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Supporting Information

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Synthesis of arylglycines via a novel α-arylation of Weinreb amides

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Supporting Information

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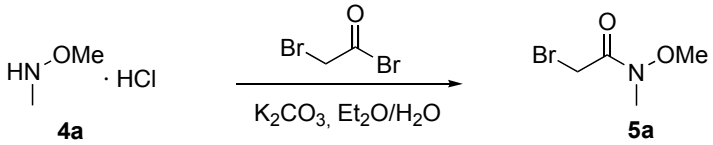
General Experimental procedure.

^{1}H and ^{13}C NMR spectra were recorded at 400 MHz (100 MHz) or 500 MHz (125 MHz) on a Bruker Avance 400 or a Bruker Avance DMX 500 instrument in $CDCl_3$ using the residual peak of $CHCl_3$ (^{1}H NMR δ = 7.26 ppm, ^{13}C NMR δ = 77.0 ppm) as internal standard. Chemical shifts are reported in the δ-scale with multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), integration and coupling constant (Hz). IR-spectra were recorded on an ATI Mattson Infinity Series FTIR and only the strongest/structurally most important peaks (ν_{max}, cm^{-1}) are listed. Optical rotations were determined on a Perkin Elmer Polarimeter 343 at the sodium D line (589 nm) and at ambient temperature. Dichloromethane (CH_2Cl_2) and tetrahydrofuran (THF) were dried by passing through a solvent column composed of activated alumina. Air- and moisture sensitive reactions were carried out in flame-dried, septum-capped flasks under an atmospheric pressure of nitrogen. All liquid reagents were transferred via oven-dried syringes. Commercially available compounds were used without further purification unless otherwise indicated. Lithium diisopropylamide (LDA) solution (1.8 M in tetrahydrofuran/heptane/ethylbenzene) was purchased from Aldrich and titrated before use.[1]

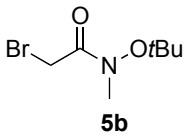
General procedure for the synthesis of bromides 5a-b: [2]

2-bromo-*N*-methoxy-*N*-methylacetamide (5a)



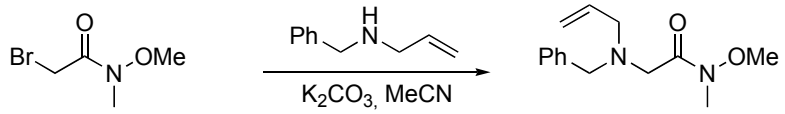
To a cold (-5 °C) solution of K_2CO_3 (6.24 g, 45.0 mmol) in 25 mL H_2O was added hydrochloride **4a** (2.00 g, 20.5 mmol) and 25 mL diethyl ether. Bromoacetyl bromide (1.96 mL, 24.6 mmol) was added dropwise, the cooling bath was removed and the mixture was stirred for 30 min. The layer were separated and the aqueous phase was extracted three times with Et_2O. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to give **5a** as pale yellow oil (2.98 g, 80%) that was directly used in the next step.

***N-tert*-butoxy-2-bromo-*N*-methylacetamide (5b)**



The general procedure was followed using **4b** (14.3 mmol, 2.00 g) and bromoacetyl bromide (4.34 g, 21.5 mmol) to give **5b** as a pale yellow oil (2.65 g, 83%) that was directly used for the next step.

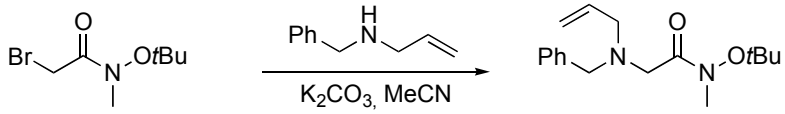
Synthesis of 2-bromo-*N*-methoxy-*N*-methylacetamide (6a)



5a **6a**

To a solution of **5a** (1.51 g, 8.31 mmol) and *N*-allyl-*N*-benzylamine (1.02 g, 6.93 mmol) in 30 mL MeCN was added K_2CO_3 (2.87 g, 20.8 mmol) and the mixture was stirred over night.. The reaction was filtered and concentrated under reduced pressure. Flash chromatography (pentane + 1% *i*PrNH$_2$, EtOAc 5 → 40%) of the residue gave **6a** as a pale yellow oil (1.27 g, 74%): ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.39-7.21 (m, 5H), 5.90 (m, 1H), 5.22 (m, 1H), 5.15 (m, 1H), 3.83 (s, 2H), 3.56 (s, 3H), 3.45 (s, 2H), 3.33 (m, 2H), 3.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 139.1, 136.1, 128.2, 126.9, 117.6, 61.1, 57.8, 57.0, 52.0, 32.1 IR (film) ν_{max} = 2936, 1671, 1454, 1175 cm^{-1}; HRMS (ESI+) calcd for $C_{14}H_{21}N_2O_2$ (M+H): 249,1598, found: 249,1601

2-(*N*-allyl-*N*-benzylamino)-*N*-*tert*-butoxy-*N*-methylacetamide (6b)

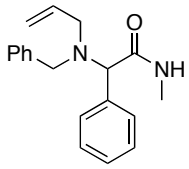


5b **6b**

To a solution of **5b** (556 mg, 2.45 mmol) and *N*-allyl-*N*-benzylamine (365 mg, 2.45 mmol) in 4 mL MeCN was added K_2CO_3 (1.03 g, 7.44 mmol) and the mixture was stirred over night. The reaction was filtered and concentrated under reduced pressure. Flash chromatography (pentane + 1% *i*PrNH$_2$, EtOAc 5 → 30%) of the residue gave **6b** as a colorless oil (579 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39-7.21 (m, 5H), 5.90 (m, 1H), 5.22 (m, 1H), 5.15 (m, 1H), 3.83 (s, 2H), 3.56 (s, 3H), 3.45 (s, 2H), 3.33 (m, 2H), 3.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 139.3, 136.3, 129.1, 128.2, 126.9, 117.5, 82.4, 57.7, 56.8, 27.5; IR (film) ν_{max} = 2936, 1671, 1454, 1175 cm^{-1}; HRMS (ESI+) calcd for $C_{17}H_{27}N_2O_2$ (M+H): 291.2067, found 291.2065.

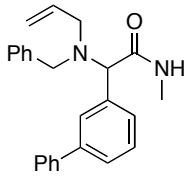
General Procedures for the α-arylation of amide 6b

Procedure A: 2-(*N*-allyl-*N*-benzylamino)-*N*-methyl-2-phenylacetamide (8a)



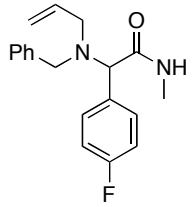
To a solution of amide **6b** (29.0 mg, 0.10 mmol) in THF (2 mL) was added LDA (1.40 M, 71 μL, 0.10 mmol) at -78 °C. The solution was stirred for 1 min and PhMgCl (2.0 M in THF, 100 μL, 0.20 mmol) was added. The reaction was allowed to reach room temperature and quenched with sat. NH_4Cl (1 mL) and brine (1 mL). The aqueous phase was extracted twice with Et_2O and the combined organic extracts were dried (K_2CO_3) and concentrated under reduced pressure. Flash chromatography (pentane + 1% *i*$PrNH_2$, EtOAc 5 → 40%) of the residue gave **8a** (25.2 mg, 86%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.39-7.25 (m, 10H), 7.20 (br, 1H), 5.84 (m, 1H), 5.18 (m, 2H), 4.2 (s, 1H), 3.82 (d, *J* = 14.0 Hz, 1H), 3.33 (d, *J* = 14.0 Hz, 1H), 3.25 (m, 1H), 2.88 (d, *J* = 4.9 Hz, 3H), 2.85 (m, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.2, 138.5, 134.7, 129.8, 128.5, 128.4, 128.1, 127.8, 127.2, 118.4, 68.9, 54.5, 53.2, 26.0; IR (film) ν_{max} = 3308, 1657, 1521, 1453 cm^{-1}; HRMS (ESI+) calcd for $C_{19}H_{23}N_2O_3$ (M+H): 295.1805, found: 295.1801.

Procedure B: 2-(*N*-allyl-*N*-benzylamino)-2-(3-biphenyl)-*N*-methylacetamide (8d)



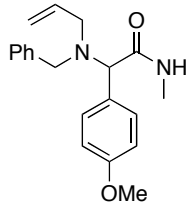
The Grignard reagent was prepared from 3-bromobiphenyl (333 μL, 2.0 mmol) and magnesium powder (73 mg, 3.0 mmol) in 5 mL THF. To a solution of amide **6b** (29.0 mg, 0.10 mmol) in THF (2 mL) was added LDA (1.40 M, 71 μL, 0.10 mmol) at 0 °C. The solution was stirred for 1 min, cooled down to -78 °C and the freshly prepared Grignard solution was added (0.27 M in THF, 0.74 mL, 0.20 mmol). The reaction was allowed to reach room temperature and quenched with sat. NH_4Cl (1 mL) and brine (1 mL). The aqueous phase was extracted twice with Et_2O and the combined organic extracts were dried (K_2CO_3) and concentrated under reduced pressure. Flash chromatography (pentane + 1% *i*$PrNH_2$, EtOAc 5 → 35%) gave **8d** (29.9 mg, 81%) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.52-711 (m, 15H), 5.79 (m, 1H), 5.12 (m, 2H), 4.42 (s, 1H), 3.79 (d, *J* = 14.0 Hz, 1H), 3.31 (d, *J* = 14.0 Hz, 1H), 3.21 (dd, *J* = 14.6, 4.9 Hz), 2.85 (m, 1H), 2.83 (d, J = 4.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.2, 141.2, 141.1, 138.6, 135.3, 135.2, 134.8, 128.8, 128.8, 128.7, 128.6, 128.6, 127.3, 127.3, 126.8, 118.6, 69.2, 54.8, 53.4, 26.2; IR (film) ν_{max} = 3310, 2928, 1660, 1521, 1411 cm^{-1}; HRMS (ESI+) calcd for $C_{25}H_{27}N_2O$ (M+H): 371.2118, found: 371.2114.

2-(*N*-allyl-*N*-benzylamino)-2-(4-fluorophenyl)-*N*-methylacetamide (8b)



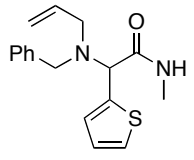
The general procedure A was followed using 1.5 equiv LDA (1.40 M, 107 μL, 0.15 mmol) and 4-FPhMgBr (1.0 M in THF, 200 μL, 0.20 mmol) to give **8b** as a colorless oil (24.1 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.29-7.12 (m, 8H), 6.95 (m, 2H), 5.74 (m,1H), 5.10 (m, 2H), 4.32 (s, 1H) , 3.72 (d, J = 14.0 Hz, 1H), 3.20 (d, J = 14.0 Hz, 1H), 3.15 (m, 1H), 2.78 (d, J = 4.8 Hz, 3H), 2.73 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.0, 163.3, 161.3, 138.3, 134.7, 131.5, 131.5, 130.3, 130.3, 128.5, 128.4, 127.3, 118.5, 115.1, 114.9, 67.9, 54.5, 53.2, 26.0; IR (film) ν_{max} = 3309, 1660, 1508, 1224 cm^{-1}; HRMS (ESI+) calcd for $C_{19}H_{22}FN_2O$ (M+H): 313.1711, found: 313.1711.

2-(*N*-allyl-*N*-benzylamino)-2-(4-methoxyphenyl)-*N*-methylacetamide (8c)



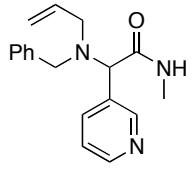
The general procedure A was followed using 4-MePhMgBr (1.0 M in THF, 200 μL, 0.20 mmol). Flash chromatography (pentane + 1% *i*PrNH$_2$, EtOAc 5→40%) gave **8c** (29.8 mg, 92%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.28-7.10 (m, 8H), 6.81 (m, 2H), 5.76 (m, 1H), 5.10 (m, 2H), 4.29 (s, 1H), 3.72 (m, 4H), 3.23 (d, J = 14.0 Hz, 1H), 3.15 (m, 1H), 2.79 (d, J = 4.1 Hz, 3H), 2.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.5, 159.1, 138.6, 134.8, 130.9, 128.47, 128.42, 127.1, 126.8, 118.3, 113.6, 68.3, 55.1, 54.5, 53.1, 26.0; IR (film) ν_{max} = 3309, 2934, 1659, 1511, 1248 cm^{-1}; HRMS (ESI+) calcd for $C_{20}H_{25}N_2O_2$ (M+H): 325.1911, found: 325.1911.

