Supplementary Information

Excited Pd-catalyzed dearomative 1,4-dicarbofunctionalization of nonactivated aromatic rings

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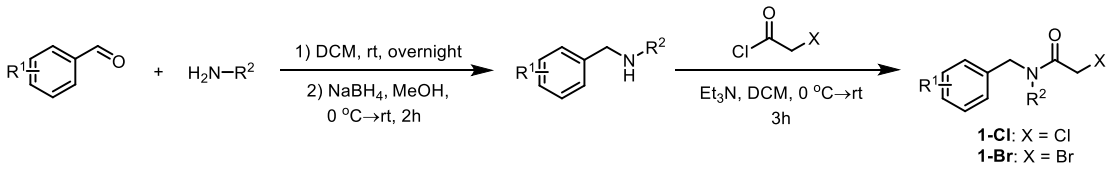
Content

1. Chemicals and apparatus

All reactions were carried out in dried tubes with magnetic stirrer. Purifications of reaction products were carried out by flash chromatography using Qingdao Haiyang Chemical Co. Ltd silica gel (200-300 mesh). ^{1}H, ^{13}C NMR spectra were recorded on a Bruker AVANCE (500 MHz or 400 MHz for ^{1}H; 125 MHz or 100 MHz for ^{13}C, 471 MHz or 376 MHz for ^{19}F), ^{1}H NMR and ^{13}C NMR shifts were determined relative to internal standard TMS at δ 0.0. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Mass spectra (MS) were obtained using thermo fisher Q Exactive HR-MS. Melting points were determined using WRS-1C from INESA intelligent technology. Infrared spectra (IR) were recorded on a Brucker TENSOR 27 FTIR spectrophotometer and were reported as wavelength numbers (cm^{-1}). Infrared spectra were recorded by preparing a KBr pellet containing the title compounds. All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature.

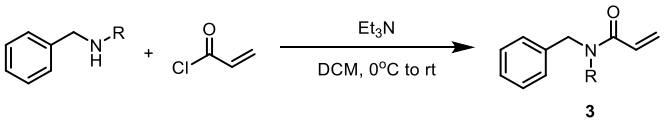
2. Procedure for the synthesis of starting materials.



Scheme S1. Synthesis route of **1**

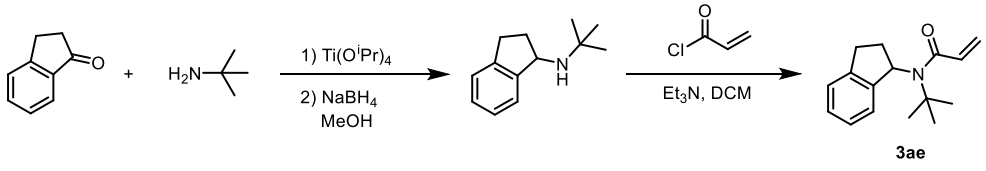
A mixture of benzaldehyde (10 mmol) and primary amine (11 mmol) in DCM (20 mL) was stirred at room temperature for 12 hours. Then the volatiles were removed by rotary evaporation under reduced pressure. The residue was redissolved by MeOH (20 mL) and stirred in ice bath for 5 minutes. After cooling down, $NaBH_4$ (20 mmol, 0.76 g) in three portion was added to the mixture stepwise, following with a continuous stir for 2 hours under room temperature. The reaction was quenched with water, and the mixture was concentrated by rotary evaporation under reduced pressure. The product was extracted by DCM (20 mL) from the mixture and washed with brine (30 mL × 3). Then the organic phase was dried by anhydrous sodium sulfate, and the solvent was then removed by rotary evaporation under reduced pressure to afford the crude secondary amine.

The resulted secondary amine was dissolved in anhydrous DCM (20 mL), following with the addition of anhydrous triethylamine (3 mL). α-Halogenated acyl chloride (15 mmol) dissolved in 5 mL anhydrous DCM was then added to the reaction mixture dropwise under 0 ℃ over 10 minutes. After stirring for 3 hours, the reaction was quenched by water. The product was extracted by DCM (20 mL) and washed with brine (50 mL × 3). Reagents **1** were afforded by the evaporation of solvent and purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (10/1, v/v) as the eluent.



Scheme S2. Synthesis route of **3**

The secondary amine was dissolved in anhydrous DCM (20 mL), following with the addition of anhydrous triethylamine (3 mL). Acryloyl chloride (15 mmol) dissolved in 5 mL anhydrous DCM was then added to the reaction mixture dropwise under 0 ℃ over 10 minutes. After stirring for 3 hours, the reaction was quenched by water. The product was extracted by DCM (20 mL) and washed with brine (50 mL × 3). Reagents **3** were afforded by the evaporation of solvent and purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (10/1, v/v) as the eluent.



Scheme S3. Synthesis route of **3ae**

2,3-dihydro-1H-inden-1-one (10 mmol) and tetraisopropyl titanate (15 mL) was placed into a 100 mL round bottle flask. Before adding *tert*-butylamine (11 mol) dropwise, the mixture was stirred and cooled down. Then, MeOH (10 mL) was added into the reaction slowly for 5 minutes, and the $NaBH_4$ (20 mmol, 0.76 g) was added to the mixture in serval portion. After 1.5 hours, the reaction was quenched by water and filtered. The crude secondary amine was collected by the extraction of DCM from the filtrate and the further removal of solvent from organic phase.

The resulted secondary amine was dissolved in anhydrous DCM (20 mL), following with the addition of anhydrous triethylamine (3 mL). Acryloyl chloride (15 mmol) dissolved in 5 mL anhydrous DCM was then added to the reaction mixture dropwise under 0 ℃ over 10 minutes. After stirring for 3 hours, the reaction was quenched by water. The product was extracted by DCM (20 mL) and washed with brine (50 mL × 3). Reagents **3ae** were afforded by the evaporation of solvent and purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (10/1, v/v) as the eluent.

3. General procedure for the Synthesis of 2 and 4

1 (0.2 mmol) was added to a 25 mL reaction tube charged with nucleophile (0.4 mmol), $Pd(PPh_3)_4$ (0.01 mmol, 11.6 mg), phosphorus ligand (0.04 mmol), K_2CO_3 (0.4 mmol, 40 mg) and anhydrous THF (2.5 mL). The tube was placed next to the blue LED light (30 W, 430-435 nm) with a fan behind for cooling (Figure S1). The reaction was carried under argon atmosphere for 20 hours. After that, the reaction was quenched by adding water, and the product was diluted with DCM (10 mL) and washed with brine (5 mL × 3). The organic layer was concentrated by the rotary evaporation and the resulting residue was further purified by chromatography on silica gel with petroleum ether/ethyl acetate as the eluent to afford the product **2**.

3 (0.2 mmol) was added to a 25 mL reaction tube charged with nucleophile (0.4 mmol), halohydrocarbon (0.4 mmol), $Pd(PPh_3)_4$ (0.01 mmol, 11.6 mg), phosphorus ligand (0.04 mmol), K_2CO_3 (0.4 mmol, 40 mg) and anhydrous DMF (2.5 mL). The tube was placed between two blue LED light (30 W, 430-435 nm) (Figure S1). The reaction was carried under argon atmosphere for 20 hours. After that, the reaction was quenched by adding water, and the product was diluted with DCM (10 mL) and washed with brine (5 mL × 3). The organic layer was concentrated by the rotary evaporation and the resulting residue was further purified by chromatography on silica gel with petroleum ether/ethyl acetate as the eluent to afford the product **4**.

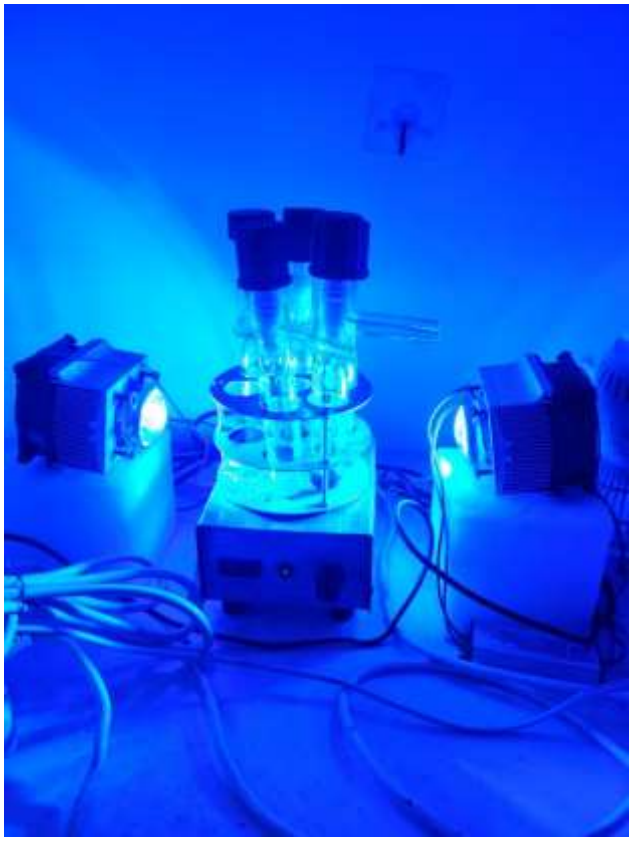
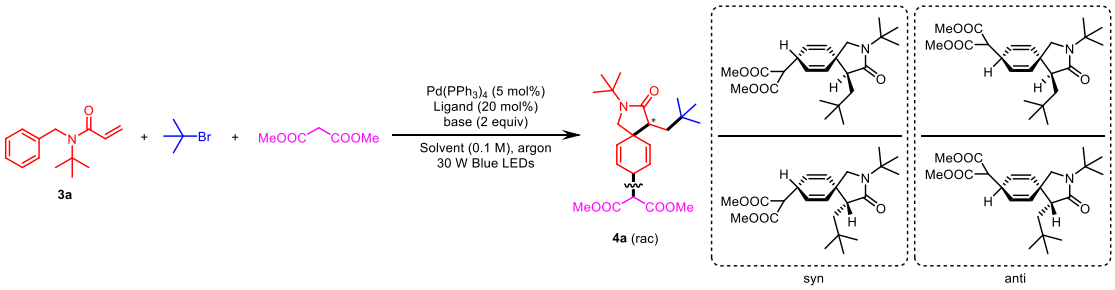


Figure S1 Device for the standard reaction

4. Optimization of the three-component reaction

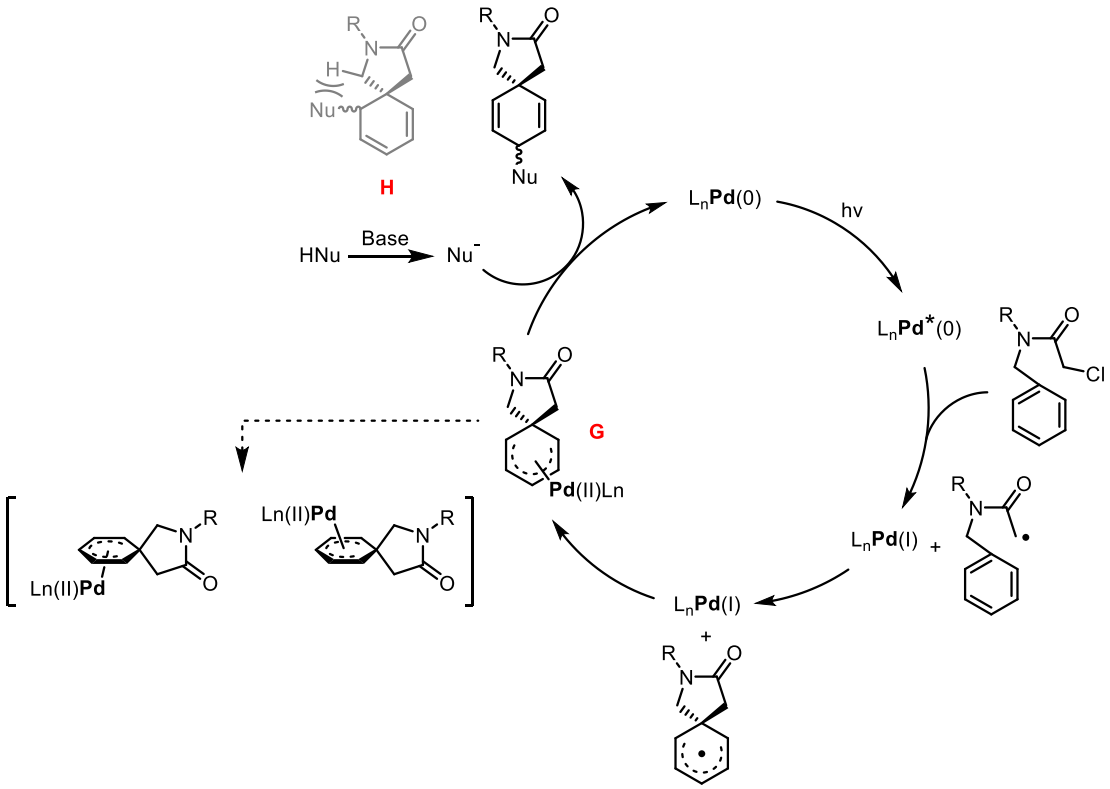
Table S1. Screen of three-component reaction conditions



Entry[a]	Solvent	Ligand	Time(h)	Yield(%)[b]
1	DMF	PPh_3	24	35
2	DMSO	PPh_3	24	trace
3	THF	PPh_3	24	trace
4	DMF	PPh_3	36	54
5	DMF	PPh_3	48	56
6[c]	DMF	PPh_3	48	37
7[d]	DMF	PPh_3	48	trace
8	DMF	Cy-Johnphos	48	trace
9	DMF	Xantphos	48	trace
10	DMF	(S)-BINAP	48	88(86)[e]
11[f]	DMF	(S)-BINAP	48	N.D.
12[g]	DMF	(S)-BINAP	48	N.D.
13[h]	DMF	-	48	26

[a]Unless noted otherwise, the reactions were carried out with 0.2 mmol **3a**, 0.4 mmol nucleophile in solvent (c = 0.1 M) under irradiation of 30 W blue LEDs and argon atmosphere at room temperature. [b]Yields of **4a** determined by ^{1}H NMR with dibromomethane as the internal standard. [c]Cs_2CO_3 instead of K_2CO_3. [d]Et_3N instead of K_2CO_3. [e]Isolated yield with the ratio of syn:anti (> 20:1). [f]In dark. [g]Without $Pd(PPh_3)_4$. [h]Without (S)-BINAP.

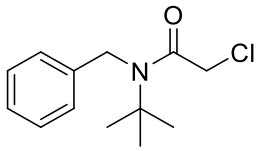
5. Possible mechanism for the two-component reaction



Scheme S4. Possible reaction cycle for the two-component reaction.

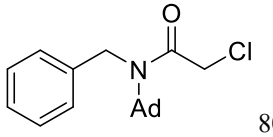
6. Structural characterization data for the compounds

N-benzyl-N-(tert-butyl)-2-chloroacetamide (1a):



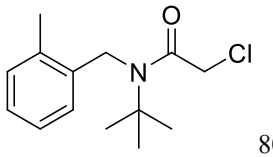
85% yield, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 2H), 7.30 – 7.27 (m, 1H), 7.21 – 7.19 (m, 2H), 4.66 (s, 2H), 3.98 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.57, 138.50, 129.06, 127.42, 125.35, 58.69, 48.72, 44.22, 28.37. The NMR data is consistent with reported literature.[1]

N-(adamantan-1-yl)-N-benzyl-2-chloroacetamide (1j):



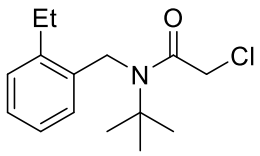
80% yield, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.40 (m, 2H), 7.30 – 7.26 (m, 1H), 7.22 – 7.20 (m, 2H), 4.67 (s, 2H), 3.96 (s, 2H), 2.23 (d, J = 3.0 Hz, 6H), 2.10 – 2.03 (m, 3H), 1.69 – 1.58 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.57, 138.86, 129.01, 127.33, 125.38, 60.18, 47.31, 44.70, 39.49, 36.26, 30.12. IR (thin film): ν_{max} (cm^{-1}) = 3299, 2909, 2857, 1660, 1448, 1305, 1149, 1003, 798, 747. HRMS (ESI) calcd for $C_{19}H_{25}ClNO$ $[M+H]^+$: 318.1619. Found: 318.1610.

N-(tert-butyl)-2-chloro-N-(2-methylbenzyl)acetamide (1m):



80% yield, yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.17 (m, 4H), 4.55 (s, 2H), 3.91 (s, 2H), 2.30 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.79, 136.18, 134.17, 130.62, 127.21, 126.61, 124.52, 58.61, 46.60, 44.00, 28.17, 18.99. IR (thin film): ν_{max} (cm^{-1}) = 2970, 1663, 1470, 1401, 1263, 1195, 798, 750, 675. HRMS (ESI) calcd for $C_{14}H_{21}ClNO$ $[M+H]^+$: 254.1306. Found: 254.1302.

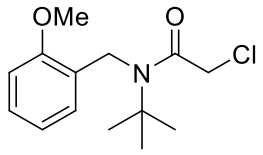
N-(tert-butyl)-2-chloro-N-(2-ethylbenzyl)acetamide (1n):



87% yield, colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.19 (m, 4H), 4.65 (s, 2H), 3.91 (s, 2H), 2.65 (q, J = 7.6 Hz, 2H), 1.49 (s, 9H), 1.27 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.74, 140.14, 135.49, 128.73, 127.44, 126.50, 124.65, 58.61, 46.16, 44.05, 28.20,

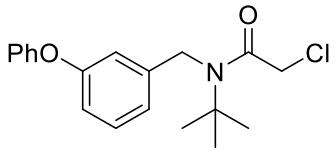
25.28, 14.28. IR (thin film): ν_{max} (cm^{-1}) = 2969, 1664, 1452, 1402, 1267, 1197, 1045, 798, 753, 675. HRMS (ESI) calcd for $C_{15}H_{23}ClNO$ $[M+H]^+$: 268.1463. Found: 268.1454.

N-(tert-butyl)-2-chloro-N-(2-methoxybenzyl)acetamide (1o):



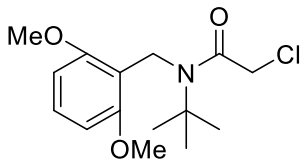
70% yield, colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 1H), 7.17 – 7.15 (m, 1H), 7.00 – 6.96 (m, 1H), 6.90 – 6.87 (m, 1H), 4.59 (s, 2H), 3.97 (s, 2H), 3.86 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.73, 156.07, 128.33, 126.49, 125.87, 120.70, 110.09, 60.39, 58.48, 55.25, 44.16, 28.18. IR (thin film): ν_{max} (cm^{-1}) = 2967, 1664, 1428, 1404, 1288, 1243, 1195, 1031, 755, 675. HRMS (ESI) calcd for $C_{14}H_{21}ClNO_2$ $[M+H]^+$: 270.1255. Found: 270.1246.

N-(tert-butyl)-2-chloro-N-(3-phenoxybenzyl)acetamide (1p):



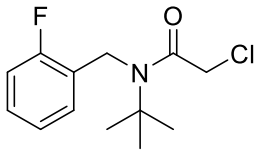
79% yield, colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 3H), 7.17 – 7.12 (m, 1H), 7.04 – 7.01 (m, 2H), 6.95 – 6.91 (m, 2H), 6.86 – 6.85 (m, 1H), 4.63 (s, 2H), 3.97 (s, 2H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.49, 158.33, 156.54, 140.79, 130.43, 129.93, 123.84, 119.80, 119.32, 117.30, 115.42, 58.70, 48.52, 44.11, 28.33. IR (thin film): ν_{max} (cm^{-1}) = 2970, 1664, 1482, 1404, 1248, 948, 756, 688. HRMS (ESI) calcd for $C_{19}H_{23}ClNO_2$ $[M+H]^+$: 332.1412. Found: 332.1402.

N-(tert-butyl)-2-chloro-N-(2,6-dimethoxybenzyl)acetamide (1q):



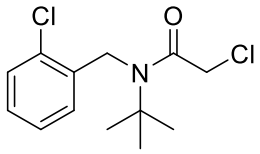
85% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.21 (m, 1H), 6.56 (d, J = 8.4 Hz, 2H), 4.66 (s, 2H), 4.40 (s, 2H), 3.82 (s, 6H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.82, 158.56, 128.92, 114.09, 103.93, 57.94, 55.53, 45.74, 40.46, 28.01. IR (thin film): ν_{max} (cm^{-1}) = 2971, 2780, 1754, 1472, 1259, 1115, 1036, 743. HRMS (ESI) calcd for $C_{15}H_{23}ClNO_3$ $[M+H]^+$: 300.1361. Found: 300.1353.

N-(tert-butyl)-2-chloro-N-(2-fluorobenzyl)acetamide (1r):



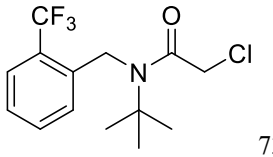
78% yield, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 1H), 7.26 – 7.22 (m, 1H), 7.20 – 7.17 (m, 1H), 7.11 – 7.06 (m, 1H), 4.70 (s, 2H), 4.00 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.68, 158.64, 129.04 (d, J_{C-F} = 8.3 Hz), 126.88 (d, J_{C-F} = 4.0 Hz), 125.60 (d, J_{C-F} = 13.8 Hz), 124.59 (d, J_{C-F} = 3.5 Hz), 115.56, 58.75, 43.99, 42.82, 28.22. ^{19}F NMR (471 MHz, $CDCl_3$) δ -118.37. IR (thin film): ν_{max} (cm^{-1}) = 2971, 1663, 1482, 1401, 1263, 1192, 1097, 1033, 760, 674. HRMS (ESI) calcd for $C_{13}H_{18}ClFNO$ $[M+H]^+$: 258.1055. Found: 258.1047.

N-(tert-butyl)-2-chloro-N-(2-chlorobenzyl)acetamide (1s):



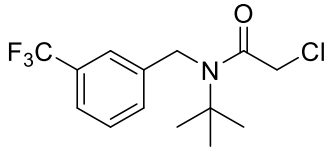
78 yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 1H), 7.34 – 7.29 (m, 1H), 7.28 – 7.22 (m, 2H), 4.67 (s, 2H), 3.92 (s, 2H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.56, 135.77, 131.83, 129.91, 128.69, 127.35, 126.59, 58.74, 46.78, 43.98, 28.20. IR (thin film): ν_{max} (cm^{-1}) = 2970, 1664, 1446, 1399, 1363, 1264, 1194, 1042, 756, 680. HRMS (ESI) calcd for $C_{13}H_{18}Cl_2NO$ $[M+H]^+$: 274.0760. Found: 274.0750.

N-(tert-butyl)-2-chloro-N-(2-(trifluoromethyl)benzyl)acetamide (1t):



73% yield, colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.70 (m, 1H), 7.64 – 7.60 (m, 1H), 7.49 – 7.40 (m, 2H), 4.83 (s, 2H), 3.92 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.67, 137.12, 132.54, 128.31, 127.55, 126.84, 126.62 (d, J_{C-F} = 5.9 Hz), 126.45, 125.59, 124.52, 58.95, 45.56, 43.91, 28.16. ^{19}F NMR (471 MHz, $CDCl_3$) δ -61.43. IR (thin film): ν_{max} (cm^{-1}) = 2972, 1669, 1452, 1407, 1312, 1270, 1164, 1116, 1043, 762. HRMS (ESI) calcd for $C_{14}H_{18}ClF_3NO$ $[M+H]^+$: 308.1024. Found: 308.1019.

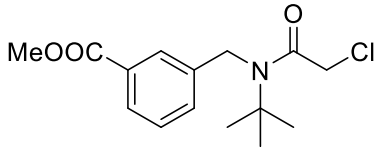
N-(tert-butyl)-2-chloro-N-(3-(trifluoromethyl)benzyl)acetamide (1u):



75% yield, colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.49 (m, 2H), 7.47 – 7.41 (m, 2H), 4.73 (s, 2H), 3.95 (s, 2H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.57, 139.84, 131.35, 129.66, 128.70, 125.22, 124.42 (q, J_{C-F} = 3.8 Hz), 122.51, 122.25 (q, J_{C-F} = 3.7 Hz),

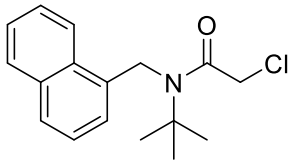
117.95, 58.87, 48.48, 43.94, 28.36. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.75. IR (thin film): ν_{max} (cm^{-1}) = 2975, 1665, 1448, 1402, 1327, 1266, 1177, 1079, 913, 799, 704, 666. HRMS (ESI) calcd for $C_{14}H_{18}ClF_3NO$ $[M+H]^+$: 308.1024. Found: 308.1019.

methyl 3-((N-(tert-butyl)-2-chloroacetamido)methyl)benzoate (1v):



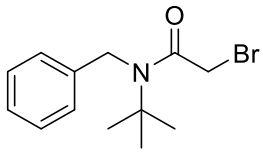
70% yield, colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.92 (m, 1H), 7.92 – 7.86 (m, 1H), 7.50 – 7.38 (m, 2H), 4.71 (s, 2H), 3.96 (s, 2H), 3.91 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.60, 166.64, 139.13, 131.05, 129.77, 129.23, 128.73, 126.52, 58.86, 52.36, 48.53, 44.06, 28.38. IR (thin film): ν_{max} (cm^{-1}) = 2964, 1722, 1664, 1442, 1288, 1193, 752, 675. HRMS (ESI) calcd for $C_{15}H_{21}ClNO_3$ $[M+H]^+$: 298.1204. Found: 298.1200.

N-(tert-butyl)-2-chloro-N-(naphthalen-1-ylmethyl)acetamide (1w):



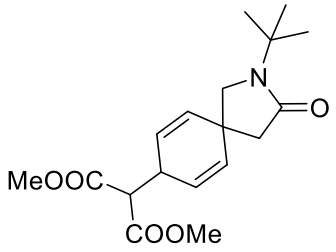
72% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.93 (m, 2H), 7.84 – 7.82 (m, 1H), 7.64 – 7.56 (m, 2H), 7.54 – 7.50 (m, 1H), 7.46 – 7.43 (m, 1H), 5.13 (s, 2H), 3.96 (s, 2H), 1.56 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.91, 133.69, 129.82, 129.16, 128.06, 126.69, 126.27, 125.57, 122.53, 121.77, 58.77, 46.49, 44.00, 28.25. IR (thin film): ν_{max} (cm^{-1}) = 2971, 1664, 1404, 1264, 1196, 1024, 799. HRMS (ESI) calcd for $C_{17}H_{21}ClNO$ $[M+H]^+$: 290.1306. Found: 290.1296.

N-benzyl-2-bromo-N-(tert-butyl)acetamide (1x):



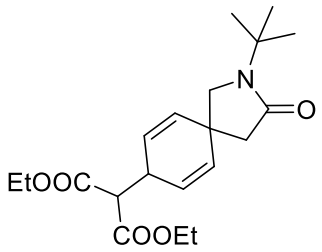
73% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 2H), 7.30 – 7.26 (m, 1H), 7.22 – 7.20 (m, 2H), 4.69 (s, 2H), 3.74 (s, 2H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.83, 138.60, 129.05, 127.40, 125.34, 58.62, 49.39, 30.17, 28.32. IR (thin film): ν_{max} (cm^{-1}) = 2969, 1655, 1443, 1398, 1365, 1262, 1194, 997, 748. HRMS (ESI) calcd for $C_{13}H_{19}BrNO$ $[M+H]^+$: 284.0645. Found: 284.0636.

dimethyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2a):



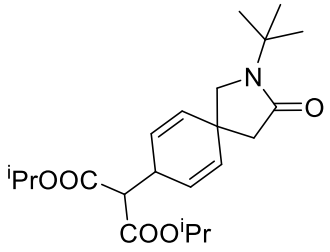
74% yield (d.r. = 1:1), yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 – 5.76 (m, 2H), 5.78 – 5.70 (m, 2H), 3.74 (d, *J* = 5.1 Hz, 6H), 3.53 – 3.46 (m, 1H), 3.40 – 3.38 (m, 1H), 3.30 (s, 1H), 3.26 (s, 1H), 2.23 (s, 1H), 2.29 (s, 1H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.05, 168.03, 132.34, 125.27, 57.85, 56.64, 56.42, 54.01, 52.46, 36.66, 35.62, 27.69. IR (thin film): ν_{max} (cm^{-1}) = 3315, 2077, 1653, 1570, 1391, 1339, 752. HRMS (ESI) calcd for $C_{18}H_{26}NO_5$ $[M+H]^+$: 336.1805. Found: 336.1807.

diethyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2b):



58% yield (d.r. = 1:1), yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 – 5.73 (m, 4H), 4.27 – 4.19 (m, 4H), 3.52 – 3.47 (m, 1H), 3.35 – 3.32 (m, 1H) 3.52 – 3.47 (m, 1H), 3.30 (s, 1H), 3.26 (s, 1H), 2.33 (s, 1H), 2.30 (s, 1H), 1.39 (s, 9H), 1.30 – 1.25 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.21, 167.68, 132.12, 125.42, 61.51, 57.88, 56.91, 54.05, 47.10, 36.67, 35.49, 27.71, 14.13. IR (thin film): ν_{max} (cm^{-1}) = 2956, 2831, 1598, 1364, 1081, 767, 545. HRMS (ESI) calcd for $C_{20}H_{30}NO_5$ $[M+H]^+$: 364.2118. Found: 364.2119.

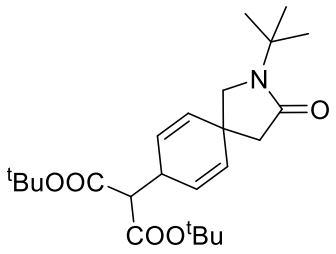
diisopropyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2c):



61% yield (d.r. = 1.3:1), yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 – 5.75 (m, 4H), 5.14 – 5.04 (m, 2H), 3.50 – 3.45 (m, 1H), 3.30 (s, 1H), 3.28 (s, 1H) 3.27 – 3.24 (m, 1H), 2.33 (s, 1H), 2.31 (s, 1H), 1.39 (s, 9H), 1.29 – 1.25 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.17, 167.16, 131.95, 125.59, 69.05, 57.85, 53.98, 47.16, 36.63, 35.38, 27.70, 21.72, 21.63. IR (thin film): ν_{max} (cm^{-1}) = 2830, 1600, 1361, 1084, 770, 546. HRMS (ESI) calcd for $C_{22}H_{34}NO_5$ $[M+H]^+$: 392.2431. Found:

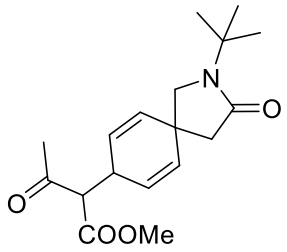
392.2435.

di-tert-butyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2d):



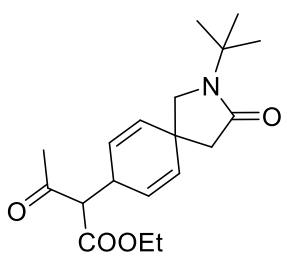
51% yield (d.r. = 1:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 – 5.76 (m, 4H), 3.45 – 3.39 (m, 1H), 3.30 (s, 1H), 3.28 (s, 1H), 3.17 – 3.11 (m, 1H), 2.33 (s, 1H), 2.32 (s, 1H), 1.48 (s, 9H), 1.47 (s, 9H), 1.39 (d, J = 4.9 Hz, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.24, 167.00, 131.64, 125.87, 81.83, 58.62, 57.99, 53.96, 47.21, 36.59, 35.38, 27.96, 27.68. IR (thin film): ν_{max} (cm^{-1}) = 2972, 2831, 1600, 1363, 1250, 1141, 767, 547. HRMS (ESI) calcd for $C_{24}H_{38}NO_5$ $[M+H]^+$: 420.2744. Found: 420.2737.

methyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2e):



55% yield (d.r. = 1.2:1), yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.76 (m, 2H), 5.74 – 5.65 (m, 2H), 3.74 (d, J = 4.6 Hz, 3H), 3.56 – 3.52 (m, 1H), 3.47 – 3.44 (m, 1H), 3.30 (s, 1H), 3.25 (s, 1H), 2.32 (s, 1H), 2.29 (s, 1H), 2.23 (d, J = 3.0 Hz, 3H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.45, 173.04, 168.48, 132.21, 125.52, 64.49, 57.89, 54.05, 52.41, 47.16, 36.66, 35.28, 30.15, 27.70. IR (thin film): ν_{max} (cm^{-1}) = 2957, 2831, 1598, 1363, 1081, 767, 544. HRMS (ESI) calcd for $C_{18}H_{26}NO_4$ $[M+H]^+$: 320.1856. Found: 320.1858.

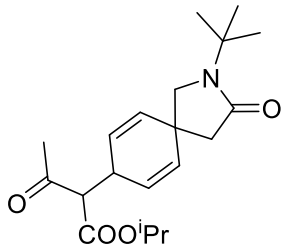
ethyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2f):



54% yield (d.r. = 1:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 – 5.77 (m, 2H), 5.74 – 5.61 (m, 2H), 4.25 – 4.18 (m, 2H), 3.57 – 3.51 (m, 1H), 3.44 – 3.41 (m, 1H), 3.30 (s, 1H), 3.26 (s, 1H), 2.32 (s, 1H), 2.29 (s, 1H), 2.23 (d, J = 2.7 Hz, 3H), 1.39 (s, 9H), 1.32 – 1.27 (m,

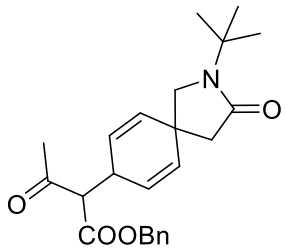
3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.43, 173.00, 167.94, 132.09, 125.71, 64.70, 61.52, 57.84, 54.00, 47.14, 36.66, 35.12, 30.06, 27.70, 14.15. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1599, 1363, 1080, 769, 545. HRMS (ESI) calcd for $C_{19}H_{28}NO_4$ $[M+H]^+$: 334.2013. Found: 334.2014.

isopropyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2g):



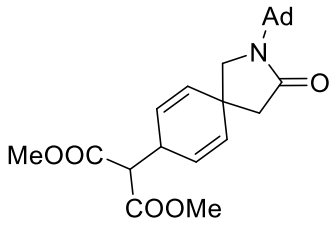
50% yield (d.r. = 1:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 – 5.76 (m, 2H), 5.74 – 5.68 (m, 2H), 5.12 – 5.02 (m, 1H), 3.54 – 3.50 (m, 1H), 3.40 – 3.37 (m, 1H), 3.29 (s, 1H), 3.25 (s, 1H), 2.32 (s, 1H), 2.30 (s, 1H), 2.22 (d, J = 3.1 Hz, 3H), 1.39 (s, 9H), 1.30 – 1.21 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.61, 173.06, 167.48, 132.06, 125.78, 69.29, 64.90, 57.87, 54.02, 47.16, 36.66, 35.17, 30.20, 27.70, 21.63. IR (thin film): ν_{max} (cm^{-1}) = 2958, 2831, 1598, 1364, 1269, 1081, 745, 541. HRMS (ESI) calcd for $C_{20}H_{30}NO_4$ $[M+H]^+$: 348.2169. Found: 348.2170.

benzyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2h):



43% yield (d.r. = 1.1:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 5H), 5.78 – 5.73 (m, 2H), 5.70 – 5.65 (m, 2H), 5.21 – 5.13 (m, 2H), 3.57 – 3.52 (m, 1H), 3.48 – 3.47 (m, 1H), 3.28 (s, 1H), 3.20 (s, 1H), 2.30 (s, 1H), 2.26 (s, 1H), 2.18 (d, J = 5.2 Hz, 3H), 1.37 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.32, 173.01, 167.87, 135.10, 132.18, 128.67, 128.60, 128.42, 125.63, 67.28, 64.36, 57.81, 54.01, 47.11, 36.64, 35.30, 30.38, 27.70. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1599, 1363, 1080, 768, 546. HRMS (ESI) calcd for $C_{24}H_{30}NO_4$ $[M+H]^+$: 396.2169. Found: 396.2169.

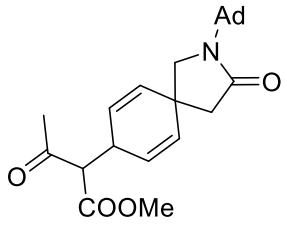
dimethyl 2-(2-(adamantan-1-yl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2j):



61% yield (d.r. = 1:1), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 –

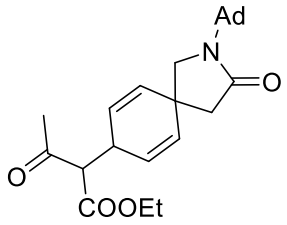
5.79 (m, 2H), 5.76 – 5.71 (m, 2H), 3.74 (d, J = 4.9 Hz, 6H), 3.52 – 3.46 (m, 1H), 3.41 – 3.36 (m, 1H), 3.30 (s, 1H), 2.26 (s, 1H), 2.32 (s, 1H), 2.28 (s, 1H), 2.11 (s, 9H), 1.74 – 1.65 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.00, 168.06, 132.42, 125.22, 56.78, 56.67, 56.44, 55.25, 52.48, 47.38, 39.65, 36.81, 36.29, 35.65, 29.56. IR (thin film): ν_{max} (cm^{-1}) = 2915, 2832, 1599, 1363, 1078, 767, 546. HRMS (ESI) calcd for $C_{24}H_{32}NO_5$ $[M+H]^+$: 414.2275. Found: 414.2277.

methyl 2-(2-(adamantan-1-yl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2k):



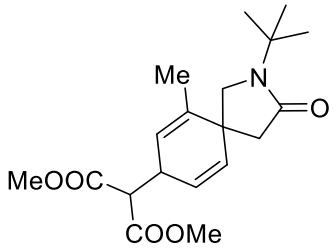
48% yield (d.r. = 1.2:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 – 5.77 (m, 2H), 5.72 – 5.66 (m, 2H), 3.74 (d, J = 6.6 Hz, 3H), 3.54 – 3.52 (m, 1H), 3.46 – 3.44 (m, 1H), 3.30 (s, 1H), 3.25 (s, 1H), 2.31 (s, 1H), 2.28 (s, 1H), 2.23 (d, J = 3.8 Hz, 3H), 2.11 (s, 9H), 1.73 – 1.64 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.52, 172.99, 168.51, 132.32, 125.63, 64.51, 56.81, 55.28, 52.46, 47.50, 39.64, 36.80, 36.28, 35.31, 30.42, 29.55. IR (thin film): ν_{max} (cm^{-1}) = 2915, 2832, 1600, 1363, 1079, 766. HRMS (ESI) calcd for $C_{24}H_{32}NO_4$ $[M+H]^+$: 398.2326. Found: 398.2328.

ethyl 2-(2-(adamantan-1-yl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2l):



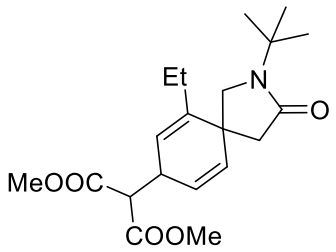
48% yield (d.r. = 1.3:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 – 5.77 (m, 2H), 5.73 – 5.66 (m, 2H), 4.28 – 4.14 (m, 2H), 3.54 – 3.52 (m, 1H), 3.43 – 3.41 (m, 1H), 3.29 (s, 1H), 3.25 (s, 1H), 2.31 (s, 1H), 2.28 (s, 1H), 2.23 – 2.22 (m, 3H), 2.11 (s, 9H), 1.75 – 1.60 (m, 6H), 1.31 – 1.24 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.52, 172.98, 167.96, 132.24, 125.70, 64.43, 61.54, 56.80, 55.24, 47.47, 39.65, 36.75, 36.29, 35.28, 30.34, 29.55, 14.16. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1601, 1361, 1268, 1074, 760, 546. HRMS (ESI) calcd for $C_{25}H_{34}NO_4$ $[M+H]^+$: 412.2482. Found: 412.2482.

dimethyl 2-(2-(tert-butyl)-6-methyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2m):



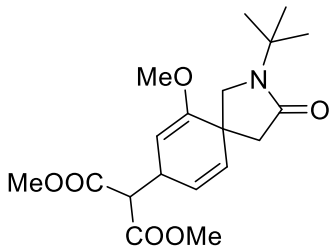
76% yield (d.r. = 1.1:1), yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 – 5.65 (m, 2H), 5.46 – 5.41 (m, 1H), 3.76 – 3.71 (m, 6H), 3.52 – 3.37 (m, 2H), 3.35 – 3.33 (m, 1H), 3.26 – 3.22 (m, 1H), 2.54 – 2.26 (m, 2H), 1.77 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.29, 168.18, 137.32, 133.85, 124.19, 122.08, 56.92, 56.67, 54.23, 52.49, 44.98, 38.10, 36.19, 27.67, 18.96. IR (thin film): ν_{max} (cm^{-1}) = 2832, 1599, 1362, 756. HRMS (ESI) calcd for $C_{19}H_{28}NO_5$ $[M+H]^+$: 350.1962. Found: 350.1964.

dimethyl 2-(2-(tert-butyl)-6-ethyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2n):



81% yield (d.r. = 1:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 – 5.65 (m, 2H), 5.49 – 5.41 (m, 1H), 3.76 – 3.67 (m, 6H), 3.53 – 3.37 (m, 2H), 3.35 – 3.33 (m, 1H), 3.24 – 3.18 (m, 1H), 2.58 – 2.44 (m, 1H), 2.26 – 2.21 (m, 1H), 2.12 – 1.98 (m, 2H), 1.39 (s, 9H), 1.07 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.35, 168.20, 142.36, 134.45, 123.84, 119.88, 57.21, 56.77, 54.19, 52.35, 45.59, 45.17, 38.29, 36.05, 27.64, 22.98, 12.64. IR (thin film): ν_{max} (cm^{-1}) = 2962, 2832, 1738, 1602, 1362, 1155, 762. HRMS (ESI) calcd for $C_{20}H_{30}NO_5$ $[M+H]^+$:364.2118. Found: 364.2121.

