Supplementary Information

Electrochemical dehydrogenative cyclization of 1,3-dicarbonyl compounds

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1. General Information

Anhydrous dichloromethane and tetrahydrofuran were obtained by distillation under argon from calcium hydride and sodium/benzophenone, respectively. Ferrocene and Et_4NPF_6 was purchased from Aldrich. $Y(OTf)_3$ (Yttrium(III) trifluoromethanesulfonate) and lithium methoxide (2.2 M solution in methanol) were purchased from Acros. Flash column chromatography was performed with silica gel (230–300 mesh). NMR spectra were acquired on Bruker AV–400 and Bruker AV–500 instruments. Data were reported as chemical shifts in ppm relative to TMS (0.00 ppm) for ^1H and $CDCl_3$ (77.2 ppm) for ^{13}C. The abbreviations used for explaining the multiplicities were as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High resolution mass spectra (ESI HRMS) were recorded on a Micromass QTOF2 Quadruple/Time–of–Flight Tandem mass spectrometer by the instrumentation center of Department of Chemistry, Xiamen University. Cyclic voltammograms were obtained on a CHI 760E potentiostat. Infrared spectra (IR) were recorded on a Nicolet AVATER FTIR330 spectrometer. Reticulated vitreous carbon (RVC, 100 pores per inch) was purchased from Goodfellow.

2. Procedures for the Electrolysis

General procedure A for the synthesis of oxindoles: A 10 mL three–necked round bottom flask was charged with Cp_2Fe (0.03 mmol, 0.1 equiv), the substrate (0.3 mmol, 1.0 equiv), Et_4NPF_6 (0.6 mmol, 2.0 equiv), LiOMe (0.15 mmol, 0.5 equiv) and $Y(OTf)_3$ (0.03 mmol, 0.1 equiv). The flask was equipped with a reticulated vitreous carbon (100 PPI) anode (1 cm x 1 cm x 1.2 cm) and a platinum plate (1 cm x 1 cm) cathode (Figure S1, left). The flask was flushed with argon. THF (4 mL) and MeOH (2 mL) were added. The constant current (7.5 mA) electrolysis was carried out at 80 °C (oil bath temperature) until complete consumption of the substrate (monitored by TLC or ^1H NMR). The solvent was removed under reduced pressure. The residue was chromatographed through silica gel eluting with AcOEt/hexane to give the desired product.

Figure S1. Electrolysis setup.

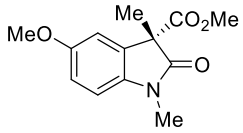
The degram scale electrolysis was conducted in a 1.0 L beaker–type cell equipped with two reticulated vitreous carbon (100 PPI) anodes (1.2 cm x 5 cm x 7.5 cm) and a platinum plate (5 cm x 5 cm x 0.1 mm) cathode (Figure S1, right). The three electrodes were placed in parallel with the Pt plate cathode sandwiched between two RVC anodes. The cell was charged with Cp_2Fe (0.85 g, 4.6 mmol, 0.1 equiv), compound **1** (10.2 g, 46.1 mmol, 1.0 equiv), Et_4NPF_6

(25.3 g, 91.9 mmol, 2 equiv), LiOMe (2.2 M; 10.5 mL, 23.1 mmol, 0.5 equiv) and $Y(OTf)_3$ (2.46 g, 4.60 mmol, 0.1 equiv) and then flushed with argon. THF (560 mL) and MeOH (280 mL) were added. The constant current (562 mA) electrolysis was carried out at 80 °C for 5.4 h. The reaction mixture was concentrated under reduced pressure. The residue was suspended in AcOEt (200 mL) and filtered through Celite. The Celite was rinsed with AcOEt (3 x 50 mL). The filtrate was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 5/1) to afford **2** as a pale yellow solid (8.47 g, 84% yield).

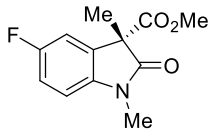
General procedure B for the synthesis of 3,4-dihydro-1*H*-quinolin-2-ones: A 10 mL three–necked round bottom flask was charged with Cp_2Fe (0.015 mmol, 5 mol %), the substrate (0.3 mmol, 1.0 equiv), $n$$Bu_4NBF_4$ (0.15 mmol, 0.5 equiv) and Na_2CO_3 (0.09 mmol, 0.3 equiv). The flask was equipped with a reticulated vitreous carbon (100 PPI) anode (1 cm x 1 cm x 1 cm) and a platinum plate (1 cm x 1 cm) cathode. The flask was flushed with argon. THF (3 mL) and MeOH (3 mL) were added. The constant current (10 mA) electrolysis was carried out at reflux until complete consumption of the substrate (monitored by TLC or ^{1}H NMR). The solvent was removed under reduced pressure. The residue was chromatographed through silica gel eluting with AcOEt/hexane to give the desired product.

3. Characterization Data for the Electrolysis Products

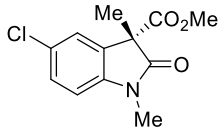
Compound **2**,[1] **17**,[1] **18**,[1] **20**,[1] **26**,[1] and **40**[2] are konwn in the literature.



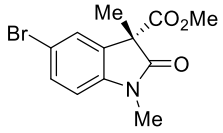
Methyl 5-methoxy-1,3-dimethyl-2-oxoindoline-3-carboxylate (3). Yield = 73%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (d, J = 2.6 Hz, 1H), 6.85 (dd, J = 8.4, 2.6 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 3.79 (s, 3H), 3.66 (s, 3H), 3.23 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 170.4, 156.4, 137.2, 131.3, 113.5, 110.6, 109.0, 56.0, 55.4, 53.2, 26.8, 20.5; IR (neat, cm^{-1}): 2935, 1746, 1712, 1601, 1498, 1355, 1326, 1111, 1038, 812; ESI HRMS m/z $(M+Na)^+$ calcd 272.0893, obsd 272.0890.



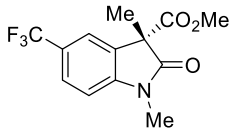
Methyl 5-fluoro-1,3-dimethyl-2-oxoindoline-3-carboxylate (4). Yield = 67%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06–7.00 (m, 2H), 6.81–6.77 (m, 1H), 3.68 (s, 3H), 3.25 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 169.9, 159.5 (d, $J_{C–F}$ = 241.8 Hz), 139.7 (d, $J_{C–F}$ = 2.2 Hz), 131.5 (d, $J_{C–F}$ = 8.3 Hz), 115.5 (d, $J_{C–F}$ = 23.4 Hz), 111.6 (d, $J_{C–F}$ = 25.4 Hz), 109.1 (d, $J_{C–F}$ = 8.2 Hz), 55.4, 53.3, 26.9, 20.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ –119.8; IR (neat, cm^{-1}): 2924, 1746, 1720, 1496, 1349, 1270, 1110, 813; ESI HRMS m/z $(M+Na)^+$ calcd 260.0693, obsd 260.0691.



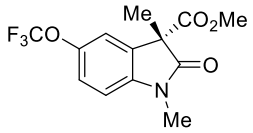
Methyl 5-chloro-1,3-dimethyl-2-oxoindoline-3-carboxylate (5). Yield = 84%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.24 (d, *J* = 2.1 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 3.68 (s, 3H), 3.24 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 169.8, 142.3, 131.6, 129.2, 128.4, 123.9, 109.5, 55.2, 53.4, 26.9, 20.4; IR (neat, cm^{-1}): 2933, 1719, 1609, 1490, 1343, 1112, 810; ESI HRMS *m/z* $(M+Na)^+$ calcd 276.0398, obsd 276.0396.



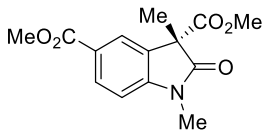
Methyl 5-bromo-1,3-dimethyl-2-oxoindoline-3-carboxylate (6). Yield = 75%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.38 (d, *J* = 1.9 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 3.68 (s, 3H), 3.24 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 169.8, 142.8, 132.1, 132.0, 126.6, 115.6, 110.1, 55.1, 53.4, 26.8, 20.4; IR (neat, cm^{-1}): 2930, 1746, 1720, 1488, 1341, 1241, 1111, 809; ESI HRMS *m/z* $(M+Na)^+$ calcd 319.9893, obsd 319.9891.



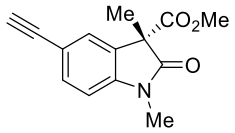
Methyl 1,3-dimethyl-2-oxo-5-(trifluoromethyl)indoline-3-carboxylate (7). Yield = 37%; Pale yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.50 (d, *J* = 1.7 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 3.69 (s, 3H), 3.29 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 169.6, 146.7, 130.6, 127.1 (q, J_{C-F} = 4.0 Hz), 125.5 (q, *J* = 32.9 Hz), 124.3 (q, *J* = 271.6 Hz), 123.2, 120.5 (q, J_{C-F} = 3.7 Hz), 108.5, 55.0, 53.5, 27.0, 20.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ –61.5; IR (neat, cm^{-1}): 2920, 1746, 1724, 1622, 1326, 1131, 1113, 821; ESI HRMS *m/z* $(M+Na)^+$ calcd 310.0661, obsd 310.0661.



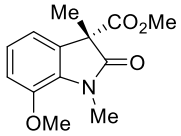
Methyl 1,3-dimethyl-2-oxo-5-(trifluoromethoxy)indoline-3-carboxylate (8). Yield = 35%; Yellow solid; ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.24–7.19 (m, 1H), 7.18–7.11 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 3.69 (s, 3H), 3.26 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 169.7, 145.1, 142.4, 131.4, 122.3, 120.7 (q, J_{C-F}= 256.9 Hz), 117.5, 109.0, 55.3, 53.4, 26.9, 20.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ –58.4; IR (neat, cm^{-1}): 3398, 2920, 1748,1724, 1496, 1257, 1076, 810; ESI HRMS *m/z* $(M+Na)^+$ calcd 326.0611, obsd 326.0609.



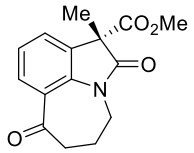
Dimethyl 1,3-dimethyl-2-oxoindoline-3,5-dicarboxylate (9). Yield = 61%; White solid; ^{1}H NMR (500 MHz,$CDCl_3$) δ 8.09 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.93 (d, *J* = 1.7 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 3.91 (s, 3H), 3.67 (s, 3H), 3.29 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 169.7, 166.7, 147.8, 131.9, 130.1, 125.2, 124.6, 108.2, 54.9, 53.3, 52.3, 27.0, 20.2; IR (neat, cm^{-1}): 2925, 1713, 1614, 1500, 1284, 1105, 767; ESI HRMS *m/z* $(M+Na)^+$ calcd 300.0842, obsd 300.0839.



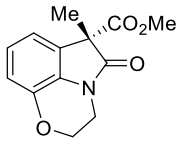
Methyl 5-ethynyl-1,3-dimethyl-2-oxoindoline-3-carboxylate (12). Yield = 62%; Yellow solid; ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.48 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.38 (d, *J* = 1.6 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 3.67 (s, 3H), 3.26 (s, 3H), 3.06 (s, 1H), 1.66 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 169.9, 144.1, 133.7, 130.3, 127.0, 116.7, 108.6, 83.4, 77.0, 54.9, 53.3, 26.9, 20.3; IR (neat, cm^{-1}): 3284, 2920, 1744, 1714, 1613, 1494, 1343, 1111, 820; ESI HRMS *m/z* $(M+Na)^+$ calcd 266.0788, obsd 266.0786.



Methyl 7-methoxy-1,3-dimethyl-2-oxoindoline-3-carboxylate (13). Yield = 85%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (dd, *J* = 8.4, 7.4 Hz, 1H), 6.91–6.84 (m, 2H), 3.87 (s, 3H), 3.65 (s, 3H), 3.52 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 170.5, 145.5, 131.6, 131.6, 123.6, 115.8, 113.0, 56.1, 55.2, 53.2, 30.0, 20.6; IR (neat, cm^{-1}): 2954, 2842, 1746, 1715, 1613, 1468, 1361, 1338, 1251, 1103, 1046, 786, 746;
ESI HRMS *m/z* $(M+Na)^+$ calcd 272.0893, obsd 272.0892.

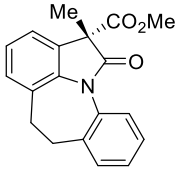


Methyl 7-methyl-1,6-dioxo-1,2,3,4,6,7-hexahydroazepino[3,2,1-*hi*]indole-7-Carboxylate (14). Yield = 61%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97–7.94 (m, 1H), 7.43–7.40 (m, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 4.07 (ddd, *J* = 14.2, 7.2, 3.4 Hz, 1H), 4.00 (ddd, *J* = 14.2, 7.2, 3.4 Hz, 1H), 3.68 (s, 3H), 3.08–3.01 (m, 2H), 2.25–2.16 (m, 2H), 1.70 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.3, 175.0, 169.9, 142.7, 131.4, 131.0, 127.9, 122.8, 121.1, 54.1, 53.4, 44.6, 44.2, 20.8, 20.6; IR (neat, cm^{-1}): 2923, 2852, 1744, 1720, 1665, 1586, 1349, 1242, 1142, 1114, 1016, 968, 878, 752; ESI HRMS *m/z* $(M+Na)^+$ calcd 296.0893, obsd 296.0894.

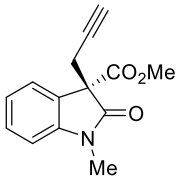


Methyl 6-methyl-5-oxo-2,3,5,6-tetrahydro-[1,4]oxazino[2,3,4-*hi*]indole-6-carboxylate (15). Yield = 85%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97–6.93 (m, 1H), 6.91–6.85 (m, 2H), 4.31 (t, *J* = 4.8 Hz, 2H), 3.96 (dt, *J* = 13.4, 4.6 Hz, 1H), 3.85 (dt, *J* = 13.4, 5.0 Hz,

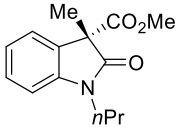
1H), 3.69 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 170.1, 141.5, 129.7, 128.5, 123.4, 116.4, 115.9, 64.9, 57.0, 53.3, 39.6, 20.1; IR (neat, cm^{-1}): 2960, 2924, 1744, 1713, 1633, 1492, 1345, 1260, 1093, 798; ESI HRMS *m/z* $(M+Na)^+$ calcd 270.0737, obsd 270.0735.



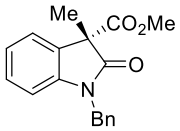
Methyl 7-methyl-6-oxo-6,7,11,12-tetrahydrobenzo[6,7]azepino[3,2,1-*hi*]indole-7-carboxyl -ate (16). Yield = 70%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 1H), 7.32–7.27 (m, 1H), 7.23–7.18 (m, 2H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.02–6.98 (m, 1H), 3.70 (s, 3H), 3.11–3.00 (m, 4H), 1.77 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.7, 170.6, 140.9, 136.8, 136.1, 131.1, 130.3, 129.8, 126.9, 126.8, 126.7, 125.1, 122.9, 121.0, 55.1, 53.3, 33.9, 33.7; IR (neat, cm^{-1}): 2960, 2963, 2852, 1747, 1721, 1600, 1494, 1449, 1352, 1260, 797; ESI HRMS *m/z* $(M+Na)^+$ calcd 330.1101, obsd 330.1098.



Methyl 1-methyl-2-oxo-3-(prop-2-yn-1-yl)indoline-3-carboxylate (19). Yield = 88%; Pale yellow solid; ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.40–7.35 (m, 1H), 7.35–7.31 (m, 1H), 7.17–7.06 (m, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 3.67 (s, 3H), 3.27 (s, 3H), 3.19 (dd, *J* = 16.7, 2.6 Hz, 1H), 3.04 (dd, *J* = 16.7, 2.6 Hz, 1H), 1.77 (t, *J* = 2.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 168.9, 144.6, 129.7, 127.3, 123.7, 123.2, 108.6, 78.1, 70.8, 58.1, 53.4, 26.8, 24.4; IR (neat, cm^{-1}): 3290, 2924, 2853, 1738, 1713, 1611, 1467, 1260, 1086, 797; ESI HRMS *m/z* $(M+Na)^+$ calcd 266.0788, obsd 266.0787.

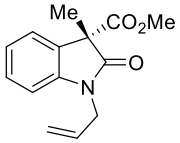


Methyl 3-methyl-2-oxo-1-propylindoline-3-carboxylate (21). Yield = 85%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.28 (m, 1H), 7.27–7.21 (m, 1H), 7.09–7.01 (m, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 3.76 (dt, *J* = 14.3, 7.3 Hz, 1H), 3.71–3.66 (m, 1H), 3.65 (s, 3H), 1.80–1.70 (m, 2H), 1.66 (s, 3H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 170.5, 143.3, 130.4, 129.1, 123.3, 122.8, 108.9, 55.0, 53.1, 41.9, 20.8, 20.3, 11.3; IR (neat, cm^{-1}): 2929, 1747, 1717, 1609, 1488, 1466, 1358, 1238, 1107, 1021, 749; ESI HRMS *m/z* $(M+Na)^+$ calcd 270.1101, obsd 270.1099.

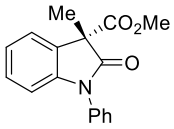


Methyl 1-benzyl-3-methyl-2-oxoindoline-3-carboxylate (22). Yield = 70%; White solid; ^{1}H

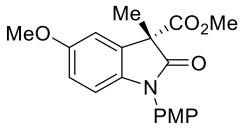
NMR (500 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.27–7.22 (m, 2H), 7.18 (td, *J* = 7.8, 1.3 Hz, 1H), 7.04–7.00 (m, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.07 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H), 3.68 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 170.4, 142.8, 135.6, 130.2, 129.1, 128.9, 127.8, 127.2, 123.2, 123.1, 109.7, 55.1, 53.2, 44.0, 20.2; IR (neat, cm^{-1}): 2930, 1744, 1715, 1608, 1488, 1357, 1237, 1179, 1108, 750; ESI HRMS *m/z* $(M+Na)^+$ calcd 318.1101, obsd 318.1100.



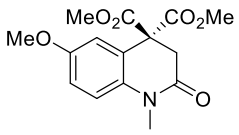
Methyl 1-allyl-3-methyl-2-oxoindoline-3-carboxylate (23). Yield = 90%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32–7.20 (m, 2H), 7.06 (t, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 5.90–5.81 (m, 1H), 5.28–5.20 (m, 2H), 4.47–4.41 (m, 1H), 4.36–4.28 (m, 1H), 3.66 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 170.4, 142.9, 131.1, 130.2, 129.1, 123.3, 123.0, 117.5, 109.5, 55.1, 53.2, 42.5, 20.3; IR (neat, cm^{-1}): 2920, 1744,1719, 1609, 1467, 1355, 1239, 1182, 1108, 926, 751; ESI HRMS *m/z* $(M+Na)^+$ calcd 268.0944, obsd 268.0943.



Methyl 3-methyl-2-oxo-1-phenylindoline-3-carboxylate (24). Yield = 75%; Yellow solid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56–7.51 (m, 2H), 7.46–7.40 (m, 3H), 7.32 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.29–7.21 (m, 1H), 7.12–7.08 (m, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 3.71 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 170.4, 143.8, 134.4, 130.0, 129.8, 129.1, 128.4, 126.7, 123.5, 109.9, 55.3, 53.3, 20.5; IR (neat, cm^{-1}): 2924, 2852, 1746, 1724, 1609, 1499, 1374, 1240, 1119, 757, 695; ESI HRMS *m/z* $(M+Na)^+$ calcd 304.0944, obsd 304.0942.

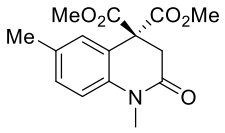


Methyl 5-methoxy-1-(4-methoxyphenyl)-3-methyl-2-oxoindoline-3-carboxylate (25). Yield = 67%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.31 (m, 2H), 7.06–7.00 (m, 2H), 6.91 (d, *J* = 2.6 Hz, 1H), 6.77 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.71 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 170.4, 159.3, 156.5, 137.6, 131.1, 127.9, 127.2, 115.0, 113.7, 110.3, 110.3, 56.0, 55.7, 55.5, 53.3, 20.6; IR (neat, cm^{-1}): 2923, 2838, 1744, 1719, 1600, 1513, 1490, 1375, 1279, 1247, 1110, 1030, 814; ESI HRMS *m/z* $(M+Na)^+$ calcd 364.1155, obsd 364.1152.

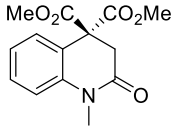


Dimethyl 2,3-dihydro-6-methoxy-1-methyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (28). Yield = 82%; White solid; ^1H NMR (500 MHz, $CDCl_3$) δ 6.96 (d, *J* = 8.9 Hz, 1H), 6.90 (dd, *J*

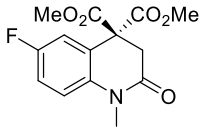
= 8.9, 2.8 Hz, 1H), 6.83 (d, *J* = 2.8 Hz, 1H), 3.81 (s, 6H), 3.80 (s, 3H), 3.31 (s, 3H), 3.22 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5, 166.3, 155.6, 133.6, 123.8, 116.4, 114.6, 113.9, 57.2, 55.8, 53.6, 38.2, 29.9; IR (neat, cm^{-1}): 2956, 2848, 1731, 1674, 1429, 1238, 1016; ESI HRMS *m/z* $(M+Na)^+$ calcd 330.0948, obsd 330.0949.



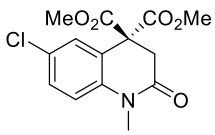
Dimethyl 2,3-dihydro-1,6-dimethyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (29). Yield = 94%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.2 Hz, 1H), 7.03 (s, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 3.81 (s, 6H), 3.31 (s, 3H), 3.22 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 166.5, 137.5, 133.0, 130.1, 128.4, 122.3, 115.4, 57.1, 53.5, 38.2, 29.7, 20.8; IR (neat, cm^{-1}): 2955, 2916, 1731, 1683, 1239, 1025; ESI HRMS *m/z* $(M+Na)^+$ calcd 314.0999, obsd 314.0995.



Dimethyl 2,3-dihydro-1-methyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (30). Yield = 92%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.36 (m, 1H), 7.28–7.24 (m, 1H), 7.15–7.10 (m, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 3.81 (s, 6H), 3.34 (s, 3H), 3.25 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 166.7, 139.9, 129.7, 128.0, 123.4, 122.5, 115.6, 57.1, 53.7, 38.1, 29.9; IR (neat, cm^{-1}): 2954, 1737, 1682, 1366, 1235, 1053; ESI HRMS *m/z* $(M+Na)^+$ calcd 300.0842, obsd 300.0844.

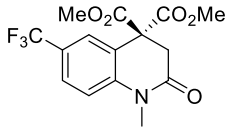


Dimethyl 6-fluoro-2,3-dihydro-1-methyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (31). Yield = 96%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12–7.02 (m, 2H), 7.00 (dd, *J* = 8.9, 4.6 Hz, 1H), 3.82 (s, 6H), 3.33 (s, 3H), 3.23 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 166.2, 158.5 (d, $J_{C–F}$ = 243.4 Hz), 136.3 (d, $J_{C–F}$ = 2.7 Hz), 124.0 (d, $J_{C–F}$ = 7.7 Hz), 116.7 (d, $J_{C–F}$ = 8.0 Hz), 116.1 (d, $J_{C–F}$ = 22.5 Hz), 115.4 (d, $J_{C–F}$ = 24.9 Hz), 56.8, 53.7, 37.8, 30.0; ^{19}F NMR (471 MHz, $CDCl_3$) δ –119.4; IR (neat, cm^{-1}): 2960, 1738, 1685, 1430, 1243, 1180, 815; ESI HRMS *m/z* $(M+Na)^+$ calcd 318.0748, obsd 318.0746.

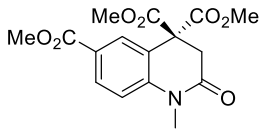


Dimethyl 6-chloro-2,3-dihydro-1-methyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (32). Yield = 93%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.26 (d, *J* = 2.4 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 1H), 3.82 (s, 6H), 3.32 (s, 3H), 3.23 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 166.3, 138.7, 129.6, 128.7, 128.2, 123.9, 116.7, 56.8, 53.9, 37.9, 30.0; IR (neat, cm^{-1}): 2957, 1737, 1687, 1358, 1239, 1139; ESI HRMS *m/z* $(M+Na)^+$

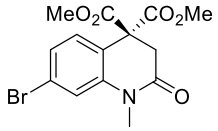
calcd 334.0453, obsd 334.0454.



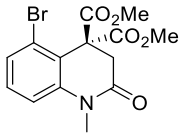
Dimethyl 2,3-dihydro-1-methyl-2-oxo-6-(trifluoromethyl) quinoline-4,4(*1H*)-dicarboxylate (33). Yield = 88%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.14 (d, *J* = 8.7 Hz, 1H), 3.83 (s, 6H), 3.37 (s, 3H), 3.26 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 166.4, 142.9, 126.9 (q, $J_{C–F}$ = 3.7 Hz), 125.4 (q, $J_{C–F}$ = 33.3 Hz), 125.4 (q, $J_{C–F}$ = 4.2 Hz), 123.9 (q, $J_{C–F}$ = 271.7 Hz), 122.8, 115.7, 56.8, 53.8, 37.7, 29.9; ^{19}F NMR (471 MHz, $CDCl_3$) δ –62.1; IR (neat, cm^{-1}): 2957, 1737, 1694, 1337, 1282, 1120; ESI HRMS *m/z* $(M+Na)^+$ calcd 368.0716, obsd 368.0711.



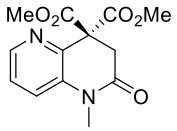
Trimethyl 2,3-dihydro-1-methyl-2-oxoquinoline-4,4,6(*1H*)-tricarboxylate (34). Yield = 82%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.96 (d, *J* = 1.9 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 1H), 3.91 (s, 3H), 3.83 (s, 6H), 3.37 (s, 3H), 3.27 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.2, 166.6, 166.1, 143.6, 131.3, 129.7, 125.0, 122.3, 115.3, 56.8, 53.7, 52.3, 37.8, 29.9; IR (neat, cm^{-1}): 2955, 1738, 1694, 1610, 1437, 1264, 1142; ESI HRMS *m/z* $(M+Na)^+$ calcd 358.0897, obsd 358.0895.



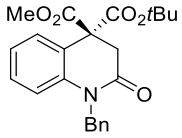
Dimethyl 7-bromo-2,3-dihydro-1-methyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (35). Yield = 30%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.17 (d, *J* = 1.9 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 3.81 (s, 6H), 3.32 (s, 3H), 3.23 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 166.5, 141.3, 129.6, 126.3, 123.6, 121.3, 118.8, 56.8, 53.8, 37.9, 29.9; IR (neat, cm^{-1}): 2916, 1741, 1651, 1351, 1256; ESI HRMS *m/z* $(M+Na)^+$ calcd 377.9948, obsd 377.9950.



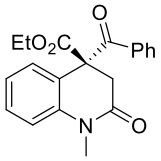
Dimethyl 5-bromo-2,3-dihydro-1-methyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (35'). Yield = 21%; Pale yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.1 Hz, 1H), 7.21 (t, *J* = 8.1 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 1H), 3.81 (s, 6H), 3.32 (s, 3H), 3.23 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 166.0, 142.4, 130.1, 129.6, 124.7, 123.6, 115.3, 58.2, 53.8, 39.4, 30.7; IR (neat, cm^{-1}): 2953, 1732, 1693, 1359, 1242; ESI HRMS *m/z* $(M+Na)^+$ calcd 377.9948, obsd 377.9950.



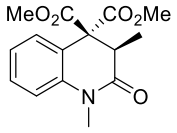
Dimethyl 2,3-dihydro-1-methyl-2-oxo-1,5-naphthyridine-4,4(*1H*)-dicarboxylate (36). Yield = 68%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34–8.27 (m, 1H), 7.34–7.29 (m, 2H), 3.83 (s, 6H), 3.43 (s, 2H), 3.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 166.5, 143.5, 143.3, 136.0, 124.0, 122.1, 59.6, 53.8, 37.8, 29.3; IR (neat, cm^{-1}): 1732, 1693, 1455, 1252, 1143; ESI HRMS *m/z* $(M+Na)^+$ calcd 301.0795, obsd 301.0794.



4-(*tert*-Butyl) 4-methyl 1-benzyl-2,3-dihydro-2-oxoquinoline-4,4(*1H*)-dicarboxylate (37). Yield = 96%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.29–7.25 (m, 2H), 7.22–7.15 (m, 4H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 5.20, 5.14 (ABq, J_{AB} = 16.3 Hz, 2H), 3.78 (s, 3H), 3.34, 3.29 (ABq, J_{AB} = 15.8 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 168.0, 167.1, 139.0, 136.6, 129.3, 128.8, 128.2, 127.3, 126.6, 123.4, 123.2, 116.3, 83.7, 57.8, 53.3, 45.9, 38.3, 27.9; IR (neat, cm^{-1}): 2978, 1731, 1683, 1456, 1371, 1247, 1156, 753; ESI HRMS *m/z* $(M+Na)^+$ calcd 418.1625, obsd 418.1631.

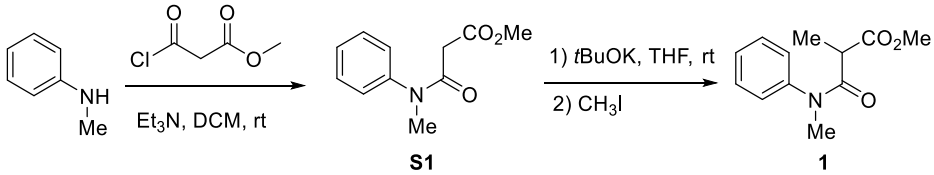


Ethyl 4-benzoyl-1,2,3,4-tetrahydro-1-methyl-2-oxoquinoline-4-carboxylate (38). Yield = 77%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.70 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.40–7.35 (m, 3H), 7.35–7.31 (m, 1H), 7.09–7.05 (m, 2H), 4.29–4.19 (m, 2H), 3.39, 3.33 (ABq, J_{AB} = 16.1 Hz, 2H), 3.35 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 170.3, 167.0, 140.3, 135.2, 133.2, 129.6, 129.4, 128.9, 128.7, 123.3, 123.3, 115.8, 62.6, 61.1, 39.2, 29.9, 14.0; IR (neat, cm^{-1}): 2958, 1734, 1684, 1458, 1136; ESI HRMS *m/z* $(M+Na)^+$ calcd 360.1206, obsd 360.1205.



Dimethyl 2,3-dihydro-1,3-dimethyl-2-oxoquinoline-4,4(*1H*)-dicarboxylate (39). Yield = 86%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.38–7.33 (m, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.34 (s, 3H), 3.30 (q, *J* = 7.2 Hz, 1H), 1.23 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 169.8, 168.3, 139.7, 129.6, 129.5, 123.2, 121.7, 115.2, 61.0, 53.3, 53.0, 41.6, 30.0, 12.6; IR (neat, cm^{-1}): 2953, 1737, 1683, 1362, 1257, 1035, 757; ESI HRMS *m/z* $(M+Na)^+$ calcd 314.0999, obsd 314.0998.

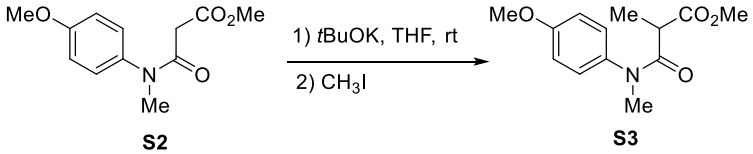
4. Synthesis and Characterization of Substrates



S1 1

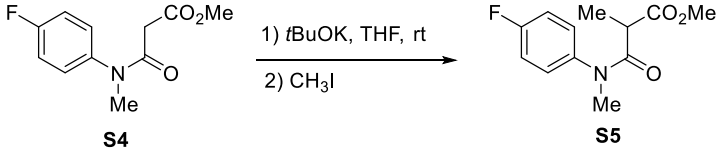
Methyl 3-(methyl(phenyl)amino)-3-oxopropanoate (S1).[1] A solution of *N*–methylaniline (1.07 g, 10.0 mmol, 1.0 equiv) and Et_3N (2.8 mL, 20 mmol, 2.0 equiv) in anhydrous CH_2Cl_2 (30 mL) was cooled to 0 °C. Methyl malonyl chloride (1.3 mL, 12 mmol, 1.2 equiv) was added dropwise. The mixture was then allowed to warm to rt and stirred for 2 h. The solvent was removed under reduced pressure. AcOEt (15 mL) was added and the mixture was filtered. The filtrate was concentrated under reduce pressure. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 3/1) to afford the known compound **S1** as colorless oil (1.84 g, 88% yield).

Methyl 2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (1). The following procedure was adapted from a reported method.[3] To a suspension of *t*BuOK (0.62 g, 5.5 mmol, 1.1 equiv) in THF (20 mL) was added a solution of **S1** (1.0 g, 5.0 mmol, 1.0 equiv) in THF (5 mL) dropwise at rt. The mixture was stirred for 10 min and treated with CH_3I (0.74 g, 5.2 mmol, 1.0 equiv). The mixture was stirred at rt until complete consumption of **S1** (monitored by TLC). HCl (10%, 30 mL) was added until the disappearance of the colorless solid. The reaction mixture was extracted with AcOEt (3 x 50 mL). The combined organic fractions were washed with brine (100 mL) and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 3/1) to afford the known compound **1**[1] as a pale yellow oil (0.87 g, 79% yield).



S2 S3

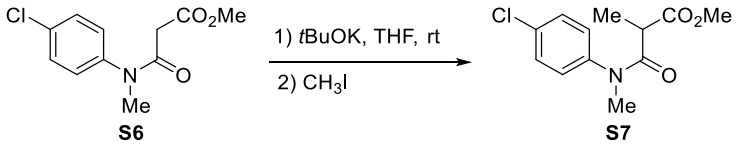
Methyl 3-((4-methoxyphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S3). The title compound was prepared from the known compound **S2**[1] by following the procedure described for the synthesis of **1**. Yield = 67%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18–7.13 (m, 2H), 6.96–6.91 (m, 2H), 3.84 (s, 3H), 3.66 (s, 3H), 3.43 (q, *J* = 7.0 Hz, 1H), 3.27 (s, 3H), 1.30 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 170.5, 159.3, 136.4, 128.6, 115.1, 55.6, 52.4, 43.5, 37.9, 14.3; IR (neat, cm^{-1}): 2950, 2840, 1747, 1659, 1512, 1457, 1384, 1248, 1030, 840; ESI HRMS *m/z* $(M+Na)^+$ calcd 274.1050, obsd 274.1046.



S4 S5

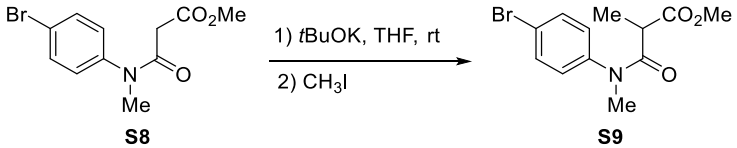
Methyl 3-((4-fluorophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S5). The title compound was prepared from the known compound **S4**[4] by following the procedure described

for the synthesis of **1**. Yield = 65%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.20 (m, 2H), 7.16–7.10 (m, 2H), 3.66 (s, 3H), 3.39 (q, *J* = 7.1 Hz, 1H), 3.28 (s, 3H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 170.2, 162.1 (d, $J_{C–F}$ = 248.9 Hz), 139.6 (d, $J_{C–F}$ = 3.3 Hz), 129.4 (d, $J_{C–F}$ = 8.7 Hz), 117.0 (d, $J_{C–F}$ = 22.7 Hz), 52.5, 43.5, 37.9, 14.3; ^{19}F NMR (471 MHz, $CDCl_3$) δ –112.6; IR (neat, cm^{-1}): 2951, 1747, 1666, 1509, 1457, 1384, 1222, 1092, 847; ESI HRMS *m/z* $(M+Na)^+$ calcd 262.0850, obsd 262.0848.



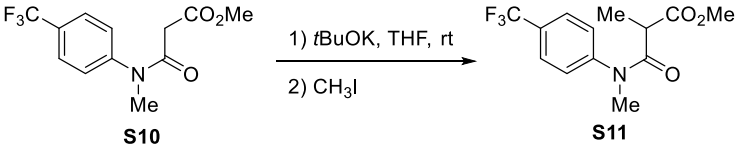
S6 **S7**

Methyl 3-((4-chlorophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S7). The title compound was prepared from the known compound **S6**[4] by following the procedure described for the synthesis of **1**. Yellow oil; Yield = 90%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.39 (m, 2H), 7.23–7.18 (m, 2H), 3.67 (s, 3H), 3.40 (q, *J* = 7.1 Hz, 1H), 3.28 (s, 3H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 170.0, 142.2, 134.3, 130.3, 129.0, 52.5, 43.5, 37.8, 14.3; IR (neat, cm^{-1}): 2950, 1747, 1665, 1490, 1382, 1203, 1091, 1015, 841; ESI HRMS *m/z* $(M+Na)^+$ calcd 278.0554, obsd 278.0551.



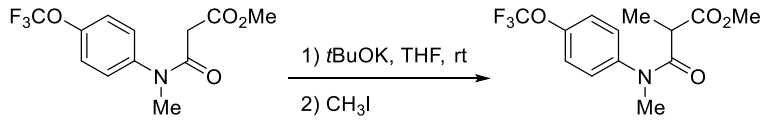
S8 **S9**

Methyl 3-((4-bromophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S9). The title compound was prepared from the known compound **S8**[4] by following the procedure described for the synthesis of **1**. Yield = 60%; Yellow oil; ^{1}H NMR (500 MHz, DCl_3) δ 7.59–7.55 (m, 2H), 7.17–7.12 (m, 2H), 3.67 (s, 3H), 3.40 (q, *J* = 7.1 Hz, 1H), 3.28 (s, 3H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 169.9, 142.7, 133.3, 129.3, 122.2, 52.5, 43.5, 37.7, 14.3; IR (neat, cm^{-1}): 2949, 1747, 1664, 1486, 1384, 1204, 1098, 1011, 838; ESI HRMS *m/z* $(M+Na)^+$ calcd 322.0049, obsd 322.0047.



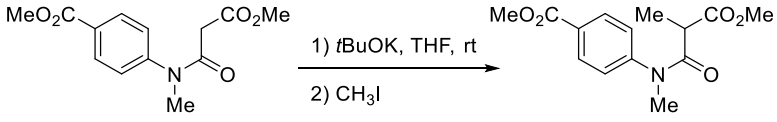
S10 **S11**

Methyl 2-methyl-3-(methyl(4-(trifluoromethyl)phenyl)amino)-3-oxopropanoate (S11). The title compound was prepared from the known compound **S10**[4] by following the procedure described for the synthesis of **1**. Yield = 97%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 3.68 (s, 3H), 3.46–3.36 (m, 1H), 3.33 (s, 3H), 1.33 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 169.9, 146.9, 130.7, 130.5, 128.1, 127.3, 123.8 (q, $J_{C–F}$ = 272.0 Hz), 52.6, 43.7, 37.8, 14.3; ^{19}F NMR (471 MHz, $CDCl_3$) δ –62.7; IR (neat, cm^{-1}): 2953, 1748, 1668, 1613, 1382, 1326, 1128, 1067, 853; ESI HRMS *m/z* $(M+Na)^+$ calcd 312.0818, obsd 312.0816.



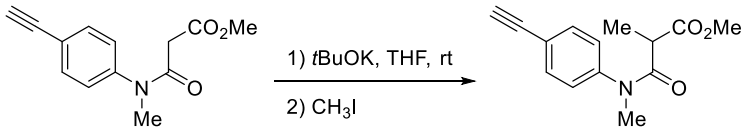
S12 **S13**

Methyl 2-methyl-3-(methyl(4-(trifluoromethoxy)phenyl)amino)-3-oxopropanoate (S13) . The title compound was prepared from the known compound **S12**[4] by following the procedure described for the synthesis of **1**. Yield = 77%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.29 (m, 4H), 3.66 (s, 3H), 3.39 (q, *J* = 7.1 Hz, 1H), 3.30 (s, 3H), 1.32 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 170.0, 148.8, 142.1, 129.3, 122.5, 120.5 (q, $J_{C–F}$ = 258.1 Hz), 52.5, 43.7, 37.9, 14.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ –58.0; IR (neat, cm^{-1}): 2953, 1748, 1667, 1506, 1384, 1259, 1020, 858; ESI HRMS *m/z* $(M+Na)^+$ calcd 328.0767, obsd 328.0764.



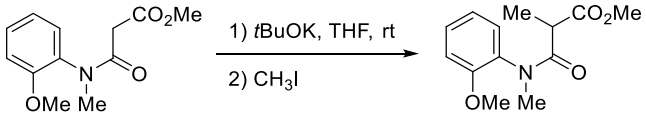
S14 **S15**

Methyl 4-(3-methoxy-N,2-dimethyl-3-oxopropanamido)benzoate (S15). The title compound was prepared from the known compound **S14**[4] by following the procedure described for the synthesis of **1**. Yield = 60%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 3.95 (s, 3H), 3.67 (s, 3H), 3.48–3.37 (m, 1H), 3.33 (s, 3H), 1.32 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 169.9, 166.2, 147.7, 131.5, 130.1, 127.5, 52.6, 52.5, 43.8, 37.7, 14.4; IR (neat, cm^{-1}): 2952, 1724, 1667, 1604, 1435, 1381, 1279, 1115, 1020, 708; ESI HRMS *m/z* $(M+Na)^+$ calcd 302.0999, obsd 302.0996.



S16 **S17**

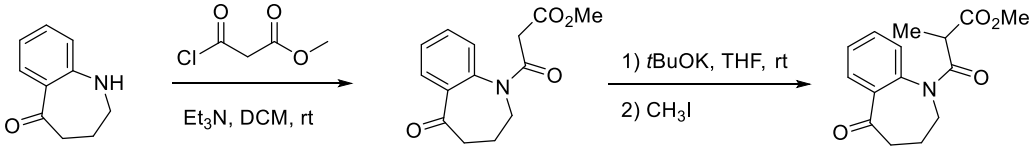
Methyl 3-((4-ethynylphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S17). The title compound was prepared from the known compound **S16**[4] by following the procedure described for the synthesis of **1**. Yield = 85%; Yellow oil; ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.57–7.54 (m, 2H), 7.23–7.20 (m, 2H), 3.67 (s, 3H), 3.40 (q, *J* = 7.0 Hz, 1H), 3.29 (s, 3H), 3.15 (s, 1H), 1.31 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 170.1, 143.9, 133.9, 127.7, 122.5, 82.5, 78.9, 52.6, 43.7, 37.8, 14.4; IR (neat, cm^{-1}): 3288, 2918, 2849, 1745, 1659, 1600, 1503, 1383, 1180, 1077, 849; ESI HRMS *m/z* $(M+Na)^+$ calcd 268.0944, obsd 268.0942.



S18 **S19**

Methyl 3-((2-methoxyphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S19). The title compound was prepared from commercial available **S18** by following the procedure described for the synthesis of **1**. Yield = 80%; Yellow oil; Ratio of isomers = 1: 0.5; 7.39–7.32 (m, 1.5H), 7.26–7.22 (m, 1H), 7.15 (dd, *J* = 7.9, 1.8 Hz, 0.5H), 7.02–6.96 (m, 3H), 3.85 (s, 4.5H), 3.64 (s, 4.5H), 3.35–3.27 (m, 1.5H), 3.21 (2s, 4.5H), 1.30 (d, *J* = 7.2 Hz, 1.5H), 1.28 (d,

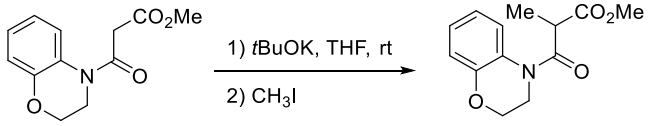
J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.6, 171.2, 170.9, 170.7, 155.4, 155.2, 131.9 (2C), 130.0, 129.9, 129.7, 129.0, 121.3, 121.2, 112.3, 112.0, 55.6 (2C), 52.3, 52.2, 43.7, 43.5, 36.5, 36.4, 14.8, 14.1; IR (neat, cm^{-1}): 2945, 2841, 1746, 1662, 1501, 1458, 1384, 1239, 1091, 1024, 754; ESI HRMS *m/z* $(M+Na)^+$ calcd 274.1050, obsd 274.1049.



S20 **S21**

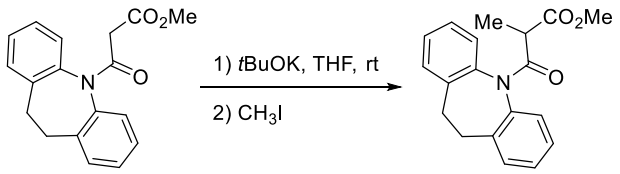
Methyl 3-oxo-3-(5-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl)propanoate (S20). The title compound was prepared from 1,2,3,4-tetrahydro-5*H*-benzo[*b*] azepin-5-one by following the procedure described for the synthesis of S**1**. Yield = 90%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.62 (td, *J* = 7.8, 1.6 Hz, 1H), 7.50 (td, *J* = 7.8, 1.2 Hz, 1H), 7.28 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.91–4.80 (m, 1H), 3.60 (s, 3H), 3.28 (d, *J* = 5.2 Hz, 2H), 3.22–3.07 (m, 1H), 2.90–2.56 (m, 2H), 2.46–2.09 (m, 1H), 2.12–1.53 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.9, 167.6, 166.2, 140.4, 135.9, 134.0, 130.2, 129.2, 128.3, 52.5, 45.5, 41.6, 39.5, 21.4; IR (neat, cm^{-1}): 2921, 2849, 1741, 1661, 1596, 1482, 1395, 1157, 1011, 776; ESI HRMS *m/z* $(M+Na)^+$ calcd 284.0893, obsd 284.0891.

Methyl 2-methyl-3-oxo-3-(5-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl)propanoate. (S21). The title compound was prepared from compound **S20** by following the procedure described for the synthesis of **1**. Yield = 82%; Yellow solid; Ratio of isomers = 1 : 0.5; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 0.5H), 7.63 (td, *J* = 7.6, 1.7 Hz, 1.5H), 7.56–7.48 (m, 1.5H), 7.43 (d, *J* = 7.9 Hz, 0.5H), 7.20 (d, *J* = 7.8 Hz, 1H), 4.93–4.78 (m, 1.5H), 3.76 (s, 1.5H), 3.49 (s, 3H), 3.43–3.33 (m, 1.5H), 3.18–3.09 (m, 1.5H), 2.81–2.64 (m, 2.5H), 2.59–2.45 (m, 0.5H), 2.27–2.16 (m, 1.5H), 1.84–1.70 (m, 1.5H), 1.38 (d, *J* = 7.0 Hz, 3H), 1.20 (d, *J* = 7.0 Hz, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.4, 202.1, 170.9, 170.8, 170.5, 170.2, 140.4, 140.2, 136.3, 136.0, 134.0, 134.0, 130.3, 130.0, 129.3, 129.2, 128.5, 128.3, 52.7, 52.3, 45.4, 45.0, 44.0, 43.6, 39.6, 39.2, 21.5, 21.4, 14.7, 14.0; IR (neat, cm^{-1}): 2925, 2852, 1747, 1659, 1595, 1452, 1392, 1195, 1088, 774; ESI HRMS *m/z* $(M+Na)^+$ calcd 298.1050, obsd 298.1047.



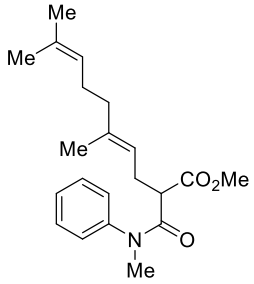
S22 **S23**

Methyl 3-(2,3-dihydro-4*H*-benzo[*b*][1,4]oxazin-4-yl)-2-methyl-3-oxopropanoate (23). The title compound was prepared from the known compound **S22**[4] by following the procedure described for the synthesis of **1**. Yield = 70%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.06 (m, 2H), 7.03–6.85 (m, 2H), 4.42–4.25 (m, 2H), 4.22 (br, 1H), 4.09–3.98 (m, 1H), 3.96–3.89 (m, 1H), 3.67 (s, 3H), 1.45 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 169.8, 147.7, 127.4, 126.0, 124.2, 120.4, 117.7, 67.0, 52.6, 43.2, 40.5, 14.4; IR (neat, cm^{-1}): 2950, 1748, 1663, 1495, 1392, 1252, 1056, 850, 755; ESI HRMS *m/z* $(M+Na)^+$ calcd 272.0893, obsd 272.0890.

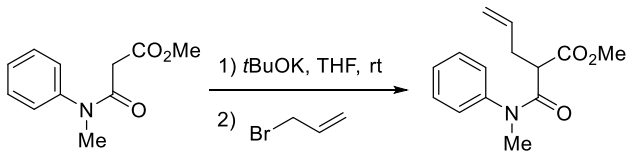


S24 **S25**

Methyl 3-(10,11-dihydro-5*H*-dibenzo[*b*,*f*]azepin-5-yl)-2-methyl-3-oxopropanoate (S25). The title compound was prepared from the known compound **S24**[4] by following the procedure described for the synthesis of **1**. Yield = 84%; Yellow solid; Ratio of isomers = 1:0.8; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.37 (m, 1.8H), 7.35–7.09 (m, 12.6H), 3.81 (s, 2.4H), 3.71–3.57 (m, 2.6H), 3.57 (s, 3H), 3.54–3.27 (m, 2.8H), 2.93–2.75 (m, 3.6H), 1.50 (d, *J* = 7.1 Hz, 3H), 1.32 (d, *J* = 7.1 Hz, 2.4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 170.9, 170.3, 170.1, 141.9, 141.4, 140.2, 139.8, 138.5, 137.9, 135.2, 134.3, 130.8 (2C), 130.6, 130.1, 129.1, 129.0, 128.8, 128.4, 127.9, 127.8 (2C), 127.7, 127.5 (2C), 126.8, 126.7, 52.7, 52.4, 43.9, 43.6, 31.2, 30.7, 30.4, 30.3, 14.6, 14.2; IR (neat, cm^{-1}): 2925, 2852, 1747, 1668, 1488, 1357, 1197, 1087, 1030, 776; ESI HRMS *m/z* $(M+Na)^+$ calcd 332.1257, obsd 332.1255.

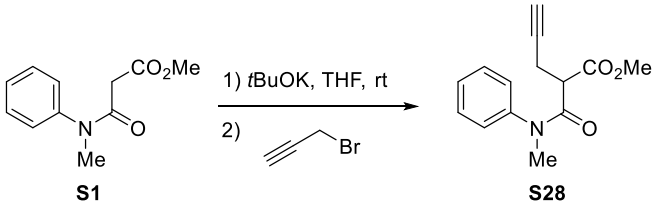


Methyl (*E*)-5,9-dimethyl-2-(methyl(phenyl)carbamoyl)deca-4,8-dienoate (S26).[5]



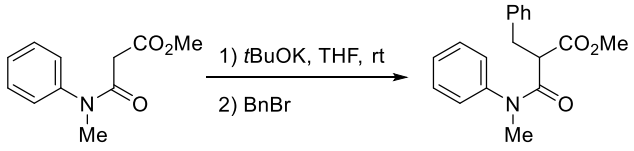
S1 **S27**

Methyl 2-(methyl(phenyl)carbamoyl)pent-4-enoate (S27). The title compound was prepared from the known compound **S1**[1] and 3-bromoprop-1-ene by following the procedure described for the synthesis of **1**. Yield = 65%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.40 (m, 2H), 7.39–7.34 (m, 1H), 7.25–7.18 (m, 2H), 5.64 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.09–4.93 (m, 2H), 3.67 (s, 3H), 3.42 (dd, *J* = 8.6, 6.2 Hz, 1H), 3.30 (s, 3H), 2.68–2.50 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 168.6, 143.5, 134.7, 130.0, 128.4, 127.9, 117.5, 52.5, 49.0, 37.8, 33.7; IR (neat, cm^{-1}): 3064, 2951, 2925, 2852, 1744, 1663, 1595, 1496, 1436, 1381, 1265, 1120, 918, 774, 701; ESI HRMS *m/z* $(M+Na)^+$ calcd 270.1101, obsd 270.1098.



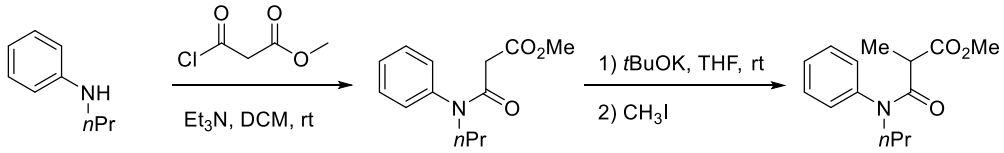
S1 **S28**

Methyl 2-(methyl(phenyl)carbamoyl)pent-4-ynoate (S28). The title compound was prepared from the known compound **S1**[1] and 3-bromoprop-1-yne by following the procedure described for the synthesis of **1**. Yield = 72%; Yellow oil; ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.48–7.42 (m, 2H), 7.41–7.35 (m, 1H), 7.34–7.29 (m, 2H), 3.68 (s, 3H), 3.64 (dd, *J* = 9.6, 5.5 Hz, 1H), 3.34 (s, 3H), 2.85 (ddd, *J* = 16.9, 9.6, 2.7 Hz, 1H), 2.68 (ddd, *J* = 16.9, 5.5, 2.7 Hz, 1H), 2.00 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 167.7, 143.3, 130.0, 128.5, 128.1, 81.0, 70.2, 52.7, 47.7, 38.0, 19.0; IR (neat, cm^{-1}): 3290, 2952, 2971, 2852, 1746, 1659, 1496, 1431, 1386, 1271, 1119, 1025, 892, 775, 701; ESI HRMS *m/z* $(M+Na)^+$ calcd 268.0944, obsd 268.0942.



S1 **S29**

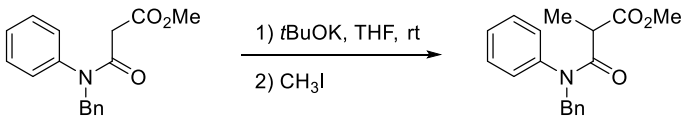
Methyl 2-benzyl-3-(methyl(phenyl)amino)-3-oxopropanoate (S29). The title compound was prepared from the known compound **S1**[1] and benzyl bromide by following the procedure described for the synthesis of **1**. Yield = 85%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.16 (m, 6H), 7.09–6.87 (m, 2H), 6.63 (br, 2H), 3.70 (s, 3H), 3.57 (dd, *J* = 10.2, 5.0 Hz, 1H), 3.22 (dd, *J* = 13.4, 10.2 Hz, 1H), 3.17 (s, 3H), 3.08 (dd, *J* = 13.4, 5.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 168.6, 143.3, 138.5, 129.7, 129.3, 128.5, 128.1, 127.6, 126.7, 52.5, 51.0, 37.5, 35.5; IR (neat, cm^{-1}): 3028, 2950, 2853, 1747, 1659, 1595, 1495, 1383, 1201, 1118, 1024, 826, 774, 756, 700; ESI HRMS *m/z* $(M+Na)^+$ calcd 320.1257, obsd 320.1256.



S30 **S31**

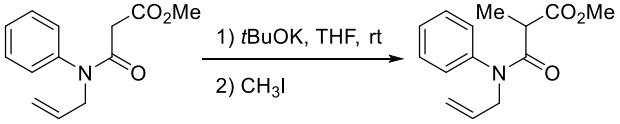
Methyl 3-oxo-3-(phenyl(propyl)amino)propanoate (S30). The title compound was prepared from *N*–propylaniline by following the procedure described for the synthesis of **S1**. Yield = 86%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.40 (m, 2H), 7.40–7.34 (m, 1H), 7.23–7.18 (m, 2H), 3.72–3.68 (m, 2H), 3.67 (s, 3H), 3.17 (s, 2H), 1.61–1.49 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 165.8, 142.2, 130.0, 128.5, 128.4, 52.3, 51.1, 41.9, 21.0, 11.3; IR (neat, cm^{-1}): 2961, 2875, 1745, 1662, 1595, 1495, 1403, 1327, 1135, 1024, 847, 702; ESI HRMS *m/z* $(M+Na)^+$ calcd 258.1101, obsd 258.1100.

Methyl 2-methyl-3-oxo-3-(phenyl(propyl)amino)propanoate (S31). The title compound was prepared from compound **S30** by following the procedure described for the synthesis of **1**. Yield = 83%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48–7.40 (m, 2H), 7.40–7.35 (m, 1H), 7.25–7.18 (m, 2H), 3.77–3.69 (m, 1H), 3.65 (s, 3H), 3.65–3.60 (m, 1H), 3.33 (q, *J* = 7.1 Hz, 1H), 1.63–1.48 (m, 2H), 1.30 (d, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 169.9, 142.3, 130.0, 128.6, 128.4, 52.4, 51.2, 44.0, 21.0, 14.4, 11.3; IR (neat, cm^{-1}): 2936, 2875, 1748, 1660, 1595, 1494, 1403, 1201, 1090, 702; ESI HRMS *m/z* $(M+Na)^+$ calcd 272.1257, obsd 272.1256.



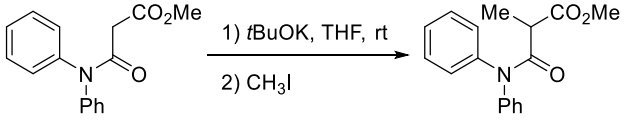
S32 **S33**

Methyl 3-(benzyl(phenyl)amino)-2-methyl-3-oxopropanoate (S33). The title compound was prepared from the known compound **S32**[4] by following the procedure described for the synthesis of **1**. Yield = 82%; White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.30 (m, 3H), 7.29–7.24 (m, 3H), 7.22–7.18 (m, 2H), 7.06–6.98 (m, 2H), 4.97 (d, *J* = 14.3 Hz, 1H), 4.85 (d, *J* = 14.3 Hz, 1H), 3.66 (s, 3H), 3.38 (q, *J* = 7.1 Hz, 1H), 1.34 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 170.2, 141.9, 137.3, 129.8, 128.9, 128.7, 128.5, 127.6, 53.4, 52.4, 44.0, 14.4; IR (neat, cm^{-1}): 3062, 3030, 2949, 2849, 1747, 1660, 1594, 1495, 1400, 1196, 1078, 849, 700; ESI HRMS *m/z* $(M+Na)^+$ calcd 320.1257, obsd 320.1253.



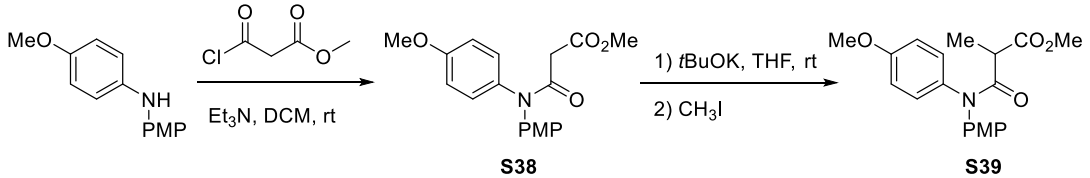
S34 **S35**

Methyl 3-(allyl(phenyl)amino)-2-methyl-3-oxopropanoate (S35). The title compound was prepared from the known compound **S34**[6] by following the procedure described for the synthesis of **1**. Yield = 80%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.41 (m, 2H), 7.40–7.35 (m, 1H), 7.27–7.23 (m, 2H), 5.92–5.82 (m, 1H), 5.32–5.26 (m, 1H), 5.25–5.20 (m, 1H), 4.61–4.50 (m, 2H), 3.45 (q, *J* = 7.0 Hz, 1H), 3.31 (s, 3H), 1.32 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 170.1, 143.7, 131.9, 130.0, 128.3, 127.6, 118.3, 65.7, 43.6, 37.7, 14.2; IR (neat, cm^{-1}): 2987, 2950, 1748, 1662, 1595, 1494, 1396, 1198, 701; ESI HRMS *m/z* $(M+Na)^+$ calcd 270.1101, obsd 270.1100.



S36 **S37**

Methyl 3-(diphenylamino)-2-methyl-3-oxopropanoate (S37). The title compound was prepared from the known compound **S36**[7] by following the procedure described for the synthesis of **1**. Yield = 86%; Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.13 (m, 10H), 3.69 (s, 3H), 3.62 (q, *J* = 7.1 Hz, 1H), 1.41 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 170.4, 142.6, 130.1, 129.1, 128.9, 128.4, 126.5, 126.5, 52.5, 44.7, 14.3; IR (neat, cm^{-1}): 2950, 2852, 1747, 1673, 1592, 1491, 1356, 1205, 1156, 1028, 882, 840, 757, 703; ESI HRMS *m/z* $(M+Na)^+$ calcd 306.1101, obsd 306.1099.

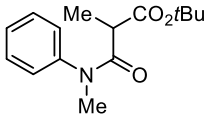


S38 **S39**

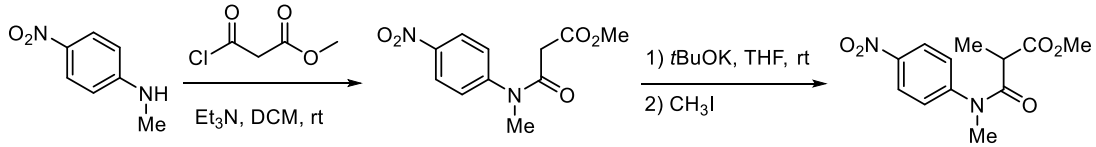
Methyl 3-(bis(4-methoxyphenyl)amino)-3-oxopropanoate (S38). The title compound was prepared from bis(4–methoxyphenyl)amine by following the procedure described for the synthesis of **S1**. Yield = 90%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24–7.19 (m, 4H),

6.90 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 9.2 Hz, 2H), 3.80 (s, 3H), 3.76 (s, 3H), 3.69 (s, 3H), 3.40 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 166.4, 159.3, 157.9, 135.6, 135.5, 129.6, 127.4, 115.2, 114.3, 55.6, 55.5, 52.4, 42.4; IR (neat, cm^{-1}): 2953, 2838, 1743, 1669, 1508, 1366, 1246, 1031, 832; ESI HRMS *m/z* $(M+Na)^+$ calcd 352.1155, obsd 352.1152.

Methyl 3-(bis(4-methoxyphenyl)amino)-2-methyl-3-oxopropanoate (S39). The title compound was prepared from **S38** by following the procedure described for the synthesis of **1**. Yield = 84%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.15 (m, 4H), 6.91 (d, J = 8.3 Hz, 2H), 6.86–6.79 (m, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 3.69 (s, 3H), 3.62 (q, J = 7.1 Hz, 1H), 1.39 (d, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 170.6, 159.3, 157.8, 135.9, 135.7, 129.8, 127.5, 115.2, 114.3, 55.7, 55.6, 52.5, 44.4, 14.3; IR (neat, cm^{-1}): 2922, 2849, 1744, 1666, 1506, 1455, 1244, 1154, 1029, 829; ESI HRMS *m/z* $(M+Na)^+$ calcd 366.1312, obsd 366.1309.