2-(*N*-allyl-*N*-benzylamino)-*N*-methyl-2-(thiophen-2-yl)acetamide) (8e)



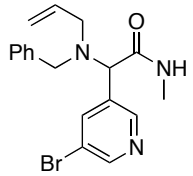
The general procedure A was followed using 1.5 equiv LDA (1.40 M, 107 μL, 0.15 mmol) to give **8e** as a colorless oil (27.3 mg, 91%).: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.37-7.25 (m, 6H), 7.16 (br, 1H), 7.02 (m, 1H), 6.98 (m, 1H), 5.86 (m, 1H), 5.23 (m, 2H), 4.71 (s, 1H), 3.83 (d, J = 13.8 Hz, 1H), 3.39 (d, J = 13.8 Hz, 1H), 3.25 (m, 1H), 2.93 (m, 1H), 2.87 (d, J = 5.0 Hz, 3H) ;^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.1, 138.4, 136.4,135.0, 128.6, 128.5, 128.4, 127.3, 126.3, 125.6, 118.4, 63.3, 54.6, 53.5, 26.1; IR (film) ν_{max} = 3307, 1661, 1522, 1409 cm^{-1}; HRMS (ESI+) calcd for $C_{17}H_{21}N_2OS$ (M+H): 301.1369, found: 301.1366.

2-(*N*-allyl-*N*-benzylamino)-*N*-methyl-2-(pyridin-3-yl)acetamide (8f)



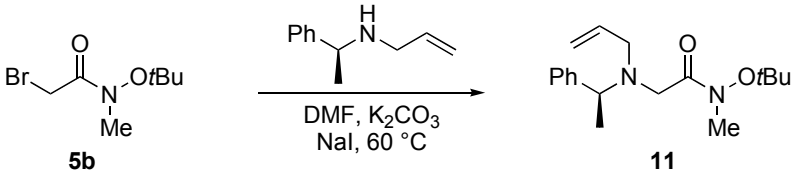
The Grignard reagent was prepared from 3-bromopyridine (19.3 μL, 0.20 mmol) and *i*PrMgCl · LiCl (1.0 M in THF, 200 μL, 0.20 mmol).[3] The general procedure B was followed. Flash chromatography (pentane + 1% *i*PrNH$_2$, EtOAc 5 → 50%) gave **8f** (22.7 mg, 77%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.48 (m, 1H), 8.41 (s, 1H), 7.54 (m, 1H), 7.33-7.12 (m, 7H), 5.76 (m, 1H), 5.15 (m, 2H), 4.40 (s, 1H), 3.77 (d, J = 13.9 Hz, 1H), 3.19 (m, 1H), 3.15 (d, J = 13.9 Hz, 1H), 2.82 (d, J = 4.9 Hz, 3H), 2.69 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.2, 151.1, 149.1, 138.0, 137.5, 134.6, 127.5, 123.0, 118.8, 65.9, 54.7, 53.4, 26.1; IR (film) ν_{max} = 3293, 2930, 1664, 1524, 1424 cm^{-1}; HRMS (ESI+) calcd for $C_{18}H_{21}N_3O$ (M+H): 296.1757, found: 296.1758.

2-(*N*-allyl-*N*-benzylamino)-2-(5-bromopyridin-3-yl)-*N*-methylacetamide (8g)



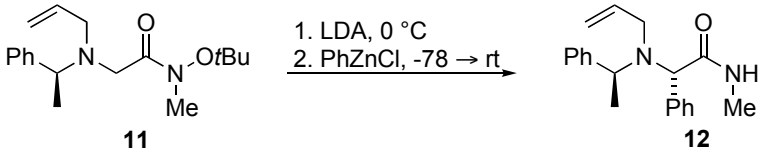
The Grignard reagent was prepared from 3,5-dibromopyridine (47.4 mg, 0.20 mmol) and *i*PrMgCl · LiCl (1.0 M in THF, 200 μL, 0.20 mmol).[3] The general procedure B was followed. Flash chromatography (pentane + 1% *i*PrNH$_2$: EtOAc 5 → 50%) gave **8g** (28.4 mg, 76%) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.56 (s, 1H), 8.32 (s, 1H), 7.68 (s, 1H), 7.33–7.19 (m, 6H), 5.76 (m, 1H), 5.18 (m, 2H), 4.38 (s, 1H), 3.78 (d, J = 13.8 Hz, 1H), 3.20 (m, 1H), 3.14 (d, J = 13.8 Hz, 1H), 2.83 (d, J = 5.3 Hz, 3H), 2.68 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 170.6, 150.2, 149.2, 140.1, 137.7, 134.5, 131.4, 128.8, 128.4, 127.7, 120.4, 119.1, 65.3, 54.8, 53.5, 26.2; IR (film) ν_{max} = 3321, 3065, 2929, 1667, 1523, 1420 cm^{-1}; HRMS (ESI+) calcd for $C_{18}H_{21}BrN_3O$ (M+H): 374.0863, found: 374.0861.

2-(*N*-allyl-*N*-((*S*)-1-phenylethyl)amino)-*N*-*tert*-butoxy-*N*-methylacetamide (11)



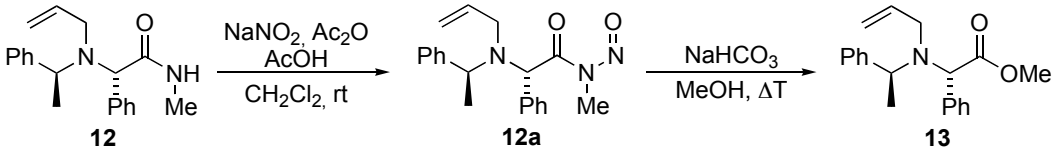
To a solution of *N*-((*S*)-1-phenylethyl)prop-2-en-1-amine (1.00 g, 6.20 mmol), bromide **5b** (1.53 g, 6.82 mmol) and sodium iodide (186 mg, 1.24 mmol) in DMF (10 mL) was added K_2CO_3 (1.71 g, 12.40 mmol). The resultant mixture was stirred for 24 h at 60 °C and quenched with H_2O (20 mL). The mixture was extracted three times with Et_2O and the combined organic extracts were washed with water, brine, dried over K_2CO_3 and concentrated under reduced pressure. Flash chromatography (pentane + 1% *i*PrNH$_2$,) of the residue gave **11** (1.72 g, 91%) as a colorless oil: $[\alpha]_D^{20}$ = -17.8 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.40-7.18 (m, 5H), 5.82 (m, 1H), 5.15 (m, 1H), 5.07 (m, 1H), 4.25 (q, *J* = 6.7 Hz, 1H), 3.67-3.43 (m, 2H), 3.33-3.21 (m, 2H), 3.19 (s, 3H),1.34 (d, 3H, *J* = 6.7 Hz), 1.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 145.0, 136.9, 128.2, 127.6, 126.7, 116.9, 82.2, 59.9, 54.1, 49.3, 39.3, 27.5, 20.0; IR (film) ν_{max} = 2977, 2935, 1677, 1366, 1523, 1157 cm^{-1}; HRMS (ESI+) calcd for $C_{18}H_{28}N_2O_2$ (M+H): 305.2224, found: 305.2228.

(*S*)-2-(*N*-allyl-*N*-((*S*)-1-phenylethyl)amino)-*N*-methyl-2-phenylacetamide (12)



To a solution of $ZnCl_2$ (327 mg, 2.40 mmol) in 5 mL THF was added PhMgCl (2.0 M in THF, 1.2 mL, 2.40 mmol) and the resultant mixture was stirred for 30 min at rt. To a solution of **11** (609 mg, 2.0 mmol) in 20 mL Et_2O was added LDA (1.39 M, 1.51 mL, 2.1 mmol) at 0 °C and the resultant yellow solution was stirred for 1 min. The mixture was cooled down to -78 °C and the freshly prepared solution of PhZnCl was added and the temperature was allowed to reach room temperature. The reaction mixture was quenched with sat. NH_4Cl (5 mL) and brine (10 mL) and the phases were separated. The aqueous layer was extracted with 2*Et_2O and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure (diastereomeric ratio: 87:13, ^{1}H-NMR analysis on the crude product). Flash chromatography (hexane, THF 2 → 18%) gave **12** as a diasteromeric mixture (458 mg, 74%). The diastereomers can be separated by flash chromatography (pentane, Et_2O 5 → 20%) to yield **12** as a colourless oil: $[\alpha]_D^{20}$ = +9.2 (*c* 0.85, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.41-7.24 (m, 10H), 6.94 (br, 1H), 5.65 (m, 1H), 5.03 (m, 2H), 4.47 (s, 1H), 4.12 (q, *J* = 6.9 Hz, 1H), 3.31 (m, 1H), 3.15 (m, 1H), 2.75 (d, *J* = 5.0 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.9, 143.6, 137.2, 129.6, 128.4, 128.4, 127.8, 127.5, 127.0, 116.8, 69.1, 57.5, 51.1, 25.8, 15.3; IR (film) ν_{max} = 2970, 2931, 1658, 1523, 1452 cm^{-1}; HRMS (ESI+) calcd for $C_{20}H_{25}N_2O$ (M+H): 309.1961, found: 309.1958.

(*S*)-2-(*N*-allyl-*N*-((*S*)-1-phenylethyl)amino)-*N*-methyl-*N*-nitroso-2-phenylacetamide (12a)

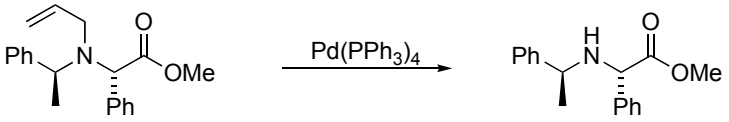


12 **12a** **13**

To a solution of amide **12** (117.4 mg, 0.38 mmol) in CH_2Cl_2 (6 mL), Ac_2O (2 mL) and acetic acid (0.2 mL) was added sodium nitrite (263 mg, 3.8 mmol) and the mixture was stirred for 6 h at rt. The reaction was diluted with toluene (20 mL), filtered and concentrated under reduced pressure to give crude nitrosoamide **12a** as a deep yellow oil, which was directly used in the next step.

(*S*)-methyl 2-(*N*-allyl-*N*-((*S*)-1-phenylethyl)amino)-2-phenylacetate (13): To a solution of crude nitrosoamide **12a** in 10 ml MeOH was added sat. $NaHCO_3$ (5 mL). The mixture was slowly heated to reflux, diluted with brine and extracted three times with Et_2O. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (pentane, Et_2O 2 → 20%) gave **13** as a colourless oil (98.2 mg, 84%): $[\alpha]_D^{20}$ = + 22.2 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.36-7.14 (m, 10H), 5.63 (m, 1H), 4.98 (m, 1H), 4.85 (m, 1H), 4.57 (s, 1H), 4.01 (q, *J* = 6.9 Hz, 1H), 3.50 (s, 3H), 3.31 (m, 2H), 1.29 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 173.1, 143.9, 139.1, 137.9, 128.6, 128.3, 128.2, 127.7, 127.6, 126.9, 115.0, 66.3, 59.1, 56.2, 50.5, 19.1; IR (film) ν_{max} = 3029, 2975, 1738, 1453, 1157 cm^{-1}; HRMS (ESI+) calcd for $C_{20}H_{24}NO_2$ (M+H): 310,1802, found: 310,1802.