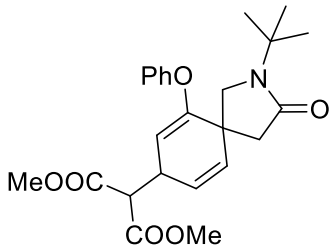
Dimethyl 2-(2-(tert-butyl)-6-methoxy-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2o):



62% yield (d.r. = 1.1:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 – 5.72 (m, 1H), 5.71 – 5.62 (m, 1H), 4.73 – 4.66 (m, 1H), 3.78 – 3.71 (m, 6H), 3.71 – 3.59 (m, 2H), 3.56 (s, 3H), 3.38 – 3.36 (m, 1H), 3.20 – 3.15 (m, 1H), 2.86 – 2.70 (m, 1H), 2.20 – 2.15 (m, 1H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.97, 168.15, 156.72, 132.73, 123.84, 93.45, 57.66, 56.29, 55.65,

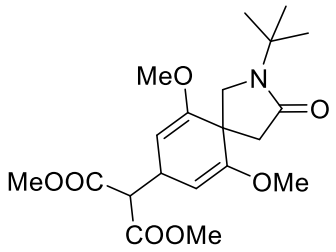
54.05, 52.40, 44.68, 43.99, 38.41, 36.81, 27.62. IR (thin film): ν_{max} (cm^{-1}) = 2832, 1600, 1361, 760. HRMS (ESI) calcd for $C_{19}H_{28}NO_6$ $[M+H]^+$: 366.1911. Found: 366.1913.

dimethyl 2-(2-(tert-butyl)-3-oxo-7-phenoxy-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2p):



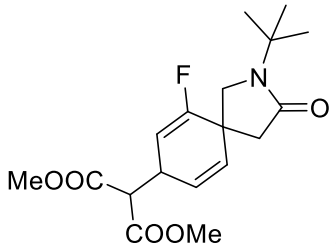
68% yield (d.r. = 1:1), colorless liquid. ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.19 – 7.13 (m, 1H), 7.08 – 7.04 (m, 2H), 5.90 – 5.80 (m, 2H), 4.75 – 4.72 (m, 1H), 4.06 – 4.04 (m, 1H), 3.80 – 3.70 (m, 7H), 3.32 – 3.20 (m, 1H), 3.20 – 3.17 (m, 1H), 2.34 – 2.31 (m, 2H), 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.03, 168.62, 154.46, 153.01, 132.39, 129.81, 124.50, 123.43, 120.82, 107.65, 58.09, 53.98, 53.40, 52.59, 52.31, 47.26, 38.86, 38.17, 27.69. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1599, 1362, 1079, 767, 546. HRMS (ESI) calcd for $C_{24}H_{30}NO_6$ $[M+H]^+$: 428.2068. Found: 428.2070.

dimethyl 2-(2-(tert-butyl)-6,10-dimethoxy-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4-2q):



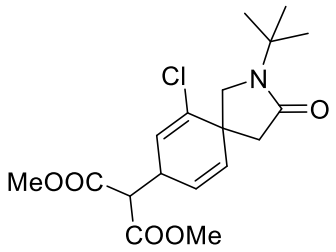
68% yield (d.r. = 1.1:1), white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 4.69 – 4.63 (m, 2H), 3.74 (d, J = 5.2 Hz, 6H), 3.73 – 3.70 (m, 1H), 3.56 (s, 6H), 3.53 (s, 1H), 3.43 (s, 1H), 3.34 – 3.31 (m, 1H), 2.61 (s, 1H), 2.53 (s, 1H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.61, 168.37, 157.06, 92.55, 58.76, 55.21, 54.76, 54.15, 52.25, 42.77, 41.38, 40.40, 35.14, 27.53. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1600, 1362, 1075, 764, 549. HRMS (ESI) calcd for $C_{20}H_{30}NO_7$ $[M+H]^+$: 396.2017. Found: 396.2020.

dimethyl 2-(2-(tert-butyl)-6-fluoro-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2r):



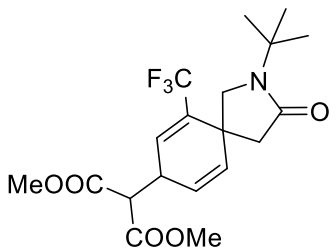
41% yield (d.r. = 1:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 – 5.75 (m, 1H), 5.72 – 5.62 (m, 1H), 5.47 – 5.31 (m, 1H), 3.79 – 3.74 (m, 6H), 3.74 – 3.64 (m, 2H), 3.43 – 3.41 (m, 1H), 3.29 – 3.24 (m, 1H), 2.84 – 2.74 (m, 1H), 2.31 – 2.21 (m, 1H), 1.41 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$) δ 172.07, 167.82, 131.89 (d, $J_{C\text{-}F}$ = 4.6 Hz), 123.91 (d, $J_{C\text{-}F}$ = 1.9 Hz), 102.94 (d, $J_{C\text{-}F}$ = 3.4 Hz), 56.25, 54.85, 54.28, 52.64, 43.25, 42.61, 37.68, 36.74, 29.70, 27.64. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.38. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1602, 1361, 761. HRMS (ESI) calcd for $C_{18}H_{25}FNO_5$ $[M+H]^+$: 354.1711. Found: 354.1713.

dimethyl 2-(2-(tert-butyl)-6-chloro-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2s):



36% yield (d.r. = 1:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.97 – 5.92 (m, 1H), 5.87 – 5.80 (m, 1H), 5.70 – 5.62 (m, 1H), 3.80 – 3.69 (m, 7H), 3.69 – 3.61 (m, 1H), 3.43 – 3.41 (m, 1H), 3.27 – 3.21 (m, 1H), 2.93 – 2.82 (m, 1H), 2.28 – 2.21 (m, 1H), 1.40 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.16, 167.61, 136.70, 132.79, 125.21, 122.80, 56.19, 55.85, 54.36, 52.69, 44.48, 40.51, 38.03, 27.63. IR (thin film): ν_{max} (cm^{-1}) = 2920, 1741, 1688, 1466, 1285, 1024, 754. HRMS (ESI) calcd for $C_{18}H_{25}ClNO_5$ $[M+H]^+$: 370.1416. Found: 370.1407.

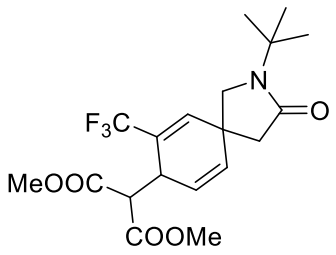
dimethyl 2-(2-(tert-butyl)-3-oxo-6-(trifluoromethyl)-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2t):



40% yield (d.r. = 1.1:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 – 6.53 (m, 1H), 5.89 – 5.82 (m, 1H), 5.73 – 5.64 (m, 1H), 3.79 – 3.71 (m, 6H), 3.70 – 3.59 (m, 2H), 3.50 – 3.48 (m, 1H), 3.29 – 3.22 (m, 1H), 2.85 – 2.77 (m, 1H), 2.31 – 2.23 (m, 1H), 1.39 (s, 9H). ^{13}C

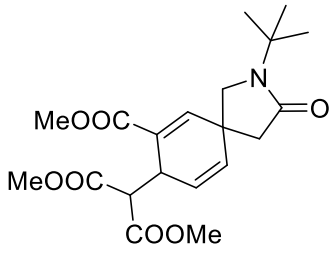
NMR (126 MHz, $CDCl_3$) δ 171.99, 167.40, 138.94, 134.49, 132.86 (d, $J_{C\text{-}F}$ = 4.6 Hz), 131.20, 125.02, 118.05, 121.84, 121.69, 56.78, 56.20, 55.45, 54.29, 52.65, 45.47, 44.90, 35.64, 27.49. ^{19}F NMR (471 MHz, $CDCl_3$) δ -60.28. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1601, 1359, 1076, 758. HRMS (ESI) calcd for $C_{19}H_{25}F_3NO_5$ $[M+H]^+$: 404.1679. Found: 404.1685.

dimethyl 2-(2-(tert-butyl)-3-oxo-7-(trifluoromethyl)-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2u):



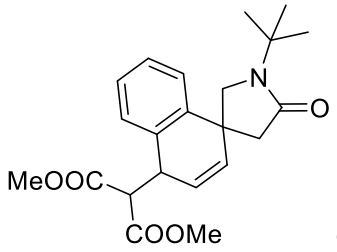
70% yield (d.r. = 1.1:1), colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 6.51 – 6.44 (m, 1H), 6.04 – 5.88 (m, 1H), 5.88 – 5.78 (m, 1H), 3.93 – 3.89 (m, 1H), 3.81 (d, *J* = 4.0 Hz, 3H), 3.79 – 3.70 (m, 1H), 3.68 (d, *J* = 5.6 Hz, 3H), 3.41 – 3.32 (m, 2H), 2.44 – 2.36 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.33, 168.28, 136.89 (d, $J_{C\text{-}F}$ = 5.6 Hz), 130.77, 128.99, 126.60, 124.67, 124.20, 123.66, 122.37, 57.05, 56.49, 54.30, 52.91, 52.30, 46.65, 45.95, 37.16, 33.97, 27.68. ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.87. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1601, 1361, 1073, 760. HRMS (ESI) calcd for $C_{19}H_{25}F_3NO_5$ $[M+H]^+$: 404.1679. Found: 404.1683.

dimethyl 2-(2-(tert-butyl)-7-(methoxycarbonyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2v):



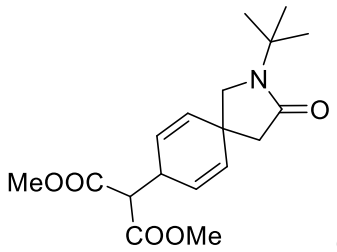
50% yield (d.r. = 1:1), colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.02 – 7.01 (m, 1H), 6.12 – 5.99 (m, 1H), 5.85 – 5.74 (m, 1H), 4.10 – 4.03 (m, 1H), 3.93 – 3.85 (m, 1H), 3.80 (s, 3H), 3.78 (d, *J* = 3.6 Hz, 3H), 3.63 (d, *J* = 3.9 Hz, 3H), 3.40 – 3.26 (m, 2H), 2.39 (s, 1H), 2.35 (s, 1H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 57.17, 54.24, 52.59, 52.12, 51.84, 46.76, 46.38, 37.87, 35.33, 27.69. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1600, 1362, 1267, 1075, 762, 546. HRMS (ESI) calcd for $C_{20}H_{28}NO_7$ $[M+H]^+$:394.1860. Found: 394.1865.

dimethyl 2-(1'-(tert-butyl)-5'-oxo-4H-spiro[naphthalene-1,3'-pyrrolidin]-4-yl)malonate (2w):



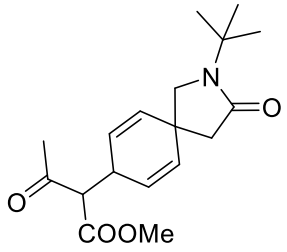
90% yield (d.r. = 1:1), yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.34 (m, 1H), 7.32 – 7.18 (m, 3H), 6.12 – 6.03 (m, 1H), 6.01 – 5.94 (m, 1H), 4.27 – 4.17 (m, 1H), 3.85 – 3.54 (m, 9H), 2.85 – 2.70 (m, 1H), 2.66 – 2.60 (m, 1H), 1.48 (s, 4.5H), 1.43 (s, 4.5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.52, 168.58, 167.72, 141.59, 134.86, 134.41, 133.70, 127.95, 126.90, 125.70, 124.78, 60.91, 59.34, 54.26, 52.57, 52.35, 49.76, 39.03, 37.88, 27.75. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1602, 1362, 1074, 761, 539. HRMS (ESI) calcd for $C_{22}H_{28}NO_5$ $[M+H]^+$:386.1962. Found: 386.1962.

dimethyl 2-(2-tert-butyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (2x):



63% yield (d.r. = 1.1:1), yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 – 5.78 (m, 2H), 5.80 – 5.71 (m, 2H), 3.75 (d, J = 4.1 Hz, 6H), 3.54 – 3.48 (m, 1H), 3.41 – 3.39 (m, 1H), 3.31 (s, 1H), 3.27 (s, 1H), 2.34 (s, 1H), 2.30 (s, 1H), 1.40 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.10, 168.08, 132.33, 125.28, 57.87, 56.63, 54.03, 52.52, 47.05, 36.66, 35.62, 27.69. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1600, 1362, 1074, 765, 546. HRMS (ESI) calcd for $C_{18}H_{26}NO_5$ $[M+H]^+$: 336.1805. Found: 336.1806.

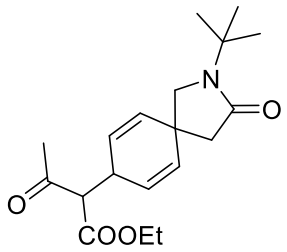
methyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2y):



51% yield (d.r. = 1.3:1), yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 – 5.78 (m, 2H), 5.74 – 5.65 (m, 2H), 3.74 (d, J = 5.6 Hz, 3H), 3.57 – 3.51 (m, 1H), 3.46 – 3.44 (m, 1H), 3.29 (s, 1H), 3.25 (s, 1H), 2.32 (s, 1H), 2.29 (s, 1H) 2.23 (d, J = 3.5 Hz, 3H), 1.39 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.49, 173.02, 168.50, 132.26, 125.68, 64.19, 57.80, 54.02, 52.44, 47.12, 36.61, 35.15, 30.18, 27.71. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1601, 1362, 1075, 763, 548. HRMS (ESI) calcd for

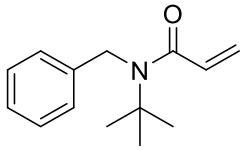
$C_{18}H_{25}NO_4$ $[M+H]^+$: 320.1856. Found: 320.1859.

ethyl 2-(2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (2z):



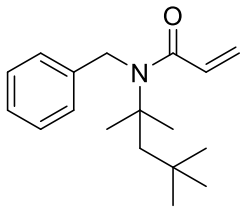
49% yield (d.r. = 1:1), yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 – 5.75 (m, 2H), 5.74 – 5.66 (m, 2H), 4.28 – 4.14 (m, 2H), 3.57 – 3.50 (m, 1H), 3.43 – 3.41 (m, 1H), 3.29 (s, 1H), 3.25 (s, 1H), 2.32 (s, 1H), 2.29 (s, 1H), 2.23 (d, J = 3.1 Hz, 3H), 1.39 (s, 9H), 1.31 – 1.24 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.59, 173.04, 168.00, 132.15, 125.65, 64.41, 61.54, 57.85, 54.01, 47.15, 36.66, 35.12, 30.34, 27.71, 14.16. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1600, 1362, 1076, 763, 547. HRMS (ESI) calcd for $C_{19}H_{28}NO_4$ $[M+H]^+$: 334.2013. Found: 334.2012.

N-benzyl-N-(tert-butyl)acrylamide (3a):



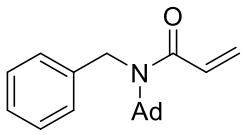
81% yield, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.35 (m, 2H), 7.30 – 7.21 (m, 3H), 6.38 (dd, J = 16.6, 10.0 Hz, 1H), 6.30 (dd, J = 16.6, 2.1 Hz, 1H), 5.53 (dd, J = 10.0, 2.1 Hz, 1H), 4.63 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.53, 139.46, 131.57, 128.79, 127.21, 127.08, 125.69, 57.72, 48.97, 28.53. The NMR data is consistent with reported literature.[2]

N-benzyl-N-(2,4,4-trimethylpentan-2-yl)acrylamide (3ab):



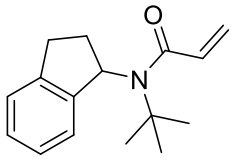
73% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 2H), 7.32 – 7.23 (m, 3H), 6.39 (dd, J = 16.6, 10.1 Hz, 1H), 6.28 (dd, J = 16.6, 2.4 Hz, 1H), 5.52 (dd, J = 10.1, 2.4 Hz, 1H), 4.69 (s, 2H), 2.07 (s, 2H), 1.50 (s, 6H), 1.03 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.64, 139.46, 131.89, 128.79, 127.09, 125.78, 61.86, 50.43, 49.86, 31.79, 31.60, 29.39. IR (thin film): ν_{max} (cm^{-1}) = 2966, 1654, 1416, 1257, 1203, 987, 798, 748. HRMS (ESI) calcd for $C_{18}H_{27}NO$ $[M+H]^+$: 272.2020. Found: 272.2023.

N-(adamantan-1-yl)-N-benzylacrylamide (3ac):



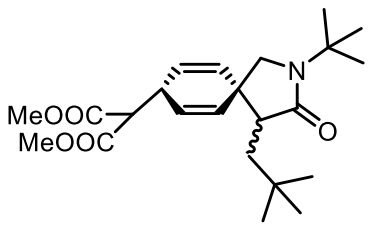
78% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.36 (m, 2H), 7.29-7.25(m, 3H), 6.39 (dd, *J* = 16.6, 10.0 Hz, 1H), 6.29 (dd, *J* = 16.6, 2.4 Hz, 1H), 5.53 (dd, *J* = 10.0, 2.4 Hz, 1H), 4.67 (s, 2H), 2.26 (d, *J* = 2.7 Hz, 6H), 2.09 – 2.06 (m, 3H), 1.71 – 1.63 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.55, 139.78, 132.05, 128.73, 127.04, 125.75, 59.24, 47.67, 39.62, 36.38, 30.07. IR (thin film): ν_{max} (cm^{-1}) = 3294, 2908, 2842, 1648, 1545, 1458, 1416, 1366, 1312, 1209, 990, 743. HRMS (ESI) calcd for $C_{20}H_{25}NO$ $[M+H]^+$: 294.1863. Found: 294.1867.

N-(tert-butyl)-N-(2,3-dihydro-1H-inden-1-yl)acrylamide (3ae):



70% yield, orange solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.04 (m, 4H), 6.04 – 5.96 (m, 1H), 5.85 – 5.70 (m, 1H), 5.30 (t, *J* = 9.3 Hz, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 3.17 – 3.03 (m, 1H), 2.97 – 2.87 (m, 1H), 2.59 – 2.45 (m, 1H), 2.33 – 2.17 (m, 1H), 1.60 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.35, 144.85, 140.79, 132.71, 127.33, 126.99, 125.17, 124.33, 123.09, 60.24, 58.41, 34.11, 29.75, 29.57. IR (thin film): ν_{max} (cm^{-1}) = 2964, 2790, 1652, 1611, 1470, 1422, 1307, 1270, 1207, 1141, 1030, 980, 800, 752. HRMS (ESI) calcd for $C_{16}H_{21}NO$ $[M+H]^+$: 242.1550. Found: 242.1549.

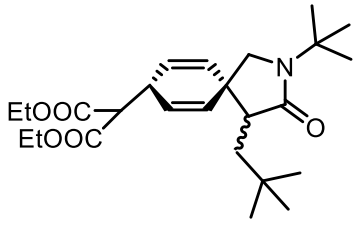
dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4a):



86% yield (d.r. > 20:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 – 5.76 (m, 2H), 5.66 – 5.56 (m, 2H), 3.76 (d, *J* = 1.5 Hz, 6H), 3.55 – 3.50 (m, 1H), 3.39 (d, *J* = 7.4 Hz, 0.05H), 3.32 (d, *J* = 8.5 Hz, 1.01H), 3.30 – 3.06 (m, 2H), 2.17 – 2.15 (m, 1H), 1.59 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.37 (s, 9H), 1.00 (dd, *J* = 14.2, 2.5 Hz, 1H), 0.87 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.66, 168.07, 132.12, 129.76, 127.62, 126.43, 57.01, 55.60, 53.82, 52.61, 49.32, 43.58, 38.14, 35.69, 30.17, 29.64, 27.75. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1600, 1361, 1074, 768, 545. HRMS (ESI) calcd for $C_{23}H_{36}NO_5$ $[M+H]^+$: 406.2588. Found: 406.2584.

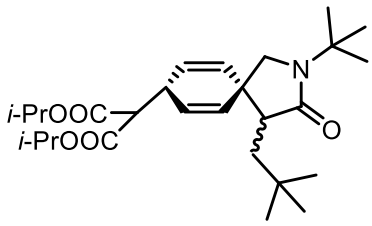
diethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate

(4b):



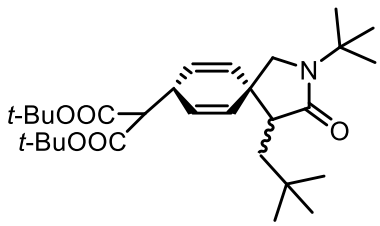
75% yield (72h, d.r. > 20:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 – 5.76 (m, 2H), 5.65 – 5.56 (m, 2H), 4.26 – 4.17 (m, 4H), 3.55 – 3.49 (m, 1H), 3.30 – 3.15 (m, 3H), 2.17 – 2.15 (m, 1H), 1.59 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.37 (s, 9H), 1.30 – 1.26 (m, 6H), 1.01 (dd, *J* = 14.2, 2.6 Hz, 1H), 0.87 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.70, 167.66, 131.98, 129.59, 127.85, 126.65, 61.56, 57.49, 55.63, 53.82, 49.35, 43.59, 38.18, 35.61, 30.18, 29.66, 27.77, 14.10. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1600, 1361, 1267, 1075, 756, 546. HRMS (ESI) calcd for $C_{25}H_{40}NO_5$ $[M+H]^+$: 434.2901. Found: 434.2906.

di isopropyl 2-((4R,5r,8R)-2-(tert-butyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4c):



67% yield (72h, d.r. > 20:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 – 5.81 (m, 2H), 5.66 – 5.52 (m, 2H), 5.19 – 4.98 (m, 2H), 3.55 – 3.45 (m, 1H), 3.29 – 3.15 (m, 3H), 2.20 – 2.13 (m, 1H), 1.60 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.38 (s, 9H), 1.28 – 1.26 (m, 12H), 1.04 (dd, *J* = 14.2, 2.5 Hz, 1H), 0.88 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.73, 167.26, 131.83, 129.42, 128.08, 126.83, 69.12, 57.91, 55.66, 53.80, 49.38, 43.58, 38.19, 35.45, 30.17, 29.66, 27.77, 21.71. IR (thin film): ν_{max} (cm^{-1}) = 2959, 2831, 1601, 1362, 1100, 763, 545. HRMS (ESI) calcd for $C_{27}H_{44}NO_5$ $[M+H]^+$: 462.3214. Found: 462.3209.

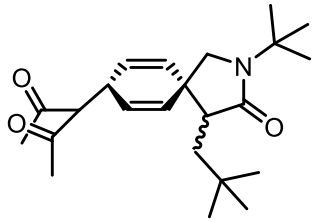
di-tert-butyl 2-((4R,5r,8R)-2-(tert-butyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4d):



52% yield (72h, d.r. > 20:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 – 5.80 (m, 2H), 5.64 – 5.54 (m, 2H), 3.44 – 3.36 (m, 1H), 3.29 – 3.15 (m, 2H), 2.98 (d, *J*

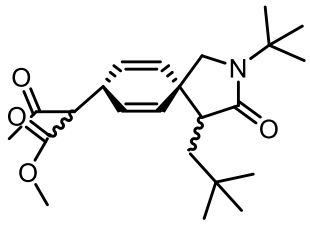
= 9.9 Hz, 1H), 2.20 – 2.12 (m, 1H), 1.60 (dd, *J* = 14.3, 6.0 Hz, 1H), 1.47 (d, *J* = 1.1 Hz, 18H), 1.37 (s, 9H), 1.05 (dd, *J* = 14.3, 2.5 Hz, 1H), 0.87 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.78, 167.16, 131.60, 129.23, 128.41, 127.18, 81.88, 59.71, 55.70, 53.82, 49.41, 43.62, 38.26, 35.46, 30.19, 29.72, 27.96, 27.79. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1600, 1363, 1267, 1077, 763, 545. HRMS (ESI) calcd for $C_{29}H_{48}NO_5$ $[M+H]^+$: 490.3527. Found: 490.3522.

3-((4R,5r,8R)-2-(tertbutyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)pentane-2,4-dione (4e):



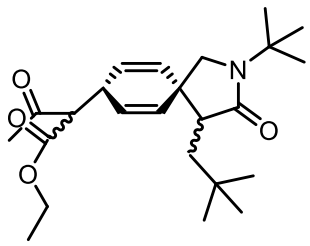
60% yield (d.r. > 20:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72 – 5.55 (m, 4H), 3.65 – 3.60 (m, 2H), 3.28 – 3.15 (m, 2H), 2.23 (d, *J* = 1.2 Hz, 6H), 2.19 – 2.13 (m, 1H), 1.63 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.37 (s, 9H), 0.97 (dd, *J* = 14.2, 2.5 Hz, 1H), 0.88 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.24, 175.44, 132.13, 129.93, 127.72, 126.52, 74.14, 55.62, 53.86, 49.23, 43.55, 38.52, 35.98, 30.63, 30.21, 29.76, 27.75. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1601, 1361, 1265, 758. HRMS (ESI) calcd for $C_{23}H_{36}NO_3$ $[M+H]^+$: 374.2690. Found: 374.2684.

methyl-2-((4R,5S,8R)-2-(tert-butyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (4f):



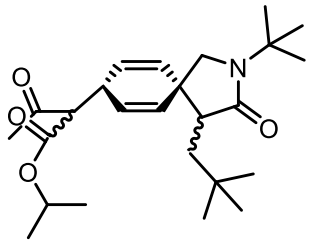
63% yield (d.r. = 1.1:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.68 (m, 2H), 5.65 – 5.53 (m, 2H), 3.75 (s, 3H), 3.58 – 3.52 (m, 1H), 3.47 – 3.38 (m, 1H), 3.30 – 3.13 (m, 2H), 2.26 (d, *J* = 1.5 Hz, 3H), 2.20 – 2.12 (m, 1H), 1.60 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.37 (s, 9H), 1.01 – 0.94 (m, 1H), 0.87 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.30, 175.54, 168.24, 132.13, 129.65, 128.01, 126.74, 64.68, 55.66, 53.82, 52.56, 49.27, 43.60, 38.40, 35.42, 30.67, 30.18, 29.72, 27.74. IR (thin film): ν_{max} (cm^{-1}) = 2956, 2834, 1684, 1600, 1362, 1156, 764, 555. HRMS (ESI) calcd for $C_{23}H_{36}NO_4$ $[M+H]^+$: 390.2639. Found: 390.2635.

ethyl-2-((4R,5S,8R)-2-(tert-butyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (4g):



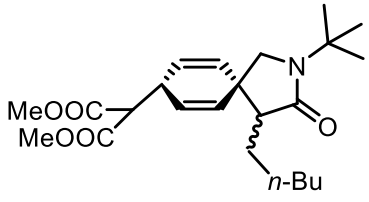
85% yield (d.r. = 4:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 – 5.69 (m, 2H), 5.69 – 5.53 (m, 2H), 4.28 – 4.13 (m, 2H), 3.59 – 3.53 (m, 1H), 3.46 – 3.36 (m, 1H), 3.28 – 3.15 (m, 2H), 2.28 – 2.24 (m, 3H), 2.19 – 2.13 (m, 1H), 1.61 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.37 (s, 9H), 1.32 – 1.24 (m, 6H), 1.04 – 0.94 (m, 1H), 0.88 – 0.84 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.36, 175.55, 167.73, 132.00, 129.71, 128.05, 126.81, 64.99, 61.62, 55.67, 53.82, 49.28, 43.61, 38.39, 35.36, 30.56, 30.18, 29.69, 27.75, 14.10. IR (thin film): ν_{max} (cm^{-1}) = 2956, 2833, 1597, 1468, 1361, 1266, 1159, 756, 555. HRMS (ESI) calcd for $C_{24}H_{38}NO_4$ $[M+H]^+$: 404.2795. Found: 404.2790.

isopropyl-2-((4R,5S,8R)-2-(tert-butyl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)-3-oxobutanoate (4h):



75% yield (72h, d.r. = 4:1), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.68 (m, 2H), 5.64 – 5.53 (m, 2H), 5.15 – 5.01 (m, 1H), 3.59 – 3.50 (m, 1H), 3.42 – 3.31 (m, 1H), 3.29 – 3.12 (m, 2H), 2.25 – 2.23 (m, 3H), 2.19 – 2.12 (m, 1H), 1.60 (dd, *J* = 14.2, 5.9 Hz, 1H), 1.37 (s, 9H), 1.30 – 1.22 (m, 6H), 1.06 – 0.93 (m, 1H), 0.87 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.32, 175.61, 167.20, 131.92, 129.58, 128.07, 126.80, 69.25, 65.59, 55.64, 53.81, 49.27, 43.55, 38.28, 35.29, 30.17, 29.71, 27.75, 21.73. IR (thin film): ν_{max} (cm^{-1}) = 2956, 2833, 1601, 1467, 1363, 1240, 1104, 766, 556. HRMS (ESI) calcd for $C_{25}H_{40}NO_4$ $[M+H]^+$: 418.2952. Found: 418.2954.

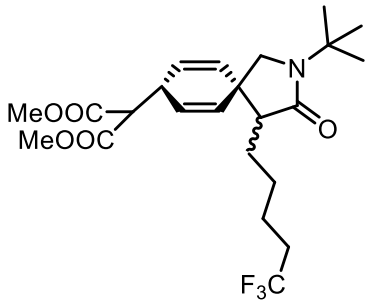
dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-3-oxo-4-pentyl-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4p):



66% yield (d.r. = 8:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 – 5.75 (m, 2H), 5.75 – 5.70 (m, 1H), 5.67 – 5.63 (m, 1H), 3.75 (d, *J* = 1.8 Hz, 6H), 3.55 – 3.50 (m, 1H), 3.40 (d, *J* = 7.3 Hz, 0.11H), 3.31 (d, *J* = 8.8 Hz, 0.92H), 3.24 – 3.02 (m, 2H), 2.16 – 2.13 (m, 1H),

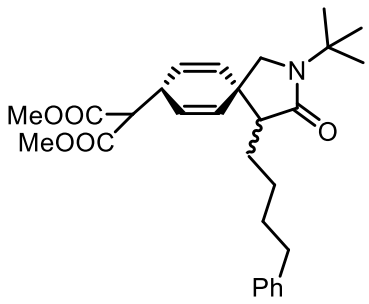
1.64 – 1.44 (m, 2H), 1.37 (s, 9H), 1.31 – 1.15 (m, 6H), 0.87 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.34, 168.10, 132.65, 129.53, 126.87, 126.12, 56.72, 55.93, 53.85, 52.92, 52.60, 42.07, 35.71, 32.00, 27.85, 27.70, 26.24, 22.50, 14.12. IR (thin film): ν_{max} (cm^{-1}) = 3291, 2921, 1742, 1685, 1461, 1265, 753. HRMS (ESI) calcd for $C_{23}H_{36}NO_5$ $[M+H]^+$: 406.2588. Found: 406.2591.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-3-oxo-4-(5,5,5-trifluoropentyl)-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4q):



61% yield (d.r. = 10:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 – 5.63 (m, 4H), 3.75 (d, J = 1.2 Hz, 6H), 3.57 – 3.50 (m, 1H), 3.33 – 3.04 (m, 3H), 2.17 – 1.99 (m, 3H), 1.60 – 1.48 (m, 4H), 1.37 (s, 9H), 1.24 – 1.17 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.93, 168.02, 132.70, 132.24, 129.24, 128.81, 127.36, 126.37, 125.46, 122.13, 60.81, 56.61, 55.89, 53.95, 52.63, 42.12, 35.73, 33.60 (q, $J_{C\text{-}F}$ = 28.8 Hz), 28.74, 27.69, 27.18, 25.82, 21.95. ^{19}F NMR (471 MHz, $CDCl_3$) δ -66.49. IR (thin film): ν_{max} (cm^{-1}) = 2831, 1643, 1571, 1370, 754. HRMS (ESI) calcd for $C_{23}H_{33}F_3NO_5$ $[M+H]^+$: 460.2305. Found: 460.2306.

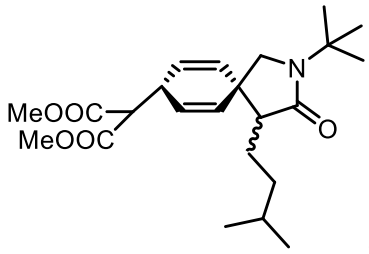
dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-3-oxo-4-(4-phenylbutyl)-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4r):



61% yield (d.r. = 9:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 2H), 7.19 – 7.15 (m, 3H), 5.83 – 5.71 (m, 3H), 5.68 – 5.61 (m, 1H), 3.76 (s, 6H), 3.58 – 3.51 (m, 1H), 3.40 (d, J = 7.0 Hz, 0.11H), 3.32 (d, J = 8.8 Hz, 0.96H), 3.26 – 3.02 (m, 2H), 2.68 – 2.55 (m, 2H), 2.18 – 2.14 (m, 1H), 1.72 – 1.52 (m, 5H), 1.39 (s, 9H), 0.96 – 0.82 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.23, 168.06, 142.89, 132.54, 129.45, 128.39, 128.21, 127.03, 126.21, 125.54, 56.75, 55.92, 53.88, 52.60, 42.11, 35.82, 31.76, 29.70, 27.91, 27.71, 26.09. IR (thin film): ν_{max} (cm^{-1}) = 2917,

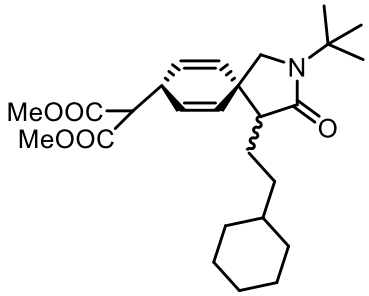
1742, 1682, 1448, 1268, 752. HRMS (ESI) calcd for $C_{28}H_{38}NO_5$ $[M+H]^+$: 468.2744. Found: 468.2748.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-isopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4s):



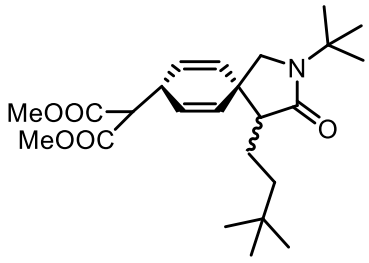
47% yield (d.r. > 20:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 – 5.70 (m, 3H), 5.70 – 5.61 (m, 1H), 3.76 (s, 6H), 3.58 – 3.51 (m, 1H), 3.32 (d, J = 9.2 Hz, 1H), 3.25 – 3.11 (m, 2H), 2.14 – 2.11 (m, 1H), 1.71 – 1.57 (m, 1H), 1.57 – 1.44 (m, 1H), 1.38 (s, 9H), 1.27 – 1.15 (m, 3H), 0.88 (d, J = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.27, 168.05, 132.75, 129.52, 126.81, 126.12, 56.76, 55.95, 53.86, 53.11, 52.60, 42.08, 37.25, 35.70, 28.27, 27.70, 24.17, 22.48. IR (thin film): ν_{max} (cm^{-1}) = 2955, 1745, 1687, 1464, 1254, 1021, 751. HRMS (ESI) calcd for $C_{23}H_{36}NO_5$ $[M+H]^+$: 406.2588. Found: 406.2592.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-(2-cyclohexylethyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4t):



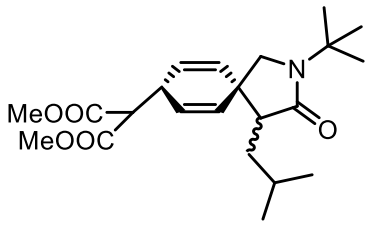
61% yield (d.r. = 6:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 – 5.70 (m, 3H), 5.68 – 5.62 (m, 1H), 3.76 (d, J = 1.5 Hz, 6H), 3.55 – 3.50 (m, 1H), 3.40 (d, J = 7.3 Hz, 0.15H), 3.32 (d, J = 9.1 Hz, 0.91H), 3.24 – 3.02 (m, 2H), 2.12 – 2.10 (m, 1H), 1.73 – 1.59 (m, 6H), 1.37 (s, 9H), 1.24 – 1.12 (m, 6H), 0.91 – 0.78 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.32, 168.05, 132.76, 129.55, 126.74, 126.08, 56.69, 55.95, 53.84, 53.12, 52.63, 42.01, 37.93, 35.70, 33.19, 29.71, 27.70, 26.72, 26.41, 23.66. IR (thin film): ν_{max} (cm^{-1}) = 2923, 2853, 1746, 1681, 1582, 1443, 1337, 1236, 1154, 1023, 747. HRMS (ESI) calcd for $C_{26}H_{40}NO_5$ $[M+H]^+$: 446.2901. Found: 446.2905.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-(3,3-dimethylbutyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4u):



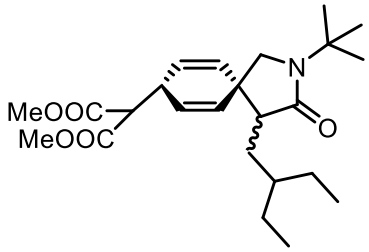
52% yield (d.r. > 20:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 – 5.71 (m, 3H), 5.69 – 5.62 (m, 1H), 3.76 (s, 6H), 3.57 – 3.50 (m, 1H), 3.31 (d, *J* = 9.8 Hz, 1H), 3.25 – 3.10 (m, 2H), 2.12 – 2.07 (m, 1H), 1.70 – 1.61 (m, 2H), 1.37 (s, 9H), 1.28 – 1.18 (m, 2H), 0.87 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.27, 168.09, 132.96, 129.53, 126.63, 126.05, 56.81, 56.02, 53.90, 53.57, 52.71, 42.35, 42.04, 35.69, 30.53, 29.26, 27.70, 21.45. IR (thin film): ν_{max} (cm^{-1}) = 2911, 1748, 1469, 1269, 1031, 751. HRMS (ESI) calcd for $C_{24}H_{38}NO_5$ $[M+H]^+$: 420.2744. Found: 420.2748.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-isobutyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4v):



80% yield (d.r. = 6:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 – 5.69 (m, 3H), 5.67 – 5.63 (m, 1H), 3.76 (s, 6H), 3.55 – 3.50 (m, 1H), 3.40 (d, *J* = 7.3 Hz, 0.15H), 3.31 (d, *J* = 8.6 Hz, 0.90H), 3.26 – 3.03 (m, 2H), 2.27 – 2.24 (m, 1H), 1.87 – 1.77 (m, 1H), 1.52 – 1.45 (m, 1H), 1.37 (s, 9H), 1.08 – 1.01 (m, 1H), 0.88 – 0.84 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.48, 168.06, 132.31, 129.54, 127.15, 126.07, 56.63, 55.87, 53.84, 52.62, 50.28, 42.22, 35.68, 35.09, 27.70, 25.35, 22.52. IR (thin film): ν_{max} (cm^{-1}) = 2957, 2833, 1743, 1636, 1364, 1248, 763. HRMS (ESI) calcd for $C_{22}H_{34}NO_5$ $[M+H]^+$: 392.2431. Found: 392.2434.

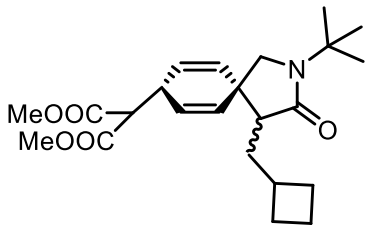
dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-(2-ethylbutyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4w):



73% yield (d.r. = 11:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 – 5.71 (m, 3H), 5.66 – 5.63 (m, 1H), 3.75 (s, 6H), 3.57 – 3.48 (m, 1H), 3.40 (d, *J* = 7.3 Hz, 0.09H),

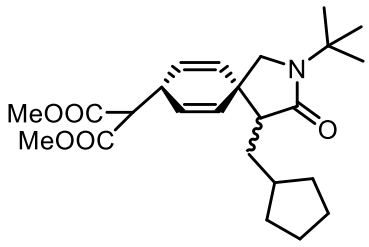
3.30 (d, J = 9.3 Hz, 1.01H), 3.27 – 3.01 (m, 2H), 2.29 – 2.26 (m, 1H), 1.57 – 1.44 (m, 2H), 1.37 (s, 9H), 1.31 – 1.21 (m, 4H), 1.17 – 1.06 (m, 1H), 0.89 – 0.75 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.55, 168.02, 132.47, 129.59, 126.97, 125.99, 56.68, 55.91, 53.83, 52.57, 49.94, 42.21, 36.94, 35.70, 29.67, 27.72, 24.87, 10.49. IR (thin film): ν_{max} (cm^{-1}) = 2960, 1746, 1687, 1447, 1260, 1023, 750. HRMS (ESI) calcd for $C_{24}H_{38}NO_5$ $[M+H]^+$: 420.2744. Found: 420.2742.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-(cyclobutylmethyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4x)



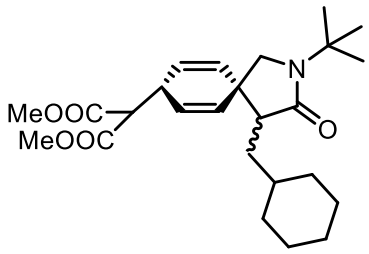
56% yield (d.r. = 9:1), colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 – 5.75 (m, 2H), 5.75 – 5.68 (m, 1H), 5.64 – 5.59 (m, 1H), 3.77 – 3.75 (m, 6H), 3.57 – 3.51 (m, 1H), 3.40 (d, J = 7.3 Hz, 0.10H), 3.36 (d, J = 8.4 Hz, 0.91H), 3.23 – 3.01 (m, 2H), 2.61 – 2.47 (m, 1H), 2.11 – 1.94 (m, 3H), 1.84 – 1.65 (m, 3H), 1.60 – 1.44 (m, 2H), 1.36 (s, 9H), 1.31 – 1.22 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.32, 168.11, 132.34, 129.45, 127.06, 126.18, 56.62, 55.87, 53.84, 52.61, 50.32, 41.99, 35.69, 33.55, 33.07, 28.08, 27.86, 27.69, 17.98. IR (thin film): ν_{max} (cm^{-1}) = 2960, 1742, 1680, 1553, 1445, 1247, 1025, 748. HRMS (ESI) calcd for $C_{23}H_{34}NO_5$ $[M+H]^+$: 404.2431. Found: 404.2435.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-(cyclopentylmethyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4y):



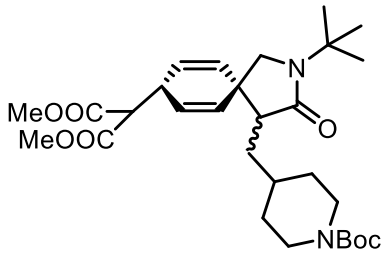
75% yield (d.r. = 6:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 – 5.61 (m, 4H), 3.74 (d, J = 1.5 Hz, 6H), 3.56 – 3.49 (m, 1H), 3.39 (d, J = 7.3 Hz, 0.14H), 3.29 (d, J = 8.7 Hz, 0.89H), 3.25 – 3.01 (m, 2H), 2.23 – 2.20 (m, 1H), 2.12 – 2.02 (m, 1H), 1.79 – 1.67 (m, 2H), 1.65 – 1.52 (m, 3H), 1.54 – 1.41 (m, 2H), 1.36 (s, 9H), 1.24 – 1.10 (m, 1H), 1.08 – 0.92 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.43, 168.04, 132.45, 129.52, 127.02, 126.09, 56.65, 55.85, 53.82, 52.59, 51.50, 42.21, 37.36, 35.69, 32.60, 32.29, 27.69, 25.12. IR (thin film): ν_{max} (cm^{-1}) = 2912, 1648, 1450, 1271, 743. HRMS (ESI) calcd for $C_{24}H_{36}NO_5$ $[M+H]^+$: 418.2588. Found: 418.2590.

dimethyl 2-((4R,5r,8R)-2-(tert-butyl)-4-(cyclohexylmethyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4z):



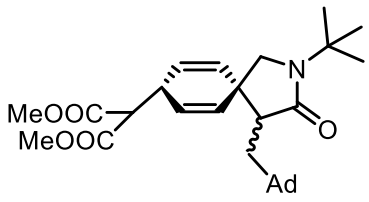
71% yield (d.r. = 8:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 – 5.68 (m, 3H), 5.65 – 5.60 (m, 1H), 3.75 (s, 6H), 3.55 – 3.48 (m, 1H), 3.39 (d, *J* = 7.3 Hz, 0.11H), 3.31 (d, *J* = 9.1 Hz, 0.90H), 3.24 – 3.02 (m, 2H), 2.32 – 2.28 (m, 1H), 1.71 – 1.58 (m, 5H), 1.54 – 1.43 (m, 2H), 1.36 (s, 9H), 1.24 – 0.98 (m, 4H), 0.91 – 0.72 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.55, 168.05, 132.38, 129.53, 127.00, 126.00, 56.74, 55.87, 53.83, 52.58, 49.37, 42.24, 35.70, 34.64, 33.66, 33.35, 33.12, 27.70, 26.67, 26.11. IR (thin film): ν_{max} (cm^{-1}) = 2921, 2856, 2794, 1743, 1682, 1449, 1265, 752. HRMS (ESI) calcd for $C_{25}H_{38}NO_5$ $[M+H]^+$: 432.2744. Found: 432.2747.

dimethyl 2-((5r,8r)-4-((1-(tert-butoxycarbonyl)piperidin-4-yl)methyl)-2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4aa):



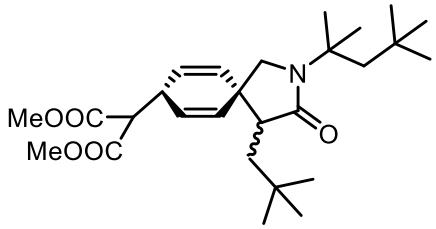
80%, yield (d.r. = 8:1), colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 – 5.74 (m, 2H), 5.70 – 5.66 (m, 1H), 5.61 – 5.57 (m, 1H), 4.18 – 3.99 (m, 2H), 3.98 – 3.87 (m, 1H), 3.72 (s, 6H), 3.52 – 3.48 (m, 1H), 3.26 (d, *J* = 8.7 Hz, 1H), 3.22 (d, *J* = 9.9 Hz, 1H), 3.13 (d, *J* = 9.9 Hz, 1H), 2.73 – 2.55 (m, 2H), 2.26 (dd, *J* = 7.7, 5.9 Hz, 1H), 2.00 – 1.78 (m, 1H), 1.76 – 1.69 (m, 1H), 1.64 – 1.57 (m, 2H), 1.53 – 1.46 (m, 1H), 1.41 (s, 9H), 1.34 (s, 9H), 1.08 – 0.98 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.16, 167.92, 167.88, 154.85, 131.97, 129.24, 127.51, 126.28, 79.09, 67.38, 56.68, 55.82, 53.91, 52.61, 49.10, 42.22, 35.67, 33.12, 32.81, 29.47, 28.43, 27.68. IR (thin film): ν_{max} (cm^{-1}) = 2920, 2860, 2798, 1741, 1686, 1450, 1262, 751. HRMS (ESI) calcd for $C_{29}H_{45}N_2O_7$ $[M+H]^+$: 533.3222. Found: 533.3224.

dimethyl 2-((4R,5r,8R)-4-(adamantan-2-ylmethyl)-2-(tert-butyl)-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4ab):



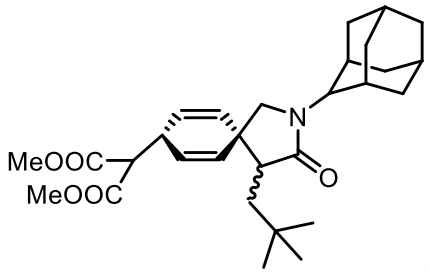
71% yield (d.r. > 20:1), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 – 5.76 (m, 2H), 5.67 – 5.54 (m, 2H), 3.77 (d, *J* = 1.4 Hz, 6H), 3.57 – 3.47 (m, 1H), 3.34 (d, *J* = 8.6 Hz, 1H), 3.31 – 3.14 (m, 2H), 2.28 – 2.21 (m, 1H), 1.97 – 1.90 (m, 3H), 1.76 – 1.56 (m, 9H), 1.53 – 1.43 (m, 4H), 1.37 (s, 9H), 0.89 – 0.82 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.82, 168.08, 132.12, 129.76, 127.64, 126.47, 57.09, 55.60, 53.82, 52.65, 47.20, 43.60, 42.53, 38.85, 37.08, 35.71, 31.90, 28.65, 27.77. IR (thin film): ν_{max} (cm^{-1}) = 2912, 1648, 1450, 1271, 743. HRMS (ESI) calcd for $C_{29}H_{42}NO_5$ $[M+H]^+$: 484.3057. Found: 484.3062.

dimethyl 2-((4R,5r,8R)-4-neopentyl-3-oxo-2-(2,4,4-trimethylpentan-2-yl)-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4ac):



68% yield (d.r. = 11:1), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 – 5.75 (m, 2H), 5.67 – 5.56 (m, 2H), 3.76 (s, 6H), 3.56 – 3.49 (m, 1H), 3.39 (d, *J* = 8.6 Hz, 0.09H), 3.32 (d, *J* = 8.5 Hz, 1H), 3.31 – 3.10 (m, 2H), 2.26 – 2.22 (m, 1H), 2.09 – 2.03 (m, 1H), 1.66 – 1.57 (m, 2H), 1.42 (s, 3H), 1.35 (s, 3H), 1.02 – 0.95 (m, 10H), 0.86 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.50, 168.05, 132.24, 129.96, 127.64, 126.38, 57.66, 56.99, 56.13, 52.59, 49.69, 43.55, 37.82, 35.66, 31.38, 30.16, 29.60, 29.14, 28.29. IR (thin film): ν_{max} (cm^{-1}) = 3297, 2961, 1743, 1679, 1446, 1230, 1156, 1024, 752. HRMS (ESI) calcd for $C_{27}H_{44}NO_5$ $[M+H]^+$: 462.3214. Found: 462.3216.

