A Multicomponent Route to Functionalized Amides and Oxazolidinones

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1. General

All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise stated. Purification was carried out according to standard laboratory methods.[1]

1.1 Purification of Solvents

i) Anhydrous toluene was obtained from a PureSolv SPS-400-5 solvent purification system.

ii) Acetonitrile and 2-MeTHF were purified by fractional distillation under vacuum from CaH_2; CPME was purified by vacuum distillation from sodium metal; Dimethyl carbonate was purified by fractional distillation under vacuum from 4 Å molecular sieves; DMF was purified by fractional distillation under vacuum from $MgSO_4$.

iii) Purified solvents were transferred to and stored in septum-sealed oven-dried flasks over previously activated 4 Å molecular sieves and purged with and stored under nitrogen.

iv) Ethyl acetate, methanol, and petroleum ether 40–60 °C for purification purposes were used as obtained from suppliers without further purification.

1.2 Purification of Starting Materials

i) Methyl benzoate and benzylamine used for optimisation reactions were purified by vacuum distillation from KOH.

ii) BEMP was purified by vacuum distillation from CaH_2; Cs_2CO_3, K_2CO_3 and K_3PO_4, were stored in a vacuum oven at 60 °C; ^{t}BuOK was purified by sublimation.

1.3 Experimental Details

i) All reactions were carried out using oven-dried 0.5 – 2 mL microwave vials, which were evacuated and purged with N_2 before use.

ii) Purging refers to a vacuum/nitrogen-refilling procedure.

iii) Room temperature was generally *ca*. 20 °C.

iv) Reactions were carried out at elevated temperatures using a temperature-regulated hotplate/stirrer.

1.4 Purification of Products

i) Thin layer chromatography was carried out using Merck silica plates coated with fluorescent indicator UV254. These were analysed under 254 nm UV light or developed using potassium permanganate solution.

ii) Flash chromatography was carried out using ZEOprep 60 HYD 40-63 µm silica gel.

iii) Strong cation exchange chromatography was carried out using Silicycle Silia*Prep*™ Propylsulfonic Acid (SCX-2) cartridges.

1.5 Analysis of Products

i) Fourier Transformed Infra-Red (FTIR) spectra were obtained using an A2 Technologies ATR 32 machine.

ii) 1H and 13C NMR spectra were obtained on a Bruker DRX 500 spectrometer at 500 and 126MHz, respectively or on a Bruker AV3 400 at 400 and 101 MHz, respectively.

Chemical shifts are reported in ppm and coupling constants are reported in Hz with $CDCl_3$ referenced at 7.26 (1H) and 77.16 ppm (13C).

iii) High-resolution mass spectra were obtained on a Thermofisher LTQ Orbitrap XL instrument at the EPSRC National Mass Spectrometry Service Centre (NMSSC), Swansea.

iv) Reverse phase HPLC data was obtained on an Agilent 1200 series HPLC using a Machery-Nagel Nucleodur C18 column.

v) Chiral HPLC data was obtained on an Agilent 1260 Infinity HPLC using a Chiralpak IA column.

vi) Optical rotations were measured at 589 nm using a Perkin Elmer 341 Polarimeter.

1.6 HPLC Methods

i) Reverse phase HPLC analysis was performed using a gradient method, eluting with 5 – 80% MeCN/H_2O over 5 minutes at a flow rate of 2 mL/min, with glycidyl phenyl ether, 1-(benzylamino)-3-phenoxypropan-2-ol, methyl benzoate and *N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)benzamide **5** eluting at 1.46, 1.71, 2.23 and 2.86 minutes respectively. Iodobenzene eluted at 3.49 minutes.

Table S1: Reverse phase HPLC gradient

Time (min)	Concentration of MeCN (%)
0	5
1	55
3.9	60
4.1	80
4.3	5

ii) For reactions employing the analytical construct, conversions were calculated directly from the ratio of peak areas.

iii) For reactions using an internal standard, prior HPLC calibration was carried out using samples containing varying molarities of product and iodobenzene, allowing calculation of the response factor by substituting values into the following equation:

$$Response\ Factor = \frac{(\frac{Area}{Molarity})Product}{(\frac{Area}{Molarity})Standard}$$

Screening reactions were carried out using a known molarity of iodobenzene internal standard as indicated in the relevant general experimental procedures.

Unknown molarities of product were calculated by rearranging the above equation, using the average value for the response factor as determined during calibration.

Conversion to product was calculated as a percentage of the theoretical molarity for the reaction.

iv) Samples for HPLC analysis were prepared by diluting a 10 µL aliquot from the reaction mixture to 1 mL with MeCN.

v) For compound **36:** Chiral HPLC was performed using an isocratic method, using a Chiralpak IA column, eluting with 10% IPA/hexanes over 60 minutes with a flow rate of 1 mL/min.
For compound **37** and **52**: Chiral HPLC was performed using an isocratic method, using a Chiralpak IA column, eluting with 5% IPA/hexanes over 120 minutes with a flow rate of 1 mL/min.

The major and minor enantiomers were found to elute as follows:

Table S2: Normal phase retention times for chiral amides and oxazolidinones

Product	Major enantiomer retention time (min)	Minor enantiomer retention time (min)
36	29.339	20.499
37	84.736	61.303
52	62.853	52.803

2. General Experimental Procedures

2.1 General Procedure A for the Optimisation of the MCR Amidation Process

To an oven-dried, purged and sealed 2 – 5 mL microwave vial was added MeCN (0.5 mL), glycidyl phenyl ether (135 µL, 1 mmol, 1 equiv.), benzylamine (109 µL, 1 mmol, 1 equiv.), BEMP (29 µL, 0.1 mmol, 0.1 equiv) and methyl benzoate (126 µL, 1 mmol, 1 equiv.). The reaction mixture was then heated at the required reaction temperature for 24 h. The reaction mixture was sampled and the conversion was determined by HPLC with reference to iodobenzene (1.4 M), which was used as an internal standard.

For isolated yield: reaction mixture concentrated *in vacuo* and purified by silica gel chromatography (30% EtOAc/pet. ether 40 – 60 °C) followed by strong cation exchange chromatography, eluting with methanol.

Table S3: Reaction Optimisation

Entry	Reaction temperature (°C)	Conversion (%)
1	20	0
2	40	17
3	60	30
4	70	52
5	100	71[a]
6[b]	100	17

[a]Isolated Yield. [b]Reaction performed using 5 mol% BEMP.

2.2 General Procedure B for Investigating the Solvent & Base Species

To an oven-dried, purged and sealed 2 – 5 mL microwave vial containing base (0.1 mmol, 0.1 equiv.) was added solvent (0.5 mL), glycidyl phenyl ether (135 µL, 1 mmol, 1 equiv.), benzylamine (109 µL, 1 mmol, 1 equiv.) and methyl benzoate (126 µL, 1 mmol, 1 equiv.). The reaction mixture was then heated at 100 °C for 24 h. The reaction mixture was sampled and the conversion was determined by HPLC with reference to iodobenzene (1.4 M), which was used as an internal standard.

Table S4: Investigating the Effect of Altering the Base and Solvent

Entry	Base	Solvent	Conversion (%)
1	BEMP	MeCN	71[a]
2	K_2CO_3	MeCN	4
3	Cs_2CO_3	MeCN	24
4	K_3PO_4	MeCN	36
5	^{t}BuOK	MeCN	19
6	BEMP	CPME	4
7	BEMP	Dimethyl carbonate	3
8	BEMP	DMF	40
9	BEMP	2-MeTHF	2
10	BEMP	Toluene	20

2.3 General Procedure C for Investigating the Scope of the MCR Amidation Process

To an oven-dried, purged and sealed 2 – 5 mL microwave vial was added MeCN (0.5 mL), epoxide (1 mmol, 1 equiv.), amine (1 mmol, 1 equiv.), BEMP (29 µL, 0.1 mmol, 0.1 equiv.) and ester (1 mmol, 1 equiv.). The reaction mixture was then heated at 100 °C for 24 h. Reaction concentrated *in vacuo* and purified by silica column chromatography and strong cation exchange chromatography.

2.4 General Procedure D for Optimisation of the Oxazolidinone MCR Process

To an oven-dried, purged and sealed 2 – 5 mL microwave vial was added dimethyl carbonate (0.5 mL), glycidyl phenyl ether (135 µL, 1 mmol, 1 equiv.), benzylamine (109 µL, 1 mmol, 1 equiv.) and BEMP (15 – 29 µL, 0.05 – 0.1 mmol, 0.05 – 0.1 equiv). The reaction mixture was then heated at the required reaction temperature for 16 - 24 h. Reaction concentrated i*n vacuo* and purified by silica column chromatography (25 – 30% EtOAc/pet. ether 40 – 60 °C) and strong cation exchange chromatography, eluting with methanol.

Table S5: Optimisation of Oxazolidinone MCR

Entry	Reaction Temperature (°C)	BEMP (mol%)	Time (h)	Yield (%)
1	40	10	16	12
2	70	10	16	48
3	120	10	16	94
4	70	10	24	96
5	70	5	24	13
6	120	5	16	78
7	70	10	24	94

[a]Reaction performed using 1 equiv. of dimethyl carbonate in MeCN (2M)

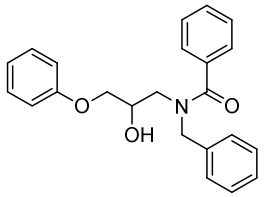
2.5 General Procedure E for Investigating the Scope of the Oxazolidinone MCR Process

To an oven-dried, purged and sealed 2 – 5 mL microwave vial was added MeCN (0.5 mL), epoxide (1 mmol, 1 equiv.), amine (1 mmol, 1 equiv.), BEMP (29 µL, 0.1 mmol, 0.1 equiv.) and dimethyl carbonate (84 µL ,1 mmol, 1 equiv.). The reaction mixture was then heated at 70 °C for 24 h. Reaction concentrated *in vacuo* and purified by silica column chromatography and, if required, strong cation exchange chromatography.

3. Characterisation Data

3.1 Characterisation Data for Amide Products

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)benzamide (5)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl benzoate (126 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a white solid (258 mg, 71%).

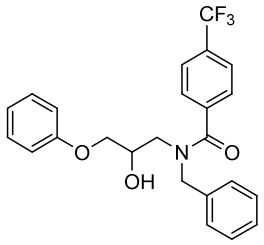
υ_{max} (neat): 3367, 3056, 3025, 2924, 1599, 1242, 693 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.47 (m, 2H), 7.42 – 7.26 (m, 8H), 7.18 (d, *J* = 6.7 Hz, 2H), 6.96 (t, *J* = 7.3 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 2H), 4.64 (q, *J* = 16.1 Hz, 2H), 4.39 (br. s, 1H), 4.26 (s, 1H), 4.04 – 3.83 (m, 3H), 3.69 (d, *J* = 13.7 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 158.5, 136.4, 135.6, 130.2, 129.7, 129.1, 128.7, 128.0, 127.2, 127.0, 121.3, 114.6, 70.2, 69.4, 54.9, 50.1.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{24}NO_3$ 362.1751, found 362.1753.

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)-4-(trifluoromethyl)benzamide (6)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 4-(trifluoromethyl)benzoate (161 µL), and purified by flash column chromatography (20% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as an off-white solid (384 mg, 89%).

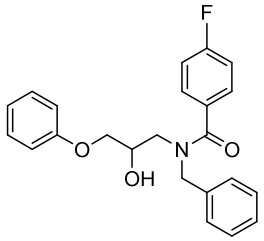
υ_{max} (neat): 3395, 3056, 3030, 2922, 1600, 1323, 1125, 753 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.39 (m, 5H), 7.16 (d, *J* = 7.3 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 2H), 4.65 – 4.58 (m, 2H), 4.33 (s, 1H), 4.03 – 3.97 (m, 1H), 3.85 (dd, *J* = 14.2, 7.5 Hz, 1H), 3.77 – 3.70 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 158.4, 139.25, 136.0, 132.1 (q, $^{2}J_{CF}$ = 32.8 Hz), 129.7, 129.2, 128.2, 127.3, 127.0, 125.83, 125.80, 123.7 (q, $^{1}J_{CF}$ = 272.8 Hz) 121.4, 114.6, 69.9, 69.6, 54.6, 49.8

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{23}F_3NO_3$ 430.1625, found 430.1623

_N_-benzyl-4-fluoro-_N_-(2-hydroxy-3-phenoxypropyl)benzamide (7)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 4-fluorobenzoate (129 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (221 mg, 58%).

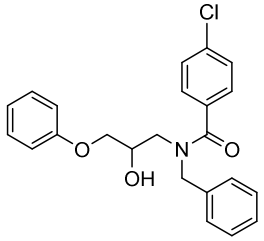
υ_{max} (neat): 3283, 3028, 2924, 1589, 1074, 1048, 842, 758, 697 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 – 7.47 (m, 2H), 7.37 (t, *J* = 7.3 Hz, 2H), 7.33 – 7.26 (m, 3H), 7.18 (s, 2H), 7.08 – 7.04 (m, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 4.7 Hz, 2H), 4.65 (q, *J* = 16.5 Hz, 2H), 4.26 (s, 1H), 4.01 – 3.95 (m, 2H), 3.84 (s, 1H), 3.69 (d, *J* = 14.4 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 158.4, 136.3, 131.6, 129.7, 129.4 (d, $^{3}J_{CF}$ = 8.7 Hz), 129.2, 128.1, 127.0, 121.4, 115.8 (d, $^{2}J_{CF}$ = 21.8 Hz), 114.6, 70.1, 69.5, 54.9, 50.3

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{23}FNO_3$ 380.1656, found 380.1656

_N_-benzyl-4-chloro-_N_-(2-hydroxy-3-phenoxypropyl)benzamide (8)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 4-chlorobenzoate (171 mg), and purified by flash column chromatography (20% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow solid (234 mg, 59%).

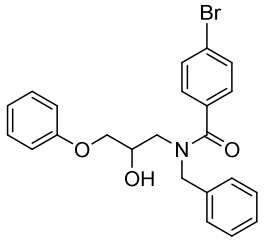
υ_{max} (neat): 3369, 3030, 2913, 1597, 1253, 1046, 753, 699 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.4 Hz, 2H), 7.39 – 7.26 (m, 7H), 7.16 (d, *J* = 6.6 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 4.63 (q, *J* = 16.4 Hz, 2H), 4.27 (s, 1H), 4.01 – 3.95 (m, 2H), 3.84 (dd, *J* = 13.8, 7.2 Hz, 1H), 3.69 (d, *J* = 13.9 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 158.4, 136.4, 136.2, 134.0, 129.7, 129.2, 129.0, 128.50, 128.1, 127.0, 121.4, 114.6, 70.1, 69.5, 54.8, 50.1

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{23}ClNO_3$ 396.1361, found 396.1361

_N_-benzyl-4-bromo-_N_-(2-hydroxy-3-phenoxypropyl)benzamide (9)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 4-bromobenzoate (215 mg), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a white solid (257 mg, 58%).

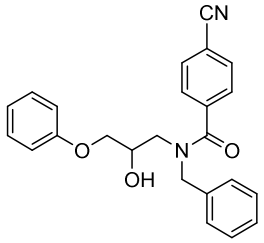
υ_{max} (neat): 3370, 3030, 2915, 1599, 1253, 1046, 751, 699 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 – 7.50 (m, 2H), 7.38 – 7.26 (m, 7H), 7.16 (d, *J* = 6.9 Hz, 2H), 6.97 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 2H), 4.62 (q, *J* = 16.4 Hz, 2H), 4.26 (s, 1H), 4.00 – 3.95 (m, 2H), 3.86 3.82 (m, 1H), 3.69 (d, *J* = 13.8 Hz)

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 158.4, 136.2, 134.5, 132.0, 129.7, 129.2, 128.7, 128.1, 127.0, 121.4, 114.6, 70.1, 69.5, 54.8, 50.1

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{23}BrNO_3$ 440.0856, found 440.0855

_N_-benzyl-4-cyano-_N_-(2-hydroxy-3-phenoxypropyl)benzamide (10)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 4-cyanobenzoate (161 mg), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (229 mg, 59%).

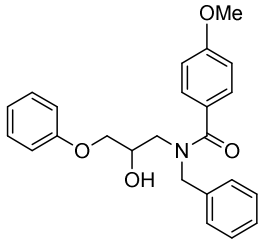
υ_{max} (neat): 3376, 3058, 3028, 2924, 2229, 1619, 1599, 1242, 755, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.26 (m, 5H), 7.14 (d, *J* = 7.3 Hz, 2H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 2H), 4.59 (s, 2H), 4.31 (s, 1H), 4.00 (d, *J* = 3.8 Hz, 2H), 3.83 (dd, *J* = 14.2, 7.4 Hz, 1H), 3.73 (dd, *J* = 14.3, 2.3 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.3, 158.4, 140.1, 135.8, 132.6, 129.8, 129.3, 128.3, 127.6, 126.9, 121.5, 118.1, 114.6, 114.0, 69.9, 69.6, 54.6, 49.8

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{23}N_2O_3$ 387.1703, found 387.1703

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)-4-methoxybenzamide (11)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 4-methoxybenzoate (166 mg), and purified by flash column chromatography (40% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (150 mg, 38%).

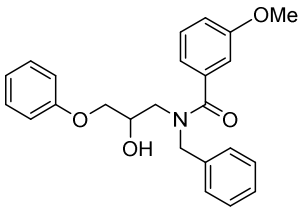
υ_{max} (neat): 3378, 2932, 1597, 1251, 1232, 1026, 725, 693 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* =8.7 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.32 – 7.25 (m, 5H), 6.95 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 4H), 4.73 – 4.68 (m, 3H), 4.23 (s, 1H), 4.00 (s, 1H), 3.91 (s, 1H), 3.85 – 3.80 (m, 4H), 3.65 – 3.63 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.5, 129.7, 129.1, 127.9, 127.1, 121.30, 114.6, 114.0, 70.1, 69.4, 55.5, 54.9, 50.6

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_4$ 392.1856, found 392.1853

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)-3-methoxybenzamide (12)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 3-methoxybenzoate (145 µL), and purified by flash column chromatography (40% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (273 mg, 70%).

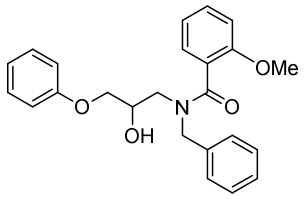
υ_{max} (neat): 3348, 2928, 1599, 1586, 1234, 1039, 753, 693 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (t, *J* = 7.2 Hz, 2H), 7.35 – 7.26 (m, 4H), 7.19 (d, *J* = 7.0 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.98 – 6.93 (m, 3H), 6.88 (d, *J* = 7.9 Hz, 2H), 4.64 (app. q, *J* = 16.3 Hz, 2H), 4.26 (s, 1H), 4.04 – 3.83 (m, 3H), 3.71 – 3.67 (m, 4H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.8, 129.9, 129.7, 129.1, 128.0, 127.1, 121.4, 119.05, 116.4, 114.6, 112.1, 70.2, 69.4, 55.4, 54.8, 50.2

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_4$ 392.1856, found 392.1854

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)-2-methoxybenzamide (13)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 2-methoxybenzoate (145 µL), and purified by flash column chromatography (40% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (130 mg, 33%).

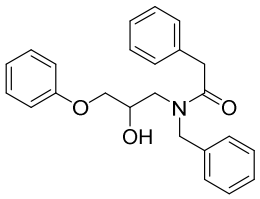
υ_{max} (neat): 3356, 3058, 3026, 2932, 1599, 1240, 753, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.22 (m, 7H), 7.15 (d, *J* = 6.8 Hz, 2H), 6.98 (dd, *J* = 15.9, 7.7 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 3H), 4.52 – 4.26 (m, 3H), 4.03 – 4.02 (m, 2H), 3.88 (d, *J* = 5.2 Hz, 1H), 3.81 (s, 3H), 3.65 – 3.62 (m, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.6, 136.5, 130.9, 129.7, 128.9, 128.8, 128.3, 127.9, 127.7, 121.2, 114.6, 111.2, 70.0, 55.7

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_4$ 392.1856, found 392.1849

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (14)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (354 mg, 94%).

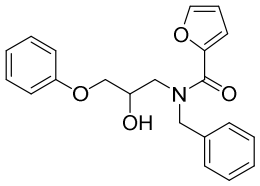
υ_{max} (neat): 3374, 3060, 3026, 1621, 1599, 1244, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.30 (m, 5H), 7.29 – 7.24 (m, 5H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.96 (t, *J* = 7.3 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 4.63 (q, *J* = 16.9 Hz, 2H), 4,22 – 4.14 (m, 1H), 3.95 (dd, *J* = 9.4, 5.3 Hz, 1H), 3.86 (dd, *J* = 10.4, 3.5 Hz, 1H), 3.78 – 3.72 (m, 3H), 3.66 – 3.63 (m, 1H)

13C NMR (126 MHz, $CDCl_3$): δ 174.6, 158.4, 136.2, 134.6, 129.7, 129.2, 129.0, 128.9, 128.0, 127.2, 126.6, 70.3, 69.2, 53.6, 51.3, 41.0,

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_3$ 376.1907, found 376.1905

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)furan-2-carboxamide (15)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl 2-furoate (107 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as an orange oil (178 mg, 51%).

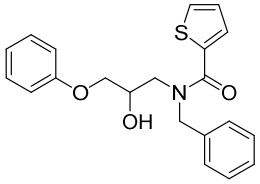
υ_{max} (neat): 3365, 3058, 3026, 2922, 1599, 1487, 1244, 753, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 (s, 1H), 7.39 – 7.36 (m, 2H), 7.33 – 7.26 (m, 5H), 7.06 (s, 1H), 6.96 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 2H), 6.48 – 6.47 (m, 1H), 4.97 (s, 2H), 4.27 (s, 1H), 4.01 (s, 1H), 3.93 (d, *J* = 6.7 Hz, 1H), 3.80 (dd, *J* = 14.4, 7.4 Hz, 1H), 3.66 – 3.64 (m, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 162.7, 158.3, 144.7, 136.5, 129.5, 128.9, 127.8, 127.1, 121.2, 117.6, 114.5, 111.2, 69.8, 69.2, 53.5, 51.4

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{22}NO_4$ 352.1543, found 352.1544

_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)thiophene-2-carboxamide (16)



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and ethyl 2-thiophenecarboxylate (134 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a yellow oil (218 mg, 59%).

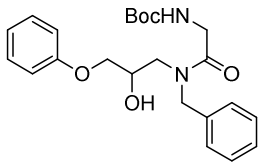
υ_{max} (neat): 3363, 3060, 3026, 2924, 1597, 1242, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.35 – 7.26 (m, 6H), 6.98 – 6.94 (m, 2H), 6.86 (d, *J* = 7.9 Hz, 2H), 4.99 – 4.91 (m, 2H), 4.30 (qd, *J* = 7.6, 2.6 Hz, 1H), 4.04 – 4.01 (m, 1H), 3.93 (dd, *J* = 9.4, 6.7 Hz, 1H), 3.86 (dd, *J* = 14.5, 7.5 Hz, 1H), 3.69 (dd, *J* = 14.5, 2.5 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.4, 137.1, 136.4, 130.3, 129.7, 129.5, 129.3, 128.0, 127.3, 126.8, 121.4, 114.3, 69.9, 69.3, 51.7

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{22}NO_3S$ 368.1315, found 368.1314

***tert*-butyl (2-(benzyl(2-hydroxy-3-phenoxypropyl)amino)-2-oxoethyl)carbamate (17)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), benzylamine (109 µL) and *N*-(*tert*-Butoxycarbonyl)glycine methyl ester (175 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (169 mg, 41%).

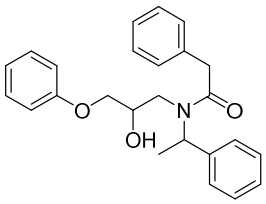
υ_{max} (neat): 3413, 2974, 2930, 1643, 1496, 1244, 1165, 755, 732, 693 cm^{-1}

1H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.23 (m, 6H, 7.16 (d, *J* = 7.1 Hz, 1H), 6.98 – 6.95 (m, 1H), 6.88 – 6.86 (m, 2H), 4.65 – 4.53 (m 2H), 4.21 – 4.17 (m, 1H), 4.06 – 4.04 (m, 2H), 3.93 (qd, *J* = 9.5, 5.8 Hz, 2H), 3.73 – 3.63 (m, 2H), 1.45 (d, *J* = 6.0 Hz, 9H)

13C NMR (101 MHz, $CDCl_3$): δ 170.80, 157.74, 134.88, 129.07, 128.66, 128.26, 127.54, 125.99, 120.78, 113.99, 69.37, 68.69, 51.64, 50.39, 41.93, 27.84

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{31}N_2O_5$ 415.2227, found 415.2222

***N*-(2-hydroxy-3-phenoxypropyl)-2-phenyl-*N*-(1-phenylethyl)acetamide (18)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), α-methylbenzylamine (129 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (20% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (204 mg, 52%).

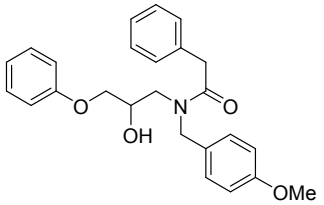
υ_{max} (neat): 3341, 3058, 3026, 2928, 1599, 755, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 – 7.21 (m, 10H), 7.11 (d, *J* = 7.5Hz, 1H), 7.04 – 7.03 (m, 1H), 6.92 (dt, *J* = 11.2, 7.4 Hz, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 5.23 (p, *J* = 6.7 Hz, 1H), 4.07 – 4.00 (m, 1H), 3.96 (d, *J* = 4.5 Hz, 1H), 3.92 (d, *J* = 6.6 Hz, 1H), 3.71 – 3.56 (m, 2.5 H), 3.39 – 3.35 (m, 0.5 H), 3.28 – 3.20 (m, 1H), 1.50 (dd, *J* = 11.1, 7.0 Hz, 3H) (1:1 mixture of diastereomers)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.8, 174.3, 158.5, 158.3, 139.6, 138.7, 134.7, 134.5, 129.5, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.1, 127.9, 127.4, 127.3, 127.2, 126.5, 121.0, 120.8, 114.4, 114.3, 72.5, 70.9, 69.6, 69.4, 56.6, 56.2, 48.8, 47.7, 41.9, 41.6, 18.3, 17.0, (1:1 mixture of diastereomers)

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{28}NO_3$ 390.2064 , found 390.2061

***N*-(2-hydroxy-3-phenoxypropyl)-*N*-(4-methoxybenzyl)-2-phenylacetamide (20)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), 4-methoxybenzylamine (131 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (220 mg, 54%).

υ_{max} (neat): 3378, 3058, 3026, 2930, 2833, 1612, 1599, 1244, 755, 693 cm^{-1}

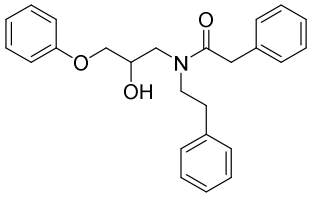
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 – 7.25 (m, 7H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.95 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 4.59 (d, *J* = 16.5 Hz, 1H), 4.50 (d *J* = 16.4 Hz, 1H), 4.39 (d, *J* = 4.1 Hz, 1H), 4.13 (s, 1H), 3.93 (dd, *J* = 9.4, 5.2 Hz, 1H), 3.80 – 3.79 (m, 5H), 3.72 (dd, *J* = 14.4, 7.1 Hz, 1H), 3.60 (dd, *J* = 14.4, 2.6 Hz, 1H)

13C NMR (126 MHz, $CDCl_3$): δ 173.9, 158.8, 157.8, 134.1, 129.0, 128.4, 128.3, 127.4, 126.6, 120.6, 113.9, 69.8, 68.5, 54.8, 52.5, 50.4, 40.4

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{28}NO_4$ 406.2013 , found 406.2008

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{28}NO_4$ 406.2013 , found 406.2009

***N*-(2-hydroxy-3-phenoxypropyl)-*N*-phenethyl-2-phenylacetamide (21)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), phenethylamine (126 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (348 mg, 89%).

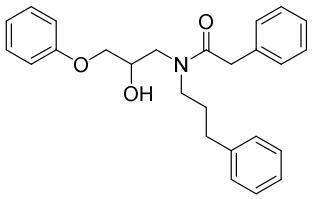
υ_{max} (neat): 3357, 3058, 3025, 2922, 1619, 1599, 1244, 753, 693 cm^{-1}

1H NMR (500 MHz, $CDCl_3$): δ 7.34 – 7.30 (m, 5H), 7.29 – 7.26 (m, 3H), 7.16 (d, *J* = 7.1 Hz, 2H), 7.11 (d, *J* = 7.1 Hz, 2H), 6.97 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 7.9 Hz, 2H), 4.53 (s, 1H), 4.21 (qd, *J* = 7.3, 2.5 Hz, 1H), 4.00 (dd, *J* = 9.4, 5.2 Hz, 1H), 3.87 – 3.84 (m, 1H), 3.74 (dd, *J* = 14.4, 6.9 Hz, 1H), 3.66 – 3.54 (m, 3H), 3.50 (s, 2H), 2.87 – 2.75 (m, 2H)

13C NMR (126 MHz, $CDCl_3$): δ 174.1, 158.3, 137.8, 134.6, 129.6, 128.9, 128.8, 128.8, 127.0, 126.9, 121.2, 114.5, 70.5, 69.0, 51.9, 51.2, 40.5, 35.0

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{28}NO_3$ 390.2064, found 390.206

***N*-(2-hydroxy-3-phenoxypropyl)-2-phenyl-*N*-(3-phenylpropyl)acetamide (22)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), 3-phenylpropylamine (142 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (375 mg, 93%).

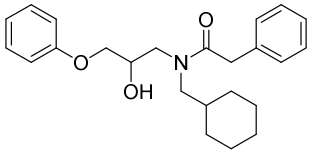
υ_{max} (neat): 3346, 3058 3025, 2924, 1619, 1599, 1244, 753, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 – 7.26 (m, 8H), 7.12 (dd, *J* = 13.5, 7.0 Hz, 4H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.87 – 6.85 (m, 2H), 4.61(d, *J* = 3.9 Hz, 1H), 4.18 – 4.14 (s, 1H), 3.99 (dd, *J* = 9.4, 5.1 Hz, 1H), 3.83 (dd, *J* = 9.4, 7.3 Hz, 1H), 3.72 (dd, *J* = 14.4, 7.0 Hz, 1H), 3.63 (s, 2H), 3.59 (dd, *J* = 14.3, 2.3 Hz, 1H), 3.40 – 3.34 (m, 1H), 3.31 – 3.24 (m, 1H) 2.59 (t, *J* = 7.3 Hz, 2H), 1.96 – 1.83 (m, 2H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.0, 158.4, 140.7, 134.7, 129.7, 128.9, 128.79, 128.75, 128.4, 127.1, 126.5, 121.3, 114.6, 70.7, 69.2, 51.4, 50.0, 41.0, 33.0, 30.2

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{30}NO_3$ 404.2220, found 404.2215

***N*-(cyclohexylmethyl)-*N*-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (23)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), cyclohexylmethylamine (130 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (20% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (366 mg, 96%).

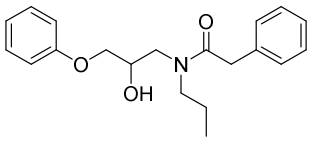
υ_{max} (neat): 3359, 3060, 3026, 2921, 2848, 1619, 1599, 1496, 1450, 1244, 753, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 – 7.31 (m, 2H), 7.29 – 7.24 (m, 5H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.88 – 6.86 (m, 2H), 4.73 (d, *J* 3.7 Hz, 1H), 4.16 – 4.14 (m, 1H), 3.99 (dd, *J* = 9.4, 5.0 Hz, 1H), 3.82 – 3.74 (m, 4H), 3.58 – 3.55 (m, 1H), 3.24 (dd, *J* = 14,7, 7.8 Hz, 1H), 3.15 (dd, *J* = 14.6, 6.7 Hz, 1H), 1.77 – 1.68 (m, 6H), 1.24 – 1.14 (m, 3H), 0.95 – 0.83 (m, 2H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.5, 158.5, 134.9, 129.7, 129.0, 128.9, 127.1, 121.3, 114.6, 70.7, 69.2, 56.9, 52.3, 40.8, 37.6, 31.2, 31.0, 26.4, 26.0, 25.9

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{32}NO_3$ 382.2377, found 382.2380

***N*-(2-hydroxy-3-phenoxypropyl)-2-phenyl-*N*-propylacetamide (24)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), 1-propylamine (82 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (313 mg, 96%).

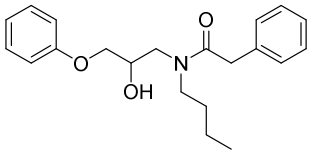
υ_{max} (neat): 3361, 3060, 3026, 2960, 2930, 2872, 1619, 1599, 1244, 1043, 755, 693 cm $^{-1}$

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 – 7.30 (m, 2H), 7.28 – 7.24 (m, 5H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.87 – 6.85 (m, 2H), 4.62 (d, *J* = 3.7 Hz, 1H), 4.16 – 4.13 (m, 1H), 3.98 (dd, *J* = 9.4, 5.1 Hz, 1H), 3.82 (dd, 9.4, 7.3 Hz, 1H), 3.74 – 3.68 (m, 3H), 3.55 (dd, *J* = 14.4, 2.5 Hz, 1H), 3.36 – 3.30 (m, 1H), 3.28 – 3.22 (m, 1H), 1.62 – 1.49 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.1, 158.5, 134.9, 129.7, 128.9, 128.9, 127.2, 121.3, 114.6, 70.7, 69.2, 52.2, 51.5, 40.9, 22.1, 11.3,

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{26}NO_3$ 328.1907, found 328.1909

***N*-butyl-*N*-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (25)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), 1-butylamine (99 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a cloudy white oil (251 mg, 73%).

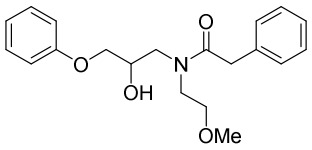
υ_{max} (neat): 3318, 3060, 3026, 2954, 2928, 2870, 1619, 1599, 1244, 755, 693 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.28 (m, 2H), 7.25 – 7.21(m, 5H), 6.94 – 6.90 (m, 1H), 6.85 – 6.83 (m, 2H), 4.64 (s, 1H), 4.15 – 4.10 (m, 1H), 3.96 (dd, *J* = 9.4, 5.1 Hz, 1H), 3.79 (dd, *J* = 9.4, 7.4 Hz, 1H), 3.72 – 3.66 (m, 3H), 3.56 – 3.51 (m, 1H), 3.37 – 3.20 (m, 2H), 1.53 – 1.43 (m, 2H), 1.24 (dd, *J* = 14.8, 7.4 Hz, 2H), 0.89 – 0.85 (m, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0, 158.3, 134.7, 129.5, 128.8, 128.7, 127.0, 121.1, 114.4, 70.6, 69.0, 51.4, 50.3, 40.7, 30.8, 20.0, 13.7

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{28}NO_3$ 342.2064, found 342.2066

***N*-(2-hydroxy-3-phenoxypropyl)-*N*-(2-methoxyethyl)-2-phenylacetamide (27)**



Synthesised according to General Experimental Procedure C using glycidyl phenyl ether (135 µL), 2-methoxyethylamine (87 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (50% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a cloudy yellow oil (312 mg, 91%).

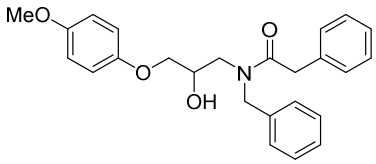
υ_{max} (neat): 3367, 3060, 3026, 2924, 2876, 1621, 1599, 1244, 1113, 756 693 cm^{-1}

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.31 – 7.27 (m, 4H), 7.23 – 7.19 (m, 3H), 6.96 – 6.89 (m, 3H), 5.25 (s, 0.5H), 4.98 (s, 0.5 H) 4.06 (s, 1H), 3.93 – 3.72 (m, 4H), 3.61 (s, 2H), 3.47 (m, 3H), 3.25 (d, *J* = 15.4 Hz, 3H) (mixture of rotamers)

13C NMR (101 MHz, DMSO-d_6): δ 171.0, 170.6, 158.5, 158.3, 135.87, 129.2, 128.8, 128.7, 127.9, 125.9, 120.5, 120.3, 114.4, 70.5, 70.1, 69.7, 69.4, 67.6, 67.5, 58.04, 57.7, 51.7, 49.2, 48.3, 45.4 (mixture of rotamers)

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{26}NO_4$ 344.1856, found 344. 1860

***N*-benzyl-*N*-(2-hydroxy-3-(4-methoxyphenoxy)propyl)-2-phenylacetamide (28)**



Synthesised according to General Experimental Procedure C using glycidyl 4-methoxyphenyl ether (180 mg), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a colourless oil (141 mg, 35%).

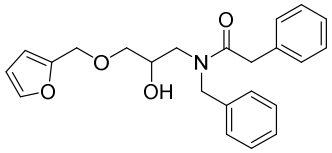
υ_{max} (neat): 3389, 3026, 2928, 2831, 1619, 1508, 1230, 1032, 825, 697 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.31 (m, 5H), 7.28 – 7.24 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.82 – 6.75 (m, 4H), 4.63 (app. q, *J* = 16.9 Hz, 2H), 4.28 (m, 1H), 4.16 – 4.14 (m, 1H), 3.89 (dd, *J* = 9.4, 5.3 Hz, 1H), 3.81 – 3.70 (m, 7H), 3.64 (dd, *J* = 14.4, 2.7 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.6, 154.2, 152.6, 136.3, 134.6, 129.2, 129.0, 128.9, 128.0, 127.2, 126.6, 115.5, 114.8, 70.4, 70.0, 55.9, 53.6, 51.3, 41.0

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{28}NO_4$ 406.2013, found 406.2008

***N*-benzyl-*N*-(3-(furan-2-ylmethoxy)-2-hydroxypropyl)-2-phenylacetamide (29)**



Synthesised according to General Experimental Procedure C using furfuryl glycidyl ether (137 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (35% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as an orange oil (106 mg, 28%).

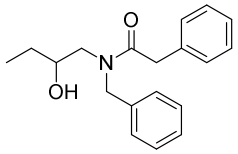
υ_{max} (neat): 3387, 3026, 2900, 2857, 1621, 1076, 734, 697 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 – 7.18 (m, 9H), 7.11 (d, *J* = 7.3 Hz, 2H), 6.32 – 6.31 (m, 1H), 6.27 – 6.26 (d, *J* = 3.2 Hz, 1H), 4.62 – 4.53 (m, 2H), 4.47 – 4.38 (m, 2H), 3.98 (s, 2H), 3.72 (s, 2H), 3.58 – 3.50 (m, 2H), 3.45 – 3.38 (m, 2H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.3, 151.5, 143.0, 136.6, 134.8, 129.1, 128.9, 128.89, 127.9, 127.1, 126.5, 110.5, 109.7, 71.6, 70.5, 65.2, 53.3, 51.2, 40.1

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{26}NO_4$ 380.1856, found 380.1858

***N*-benzyl-*N*-(2-hydroxybutyl)-2-phenylacetamide (30)**



Synthesised according to General Experimental Procedure C using 1,2-epoxybutane (87 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (87 mg, 29%).

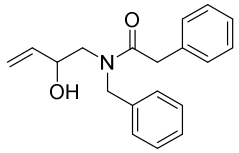
υ_{max} (neat): 3387, 3060, 3026, 2960, 2930, 2874, 1621, 1452, 697 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.32 (m, 6H), 7.25 – 7.23 (m, 2H), 7.12 (d, *J* = 7.0 Hz, 2H), 4.66 – 4.56 (m, 2H), 3.75 (s, 2H), 3.71 – 3.68 (m, 1H), 3.64 (dd, *J* = 8.8, 5.0 Hz, 1H), 3.22 (dd, *J* = 13.8, 1.7 Hz, 1H), 1.44 – 1.39 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0, 136.2, 134.6, 129.0, 128.8, 128.7, 127.8, 127.0, 126.4, 73.0, 53.6, 53.2, 40.9, 28.5, 9.7

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{24}NO_2$ 298.1802, found 298.1801

***N*-benzyl-*N*-(2-hydroxybut-3-en-1-yl)-2-phenylacetamide (32)**



Synthesised according to General Experimental Procedure C using butadiene monoxide (81 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (161 mg, 54%).

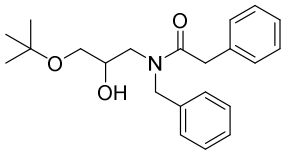
υ_{max} (neat): 3376, 3060, 3026, 2930, 1621, 1452, 697 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.29 (m, 6H), 7.25 – 7.23 (m, 2H), 7.12 (d, *J* = 7.4 Hz, 2H), 5.82 – 5.76 (m, 1H), 5.30 (d, *J* = 17.1 Hz, 1H), 5.12 (d, *J* = 10.5 Hz, 1H), 4.65 (d, *J* = 17.0 Hz, 1H), 4.57 (d, *J* = 17.0 Hz, 1H), 4.35 (s, 1H), 3.83 (s, 1H), 3.75 (s, 2H), 3.59 (dd, *J* = 14.3, 7.9 Hz,1 H), 3.45 (dd, *J* = 14.2, 2.9 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.3, 138.4, 136.3, 134.7, 129.2, 128.9(2), 128.0, 127.2, 126.5, 115.9, 72.7, 53.6, 53.5, 41.0

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{22}NO_2$ 296.1645, found 296.1646

***N*-benzyl-*N*-(3-(*tert*-butoxy)-2-hydroxypropyl)-2-phenylacetamide (33)**



Synthesised according to General Experimental Procedure C using *tert*-butyl glycidyl ether (142 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow solid (86 mg, 24%).

