Electronic Supplementary Information

Catalytic stereoselective total synthesis of (+)-3'-(4-oxoquinazolin-3yl)spiro[1*H*-indole-3,5'-oxolane]-2,2'-dione, and pentacyclic core of tryptoquivalines

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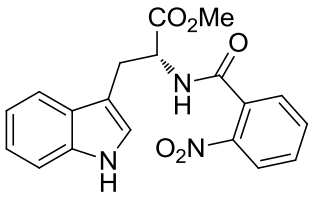
1. General information

All reagents bought from commercial sources were used as received. Organic solvents were evaporated under reduced pressure using a Büchi rotary evaporator. All solvents were commercially supplied or dried by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic, Sigma-Aldrich) columns. Petrol ether (PE) refers to distilled light petroleum of fraction 30 - 40 °C. Toluene was distilled twice over calcium hydride. All reactions were followed by thin-layer chromatography (TLC) when practical, using Merck Kieselgel 60 F_{254} fluorescent treated silica. Visualisation was accomplished under UV light (λmax= 254 nm) and by staining with $KMnO_4$ staining dip. Chromatographic purification was performed on VWR 60 silica gel 40-63 μm using HPLC grade solvents that were used as supplied. High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics MicroTOF mass spectrometer equipped with an ESI source or on a Micromass GCT equipped with an EI source unless otherwise specified. Infrared absorption spectra (IR) were recorded on a Bruker Tensor 27 FT-IR spectrometer from a thin film on a diamond ATR module. Only selected bands (ν_{max}) are reported in wavenumbers (cm^{-1}). NMR spectra were recorded on Bruker spectrometers operating at 400 or 500 MHz (^1H resonance). Proton chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane (TMS) with the solvent resonance ($CDCl_3$, δ = 7.26 ppm) as internal standard. The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet, br = broad signal. Coupling constants (*J*) are given in Hertz (Hz). ^{13}C-NMR spectra were recorded with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the solvent resonance ($CDCl_3$, δ = 77.16 ppm) as internal standard.

2. Synthetic procedures

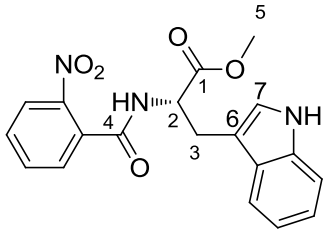
Compound 2



D-Tryptophan methyl ester hydrochloride (10 g, 39 mmol, 1.0 eq) and sodium hydrogen carbonate (13 g, 156 mmol, 4.0 eq) was dissolved in 130 mL of water and 130 mL of CH_2Cl_2; while stirring 2-nitrobenzoyl chloride (7.2 g, 39 mmol, 1.0 eq) was added into the reaction mixture dropwise. After stirring for 15 min, the bi-phase reaction mixture was separated, and the aqueous phase was extract with CH_2Cl_2, combined organic parts, washed with 1 N HCl, brine and dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified with FCC CH_2Cl_2/Et_2O (from 100/1 to 8/1) to give a light yellow foam 14.28 g (99%).

m.p. 50 – 55 ^oC; $\mathbf{[\alpha]_D^{25}}$ –58.4 (*c* 0.48, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 3405, 3346, 1738, 1652, 1528, 1458, 1439, 1349, 1311, 1253, 1217, 1101, 1011, 910, 850, 789, 735, 699, 648;

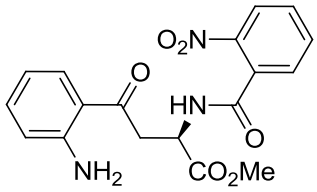


^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.19 (s, 1H, Indole), 7.98 (dd, *J* = 7.9, 1.4 Hz, 1H, $C_{[ar]}H$), 7.68 – 7.44 (m, 3H, $C_{[ar]}H$), 7.36 – 7.27 (m, 2H, $C_{[ar]}H$), 7.15 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H, C[ar]H), 7.09 – 7.03 (m, 2H, $C_{[ar]}H$), 6.43 (d, *J* = 8.0 Hz, 1H, CON*H*), 5.15 (dt, *J* = 8.0, 5.2 Hz, 1H, $C_{[2]}H$), 3.70 (s, 3H, $C_{[5]}H$), 3.45 (d, *J* = 5.3 Hz, 2H, $C_{[3]}H$);

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 172.2 ($C_{[1]}$), 166.0 ($C_{[4]}$), 146.8 ($C_{[ar]}$), 136.3 ($C_{[ar]}$), 133.8 ($C_{[ar]}$), 132.5 ($C_{[ar]}$), 130.8 ($C_{[ar]}$), 128.9 ($C_{[ar]}$), 127.8 ($C_{[ar]}$), 124.7 ($C_{[ar]}$), 123.4 ($C_{[ar]}$), 122.4 ($C_{[ar]}$), 119.9 ($C_{[ar]}$), 118.7 ($C_{[ar]}$), 111.5 ($C_{[ar]}$), 109.8 ($C_{[ar]}$), 53.5 ($C_{[2]}$), 52.8 ($C_{[5]}$), 27.6 ($C_{[3]}$);

HRMS (ESI) $[C_{19}H_{17}N_3O_5+H]^+$ requires *m/z* 368.1241, found *m/z* 368.1238.

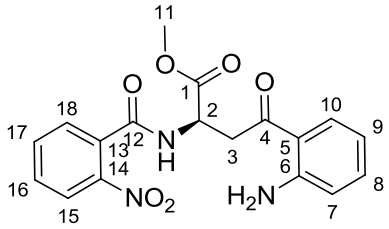
Compound 3



Compound **2** (3.67 g, 10.0 mmol, 1.0 eq) was dissolved in a mixture of 250 mL methanol and 100 mL of water. Sodium periodate (8.6 g, 40.0 mmol, 4.0 eq) was added in one portion at room temperature. The reaction was stirred at r.t. for 3 days before 300 mL of water was added, then extracted with chloroform three times, washed with sat. $NaHCO_3$, brine, and dried with $MgSO_4$. The organic layers were concentrated and the residue was dissolved in 150 mL methanol and 100 mL of water, sodium periodate (6.45 g, 30 mmol) was added. The reaction was stirred at room temperature for another 3 days, before 300 mL water was added, then extracted with chloroform three times, washed with sat. $NaHCO_3$, brine, and dried with $MgSO_4$. The organic layers were concentrated and the residue which was dissolved in 240 mL methanol and 80 mL of dioxane, and 20 mL of 4 M HCl was added. Then the reaction was stirred for 1 h at room temperature, before basified with saturated $NaHCO_3$, and extracted with CH_2Cl_2 for three times, washed with brine and dried over $MgSO_4$, concentrated, the residue was purified with FCC (methanol / CH_2Cl_2 from 1/200 to 1/50) to give the yellow thick oil 3.12 g (84 %).

$[\alpha]_D^{25}$ – 62.6 (*c 1.01*, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 3470, 3350, 1742, 1648, 1616, 1584, 1529, 1485, 1451, 1349, 1313, 1216, 1162, 1114, 1042, 980, 905, 856, 790, 735, 700;

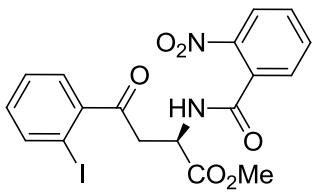


^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.99 (dd, *J* = 8.1, 1.2 Hz, 1H, $C_{[ar]}H$), 7.70 (dd, *J* = 8.2, 1.5 Hz, 1H, $C_{[ar]}H$), 7.63 (td, *J* = 7.5, 1.2 Hz, 1H, $C_{[ar]}H$), 7.59 – 7.47 (m, 2H, $C_{[ar]}H$), 7.25 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H, $C_{[ar]}H$), 7.04 (d, *J* = 8.5 Hz, 1H, CON*H*), 6.65 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H, $C_{[ar]}H$), 6.60 (dd, *J* = 8.4, 1.1 Hz, 1H, $C_{[ar]}H$), 6.19 (s, 2H, N*H*$_2$), 5.13 (dt, *J* = 8.1, 3.9 Hz, 1H, $C_{[2]}H$), 3.87 – 3.68 (m, 5H, $C_{[11]}H$+$C_{[3]}H$);

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 199.6 ($C_{[4]}$), 171.8 ($C_{[1]}$), 166.2 ($C_{[12]}$), 150.7 ($C_{[ar]}$), 146.7 ($C_{[ar]}$), 135.3 ($C_{[ar]}$), 133.9 ($C_{[ar]}$), 132.6 ($C_{[ar]}$), 131.3 ($C_{[ar]}$), 130.8 ($C_{[ar]}$), 128.9 ($C_{[ar]}$), 124.7 ($C_{[ar]}$), 117.6 ($C_{[ar]}$), 117.2 ($C_{[ar]}$), 116.3 ($C_{[ar]}$), 53.0 ($C_{[11]}$), 48.9 ($C_{[2]}$), 40.7 ($C_{[3]}$);

HRMS (ESI) $[C_{18}H_{17}N_3O_6+H]^+$ requires *m/z* 372.1190, found *m/z* 372.1184.

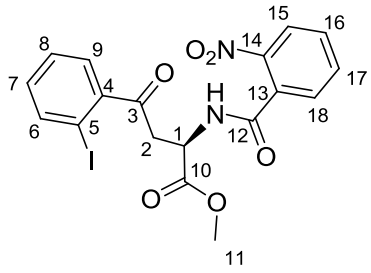
Compound 4



The aniline compound **3** (1.6 g, 4.3 mmol, 1.0 eq) was dissolved in EtOH 15 mL and 48% HBF_4 (1.13 mL, 8.6 mmol, 2.0 eq), which was stirred for 30 min before at 0 ^oC 2-methyl-2-nitropropane (1.0 mL, 9.5 mmol, 2.2 eq) was added dropwise. Then at the same temperature, 50 mL of acetone was added to dissolve the participation, which solution was kept stirring for another 1 hour. At 0 ^oC, the above solution was added into a potassium iodide (9.7 g, 58.6 mmol, 14 eq) in 50 mL of acetone, and the reaction was kept stirring at the same temperature for another 1 hours. Then the reaction was exacted with ethyl acetate for three times, washed with sat. $Na_2S_2O_3$ and brine, dried with $MgSO_4$, filtered and concentrated under vacuum, and the residue was purified with FCC ethyl acetate / petrol ether (from 1/2 to 1/1) to give light yellow foam 1.30 g (63%).

m.p. 46 – 47 ^oC; **$[\alpha]_D^{25}$** –9.9 (*c* 0.95, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 1745, 1690, 1653, 1615, 1578, 1530, 1437, 1349, 1312, 1220, 1219, 1041, 990, 963, 911, 854, 760, 733, 698;

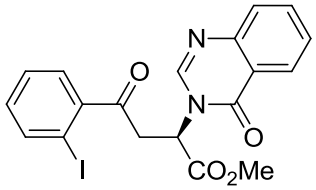


^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm): 8.07 (dd, *J* = 8.6, 1.2 Hz, 1H, $C_{[ar]}H$), 7.93 (dd, *J* = 7.9, 1.1 Hz, 1H, $C_{[ar]}H$), 7.74 – 7.65 (m, 1H, $C_{[ar]}H$), 7.63 – 7.53 (m, 3H, $C_{[ar]}H$), 7.44 (td, *J* = 7.6, 1.1 Hz, 1H, $C_{[ar]}H$), 7.20 – 7.10 (m, 1H, $C_{[ar]}H$), 7.01 (d, *J* = 8.1 Hz, 1H, CON*H*), 5.09 (dt, *J* = 7.9, 3.9 Hz, 1H, $C_{[1]}H$), 3.82 (s, 3H, $C_{[11]}H$), 3.76 (dd, *J* = 3.9, 2.8 Hz, 2H, $C_{[2]}H$);

^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): 202.2 ($C_{[3]}$), 171.0 ($C_{[10]}$), 166.3 ($C_{[12]}$), 146.6 ($C_{[ar]}$), 142.2 ($C_{[ar]}$), 141.3 ($C_{[ar]}$), 134.1 ($C_{[ar]}$), 132.7 ($C_{[ar]}$), 132.5 ($C_{[ar]}$), 131.0 ($C_{[ar]}$), 128.9 ($C_{[ar]}$), 128.9 ($C_{[ar]}$), 128.5 ($C_{[ar]}$), 124.9 ($C_{[ar]}$), 91.3 ($C_{[5]}$), 53.3 ($C_{[11]}$), 49.2 ($C_{[1]}$), 43.0 ($C_{[2]}$);

HRMS (ESI) $[C_{18}H_{15}N_2O_6I+Na]^+$ requires *m/z* 504.9867, found *m/z* 504.9866.

Compound 5



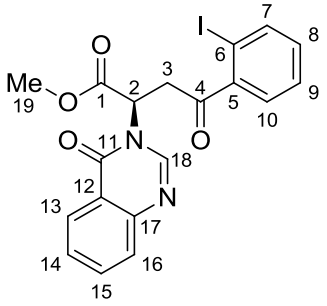
Fe powder (2.3 g, 41 mmol, 10.0 eq) and NH_4Cl (4.4 g, 82 mmol, 20.0 eq) was suspended in 40 mL of ethanol and 40 mL of water, which was heated at 70 ºC for 15 min; then at the same temperature the iodide compound **4** (2.0 g, 4.1 mmol, 1.0 eq) in 40 mL of ethanol was added. After 60 min, the reaction is finished. The mixture was filtered through Celite, washed with methanol, and the solid residue was reflux in ethyl acetate / methanol for 60 min and filtered through Celite again. The combined solution was extracted with ethyl acetate and washed with brine, dried with $MgSO_4$, filtered and concentrated to give a light yellow foam 1.85 g, which was used directly without further purification.

The aniline from above, yellow foam, (1.85 g) and p-toluenesulfonic acid monohydrate (450 mg) was dissolved in 30 mL of methanol and 30 mL trimethyl orthoformate. The mixture was stirred at 70 ºC for 2.5 hours. The volatiles were removed and the residue was dissolved in CH_2Cl_2, washed with sat. $NaHCO_3$, brine, dried with $MgSO_4$, filtered and concentrated under

vacuum. The residue was purified with FCC ethyl acetate / petrol ether (from 1/2 to 1/1) to give colorless solid 1.56 g (82%).

m.p. 137 – 140 ^{o}C; **$[\alpha]_D^{25}$** +115.8 (*c 0.67*, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 1747, 1674, 1608, 1581, 1564, 1473, 1434, 1382, 1354, 1287, 1232, 1213, 1196, 1163, 1108, 1084, 1015, 998, 978, 913, 776, 760, 731, 701, 675, 644;

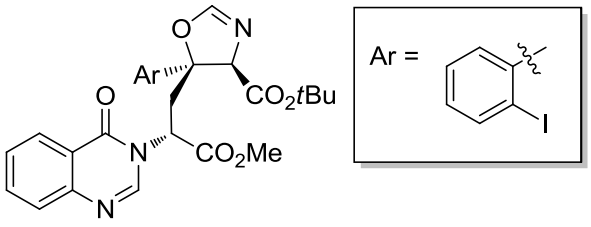


^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm): 8.29 (s, 1H, $C_{[18]}H$), 8.24 (dd, *J* = 8.0, 1.4 Hz, 1H, $C_{[ar]}H$), 7.88 (dd, *J* = 8.0, 1.1 Hz, 1H, $C_{[ar]}H$), 7.80 – 7.69 (m, 2H, $C_{[ar]}H$), 7.54 – 7.44 (m, 2H, $C_{[ar]}H$), 7.38 (td, *J* = 7.6, 1.1 Hz, 1H, $C_{[ar]}H$), 7.11 (td, *J* = 7.7, 1.7 Hz, 1H, $C_{[ar]}H$), 5.35 (dd, *J* = 8.0, 4.3 Hz, 1H, $C_{[2]}H$), 4.06 (dd, *J* = 19.1, 4.3 Hz, 1H, $C_{[3]}H'$), 3.86 (dd, *J* = 19.1, 8.0 Hz, 1H, $C_{[3]}H''$), 3.76 (s, 3H, $C_{[19]}H$);

^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.7 ($C_{[4]}$), 168.8 ($C_{[1]}$), 161.2 ($C_{[11]}$), 148.2 ($C_{[ar]}$), 147.2 ($C_{[18]}$), 142.5 ($C_{[ar]}$), 141.2 ($C_{[ar]}$), 134.9 ($C_{[ar]}$), 132.6 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.4 ($C_{[ar]}$), 127.9 ($C_{[ar]}$), 127.7 ($C_{[ar]}$), 126.8 ($C_{[ar]}$), 122.2 ($C_{[ar]}$), 91.3 ($C_{[6]}$), 57.4 ($C_{[2]}$), 53.5 ($C_{[19]}$), 41.8 ($C_{[3]}$);

HRMS (ESI) $[C_{19}H_{15}N_2O_4I+H]^+$ requires *m/z* 463.0149, found *m/z* 463.0149.

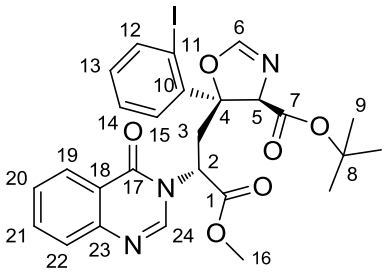
Compound 9



The ketone compound **5** (950 mg, 2.06 mmol, 1.0 eq), Ligand-1 (63 mg, 0.1 mmol, 5% eq), silver acetate (16.6 mg, 0.1 mmol, 5% eq), 4A molecular sieve (950 mg) was dissolved in 60 mL of ethyl acetate. The mixture was stirred at room temperature for 20 min, and at 0 ^{o}C, *tert*-butyl isocyanoacetate (435 mg, 3.1 mmol, 1.5 eq) in 3.5 mL of ethyl acetate was injected into the reaction, which was stirred at the same temperature for 48 h., before filtered through celite, concentrated and purified with FCC petrol ether / ethyl acetate (from 60/40 to 30/70,then 100% ethyl acetate) to give colorless foam 1.12 g (91%, dr = 14:1), which is unstable in solvents.

m.p. 42 – 45 ^{o}C; **[α]$_{D}^{25}$** +0.6 (*c 0.83*, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 1735, 1678, 1636, 1609, 1565, 1473, 1435, 1389, 1370, 1326, 1265, 1213, 1153, 1106, 1073, 1037, 1005, 949, 904, 848, 755, 700, 669, 643;



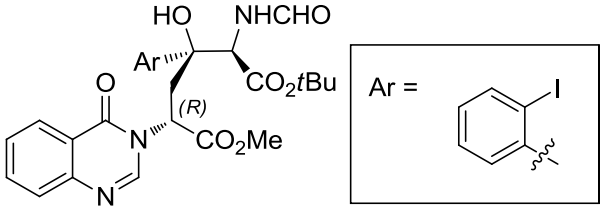
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.01 (d, *J* = 7.7 Hz, 1H, $C_{[ar]}H$), 7.65 (t, *J* = 7.6 Hz, 1H, $C_{[ar]}H$), 7.45 – 7.54 (m, 3H, $C_{[ar]}H$), 7.37 (t, *J* = 7.6 Hz, 1H, $C_{[ar]}H$), 7.30 (d, *J* = 7.7 Hz, 1H, $C_{[ar]}H$), 7.22 (s, 1H, $C_{[24]}H$), 6.91 (t, *J* = 7.7 Hz, 1H, $C_{[ar]}H$), 6.37 (t, *J* = 7.6 Hz, 1H, $C_{[6]}H$), 5.10

(d, J = 10.1 Hz, 1H, $C_{[2]}H$), 4.80 (s, 1H, $C_{[5]}H$), 3.98 (t, J = 13.0 Hz, 1H, $C_{[3]}H'$), 3.69 (s, 3H, $C_{[16]}H$), 3.16 (d, J = 15.9 Hz, 1H, $C_{[3]}H''$), 1.57 (s, 9H, $C_{[9]}H$);

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 170.8 ($C_{[1]}$), 169.3 ($C_{[7]}$), 167.4 ($C_{[17]}$), 160.3 ($C_{[ar]}$), 155.3 ($C_{[24]}$), 147.4 ($C_{[ar]}$), 145.6 ($C_{[ar]}$), 142.9 ($C_{[ar]}$), 140.6 ($C_{[ar]}$), 134.0 ($C_{[ar]}$), 129.5 ($C_{[6]}$), 128.2 ($C_{[ar]}$), 127.2 ($C_{[ar]}$), 126.7 ($C_{[ar]}$), 121.6 ($C_{[ar]}$), 92.7 ($C_{[11]}$), 89.7 ($C_{[4]}$), 83.5 ($C_{[8]}$), 77.4 ($C_{[5]}$), 56.8 ($C_{[2]}$), 53.4 ($C_{[16]}$), 32.8 ($C_{[3]}$), 28.3 ($C_{[9]}$);

HRMS (ESI) $[C_{26}H_{26}N_3O_6I+H]^+$ requires *m/z* 604.0939, found *m/z* 604.0935.

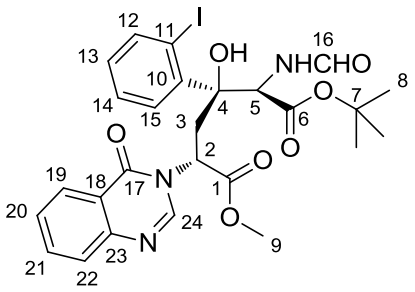
Compound 10



The oxazoline compound **9** (710 mg, 1.17 mmol) was dissolved in 30 mL of THF, and 3 mL of 1 N HCl was added. The reaction was stirred at room temperature for 5 min. The reaction was extract with ethyl acetate, washed with brine, dried with $MgSO_4$, concentrated and purified with FCC CH_2Cl_2 / methanol (from 200/1 to 200/6) to give a white solid 728 mg (99%).

m.p. 88 – 92 ^oC; **$[\alpha]_D^{25}$** +62.7 (*c* 0.51, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 3417, 2979, 2922, 1743, 1678, 1610, 1505, 1474, 1457, 1437, 1374, 1346, 1325, 1266, 1234, 1154, 1037, 1104, 912, 841, 774, 732, 700, 646;

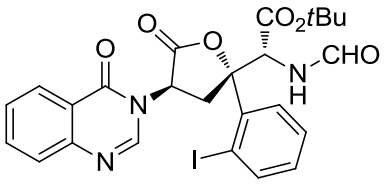


^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm): 8.02 (dd, *J* = 8.0, 1.5 Hz, 1H, $C_{[ar]}H$), 7.84 – 7.70 (m, 3H, NHC*H*O, $C_{[ar]}H$), 7.56 (s, 1H, $C_{[24]}H$), 7.52 (d, *J* = 8.1 Hz, 2H, $C_{[ar]}H$), 7.46 (t, *J* = 7.6 Hz, 1H, $C_{[ar]}H$), 7.38 (d, *J* = 8.4 Hz, 1H, N*H*CHO), 7.08 (t, *J* = 7.7 Hz, 1H, $C_{[ar]}H$), 6.53 (t, *J* = 7.6 Hz, 1H, $C_{[ar]}H$), 5.68 (s, 1H, $C_{[5]}H$), 5.08 (d, *J* = 5.8 Hz, 1H, $C_{[2]}H$), 4.14 – 3.89 (m, 1H, $C_{[3]}H$), 3.65 (s, 3H, $C_{[9]}H$), 3.30 (dd, *J* = 15.7, 3.0 Hz, 1H, $C_{[3]}H'$), 1.59 (s, 9H, $C_{[8]}H$);

^{13}C NMR (Acetone-d_6, 125 MHz) δ (ppm): 171.2 ($C_{[1]}$), 169.4 ($C_{[6]}$), 161.9 ($C_{[16]}$), 161.0 ($C_{[17]}$), 148.9 ($C_{[ar]}$), 147.8 ($C_{[24]}$), 143.2 ($C_{[ar]}$), 143.0 ($C_{[ar]}$), 134.9 ($C_{[ar]}$), 130.4 ($C_{[ar]}$), 129.7 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.1 ($C_{[ar]}$), 127.6 ($C_{[ar]}$), 127.0 ($C_{[ar]}$), 122.8 ($C_{[ar]}$), 94.5 ($C_{[11]}$), 83.3 ($C_{[7]}$), 77.8 ($C_{[4]}$), 59.0 ($C_{[5]}$), 57.9 ($C_{[2]}$), 53.2 ($C_{[9]}$), 35.5 ($C_{[3]}$), 28.3 ($C_{[8]}$);

HRMS (ESI) $[C_{26}H_{28}N_3O_7I+H]^+$ requires *m/z* 622.1045, found *m/z* 622.1042.