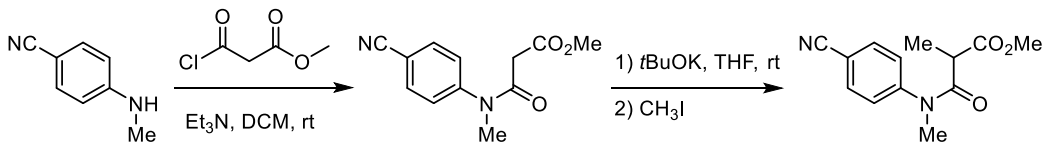
***tert*-Butyl 2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (S40).**[8]



S41 **S42**

Methyl 3-(methyl(4-nitrophenyl)amino)-3-oxopropanoate (S41). The title compound was prepared from the known compound *N*-methyl-4-nitroaniline by following procedure described for the synthesis of **S1**. Yield = 80%; Pale yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33–8.29 (m, 2H), 7.49–7.44 (m, 2H), 3.71 (s, 3H), 3.37 (s, 3H), 3.32 (s, 2H); ^{13}C NMR (126 MHz, CDCl3) δ 167.8, 165.5, 149.2, 128.0, 125.4, 52.8, 41.5, 37.8. IR (neat, cm^{-1}): 3368, 2920, 1736, 1597, 1305, 1189, 1135, 1075, 1017, 633, 581; ESI HRMS *m/z* $(M+Na)^+$ calcd 275.0638, obsd 275.0639.

Methyl 2-methyl-3-(methyl(4-nitrophenyl)amino)-3-oxopropanoate (S42). The title compound was prepared from compound **S42** by following the procedure described for the synthesis of **1**. Yield = 88%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34–8.27 (m, 2H), 7.49–7.49 (m, 2H), 3.70 (s, 3H), 3.46 (br, 1H), 3.37 (s, 3H), 1.36 (d, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 169.7, 149.3, 147.0, 128.3, 125.4, 52.7, 43.9, 37.9, 14.4; IR (neat, cm^{-1}): 3389, 2938, 1745, 1660, 1592, 1523, 1344, 1196, 1132, 1076, 859, 699; ESI HRMS *m/z* $(M+Na)^+$ calcd 289.0795, obsd 289.0795.

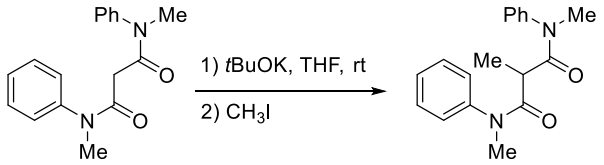


S43 **S44**

Methyl 3-((4-cyanophenyl)(methyl)amino)-3-oxopropanoate (S43). The title compound was prepared from the known compound 4-(methylamino)benzonitrile by following the procedure described for the synthesis of **S1**. Yield = 70%; Pale yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.5Hz, 2H), 3.70 (s, 3H), 3.34 (s, 3H),

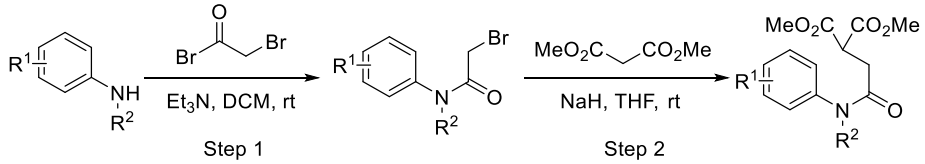
3.27 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 165.4, 147.3, 133.8, 128.1, 117.8, 112.2, 52.5, 41.3, 37.5; IR (neat, cm^{-1}): 2593, 2228, 1750, 1655, 1602, 1507, 1388, 1253, 1164, 1013, 861, 580; ESI HRMS *m/z* $(M+Na)^+$ calcd 255.0740, obsd 255.0739.

Methyl 3-((4-cyanophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S44). The title compound was prepared from compound **S43** by following the procedure described for the synthesis of **1**. Yield = 78%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.43–7.40 (m, 2H), 3.68 (s, 3H), 3.41 (s, 1H), 3.34 (s, 3H), 1.34 (d, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 169.7, 147.6, 134.0, 128.4, 118.0, 112.1, 52.7, 43.8, 37.8, 14.3; IR (neat, cm^{-1}): 2948, 2228, 1741, 1680, 1601, 1506, 1382, 1201, 1126, 1021, 853, 580; ESI HRMS *m/z* $(M+Na)^+$ calcd 269.0897, obsd 269.0895



S45

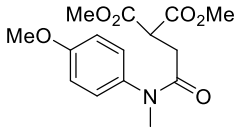
***N*^{1},*N*^{3},2-trimethyl-*N*^{1},*N*^{3}-diphenylmalonamide (S45).** The title compound was prepared from known compound *N*^{1},*N*^{3}-dimethyl-*N*^{1},*N*^{3}-diphenylmalonamide[9] by following the general procedure C. Yield = 78%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.31 (m, 6H), 6.72 (s, 4H), 3.30 (q, J = 7.1 Hz, 1H), 3.16 (s, 6H), 1.14 (d, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 143.6, 129.8, 128.2, 128.1, 43.2, 38.2, 14.9; IR (neat, cm^{-1}): 2992, 2982, 2937, 1666, 1646, 1593, 1490, 1380, 1302, 1244, 1130, 1030, 784, 707, 562; ESI HRMS *m/z* $(M+Na)^+$ calcd 319.1417, obsd 319.1416.



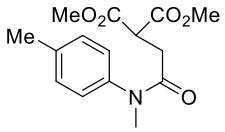
General procedure D:

Step 1: A solution of aniline (4.0 mmol, 1.0 equiv) and Et_3N (6.0 mmol, 1.5 equiv) in anhydrous CH_2Cl_2 (10 mL) was cooled to 0 °C. Bromoacetyl bromide (8.0 mmol, 2.0 equiv) was added dropwise. The mixture was then allowed to warm to rt and stirred for 1 h. The mixture was washed with HCl (20 mL, 2 N) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layer was washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was used in the next step without further purification.

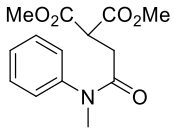
Step 2: To a suspension of NaH (60% dispersion in mineral oil, 8.0 mmol, 2.0 equiv) in THF (25 mL) was added dimethyl malonate (8.0 mmol, 2.0 equiv) dropwise at rt. The mixture was stirred for 15 min and the product of step 1 in THF (5 mL) was added dropwise. The mixture was stirred at rt for 3 h. Water (20 mL) was added to quench the reaction. The mixture was extracted with AcOEt (3 x 20 mL). The combined organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with hexane/AcOEt to afford the desired product.



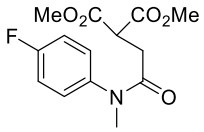
Dimethyl 2-(2-((4-methoxyphenyl)(methyl)amino)-2-oxoethyl)malonate (S46). The title compound was prepared from 4-methoxy-*N*-methylaniline by following general procedure D. Yield = 71%; Brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18–7.13 (m, 2H), 6.96–6.92 (m, 2H), 3.97 (t, *J* = 7.3 Hz, 1H), 3.83 (s, 3H), 3.72 (s, 6H), 3.22 (s, 3H), 2.66 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 169.7, 159.3, 136.2, 128.6, 115.2, 55.6, 52.8, 48.1, 37.7, 33.7; IR (neat, cm^{-1}): 2954, 2843, 1738, 1659, 1512, 1435, 1248, 1029; ESI HRMS *m/z* $(M+Na)^+$ calcd 332.1105, obsd 332.1104.



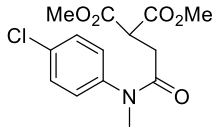
Dimethyl 2-(2-(methyl(*p*-tolyl)amino)-2-oxoethyl)malonate (S47). The title compound was prepared from *N*,4-dimethylaniline by following general procedure D. Yield = 85%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 3.97 (t, *J* = 7.3 Hz, 1H), 3.72 (s, 6H), 3.23 (s, 3H), 2.67 (d, *J* = 7.3 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 169.6, 140.7, 138.1, 130.6, 127.1, 52.7, 47.9, 37.5, 33.6, 21.1; IR (neat, cm^{-1}): 2954, 1739, 1661, 1515, 1235, 1021, 829; ESI HRMS *m/z* $(M+Na)^+$ calcd 316.1155, obsd 316.1149.



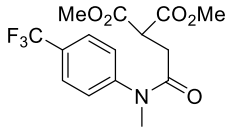
Dimethyl 2-(2-(methyl(phenyl)amino)-2-oxoethyl)malonate (S48). The title compound was prepared from *N*-methylaniline by following general procedure D. Yield = 74%; Yellow oil; ^{1}HMR (500 MHz, $CDCl_3$) δ 7.48–7.42 (m, 2H), 7.40–7.34 (m, 1H), 7.27–7.23 (m, 2H), 3.98 (t, *J* = 7.4 Hz, 1H), 3.72 (s, 6H), 3.26 (s, 3H), 2.67 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7 (2C), 143.4, 130.2, 128.3, 127.5, 52.9, 48.0, 37.6, 33.8; IR (neat, cm^{-1}): 2954, 1738, 1660, 1496, 1235, 702; ESI HRMS *m/z* $(M+Na)^+$ calcd 302.0999, obsd 302.0998.



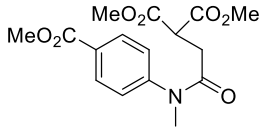
Dimethyl 2-(2-((4-fluorophenyl)(methyl)amino)-2-oxoethyl)malonate (S49). The title compound was prepared from 4-fluoro-*N*-methylaniline by following general procedure D. Yield = 82%; Yellow oil; 1H NMR (500 MHz, $CDCl_3$) δ 7.26–7.21 (m, 2H), 7.16–7.10 (m, 2H), 3.98 (t, *J* = 7.3 Hz, 1H), 3.73 (s, 6H), 3.23 (s, 3H), 2.64 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 169.7, 162.1 (d, $J_{C–F}$ = 248.7 Hz), 139.5 (d, $J_{C–F}$ = 3.2 Hz), 129.4 (d, $J_{C–F}$ = 8.7 Hz), 117.1 (d, $J_{C–F}$ = 22.7 Hz), 52.9, 48.0, 37.7, 33.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ –112.9; IR (neat, cm^{-1}): 2955, 1738, 1660, 1511, 1223, 847; ESI HRMS *m/z* $(M+Na)^+$ calcd 320.0905, obsd 320.0899.



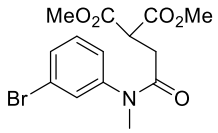
Dimethyl 2-(2-((4-chlorophenyl)(methyl)amino)-2-oxoethyl)malonate (S50). The title compound was prepared from 4-chloro-*N*-methylaniline by following general procedure D. Yield = 99%; Yellow solid; 1H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 3.98 (t, *J* = 7.4 Hz, 1H), 3.73 (s, 6H), 3.23 (s, 3H), 2.65 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 169.6, 141.9, 134.2, 130.4, 129.0, 53.0, 48.0, 37.6, 33.7; IR (neat, cm^{-1}): 2953, 1738, 1661, 1514, 1077; ESI HRMS *m/z* $(M+Na)^+$ calcd 336.0609, obsd 336.0607.



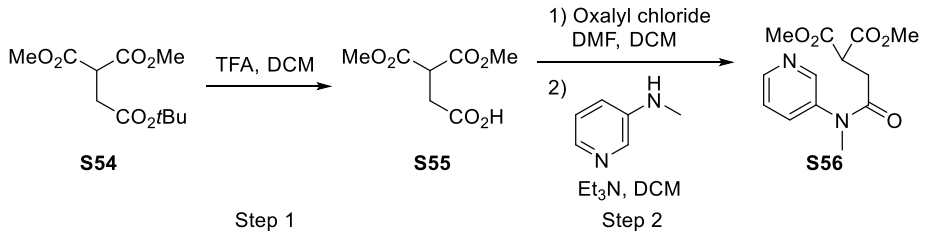
Dimethyl 2-(2-(methyl(4-(trifluoromethyl)phenyl)amino)-2-oxoethyl)malonate (S51). The title compound was prepared from *N*-methyl-4-(trifluoromethyl)aniline by following general procedure D. Yield = 91%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 4.01 (t, *J* = 7.3 Hz, 1H), 3.73 (s, 6H), 3.29 (s, 3H), 2.68 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4, 146.5, 128.0, 127.2, 123.9 (q, J_{C-F} = 276.1 Hz), 52.8, 47.9, 37.5, 33.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ –62.6; IR (neat, cm^{-1}): 2956, 1739, 1667, 1327, 1068; ESI HRMS *m/z* $(M+Na)^+$ calcd 370.0873, obsd 370.0863.



Dimethyl 2-(2-((4-(methoxycarbonyl)phenyl)(methyl)amino)-2-oxoethyl)malonate (S52). The title compound was prepared from methyl 4-(methylamino)benzoate by following general procedure D. Yield = 87%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.2 Hz, 2H), 7.37–7.32 (m, 2H), 3.99 (t, *J* = 7.3 Hz, 1H), 3.94 (s, 3H), 3.73 (s, 6H), 3.29 (s, 3H), 2.69 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5 (2C), 166.2, 147.5, 131.5, 129.9, 127.4, 52.9, 52.5, 48.0, 37.5, 33.8; IR (neat, cm^{-1}): 2955, 1731, 1666, 1604, 1435, 1281, 1117; ESI HRMS *m/z* $(M+Na)^+$ calcd 360.1054, obsd 360.1054.

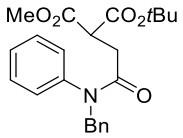


Dimethyl 2-(2-((3-bromophenyl)(methyl)amino)-2-oxoethyl)malonate (S53). The title compound was prepared from 3-bromo-*N*-methylaniline by following general procedure D. Yield = 82%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 2.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 3.99 (t, *J* = 7.3 Hz, 1H), 3.73 (s, 6H), 3.24 (s, 3H), 2.67 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5, 144.7, 131.6, 131.4, 130.8, 126.4, 123.3, 52.9, 48.0, 37.6, 33.7; IR (neat, cm^{-1}): 2954, 1737, 1661, 1434, 1157; ESI HRMS *m/z* $(M+Na)^+$ calcd 380.0104, obsd 380.0106.

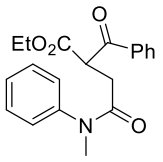


Step 1: To a solution of **S54** (1.72 g, 7.0 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added TFA (5 mL) dropwise. The mixture was stirred at rt for 1 h and concentrated under reduced pressure. The residue was washed with HCl (20 mL, 0.1 M) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layer was washed with brine (15 mL) and dried over anhydrous $MgSO_4$, filtered and evaporated under vacuum to afford the crude product **S55**, which was used in the next step without further purification.

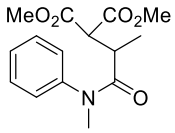
Step 2: **S55** was dissolved in CH_2Cl_2 (25 mL) and cooled to 0 °C. Oxalyl chloride (0.72 mL, 8.5 mmol, 1.2 equiv) and DMF (10 drops) were added dropwise sequentially. The resulting reaction mixture was stirred at rt for 3 h. A solution of *N*-methyl-3-pyridinamine (0.54 g, 5.0 mmol, 1.0 equiv) and Et_3N (1.39 mL, 10.0 mmol, 2.0 equiv) in CH_2Cl_2 (10 mL) was added dropwise at 0 °C. The result mixture was allowed to warm to rt and stirred until complete consumption of the pyridinamine. The solvent was removed under reduced pressure. Saturated $NaHCO_3$ solution (30 mL) was added and the mixture was extracted with AcOEt (3 x 30 mL). The combined organic solution was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/CH_2Cl_2 = 1/1) to afford **S56** as a brown oil (0.61 g, 43% yield over 2 steps); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.58 (s, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.44 (t, *J* = 6.4 Hz, 1H), 4.00 (t, *J* = 7.4 Hz, 1H), 3.73 (s, 6H), 3.29 (s, 3H), 2.64 (d, *J* = 7.4 Hz, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5, 169.2, 149.3, 148.9, 139.9, 135.0, 124.5, 52.8, 47.8, 37.6, 33.6; IR (neat, cm^{-1}): 2955, 1737, 1665, 1435, 1023; ESI HRMS *m/z* $(M+Na)^+$ calcd 303.0951, obsd 303.0948.



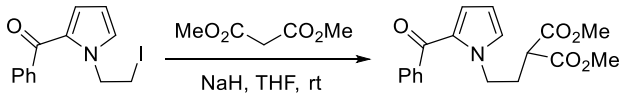
1-(*tert*-Butyl) 3-methyl 2-(2-(benzyl(phenyl)amino)-2-oxoethyl)malonate (S57). The title compound was prepared from *tert*-butyl methyl malonate by following general procedure D. Yield = 67%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.28 (m, 3H), 7.27–7.20 (m, 3H), 7.17 (d, *J* = 7.4 Hz, 2H), 7.04 (d, *J* = 6.8 Hz, 2H), 4.94 (d, *J* = 14.4 Hz, 1H), 4.79 (d, *J* = 14.4 Hz, 1H), 3.95 (t, *J* = 7.4 Hz, 1H), 3.71 (s, 3H), 2.62 (d, *J* = 7.4 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 170.0, 168.2, 141.9, 137.4, 129.9, 128.9, 128.6, 128.5, 128.4, 127.5, 82.2, 53.4, 52.6, 49.3, 33.9, 28.0; IR (neat, cm^{-1}): 2979, 1731, 1661, 1495, 1278, 1147, 701; ESI HRMS *m/z* $(M+Na)^+$ calcd 420.1781, obsd 420.1789.



Ethyl 2-benzoyl-4-(methyl(phenyl)amino)-4-oxobutanoate (S58). The title compound was prepared from ethyl benzoylacetate by following general procedure D. Yield = 91%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.4 Hz, 2H), 7.59–7.55 (m, 1H), 7.49–7.42 (m, 4H), 7.38–7.34 (m, 1H), 7.31–7.25 (m, 2H), 5.04 (t, *J* = 7.0 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.24 (s, 3H), 2.82 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.75 (dd, *J* = 16.8, 6.4 Hz, 1H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 170.2, 169.6, 143.5, 136.2, 133.6, 130.1, 129.1, 128.8, 128.3, 127.6, 61.7, 50.1, 37.7, 34.0, 14.0; IR (neat, cm^{-1}): 2981, 1736, 1655, 1496, 1124, 701; ESI HRMS *m/z* $(M+Na)^+$ calcd 362.1363, obsd 362.1364.



Dimethyl 2-(1-(methyl(phenyl)amino)-1-oxopropan-2-yl)malonate (S59). The title compound was prepared from 2-bromopropionyl bromide (1 equiv) and dimethyl malonate (3 equiv) by following general procedure D. Yield = 70%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (t, *J* = 7.6 Hz, 2H), 7.42–7.35 (m, 3H), 3.93 (d, *J* = 10.9 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.26 (s, 3H), 3.14 (dq, *J* = 10.9, 7.0 Hz, 1H), 0.97 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 169.2 (2C), 143.6, 130.0, 128.1, 127.8, 77.5, 77.2, 76.9, 55.1, 52.8, 52.7, 37.9, 36.8, 15.9; IR (neat, cm^{-1}): 2954, 1737, 1658, 1435, 1199, 702; ESI HRMS *m/z* $(M+Na)^+$ calcd 316.1155, obsd 316.1152.



S60 **S61**

Dimethyl 2-(2-(2-benzoyl-*1H*-pyrrol-1-yl)ethyl)malonate (S61). The title compound was prepared from **S60** by following a previously reported method.[10] Yield = 72%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.9 Hz, 2H), 7.55–7.50 (m, 1H), 7.47–7.42 (m, 2H), 6.99–6.96 (m, 1H), 6.76–6.72 (m, 1H), 6.20–6.16 (m, 1H), 4.50 (t, *J* = 7.0 Hz, 2H), 3.73 (s, 6H), 3.40 (t, *J* = 7.4 Hz, 1H), 2.45 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.2, 169.5, 140.1, 131.5, 131.0, 130.0, 129.3, 128.2, 123.8, 108.8, 52.9, 49.0, 47.0, 30.8; IR (neat, cm^{-1}): 2921, 1738, 1622, 1430, 1132, 1076; ESI HRMS *m/z* $(M+Na)^+$ calcd 352.1155, obsd 352.1151.

5. References

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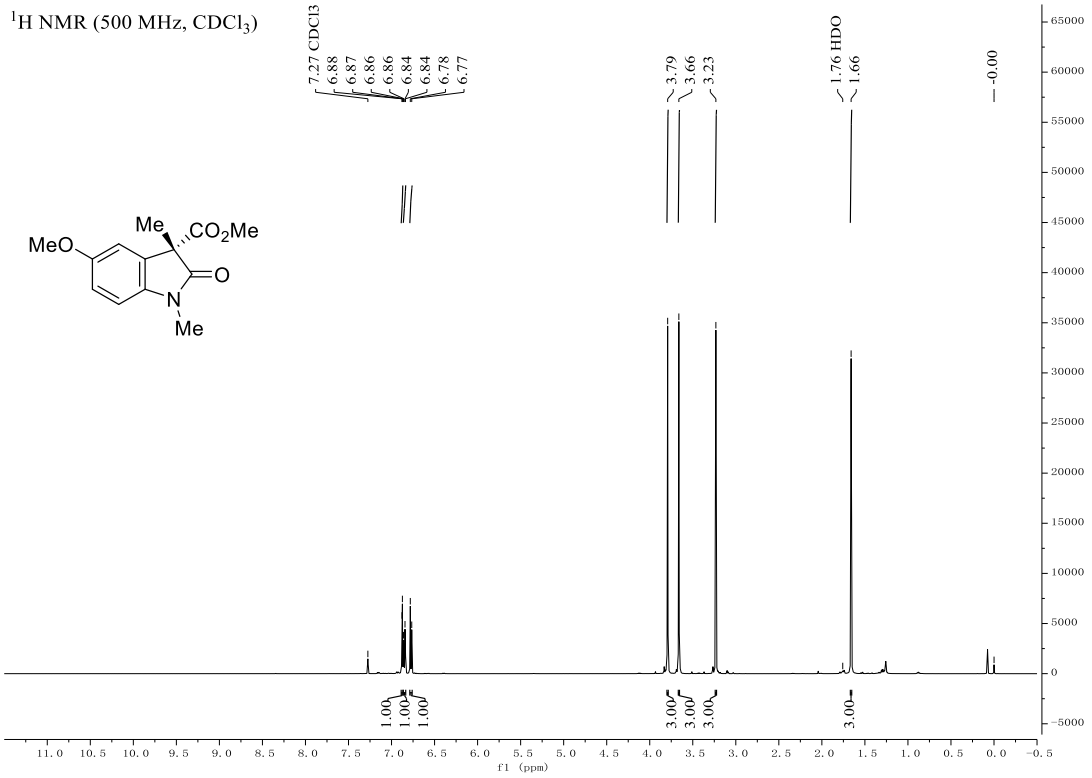
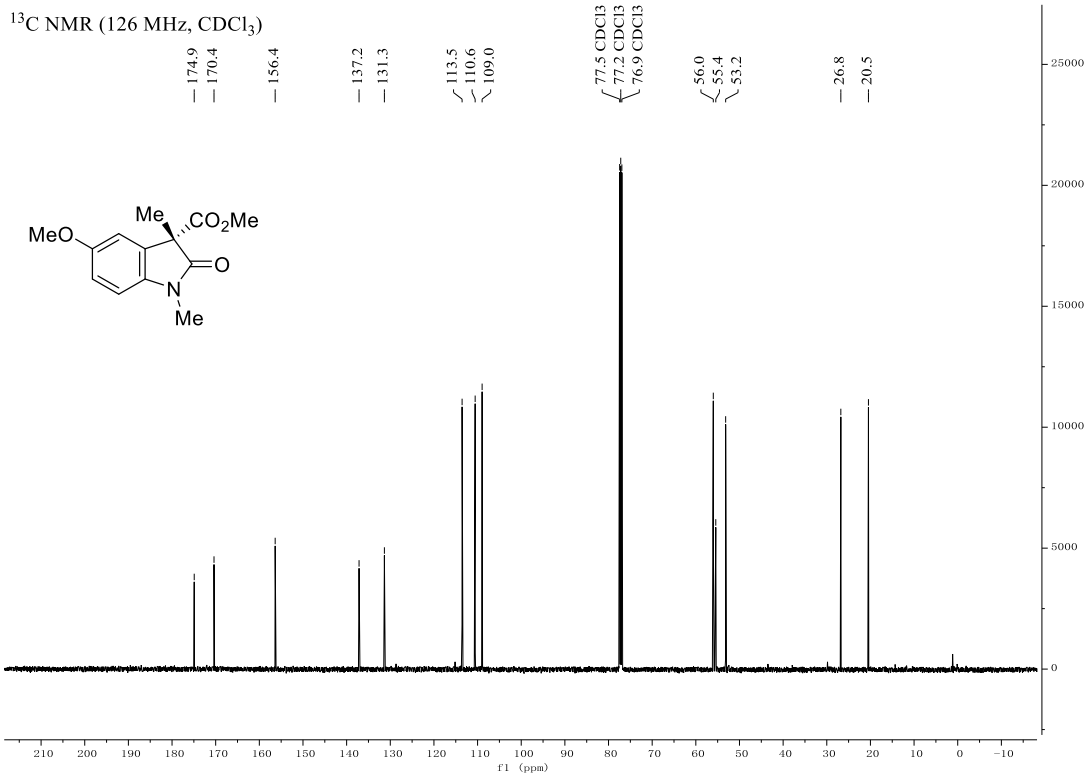
Compound 3

^{1}H NMR (500 MHz, $CDCl_3$)

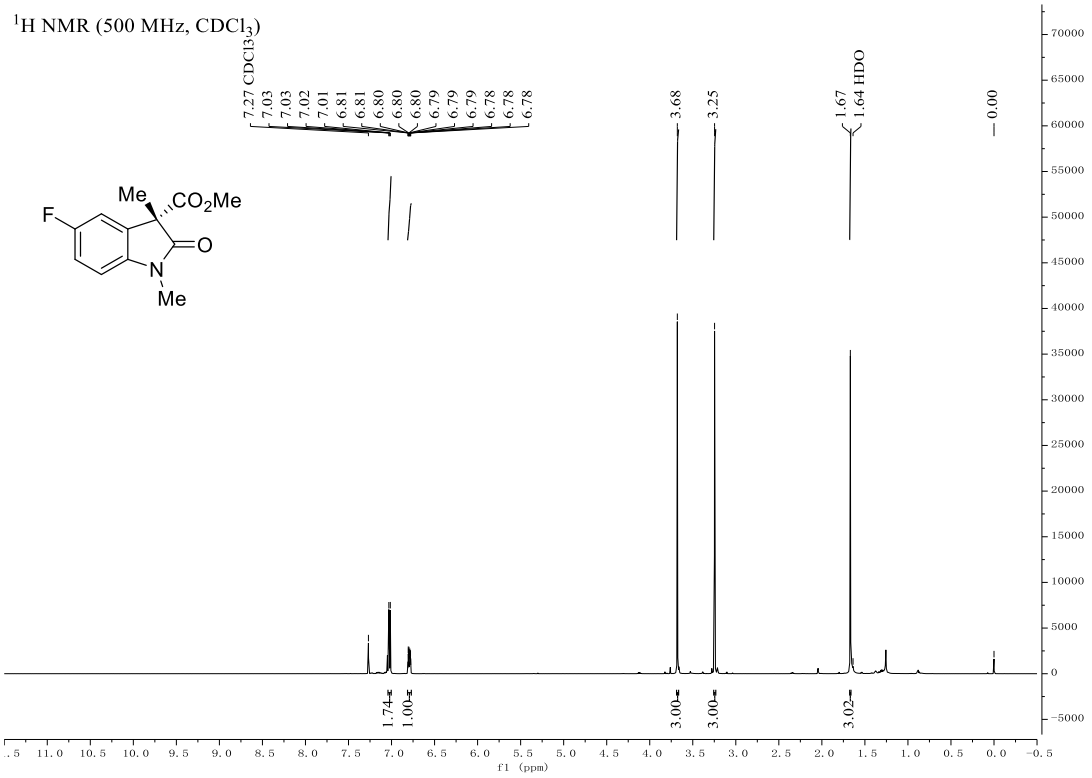


^{13}C NMR (126 MHz, $CDCl_3$)

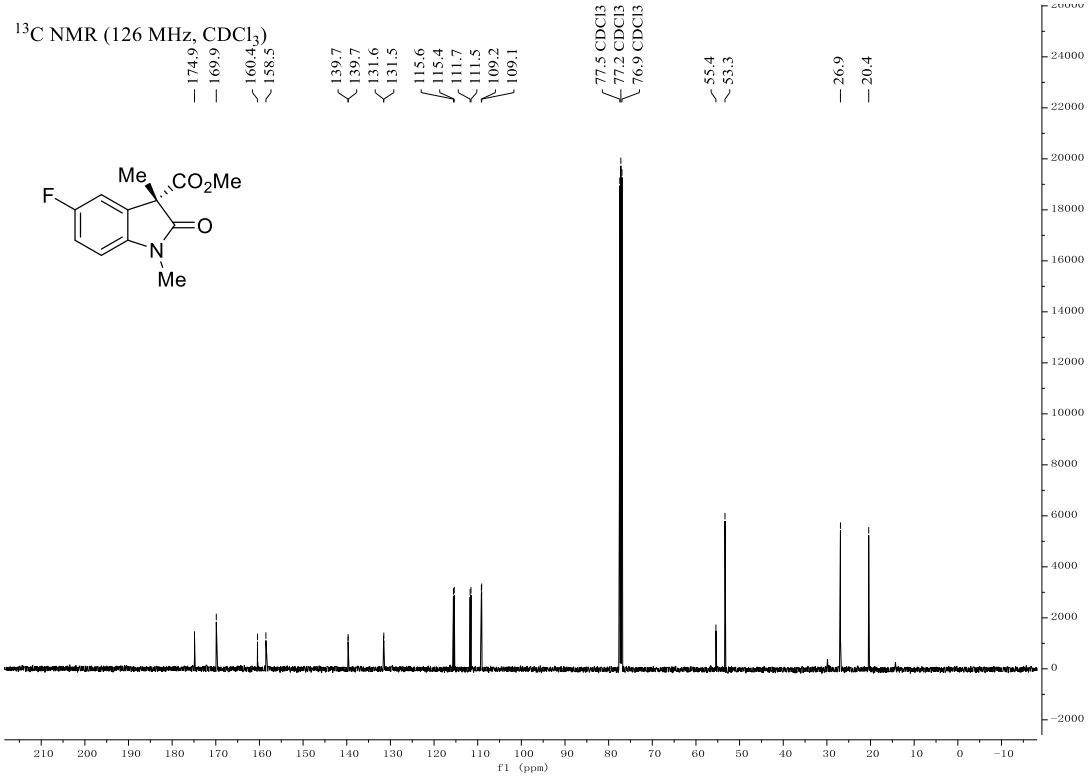


Compound 4

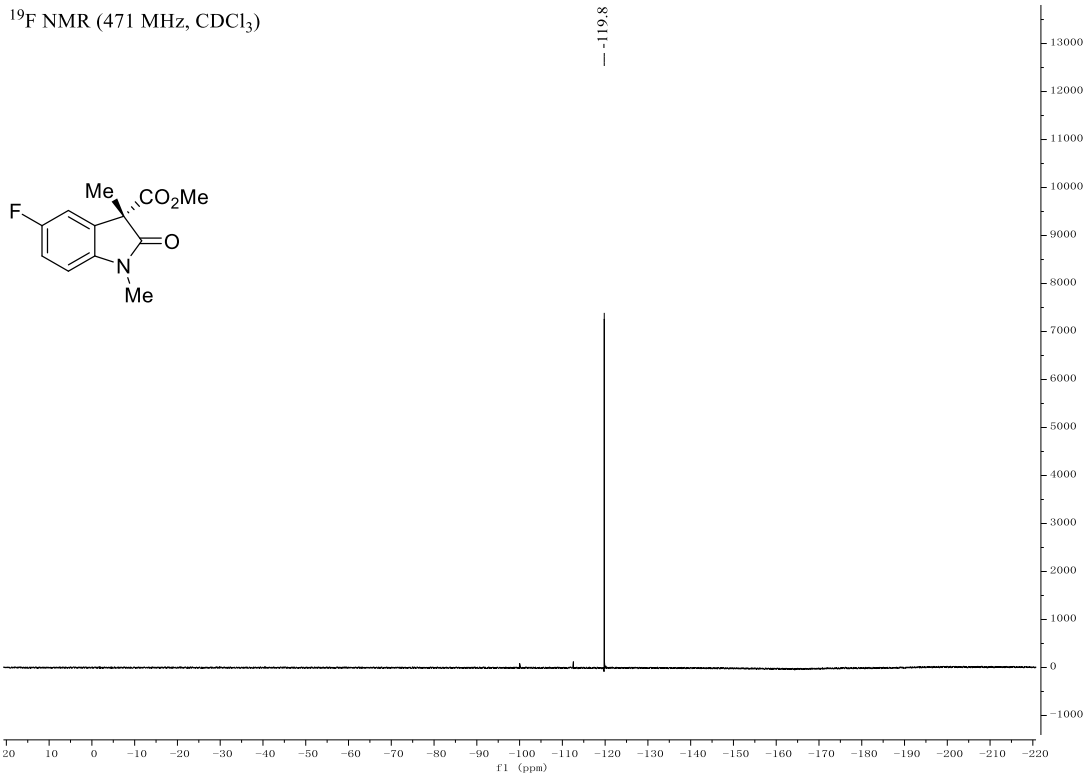
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

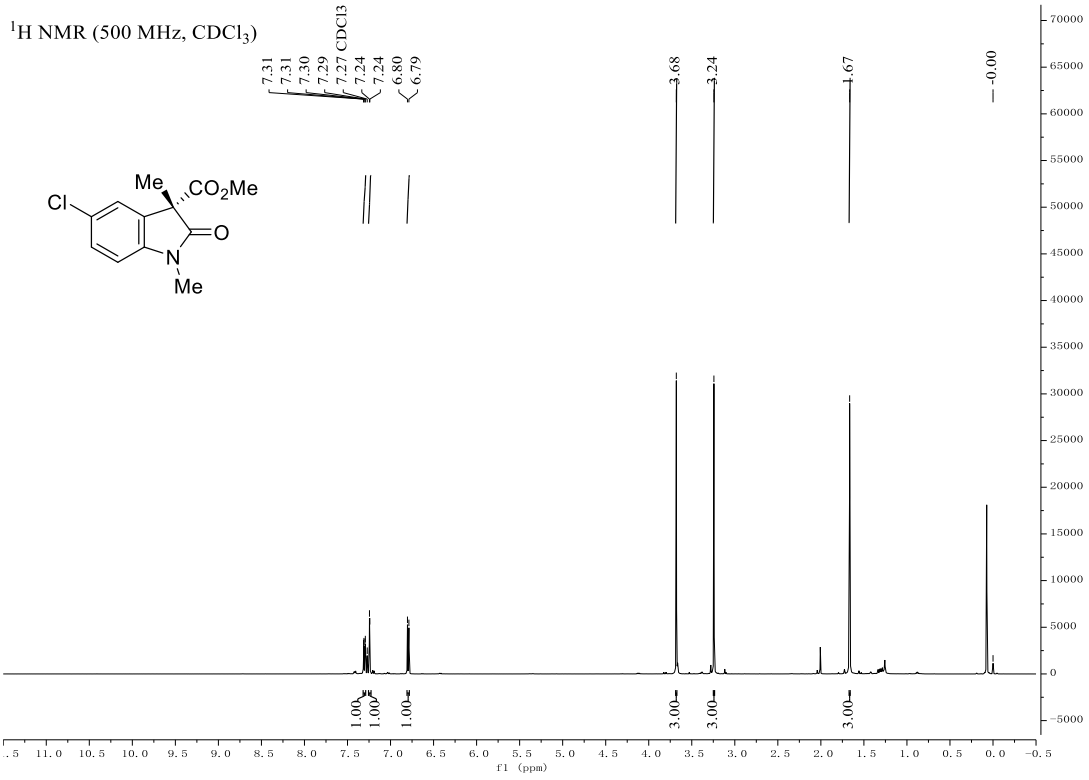


^{19}F NMR (471 MHz, $CDCl_3$)

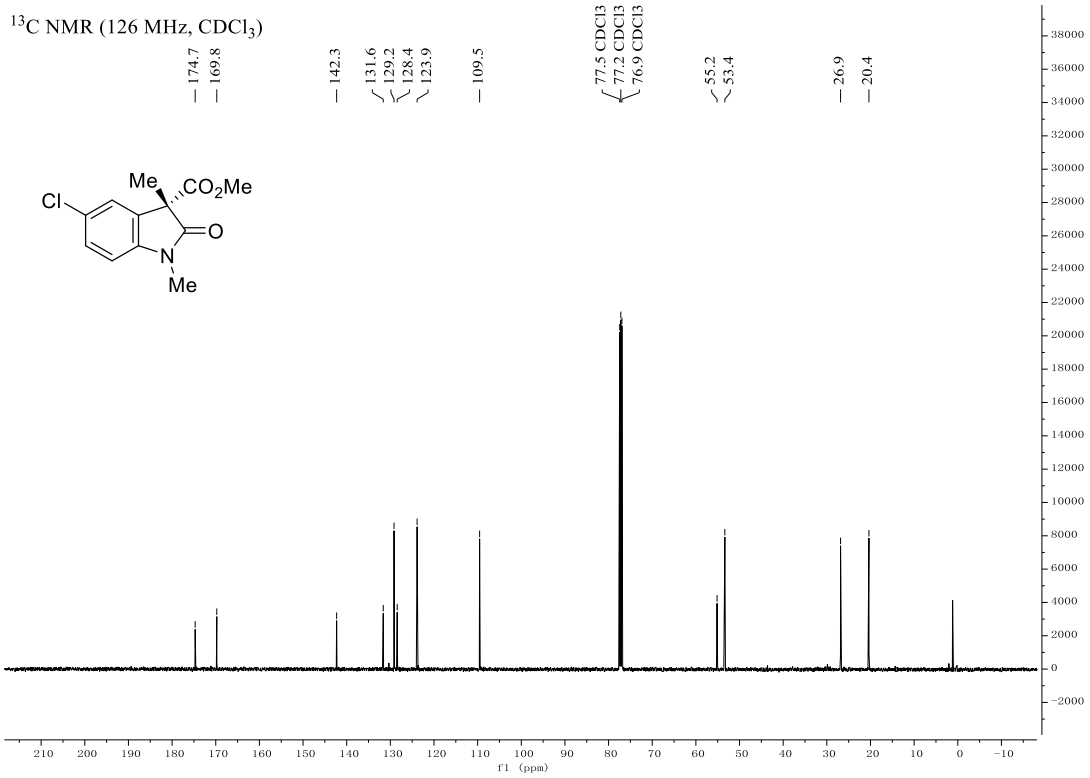


Compound 5

^{1}H NMR (500 MHz, $CDCl_3$)

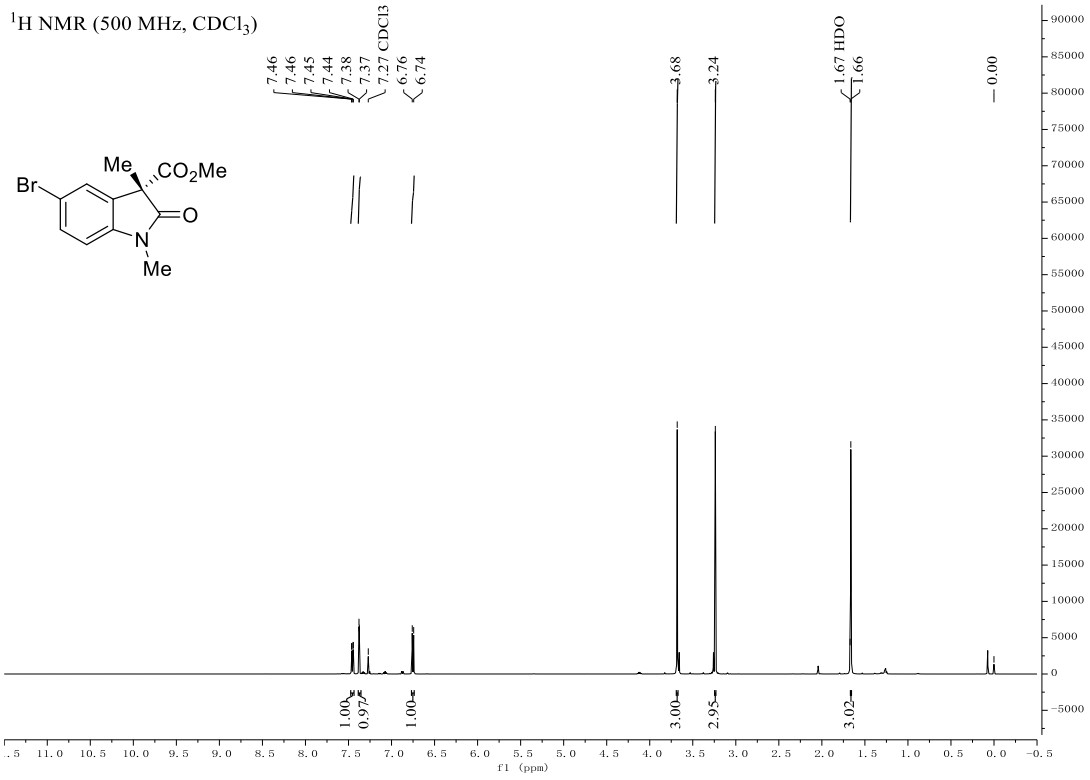


^{13}C NMR (126 MHz, $CDCl_3$)

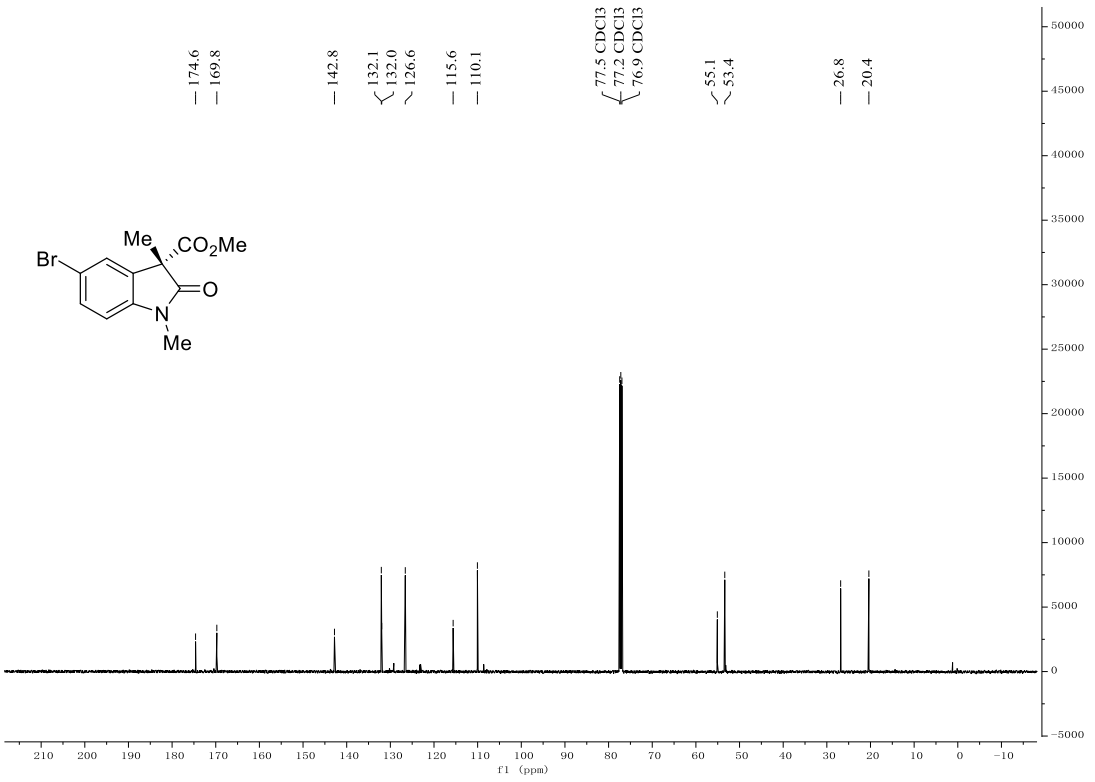


Compound 6

^{1}H NMR (500 MHz, $CDCl_3$)

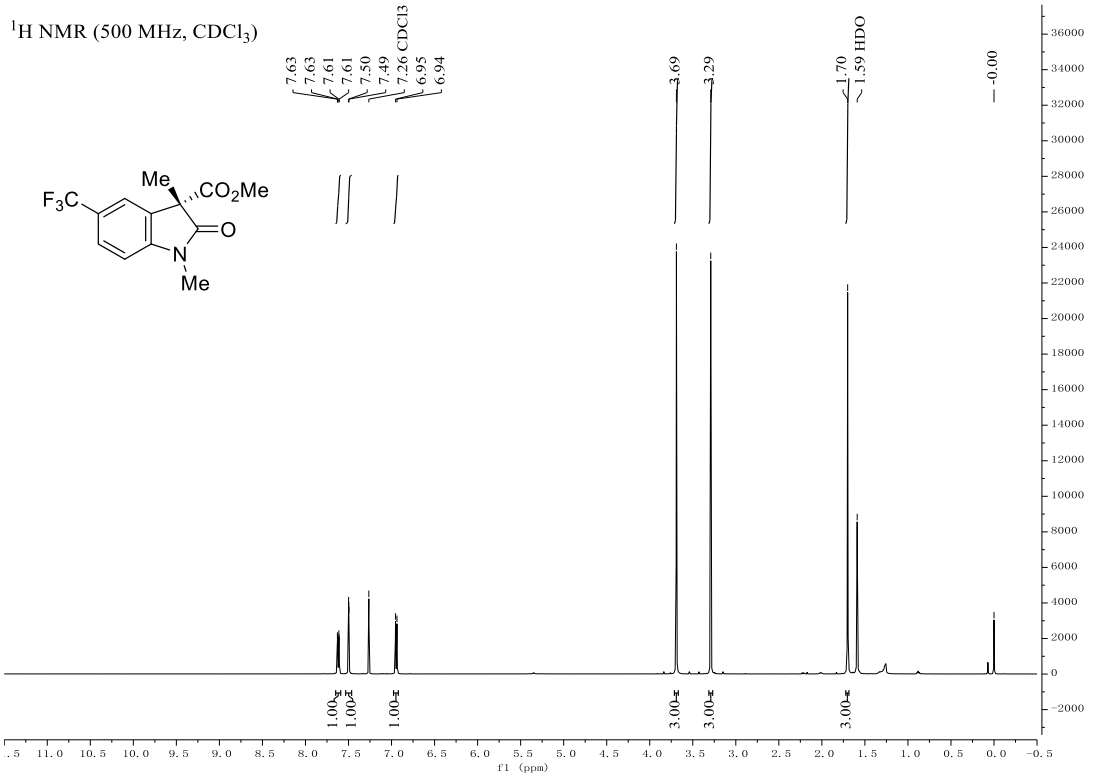


^{13}C NMR (126 MHz, $CDCl_3$)

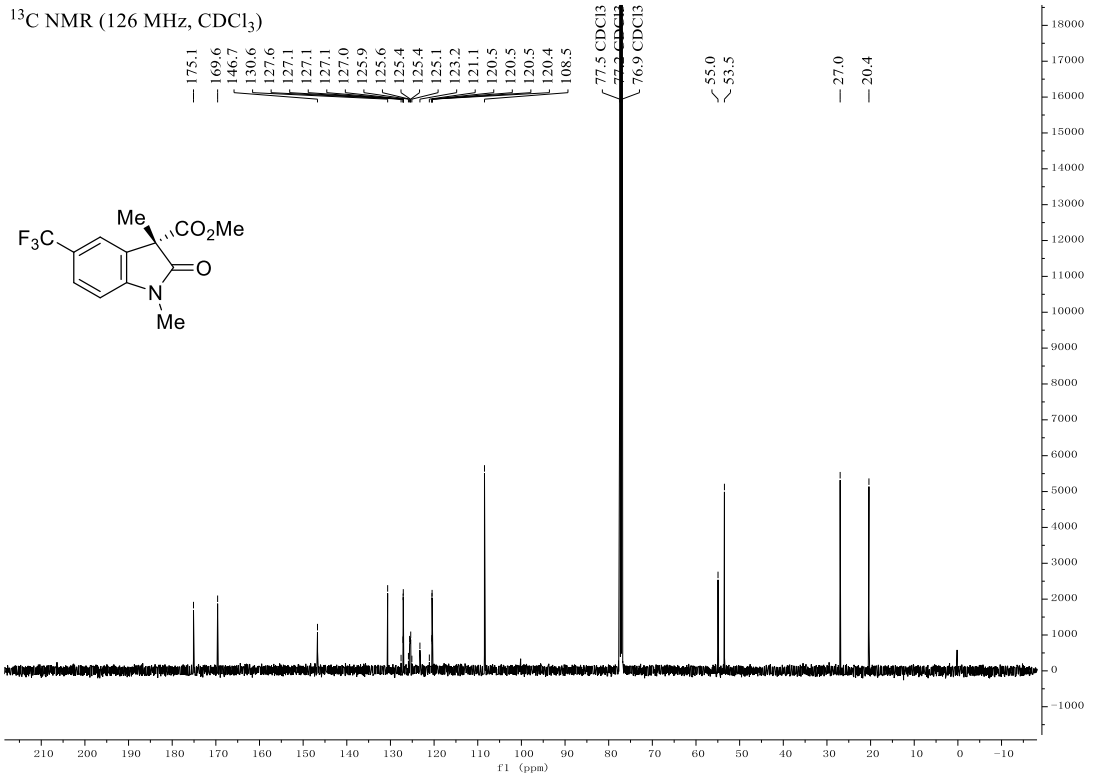


Compound 7

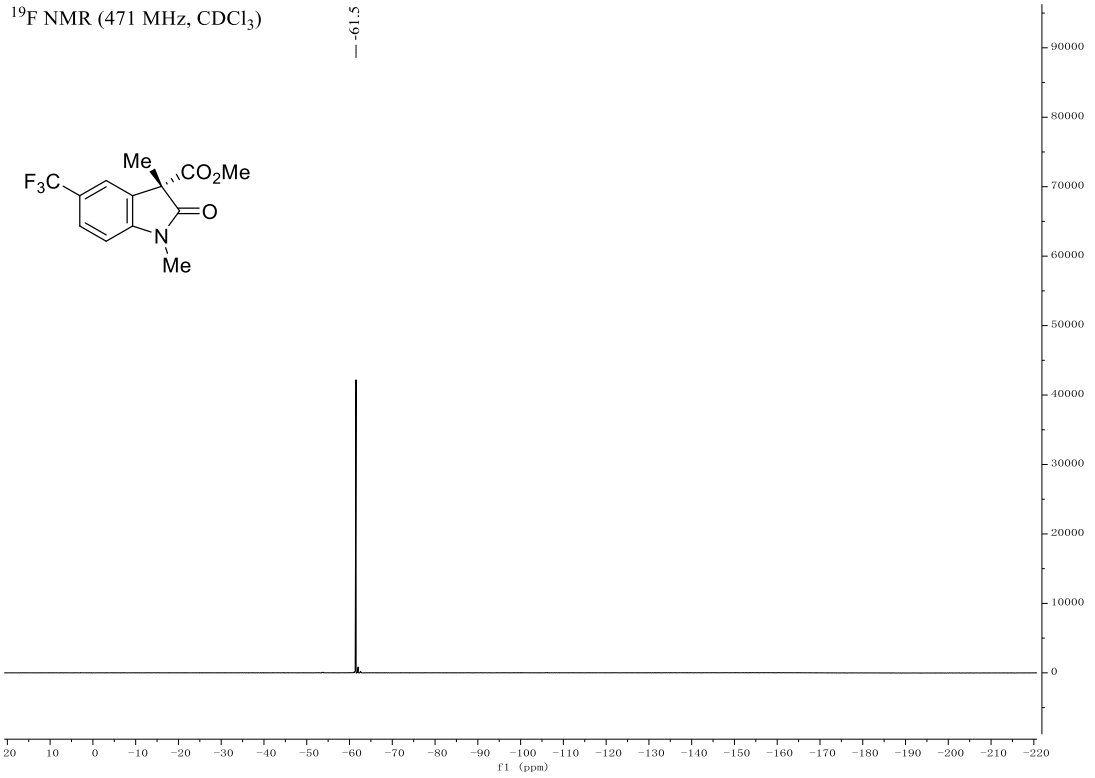
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

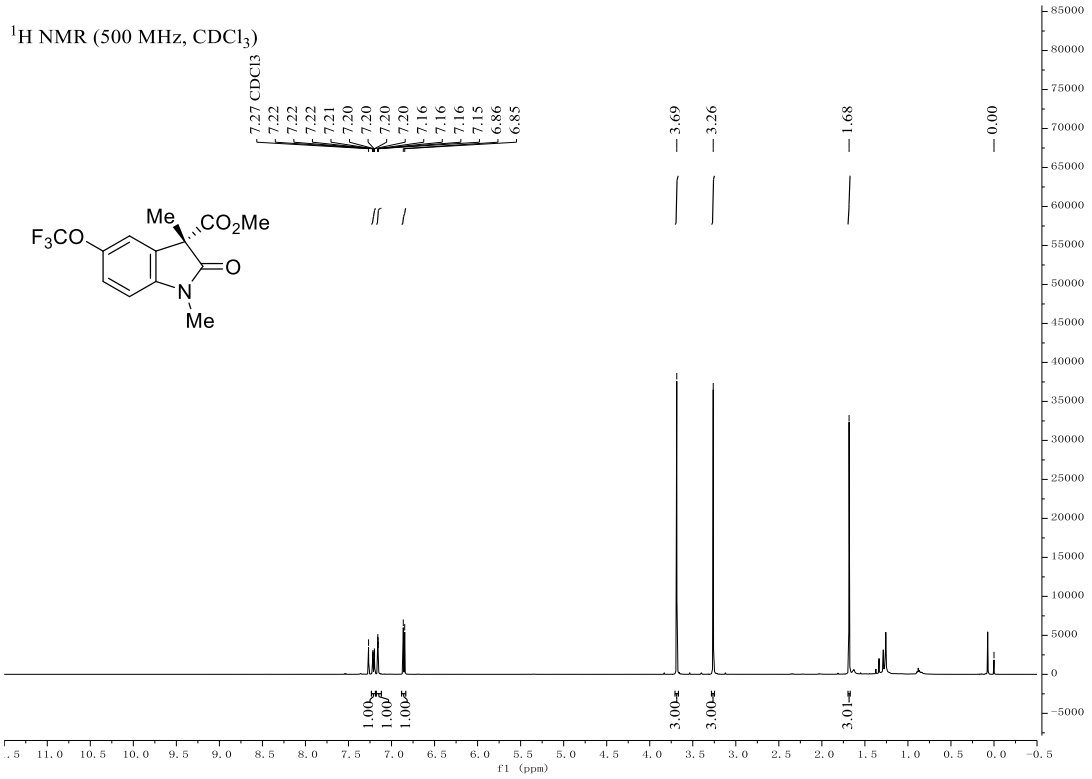


^{19}F NMR (471 MHz, $CDCl_3$)

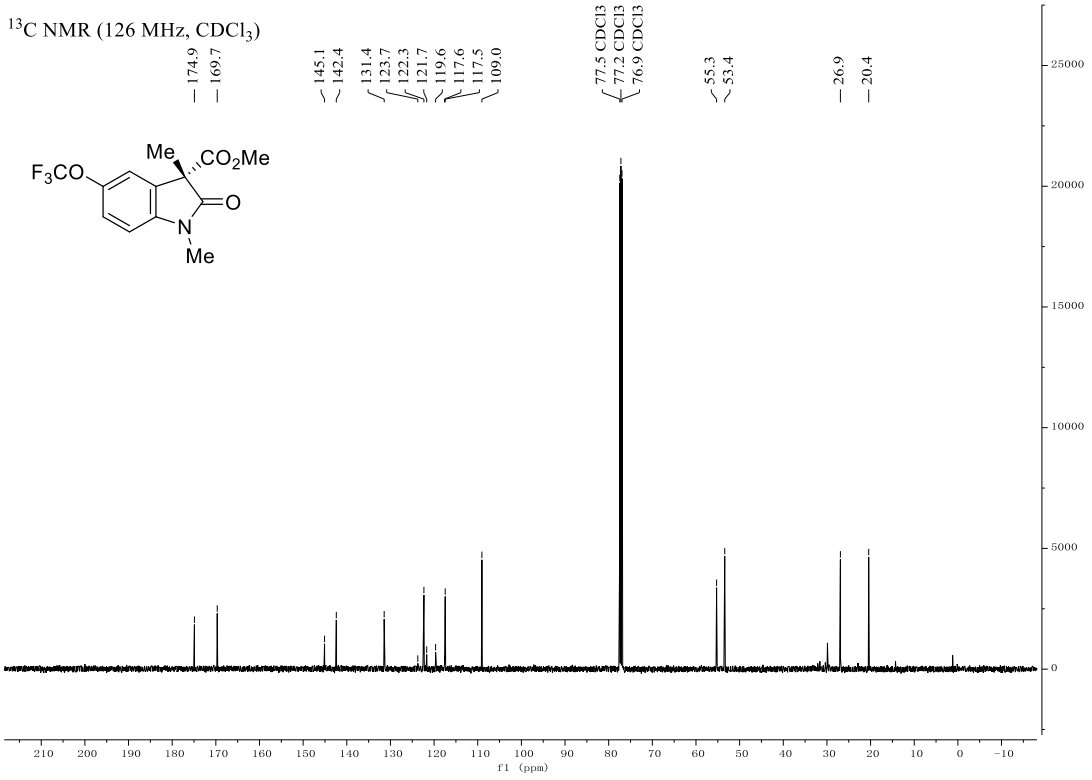


Compound 8

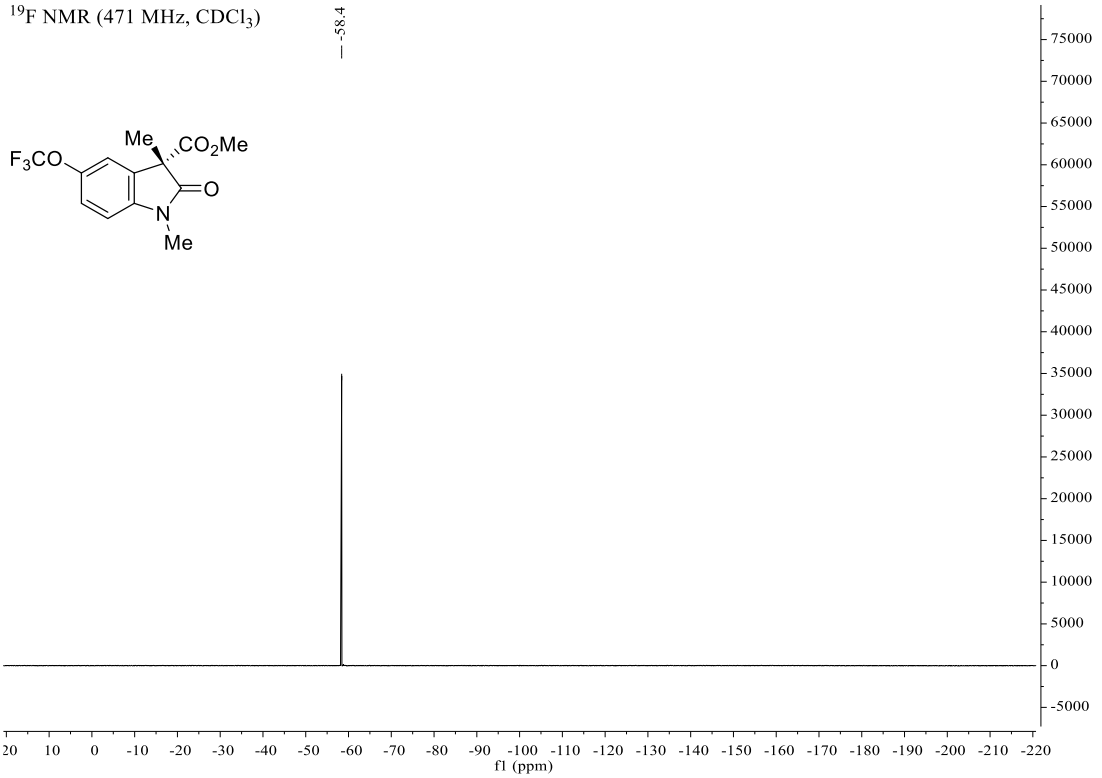
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

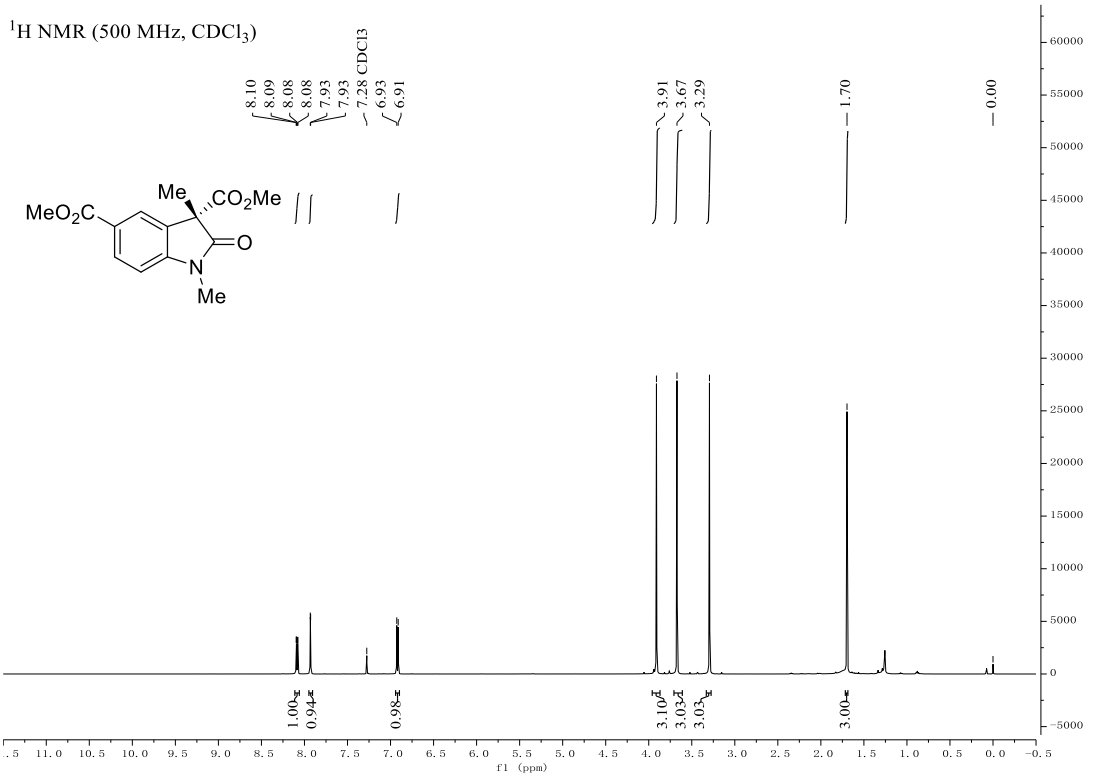


^{19}F NMR (471 MHz, $CDCl_3$)