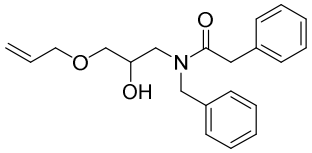
υ_{max} (neat): 3365, 3062, 3030, 2969, 2921, 2870, 1627, 1072, 699 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.35 (m, 2H), 7.31 – 7.30 (m, 4H), 7.24 – 7.23 (m, 2H), 7.14 (d, *J* = 7.3 Hz, 2H), 4.66 (s, 2H), 3.74 (s, 2H), 3.32 – 3.26 (m, 2H), 1.19 (s, 3H), 1.13 (s, 9H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 173.7, 137.7, 136.6, 135.4, 134.8, 129.0, 128.8, 128.7, 128.6, 128.5, 128.1, 127.7, 127.3, 127.0, 126.8, 126.4, 73.6, 73.1, 71.1, 69.1, 63.4, 62.9, 53.2, 50.8, 49.8, 48.9, 40.9, 40.8, 27.5, 27.48 (mixture of rotamers)

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{30}NO_3$ 356.2220, found 356.2221

***N*-(3-(allyloxy)-2-hydroxypropyl)-*N*-benzyl-2-phenylacetamide (34)**



Synthesised according to General Experimental Procedure C using allyl glycidyl ether (119 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (128 mg, 41%).

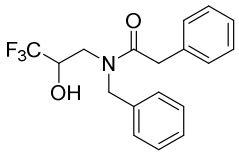
υ_{max} (neat): 3385, 3026, 2915, 2848, 1621, 1078, 697 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.33 (m, 2H), 7.31 (d, *J* = 7.6 Hz, 3H), 7.26 – 7.22 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 2H), 5.88 – 5.80 (m, 1H), 5.22 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.15 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.68 – 4.60 (m, 2H), 4.00 – 3.98 (m, 1H), 3.94 (d, *J* = 5.6 Hz, 2H), 3.90 – 3.88 (m, 1H), 3.74 (s, 2H), 3.60 – 3.52 (m, 2H), 3.40 – 3.37 (m, 2H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.1, 136.3, 134.8, 134.5, 129.3, 129.1, 128.9, 128.9, 128.8, 128.7, 128.2, 127.9, 127.5, 127.1, 126.9, 126.5, 117.8, 117.3, 72.5, 72.4, 72.0, 71.6, 70.6, 69.1, 53.4, 51.2, 49.8, 49.1, 41.1, 40.9 (mixture of rotamers)

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{26}NO_3$ 340.1907, found 340.1906

***N*-benzyl-2-phenyl-*N*-(3,3,3-trifluoro-2-hydroxypropyl)acetamide (35)**



Synthesised according to General Experimental Procedure C using 2-(trifluoromethyl)oxirane (86 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (20% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (233 mg, 69%).

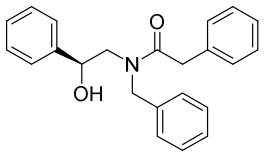
υ_{max} (neat): 3322, 3028, 1623, 1268, 1165, 1119, 695 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.33 (m, 5H), 7.30 – 7.27 (m, 1H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.10 (d, *J* = 7.2 Hz, 2H), 5.11 (d, *J* = 5.0 Hz, 1H), 4.67 (d, *J* = 16.8 Hz, 1H), 4.55 (d, *J* = 16.8 Hz, 1H), 4.05 – 4.00 (m, 1H), 3.91 (dd, *J* = 14.6, 8.5 Hz, 1H), 3.80 (s, 2H), 3.48 (dd, *J* = 14.6, 2.1 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 175.4, 135.2, 133.9, 129.3, 129.0, 128.8, 128.3, 127.3, 126.5, 125.5 (q, $^1J_{CF}$ = 282.6 Hz), 70.5 (q, $^2J_{CF}$ = 30.6 Hz), 53.6, 48.3, 40.8

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{19}F_3NO_2$ 338.1362, found 338.1362

(S)-*N*-benzyl-*N*-(2-hydroxy-2-phenylethyl)-2-phenylacetamide (36)



Synthesised according to General Experimental Procedure C using (S)-phenyloxirane (114 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a clear oil (310 mg, 90%).

υ_{max} (neat): 3374, 3056, 3025, 1619, 1452, 697 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 – 7.33 (m, 4H), 7.31 – 7.22 (m, 9H), 7.06 (d, *J* = 7.2 Hz, 2H), 4.93 (dd, *J* = 7.6, 2.6 Hz, 1H), 4.51 (d, *J* = 16.9 Hz, 1H), 4.20 (d, *J* = 16.9 Hz, 1H), 3.76 (s, 2H), 3.71 (dd, *J* = 14.4, 7.7 Hz, 1H), 3.59 (dd, *J* = 14.3, 2.8 Hz, 1H)

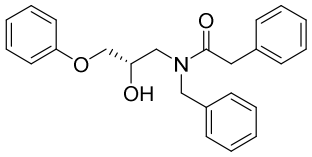
^{13}C NMR (126 MHz, $CDCl_3$): δ 174.7, 142.4, 136.1, 134.6, 129.2, 129.0, 128.96, 128.5, 128.0, 127.7, 127.2, 126.6, 125.9, 74.2, 56.0, 53.47, 41.0

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{24}NO_2$ 346.1802, found 346.1802

ee: >99%

$[\alpha]_D^{20}$ = 51.6 (c = 1, DCM)

(S)-*N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (37)



Synthesised according to General Experimental Procedure C using (S)-glycidyl phenyl ether (135 µL), benzylamine (109 µL) and methyl phenylacetate (140 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow oil (260 mg, 69%).

υ_{max} (neat): 3361, 3058, 3025, 2924, 1621, 1599, 1495, 1242, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.31 (m, 5H), 7.30 – 7.24 (m, 5H), 7.13 (d, *J* = 7.2 Hz, 2H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 7.9 Hz, 2H), 4.67 (d, *J* =16.9 Hz, 1H), 4.59 (d, *J* = 16.9 Hz, 1H), 4.19 – 4.15 (m, 1H), 3.95 (dd, *J* = 9.4, 5.3 Hz, 1H), 3.84 (dd, *J* = 9.5, 6.9 Hz, 1H), 3.78 – 3.72 (m, 3H), 3.66 – 3.63 (m, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.5, 158.3, 136.1, 134.5, 129.5, 129.1, 128.9, 128.8, 127.9, 127.2, 126.5, 121.2, 114.5, 70.3, 69.1, 53.5, 51.2, 40.9

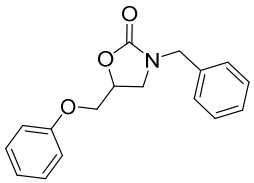
HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_3$ 376.1907, found 376.1908

ee: >99%

$[\alpha]_D^{20}$ = -9.26 (c = 1, DCM)

3.2 Characterisation Data for Oxazolidinone Products

3-benzyl-5-(phenoxymethyl)oxazolidin-2-one (38)[2]



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and benzylamine (109 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) to afford the title compound as a white solid (266 mg, 94%).

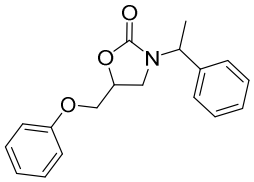
υ_{max} (neat): 3059, 3042, 2959, 2923, 1735, 1489, 1447, 1246, 1063, 755, 740 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.35 (m, 2H), 7.33 – 7.26 (m, 5H), 7.00 – 6.97 (m, 1H), 6.85 (dd, *J* = 8.7, 0.9 Hz, 2H), 4.82 (ddd, *J* = 9.0, 4.5, 1.2 Hz, 1H), 4.50 (d, *J* = 15.0 Hz, 1H), 4.45 (d, *J* = 14.9 Hz, 1H) 4.10 – 4.09 (m, 2H), 3.57 (t, *J* = 8.9 Hz, 1H), 3.44 (dd, *J* = 8.8, 6.0 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.2, 157.8, 135.8, 129.7, 129.0, 128.3, 128.2, 121.8, 114.1, 71.0, 68.2, 48.5, 46.3

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{18}NO_3$ 284.1281, found 284.1283

5-(phenoxymethyl)-3-(1-phenylethyl)oxazolidin-2-one (39)



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and α-methylbenzylamine (129 µL), and purified by flash column chromatography (20% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a white solid (146 mg, 49%).

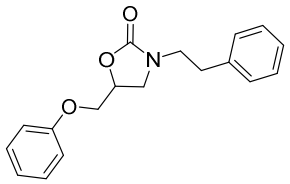
υ_{max} (neat): 3059, 3042, 2959, 2923, 1735, 1489, 1447, 1246, 1063, 755, 740 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 – 7.36 (m, 4H), 7.33 – 7.27 (m, 3H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.80 (dd, *J* = 8.6, 0.8 Hz, 2H), 5.28 (q, *J* = 7.1 Hz, 1H), 4.86 – 4.81 (m, 1H), 4.06 – 4.00 (m, 2H), 3.67 (t, *J* = 8.9 Hz, 1H), 3.21 (dd, *J* = 8.7, 5.9 Hz, 1H), 1.63 (d, *J* = 7.1 Hz , 3H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.2, 157.3, 139.6, 129.7, 128.9, 128.0, 127.1, 121.7, 114.7, 71.1, 68.2, 51.6, 42.4, 16.6

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1438, found 298.1440

3-phenethyl-5-(phenoxymethyl)oxazolidin-2-one (41)



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and phenethylamine (126 µL), and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) to afford the title compound as a white solid (223 mg, 75%).

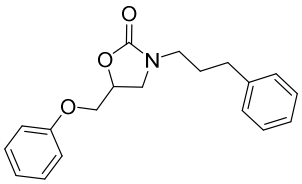
υ_{max} (neat): 3055, 3029, 2921, 1739, 1240, 1058, 755 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 – 7.29 (m, 4H), 7.27 – 7.24 (m, 3H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 2H), 4.78 (dq, *J* = 10.3, 5.3 Hz, 1H), 4.08 (dd, *J* = 9.9, 4.3 Hz, 1H), 4.00 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.66 – 3.53 (m, 3H), 3.43 (dd, *J* = 8.6, 5.7 Hz, 1H), 2.95 (t, *J* = 7.3 Hz, 2H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.2, 157.5, 138.4, 129.7, 129.7, 128.8, 126.8, 121.8, 114.7, 70.9, 68.0, 47.4, 45.5, 34.1,

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1438, found 298.1440

5-(phenoxymethyl)-3-(3-phenylpropyl)oxazolidin-2-one (42)



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and 3-phenylpropylamine (142 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a white solid (134 mg, 43%).

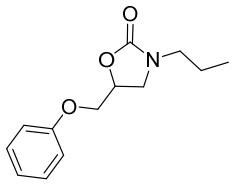
υ_{max} (neat): 3063, 3029, 2949, 2921, 2856, 1742, 1244, 1225, 1065, 755 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.27 (m, 4H), 7.19 (dd, *J* = 7.2, 5.4 Hz, 3H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 2H), 4.78 (dt, *J* = 9.9, 5.6 Hz, 1H), 4.10 (ddd, *J* = 15.5, 10.0, 4.8 Hz, 2H), 3.66 (t, *J* = 8.8 Hz, 1H), 3.53 (dd, *J* = 8.7, 5.9 Hz, 1H), 3.41 – 3.30 (m, 2H), 2.68 (td, *J* = 7.3, 2.1 Hz, 2H), 1.95 – 1.89 (m, 2H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.2, 157.7, 141.3, 129.8, 128.7, 128.5, 126.2, 121.8, 114.7, 70.8, 68.2, 46.8, 44.0, 33.1, 29.1

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1594, found 312.1598

5-(phenoxymethyl)-3-propyloxazolidin-2-one (43)[3]



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and 1-propylamine (82 µL), and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a clear oil (101 mg, 58%).

υ_{max} (neat): 2962, 2931, 2873, 1739, 1240, 1056, 755 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.28 (m, 2H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 2H), 4.83 (dt, *J* = 9.9, 5.6 Hz, 1H), 4.12 (qd, *J* = 10.0, 4.8 Hz, 2H), 3.70 (t, *J* = 8.8 Hz, 1H), 3.55 (dd, *J* = 8.7, 5.8 Hz, 1H), 3.32 – 3.21 (m, 2H), 1.64 – 1.57 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H)

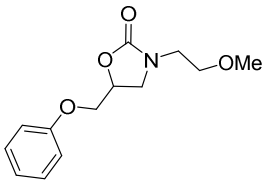
^{13}C NMR (126 MHz, $CDCl_3$): δ 158.3, 157.8, 129.8, 121.8, 114.7, 70.8, 68.2, 46.8, 45.9, 20.7, 11.2

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{18}NO_3$ 236.1281, found 236.1285

68.21, 46.84, 43.98, 29.49, 19.94, 13.83

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{20}NO_3$ 250.1438, found 250.1440

3-(2-methoxyethyl)-5-(phenoxymethyl)oxazolidin-2-one (44)



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and 2-methoxyethylamine (87 µL) and purified by flash column chromatography (40% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as an orange oil (241 mg, 96%).

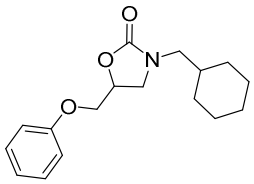
υ_{max} (neat): 2923, 1742, 1491, 1242, 1116, 1050, 757, 693 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.28 (m, 2H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 2H), 4.83 (dt, *J* = 10.4, 5.6 Hz, 1H), 4.12 (qd, *J* = 10.0, 5.0 Hz, 2H), 3.85 (t, *J* = 8.9 Hz, 1H), 3.65 (dd, *J* = 9.0, 6.1 Hz, 1H), 3.57 (t, *J* = 5.0 Hz, 2H), 3.52 – 3.42 (m, 2H), 3.35 (s, 3H),

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.3, 157.8, 129.7, 121.7, 114.8, 71.2, 71.1, 68.3, 58.9, 48.3, 44.2

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{18}NO_4$ 252.1230, found 252.1230

3-(cyclohexylmethyl)-5-(phenoxymethyl)oxazolidin-2-one (45)



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and cyclohexylmethylamine (130 µL) and purified by flash column chromatography (35% EtOAc/Petroleum ether 40 – 60 °C) to afford the title compound as a pale yellow solid (255 mg, 88%).

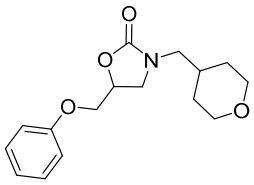
υ_{max} (neat): 2921, 2849, 1740, 1447, 1240, 1049, 757 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.28 (m, 2H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.90 – 6.89 (m, 2H), 4.85 – 4.80 (m, 1H), 4.14 – 4.10 (m, 2H), 3.70 (t, *J* = 8.9 Hz, 1H), 3.57 (dd, *J* = 8.7, 5.8 Hz, 1H), 3.16 (dd, *J* = 13.9, 7.7 Hz, 1H), 3.07 (dd, *J* = 13.9, 7.1 Hz, 1H), 1.75 – 1.69 (m, 4H), 1.26 – 1.19 (m, 3H), 1.03 – 0.96 (m, 2H), 0.94 – 0.87 (m, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.3, 158.0, 129.8, 121.8, 114.7, 70.7, 68.2, 50.7, 47.6, 36.2, 30.8, 30.7, 26.4, 25.9, 25.8

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{24}NO_3$ 290.1751, found 290.175

5-(phenoxymethyl)-3-((tetrahydro-2*H*-pyran-4-yl)methyl)oxazolidin-2-one (46)



Synthesised according to General Experimental Procedure E using glycidyl phenyl ether (135 µL) and 4-(Aminomethyl)tetrahydropyran (113 µL) and purified by flash column chromatography (40% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a yellow solid (137 mg, 47%).

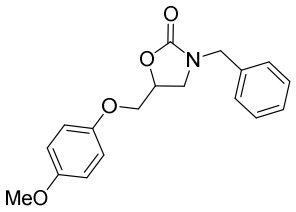
υ_{max} (neat): 2925, 2854, 1739, 1445, 1240, 757 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 2H), 6.98 (td, *J* = 7.4, 0.6 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.82 (dq, *J* = 9.5, 4.7 Hz, 1H), 4.14 – 4.09 (m, 2H), 3.99 – 3.96 (m, 2H), 3.71 (t, *J* = 8.8 Hz, 1H), 3.59 (dd, *J* = 8.0, 6.4 Hz, 1H), 3.36 (t, *J* = 11.2 Hz, 2H), 3.21 (dd, *J* = 13.9, 7.5 Hz, 1H), 3.11 (dd, *J* = 14.0, 7.1 Hz, 1H), 1.92 – 1.83 (m, 1H), 1.63 – 1.59 (m, 2H) 1.41 – 1.32 (m, 2H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.1, 157.9, 129.7, 121.7, 114.5, 70.7, 68.0, 67.5, 50.1, 47.8, 33.8, 30.6, 30.5

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{22}NO_4$ 292.1543, found 292.1546

3-benzyl-5-((4-methoxyphenoxy)methyl)oxazolidin-2-one (47)



Synthesised according to General Experimental Procedure E using glycidyl 4-methoxyphenyl ether (180 mg) and benzylamine (109 µL) and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a yellow solid (270 mg, 86%).

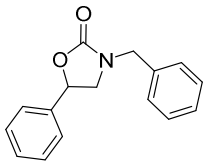
υ_{max} (neat): 3066, 3029, 3003, 2934, 2918, 2836, 1739, 1508, 1233, 1067, 1026, 829, 749, 701 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.35 (m, 2H), 7.31 (app. t, *J* = 6.5 Hz, 3H), 6.83 – 6.78 (m, 4H), 4.78 (qd *J* = 9.3, 4.7 Hz, 1H), 4.46 (m, 2H), 4.04 (d, *J* = 4.7 Hz, 2H), 3.76 (s, 3H), 3.56 (t, *J* = 8.9 Hz, 1H), 3.43 (dd, *J* = 8.8, 6.0 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 157.8, 154.6, 152.4, 135.8, 129.0, 128.3, 128.2, 115.9, 114.9, 71.1, 69.1, 55.9, 48.5, 46.2

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{20}NO_4$ 314.1387, found 314.1391

3-benzyl-5-phenyloxazolidin-2-one (48)[2]



Synthesised according to General Experimental Procedure E using phenyloxirane (114 µL) and benzylamine (109 µL) and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) and strong cation exchange chromatography (MeOH) to afford the title compound as a pale yellow solid (243 mg, 96%).

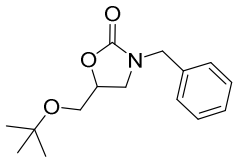
υ_{max} (neat): 3061. 3029, 1742, 1422, 1248, 1028, 768, 699 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.28 (m, 10H), 5.47 (t, *J* = 8.1 Hz, 1H), 4.54 (d, *J* = 14.8 Hz, 1H), 4.41 (d, *J* = 14.9 Hz, 1H), 3.77 (t, *J* = 8.8 Hz, 1H), 3.31 (dd, *J* = 8.6, 7.7 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.1, 138.7, 135.8, 129.4, 129.0, 128.9, 128.3, 128.1 127.4, 125.6, 74.6, 51.6, 48.5

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{16}NO_2$ 254.1176, found 254.1178

3-benzyl-5-(tert-butoxymethyl)oxazolidin-2-one (49)



Synthesised according to General Experimental Procedure E using *tert*-butyl glycidyl ether (142 µL) and benzylamine (109 µL) and purified by flash column chromatography (30% EtOAc/Petroleum ether 40 – 60 °C) to afford the title compound as a clear oil (103 mg, 39%).

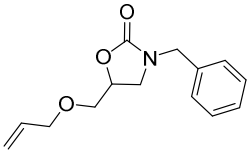
υ_{max} (neat): 2970, 2929, 2867, 1742, 1192, 1090, 1062, 701 cm^{-1}

1H NMR (500 MHz, $CDCl_3$): δ 7.36 – 7.33 (m, 2H), 7.31 – 7.28 (m, 3H), 4.57 – 4.52 (m, 1H), 4.48 (d, *J* = 15.0 Hz, 1H), 4.37 (d, *J* = 15.0 Hz, 1H), 3.48 (m, 2H), 3.43 (t, *J* = 8.7 Hz, 1H), 3.30 (dd, *J* = 8.6, 5.8 Hz, 1H), 1.15 (s, 9H)

13C NMR (126 MHz, $CDCl_3$): δ 158.2, 136.0, 128.9, 128.1, 128.0, 73.7, 72.2, 62.6, 48.3, 46.4, 27.5

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{22}NO_3$ 264.1594, found 264.1597

5-((allyloxy)methyl)-3-benzyloxazolidin-2-one (50)



Synthesised according to General Experimental Procedure E using allyl glycidyl ether (119 µL) and benzylamine (109 µL) and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) to afford the title compound as a yellow oil (228 mg, 92%).

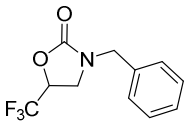
υ_{max} (neat): 3061, 3027, 2920, 2856, 1739, 1441, 1249, 1058, 701 cm^{-1}

1H NMR (500 MHz, $CDCl_3$): δ 7.36 – 7.27 (m, 5H), 5.84 (ddd, *J* = 16.1, 10.8, 5.7 Hz, 1H), 5.24 (dd, *J* = 17.2, 1.6 hz, 1H), 5.18 (dd, *J* = 10.4, 1.3 Hz, 1H), 4.63 – 4.57 (m, 1H), 4.43 (s, 2H), 4.01 (dd, *J* = 5.6, 1.1 Hz, 2H), 3.59 – 3.54 (m, 2H), 3.45 (t, *J* = 8.8 Hz, 1H), 3.30 (dd, *J* = 8.6, 6.2 Hz, 1H)

13C NMR (126 MHz, $CDCl_3$): δ 158.0, 135.9, 134.2, 128.9, 128.2, 128.3, 117.7, 72.7, 72.0, 70.4, 48.4, 46.2

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}NO_3$ 248.1281, found 248.1282

3-benzyl-5-(trifluoromethyl)oxazolidin-2-one (51)[5]



To an oven-dried, purged and sealed 2 – 5 mL microwave vial was added dimethylcarbonate(0.5 mL), 1,2-epoxy-3,3,3-trifluoropropane (86 µL, 1 mmol, 1 equiv.), benzylamine (109 µL, 1 mmol, 1 equiv.) and BEMP (29 µL, 0.1 mmol, 0.1 equiv.). The reaction mixture was then heated at 70 °C for 24 h. Reaction concentrated *in vacuo* and purified by silica column chromatography (2% MeOH/DCM) and strong cation exchange chromatography (MeOH) to afford the title compound as a (180 mg, 92%).

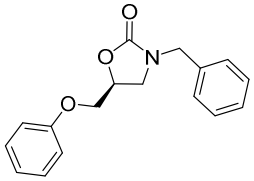
υ_{max} (neat): 3065, 3031, 2928, 1759, 1181, 1147, 1058, 701 cm^{-1}

1H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.34 (m, 3H), 7.28 – 7.25 (m, 2H), 4.78 – 4.69 (m, 1H), 4.51 – 4.42 (m, 2H), 3.61 (t, *J* = 9.6 Hz, 1H), 3.46 (dd, *J* = 9.7, 5.1 Hz, 1H)

13C NMR (126 MHz, $CDCl_3$): δ 155.9, 134.7, 129.2, 128.5, 128.2, 123.0 (q, $^1J_{CF}$ = 280.0 Hz), 69.2 (q, $^2J_{CF}$ = 35.4 Hz), 53.5, 48.4, 43.4

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{11}F_3NO_2$ 246.0736, found 246.0740

(*S*)-3-benzyl-5-(phenoxymethyl)oxazolidin-2-one (52)



Synthesised according to General Experimental Procedure E using (*S*)-glycidyl phenyl ether (135 µL) and benzylamine (109 µL) and purified by flash column chromatography (25% EtOAc/Petroleum ether 40 – 60 °C) to afford the title compound as a white solid (270 mg, 95%).

υ_{max} (neat): 3057, 3040, 2959, 2923, 2866, 1733, 1447, 1244, 1063, 755, 740 cm^{-1}

1H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.35 (m, 2H), 7.33 – 7.26 (m, 5H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.86 – 6.84 (m, 2H), 4.81 (ddd, *J* = 10.6, 9.2, 4.7 Hz, 1H), 4.50 (d, *J* = 15.0 Hz, 1H), 4.44 (d, *J* = 15.0 Hz, 1H), 4.12 – 4.07 (m, 2H), 3.57 (t, *J* = 8.9 Hz, 1H), 3.44 (dd, *J* = 8.8, 6.0 Hz, 1H)

13C NMR (126 MHz, $CDCl_3$): δ 158.2, 157.8, 135.7, 129.7, 129.0, 128.3, 128.2, 121.7, 114.7, 71.0, 68.2, 48.5, 46.2

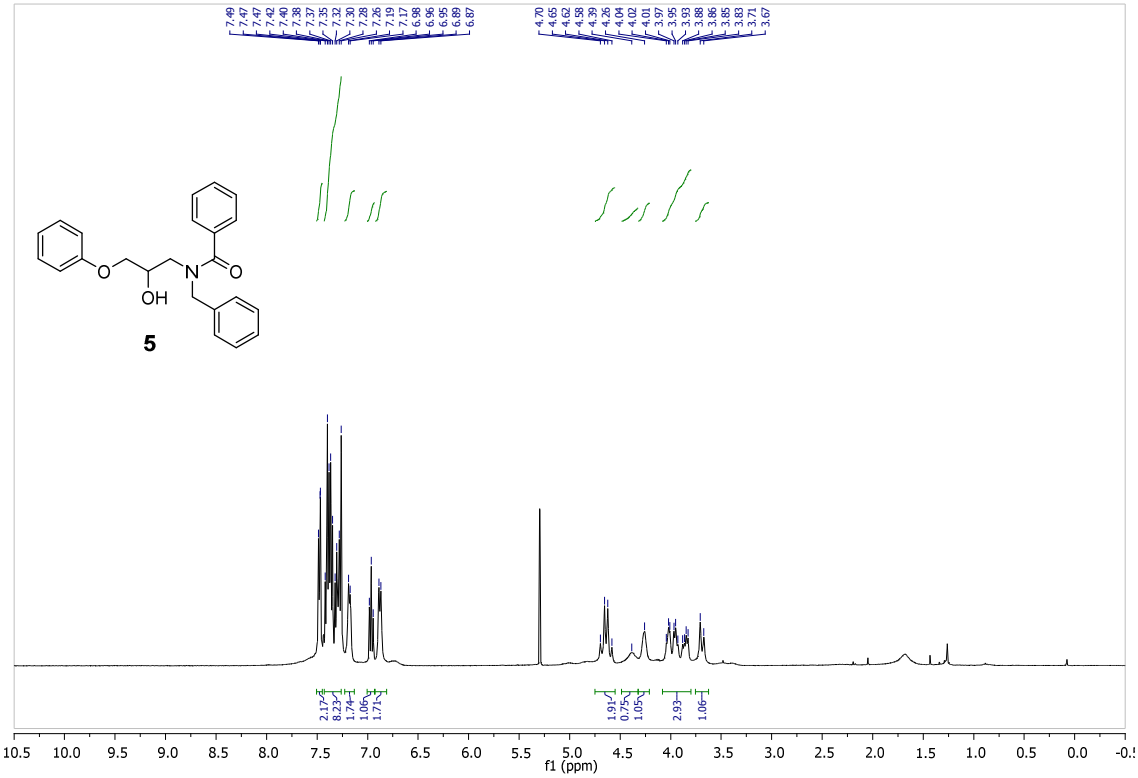
HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{18}NO_3$ 284.1281, found 284.1281

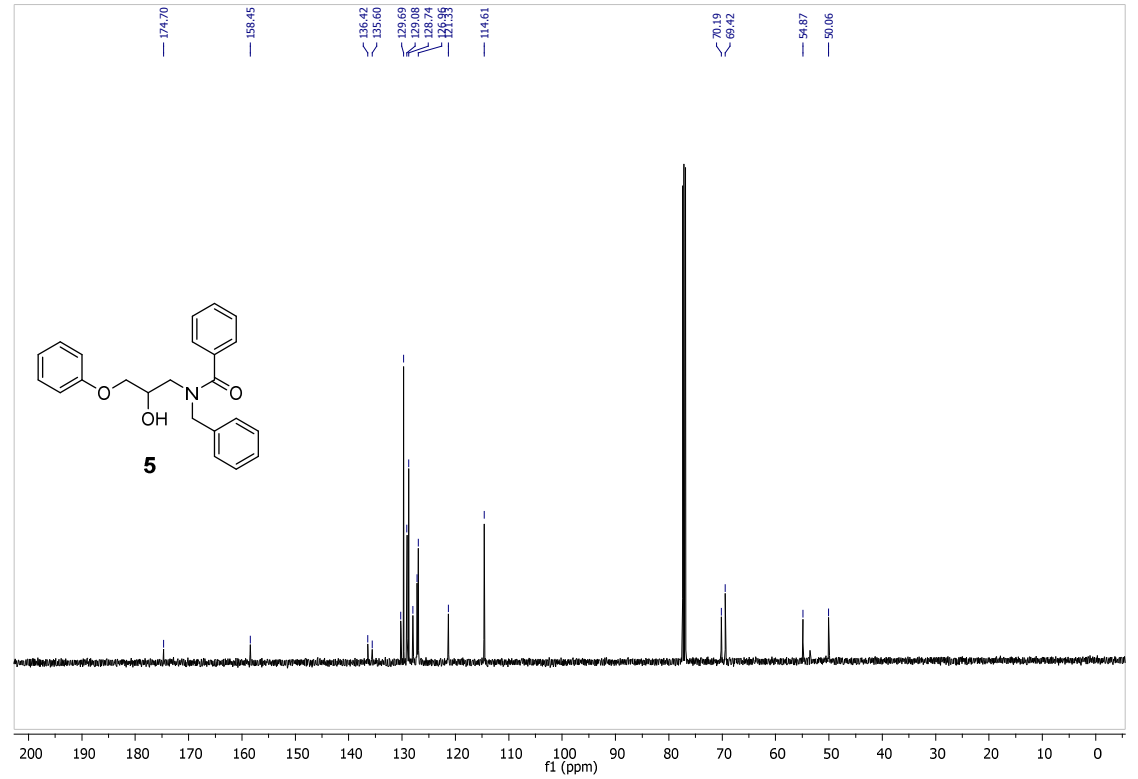
ee: 99%

$[\alpha]_D^{20}$ = 69.67 (c=1, DCM)

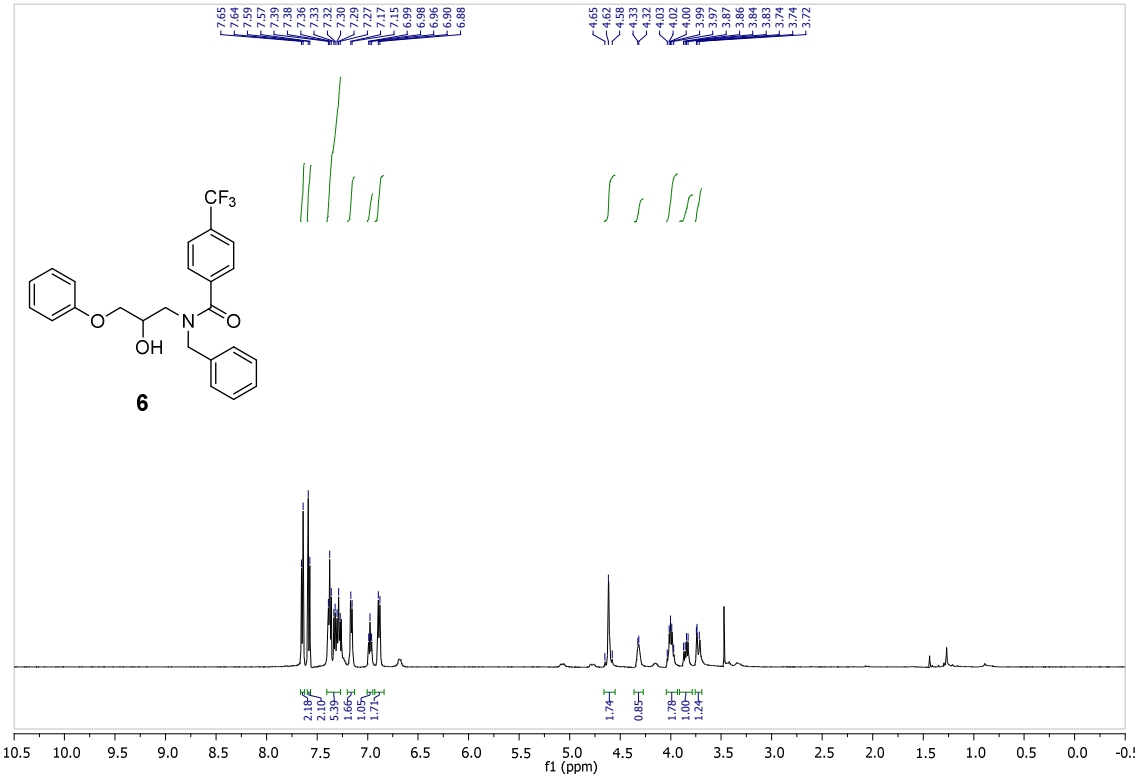
4. ^{1}H and ^{13}C Spectra for Exemplified Compounds

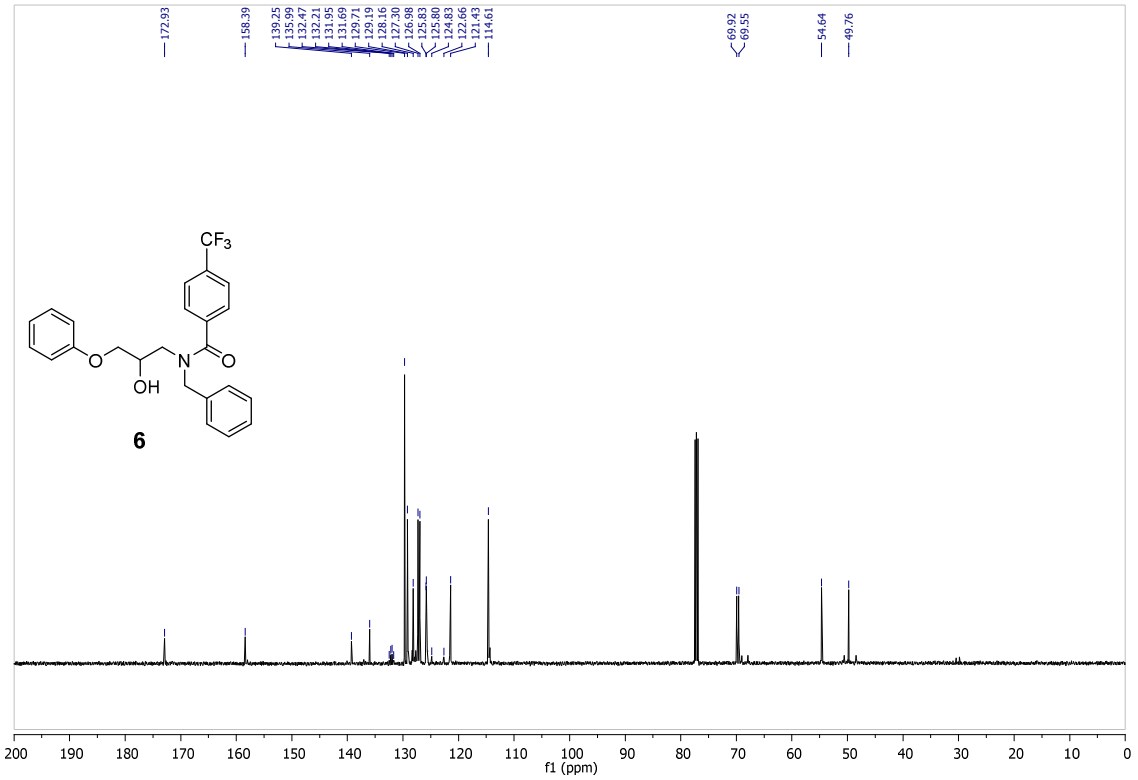
***N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)benzamide (5)**



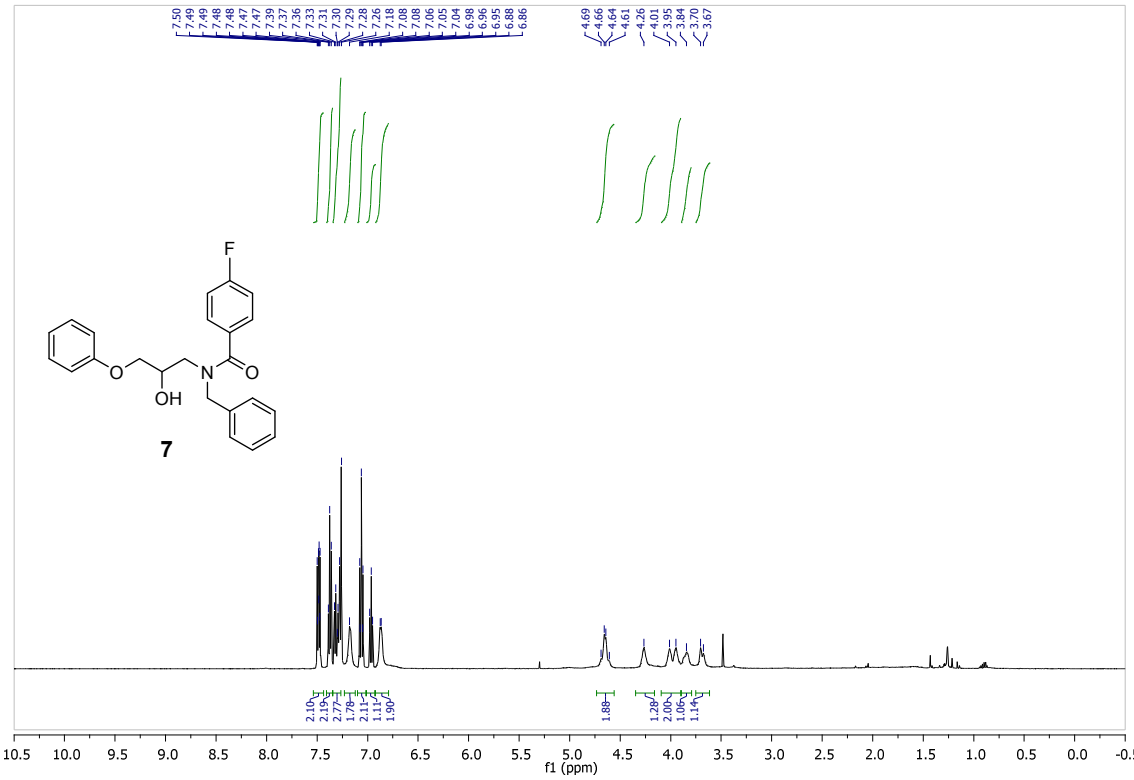


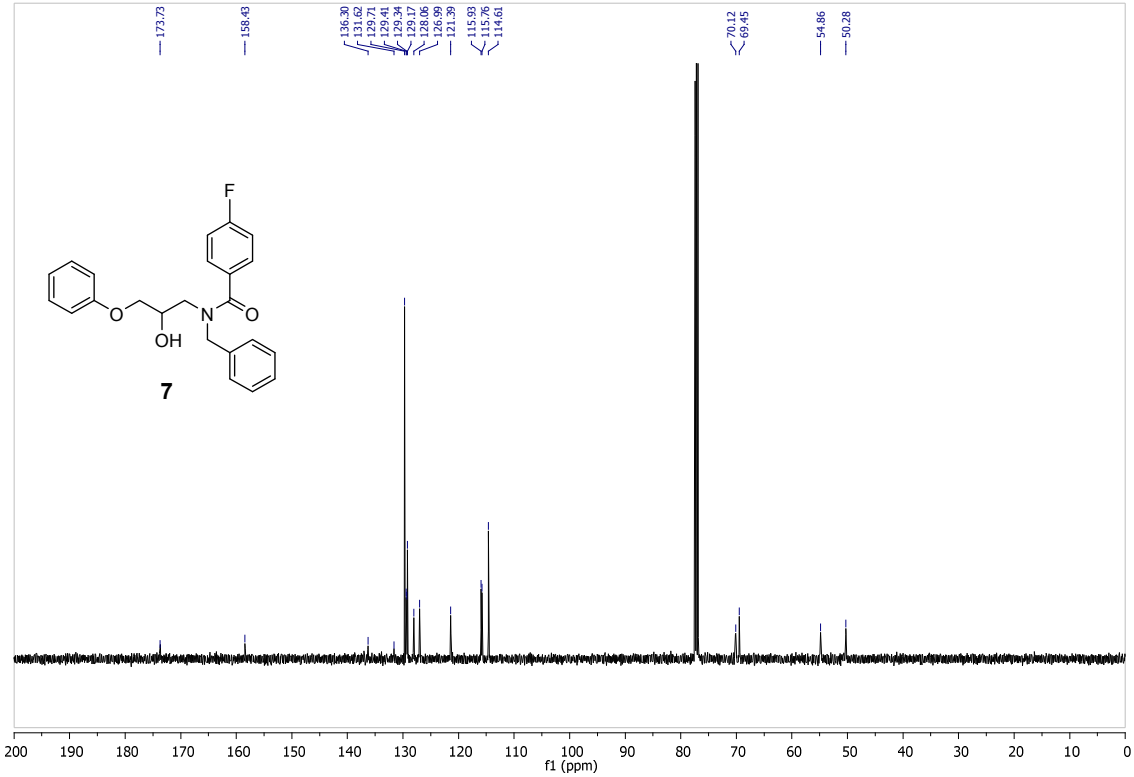
***N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)-4-(trifluoromethyl)benzamide (6)**