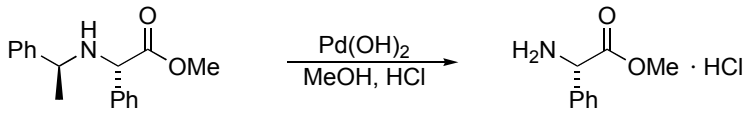
(*S*)-methyl 2-((*S*)-1-phenylethylamino)-2-phenylacetate (13a)



13 **13a**

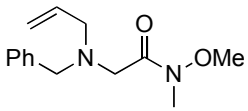
A solution of methyl ester **13** (60.0 mg, 0.194 mmol), $Pd(PPh_3)_4$ (11.2 mg, 0.010 mmol) and *N*,*N*-dimethylbarbituric acid (151.4 mg, 0.97 mmol) in 1 mL CH_2Cl_2 was refluxed for 3 h. The mixture was diluted with Et_2O, filtered and concentrated under reduced pressure. Flash chromatography (heptane + 1% *i*PrNH$_2$, Et_2O 3 → 20%) gave **13a** as a colorless oil (48.7 mg, 93%): $[\alpha]_D^{20}$ = +26.3 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.28-7.17 (m, 10H), 4.15 (s, 1H), 3.73 (q, *J* = 6.5 Hz, 1H), 3.64 (s, 1H), 2.25 (br, 1H), 1.31 (d, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 174.2, 144.7, 138.4, 128.7, 128.5, 127.9, 127.2, 127.1, 126.9, 62.9, 56.5, 52.1, 24.6; IR (film) ν_{max} = 2954, 1736, 1688, 1453, 1170 cm^{-1}; HRMS (ESI+) calcd for $C_{20}H_{25}N_2O$ (M+H): 270,1489, found: 270,1487.

(*S*)-methyl 2-amino-2-phenylacetate hydrochloride (14)

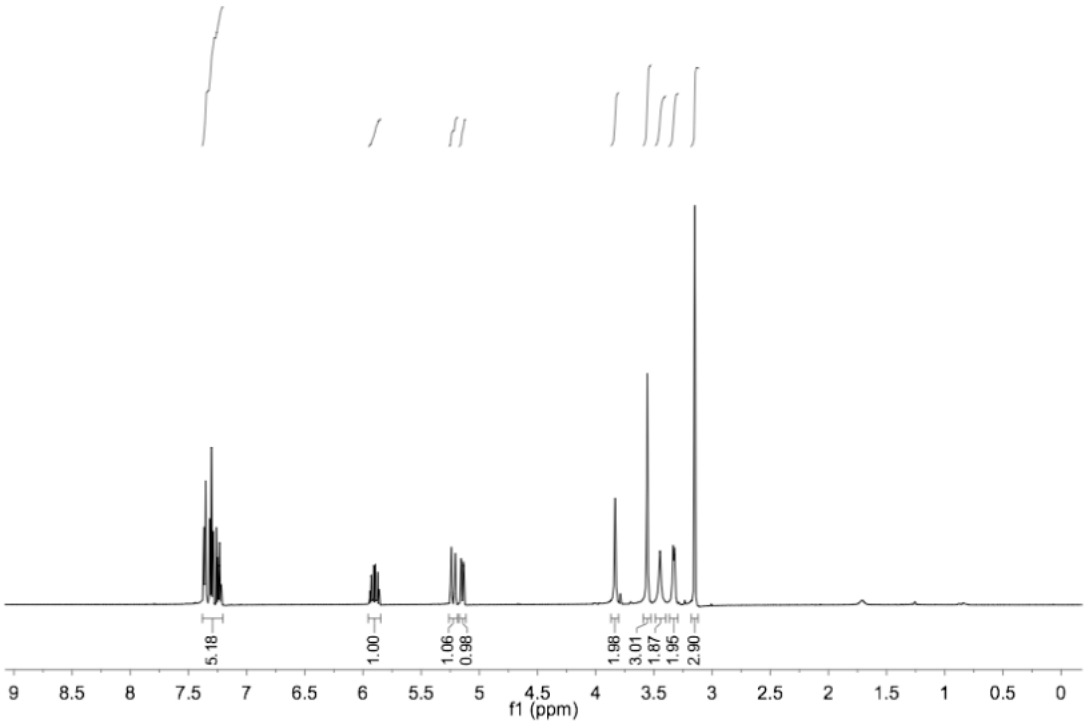


13a **14**

To a solution of **13a** (5.7 mg, 0.021 mmol) in MeOH (5 mL) and conc. HCl (250 μL) was added a catalytic amount of $Pd(OH)_2$ (20% on C). The resultant mixture was stirred under H_2-atmosphere (1 atm) for 15 h, filtered through a pad of celite and evaporated under reduced pressure to give **14** as a white solid (4.3 mg, 100%) with spectral data characterizations in accordance with those previously reported in the literature: $[\alpha]_D^{20} = +125.6$ (*c* 0.43, MeOH).[4]


Ph
N
O
N
OMe

6a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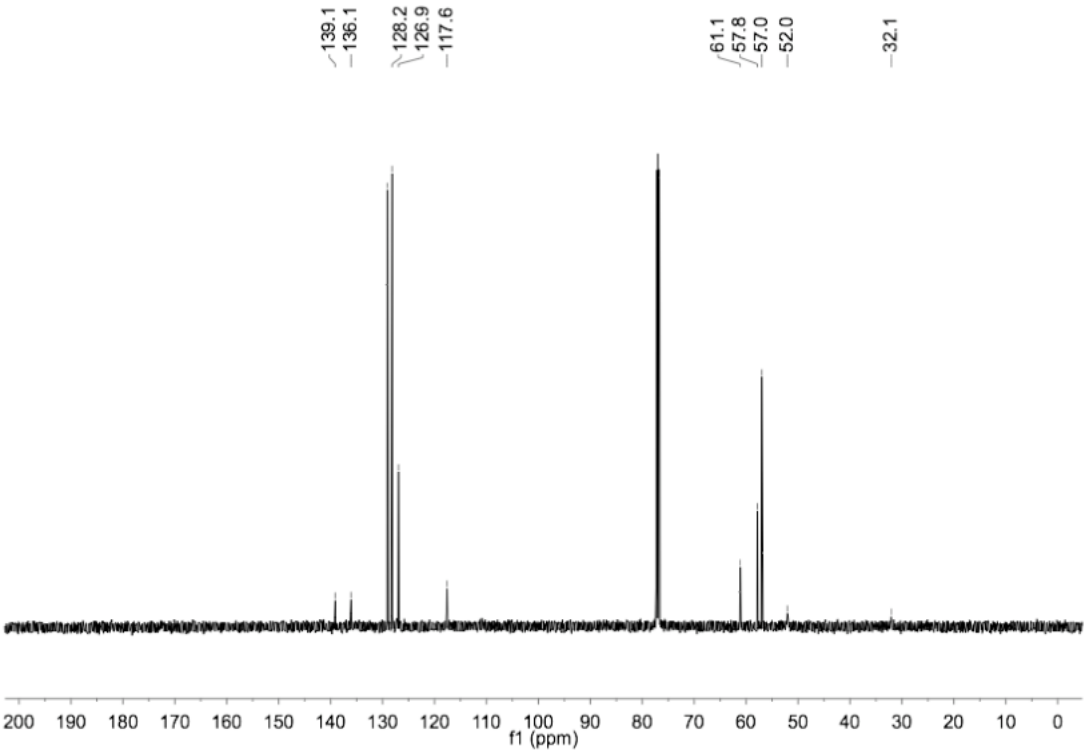
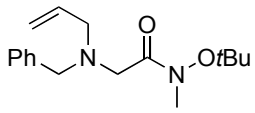
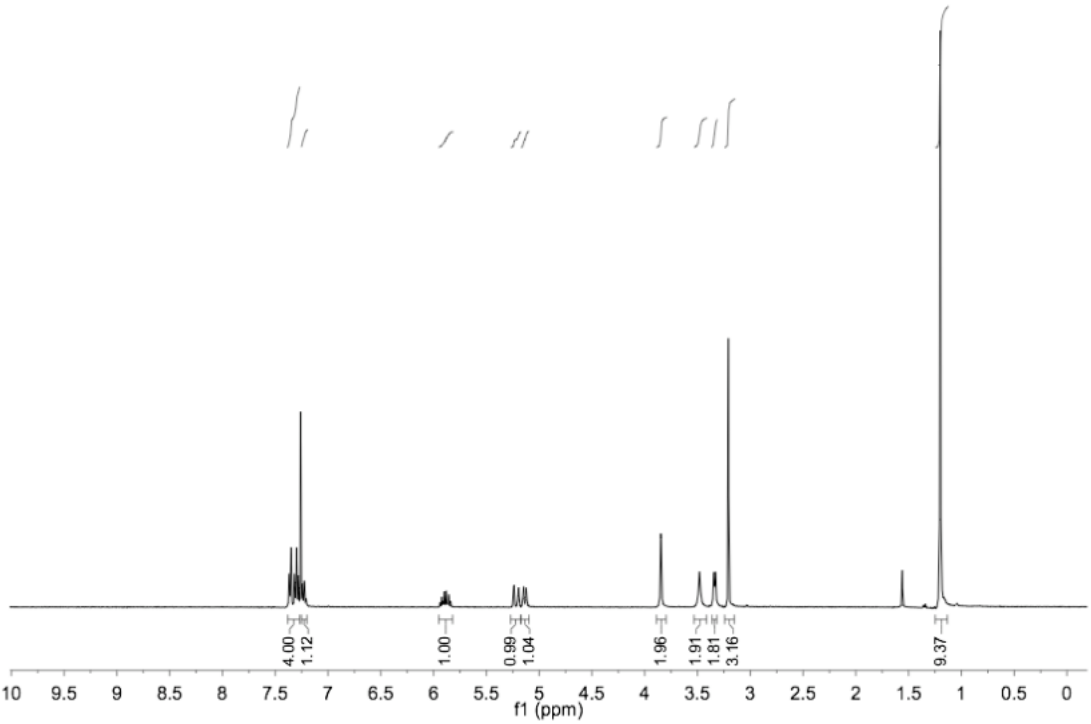
1.00
1.06
0.98
1.98
3.01
1.87
1.95
2.90
9 8.5 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0
f1 (ppm)


139.1
136.1
128.2
126.9
117.6
61.1
57.8
57.0
52.0
32.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
N
O
N
OtBu