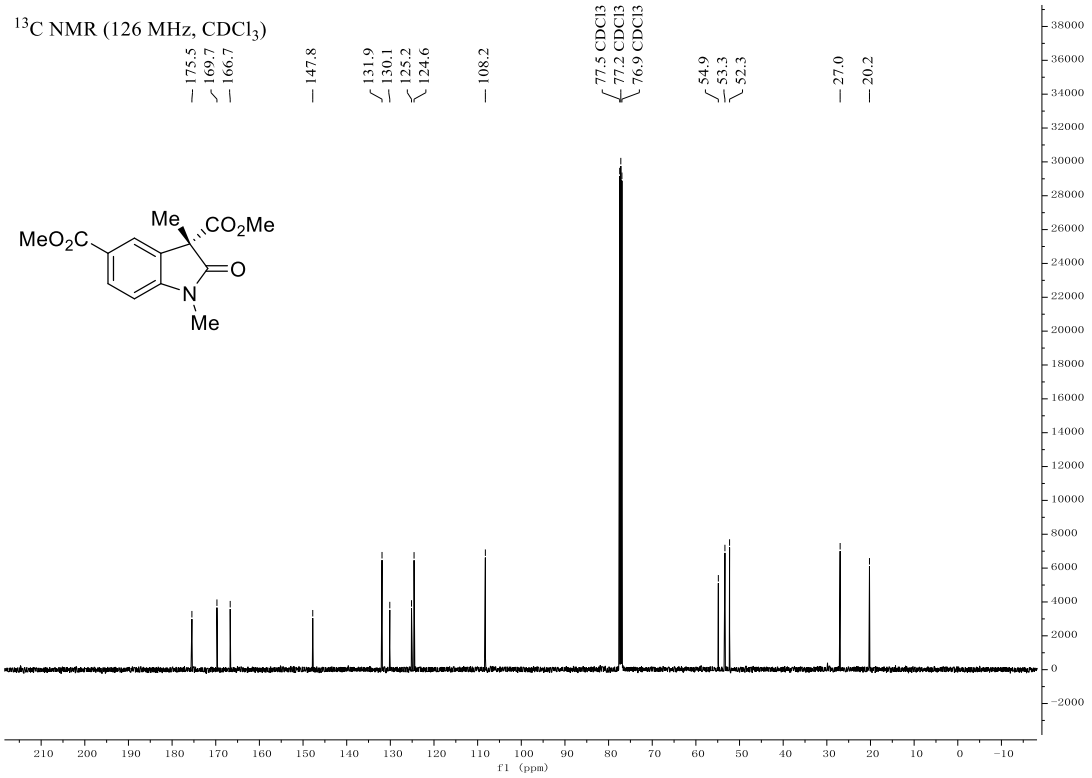


Compound 9

^{1}H NMR (500 MHz, $CDCl_3$)

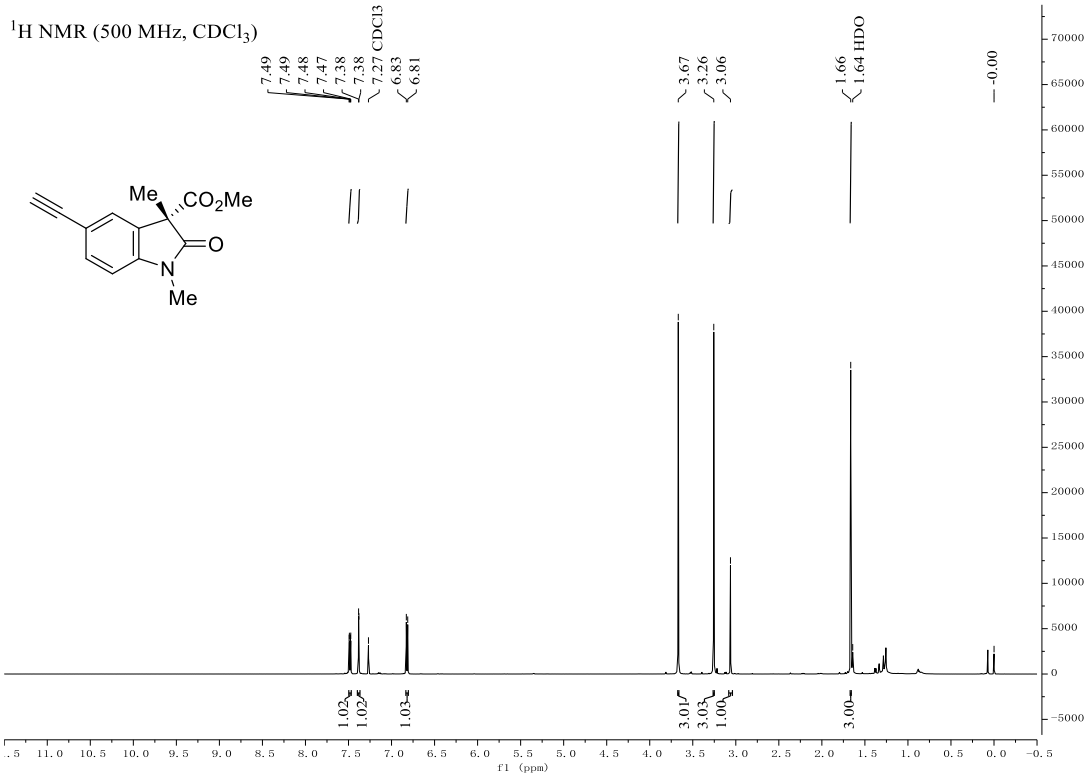


^{13}C NMR (126 MHz, $CDCl_3$)

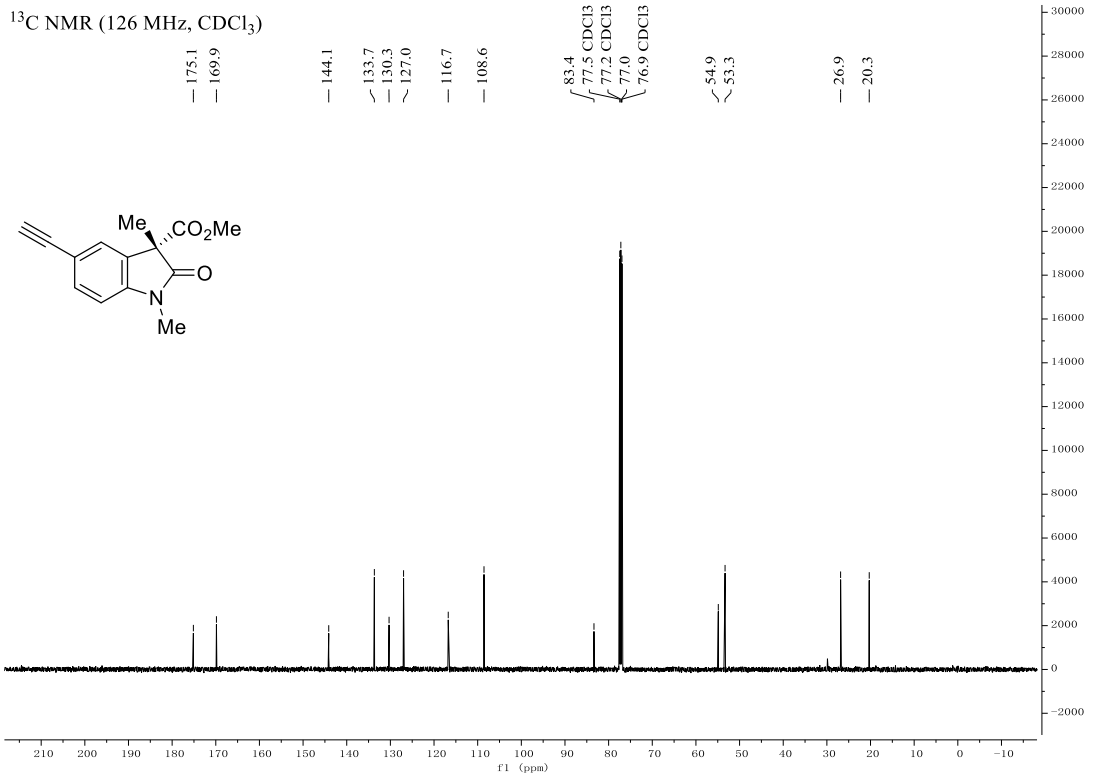


Compound 12

^{1}H NMR (500 MHz, $CDCl_3$)

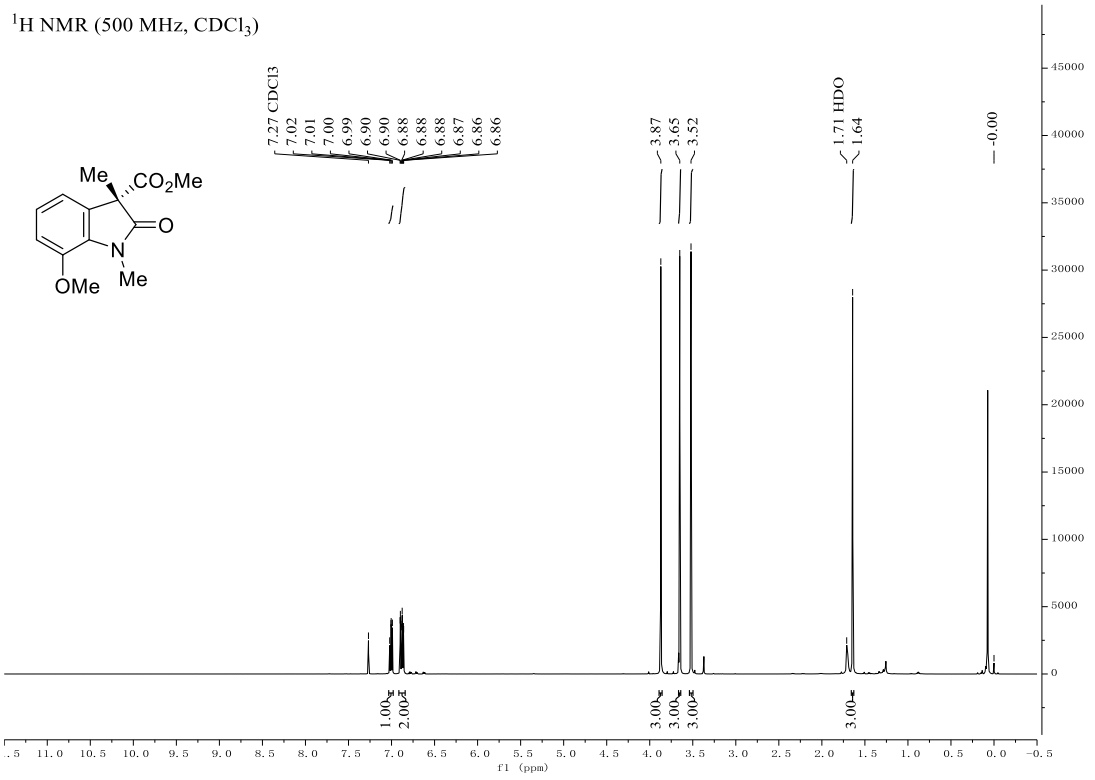


^{13}C NMR (126 MHz, $CDCl_3$)



Compound 13

^{1}H NMR (500 MHz, $CDCl_3$)



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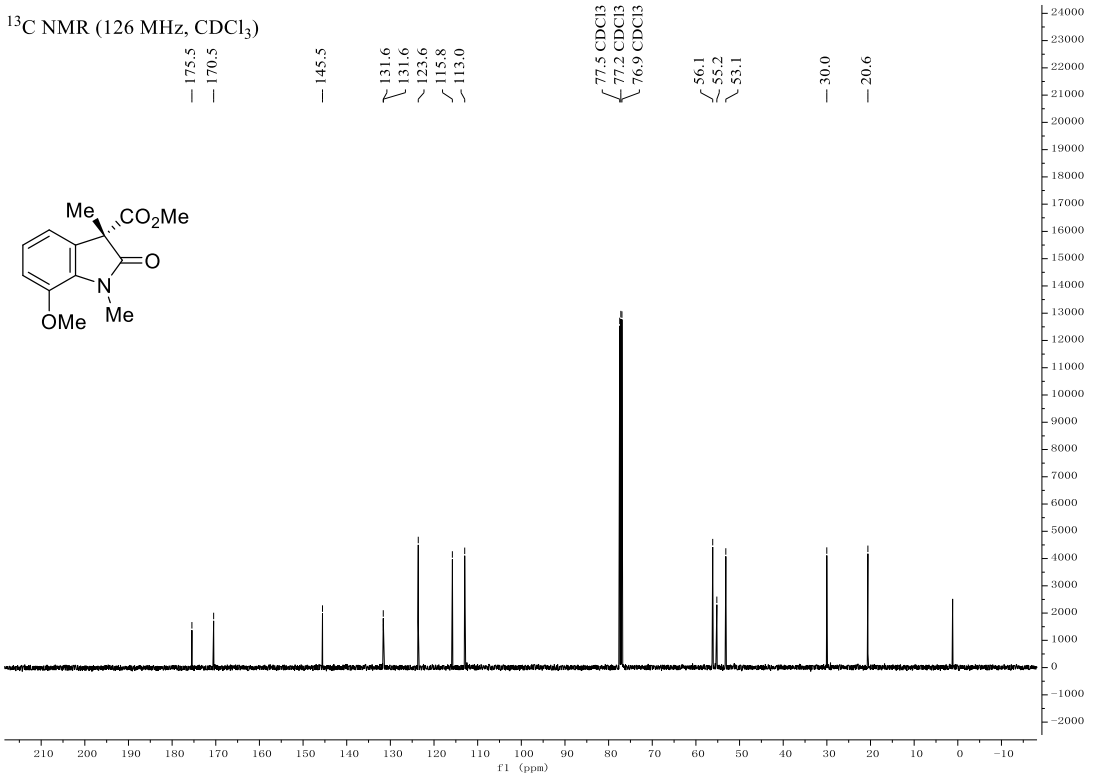
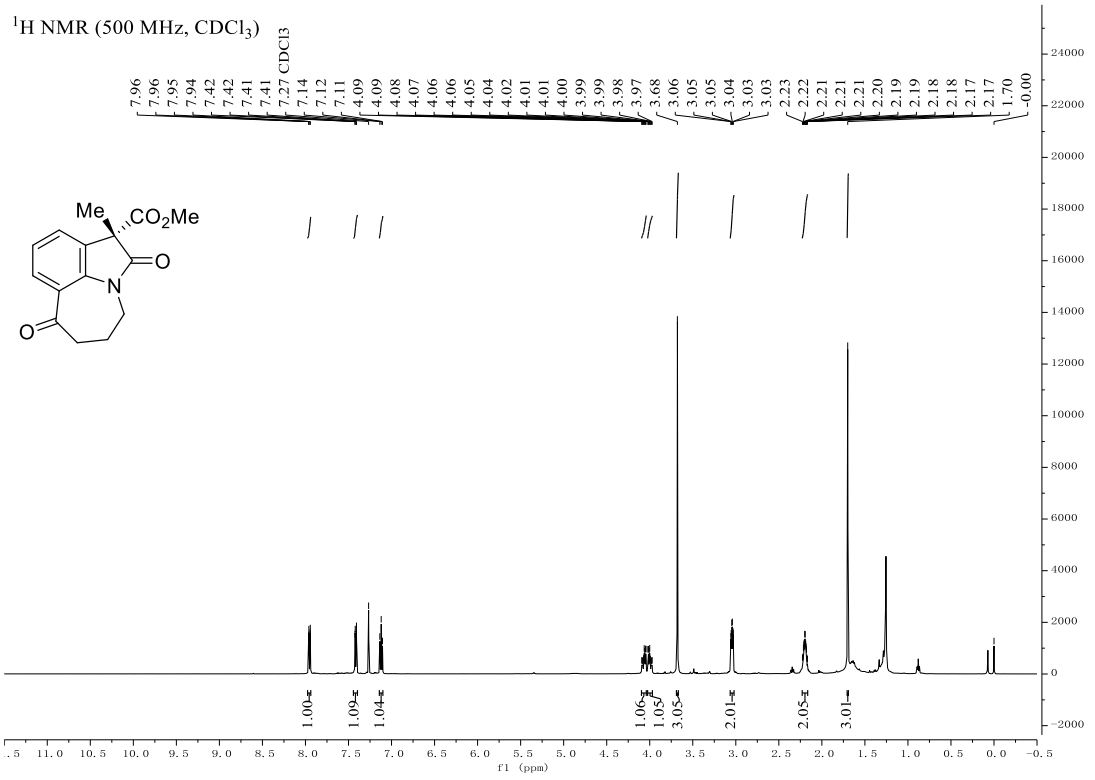
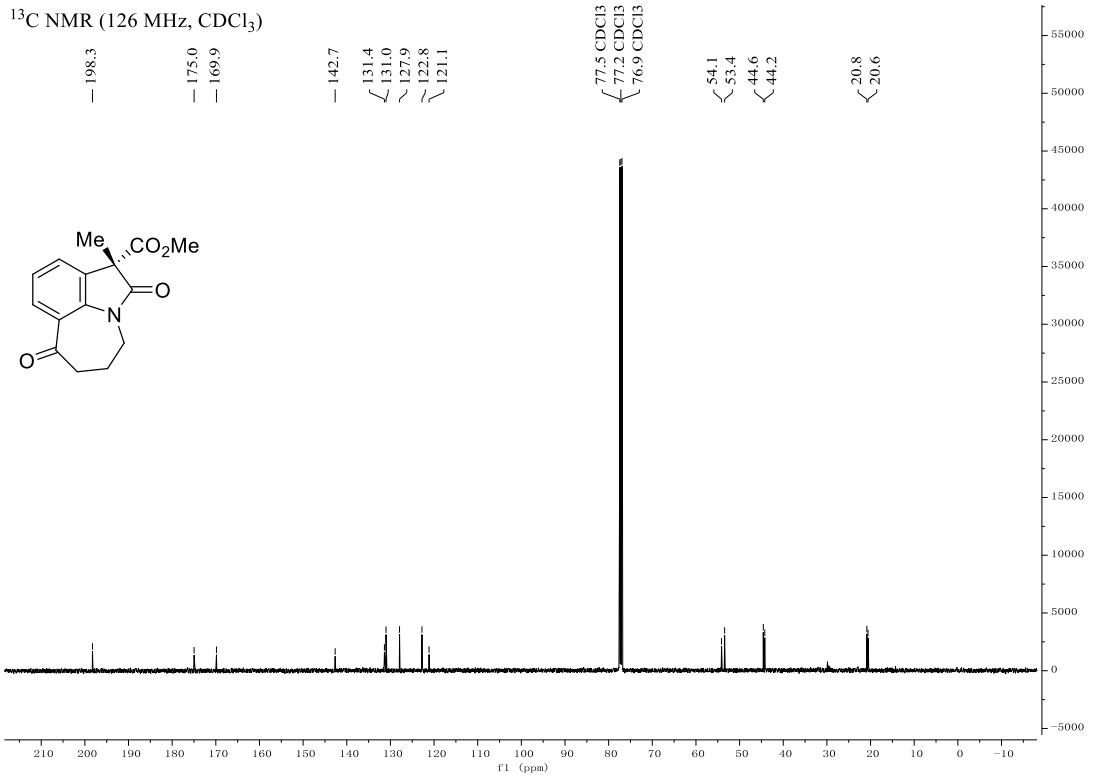


Compound 14

^{1}H NMR (500 MHz, $CDCl_3$)

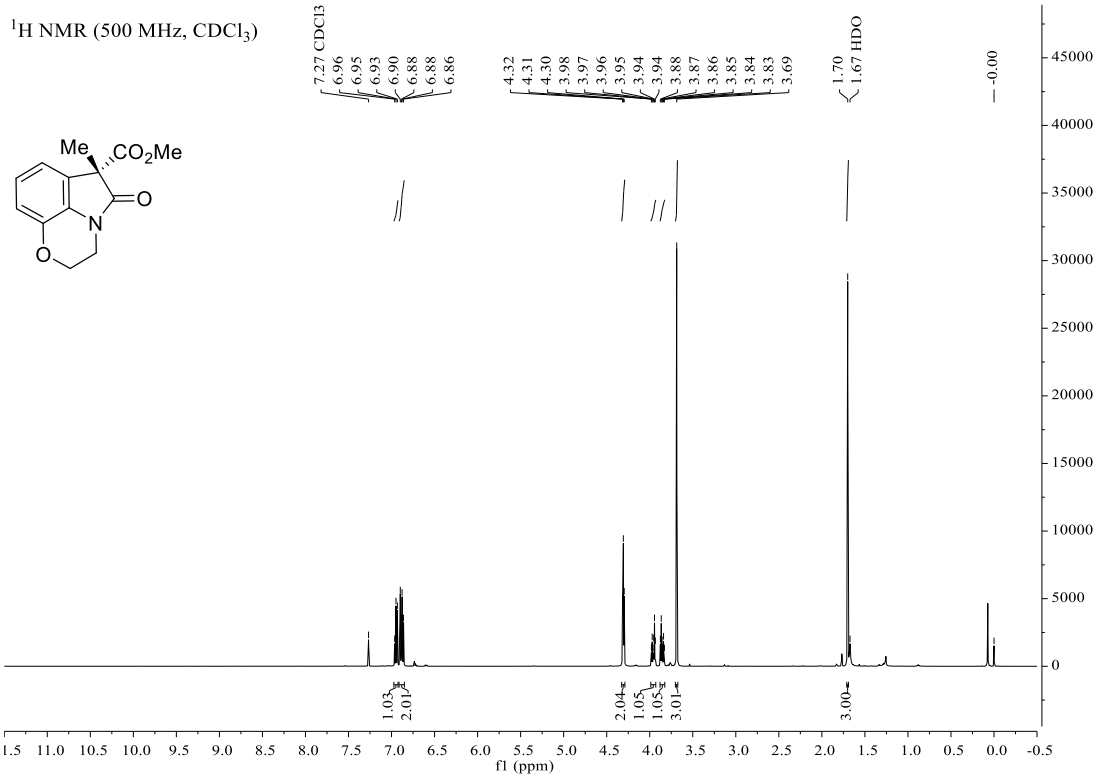


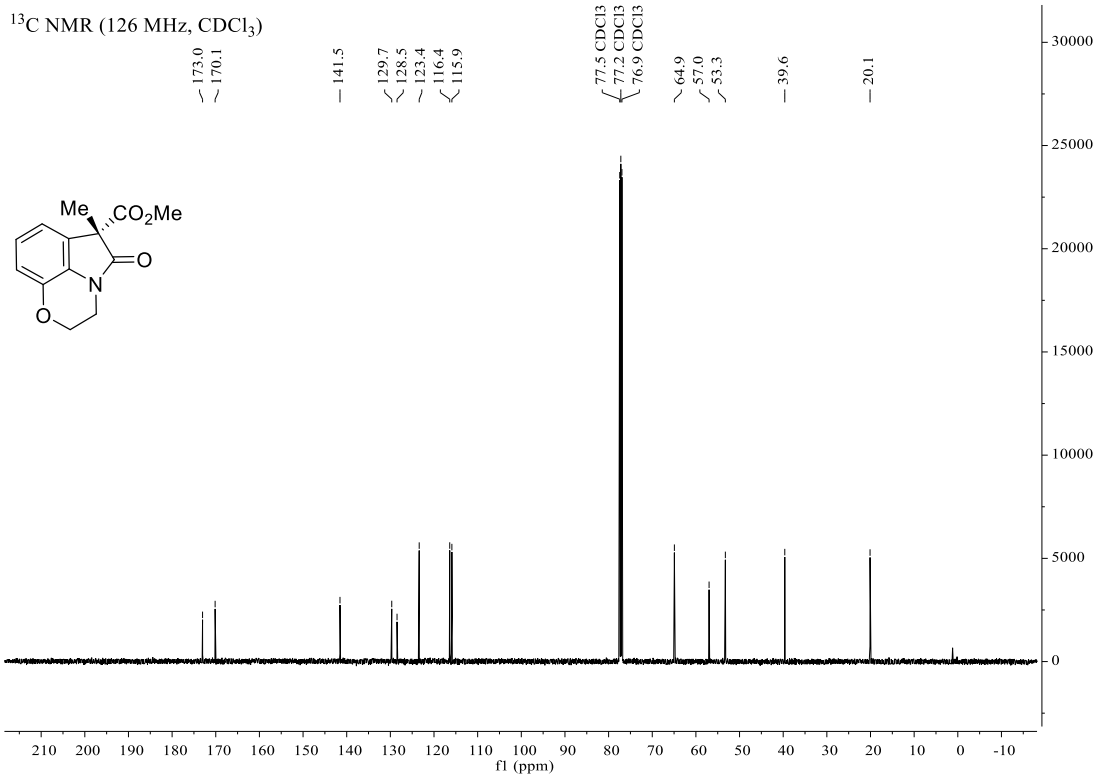
^{13}C NMR (126 MHz, $CDCl_3$)



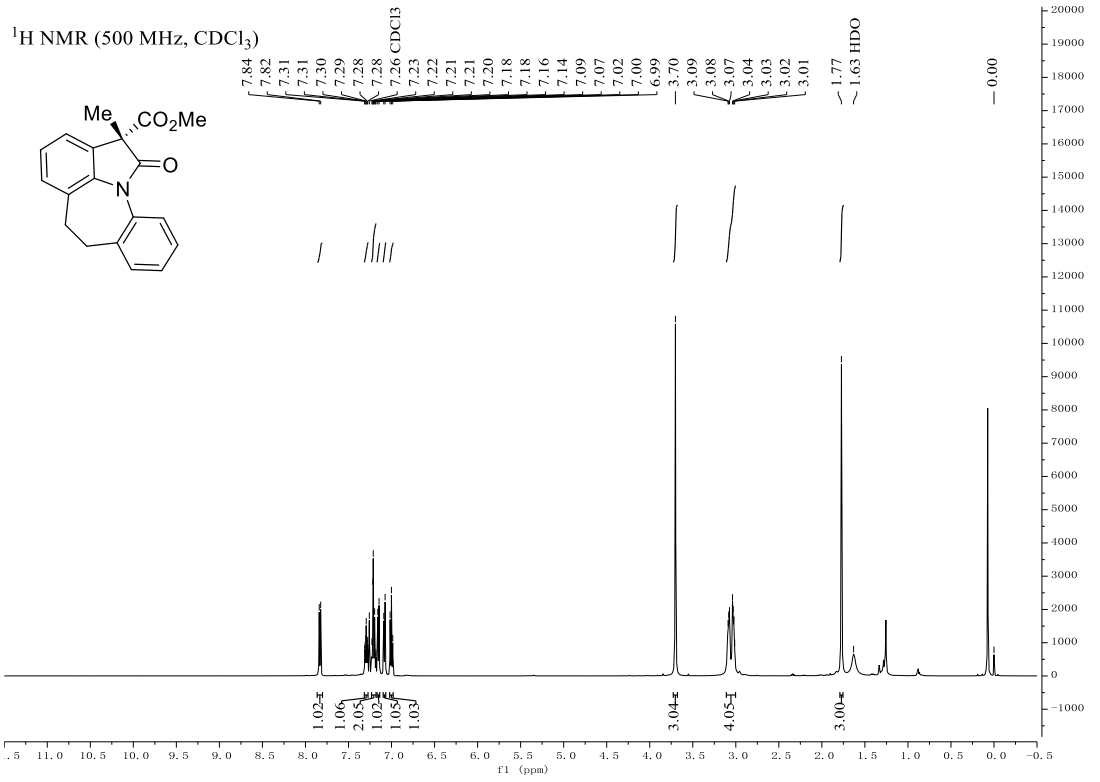
Compound 15

^{1}H NMR (500 MHz, $CDCl_3$)

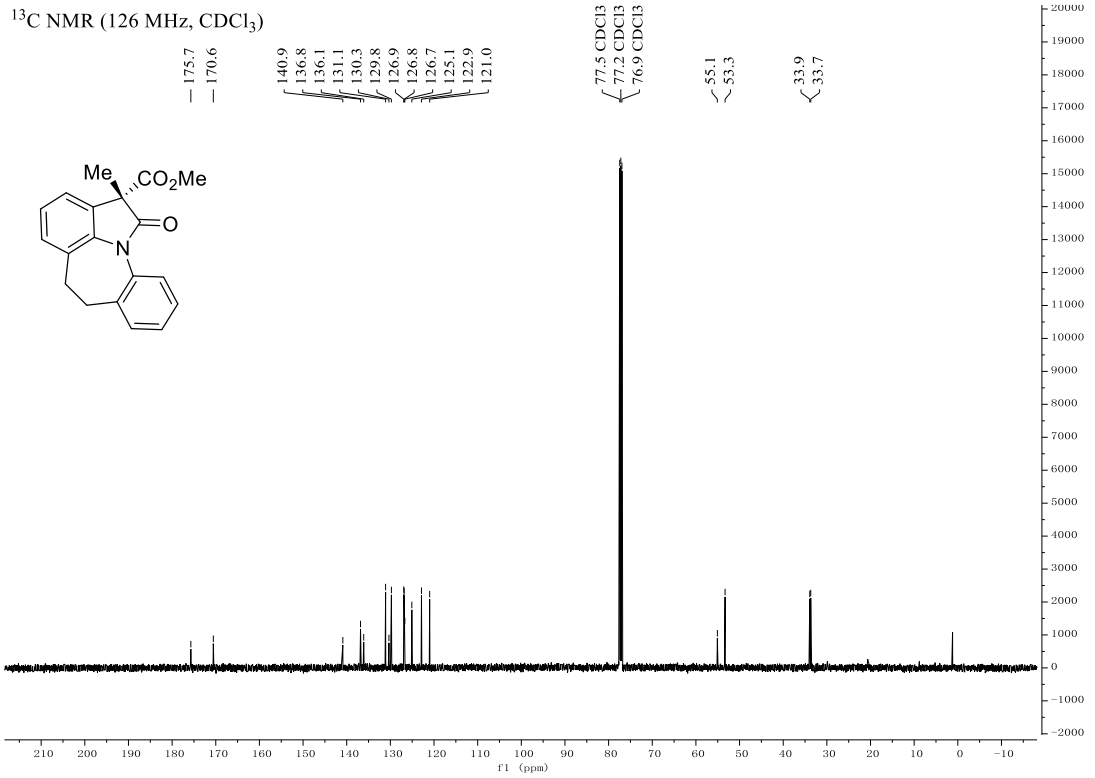



13C NMR (126 MHz, CDCl3)
173.0
170.1
141.5
129.7
128.5
123.4
116.4
115.9
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
64.9
57.0
53.3
39.6
20.1
Me
CO2Me
O
N
O
f1 (ppm)

Compound 16

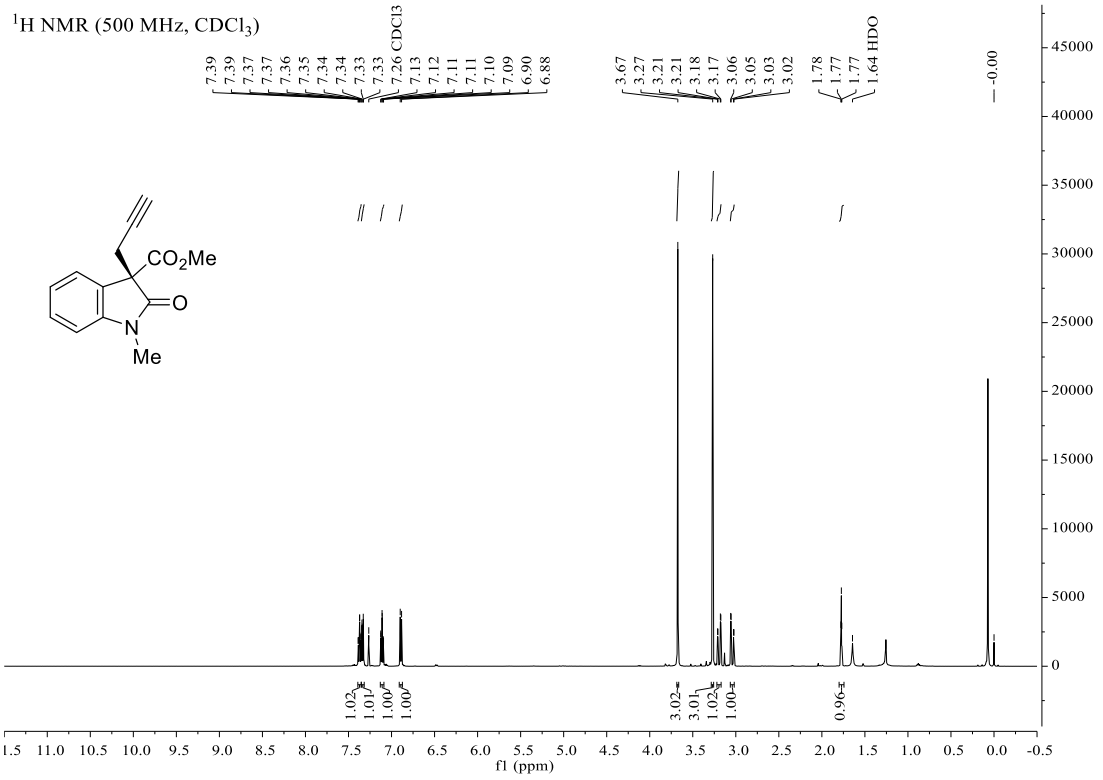

1H NMR (500 MHz, CDCl3)
7.84
7.82
7.31
7.31
7.30
7.29
7.28
7.28
7.26 CDCl3
7.23
7.22
7.21
7.21
7.20
7.18
7.18
7.16
7.14
7.09
7.07
7.02
7.00
6.99
3.70
3.09
3.08
3.07
3.04
3.03
3.02
3.01
1.77
1.63 HDO
0.00
Me
CO2Me
O
N
1.02
1.06
2.05
1.02
1.05
1.03
3.04
4.05
3.00
f1 (ppm)

^{13}C NMR (126 MHz, $CDCl_3$)

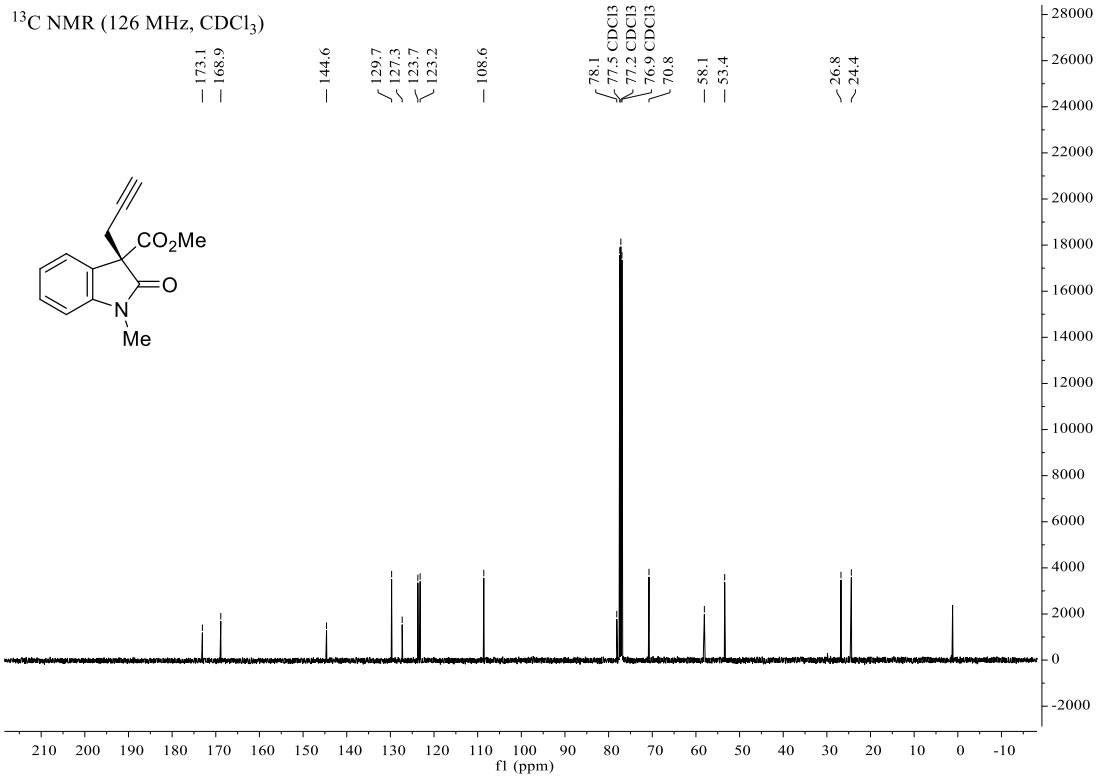


Compound 19

^{1}H NMR (500 MHz, $CDCl_3$)

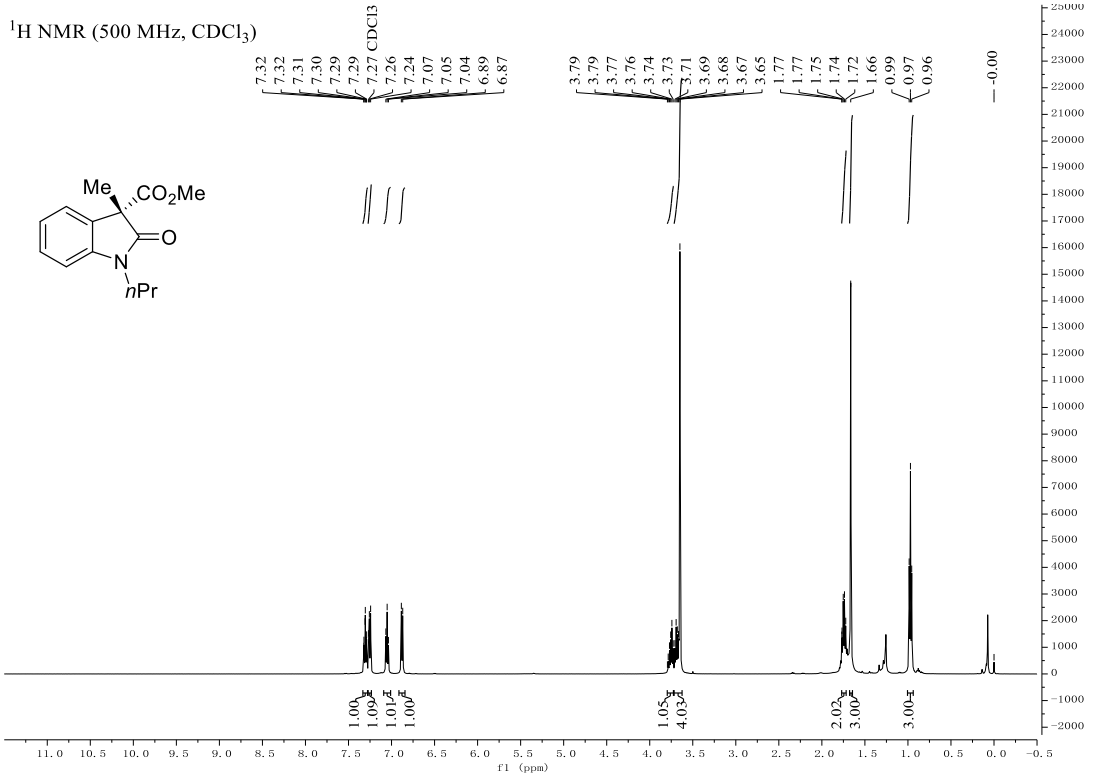


^{13}C NMR (126 MHz, $CDCl_3$)

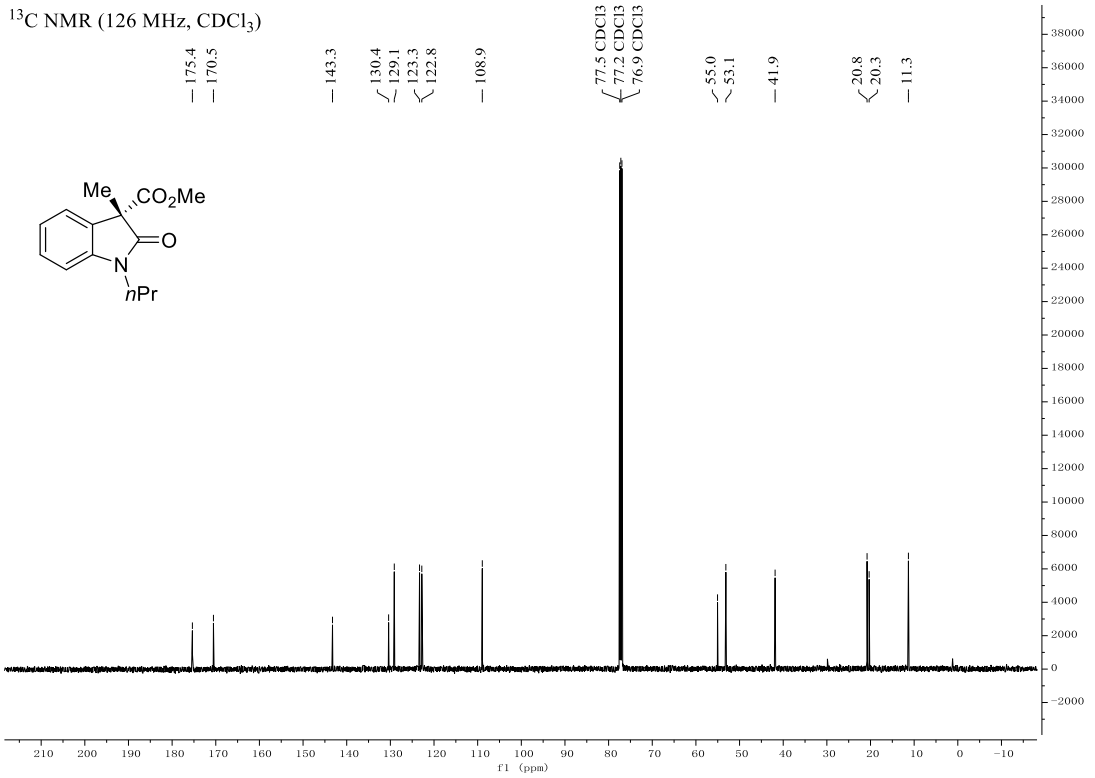


Compound 21

^{1}H NMR (500 MHz, $CDCl_3$)

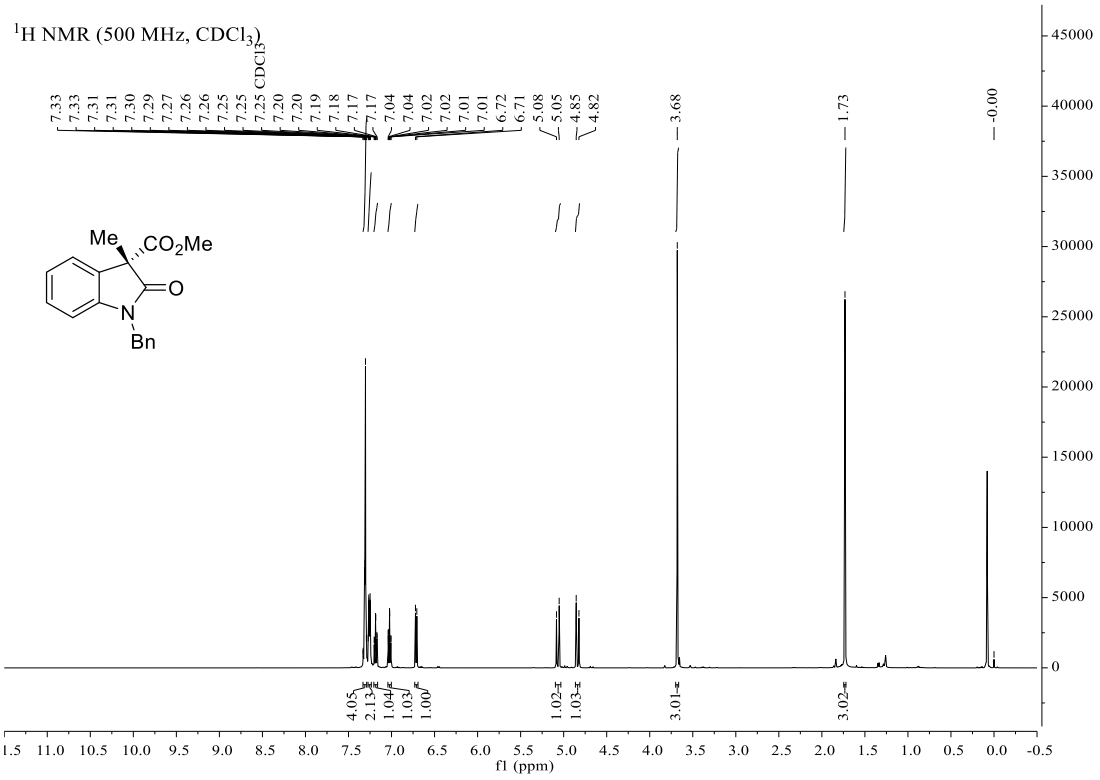


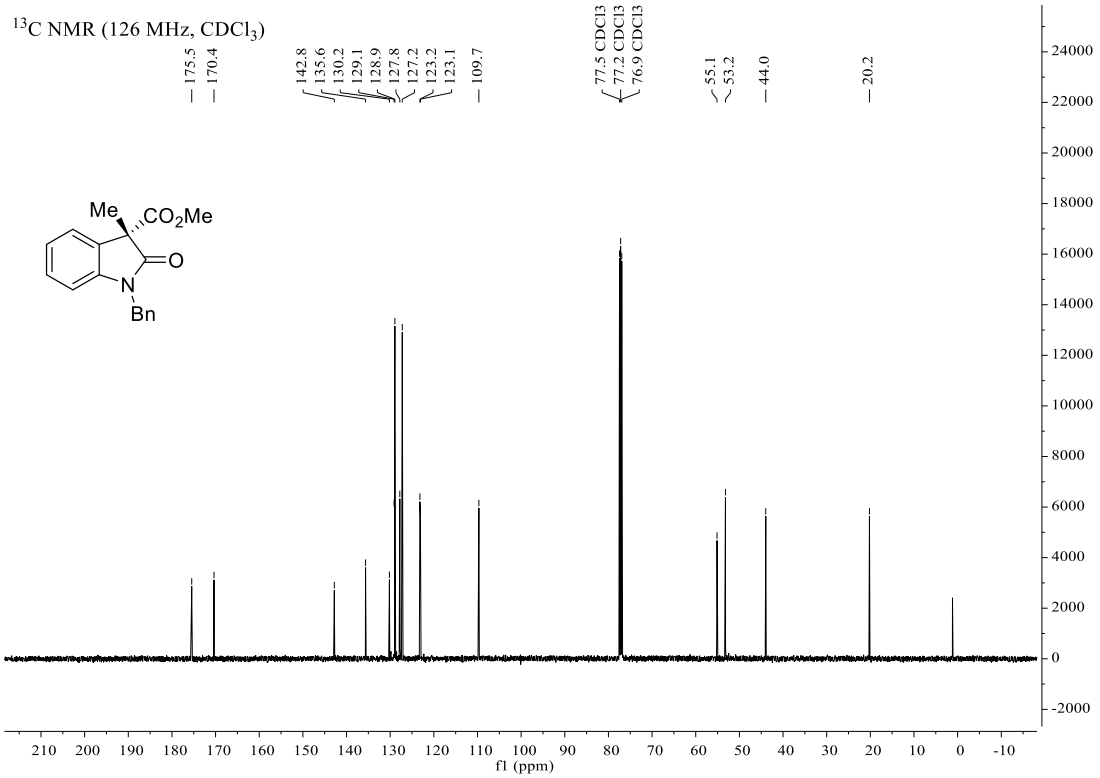
^{13}C NMR (126 MHz, $CDCl_3$)



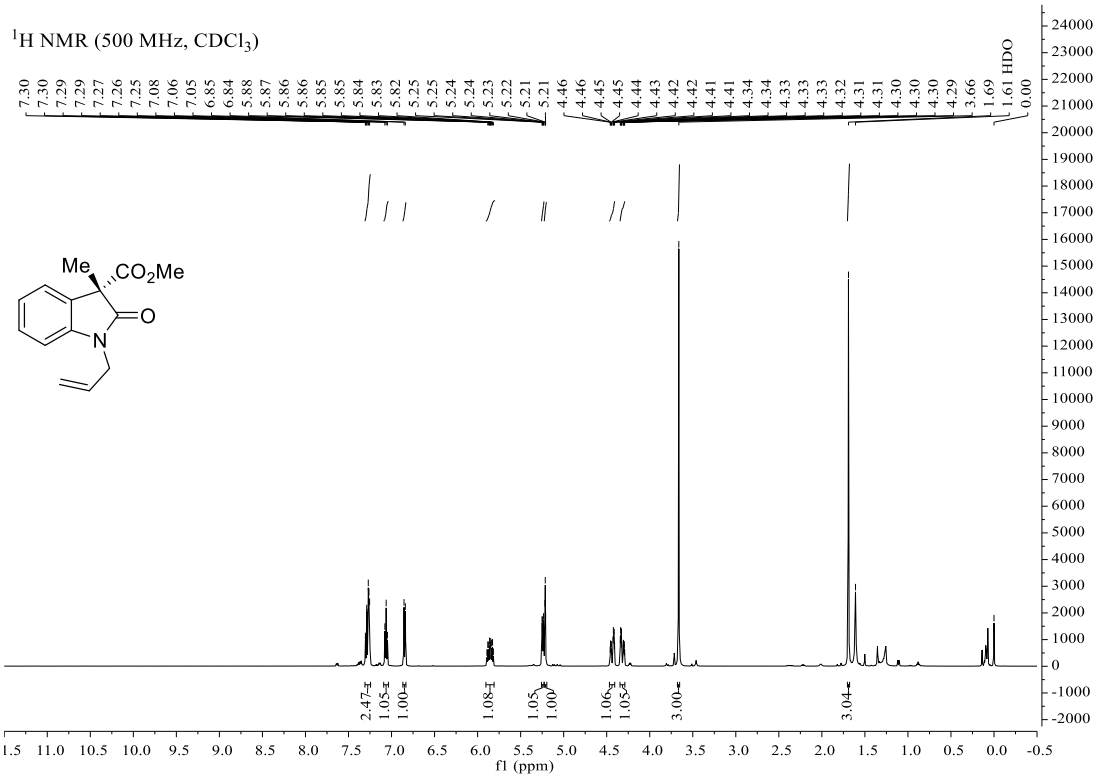
Compound 22

^{1}H NMR (500 MHz, $CDCl_3$)

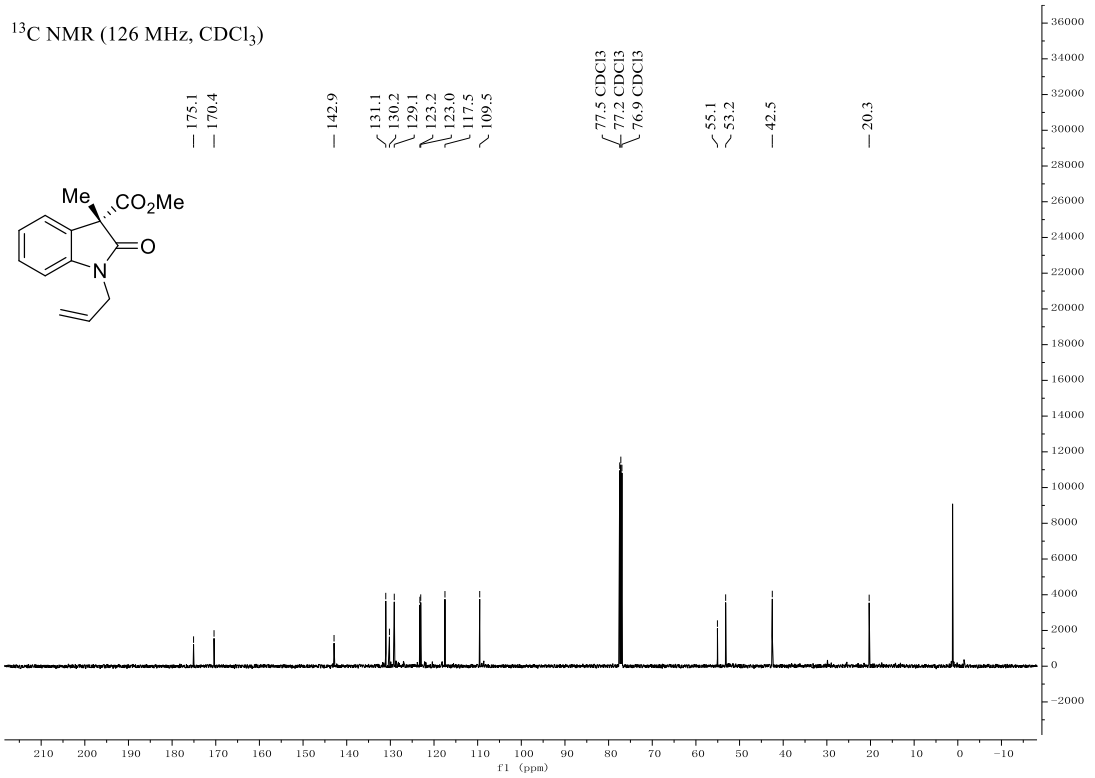



13C NMR (126 MHz, CDCl3)
175.5
170.4
142.8
135.6
130.2
129.1
128.9
127.8
127.2
123.2
123.1
109.7
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
55.1
53.2
44.0
20.2
Me
CO2Me
O
N
Bn
f1 (ppm)

Compound 23

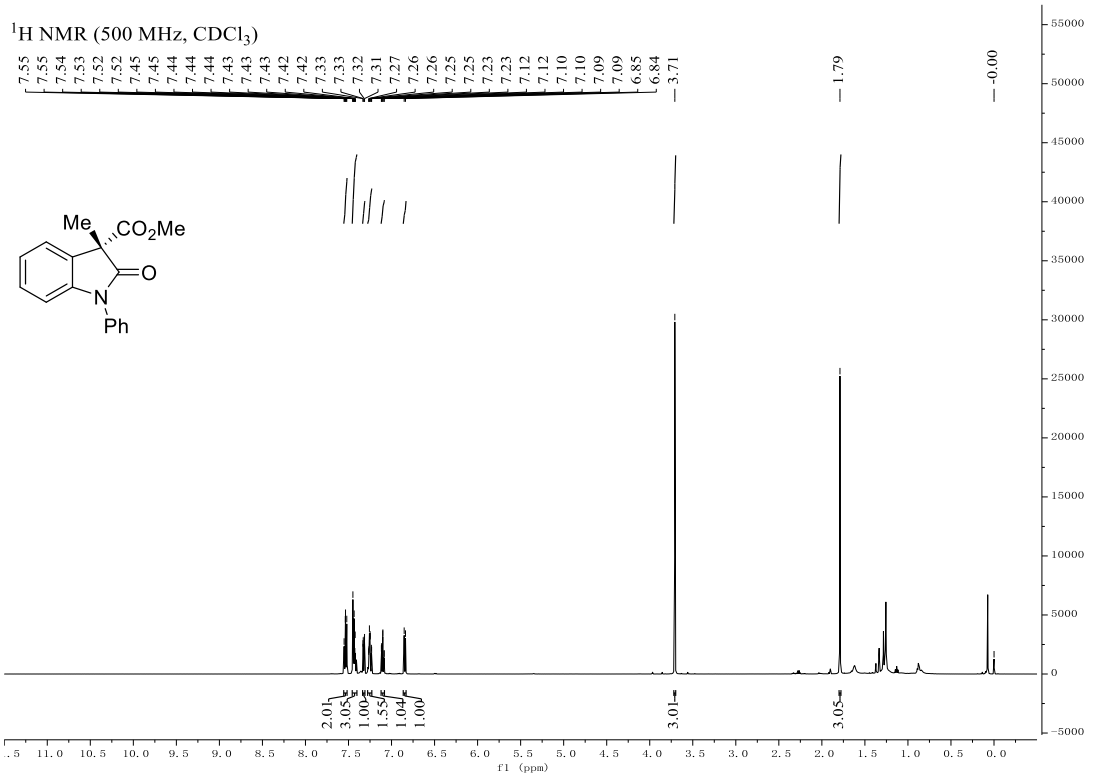

1H NMR (500 MHz, CDCl3)
7.30
7.30
7.29
7.29
7.27
7.26
7.25
7.08
7.06
7.05
6.85
6.84
5.88
5.87
5.86
5.86
5.85
5.85
5.84
5.83
5.82
5.25
5.25
5.24
5.24
5.23
5.22
5.21
5.21
4.46
4.46
4.45
4.45
4.44
4.43
4.42
4.42
4.41
4.41
4.34
4.34
4.33
4.33
4.33
4.32
4.31
4.31
4.30
4.30
4.30
4.29
3.66
1.69
1.61 HDO
0.00
Me
CO2Me
O
N
2.47
1.05
1.00
1.08
1.05
1.00
1.06
1.05
3.00
3.04
f1 (ppm)

^{13}C NMR (126 MHz, $CDCl_3$)

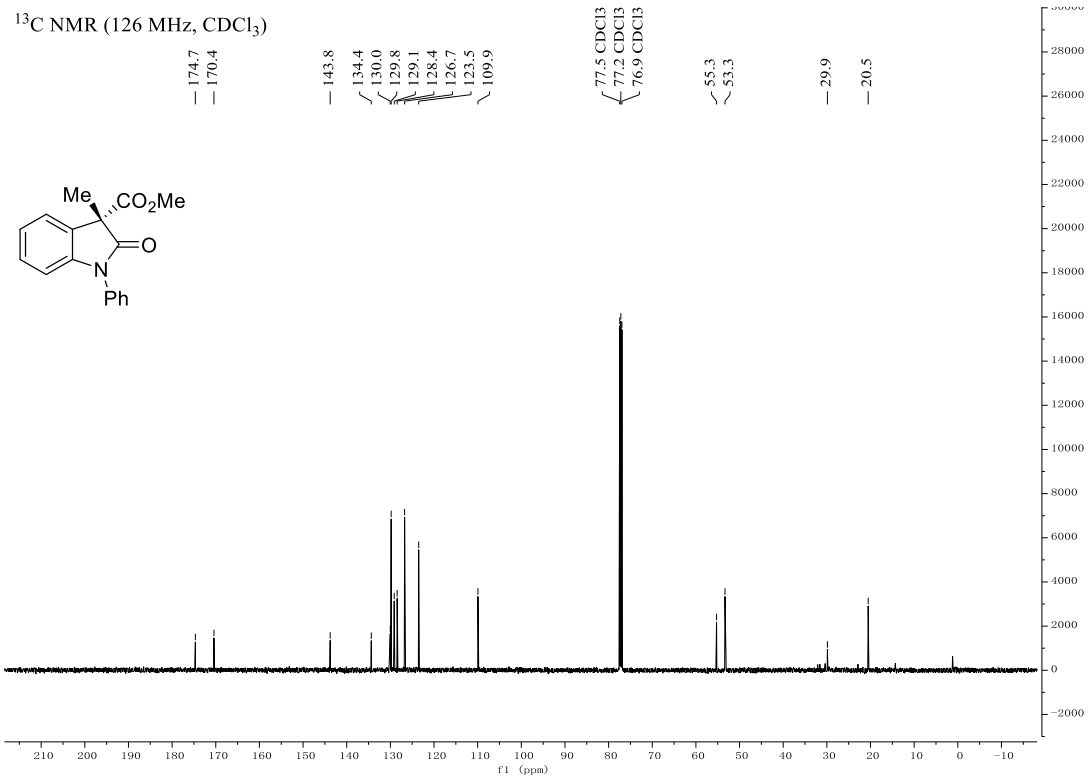


Compound 24

^{1}H NMR (500 MHz, $CDCl_3$)

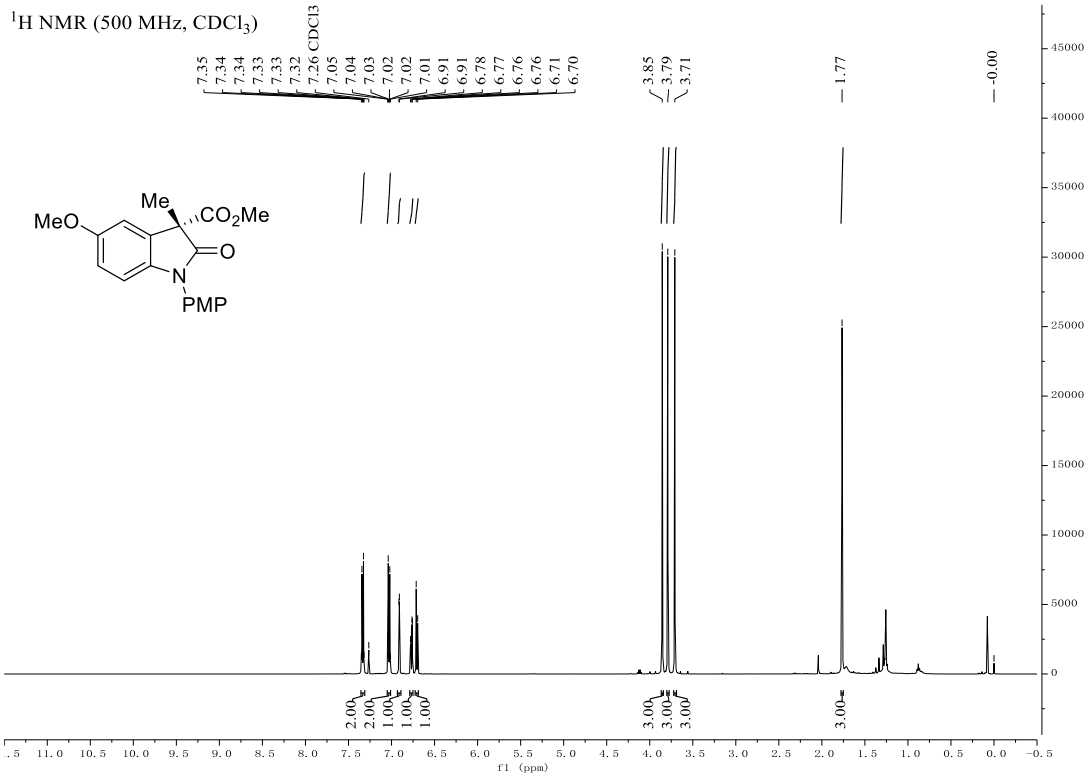


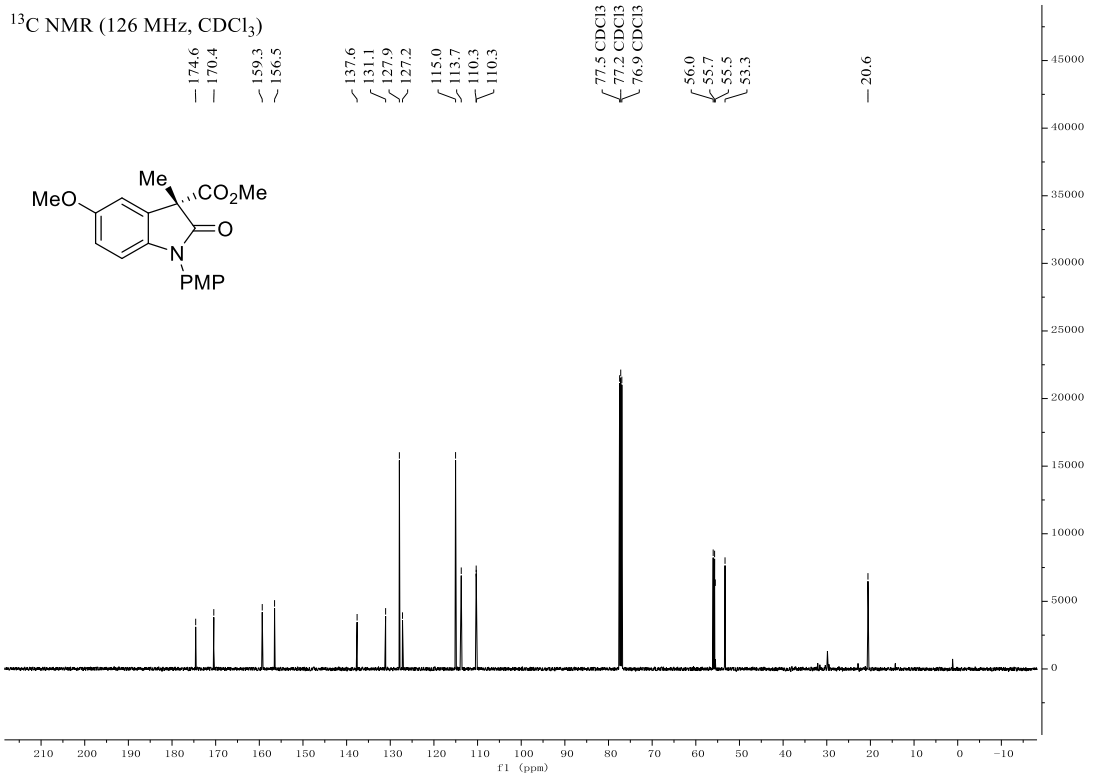
^{13}C NMR (126 MHz, $CDCl_3$)