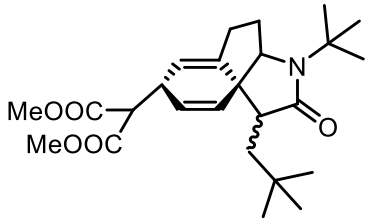
dimethyl 2-((4R,5r,8R)-2-(adamantan-1-yl)-4-neopentyl-3-oxo-2-azaspiro[4.5]deca-6,9-dien-8-yl)malonate (4ad):



54% yield (d.r. = 12:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 – 5.75 (m, 2H), 5.67 – 5.56 (m, 2H), 3.76 (d, *J* = 2.0 Hz, 6H), 3.55 – 3.50 (m, 1H), 3.38 (d, *J* = 7.4 Hz, 0.08H), 3.31 (d, *J* = 8.5 Hz, 0.97H), 3.28 – 3.10 (m, 2H), 2.20 – 2.14 (m, 1H), 2.12 – 2.06 (m,

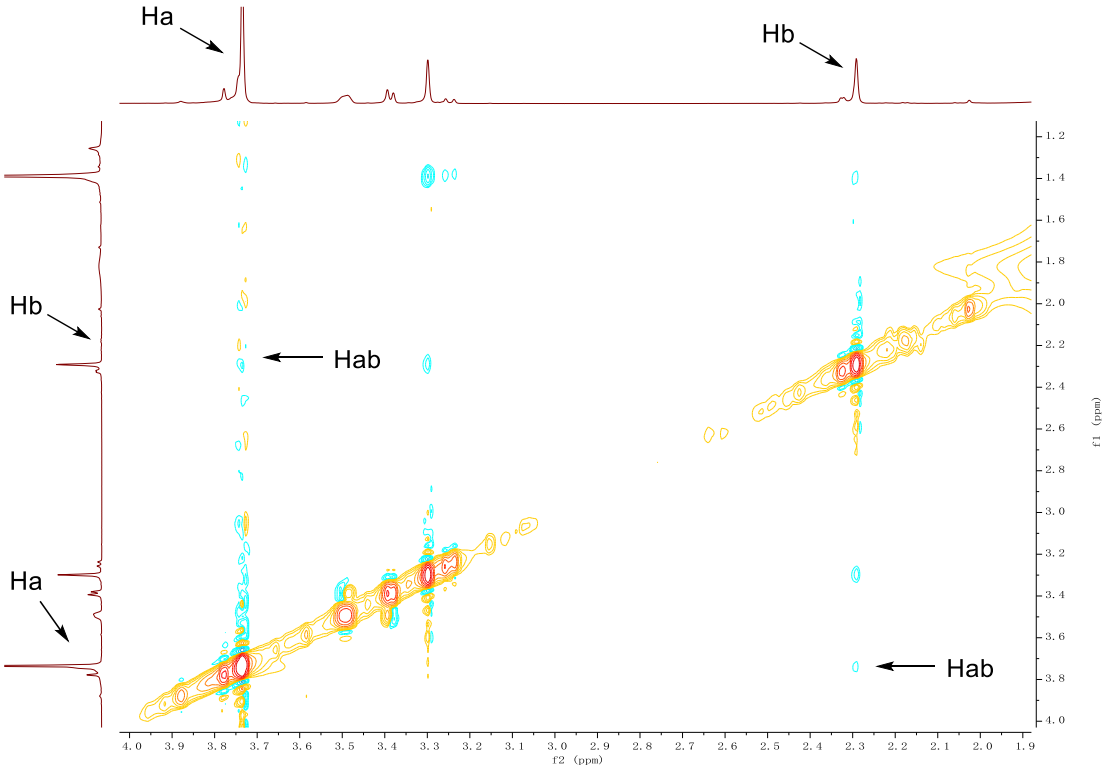
9H), 1.72 – 1.62 (m, 6H), 1.57 (dd, *J* = 14.2, 6.1 Hz, 1H), 0.98 (dd, *J* = 14.2, 2.5 Hz, 1H), 0.86 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.65, 168.03, 132.16, 129.88, 127.57, 126.36, 57.05, 54.97, 54.48, 52.63, 49.59, 43.70, 39.73, 38.18, 36.33, 35.72, 30.17, 29.65, 29.57. IR (thin film): ν_{max} (cm^{-1}) = 2954, 1745, 1689, 1468, 1248, 1026, 749. HRMS (ESI) calcd for $C_{29}H_{42}NO_5$ $[M+H]^+$: 484.3057. Found: 484.3062.

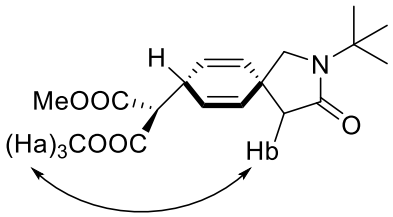
dimethyl 2-((1R,3aR,7R,9aS)-3-(tert-butyl)-1-neopentyl-2-oxo-2,3,3a,4,5,7-hexahydro-1H-indeno[1,7a-b]pyrrol-7-yl)malonate (4ae)



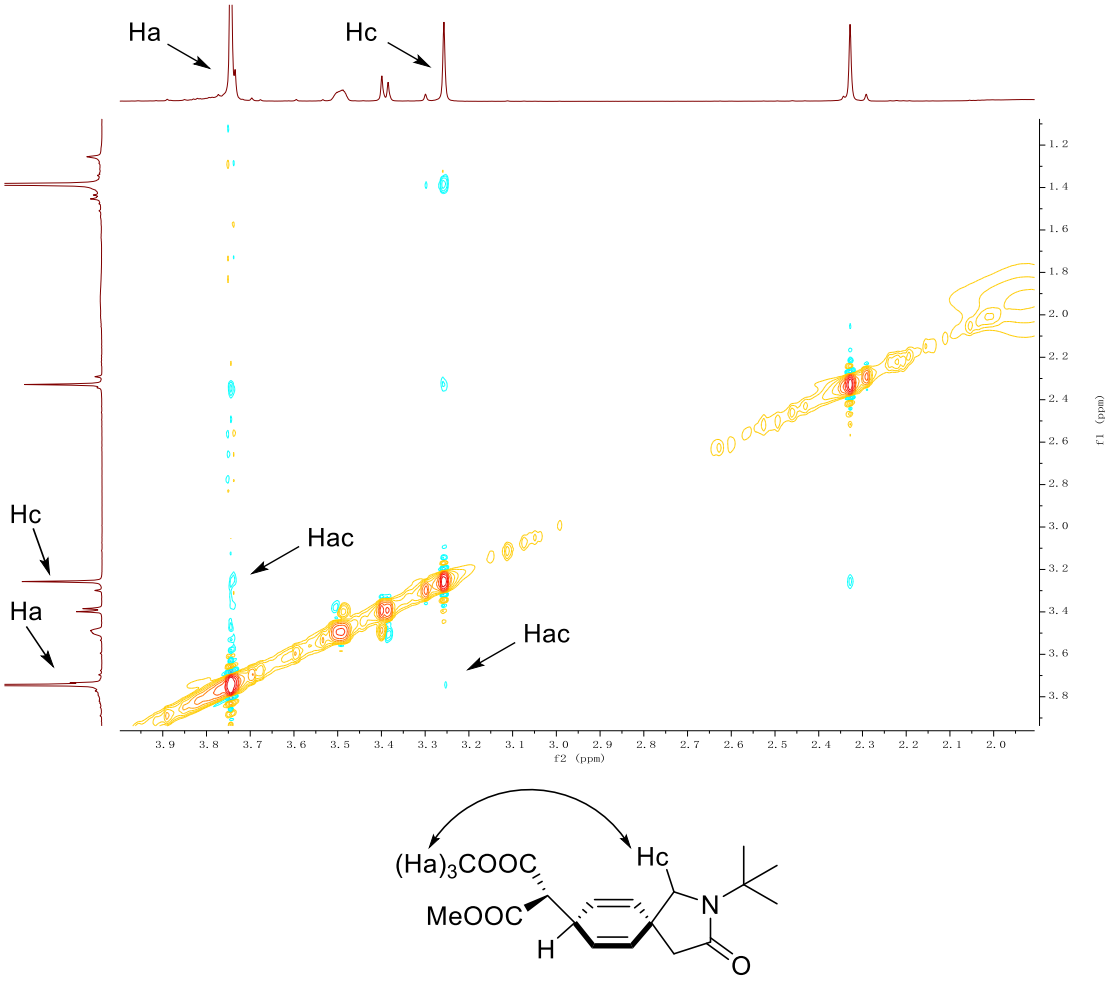
50% yield (d.r. = 1:1), white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 – 5.82 (m, 1H), 5.66 – 5.62 (m, 1H), 5.57 – 5.56 (m, 1H), 3.77 (d, *J* = 9.4 Hz, 6H), 3.62 – 3.59 (m, 1H), 3.56 – 3.52 (m, 1H), 3.19 (s, 0.5H), 3.17 (s, 0.5H), 2.79 – 2.72 (m, 1H), 2.42 – 2.34 (m, 2H), 2.14 – 2.05 (m, 1H), 1.86 – 1.79 (m, 1H), 1.61 (dd, *J* = 14.5, 6.2 Hz, 1H), 1.39 (s, 9H), 1.06 (dd, *J* = 14.5, 2.3 Hz, 1H), 0.87 (s, 9H) ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.49, 168.08, 143.03, 129.63, 127.13, 119.64, 64.56, 58.52, 53.81, 53.20, 52.69, 44.50, 38.54, 37.02, 30.67, 30.23, 30.06, 29.51, 28.32. IR (thin film): ν_{max} (cm^{-1}) = 2954, 1746, 1688, 1462, 1257, 1021, 752. HRMS (ESI) calcd for $C_{25}H_{38}NO_5$ $[M+H]^+$: 432.2744. Found: 432.2749.

2D-NMR of compounds

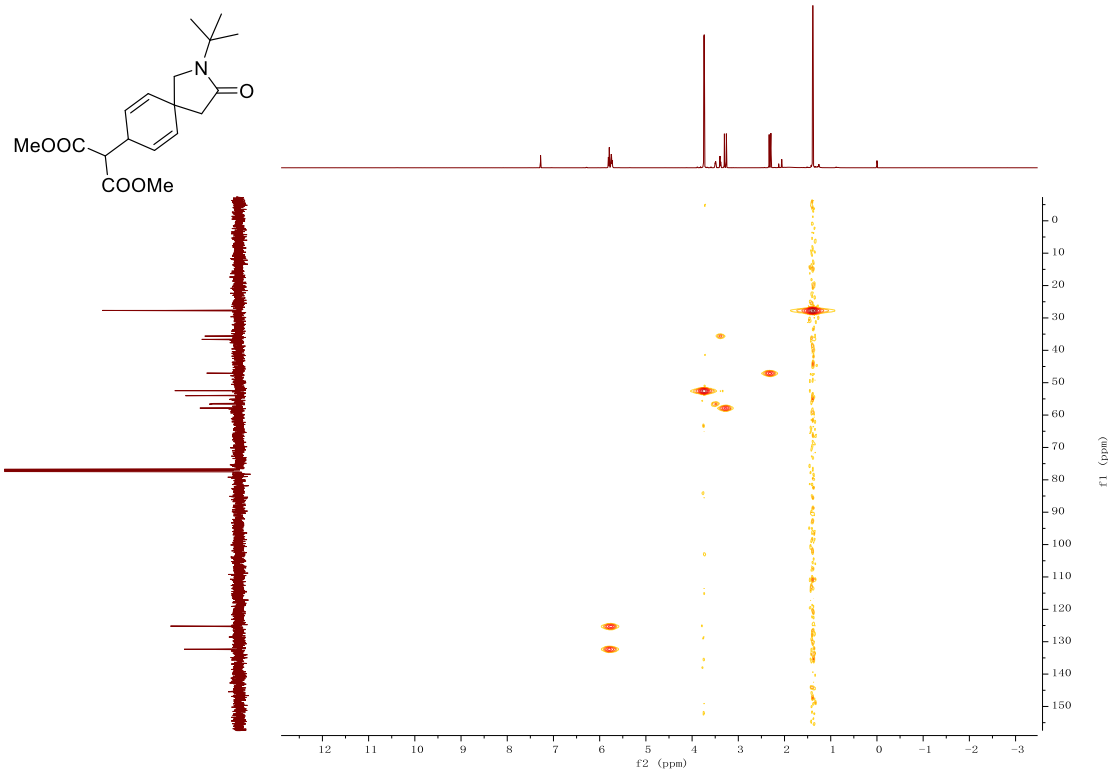




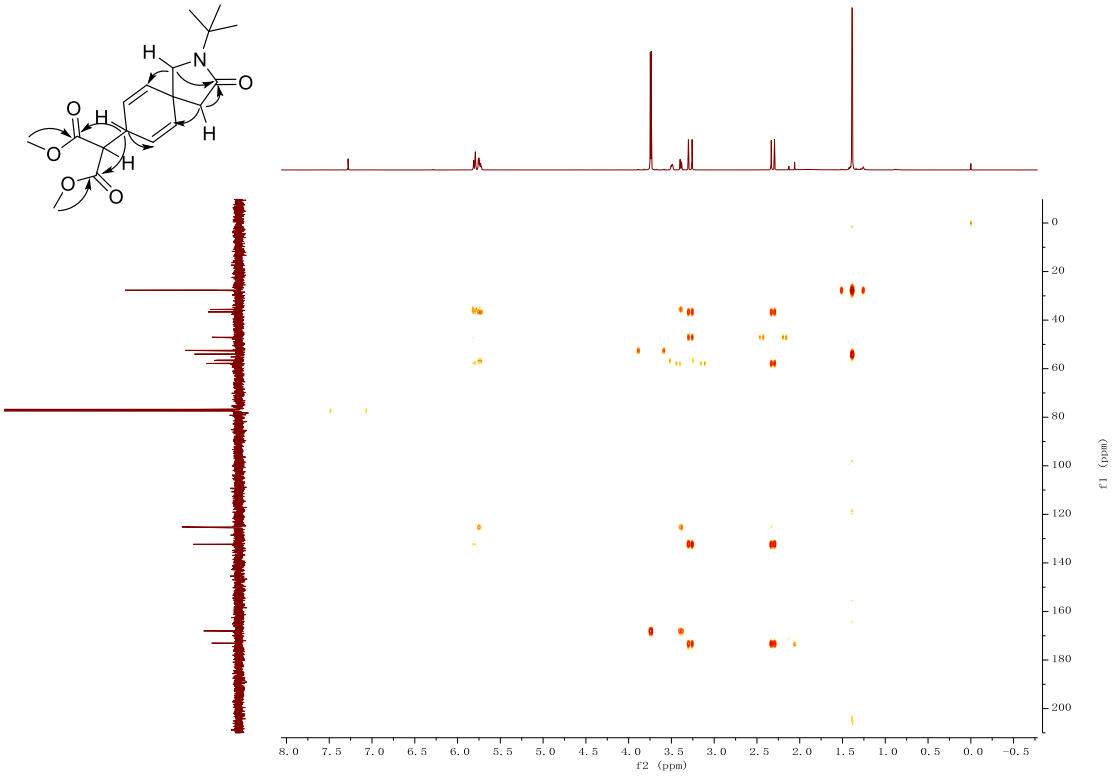
NOESY of **2a-syn**



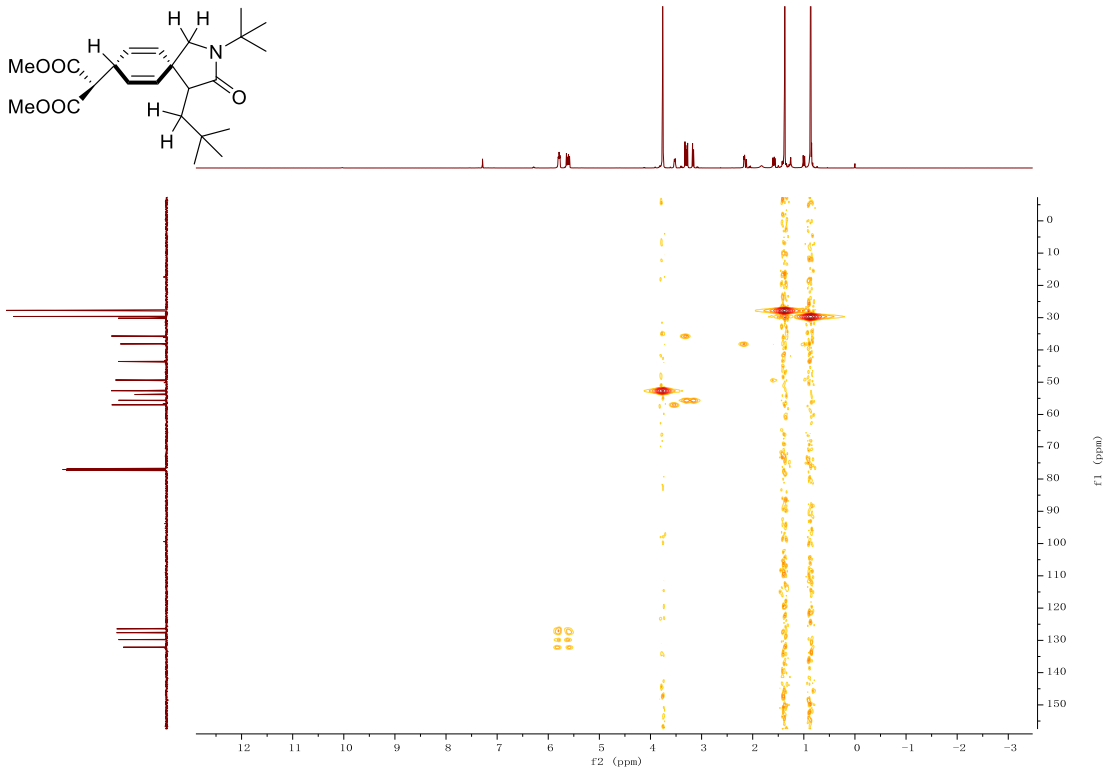
NOESY of **2a-anti**



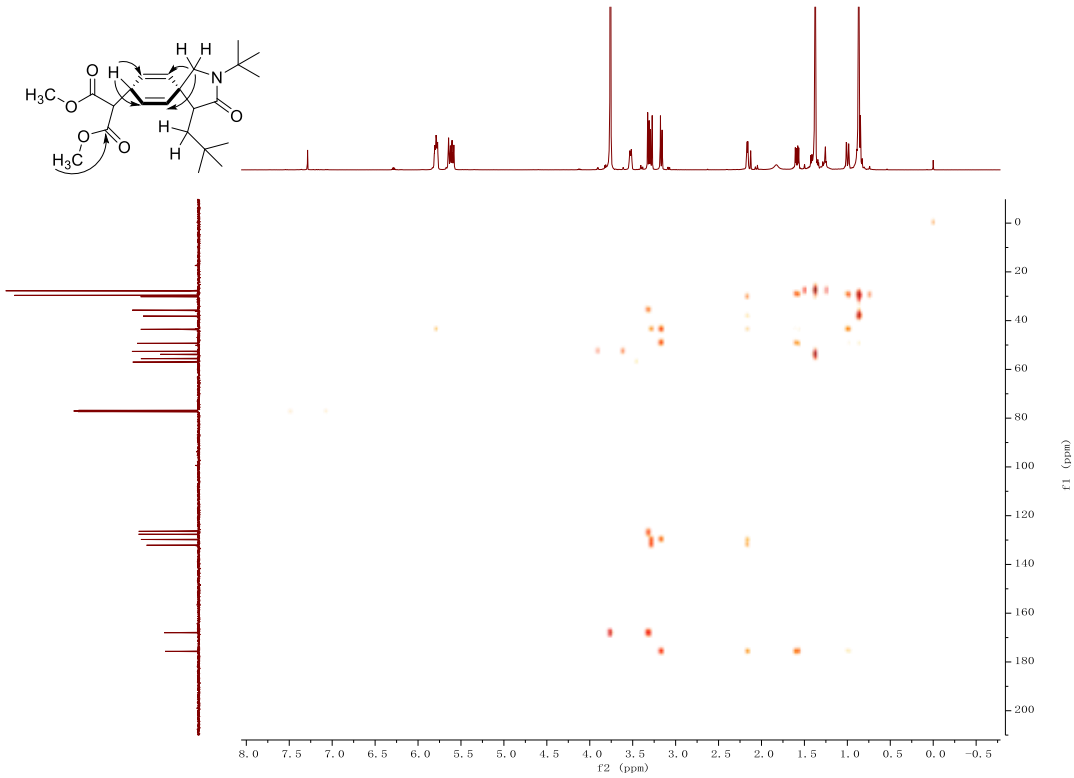
^{1}H-^{13}C HSQC NMR of **2a**



^{1}H-^{13}C HMBC NMR of **2a**



^{1}H-^{13}C HSQC NMR of **4a**

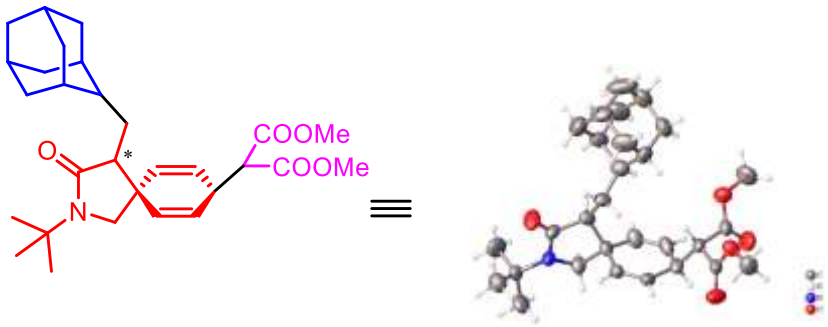


^{1}H-^{13}C HMBC NMR of **4a**

Crystal structure of 4ab

The crystal data was collected on a Agilent Gemini E diffractometer (Mo, 50kV 40mA) and reducted by CrysAlisPro (Rigaku). The structures were solved by direct methods using SHELXS-97. Refinements were performed with SHELXL-2013 using full matrix least-squares calculations on F2, with anisotropic displacement parameters for all the nonhydrogen atoms.

Single crystals suitable for X-ray diffraction were obtained by evaporation of the mixed solvent from chloroform at room temperature. Crystal data have been deposited to CCDC number 2389530.



4ab CCDC: 2389530

Table S2. Crystal data and structure refinement for **4ab**

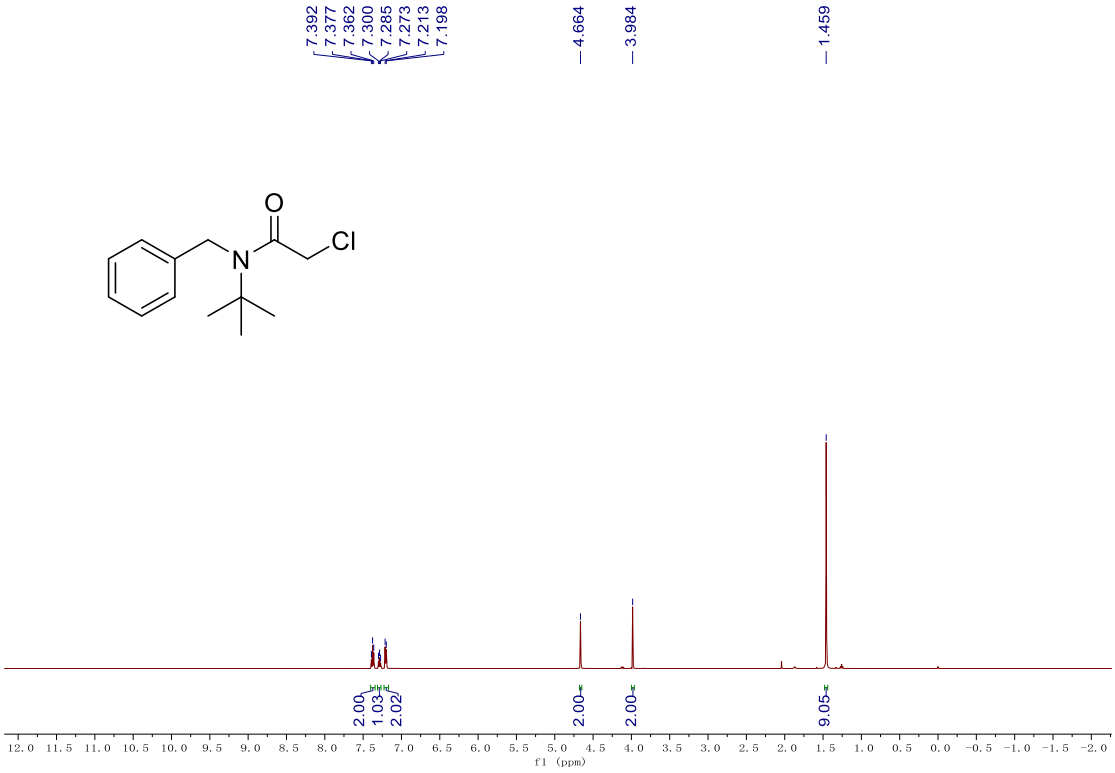
Identification code	**4ab**
Empirical formula	$C_{29}H_{41}NO_5$
Formula weight	483.63
Temperature/K	293(2)
Crystal system	monoclinic
Space group	I2/a
a/Å	33.370(2)
b/Å	6.4924(3)
c/Å	25.4956(14)
α/°	90
β/°	104.957(6)
γ/°	90
Volume/Å^3	5336.4(5)
Z	8
ρ_{calc}g/cm^3	1.204
μ/mm^{-1}	0.081
F(000)	2096.0
Crystal size/mm^3	0.22 × 0.18 × 0.11
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.652 to 49
Index ranges	-38 ≤ h ≤ 38, -7 ≤ k ≤ 7, -29 ≤ l ≤ 29
Reflections collected	20949
Independent reflections	4301 [R_{int} = 0.0448, R_{sigma} = 0.0401]
Data/restraints/parameters	4301/4/321
Goodness-of-fit on F^2	1.033
Final R indexes [I>=2σ (I)]	R_1 = 0.0818, wR_2 = 0.2014
Final R indexes [all data]	R_1 = 0.1111, wR_2 = 0.2247
Largest diff. peak/hole / e Å^{-3}	0.76/-0.22

7. References

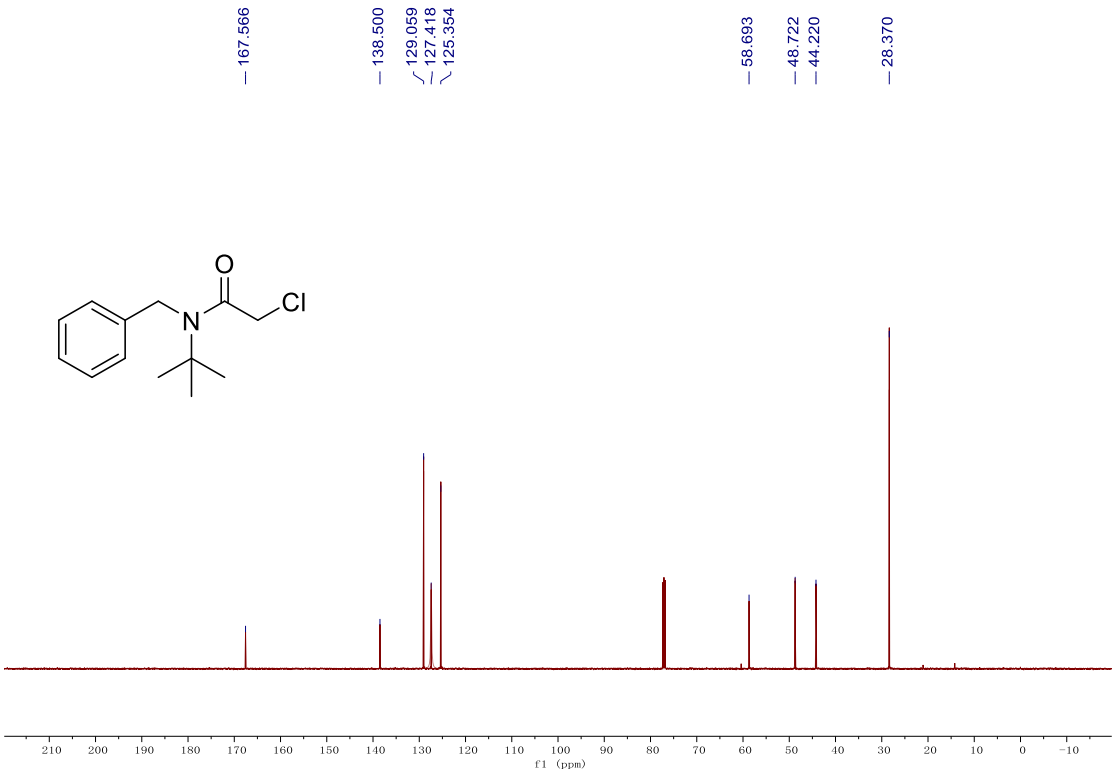
1. Mcdaniel K. A., Blood A. R., Smith G. C., Jui N. T. Dearomatization of Unactivated Arenes via Catalytic Hydroalkylation. ACS Catal., 2021, 11(9): 4968-4972.
2. Clayden J., Turnbull R., Pinto I. Nucleophilic addition to electron-rich heteroaromatics: Dearomatizing anionic cyclizations of pyrrolecarboxamides. Org. Lett., 2004, 6(4): 609-611.

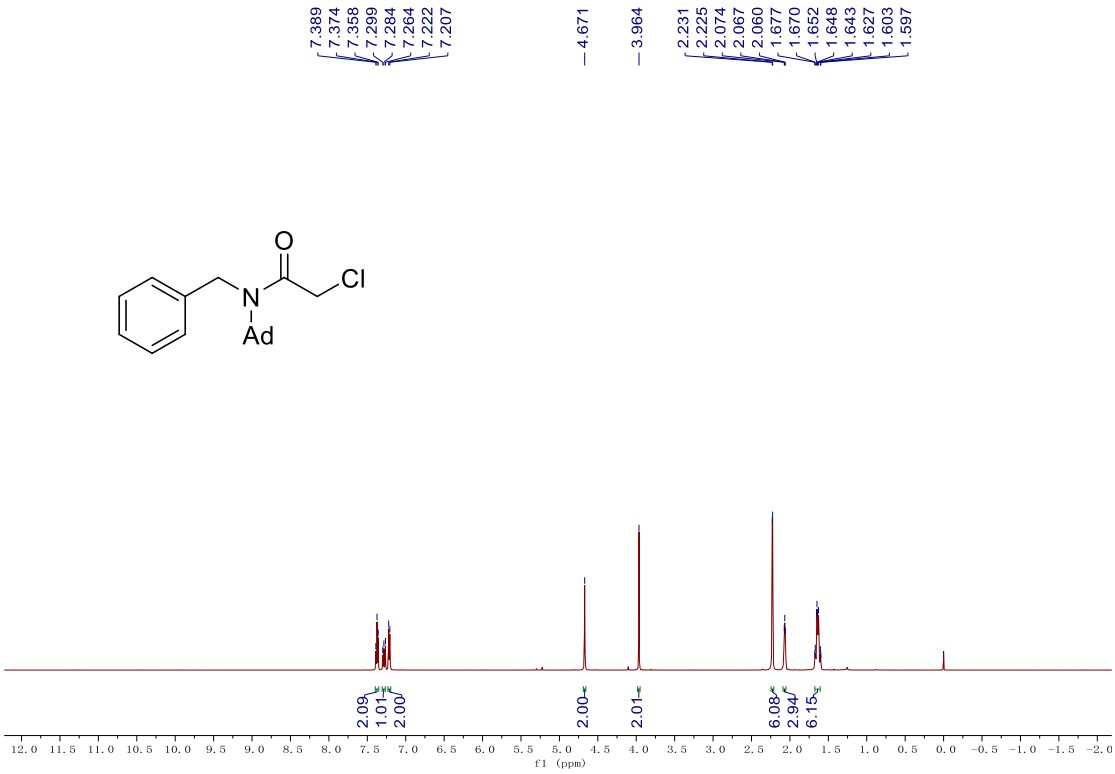
8. Copies of NMR spectra for the compounds

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

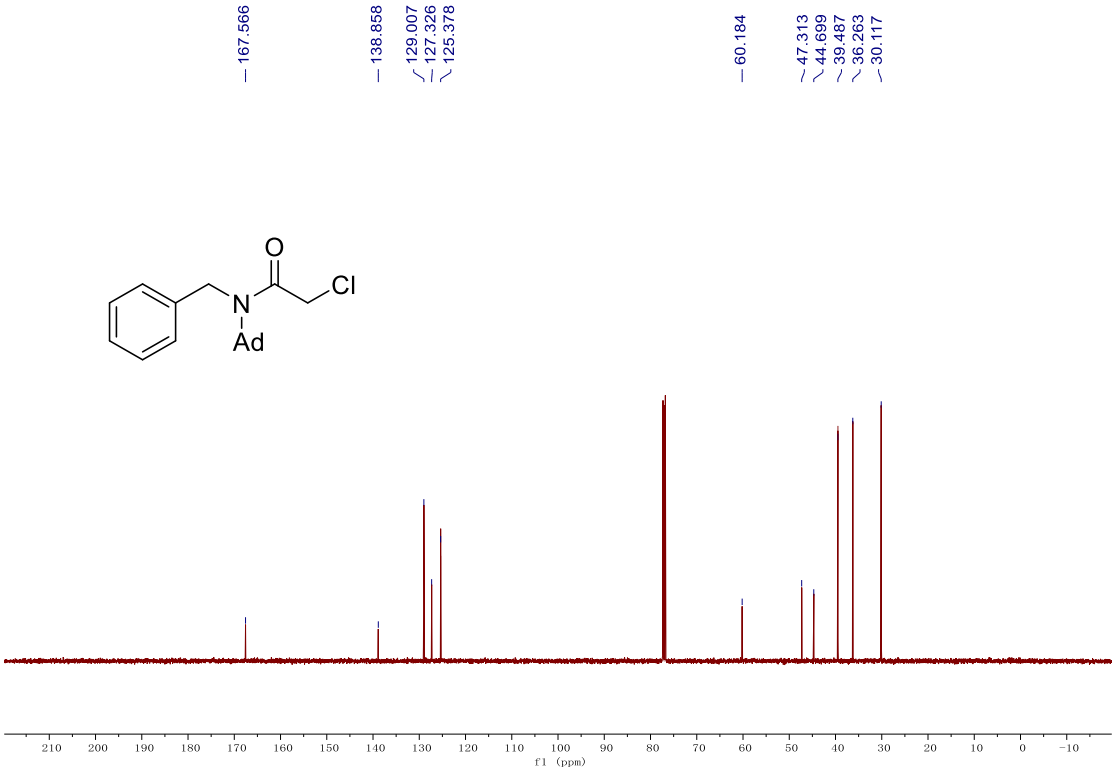


^{13}C NMR (125 MHz, $CDCl_3$) of **1a**

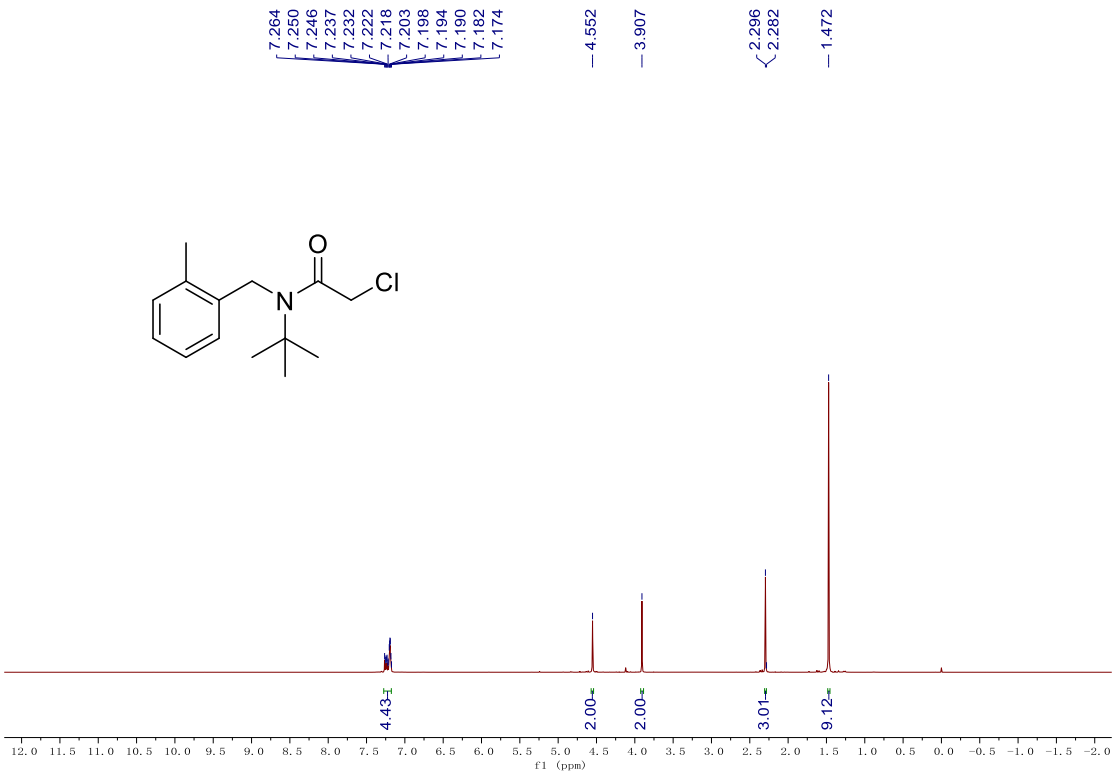




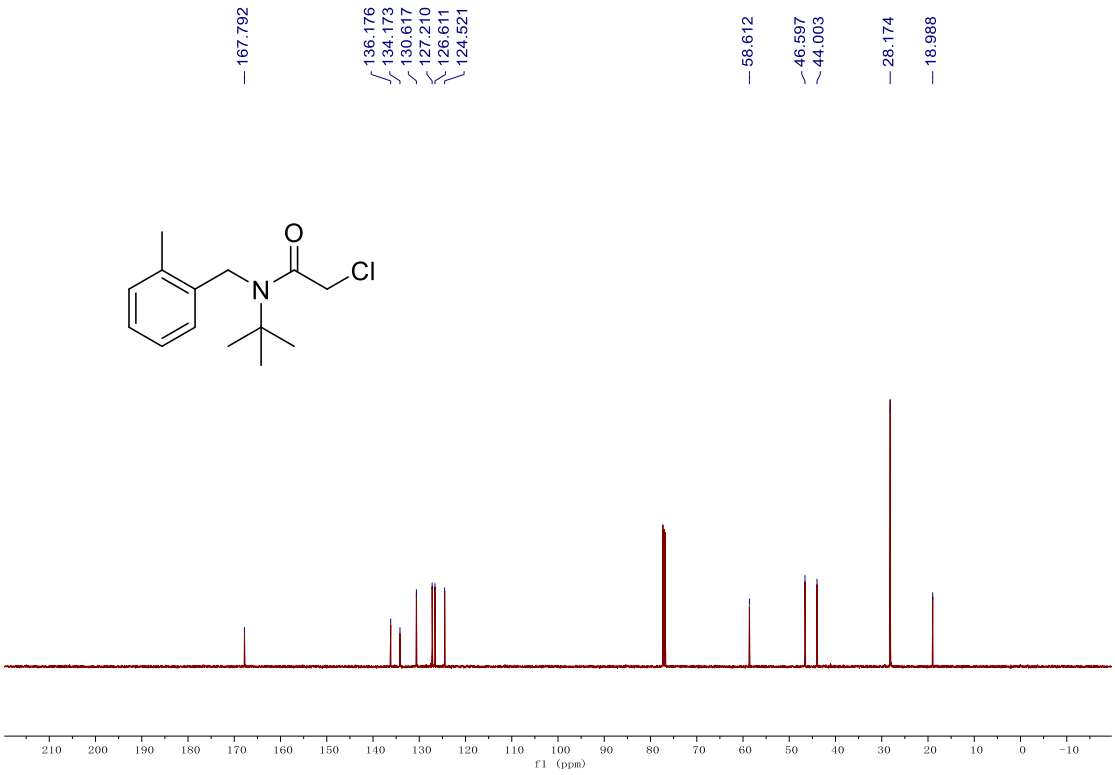
^{1}H NMR spectrum of **1j** ($CDCl_3$, 500MHz)