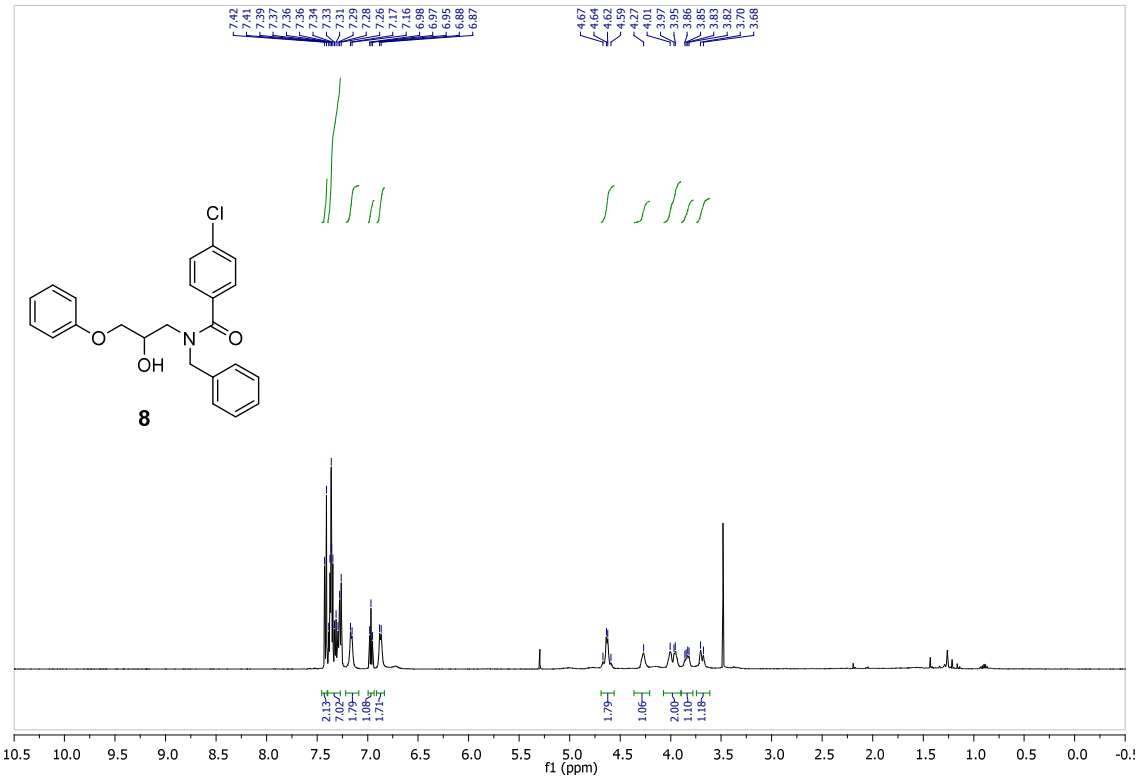


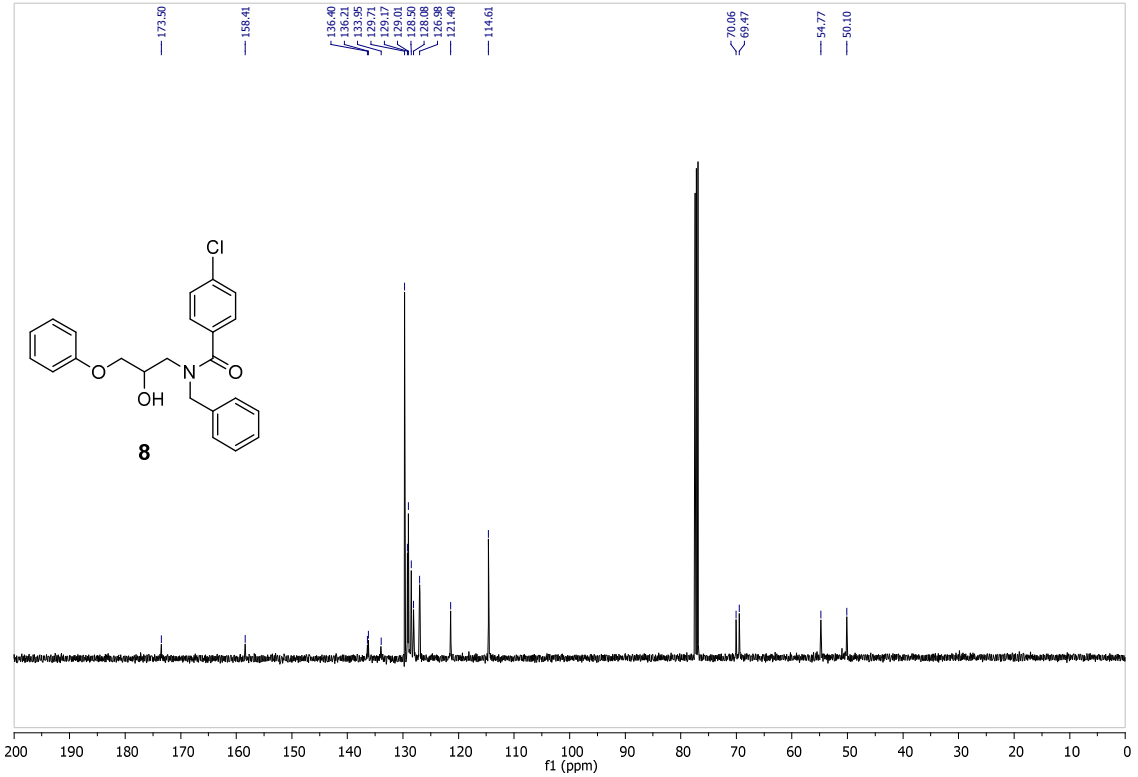
***N*-benzyl-4-fluoro-*N*-(2-hydroxy-3-phenoxypropyl)benzamide (7)**



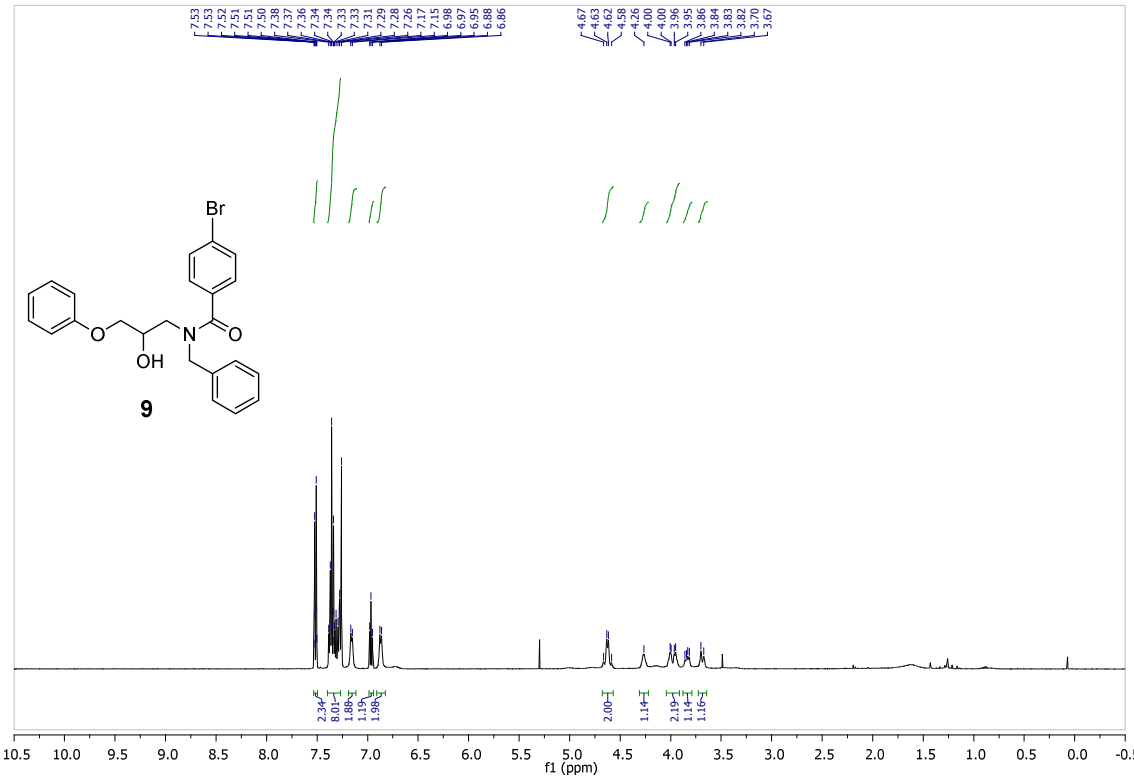


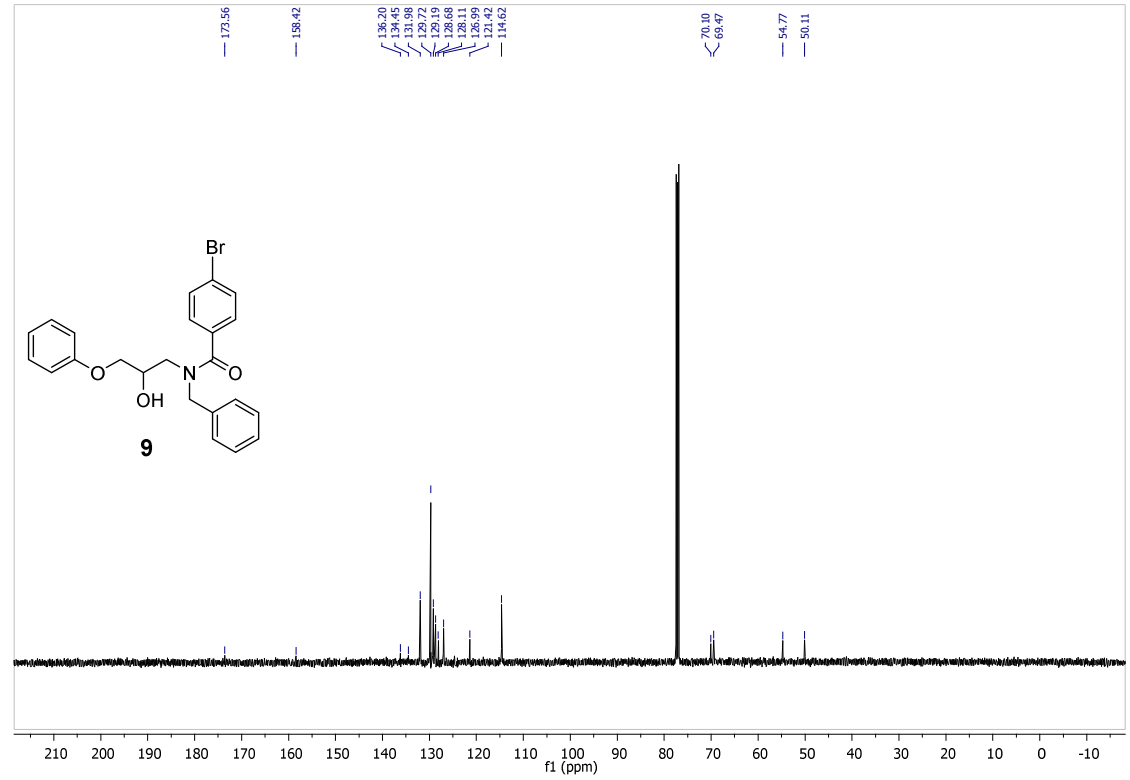
***N*-benzyl-4-chloro-*N*-(2-hydroxy-3-phenoxypropyl)benzamide (8)**



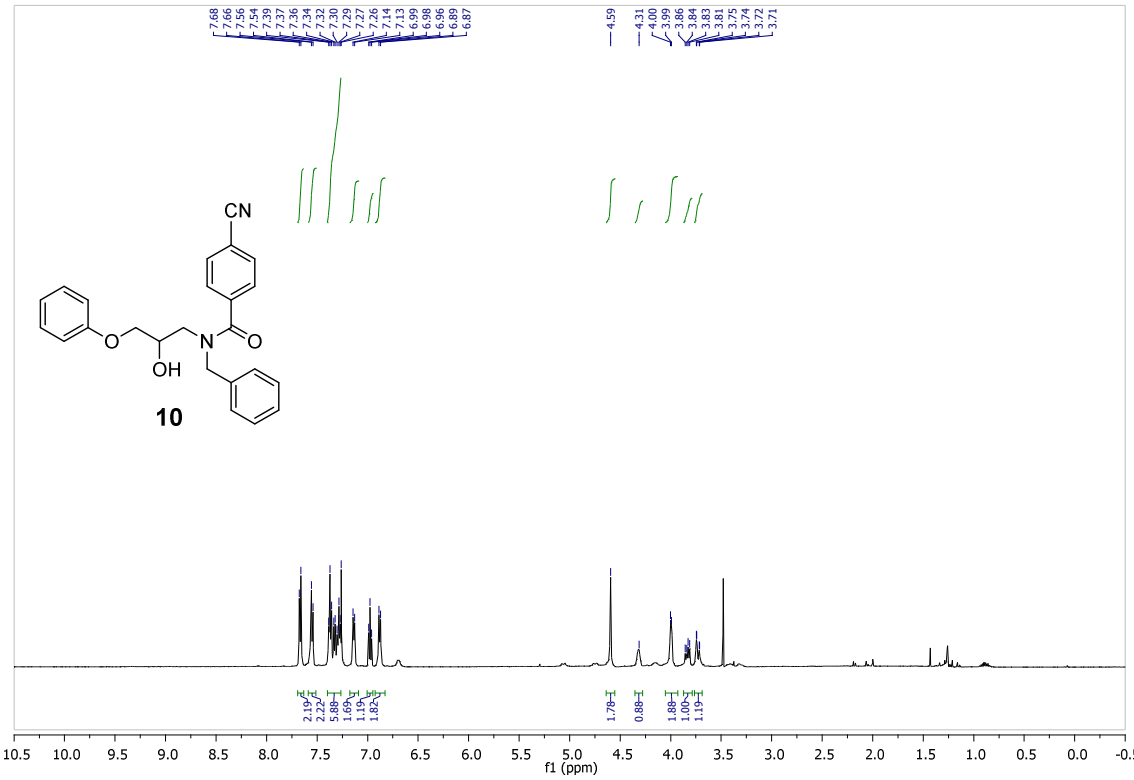


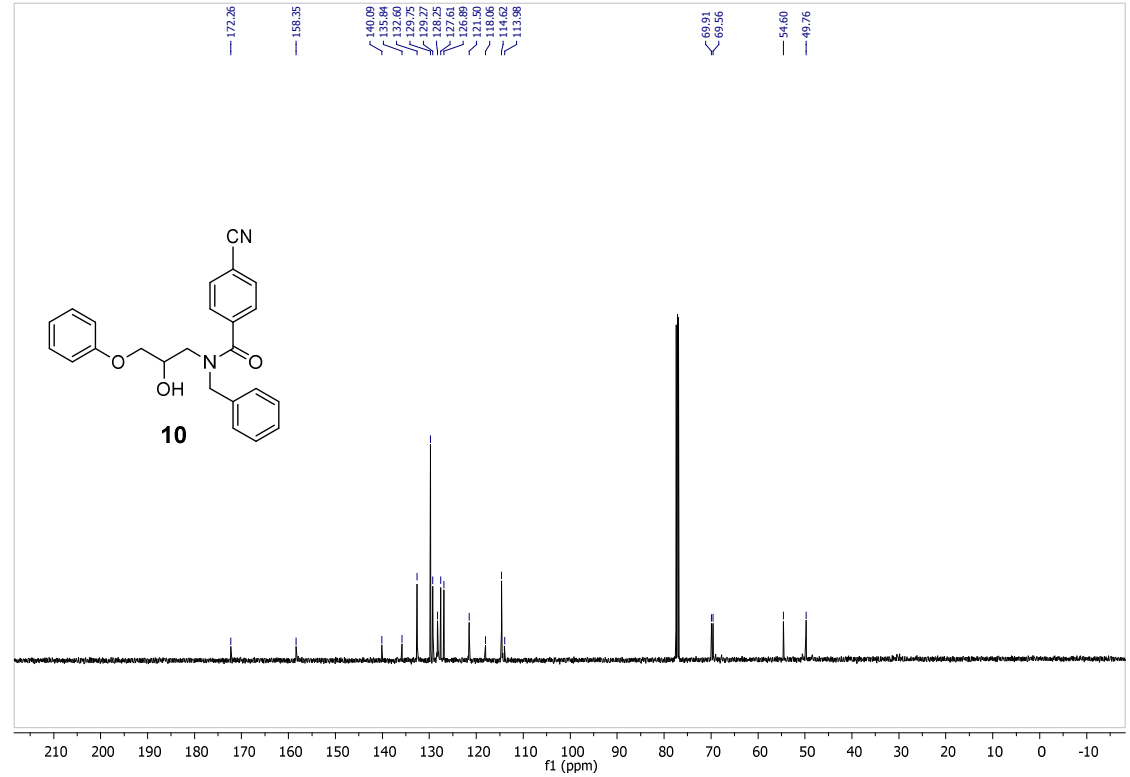
***N*-benzyl-4-bromo-*N*-(2-hydroxy-3-phenoxypropyl)benzamide (9)**



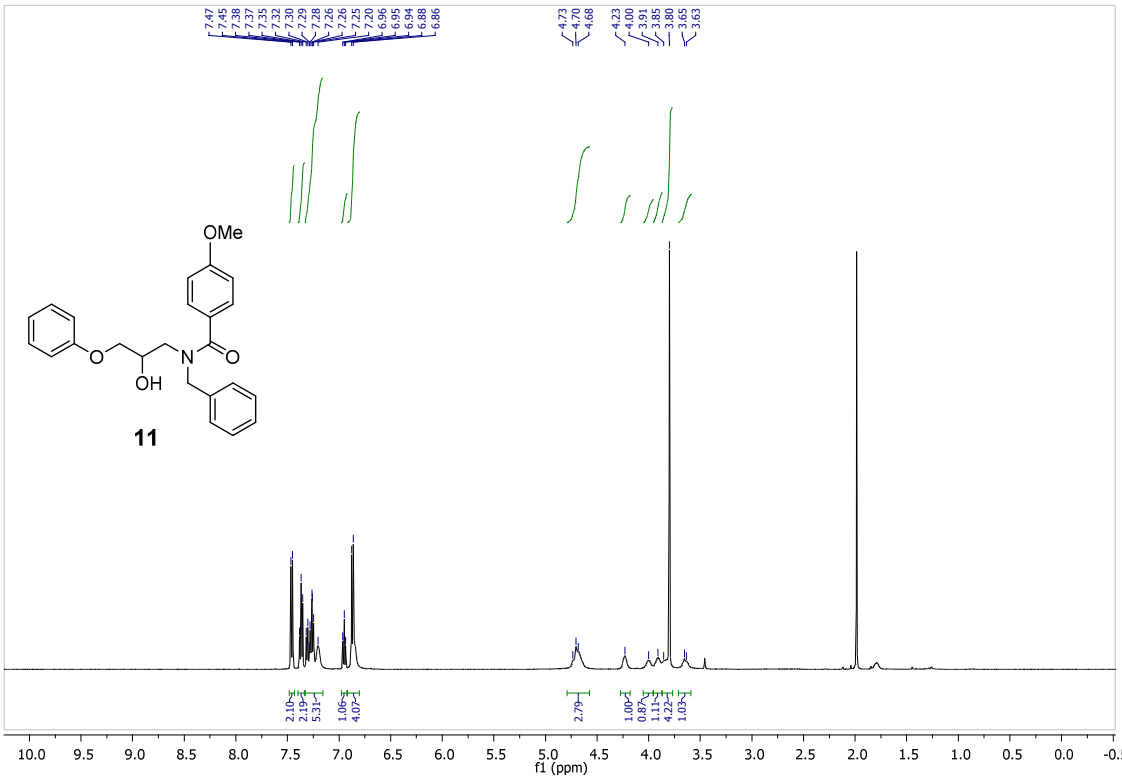


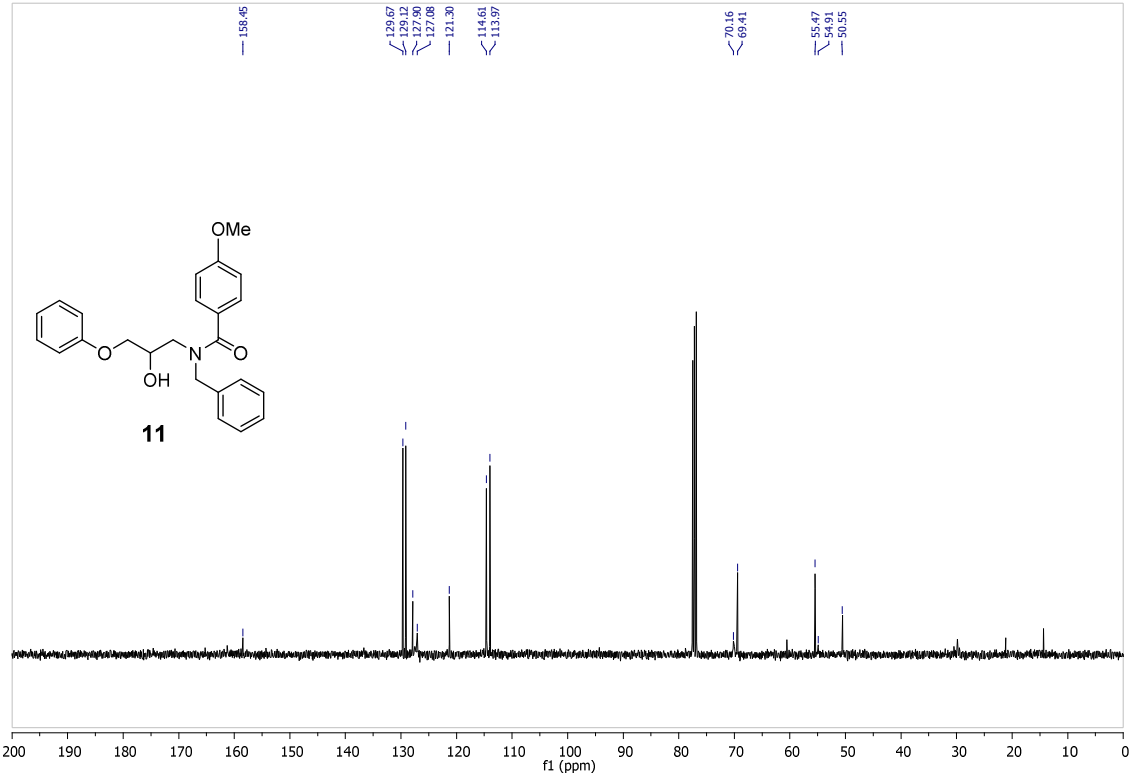
***N*-benzyl-4-cyano-*N*-(2-hydroxy-3-phenoxypropyl)benzamide (10)**



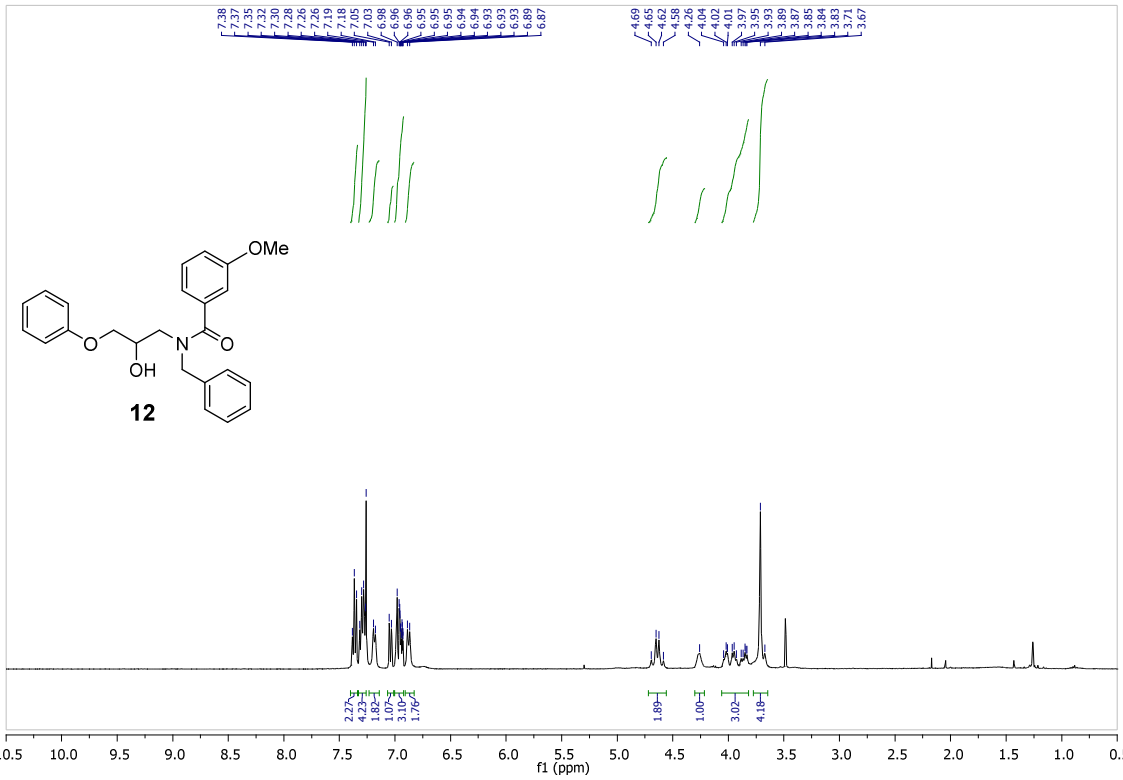


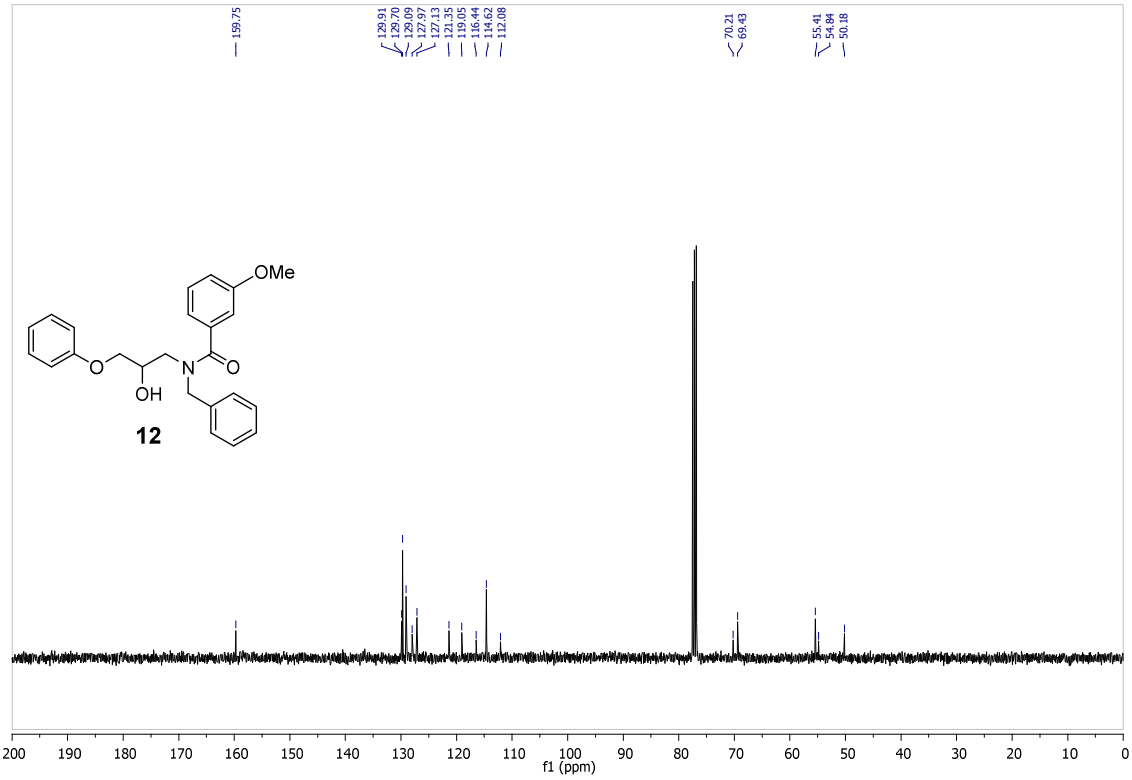
***N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)-4-methoxybenzamide (11)**



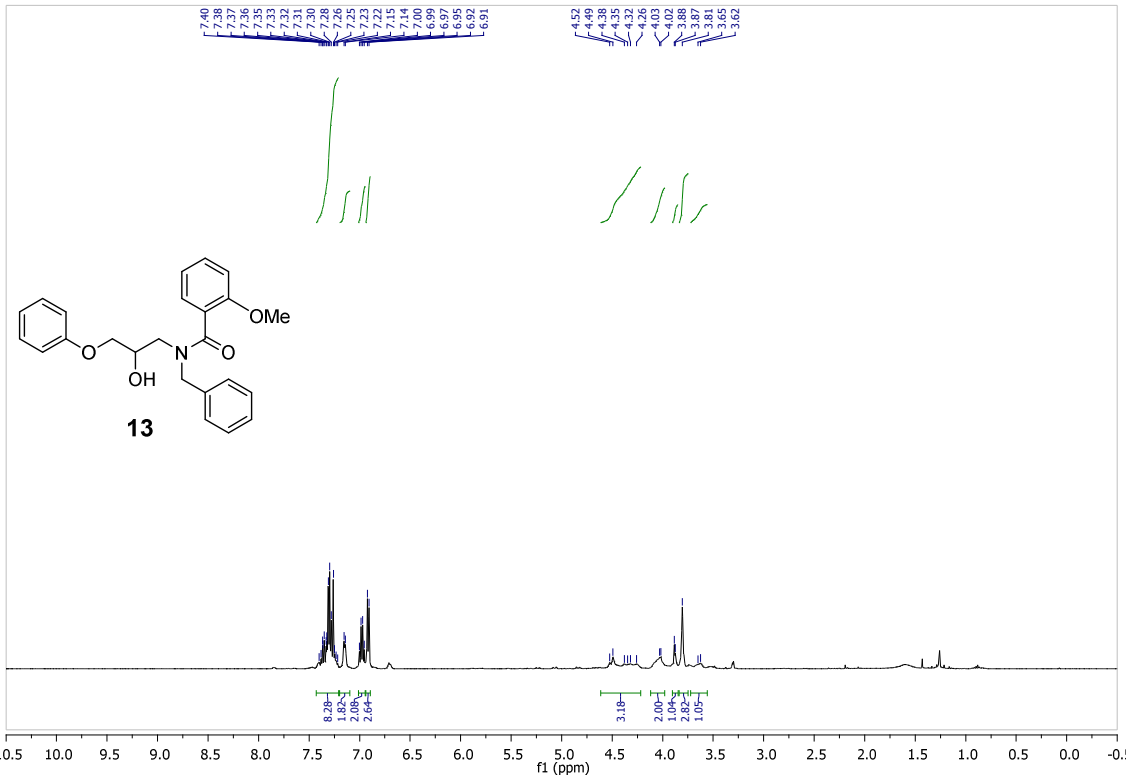


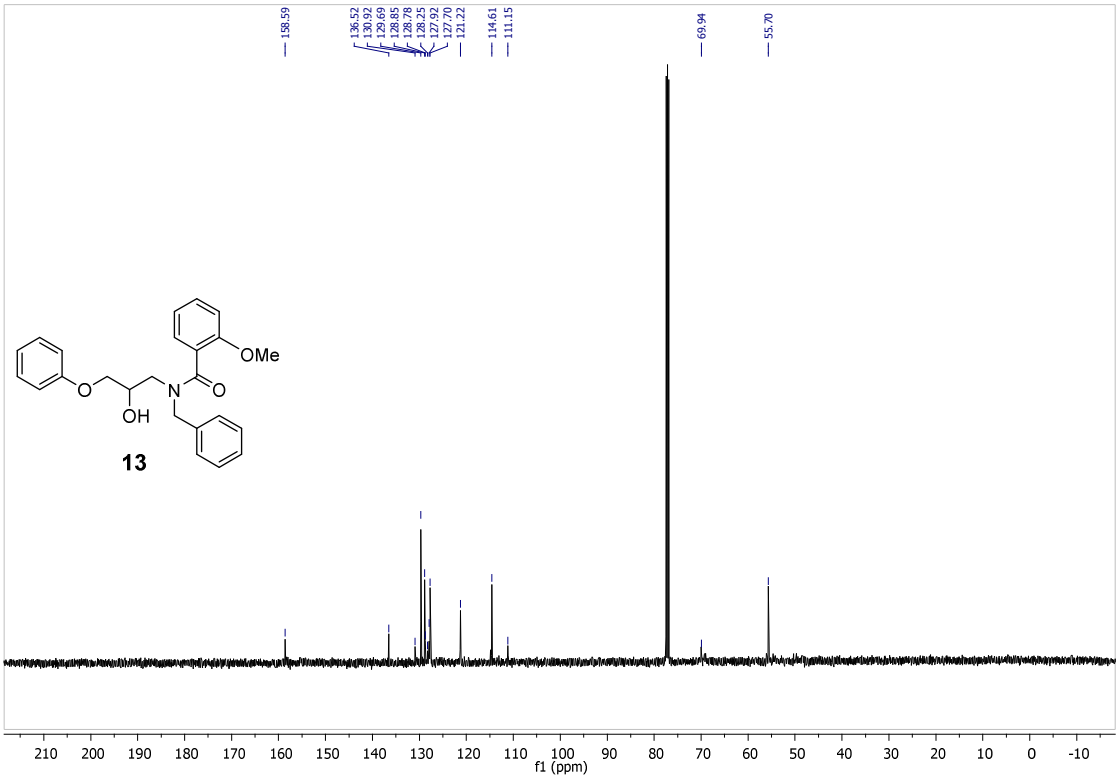
***N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)-3-methoxybenzamide (12)**



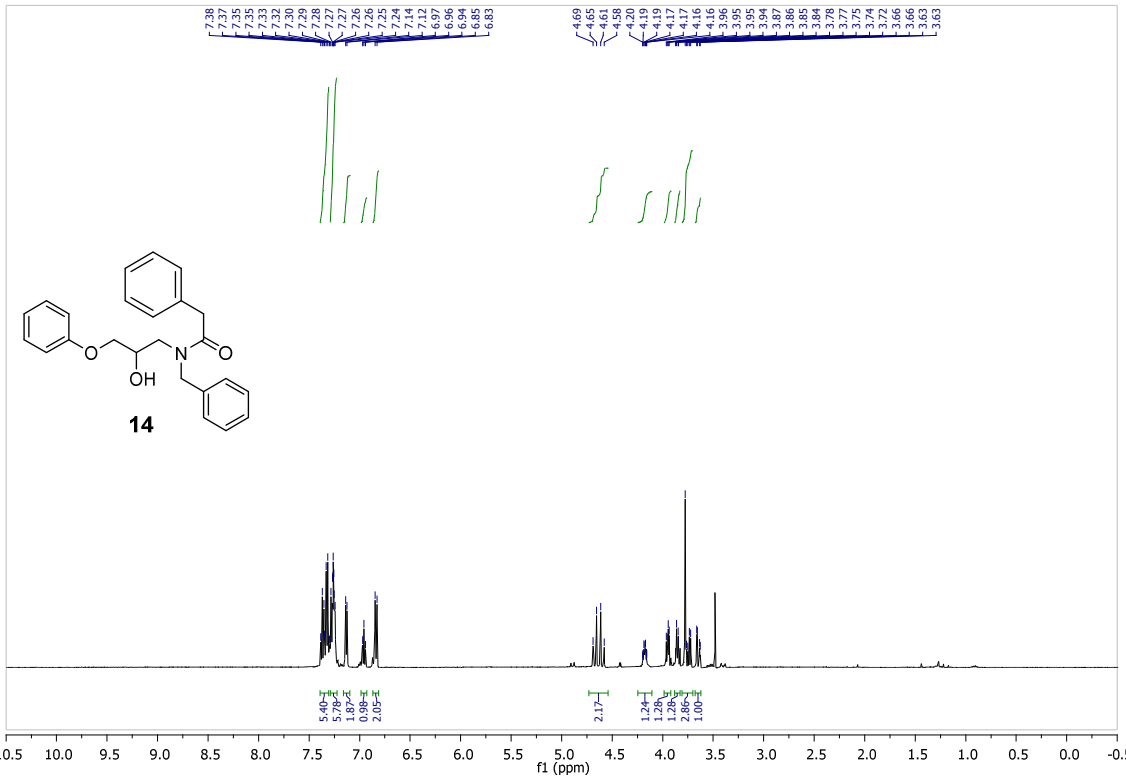


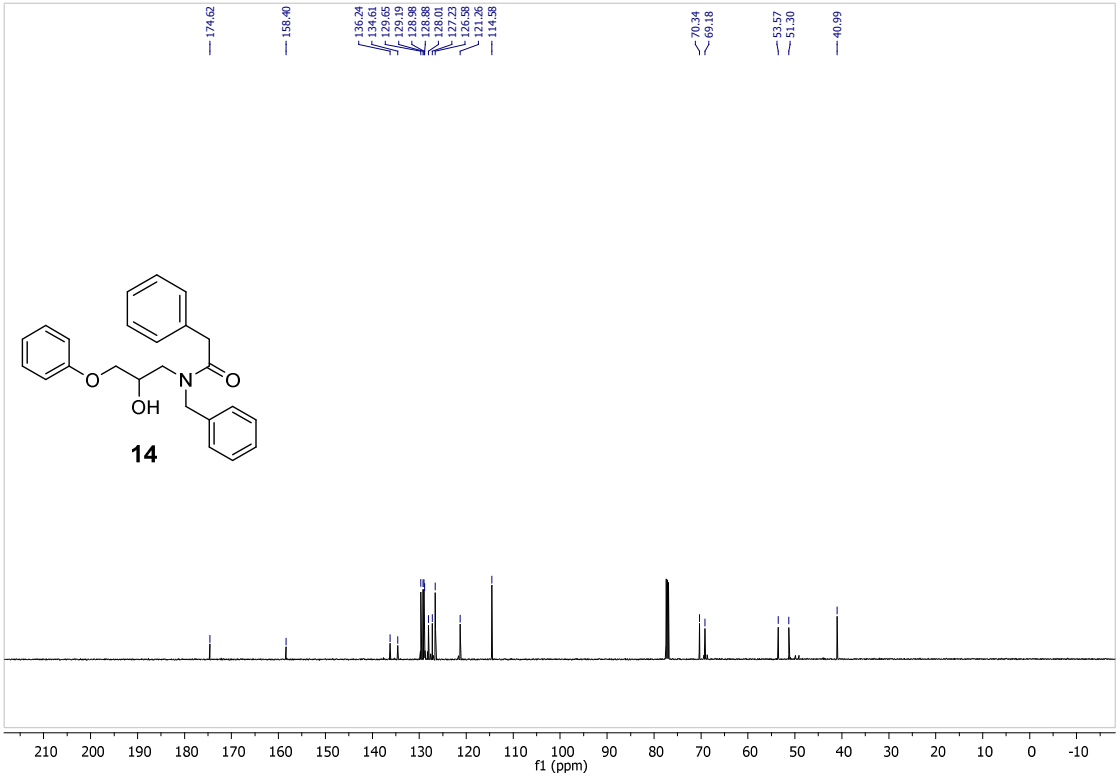
***N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)-2-methoxybenzamide (13)**