Compound 11

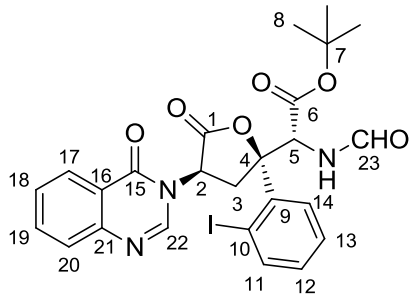


The ester-formamide compound **10** (730 mg, 1.18 mmol) was dissolved in 50 mL of toluene and 2.3 mL of acetic acid, which was stirred at 75 °C for 3 days until all starting material is

consumed. The reaction was concentrated under vacuum and re-dissolved in ethyl acetate, washed with sat. $NaHCO_3$, brine, dried with $MgSO_4$, filtered and concentrated again. The residue was purified with FCC CH_2Cl_2 / methanol (from 200:1 to 200:4) to give product as white solid 485 mg (70%).

m.p. 100 – 112 ^oC; $\mathbf{[\alpha]_D^{25}}$ –34.0 (*c* 1.33, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 2925, 1796, 1723, 1682, 1610, 1517, 1475, 1460, 1424, 1386, 1370, 1324, 1298, 1252, 1200, 1187, 1153, 1108, 1029, 1005, 967, 929, 892, 774, 753, 699;

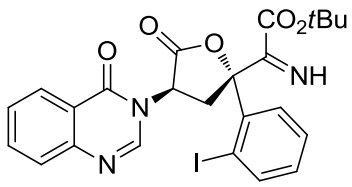


^{1}H NMR (Acetone-d_6, 500 MHz) δ (ppm): 8.24 (s, 1H, $C_{[22]}H$), 8.20 (dd, *J* = 8.1, 1.4 Hz, 1H, $C_{[ar]}H$), 8.09 (dd, *J* = 7.9, 1.3 Hz, 1H, $C_{[ar]}H$), 7.96 (d, *J* = 1.0 Hz, 1H, $C_{[23]}H$), 7.87 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H, $C_{[ar]}H$), 7.70 (d, *J* = 8.1 Hz, 1H, $C_{[ar]}H$), 7.68 (s, 1H, N*H*CHO), 7.61 – 7.55 (m, 2H, $C_{[ar]}H$), 7.53 – 7.49 (m, 1H, C[ar]H), 7.15 (td, *J* = 7.5, 1.7 Hz, 1H, $C_{[ar]}H$), 6.03 (d, *J* = 9.5 Hz, 1H, $C_{[5]}H$), 5.16 (dd, *J* = 11.3, 9.0 Hz, 1H, $C_{[2]}H$), 3.81 – 3.71 (m, 2H, $C_{[3]}H$), 1.56 (s, 9H, $C_{[8]}H$);

^{13}C NMR (Acetone-d_6, 125 MHz) δ (ppm): 170.7 ($C_{[1]}$), 167.6 ($C_{[6]}$), 161.1 ($C_{[23]}$), 160.6 ($C_{[15]}$), 149.0 ($C_{[ar]}$), 147.7 ($C_{[22]}$), 144.1 ($C_{[ar]}$), 140.9 ($C_{[ar]}$), 135.6 ($C_{[ar]}$), 131.4 ($C_{[ar]}$), 129.2 ($C_{[ar]}$), 129.0 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.4 ($C_{[ar]}$), 127.2 ($C_{[ar]}$), 122.9 ($C_{[ar]}$), 94.9 ($C_{[10]}$), 87.8 ($C_{[4]}$), 83.9 ($C_{[7]}$), 57.3 ($C_{[2]}$), 56.6 ($C_{[5]}$), 34.5 ($C_{[3]}$), 28.4 ($C_{[8]}$);

HRMS (ESI) $[C_{25}H_{24}N_3O_6I+H]^+$ requires *m/z* 590.0783, found *m/z* 590.0783.

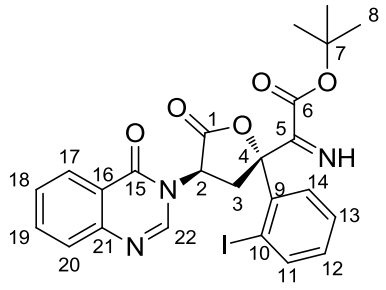
Compound 12



The formamide compound **11** (75 mg, 0.13 mmol, 1.0 eq) was dissolved in 7 mL of methanol, and 0.5 mL of thionyl chloride was added dropwise at 0 °C, the reaction was stirred for 2 h at r.t. before all volatiles were removed under vacuum and residue was dried overnight under high vacuum; then the solid was suspended in 10 mL of sat. $NaHCO_3$ and 10 mL of CH_2Cl_2 was added, after stirring for 1 min at r.t. the organic phase was collected and the aqueous phase was exacted with CH_2Cl_2 and ethyl acetate. The combined organic phase washed with brine and was dried with Na_2SO_4, filtered and concentrated； then 5 mL of CH_2Cl_2 and 2-iodoxybenzoic acid (42 mg, 0.15 mmol, 1.2 eq), then DMSO (1.0 mL) was added at 0 °C. The reaction was stirred at 0°C overnight before diluted with CH_2Cl_2 and washed with water and brine, dried with Na_2SO_4, filtered and concentrated under vacuum. The residue was purified with FCC methanol / CH_2Cl_2 (from 1/200 to 2.5/200) to give a white solid 55 mg (77%).

m.p. 95 – 105 °C; **[α]D^{25}** – 76.2 (*c* 0.83, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 2980, 2931, 1797, 1725, 1679, 1610, 1565, 1474, 1425, 1370, 1325, 1251, 1203, 1187, 1154, 1103, 1029, 1006, 963, 909, 840, 760, 699;

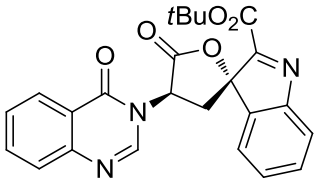


^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm): 12.36 (s, 1H, N*H*), 8.32 (s, 1H, $C_{[22]}$), 8.22 (ddd, *J* = 8.0, 1.6, 0.6 Hz, 1H, $C_{[ar]}$H), 8.06 (dd, *J* = 7.9, 1.3 Hz, 1H, $C_{[ar]}$H), 7.87 (ddd, *J* = 8.2, 7.2, 1.6 Hz, 1H, $C_{[ar]}$H), 7.75 – 7.68 (m, 2H, $C_{[ar]}$H), 7.65 – 7.54 (m, 2H, $C_{[ar]}$H), 7.20 (td, *J* = 7.6, 1.7 Hz, 1H, $C_{[ar]}$H), 5.35 (dd, *J* = 11.3, 9.3 Hz, 1H, $C_{[2]}$H), 4.53 (dd, *J* = 12.8, 11.3 Hz, 1H, $C_{[3]}$H'), 3.17 (dd, *J* = 12.8, 9.3 Hz, 1H, $C_{[3]}$H''), 1.25 (s, 9H, $C_{[8]}$H);

^{13}C NMR (Acetone-d_6, 125 MHz) δ (ppm): 171.6 ($C_{[1]}$), 168.0 ($C_{[6]}$), 160.6 ($C_{[15]}$), 159.9 ($C_{[5]}$), 149.1 ($C_{[ar]}$), 148.0* ($C_{[22]}$), 143.6 ($C_{[ar]}$H), 143.2* ($C_{[ar]}$H), 135.5* ($C_{[ar]}$H), 131.0 ($C_{[ar]}$H), 129.5 ($C_{[ar]}$H), 128.6 ($C_{[ar]}$H), 128.3 ($C_{[ar]}$H), 128.3 ($C_{[ar]}$H), 127.3* ($C_{[ar]}$H), 123.0 ($C_{[ar]}$H), 93.2 ($C_{[10]}$), 86.9 ($C_{[4]}$), 84.5 ($C_{[7]}$), 57.1 ($C_{[2]}$), 35.1 ($C_{[3]}$), 27.7 ($C_{[8]}$), * peak splits;

HRMS (ESI) $[C_{24}H_{22}N_3O_5I+H]^+$ requires *m/z* 560.0677, found *m/z* 560.0654.

Compound 13

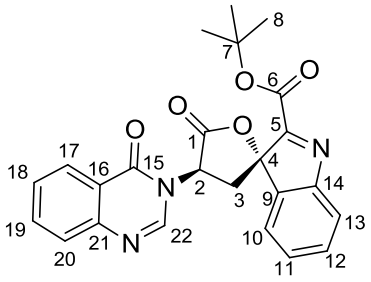


The imine compound **12** (11 mg, 0.02 mmol, 1.0 eq), copper(I) iodide (4.6 mg, 0.024 mmol, 1.2 eq) and magnesium acetate tetrahydrate (6.4 mg, 0.03 mmol, 1.5 eq) was put in a dry flask and

charged with argon. Then 1.2 mL of dry DMSO was injected. The solution was stirred in the r.t. for 5 hours before quenched with sat. NH_4Cl and exacted with CH_2Cl_2, washed with water and dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified with FCC diethyl ether / CH_2Cl_2 (1 / 10) to give the cyclized product as white solid 4.5 mg (52%).

m.p. T_{dec} >210 °C; **$[\alpha]_D^{25}$** + 175.5 (*c* 0.38, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 2979, 2922, 2852, 1795, 1730, 1677, 1610, 1567, 1472, 1370, 1326, 1254, 1196, 1135, 1059, 1033, 971, 910, 841, 773, 698;

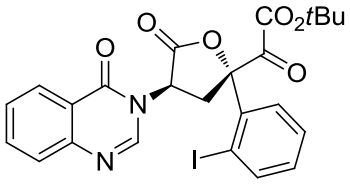


^{1}H NMR (Acetone-d_6, 500 MHz) δ (ppm): 8.61 (s, 1H, $C_{[22]}H$), 8.34 (dd, *J* = 8.0, 1.5 Hz, 1H, $C_{[ar]}H$), 8.27 – 8.11 (m, 1H, $C_{[ar]}H$), 7.91 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H, $C_{[ar]}H$), 7.76 (dt, *J* = 8.1, 1.0 Hz, 1H, $C_{[ar]}H$), 7.75 – 7.68 (m, 1H, $C_{[ar]}H$), 7.65 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H, $C_{[ar]}H$), 7.60 – 7.54 (m, 2H, $C_{[ar]}H$), 5.78 (dd, *J* = 10.7, 8.5 Hz, 1H, $C_{[2]}H$), 3.33 (dd, *J* = 14.0, 10.7 Hz, 1H, $C_{[3]}H$'), 3.17 (dd, *J* = 14.0, 8.6 Hz, 1H, $C_{[3]}H$''), 1.65 (s, 9H, $C_{[8]}H$);

^{13}C NMR (Acetone-d_6, 125 MHz) δ (ppm): 173.1 ($C_{[1]}$), 170.7 ($C_{[6]}$), 161.6 ($C_{[5]}$), 161.4 ($C_{[15]}$), 152.8 ($C_{[ar]}$), 149.4 ($C_{[ar]}$), 148.5 ($C_{[22]}$), 139.9 ($C_{[ar]}$), 135.8 ($C_{[ar]}$), 132.3 ($C_{[ar]}$), 131.0 ($C_{[ar]}$), 128.7 ($C_{[ar]}$), 128.4 ($C_{[ar]}$), 127.2 ($C_{[ar]}$), 125.8 ($C_{[ar]}$), 124.3 ($C_{[ar]}$), 123.0 ($C_{[ar]}$), 89.8 ($C_{[4]}$), 84.8 ($C_{[7]}$), 59.3 ($C_{[2]}$), 32.6 ($C_{[3]}$), 28.3 ($C_{[8]}$);

HRMS (ESI) $[C_{24}H_{21}N_3O_5+H]^+$ requires *m/z* 432.1554, found *m/z* 432.1555.

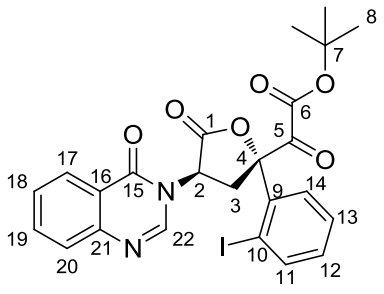
Compound 14



The imine compound **12** (70 mg, 0.13 mmol) was dissolved in 4 mL of THF and 3 mL of H_2O, 0.15 mL of acetic acid was added, and the reaction was stirred at 50 ^oC for 5 hours. The reaction was extracted with ethyl acetate and washed with brine and dried with Na_2SO_4, filtered and concentrated under vacuum, the residue was purified with FCC methanol / CH_2Cl_2 (1/70 to 1/50) to give white solid 55 mg (73%).

m.p. 105 – 108 ^oC; **$[\alpha]_D^{25}$** –77.4 (*c* 0.65, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 3063, 2981, 2926, 2853, 2362, 2335, 1802, 1742, 1680, 1609, 1565, 1469, 1428, 1372, 1296, 1252, 1196, 1162, 1108, 964, 904, 837, 757, 697, 662;



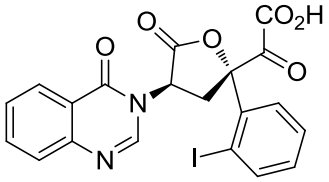
^{1}H NMR (CD_3CN-d_3, 500 MHz) δ (ppm): 8.22 (dd, *J* = 8.0, 1.6 Hz, 1H, $C_{[ar]}H$), 8.04 (dd, *J* = 7.9, 1.3 Hz, 1H, $C_{[ar]}H$), 8.01 (s, 1H, $C_{[22]}H$), 7.85 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H, $C_{[ar]}H$), 7.72 (dt, *J* = 8.3, 0.8 Hz, 1H, $C_{[ar]}H$), 7.67 (dd, *J* = 8.0, 1.6 Hz, 1H, $C_{[ar]}H$), 7.62 – 7.53 (m, 2H, $C_{[ar]}H$), 7.21

(td, *J* = 7.7, 1.7 Hz, 1H, $C_{[ar]}H$), 5.04 (dd, *J* = 10.4, 9.6 Hz, 1H, $C_{[2]}H$), 3.83 (dd, *J* = 13.3, 10.5 Hz, 1H, $C_{[3]}H'$), 3.13 (dd, *J* = 13.3, 9.6 Hz, 1H, $C_{[3]}H''$), 1.30 (s, 9H, $C_{[8]}H$);

^{13}C NMR (CD_3CN-d_3, 125 MHz) δ (ppm): 187.5 ($C_{[5]}$), 171.2 ($C_{[1]}$), 161.0 ($C_{[15]}$), 160.4 ($C_{[6]}$), 149.0 ($C_{[ar]}$), 147.6 ($C_{[22]}$), 142.9 ($C_{[ar]}$), 140.9 ($C_{[ar]}$), 136.0 ($C_{[ar]}$), 132.0 ($C_{[ar]}$), 129.9 ($C_{[ar]}$), 128.8 ($C_{[ar]}$), 128.7 ($C_{[ar]}$), 128.7 ($C_{[ar]}$), 127.2 ($C_{[ar]}$), 122.9 ($C_{[ar]}$), 94.0 ($C_{[10]}$), 88.0 ($C_{[4]}$), 86.3 ($C_{[7]}$), 57.5 ($C_{[2]}$), 34.1 ($C_{[3]}$), 27.8 ($C_{[8]}$);

HRMS (ESI) $[C_{24}H_{21}N_2O_6I+H]^+$ requires *m/z* 561.0517, found *m/z* 561.0516.

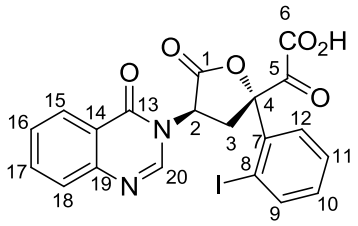
Compound 15



The ketone ester compound **14** (55 mg) was dissolved in 1.5 mL of CH_2Cl_2 and 3.0 mL of trifluoroacetic acid, the reaction was stirred at r.t. for 2 hours, and then all volatiles was removed, the residue was dried under high vacuum overnight to give light yellow solid 50 mg (quant.) which is used for next reaction without further purification.

m.p. 178 – 184 ^oC; **$[\alpha]_D^{25}$** –66.2 (*c* 1.21, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 3065, 2973, 2923, 2853, 2362, 2335, 1799, 1727, 1680, 1612, 1470, 1429, 1389, 1322, 1251, 1198, 1114, 1073, 1030, 961, 760, 698;

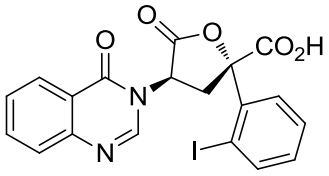


^{1}H NMR ($CDCl_3$, with one drop D_2O, 400 MHz) δ (ppm): 8.76 (s, 1H, $C_{[20]}H$), 8.45 – 8.23 (m, 1H, $C_{[ar]}H$), 8.04 (dd, *J* = 7.9, 1.3 Hz, 1H, $C_{[ar]}H$), 7.91 – 7.78 (m, 2H, $C_{[ar]}H$), 7.70 – 7.56 (m, 2H, $C_{[ar]}H$), 7.51 (td, *J* = 7.6, 1.3 Hz, 1H, $C_{[ar]}H$), 7.18 (td, *J* = 7.6, 1.7 Hz, 1H), 5.88 (t, *J* = 10.6 Hz, 1H, $C_{[2]}H$), 3.64 (d, *J* = 10.6 Hz, 2H, $C_{[3]}H$);

^{13}C NMR ($CDCl_3$, with one drop of D_2O, 125 MHz) δ (ppm): 186.7 ($C_{[5]}$), 170.6 ($C_{[1]}$), 162.4 ($C_{[6]}$), 160.3 ($C_{[13]}$), 146.1 ($C_{[20]}$), 145.0 ($C_{[ar]}$), 142.3 ($C_{[ar]}$), 139.0 ($C_{[ar]}$), 136.1 ($C_{[ar]}$), 131.4 ($C_{[ar]}$), 129.1 ($C_{[ar]}$), 128.8 ($C_{[ar]}$), 127.7 ($C_{[ar]}$), 127.6 ($C_{[ar]}$), 125.9 ($C_{[ar]}$), 120.7 ($C_{[ar]}$), 96.0 ($C_{[8]}$), 87.7 ($C_{[4]}$), 52.3 ($C_{[3]}$), 37.5 ($C_{[3]}$);

HRMS (ESI) $[C_{20}H_{13}N_2O_6I+H]^+$ requires *m/z* 504.9891, found *m/z* 504.9889.

Compound 16

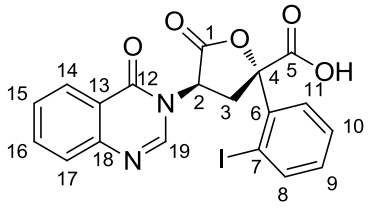


The α-ketone acid compound **15** (50 mg, 0.1 mmol, 1.0 eq) and (diacetoxyiodo)benzene (50 mg, 0.15 mmol, 1.5 eq) was dissolved in 3.6 mL of acetic acid and 0.4 mL of water, the reaction was stirred for 20 hours at r.t., before all volatiles was removed under vacuum and the residue was

purified with FCC methanol / CH_2Cl_2 (1 / 100 to 1 / 9 with acetic acid) to give a white solid 39 mg (80%).

m.p. 183 – 187 ºC; **$[\alpha]_D^{25}$** +45.6 (*c* 0.54, Acetone);

IR (film) ν_{max}/cm^{-1}: 2979, 2362, 2335, 1799, 1728, 1681, 1614, 1567, 1476, 1429, 1393, 1318, 1275, 1239, 1201, 1083, 1003, 978, 927, 769, 733, 693;

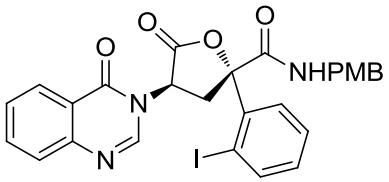


^{1}H NMR (Acetone-d_6, 500 MHz) δ (ppm): 8.31 (s, 1H, $C_{[19]}H$), 8.23 (dd, *J* = 8.1, 1.5 Hz, 1H, $C_{[ar]}H$), 8.07 (dd, *J* = 7.8, 1.2 Hz, 1H, $C_{[ar]}H$), 7.87 (ddd, *J* = 8.5, 7.2, 1.5 Hz, 1H, $C_{[ar]}H$), 7.72 (dd, *J* = 8.3, 1.2 Hz, 1H, $C_{[ar]}H$), 7.65 – 7.53 (m, 3H, $C_{[ar]}H$), 7.22 (td, *J* = 7.5, 1.9 Hz, 1H, $C_{[ar]}H$), 5.30 (dd, *J* = 10.9, 9.3 Hz, 1H, $C_{[2]}H$), 4.06 (dd, *J* = 12.9, 10.9 Hz, 1H, $C_{[3]}H'$), 3.28 (dd, *J* = 12.9, 9.4 Hz, 1H, $C_{[3]}H''$), COO*H* does not appear;

^{13}C NMR (Acetone-d_6, 125 MHz) δ (ppm): 171.3 ($C_{[1]}$), 168.4 ($C_{[5]}$), 160.7 ($C_{[12]}$), 149.1 ($C_{[ar]}$), 148.0 ($C_{[19]}$), 142.7 ($C_{[ar]}$), 142.3 ($C_{[ar]}$), 135.6 ($C_{[ar]}$), 131.3 ($C_{[ar]}$), 129.4 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.4 ($C_{[ar]}$), 127.6 ($C_{[ar]}$), 127.2 ($C_{[ar]}$), 123.0 ($C_{[ar]}$), 95.1 ($C_{[7]}$), 87.6 ($C_{[4]}$), 57.3 ($C_{[2]}$), 35.4 ($C_{[3]}$);

HRMS (ESI) $[C_{19}H_{13}O_5N_2I+H]^+$ requires *m/z* 476.9942, found *m/z* 476.9942.

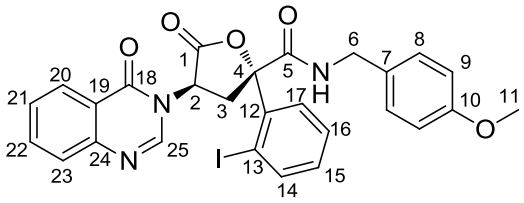
Compound 17



The acid compound **16** (9.5 mg, 0.02 mmol, 1.0 eq), 4-methoxybenzylamine (4.11 mg, 0.03 mmol, 1.5 eq), HATU (11.4 mg, 0.03 mmol, 1.5 eq) and *N*,*N*-diisopropylethylamine (6.45 mg, 0.05 mmol, 2.5 eq) was dissolved in 1.8 mL of CH_2Cl_2 and 0.2 mL of DMF. The reaction was stirred for 40 min at r.t. before quenched with 1 N HCl, exacted with CH_2Cl_2 and ethyl acetate, washed with brine and dried with Na_2SO_4, filtered and concentrated under vacuum. The residue was purified with FCC methanol / CH_2Cl_2 (1 / 100 to 1 / 50) to give white solid 8.5 mg (70%).

m.p. 90 – 95 ^{o}C; **$[\alpha]_D^{25}$** –39.1 (*c* 0.54, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 3027, 2878, 2802, 1746, 1679, 1610, 1520, 1495, 1471, 1451, 1348, 1262, 1203, 1074, 1049, 1035, 996, 880, 794, 756, 726, 699;



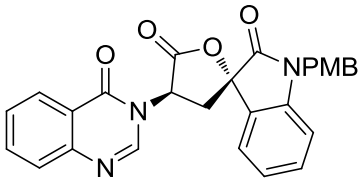
^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm): 8.26 (dd, *J* = 8.0, 1.5 Hz, 1H, $C_{[ar]}H$), 8.08 (s, 1H, $C_{[25]}H$), 8.01 (dd, *J* = 7.9, 1.3 Hz, 1H, $C_{[ar]}H$), 7.79 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H, $C_{[ar]}H$), 7.74 (dd, *J* = 8.2, 1.2 Hz, 1H, $C_{[ar]}H$), 7.58 (dd, *J* = 7.9, 1.6 Hz, 1H, $C_{[ar]}H$), 7.52 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H, $C_{[ar]}H$), 7.43 (td, *J* = 7.7, 1.3 Hz, 1H, $C_{[ar]}H$), 7.24 – 7.26 (d, *J* = 8.4 Hz, 2H, $C_{[ar]}H$), 7.10 (td, *J* = 7.6, 1.6 Hz, 1H, $C_{[ar]}H$), 6.84 (d, *J* = 8.6 Hz, 2H, $C_{[ar]}H$), 6.39 (t, *J* = 5.6 Hz, 1H, CON*H*), 5.23

(dd, J = 10.6, 9.3 Hz, 1H, $C_{[2]}H$), 4.49 (dd, J = 11.2, 5.6 Hz, 2H, $C_{[6]}H$), 3.77 (s, 3H, $C_{[11]}H$), 3.77 – 3.72 (m, 1H, $C_{[3]}H'$), 3.23 (dd, J = 14.0, 10.7 Hz, 1H, $C_{[3]}H''$);

^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): 170.9 ($C_{[1]}$), 167.4 ($C_{[5]}$), 160.6 ($C_{[18]}$), 159.4 ($C_{[10]}$), 148.0 ($C_{[ar]}$), 144.9 ($C_{[25]}$), 142.8 ($C_{[ar]}$), 139.7 ($C_{[ar]}$), 135.2 ($C_{[ar]}$), 131.2 ($C_{[ar]}$), 129.7 ($C_{[ar]}$), 129.4 ($C_{[ar]}$), 129.0 ($C_{[ar]}$), 128.1 ($C_{[ar]}$), 128.0 ($C_{[ar]}$), 128.0 ($C_{[ar]}$), 127.2 ($C_{[ar]}$), 121.7 ($C_{[ar]}$), 114.3 ($C_{[ar]}$), 94.8 ($C_{[13]}$), 87.9 ($C_{[4]}$), 55.5 ($C_{[2]}$ & $C_{[11]}$), 44.4 ($C_{[6]}$), 36.4 ($C_{[3]}$);

HRMS (ESI) $[C_{27}H_{22}O_5N_3I+H]^+$ requires *m/z* 596.0677, found *m/z* 596.0676.