6b


4.00
1.12
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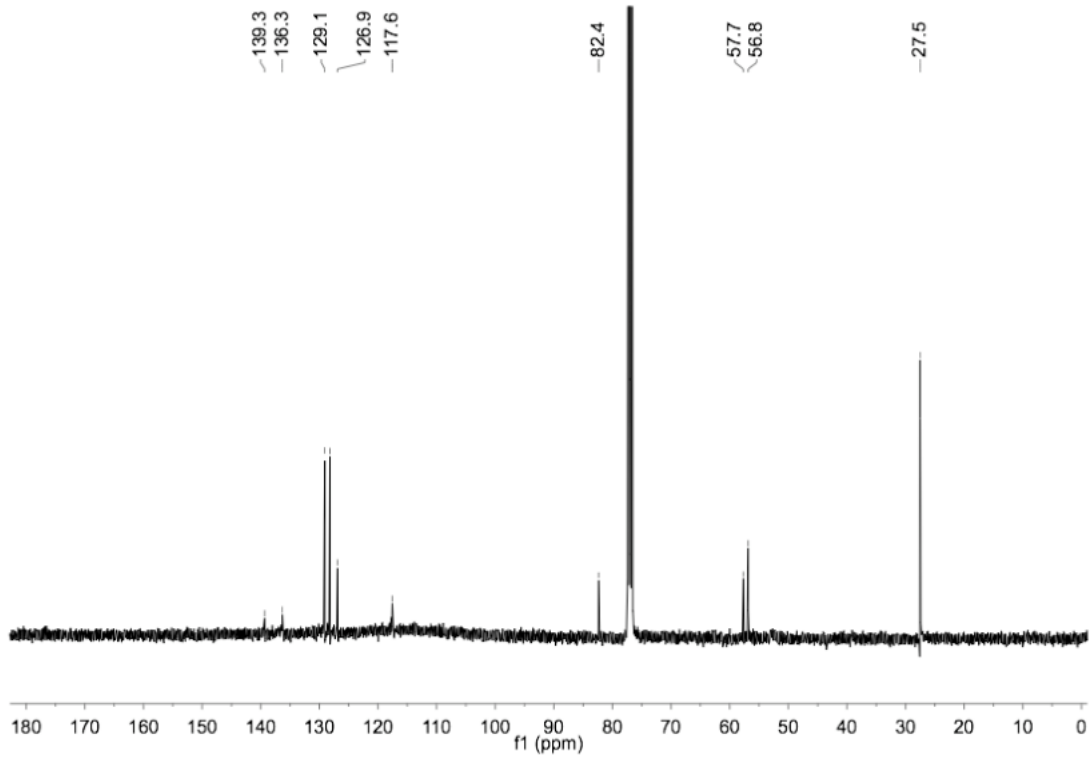
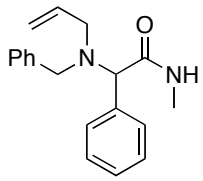
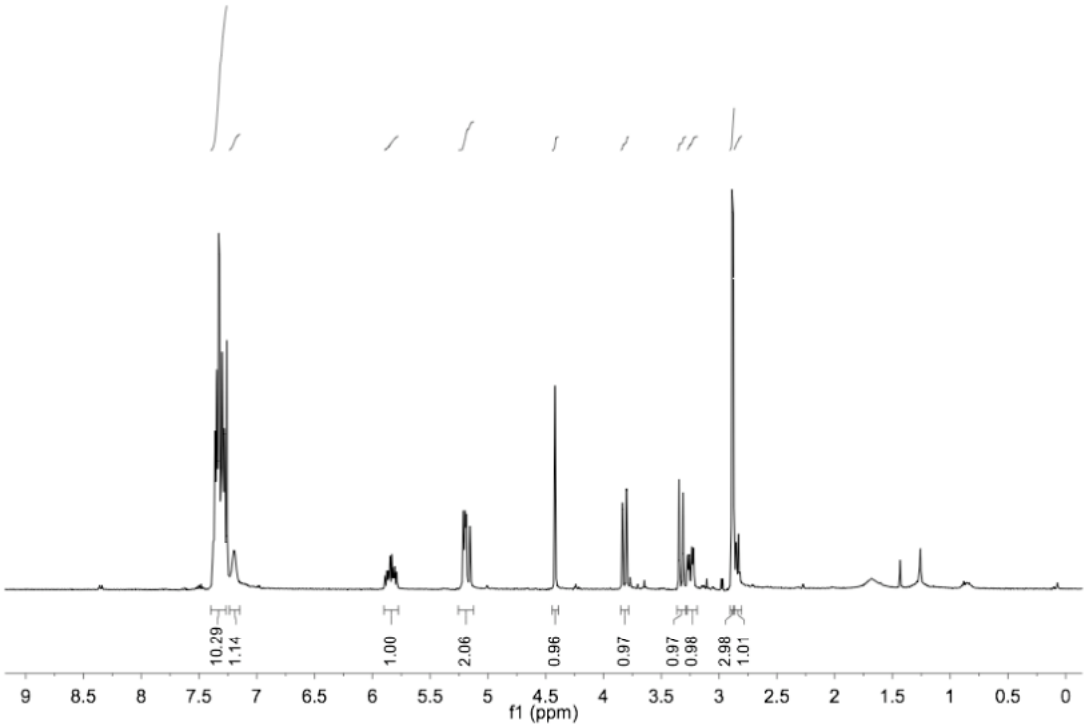
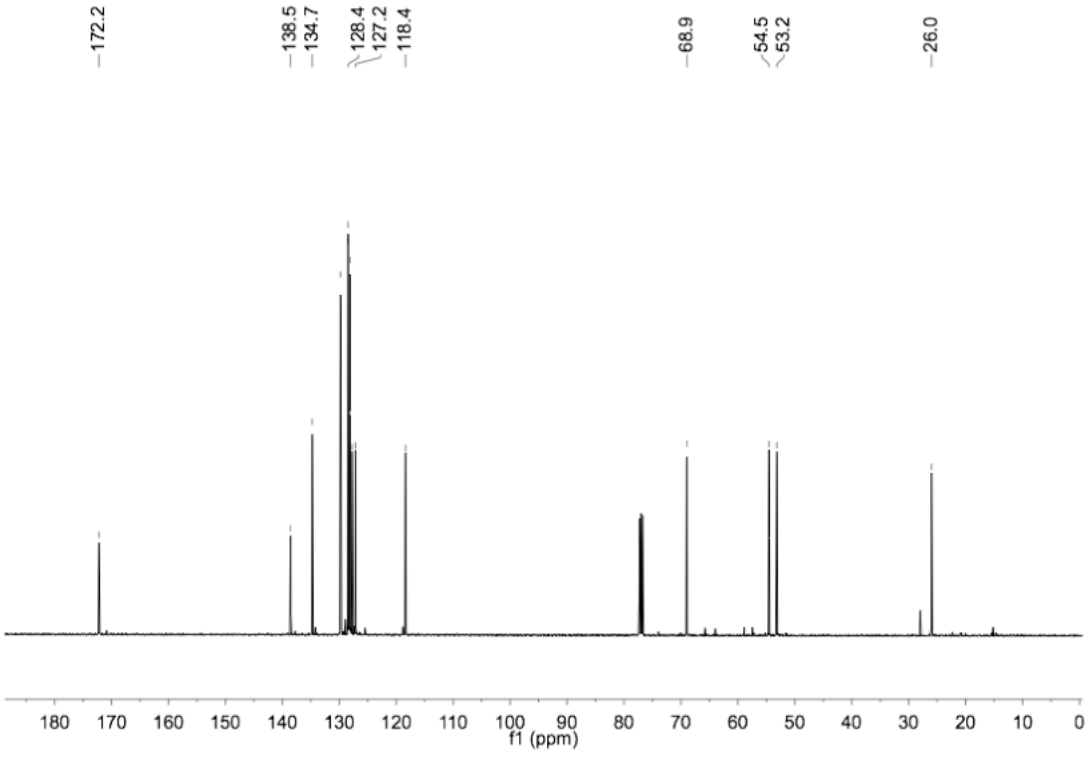
0.99
1.04
1.96
1.91
1.81
3.16
9.37
10 9.5 9 8.5 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0
f1 (ppm)

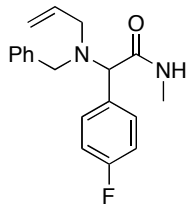

139.3
136.3
129.1
126.9
117.6
82.4
57.7
56.8
27.5
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
N
O
NH

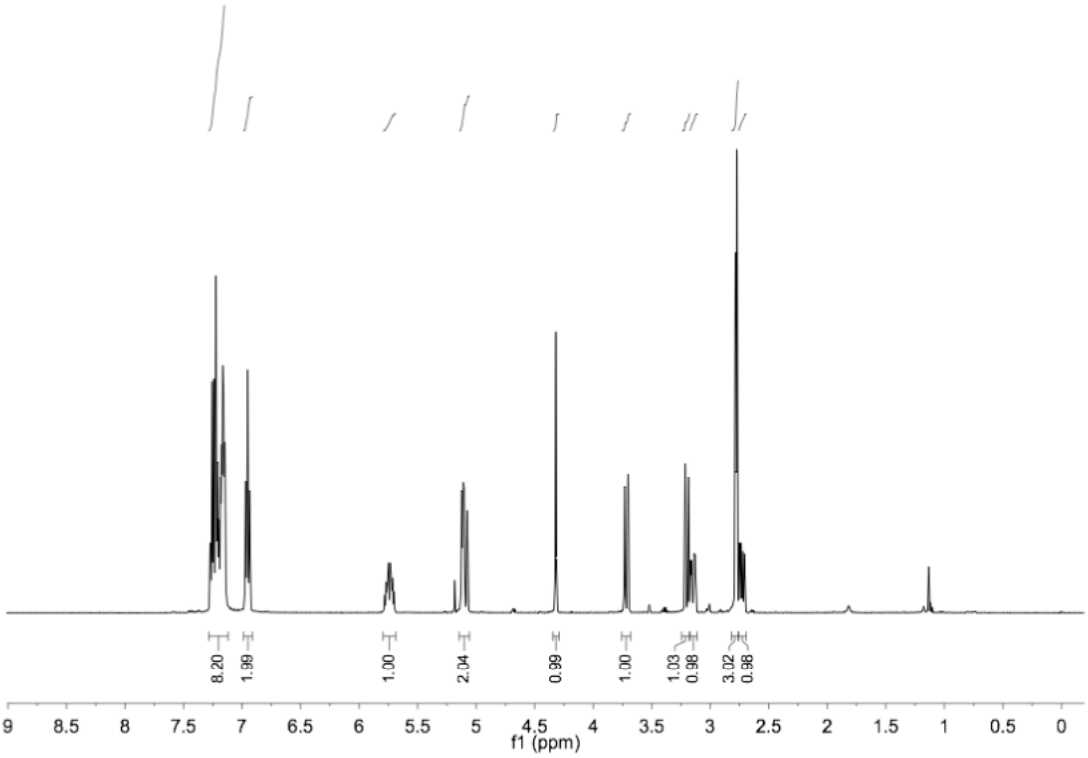
8a


10.29
1.14
1.00
2.06
0.96
0.97
0.97
0.98
2.98
1.01
9 8.5 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0
f1 (ppm)


172.2
138.5
134.7
128.4
127.2
118.4
68.9
54.5
53.2
26.0
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
N
O
NH
F

8b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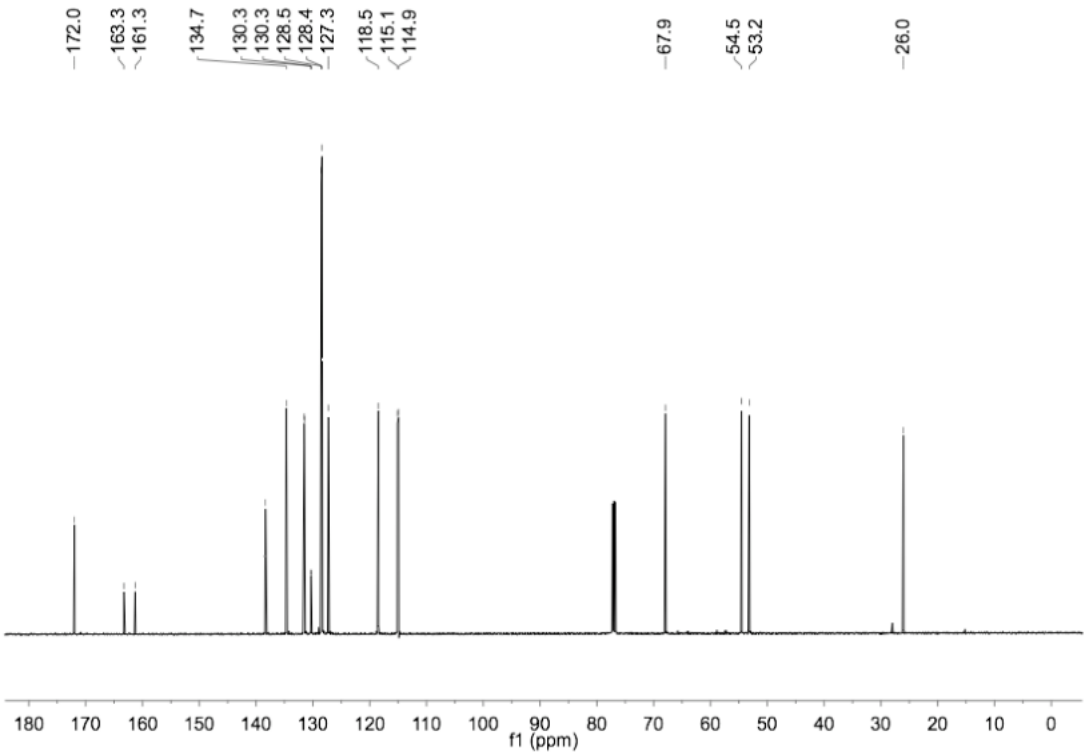
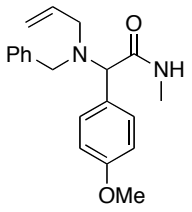
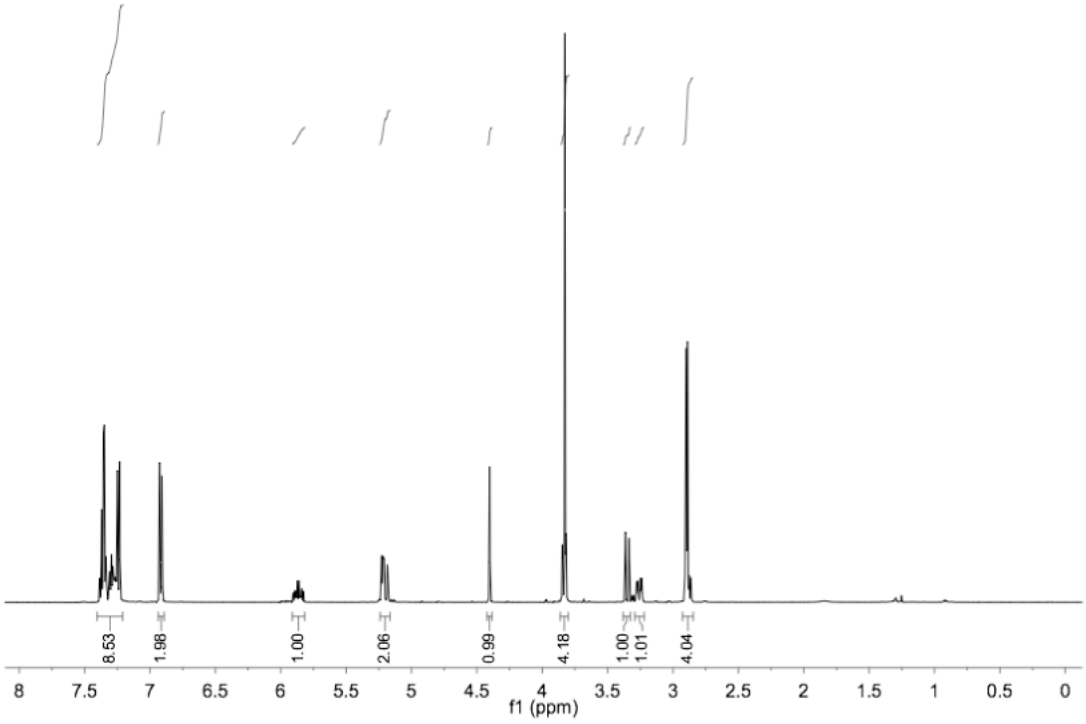
0.99
1.00
1.03
0.98
3.02
0.98
f1 (ppm)