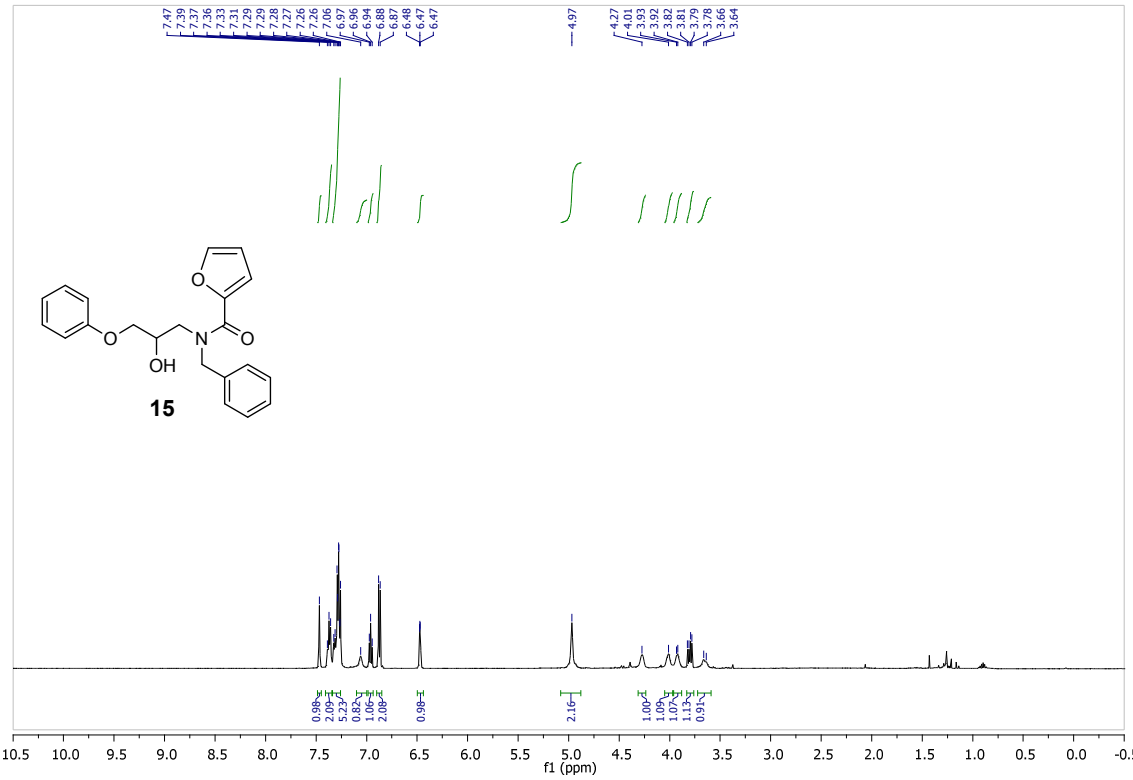


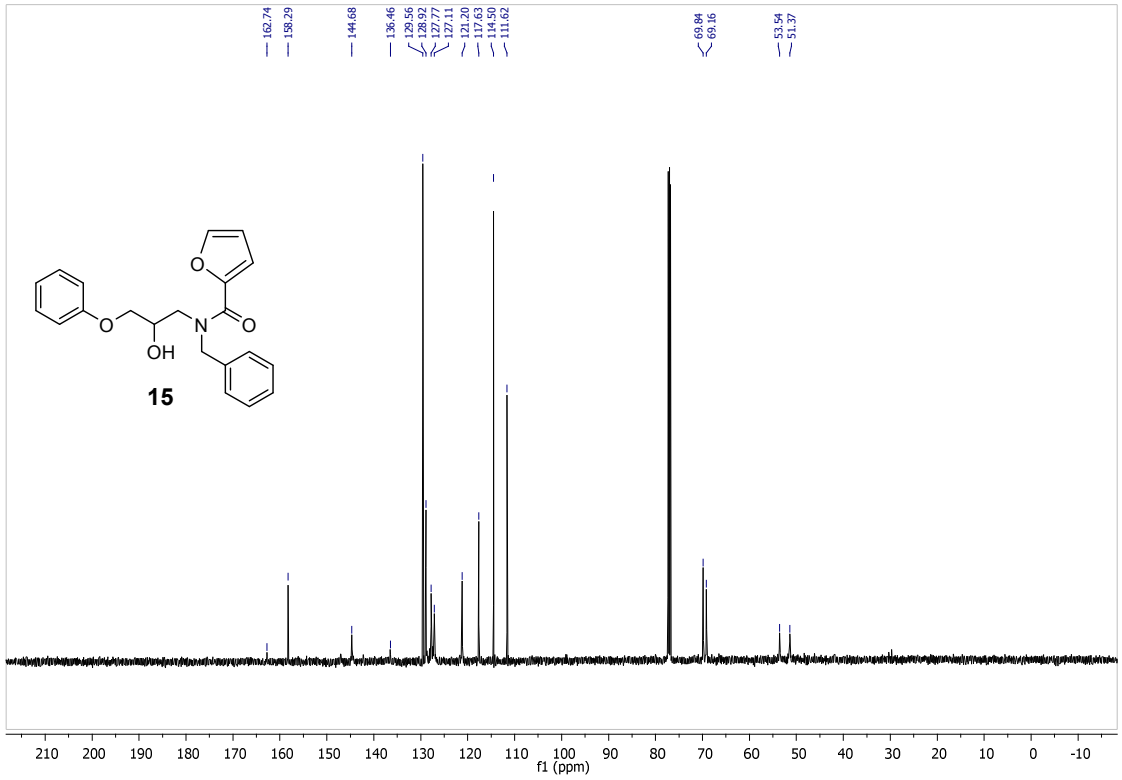
_N_-benzyl-_N_-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (14)



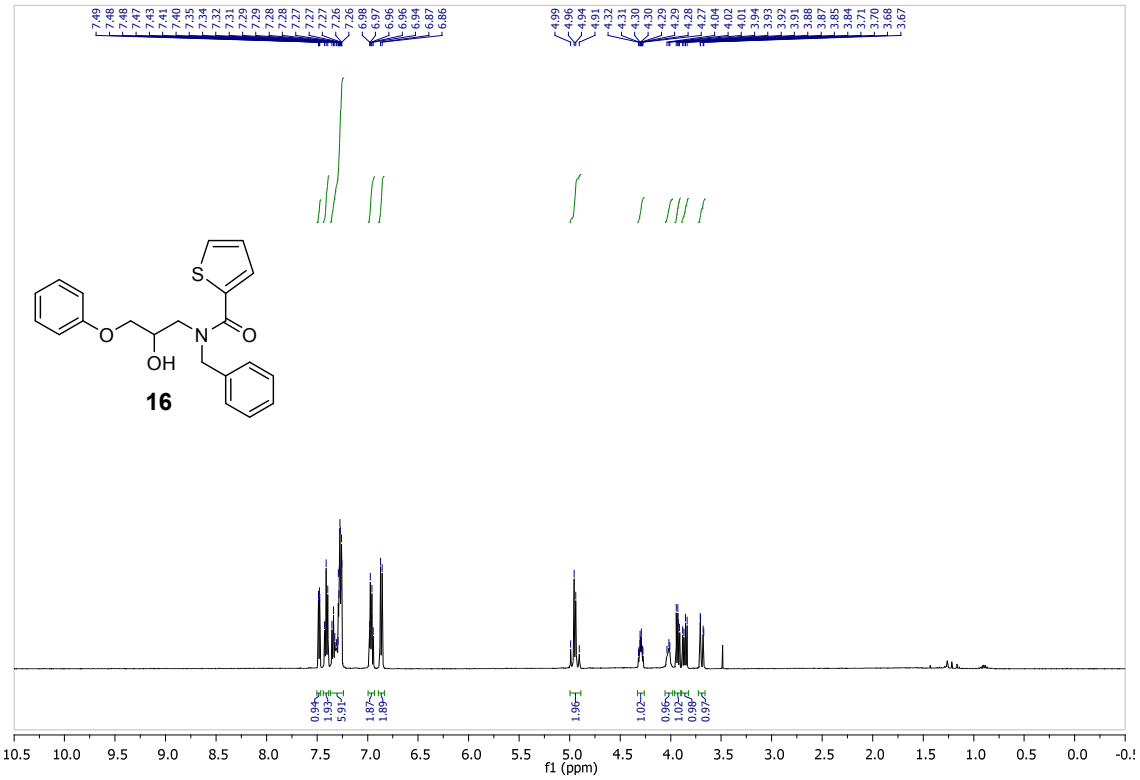


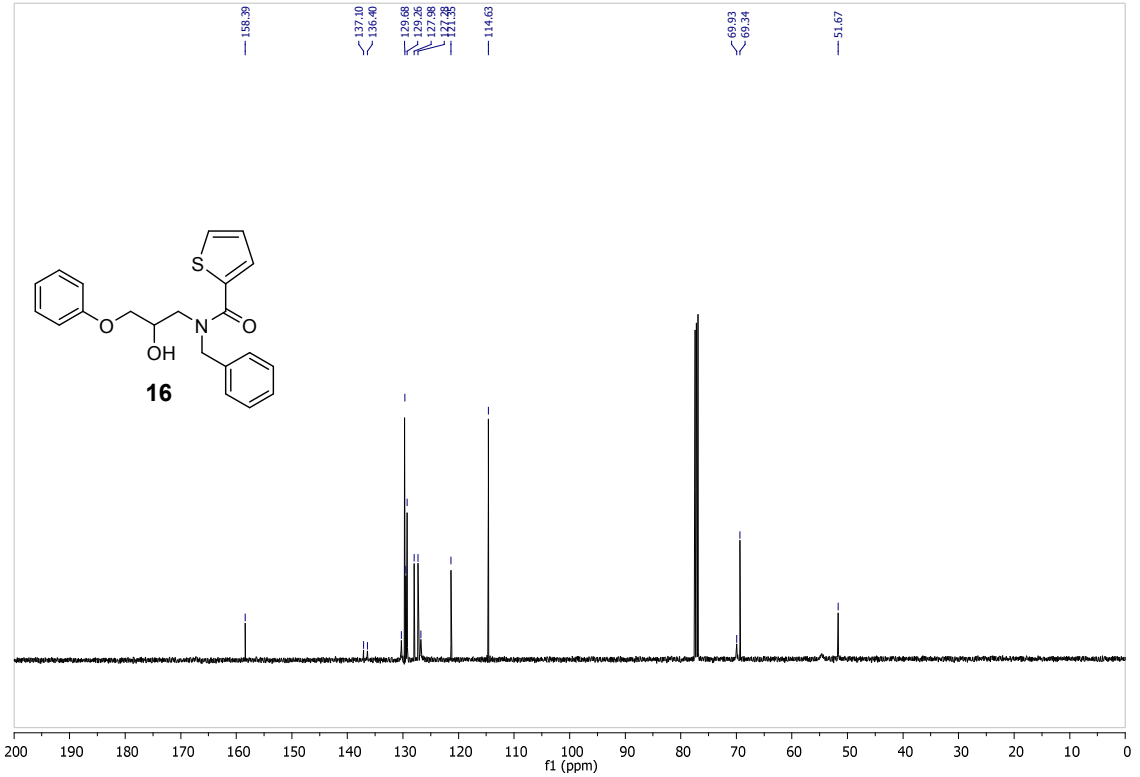
***N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)furan-2-carboxamide (15)**



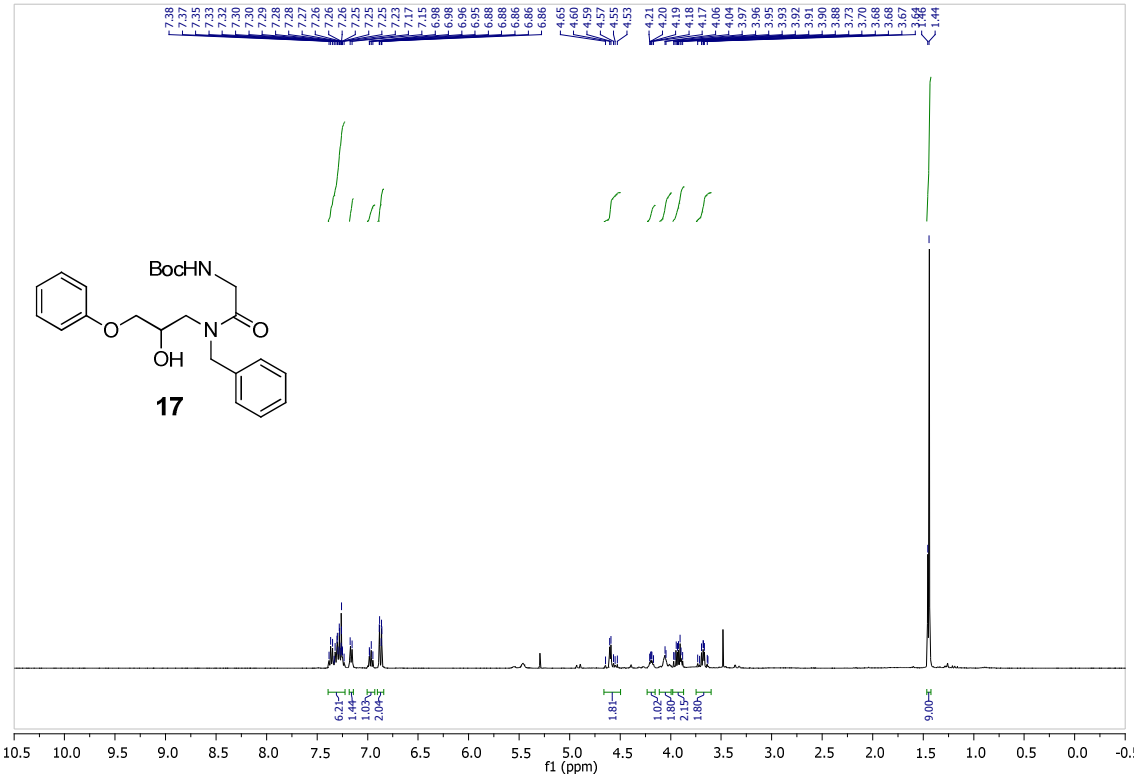


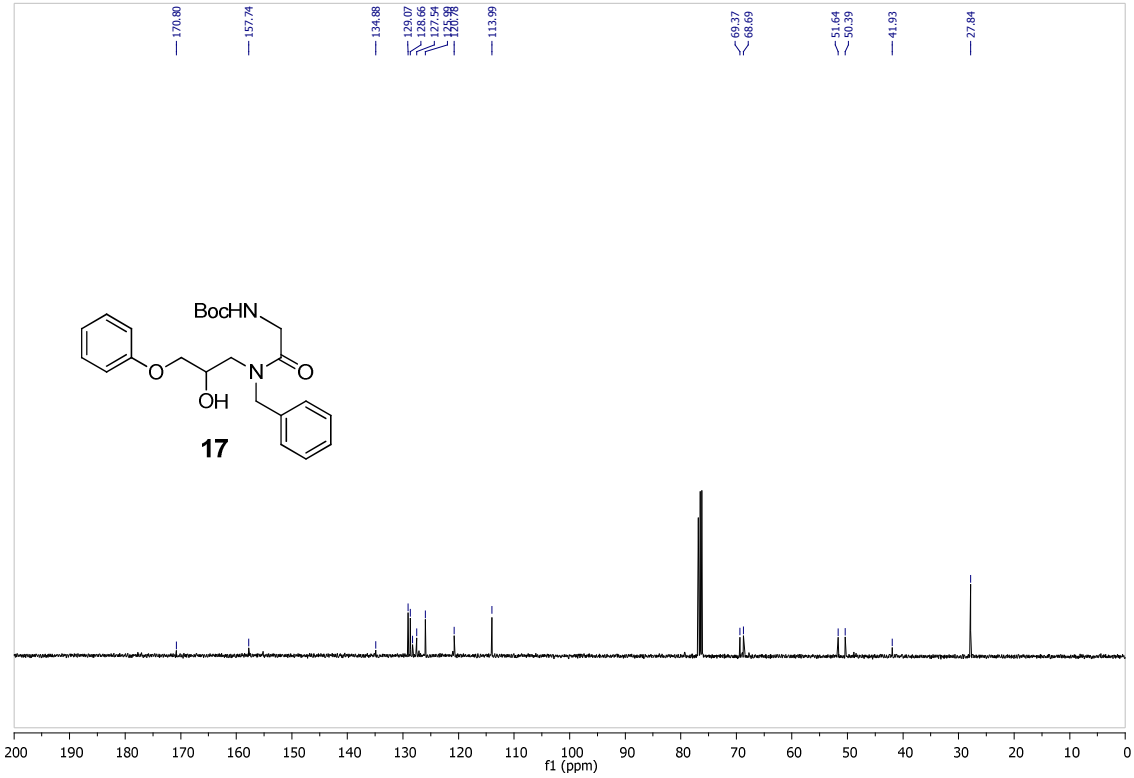
***N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)thiophene-2-carboxamide (16)**



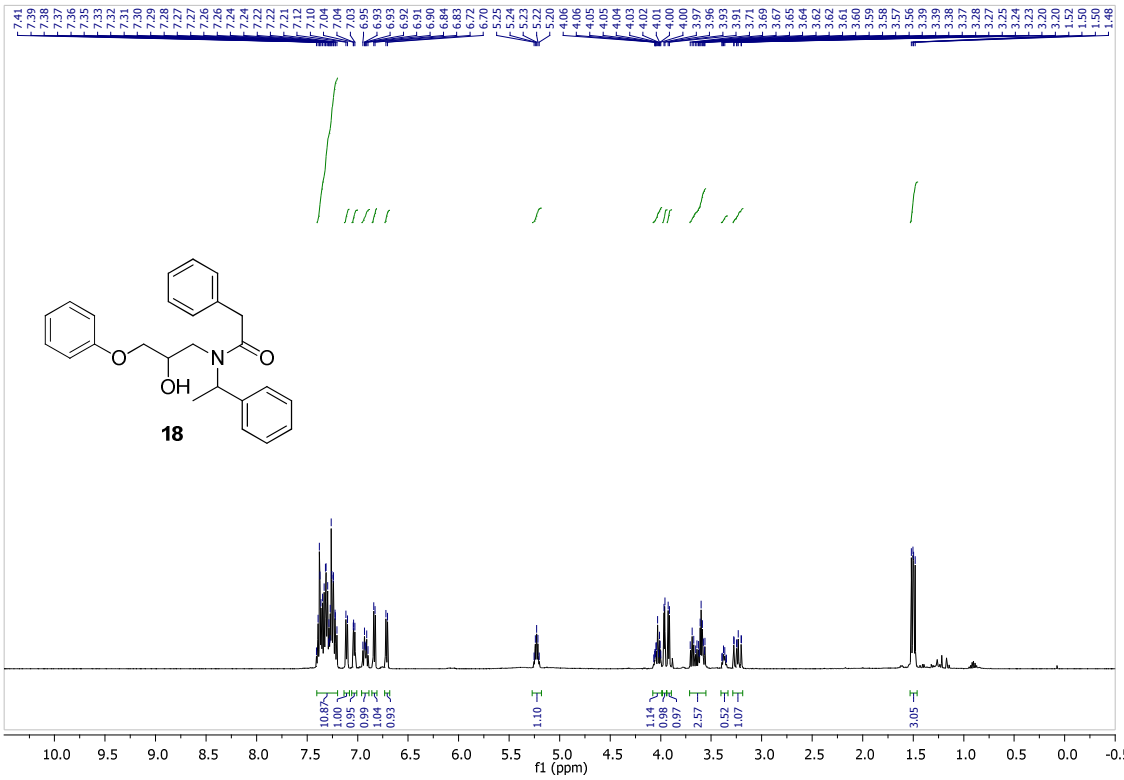


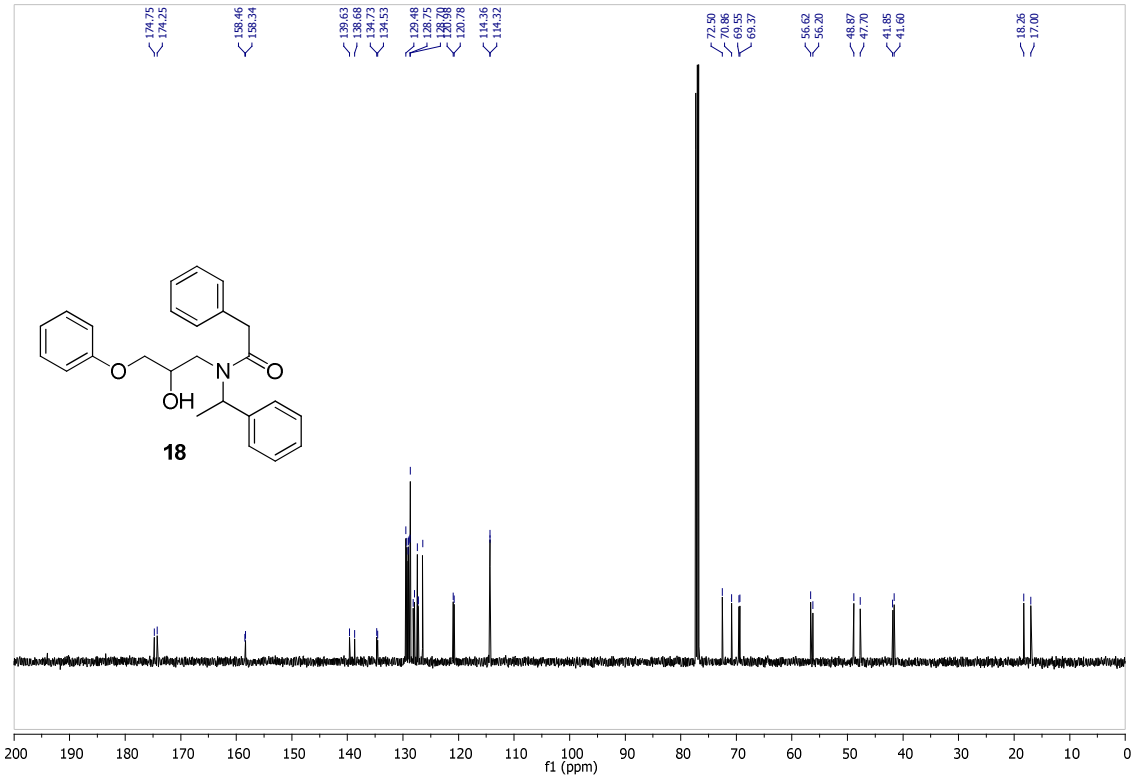
***tert*-butyl (2-(benzyl(2-hydroxy-3-phenoxypropyl)amino)-2-oxoethyl)carbamate (17)**



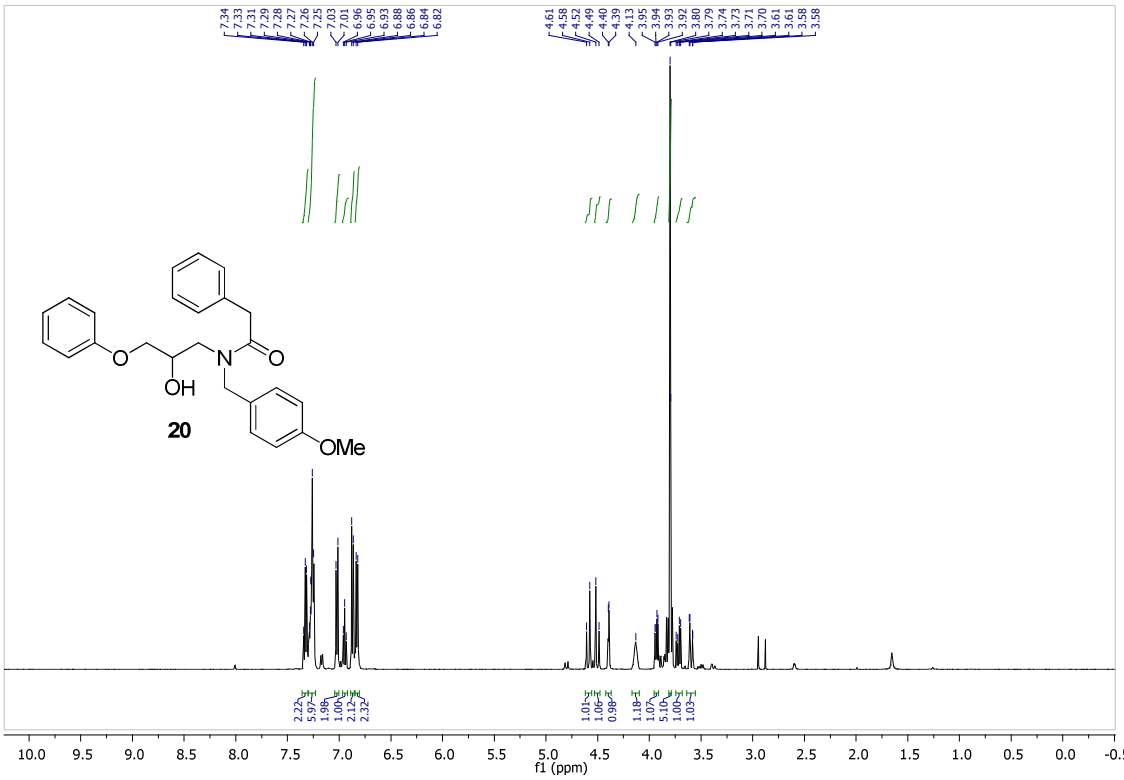


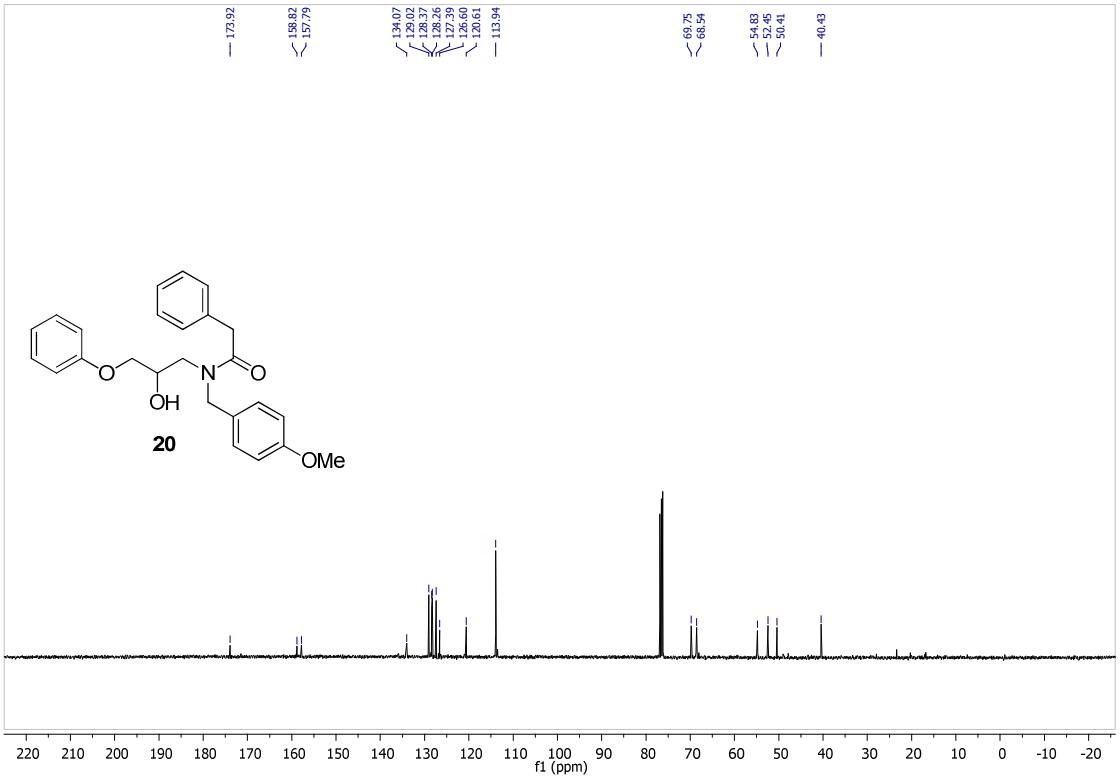
***N*-(2-hydroxy-3-phenoxypropyl)-2-phenyl-*N*-(1-phenylethyl)acetamide (18)**



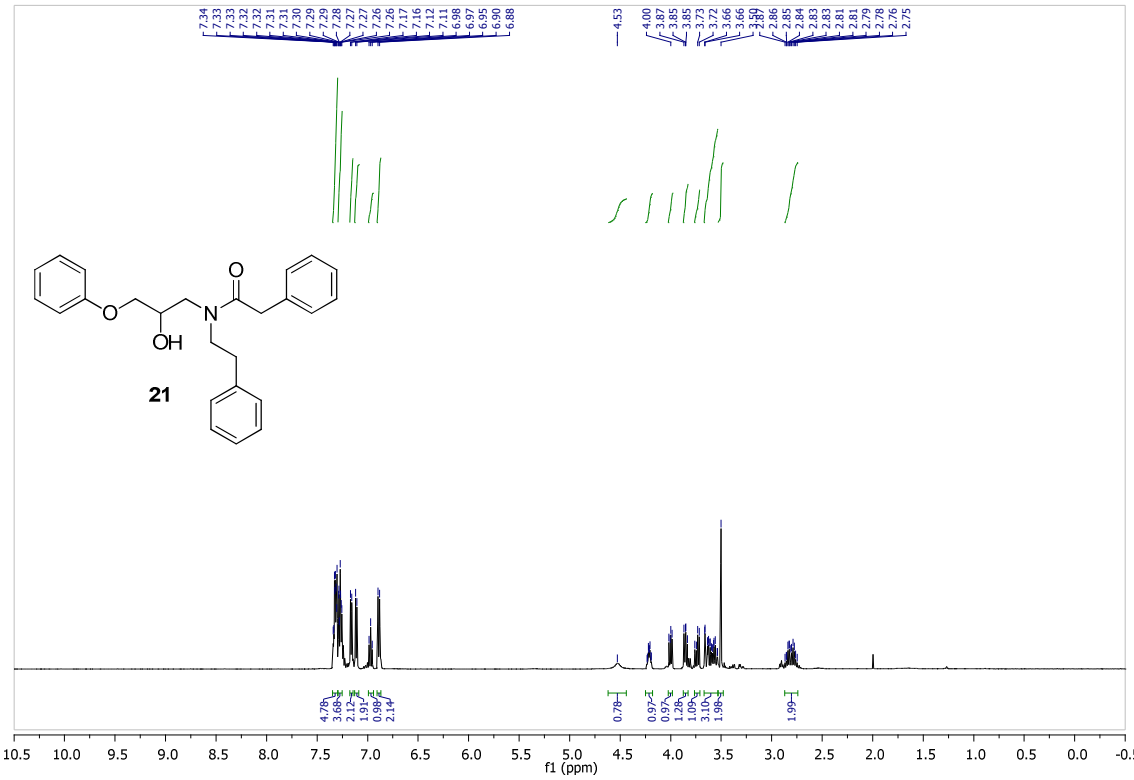


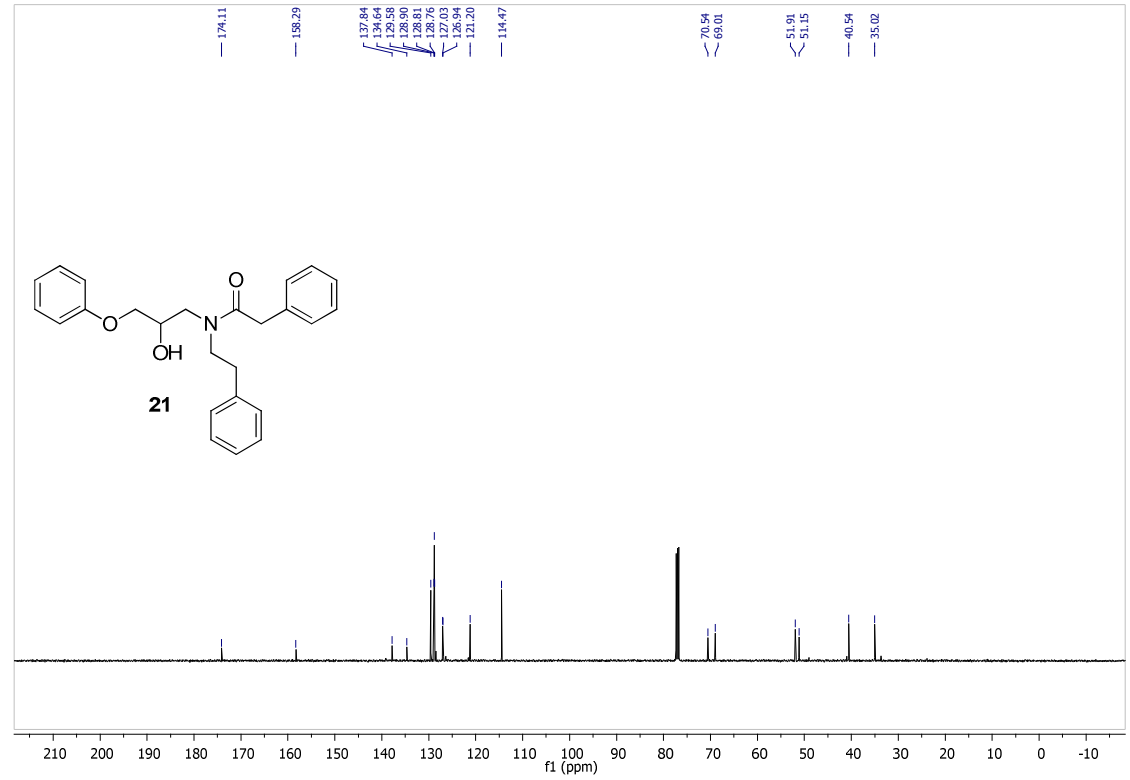
***N*-(2-hydroxy-3-phenoxypropyl)-*N*-(4-methoxybenzyl)-2-phenylacetamide (20)**



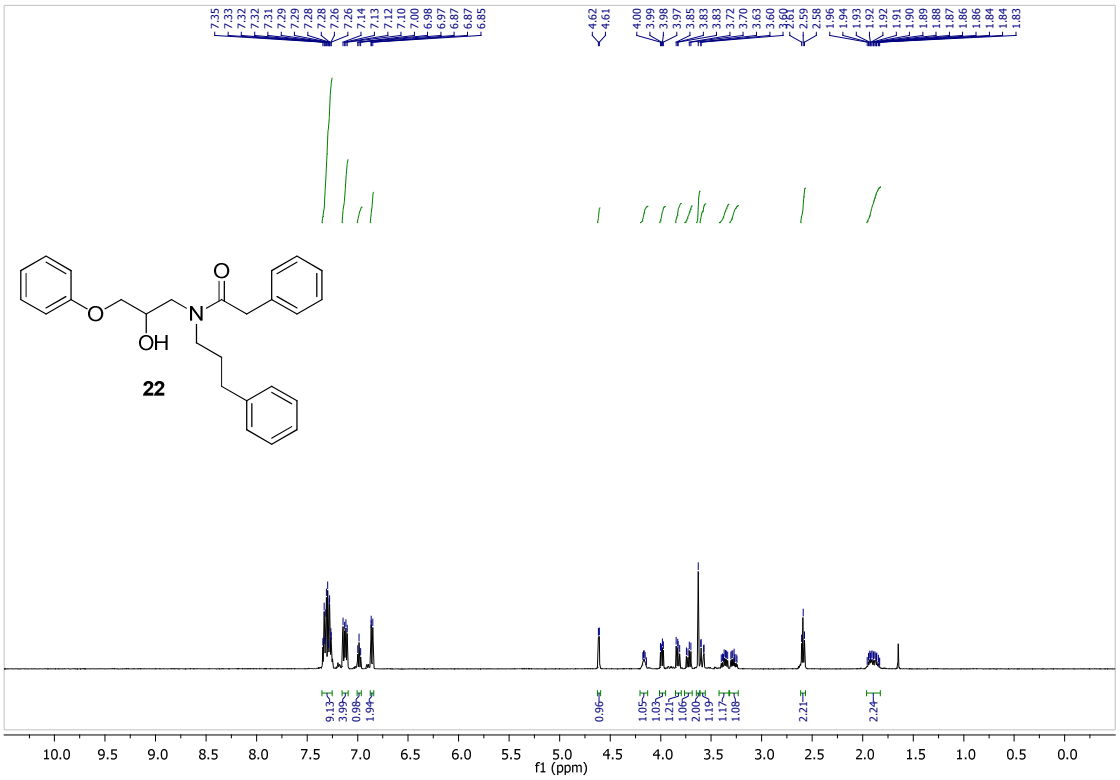


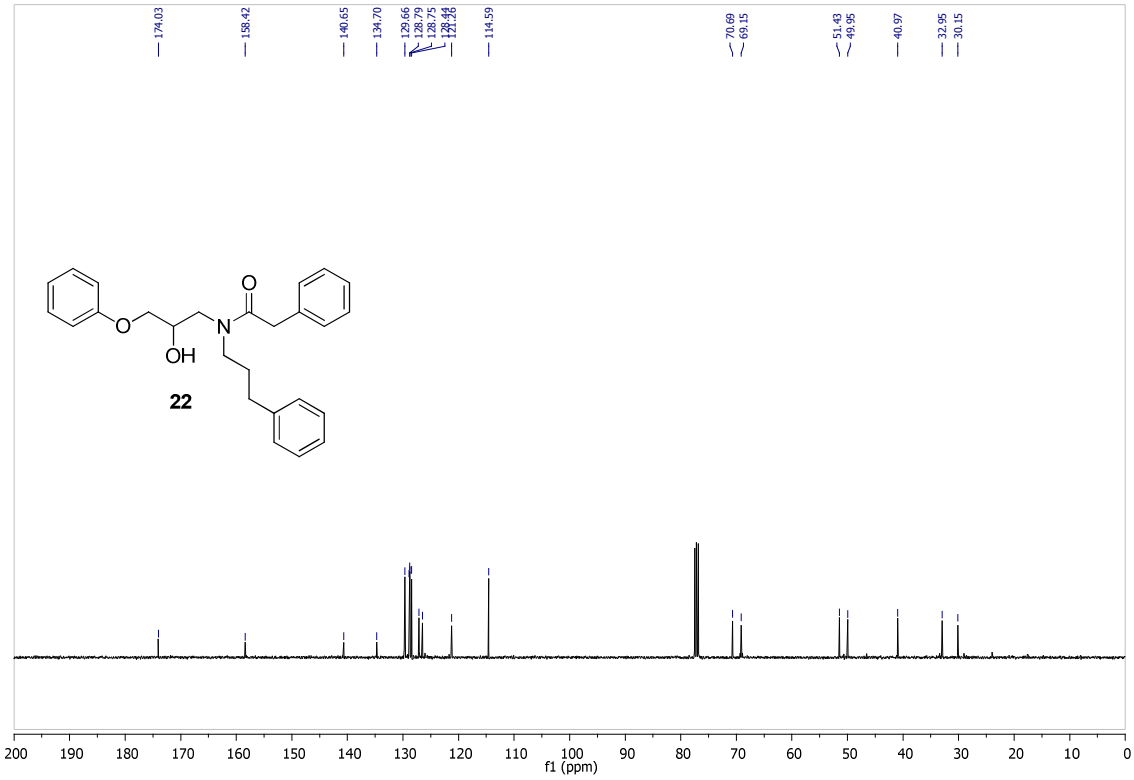
***N*-(2-hydroxy-3-phenoxypropyl)-*N*-phenethyl-2-phenylacetamide (21)**



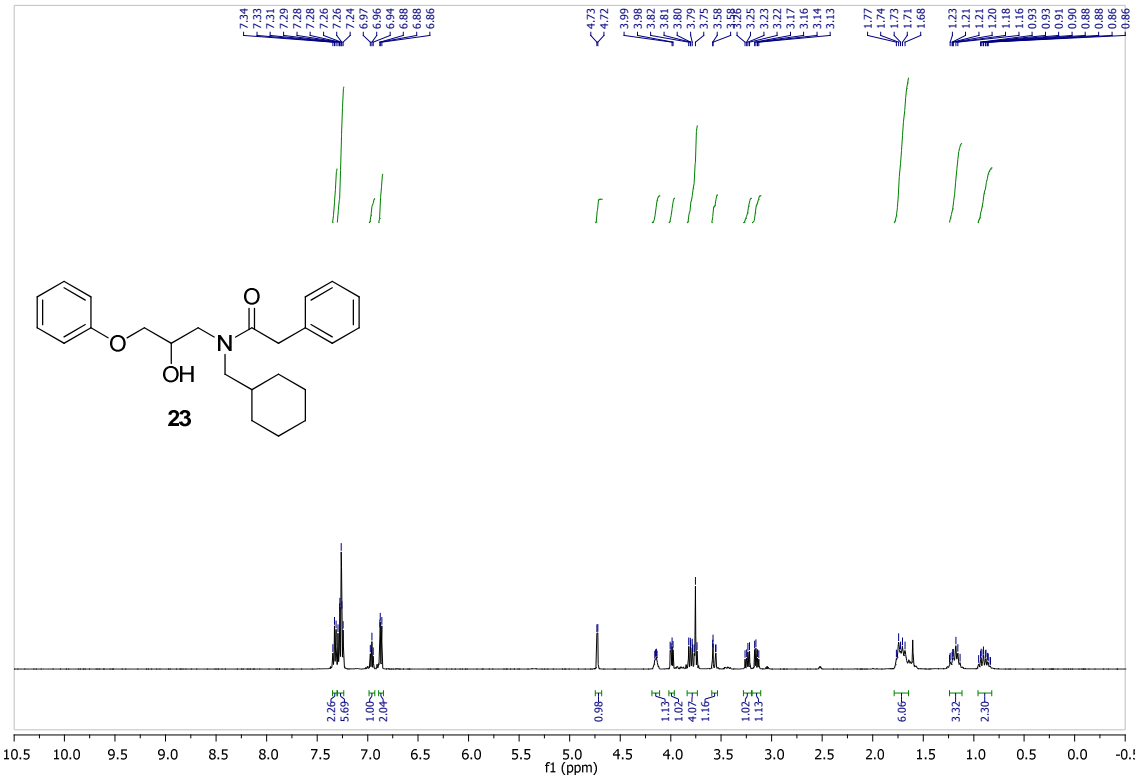


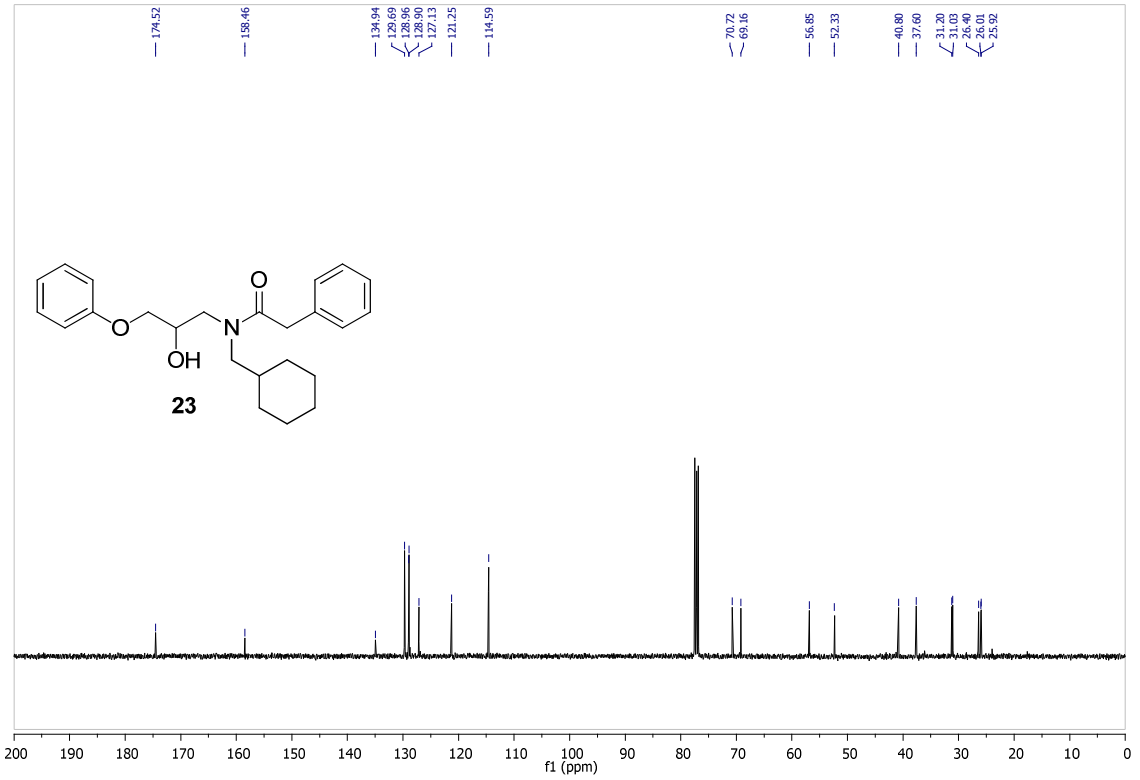
***N*-(2-hydroxy-3-phenoxypropyl)-2-phenyl-*N*-(3-phenylpropyl)acetamide (22)**



