroxazone precursor ([^{14}C]23)



$C_7{}^{14}CH_7NO_2$
MW: 151.14 g.mol^{-1}
RCYield: 30 %

Mesure AS4-189-14C-final_01.rta raytest GmbH
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS4-189-14C-FINAL_01



Description de l'échantillon

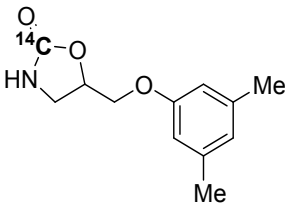
Etude:	ANTOINE		
Mesure:	AS4-189-14C-final_01.rta, commencé:	19/07/2019	15:08
Méthode:	C14		
Origine:	20 mm	Front 89 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		

Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

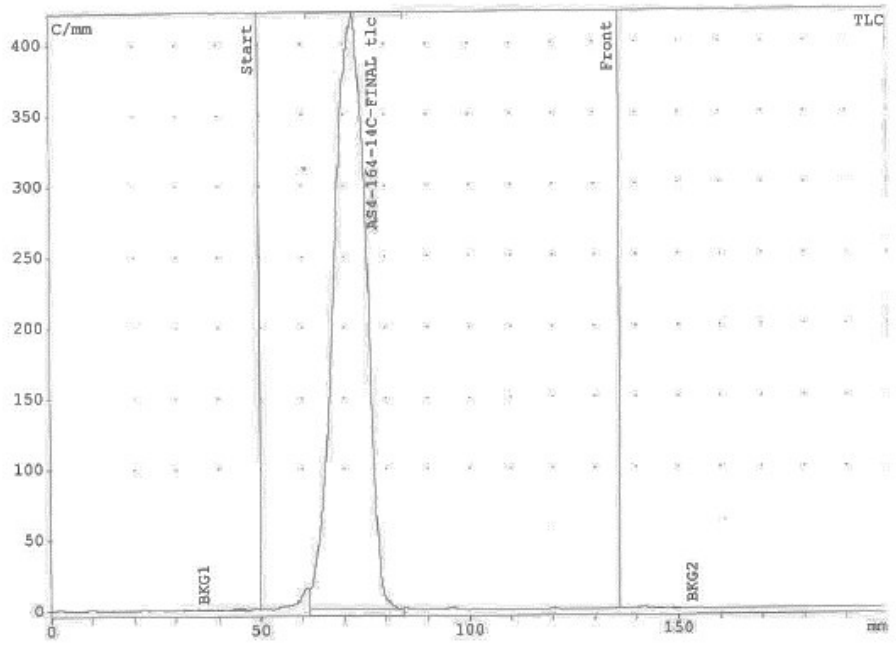
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS4-18914C-fina	0,383	DD	2370,244	100,00
Sum in ROI			2370,244	
Aire totale			2411,125	
Aire RF			2397,000	
BKG1			0,1705	
2 ROIs BKG			0,0974	
Remainder RF			26,76	1,12
Remainder (Tot)			40,88	1,70

[^{14}C] Metaxalone ([^{14}C]24)



$C_{11}{}^{14}CH_{15}NO_3$
MW: 223.25 g.mol^{-1}
Radioactive Yield: 59 %

Mesure AS4-164-14C-FINAL_02.rta raytest GmbH Page 1/1
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS4-164-14C-FINAL_02.RTADate d'impression : 0



Description de l'échantillon

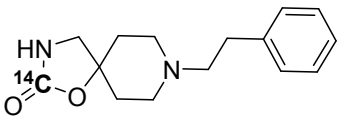
Etude:	ANTOINE		
Mesure:	AS4-164-14C-FINAL_02.rta, commencé:		03/05/2019 16:06
Méthode:	C14		
Origine:	50 mm	Front 136 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Tray number:	1,0	Position de scan:	215,0 mm
Haute tension:	1620,0 V		

Invalid parameters.
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

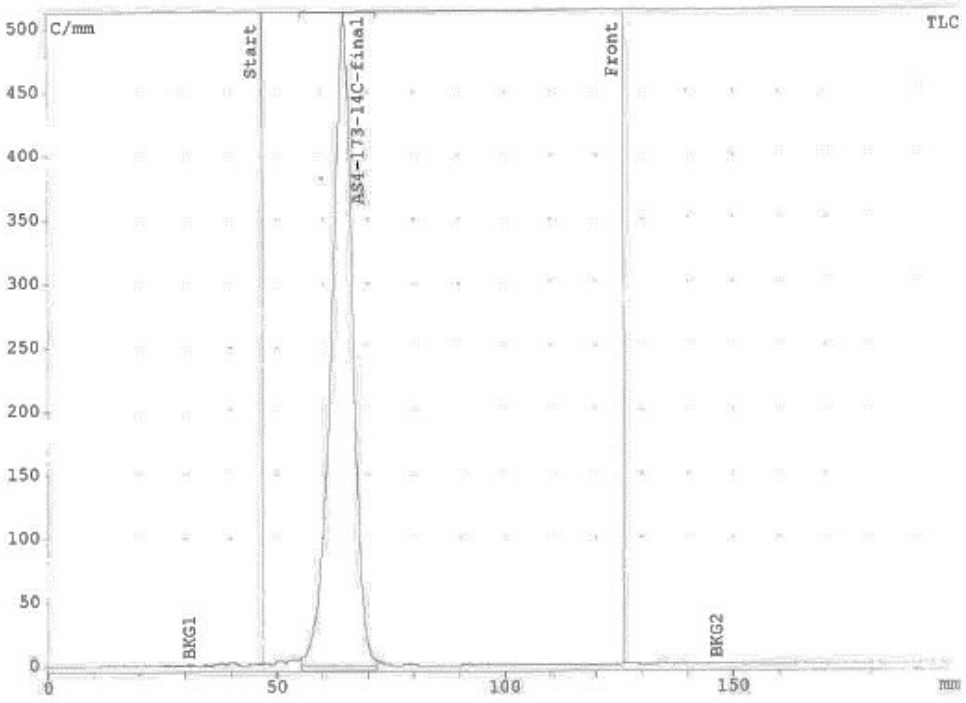
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS4-164-14C-FIN	0,260	DD	3748,832	100,00
Sum in ROI			3748,832	
Aire totale			3799,004	
Aire RF			3798,140	
BKG1			0,3519	
BKG2			0,0957	
Remainder RF			49,31	1,30
Remainder (Tot)			50,17	1,32

[^{14}C] Fenspiride ([^{14}C]25)



$C_{14}{}^{14}CH_{20}N_2O_2$
MW: 262.33 g.mol^{-1}
RCYield: 45 %

Mesure AS4-173-14C-tlc final_01.rta raytest GmbH Page 1/1
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS4-173-14C-TLC FINAL_01.RTADate d'impression



Description de l'échantillon

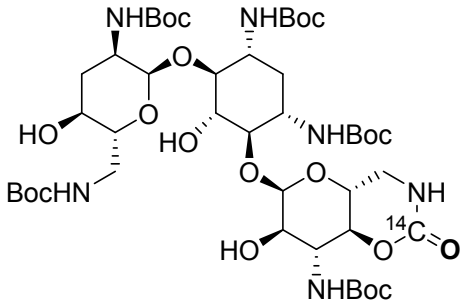
Etude:	ANTOINE		
Mesure:	AS4-173-14C-tlc final_01.rta, commencé:		04/06/2019 16:
Méthode:	C14		
Origine:	47 mm	Front 126 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		

Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

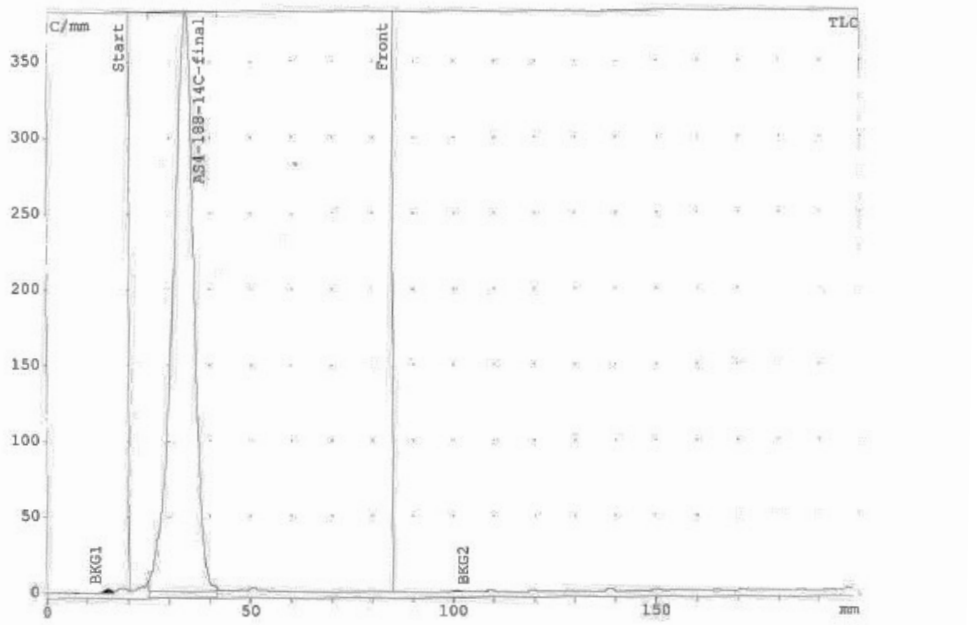
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS4-173-14C-fin	0,227	DD	2719,569	100,00
Sum in ROI			2719,569	
Aire totale			2771,552	
Aire RF			2755,000	
BKG1			0,3762	
2 ROIs BKG			0,2098	
Remainder RF			35,43	1,29
Remainder (Tot)			51,98	1,88

[^{14}C] Tobramycine derivative ([^{14}C]26)



$C_{43}{}^{14}CH_{76}N_6O_{19}$
MW: 995.11 g.mol^{-1}
Radioactive Yield: 35 %

Mesure AS4-188-14C-final_01.rta raytest GmbH Page 1/1
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS4-188-14C-FINAL_01.RTADate d'impression : 1



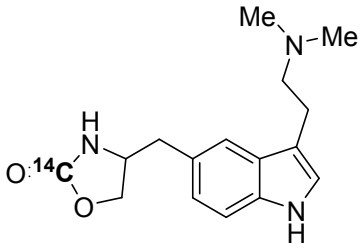
Description de l'échantillon

Etude:	ANTOINE		
Mesure:	AS4-188-14C-final_01.rta, commencé:	15/07/2019	16:00
Méthode:	C14		
Origine:	20 mm	Front 85 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		
Détecteur de radioactivité: raytest RITA			
Autre Square flow cell #0			
Cell volume 0 ul			