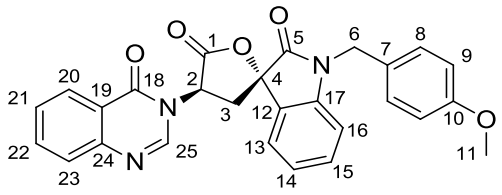
Compound 18



The amide compound **17** (7.5 mg, 0.013 mmol, 1.0 eq), Copper(I) iodide (2.9 mg, 0.015 mmol, 1.2 eq) and magnesium acetate tetrahydrate (4.1 mg, 0.019 mmol, 1.5 eq) was put in a dry flask and charged with argon, then 0.76 mL of dry DMSO was injected. The solution was stirred at r.t. for 3 hours before being quenched with sat. NH_4Cl and exacted with CH_2Cl_2 and ethyl acetate, washed with water and dried with Na_2SO_4, filtered and concentrated under vacuum. The residue was purified with FCC methanol / CH_2Cl_2 (1 / 150) to give the protected oxindole product as white solid 4.2 mg (70%).

m.p. 204 – 210 ^oC; **$[\alpha]_D^{25}$** –33.9 (*c* 0.23, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 2926, 1779, 1731, 1673, 1611, 1514, 1469, 1373, 1322, 1300, 1256, 1191, 1109, 1047, 977, 908, 839, 812, 774, 748, 690;

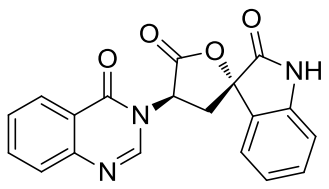


^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm): 8.38 (d, *J* = 1.6 Hz, 1H, $C_{[ar]}H$), 8.37 (d, *J* = 1.4 Hz, 1H, $C_{[ar]}H$), 7.89 – 7.78 (m, 2H, $C_{[ar]}H$), 7.58 (ddd, *J* = 8.2, 6.9, 1.5 Hz, 1H, $C_{[ar]}H$), 7.47 (dd, *J* = 7.5, 1.2 Hz, 1H, $C_{[ar]}H$), 7.37 (td, *J* = 7.8, 1.2 Hz, 1H, $C_{[ar]}H$), 7.27 (d, *J* = 8.7 Hz, 2H, $C_{[ar]}H$), 7.18 (td, *J* = 7.6, 0.9 Hz, 1H, $C_{[ar]}H$), 6.92 – 6.84 (m, 3H, $C_{[ar]}H$), 6.18 (t, *J* = 10.1 Hz, 1H, $C_{[2]}H$), 4.94 (d, *J* = 15.4 Hz, 1H, $C_{[6]}H'$), 4.84 (d, *J* = 15.4 Hz, 1H, $C_{[6]}H''$), 3.80 (s, 3H, $C_{[11]}H$), 3.08 (dd, *J* = 13.6, 10.4 Hz, 1H, $C_{[3]}H'$), 3.00 (dd, *J* = 13.6, 9.8 Hz, 1H, $C_{[3]}H''$);

^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): 172.7 ($C_{[5]}$), 171.2 ($C_{[1]}$), 160.9 ($C_{[18]}$), 159.6 ($C_{[10]}$), 147.9 ($C_{[ar]}$), 144.2 ($C_{[25]}$), 143.2 ($C_{[ar]}$), 135.2 ($C_{[ar]}$), 131.9 ($C_{[ar]}$), 129.0 ($C_{[ar]}$), 128.2 ($C_{[ar]}$), 128.1 ($C_{[ar]}$), 127.3 ($C_{[ar]}$), 126.8 ($C_{[ar]}$), 126.4 ($C_{[ar]}$), 124.3 ($C_{[ar]}$), 124.1 ($C_{[ar]}$), 121.6 ($C_{[ar]}$), 114.6 ($C_{[ar]}$), 110.7 ($C_{[ar]}$), 80.7 ($C_{[4]}$), 55.5 ($C_{[11]}$), 52.9 ($C_{[2]}$), 44.1 ($C_{[6]}$), 36.5 ($C_{[3]}$);

HRMS (ESI) $[C_{27}H_{21}O_5N_3+H]^+$ requires *m/z* 468.1554, found *m/z* 468.1555.

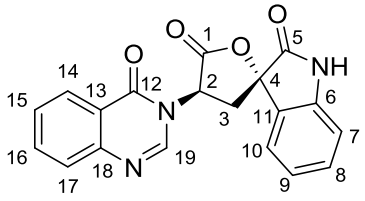
Compound 1



The protected cyclic amide compound **18** (2.5 mg) was dissolved in 1.5 mL of CH_2Cl_2, and trifluoromethanesulfonic acid (15 μL) was added at r.t., the reaction was stirred at r.t. for another 5 min until the starting material disappeared completely on TLC. After quench with aq. $NaHCO_3$, the mixture was extracted with chloroform and ethyl acetate, washed with brine and dried with Na_2SO_4, filtered and concentrated under vacuum, the residue was purified with FCC methanol / CH_2Cl_2 (1 / 100 to 1 / 30) to give a white solid 1.3 mg (64%).

m.p. 271 – 276 °C; **$[\alpha]_D^{25}$** +278.6 (*c* 0.03, MeOH);

IR (film) ν_{max}/cm^{-1}: 2920, 2851, 1787, 1743, 1673, 1612, 1563, 1473, 1439, 1387, 1327, 1280, 1251, 1207, 1186, 1112, 1058, 776, 752, 700;



^{1}H NMR (DMSO, 500 MHz) δ (ppm): 10.90 (s, 1H, CON*H*), 8.64 (s, 1H, $C_{[19]}H$), 8.24 (dd, *J* = 7.9, 1.5 Hz, 1H, $C_{[14]}H$), 7.93 (ddd, *J* = 8.4, 7.1, 1.6 Hz, 1H, $C_{[16]}H$), 7.76 (d, *J* = 8.2 Hz, 1H, $C_{[17]}H$), 7.68 – 7.62 (m, 2H, $C_{[10]}H$ & $C_{[15]}H$), 7.42 (td, *J* = 7.7, 1.3 Hz, 1H, $C_{[8]}H$), 7.18 (td, *J* = 7.6, 1.0 Hz, 1H, $C_{[9]}H$), 6.96 (d, *J* = 7.8 Hz, 1H, $C_{[7]}H$), 5.86 (t, *J* = 10.0 Hz, 1H, $C_{[2]}H$), 3.01 (dd, *J* = 10.1, 3.1 Hz, 2H, $C_{[3]}H$);

^{13}C NMR (DMSO, 125 MHz) δ (ppm): 175.4 ($C_{[5]}$), 171.9 ($C_{[1]}$), 159.9 ($C_{[12]}$), 147.8 ($C_{[19]}$), 147.7 ($C_{[18]}$), 142.8 ($C_{[6]}$), 135.1 ($C_{[16]}$), 131.7 ($C_{[8]}$), 127.7 ($C_{[15]}$), 127.5 ($C_{[17]}$), 126.4 ($C_{[11]}$), 126.1 ($C_{[14]}$), 125.3 ($C_{[10]}$), 123.1 ($C_{[9]}$), 121.4 ($C_{[13]}$), 110.7 ($C_{[7]}$), 80.9 ($C_{[4]}$), 56.5 ($C_{[2]}$), 33.4 ($C_{[3]}$);

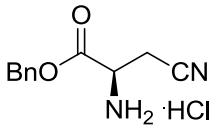
HRMS (ESI) $[C_{19}H_{13}O_4N_3+H]^+$ requires *m/z* 348.0979, found *m/z* 348.0979.

Spectroscopic and other data for synthetic compound **1** are in good agreement with reported data[1], where compound **1**'s melting point was 267 – 269 °C and $\mathbf{[\alpha]_D^{20}}$ was +250 (*c* 0.3, MeOH).

Carbon No.	Isolated	Synthetic	Difference
5	175.4	175.4	0
1	171.9	171.9	0
12	159.8	159.9	-0.1
19	147.8	147.8	0
18	147.7	147.7	0
6	142.9	142.8	0.1
16	135.1	135.1	0
8	131.6	131.7	-0.1
15	127.7	127.7	0
17	127.4	127.5	-0.1
11	126.4	126.4	0
14	126.1	126.1	0
10	125.2	125.3	-0.1
9	123.0	123.1	-0.1
13	121.4	121.4	0
7	110.8	110.7	0.1
4	80.9	80.9	0
2	56.5	56.5	0

3	33.4	33.4	0

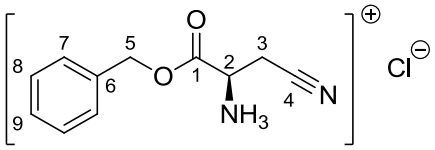
Compound S1



Compound **S1** was synthesized from *D*-Asparagine following the same procedure as described by Rapoport *et al*[2].

m.p. 157 – 160 °C; **$[\alpha]_D^{25}$** +14.0 (*c* 1.00, MeOH)

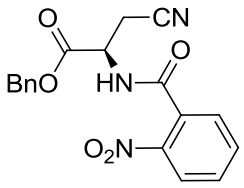
IR (neat) ν_{max}/cm^{-1}: 2830, 1743, 1486, 1413, 1223, 1152, 1069, 935, 753, 701;



^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm): 8.92 (s, 3H, N$\underline{H}_3$), 7.34 – 7.50 (m, 5H, $C_{[7][8][9]}H$), 5.29 (s, 2H, $C_{[5]}H$), 4.60 (dd, *J* = 6.7, 5.3 Hz, 1H, $C_{[2]}H$), 3.14 – 3.31 (m, 2H, $C_{[3]}H$);

^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm): 166.6 ($C_{[1]}$), 134.3 ($C_{[6]}$), 128.0 ($C_{[7]}$), 127.9 ($C_{[9]}$), 127.7 ($C_{[8]}$), 115.8 ($C_{[4]}$), 67.3 ($C_{[5]}$), 47.7 ($C_{[2]}$), 18.1 ($C_{[3]}$).

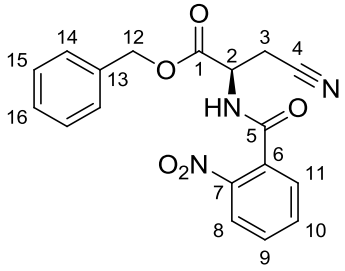
Compound S2



Compound **S1** (3.22 g, 13.4 mmol, 1.0 eq) was dissolved in H_2O 50 mL and CH_2Cl_2 100 mL. To the heterogeneous mixture, $NaHCO_3$ (3.37 g, 40.1 mmol, 3.0 eq) was added portionwise, and 2-nitrobenzoyl chloride (2.98 g, 2.1 mL, 16.1 mmol, 1.2 eq) was added dropwise. After stirred at room temperature for 30 min, the mixture was separated, and the aqueous phase was extract by 20 mL of CH_2Cl_2 for twice. Combined organic phase was washed by 20 mL of 0.5 M NaOH and brine, dried with $MgSO_4$. The combined layers were filtered and the solvent removed under vacuum to give 4.70 g of crude product, which was recrystallized from PE/EA to give 4.18 g (88%) of white solid.

m.p. 162 – 164 ^oC; $\mathbf{[\alpha]_D^{25}}$ –31.4 (*c* 1.00, $CHCl_3$)

IR (film) ν_{max}/cm^{-1}: 2922, 2852, 1742, 1669, 1532, 1349, 1214, 770, 630;

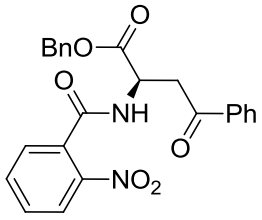


^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm): 9.61 (d, *J* = 7.8 Hz, 1H, CONH), 8.07 (dd, *J* = 8.1, 1.2 Hz, 1H, $C_{[8]}H$), 7.70 – 7.85 (m, 2H, $C_{[9][11]}H$), 7.52 (dd, *J* = 7.5, 1.5 Hz, 1H, $C_{[10]}H$), 7.32 – 7.44 (m, 5H, $C_{[14][15][16]}H$), 5.20 (d, *J* = 5.6 Hz, 2H, $C_{[12]}H$), 4.86 (td, *J* = 8.1, 5.4 Hz, 1H, $C_{[2]}H$), 3.13 (dd, *J* = 17.0, 5.5 Hz, 1H, $C_{[3]}H'$), 3.05 (dd, *J* = 17.0, 8.4 Hz, 1H, $C_{[3]}H''$);

^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm): 168.2 ($C_{[1]}$), 165.2 ($C_{[5]}$), 146.4 ($C_{[7]}$), 135.0 ($C_{[ar]}$), 133.2 ($C_{[ar]}$), 130.8 ($C_{[ar]}$), 130.7 ($C_{[ar]}$), 128.5 ($C_{[ar]}$), 127.9 ($C_{[ar]}$), 127.7 ($C_{[ar]}$), 127.4 ($C_{[ar]}$), 123.8 ($C_{[ar]}$), 117.2 ($C_{[4]}$), 66.4 ($C_{[12]}$), 48.4 ($C_{[2]}$), 18.9 ($C_{[3]}$);

HRMS (ESI) $[C_{18}H_{15}N_3O_5+Na]^+$ requires *m/z* 376.0915, found *m/z* 376.0914.

Compound 6

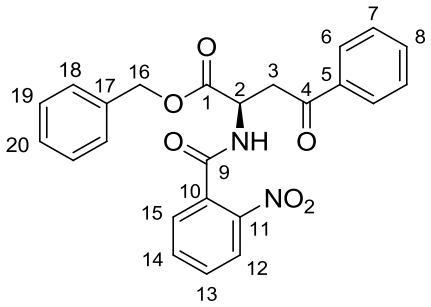


Compound **6** was synthesized following a modified procedure described by Wu *et al*[3].

Compound **S2** (3.25g, 9.2 mmol, 1.0 eq), potassium phenyltrifluoroborate (3.38g, 18.4 mmol, 2.0 eq), palladium(II) acetate (155 mg, 0.69 mmol, 0.075 eq) and 2,2'-Bipyridyl (215 mg, 1.38 mmol, 0.15 eq) were dissolved in the mixture of THF 69 mL and H_2O 13.8 mL. To this solution, TFA (10.5 g, 7.0 mL, 92.0 mmol, 10.0 eq) was added. Then the reaction was stirred at 70 ^oC under Argon atmosphere for 15 hours. Then the mixture was diluted with ethyl acetate 100 mL, washed with 1 M HCl, 0.5 M NaOH and brine, dried with $MgSO_4$, filtered and concentrated to give a dark yellow solid residue, which was purified by the first FCC Et_2O/CH_2Cl_2 (from 1/50 to 1/20) to give crude product 3.61 g. Recrystallization from $EtOH/H_2O$ (70 mL / 35 mL) gave a yellow crystal 3.35 g, which was purified by the second FCC Et_2O / CH_2Cl_2 (1/20) to give a white solid 3.30 g (83%).

m.p. 121 – 122 °C; **[α]$_D^{25}$** +53.6 (*c* 1.00, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 1742, 1674, 1529, 1451, 1348, 1215, 1111, 1039, 995, 909, 734, 696;

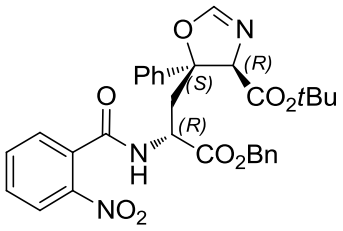


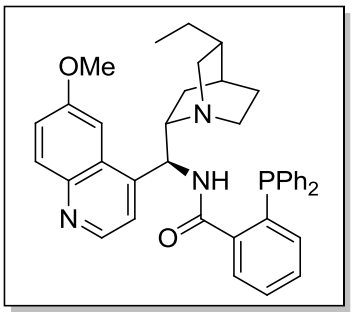
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.04 (dd, *J* = 8.1, 1.2 Hz, 1H, $C_{[12]}H$), 7.95 – 8.02 (m, 2H, $C_{[ar]}H$), 7.58 – 7.72 (m, 3H, $C_{[ar]}H$), 7.50 – 7.58 (m, 3H, $C_{[ar]}H$), 7.37 (s, 5H, $C_{[ar]}H$), 7.12 (d, *J* = 8.3 Hz, 1H, N<u>H</u>CO), 5.23 (dd, *J* = 11.2, 5.1 Hz, 1H, $C_{[16]}H$), 3.95 (dd, *J* = 18.5, 4.0 Hz, 1H, $C_{[3]}H$'), 3.88 (dd, *J* = 18.4, 3.9 Hz, 1H, $C_{[3]}H$'');

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 198.2 ($C_{[4]}$), 170.6 ($C_{[1]}$), 166.1 ($C_{[9]}$), 146.4 ($C_{[11]}$), 135.9 ($C_{[ar]}$), 135.1 ($C_{[ar]}$), 133.8 ($C_{[ar]}$), 133.7 ($C_{[ar]}$), 132.3 ($C_{[ar]}$), 130.6 ($C_{[ar]}$), 128.7 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.5 ($C_{[ar]}$), 128.4 ($C_{[ar]}$), 128.3 ($C_{[ar]}$), 128.2 ($C_{[ar]}$), 124.6 ($C_{[ar]}$), 67.6 ($C_{[16]}$), 48.9 ($C_{[2]}$), 39.9 ($C_{[3]}$);

HRMS (ESI) $[C_{24}H_{20}N_2O_6+Na]^+$ requires *m/z* 455.1214, found *m/z* 455.1213.

Compound 7



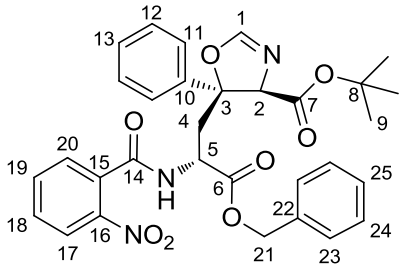


Ligand-1

The ketone compound **6**, (432 mg, 1.0 mmol, 1.0 eq), Ligand-**1** (30 mg, 0.05 mmol, 0.05 eq), AgOAc (8 mg, 0.05 mmol, 0.05 eq) and activated 4A molecular sieve 300 mg were dissolved in 18 mL ethyl acetate. After stirring at 0 ^{o}C for 30 min, *tert*-butyl isocyanoacetate (216 mg, 1.5 mmol, 1.5 eq) in 2 mL of ethyl acetate was added into the reaction mixture. The reaction was stirring at 0 ^{o}C for 5 days. The reaction was filtered through the Celite, concentrated and purified by FCC Et_2O/CH_2Cl_2 (from 1/10 to 1/8) to give a colourless foam 410 mg (71%, d.r. = 12.5:1).

m.p. 64 – 66 ^{o}C; **[α]$_D^{25}$** –40.4 (*c* 1.27, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 1742, 1670, 1636, 1533, 1450, 1350, 1312, 1154, 1024, 960, 913, 846, 790, 735, 700;



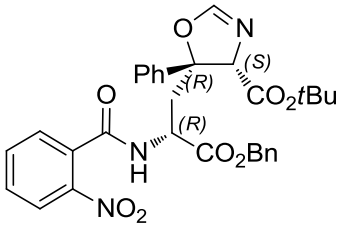
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.94 – 8.05 (m, 1H, $C_{[17]}H$), 7.50 – 7.60 (m, 2H, $C_{[ar]}H$), 7.41 – 7.48 (m, 2H, $C_{[ar]}H$), 7.32 – 7.40 (m, 7H, $C_{[ar]}H$), 7.27 – 7.32 (m, 1H, $C_{[ar]}H$), 7.07 – 7.12 (m, 1H, $C_{[ar]}H$), 6.87 (d, *J* = 1.5 Hz, 1H, CONH), 6.09 (d, *J* = 7.6 Hz, 1H, $C_{[1]}H$), 5.00 (d, *J* = 3.4

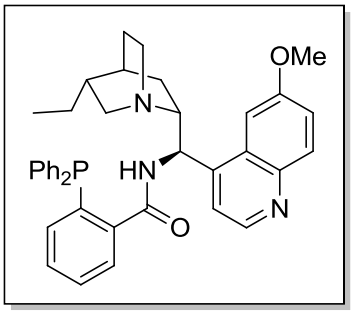
Hz, 2H, $C_{[21]}H$), 4.75 (q, *J* = 6.5 Hz, 1H, $C_{[5]}H$), 4.59 (s, 1H, $C_{[2]}H$), 2.77 (dd, *J* = 14.5, 6.2 Hz, 1H, $C_{[4]}H$'), 2.58 (dd, *J* = 14.4, 6.6 Hz, 1H, $C_{[4]}H$''), 1.54 (s, 9H, $C_{[9]}H$);

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 170.7 ($C_{[6]}$), 167.7 ($C_{[7]}$), 165.3 ($C_{[14]}$), 154.7 ($C_{[1]}$), 146.5 ($C_{[16]}$), 142.1 ($C_{[10]}$), 134.9 ($C_{[ar]}$), 133.3 ($C_{[ar]}$), 131.8 ($C_{[ar]}$), 130.7 ($C_{[ar]}$), 128.9 ($C_{[ar]}$), 128.7 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.5 ($C_{[ar]}$), 128.5 ($C_{[ar]}$), 128.1 ($C_{[ar]}$), 124.6 ($C_{[ar]}$), 124.5 ($C_{[ar]}$), 87.9 ($C_{[3]}$), 83.3 ($C_{[8]}$), 80.4 ($C_{[2]}$), 67.5 ($C_{[21]}$), 50.2 ($C_{[5]}$), 38.0 ($C_{[4]}$), 28.0 ($C_{[9]}$);

HRMS (ESI) $[C_{31}H_{31}N_3O_8+Na]^+$ requires *m/z* 596.2003, found *m/z* 596.2000.

Compound 8



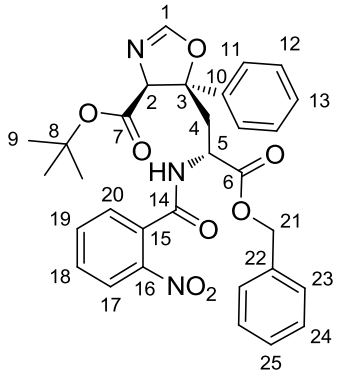


Ligand-2

The ketone compound **6** (432 mg, 1.0 mmol, 1.0 eq), Ligand-**2** (30 mg, 0.05 mmol, 0.05 eq), AgOAc (8 mg, 0.05 mmol, 0.05 eq) and activated 4A molecular sieve 300 mg were dissolved in 18 mL ethyl acetate. After stirring at 0 ^oC for 30 min, *tert*-butyl isocyanoacetate (216 mg, 1.5 mmol, 1.5 eq) in 2 mL of ethyl acetate was added into the reaction mixture. The reaction was stirring at 0 ^oC for 5 days, then filtered through the Celite, concentrated and purified by FCC Et_2O/CH_2Cl_2 (from 1/10 to 1/8) gave the colourless foam 430 mg (75%, d.r. > 20:1).

m.p. 55 – 58 ^oC; **$[\alpha]_D^{25}$** +10.7 (*c* 1.50, $CHCl_3$);

IR (film) ν_{max}/cm^{-1}: 1739, 1672, 1635, 1531, 1456, 1369, 1349, 1214, 1153, 1019, 963, 912, 843, 791, 733, 700, 647;

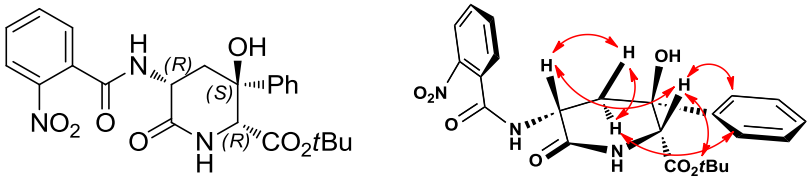


^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.92 – 8.01 (m, 1H, $C_{[17]}H$), 7.50 –7.60 (m, 2H, $C_{[ar]}H$), 7.45 (d, *J* = 7.4 Hz, 2H, $C_{[ar]}H$), 7.32 – 7.41 (m, 7H, $C_{[ar]}H$), 7.23 – 7.28 (m, 1H, $C_{[ar]}H$), 7.04 – 7.10 (m, 1H, $C_{[ar]}H$), 6.68 (d, *J* = 1.9 Hz, 1H, CONH), 6.21 (d, *J* = 7.0 Hz, 1H, $C_{[1]}H$), 5.22 (d, *J* = 12.1 Hz, 1H, $C_{[21]}H'$), 5.09 (d, *J* = 12.1 Hz, 1H, $C_{[21]}H''$), 4.63 (d, *J* = 2.1 Hz, 1H, $C_{[2]}H$), 4.60 (dt, *J* = 7.6, 3.9 Hz, 1H, $C_{[5]}H$), 2.81 (dd, *J* = 14.8, 3.8 Hz, 1H, $C_{[4]}H'$), 2.50 (dd, *J* = 14.8, 7.9 Hz, 1H, $C_{[4]}H''$), 1.51 (s, 9H, $C_{[9]}H$);

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 170.7 ($C_{[6]}$), 167.7 ($C_{[7]}$), 165.4 ($C_{[14]}$), 154.6 ($C_{[1]}$), 146.7 ($C_{[16]}$), 142.1 ($C_{[10]}$), 135.1 ($C_{[ar]}$), 133.2 ($C_{[ar]}$), 131.8 ($C_{[ar]}$), 130.6 ($C_{[ar]}$), 129.1 ($C_{[ar]}$), 128.8 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.6 ($C_{[ar]}$), 128.2 ($C_{[ar]}$), 124.4 ($C_{[ar]}$), 88.5 ($C_{[3]}$), 83.3 ($C_{[8]}$), 80.3 ($C_{[2]}$), 67.5 ($C_{[21]}$), 50.3 ($C_{[5]}$), 37.4 ($C_{[4]}$), 28.0 ($C_{[9]}$);

HRMS (ESI) $[C_{31}H_{31}N_3O_8+H]^+$ requires *m/z* 574.2184, found *m/z* 574.2182.