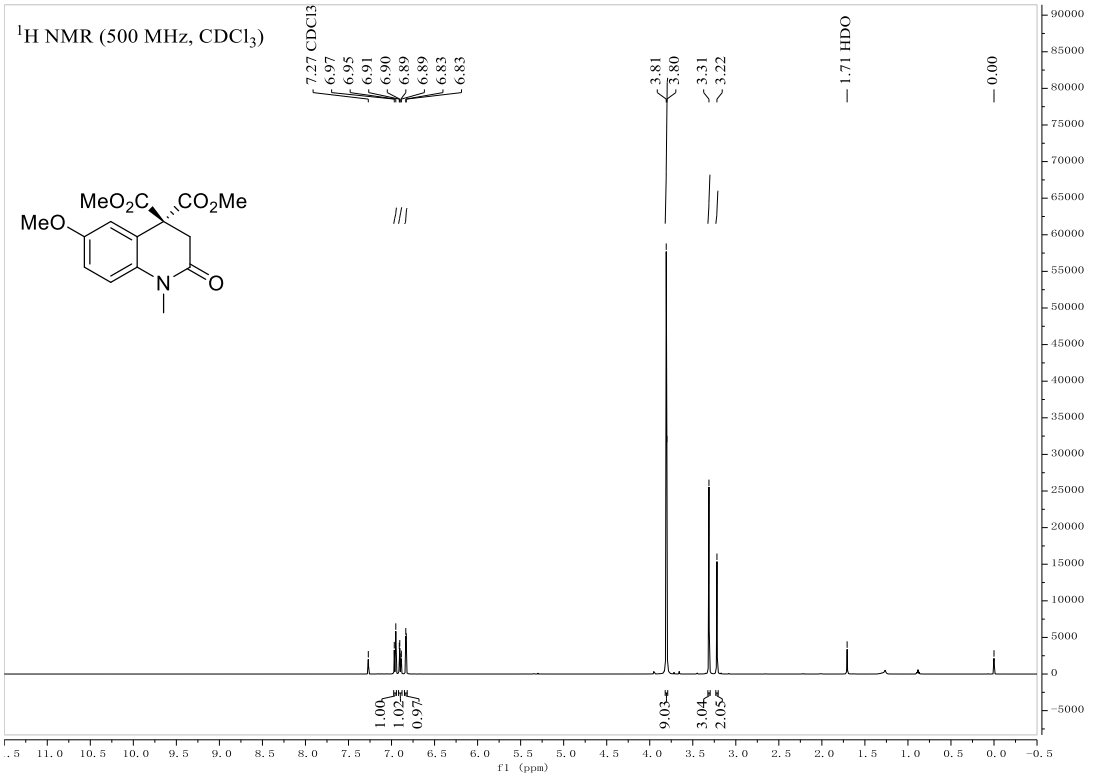
Compound 25

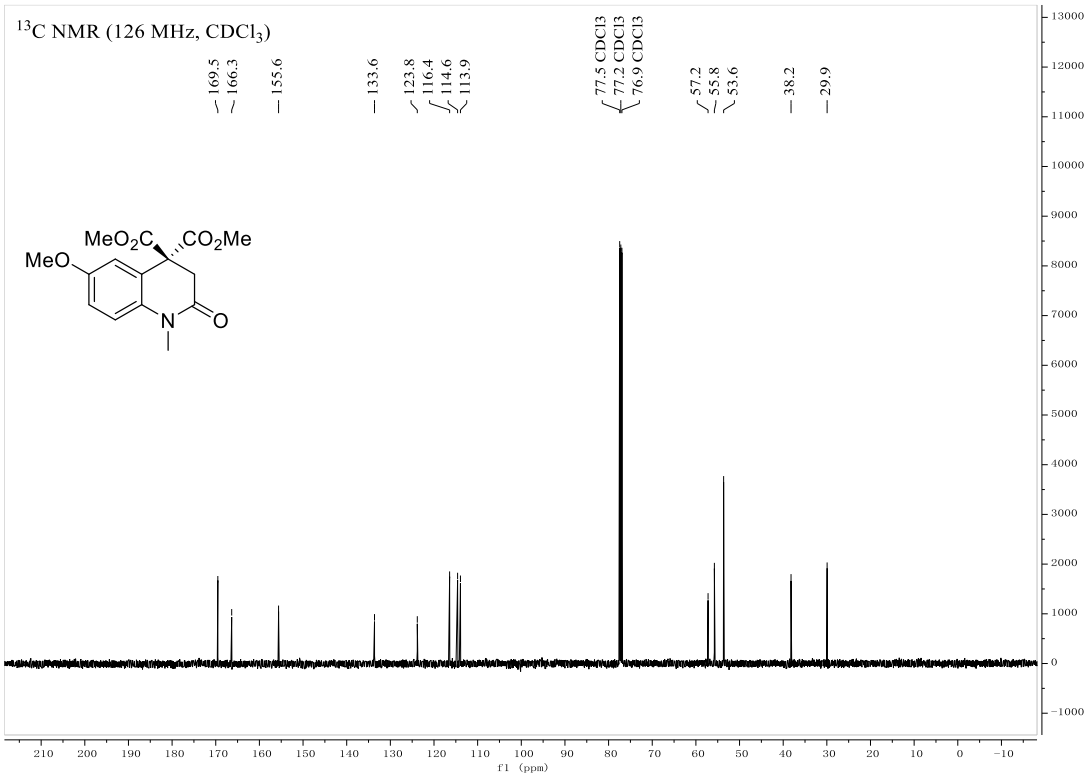
^{1}H NMR (500 MHz, $CDCl_3$)



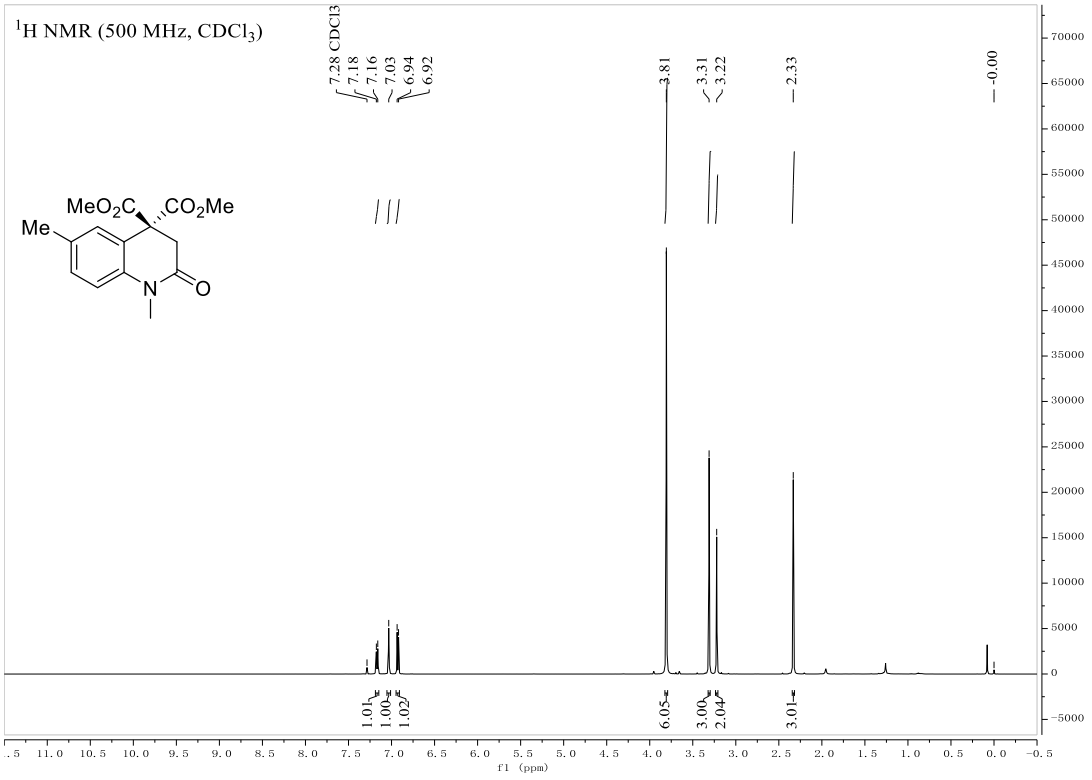

13C NMR (126 MHz, CDCl3)
174.6
170.4
159.3
156.5
137.6
131.1
127.9
127.2
115.0
113.7
110.3
110.3
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
56.0
55.7
55.5
53.3
20.6
Me
CO2Me
MeO
O
N
PMP
f1 (ppm)

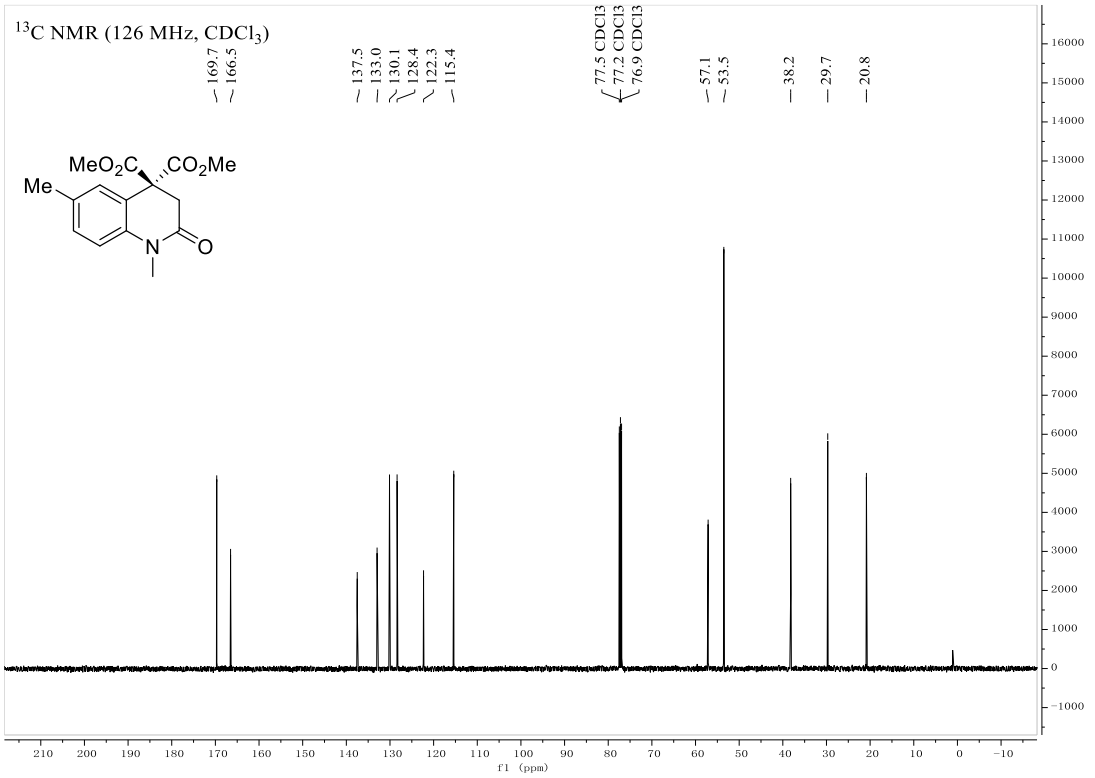
Compound 28


1H NMR (500 MHz, CDCl3)
7.27 CDCl3
6.97
6.95
6.91
6.90
6.89
6.89
6.83
6.83
3.81
3.80
3.31
3.22
1.71 HDO
0.00
MeO2C
CO2Me
MeO
N
O
1.00
1.02
0.97
9.03
3.04
2.05
f1 (ppm)

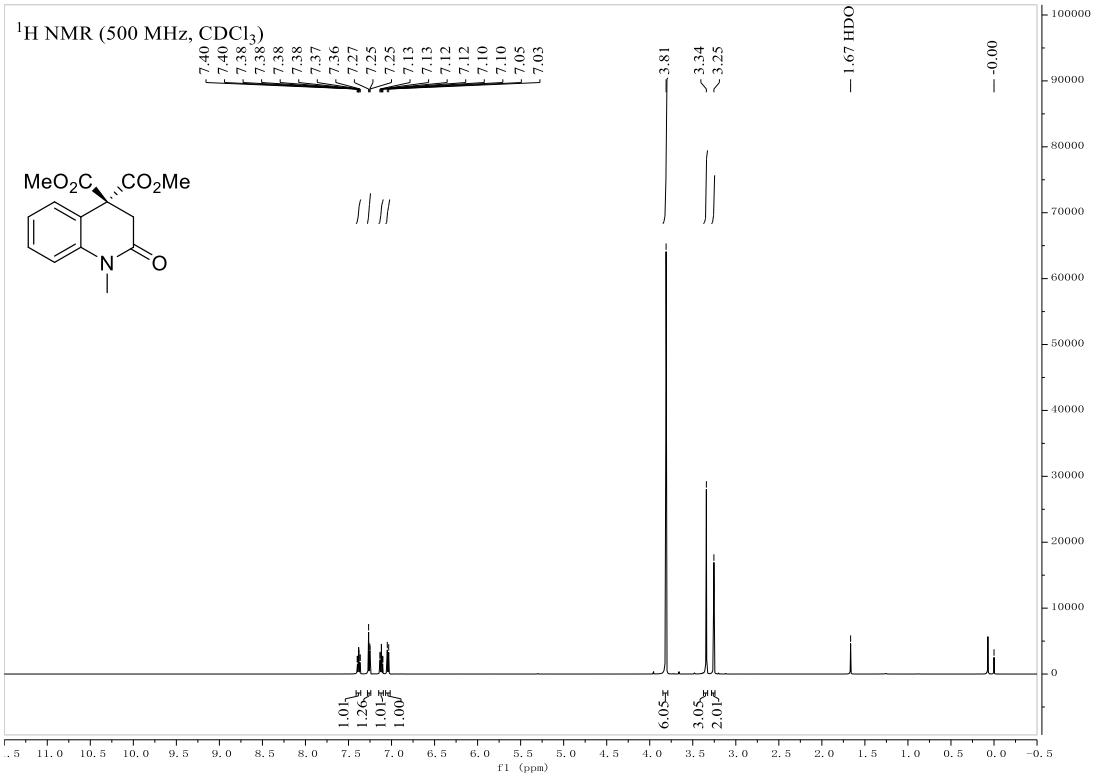

13C NMR (126 MHz, CDCl3)
169.5
166.3
155.6
133.6
123.8
116.4
114.6
113.9
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
57.2
55.8
53.6
38.2
29.9
MeO2C
CO2Me
MeO
N
O
f1 (ppm)

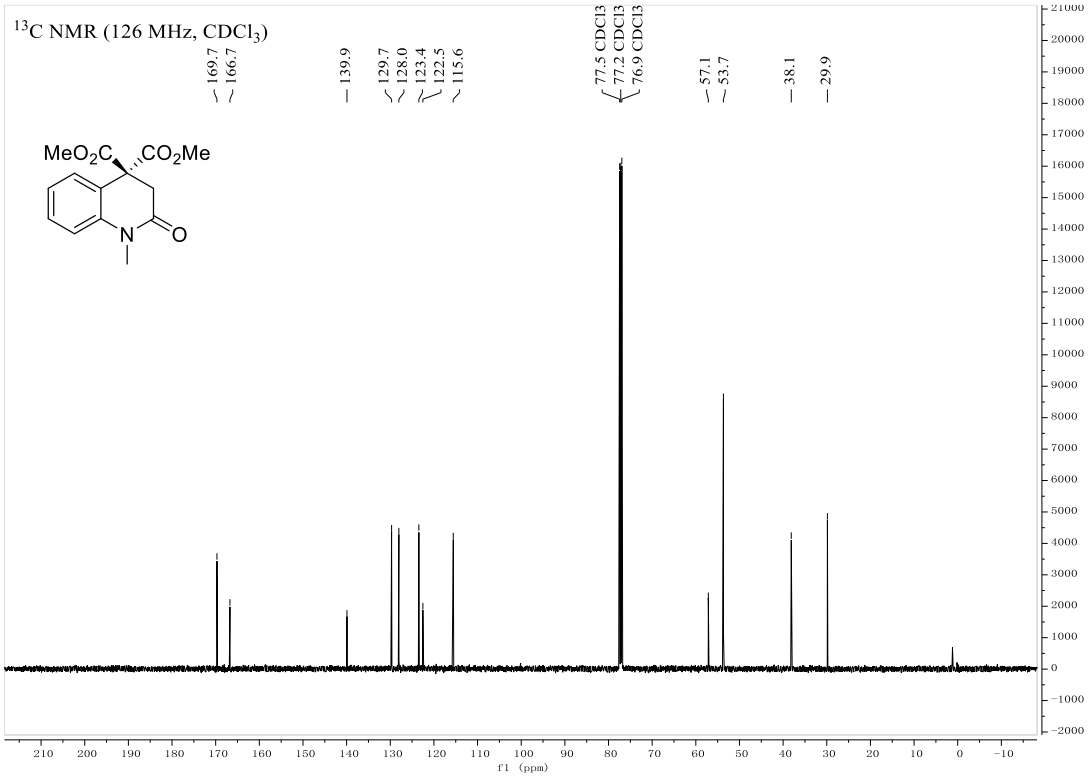
Compound 29


1H NMR (500 MHz, CDCl3)
7.28 CDCl3
7.18
7.16
7.03
6.94
6.92
3.81
3.31
3.22
2.33
-0.00
MeO2C
CO2Me
Me
N
O
1.01
1.00
1.02
6.05
3.00
2.04
3.01
f1 (ppm)

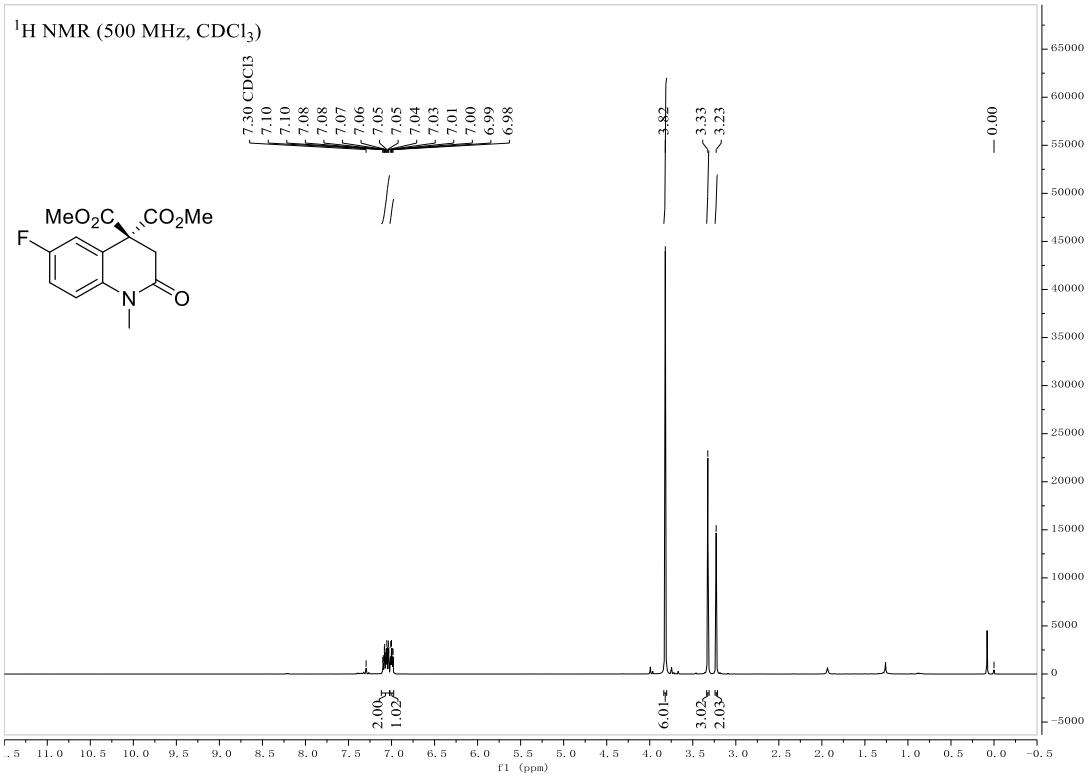

13C NMR (126 MHz, CDCl3)
169.7
166.5
137.5
133.0
130.1
128.4
122.3
115.4
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
57.1
53.5
38.2
29.7
20.8
MeO2C
CO2Me
Me
N
O
f1 (ppm)

Compound 30

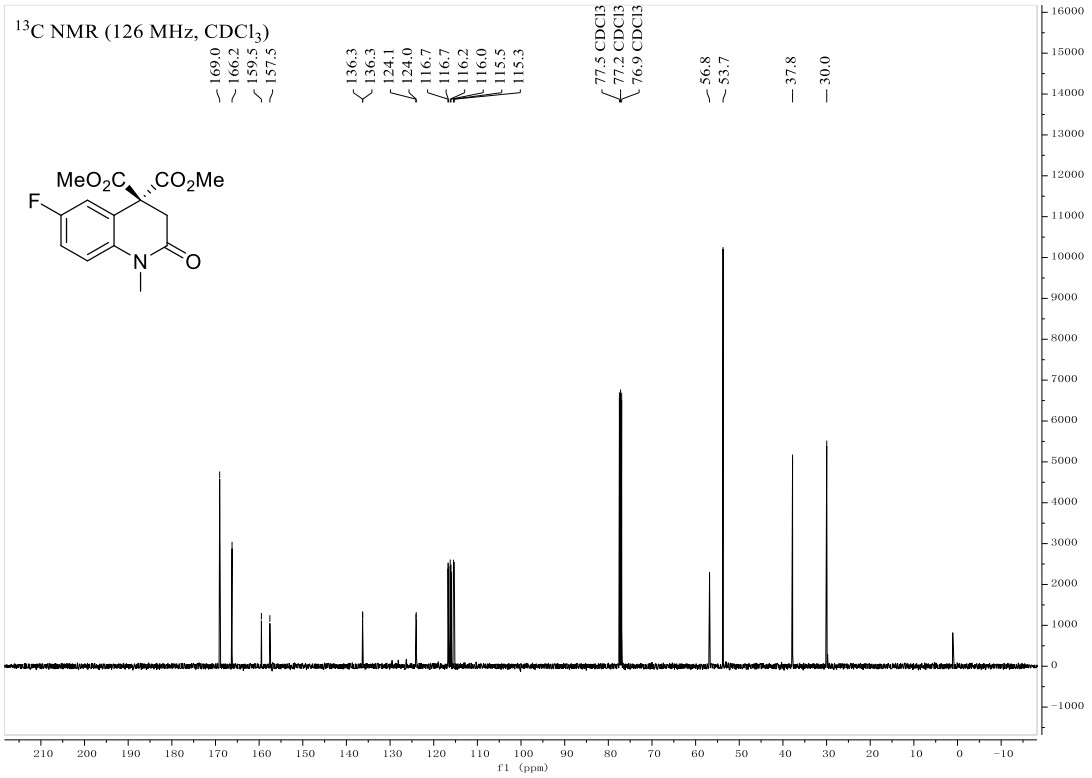

1H NMR (500 MHz, CDCl3)
7.40
7.40
7.38
7.38
7.38
7.38
7.37
7.36
7.27
7.25
7.25
7.13
7.13
7.12
7.12
7.10
7.10
7.05
7.03
3.81
3.34
3.25
1.67 HDO
-0.00
MeO2C
CO2Me
N
O
1.01
1.26
1.01
1.00
6.05
3.05
2.01
f1 (ppm)


13C NMR (126 MHz, CDCl3)
169.7
166.7
139.9
129.7
128.0
123.4
122.5
115.6
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
57.1
53.7
38.1
29.9
MeO2C
CO2Me
N
O
f1 (ppm)

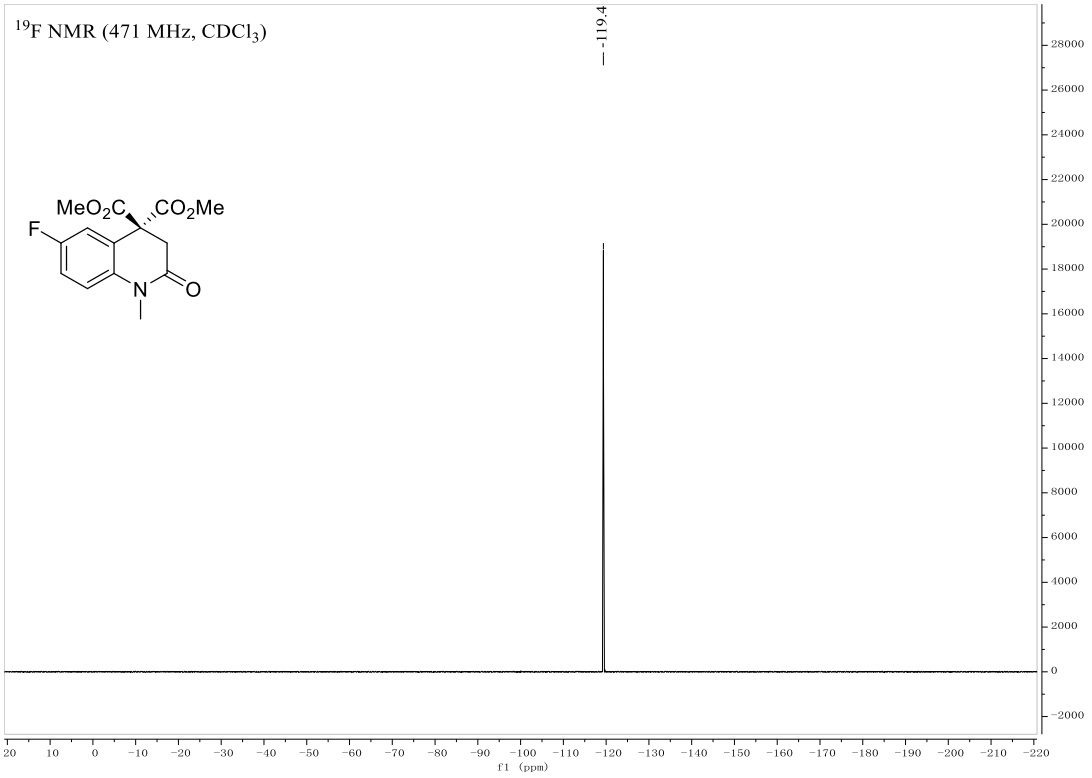
Compound 31


1H NMR (500 MHz, CDCl3)
7.30 CDCl3
7.10
7.10
7.08
7.08
7.07
7.06
7.05
7.05
7.04
7.03
7.01
7.00
6.99
6.98
3.82
3.33
3.23
0.00
MeO2C
CO2Me
F
N
O
2.00
1.02
6.01
3.02
2.03
f1 (ppm)

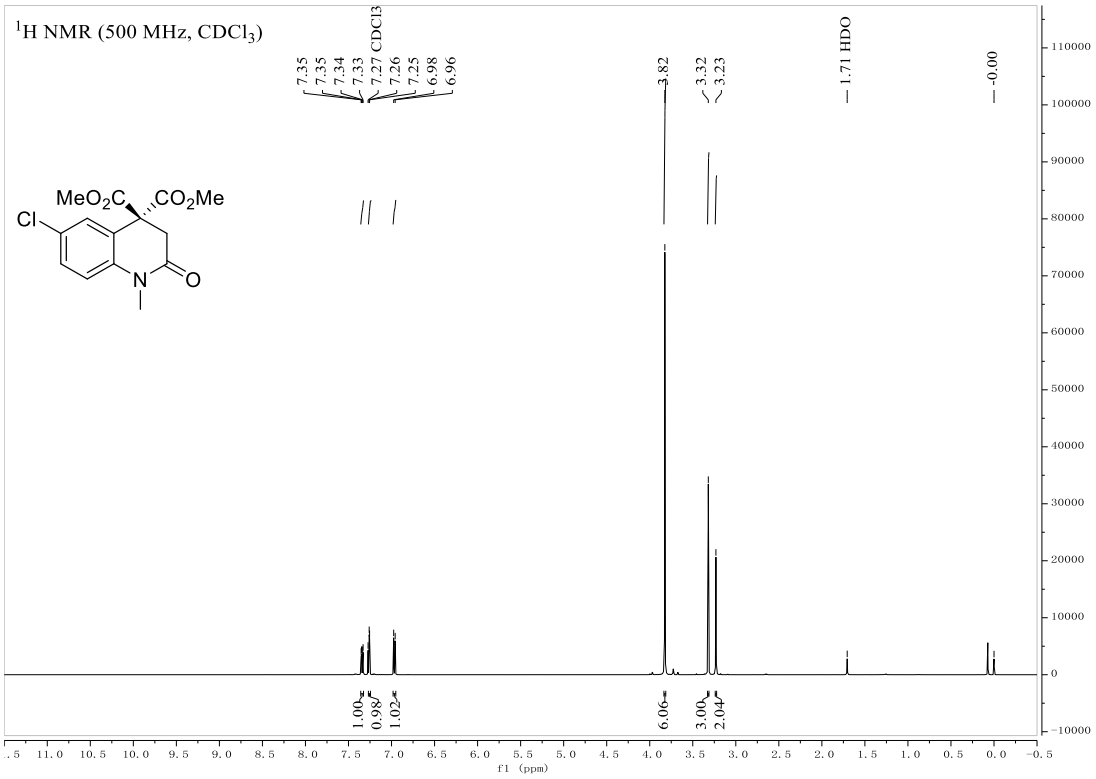
^{13}C NMR (126 MHz, $CDCl_3$)

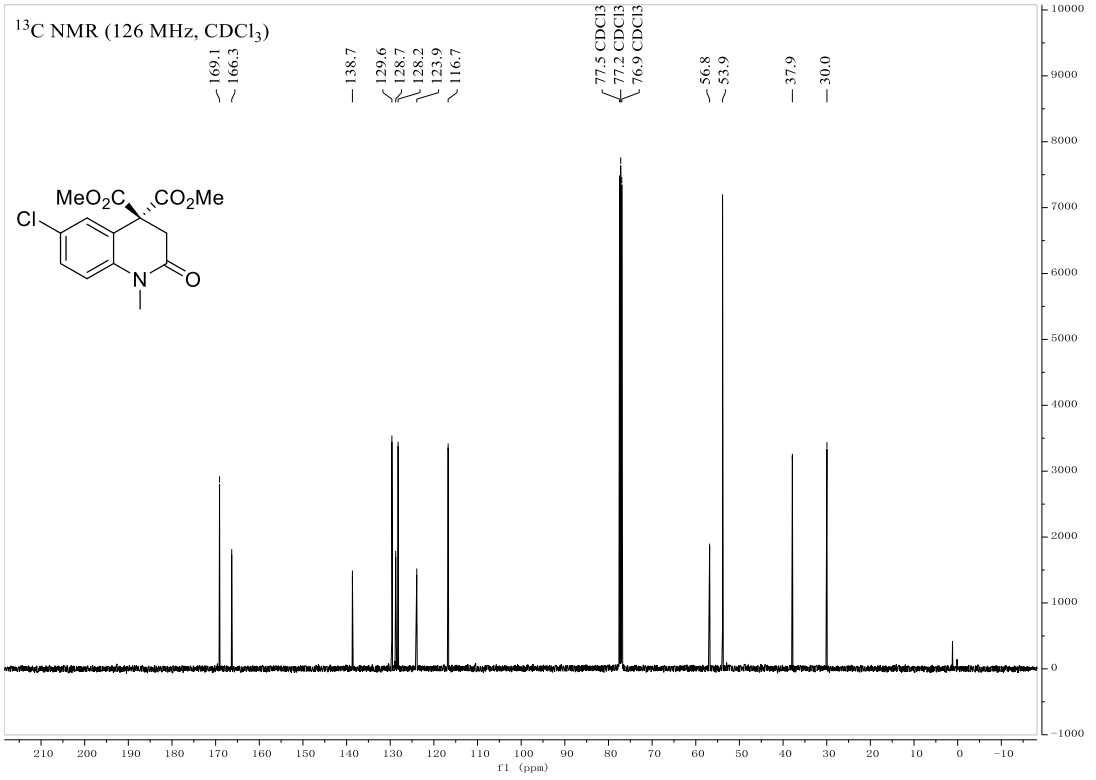


^{19}F NMR (471 MHz, $CDCl_3$)

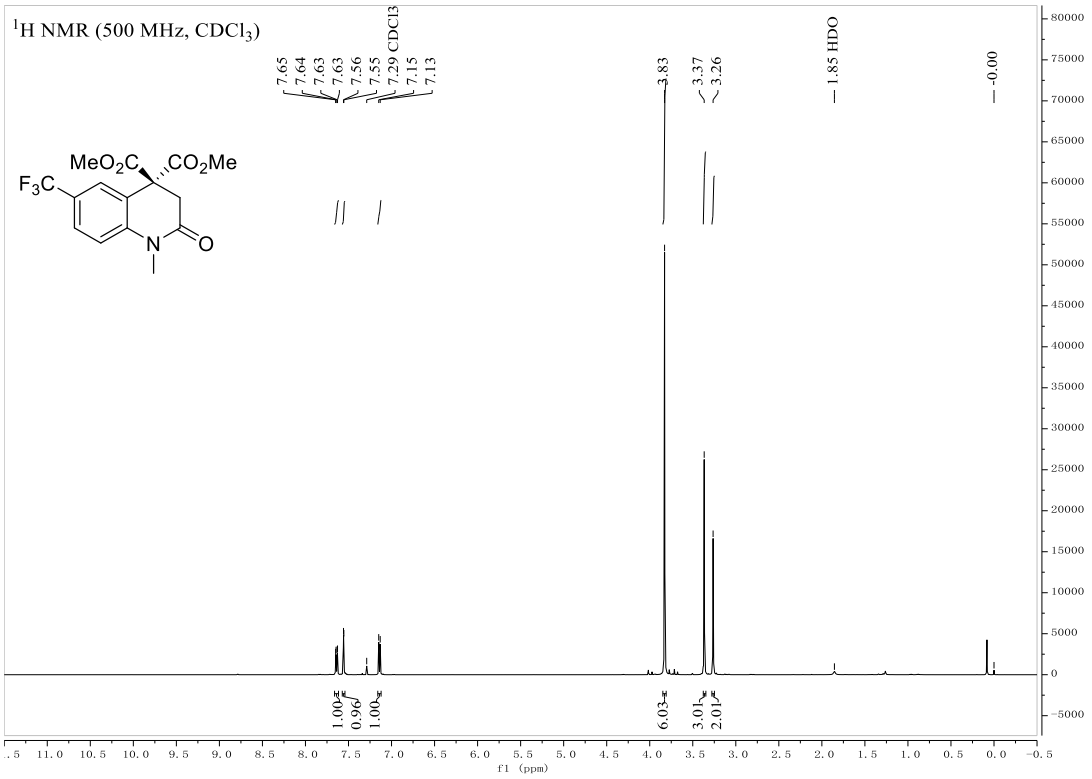


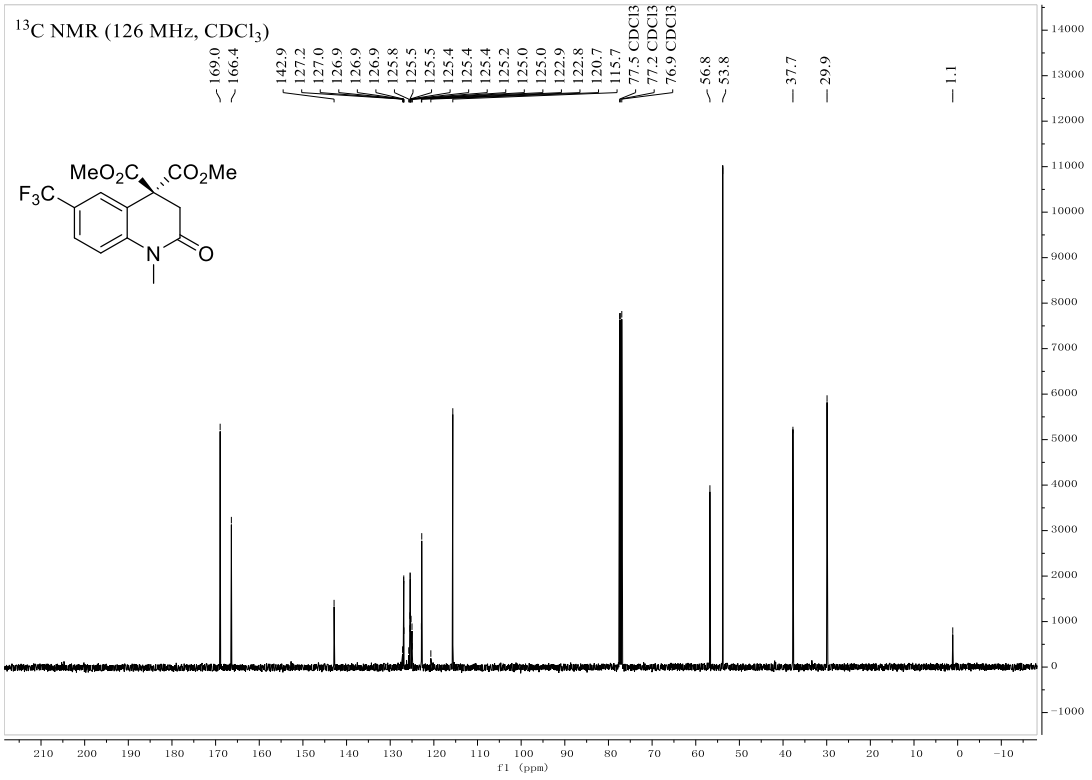
Compound 32

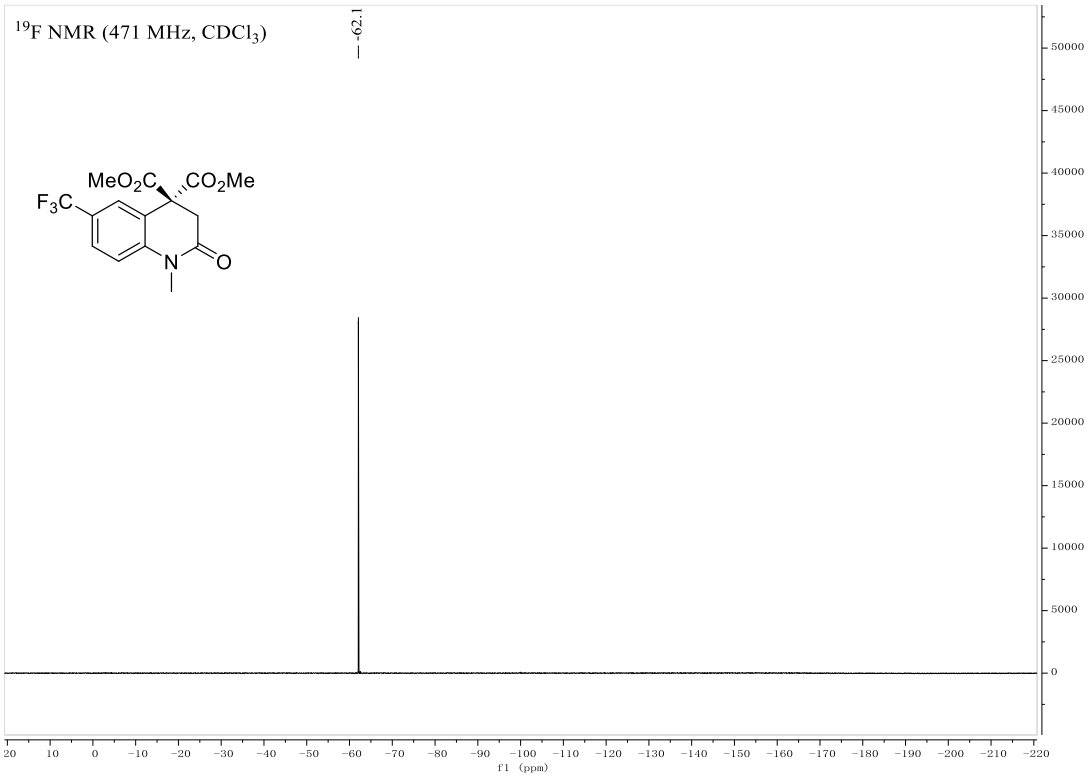

^{1}H NMR (500 MHz, $CDCl_3$)
7.35
7.35
7.34
7.33
7.27 CDCl3
7.26
7.25
6.98
6.96
3.82
3.32
3.23
1.71 HDO
-0.00
MeO2C
CO2Me
Cl
N
O
1.00
0.98
1.02
6.06
3.00
2.04
f1 (ppm)


^{13}C NMR (126 MHz, $CDCl_3$)
169.1
166.3
138.7
129.6
128.7
128.2
123.9
116.7
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
56.8
53.9
37.9
30.0
MeO2C
CO2Me
Cl
N
O
f1 (ppm)

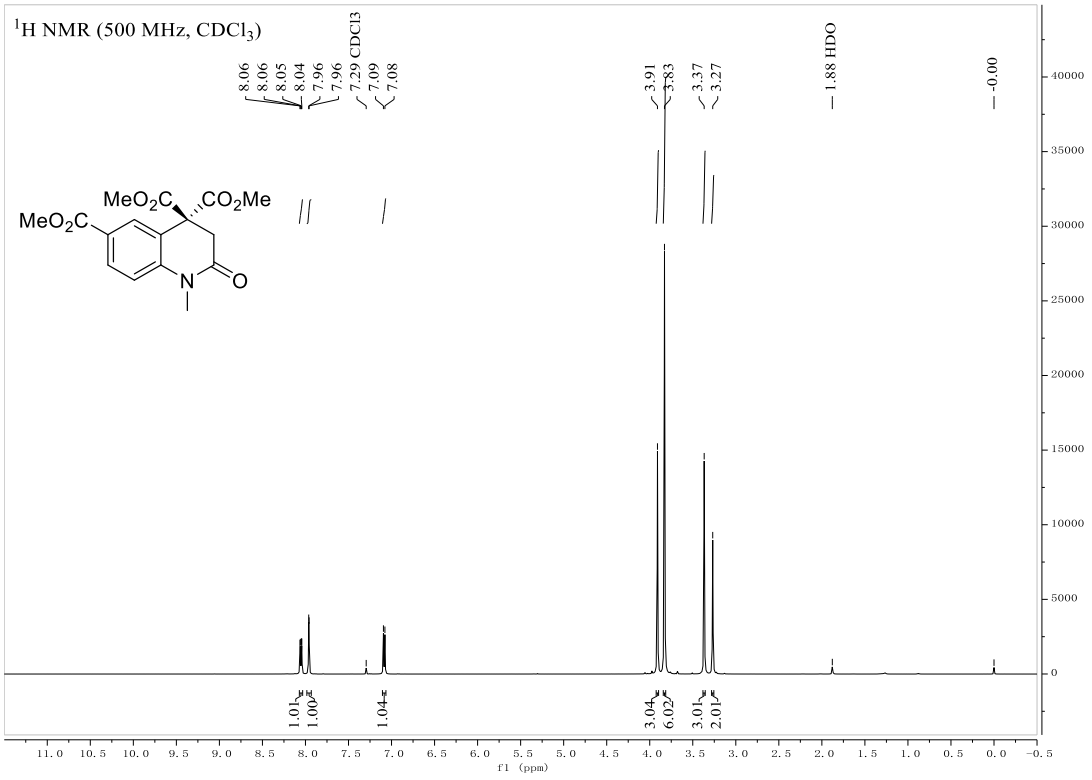
Compound 33

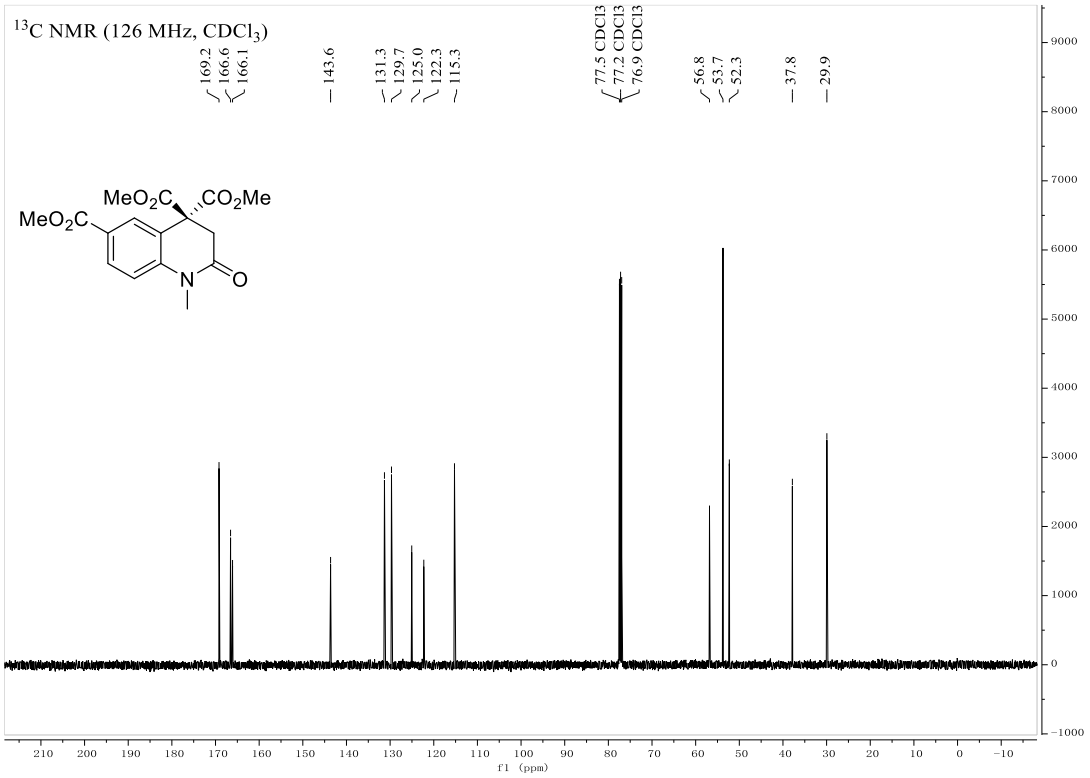

^{1}H NMR (500 MHz, $CDCl_3$)
7.65
7.64
7.63
7.63
7.56
7.55
7.29 CDCl3
7.15
7.13
3.83
3.37
3.26
1.85 HDO
0.00
MeO2C
CO2Me
F3C
N
O
1.00
0.96
1.00
6.03
3.01
2.01
f1 (ppm)


^{13}C NMR (126 MHz, $CDCl_3$)
169.0
166.4
142.9
127.2
127.0
126.9
126.9
126.9
125.8
125.5
125.5
125.4
125.4
125.4
125.2
125.0
125.0
122.9
122.8
120.7
115.7
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
56.8
53.8
37.7
29.9
1.1
MeO2C
CO2Me
F3C
N
O
f1 (ppm)

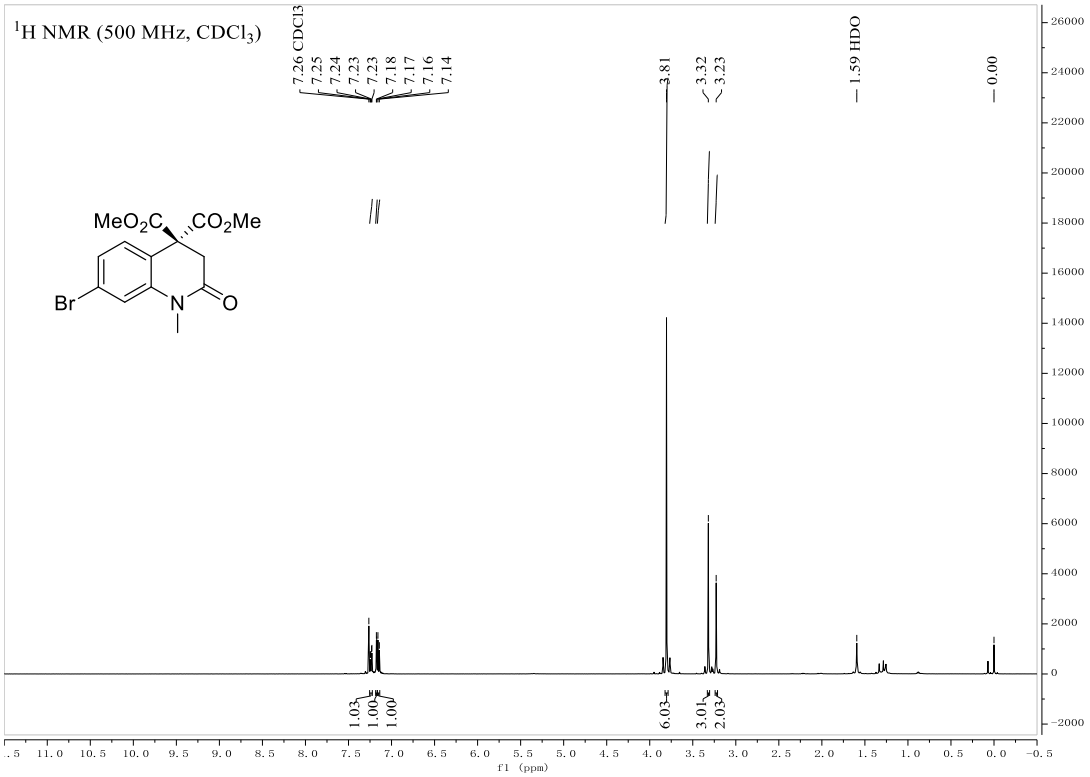

^{19}F NMR (471 MHz, $CDCl_3$)
-62.1
MeO_2C
CO_2Me
F_3C
N
O
f1 (ppm)

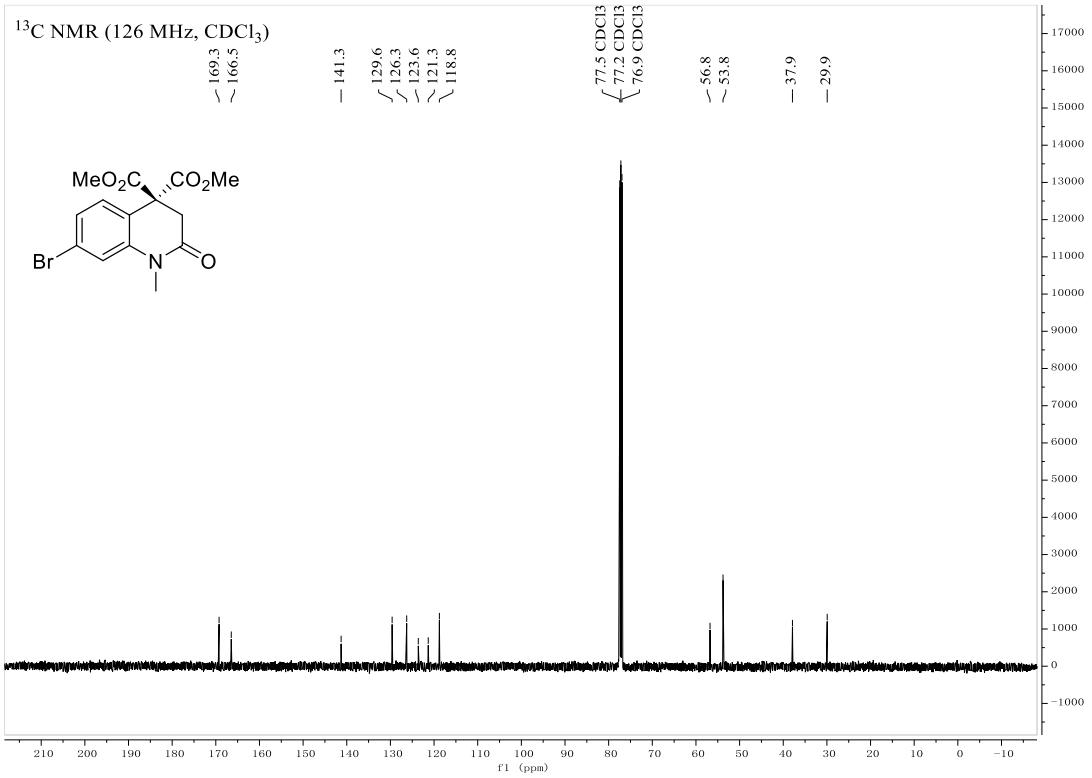
Compound 34


^{1}H NMR (500 MHz, $CDCl_3$)
8.06
8.06
8.05
8.04
7.96
7.96
7.29 CDCl3
7.09
7.08
3.91
3.83
3.37
3.27
1.88 HDO
-0.00
MeO_2C
CO_2Me
MeO_2C
N
O
1.01
1.00
1.04
3.04
6.02
3.01
2.01
f1 (ppm)

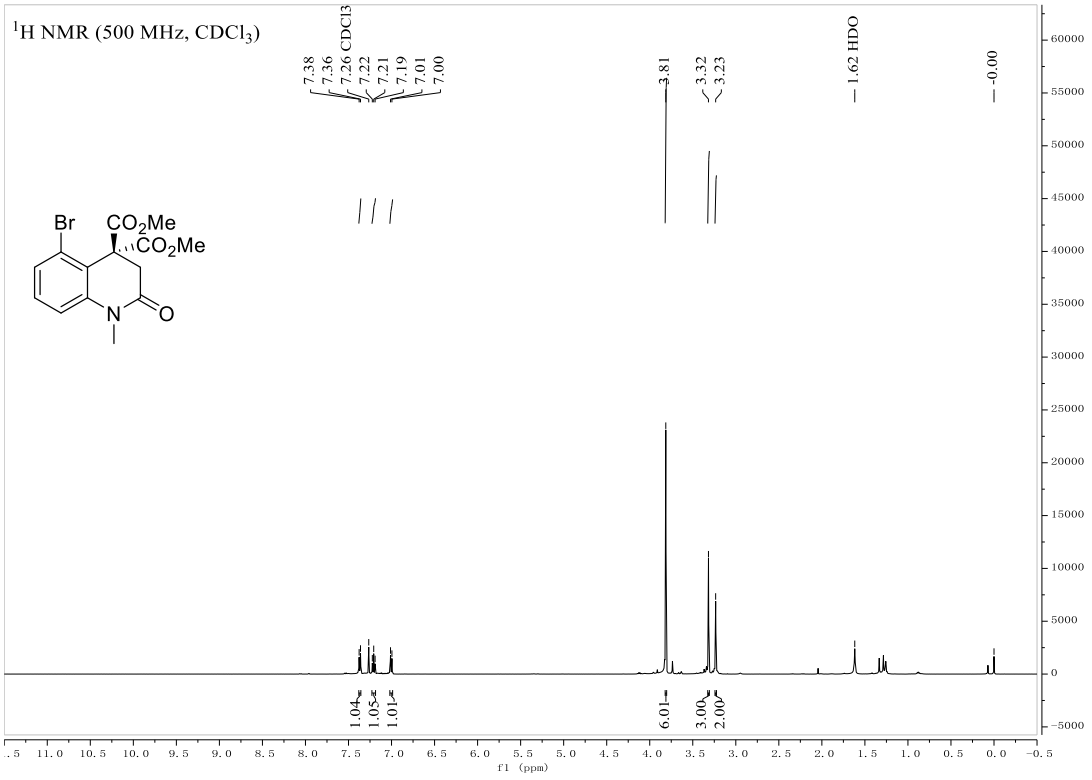

13C NMR (126 MHz, CDCl3)
169.2
166.6
166.1
143.6
131.3
129.7
125.0
122.3
115.3
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
56.8
53.7
52.3
37.8
29.9
MeO2C
CO2Me
MeO2C
N
O
f1 (ppm)

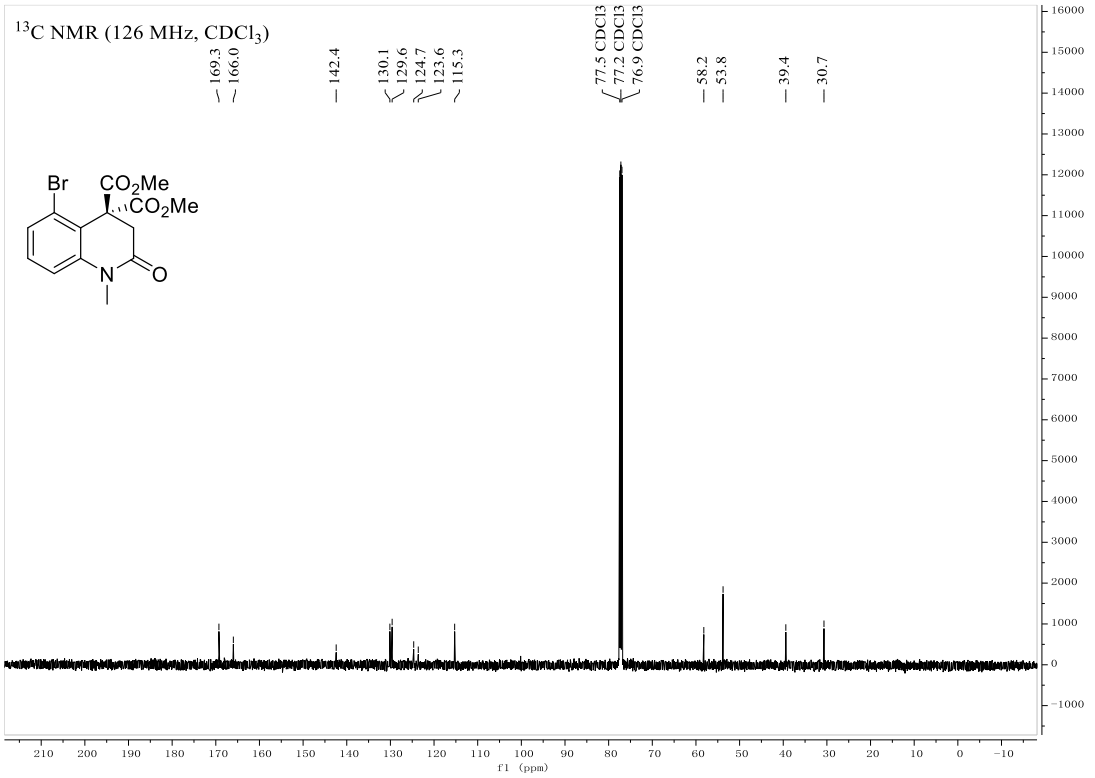
Compound 35


1H NMR (500 MHz, CDCl3)
7.26 CDCl3
7.25
7.24
7.23
7.23
7.18
7.17
7.16
7.14
3.81
3.32
3.23
1.59 HDO
0.00
MeO2C
CO2Me
Br
N
O
1.03
1.00
1.00
6.03
3.01
2.03
f1 (ppm)

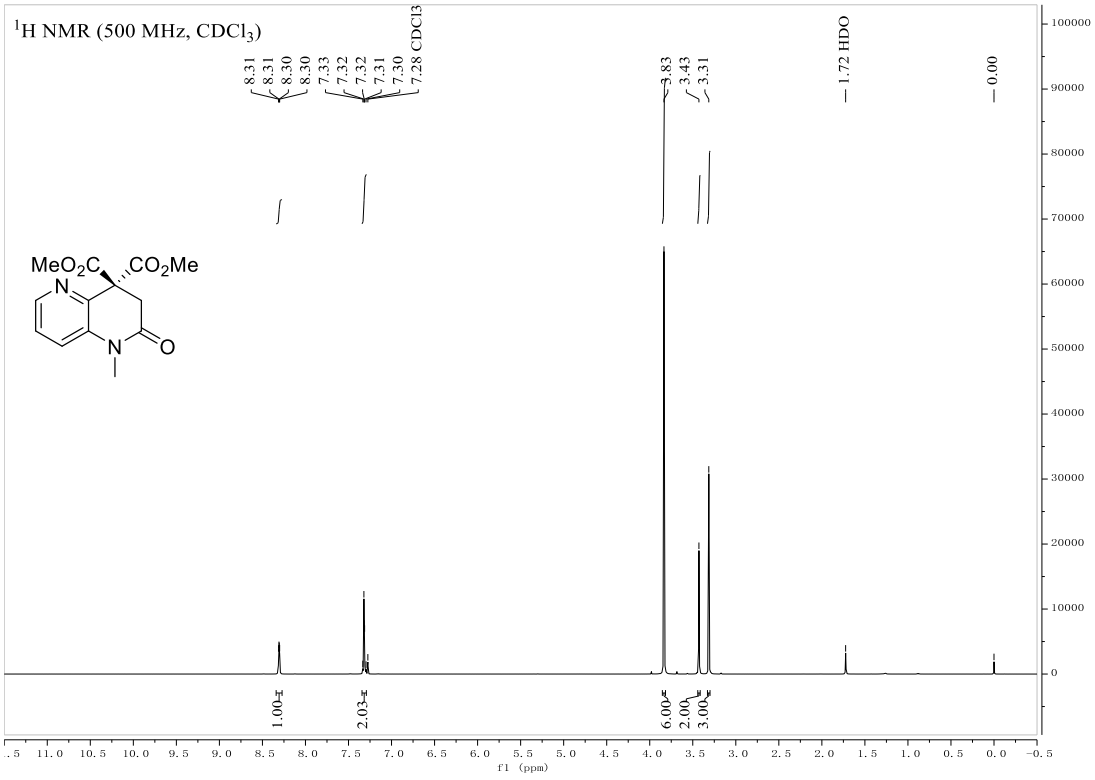

13C NMR (126 MHz, CDCl3)
169.3
166.5
141.3
129.6
126.3
123.6
121.3
118.8
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
56.8
53.8
37.9
29.9
MeO2C
CO2Me
Br
N
O
f1 (ppm)