Intégration TLC

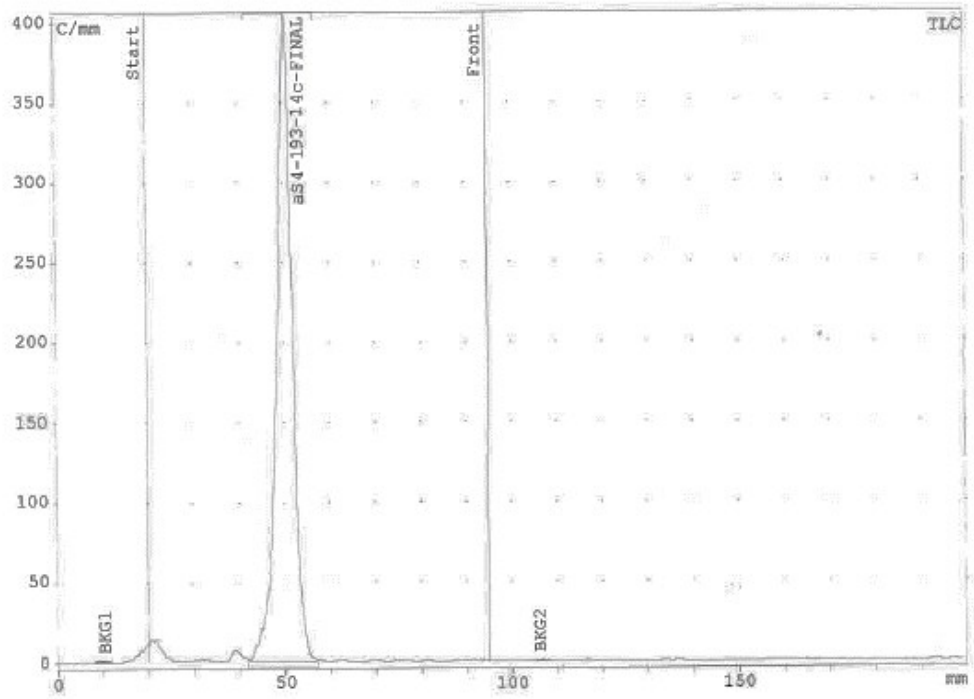
Substance	R/F	Type	Aire	%Aire
			Counts	%
AS4-188-14C-fin	0,215	DD	2264,585	100,00
Sum in ROI			2264,585	
Aire totale			2299,288	
Aire RF			2286,882	
BKG1			0,6061	
BKG2			0,1604	
Remainder RF			22,30	0,98
Remainder (Tot)			34,70	1,51

[^{14}C] Zolmitriptan ([^{14}C]30)



$C_{15}{}^{14}CH_{21}N_3O_2$
MW: 289.16 g.mol^{-1}
RCYield: 8.3 %

Mesure as4-193-14c-FINAL_01.rta raytest GmbH Page 1/1
C:\PROGRA~1\raytest\Rita Control\list\ANTOINE\C14\AS4-193-14C-FINAL_01.RTADate d'impression : 0



Description de l'échantillon

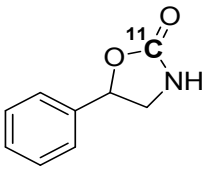
Etude:	ANTOINE		
Mesure:	as4-193-14c-FINAL_01.rta, commencé:	01/08/2019	18:25
Méthode:	C14		
Origine:	20 mm	Front 95 mm	
Meas. time:	0,2 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		
Détecteur de radioactivité: raytest RITA			
Autre Square flow cell #0			
Cell volume 0 ul			

Intégration TLC

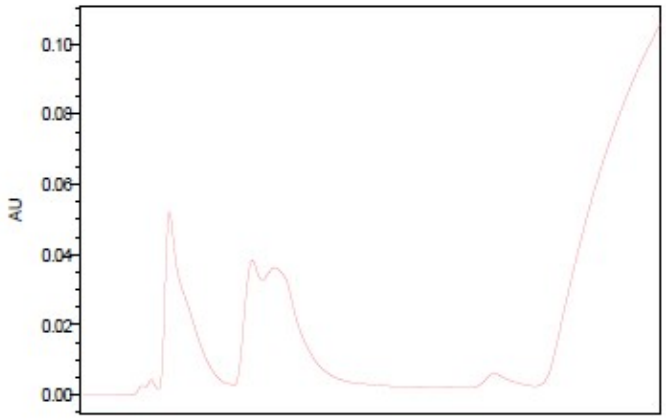
Substance	R/F	Type	Aire	%Aire
			Counts	%
aS4-193-14c-FIN	0,407	DD	1615,584	100,00
Sum in ROI			1615,584	
Aire totale			1687,600	
Aire RF			1687,714	
BKG1			0,5455	
BKG2			0,3896	
Remainder RF			72,13	4,27
Remainder (Tot)			72,02	4,27

6. Radio-HPLC Analysis for ^{11}C-Labeled Compounds

[^{11}C] 5-phenyloxazolidin-2-one **([^{11}C]2)**

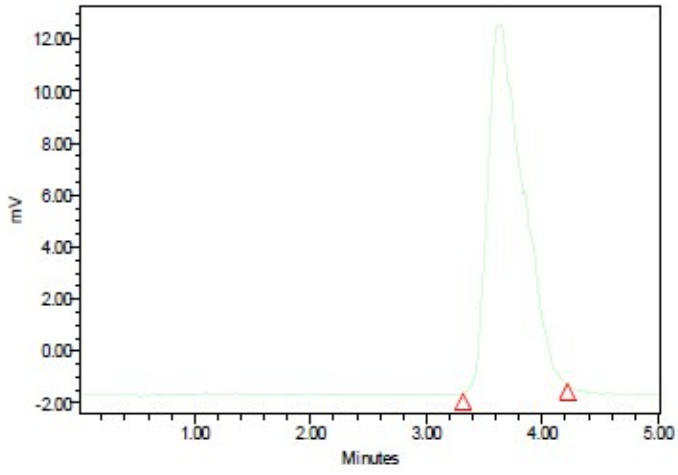


$C_8{}^{11}CH_9NO_2$
RCYield: 76%



Peak Results
Channel Name: 270nm

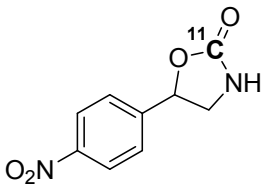
	Name	RT	Area	% Area	Channel Name	Amount
1					270nm	



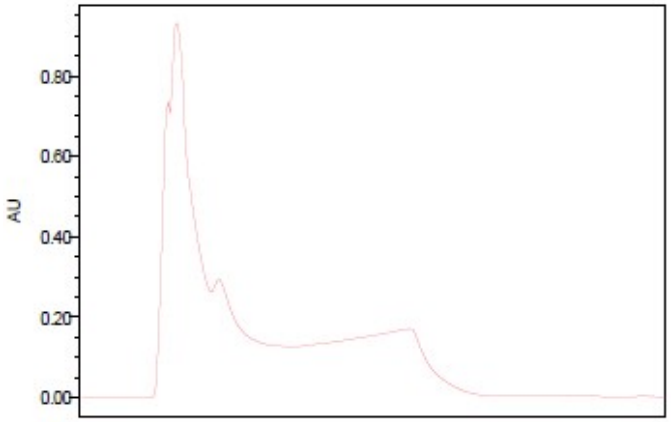
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		3.636	298160	100.00	SATIN	

[^{11}C] 5-(4-nitrophenyl)oxazolidin-2-one ([^{11}C]3)

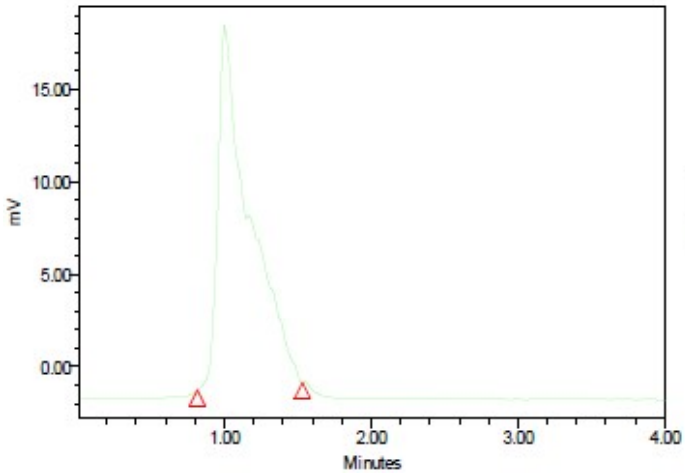


$C_8{}^{11}CH_8N_2O_2$
RCYield: 80%



Peak Results
Channel Name: 269nm

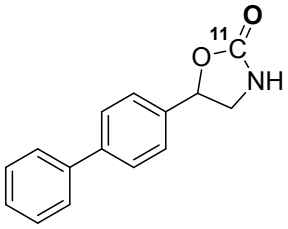
	Name	RT	Area	% Area	Channel Name	Amount
1					269nm	



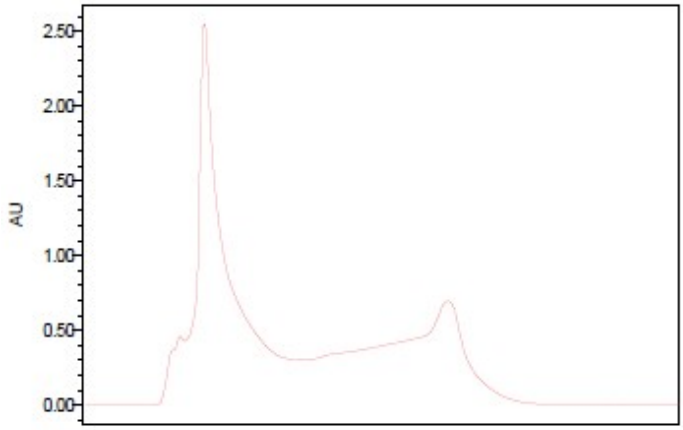
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		1.008	291705	100.00	SATIN	

[^{11}C] 5-([1,1'-biphenyl]-4-yl)oxazolidin-2-one ([^{11}C]4)

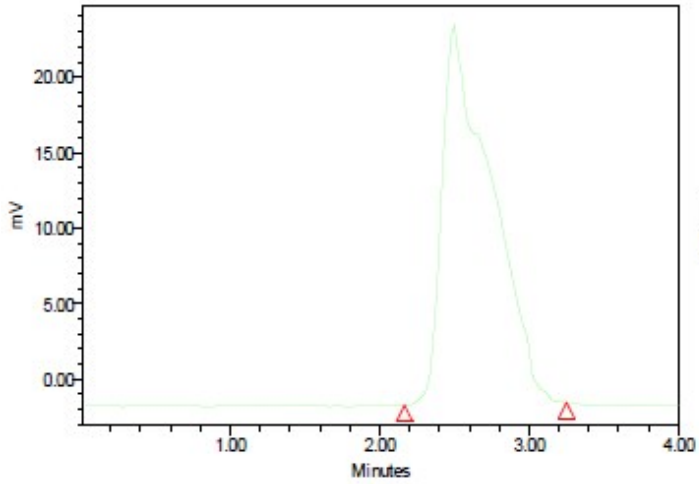


$C_{14}{}^{11}CH_{13}NO_2$
RCYield: 77%



Peak Results
Channel Name: 253nm

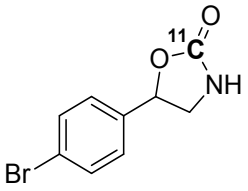
	Name	RT	Area	% Area	Channel Name	Amount
1					253nm	