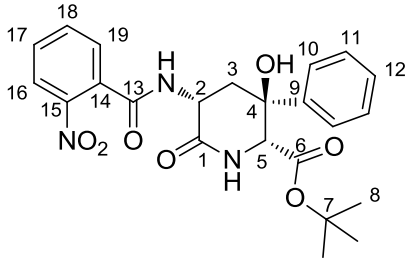
Compound S3



The oxazoline Compound **7** (660 mg, 1.15 mmol) was dissolved in methanol 40 mL, and added 3.0 mL of thionyl chloride at – 78 °C; removed the cold bath and stirred at r.t. for 90 min, the reaction was quenched by saturated $NaHCO_3$, exacted by Ethyl acetate 20 mL for three times, combined the organic phase, washed with brine 15 mL, dried with Magnesium sulfate, removed solvent and re-dissolved in Ethyl acetate 10 mL and 1 mL of Triethylamine; the mixture was stirred at 70 °C for 90 min. After cooling down, filtered the mixture and washed the solid with Ether to give white solid 430 mg (82%, single diastereomer).

m.p. 206 – 208 °C; **[α]$_D^{25}$** –101.3 (*c* 0.63, MeOH);

IR (neat) ν_{max}/cm^{-1}: 3392, 1736, 78, 1658, 1640, 1541, 1482, 1410, 1356, 1325, 1273, 1223, 1157, 1094, 1068, 1046, 957, 943, 912, 899, 855, 790, 759, 733, 696, 643;



^{1}H NMR (MeOD-d_4, 500 MHz) δ (ppm): 8.14 (dd, *J* = 8.0, 0.9 Hz, 1H, $C_{[16]}H$), 7.78 – 7.83 (m, 2H, $C_{[ar]}H$), 7.70 (ddd, *J* = 8.2, 5.5, 3.5 Hz, 1H, $C_{[ar]}H$), 7.51 – 7.56 (m, 2H, $C_{[ar]}H$), 7.38 – 7.44 (m, 2H, $C_{[ar]}H$), 7.33 – 7.38 (m, 1H, $C_{[ar]}H$), 5.21 (dd, *J* = 12.0, 6.1 Hz, 1H, $C_{[2]}H$), 4.17 (d, *J* = 1.6 Hz, 1H, $C_{[5]}H$), 2.99 (dd, *J* = 12.9, 12.1 Hz, 1H, $C_{[3]}H$'), 2.57 (ddd, *J* = 12.8, 6.2, 1.7 Hz, 1H, $C_{[3]}H$''), 1.03 (s, 9H, $C_{[8]}H$);

^{13}C NMR (MeOD-d_4, 125 MHz) δ (ppm): 172.9 ($C_{[6]}$), 171.1 ($C_{[1]}$), 169.7 ($C_{[13]}$), 148.1 ($C_{[15]}$), 144.2 ($C_{[9]}$), 135.2 ($C_{[ar]}$), 134.1 ($C_{[ar]}$), 132.0 ($C_{[ar]}$), 130.6 ($C_{[ar]}$), 130.0 ($C_{[ar]}$), 127.7 ($C_{[ar]}$), 125.6 ($C_{[ar]}$), 83.2 ($C_{[7]}$), 72.9 ($C_{[4]}$), 67.4 ($C_{[5]}$), 48.6 ($C_{[2]}$), 35.6 ($C_{[3]}$), 27.8 ($C_{[8]}$);

HRMS (ESI) $[C_{23}H_{25}N_3O_7+Na]^+$ requires *m/z* 478.1585, found *m/z* 478.1581.

3. References

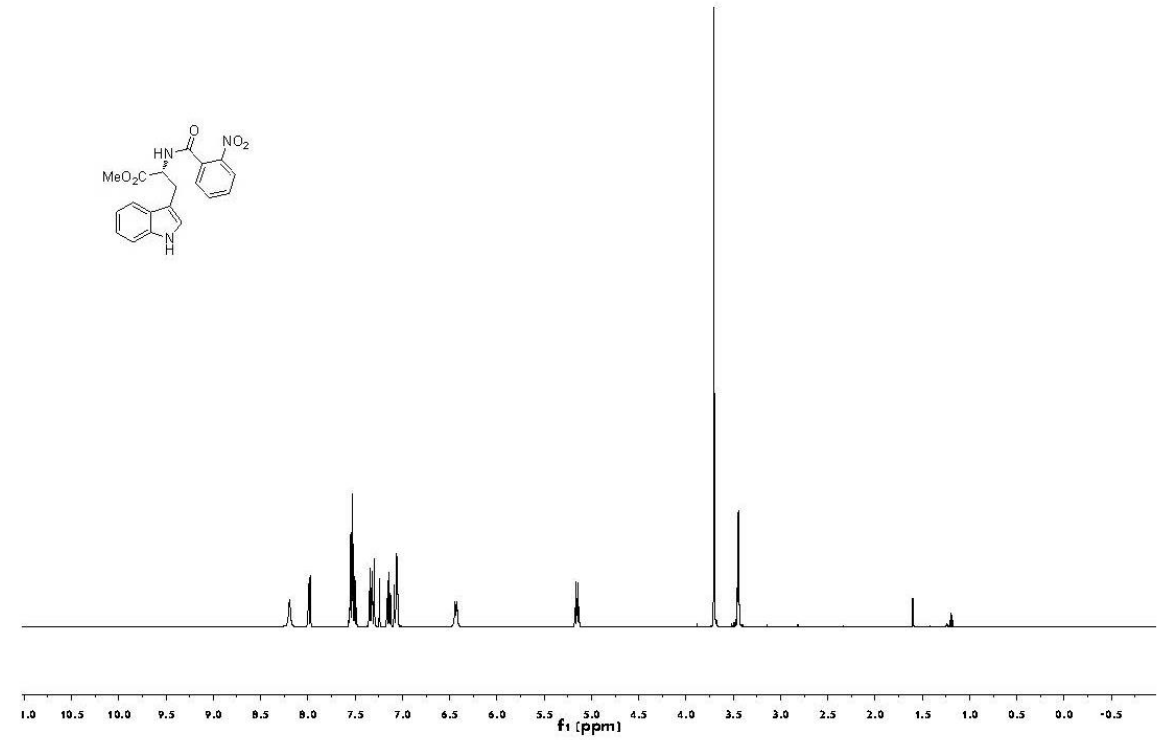
1 S. Buttachon, A. Chandrapatya, L. Manoch, A. Silva, L. Gales, C. Bruyère, R. Kiss and A. Kijjoa, *Tetrahedron*, 2012, **68**, 3253–3262.

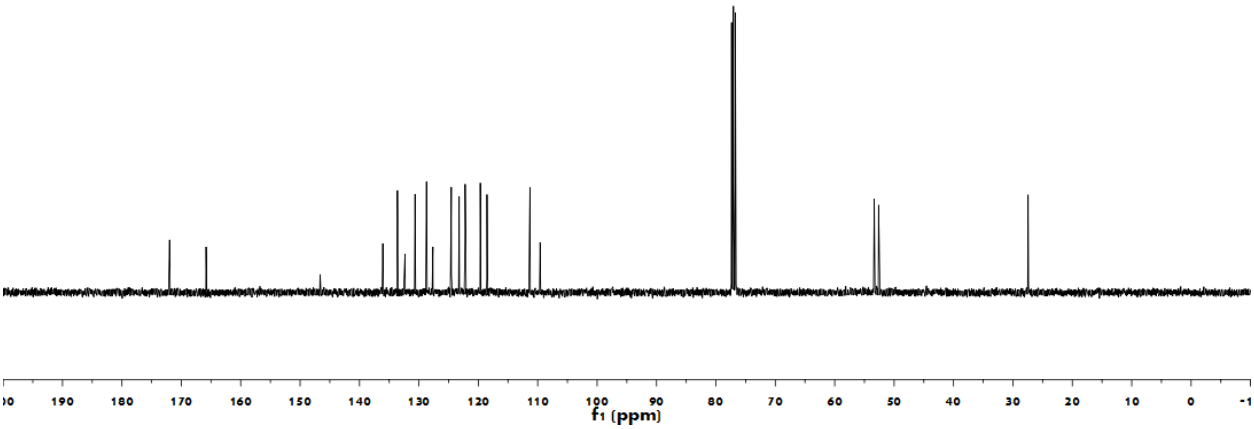
2 B. D. Christie and H. Rapoport, *J. Org. Chem.*, 1985, **50**, 1239–1246.