172.0
163.3
161.3
134.7
130.3
130.3
128.5
128.4
127.3
118.5
115.1
114.9
67.9
54.5
53.2
26.0
f1 (ppm)


Ph
N
O
NH
OMe

8c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1.00
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0.99
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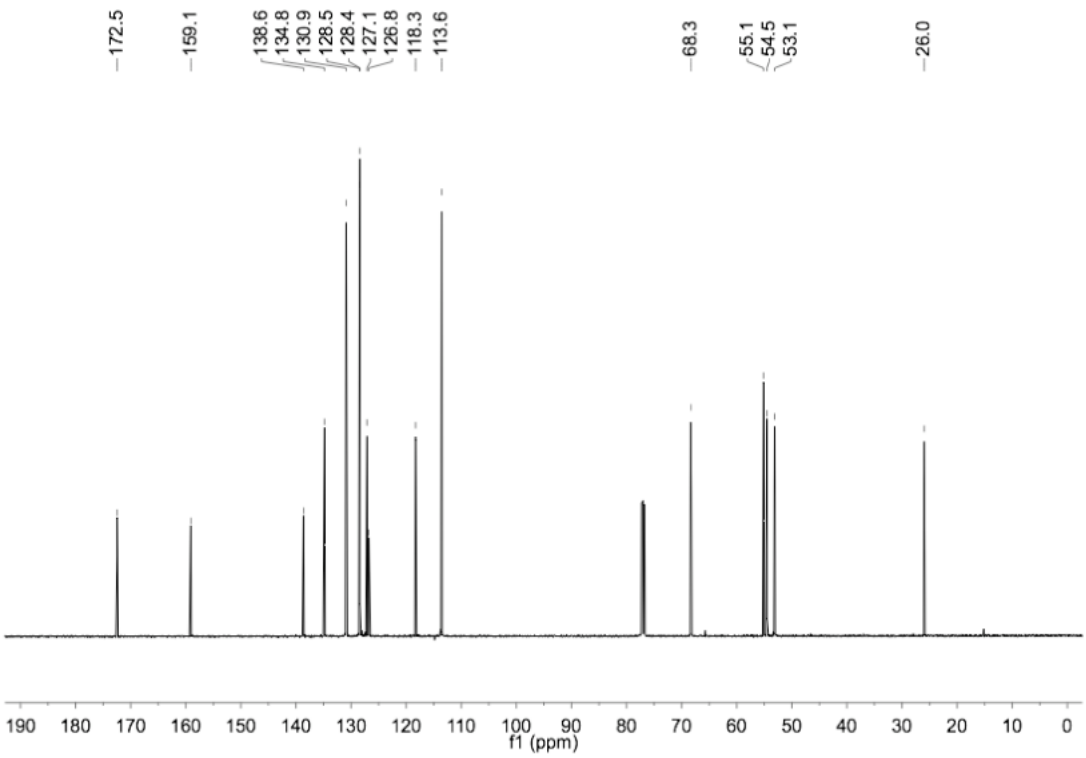
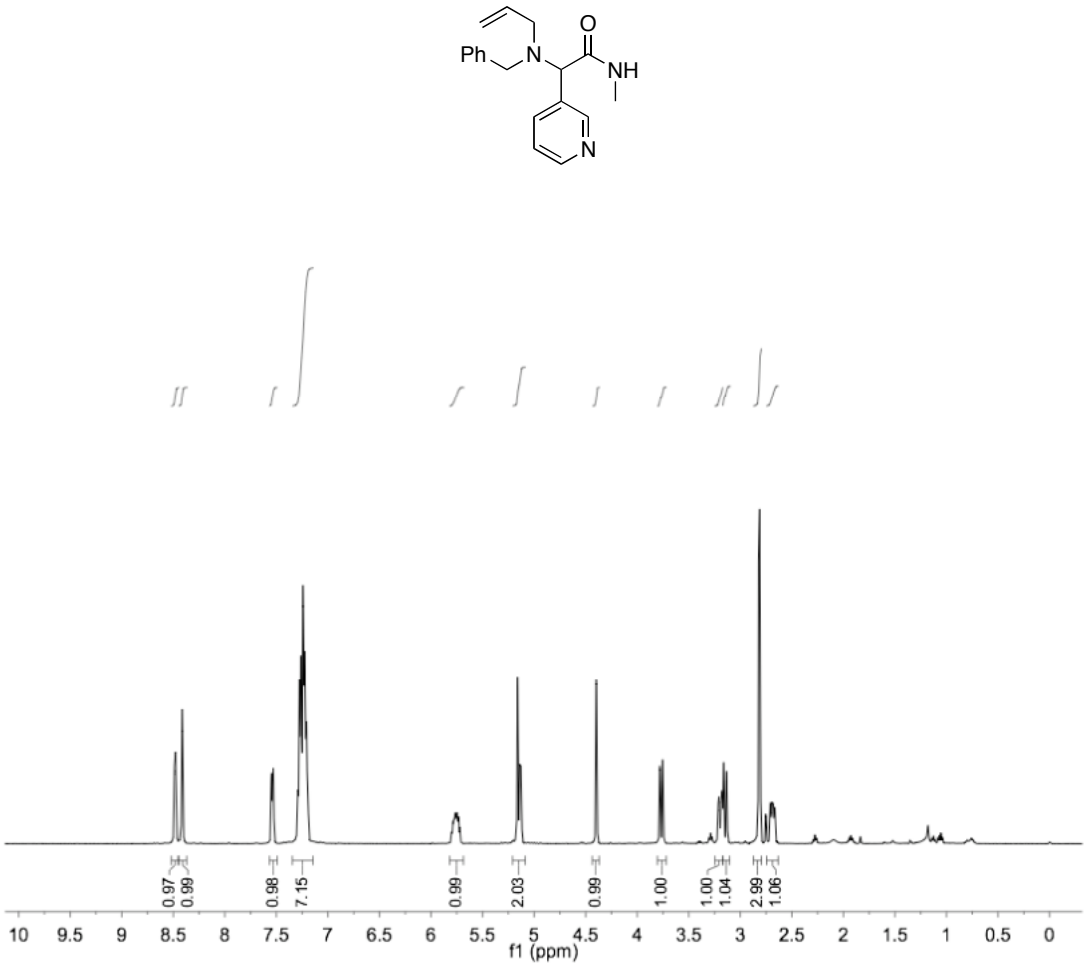
1.00
1.01
4.04
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
f1 (ppm)


172.5
159.1
138.6
134.8
130.9
128.5
128.4
127.1
126.8
118.3
113.6
68.3
55.1
54.5
53.1
26.0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Ph
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O
NH
N
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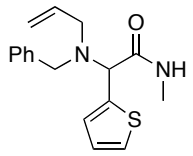
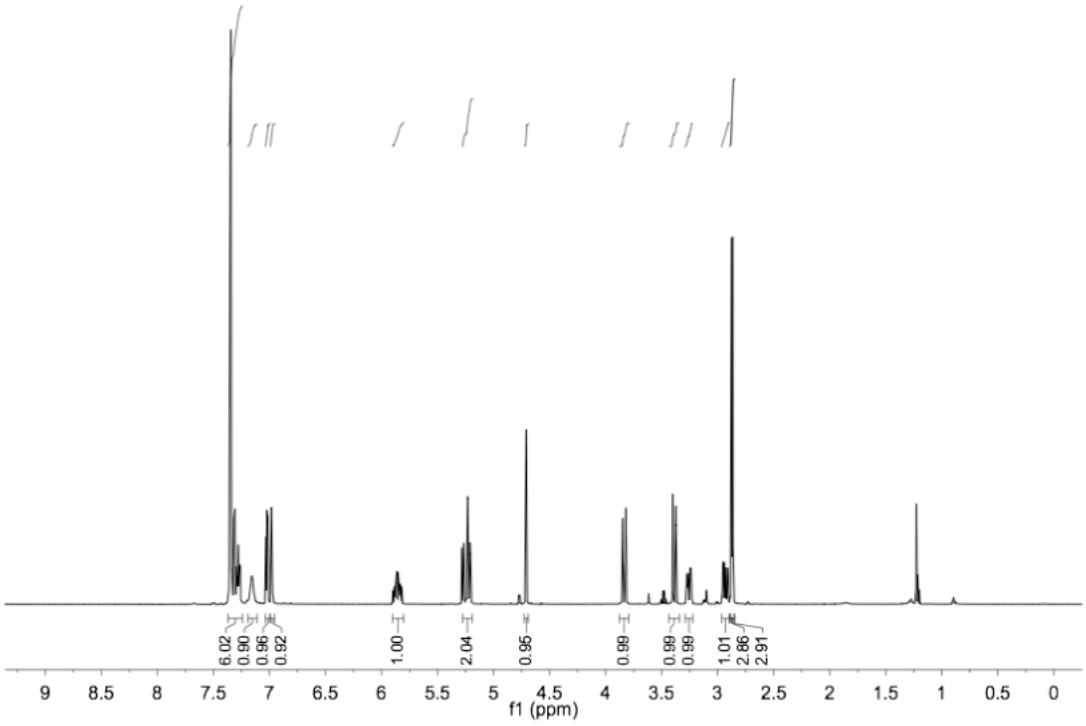
0.99
0.98
7.15
0.99
2.03
0.99
1.00
1.00
1.04
2.99
1.06
f1 (ppm)
171.2
151.1
149.1
138.0
137.5
134.6
127.5
123.0
118.8
65.9
54.7
53.4
26.1
f1 (ppm)