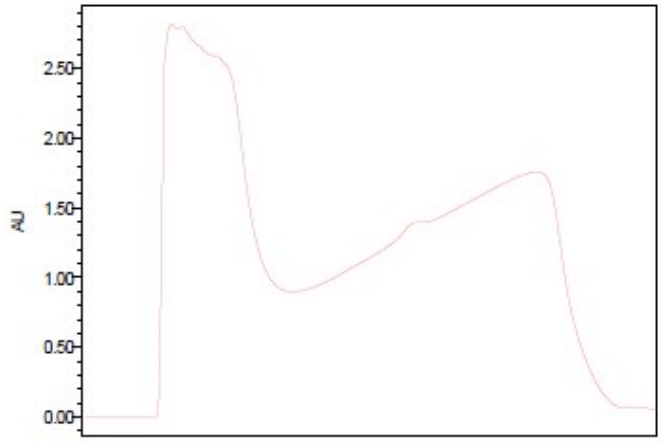
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		2.498	577125	100.00	SATIN	

[^{11}C] 5-(4-bromophenyl)oxazolidin-2-one ([^{11}C]5)

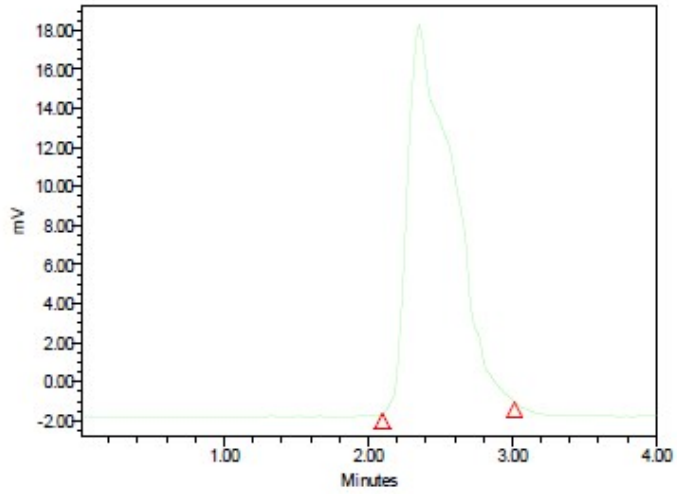


$C_8{}^{11}C\ H_8BrNO_2$
RCYield: 74%



Peak Results
Channel Name: 223nm

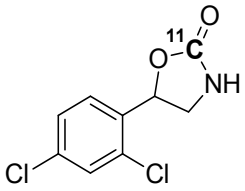
	Name	RT	Area	% Area	Channel Name	Amount
1					223nm	



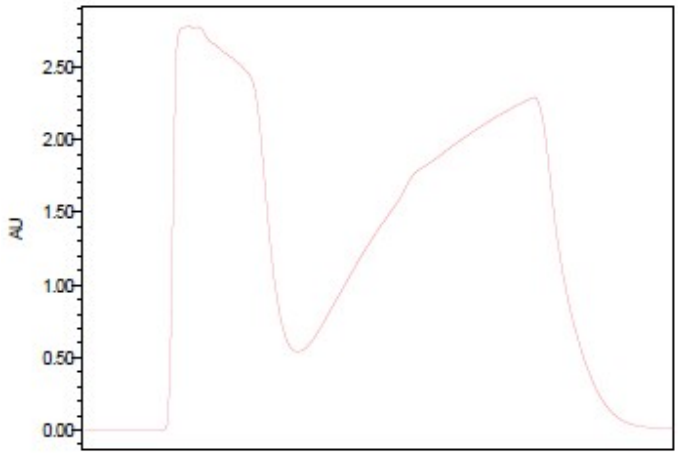
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		2.354	432713	100.00	SATIN	

[^{11}C] 5-(2,4-dichlorophenyl)oxazolidin-2-one ([^{11}C]6)

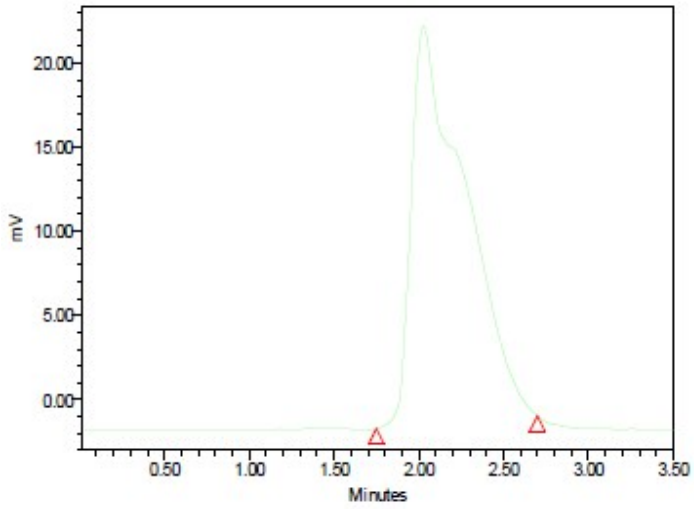


$C_8{}^{11}CH_7Cl_2NO_2$
RCYield: 79%



Peak Results
Channel Name: 222nm

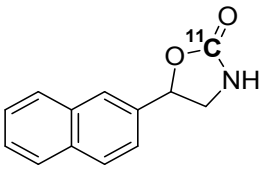
	Name	RT	Area	% Area	Channel Name	Amount
1					222nm	



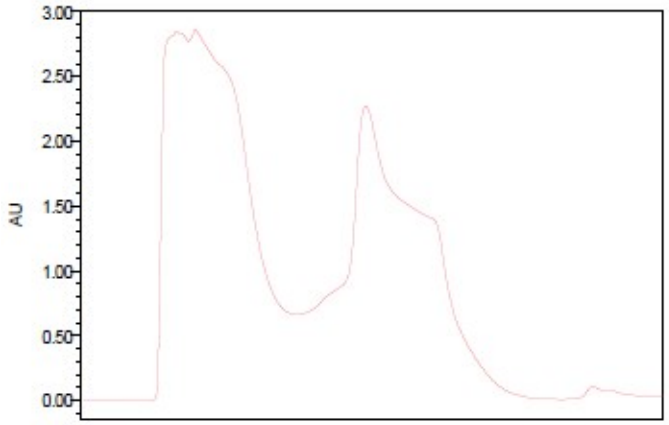
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		2.030	523463	100.00	SATIN	

[^{11}C] 5-(naphthalen-2-yl)oxazolidin-2-one ([^{11}C]7)

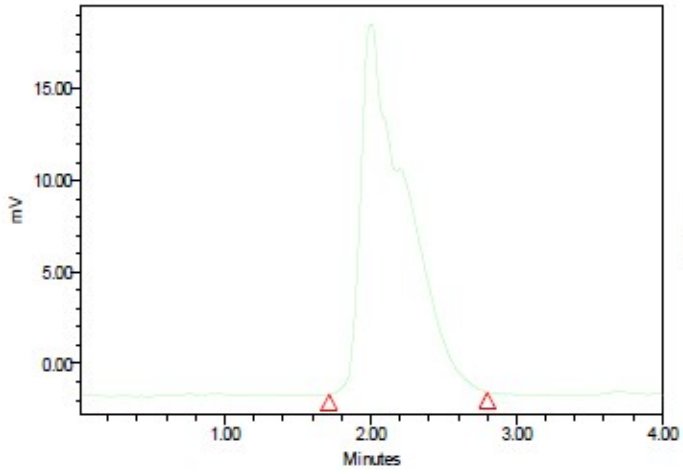


$C_{12}{}^{11}CH_{11}NO_2$
RCYield: 68%



Peak Results
Channel Name: 222nm

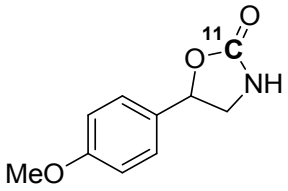
	Name	RT	Area	% Area	Channel Name	Amount
1					222nm	



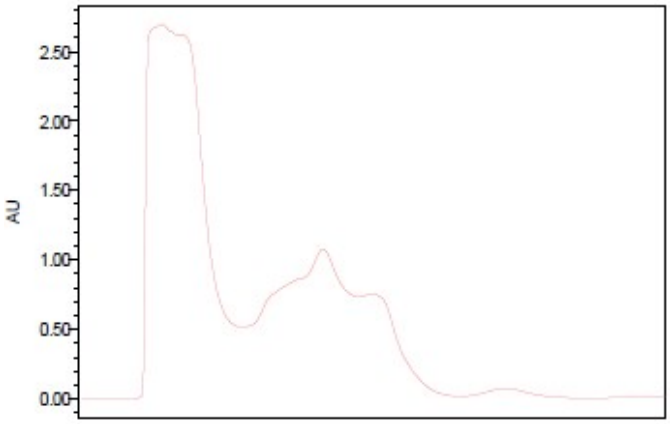
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		2.002	433764	100.00	SATIN	

[^{11}C] 5-(4-methoxyphenyl)oxazolidin-2-one ([^{11}C]8)

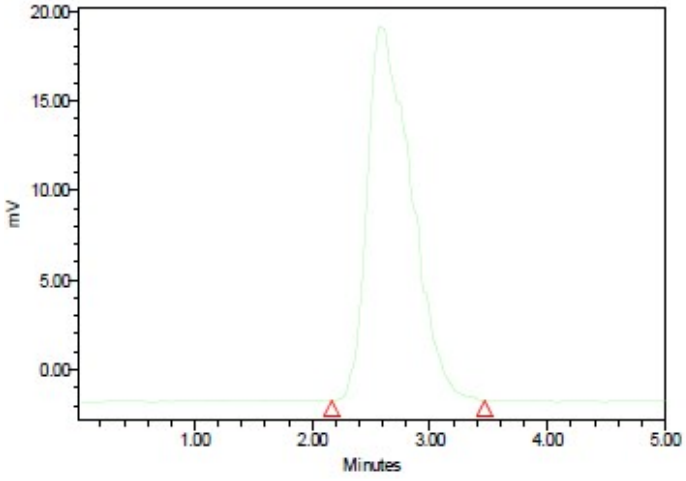


$C_9{}^{11}CH_{11}NO_3$
RCYield: 83%



Peak Results
Channel Name: 227nm

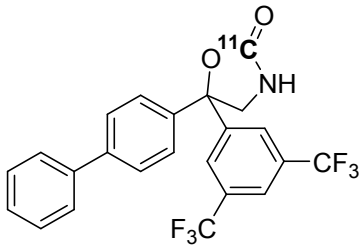
	Name	RT	Area	% Area	Channel Name	Amount
1					227nm	