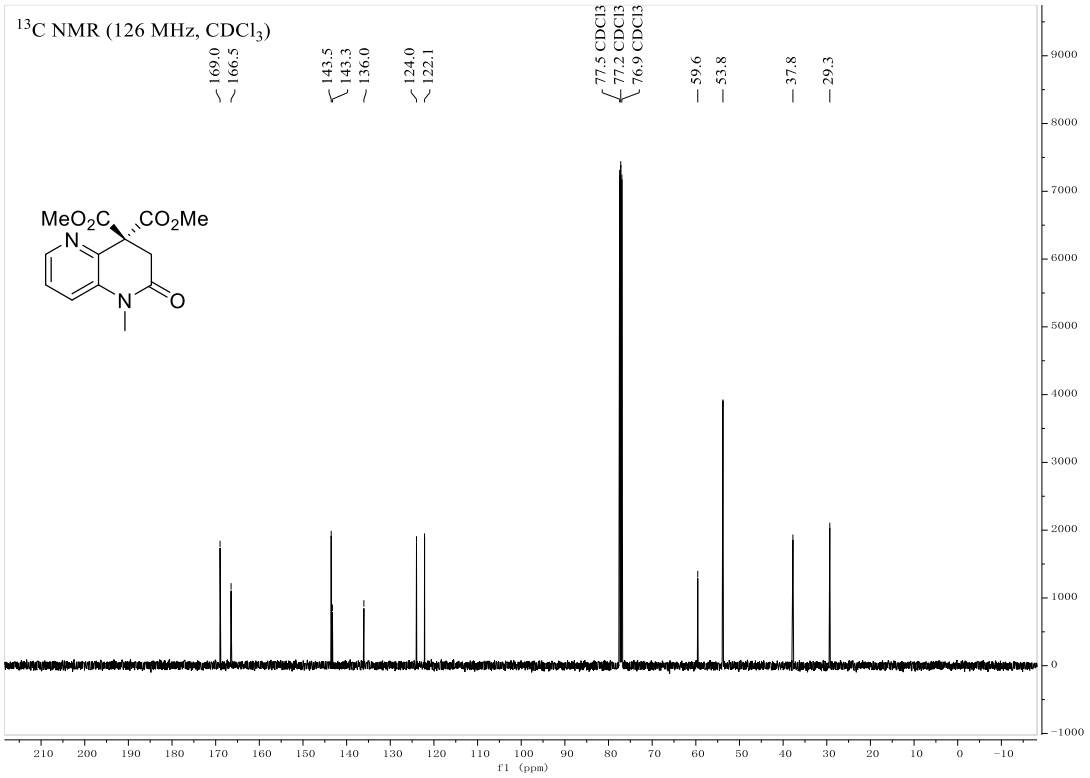
Compound 35’


1H NMR (500 MHz, CDCl3)
7.38
7.36
7.26 CDCl3
7.22
7.21
7.19
7.01
7.00
3.81
3.32
3.23
1.62 HDO
0.00
Br
CO2Me
CO2Me
N
O
1.04
1.05
1.01
6.01
3.00
2.00
f1 (ppm)

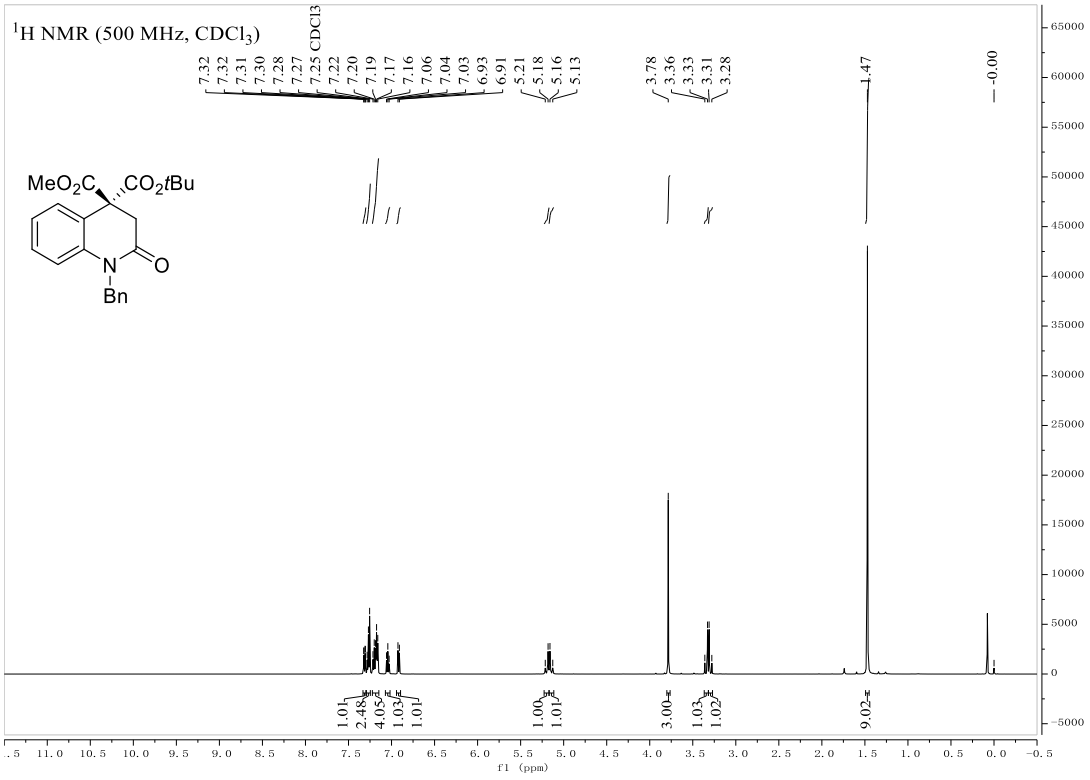

13C NMR (126 MHz, CDCl3)
169.3
166.0
142.4
130.1
129.6
124.7
123.6
115.3
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
58.2
53.8
39.4
30.7
Br
CO2Me
CO2Me
N
O
f1 (ppm)

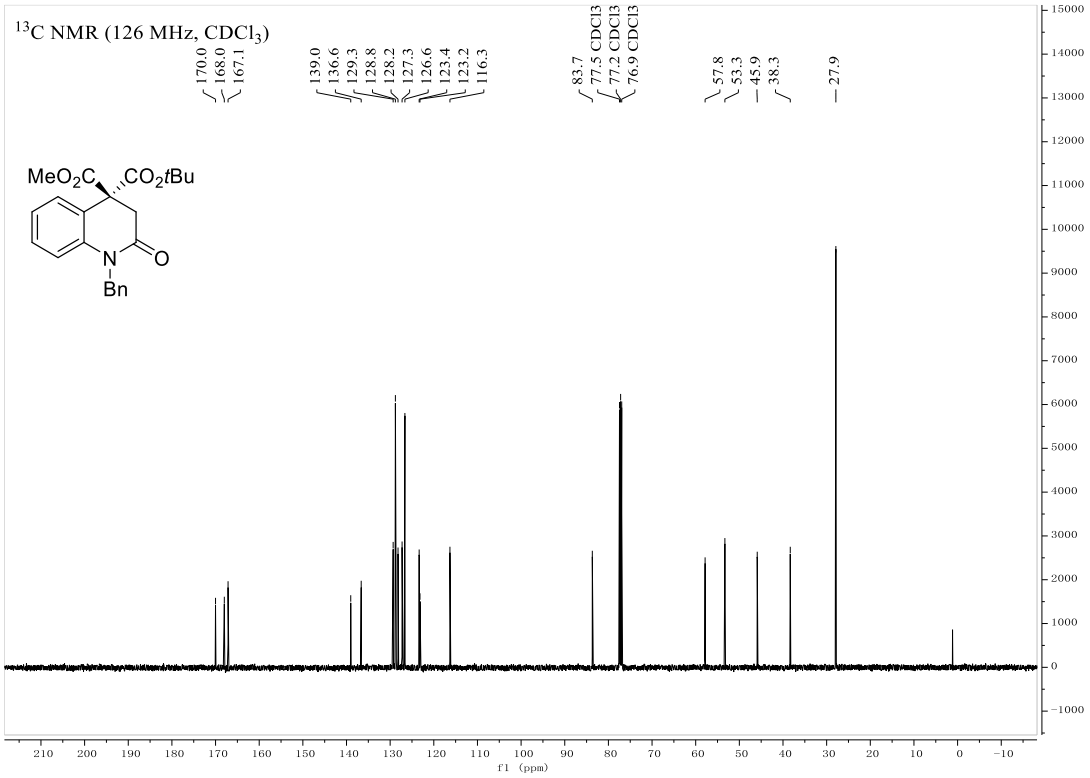
Compound 36


1H NMR (500 MHz, CDCl3)
8.31
8.31
8.30
8.30
7.33
7.32
7.32
7.31
7.30
7.28 CDCl3
3.83
3.43
3.31
1.72 HDO
0.00
MeO2C
CO2Me
N
N
O
1.00
2.03
6.00
2.00
3.00
f1 (ppm)

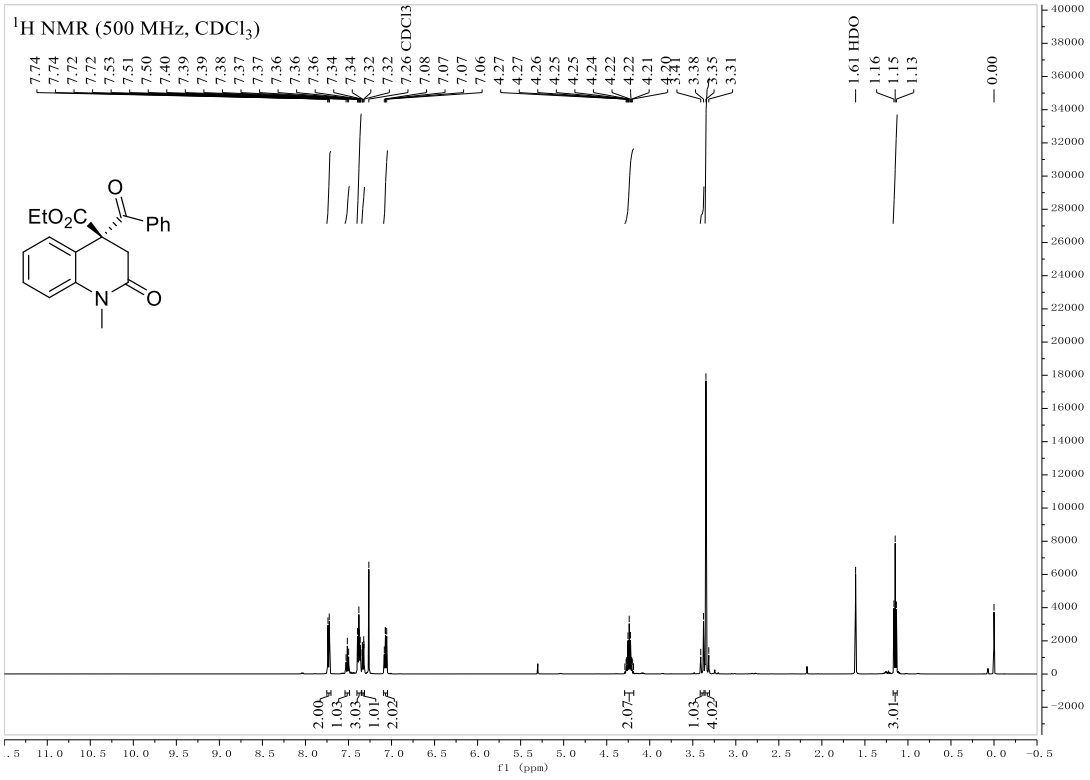

13C NMR (126 MHz, CDCl3)
169.0
166.5
143.5
143.3
136.0
124.0
122.1
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
59.6
53.8
37.8
29.3
MeO2C
CO2Me
N
O
f1 (ppm)

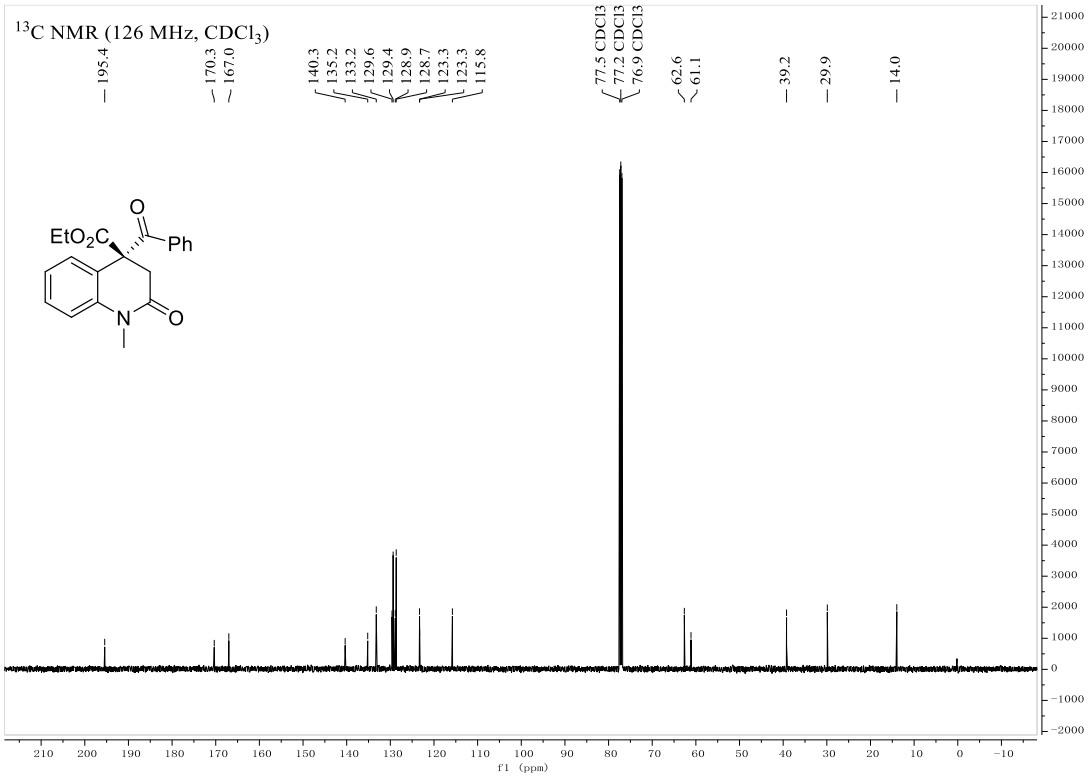
Compound 37


1H NMR (500 MHz, CDCl3)
7.32
7.32
7.31
7.30
7.28
7.27
7.25 CDCl3
7.22
7.20
7.19
7.17
7.16
7.06
7.04
7.03
6.93
6.91
5.21
5.18
5.16
5.13
3.78
3.36
3.33
3.31
3.28
1.47
-0.00
MeO2C
CO2tBu
N
O
Bn
1.01
2.48
4.05
1.03
1.01
1.00
1.01
3.00
1.03
1.02
9.02
f1 (ppm)

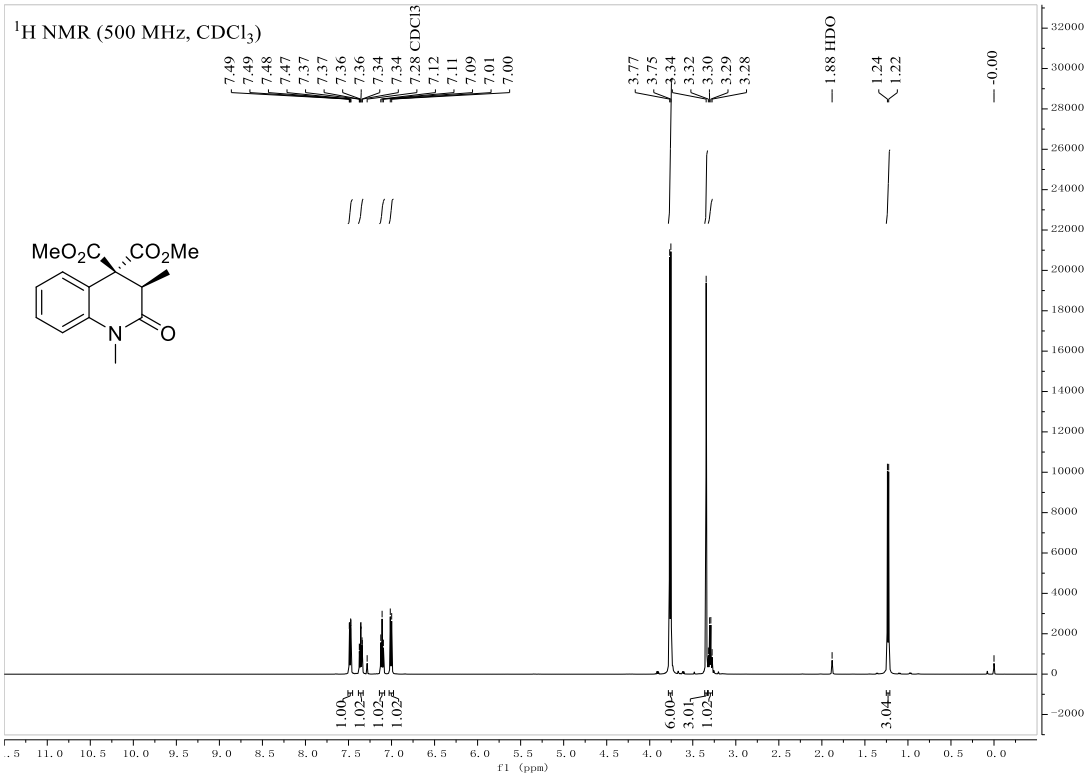

13C NMR (126 MHz, CDCl3)
170.0
168.0
167.1
139.0
136.6
129.3
128.8
128.2
127.3
126.6
123.4
123.2
116.3
83.7
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
57.8
53.3
45.9
38.3
27.9
MeO2C
CO2tBu
N
Bn
O
f1 (ppm)

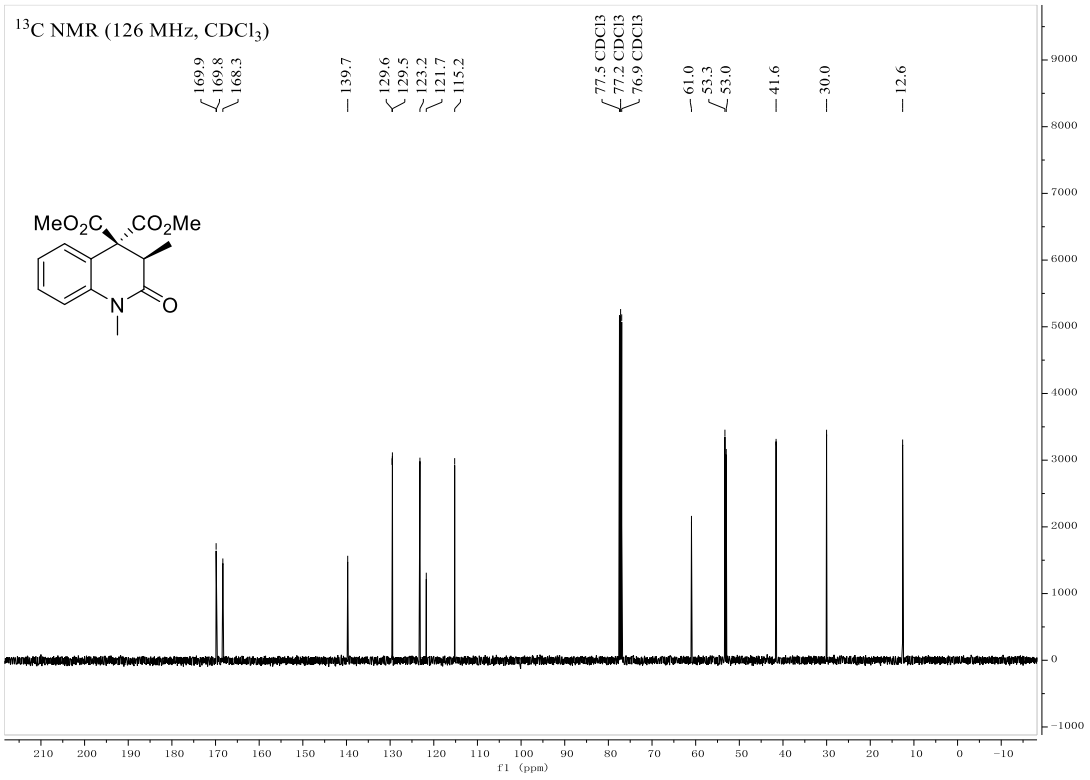
Compound 38


1H NMR (500 MHz, CDCl3)
7.74
7.74
7.72
7.72
7.53
7.51
7.50
7.40
7.39
7.39
7.38
7.37
7.37
7.36
7.36
7.36
7.34
7.34
7.32
7.26 CDCl3
7.08
7.07
7.07
7.06
4.27
4.27
4.26
4.25
4.25
4.24
4.22
4.22
4.21
4.20
3.41
3.38
3.35
3.31
1.61 HDO
1.16
1.15
1.13
0.00
EtO2C
Ph
O
N
O
2.00
1.03
3.03
1.01
2.02
2.07
1.03
4.02
3.01
f1 (ppm)


13C NMR (126 MHz, CDCl3)
195.4
170.3
167.0
140.3
135.2
133.2
129.6
129.4
128.9
128.7
123.3
123.3
115.8
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
62.6
61.1
39.2
29.9
14.0
EtO2C
Ph
O
N
O
f1 (ppm)

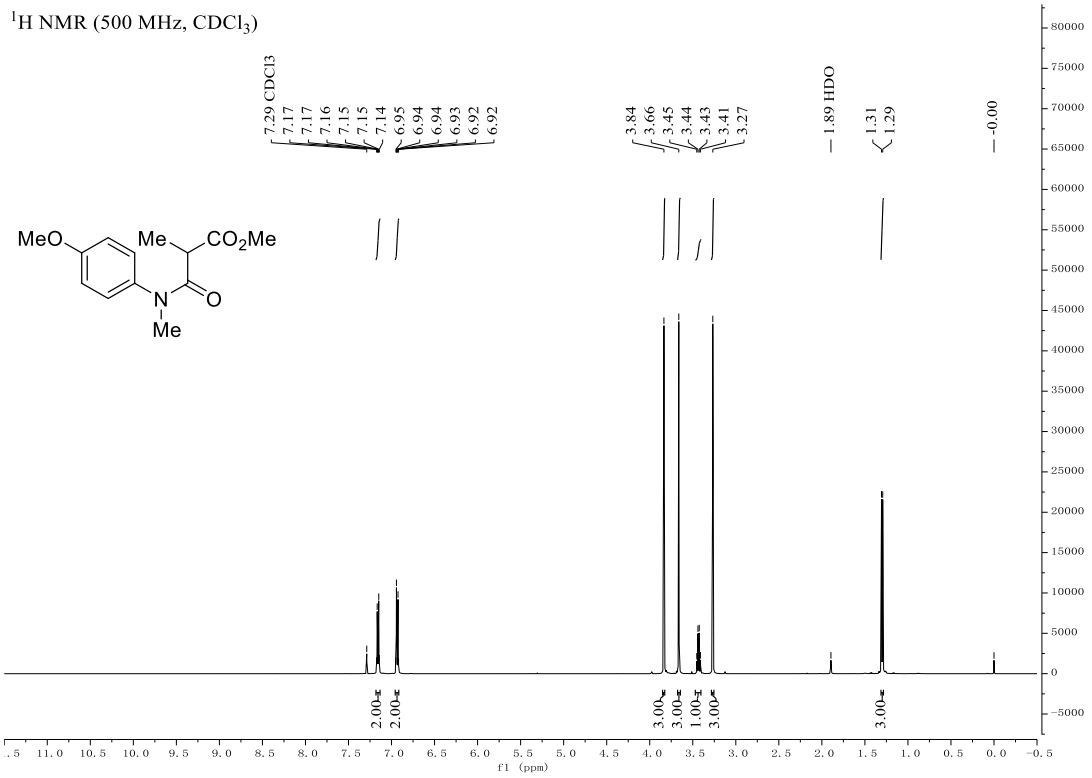
Compound 39


1H NMR (500 MHz, CDCl3)
7.49
7.49
7.48
7.47
7.37
7.37
7.36
7.36
7.34
7.34
7.28 CDCl3
7.12
7.11
7.09
7.01
7.00
3.77
3.75
3.34
3.32
3.30
3.29
3.28
1.88 HDO
1.24
1.22
-0.00
MeO2C
CO2Me
N
O
1.00
1.02
1.03
1.02
6.00
3.01
1.02
3.04
f1 (ppm)

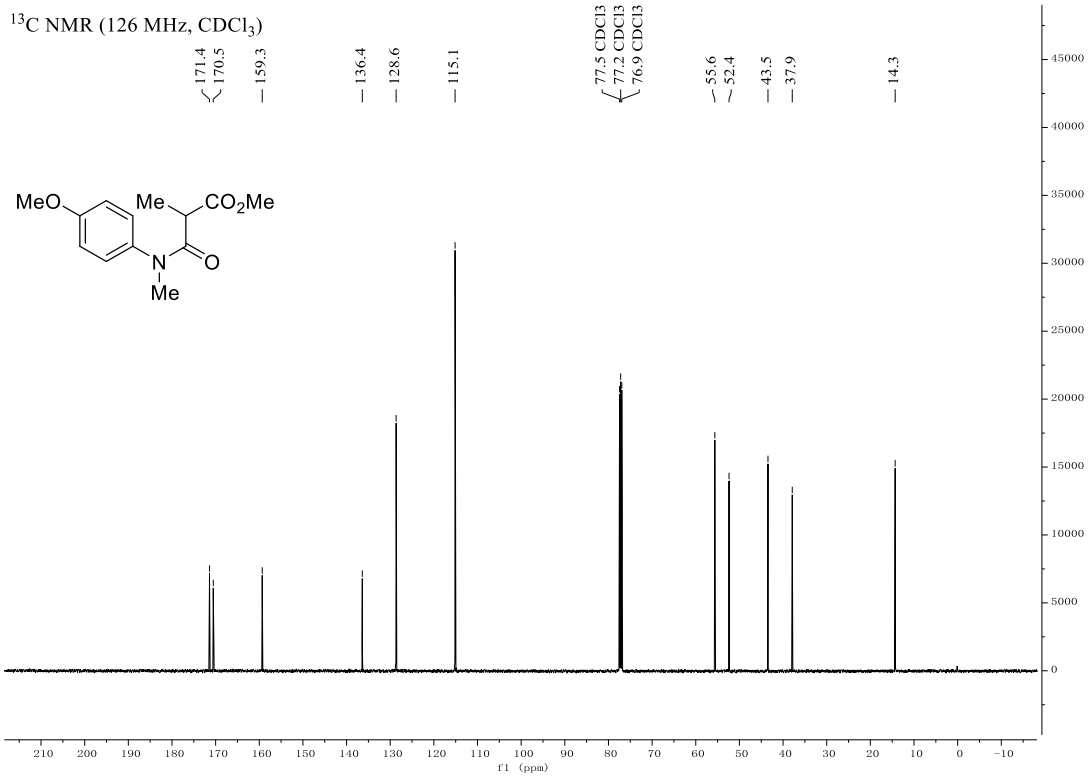

13C NMR (126 MHz, CDCl3)
169.9
169.8
168.3
139.7
129.6
129.5
123.2
121.7
115.2
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
61.0
53.3
53.0
41.6
30.0
12.6
MeO2C
CO2Me
N
O
f1 (ppm)

Compound S3

^{1}H NMR (500 MHz, $CDCl_3$)

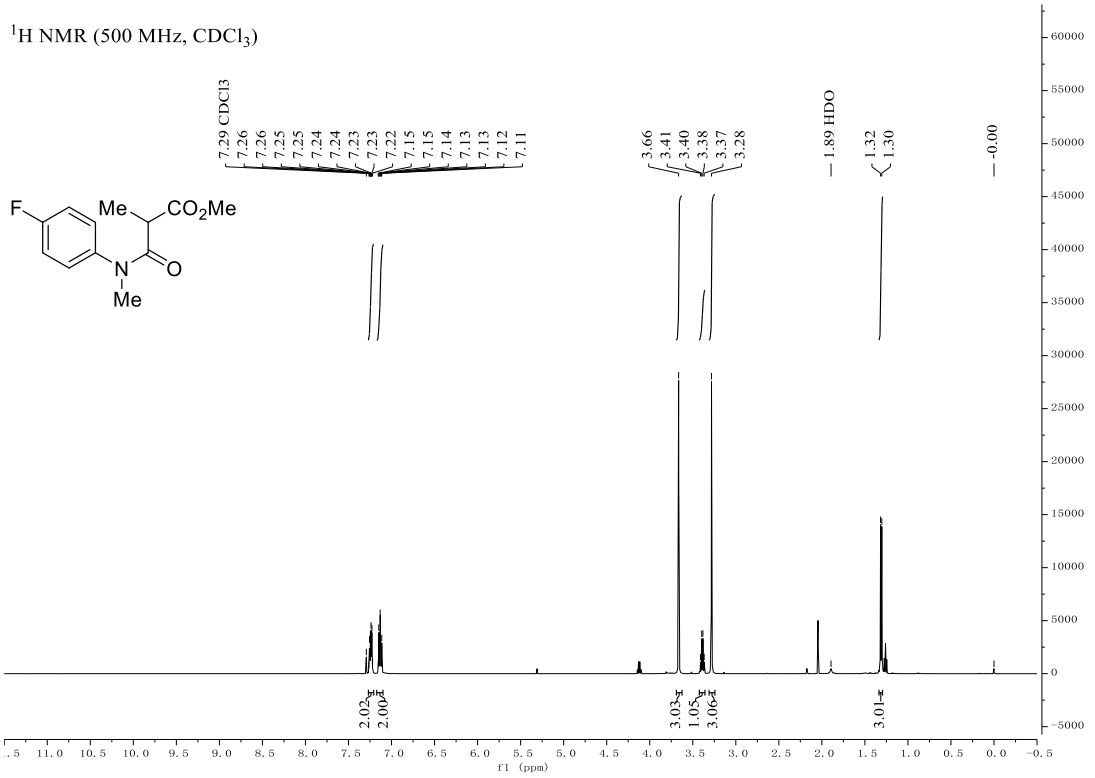


^{13}C NMR (126 MHz, $CDCl_3$)

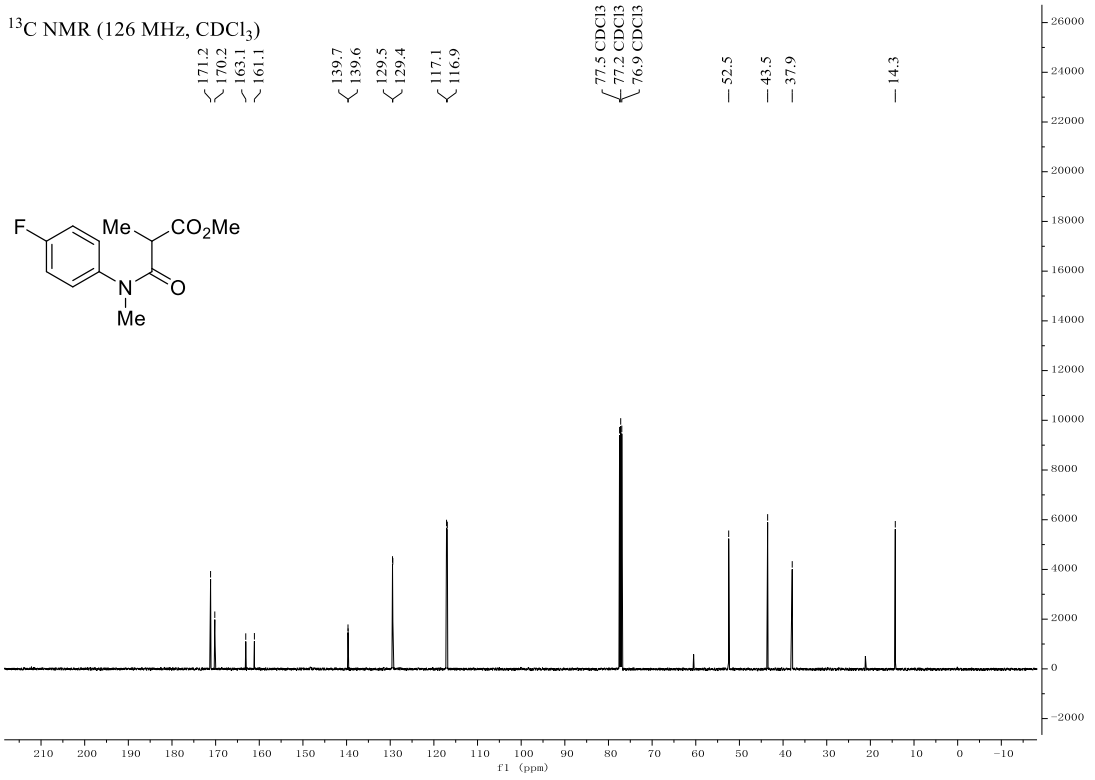


Compound S5

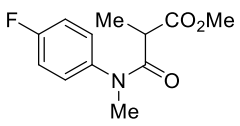
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

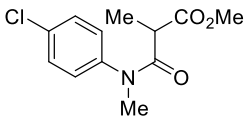


^{19}F NMR (471 MHz, $CDCl_3$)

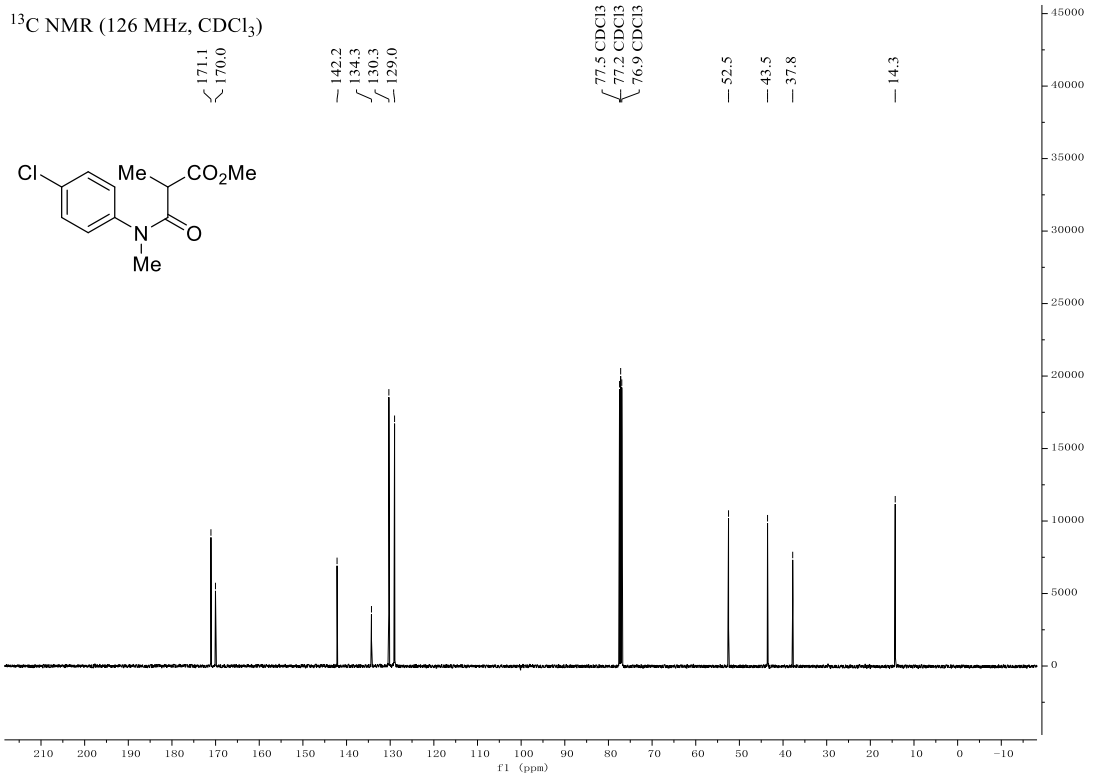


Compound S7

^{1}H NMR (500 MHz, $CDCl_3$)

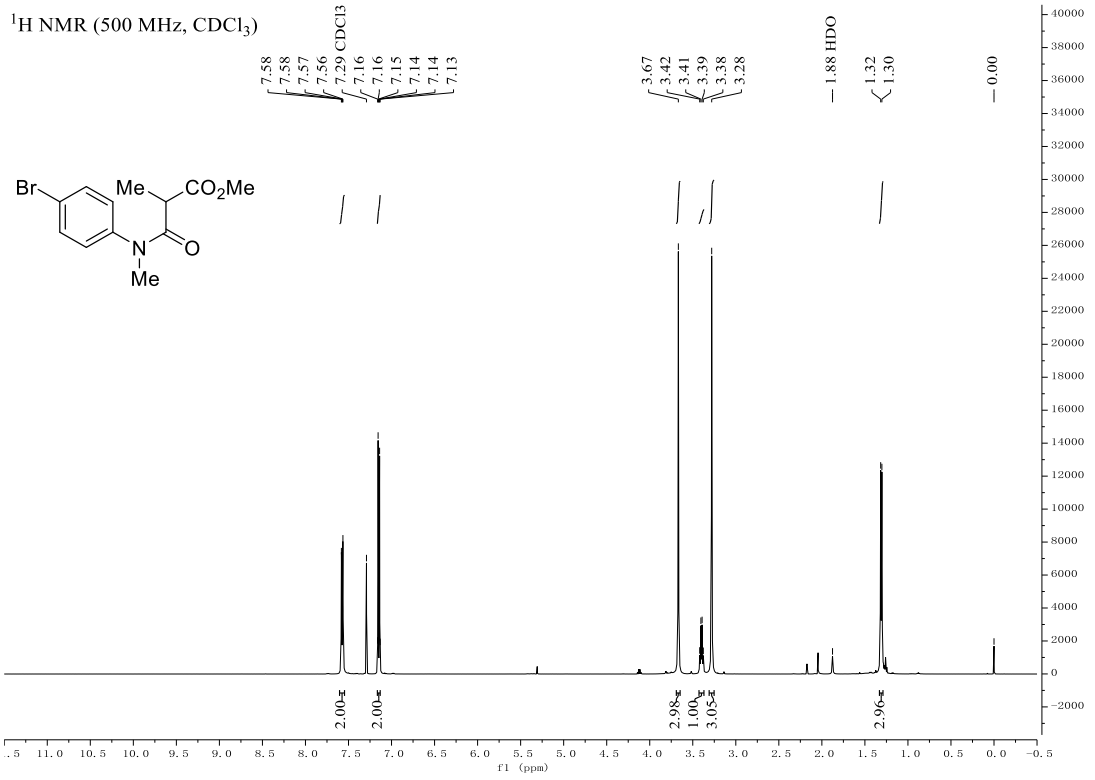


^{13}C NMR (126 MHz, $CDCl_3$)

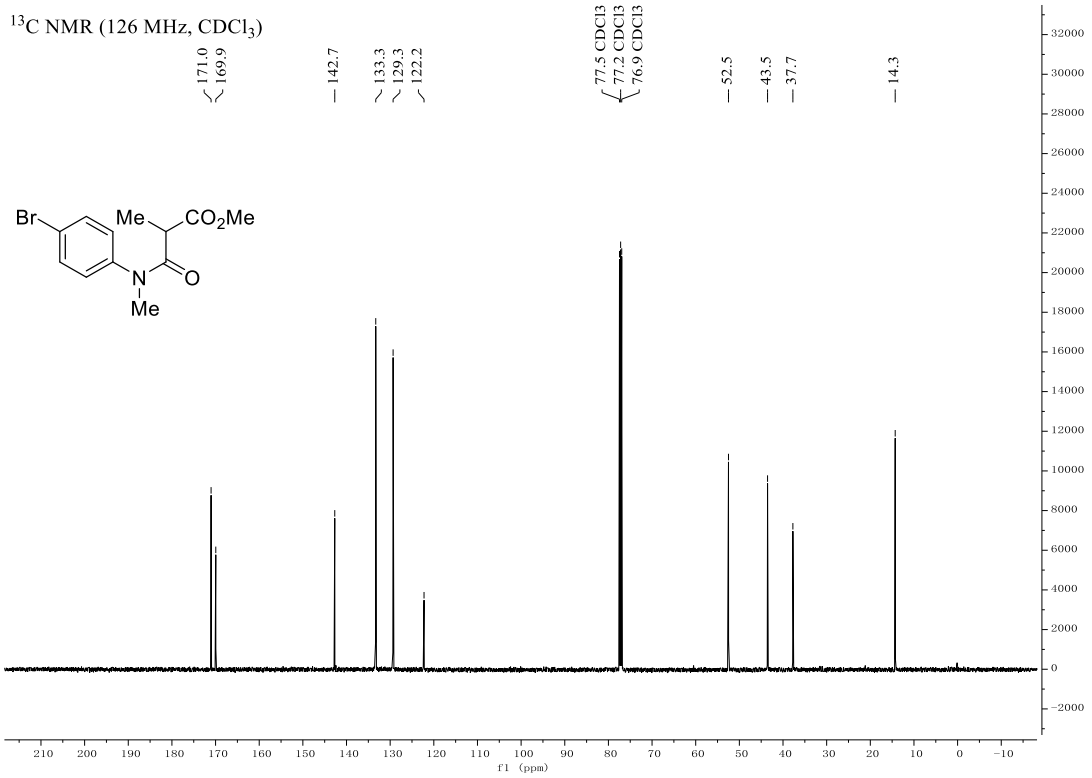


Compound S9

^{1}H NMR (500 MHz, $CDCl_3$)

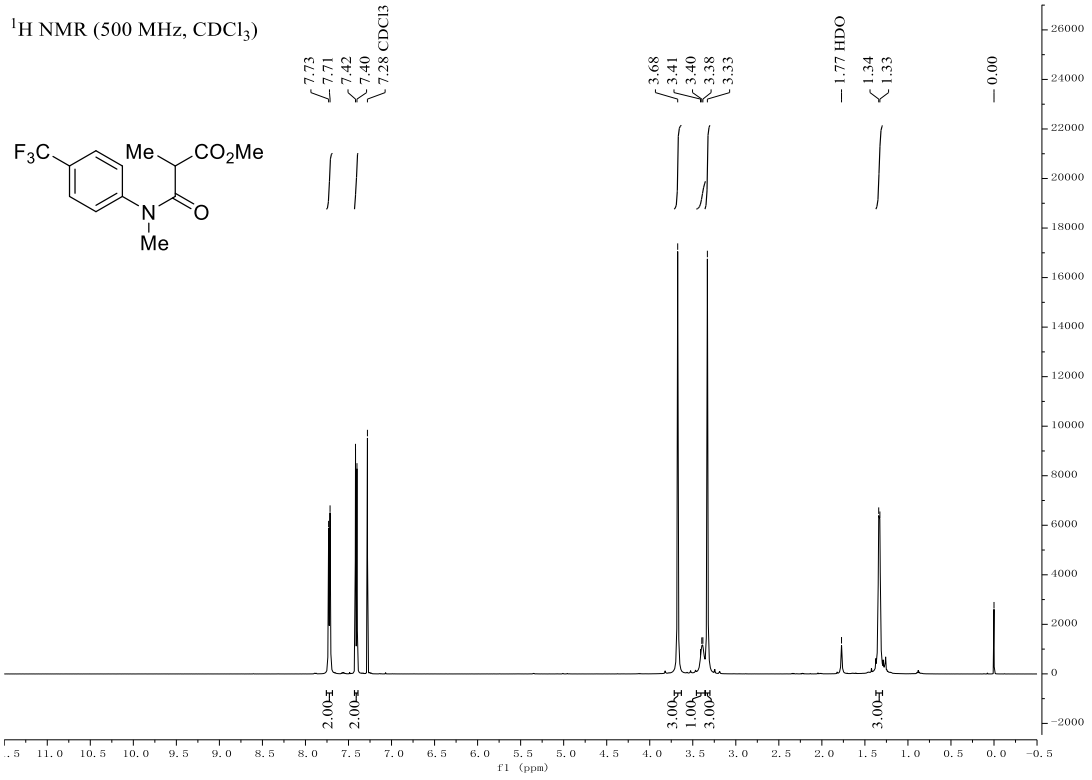


^{13}C NMR (126 MHz, $CDCl_3$)

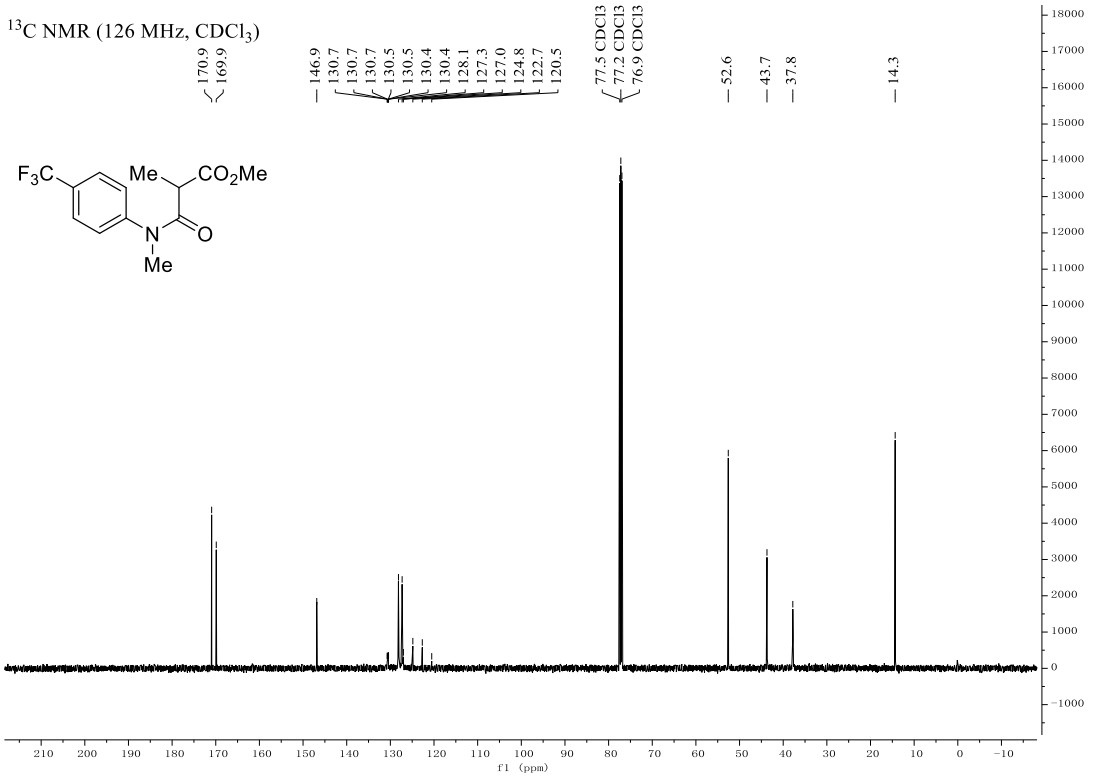


Compound S11

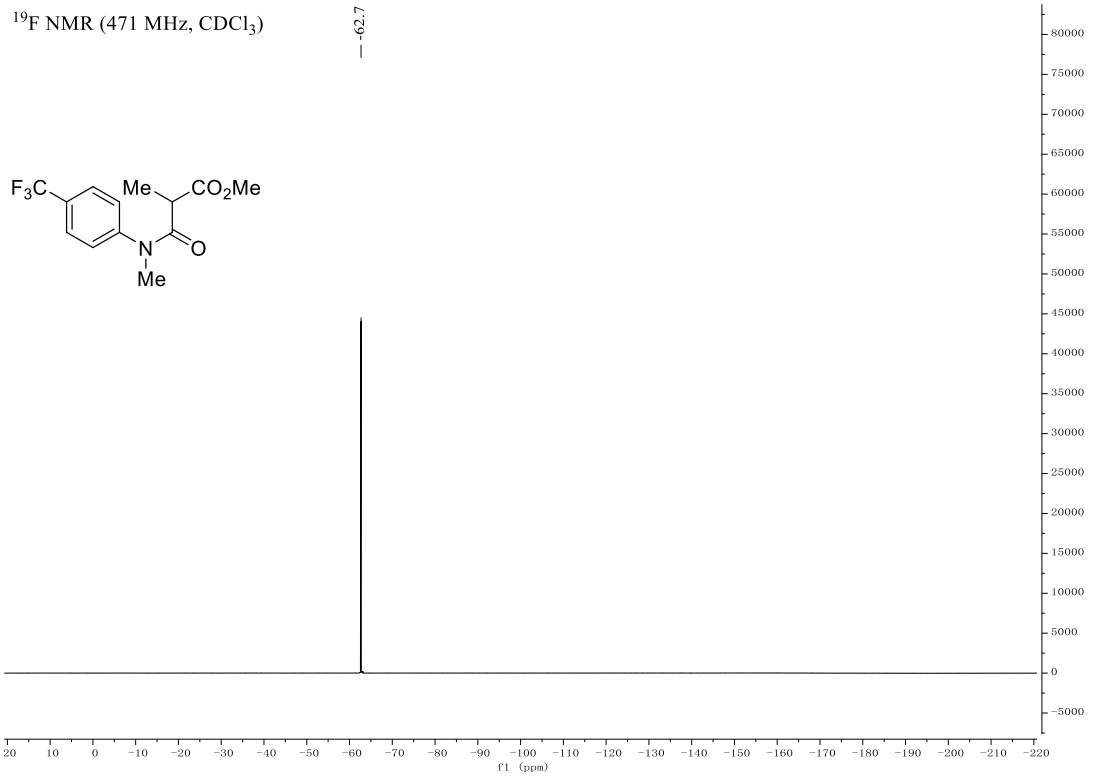
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

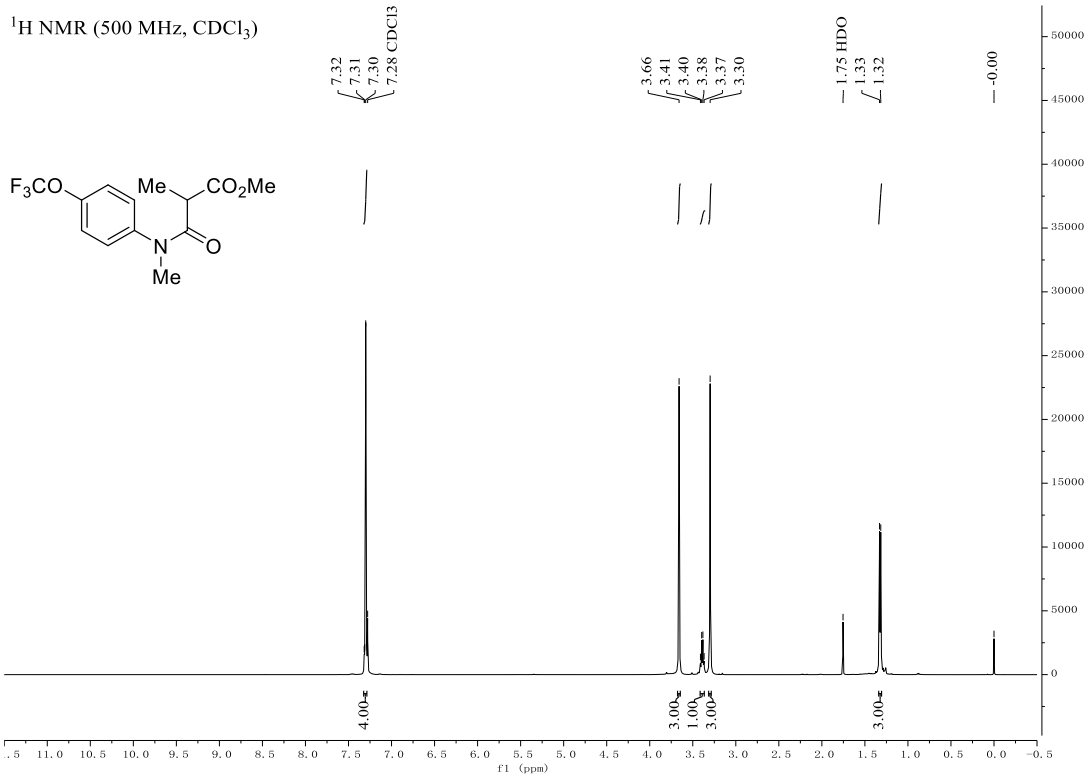


^{19}F NMR (471 MHz, $CDCl_3$)

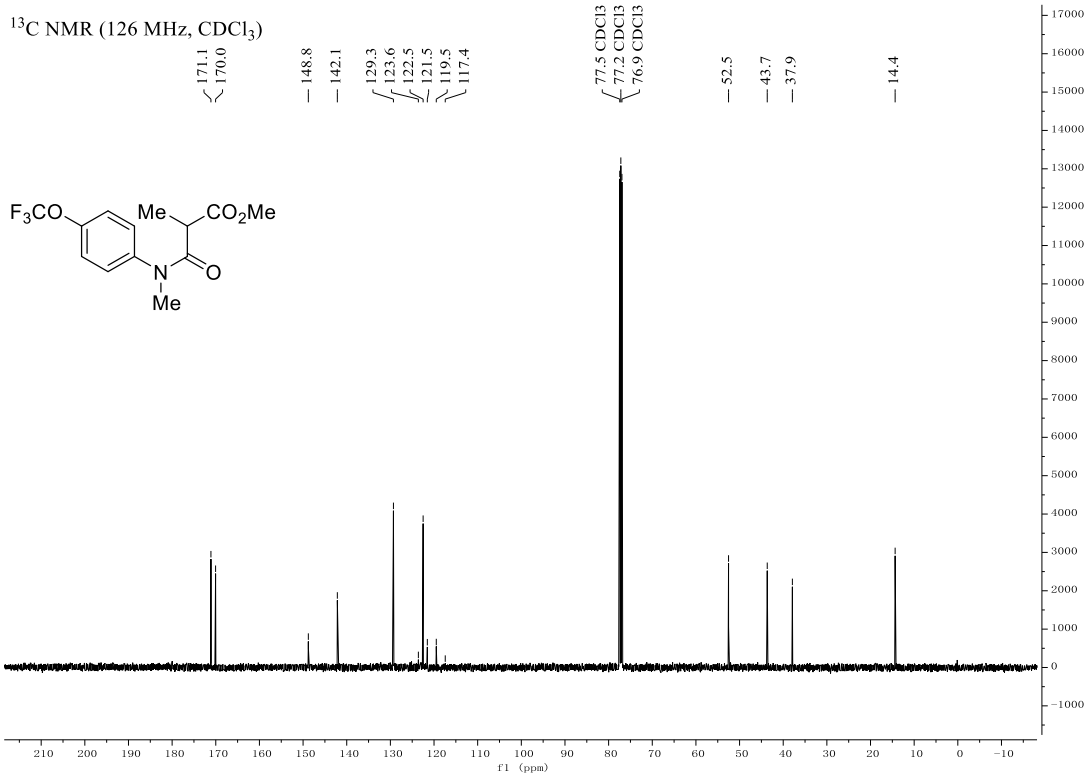


Compound S13

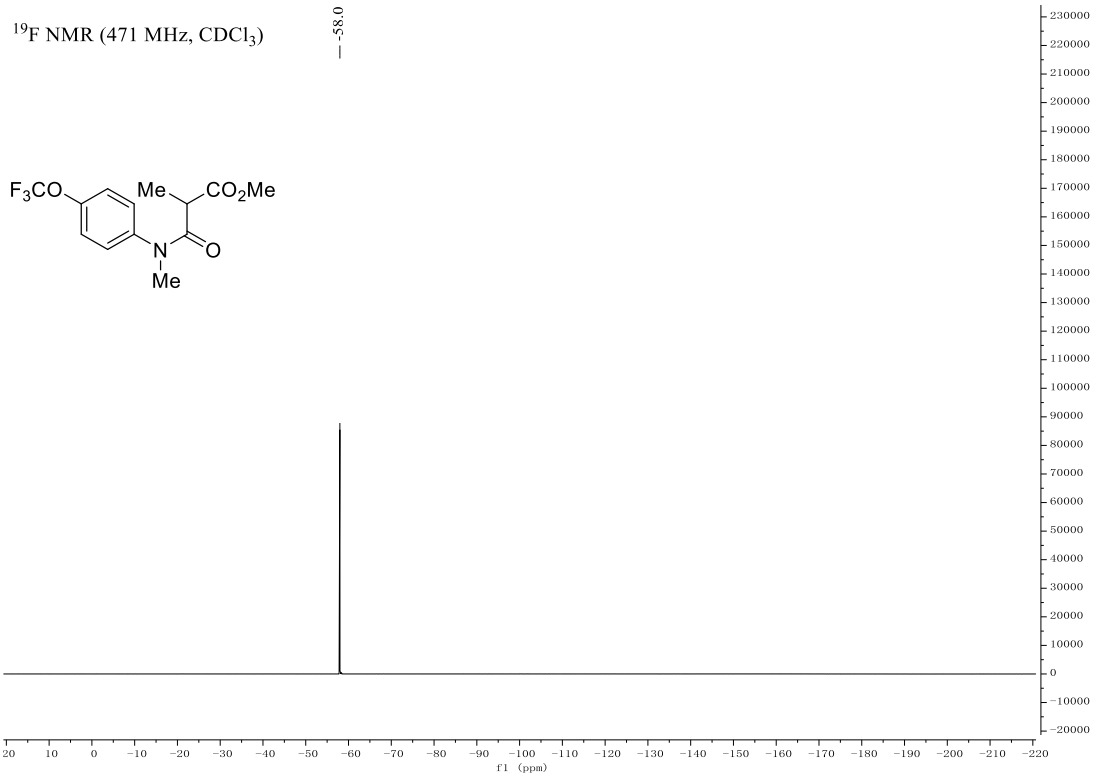
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

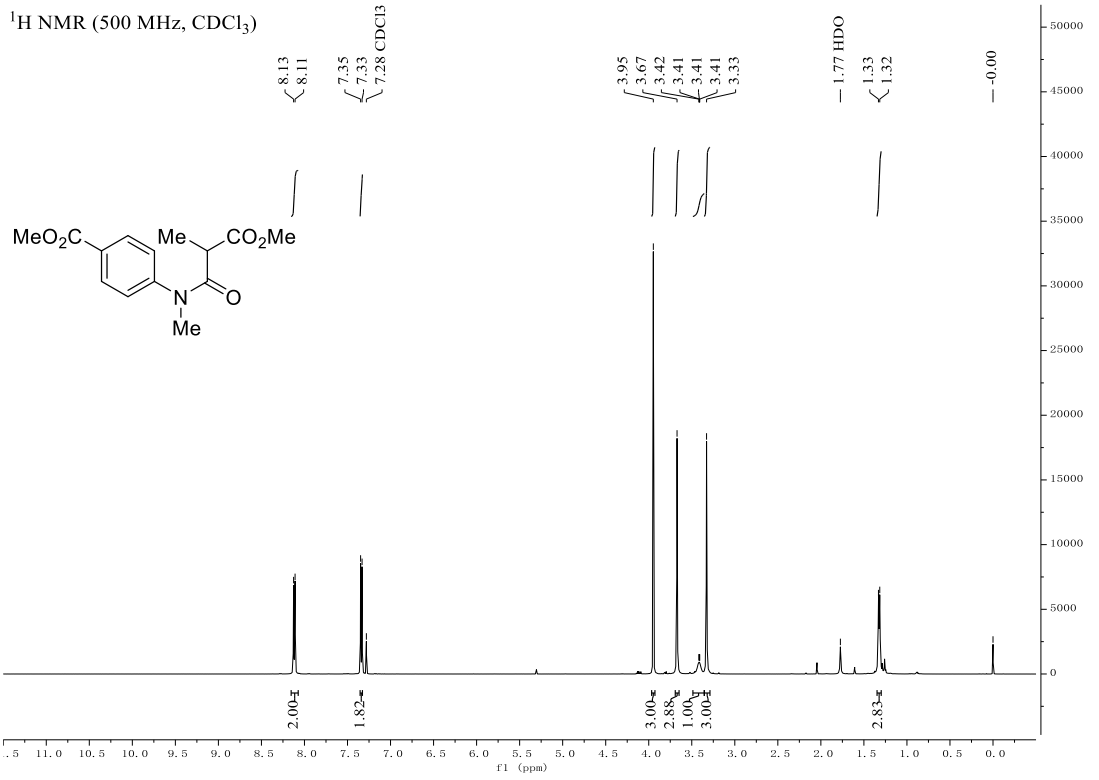


^{19}F NMR (471 MHz, $CDCl_3$)

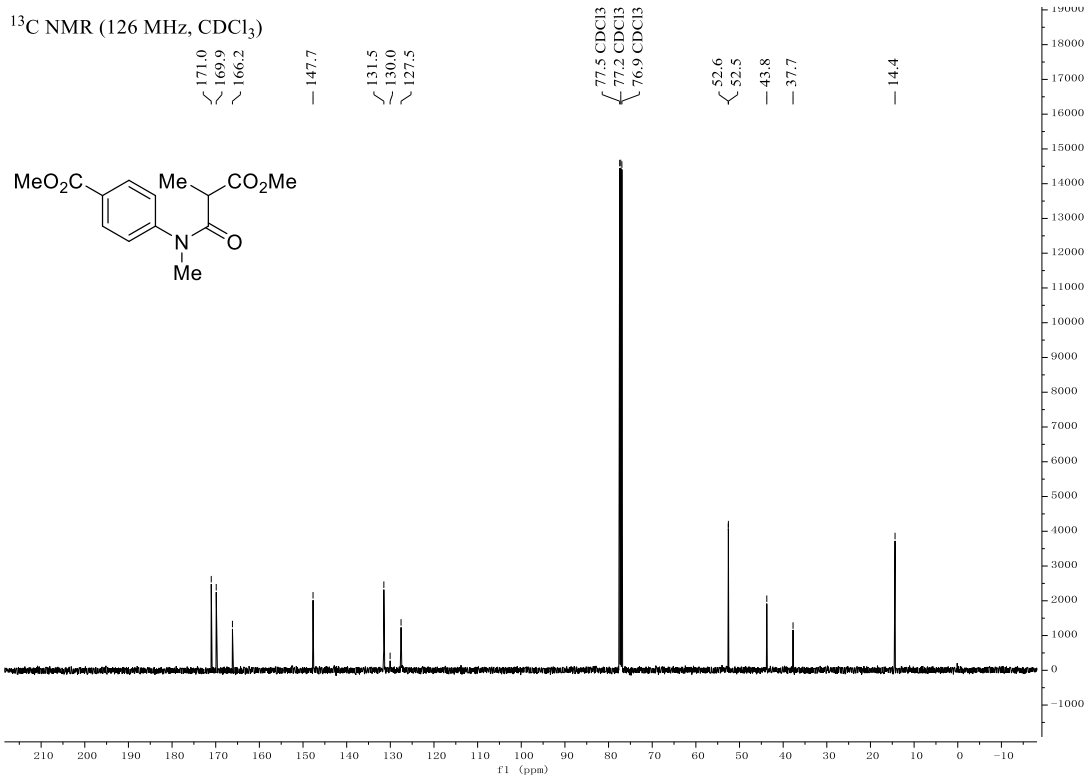


Compound S15

^{1}H NMR (500 MHz, $CDCl_3$)