Ph
N
O
NH
S

8e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2.04
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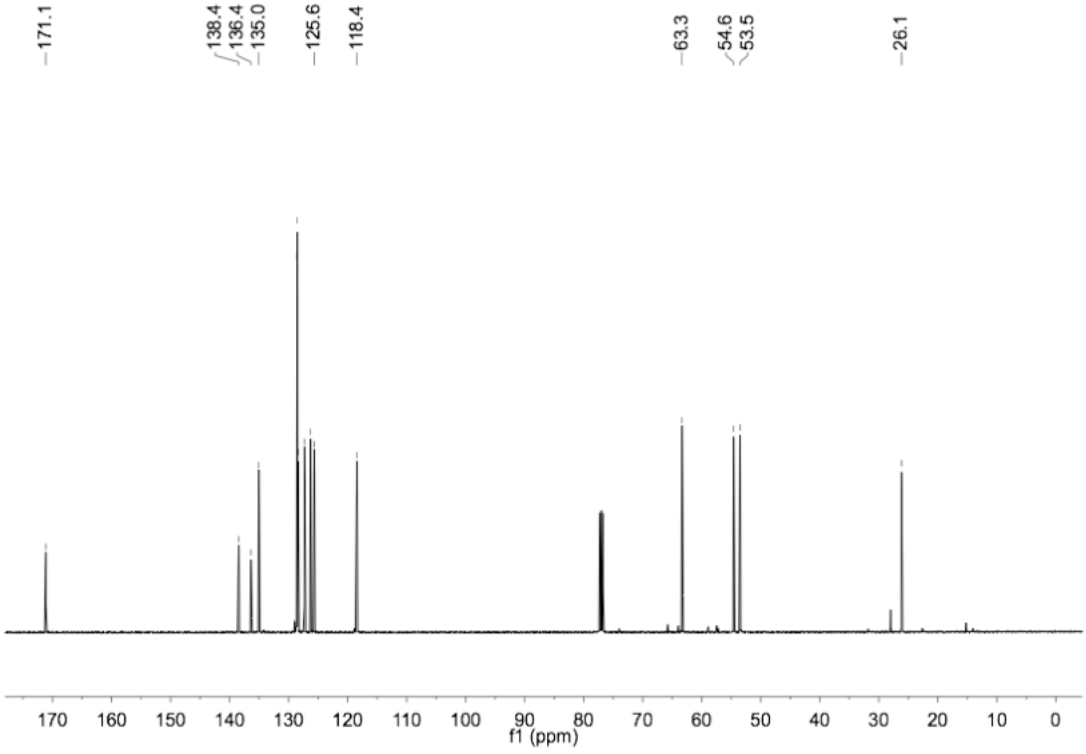
0.99
0.99
0.99
1.01
2.86
2.91
f1 (ppm)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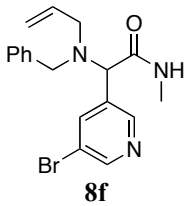
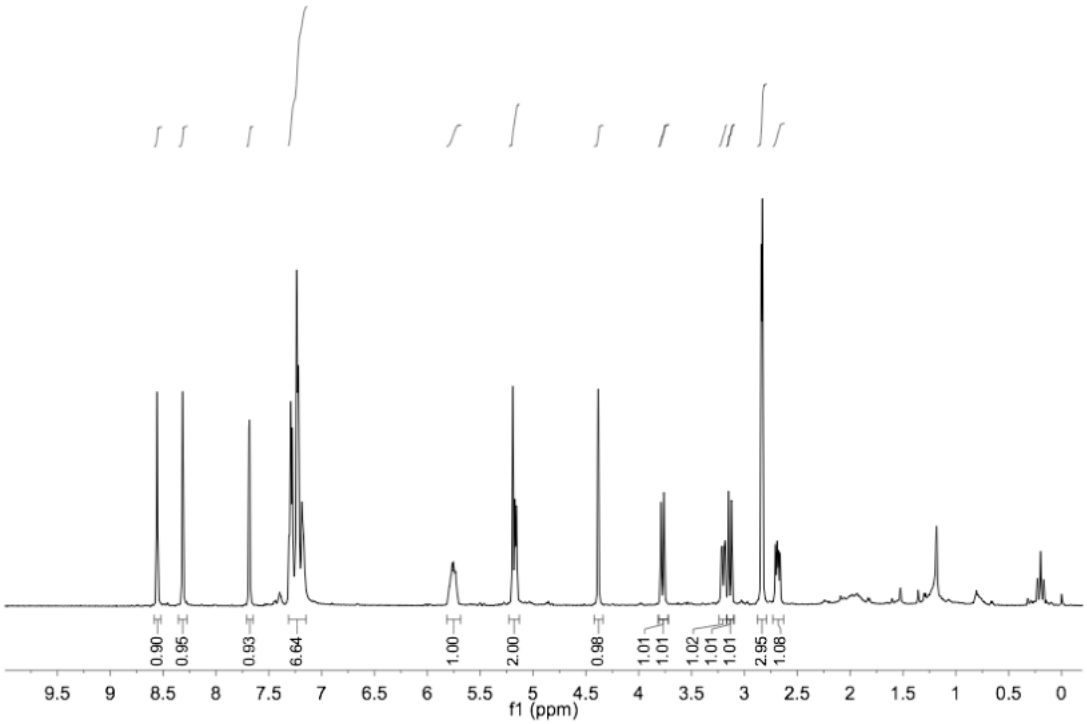
54.6
53.5
26.1
f1 (ppm)


Ph
N
O
NH
N
Br

8f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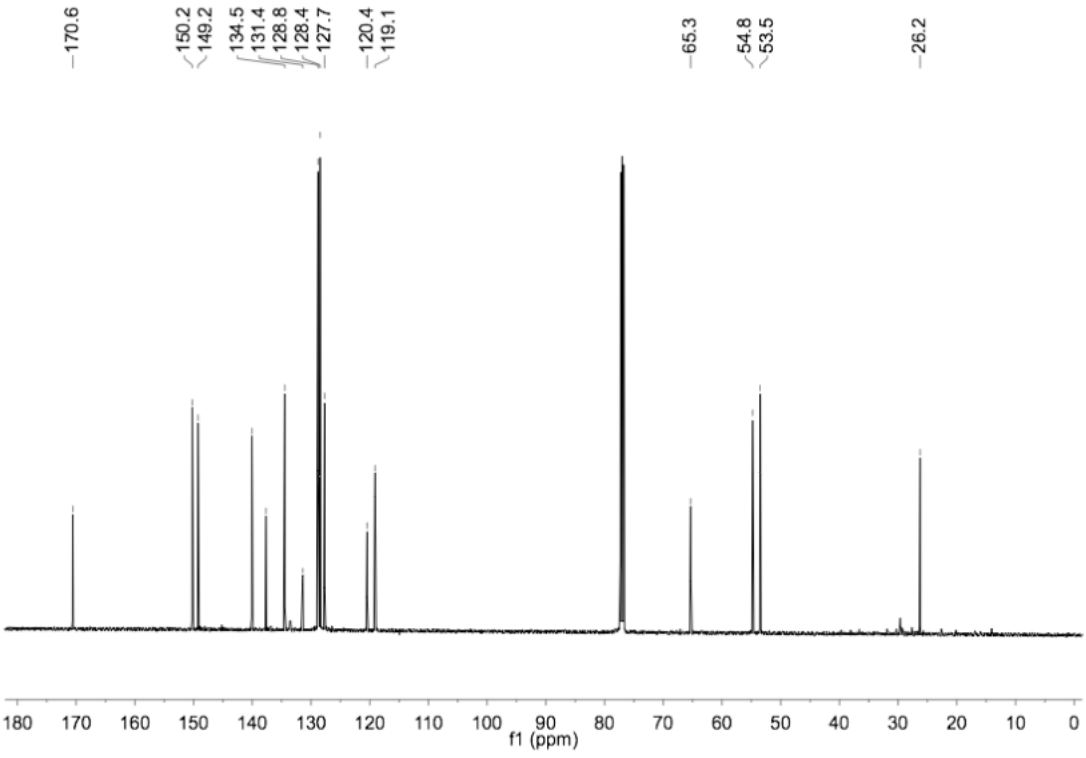
1.01
1.02
1.01
1.01
2.95
1.08
9.5 9 8.5 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0
f1 (ppm)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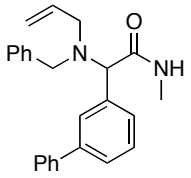
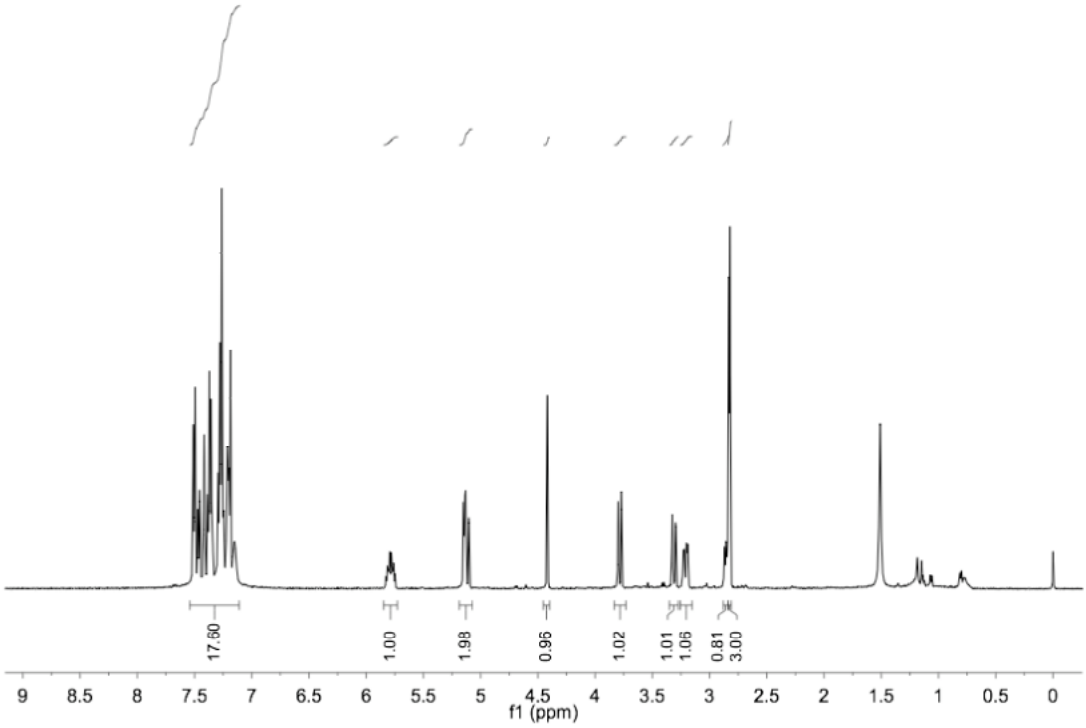
131.4
128.8
128.4
127.7
120.4
119.1
65.3
54.8
53.5
26.2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
Ph
N
NH
Ph