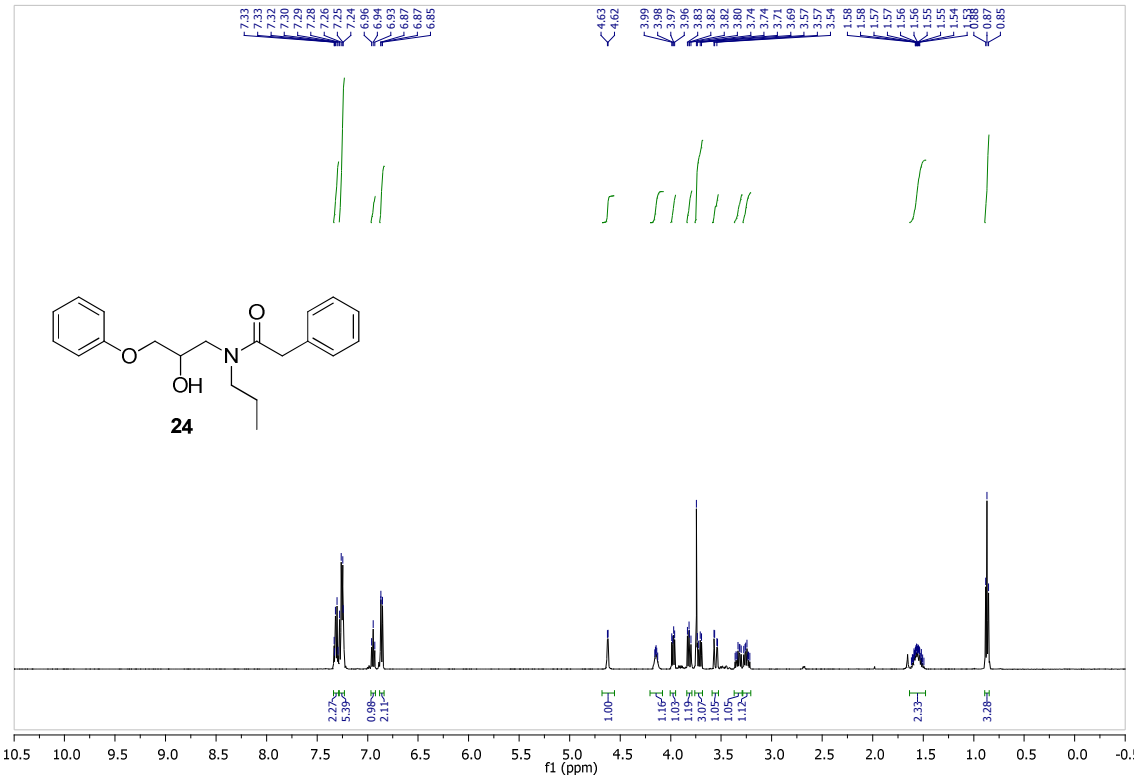


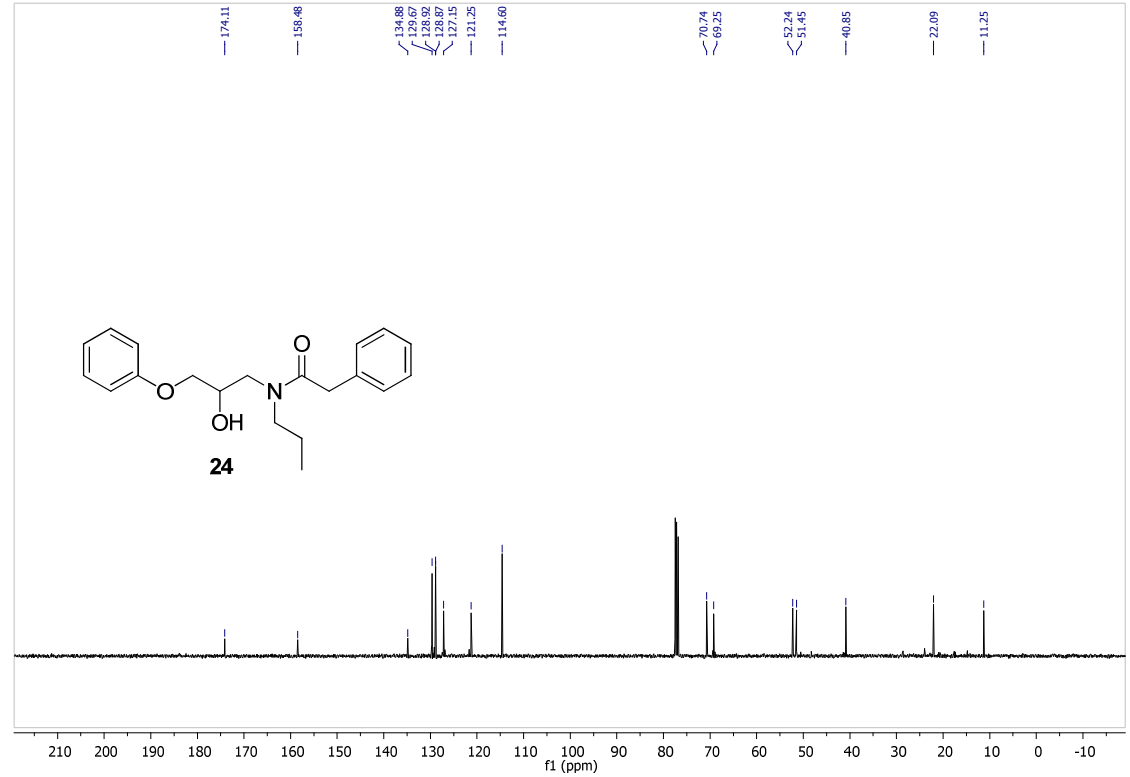
***N*-(cyclohexylmethyl)-*N*-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (23)**



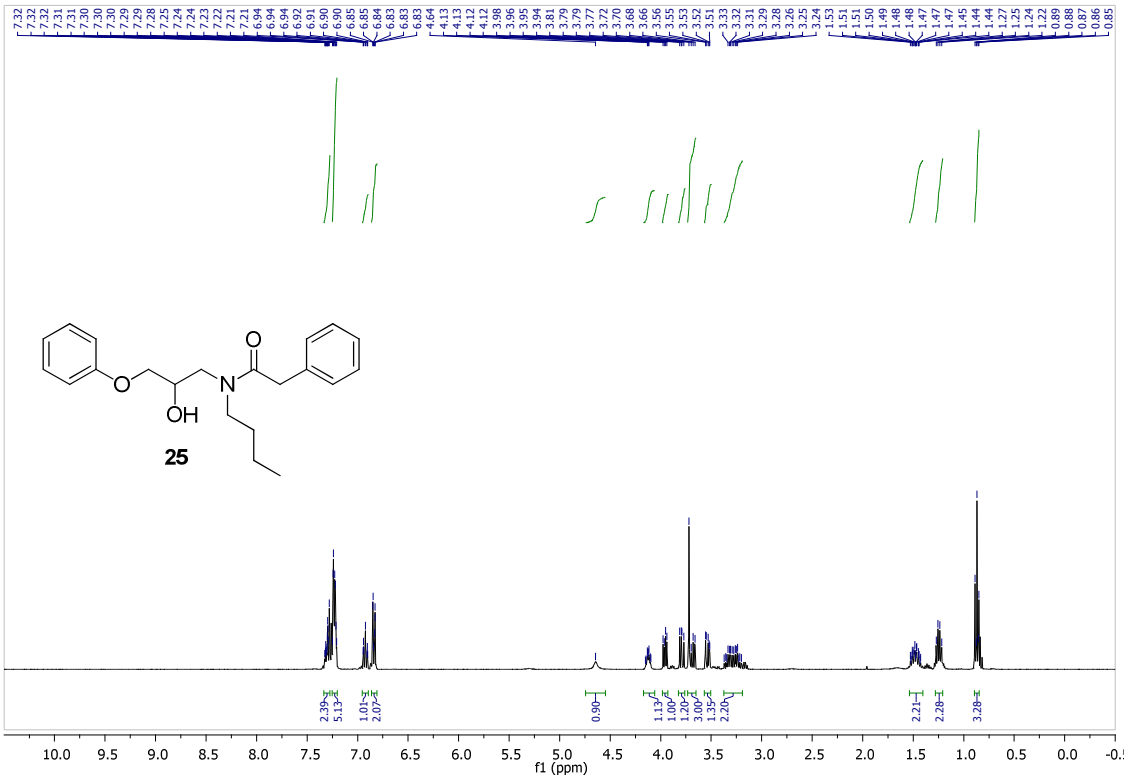


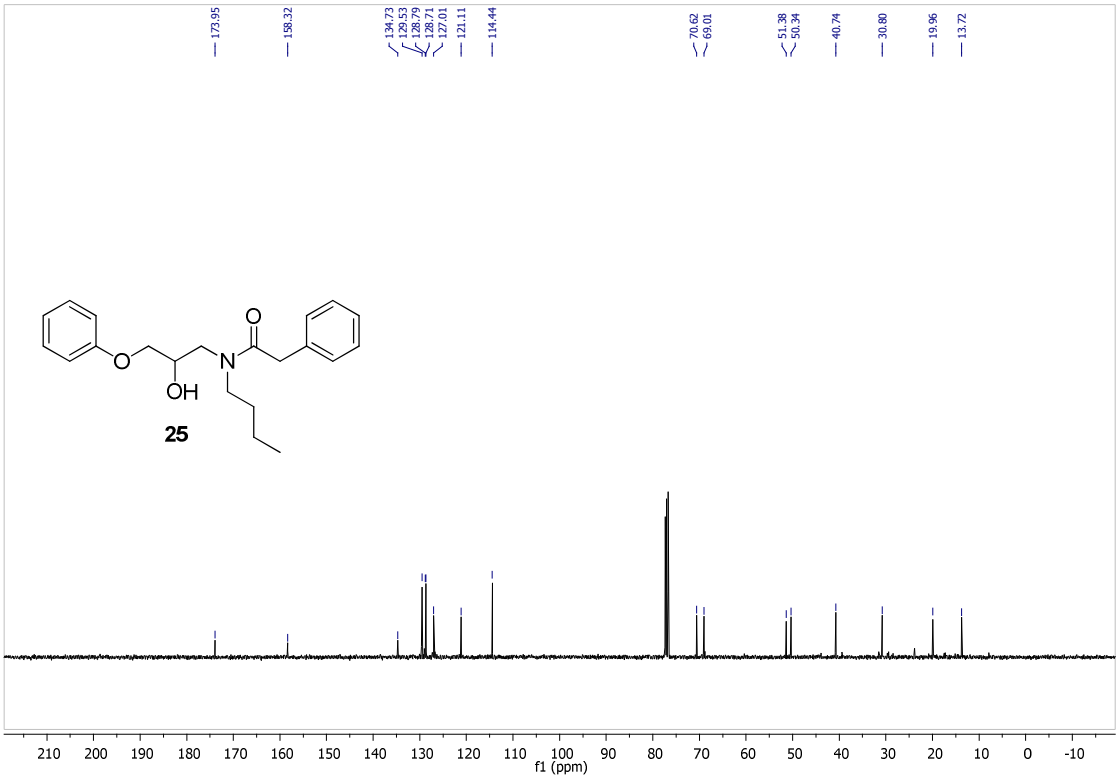
_N_-(2-hydroxy-3-phenoxypropyl)-2-phenyl-_N_-propylacetamide (24)



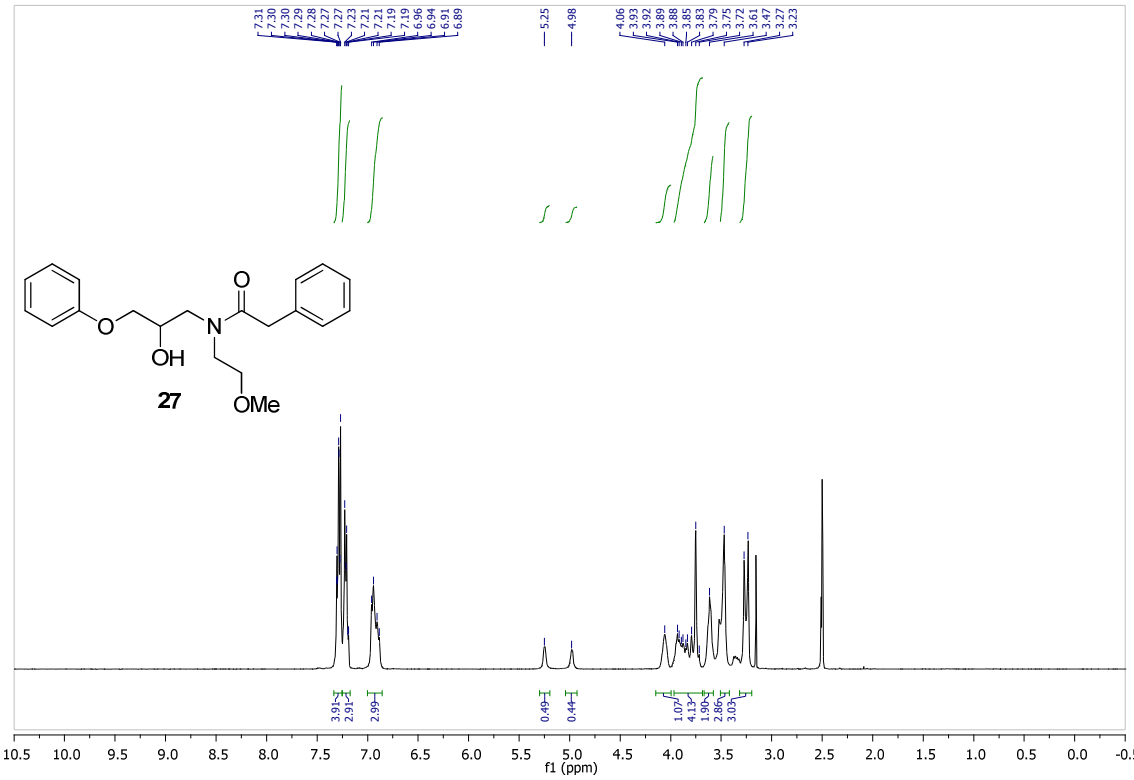


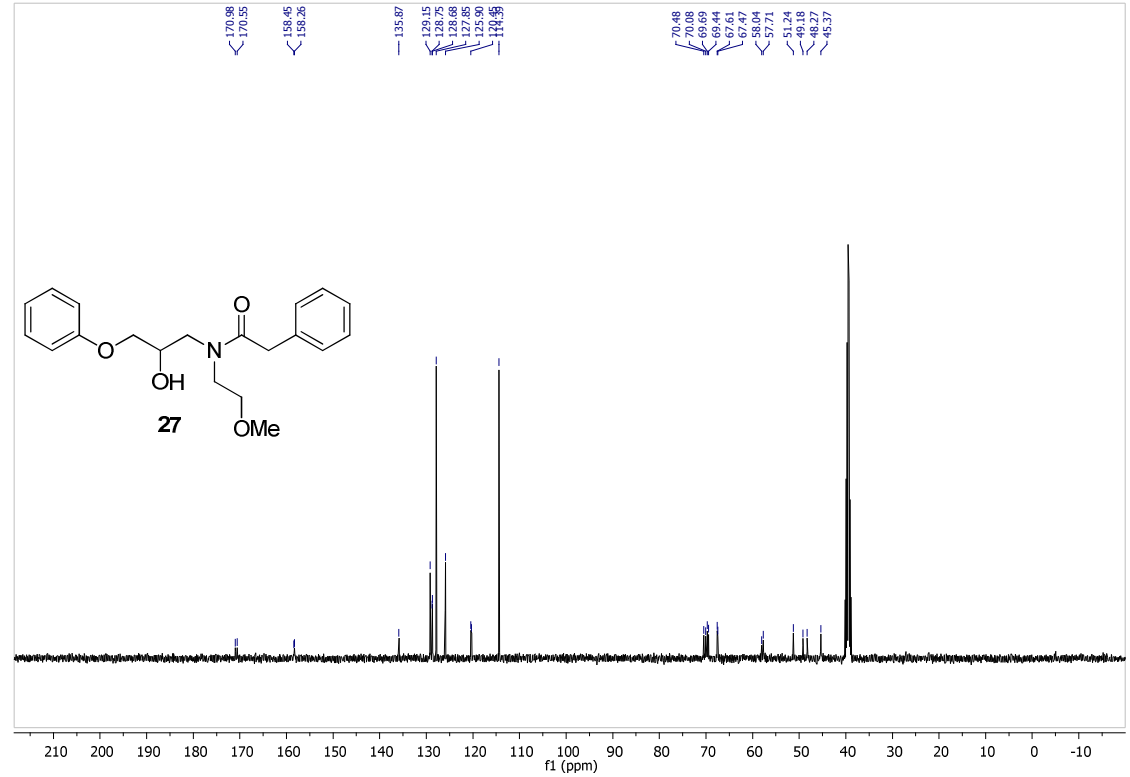
***N*-butyl-*N*-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (25)**



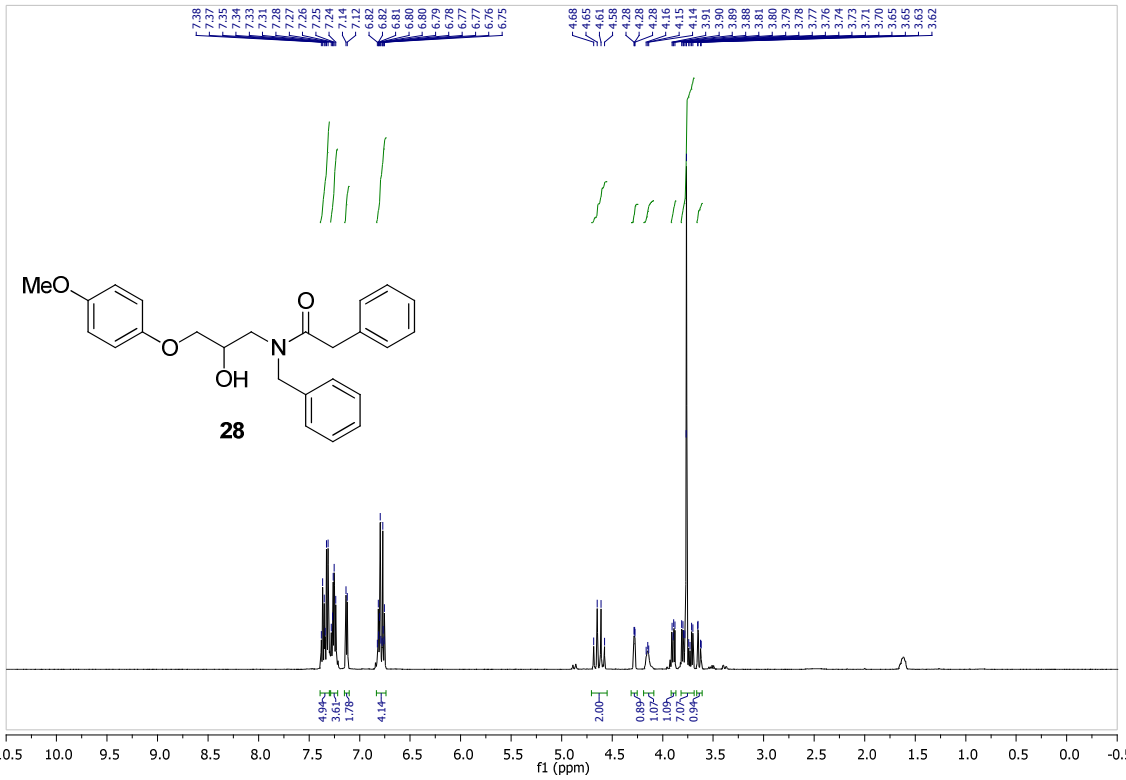


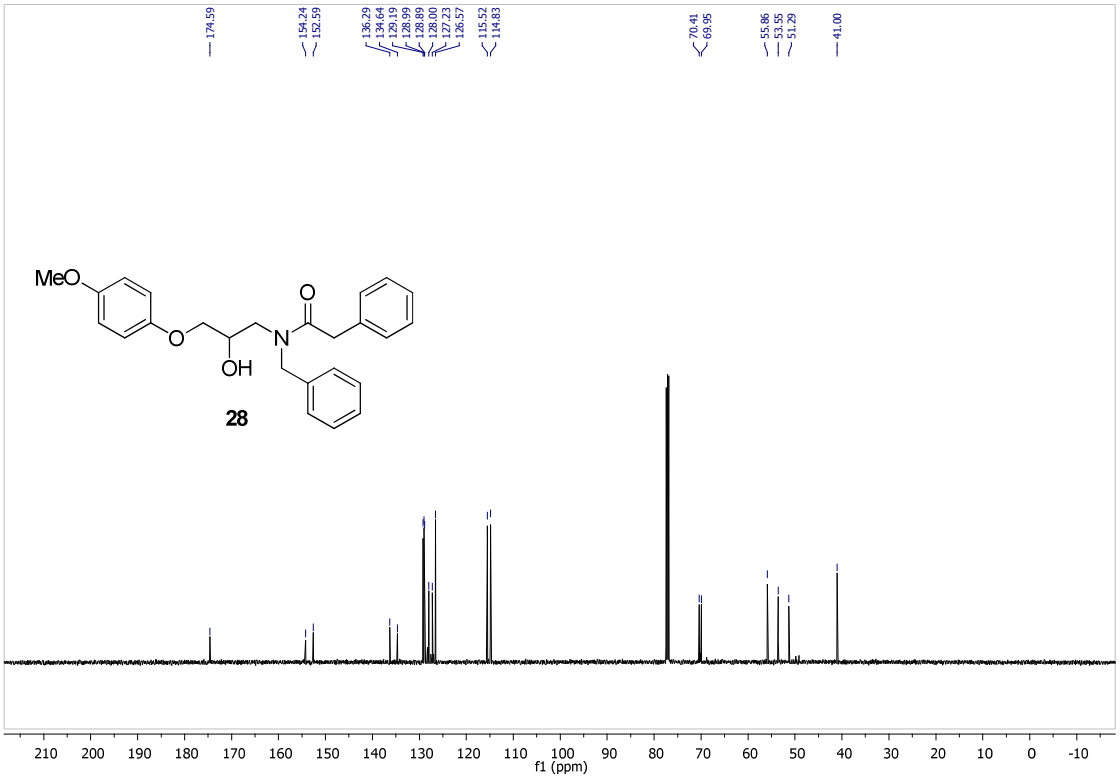
***N*-(2-hydroxy-3-phenoxypropyl)-*N*-(2-methoxyethyl)-2-phenylacetamide (27)**



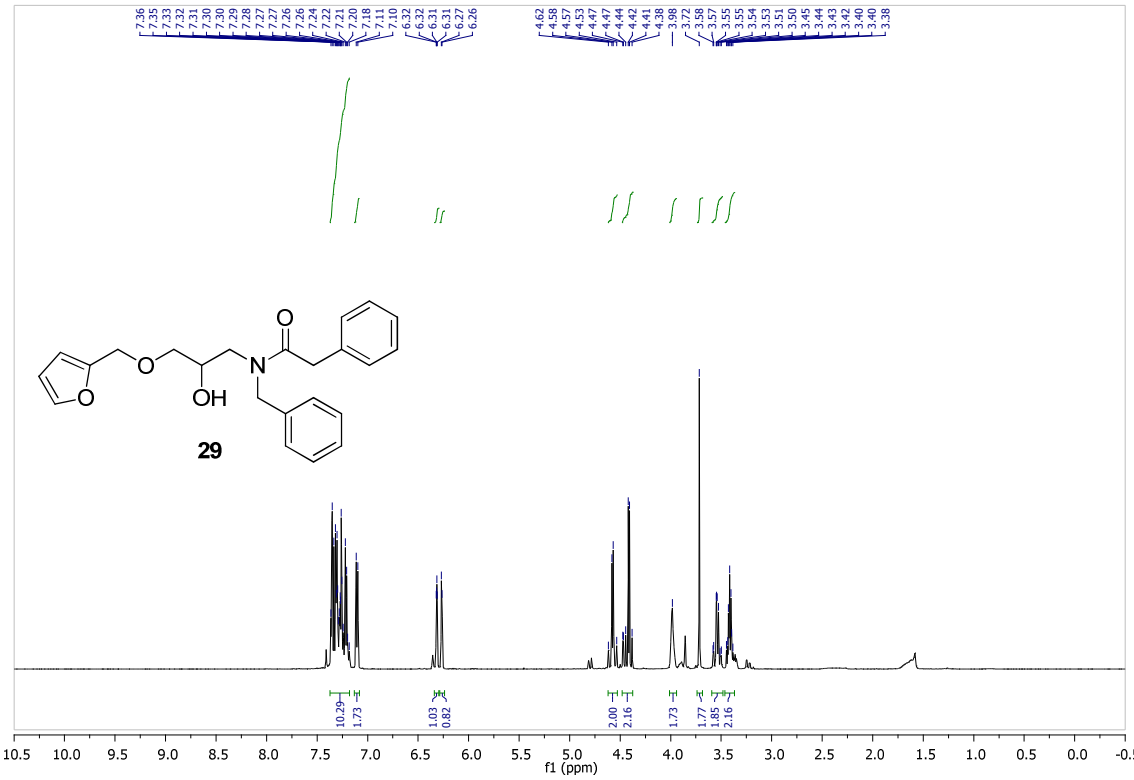


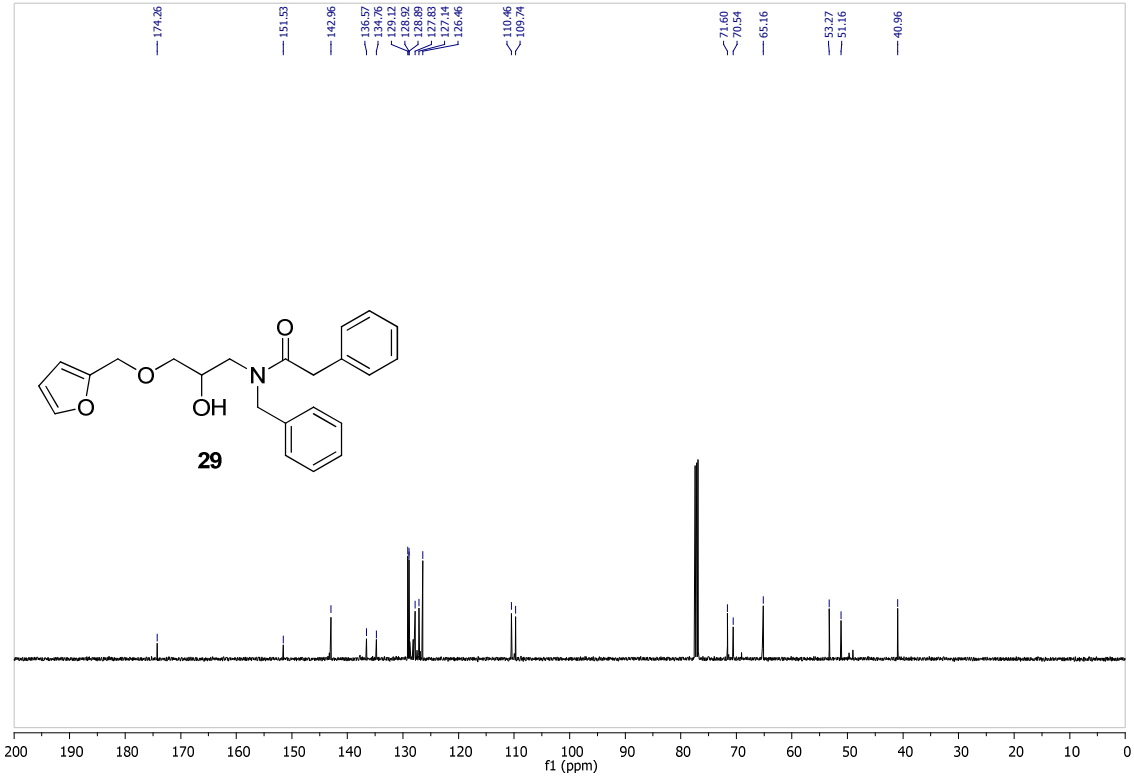
***N*-benzyl-*N*-(2-hydroxy-3-(4-methoxyphenoxy)propyl)-2-phenylacetamide (28)**



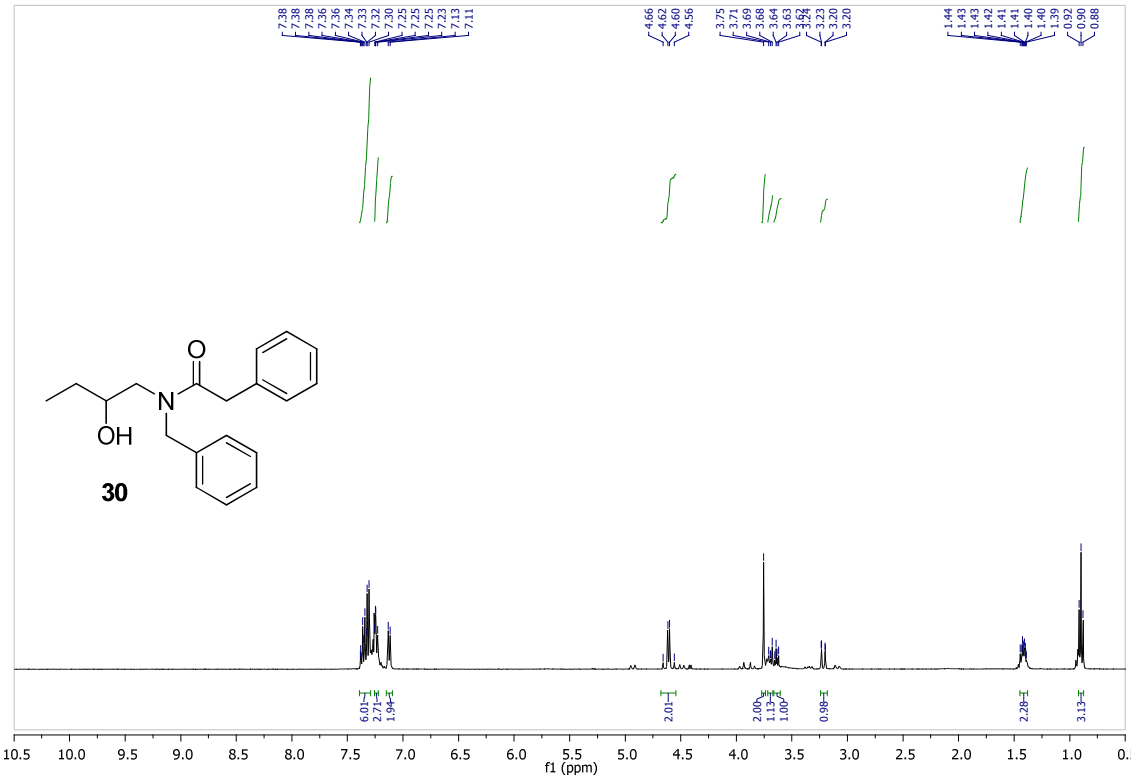


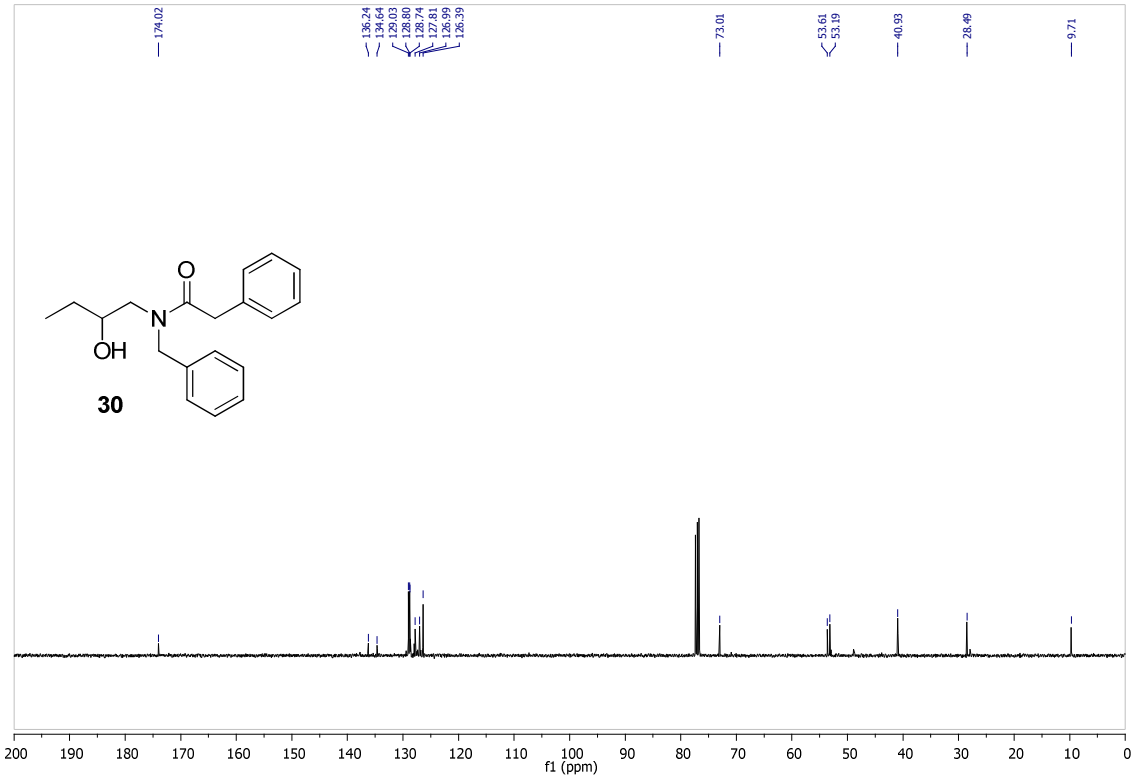
***N*-benzyl-*N*-(3-(furan-2-ylmethoxy)-2-hydroxypropyl)-2-phenylacetamide (29)**



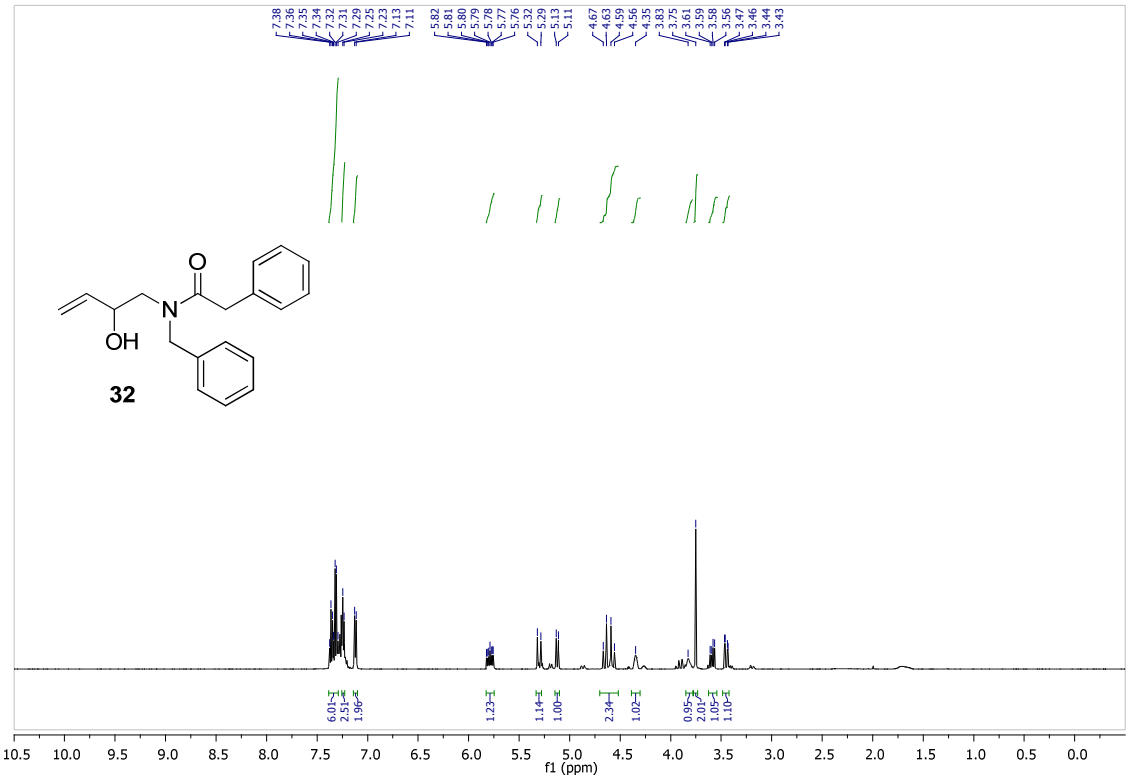


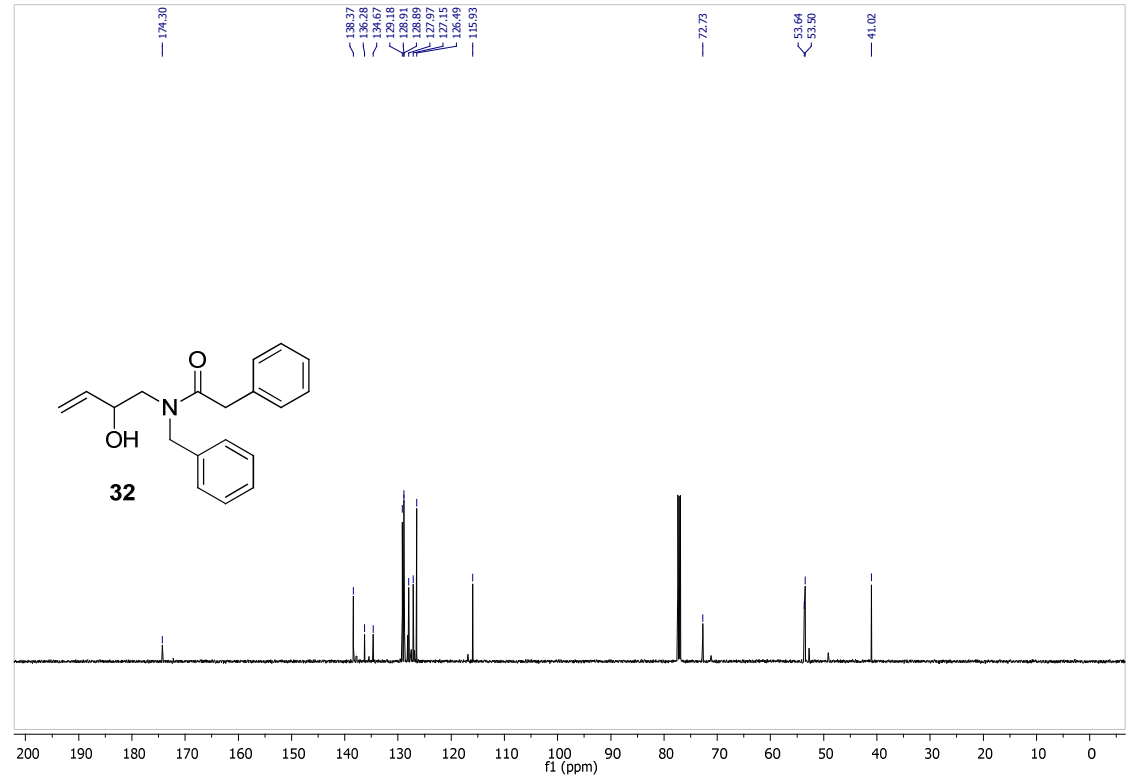
***N*-benzyl-*N*-(2-hydroxybutyl)-2-phenylacetamide (30)**