3 X. Wang, M. Liu, L. Xu, Q. Wang, J. Chen, J. Ding and H. Wu, *J. Org. Chem.*, 2013, **78**, 5273–81.

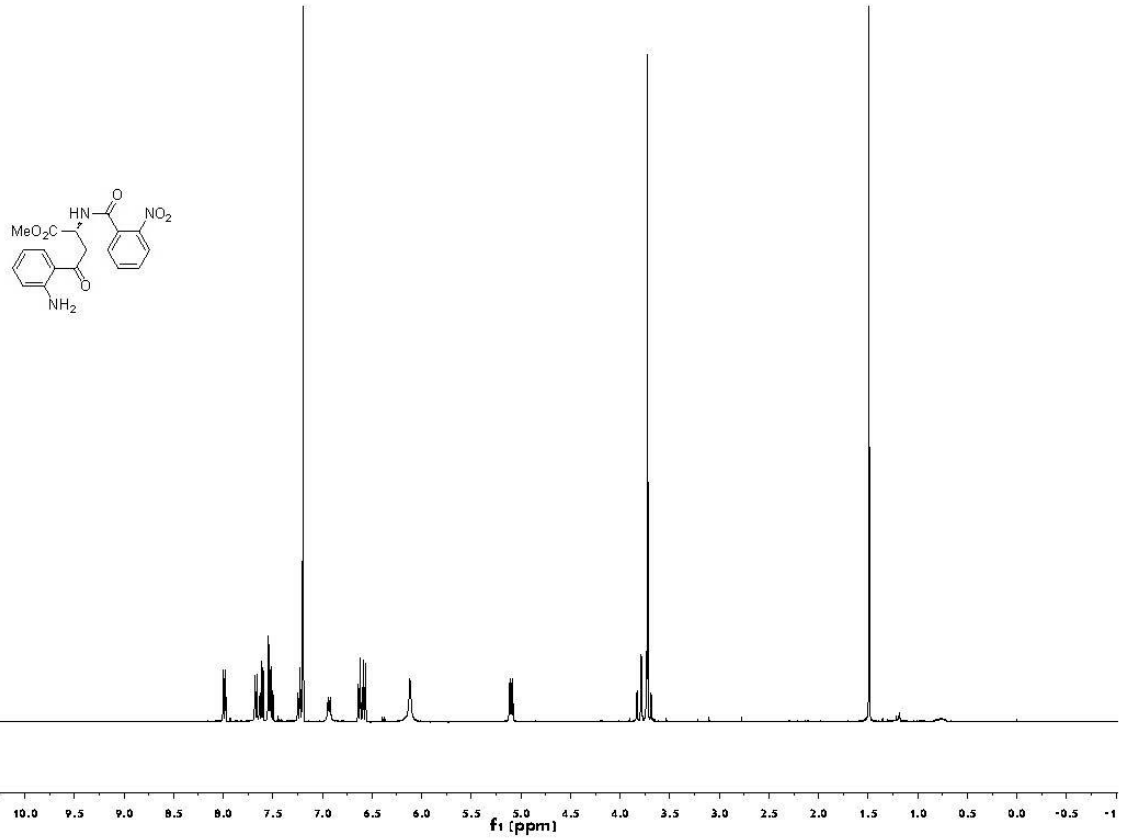
4. NMR spectra

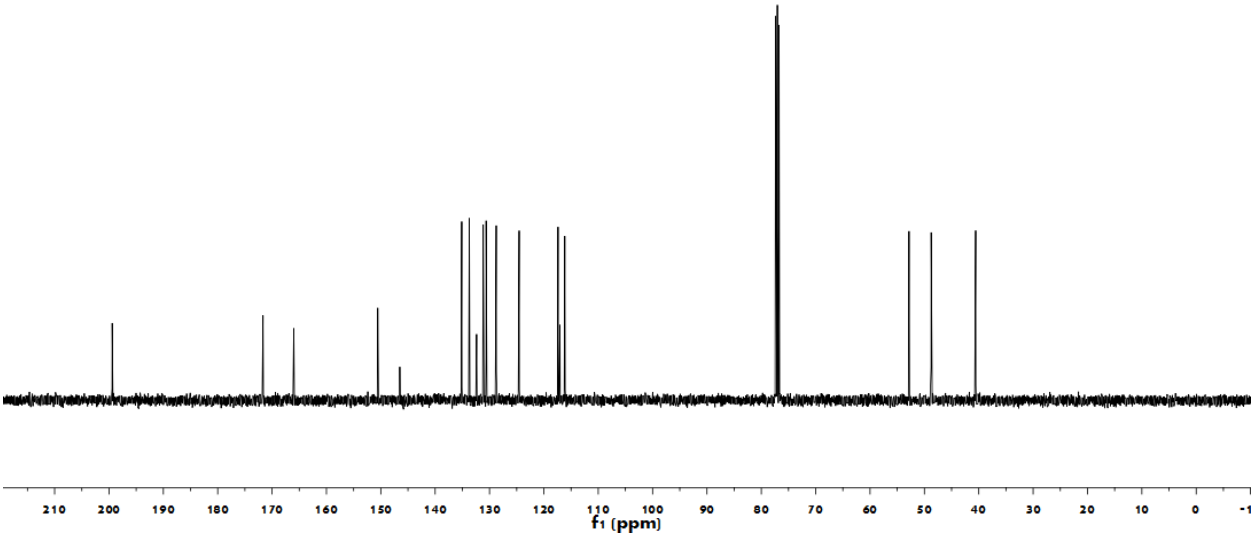
Compound 2



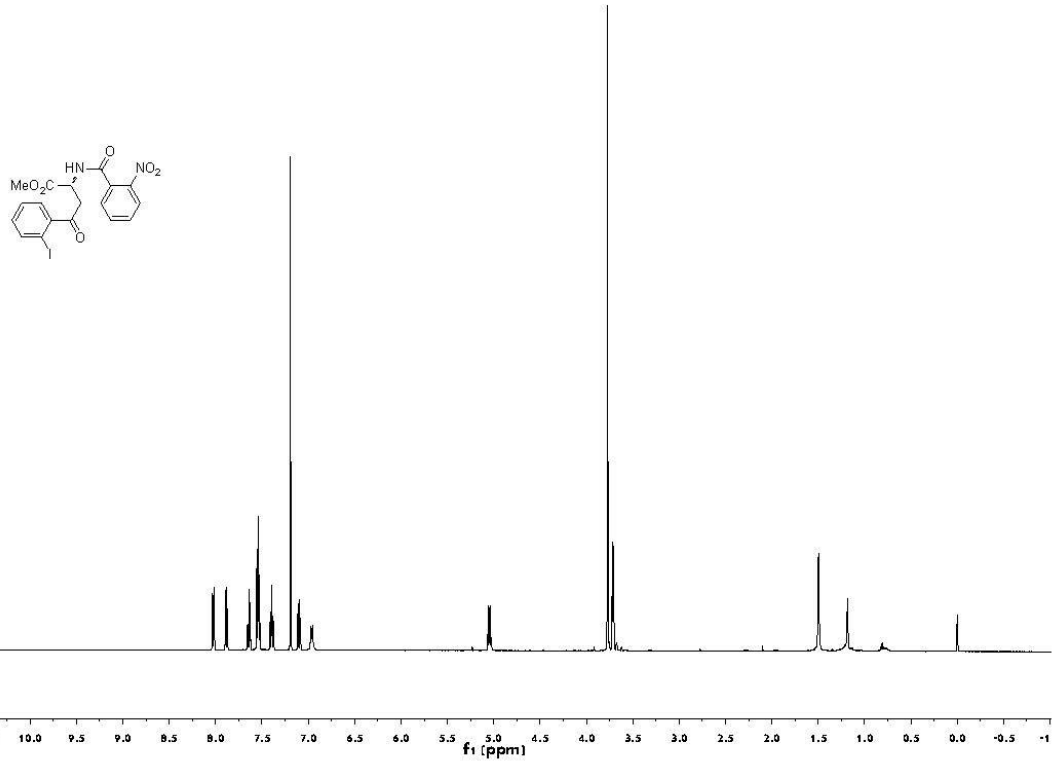


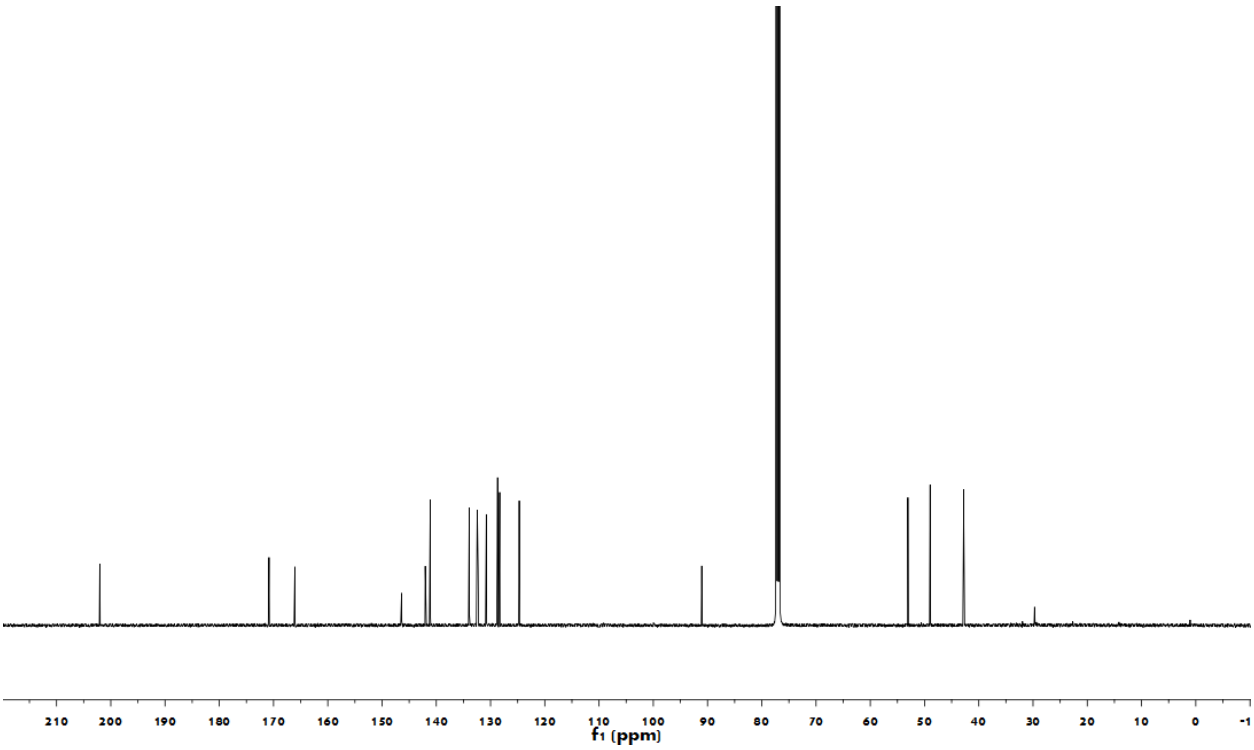
Compound 3


HN
O
NO2
MeO2C
O
NH2
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

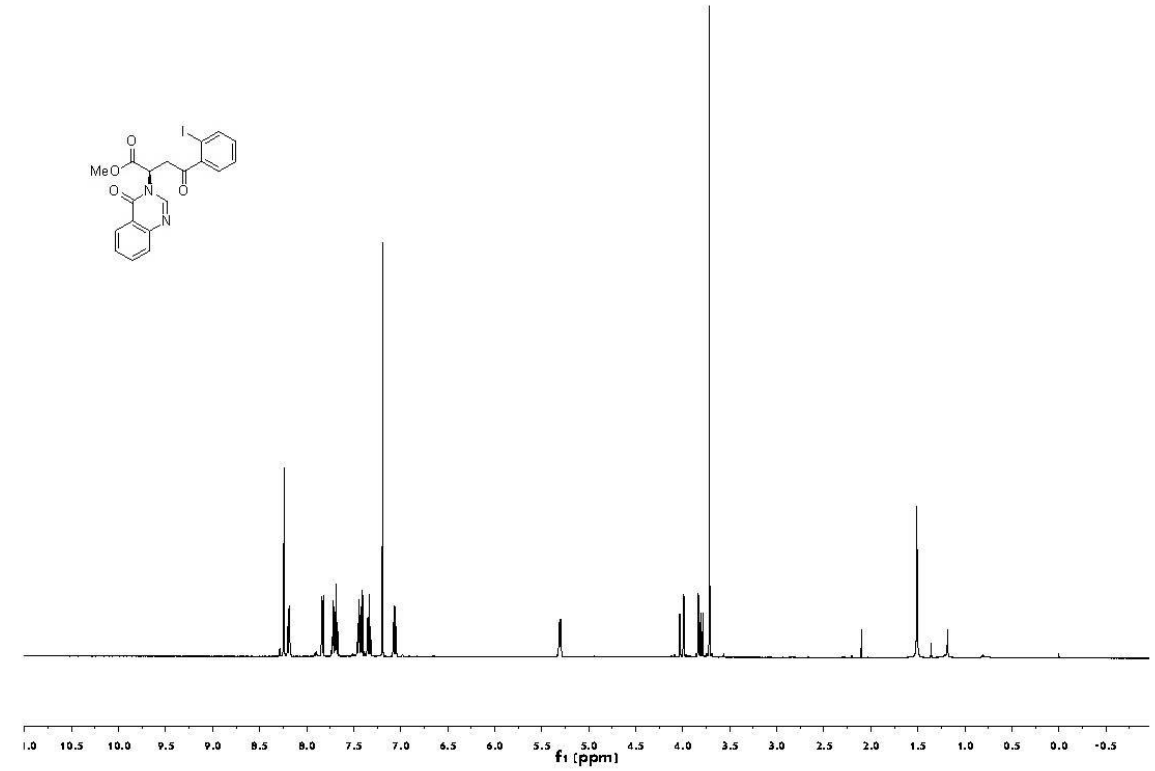

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

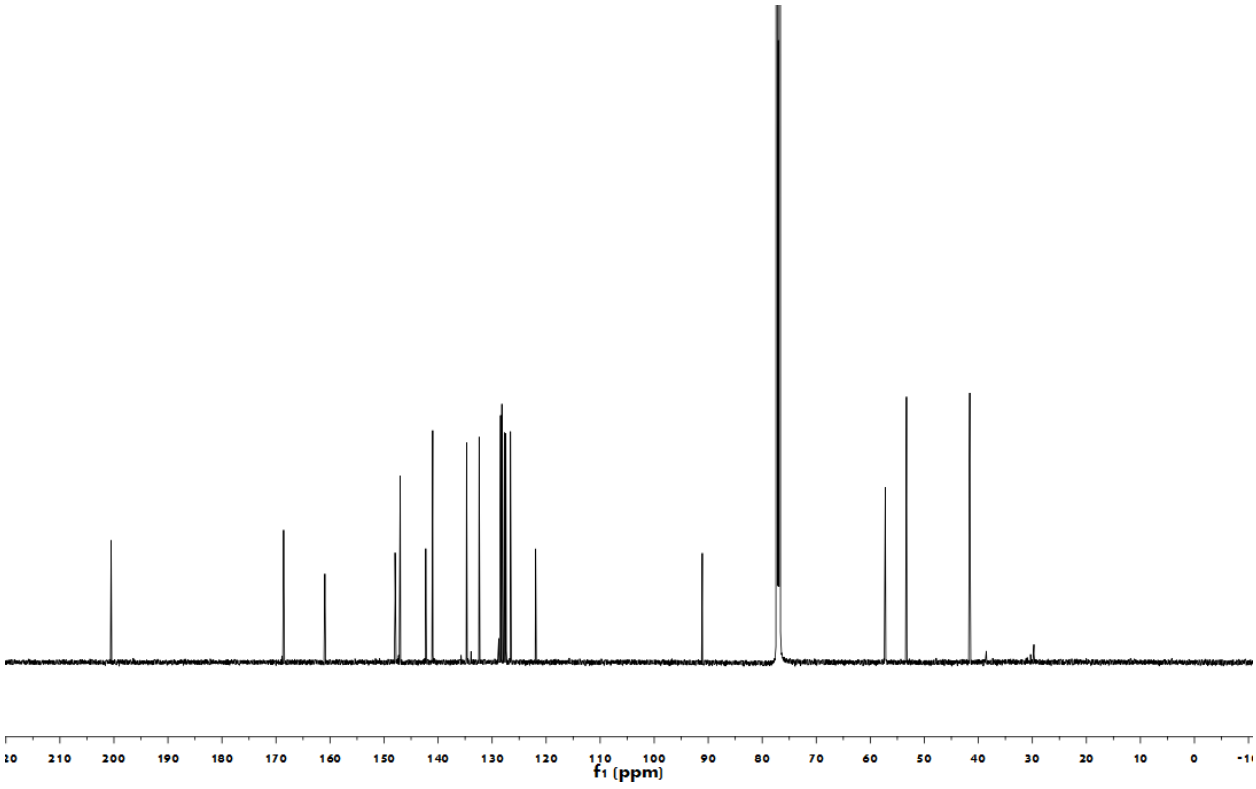
Compound 4



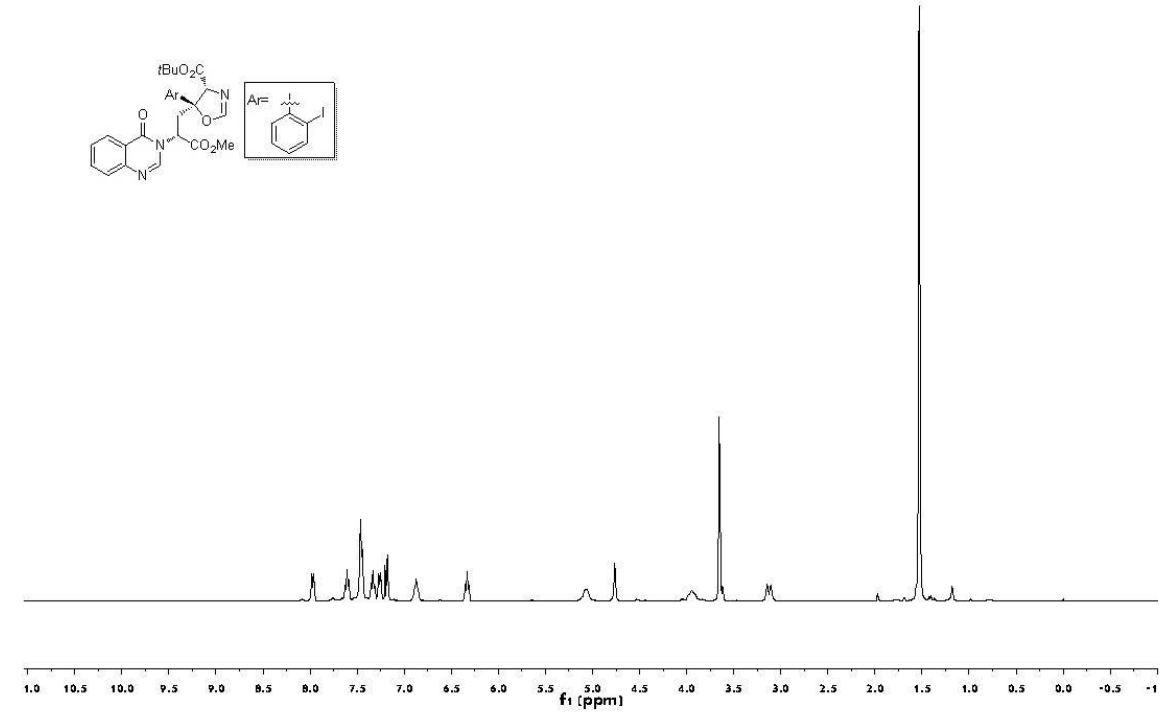


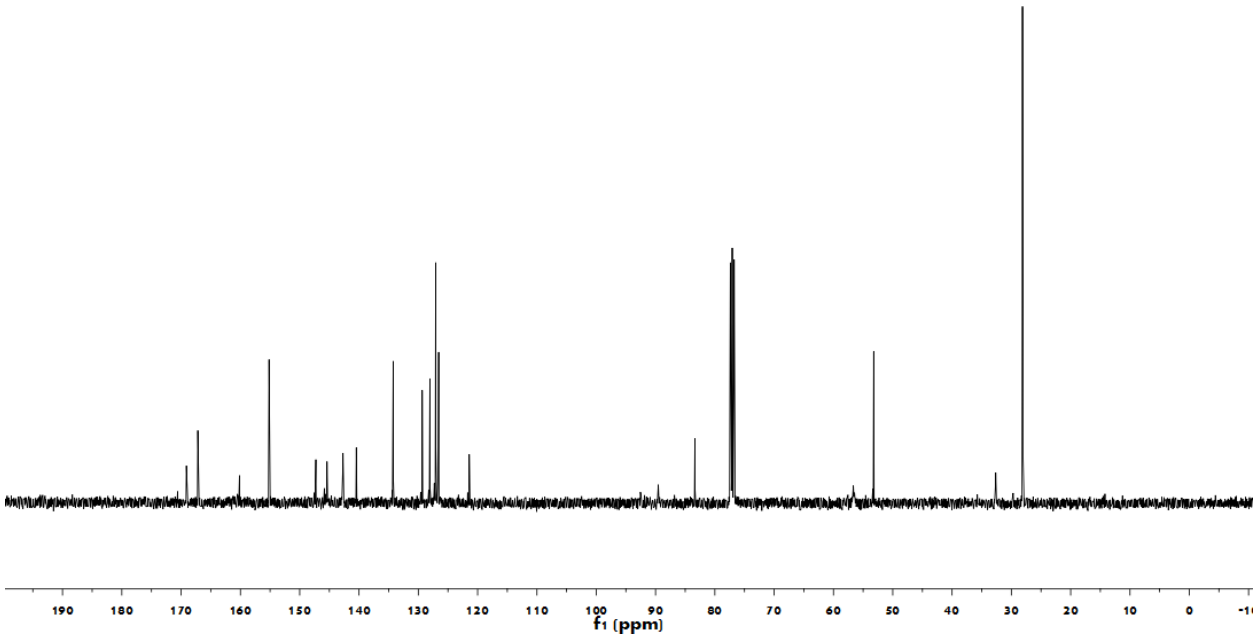
Compound 5



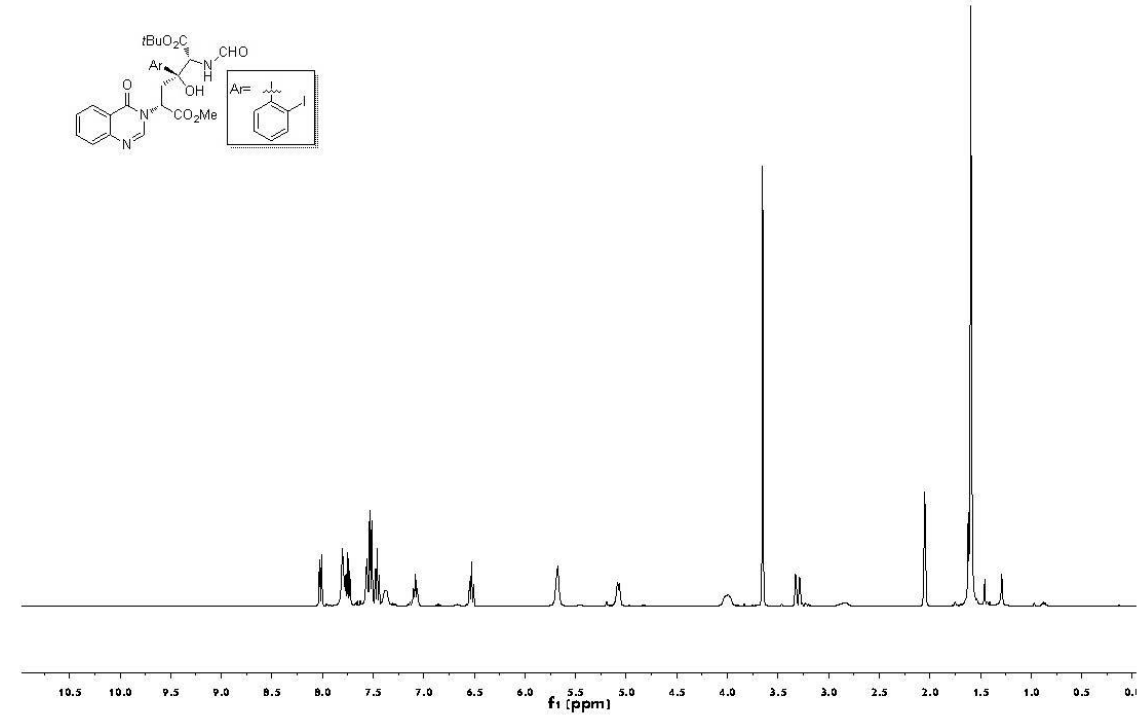


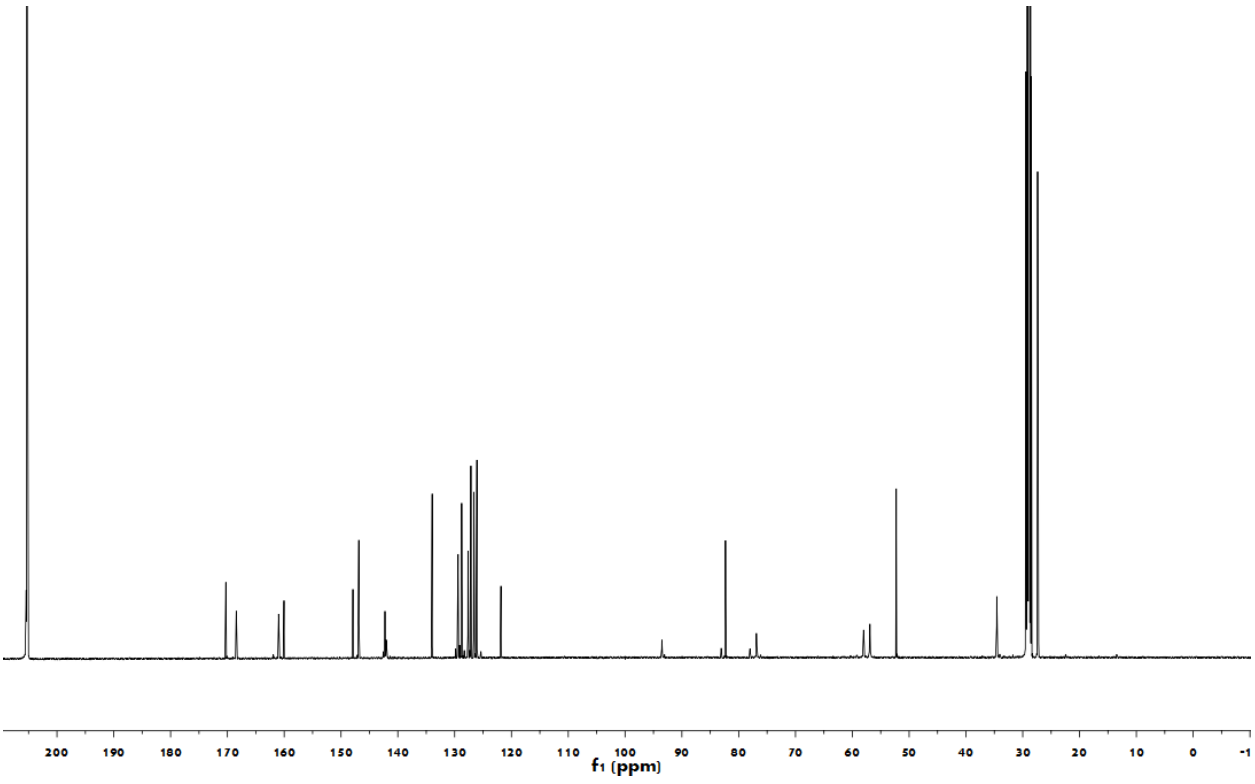
Compound 9


tBuO2C
Ar
N
O
O
N
N
CO2Me
Ar=
I
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Compound 10


tBuO2C
CHO
Ar
N
H
OH
O
N
CO2Me
N
Ar=
I
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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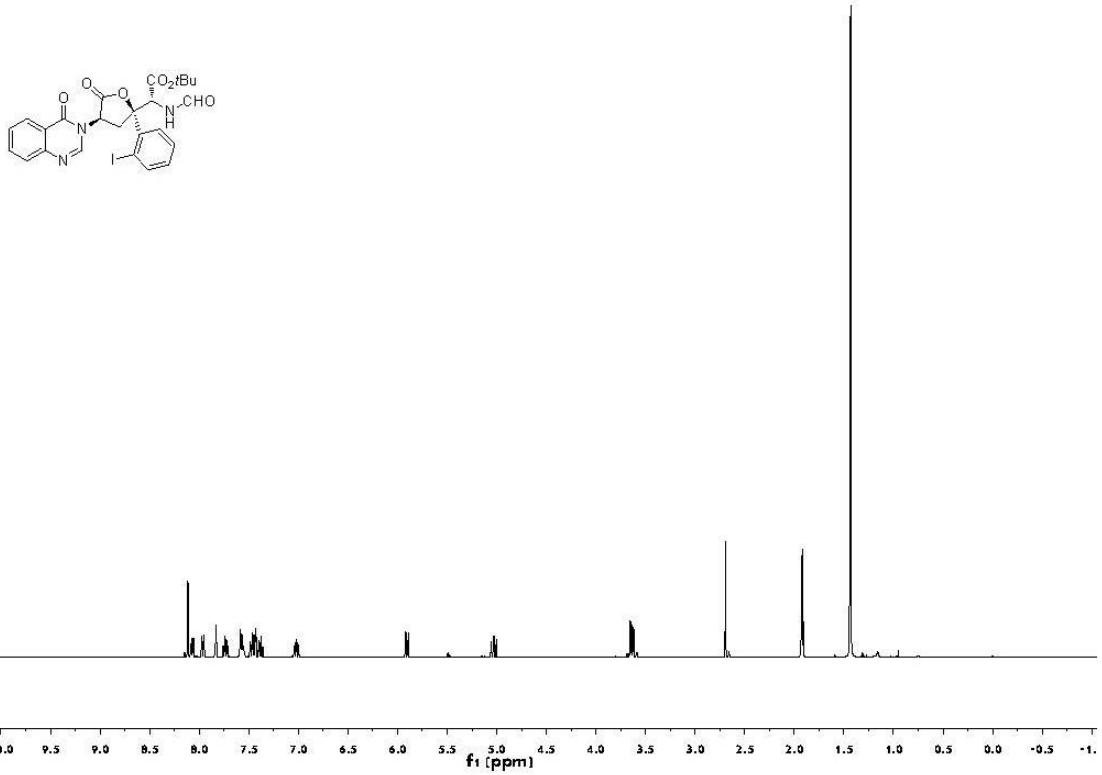
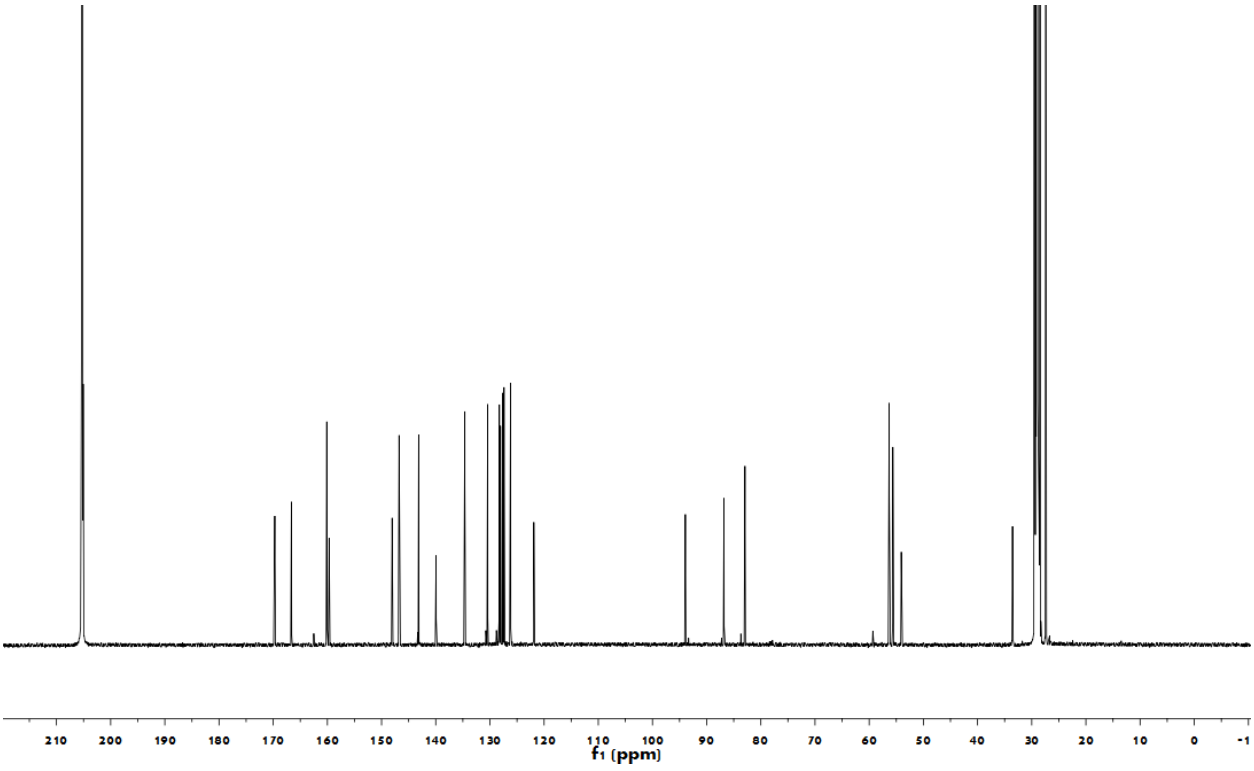
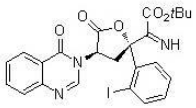
f1 (ppm)