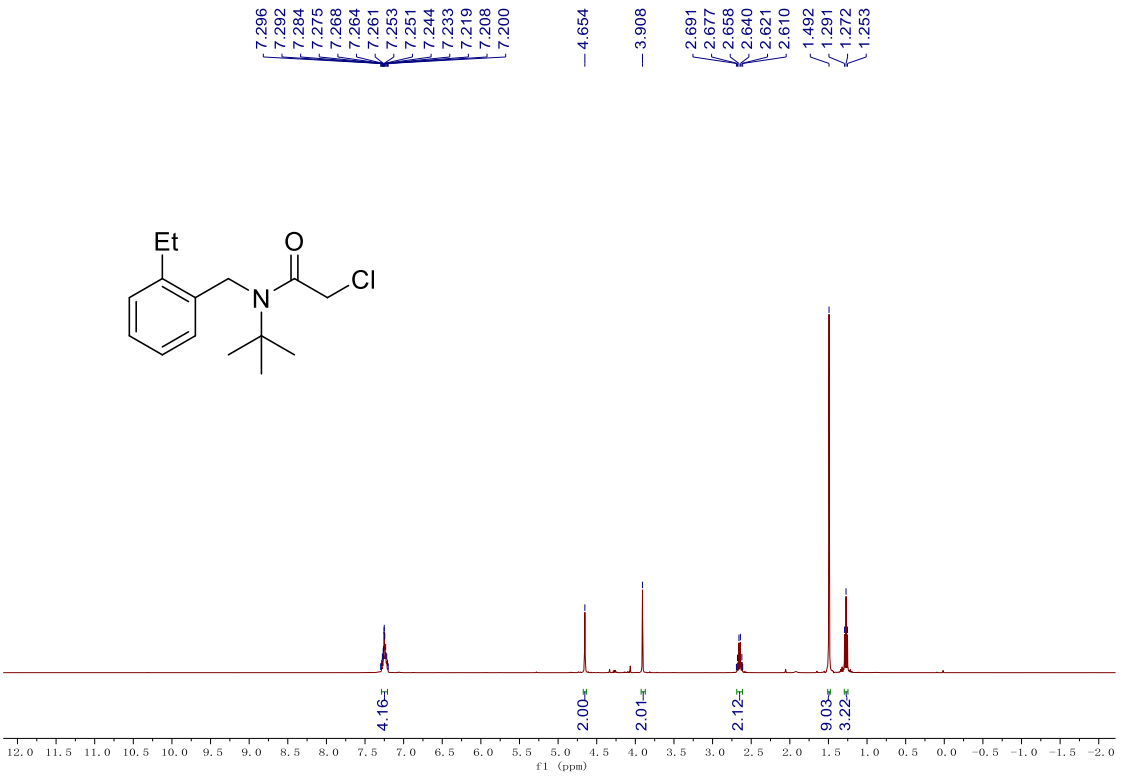
^{13}C NMR spectrum of **1j** ($CDCl_3$, 126MHz)



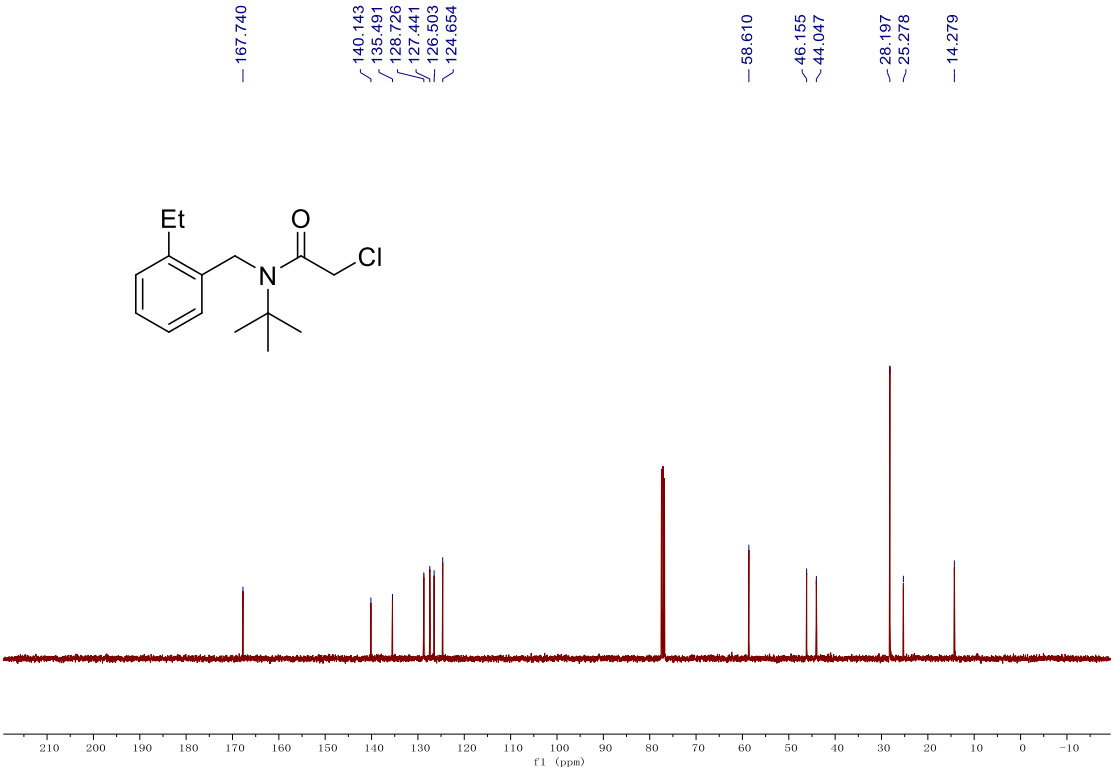
^{1}H NMR spectrum of **1m** ($CDCl_3$, 500MHz)



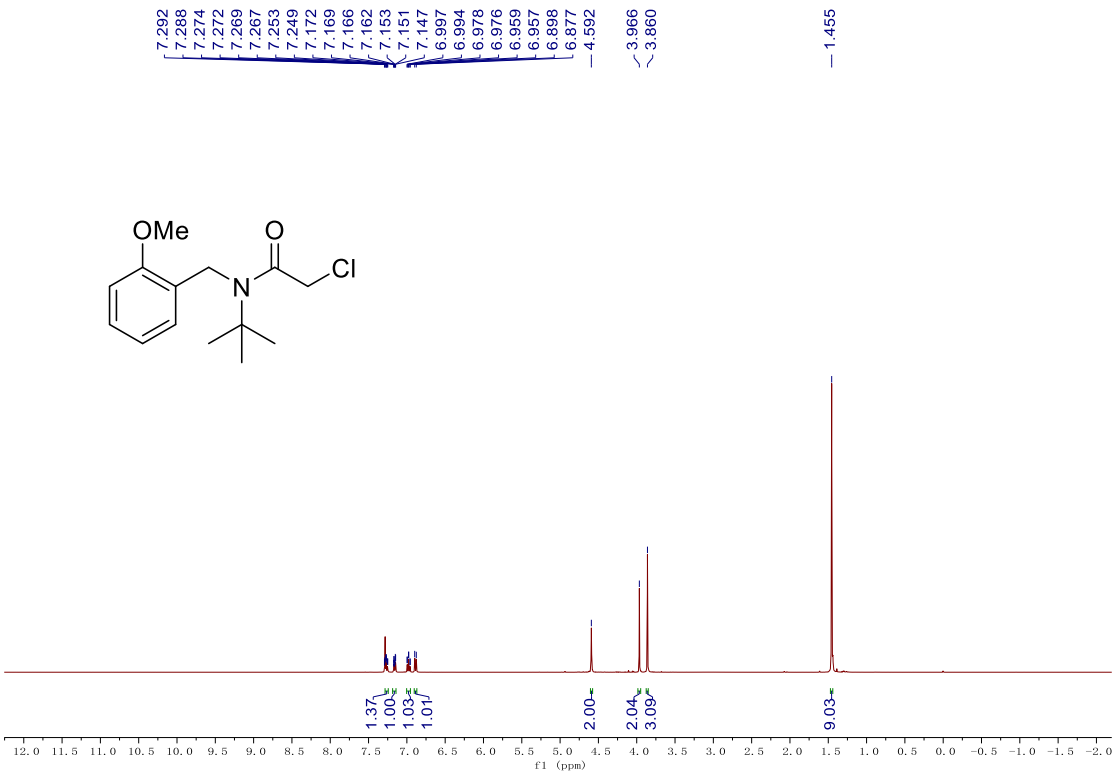
^{13}C NMR spectrum of **1m** ($CDCl_3$, 126MHz)



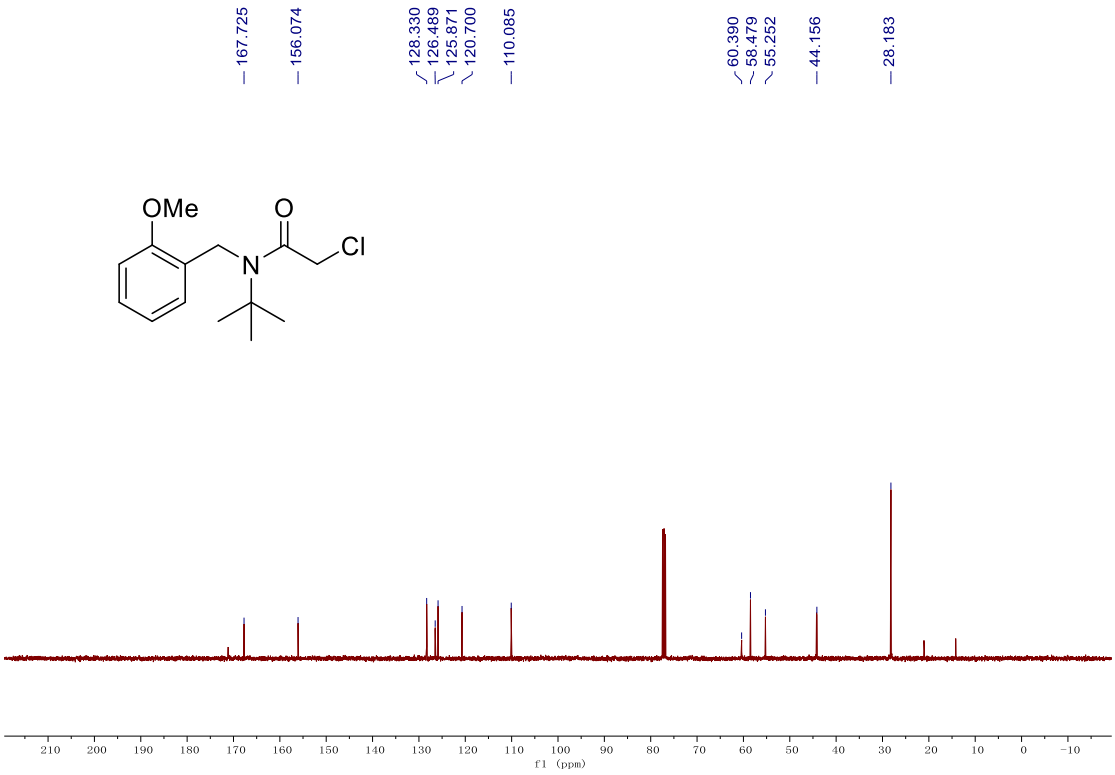
^{1}H NMR spectrum of **1n** ($CDCl_3$, 400MHz)



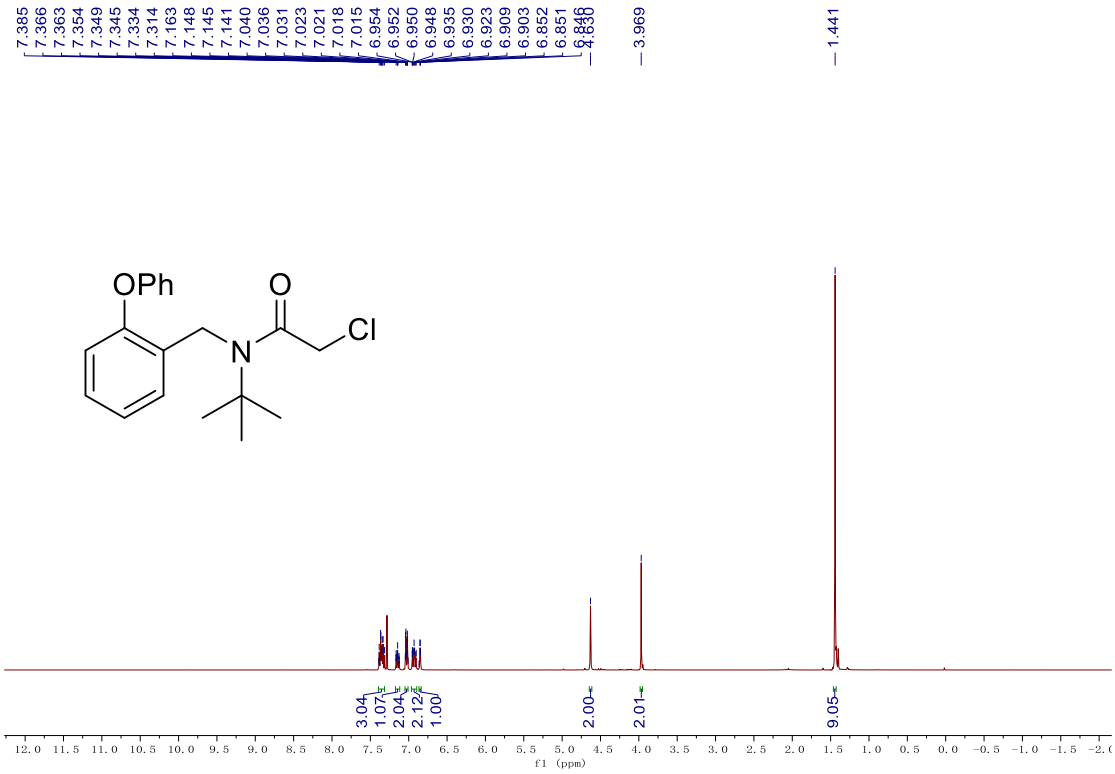
^{13}C NMR spectrum of **1n** ($CDCl_3$, 101MHz)



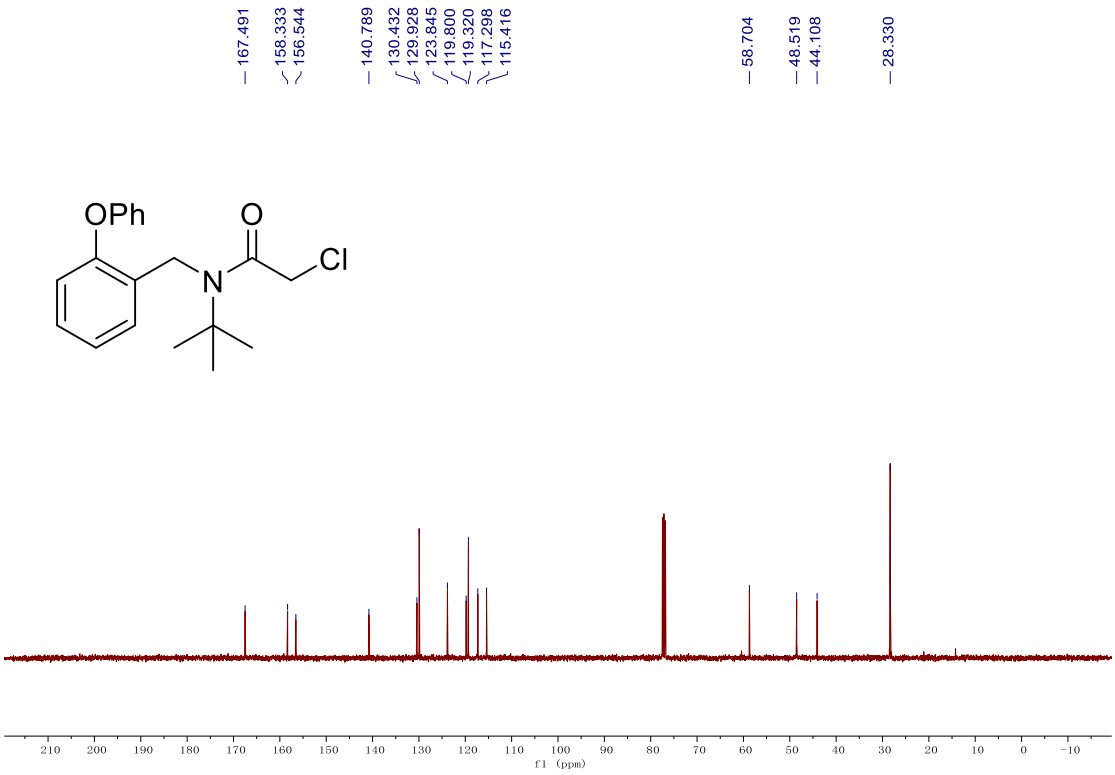
^{1}H NMR spectrum of **1o** ($CDCl_3$, 400MHz)



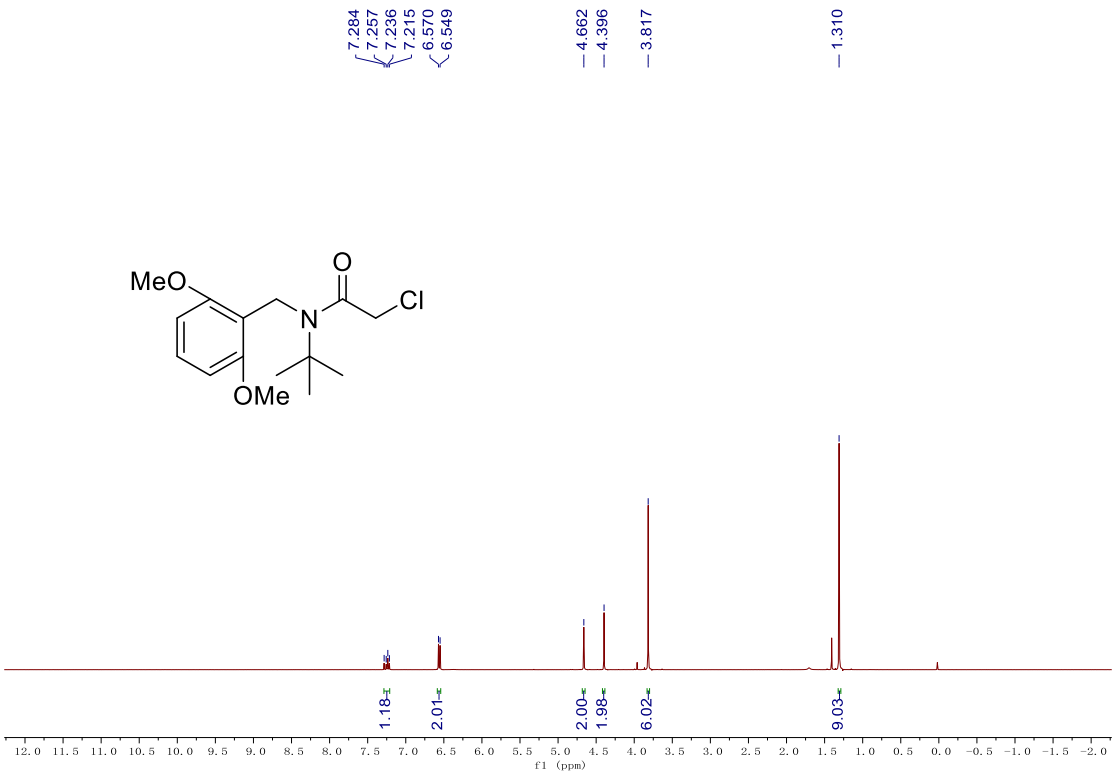
^{13}C NMR spectrum of **1o** ($CDCl_3$, 101MHz)



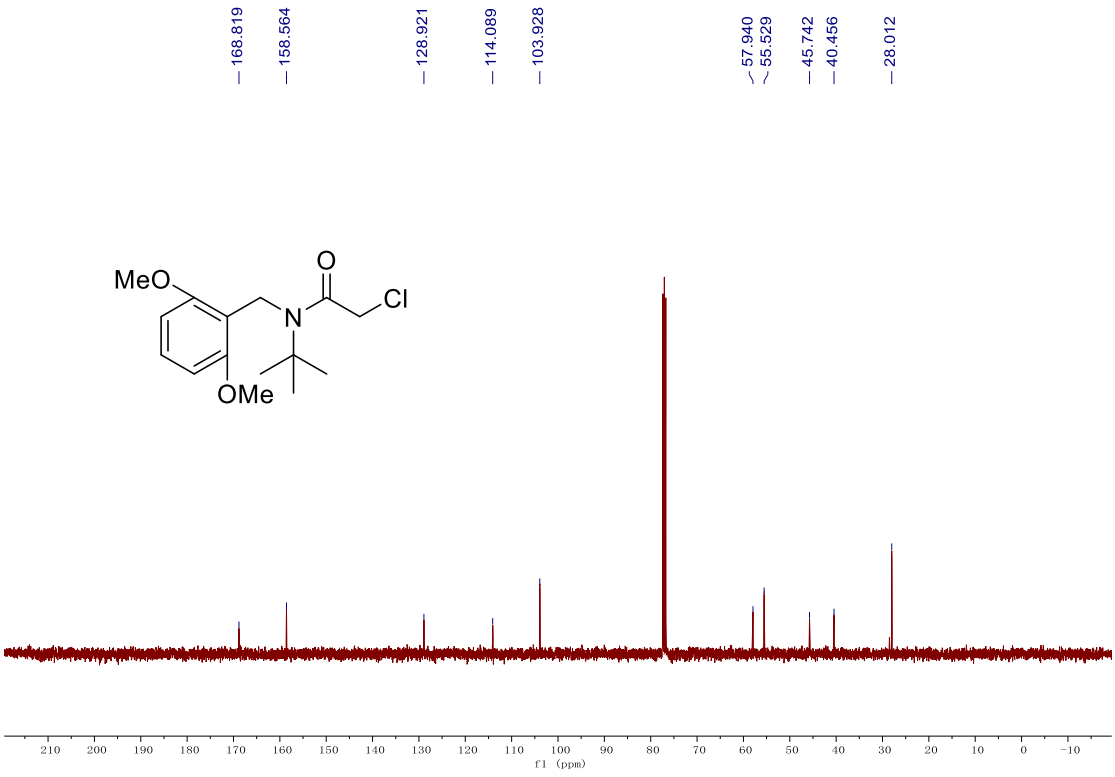
^{1}H NMR spectrum of **1p** ($CDCl_3$, 400MHz)



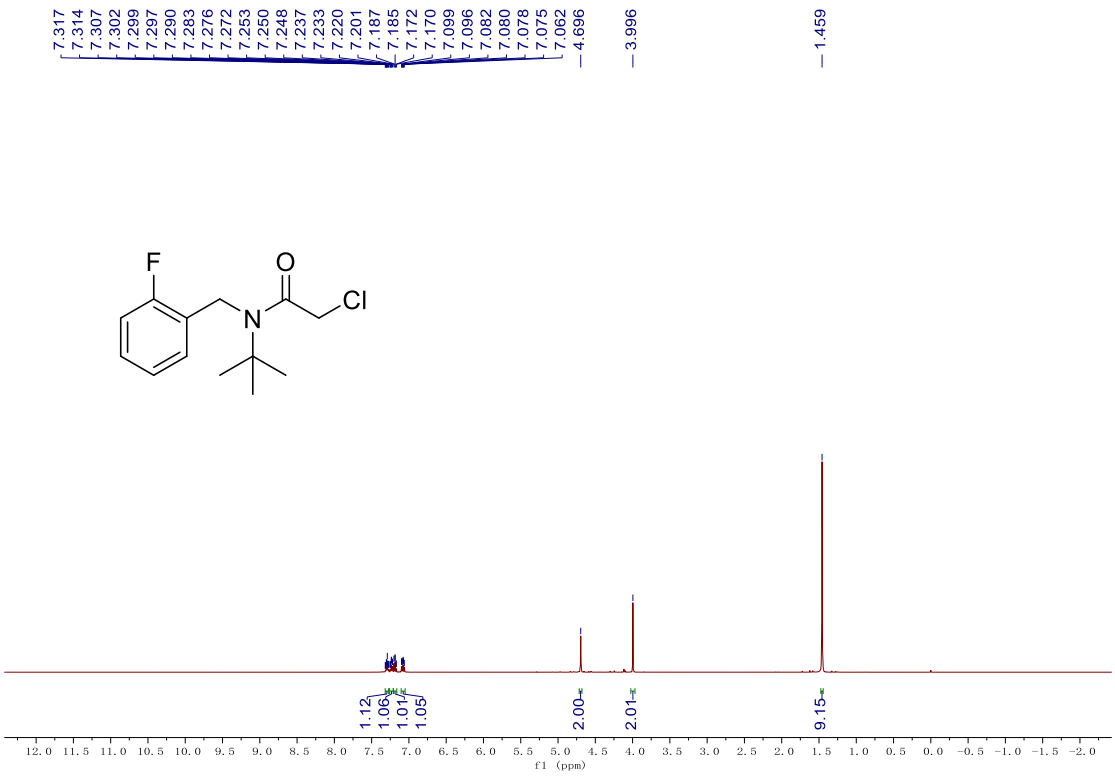
^{13}C NMR spectrum of **1p** ($CDCl_3$, 101MHz)



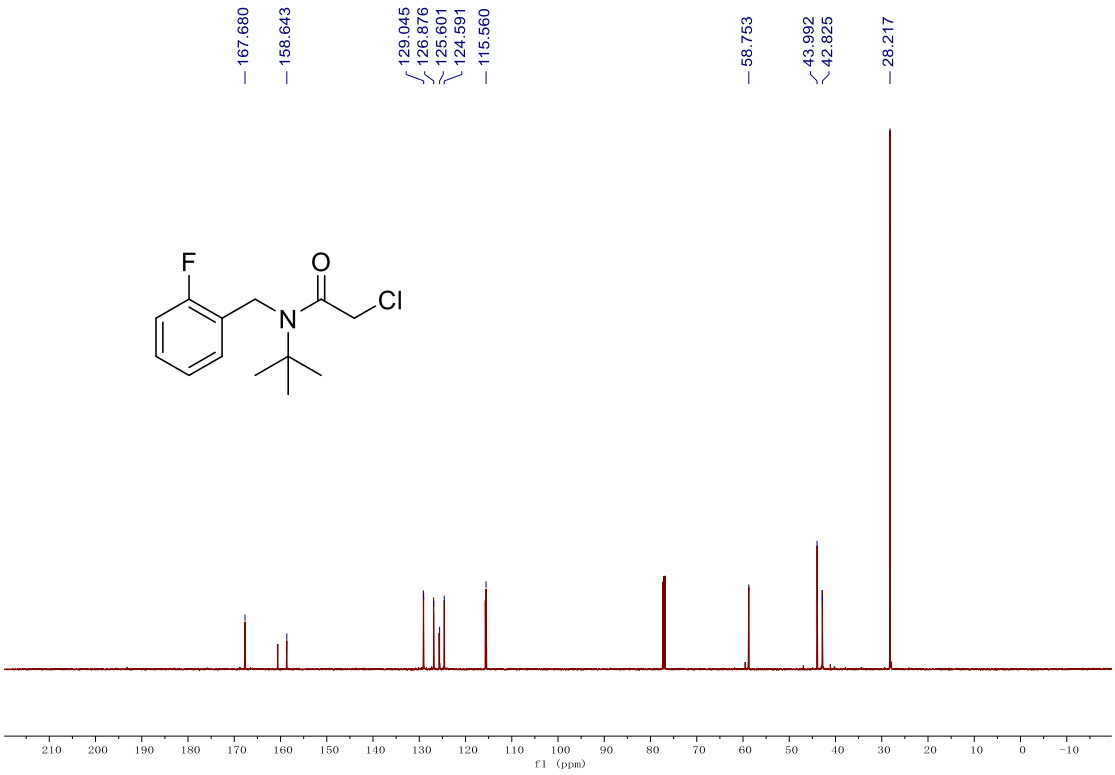
^{1}H NMR spectrum of **1q** ($CDCl_3$, 400MHz)



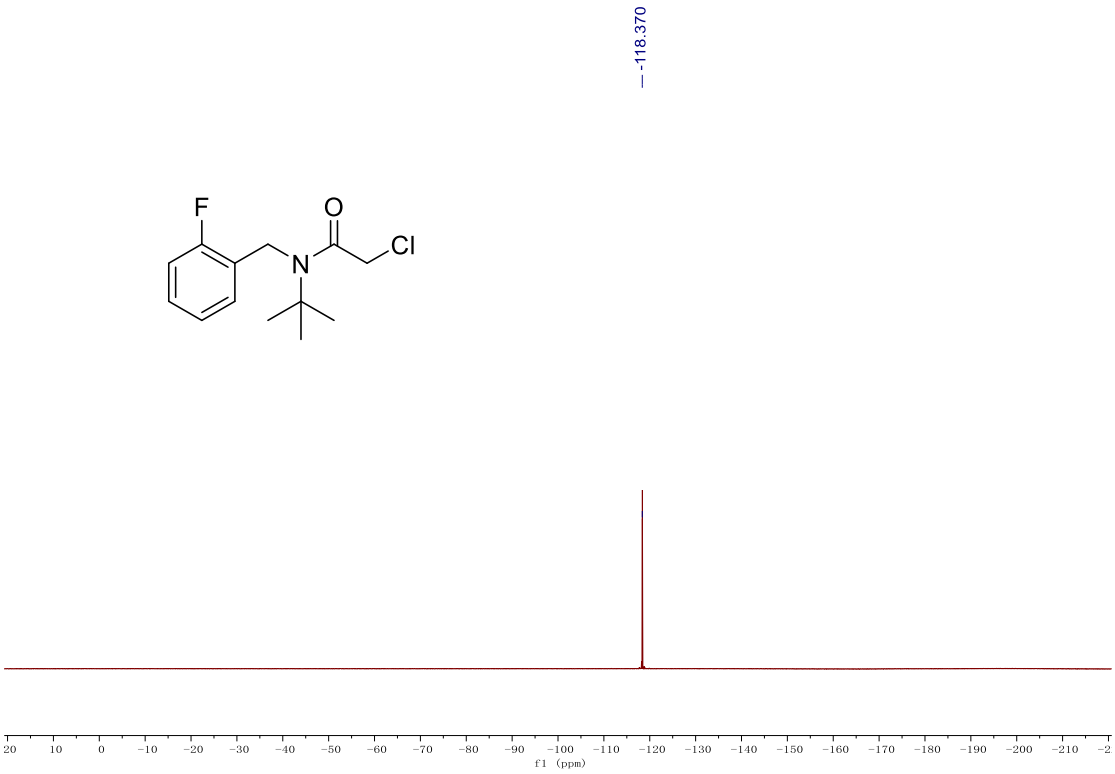
^{13}C NMR spectrum of **1q** ($CDCl_3$, 101MHz)



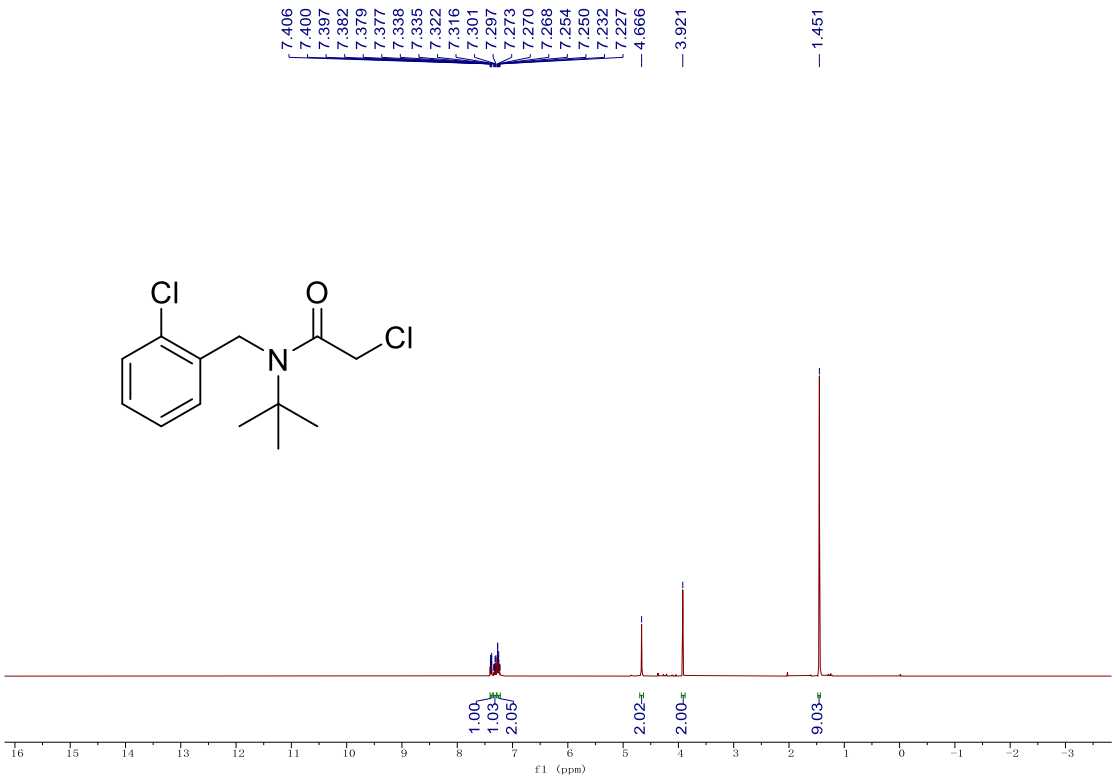
^{1}H NMR spectrum of **1r** ($CDCl_3$, 500MHz)



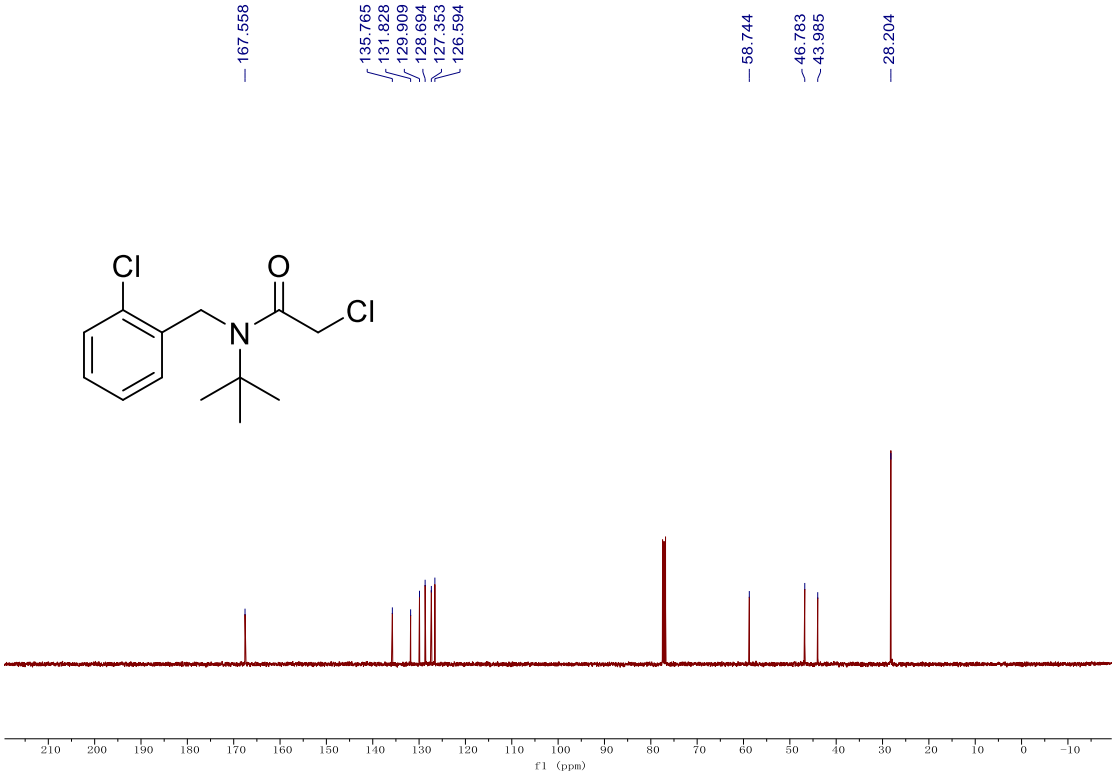
^{13}C NMR spectrum of **1r** ($CDCl_3$, 126MHz)



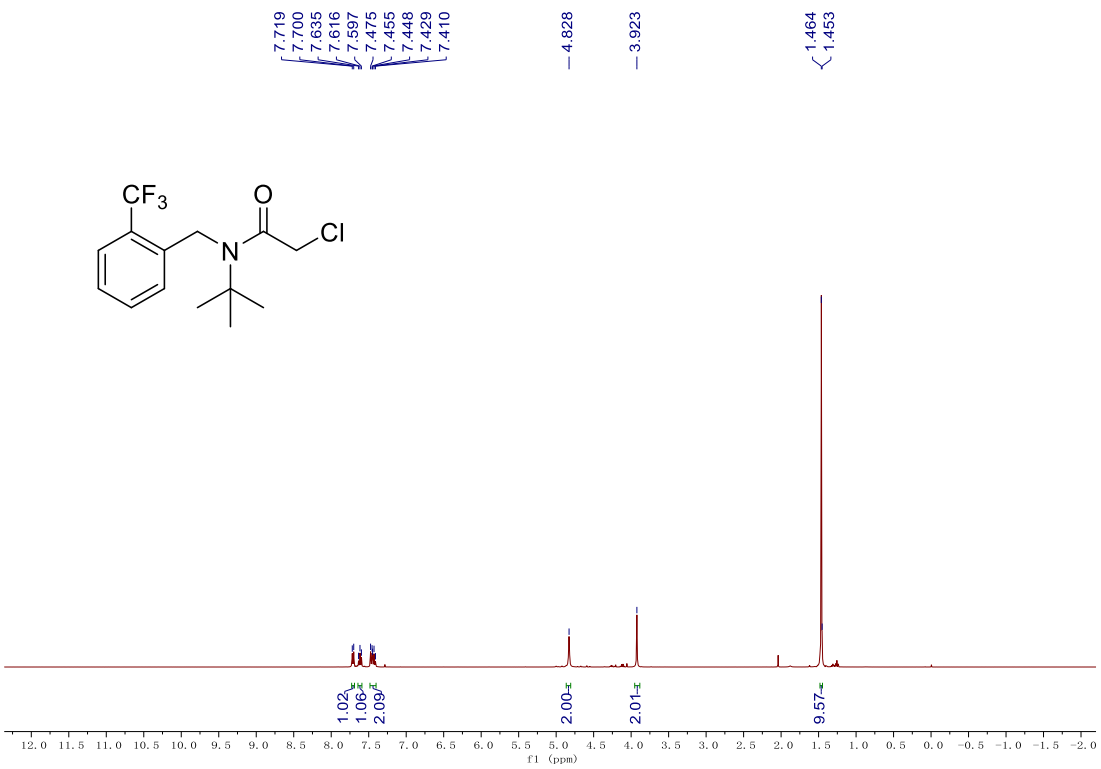
^{19}F NMR spectrum of **1r** ($CDCl_3$, 471MHz)



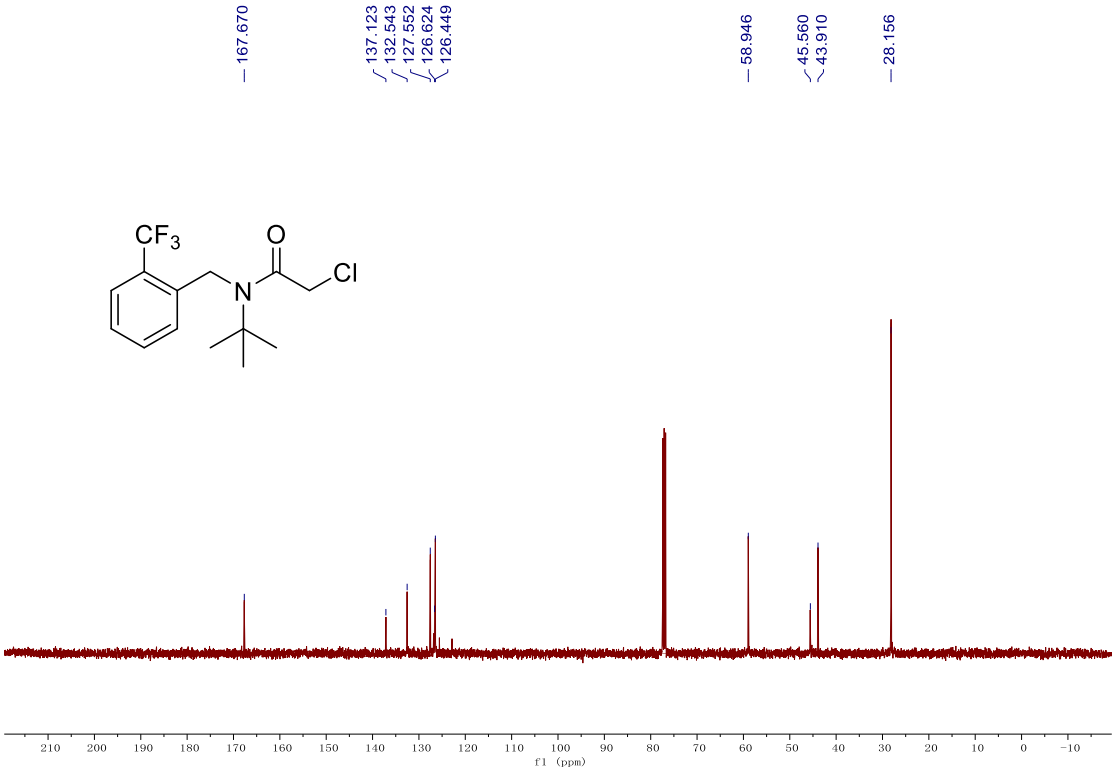
^{1}H NMR spectrum of **1s** ($CDCl_3$, 400MHz)



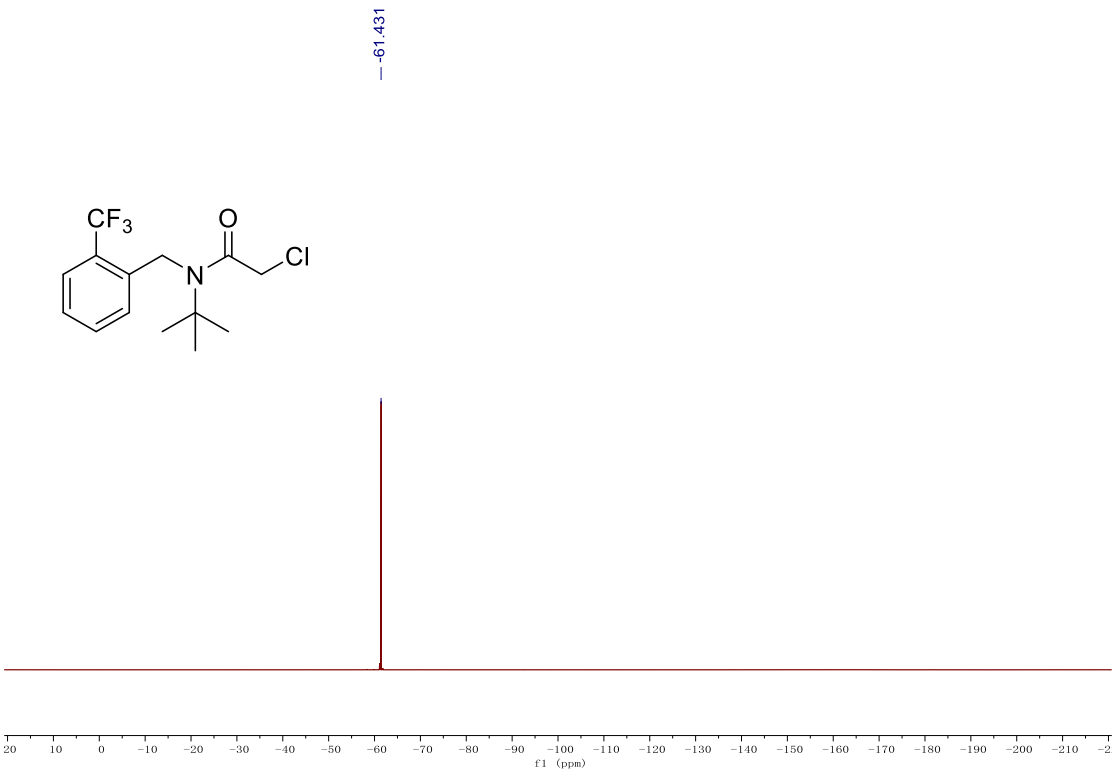
^{13}C NMR spectrum of **1s** ($CDCl_3$, 101MHz)