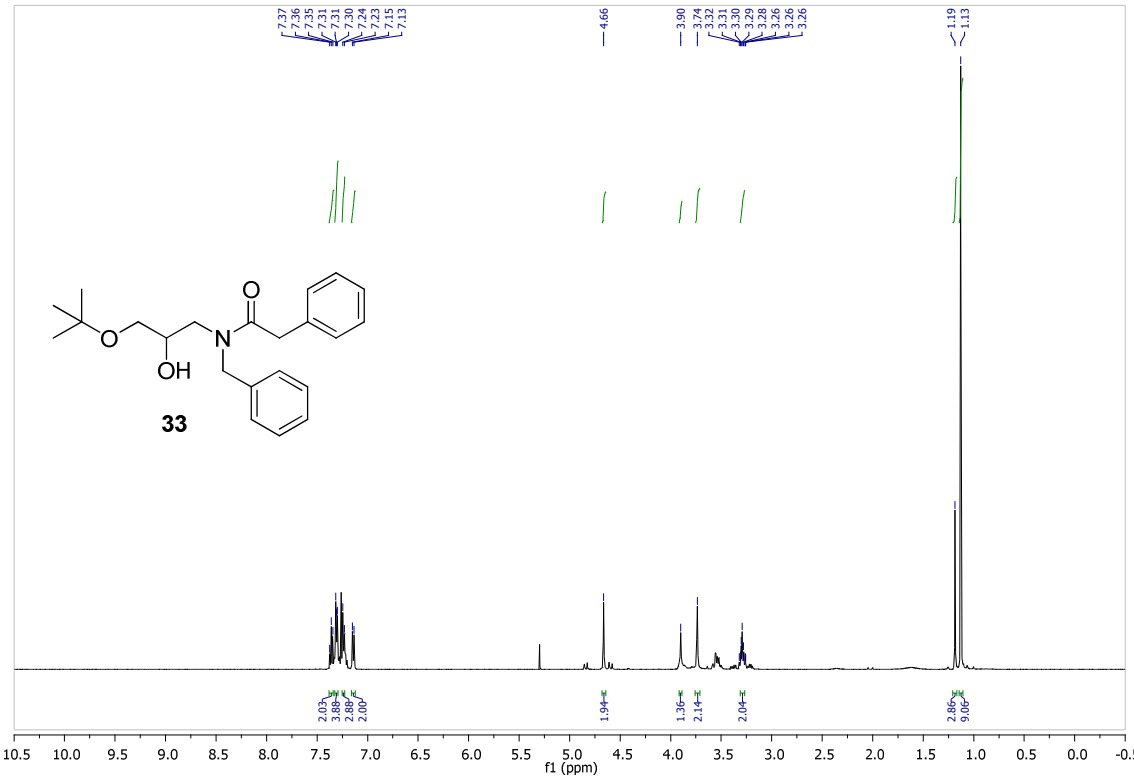


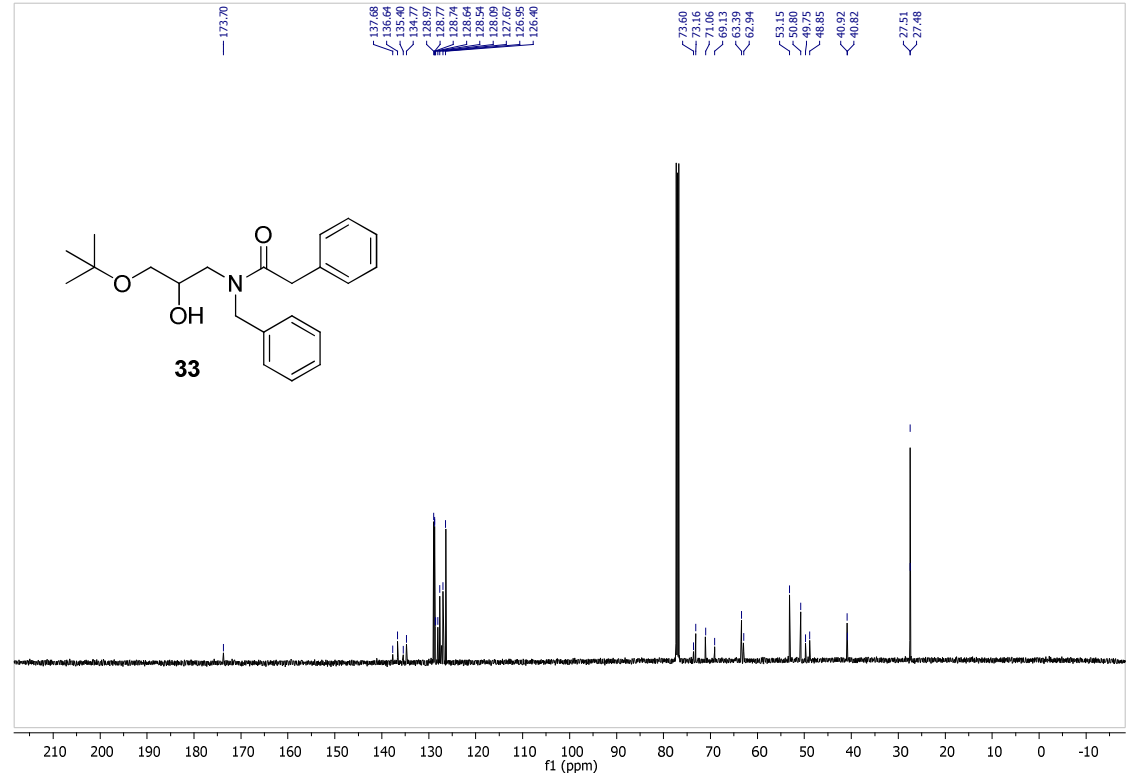
***N*-benzyl-*N*-(2-hydroxybut-3-en-1-yl)-2-phenylacetamide (32)**



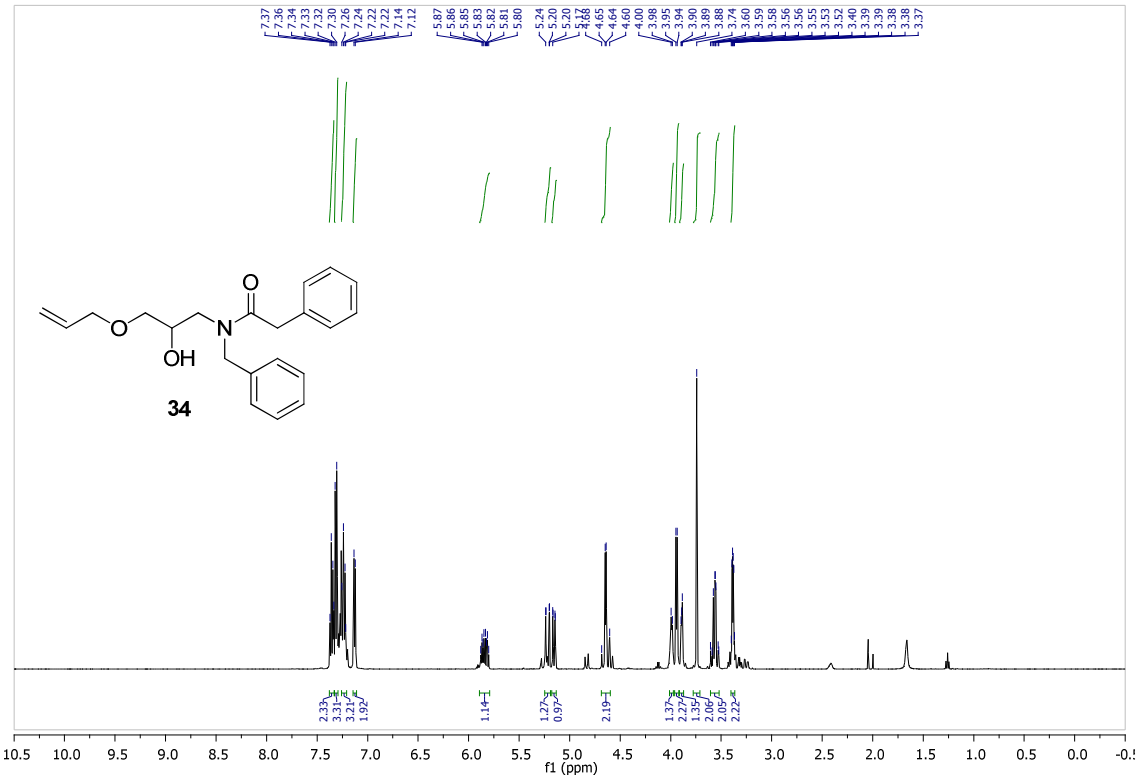


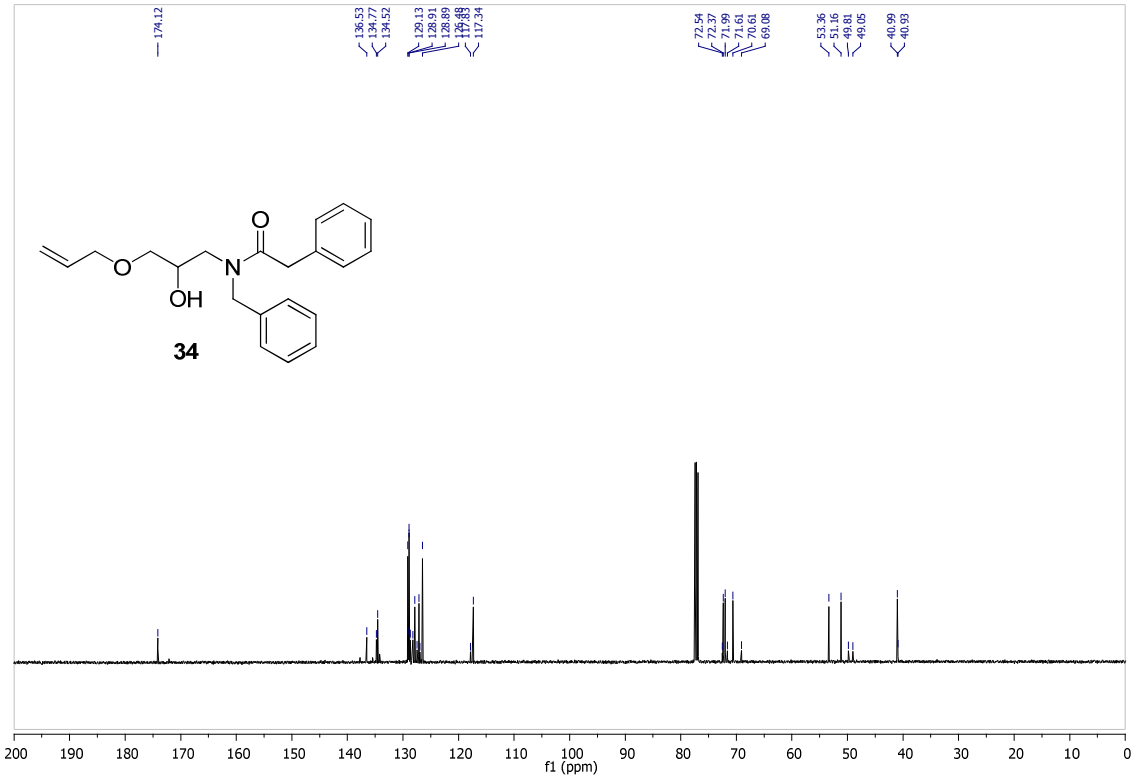
***N*-benzyl-*N*-(3-(*tert*-butoxy)-2-hydroxypropyl)-2-phenylacetamide (33)**



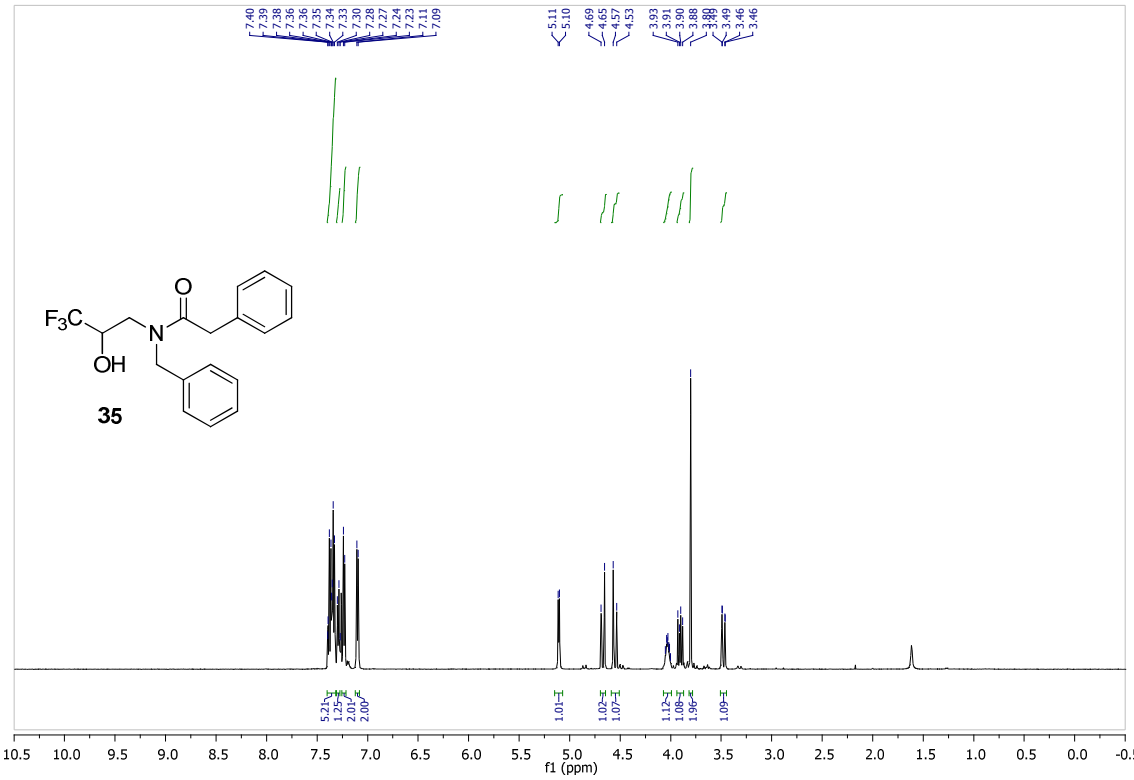


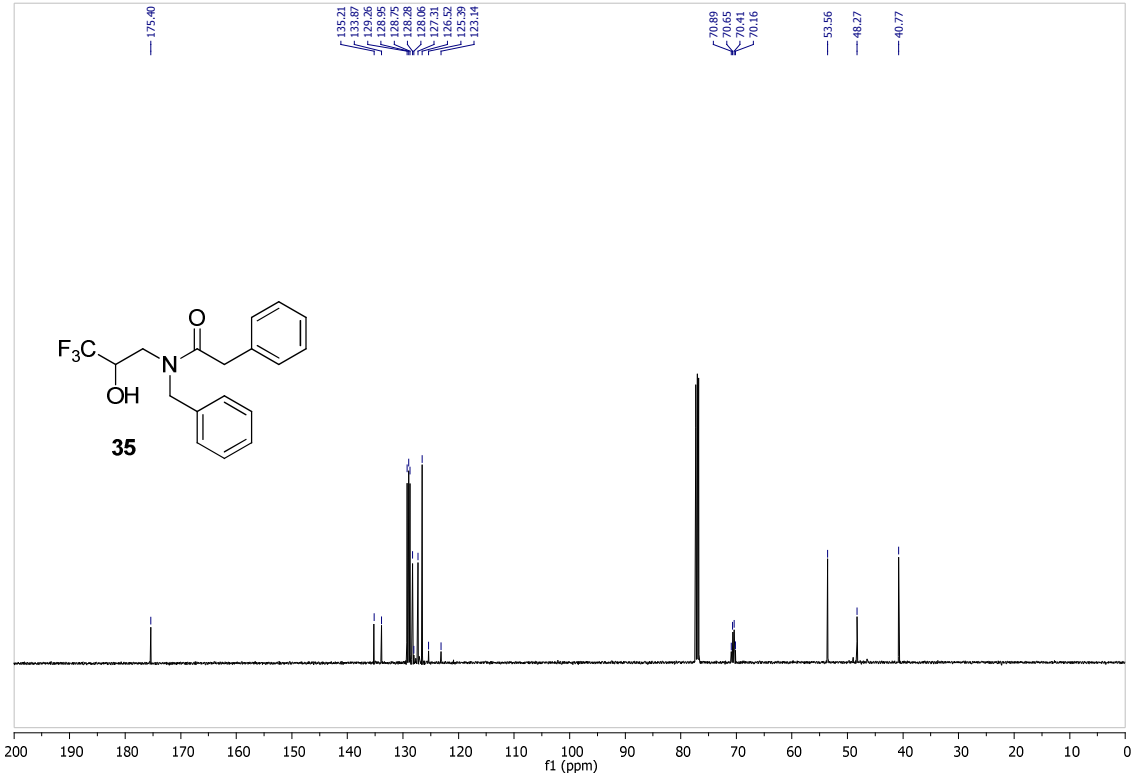
***N*-(3-(allyloxy)-2-hydroxypropyl)-*N*-benzyl-2-phenylacetamide (34)**



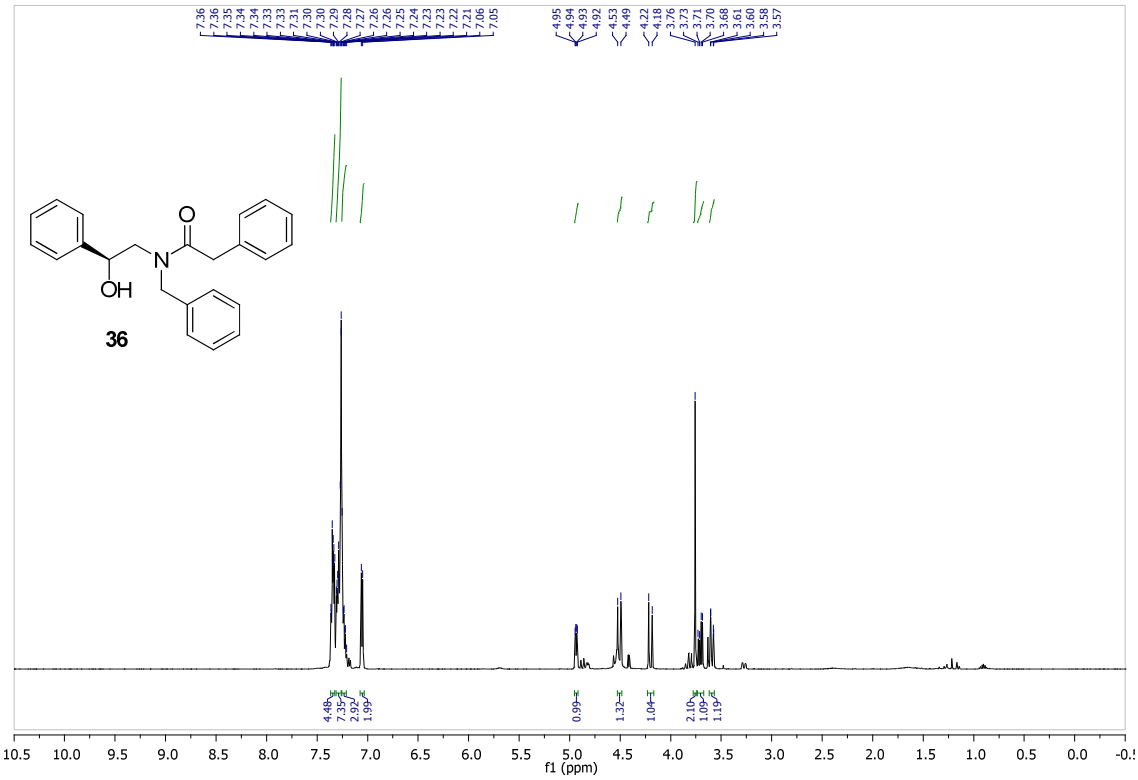


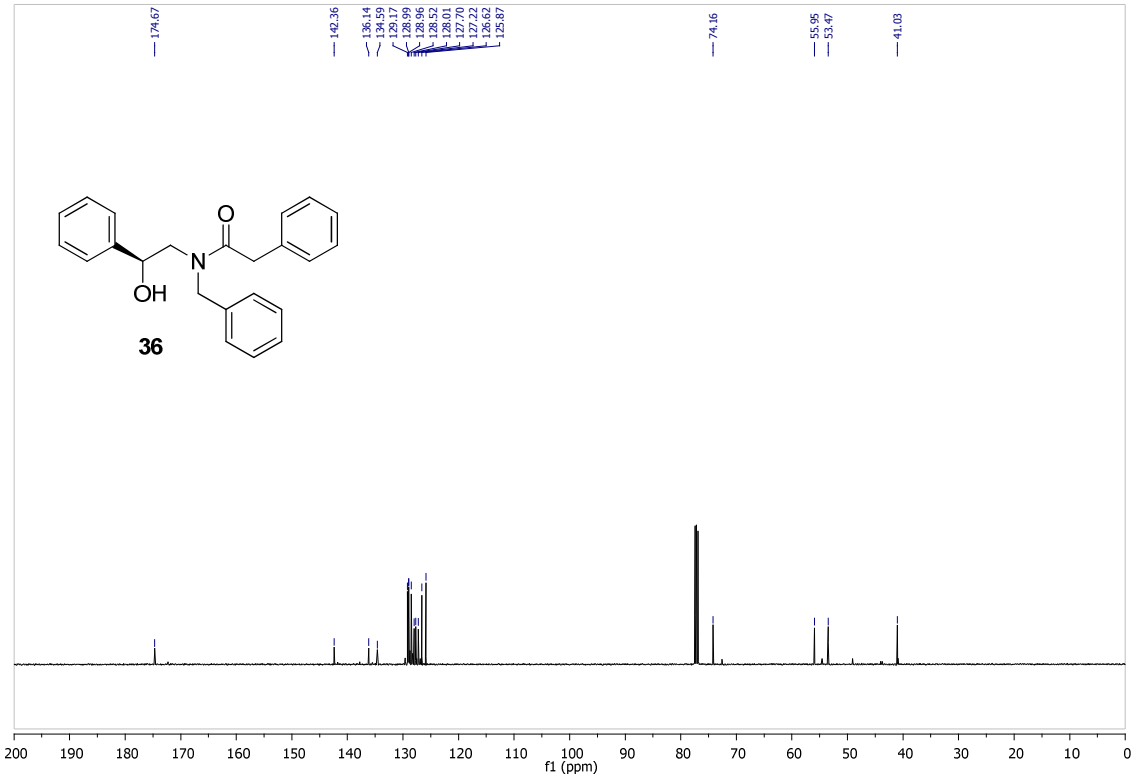
***N*-benzyl-2-phenyl-*N*-(3,3,3-trifluoro-2-hydroxypropyl)acetamide (35)**



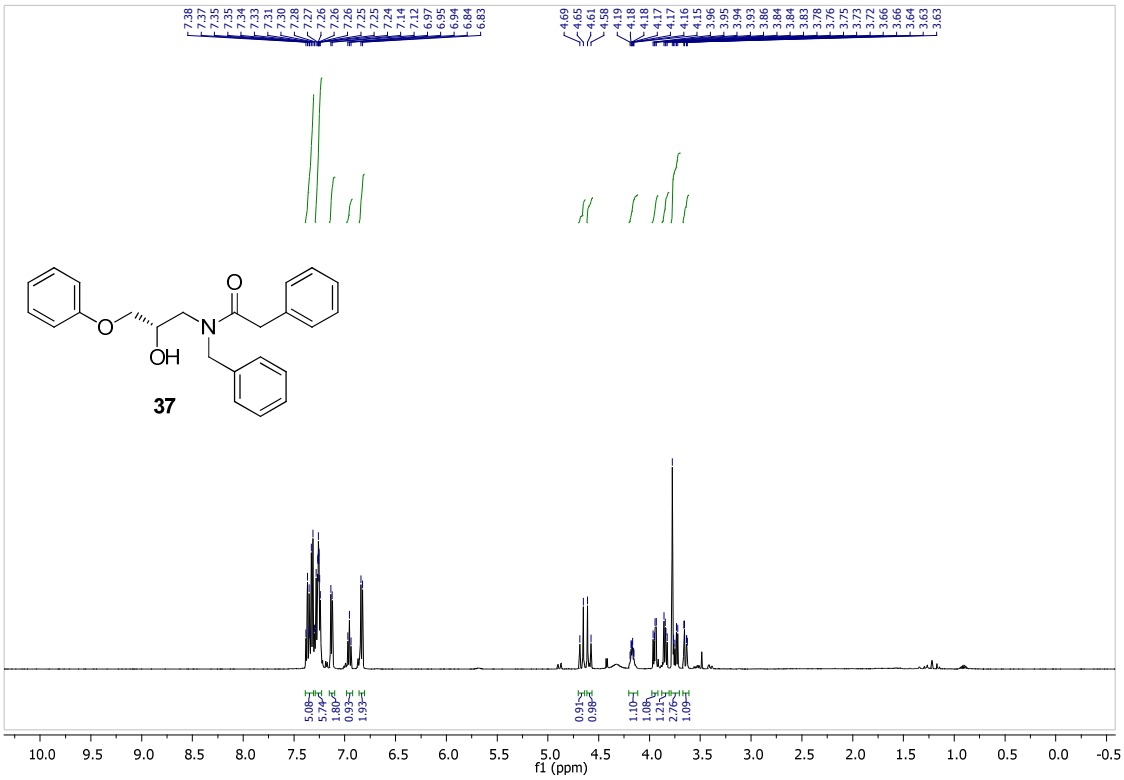


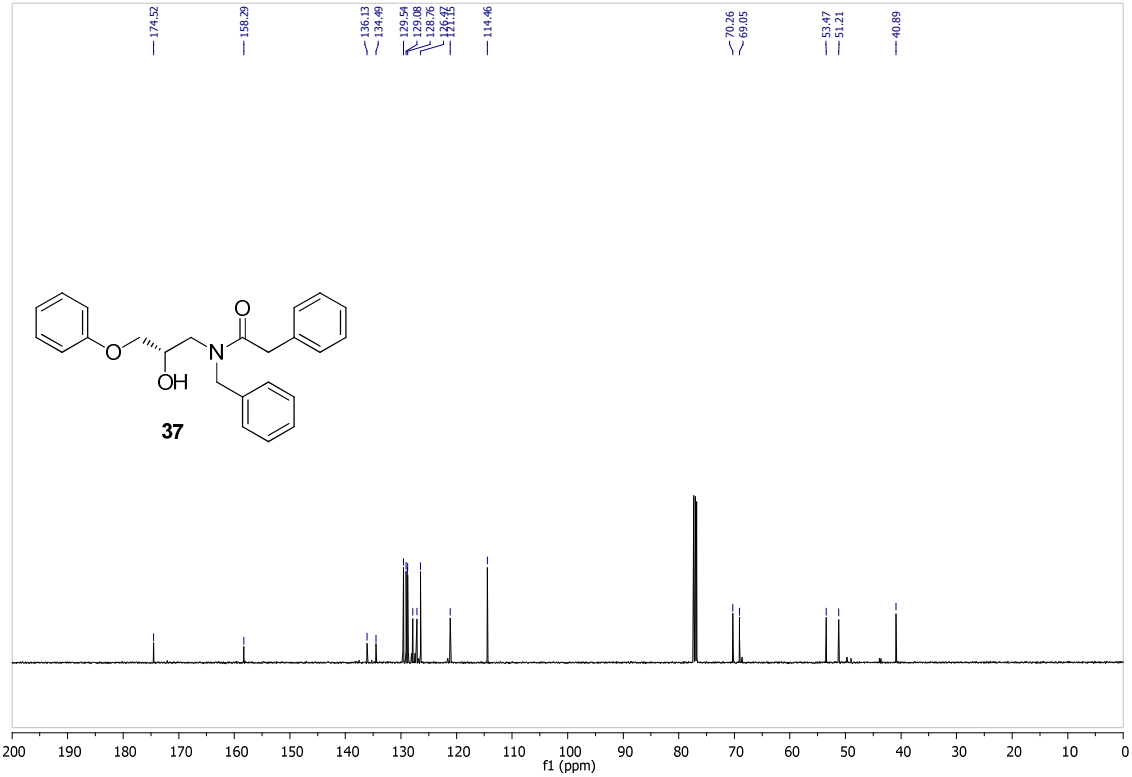
(*S*)-*N*-benzyl-*N*-(2-hydroxy-2-phenylethyl)-2-phenylacetamide (36)



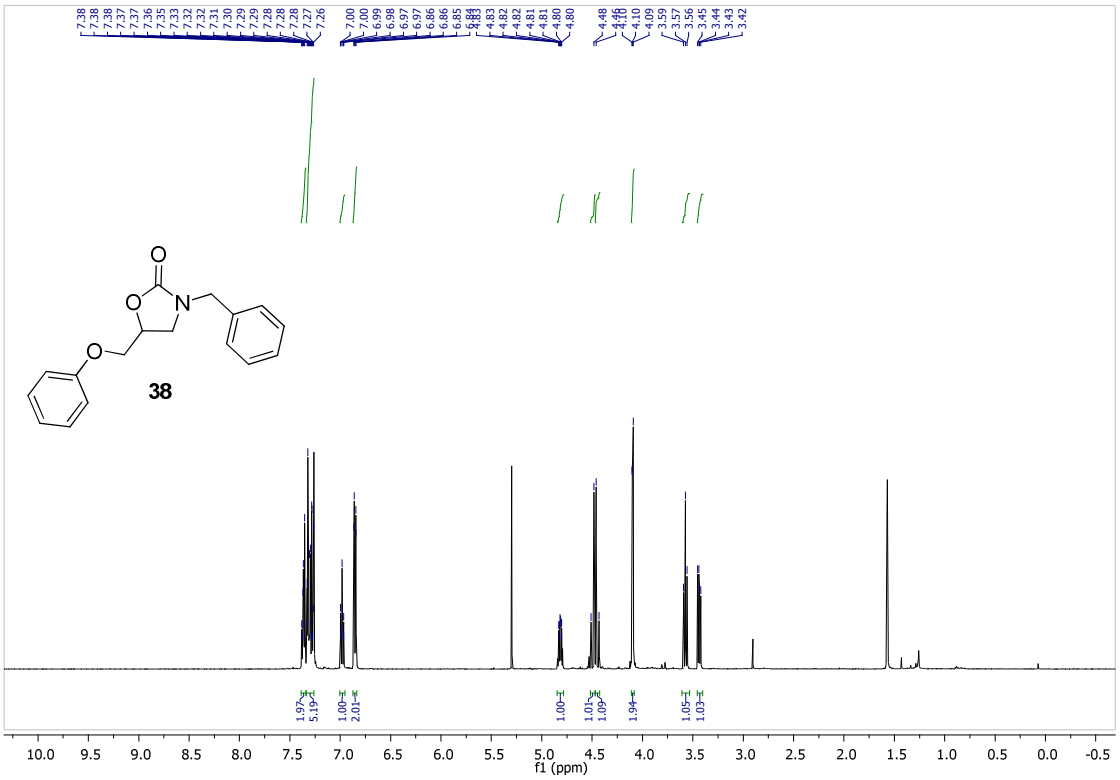


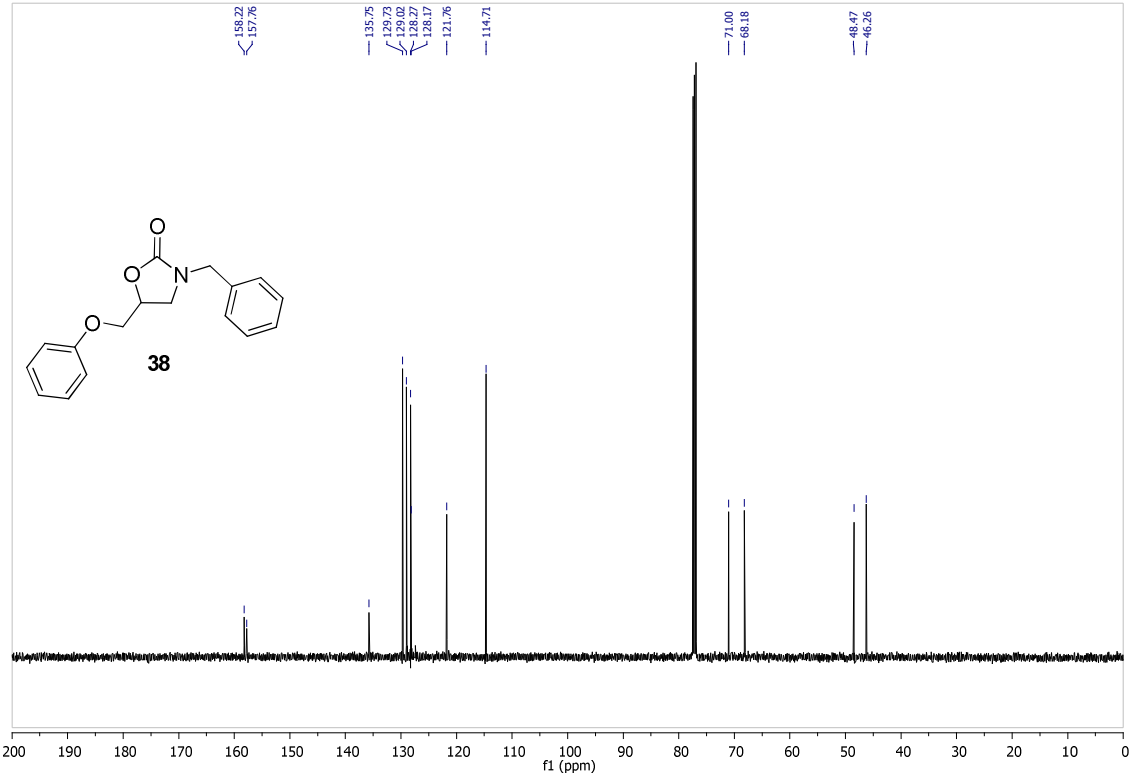
(*S*)-*N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (37)



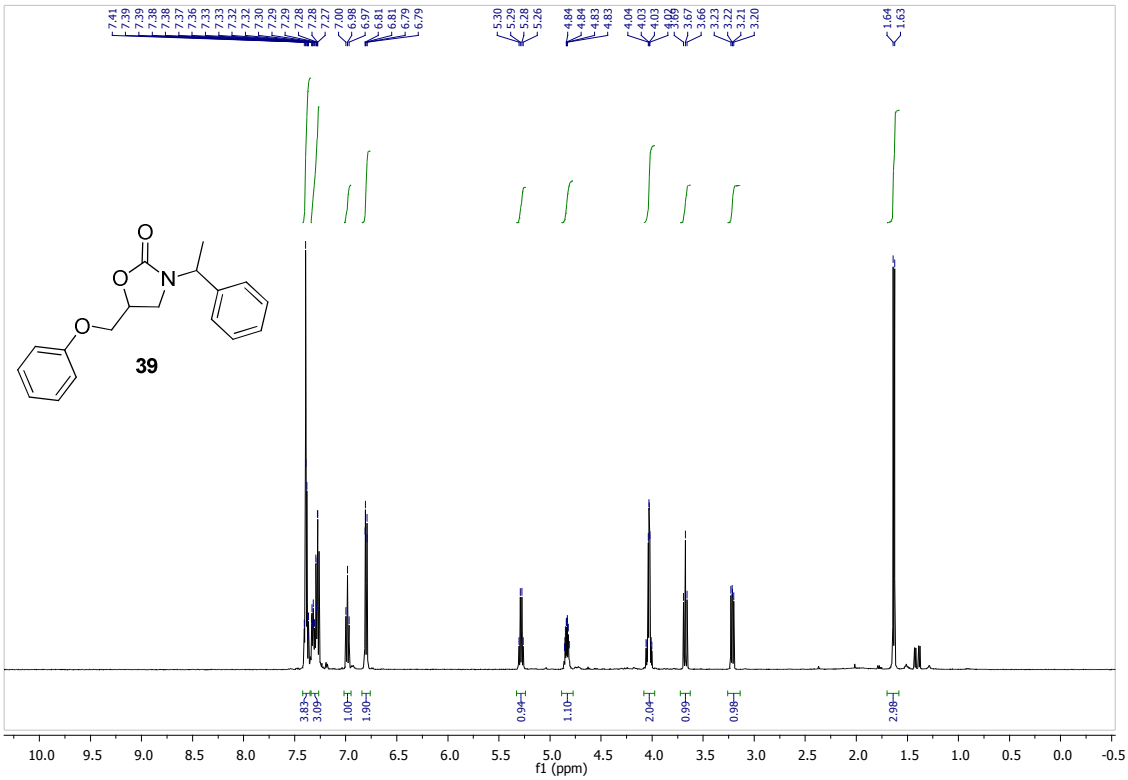


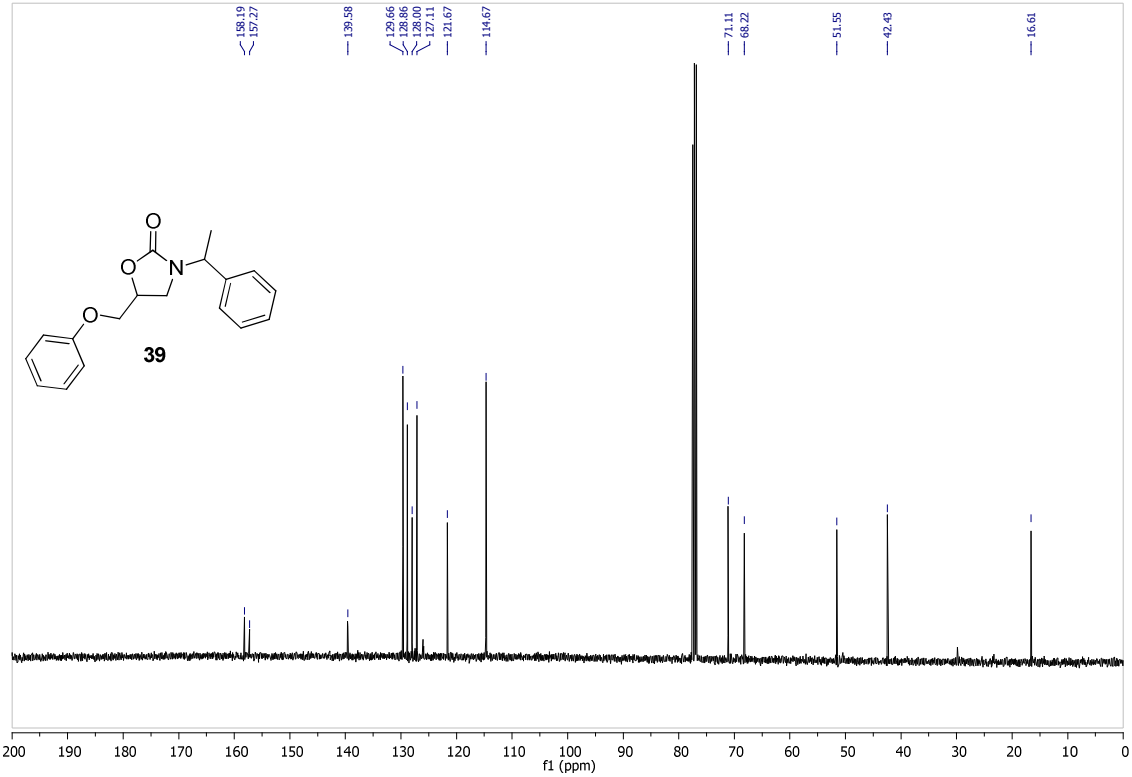
3-benzyl-5-(phenoxymethyl)oxazolidin-2-one (38)