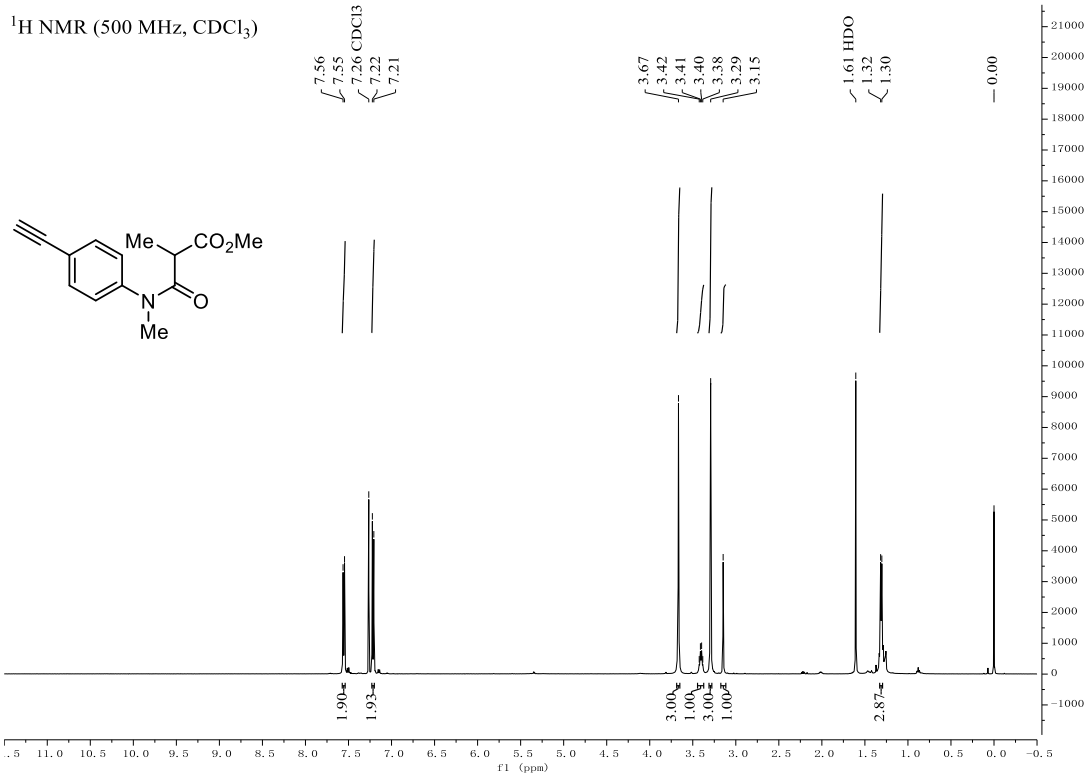


^{13}C NMR (126 MHz, $CDCl_3$)

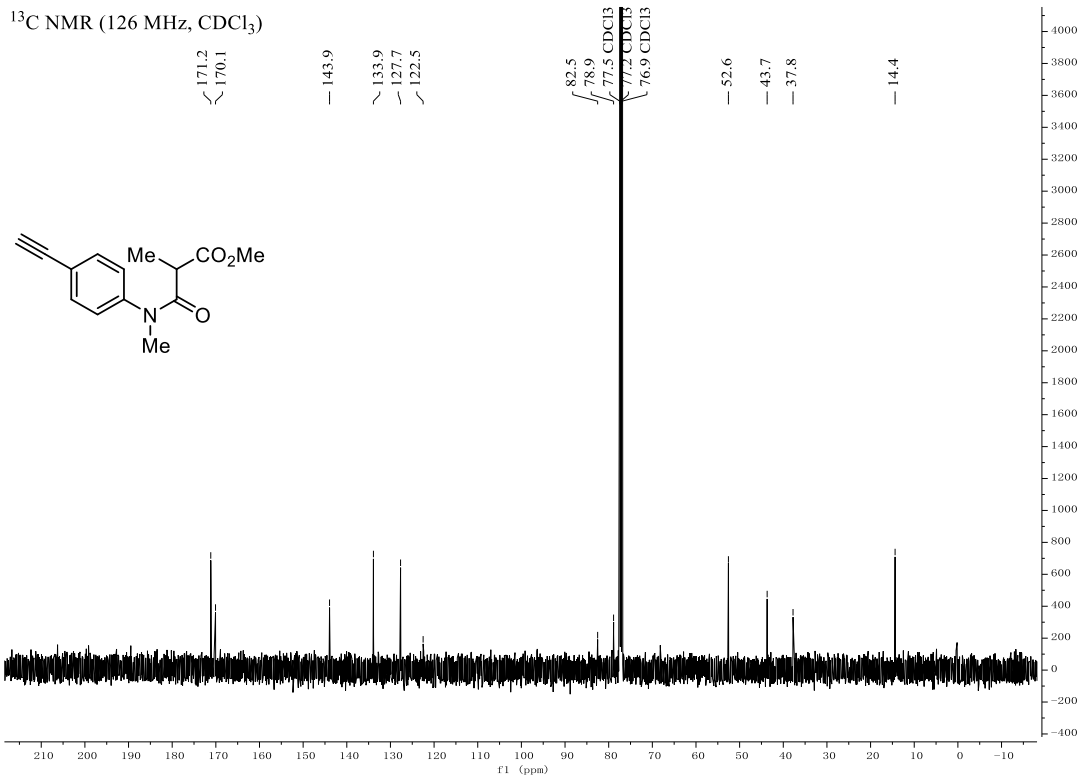


Compound S17

^{1}H NMR (500 MHz, $CDCl_3$)

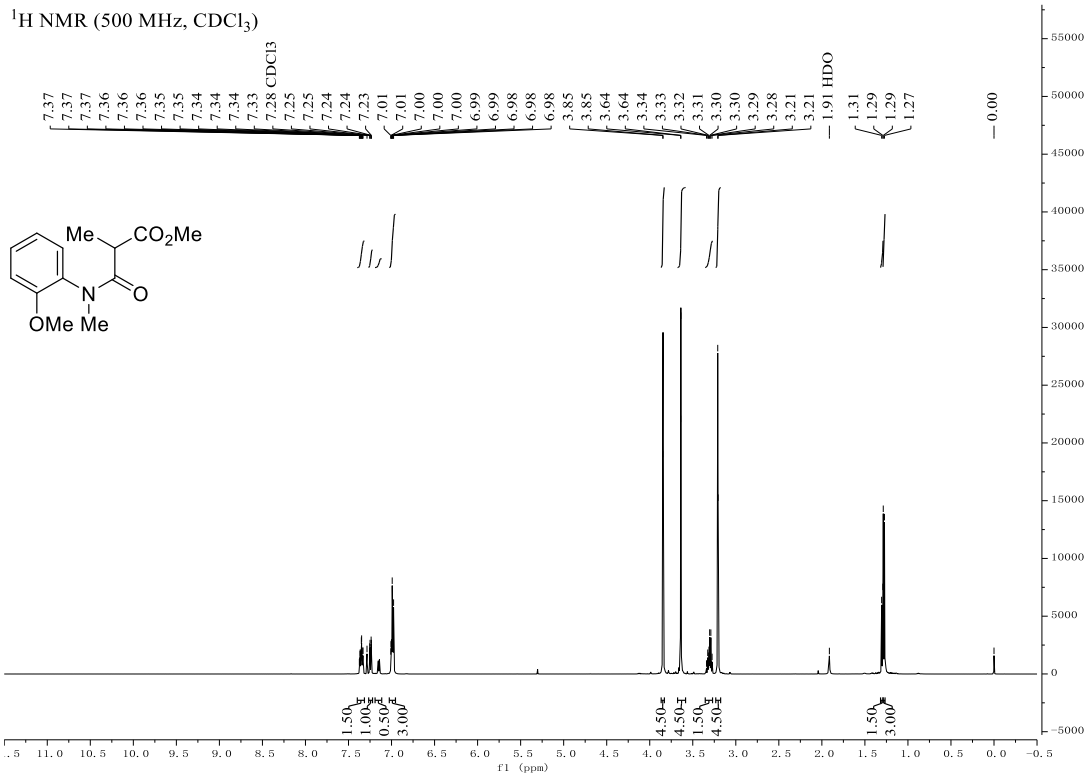


^{13}C NMR (126 MHz, $CDCl_3$)

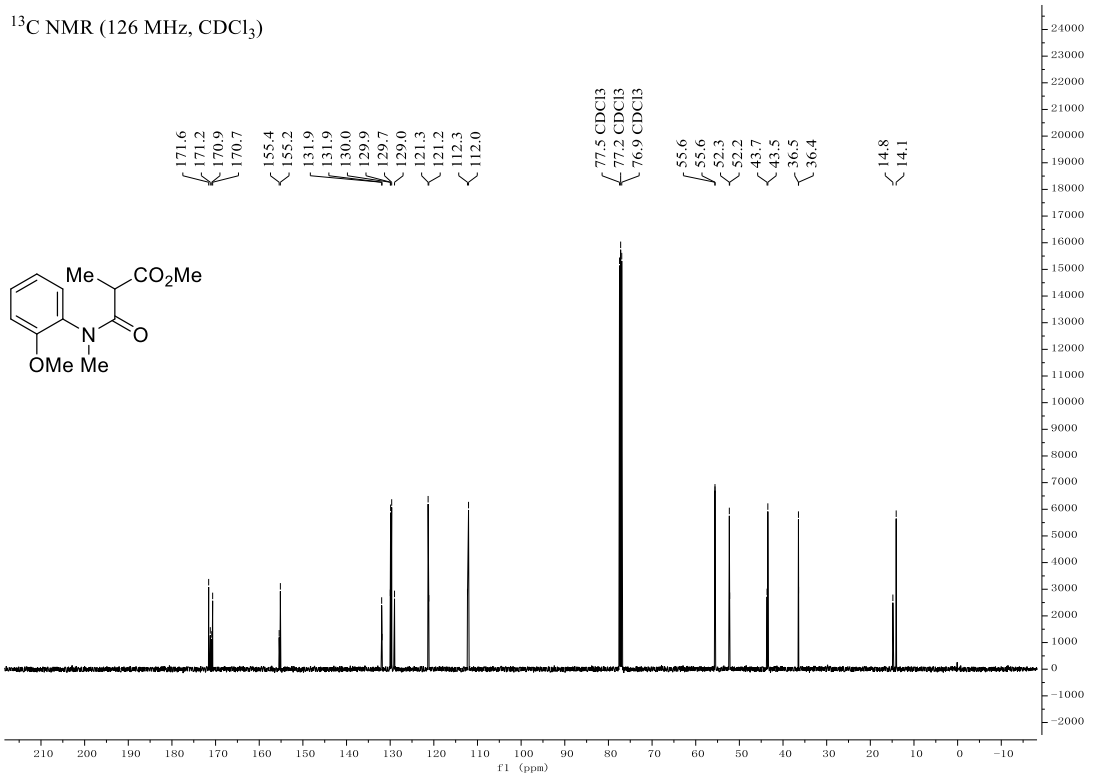


Compound S19

^{1}H NMR (500 MHz, $CDCl_3$)

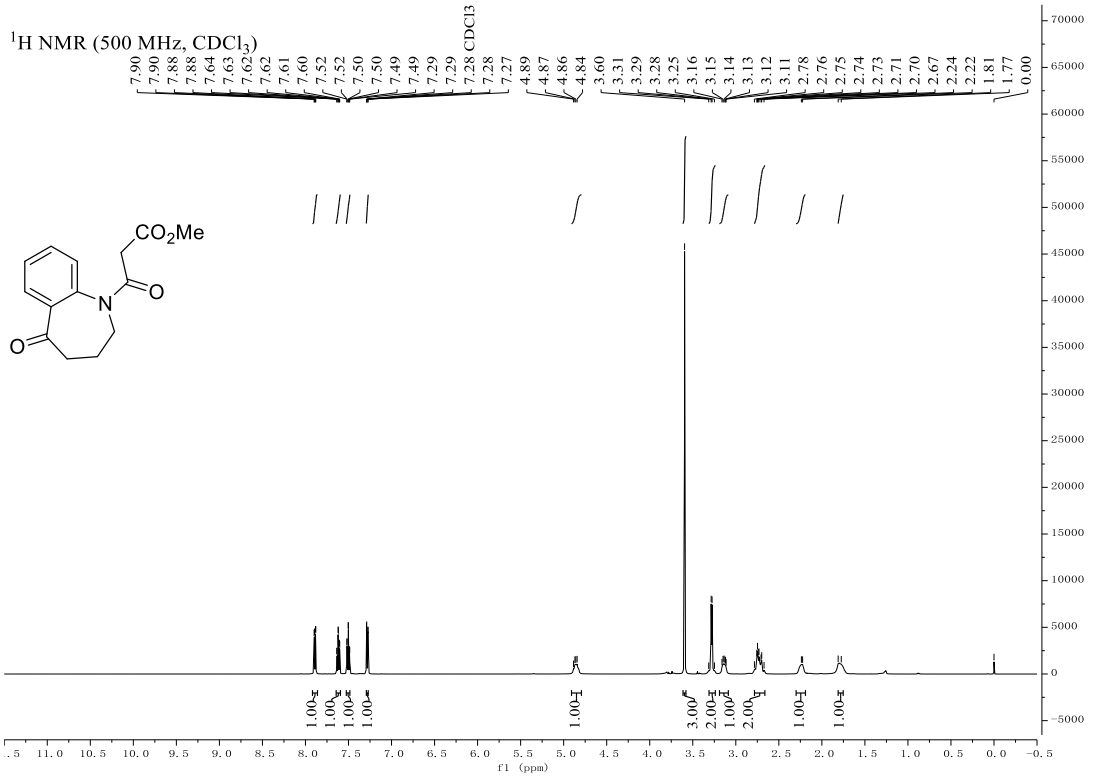


^{13}C NMR (126 MHz, $CDCl_3$)

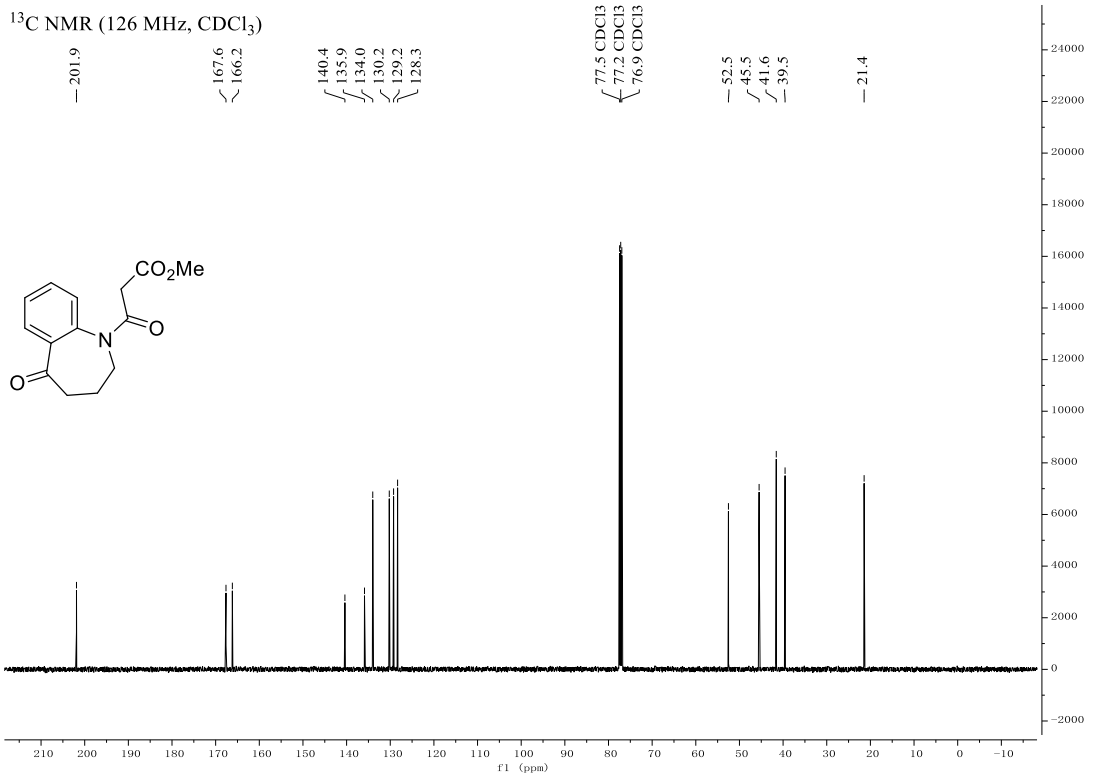


Compound S20

^{1}H NMR (500 MHz, $CDCl_3$)

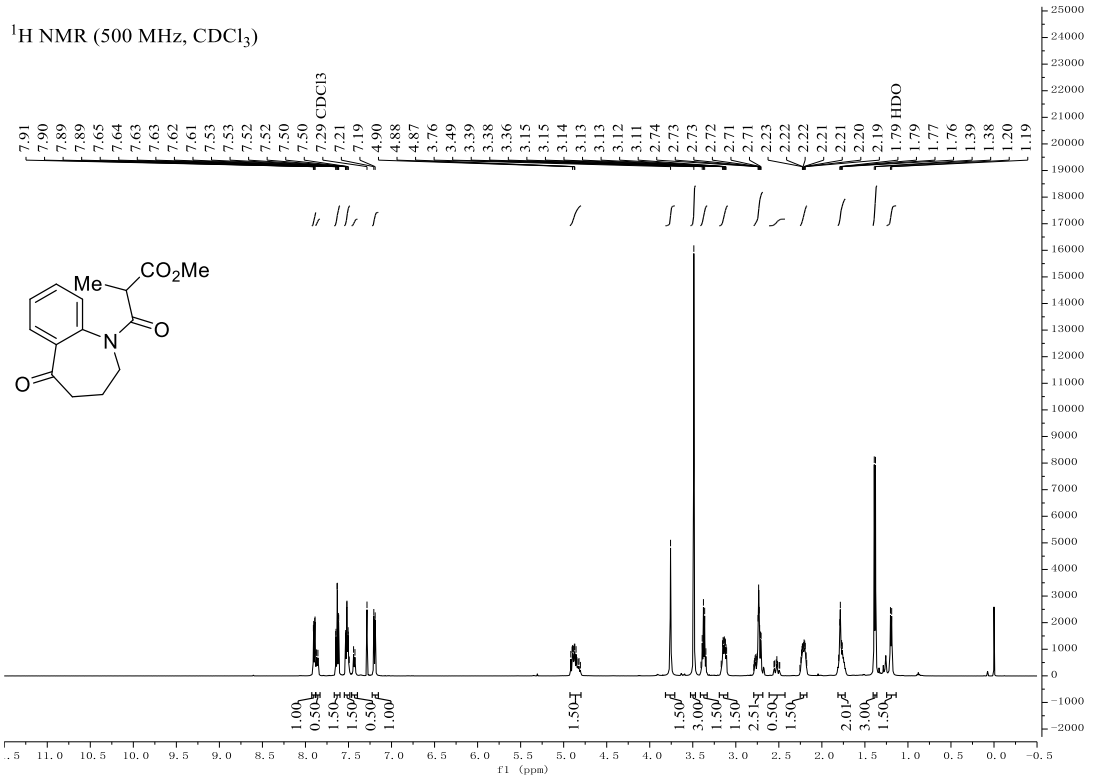


^{13}C NMR (126 MHz, $CDCl_3$)

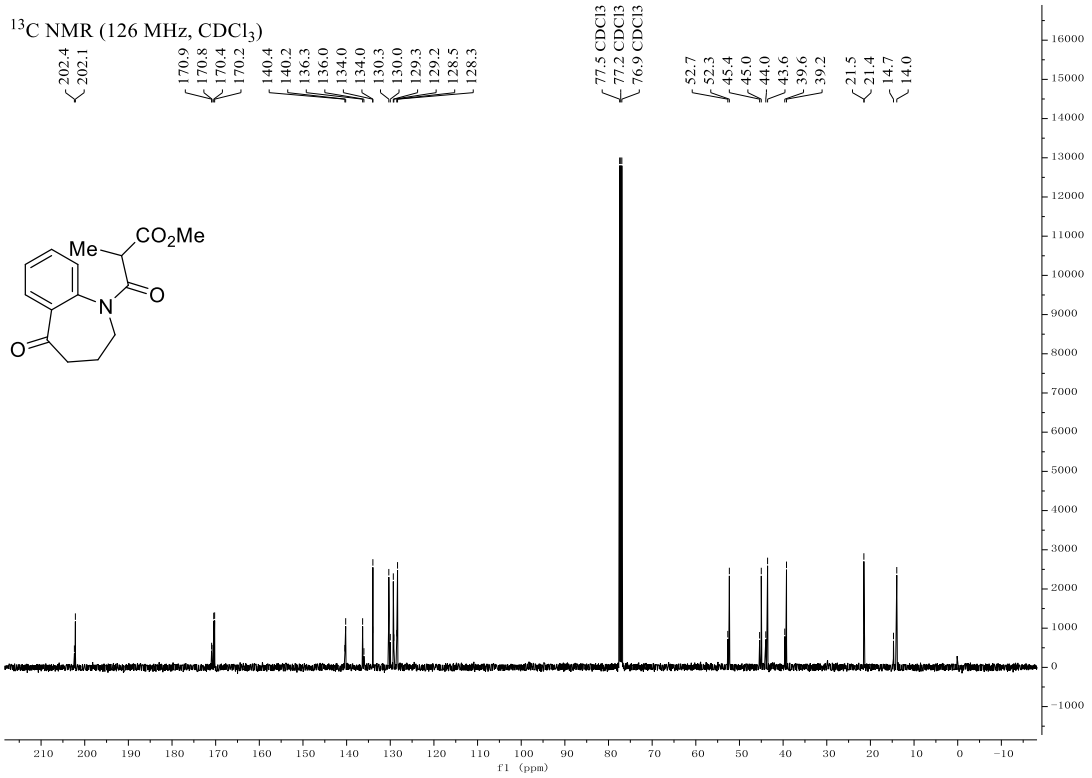


Compound S21

^{1}H NMR (500 MHz, $CDCl_3$)

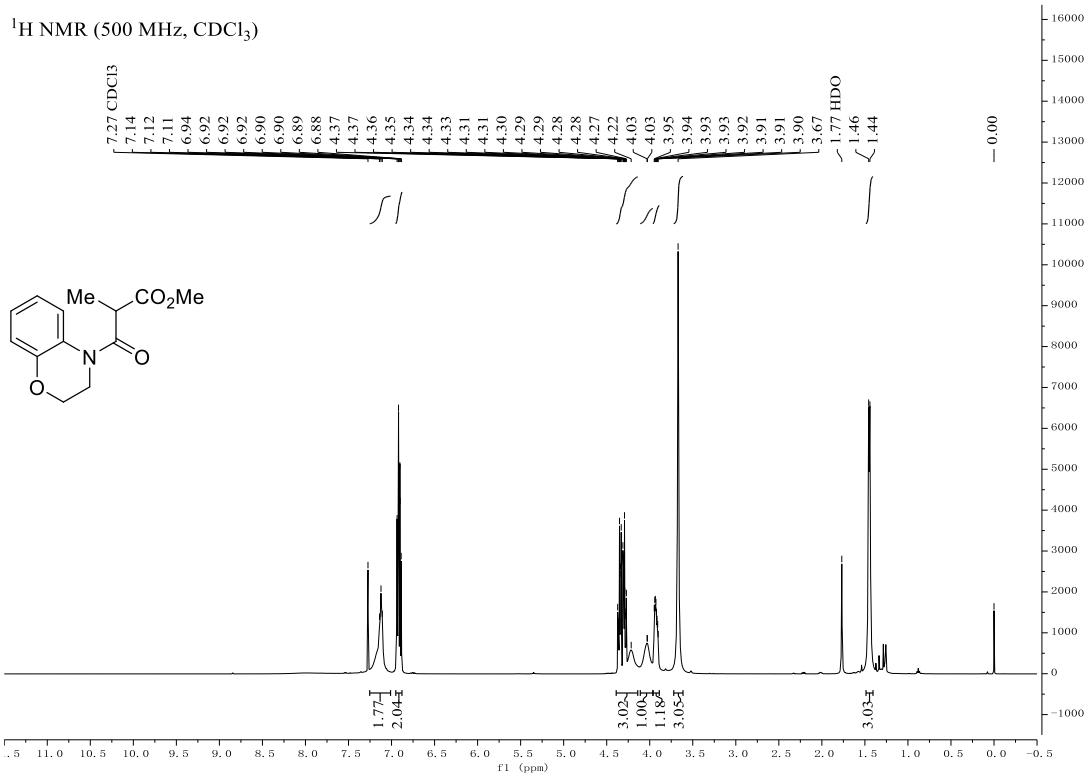


^{13}C NMR (126 MHz, $CDCl_3$)

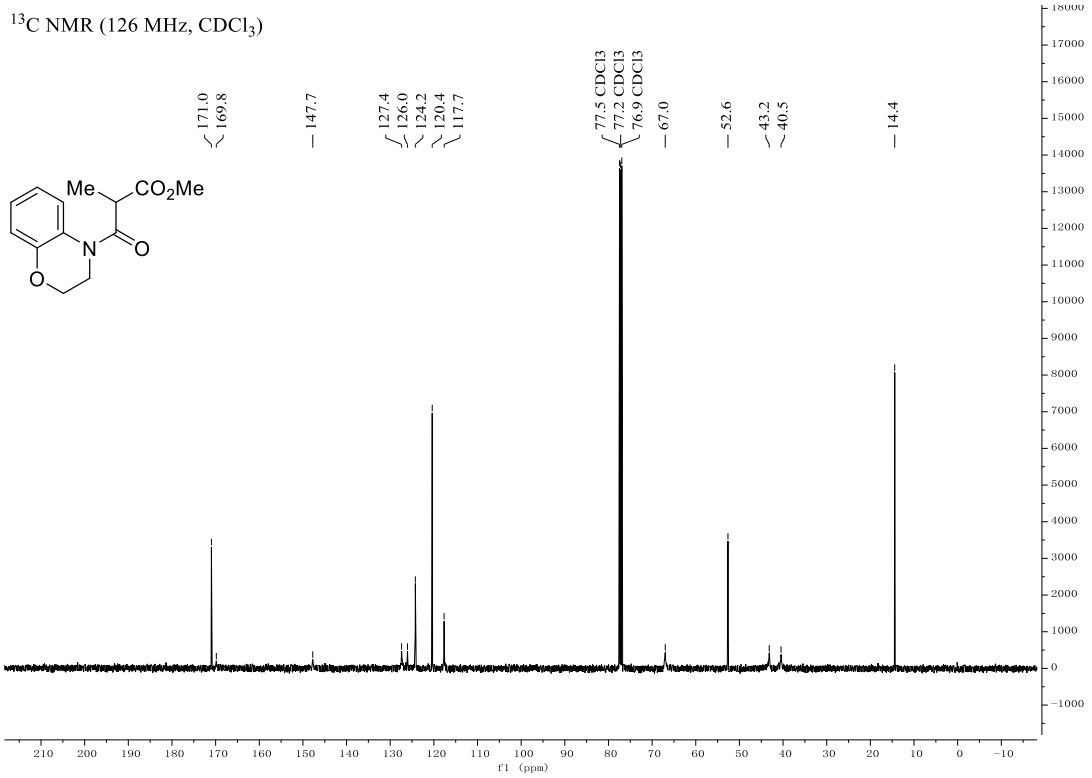


Compound S23

^{1}H NMR (500 MHz, $CDCl_3$)

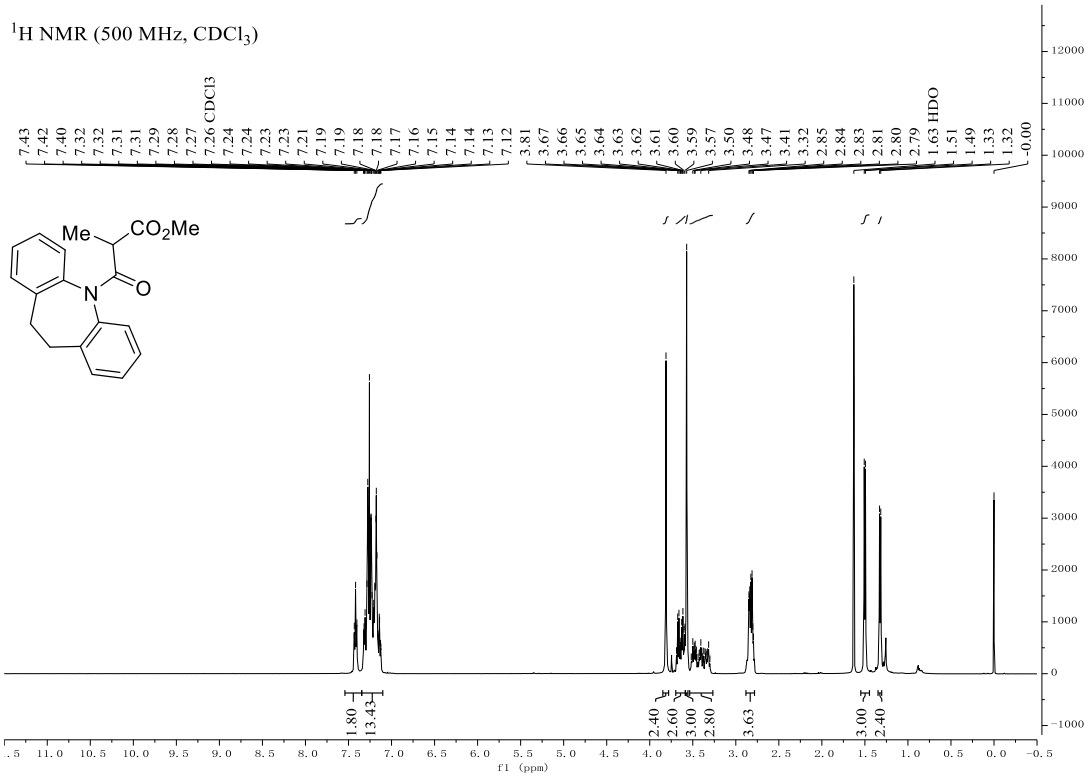


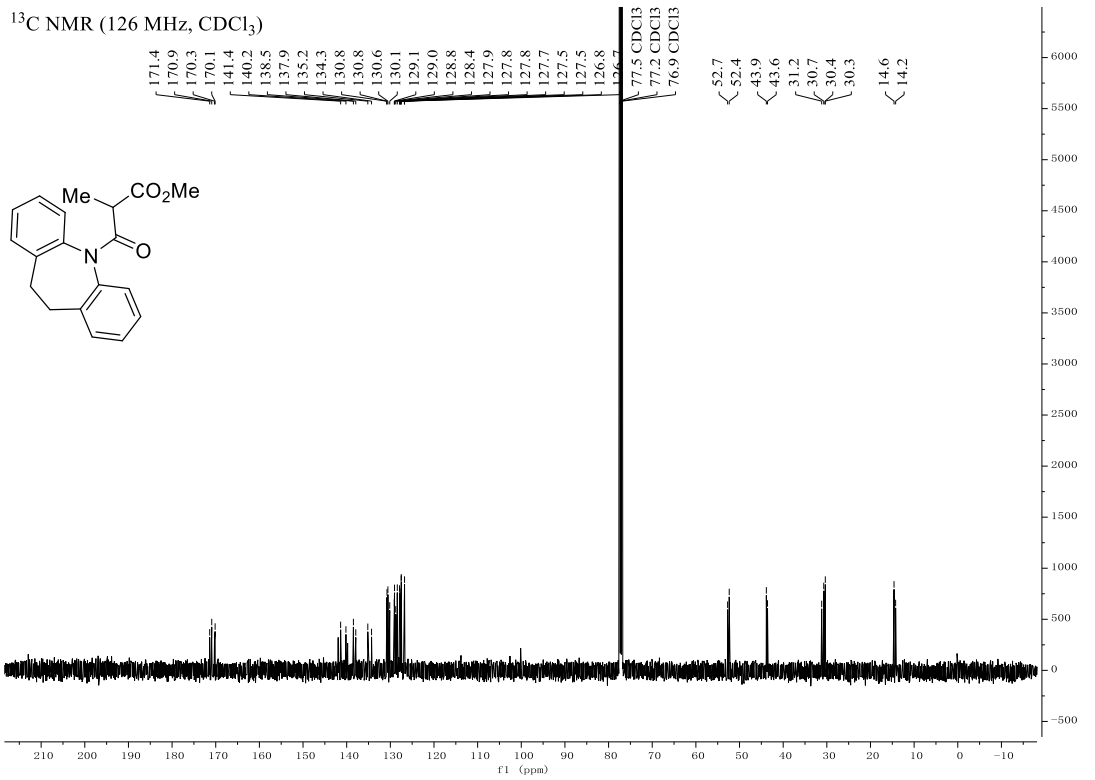
^{13}C NMR (126 MHz, $CDCl_3$)



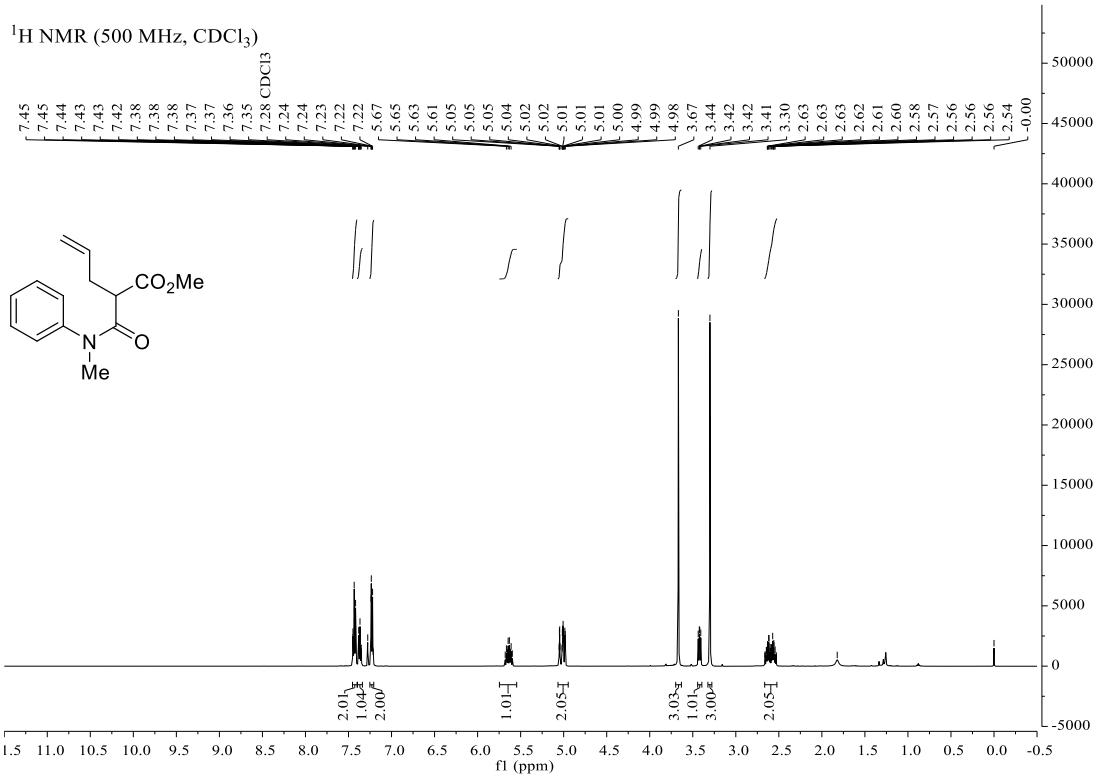
Compound S25

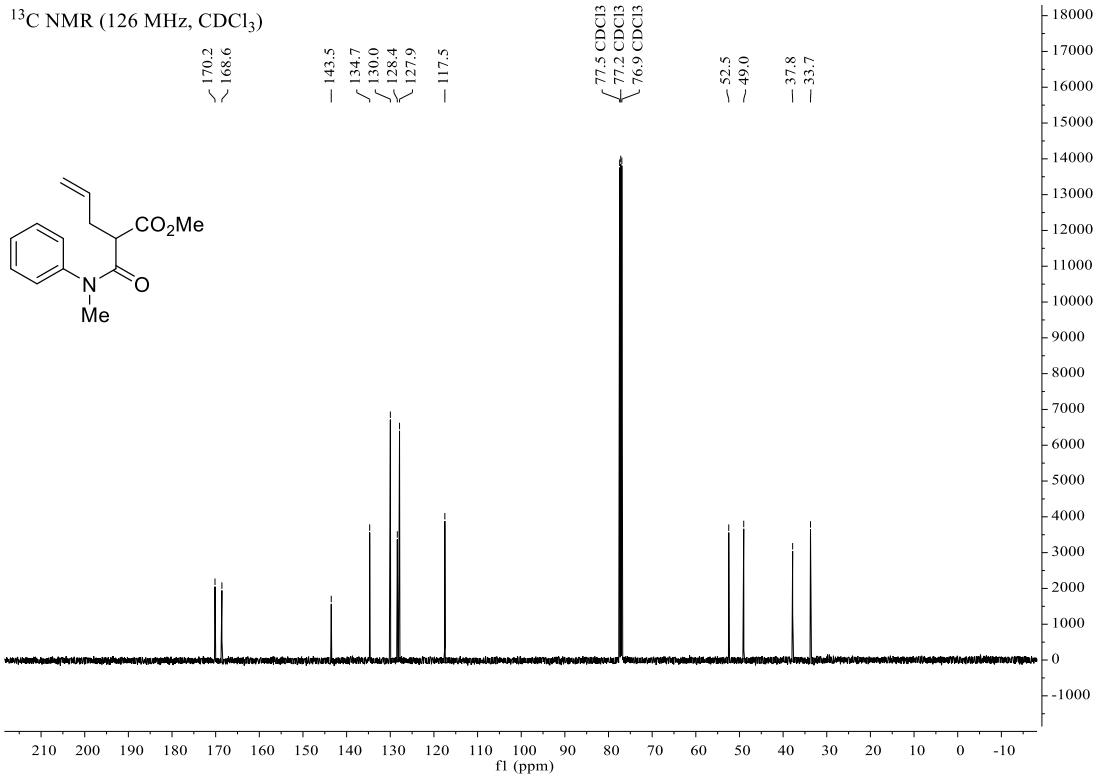
^{1}H NMR (500 MHz, $CDCl_3$)



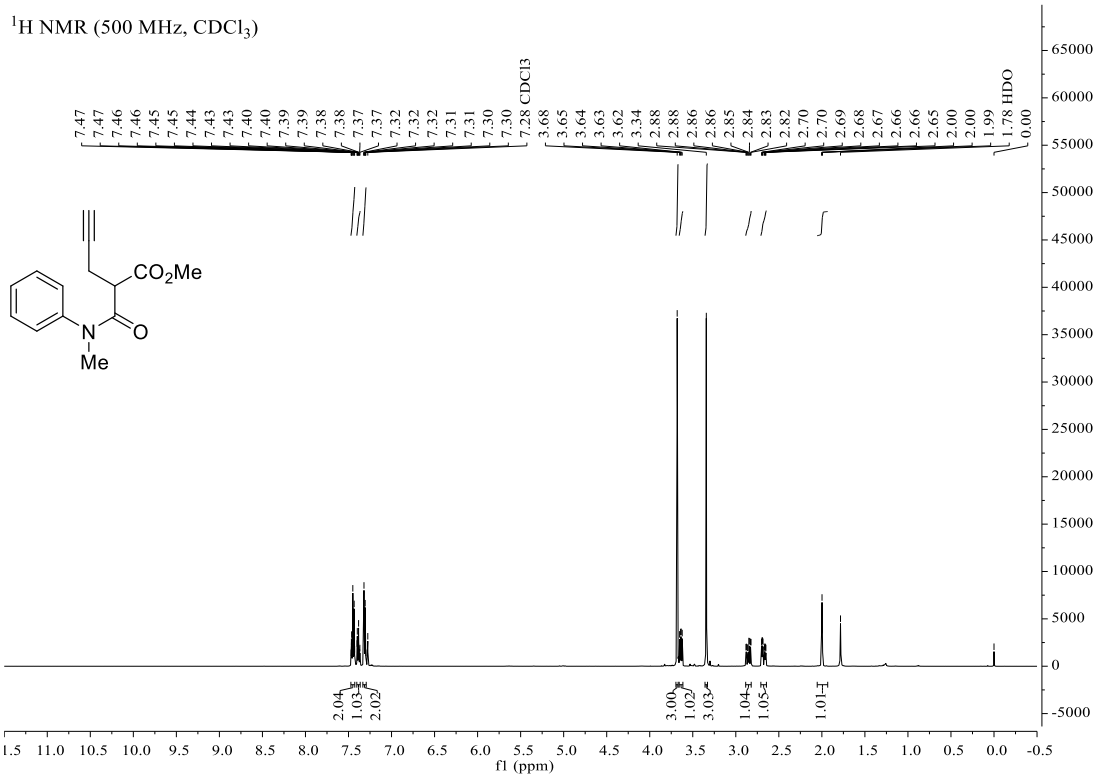


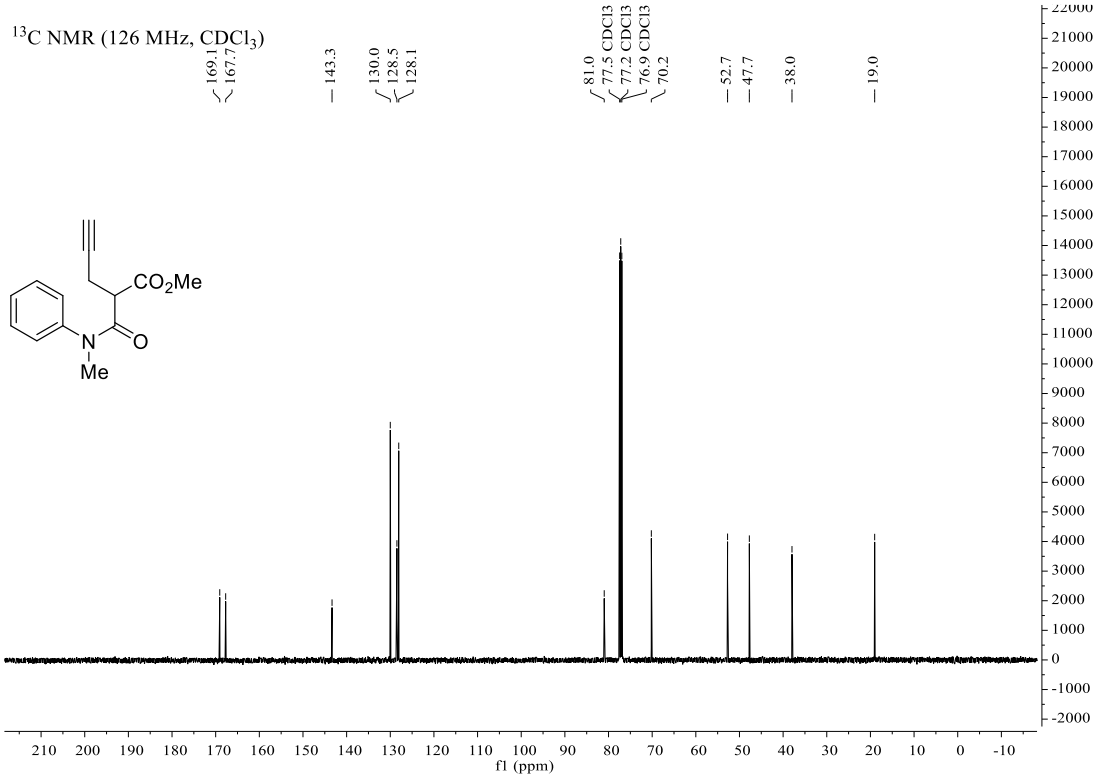
Compound S27



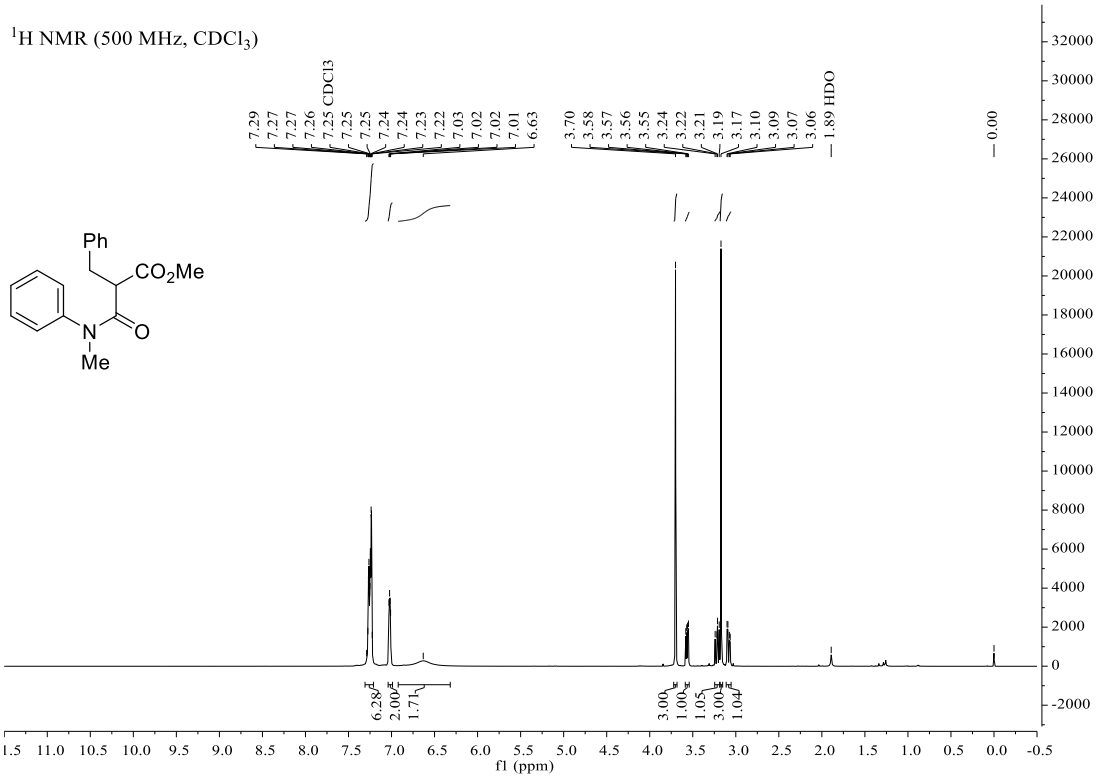


Compound S28

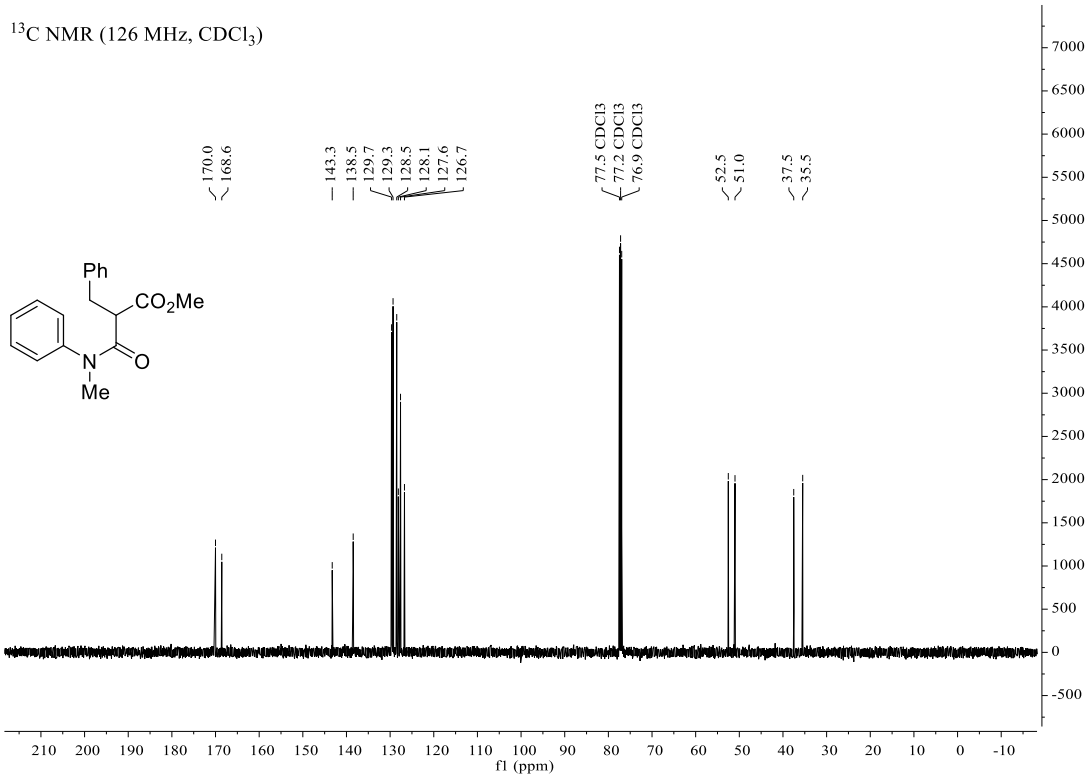




Compound S29

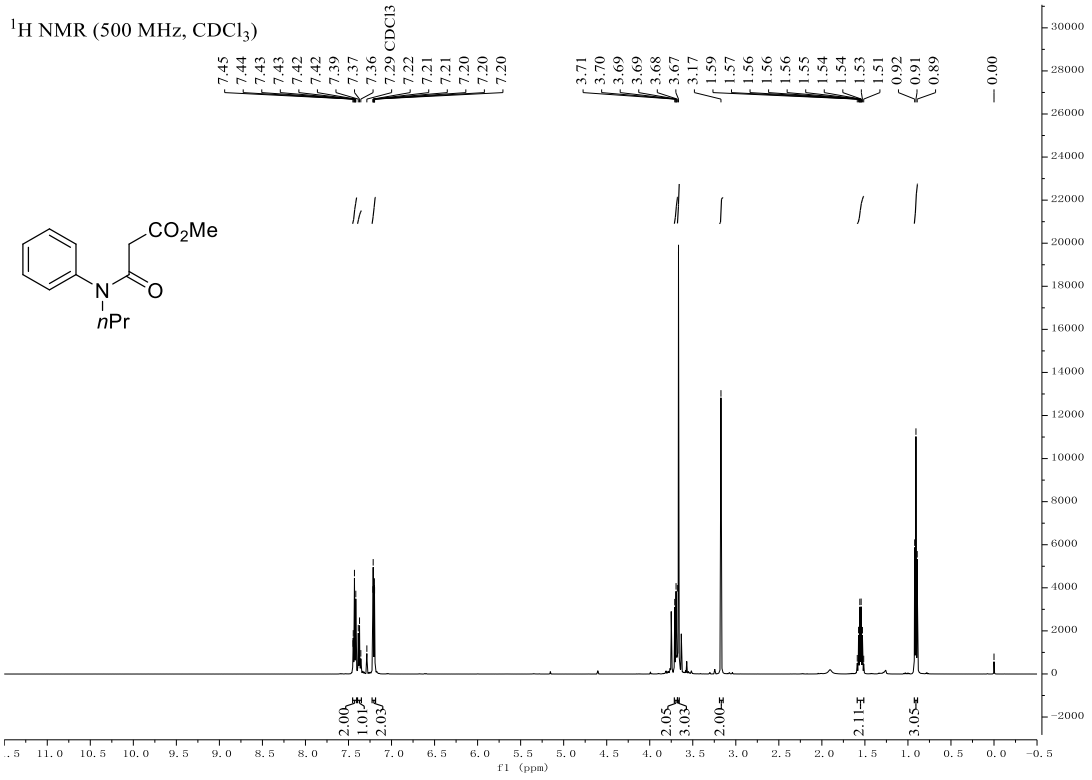


^{13}C NMR (126 MHz, $CDCl_3$)

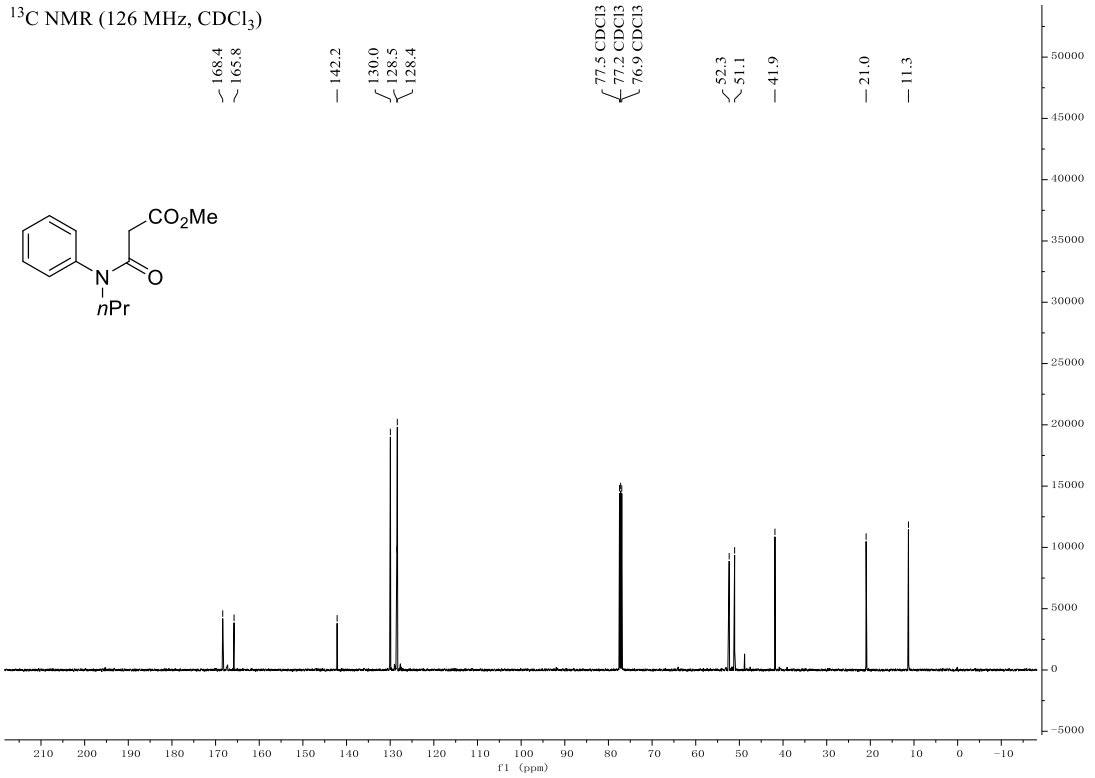


Compound S30

^{1}H NMR (500 MHz, $CDCl_3$)

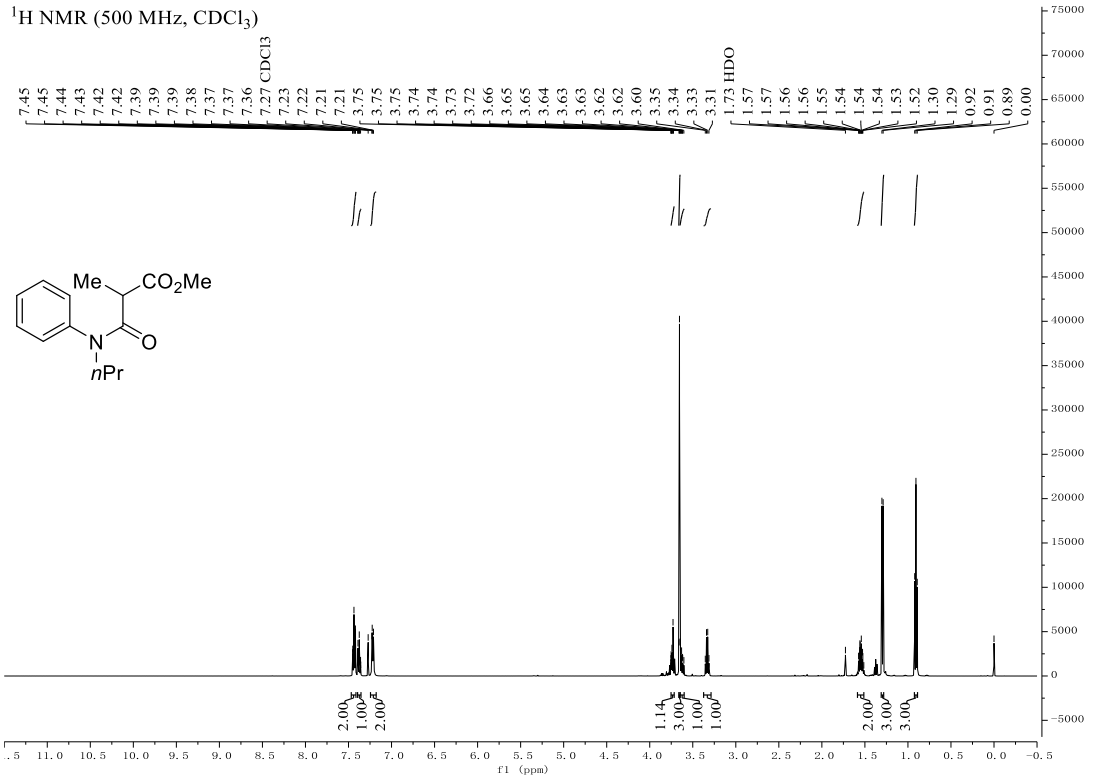


^{13}C NMR (126 MHz, $CDCl_3$)

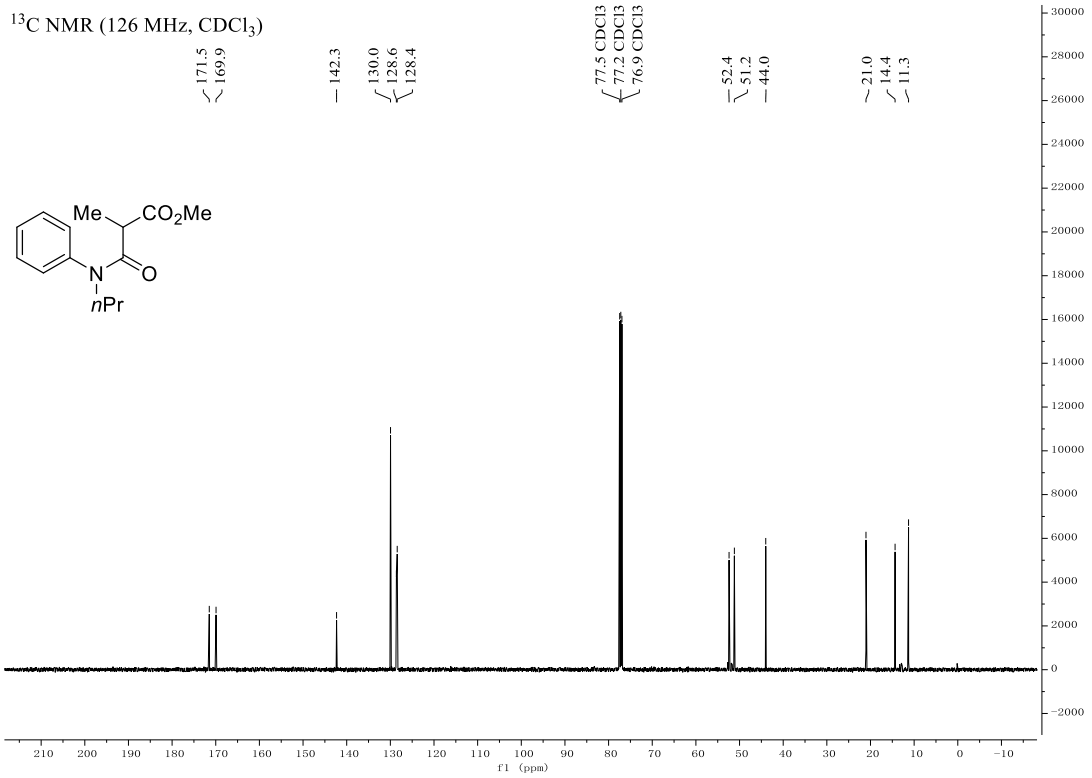


Compound S31

^{1}H NMR (500 MHz, $CDCl_3$)

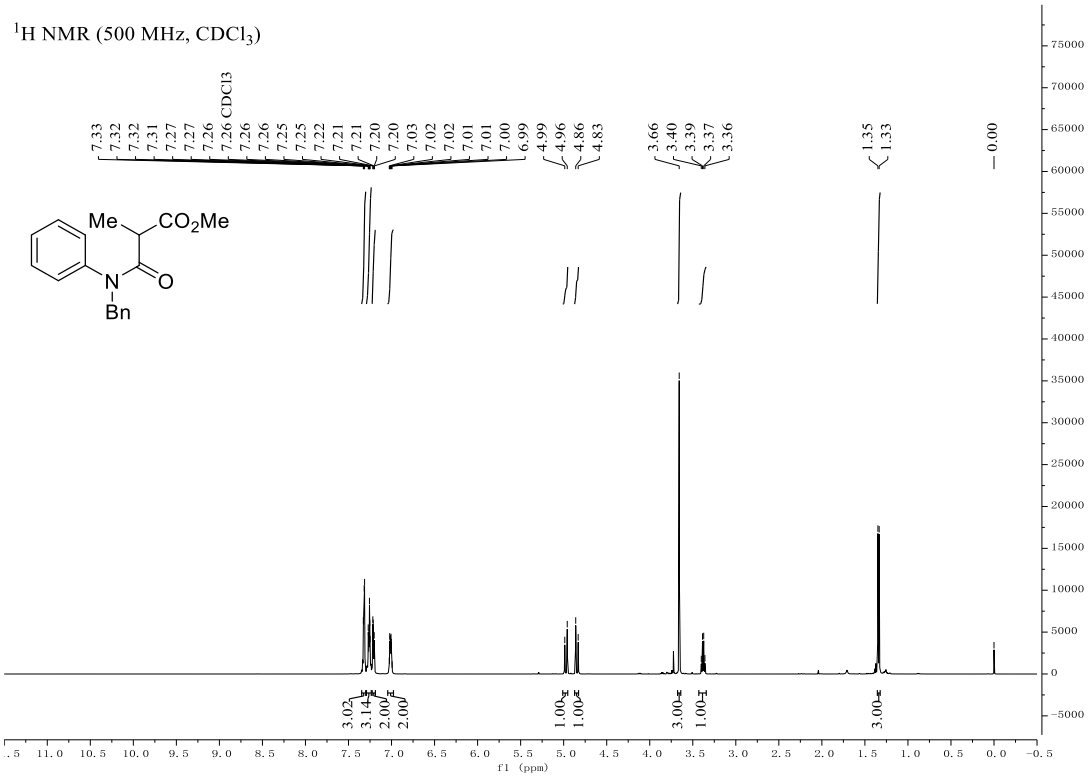


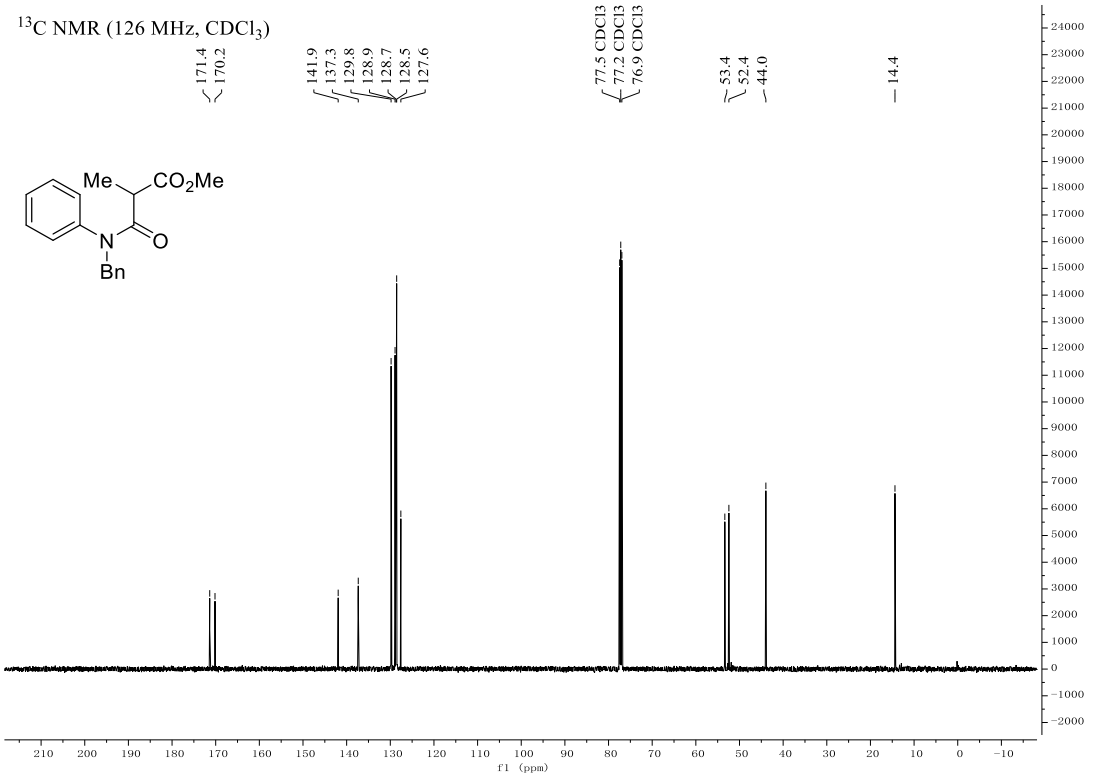
^{13}C NMR (126 MHz, $CDCl_3$)