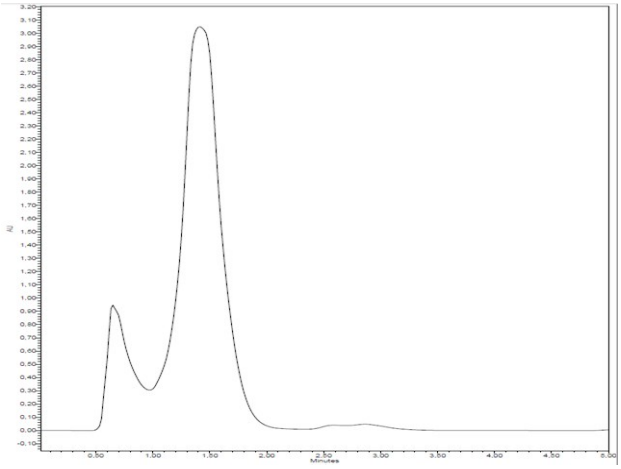
Peak Results
Channel Name: SATIN

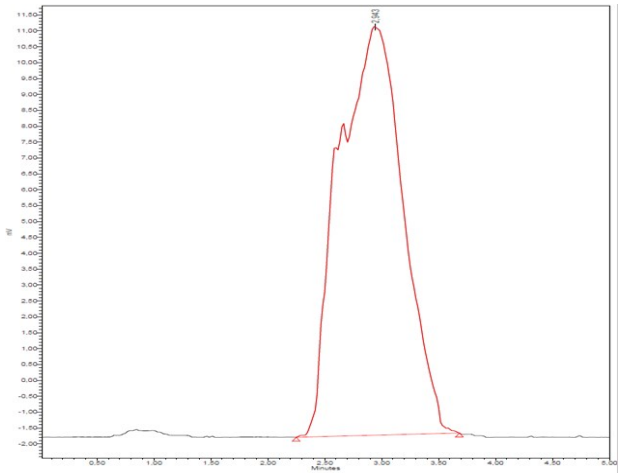
	Name	RT	Area	% Area	Channel Name	Amount
1		2.590	543655	100.00	SATIN	

***[^{11}C] 5-([1,1'-biphenyl]-4-yl)-5-(3,5-bis(trifluoromethyl)phenyl)oxazolidin-2-one* ([^{11}C]9)**



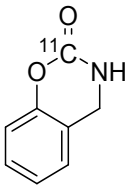
$C_{22}{}^{11}CH_{15}F_6NO_2$
RCYield: 82%





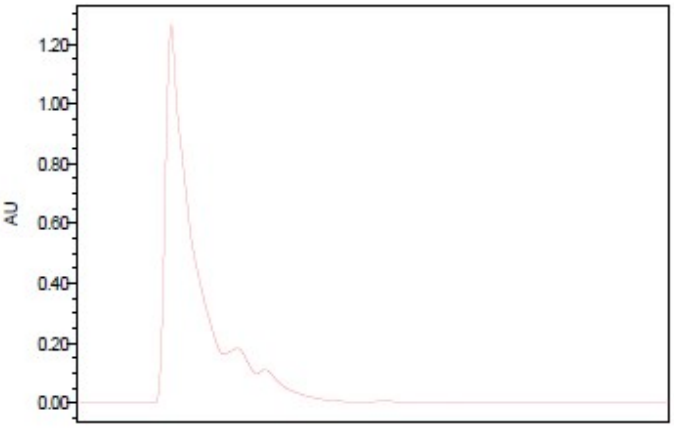
	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)
1		2,943	504207	100,00	12839

[^{11}C] 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one **([^{11}C]10)**



$C_7{}^{11}CH_7NO_2$
RCYield: 57%

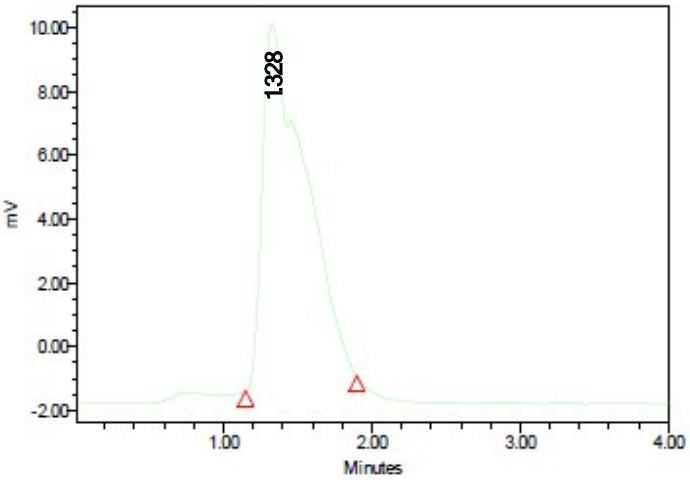
UV



Peak Results
Channel Name: 240nm

	Name	RT	Area	% Area	Channel Name	Amount
1					240nm	

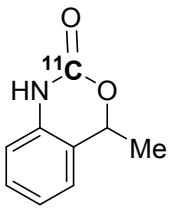
Gamma



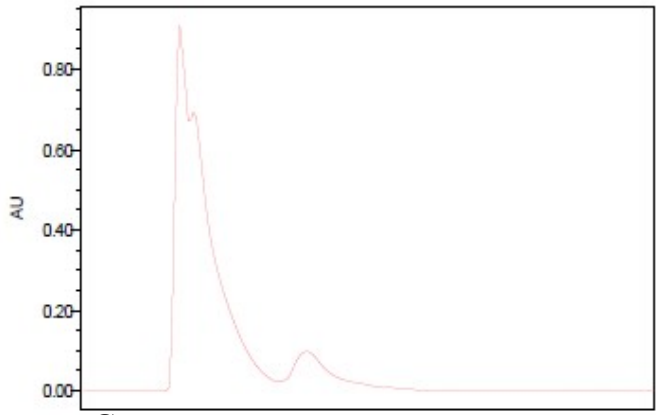
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		1.328	229420	100.00	SATIN	

***[^{11}C] 4-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{11}C]11)**



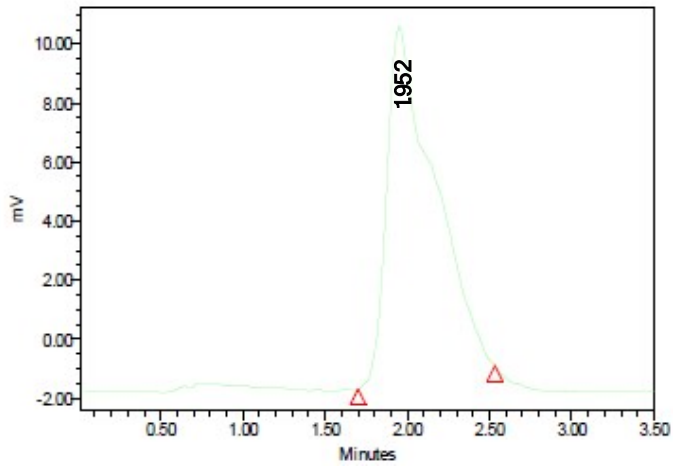
UV



Peak Results
Channel Name: 275nm

	Name	RT	Area	% Area	Channel Name	Amount
1					275nm	

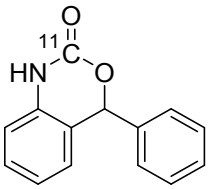
Gamma



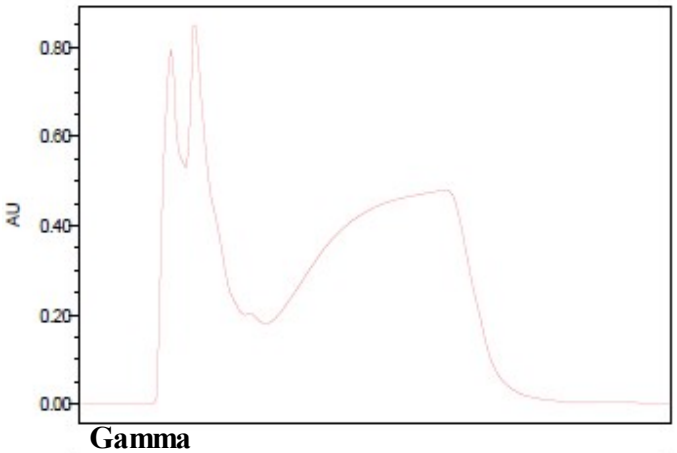
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		1.952	241955	100.00	SATIN	

***[^{11}C] 4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{11}C]12)**



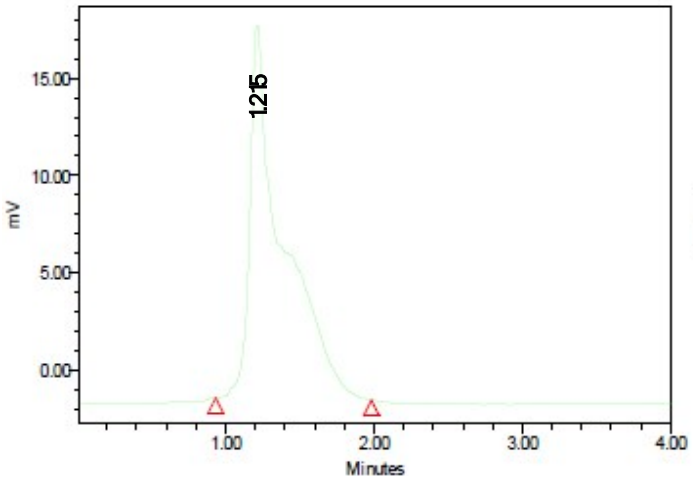
UV



Peak Results
Channel Name: 242nm

	Name	RT	Area	% Area	Channel Name	Amount
1					242nm	

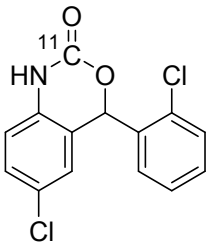
Gamma

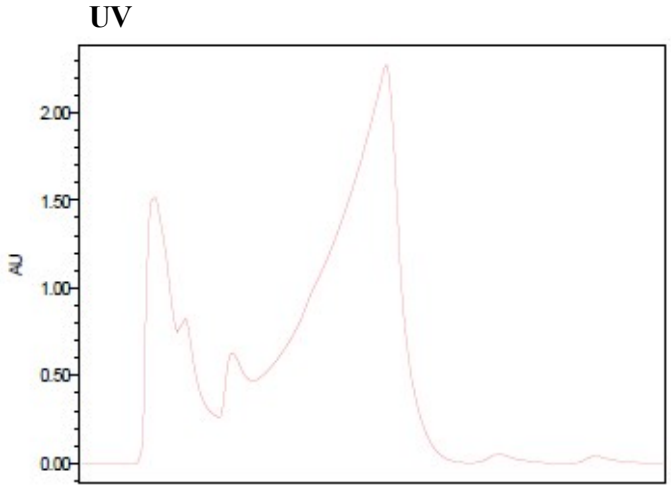


Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		1.215	294992	100.00	SATIN	

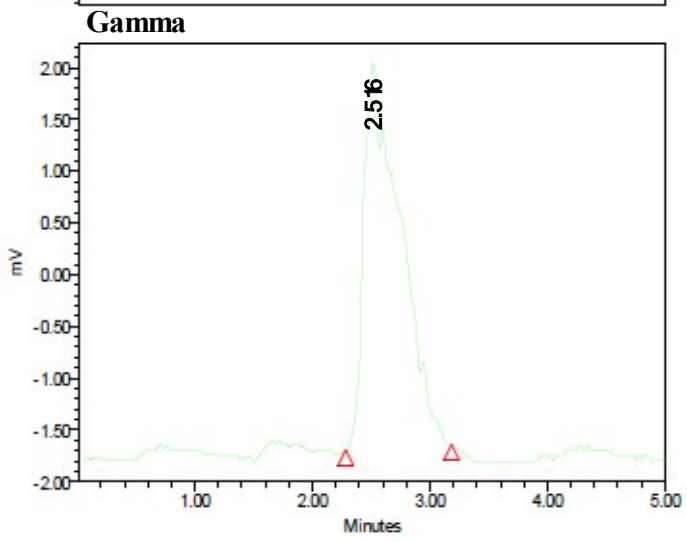
***[^{11}C] 6-chloro-4-phenyl-1H-benzo[d][1,3]oxazin-2(4H)-one* ([^{11}C]14)**