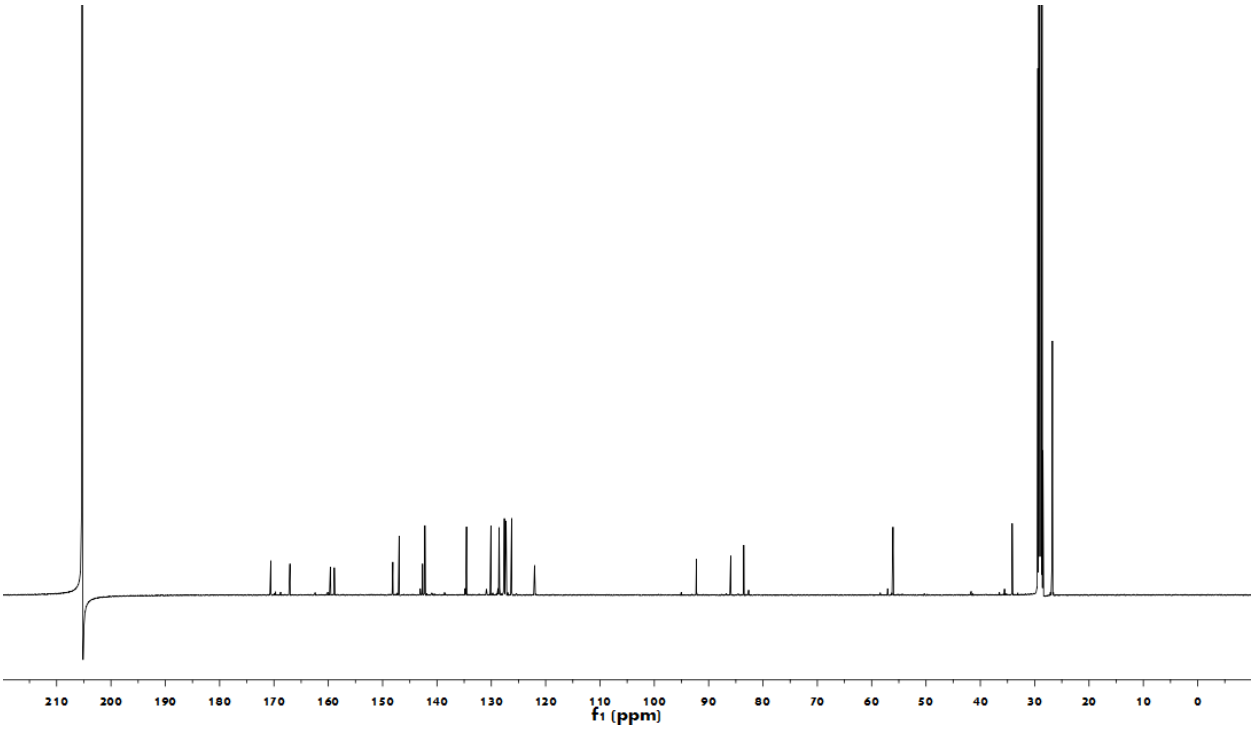
Compound 11


CO2tBu
CHO
N
H
O
O
O
N
N
I
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

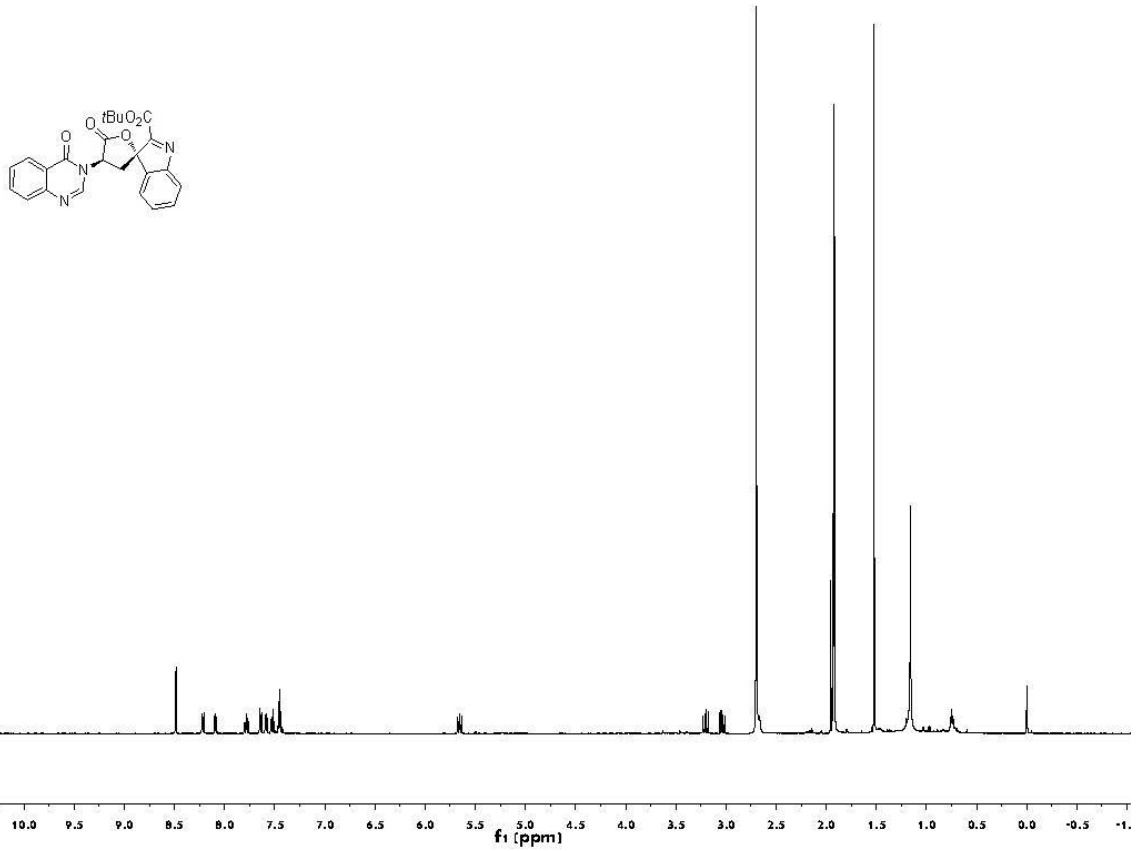

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

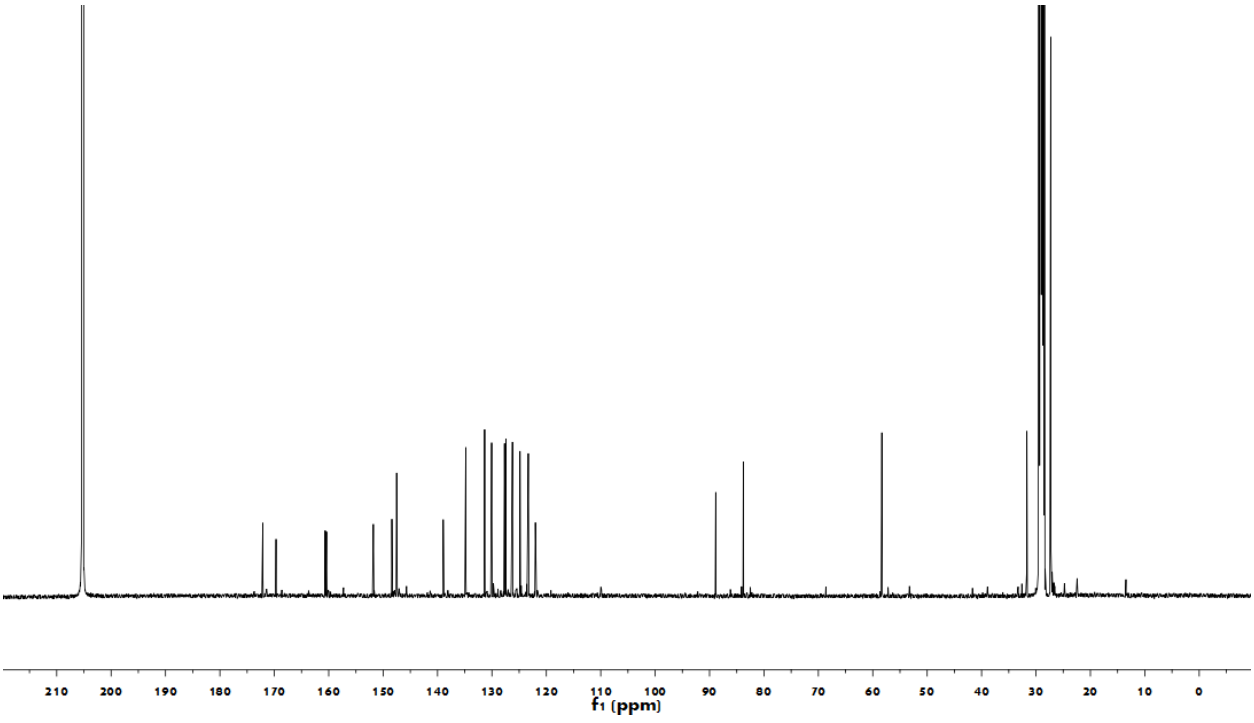
Compound 12





Compound 13


tBuO2C
O
O
O
N
N
N
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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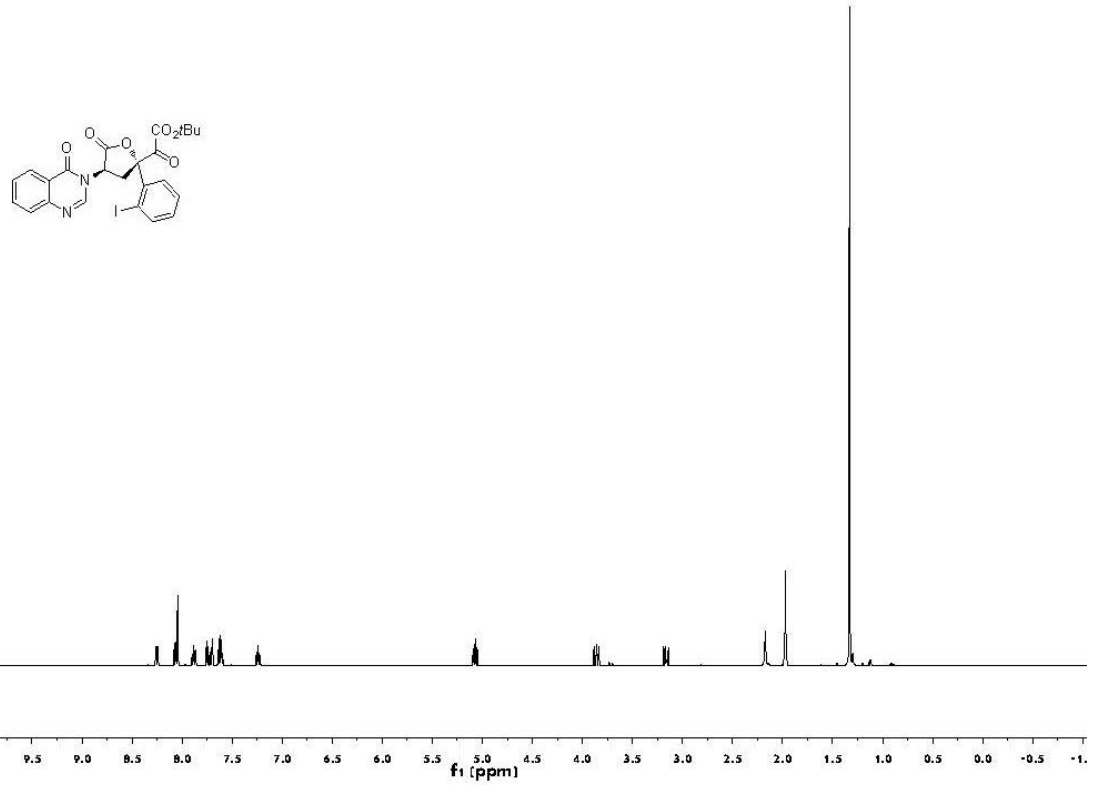
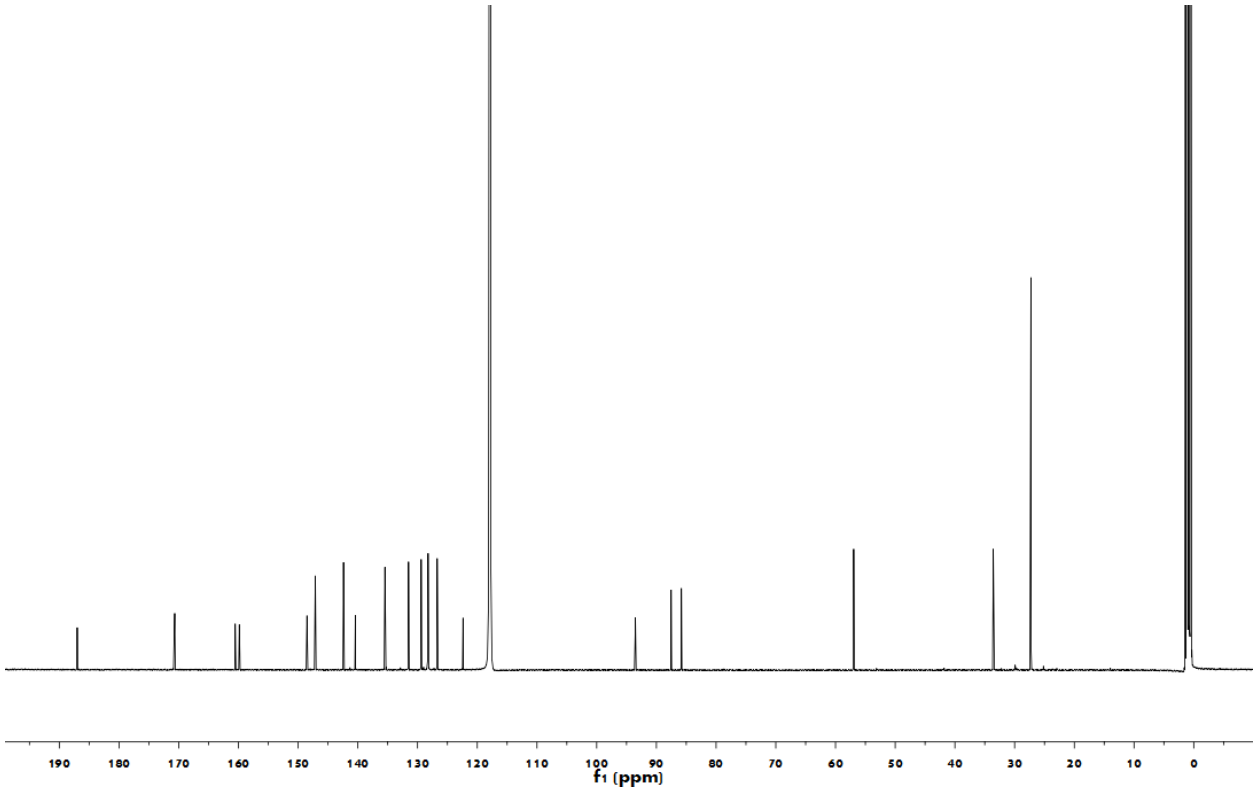
f1 (ppm)

Compound 14


CO2tBu
O
O
O
N
N
I
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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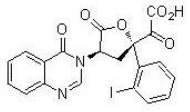
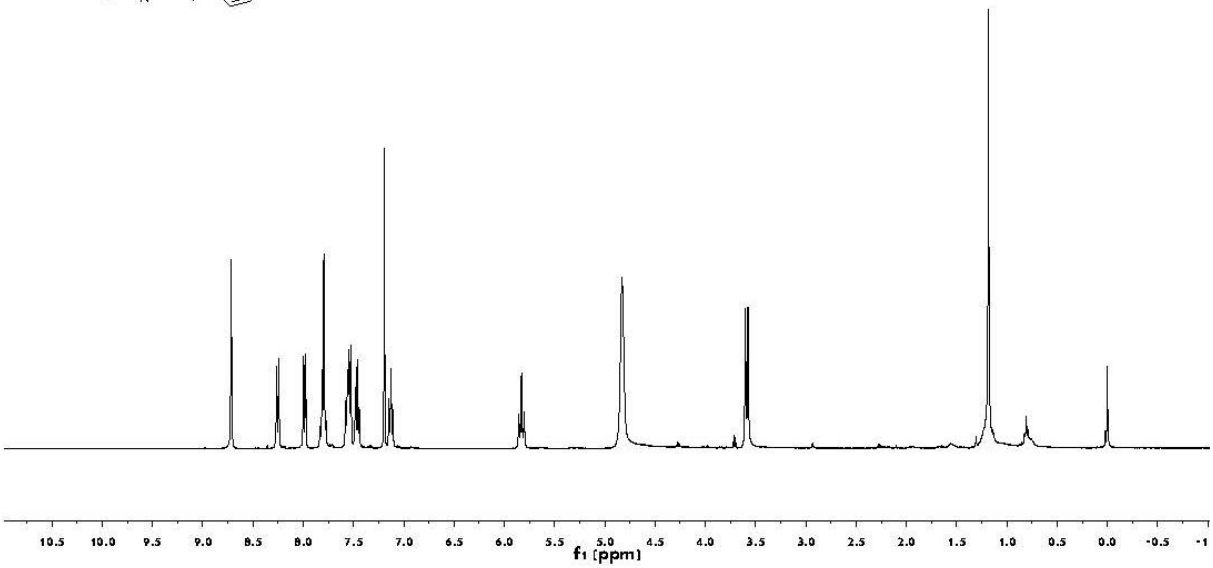
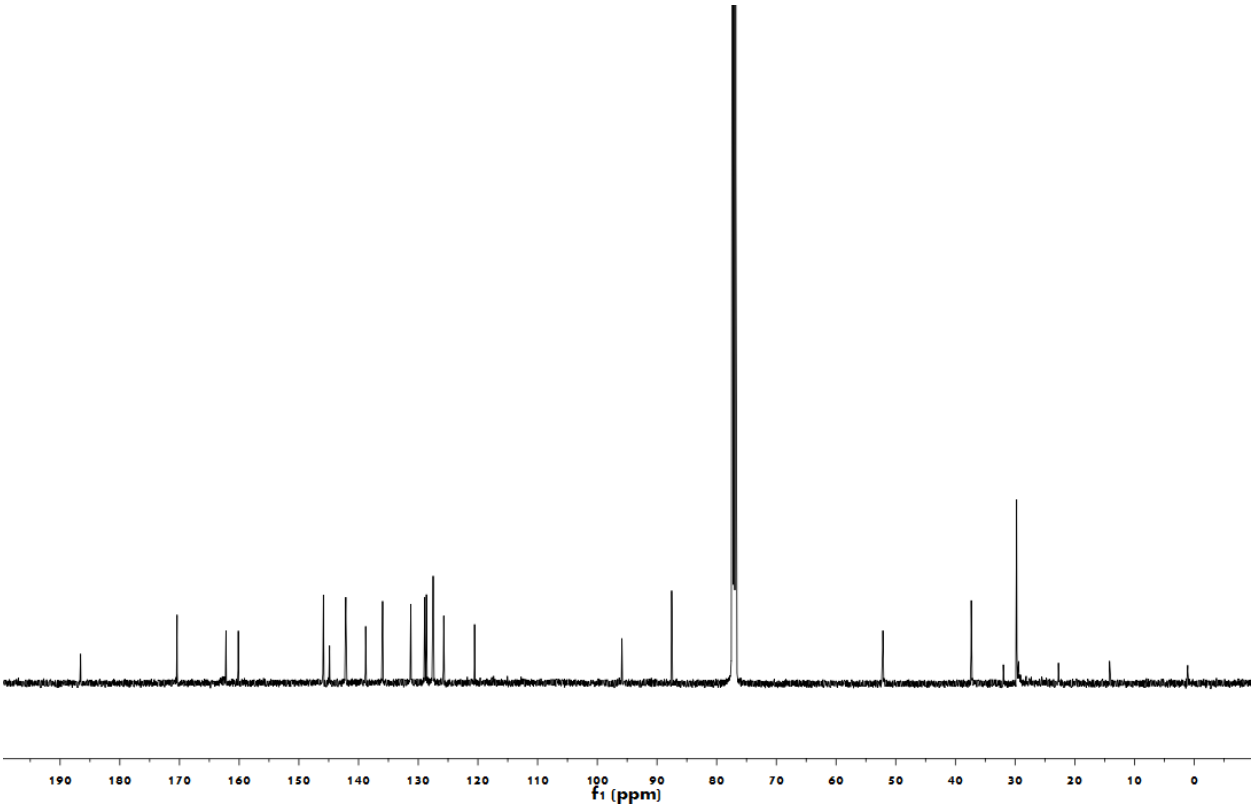
f1 (ppm)

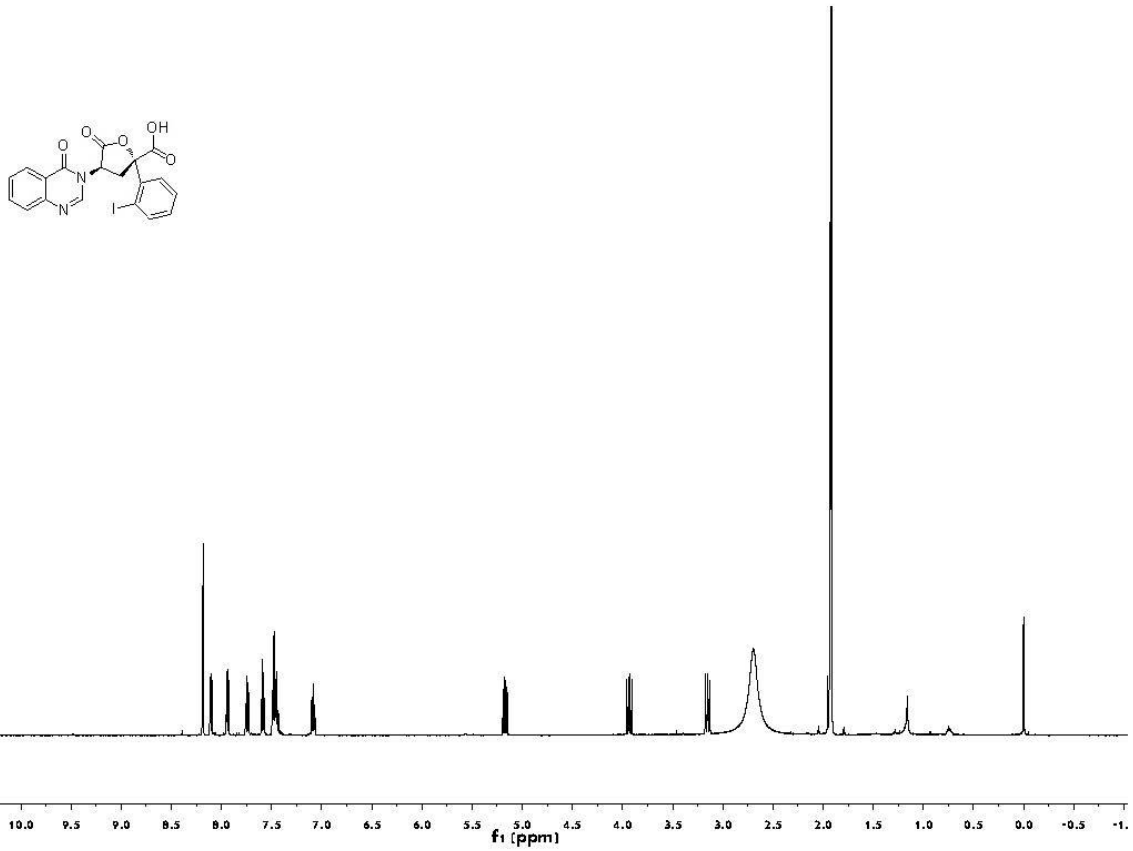
Compound 15

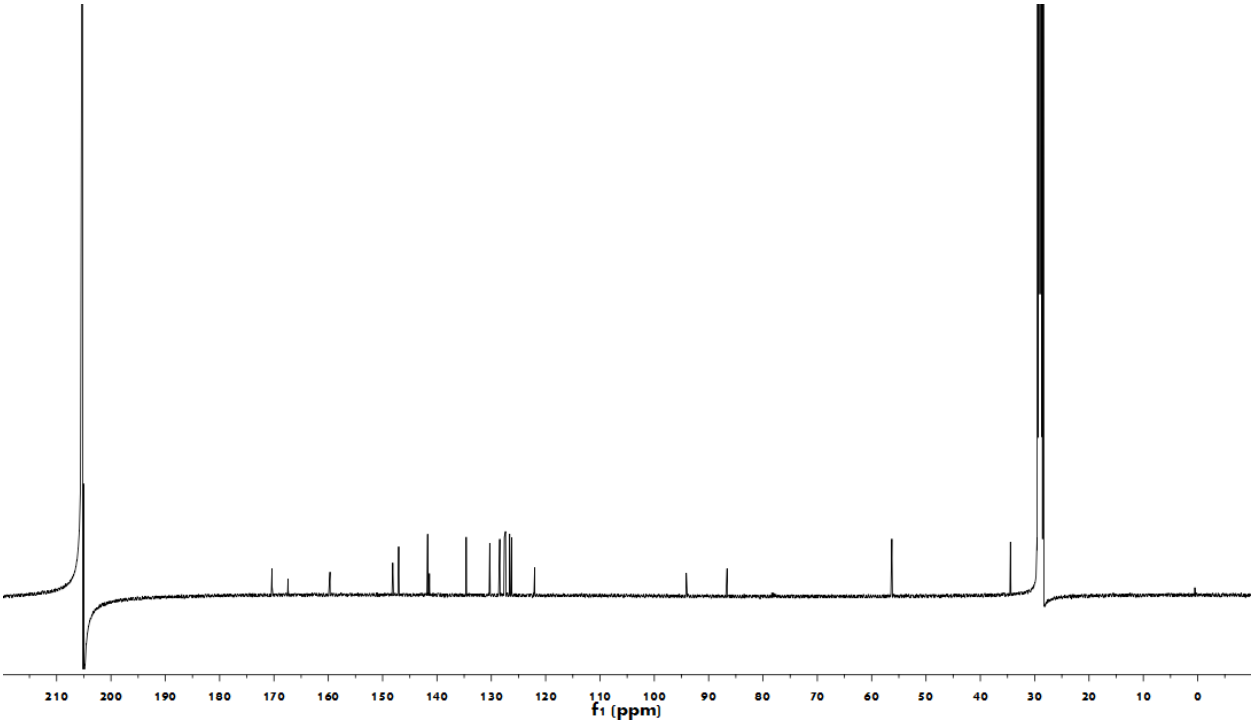

O
O
O
CO2H
O
N
N
I


10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Compound 16


10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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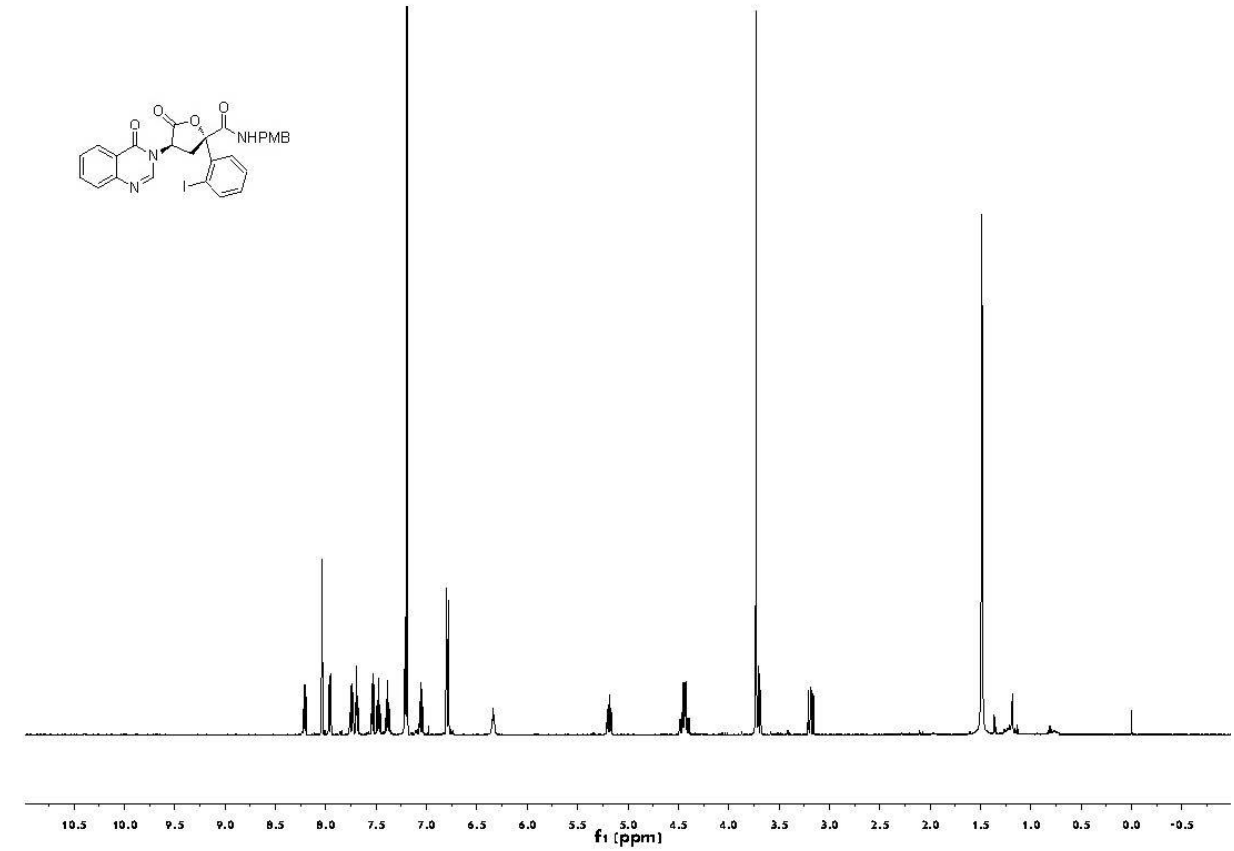
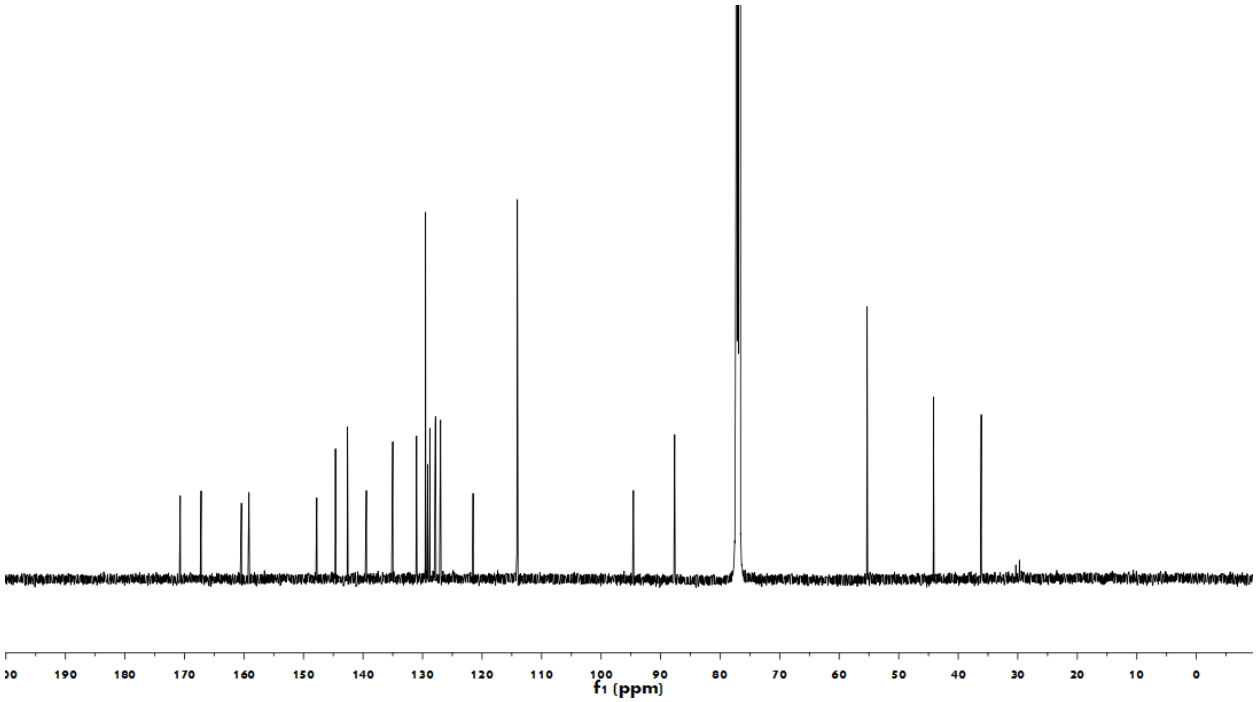
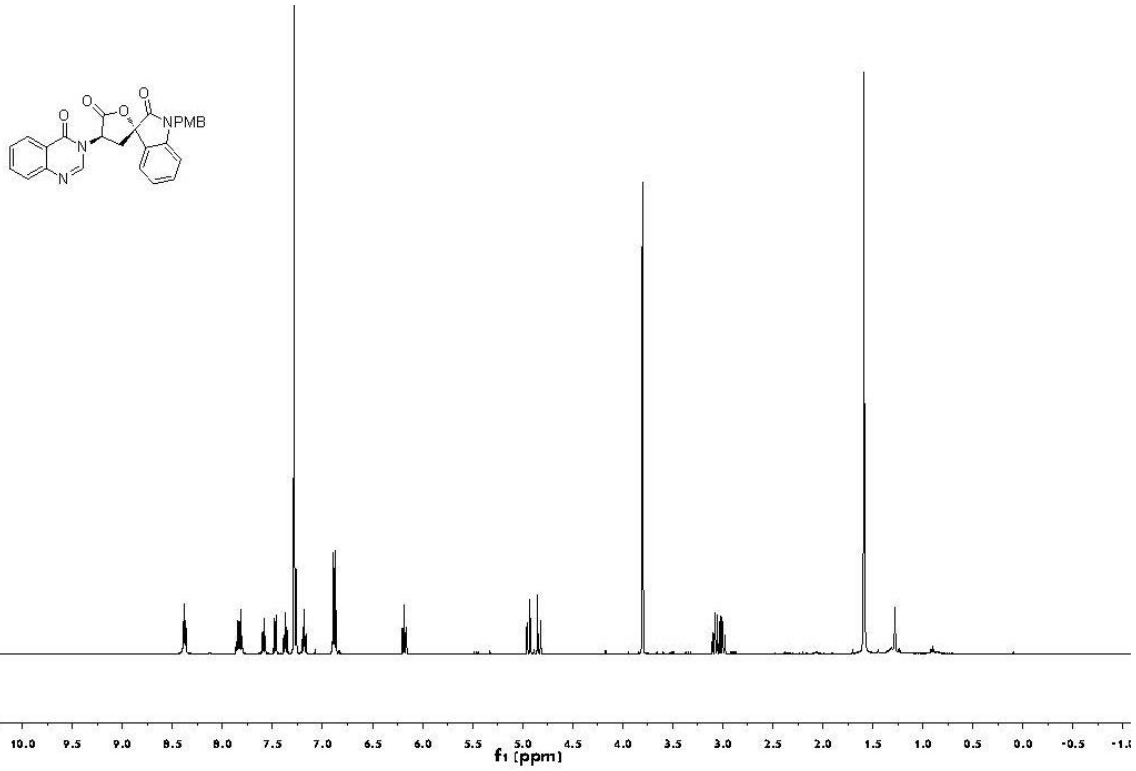
f1 (ppm)