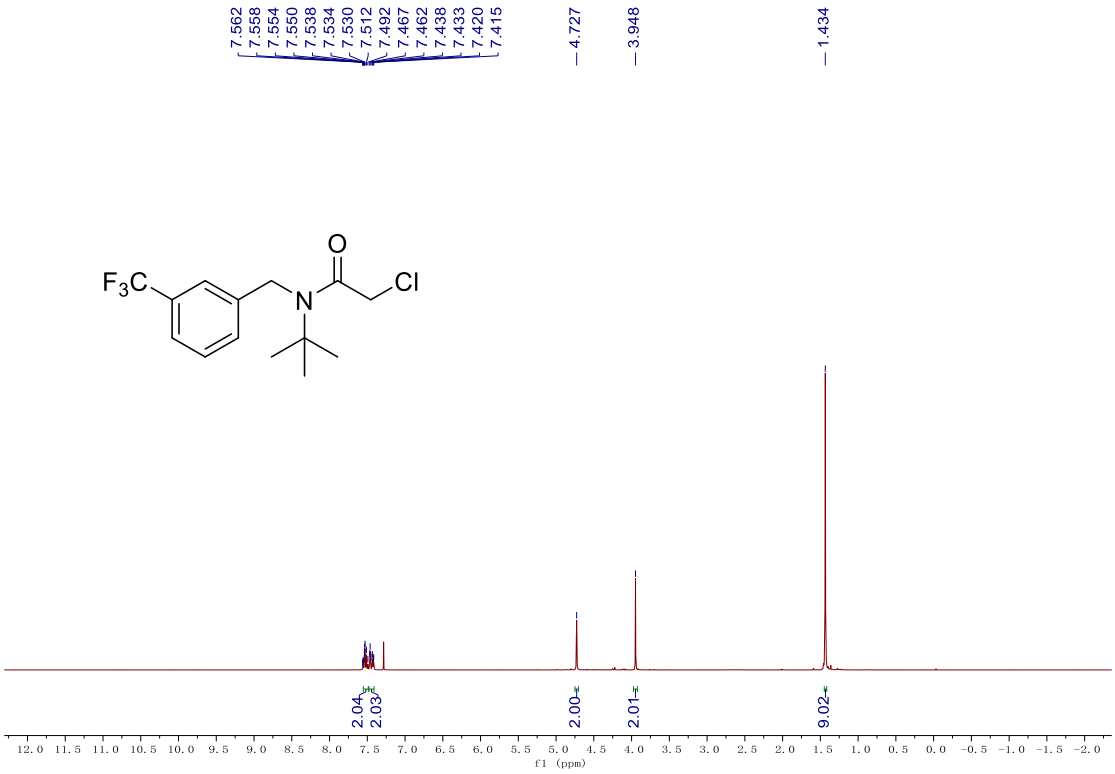
^{1}H NMR spectrum of **1t** ($CDCl_3$, 400MHz)



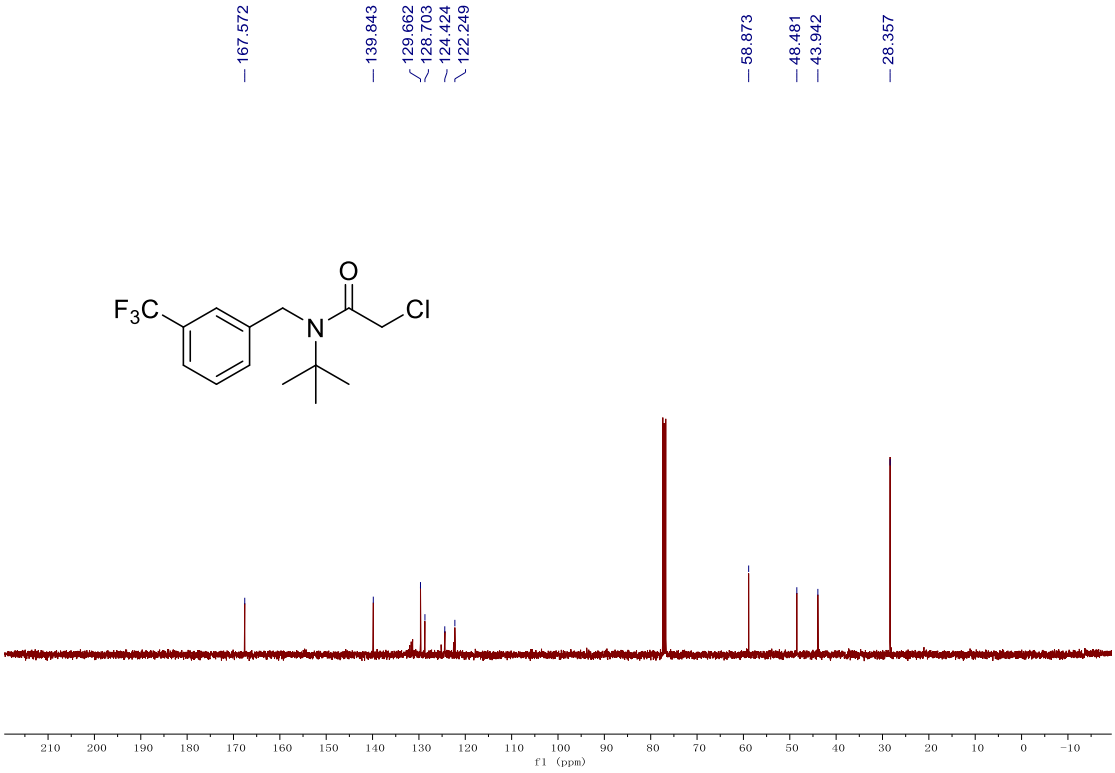
^{13}C NMR spectrum of **1t** ($CDCl_3$, 101MHz)



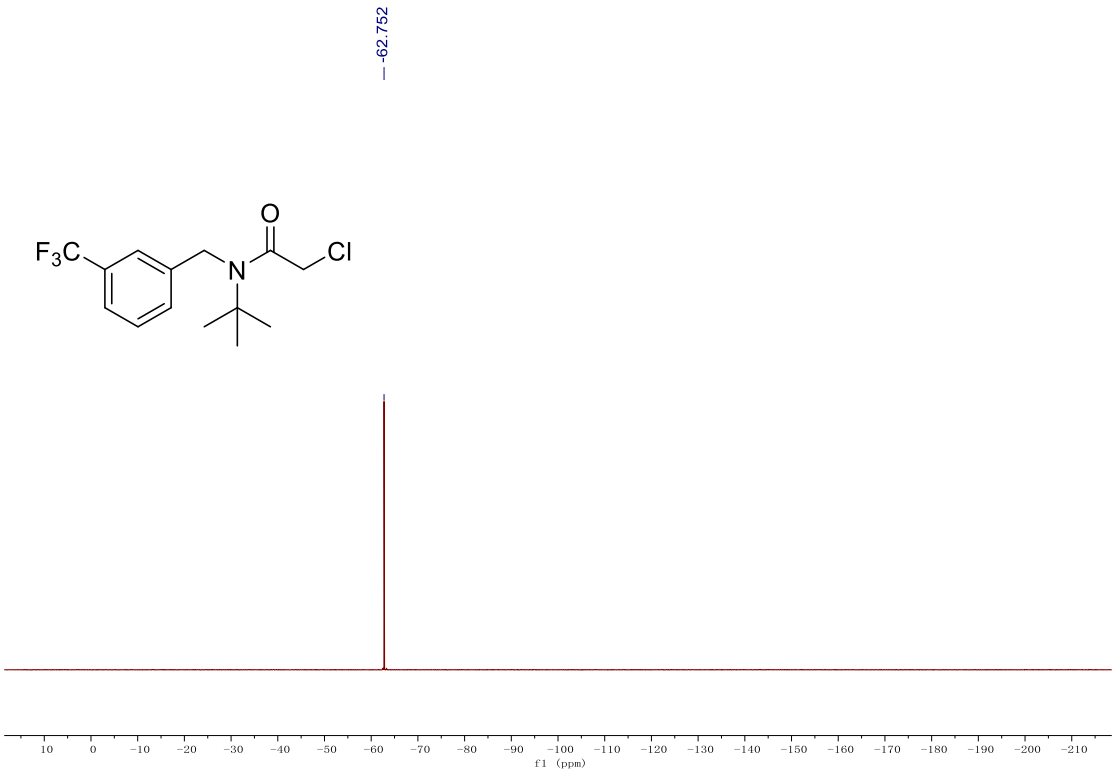
^{19}F NMR spectrum of **1t** ($CDCl_3$, 471MHz)



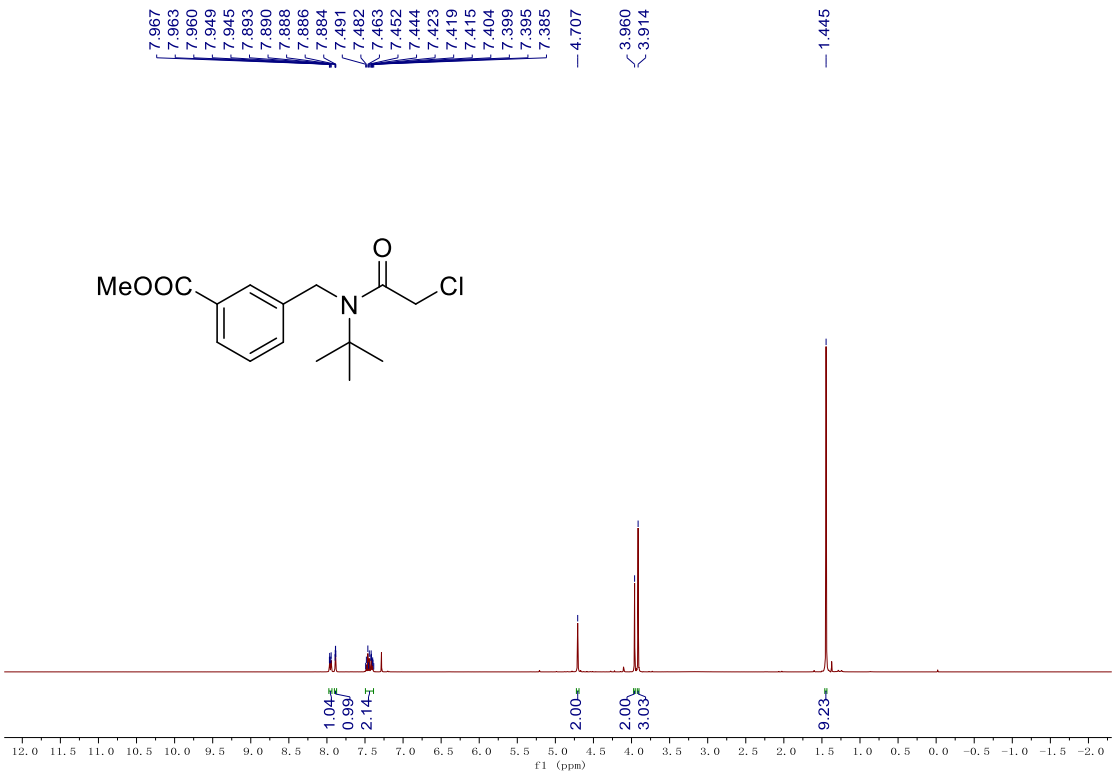
^{1}H NMR spectrum of **1u** ($CDCl_3$, 400MHz)



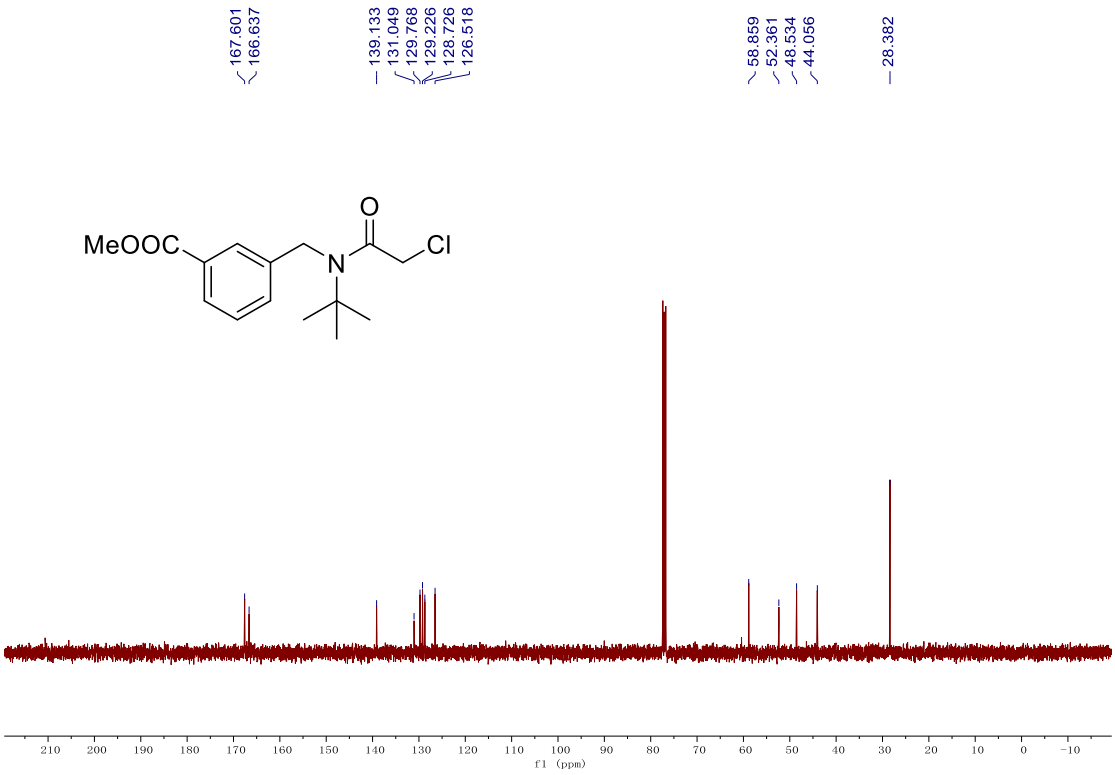
^{13}C NMR spectrum of **1u** ($CDCl_3$, 101MHz)



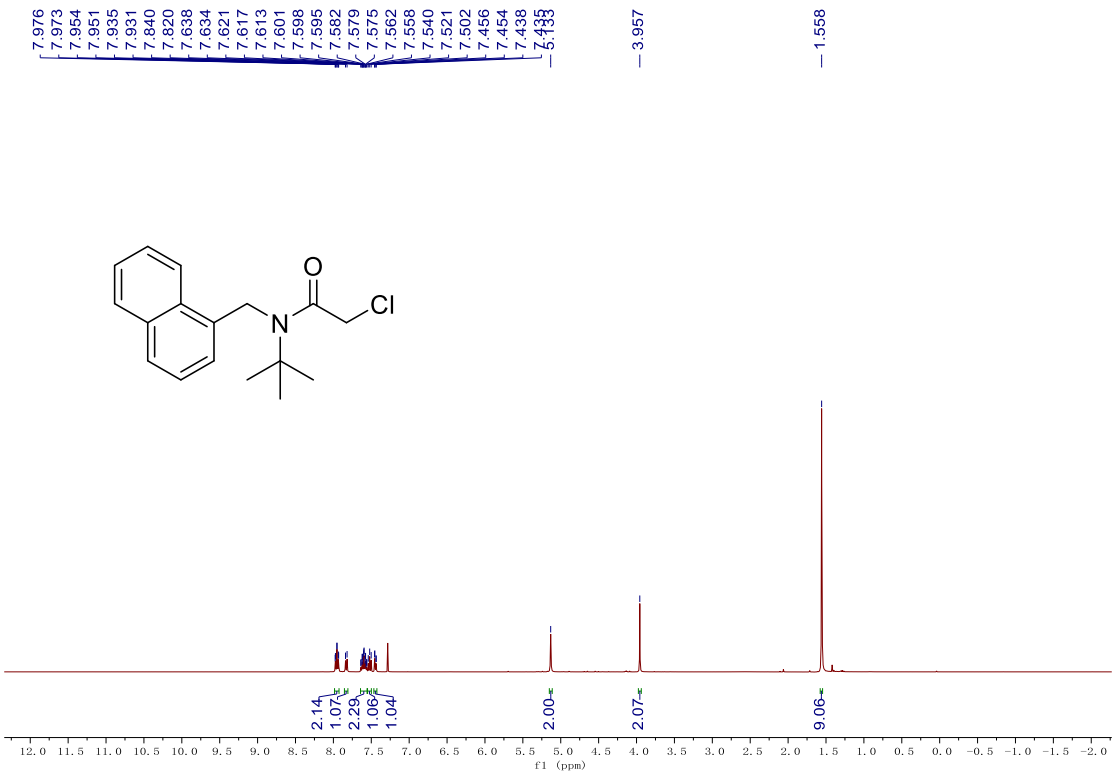
^{19}F NMR spectrum of **1u** ($CDCl_3$, 376MHz)



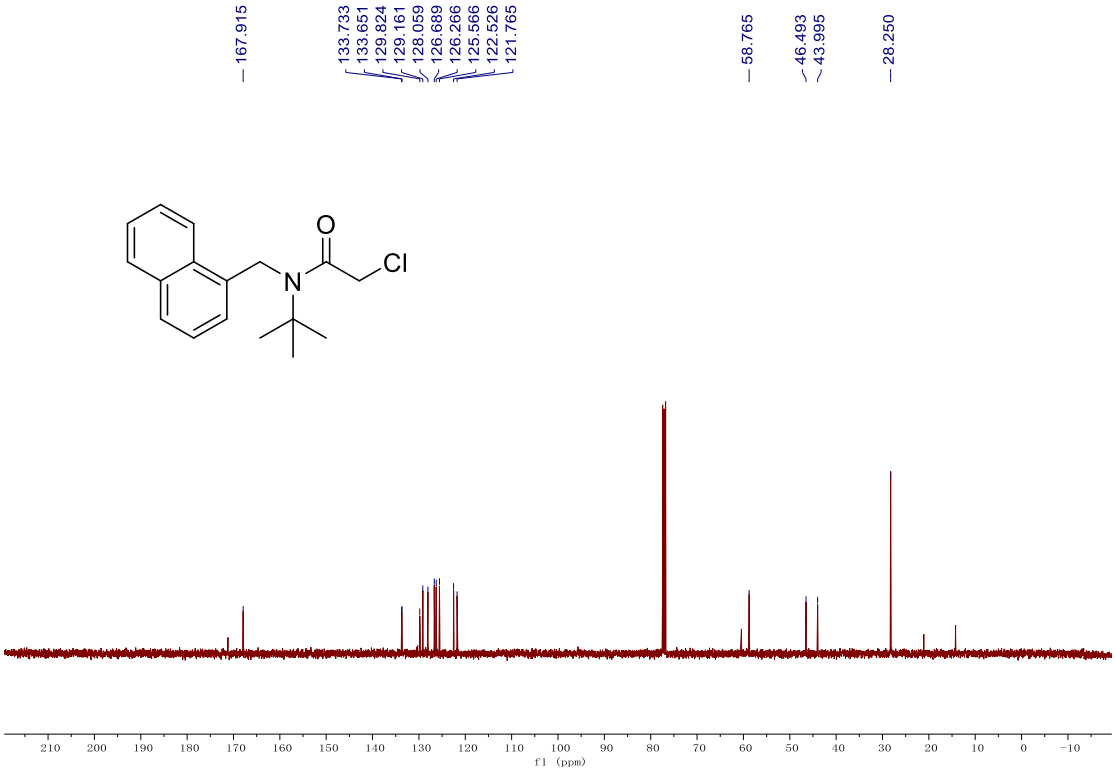
^{1}H NMR spectrum of **1v** ($CDCl_3$, 400MHz)



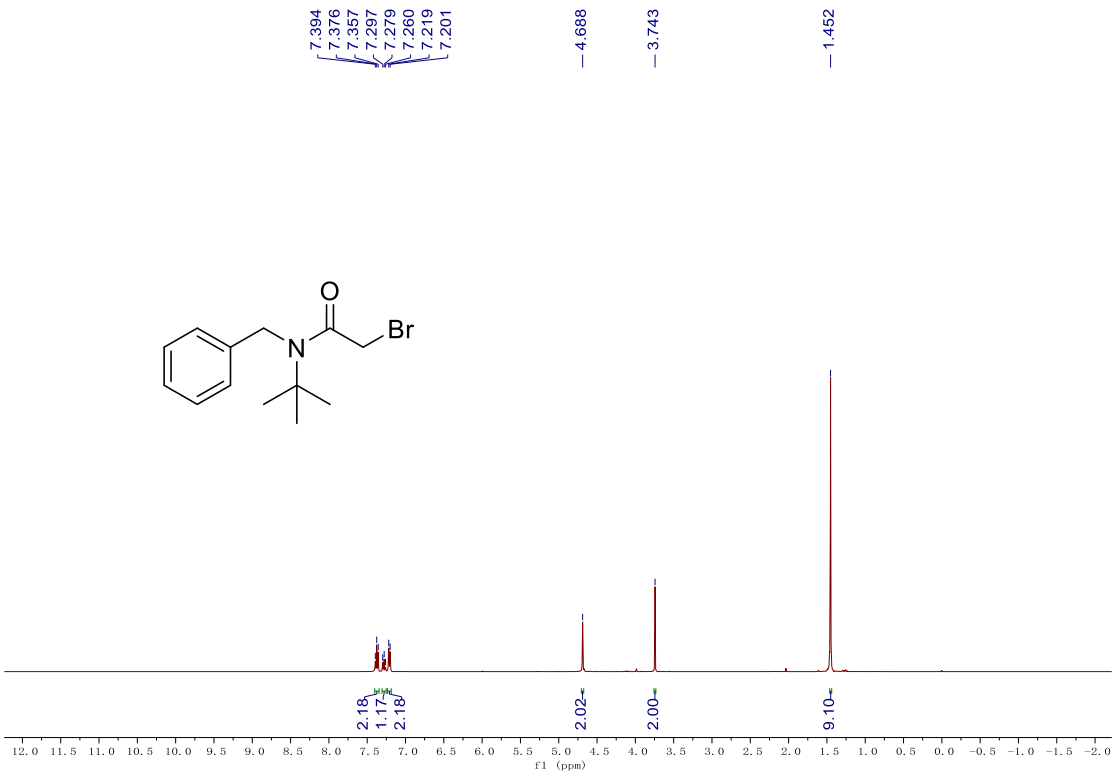
^{13}C NMR spectrum of **1v** ($CDCl_3$, 101MHz)



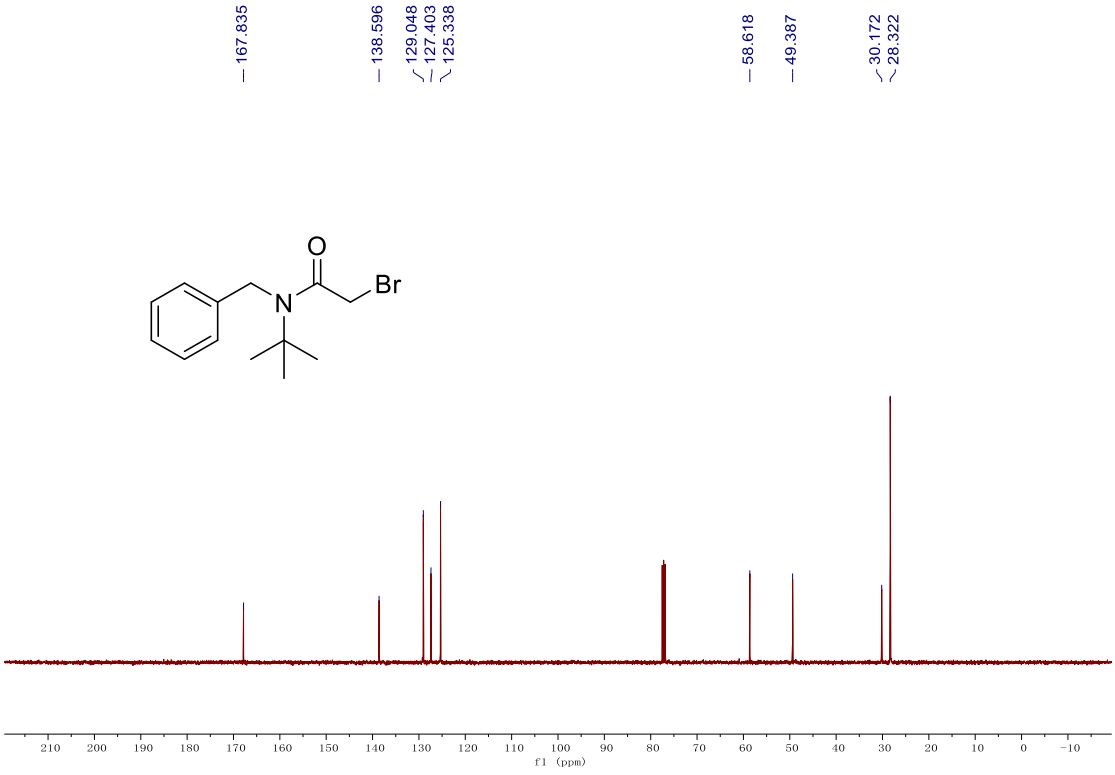
^{1}H NMR spectrum of **1w** ($CDCl_3$, 400MHz)



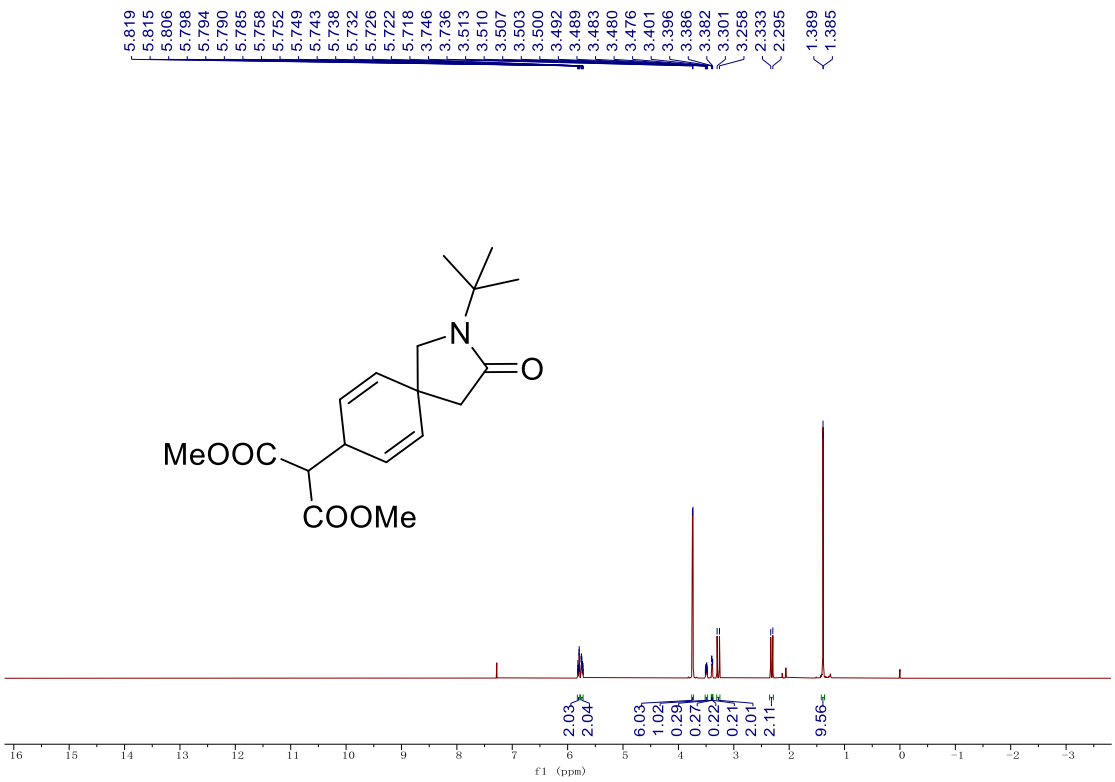
^{13}C NMR spectrum of **1w** ($CDCl_3$, 101MHz)



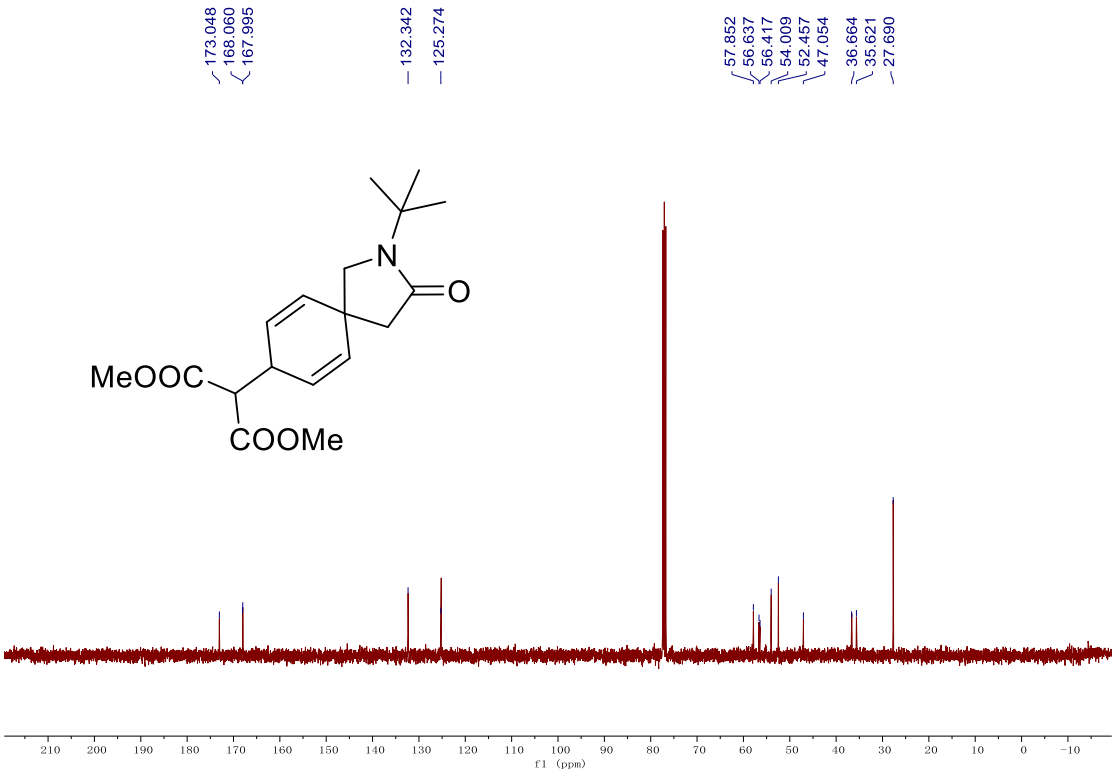
^{1}H NMR spectrum of **1x** ($CDCl_3$, 400MHz)



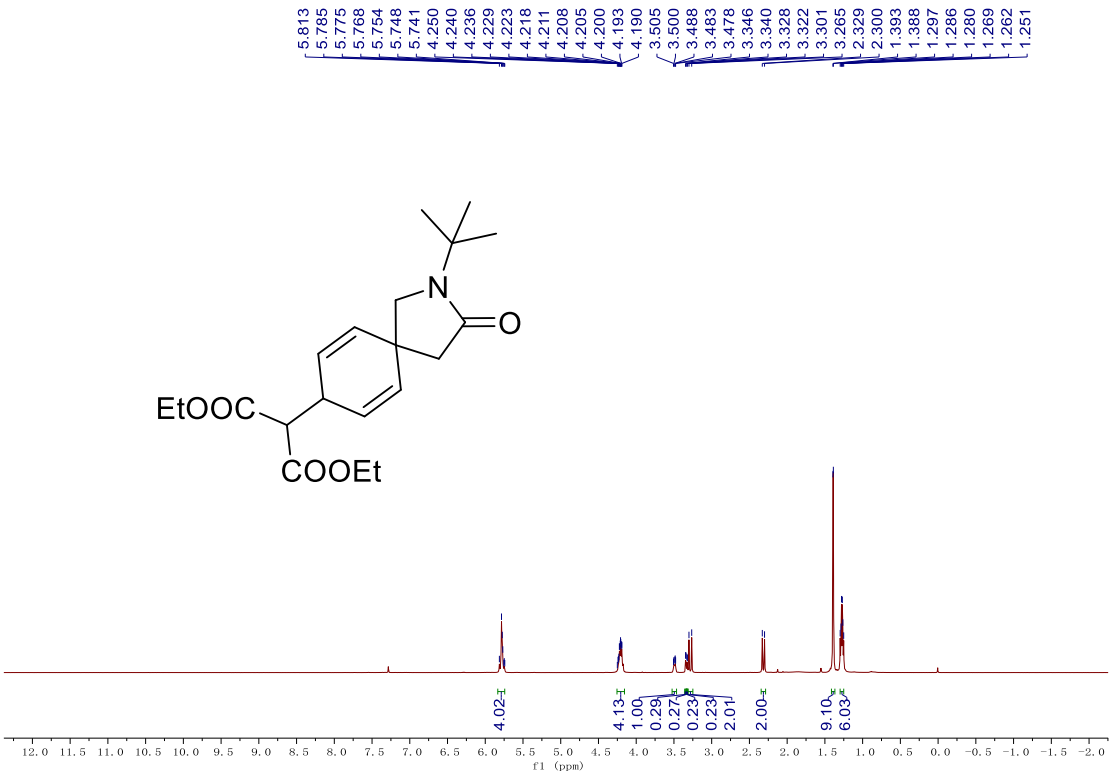
^{13}C NMR spectrum of **1x** ($CDCl_3$, 101MHz)



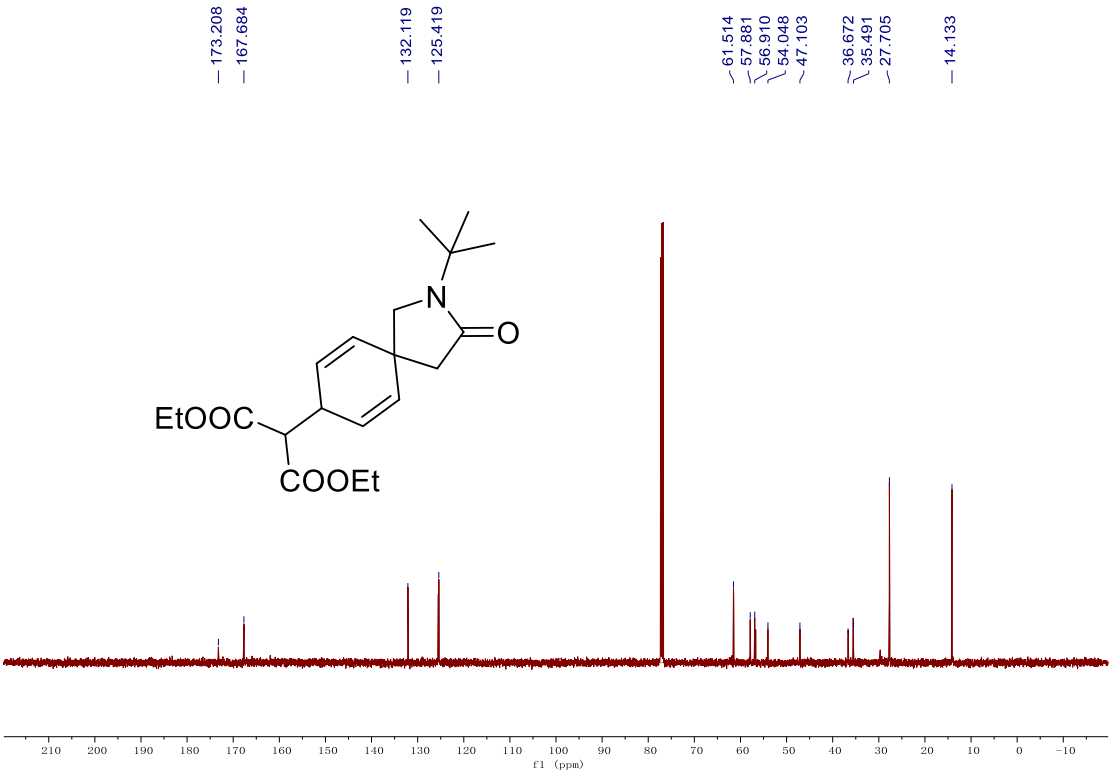
^{1}H NMR spectrum of **2a** ($CDCl_3$, 500MHz)



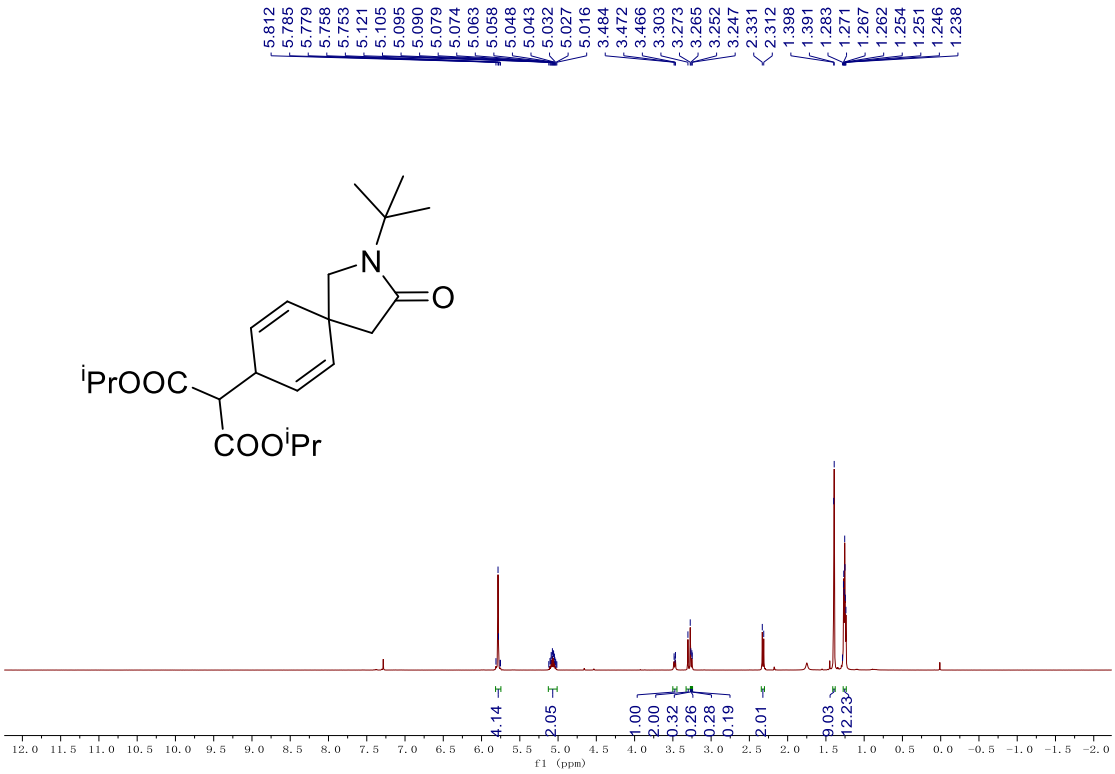
^{13}C NMR spectrum of **2a** ($CDCl_3$, 101MHz)



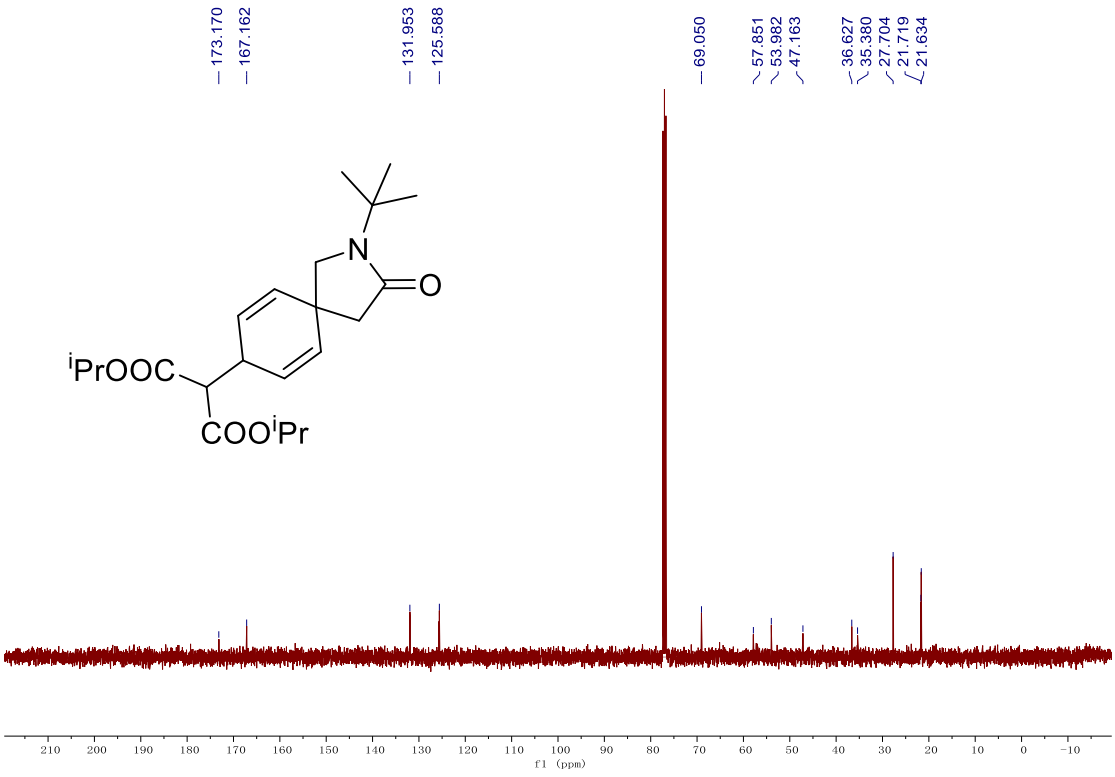
^{1}H NMR spectrum of **2b** ($CDCl_3$, 400MHz)



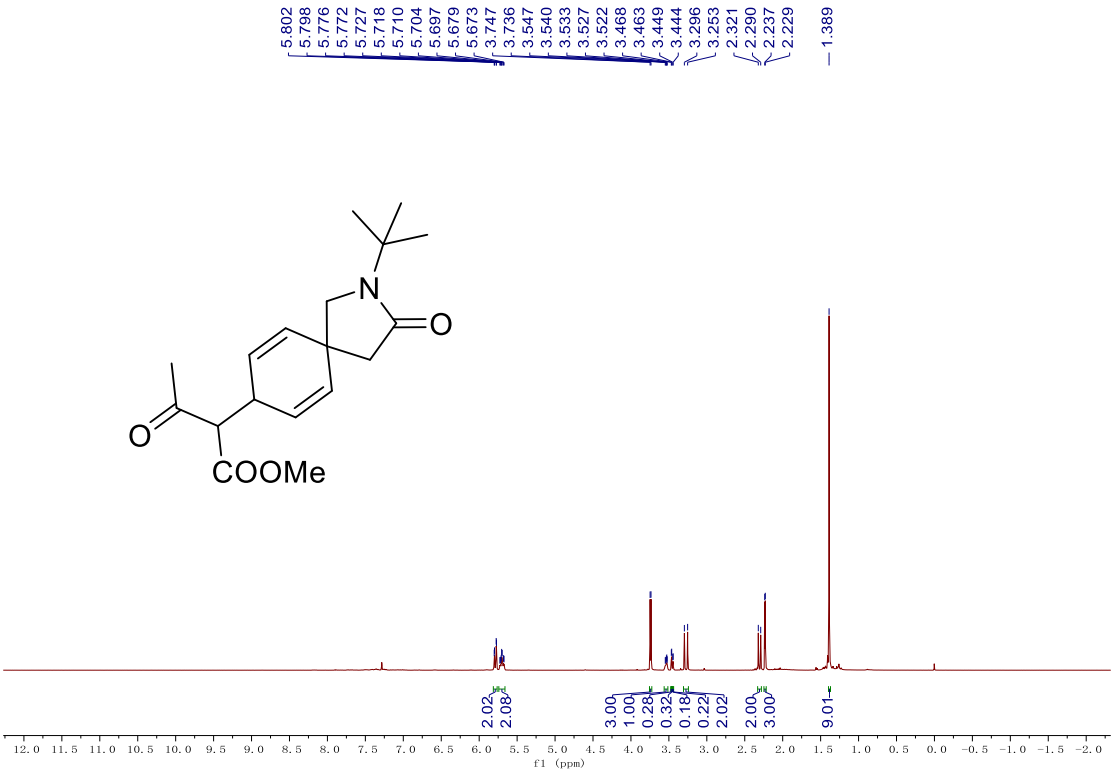
^{13}C NMR spectrum of **2b** ($CDCl_3$, 126MHz)