Peak Results
Channel Name: 242nm

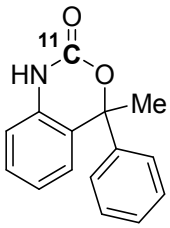
	Name	RT	Area	% Area	Channel Name	Amount
1					242nm	



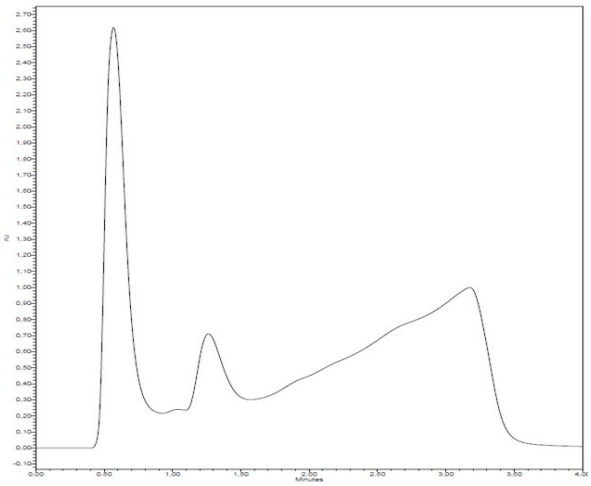
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		2.516	80569	100.00	SATIN	

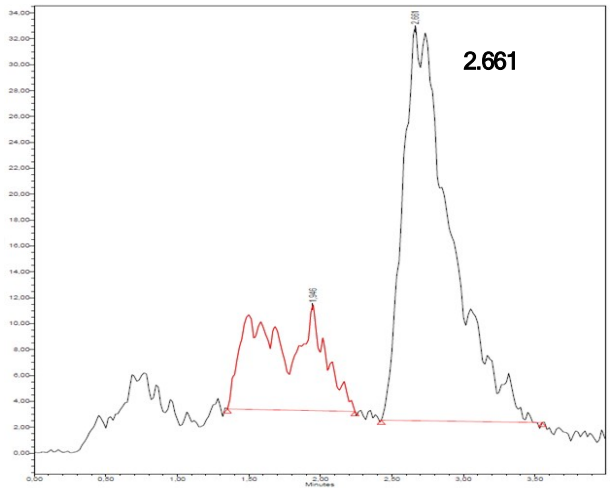
***[^{11}C] 4-methyl-4-phenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{11}C]15)**



UV

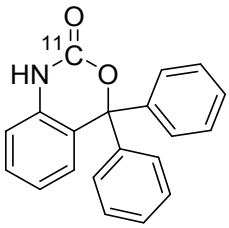


Gamma

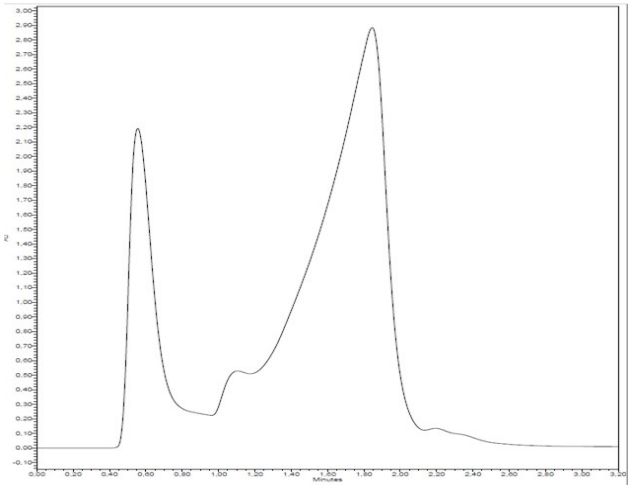


	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)
1		1,946	236655	24,89	8083
2		2,661	714282	75,11	30354

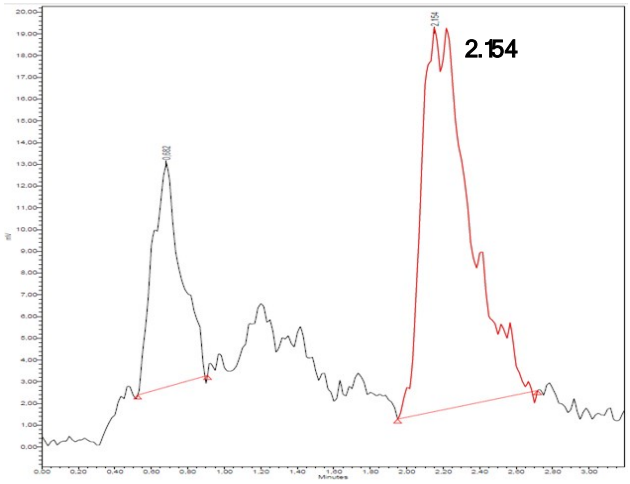
***[^{11}C] 4,4-diphenyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one* ([^{11}C]16)**



UV

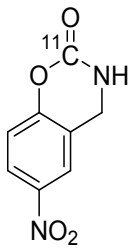


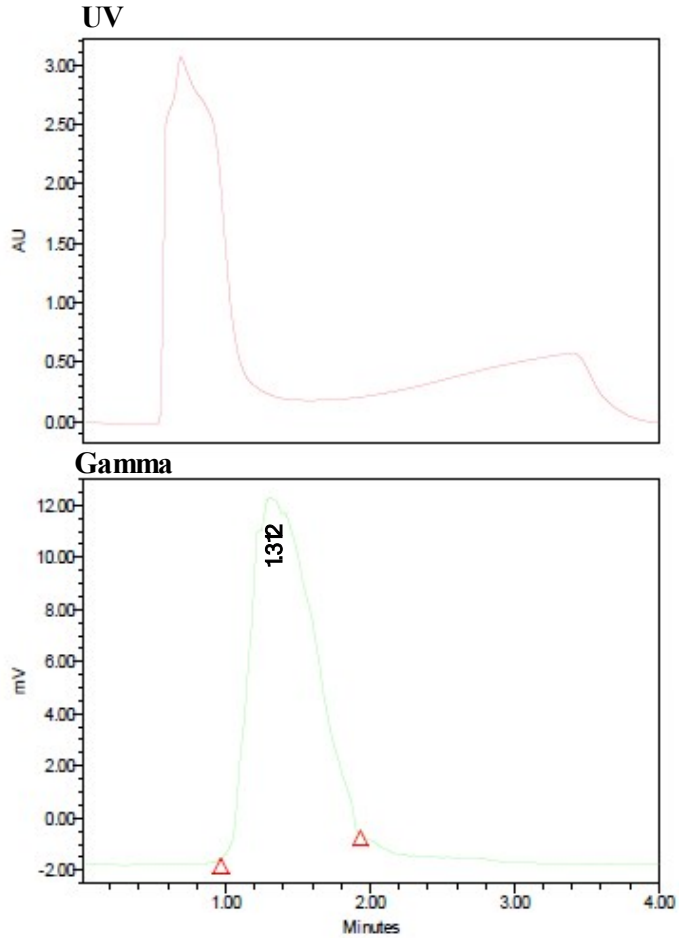
Gamma



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)
1		0,682	113304	25,28	10213
2		2,154	334813	74,72	17696

***[^{11}C] 6-nitro-3,4-dihydro-2H-benzo[e][1,3]oxazin-2-one* ([^{11}C]17)**





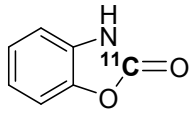
Peak Results
Channel Name: 227nm

	Name	RT	Area	% Area	Channel Name	Amount
1					227nm	

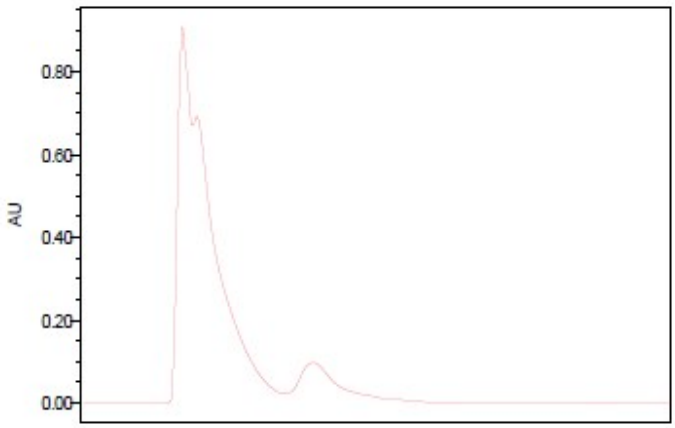
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		1.312	401896	100.00	SATIN	