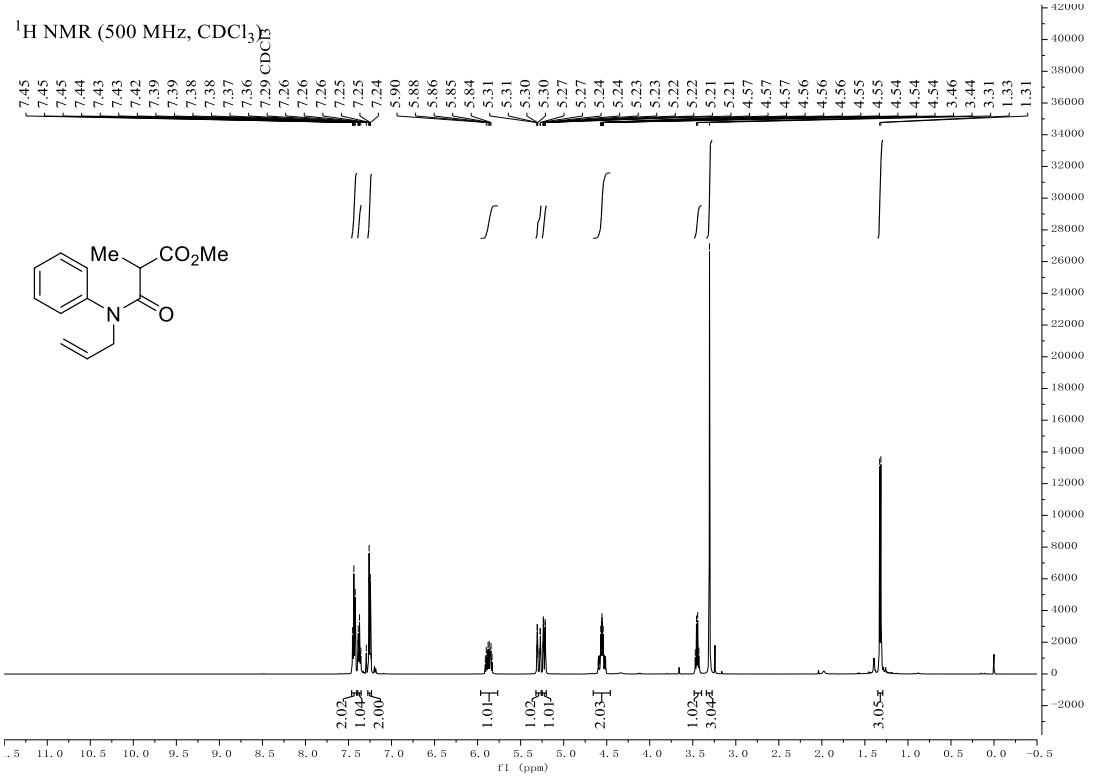
Compound S33

^{1}H NMR (500 MHz, $CDCl_3$)

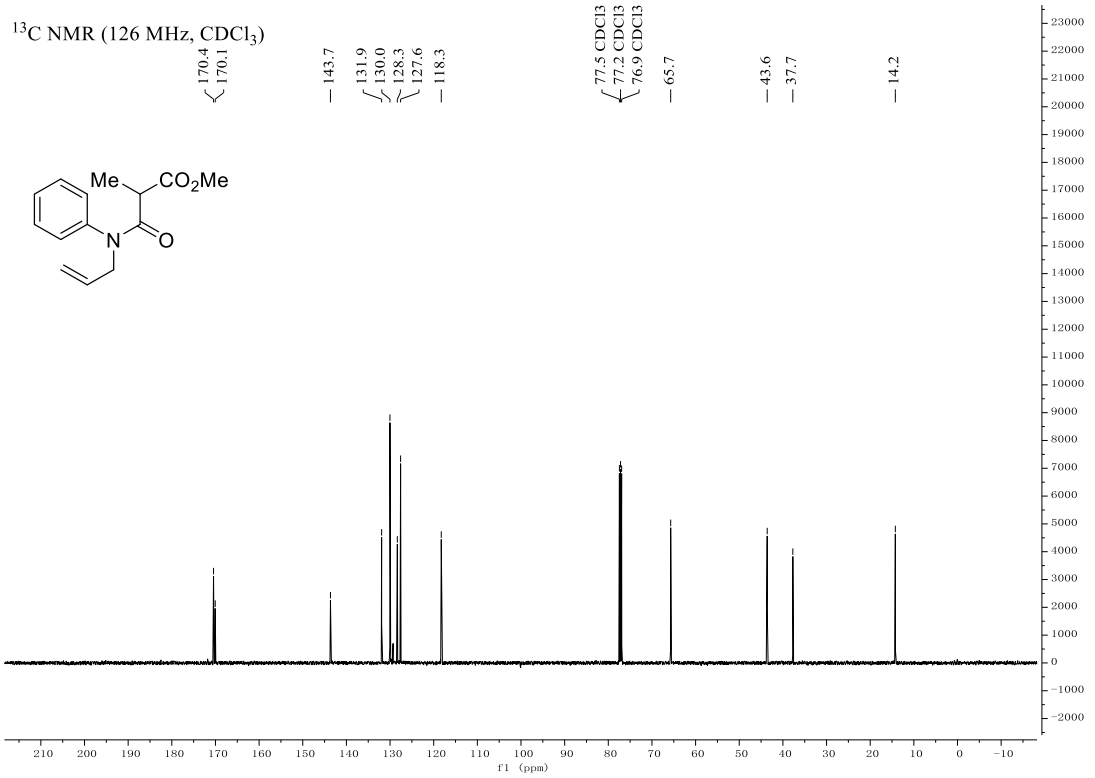




Compound S35

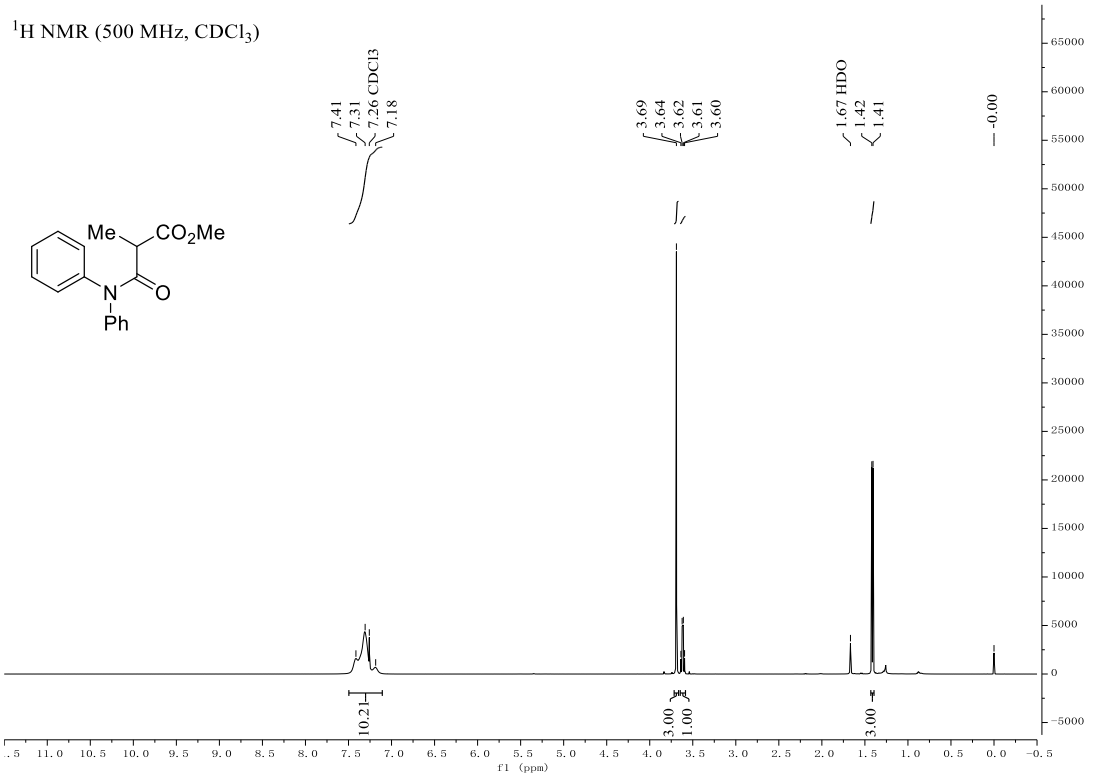


^{13}C NMR (126 MHz, $CDCl_3$)

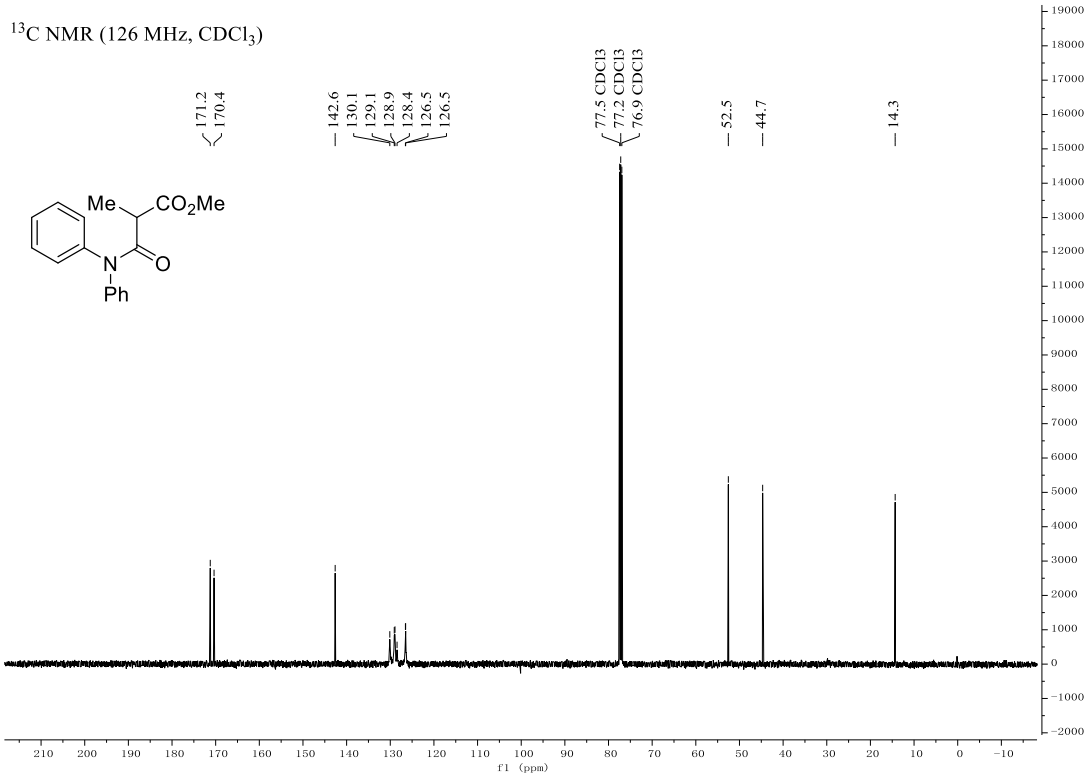


Compound S37

^{1}H NMR (500 MHz, $CDCl_3$)

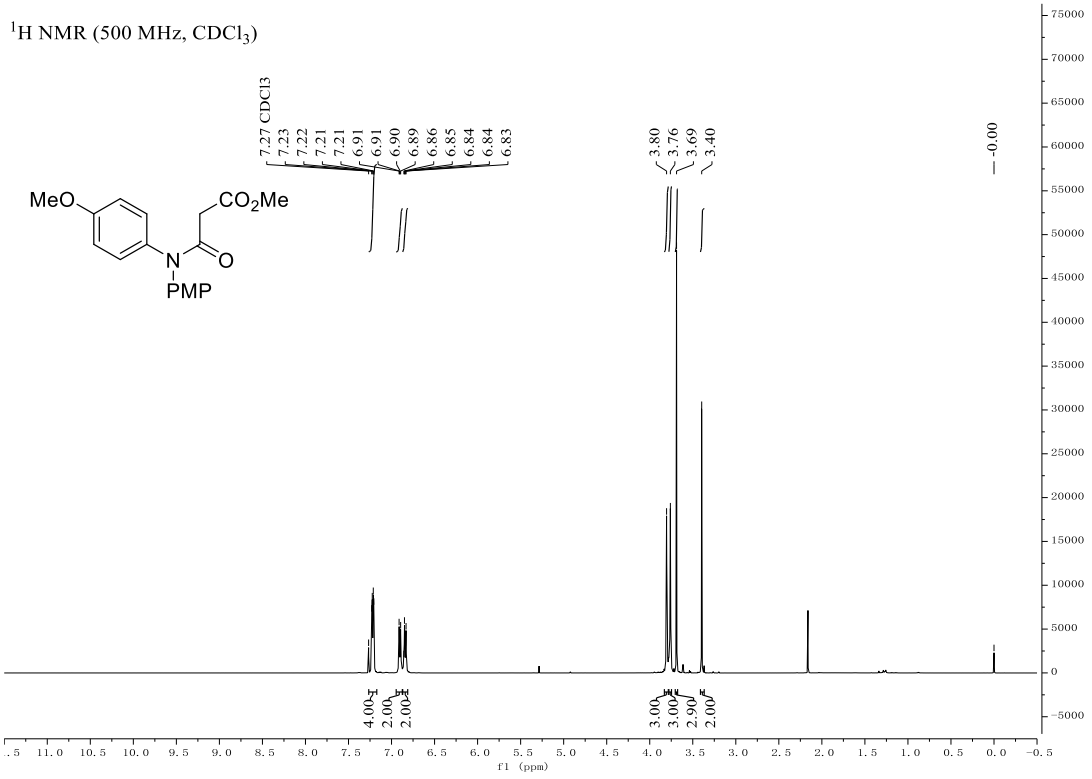


^{13}C NMR (126 MHz, $CDCl_3$)

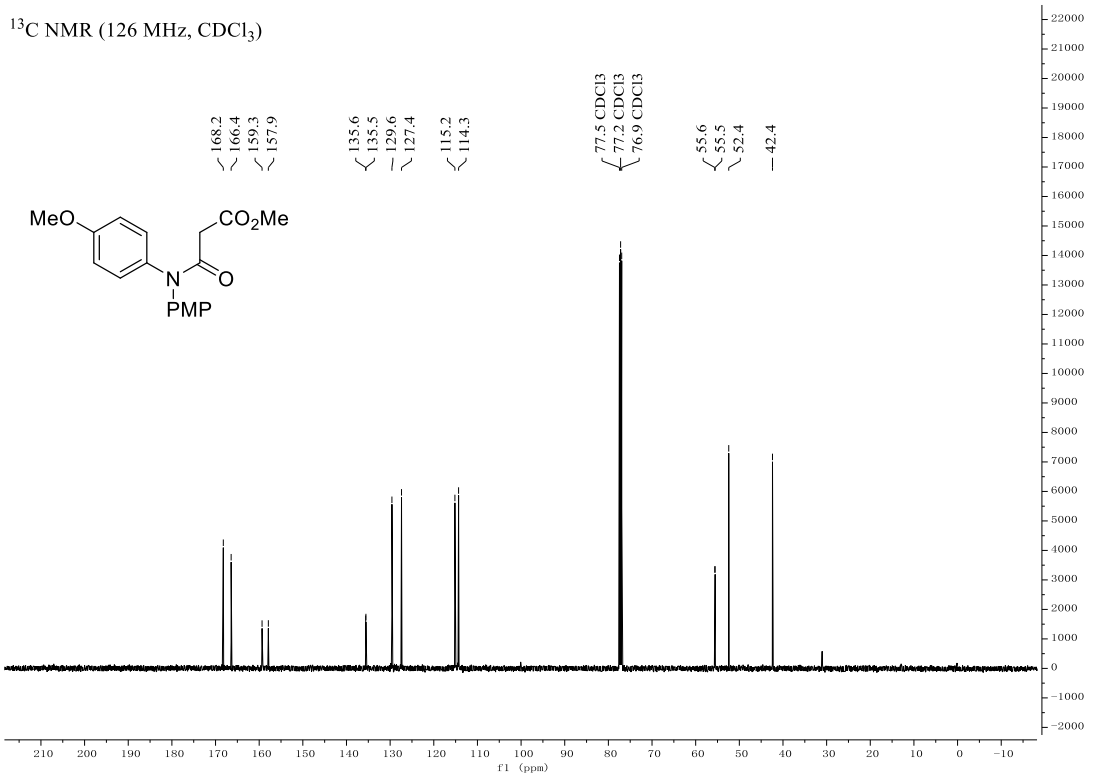


Compound S38

^{1}H NMR (500 MHz, $CDCl_3$)

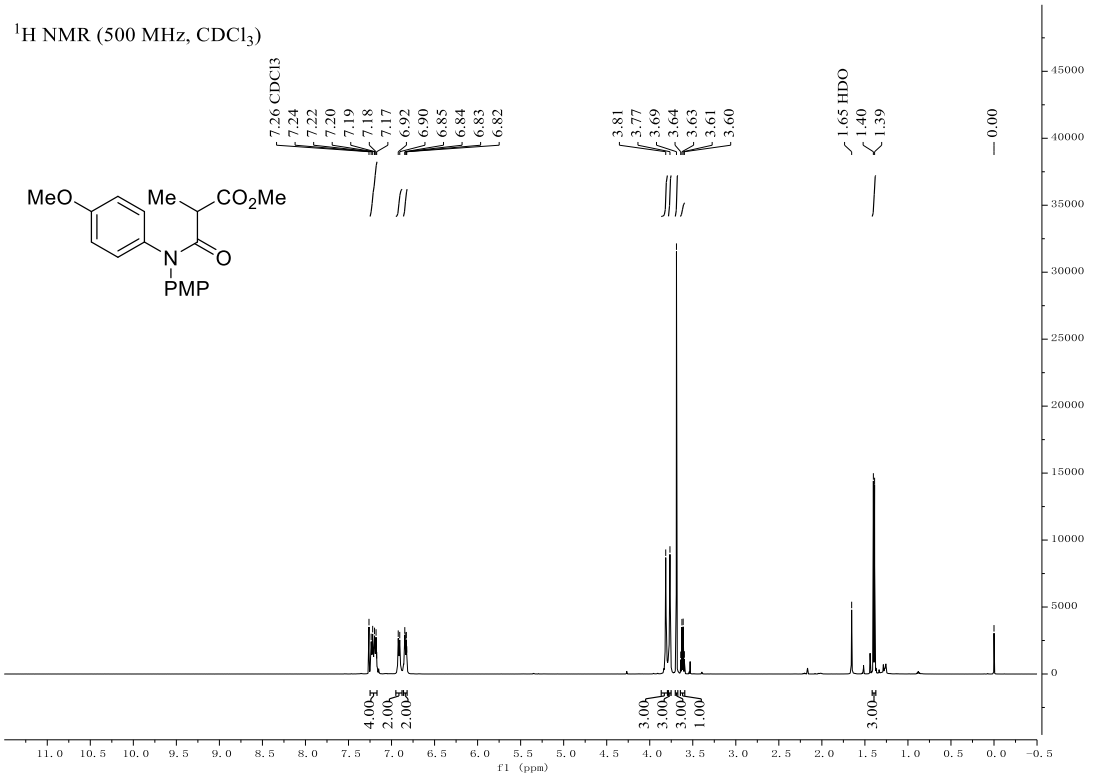


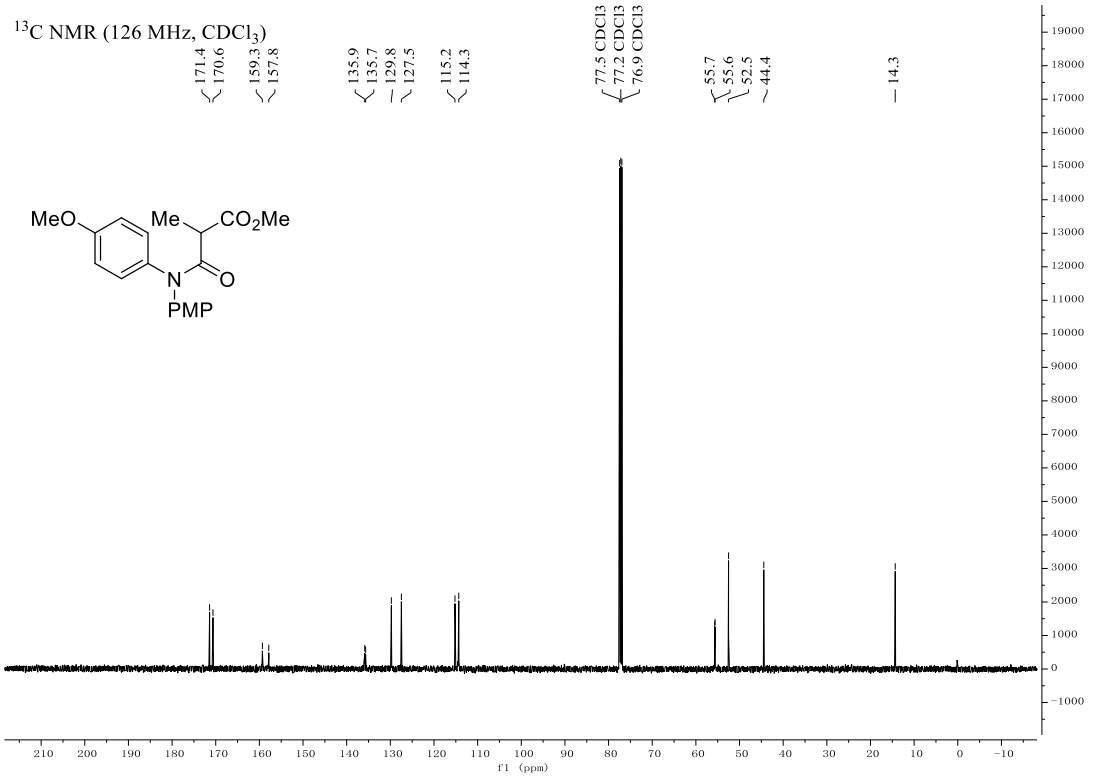
^{13}C NMR (126 MHz, $CDCl_3$)



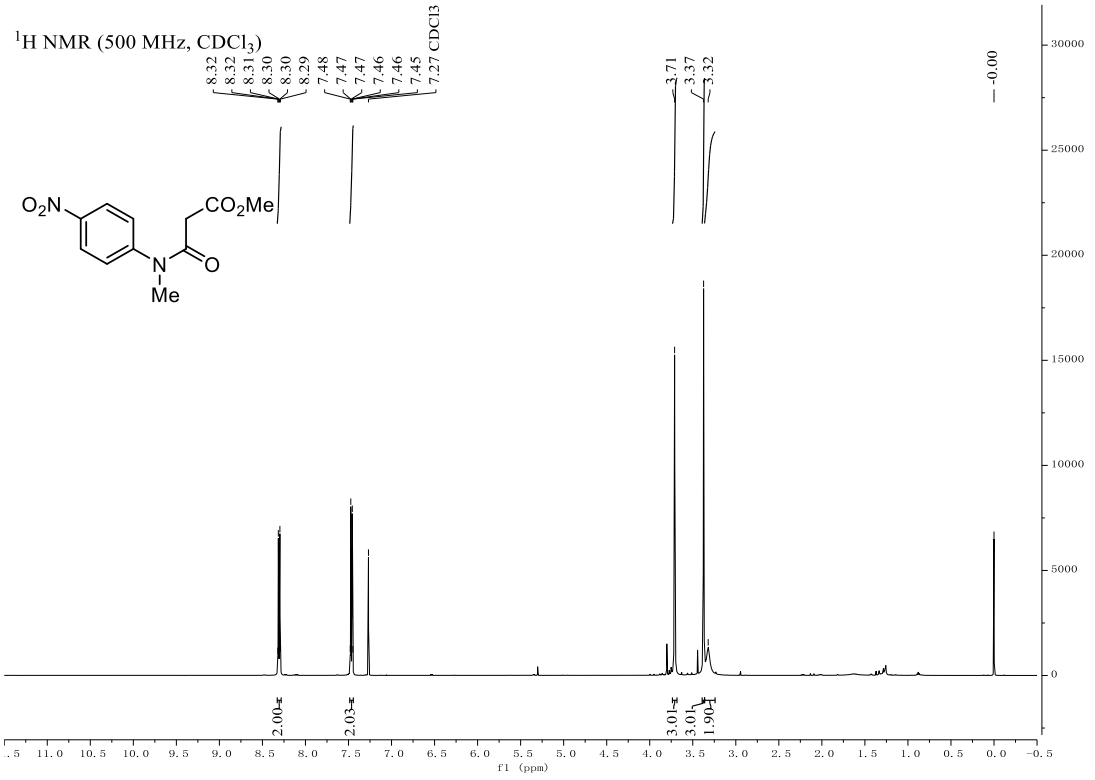
Compound S39

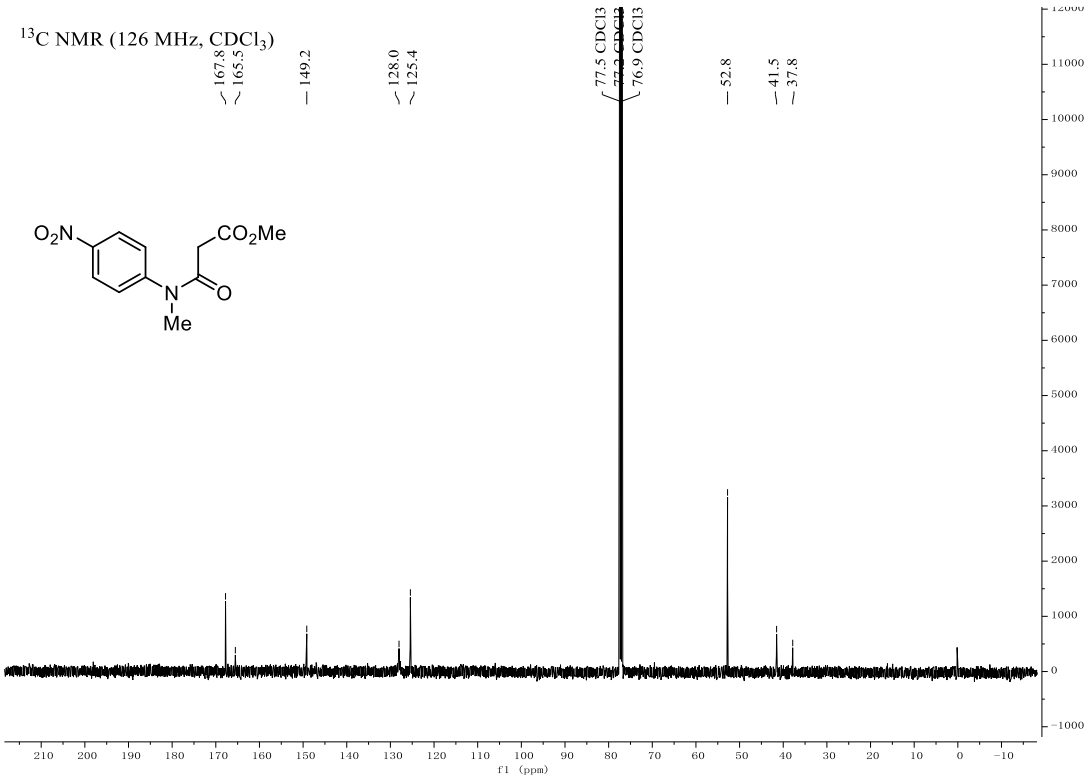
^{1}H NMR (500 MHz, $CDCl_3$)