Compound 17





Compound 18


NPMB
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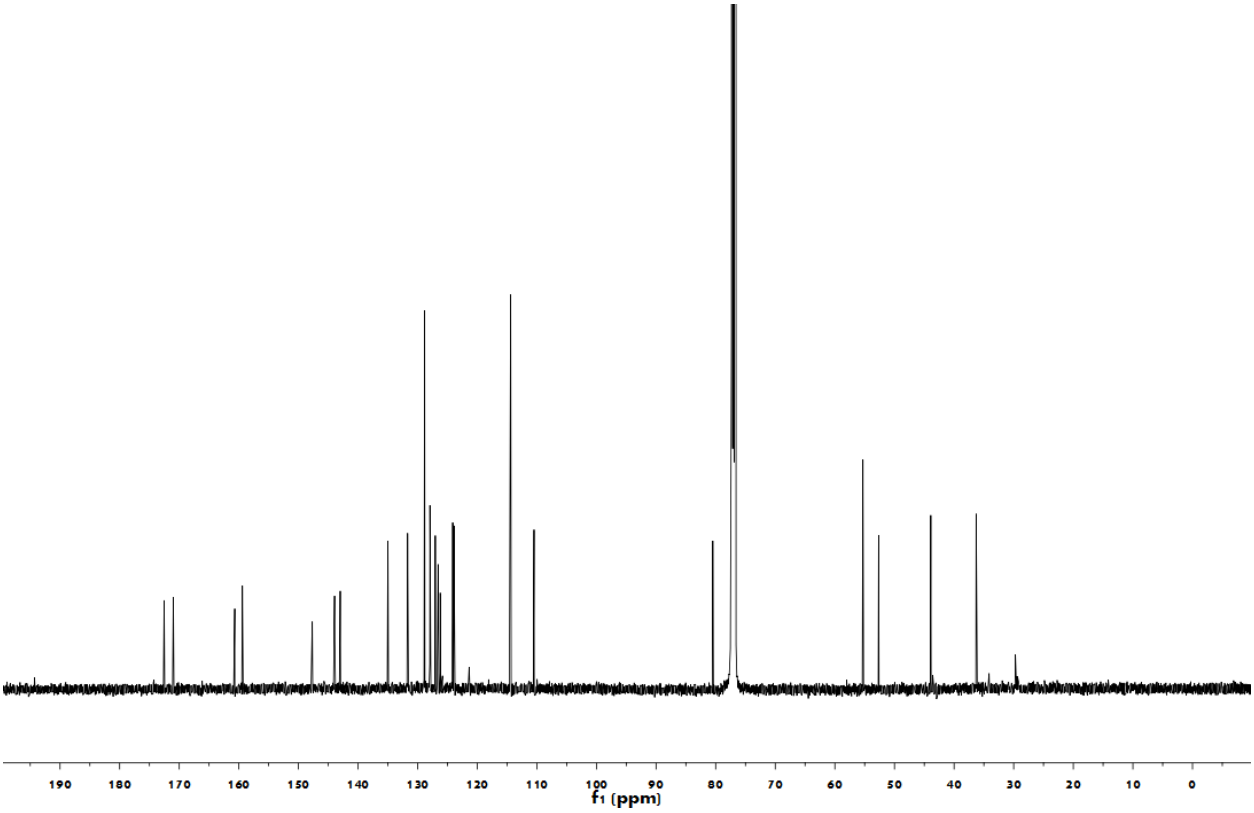
f1 (ppm)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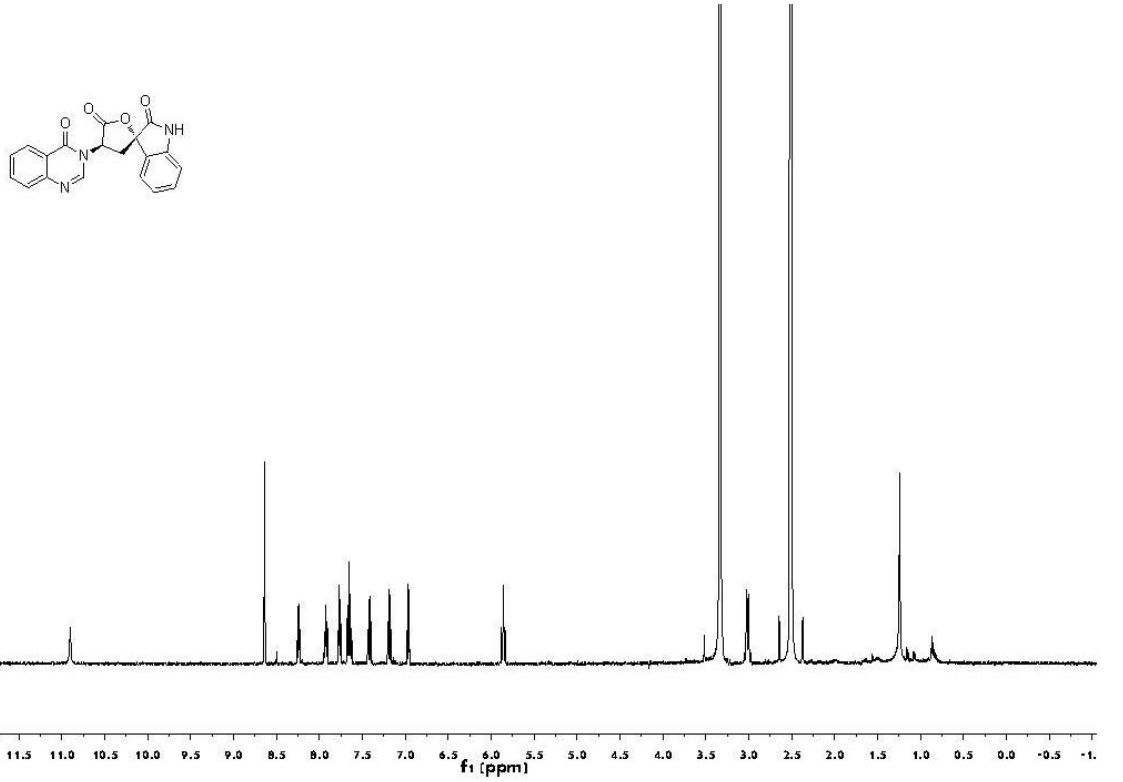
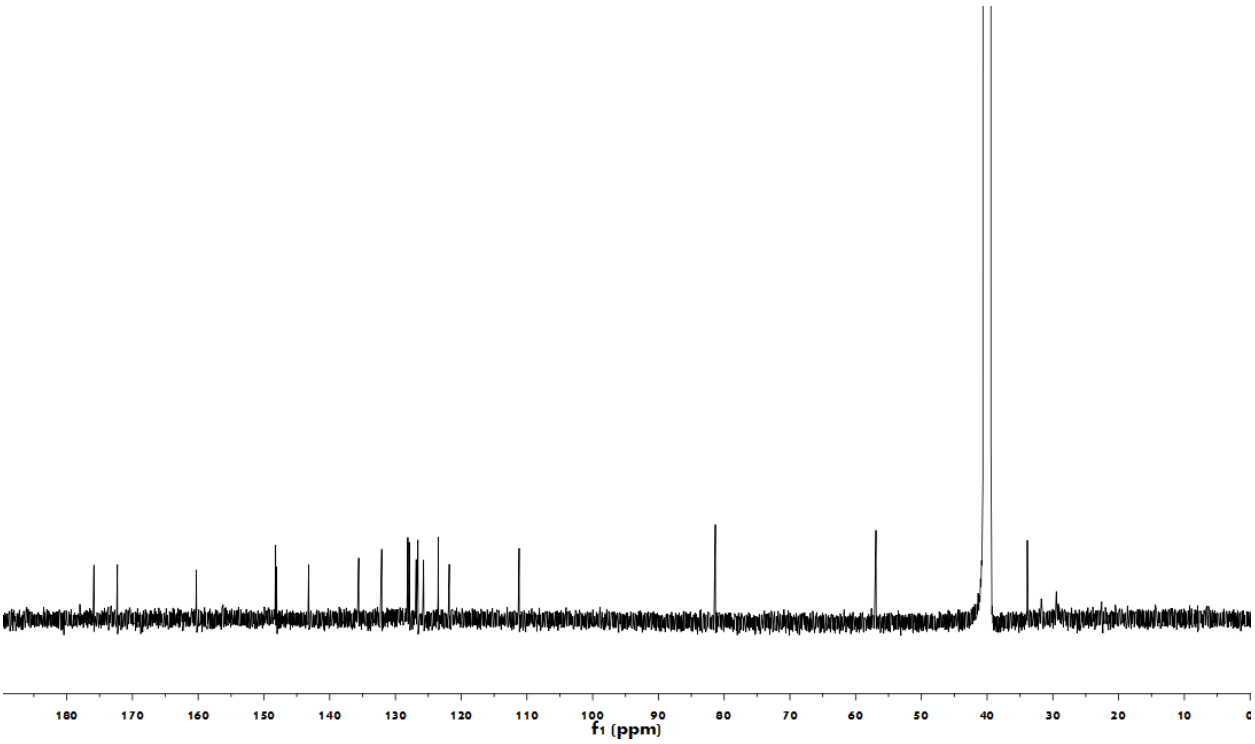
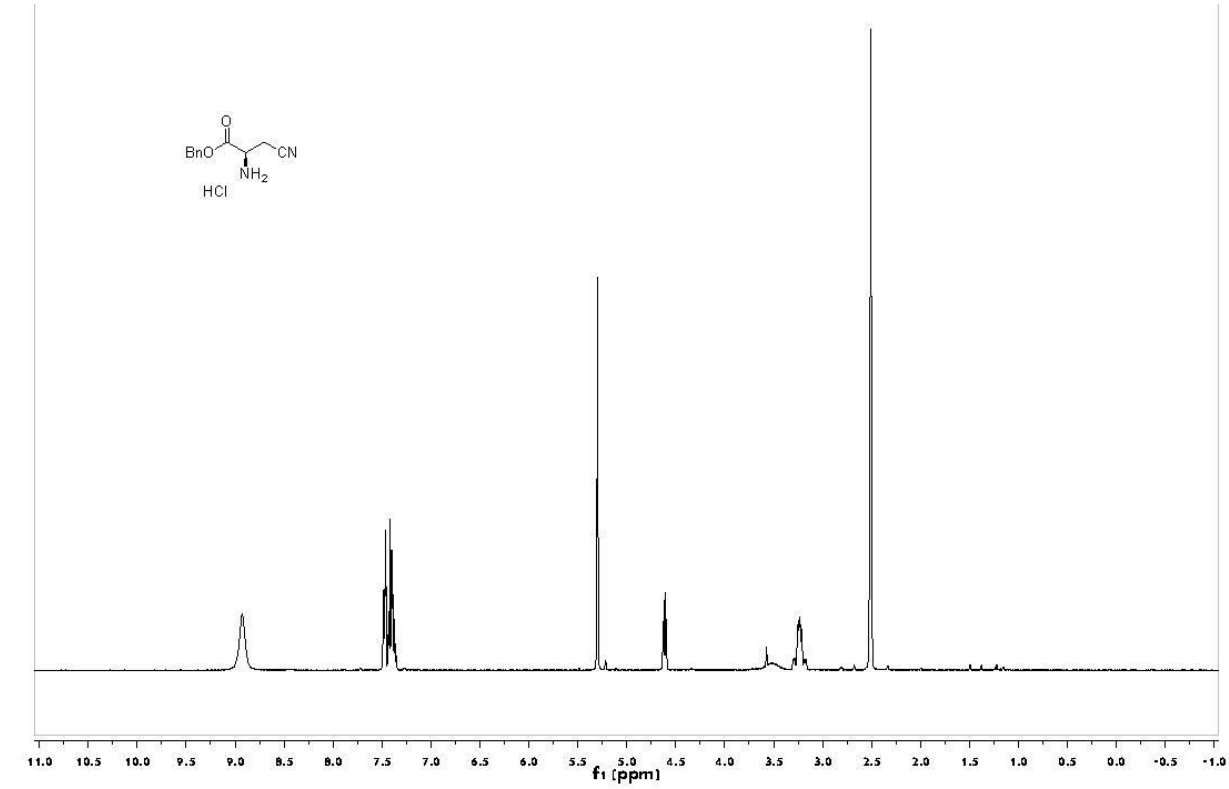
f1 (ppm)