***[^{11}C] benzo[d]oxazol-2(3H)-one* ([^{11}C]18)**



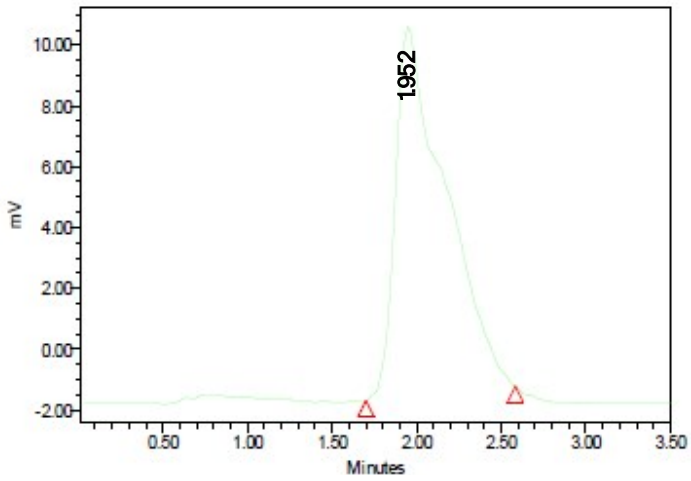
UV



Peak Results
Channel Name: 275nm

	Name	RT	Area	% Area	Channel Name	Amount
1					275nm	

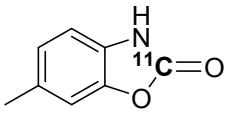
Gamma

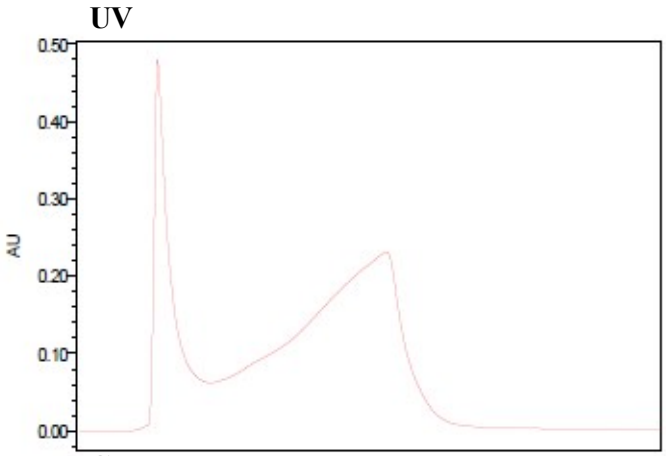


Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		1.952	251022	100.00	SATIN	

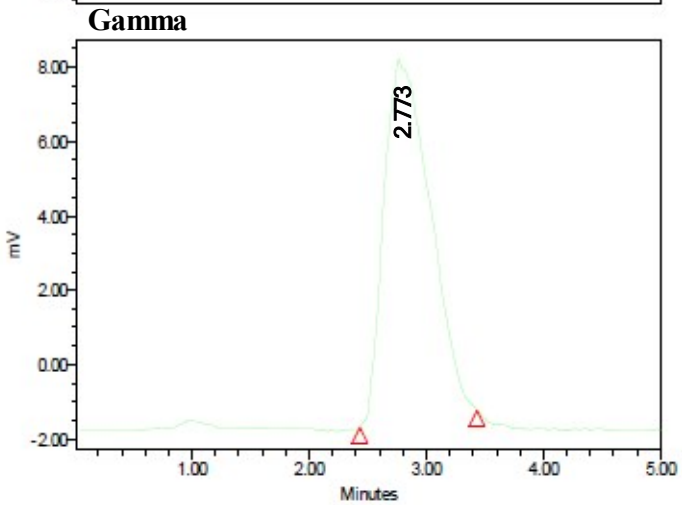
***[^{11}C] 5-methylbenzo[d]oxazol-2(3H)-one* ([^{11}C]19)**





Peak Results
Channel Name: 270nm

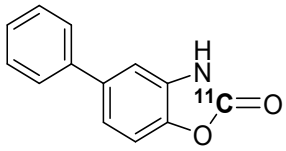
	Name	RT	Area	% Area	Channel Name	Amount
1					270nm	



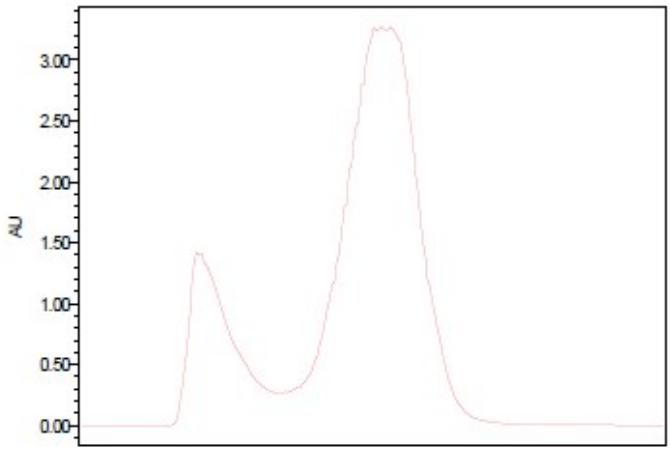
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		2.773	267129	100.00	SATIN	

***[^{11}C] 5-phenylbenzo[d]oxazol-2(3H)-one* ([^{11}C]20)**



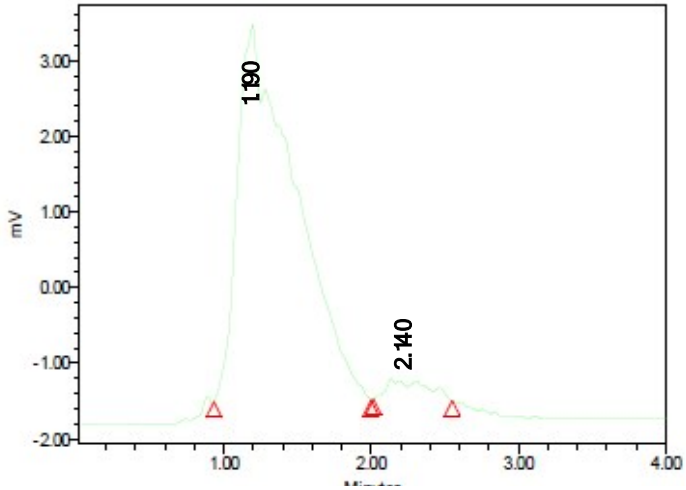
UV



Peak Results
Channel Name: 242nm

	Name	RT	Area	% Area	Channel Name	Amount
1					242nm	

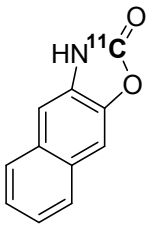
Gamma



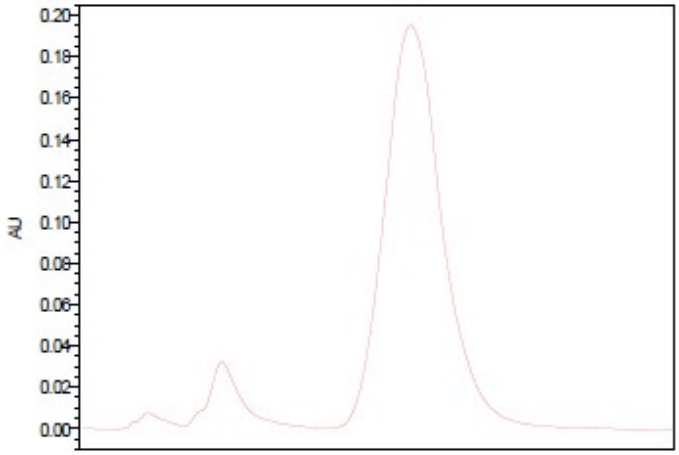
Peak Results
Channel Name: SATIN

	Name	RT	Area	% Area	Channel Name	Amount
1		1.190	136219	96.43	SATIN	
2		2.140	5046	3.57	SATIN	

***[^{11}C] naphtho[2,3-d]oxazol-2(3H)-one* ([^{11}C]21)**



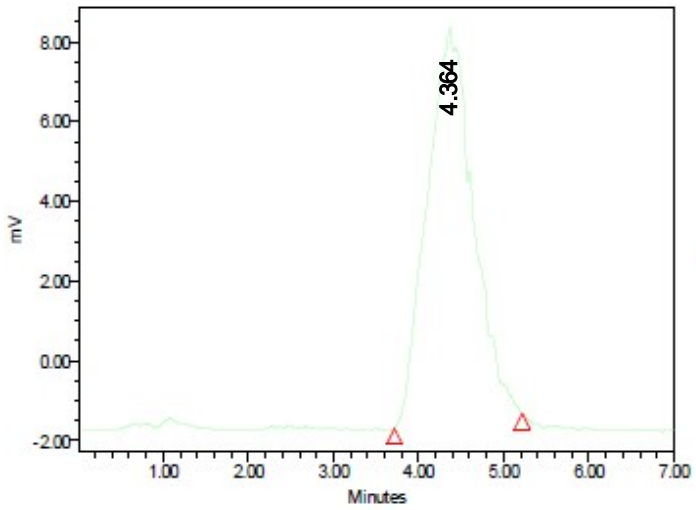
UV



Peak Results
Channel Name: 270nm

	Name	RT	Area	% Area	Channel Name	Amount
1					270nm	

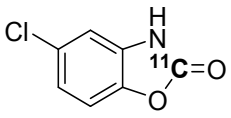
Gamma



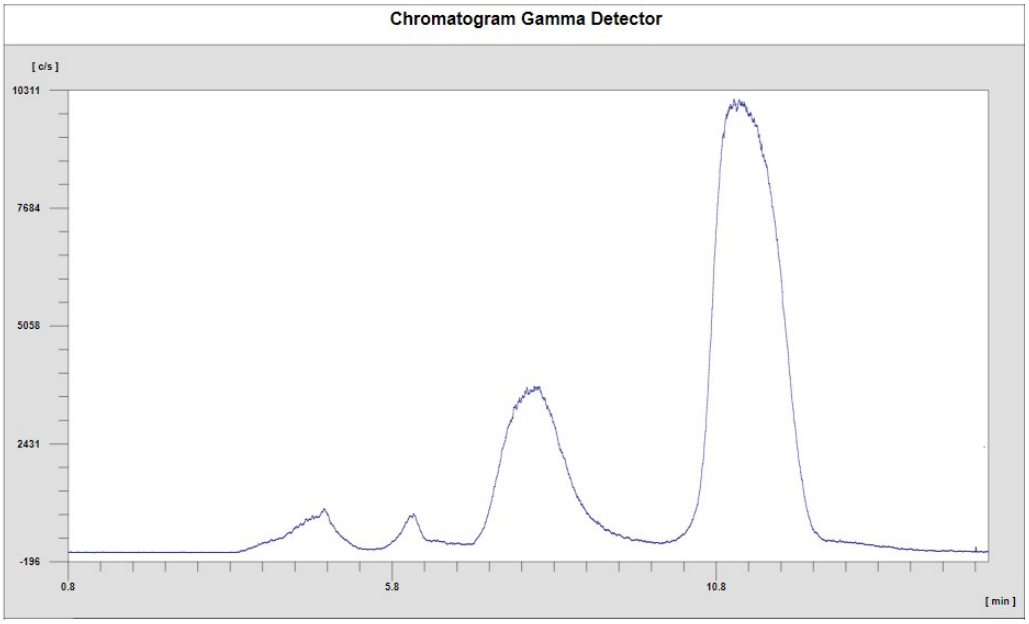
Peak Results
Channel Name: SATIN

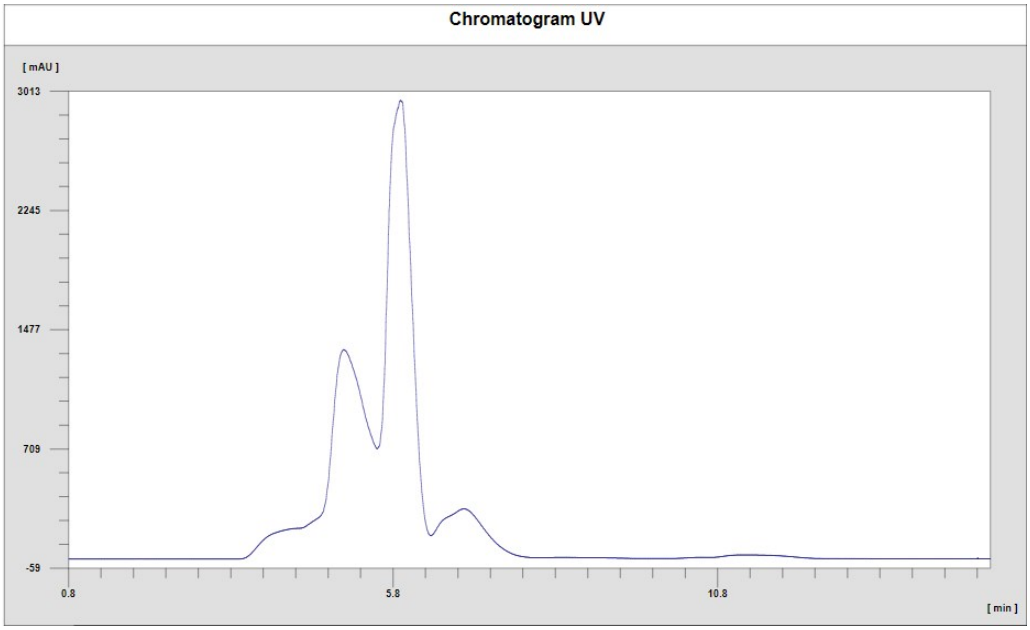
	Name	RT	Area	% Area	Channel Name	Amount
1		4.364	372328	100.00	SATIN	