8d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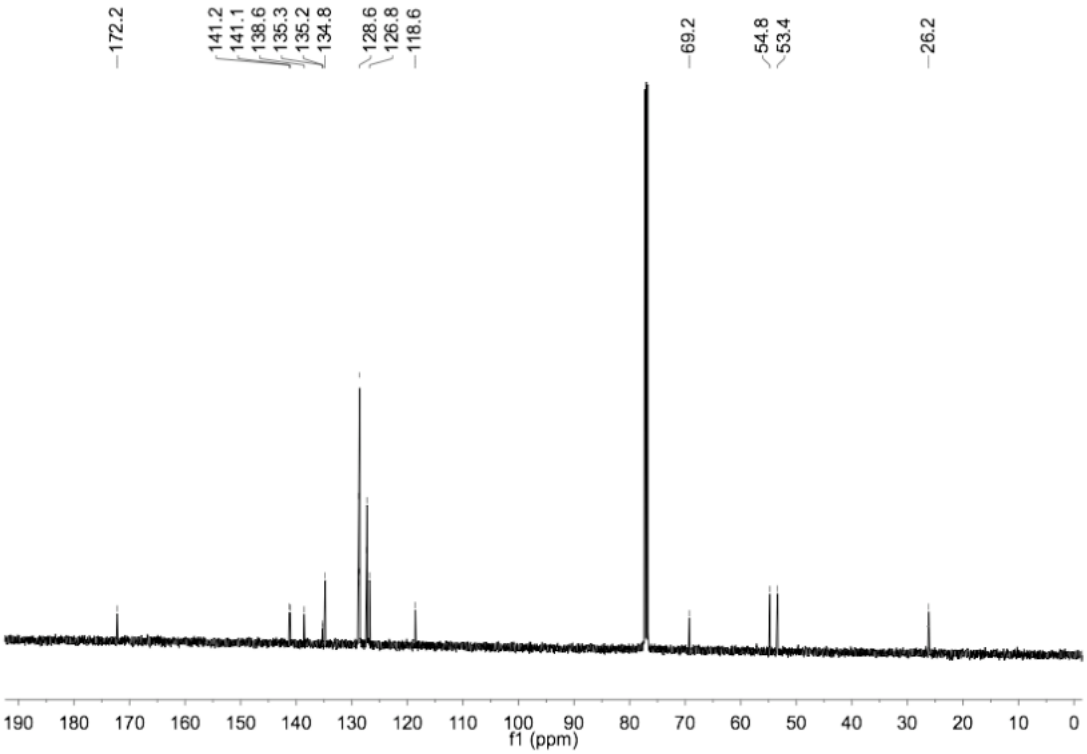
0.96
1.02
1.01
1.06
0.81
3.00
9 8.5 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0
f1 (ppm)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138.6
135.3
135.2
134.8
128.6
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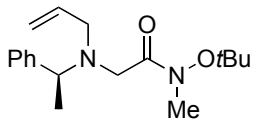
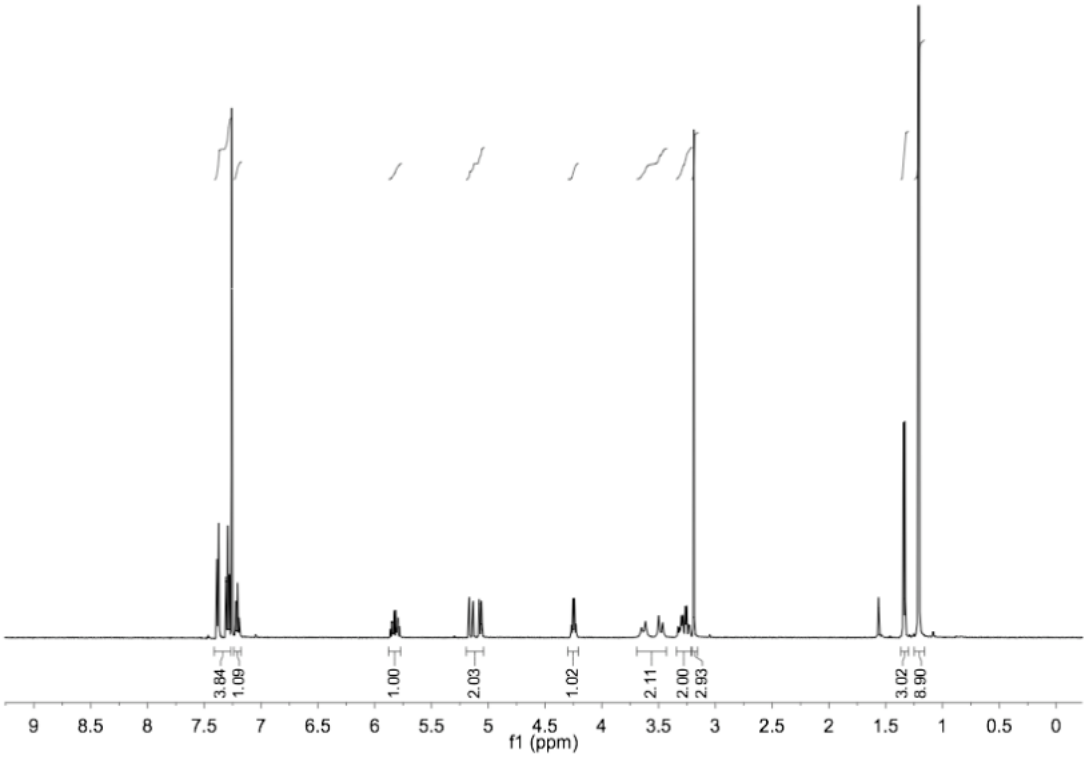
118.6
69.2
54.8
53.4
26.2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
N
O
N
OtBu
Me

11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1.02
2.11
2.00
2.93
3.02
8.90
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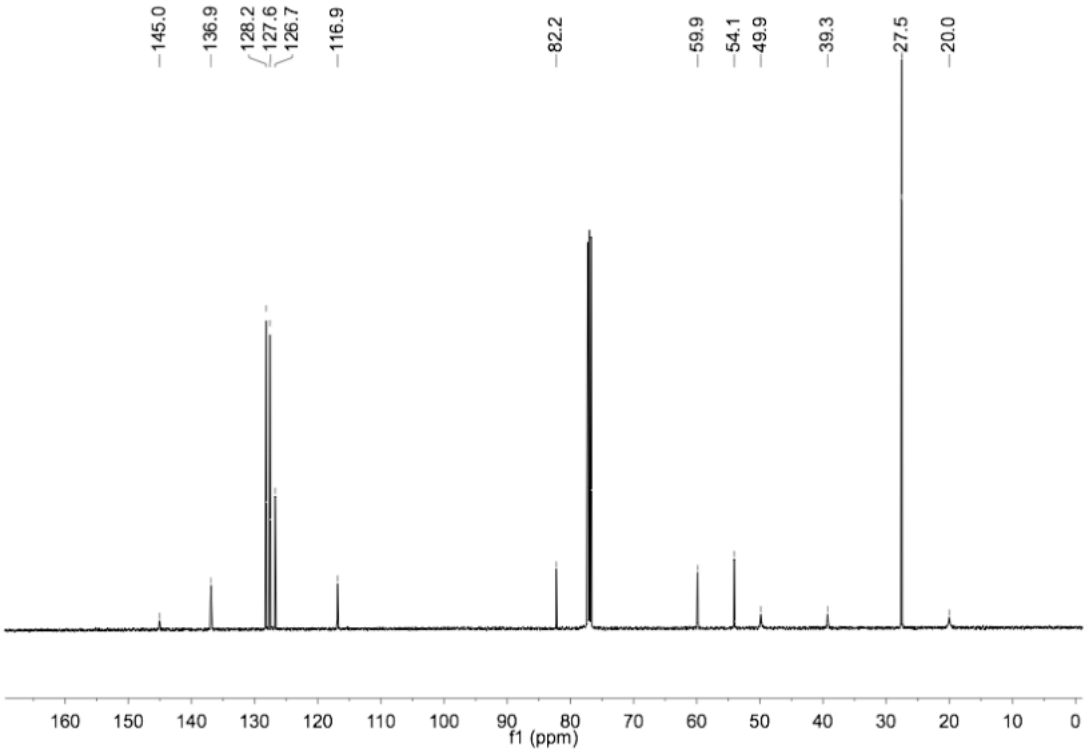
f1 (ppm)


145.0
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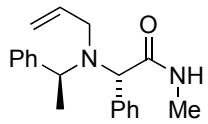
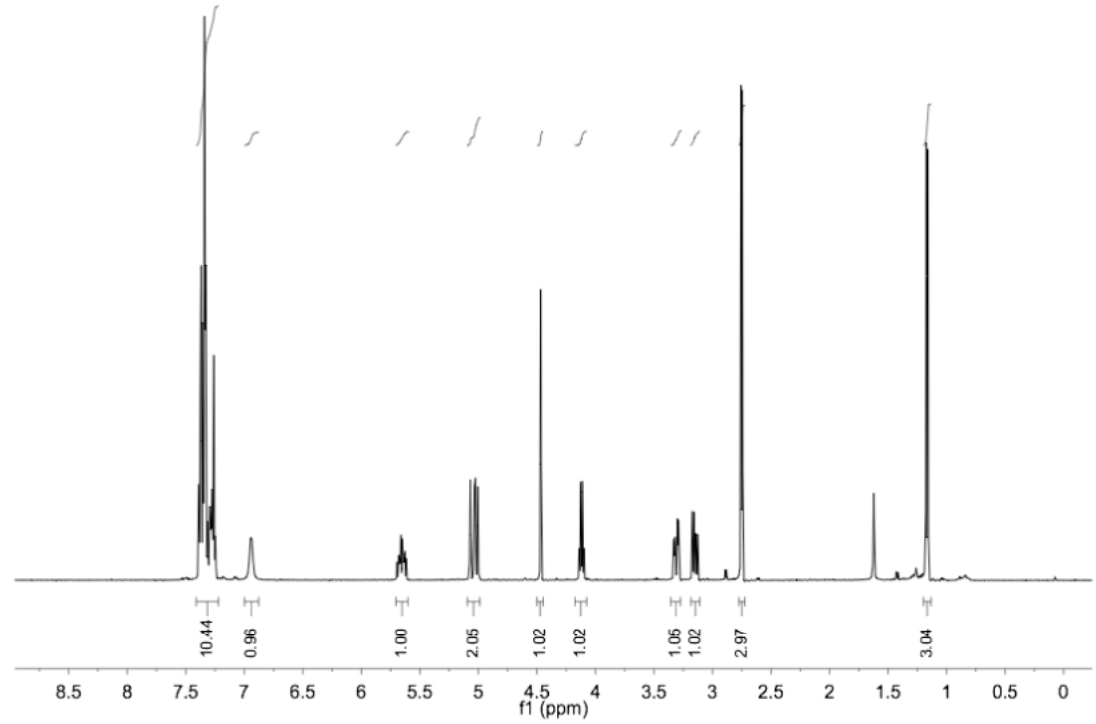
127.6
126.7
116.9
82.2
59.9
54.1
49.9
39.3
27.5
20.0
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
N
O
NH
Me
Ph