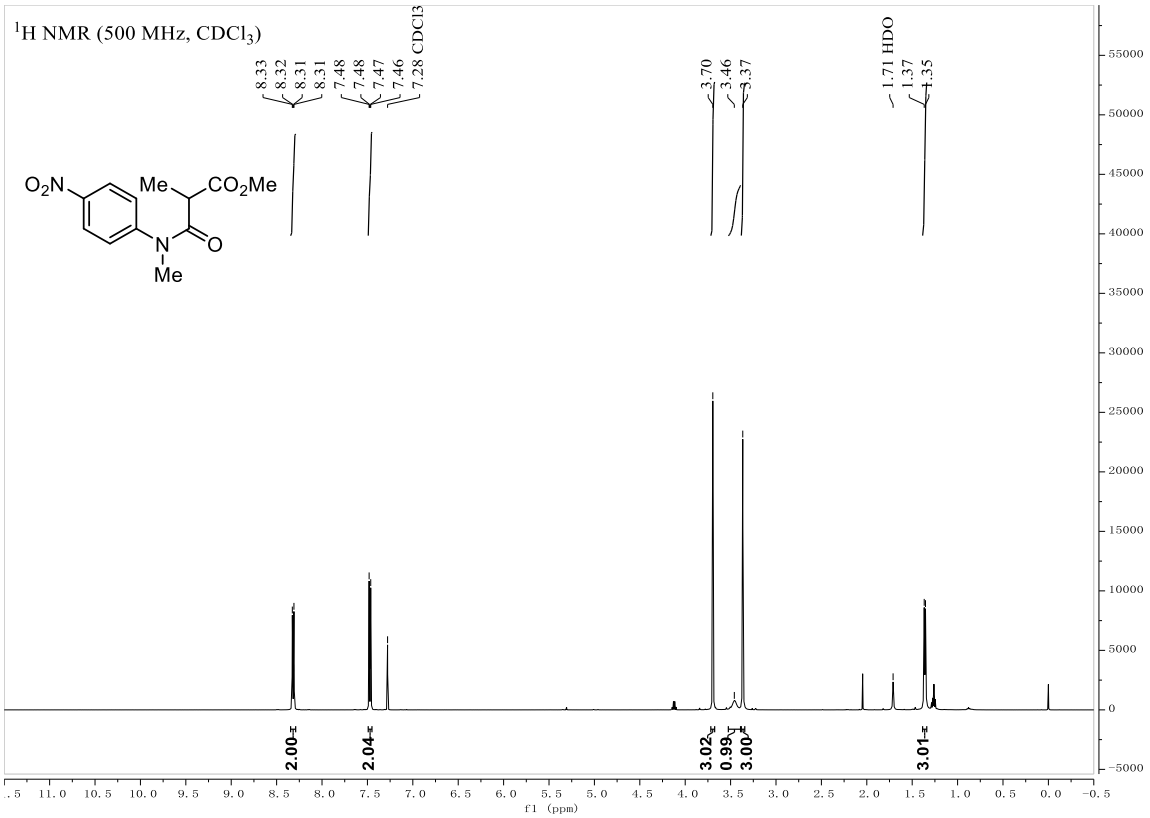


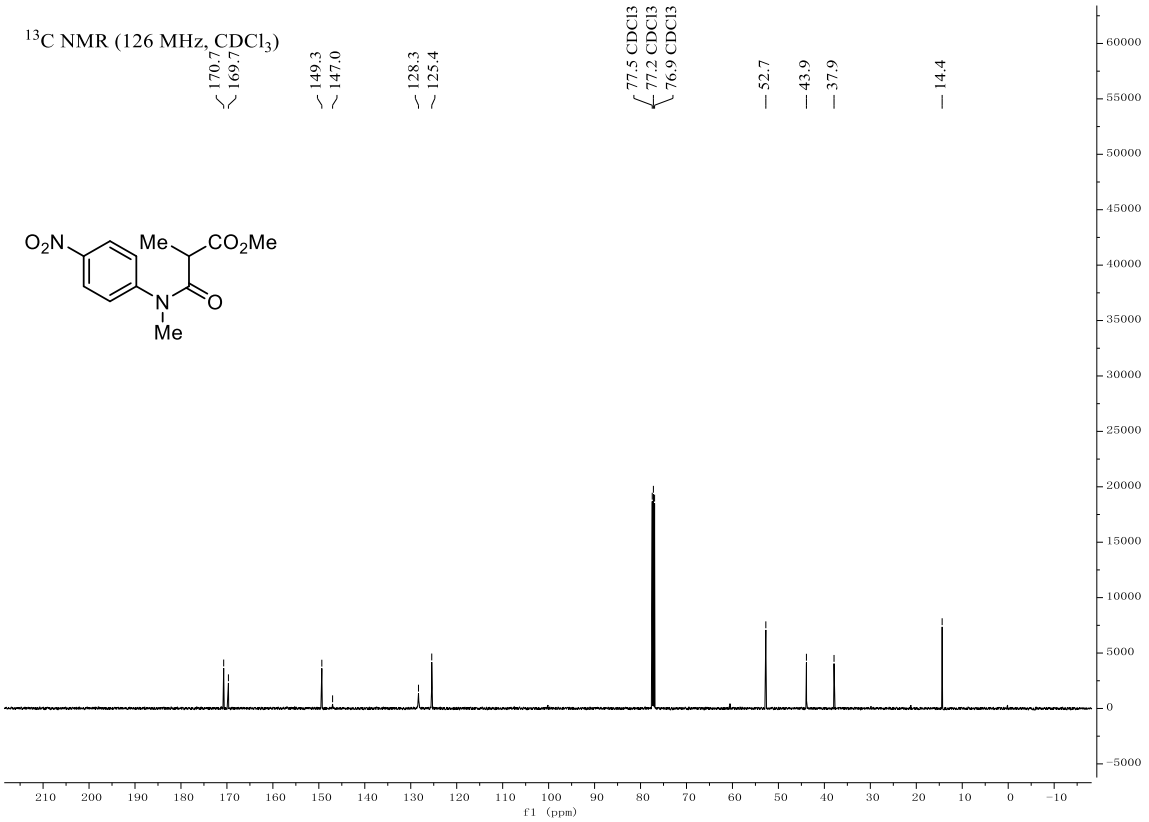
Compound S41



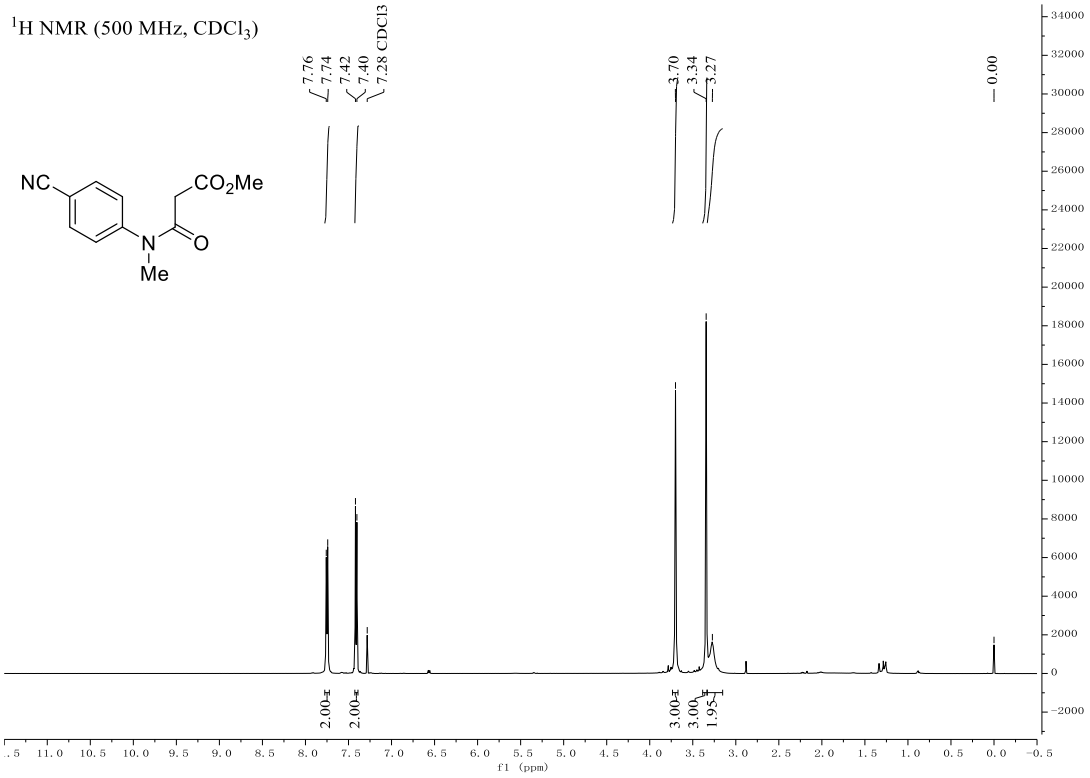


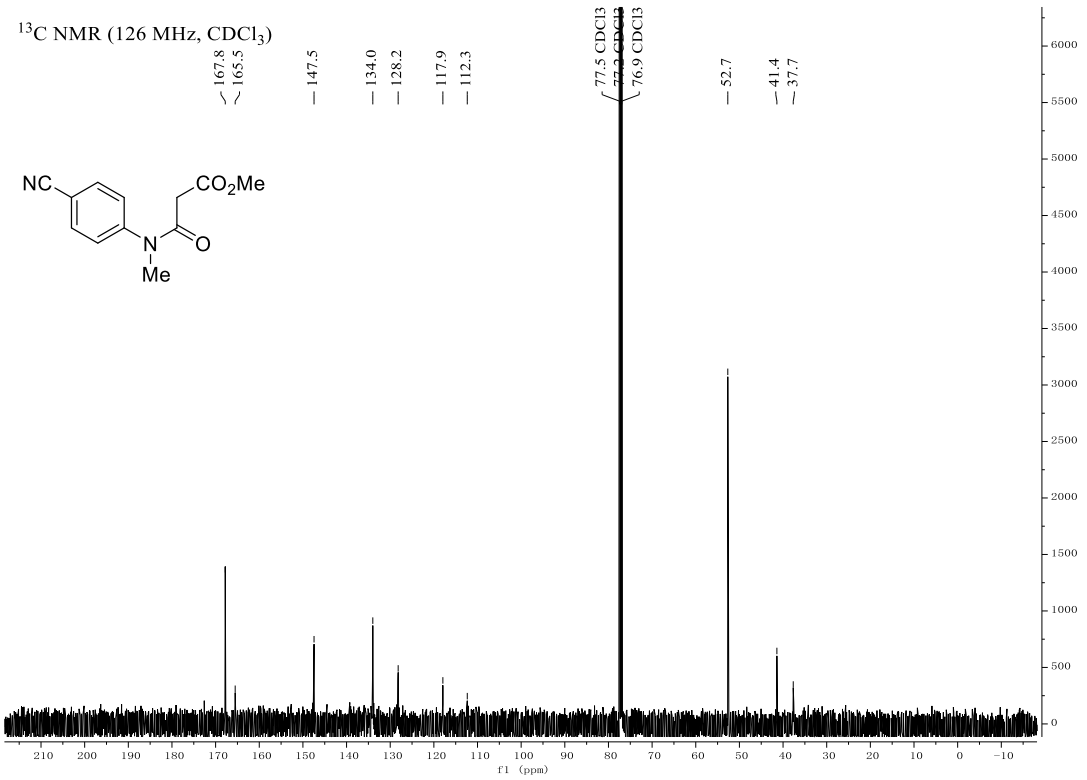
Compound S42



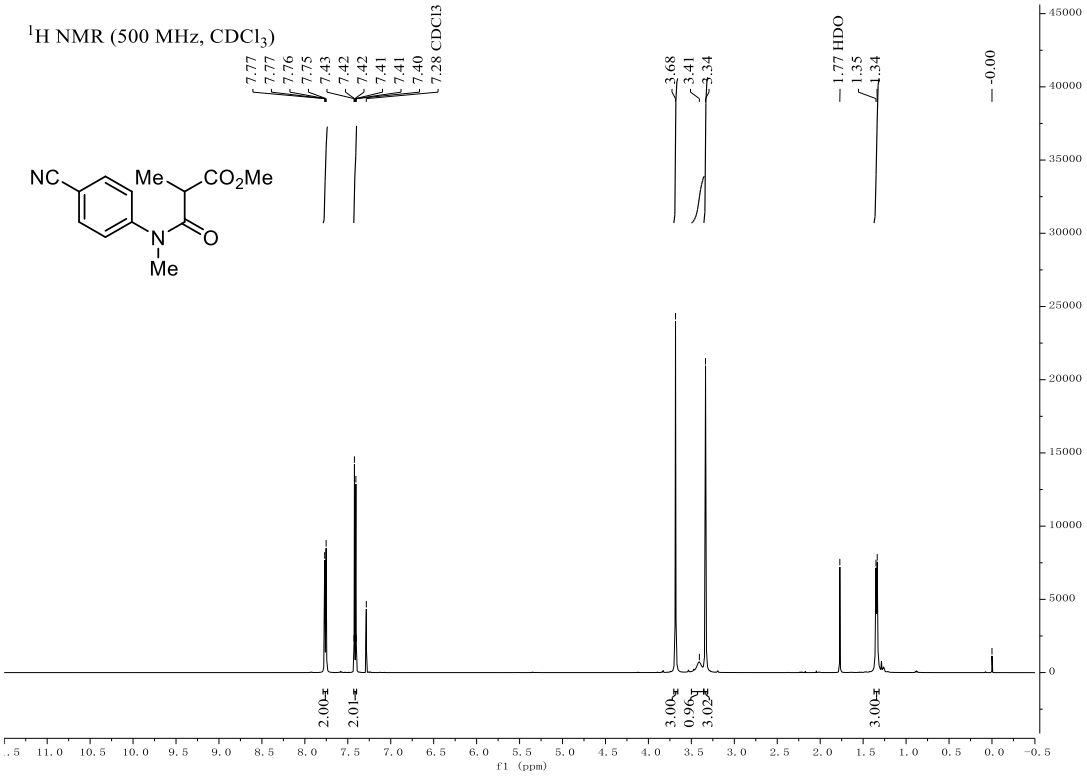


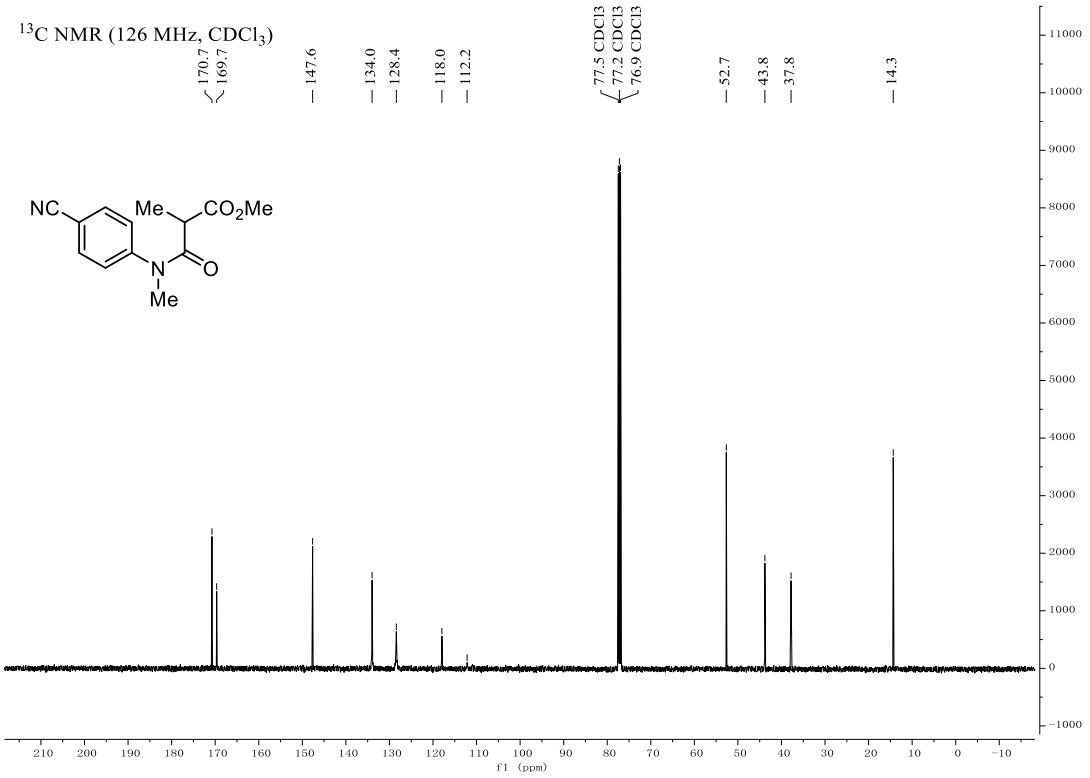
Compound S43



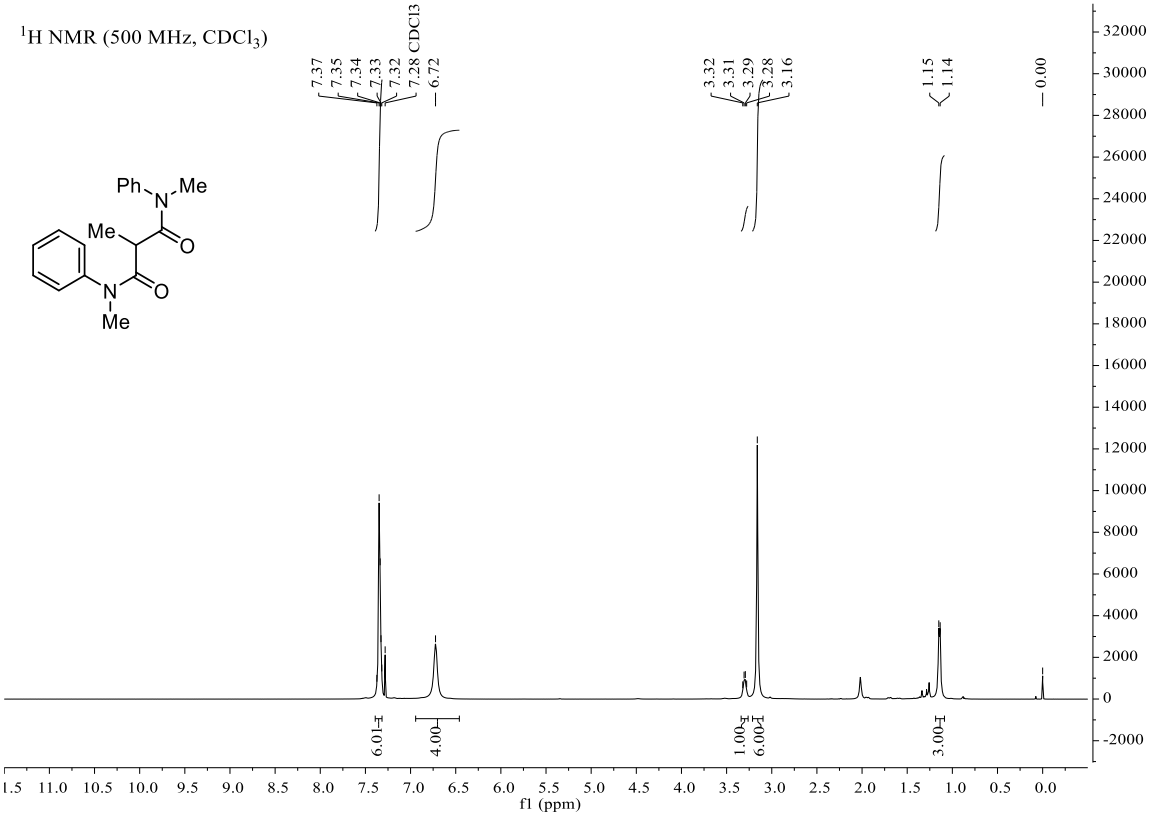


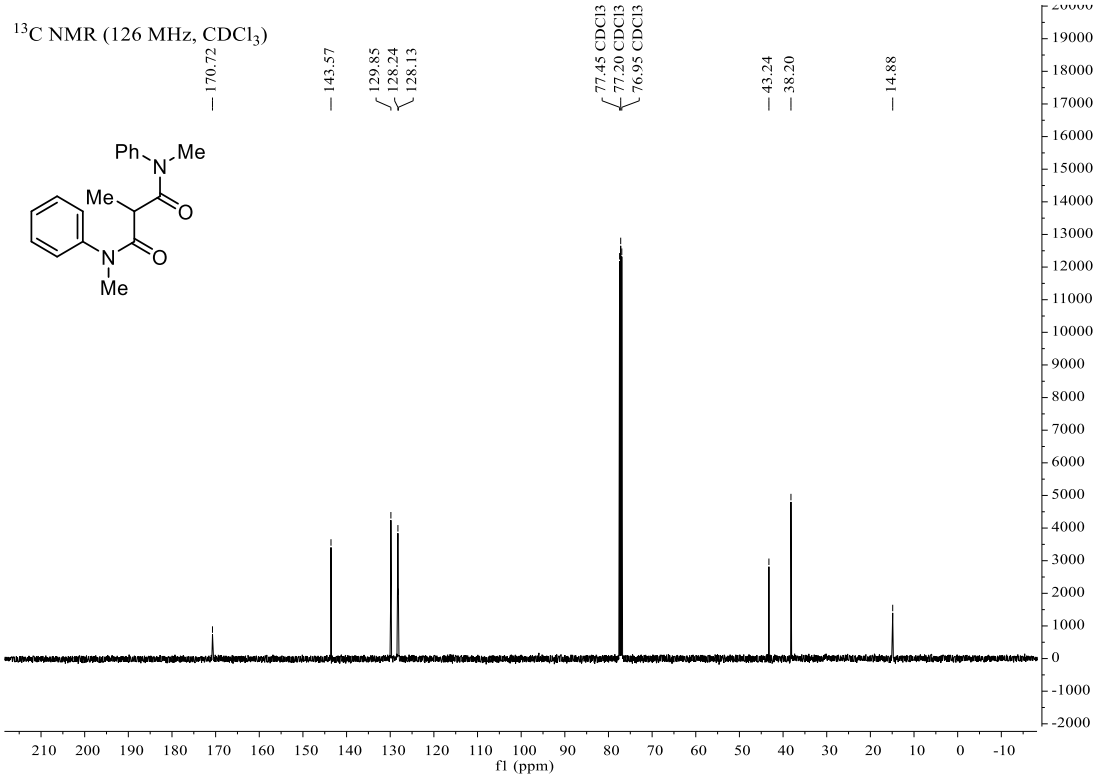
Compound S44



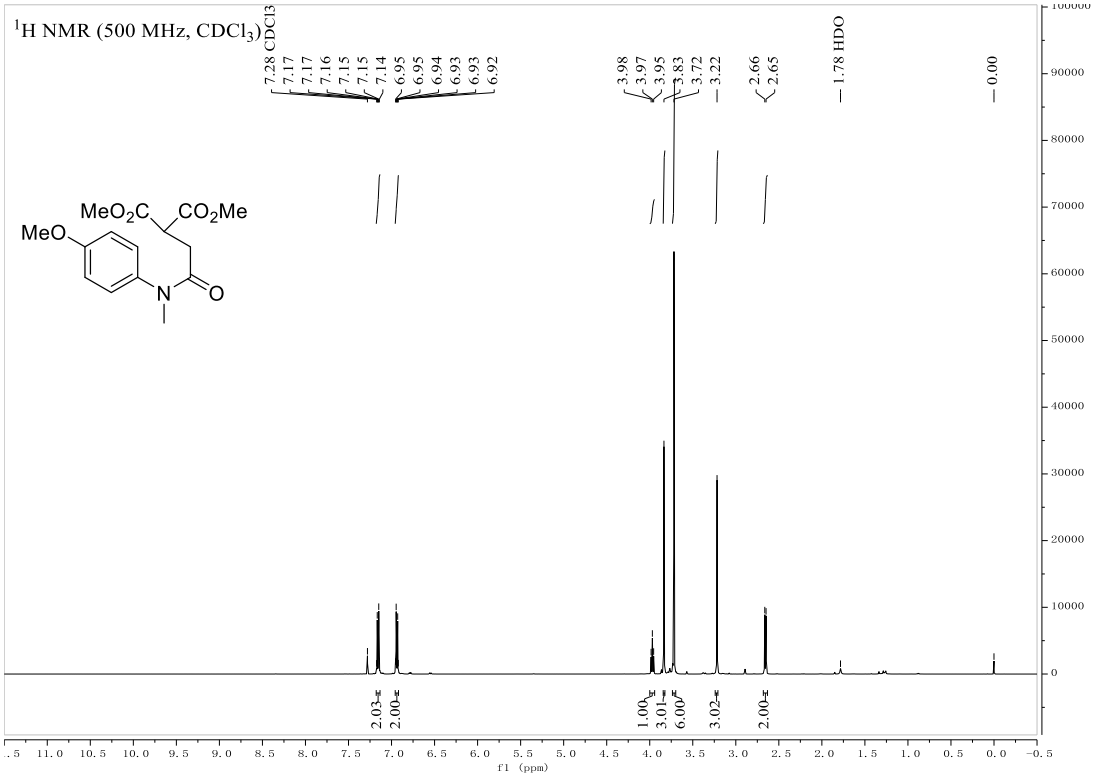


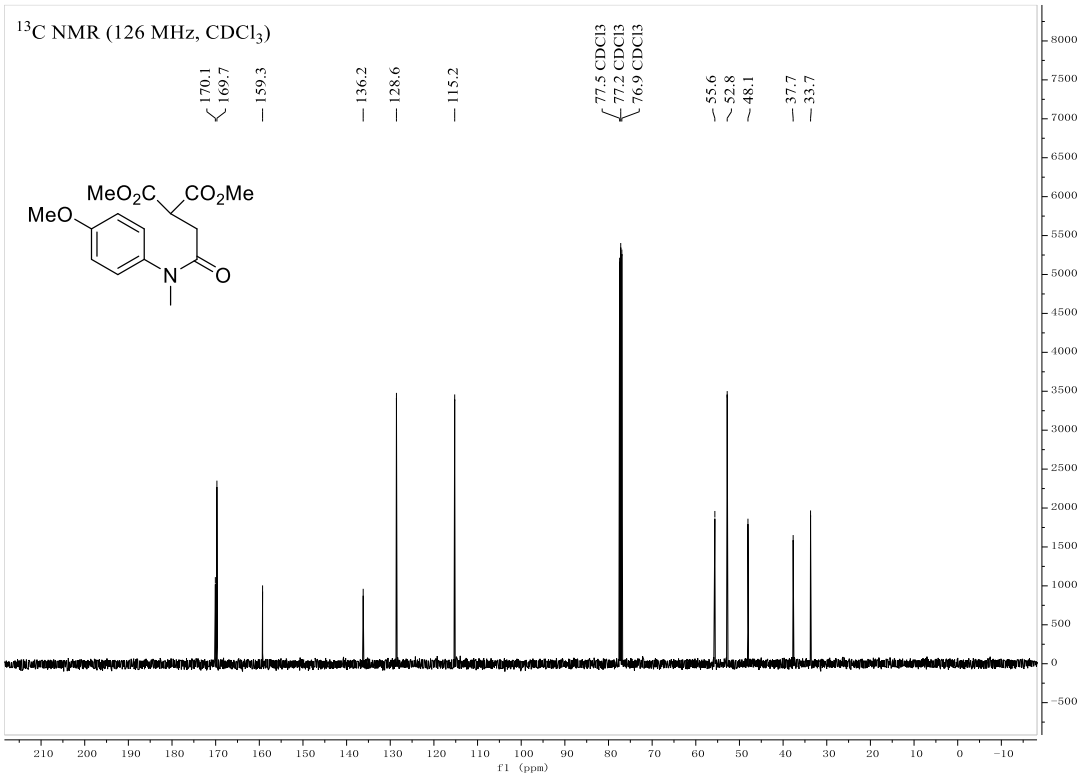
Compound S45



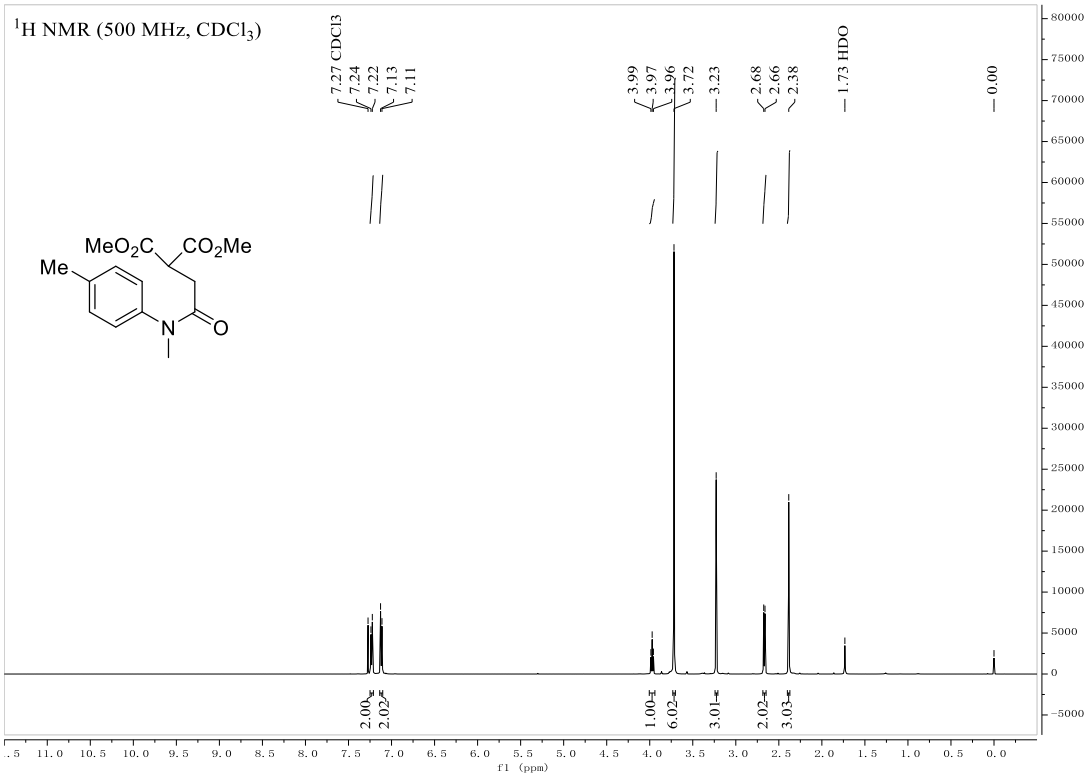


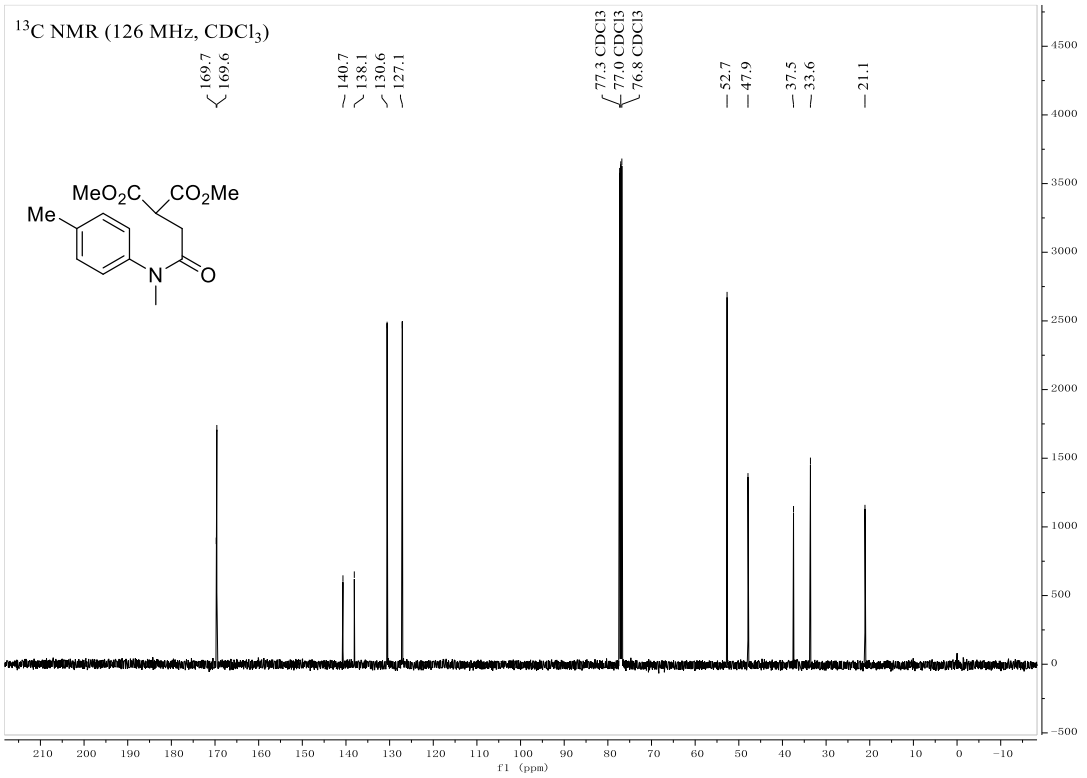
Compound S46



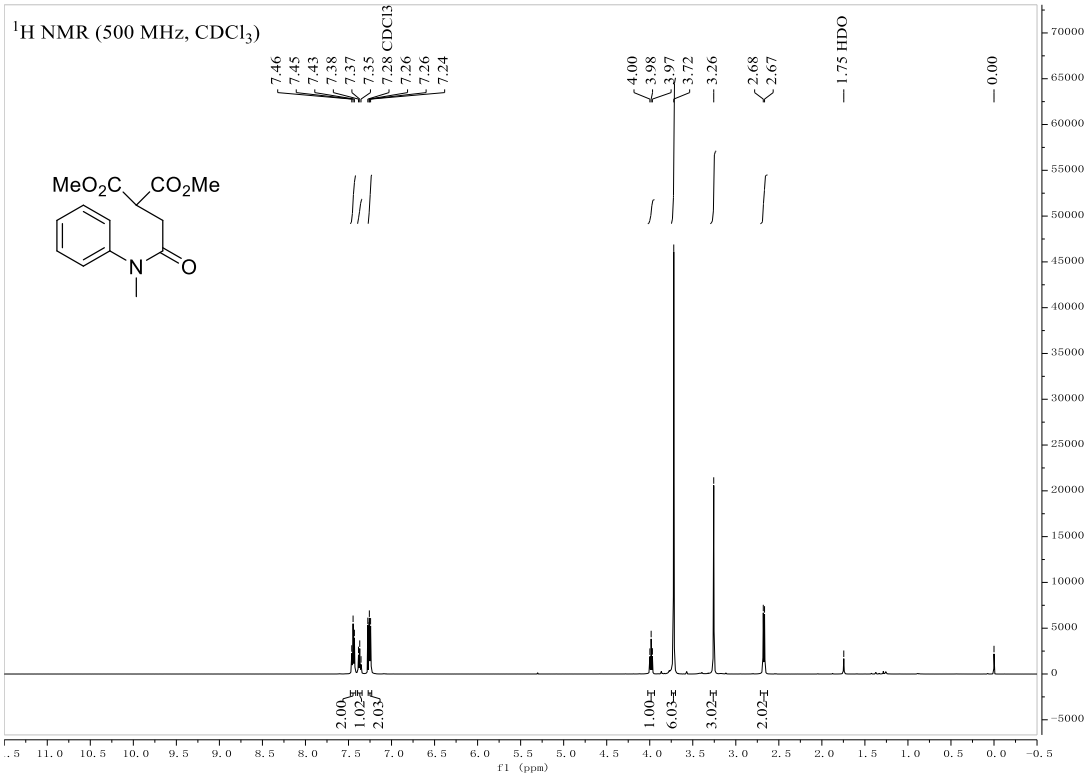


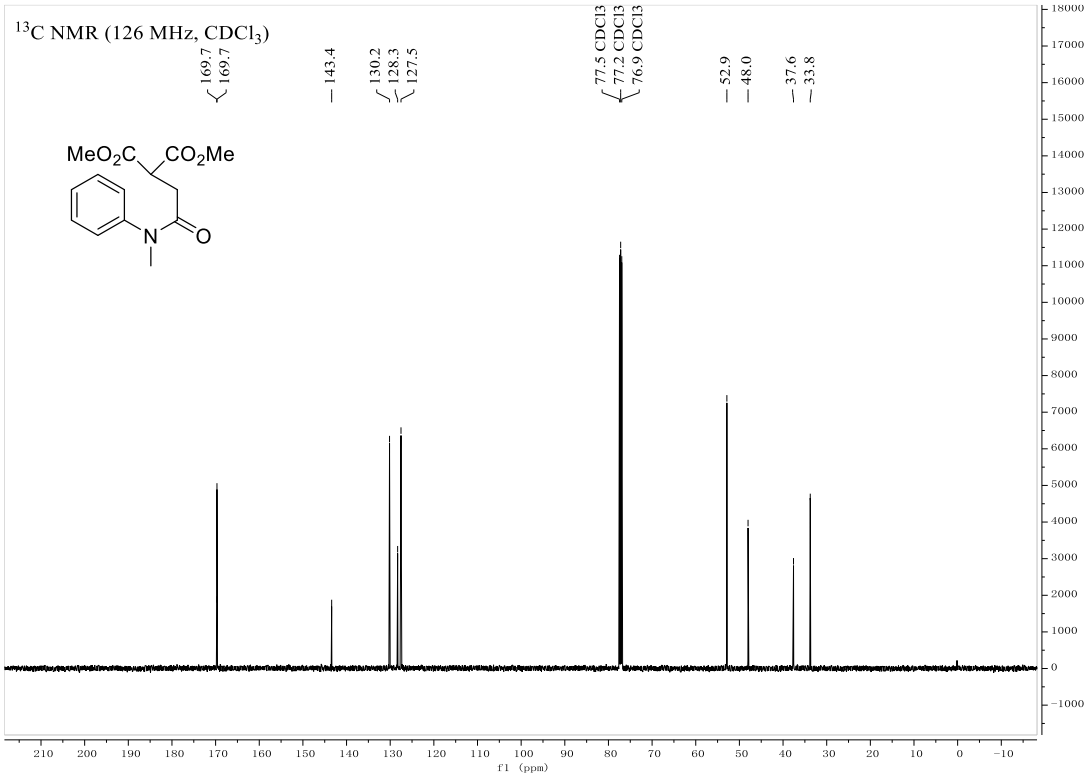
Compound S47



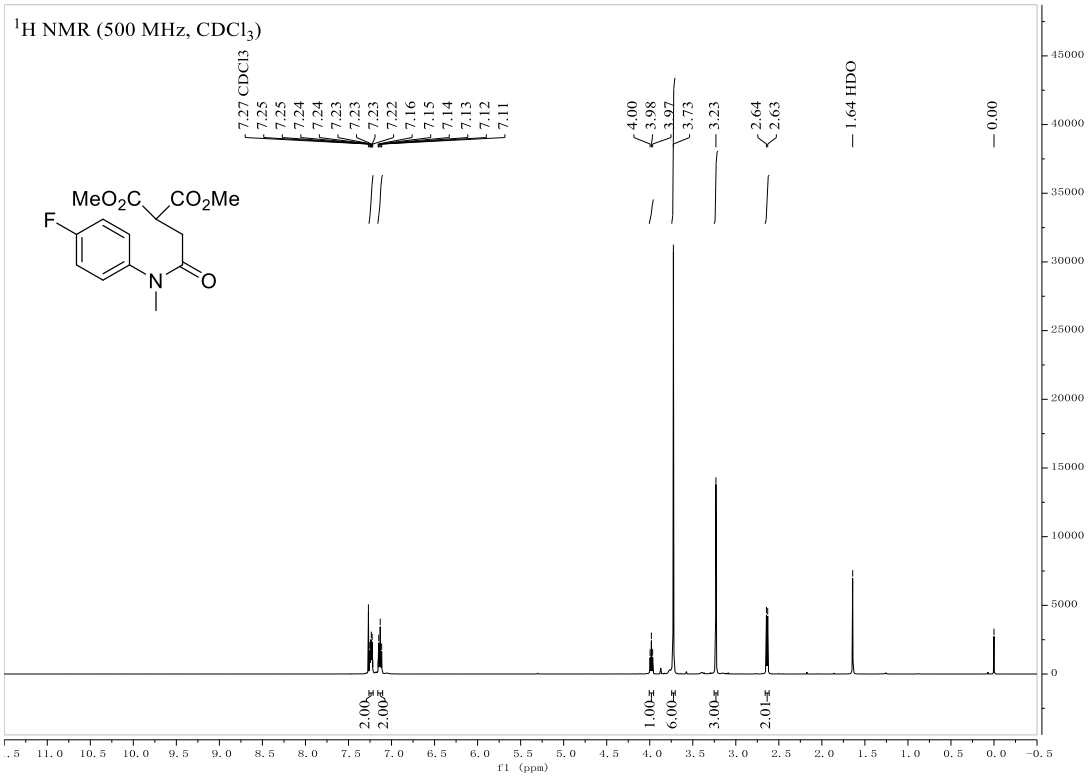


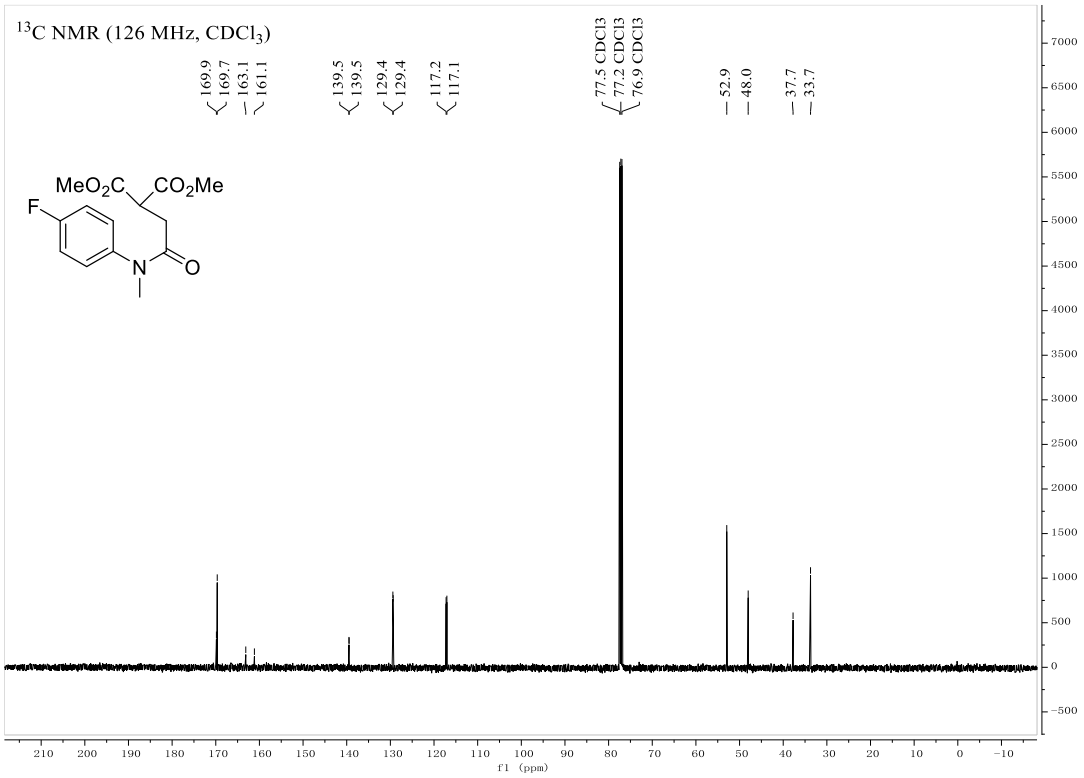
Compound S48

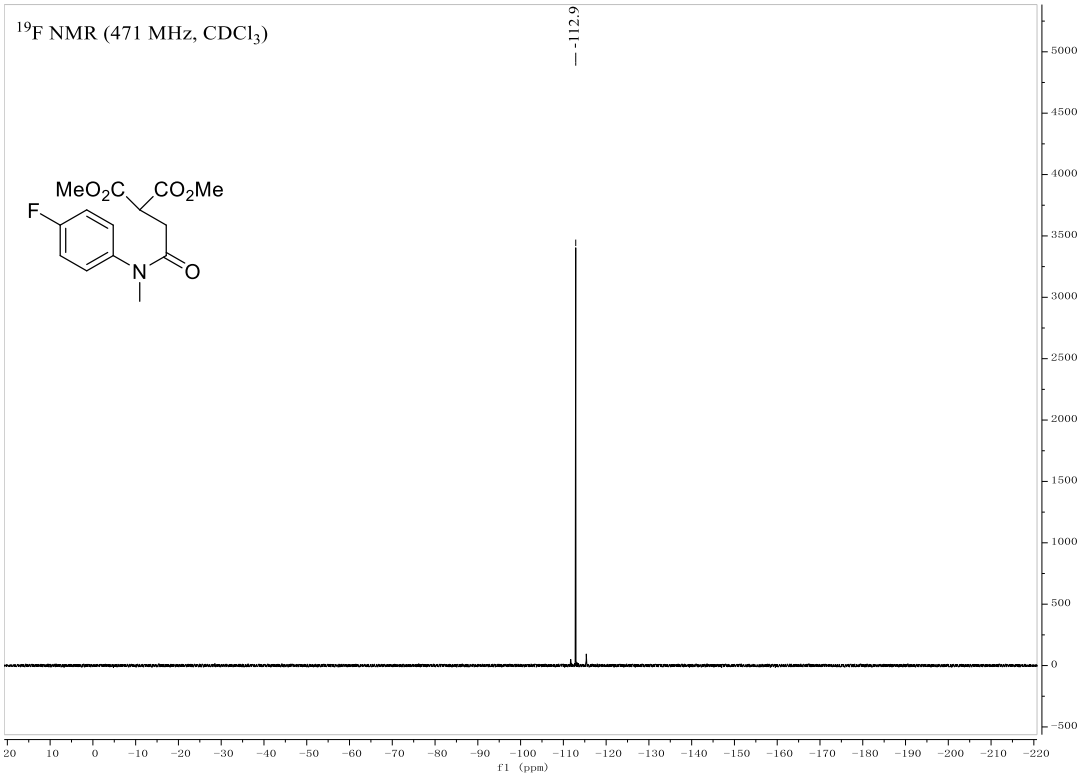




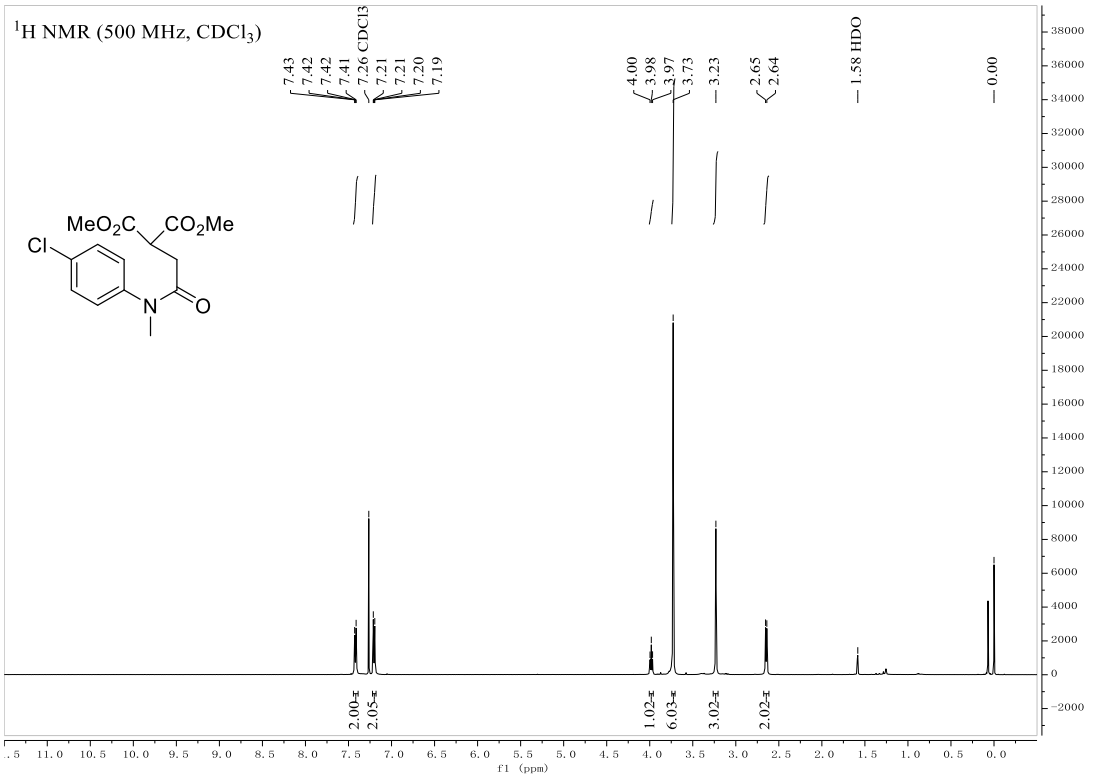
Compound S49

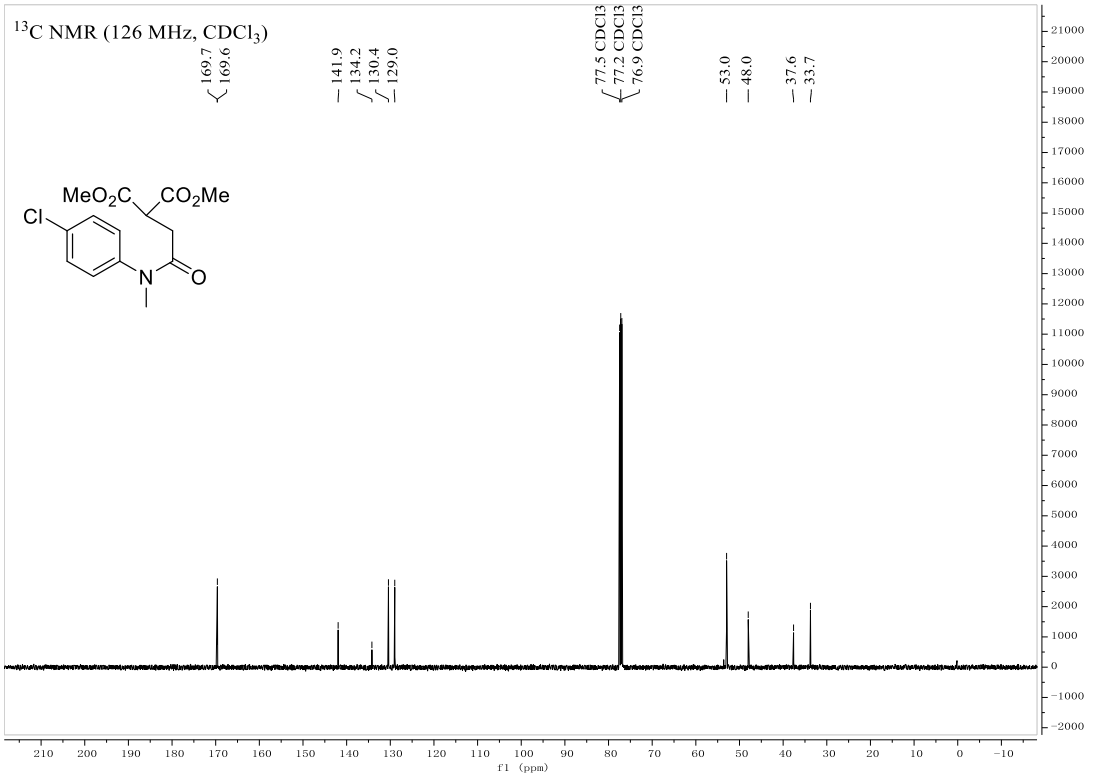



13C NMR (126 MHz, CDCl3)
169.9
169.7
163.1
161.1
139.5
139.5
129.4
129.4
117.2
117.1
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
52.9
48.0
37.7
33.7
MeO2C
CO2Me
F
N
O
f1 (ppm)

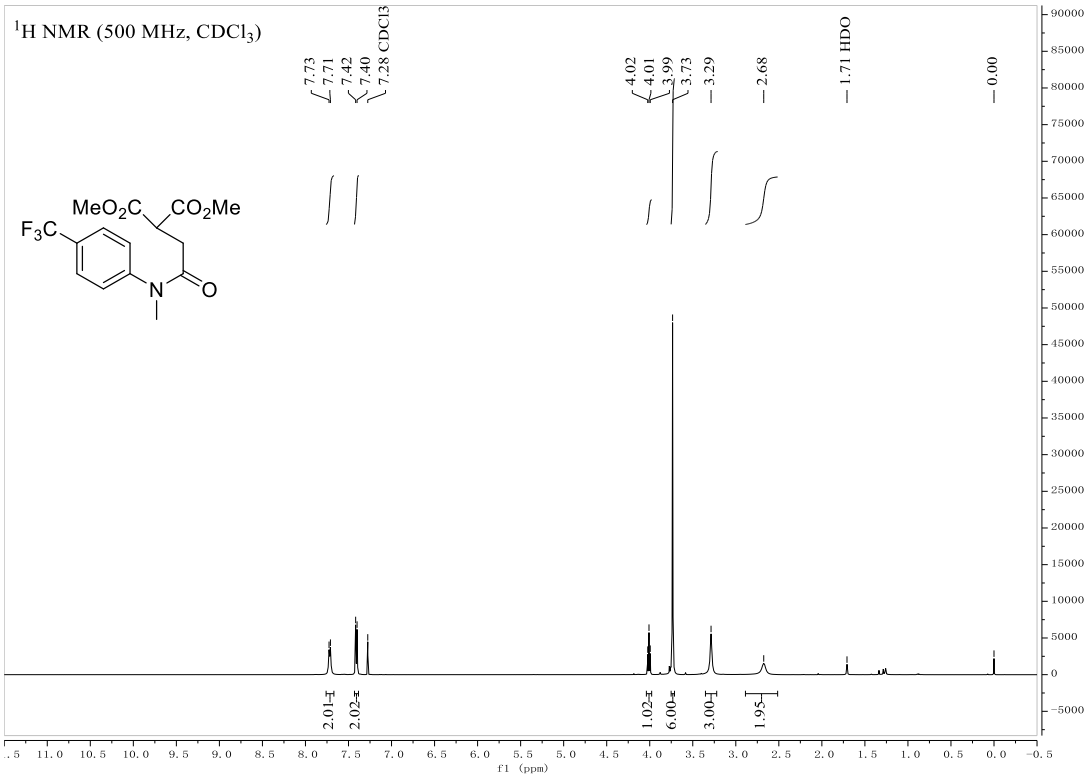

19F NMR (471 MHz, CDCl3)
-112.9
MeO2C
CO2Me
F
N
O
f1 (ppm)

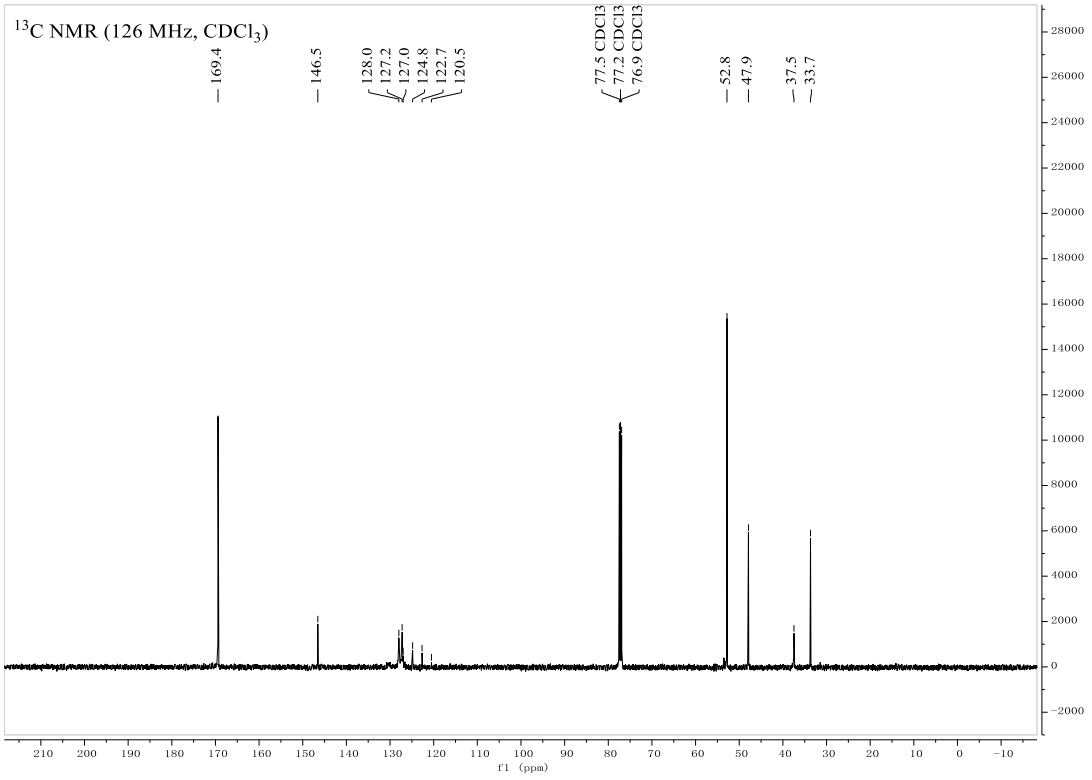
Compound S50

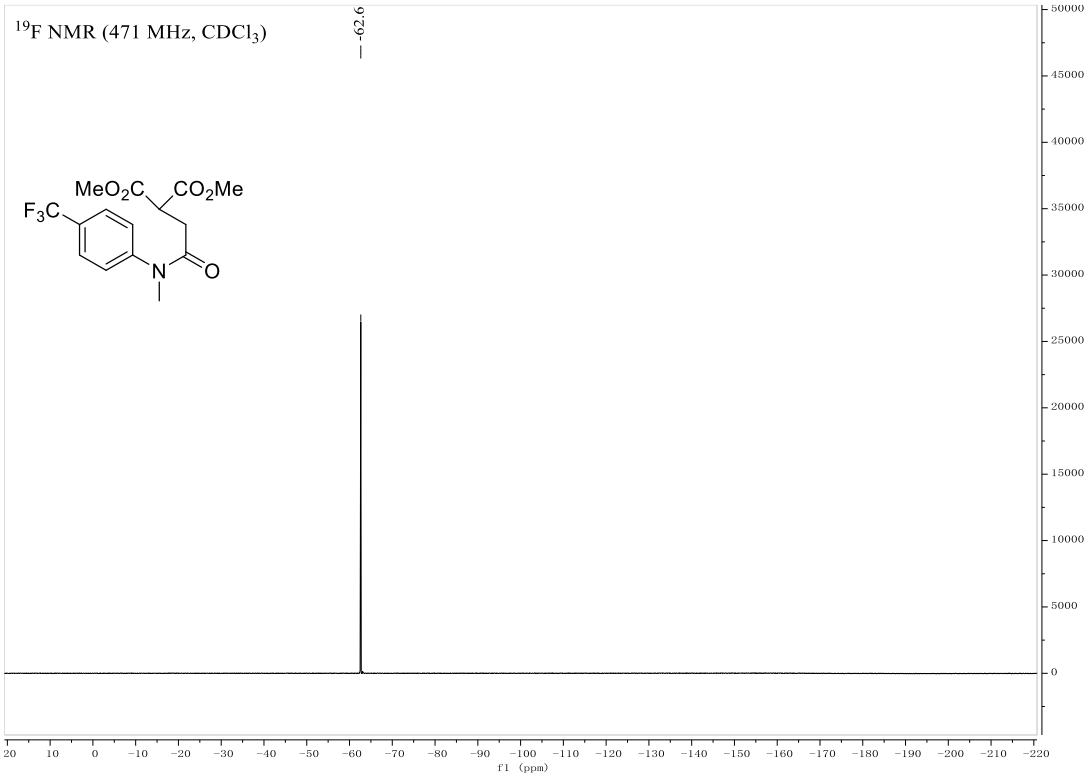




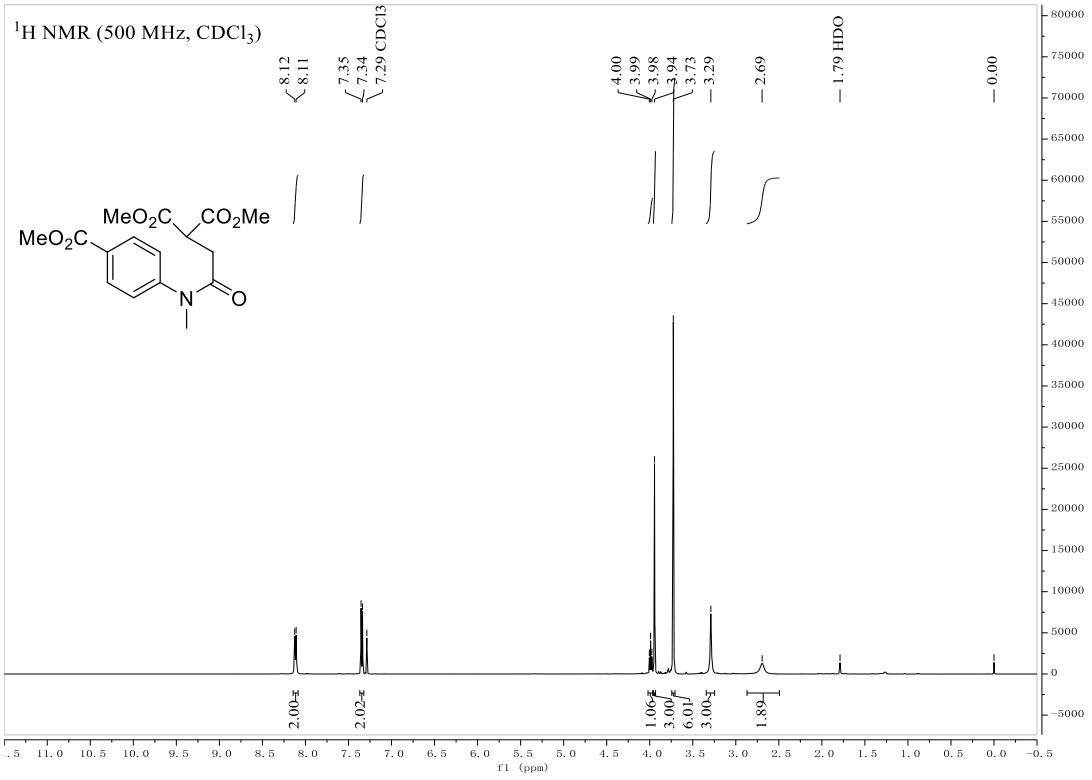
Compound S51

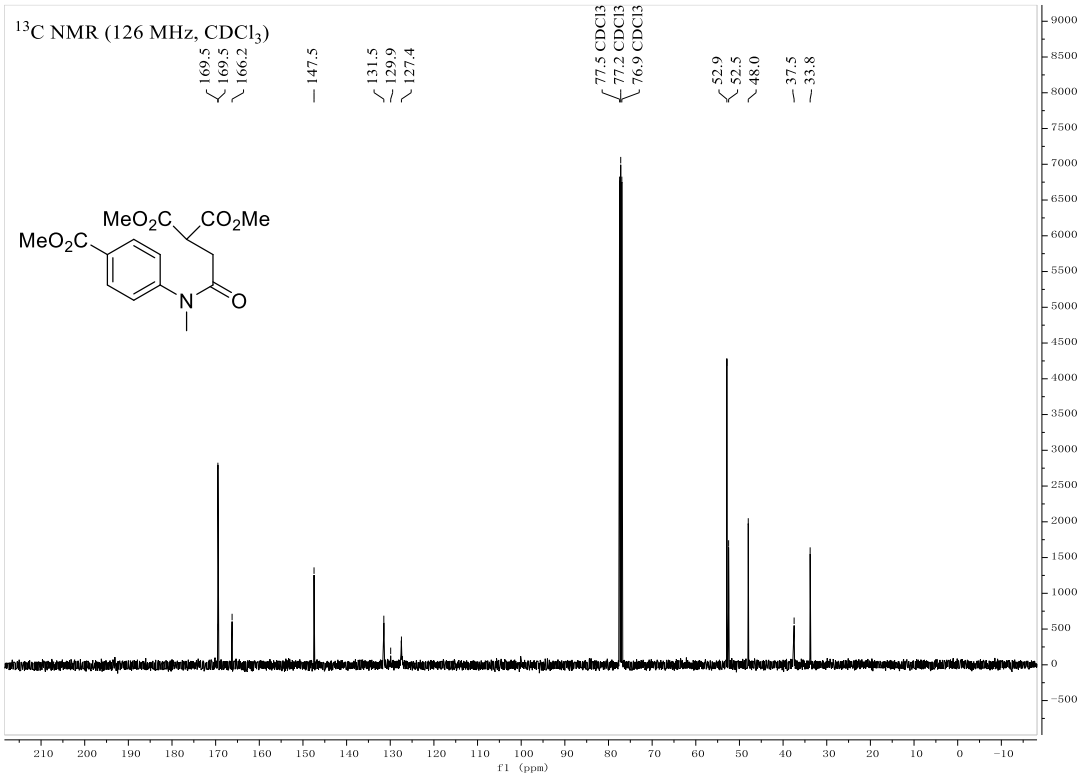




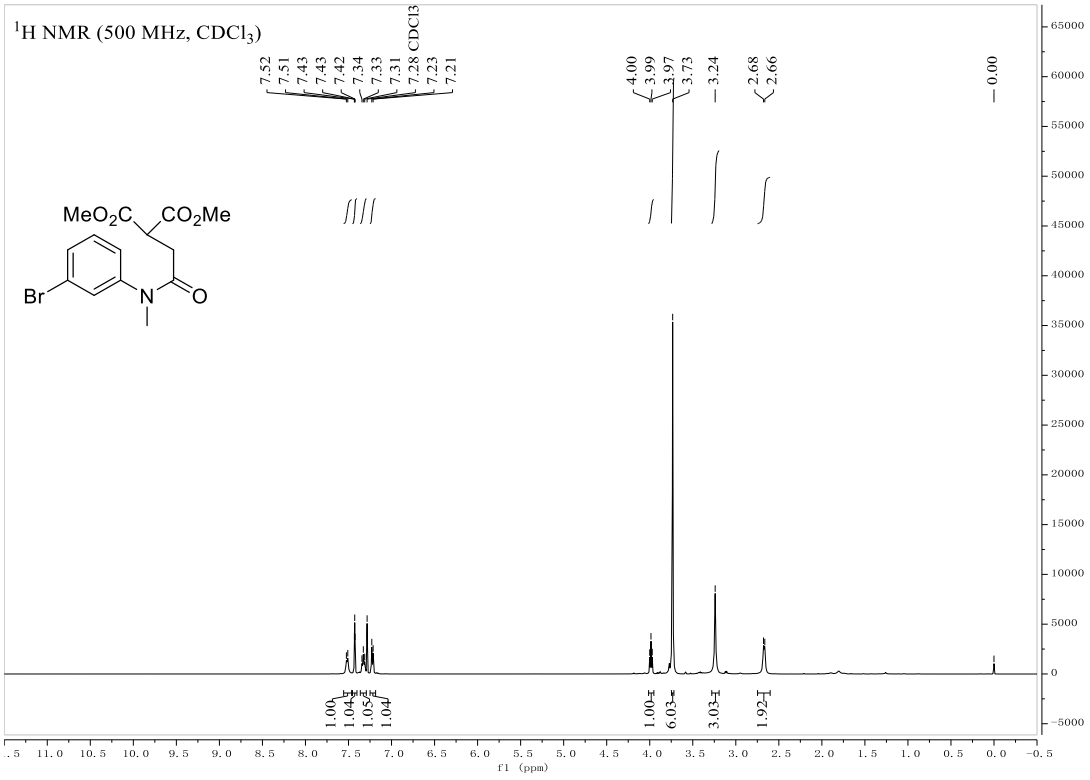


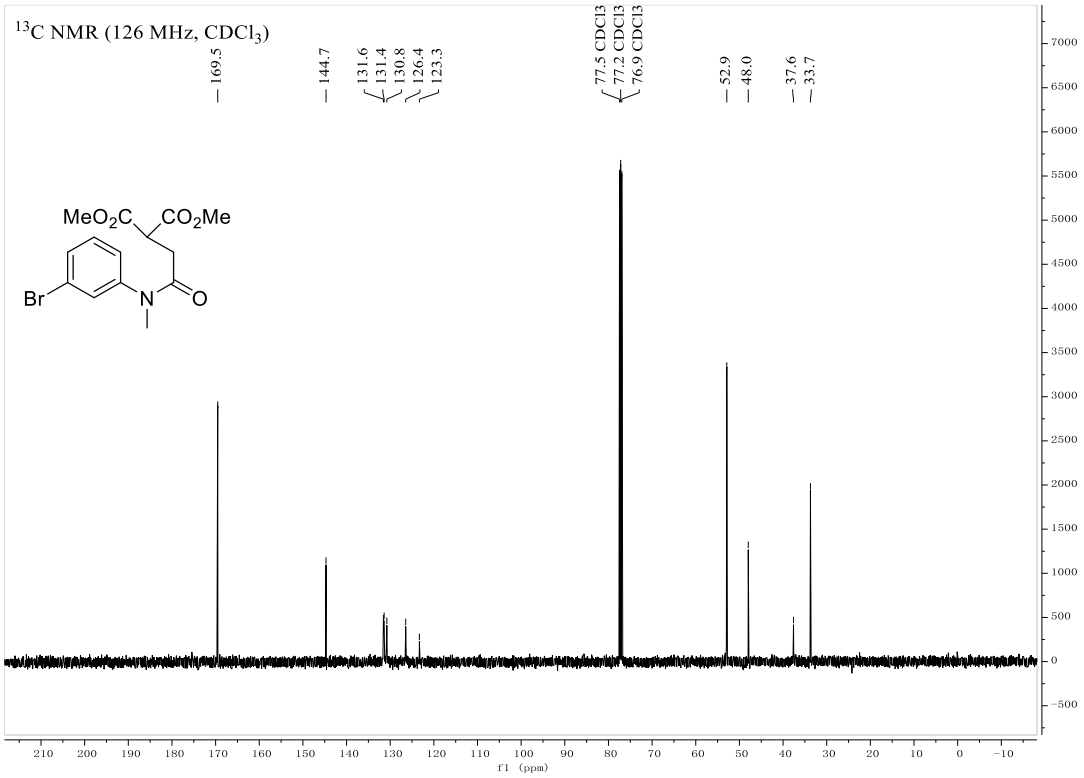
Compound S52



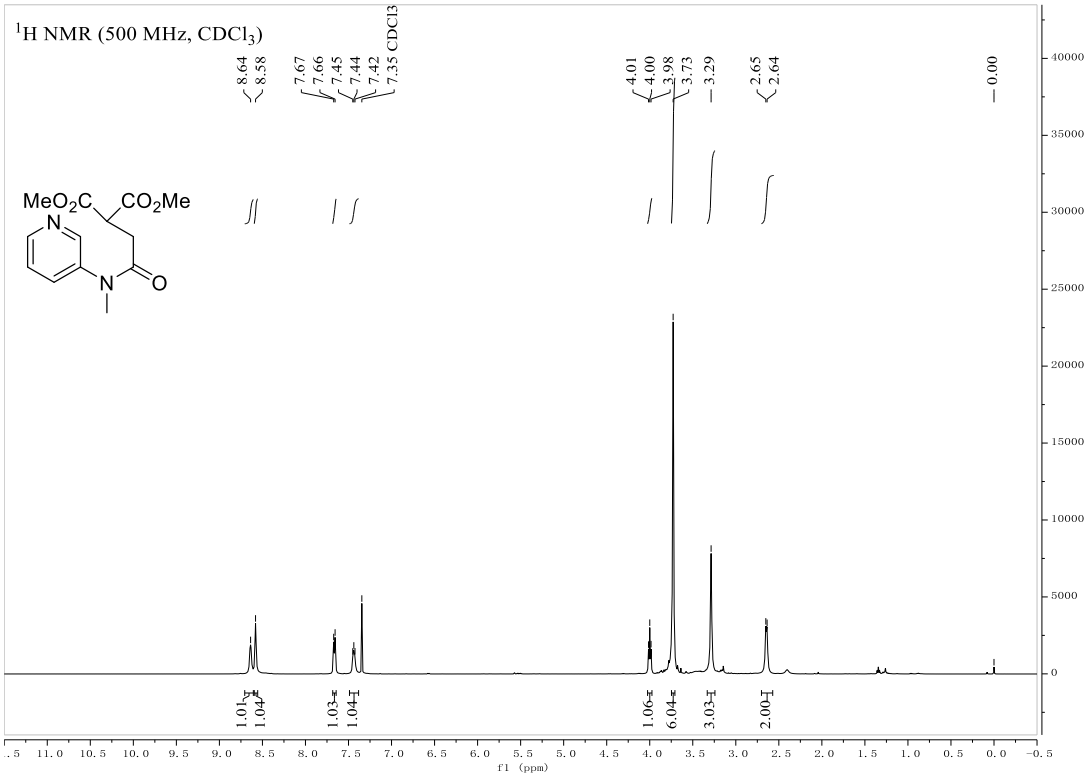


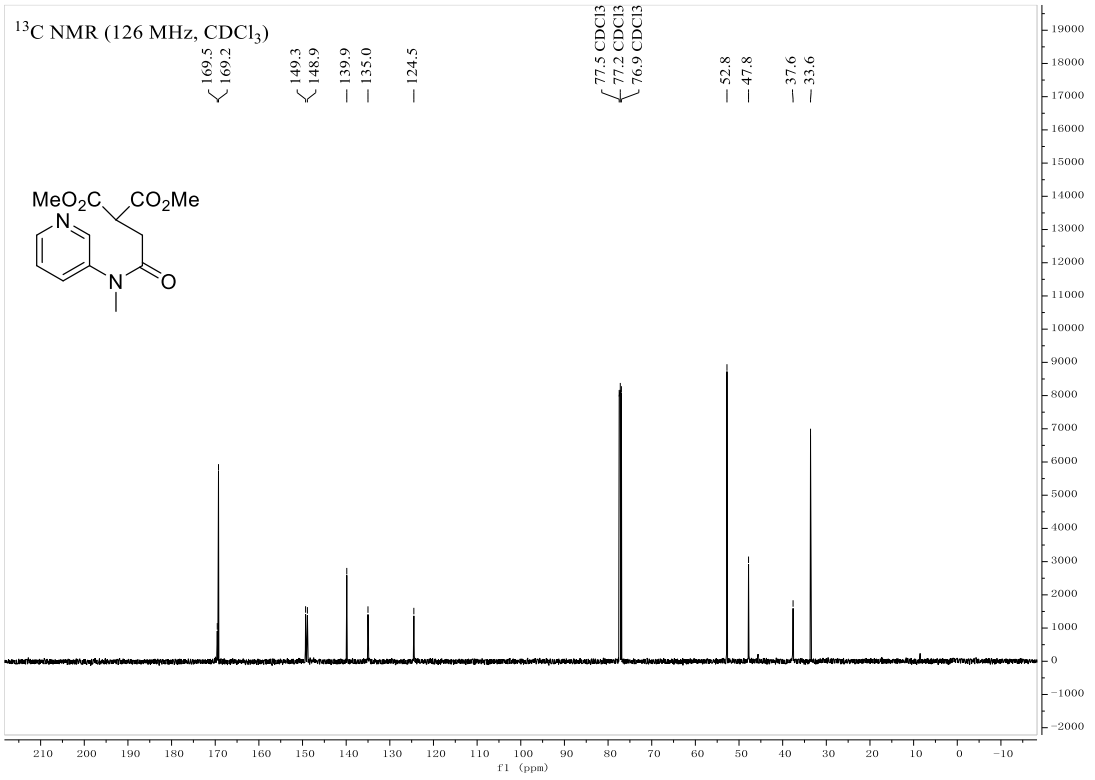
Compound S53



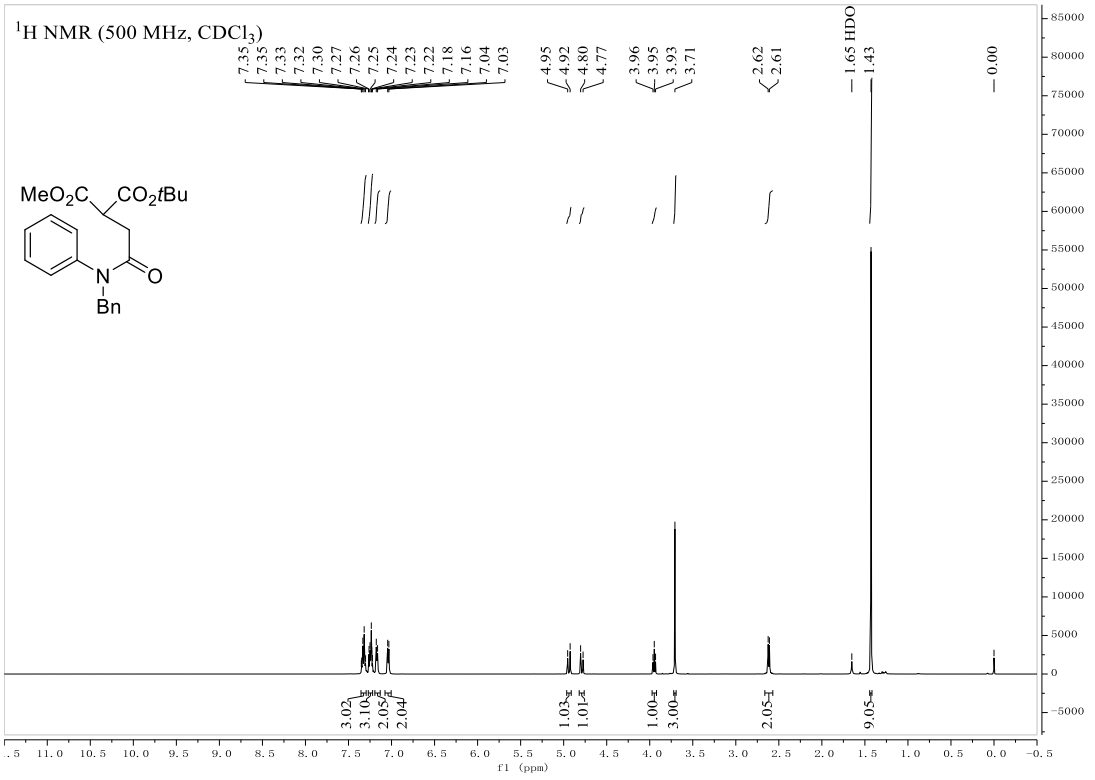


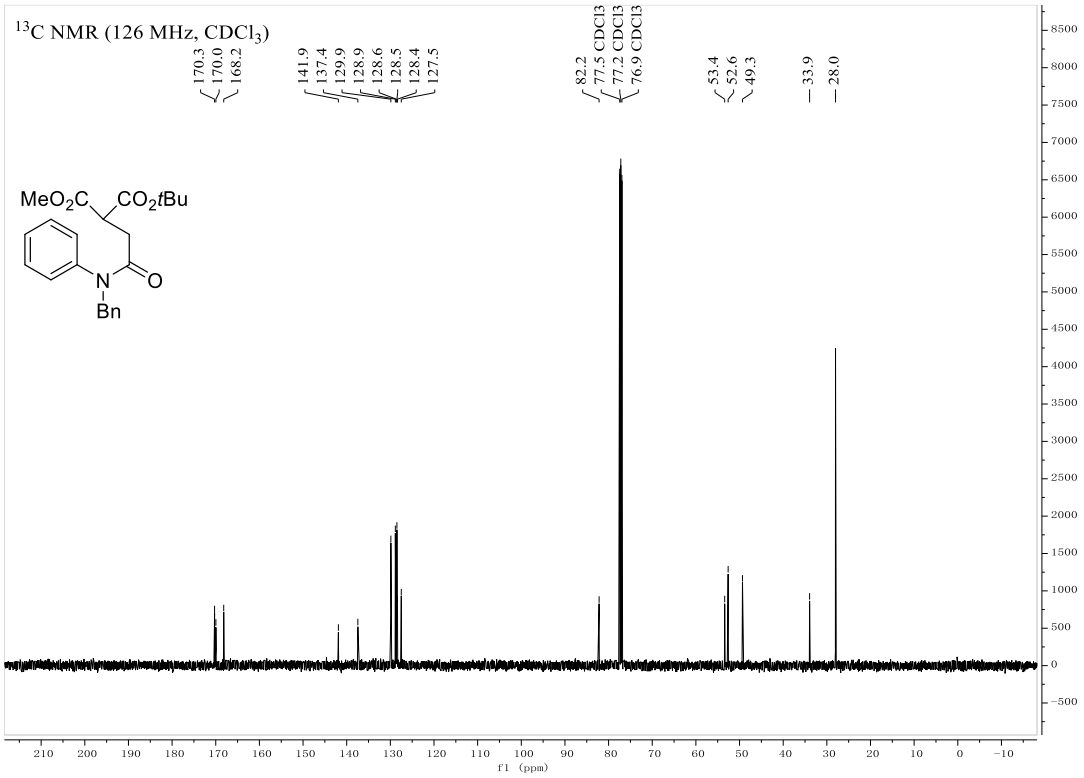
Compound S56



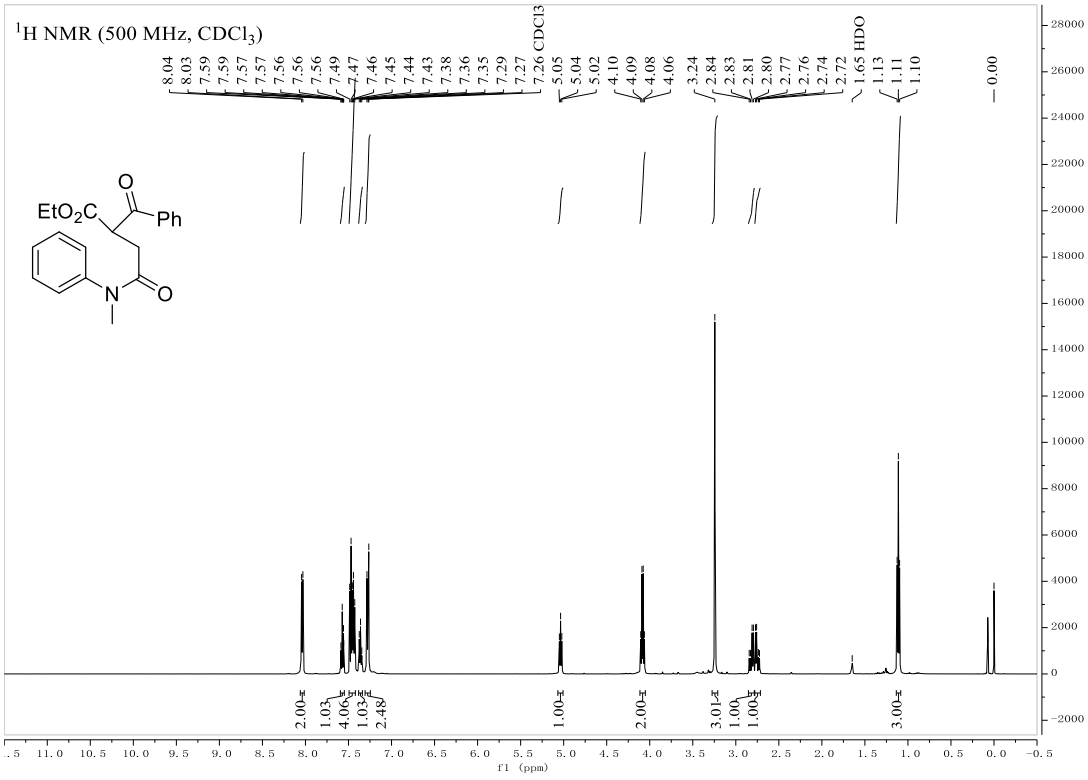


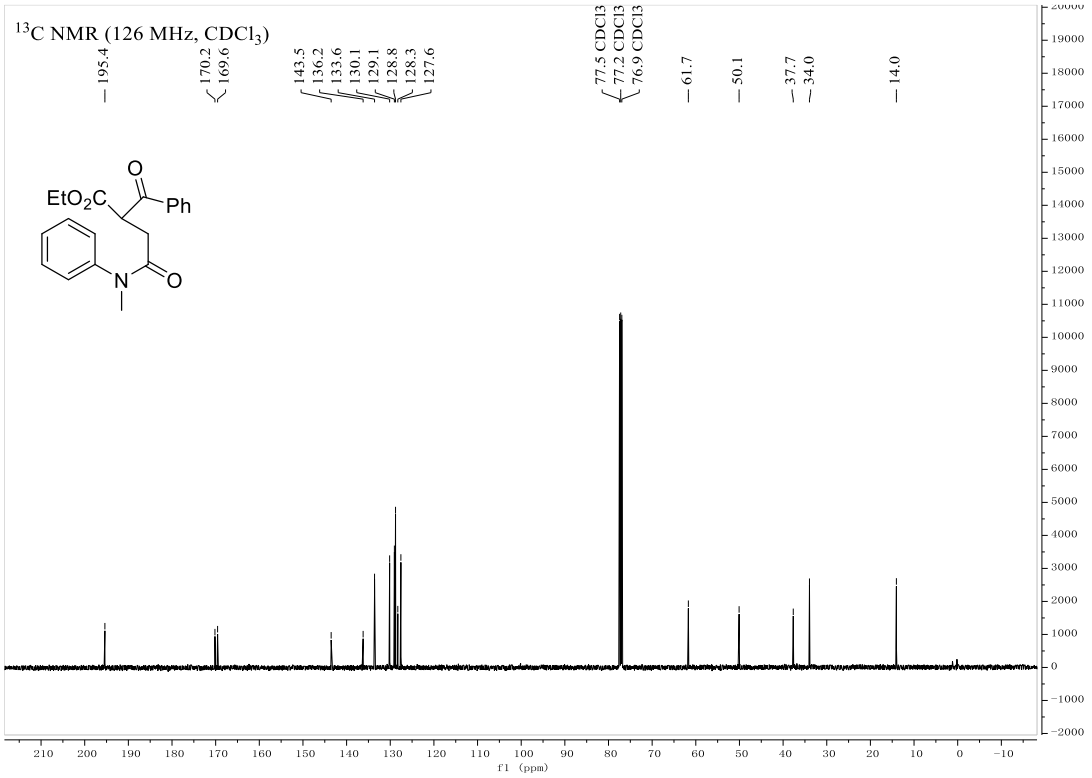
Compound S57



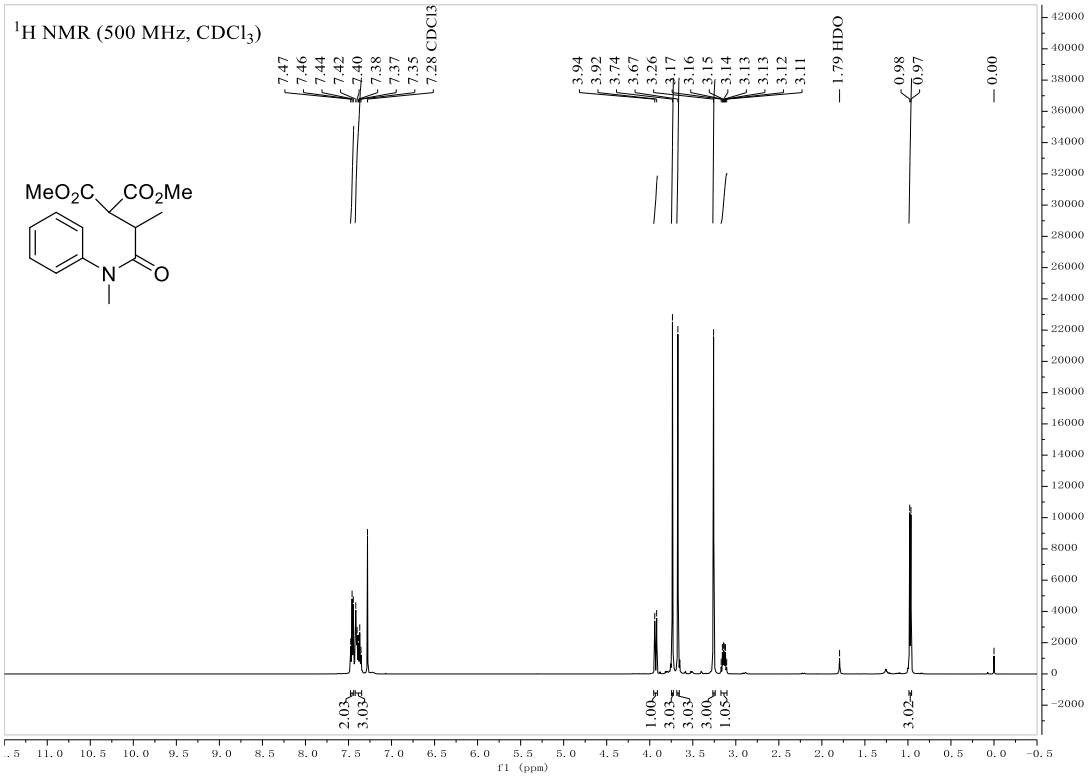


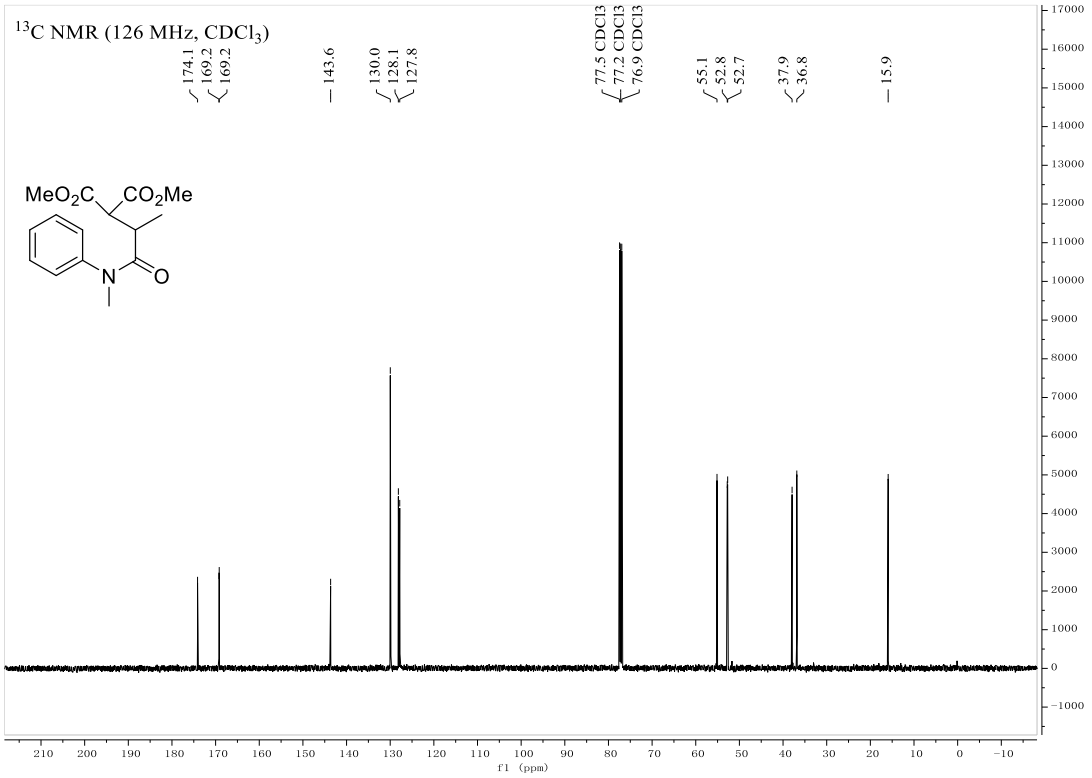
Compound S58



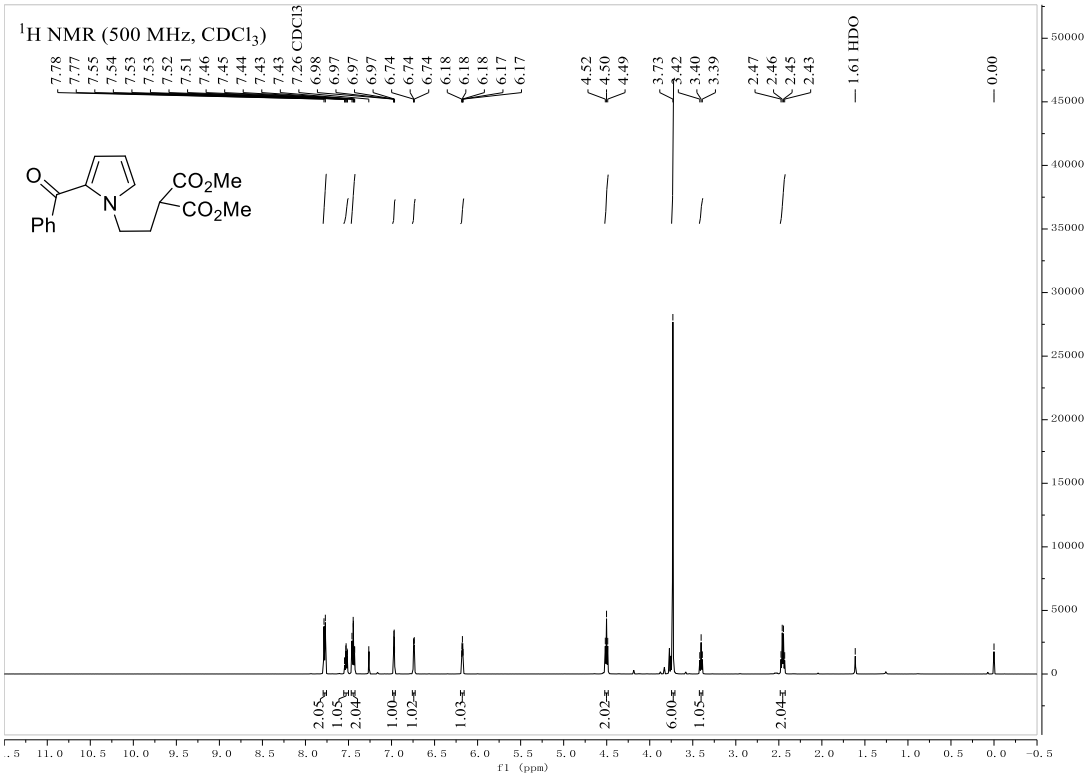


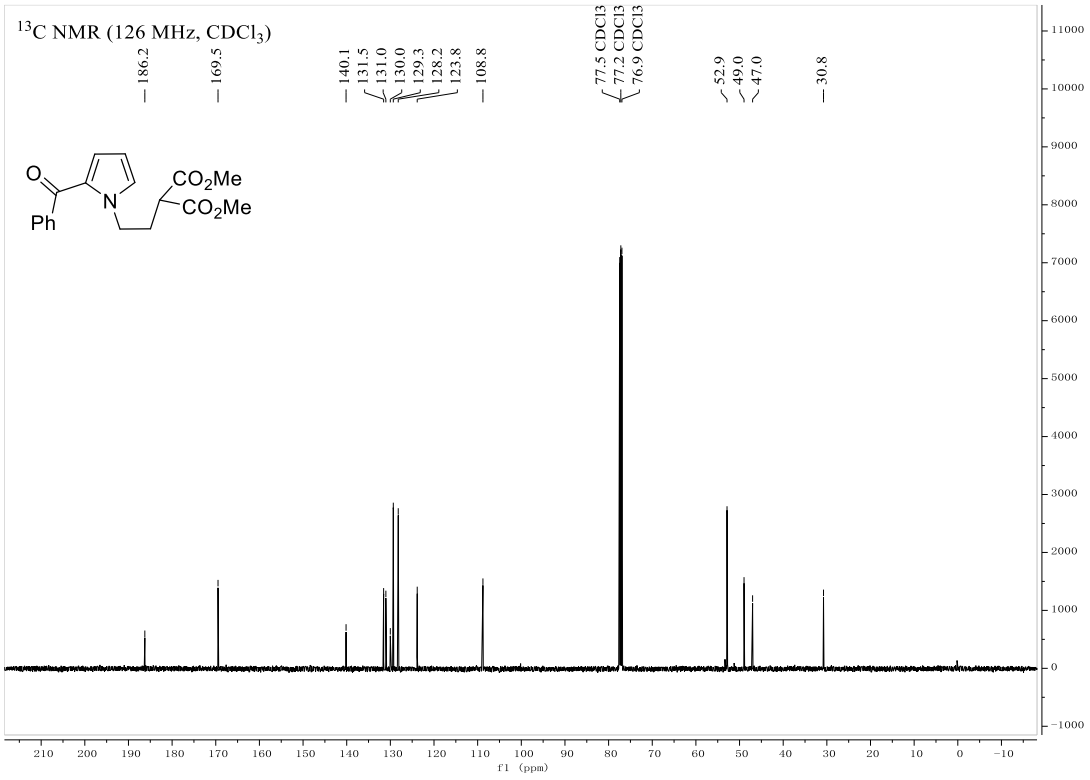
Compound S59





Compound S61




13C NMR (126 MHz, CDCl3)
186.2
169.5
140.1
131.5
131.0
130.0
129.3
128.2
123.8
108.8
77.5 CDCl3
77.2 CDCl3
76.9 CDCl3
52.9
49.0
47.0
30.8
O
N
Ph
CO2Me
CO2Me
f1 (ppm)