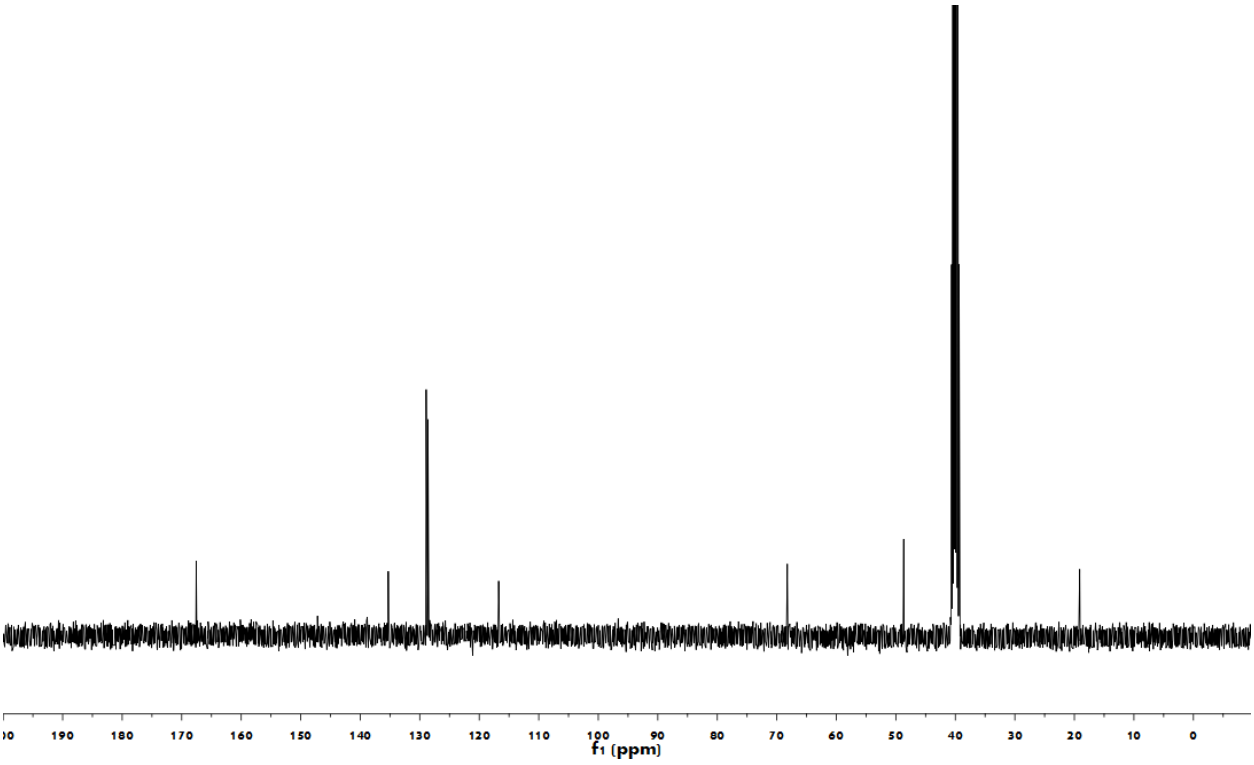
Compound 1


O
O
O
NH
N
N
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

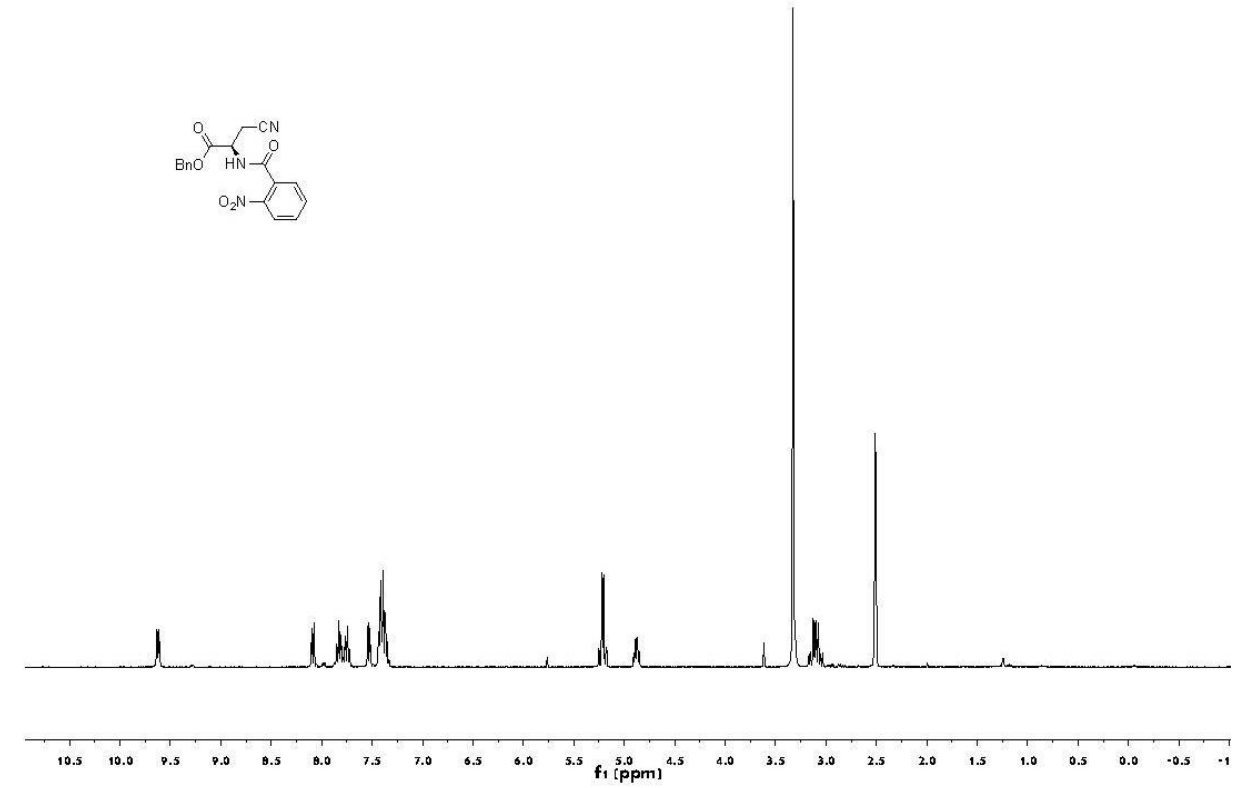

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

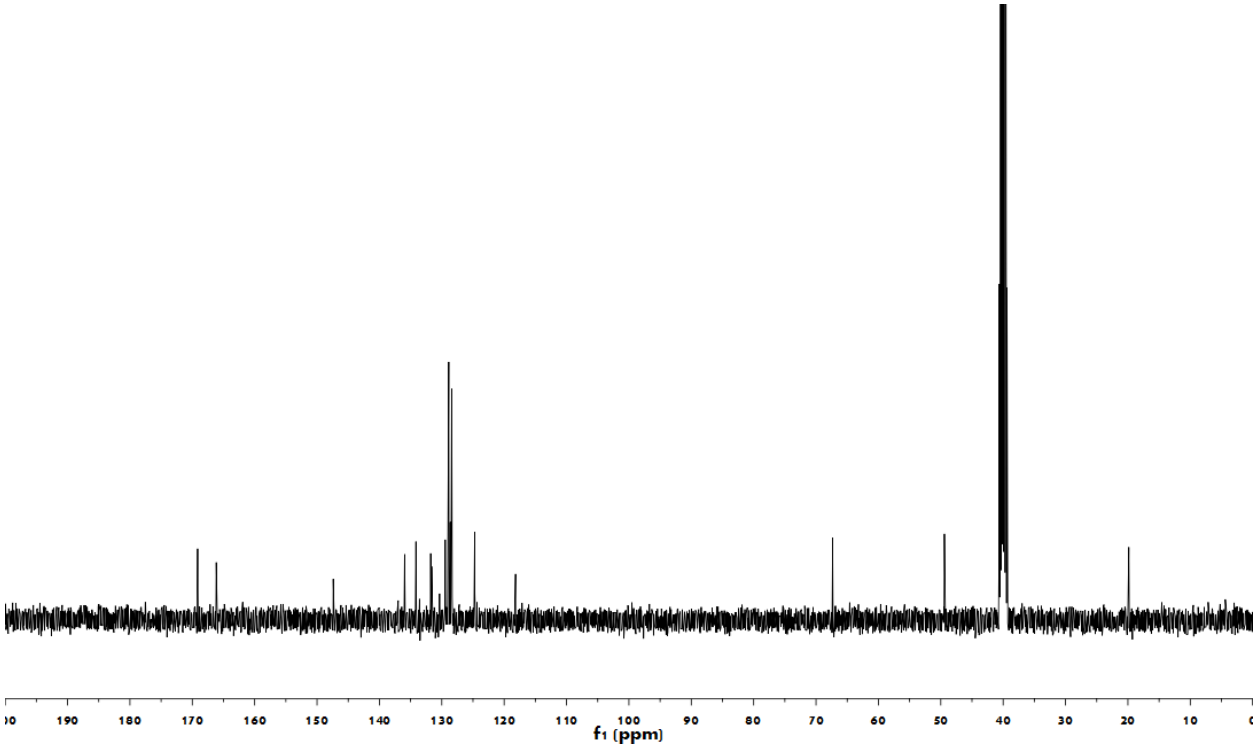
Compound S1





Compound S2


O
CN
BnO
HN
O
O2N
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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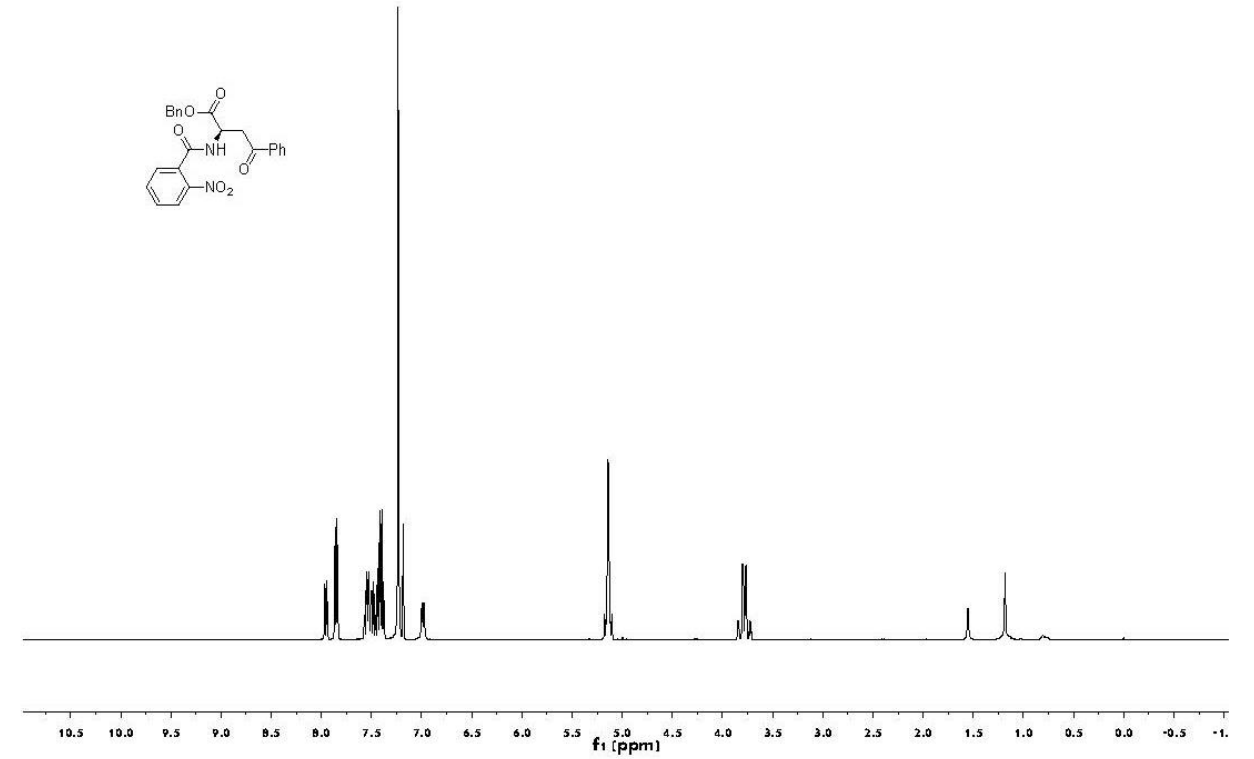
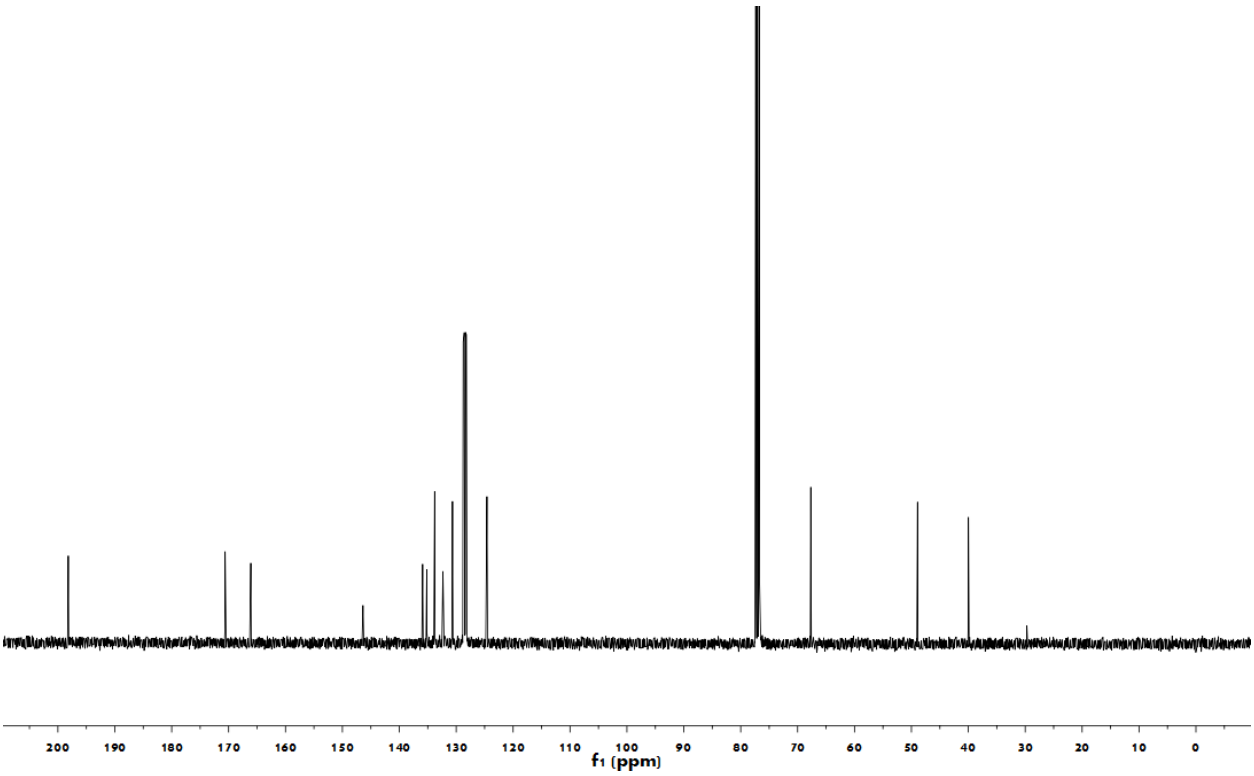
f1 (ppm)

Compound 6


BnO
O
O
NH
O
Ph
NO2
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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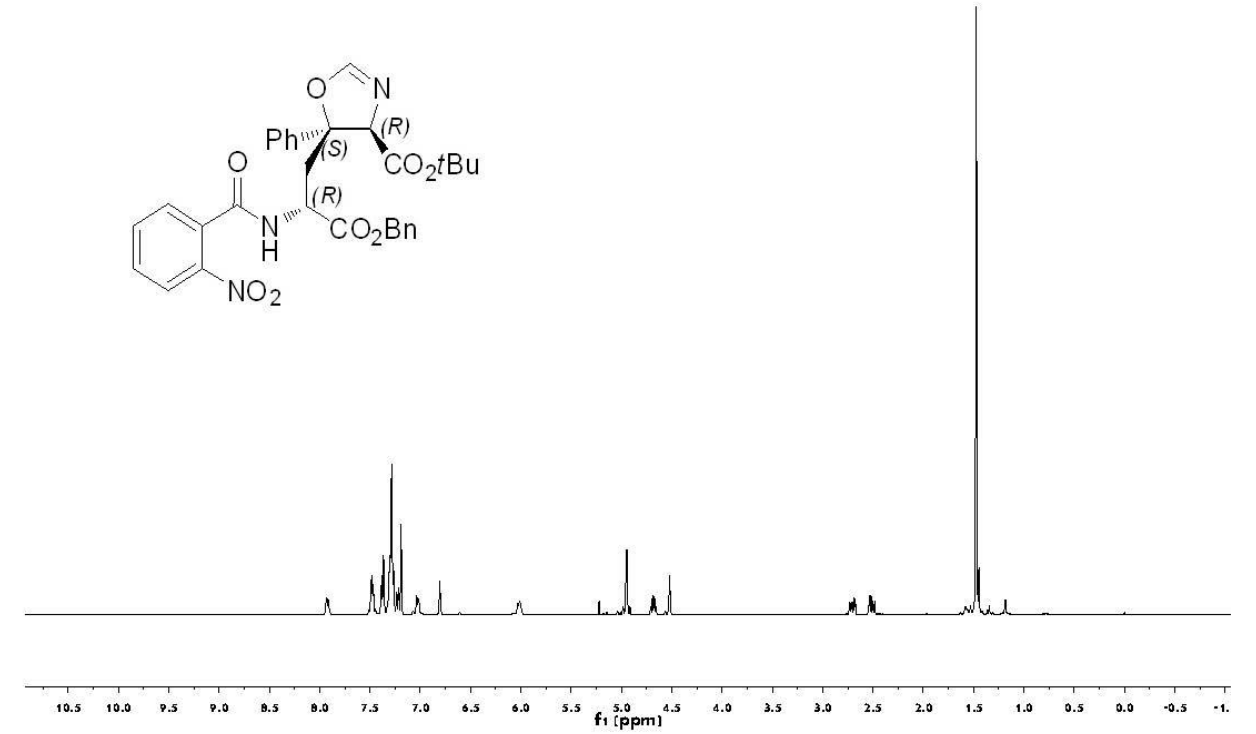
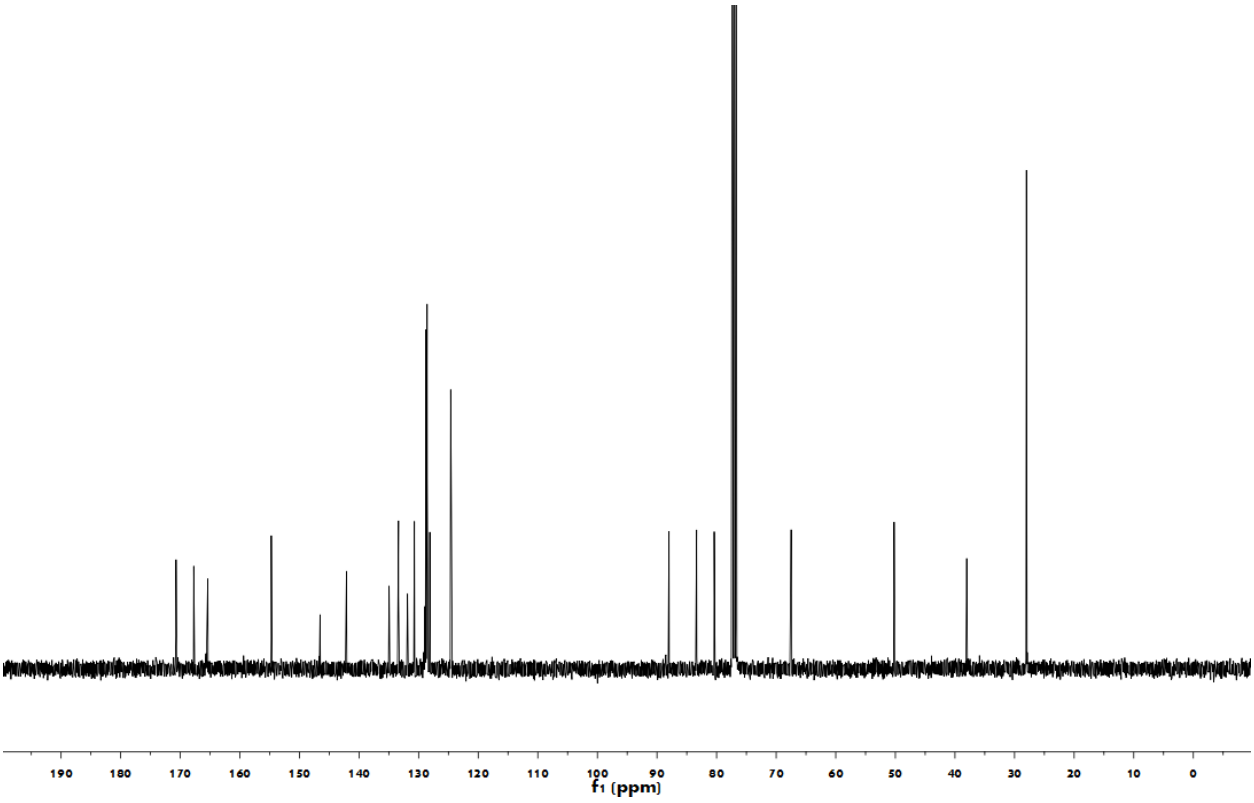
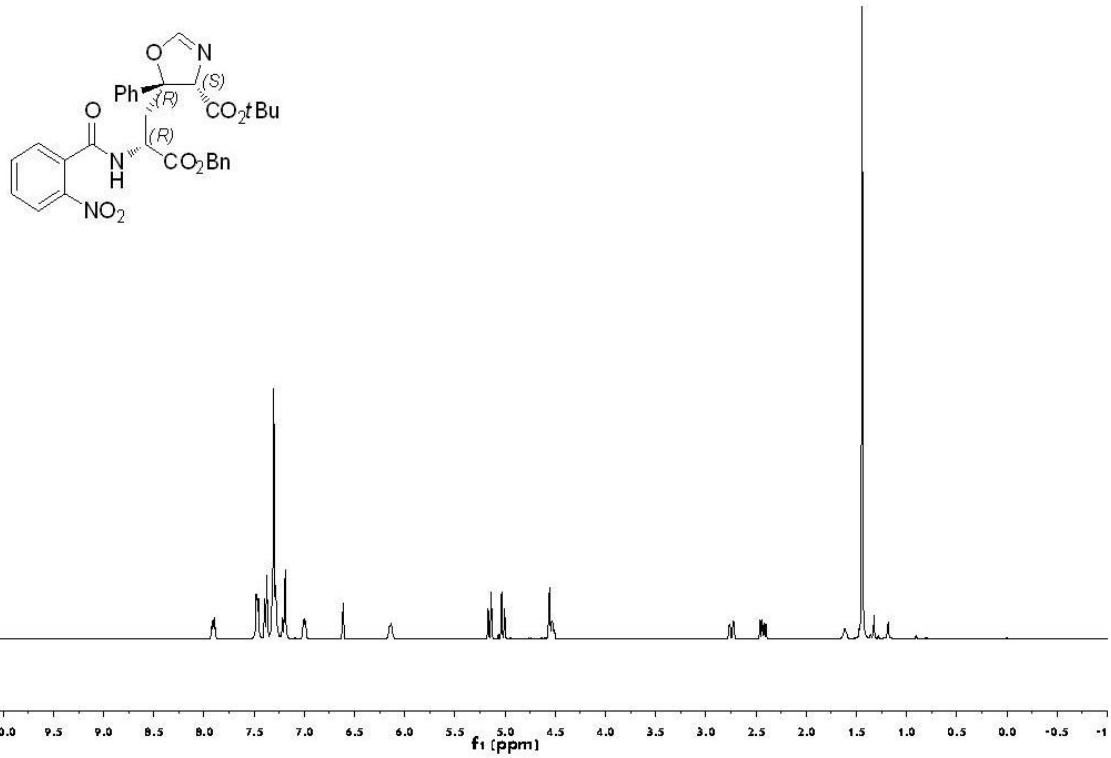
f1 (ppm)

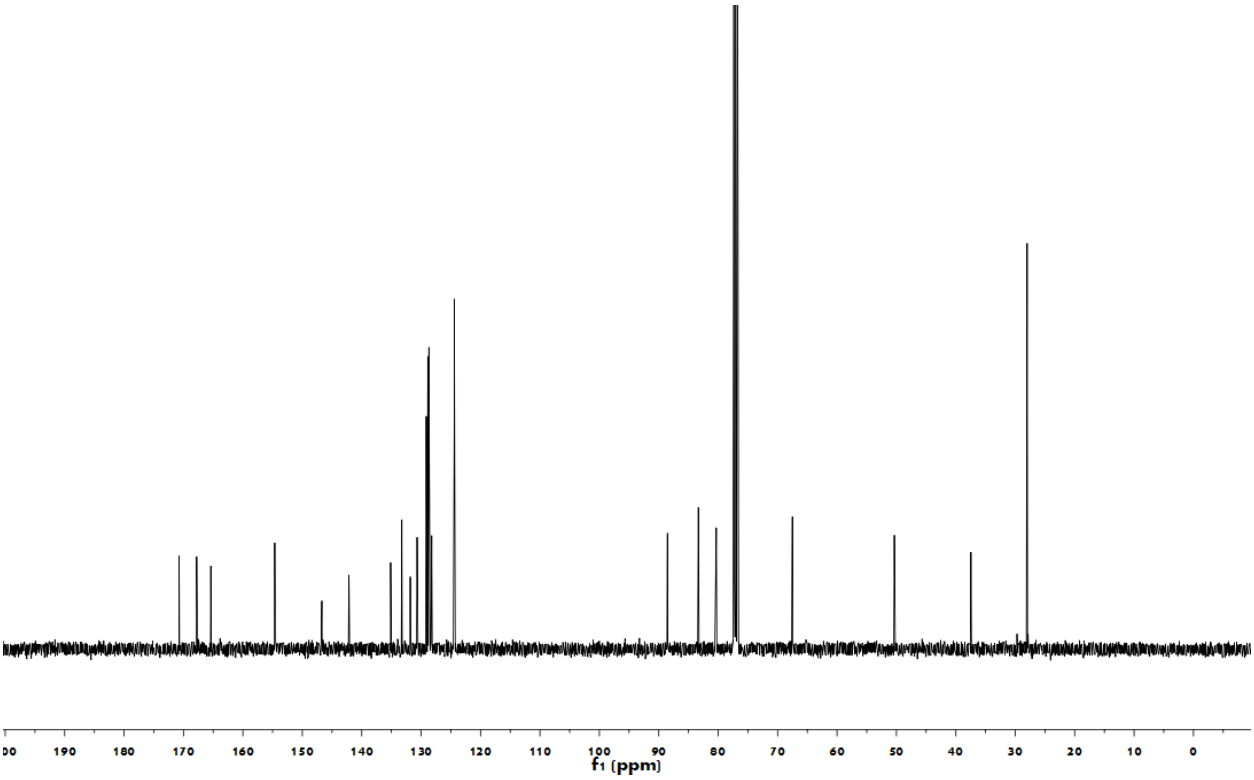
Compound 7



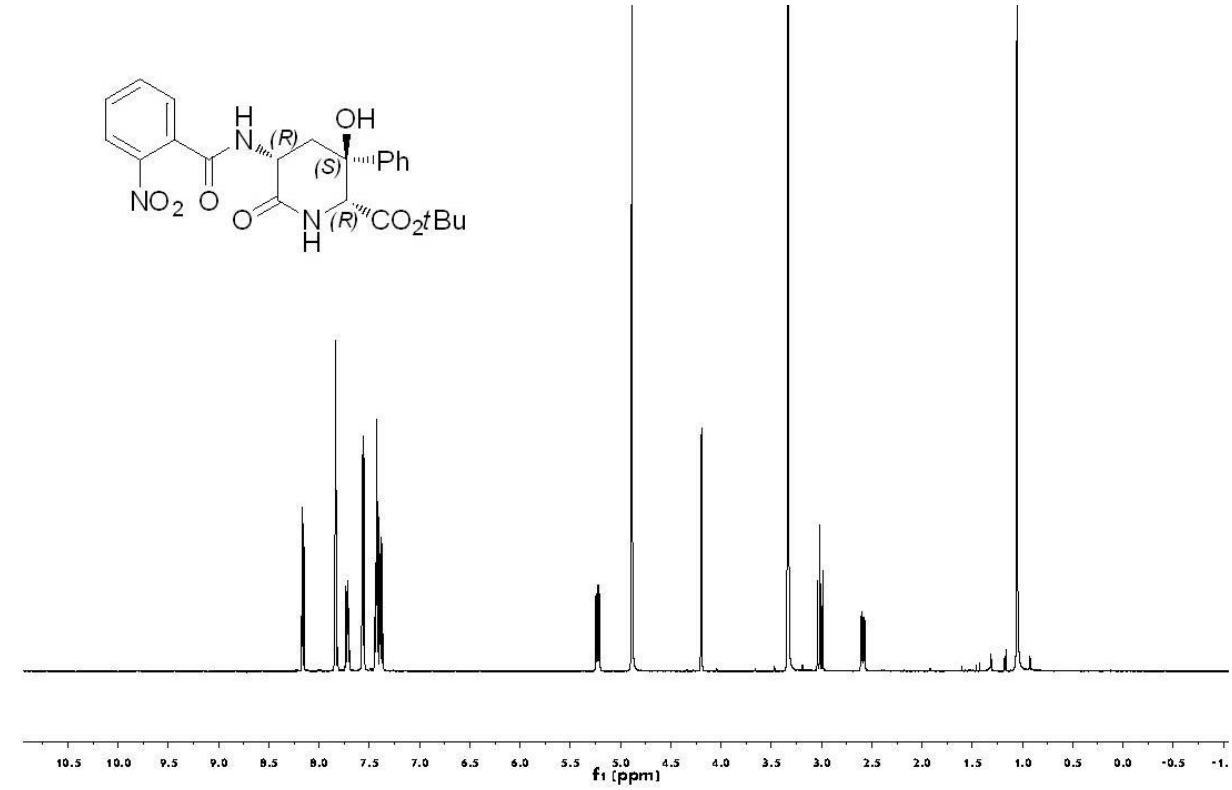


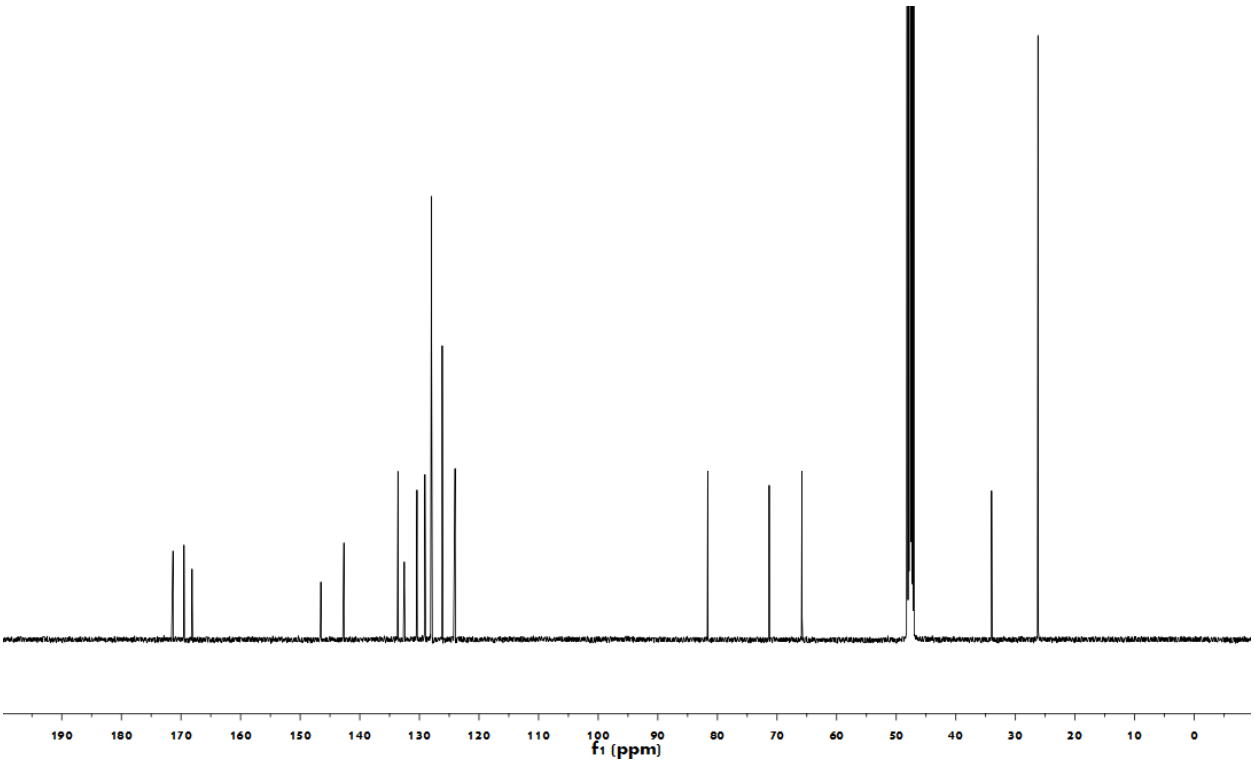
Compound 8





Compound S3


H
N
(R)
OH
(S)
Ph
NO2
O
O
N
H
(R)
CO2tBu
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Compound S3 nOe