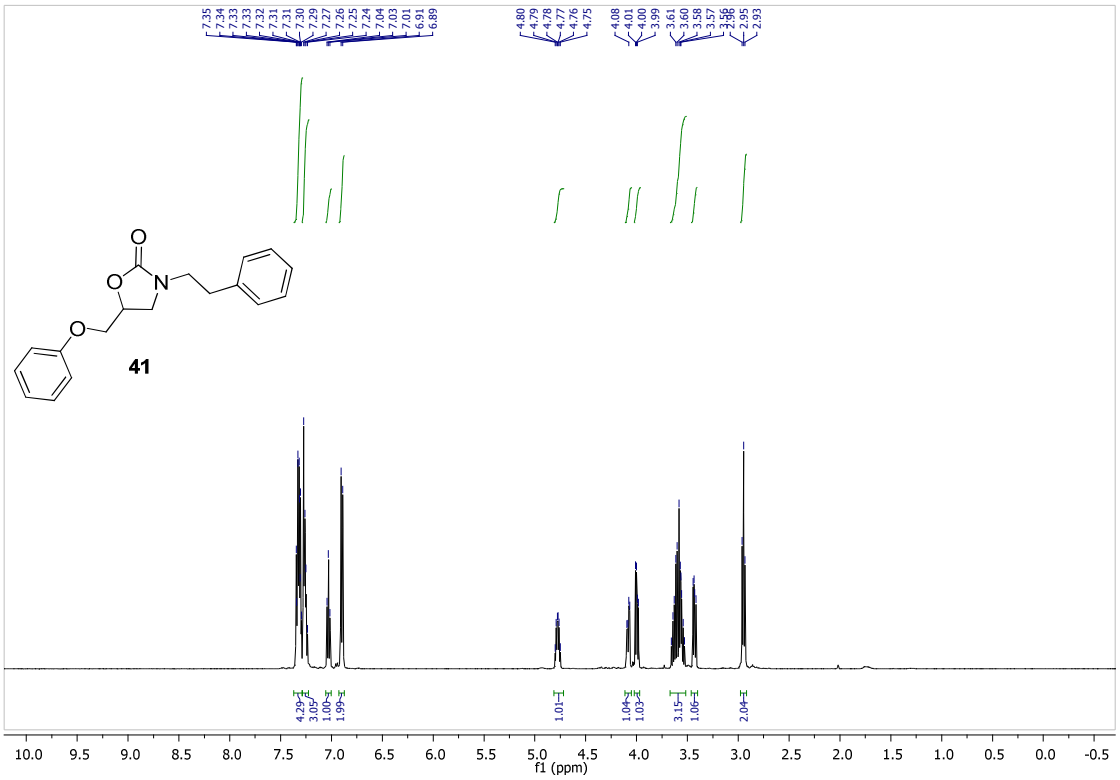


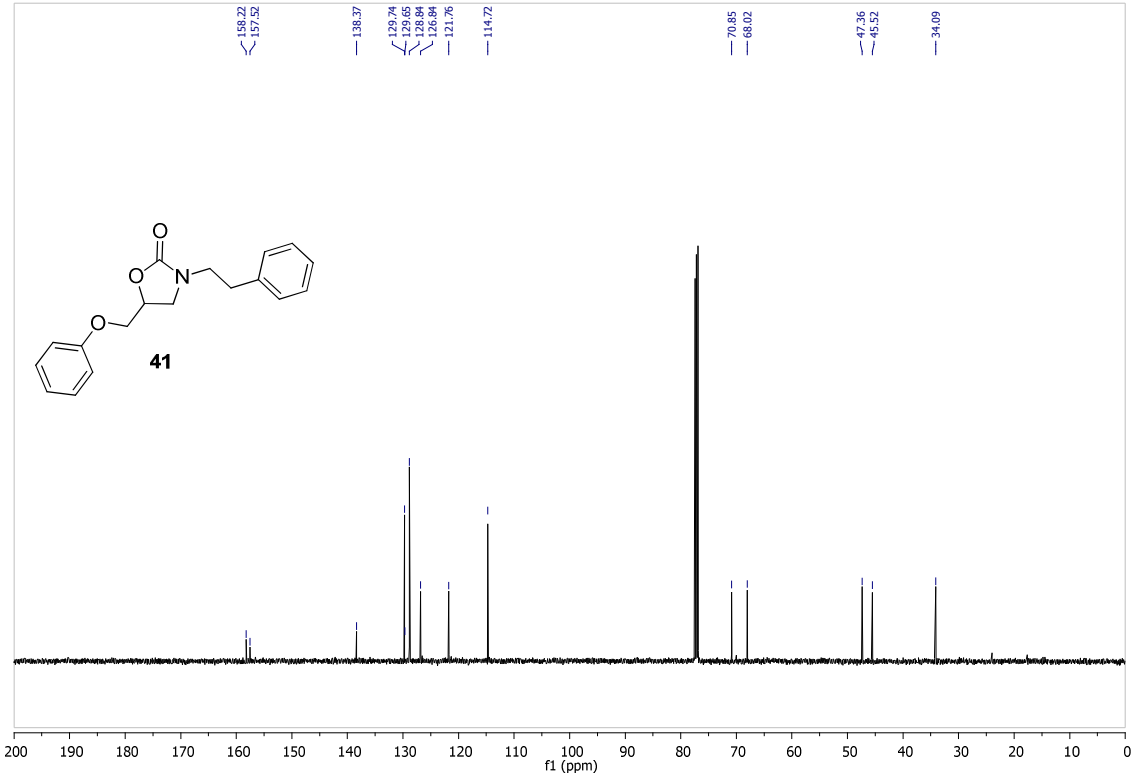
5-(phenoxymethyl)-3-(1-phenylethyl)oxazolidin-2-one (39)



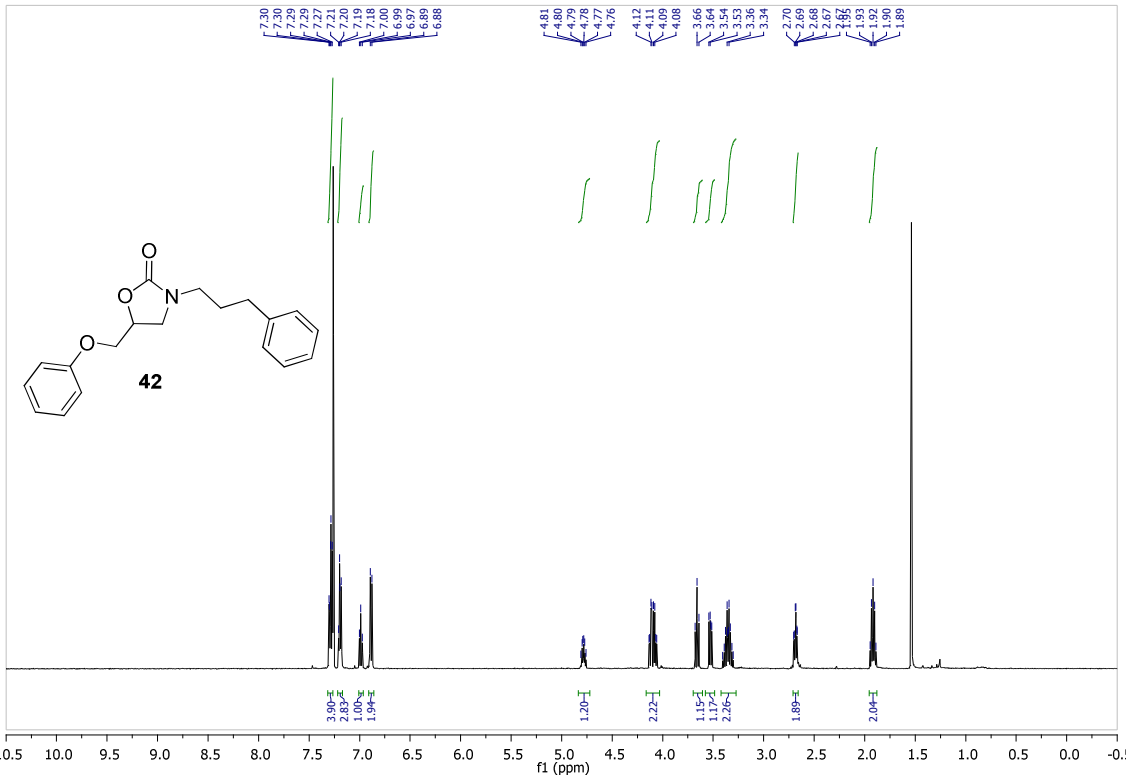


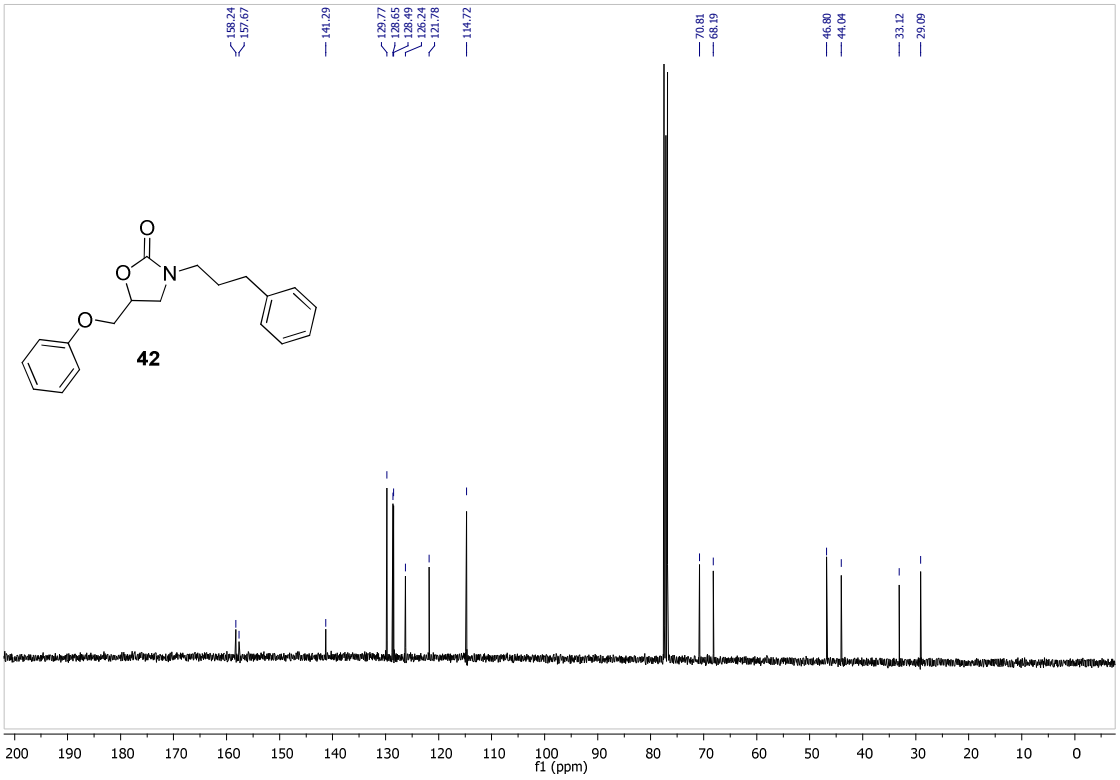
3-phenethyl-5-(phenoxymethyl)oxazolidin-2-one (41)



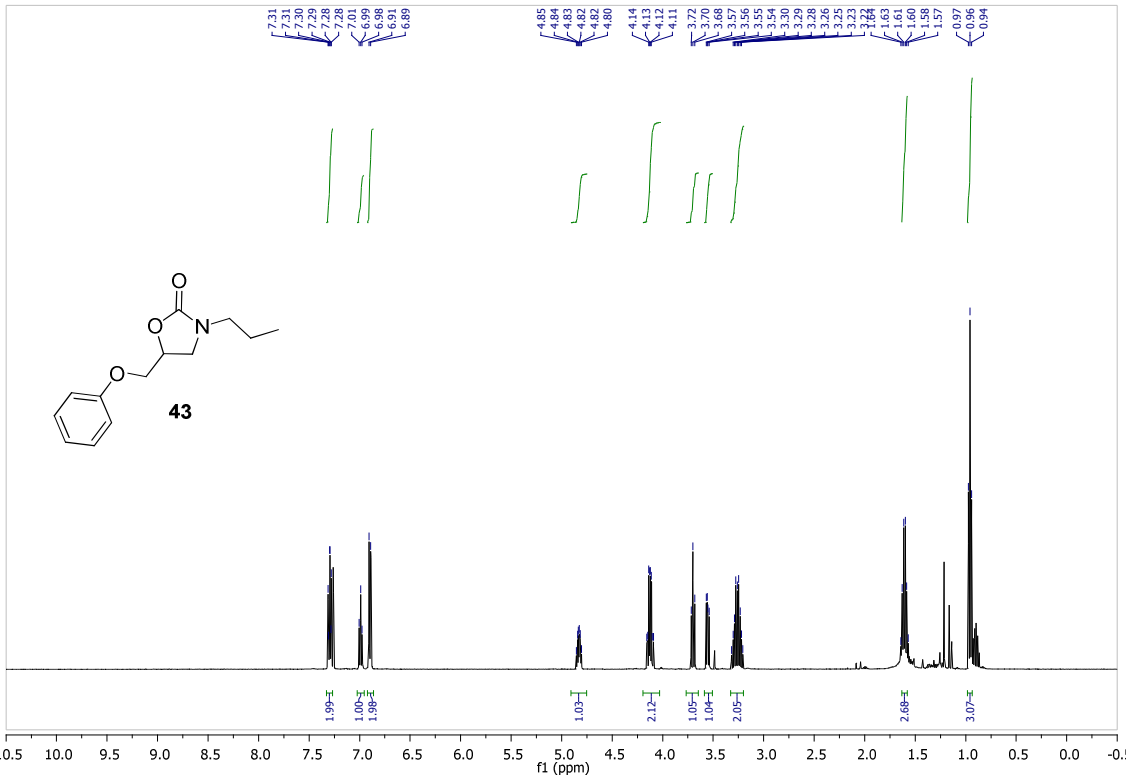


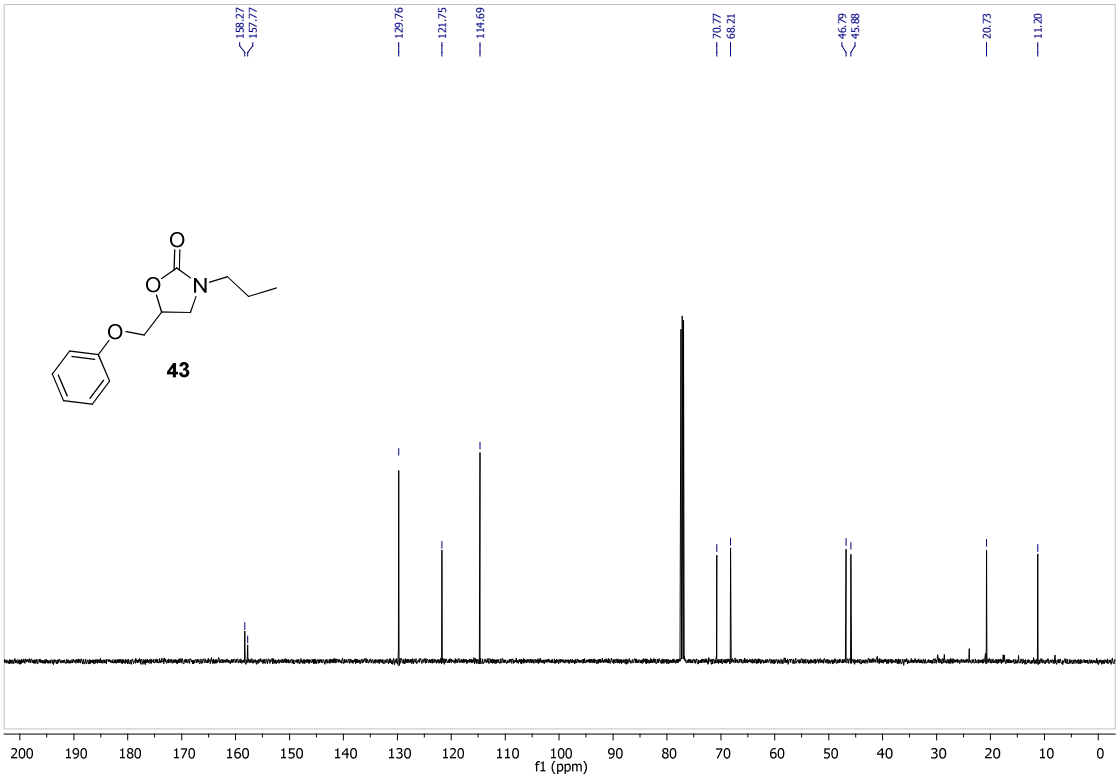
5-(phenoxymethyl)-3-(3-phenylpropyl)oxazolidin-2-one (42)



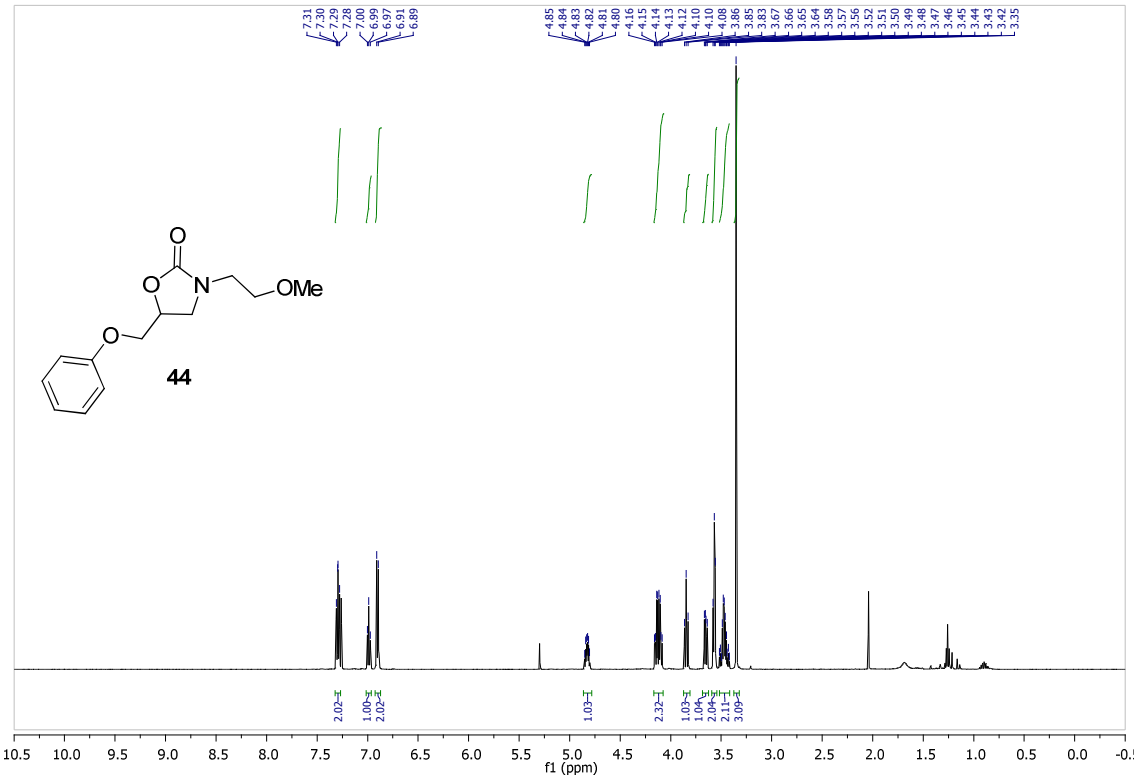


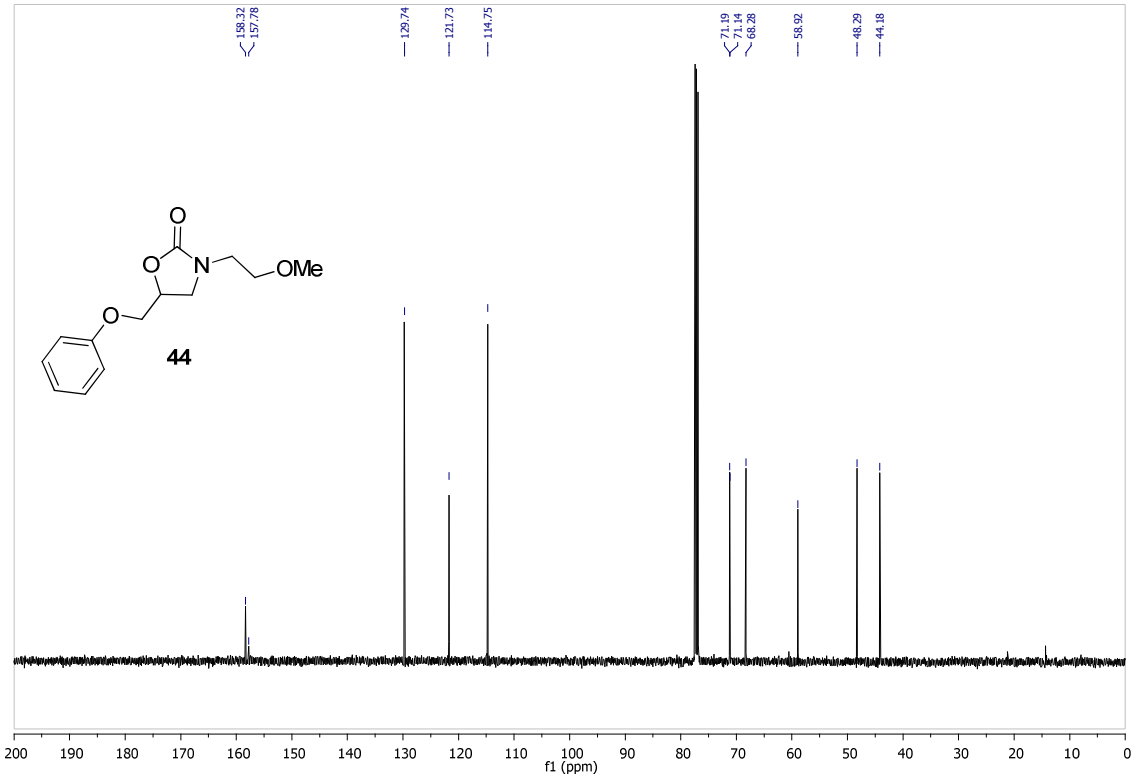
5-(phenoxymethyl)-3-propyloxazolidin-2-one (43)



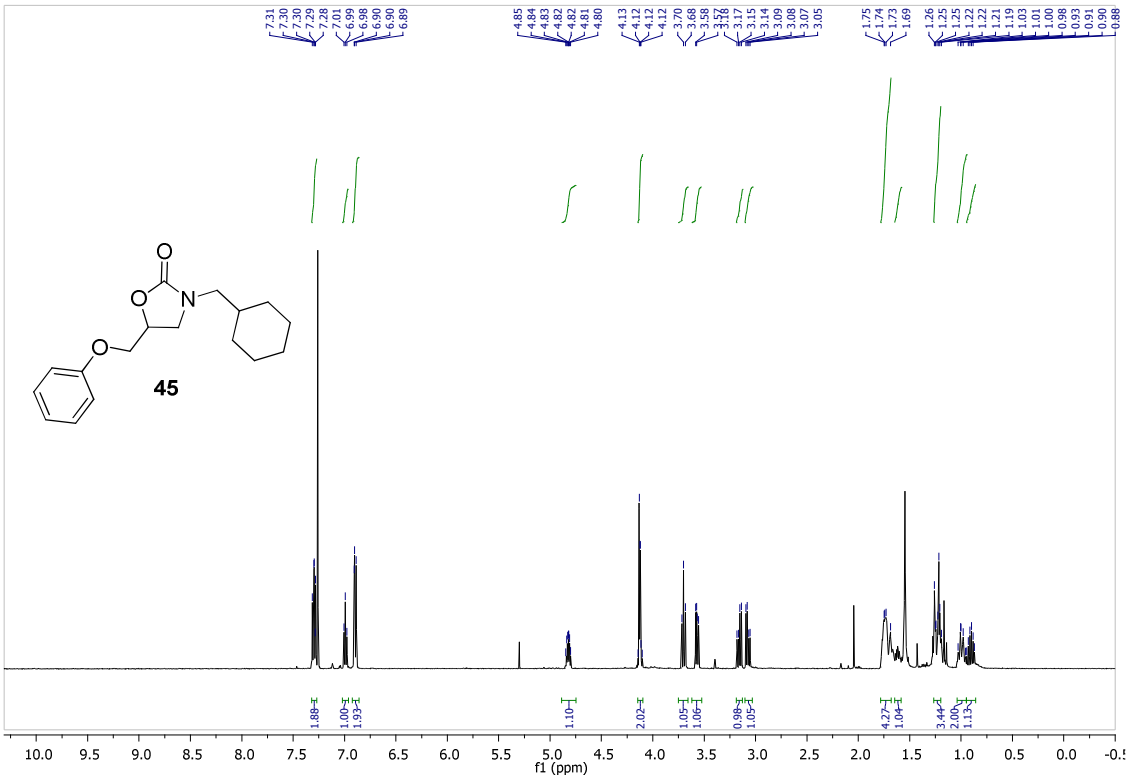


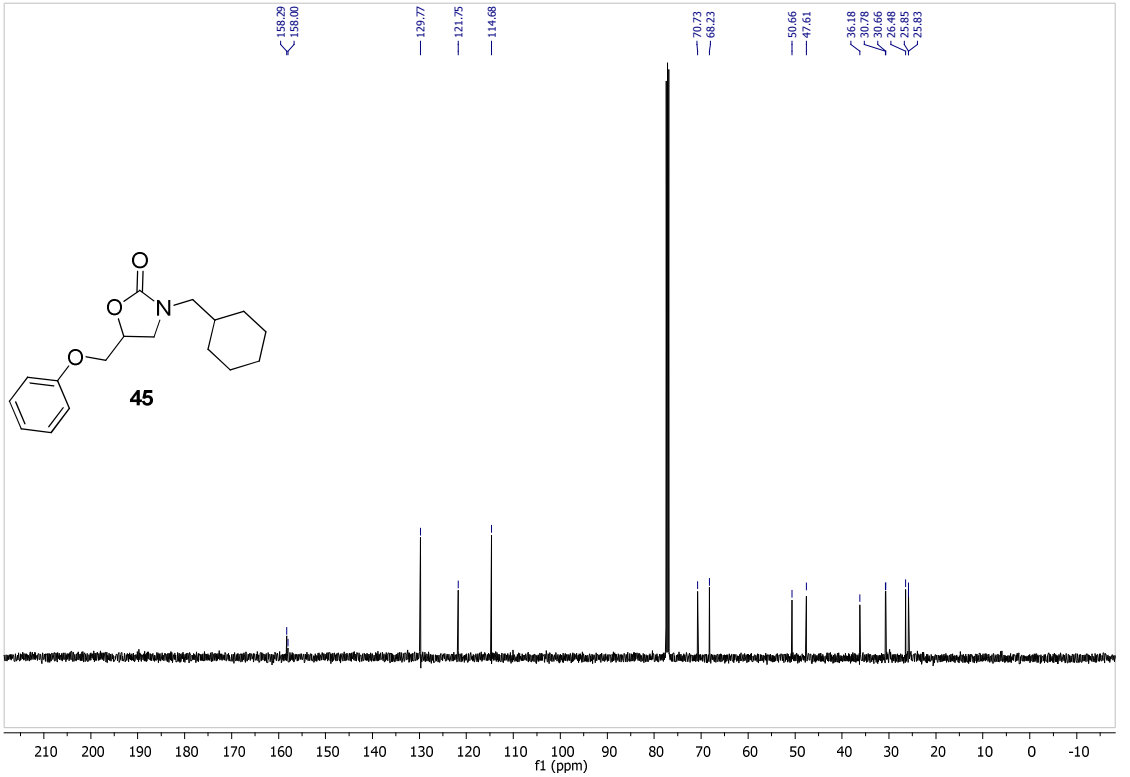
3-(2-methoxyethyl)-5-(phenoxymethyl)oxazolidin-2-one (44)



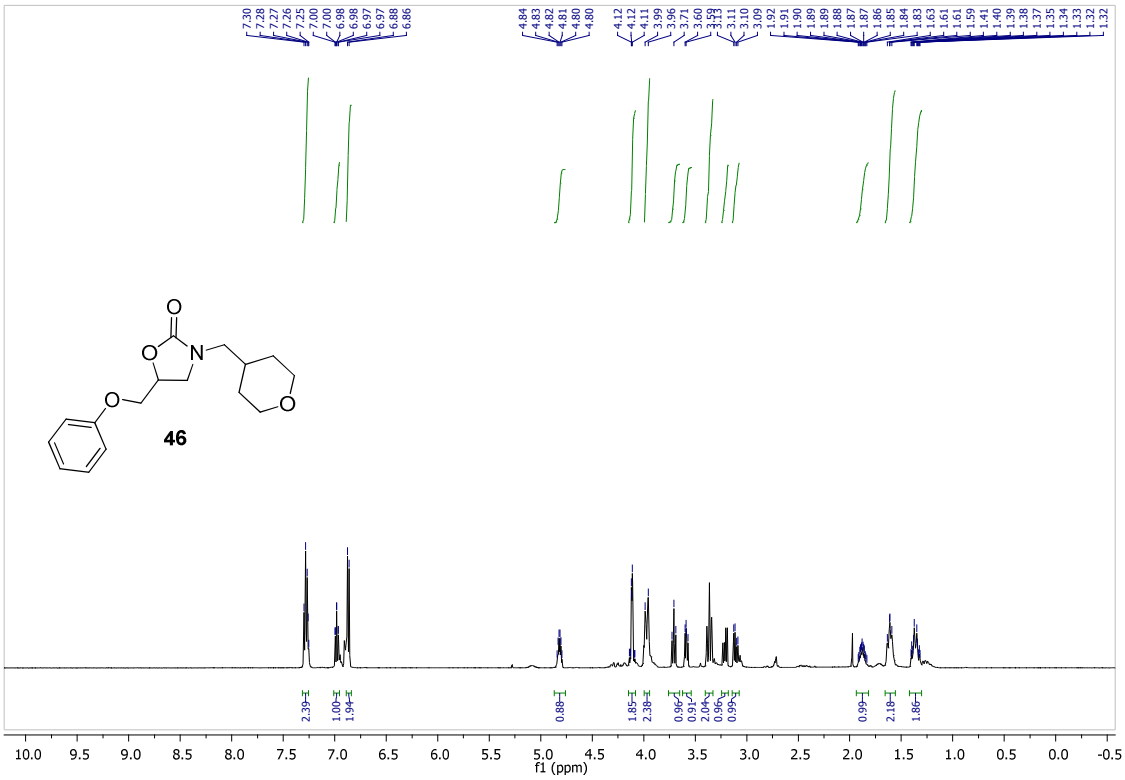


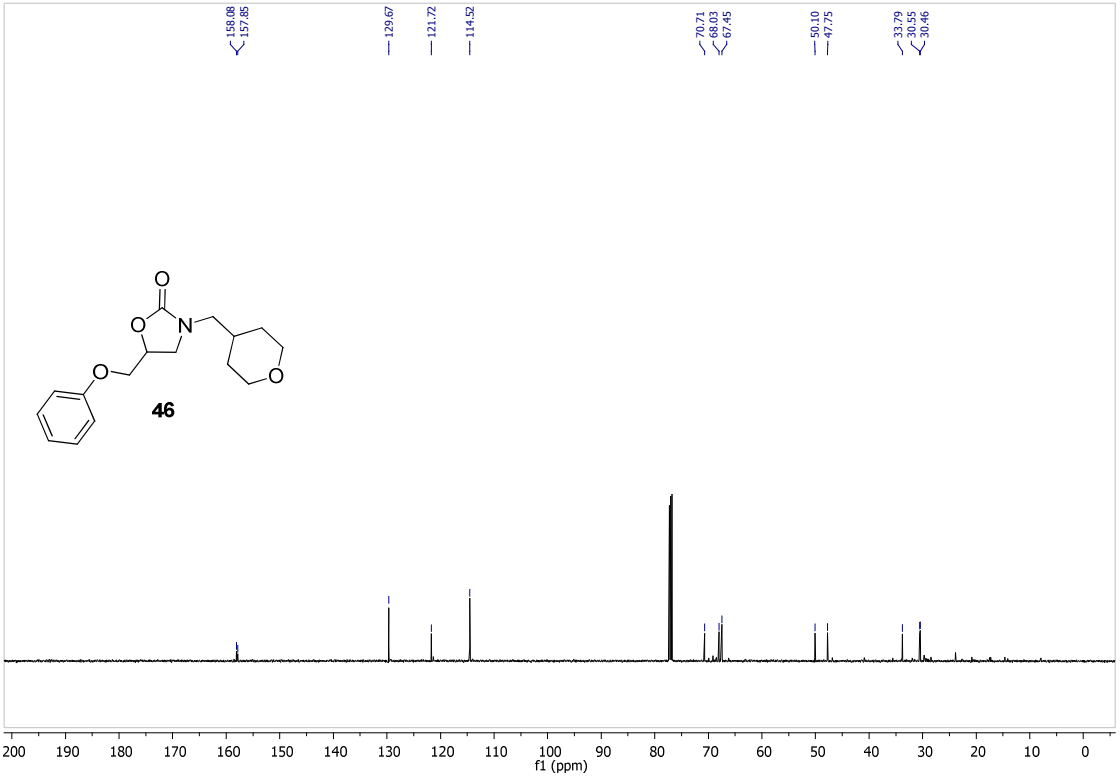
3-(cyclohexylmethyl)-5-(phenoxymethyl)oxazolidin-2-one (45)



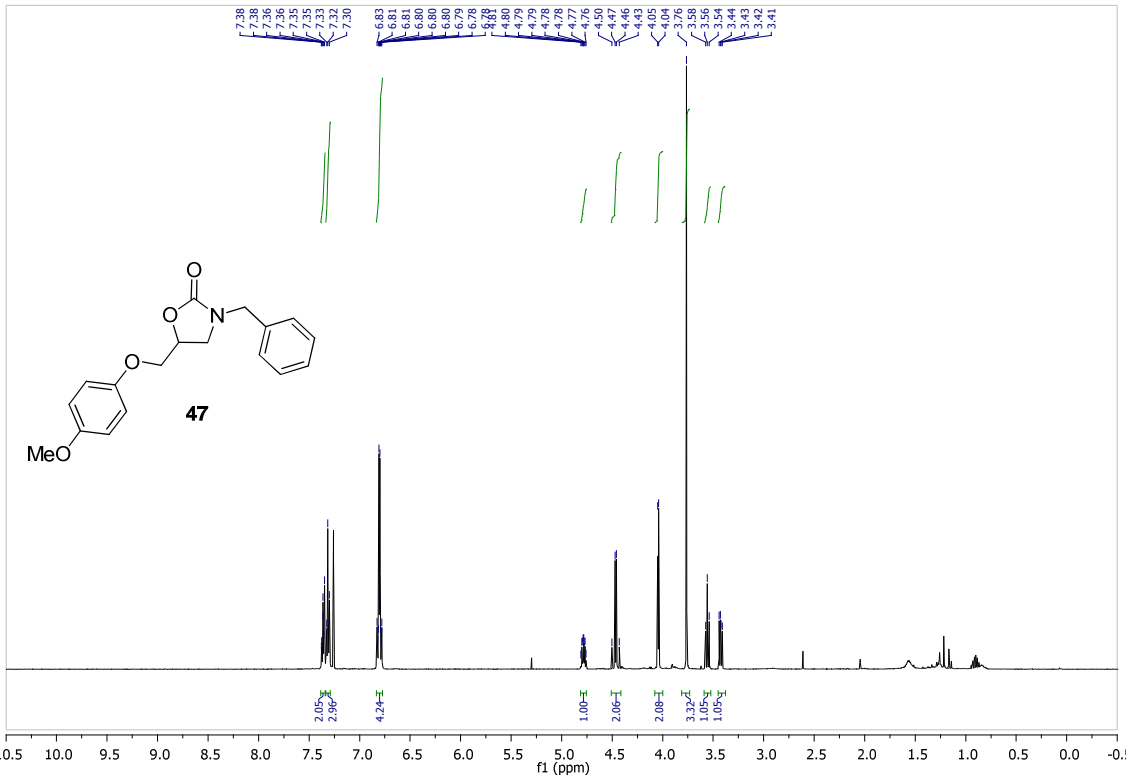


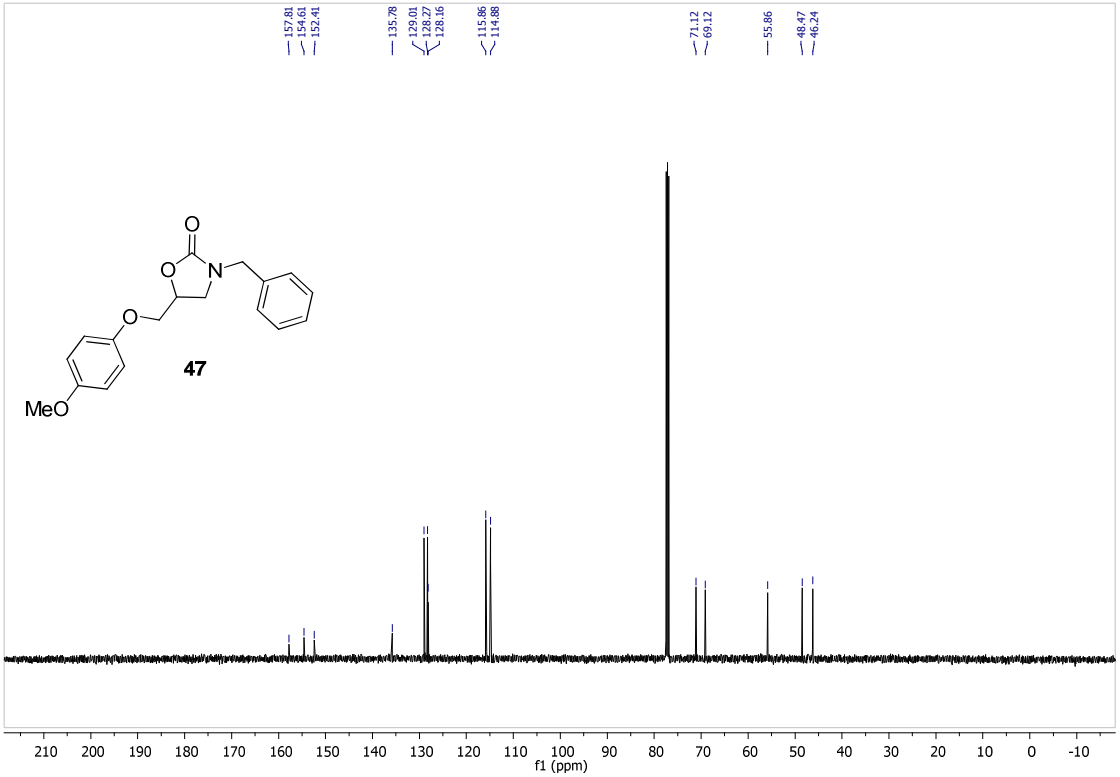
5-(phenoxymethyl)-3-((tetrahydro-2H-pyran-4-yl)methyl)oxazolidin-2-one (46)