[^{11}C]Chloroxazone ([^{11}C]**22**)

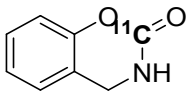


$C_6{}^{11}CH_4ClNO_2$
RCYield: 37 ± 2%

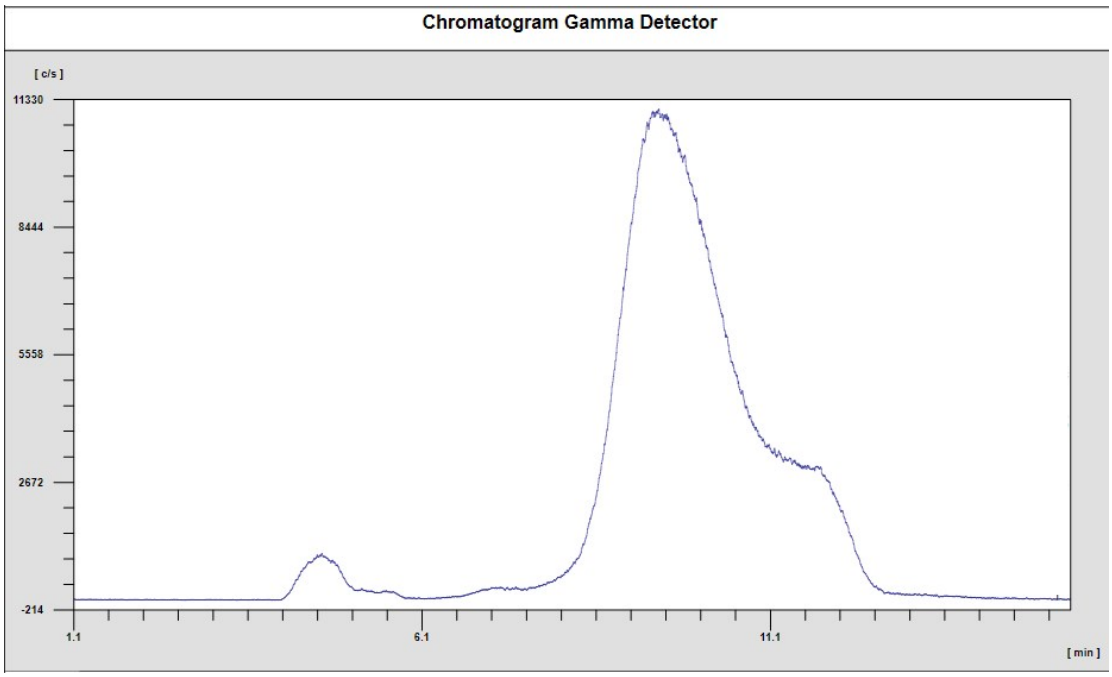


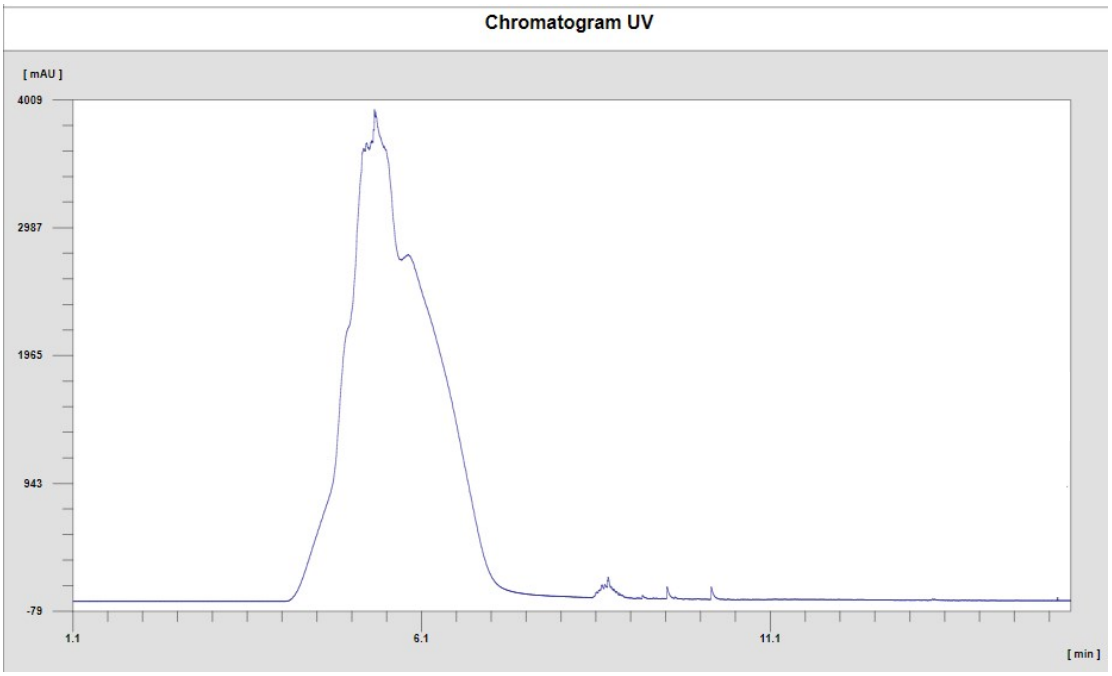


[^{11}C] Caroxazone precursor ([^{11}C]**23**)

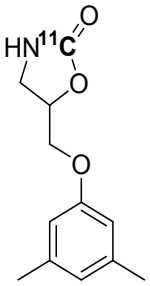


$C_7{}^{11}CH_7NO_2$
RCYield: 25 ± 5%

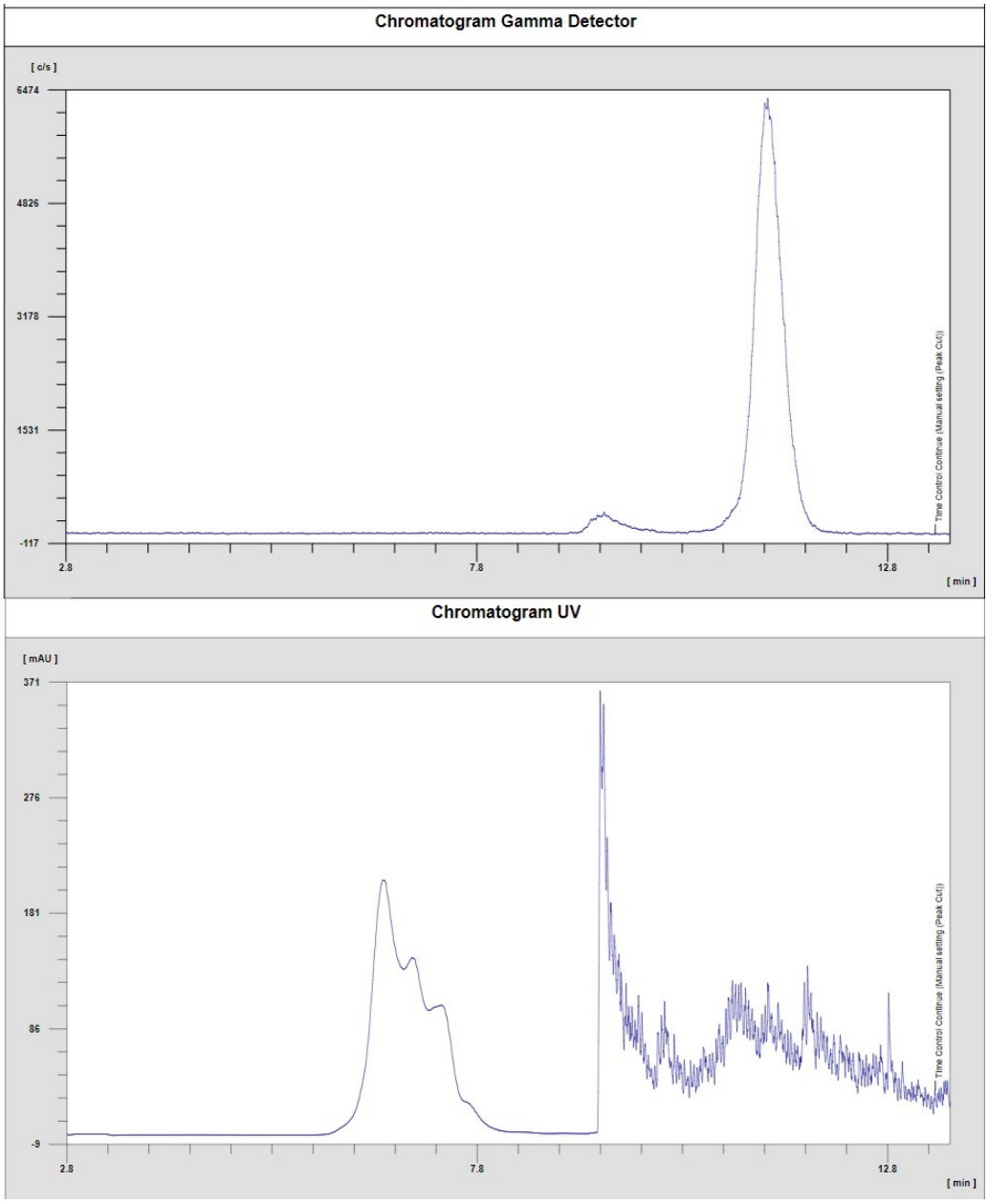




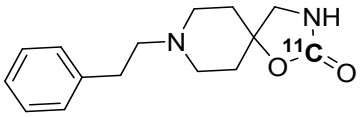
[^{11}C]Metaxalone ([^{11}C]24)