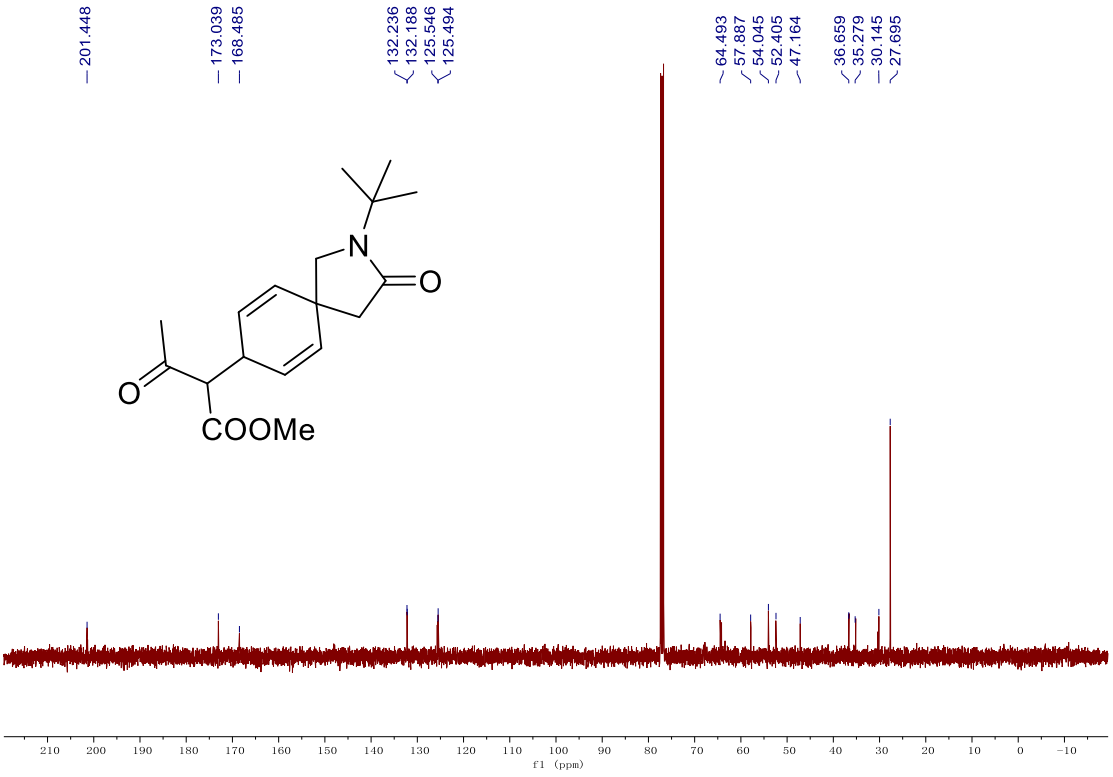
^{1}H NMR spectrum of **2c** ($CDCl_3$, 400MHz)



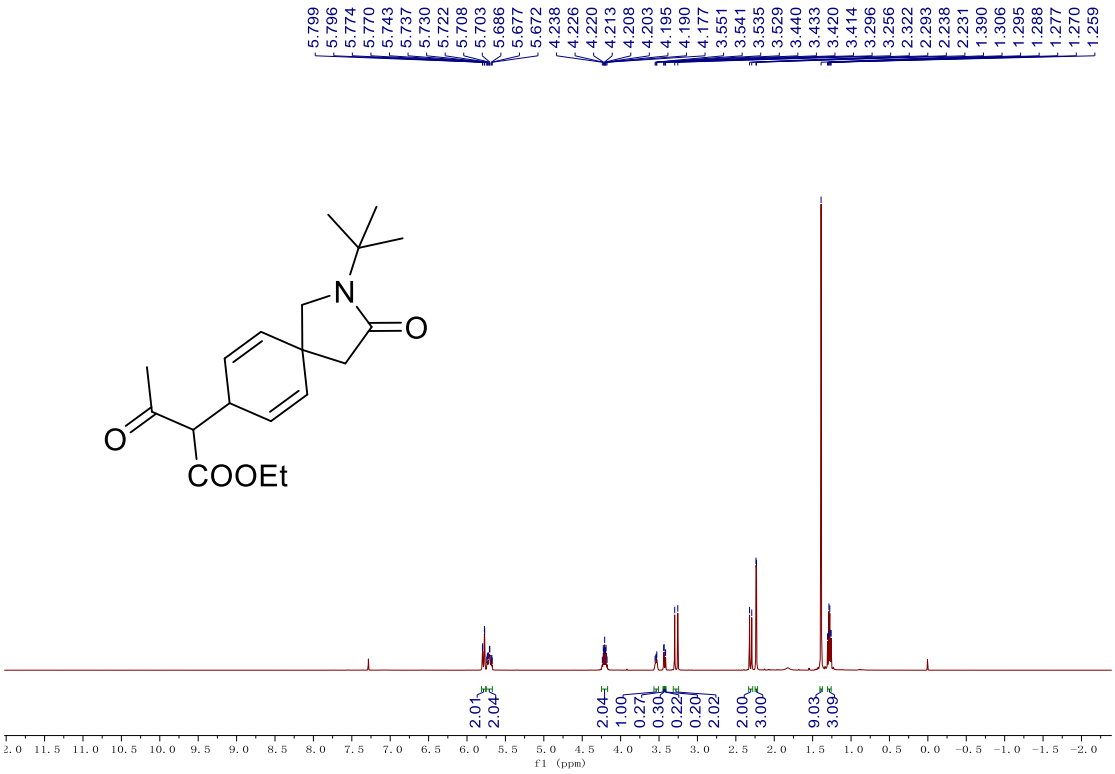
^{13}C NMR spectrum of **2c** ($CDCl_3$, 101MHz)



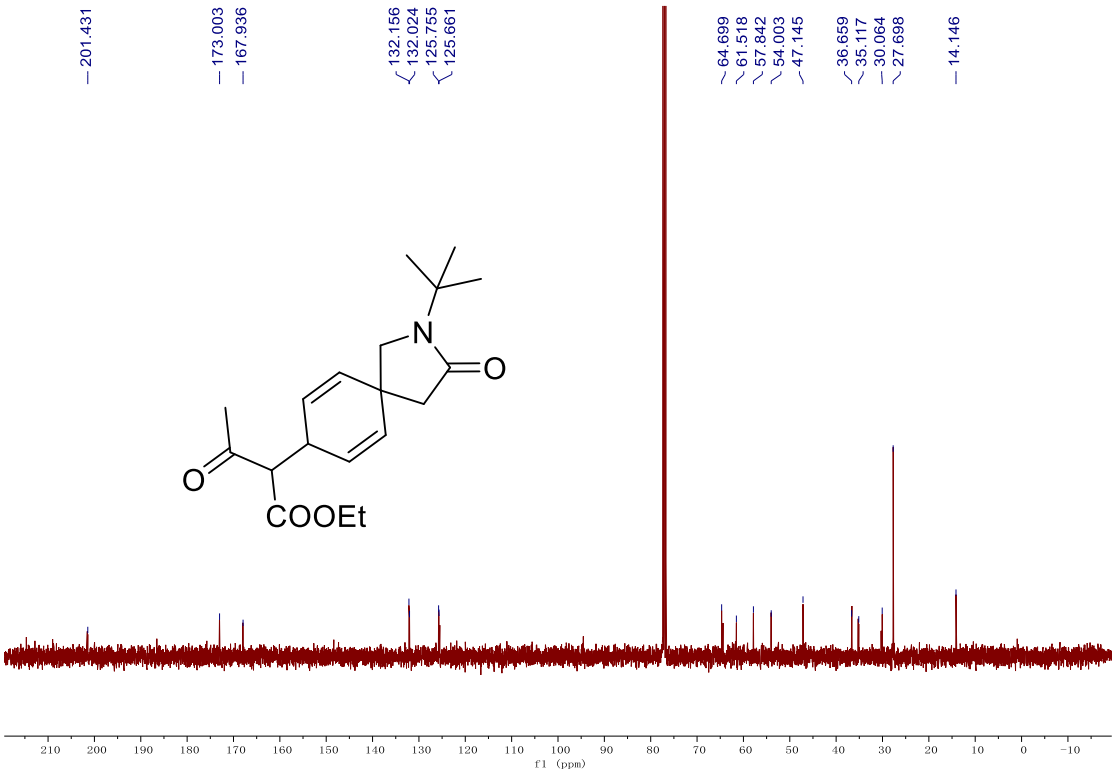
^{1}H NMR spectrum of **2e** ($CDCl_3$, 400MHz)



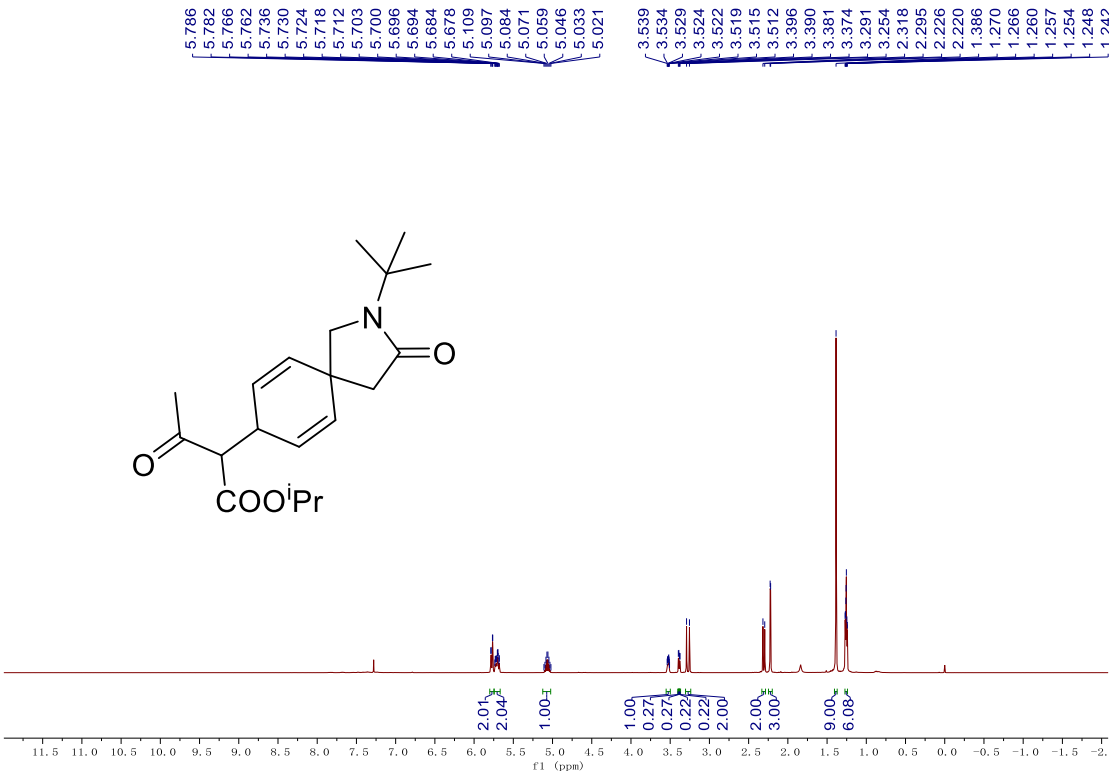
^{13}C NMR spectrum of **2e** ($CDCl_3$, 101MHz)



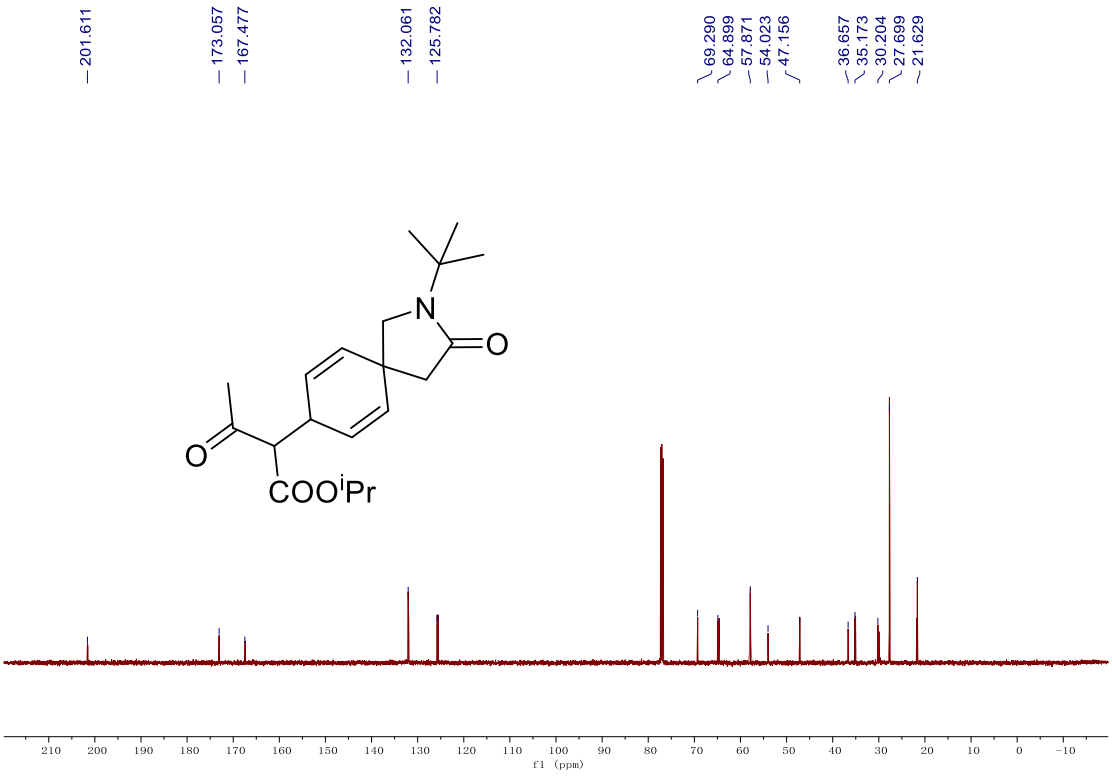
^{1}H NMR spectrum of **2f** ($CDCl_3$, 400MHz)



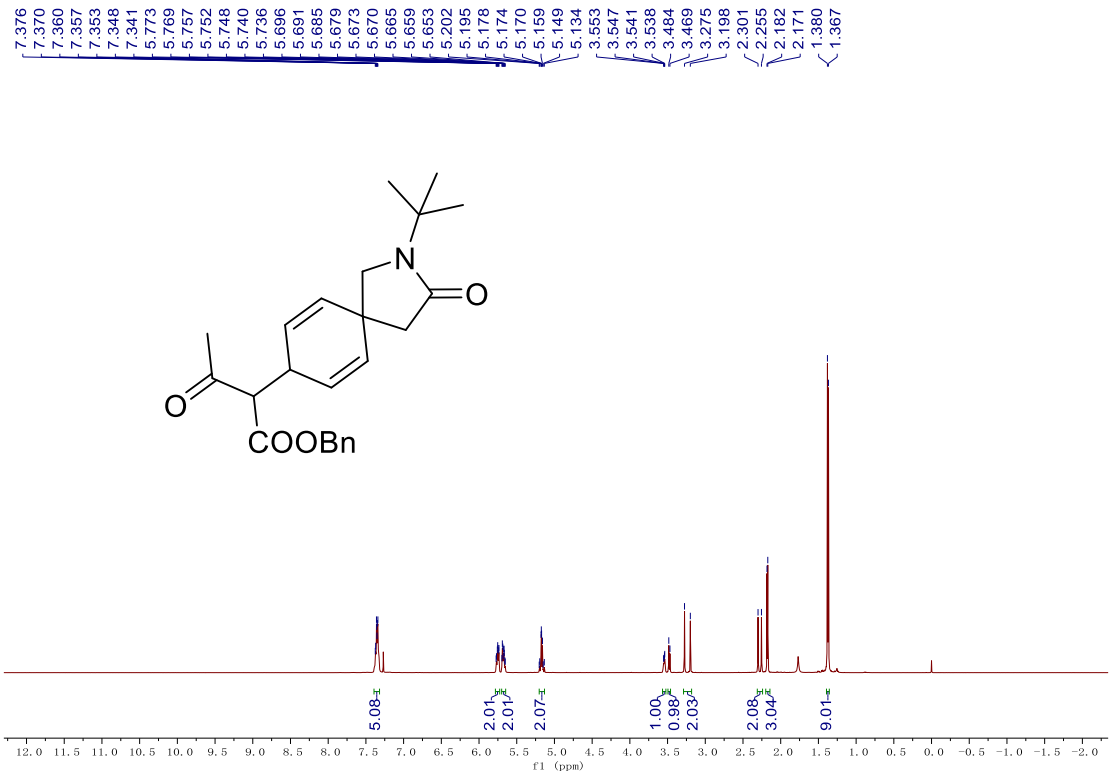
^{13}C NMR spectrum of **2f** ($CDCl_3$, 101MHz)



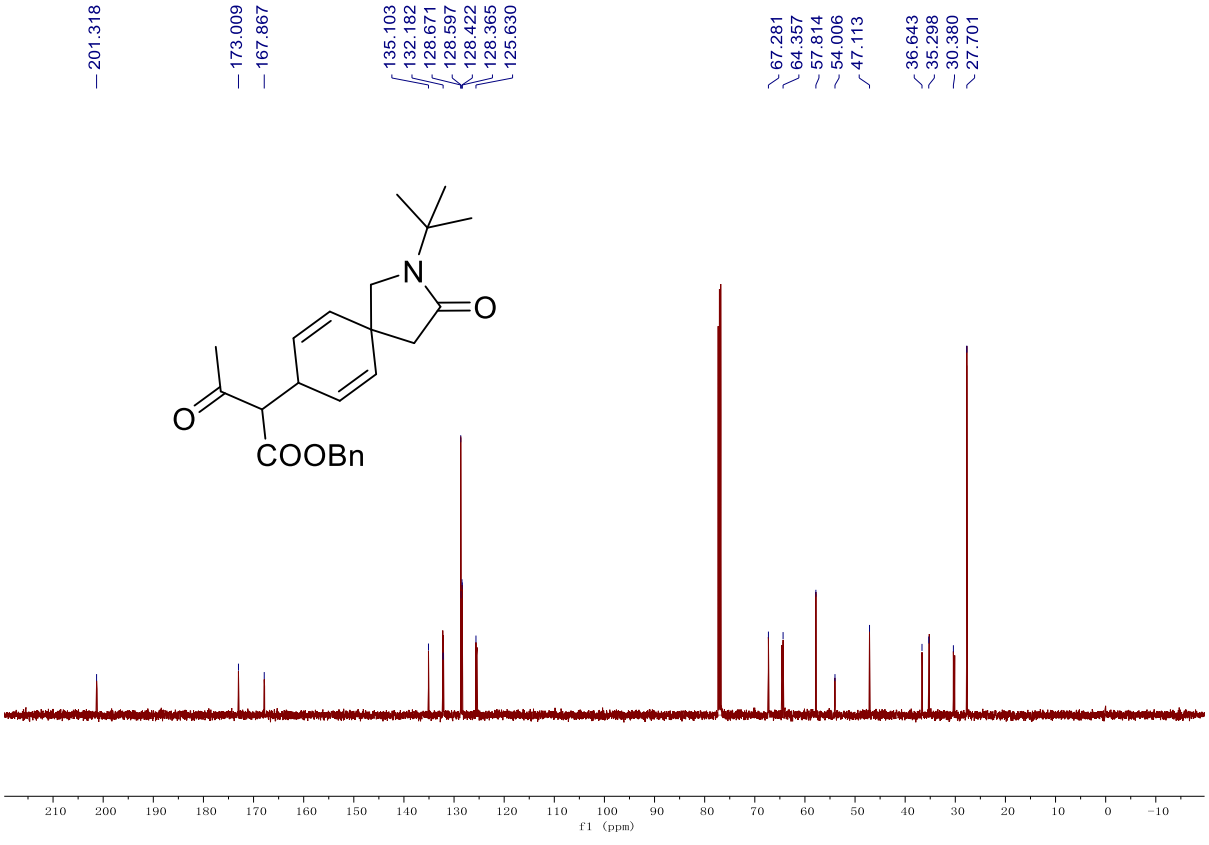
^{1}H NMR spectrum of **2g** ($CDCl_3$, 500MHz)



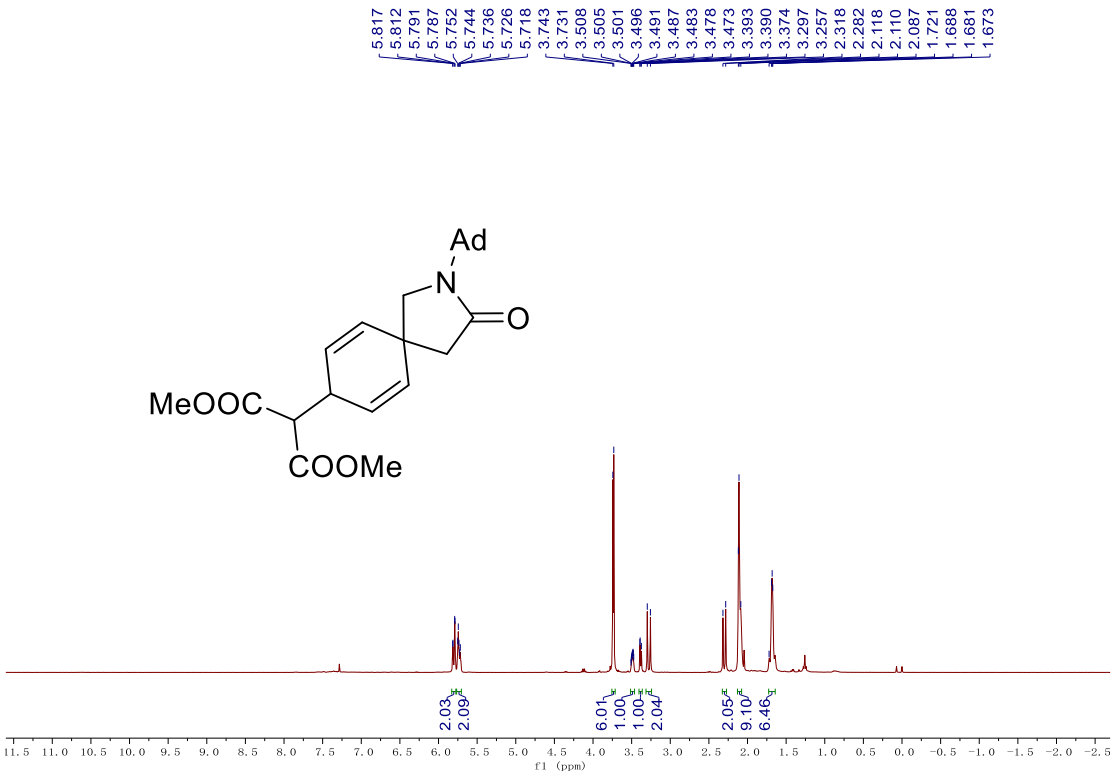
^{13}C NMR spectrum of **2g** ($CDCl_3$, 126MHz)



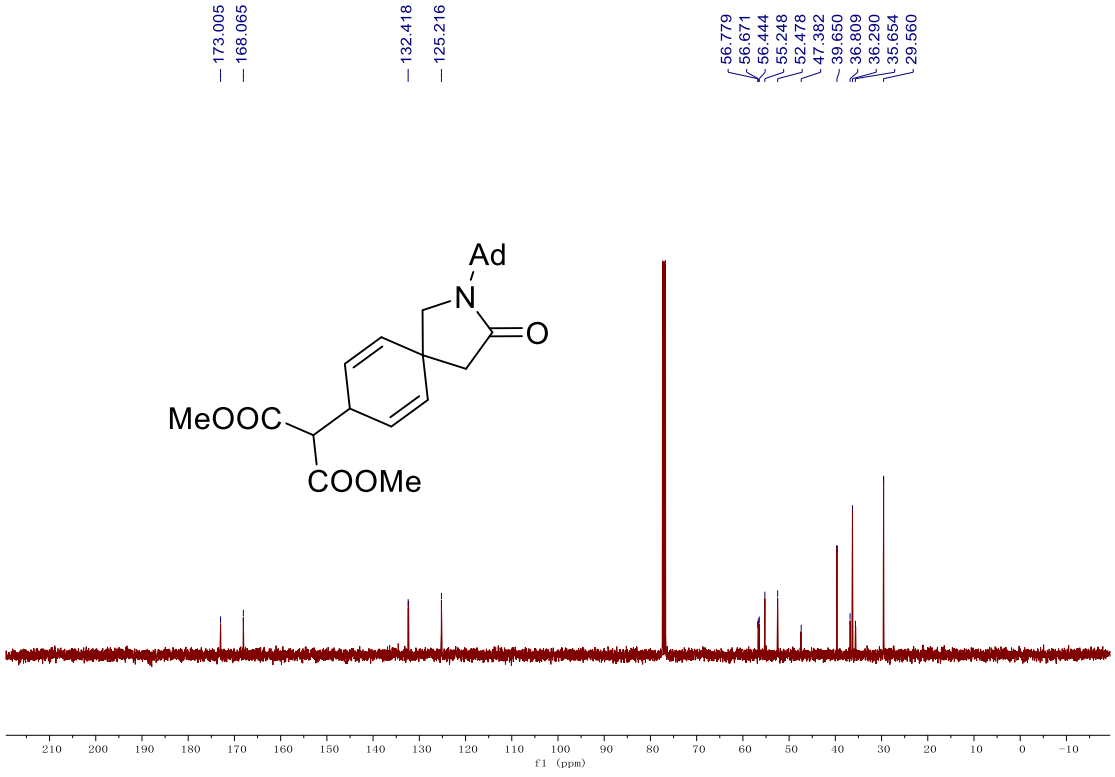
^{1}H NMR spectrum of **2h** ($CDCl_3$, 500MHz)



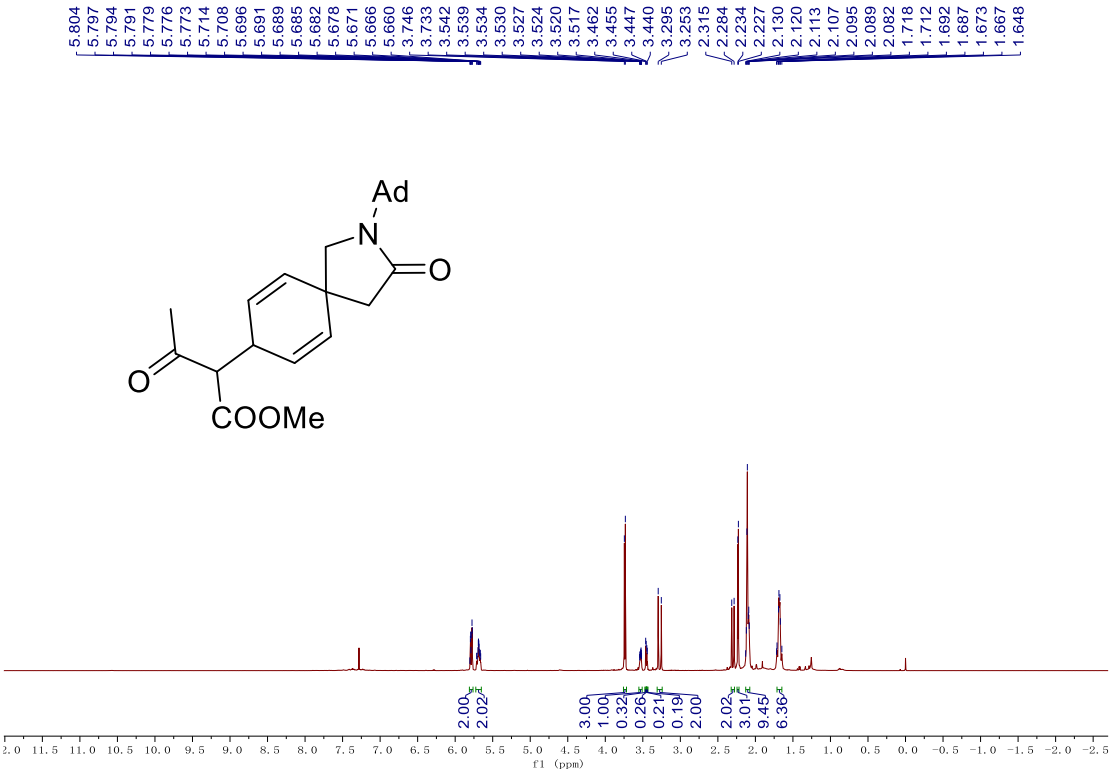
^{13}C NMR spectrum of **2h** ($CDCl_3$, 126MHz)



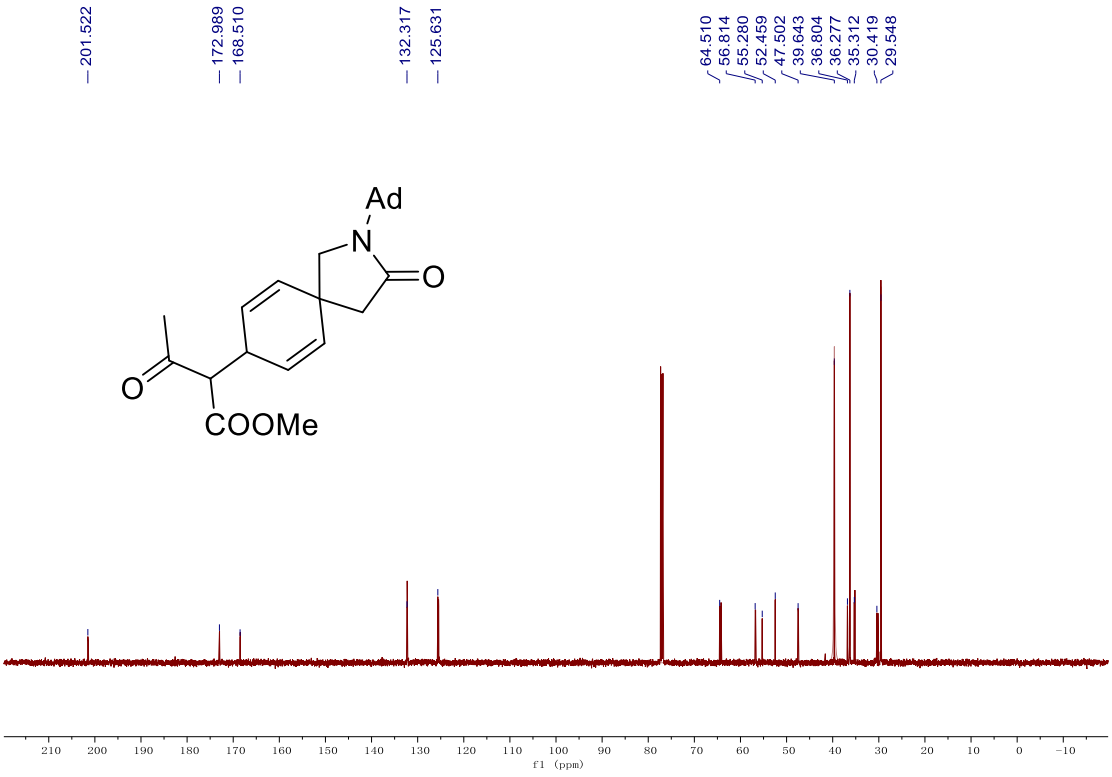
^{1}H NMR spectrum of **2j** ($CDCl_3$, 400MHz)



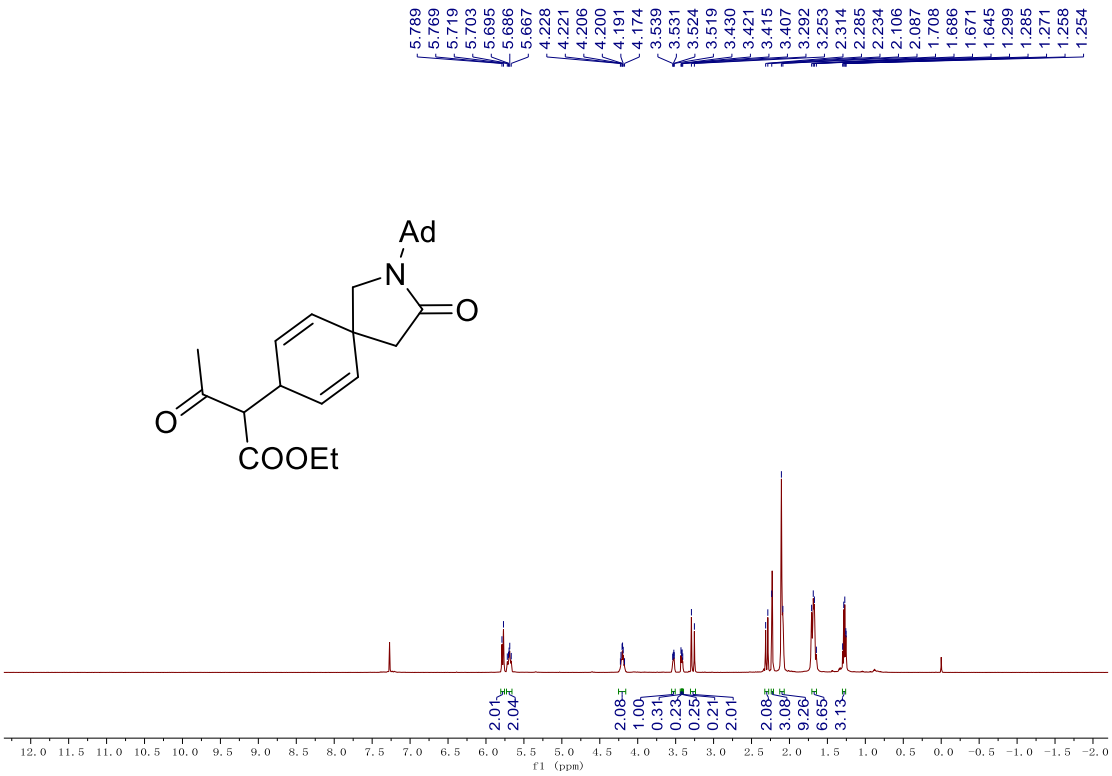
^{13}C NMR spectrum of **2j** ($CDCl_3$, 101MHz)



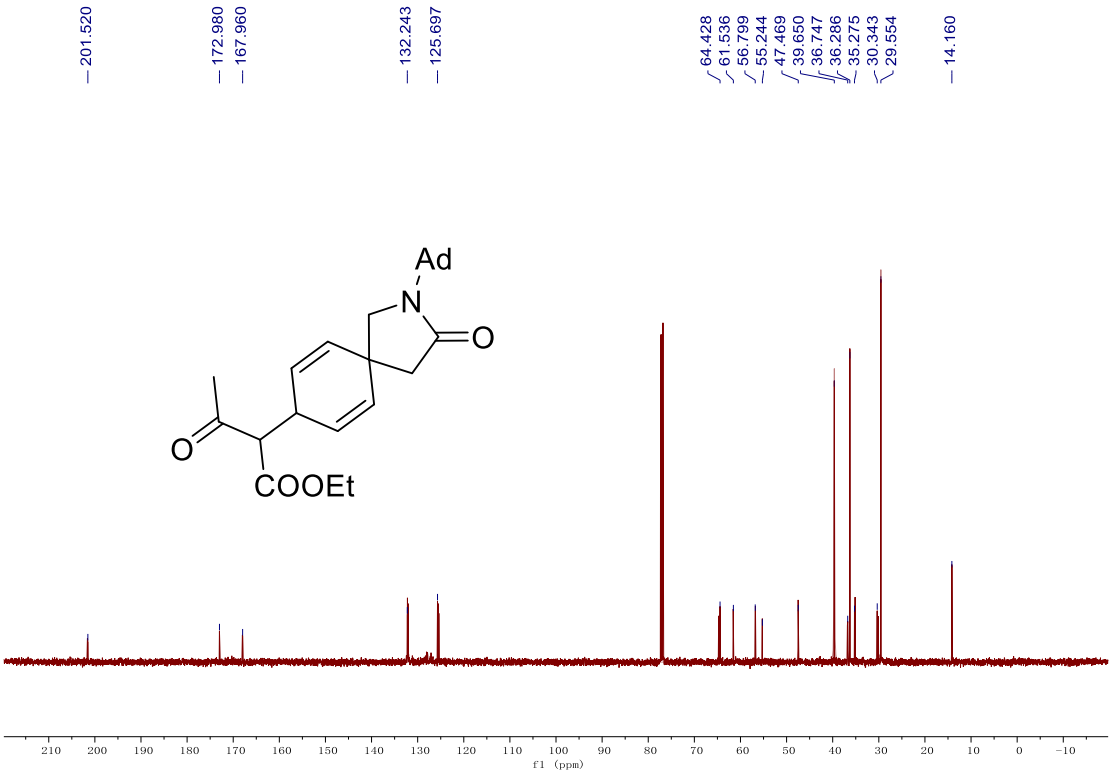
^{1}H NMR spectrum of **2k** ($CDCl_3$, 500MHz)



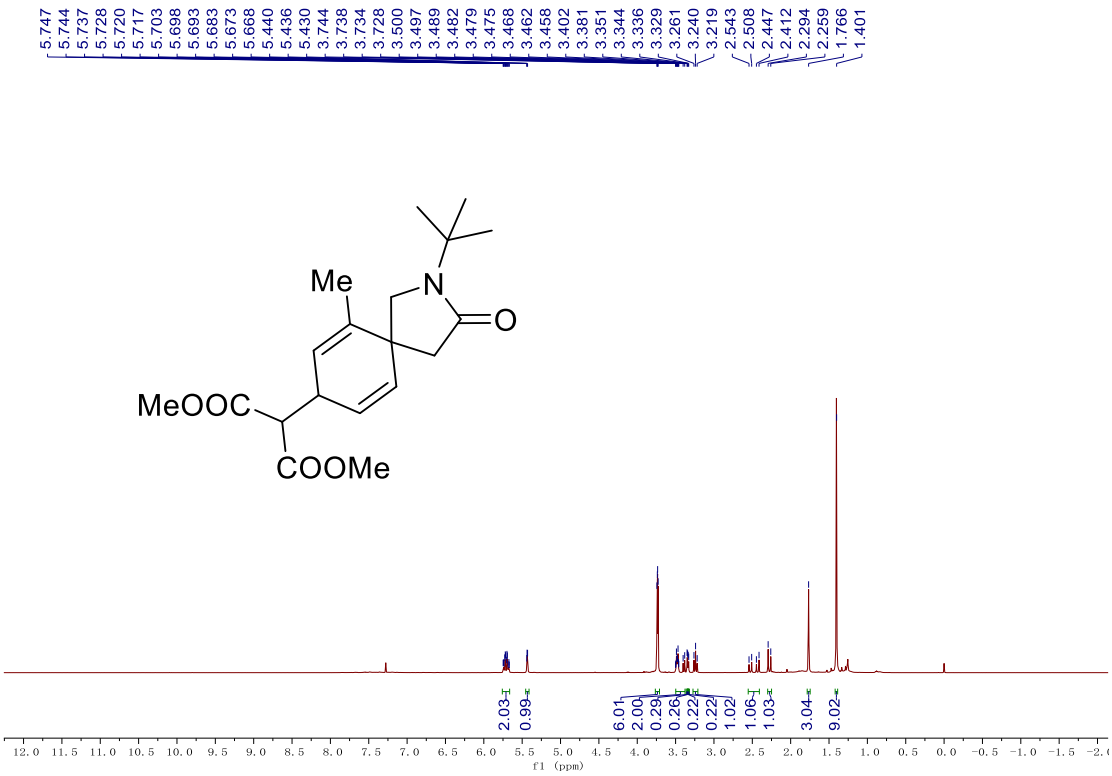
^{13}C NMR spectrum of **2k** ($CDCl_3$, 126MHz)



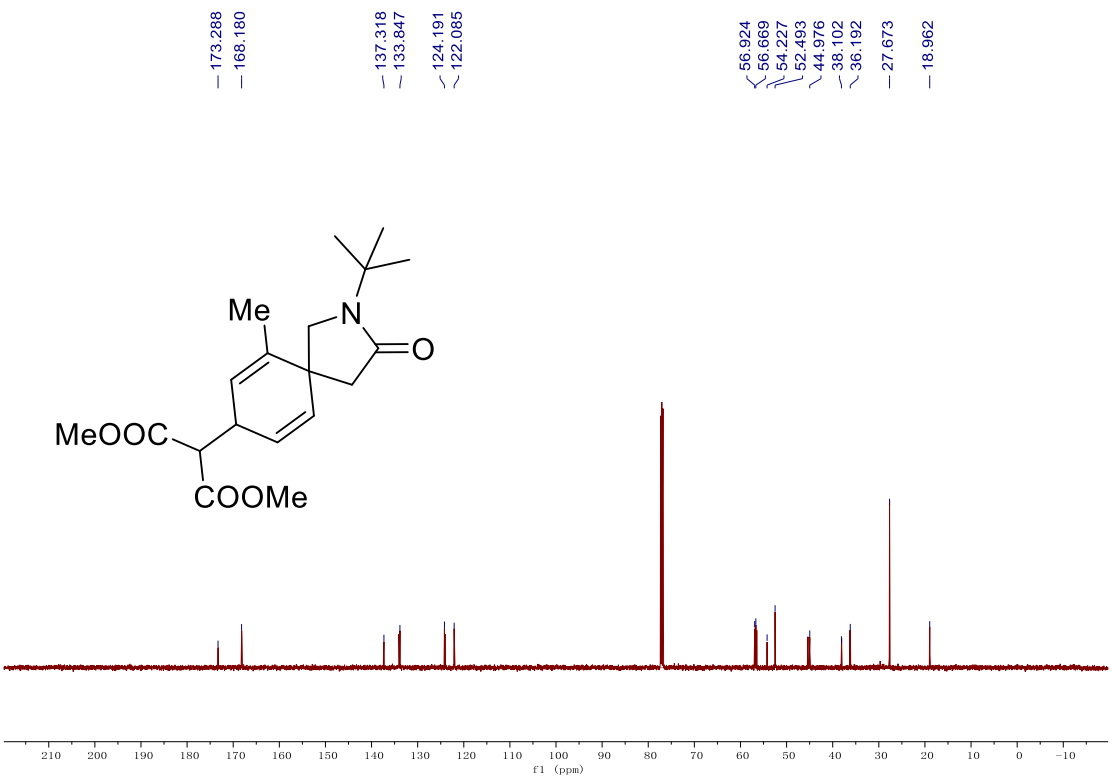
^{1}H NMR spectrum of **2l** ($CDCl_3$, 500MHz)