12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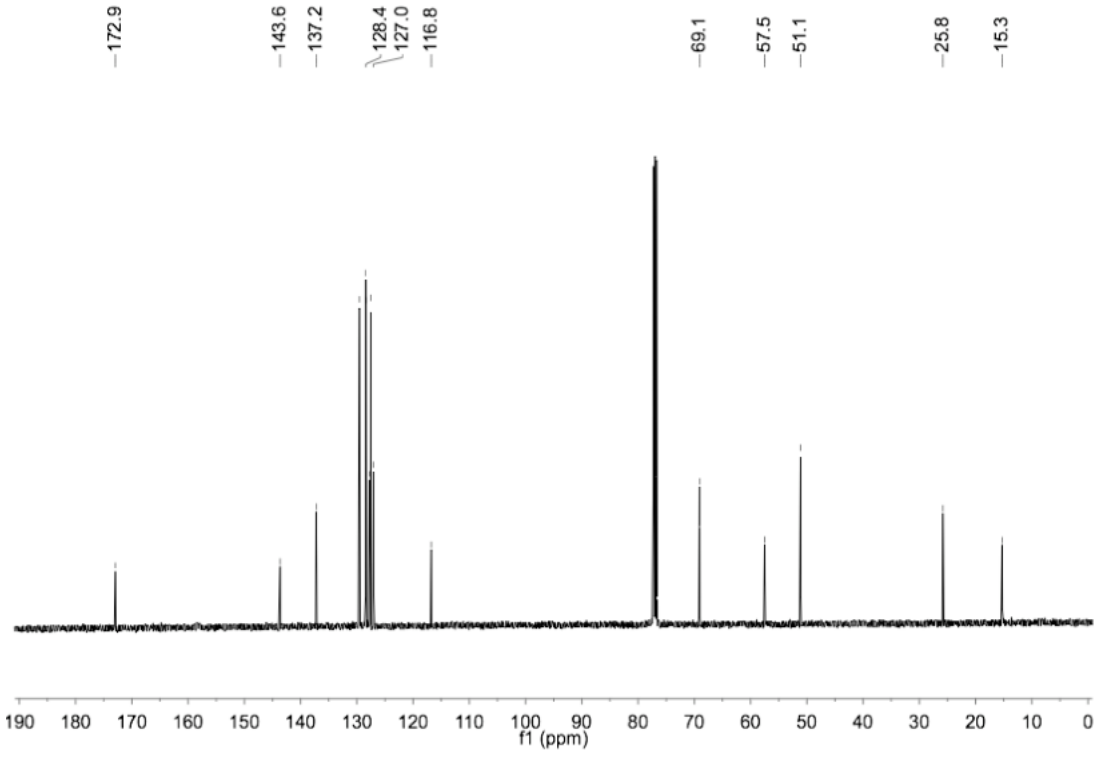
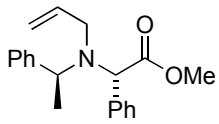
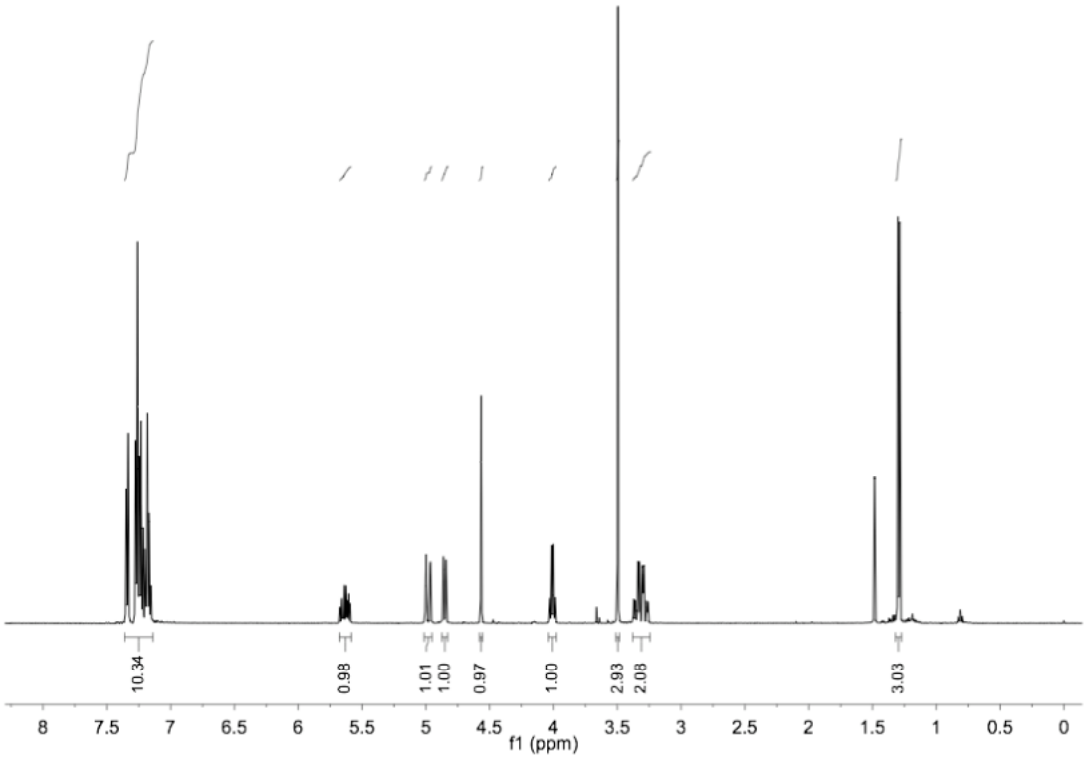
1.02
1.02
1.06
1.02
2.97
3.04
8.5 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0
f1 (ppm)


172.9
143.6
137.2
128.4
127.0
116.8
69.1
57.5
51.1
25.8
15.3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
N
O
OMe
Ph

13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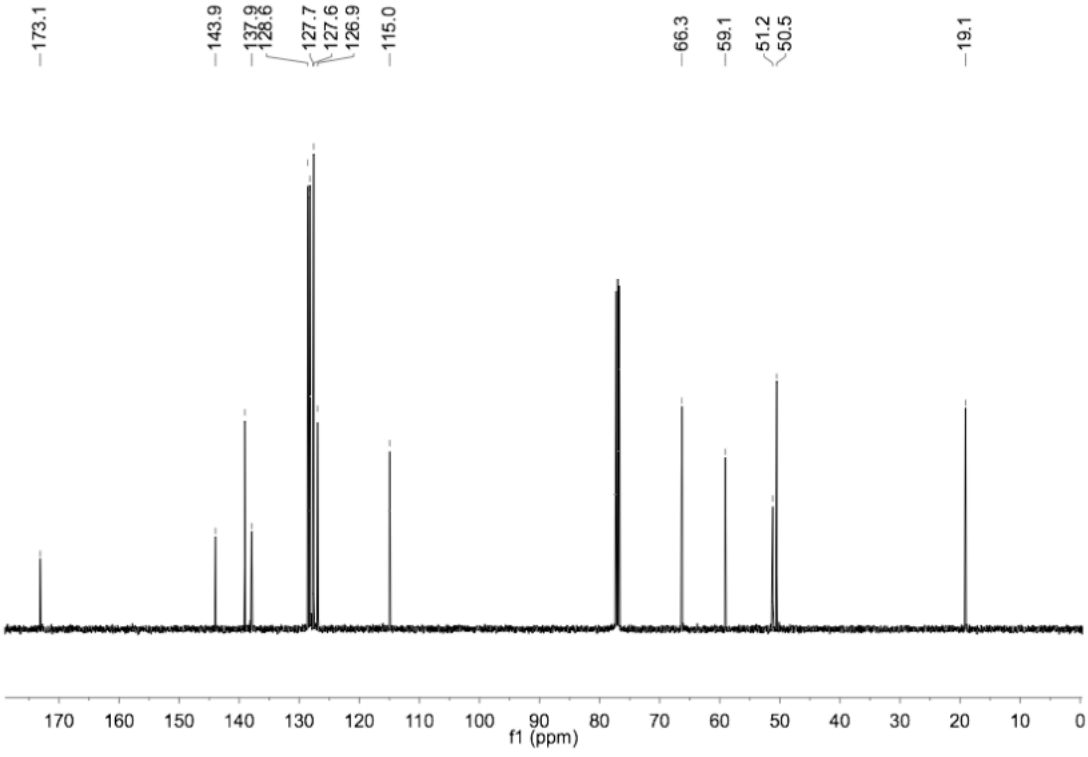
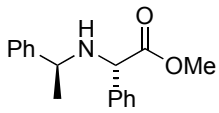
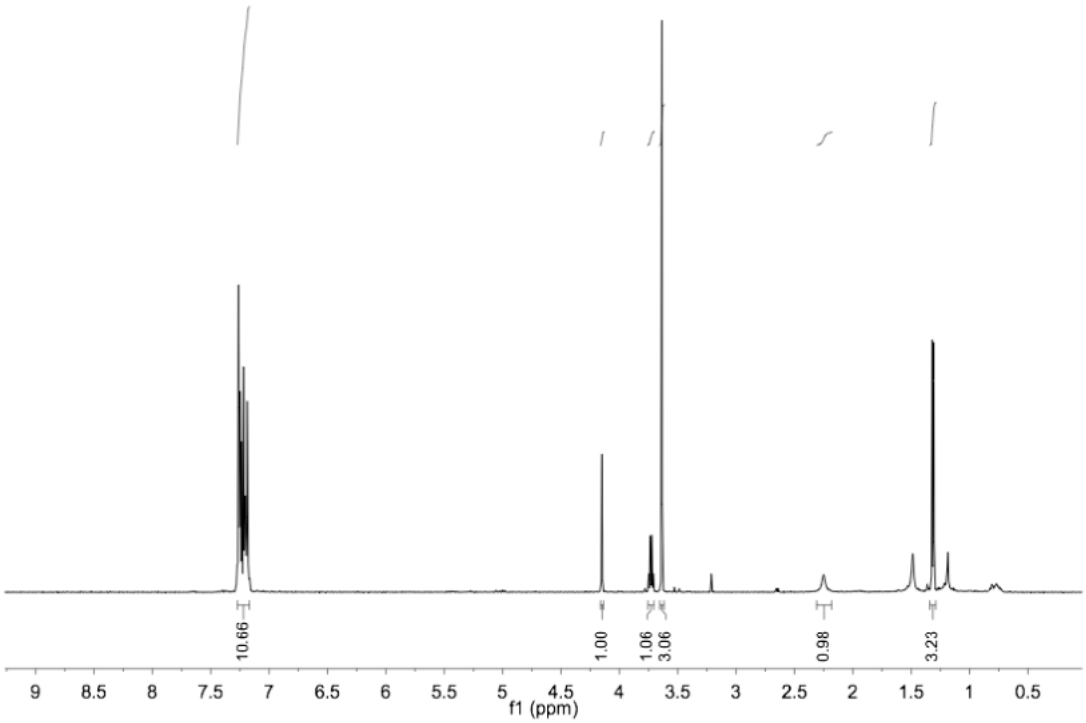
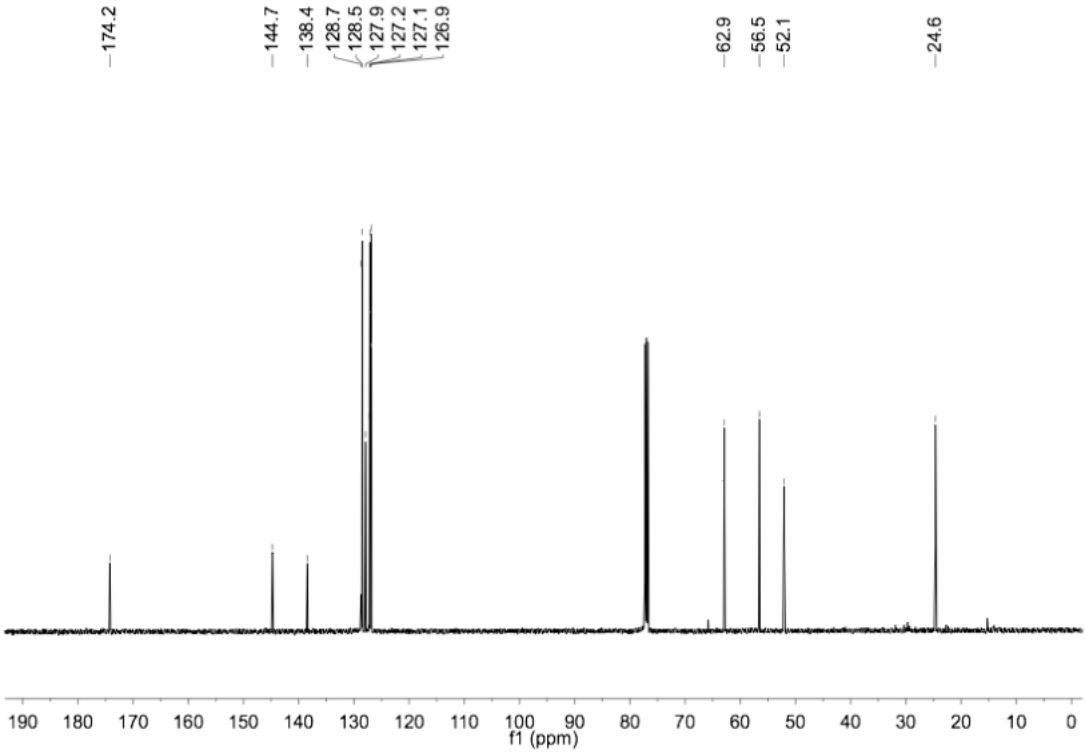
1.00
0.97
1.00
2.93
2.08
3.03
f1 (ppm)


173.1
143.9
137.9
128.6
127.7
127.6
126.9
115.0
66.3
59.1
51.2
50.5
19.1
f1 (ppm)


Ph
H
N
O
OMe
Ph

13a


10.66
1.00
1.06
3.06
0.98
3.23
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
f1 (ppm)


174.2
144.7
138.4
128.7
128.5
127.9
127.2
127.1
126.9
62.9
56.5
52.1
24.6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

References

[1] A. F. Burchat, J. M. Chong, N. Nielsen, *J. Organomet. Chem*. **1997**, *542*, 281.
[2] R. Tillyer, L. F. Frey1, D. M. Tschaen, U.-H. Dolling, *Synlett* **1996**, 225-226.
[3] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333-3336.
[4] G.-I. Li, G. Zhao, *Org. Lett.* **2006**, *8*, 633-636.