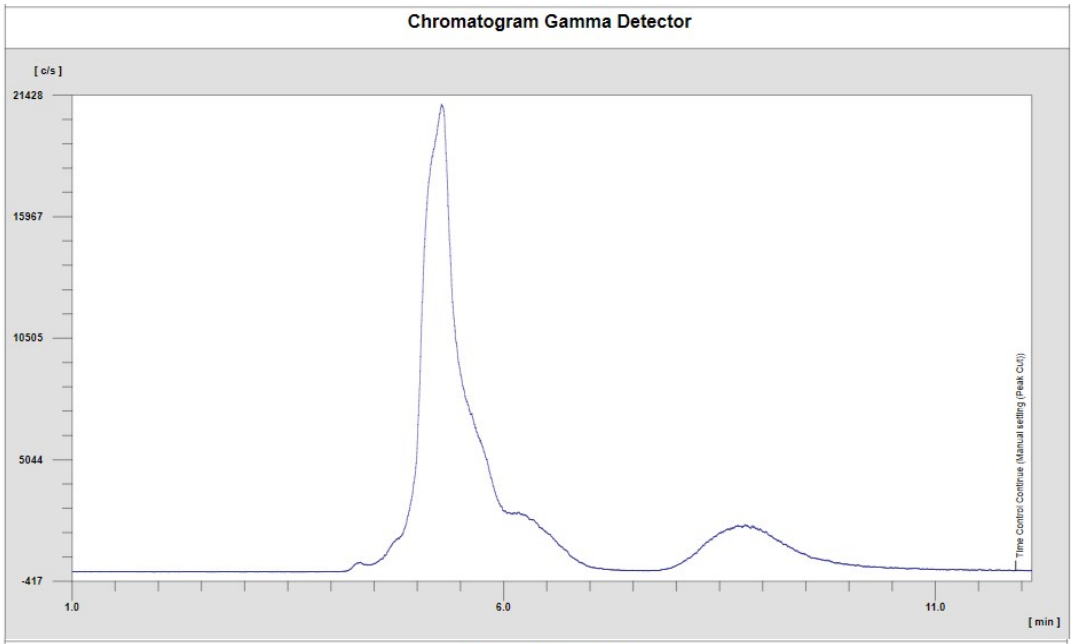
$C_{11}{}^{11}CH_{15}NO_3$
RCYield: 44 ± 3%

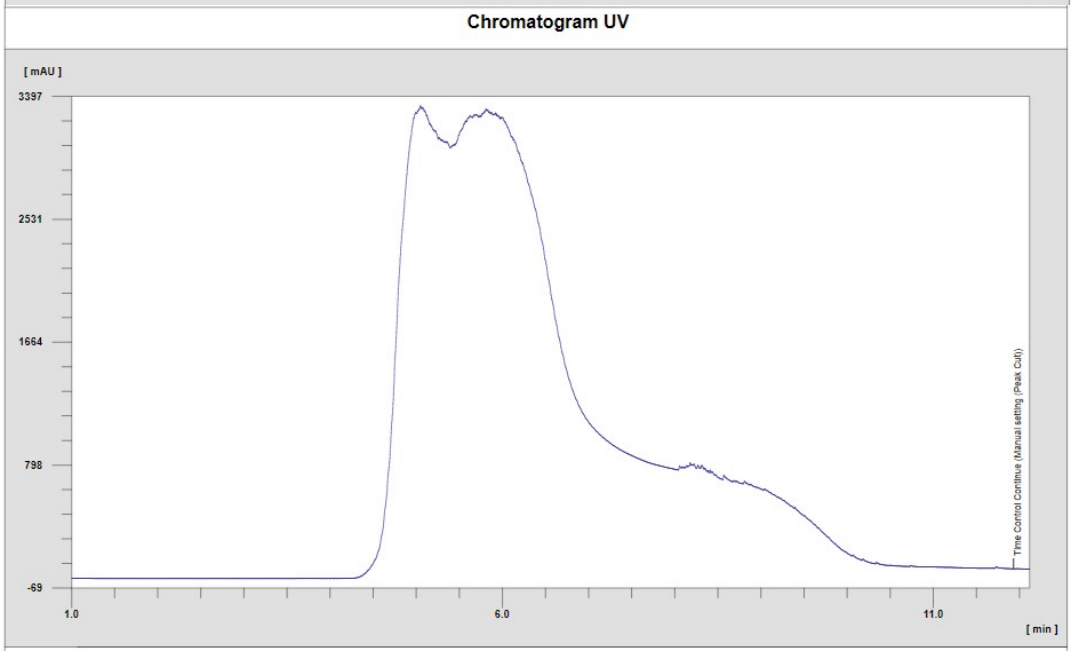


[^{11}C]Fenspiride ([^{11}C]25)

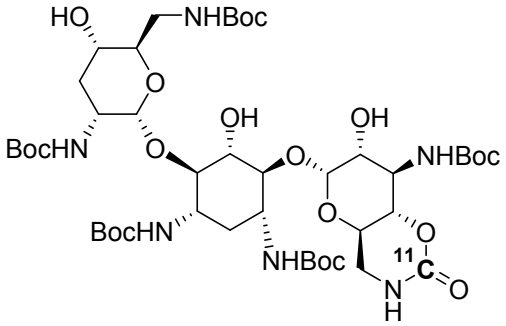


$C_{14}{}^{11}CH_{20}N_2O_2$
RCYield: 23 ± 3%

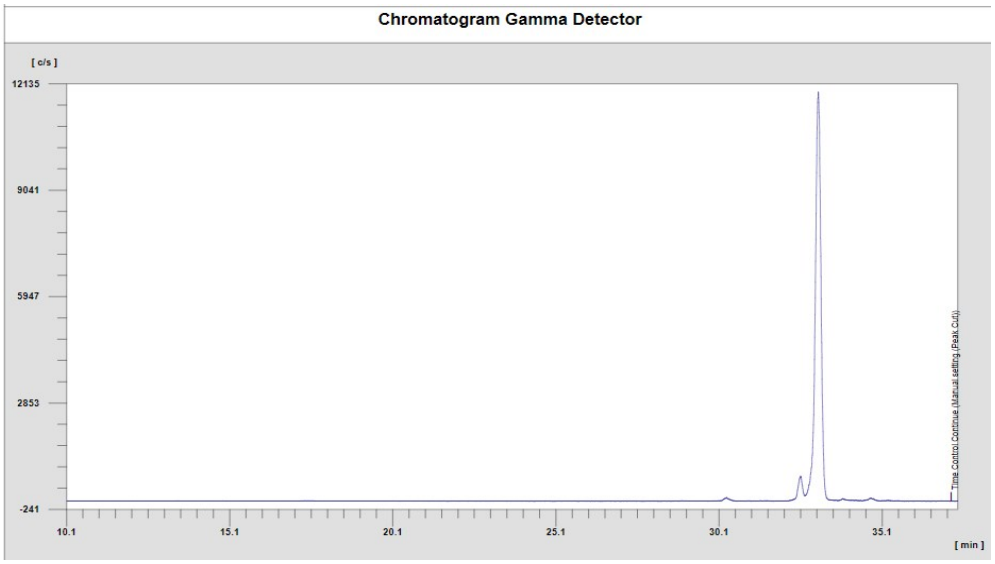


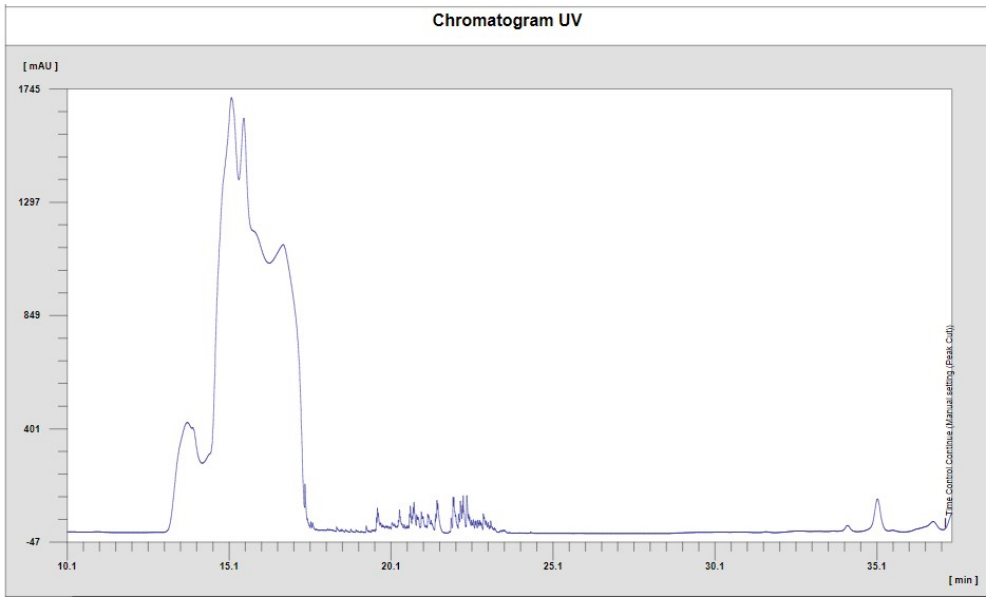


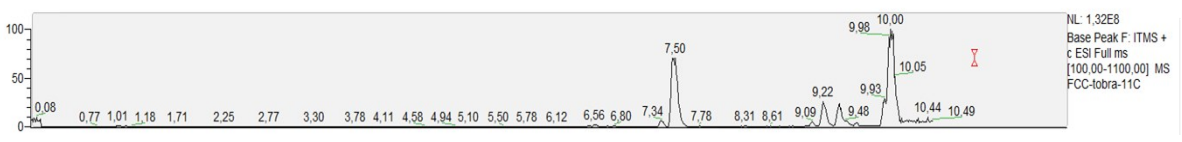
[^{11}C]-5-Boc-Tobramycine carbamate ([^{11}C]**26**)

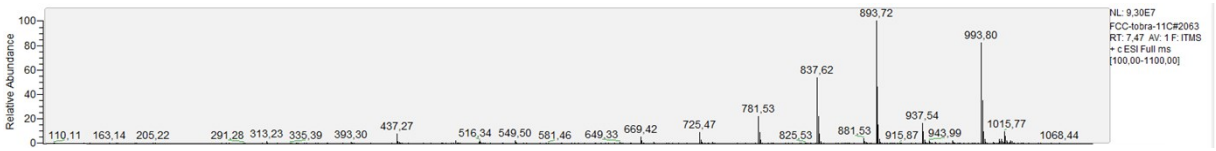


$C_{43}{}^{11}CH_{76}N_6O_{19}$
RCYield: 68 ± 2%

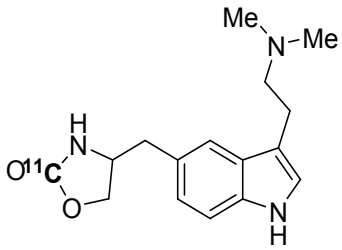








[^{11}C] Zolmitriptan ([^{11}C]30)



$C_{15}{}^{11}CH_{21}N_3O_2$
RCYield: 25 ± 2%
White solid