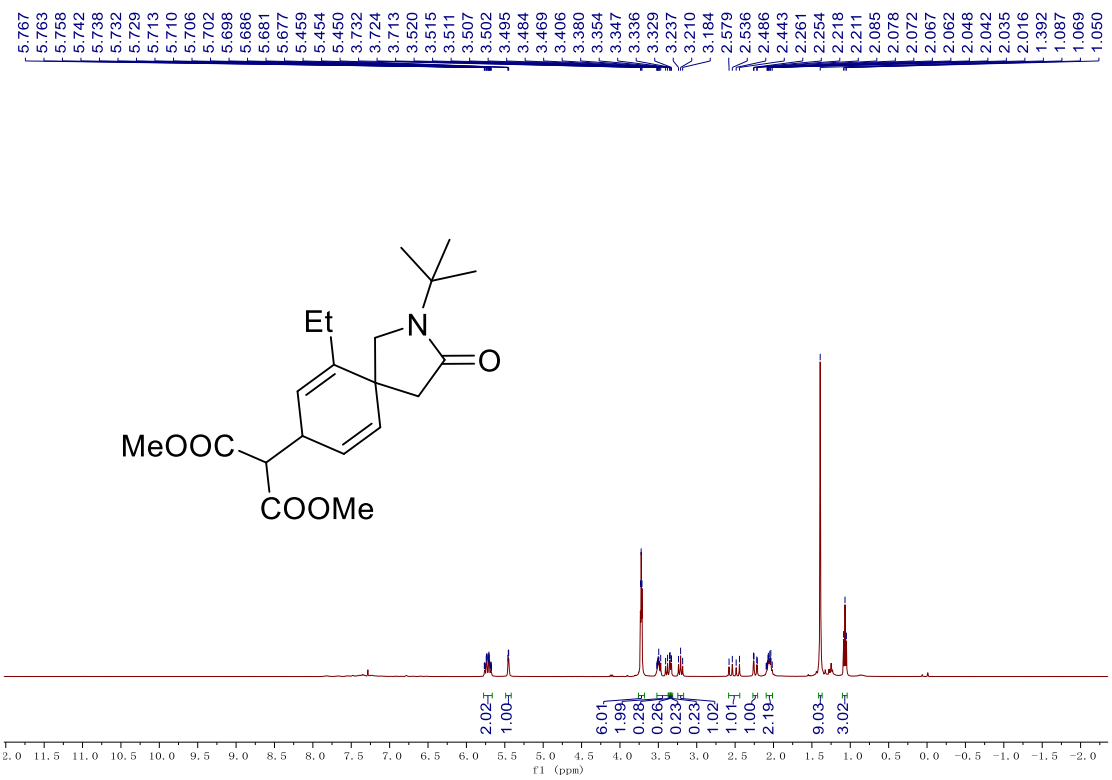
^{13}C NMR spectrum of **2l** ($CDCl_3$, 126MHz)



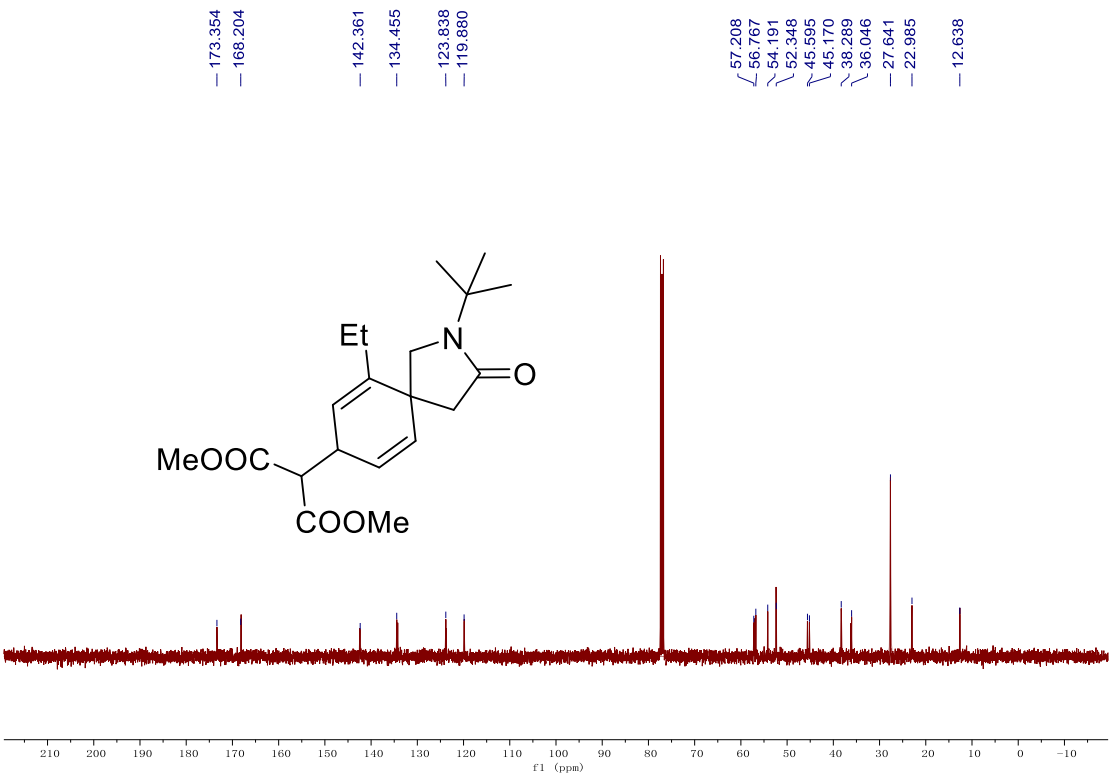
^{1}H NMR spectrum of **2m** ($CDCl_3$, 500MHz)



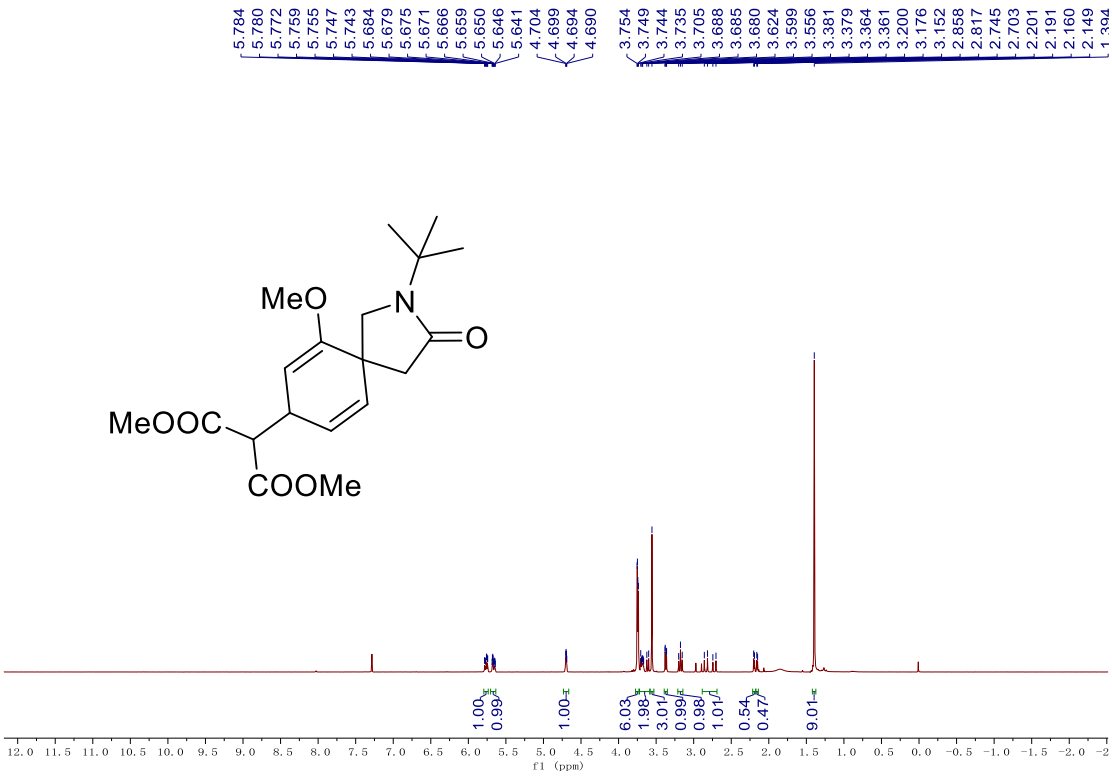
^{13}C NMR spectrum of **2m** ($CDCl_3$, 126MHz)



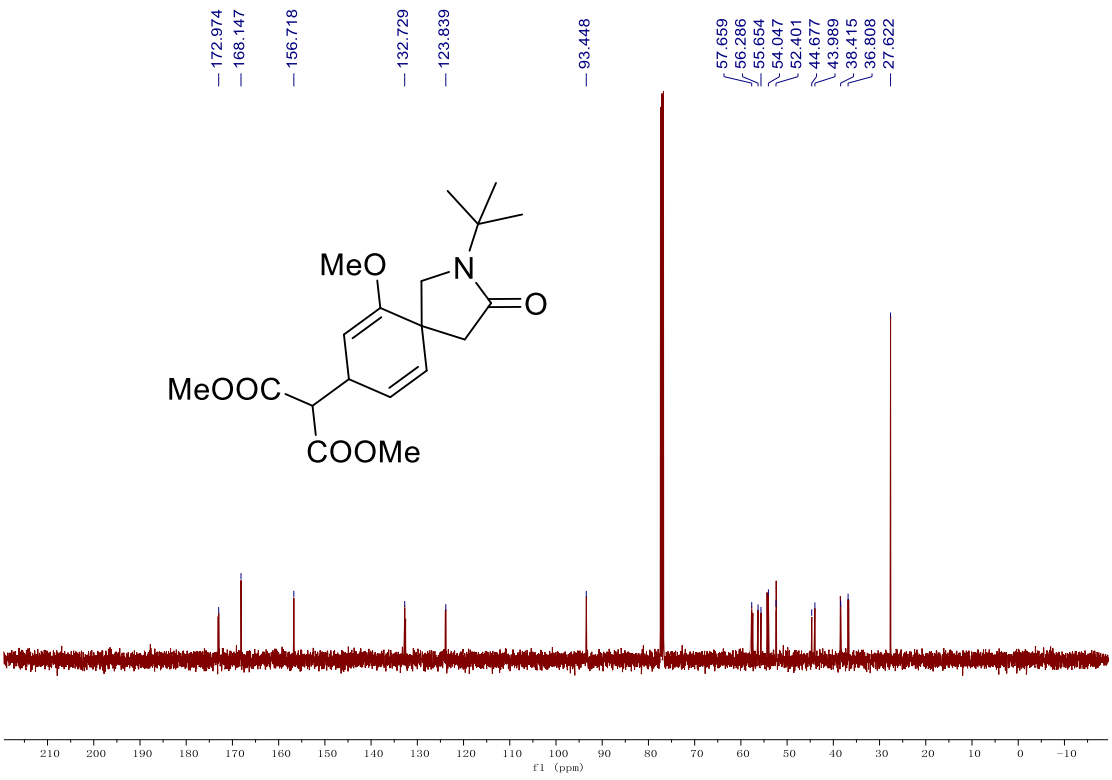
^{1}H NMR spectrum of **2n** ($CDCl_3$, 400MHz)



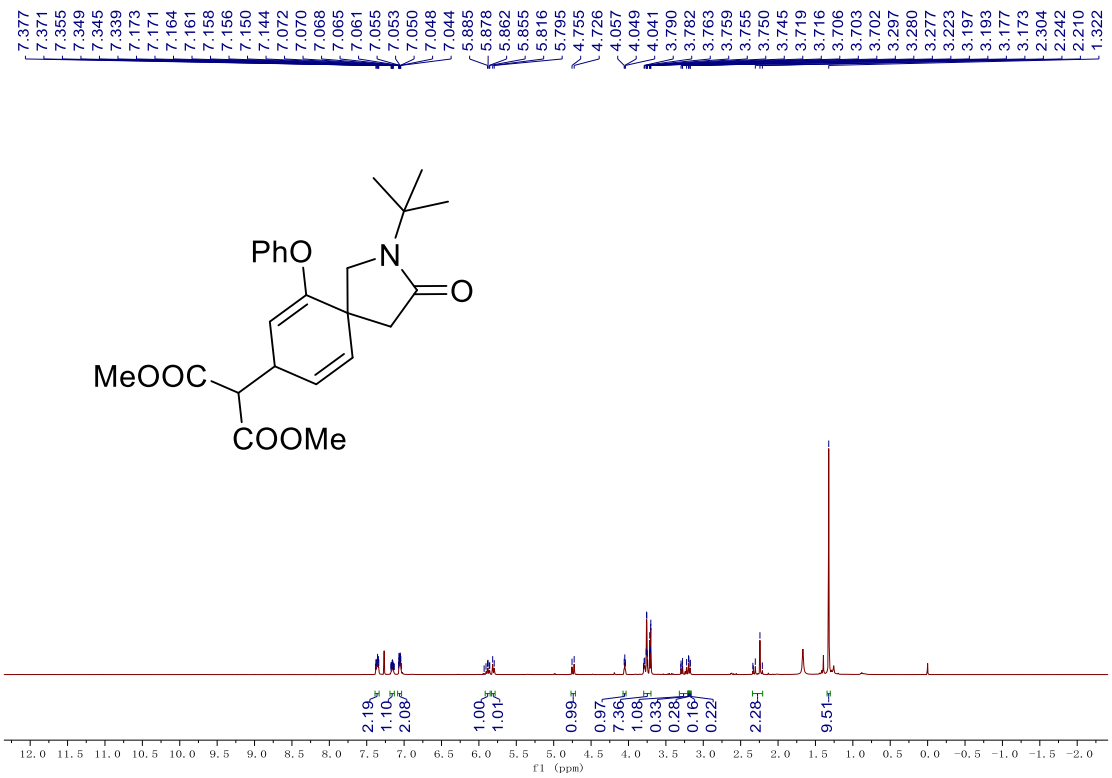
^{13}C NMR spectrum of **2n** ($CDCl_3$, 101MHz)



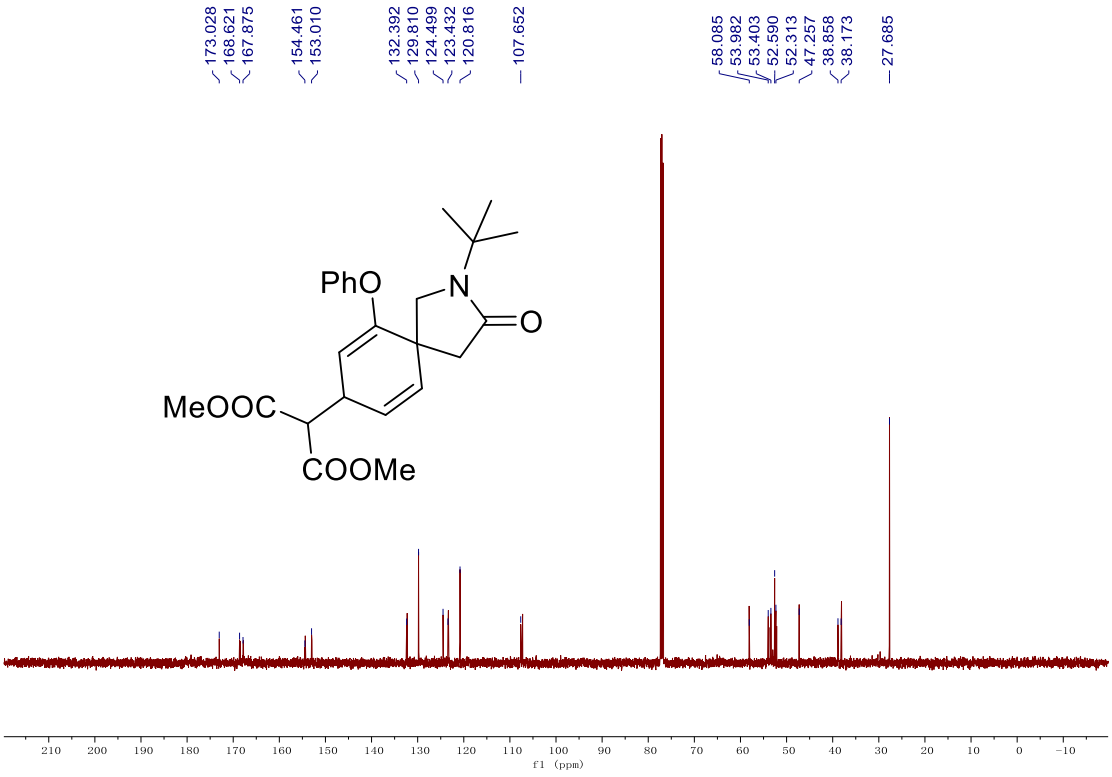
^{1}H NMR spectrum of **2o** ($CDCl_3$, 400MHz)



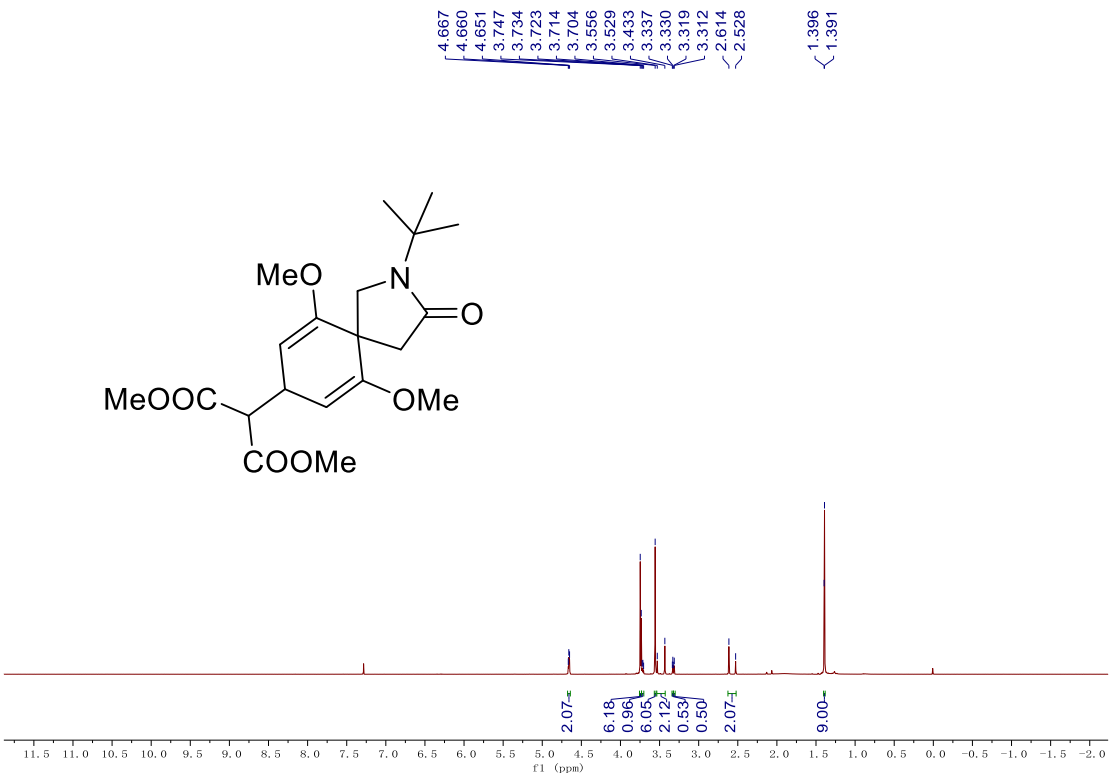
^{13}C NMR spectrum of **2o** ($CDCl_3$, 101MHz)



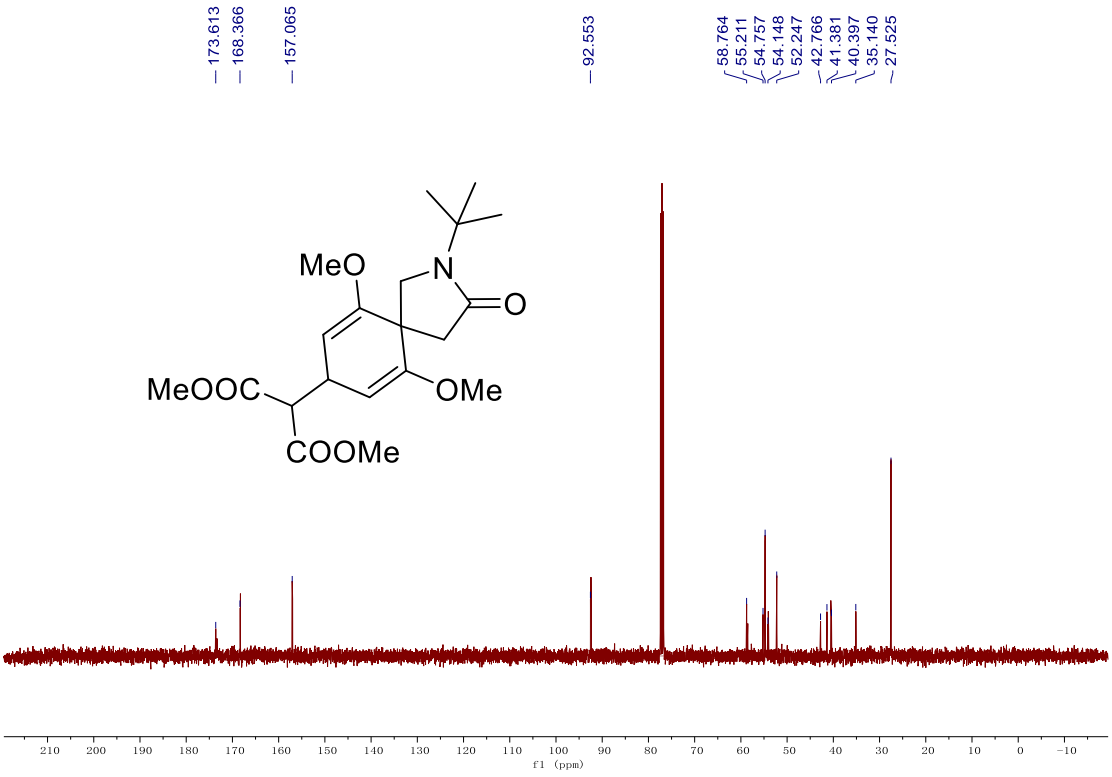
^{1}H NMR spectrum of **2p** ($CDCl_3$, 500MHz)



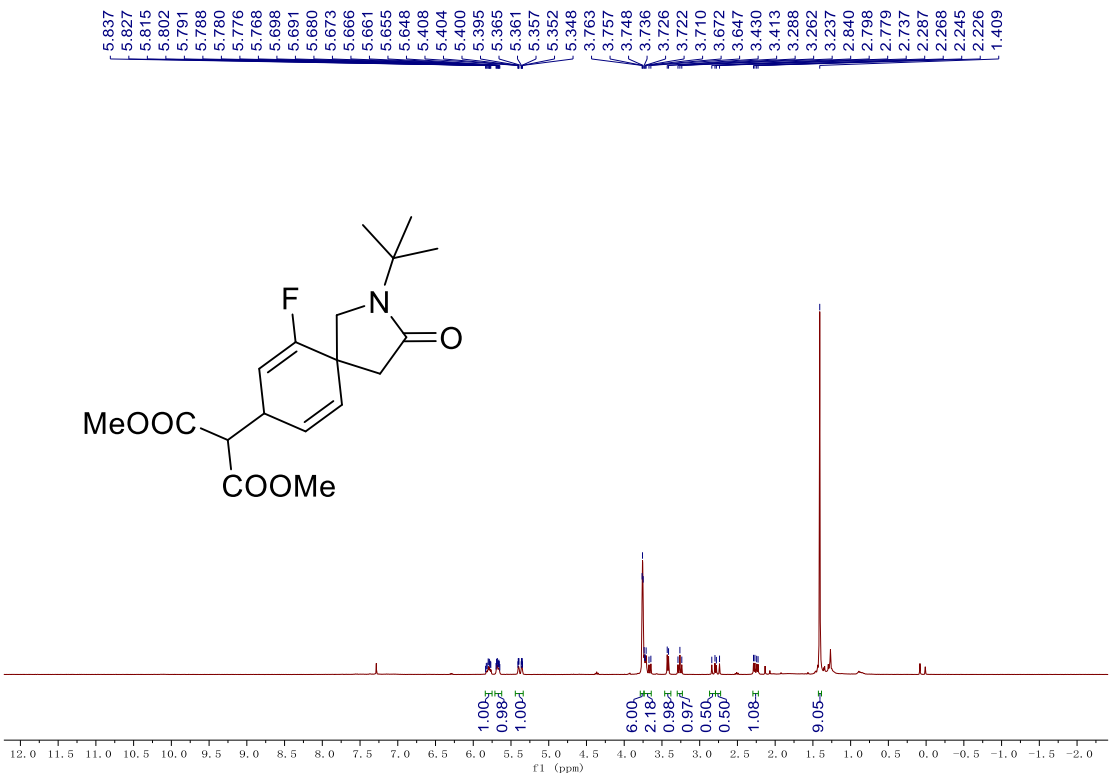
^{13}C NMR spectrum of **2p** ($CDCl_3$, 126MHz)



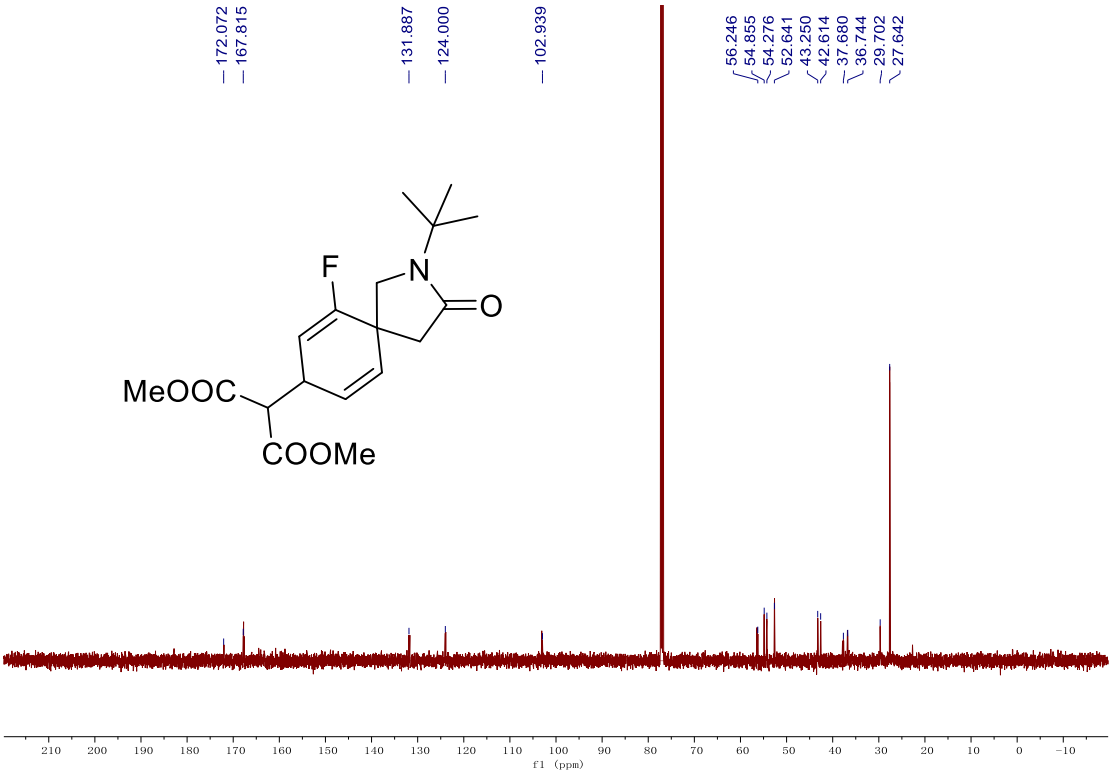
^{1}H NMR spectrum of **2q** ($CDCl_3$, 400MHz)



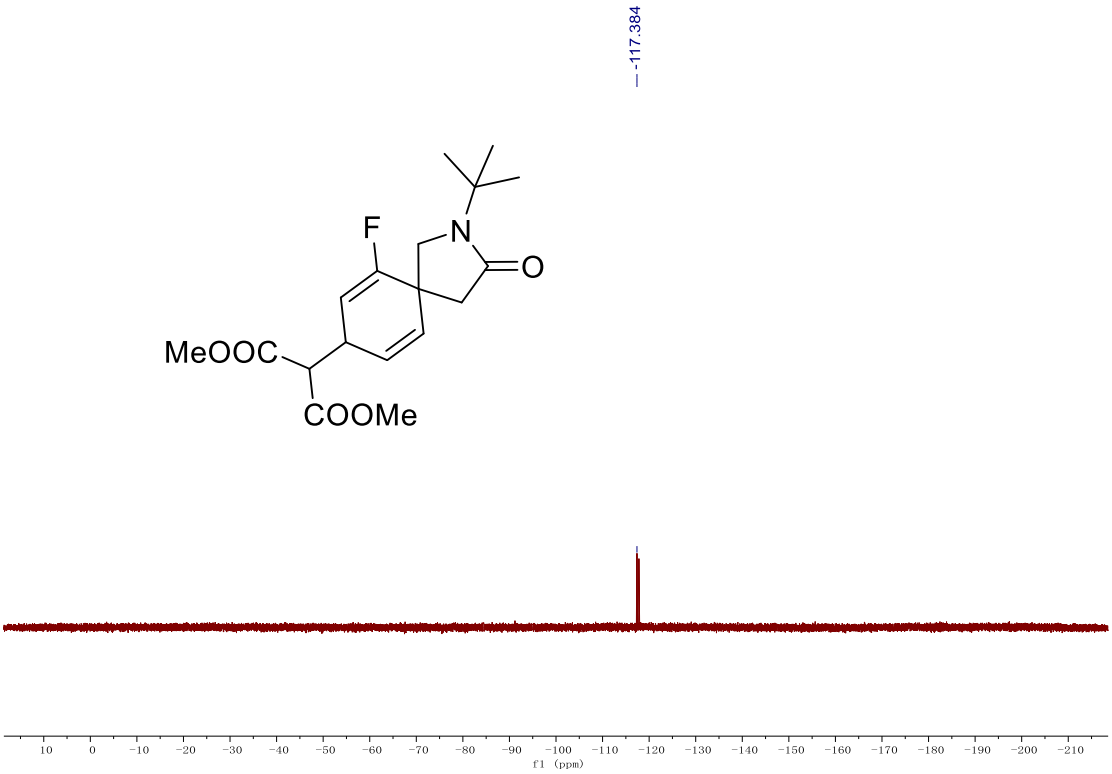
^{13}C NMR spectrum of **2q** ($CDCl_3$, 101MHz)



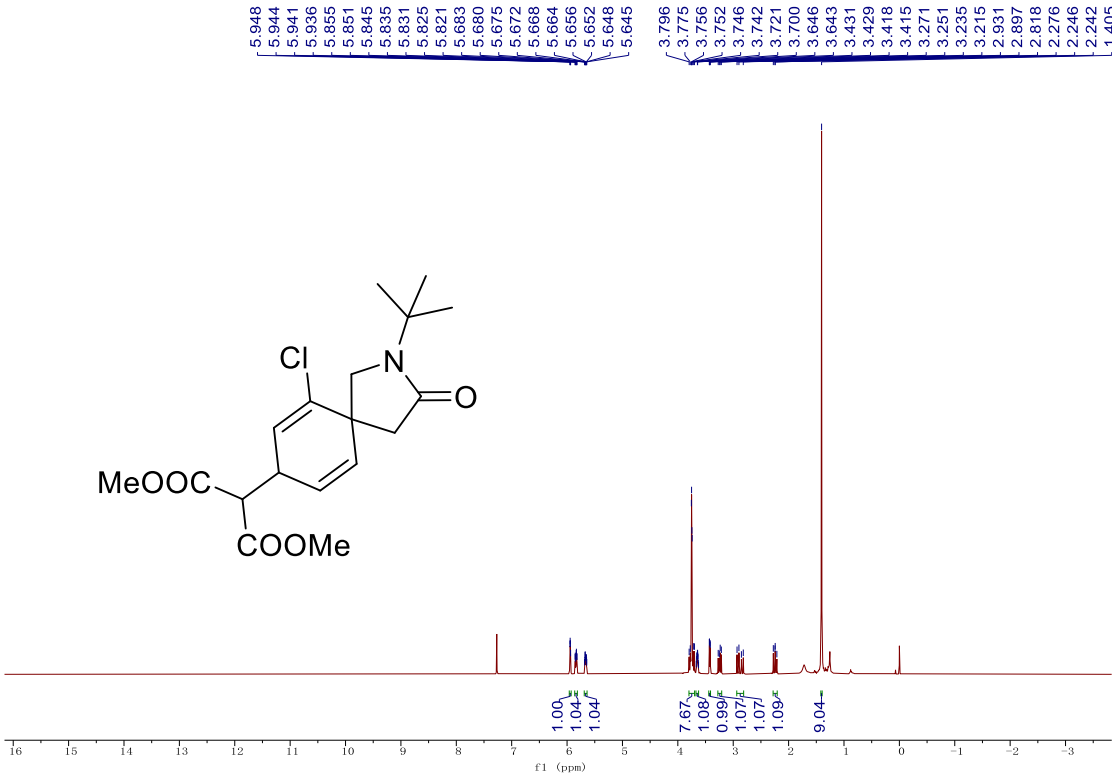
^{1}H NMR spectrum of **2r** ($CDCl_3$, 400MHz)



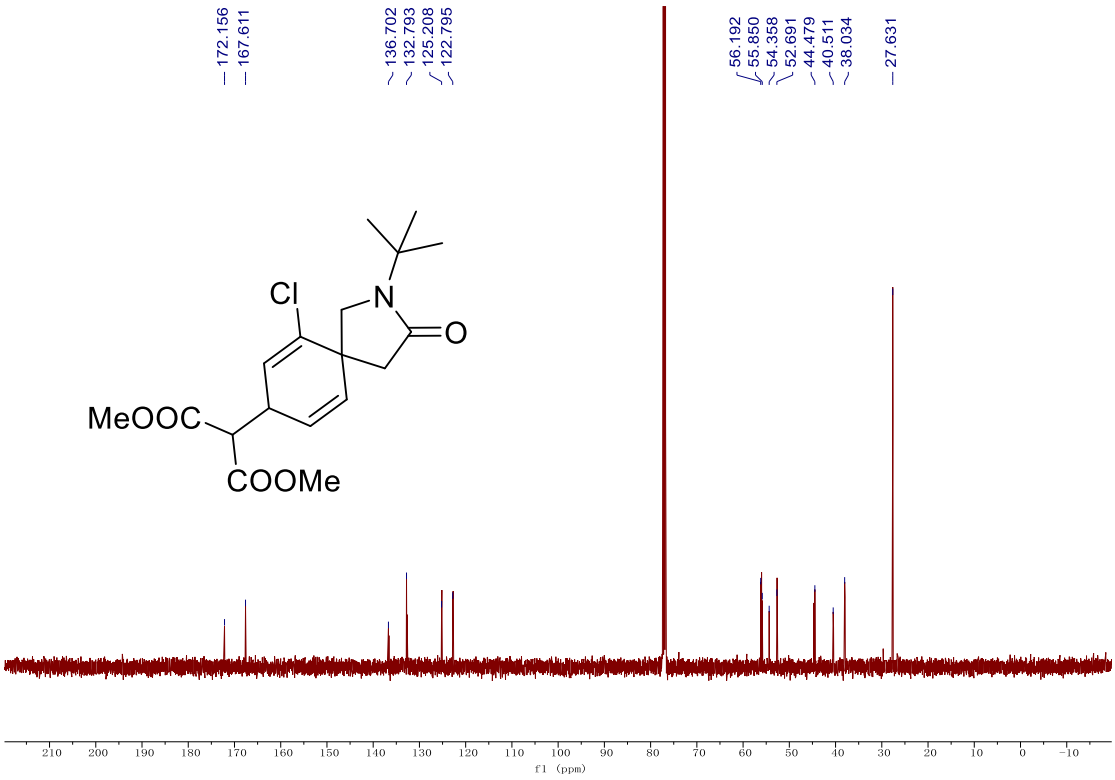
^{13}C NMR spectrum of **2r** ($CDCl_3$, 126MHz)



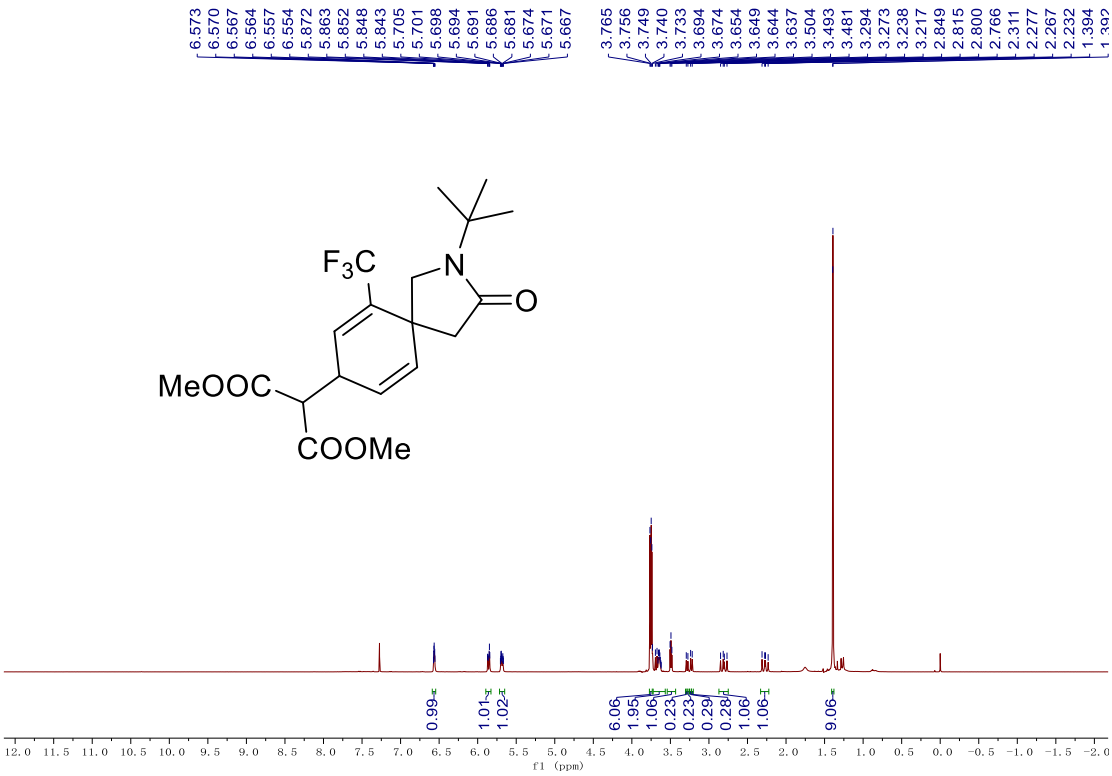
^{19}F NMR spectrum of **2r** ($CDCl_3$, 376MHz)



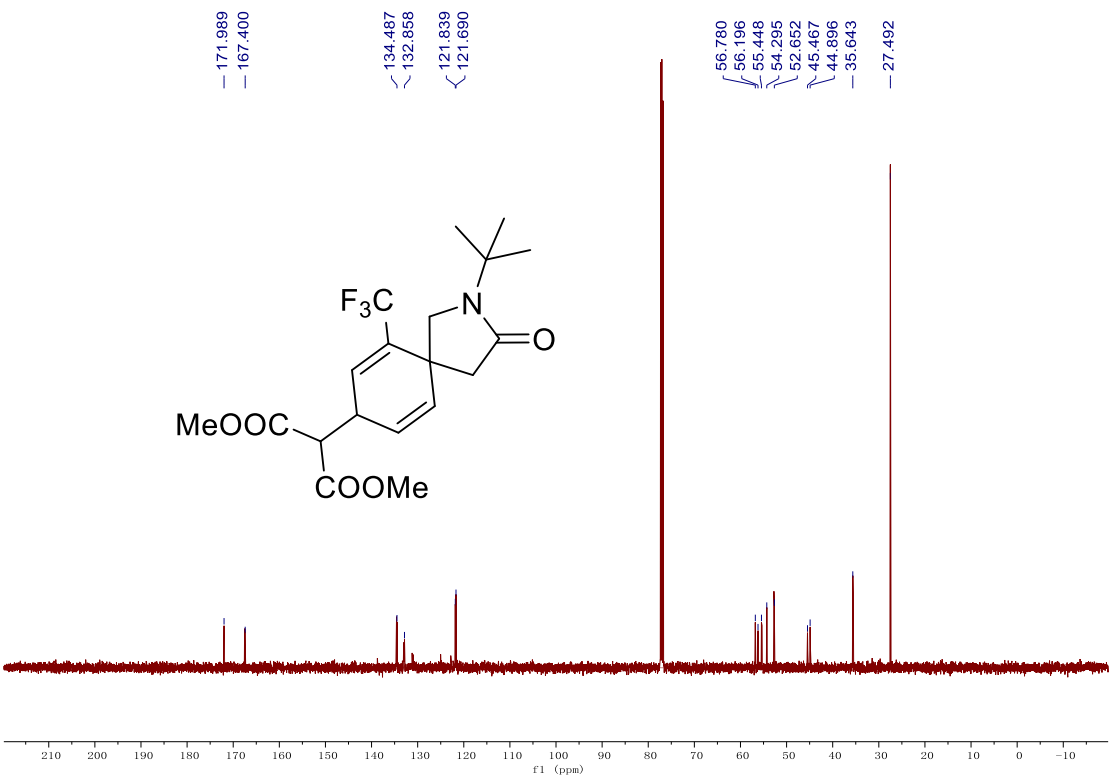
^{1}H NMR spectrum of **2s** ($CDCl_3$, 500MHz)



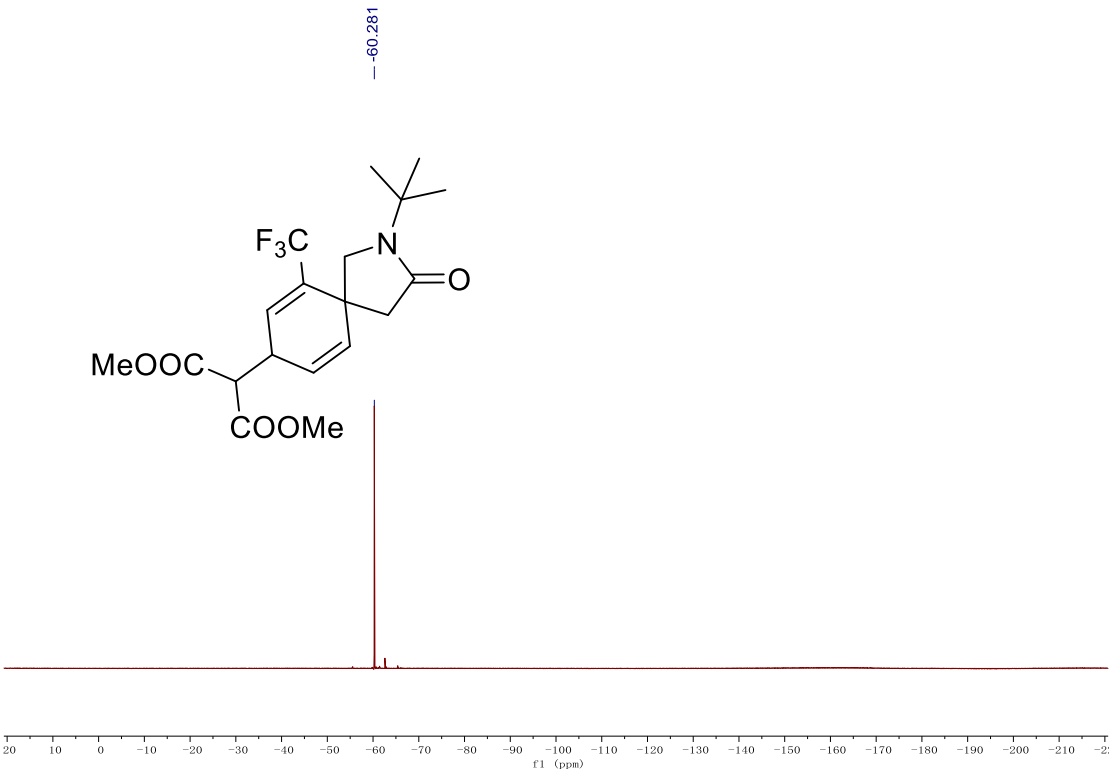
^{13}C NMR spectrum of **2s** ($CDCl_3$, 126MHz)