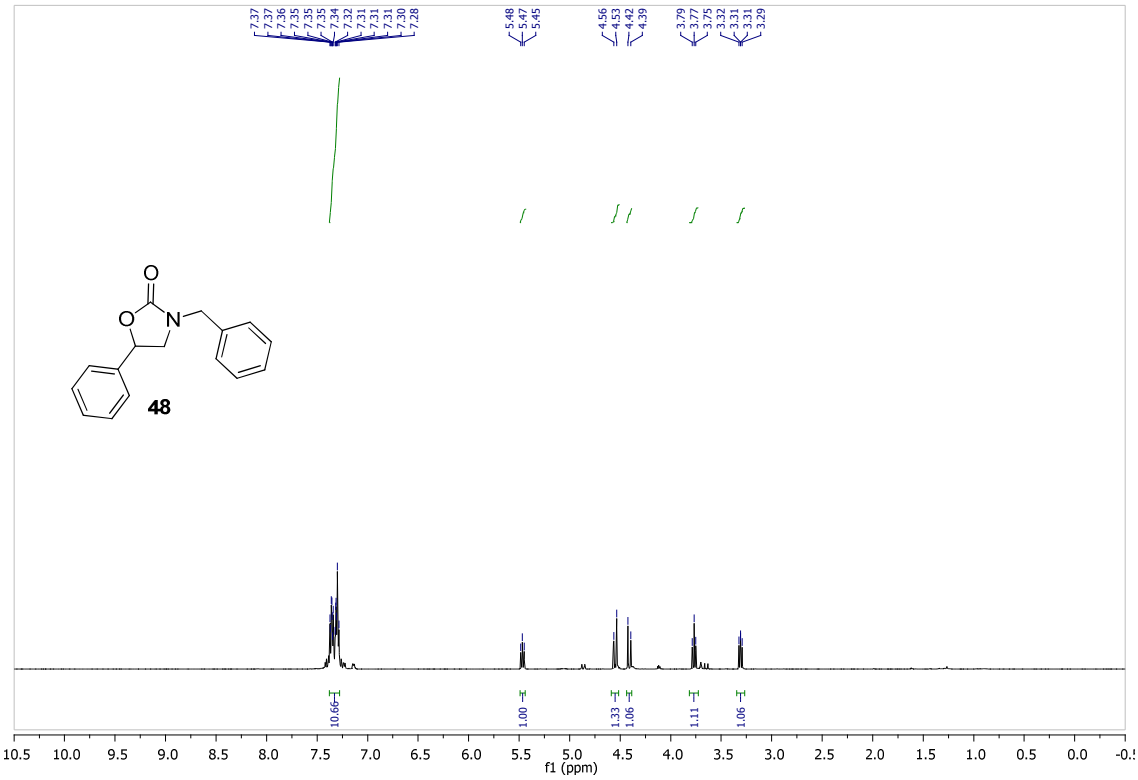


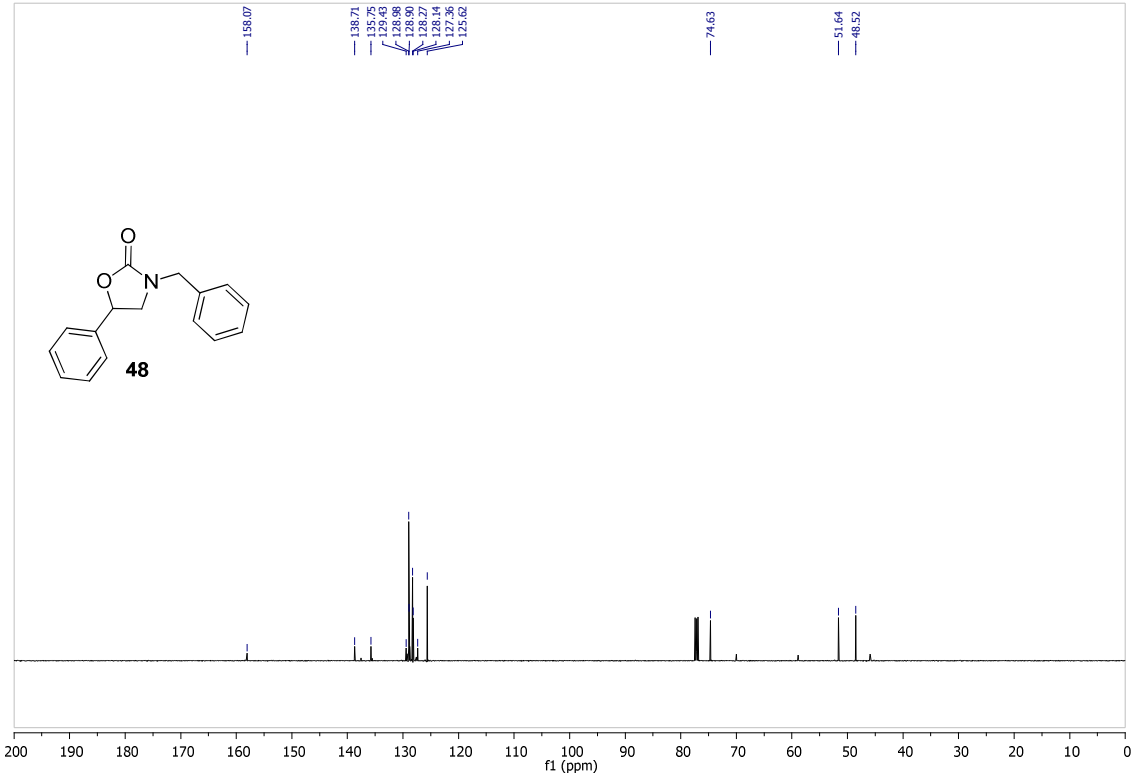
3-benzyl-5-((4-methoxyphenoxy)methyl)oxazolidin-2-one (47)



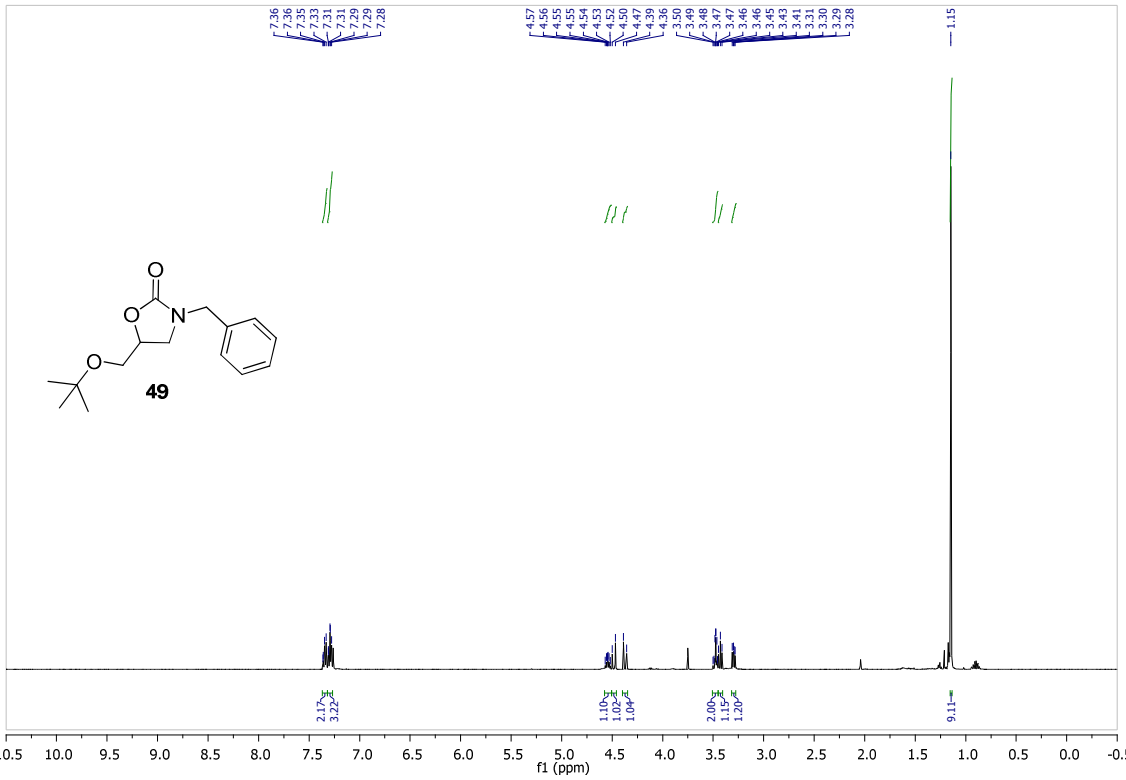


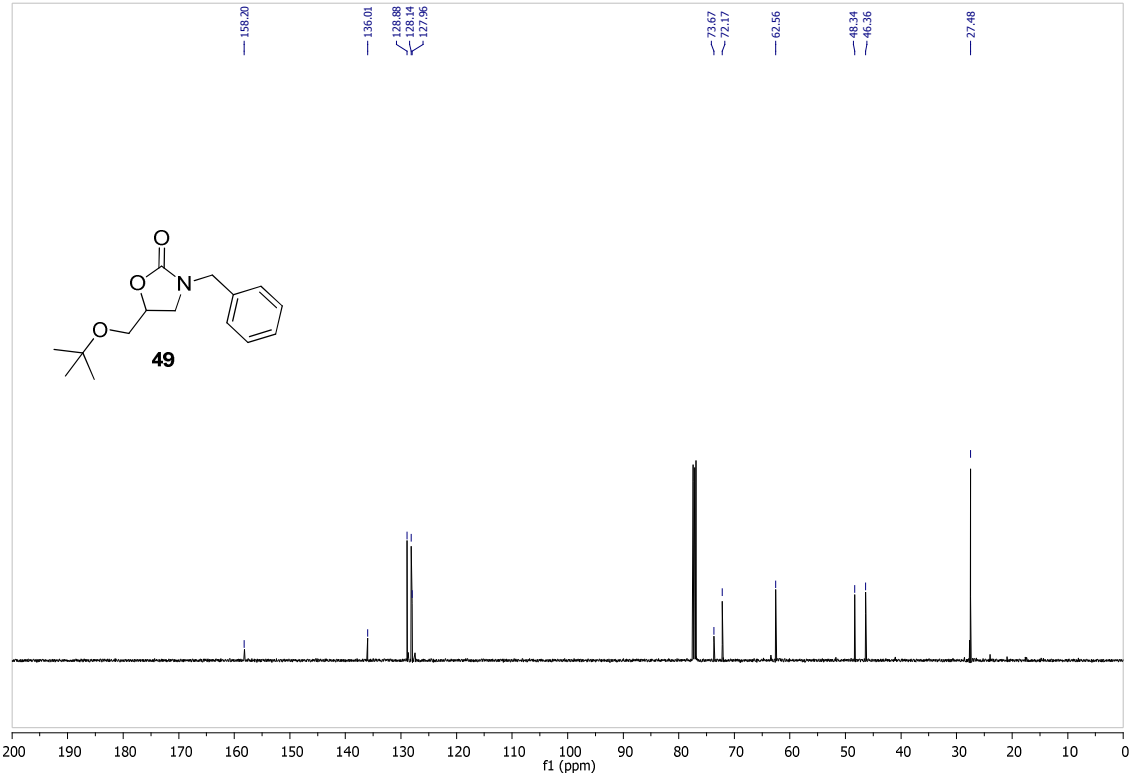
3-benzyl-5-phenyloxazolidin-2-one (48)



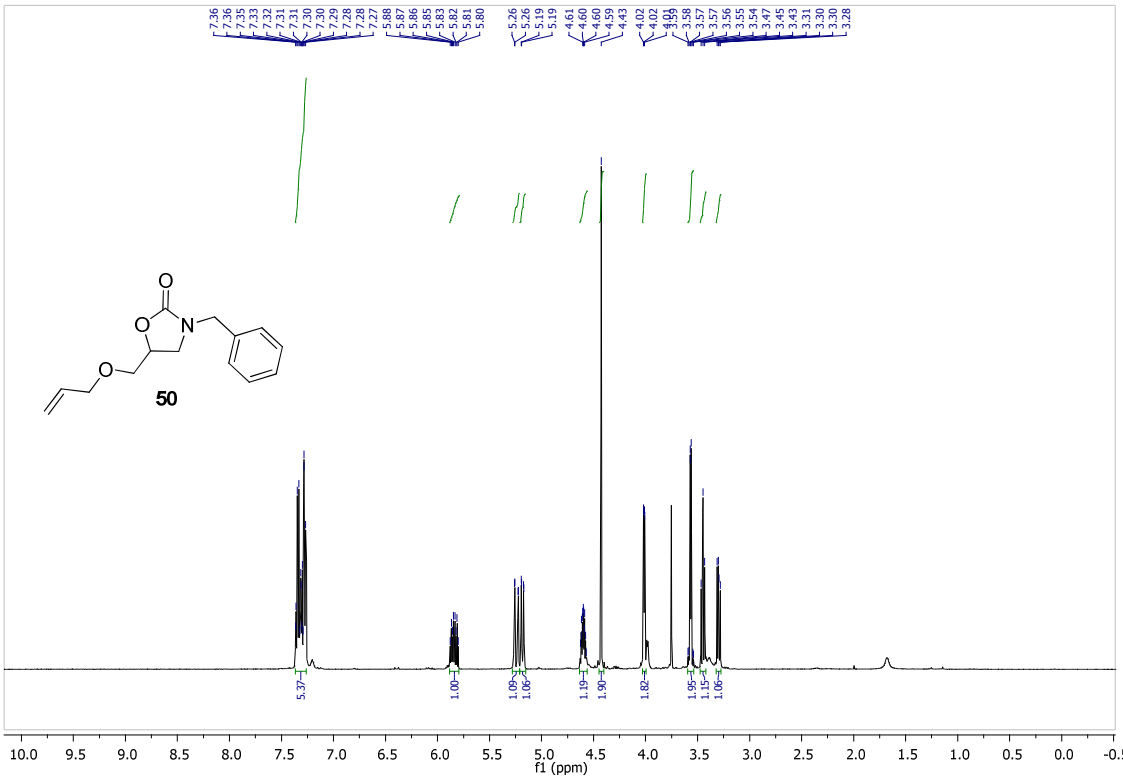


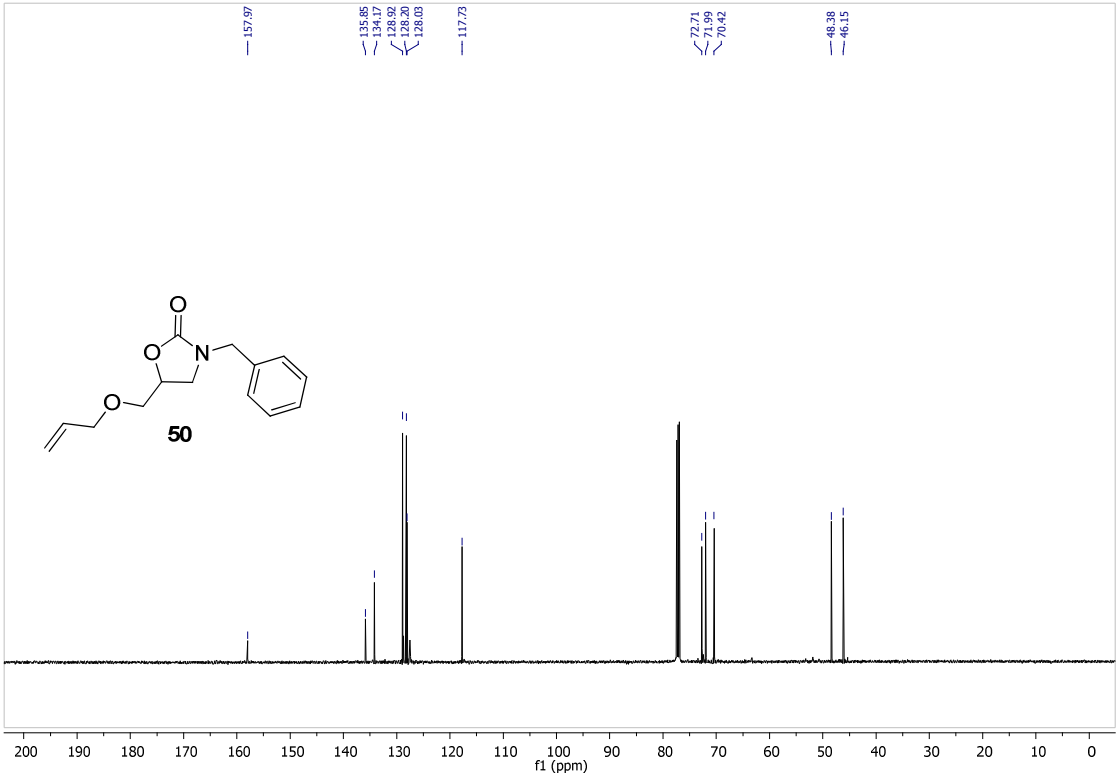
3-benzyl-5-(tert-butoxymethyl)oxazolidin-2-one (49)



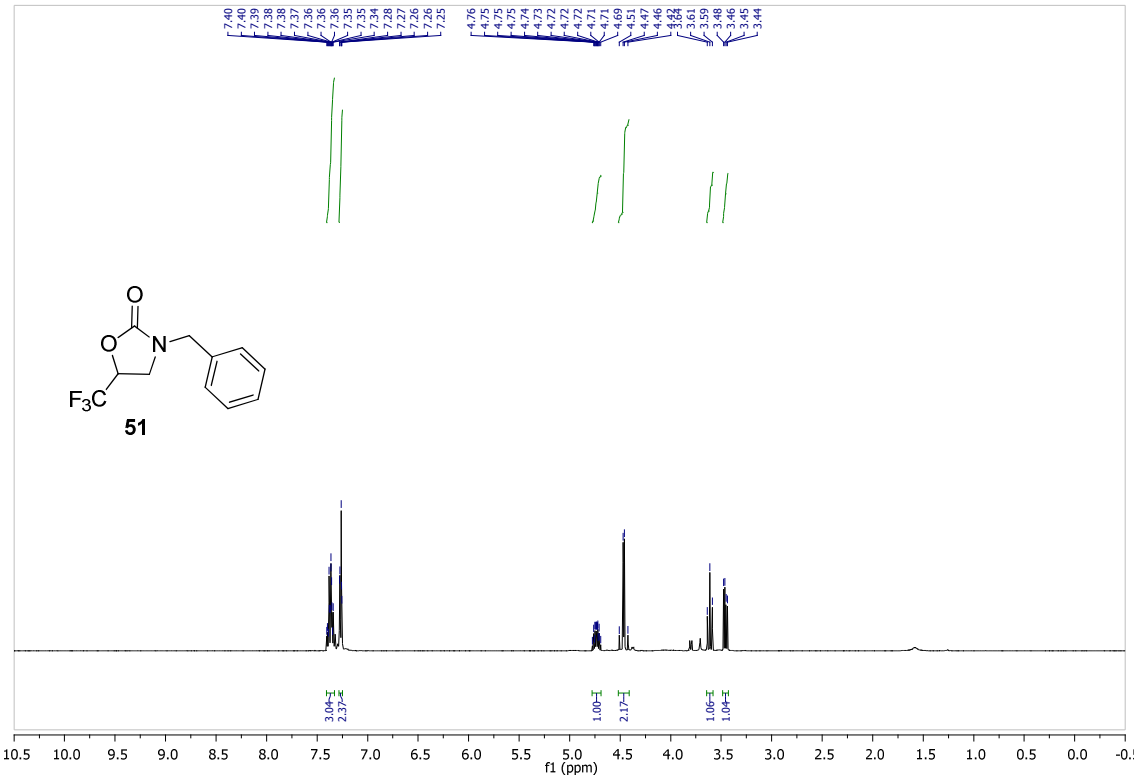


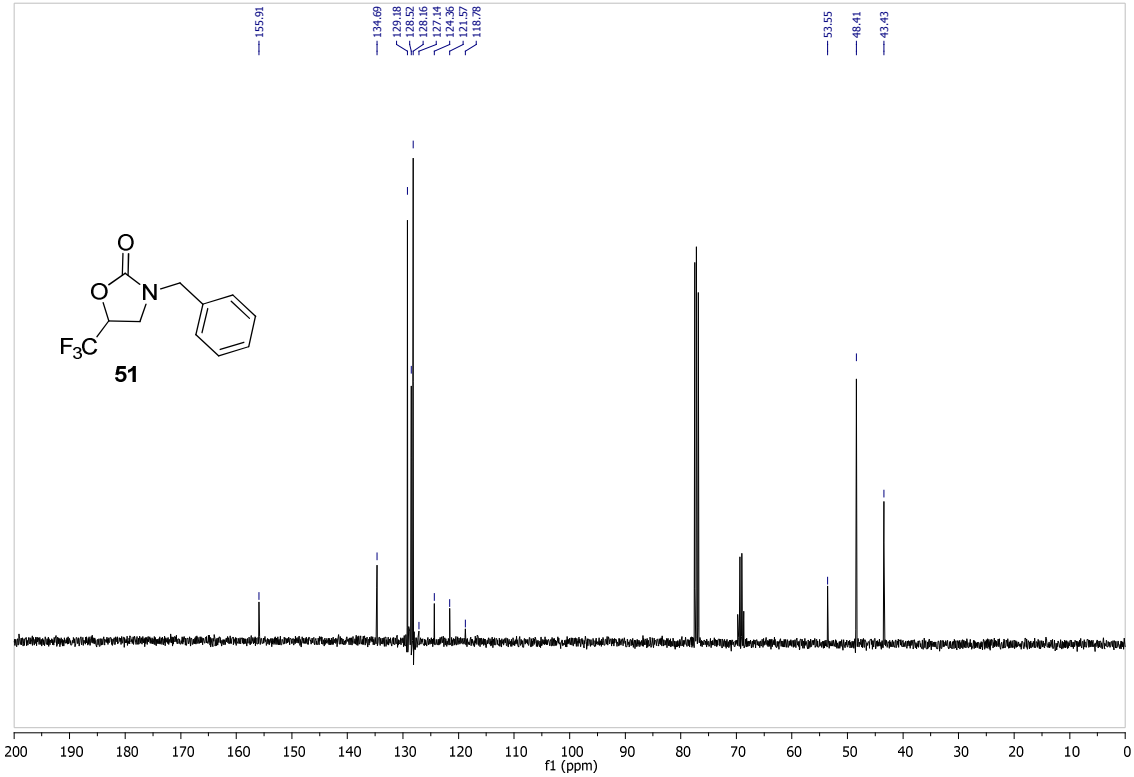
5-((allyloxy)methyl)-3-benzyloxazolidin-2-one (50)



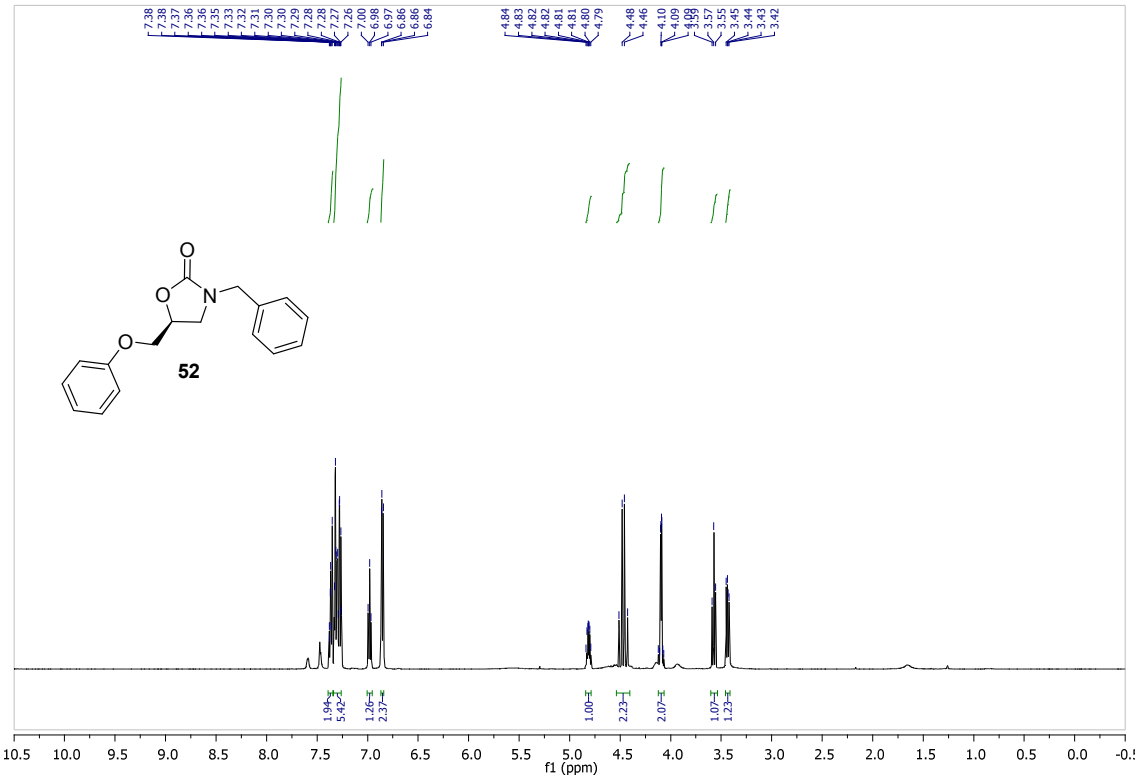


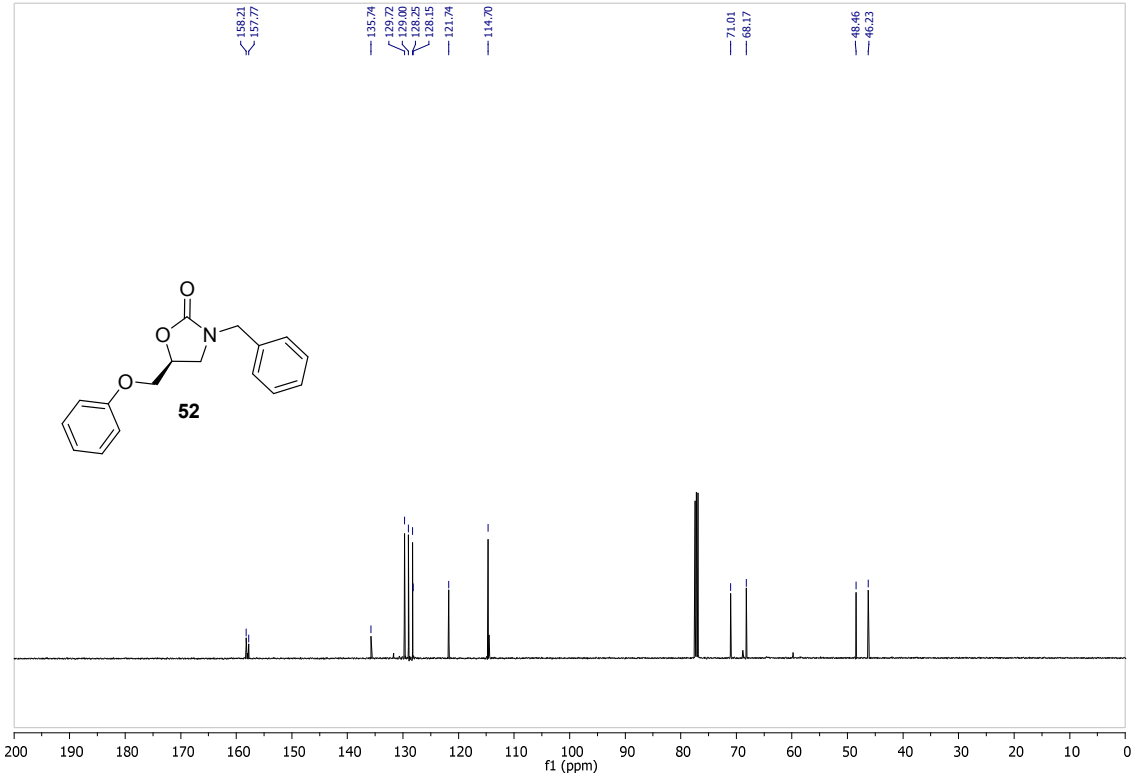
3-benzyl-5-(trifluoromethyl)oxazolidin-2-one (51)





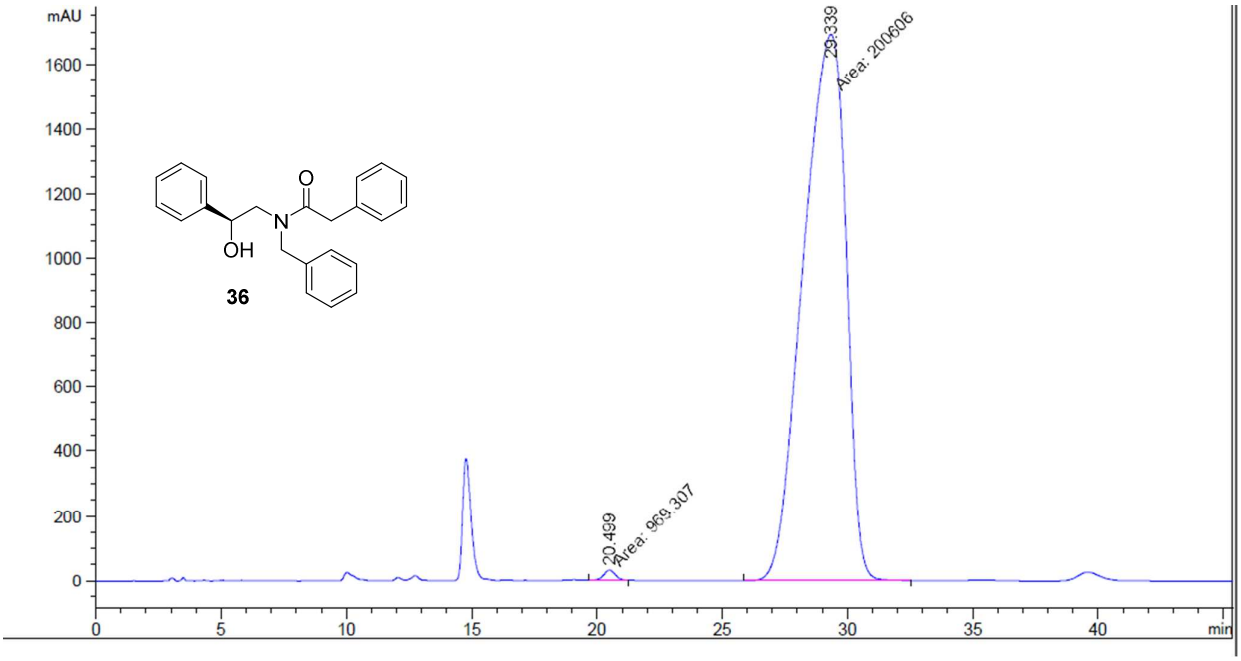
(*S*)-3-benzyl-5-(phenoxymethyl)oxazolidin-2-one (52)

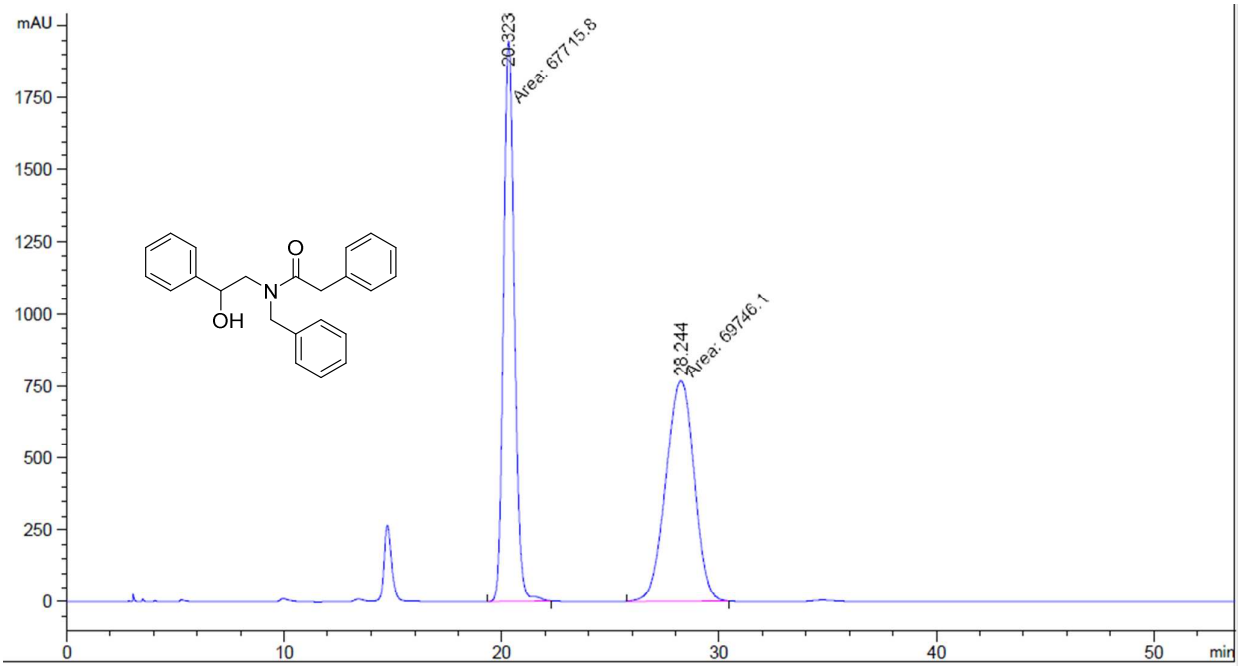




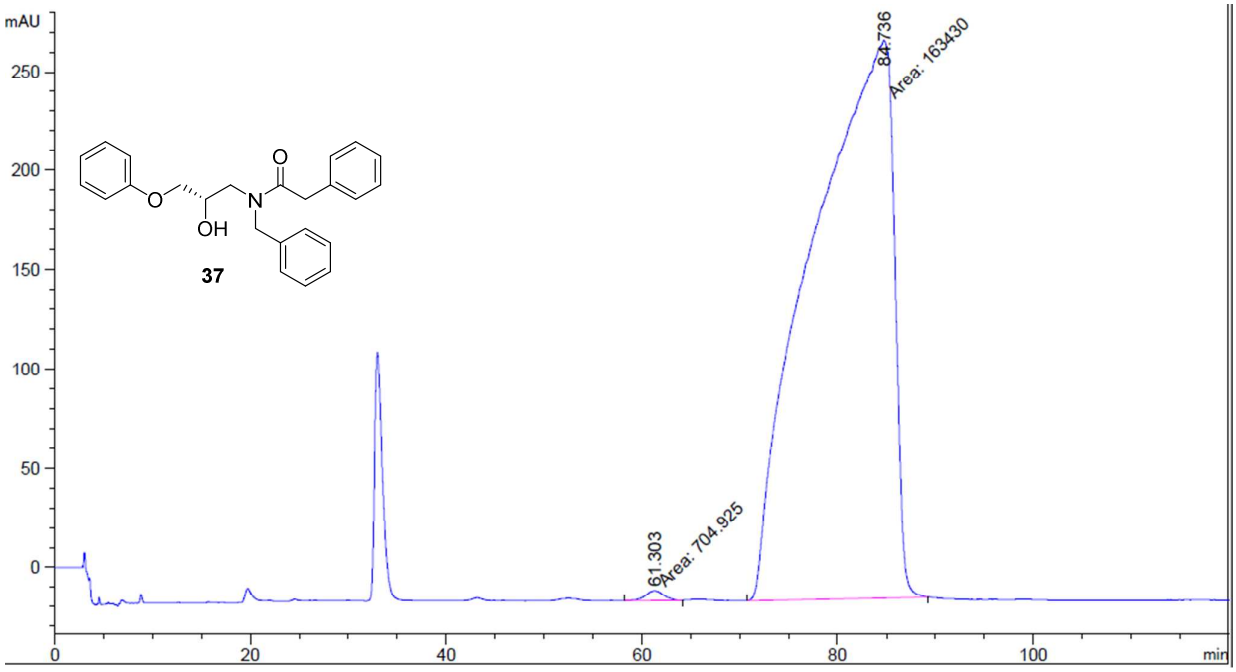
5. Chiral HPLC Spectra

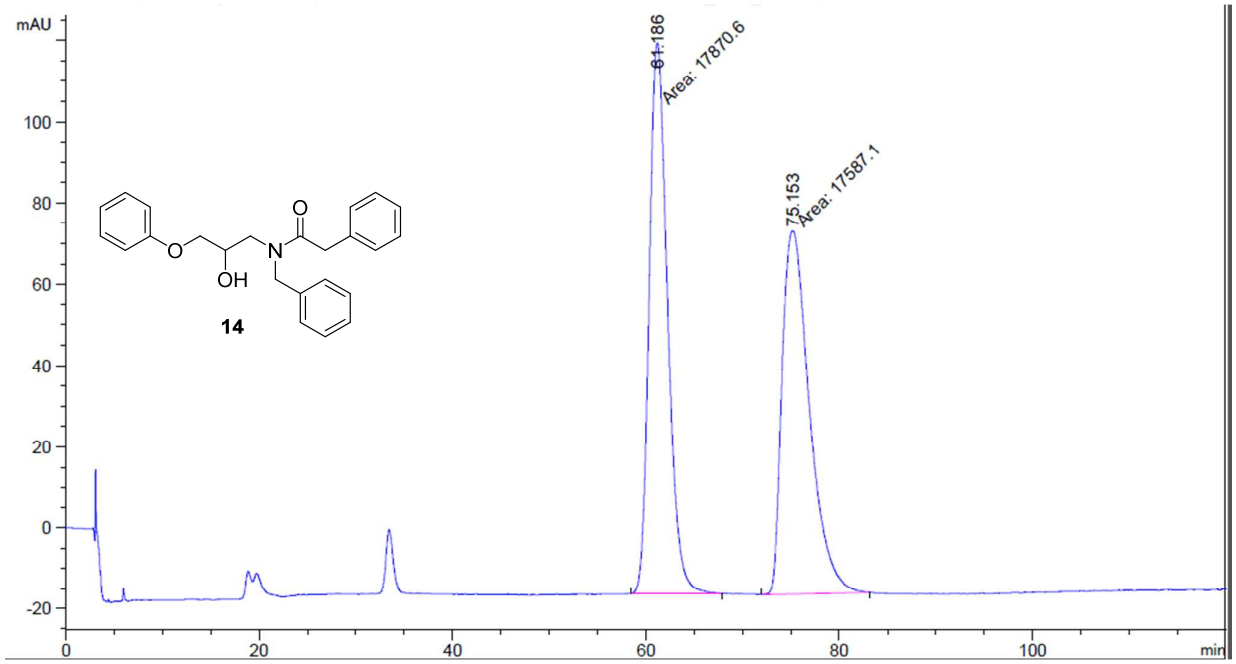
(*S*)-*N*-benzyl-*N*-(2-hydroxy-2-phenylethyl)-2-phenylacetamide (36)



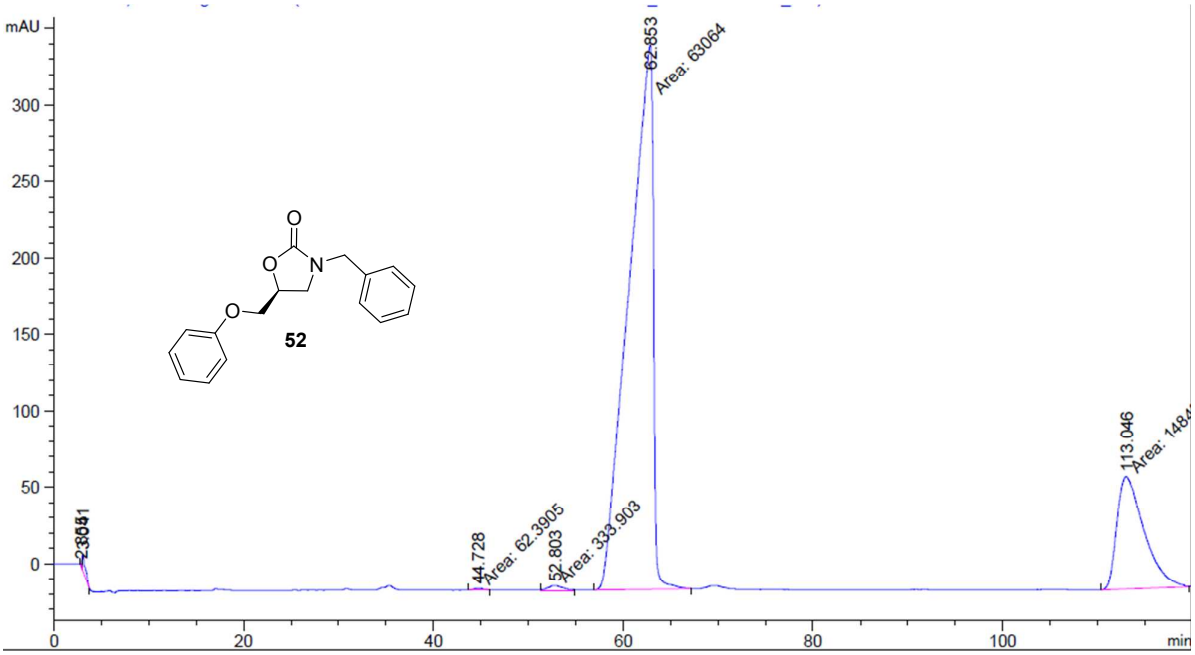


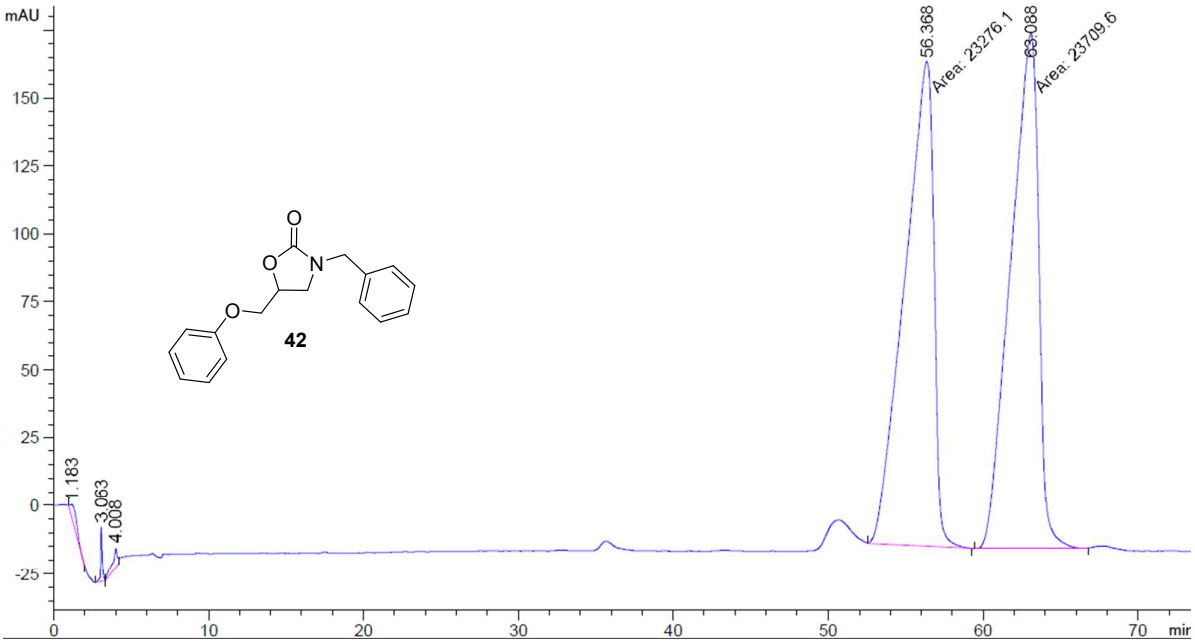
(*S*)-*N*-benzyl-*N*-(2-hydroxy-3-phenoxypropyl)-2-phenylacetamide (37)





(*S*)-3-benzyl-5-(phenoxymethyl)oxazolidin-2-one (52)





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