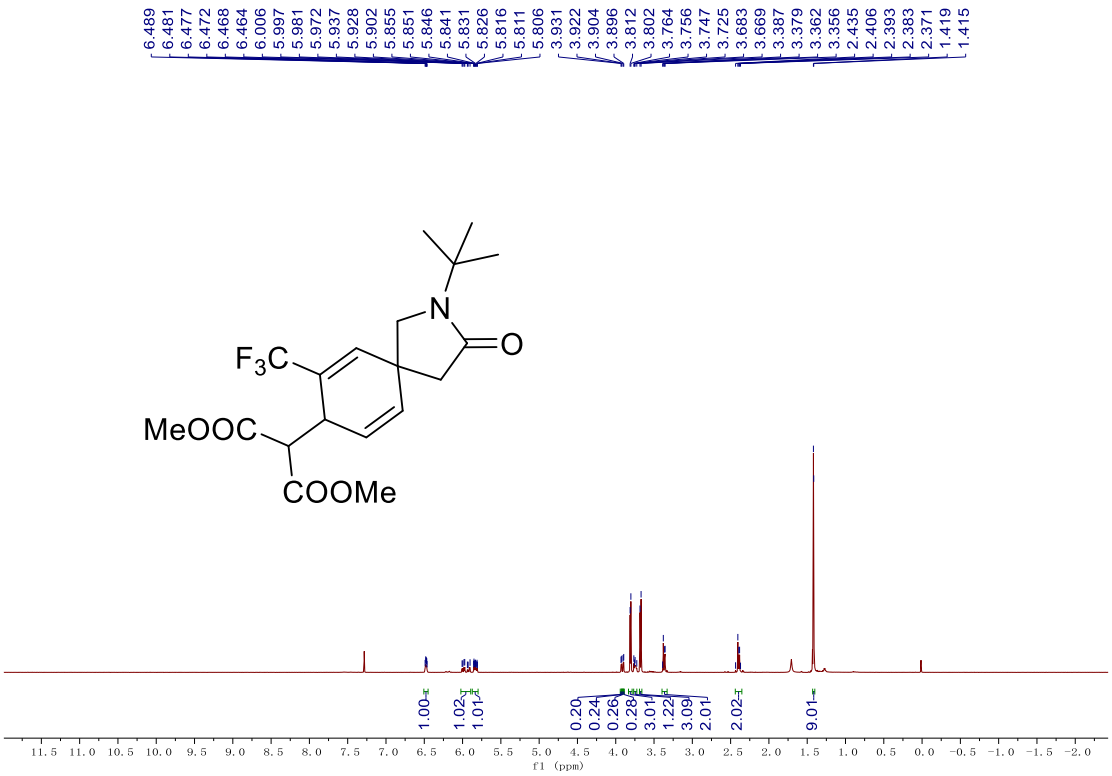
^{1}H NMR spectrum of **2t** ($CDCl_3$, 500MHz)



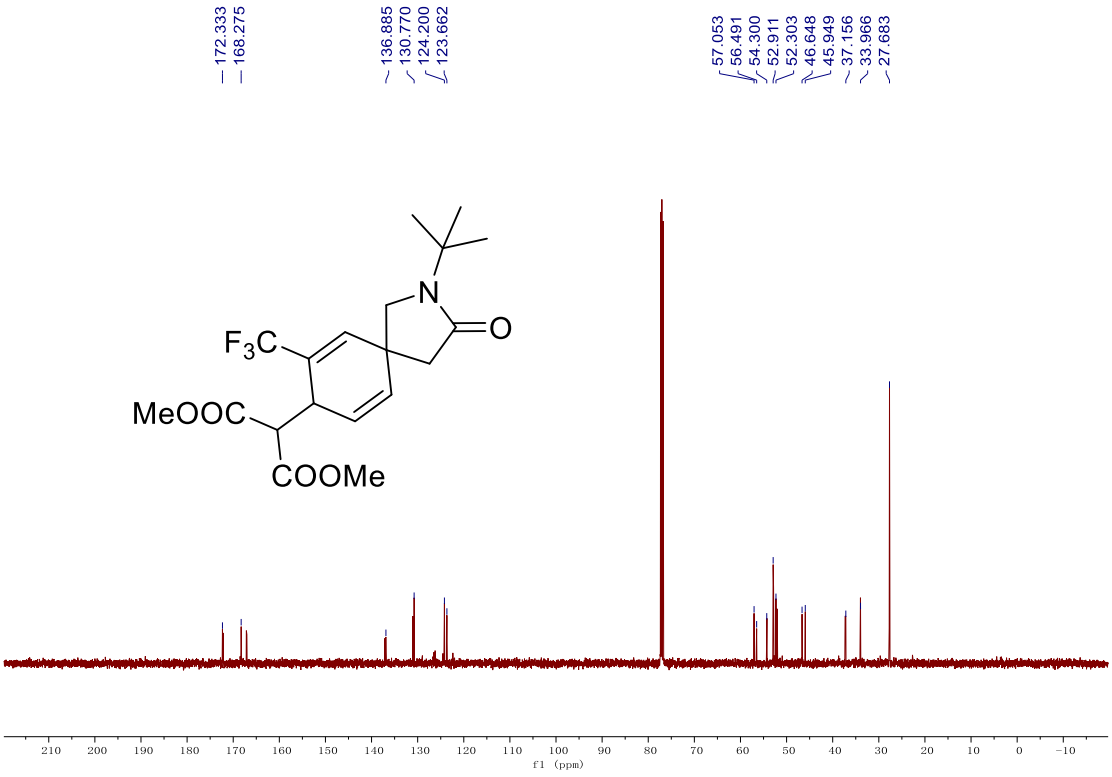
^{13}C NMR spectrum of **2t** ($CDCl_3$, 126MHz)



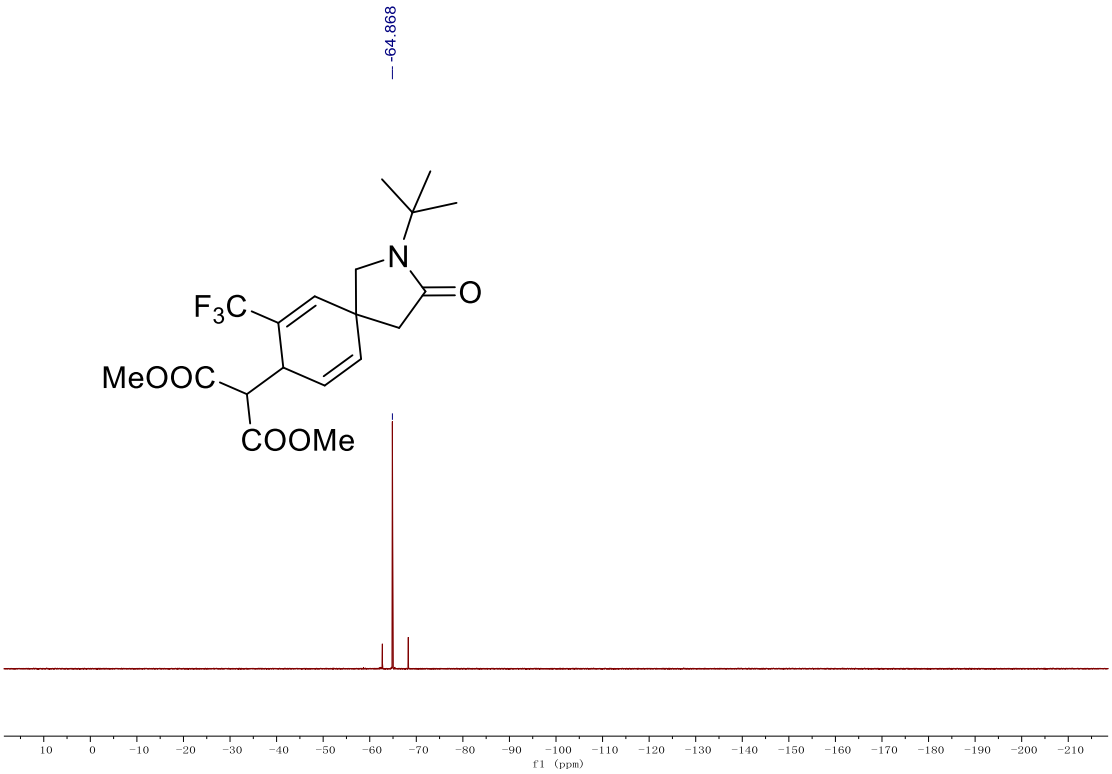
^{19}F NMR spectrum of **2t** ($CDCl_3$, 471MHz)



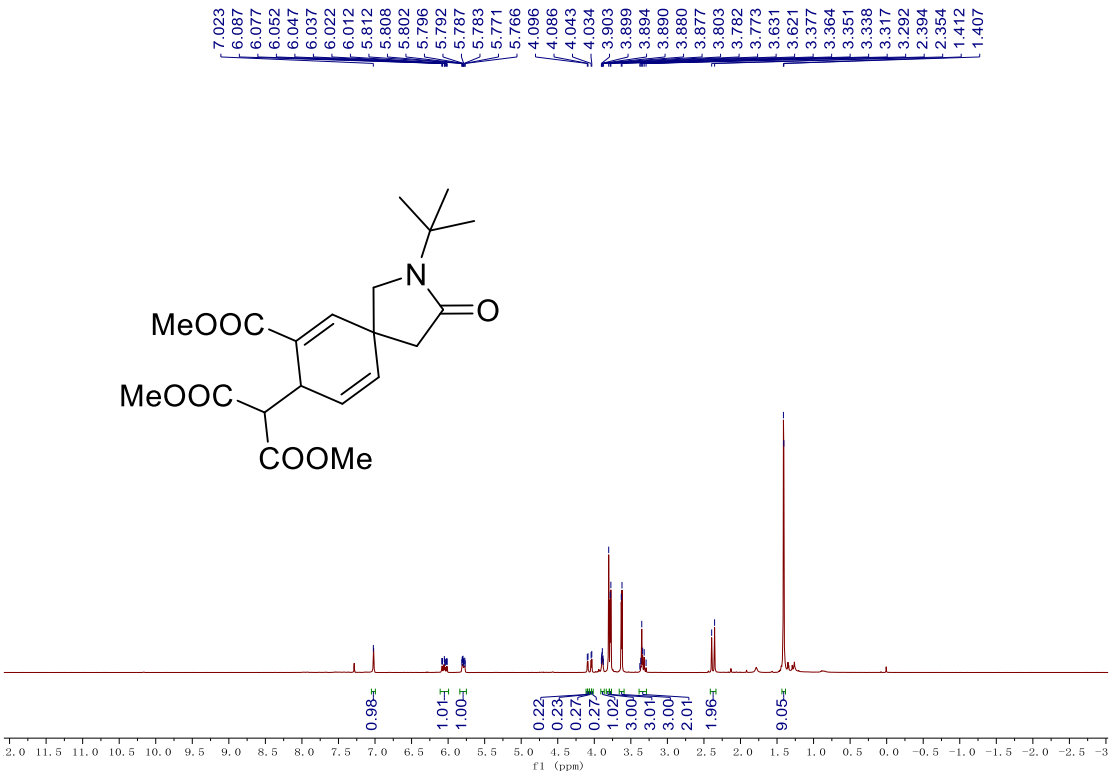
^{1}H NMR spectrum of **2u** ($CDCl_3$, 400MHz)



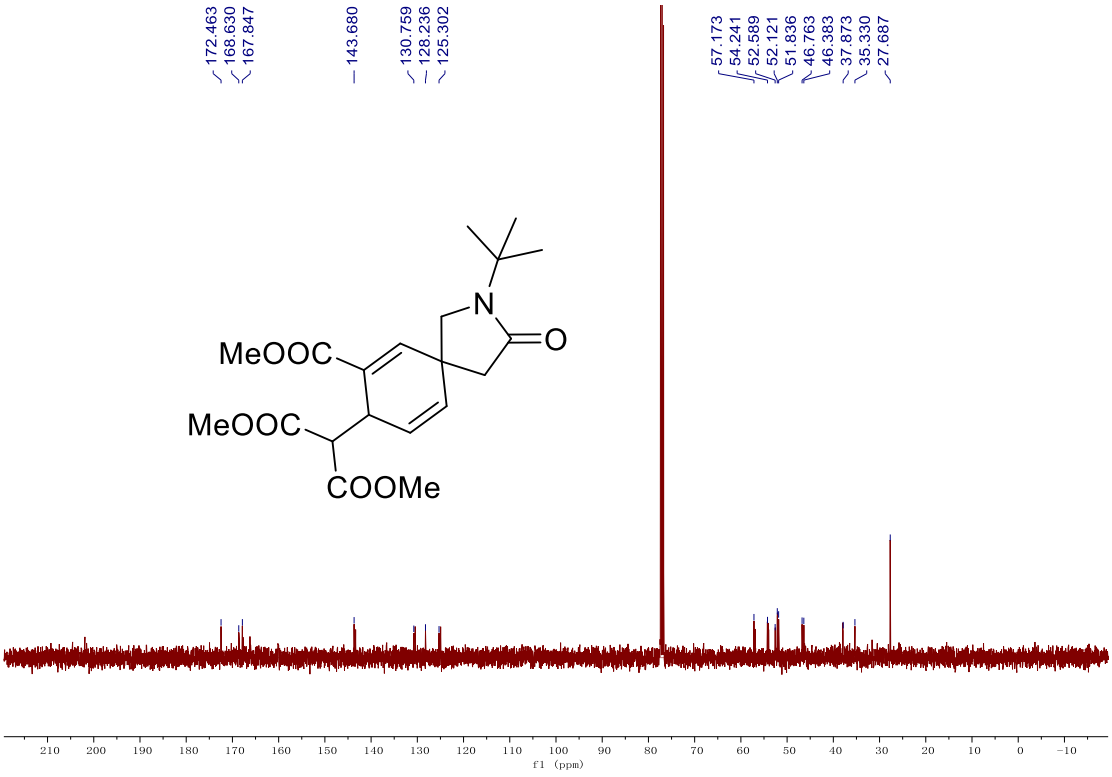
^{13}C NMR spectrum of **2u** ($CDCl_3$, 126MHz)



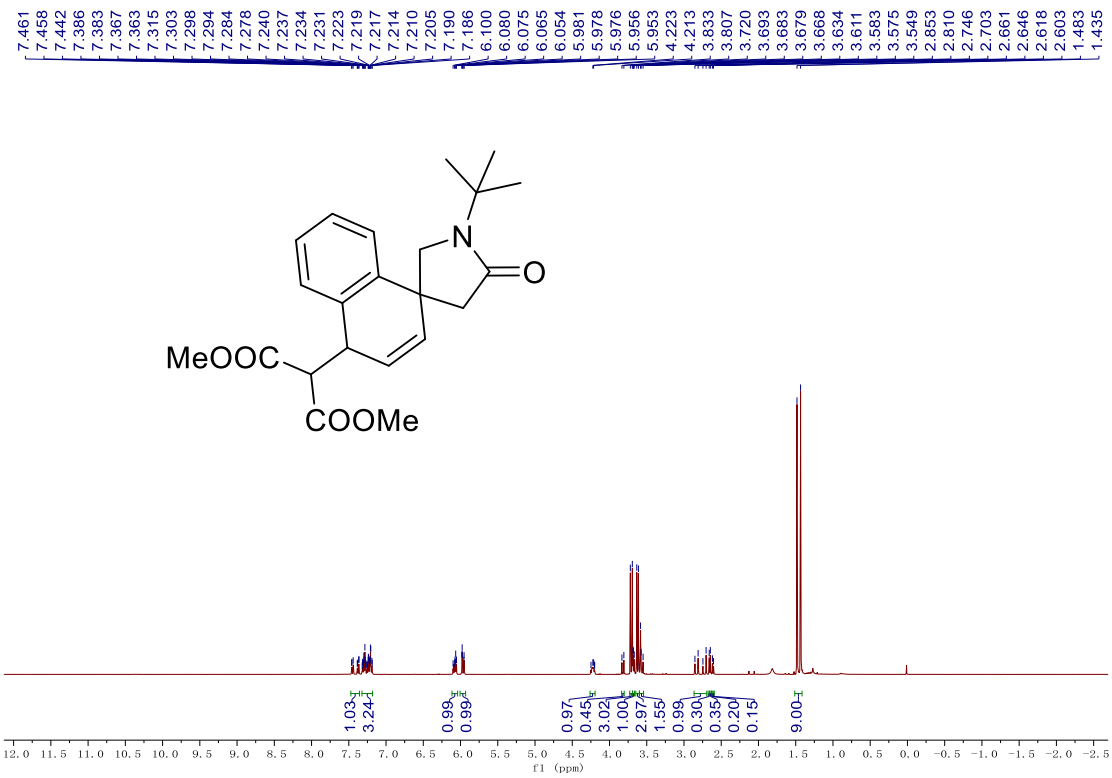
^{19}F NMR spectrum of **2u** ($CDCl_3$, 376MHz)



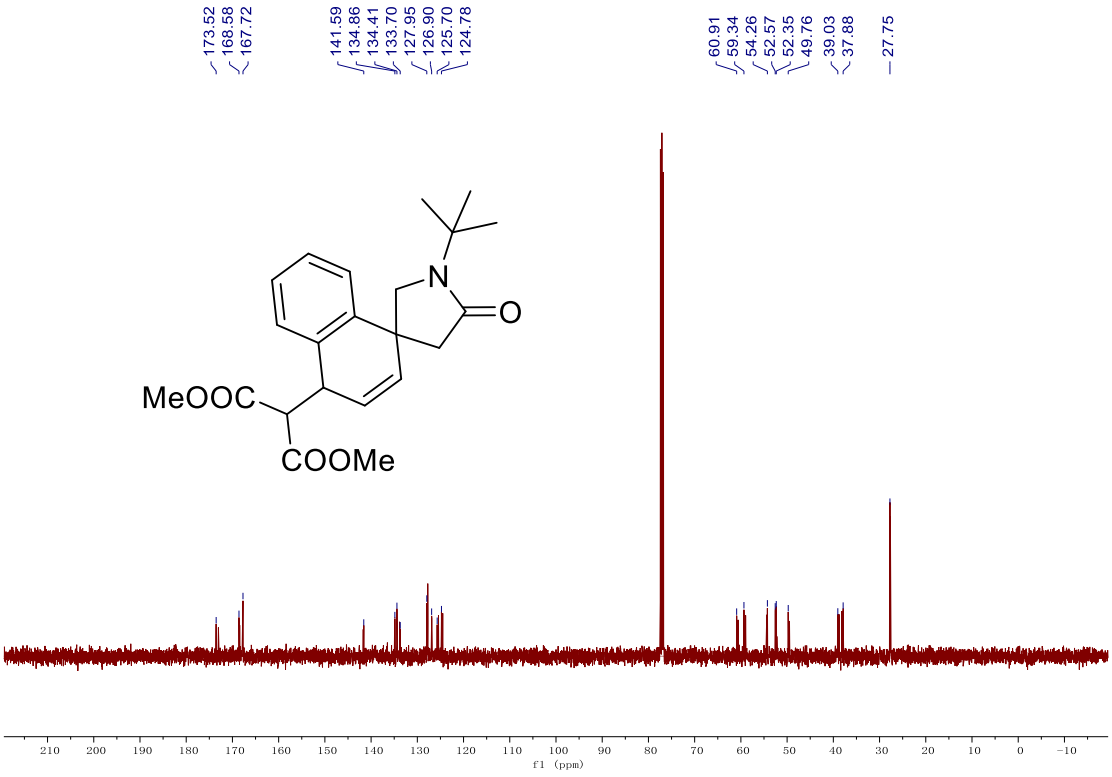
^{1}H NMR spectrum of **2v** ($CDCl_3$, 400MHz)



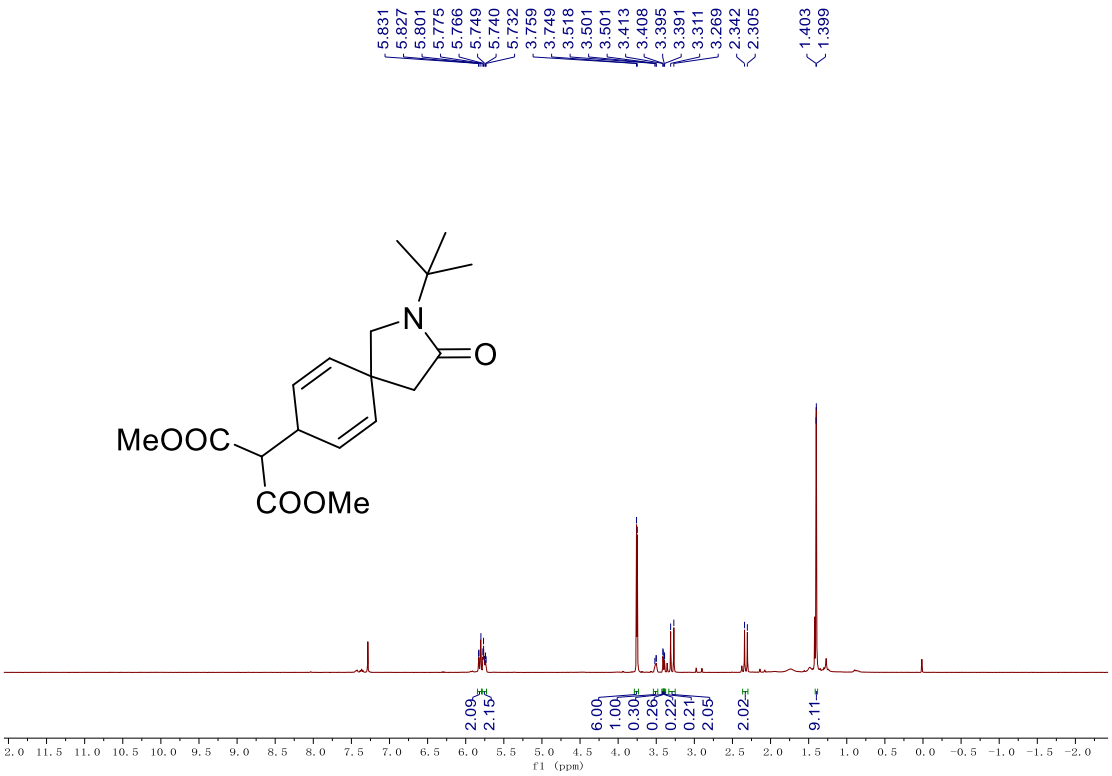
^{13}C NMR spectrum of **2v** ($CDCl_3$, 101MHz)



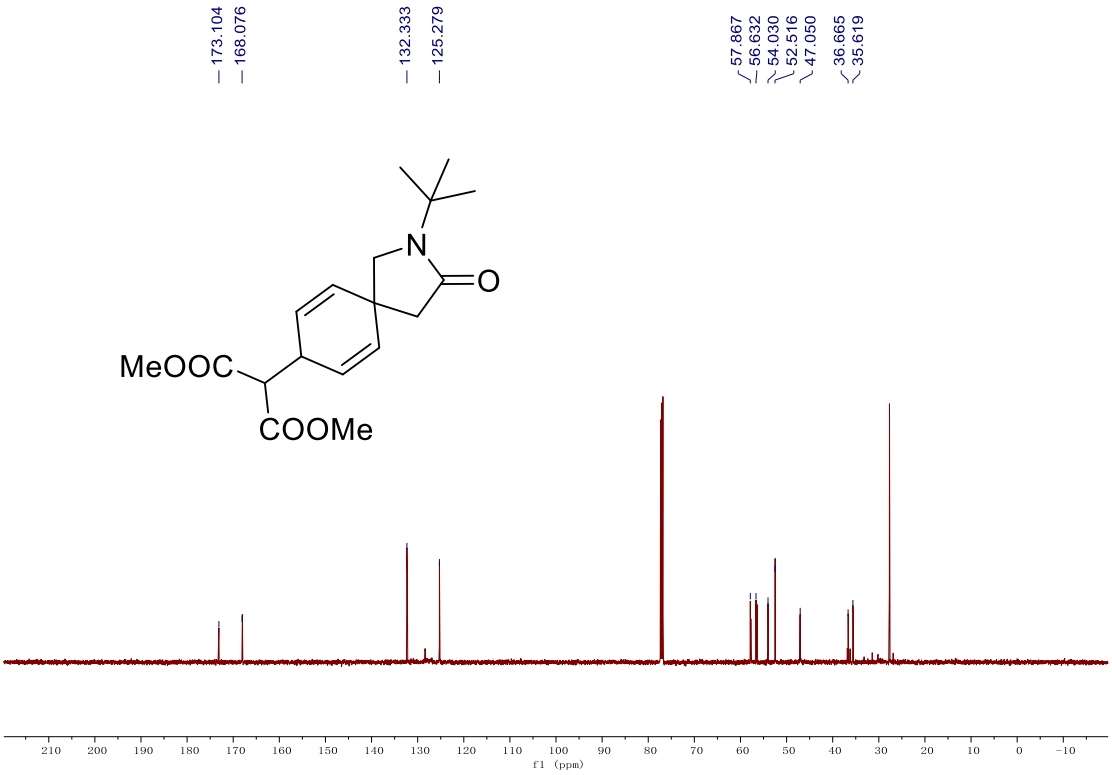
^{1}H NMR spectrum of **2w** ($CDCl_3$, 400MHz)



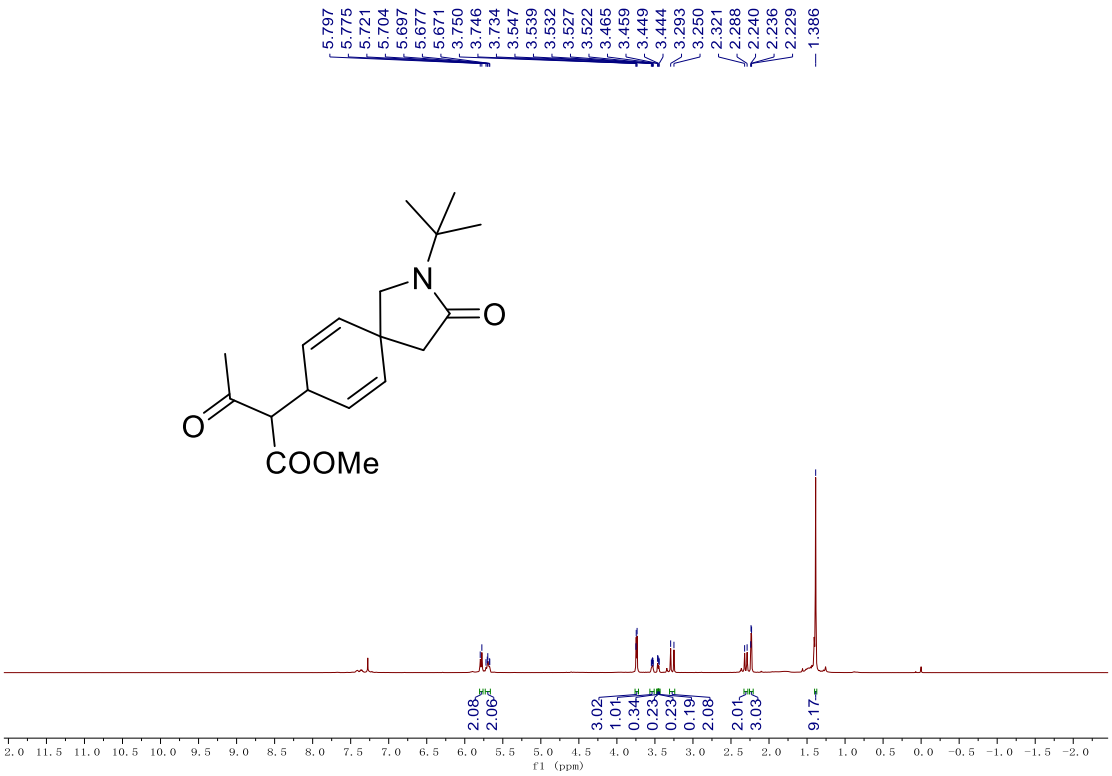
^{13}C NMR spectrum of **2w** ($CDCl_3$, 101MHz)



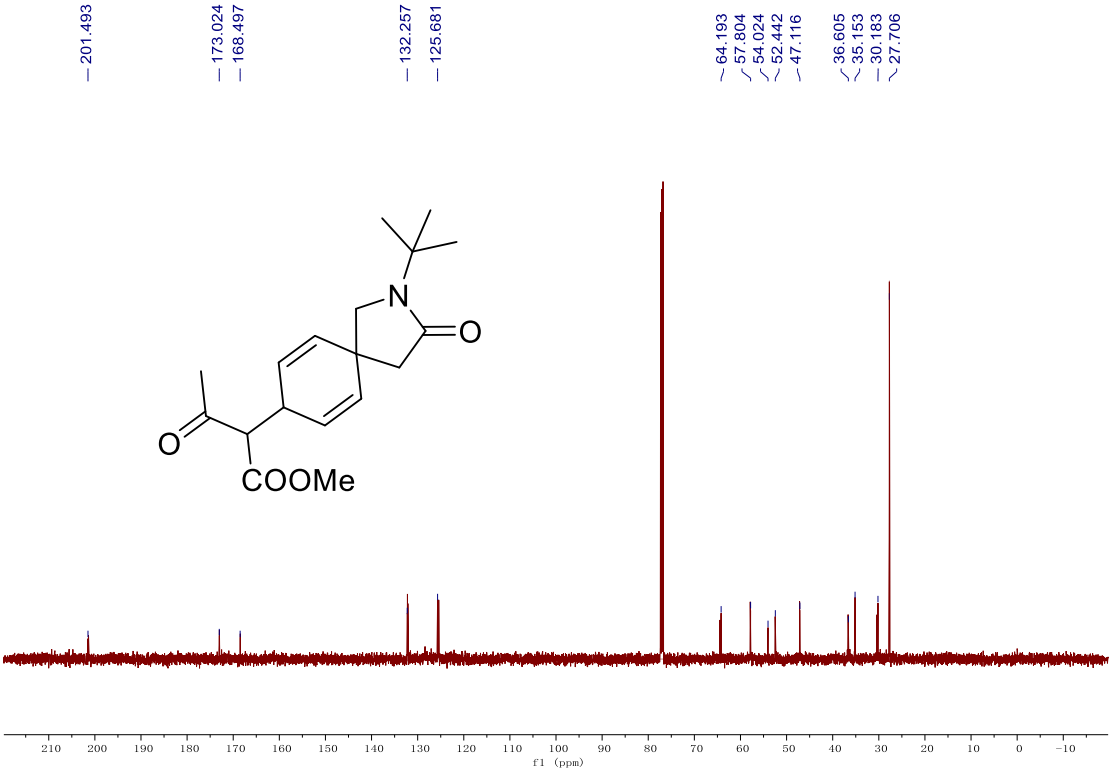
^{1}H NMR spectrum of **2x** ($CDCl_3$, 400MHz)



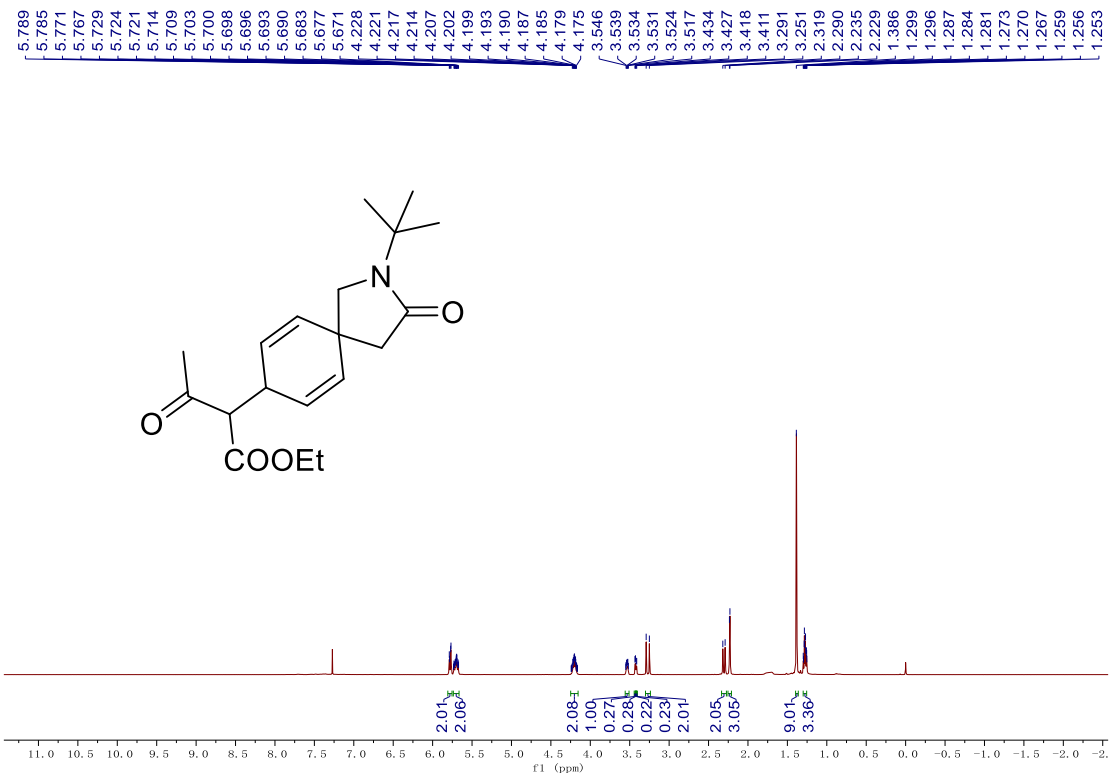
^{13}C NMR spectrum of **2x** ($CDCl_3$, 126MHz)



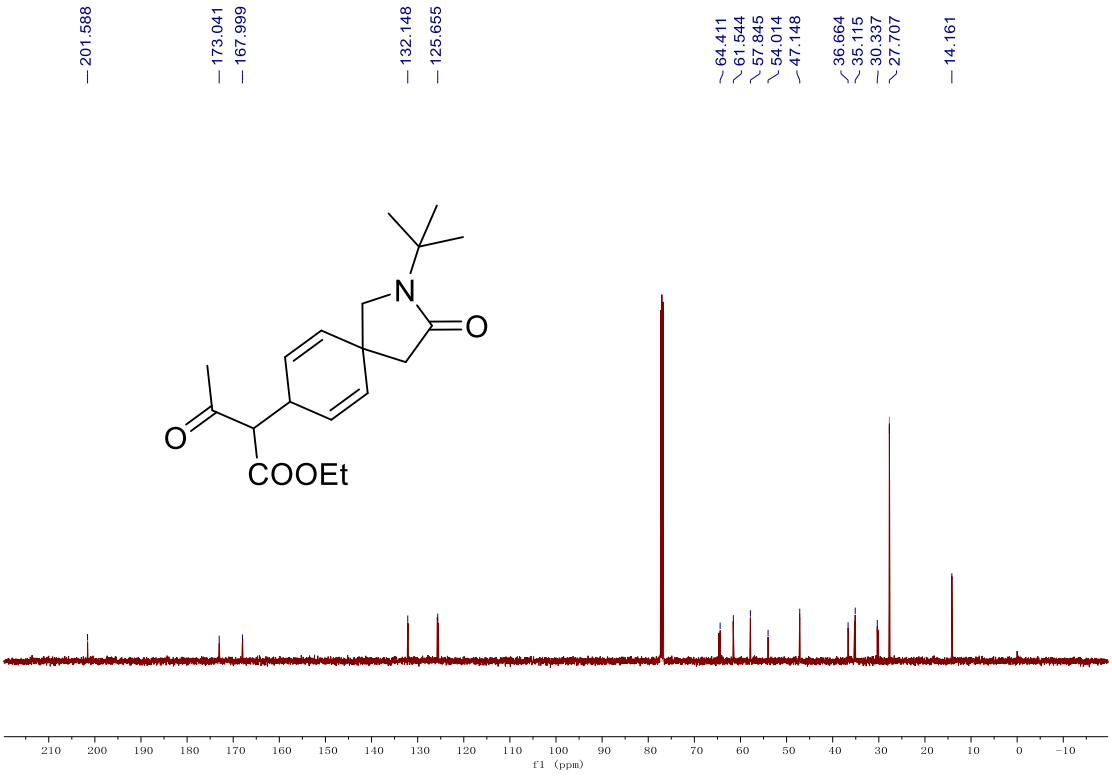
^{1}H NMR spectrum of **2y** ($CDCl_3$, 500MHz)



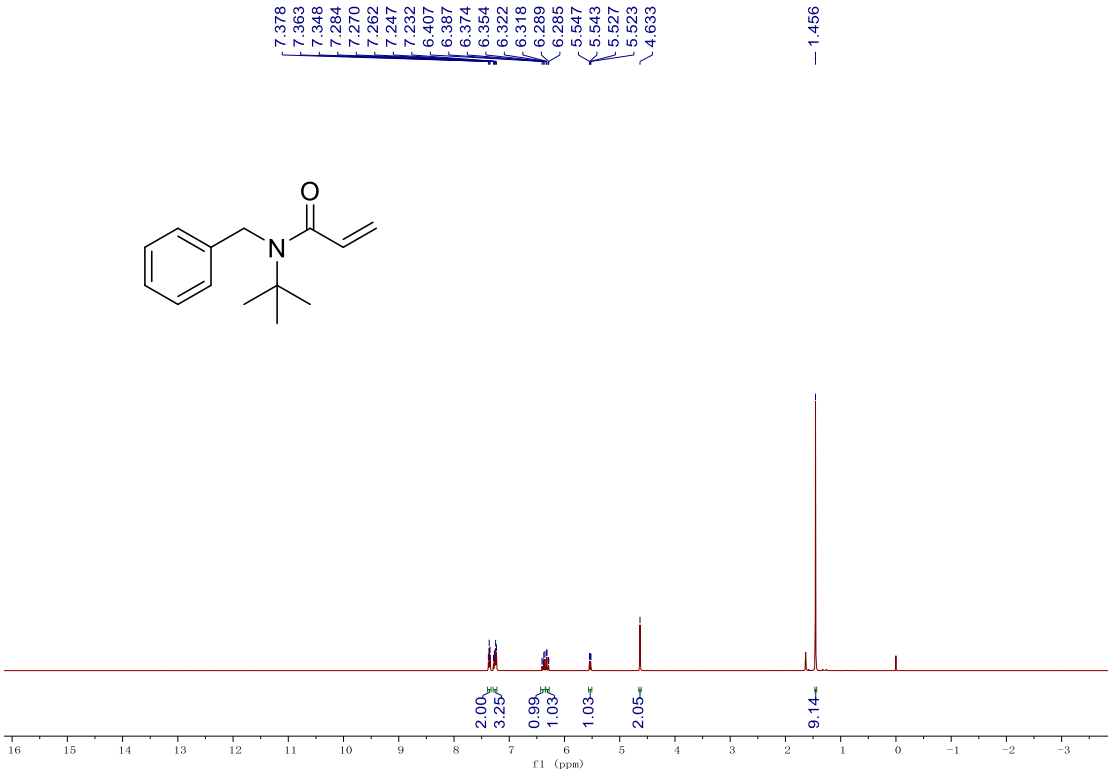
^{13}C NMR spectrum of **2y** ($CDCl_3$, 126MHz)



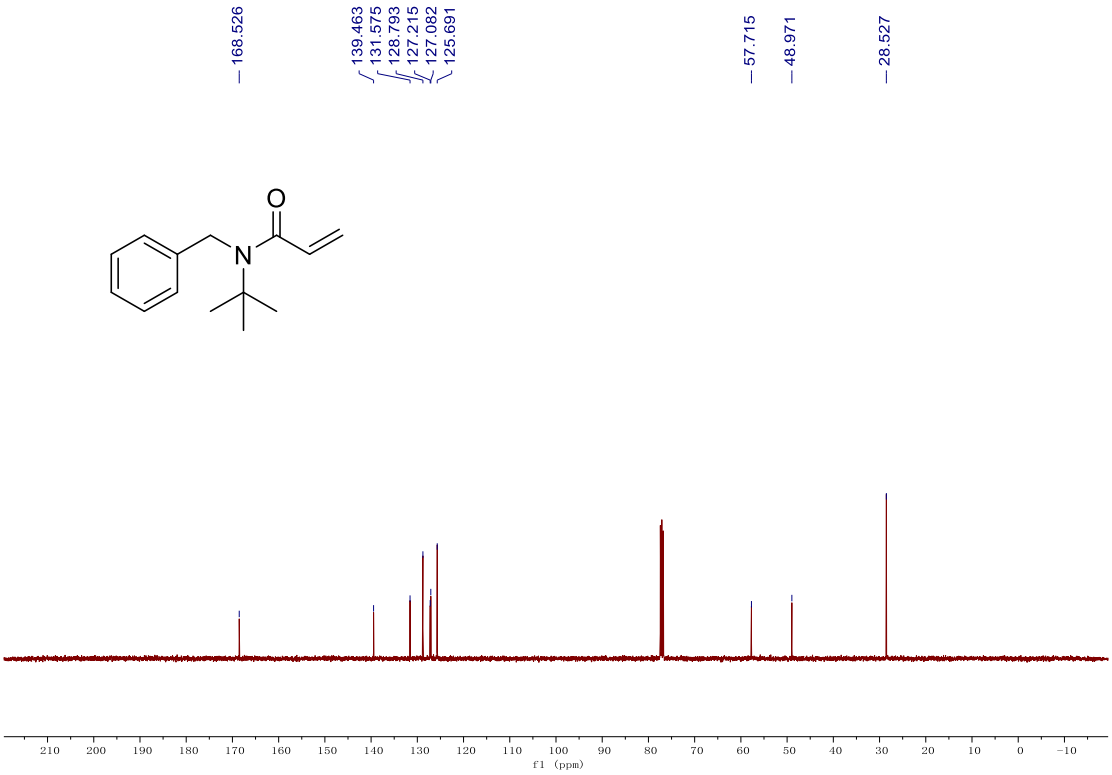
^{1}H NMR spectrum of **2z** ($CDCl_3$, 500MHz)



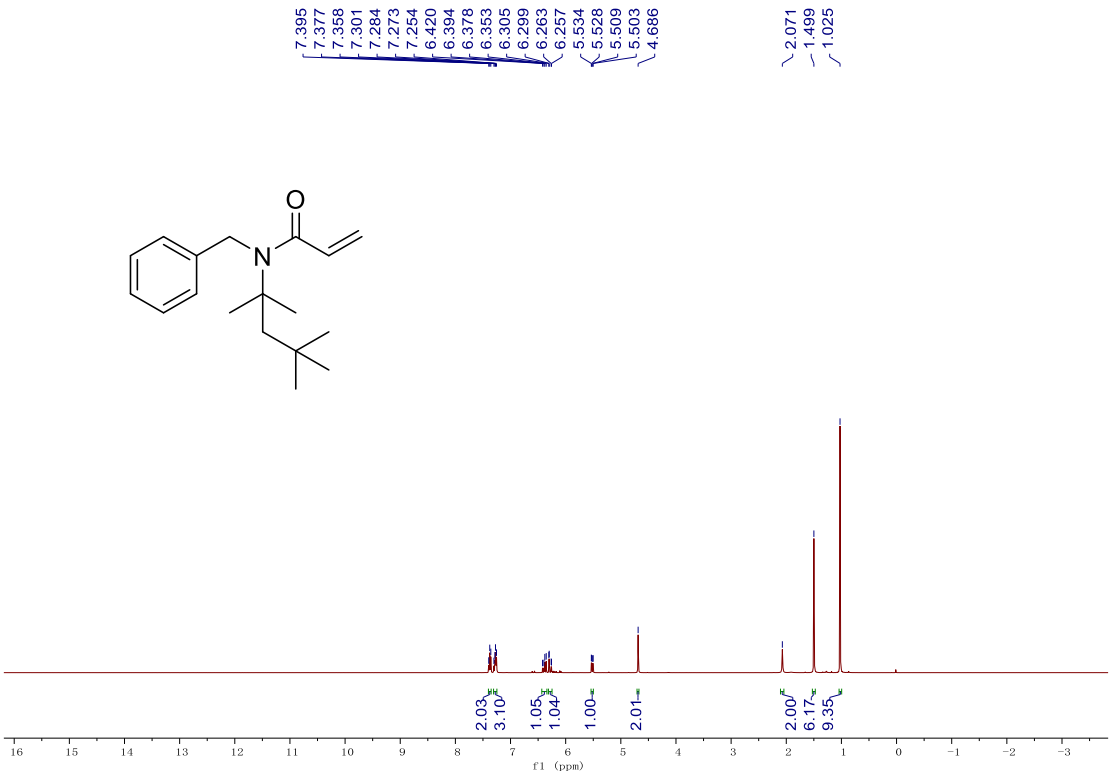
^{13}C NMR spectrum of **2z** ($CDCl_3$, 126MHz)



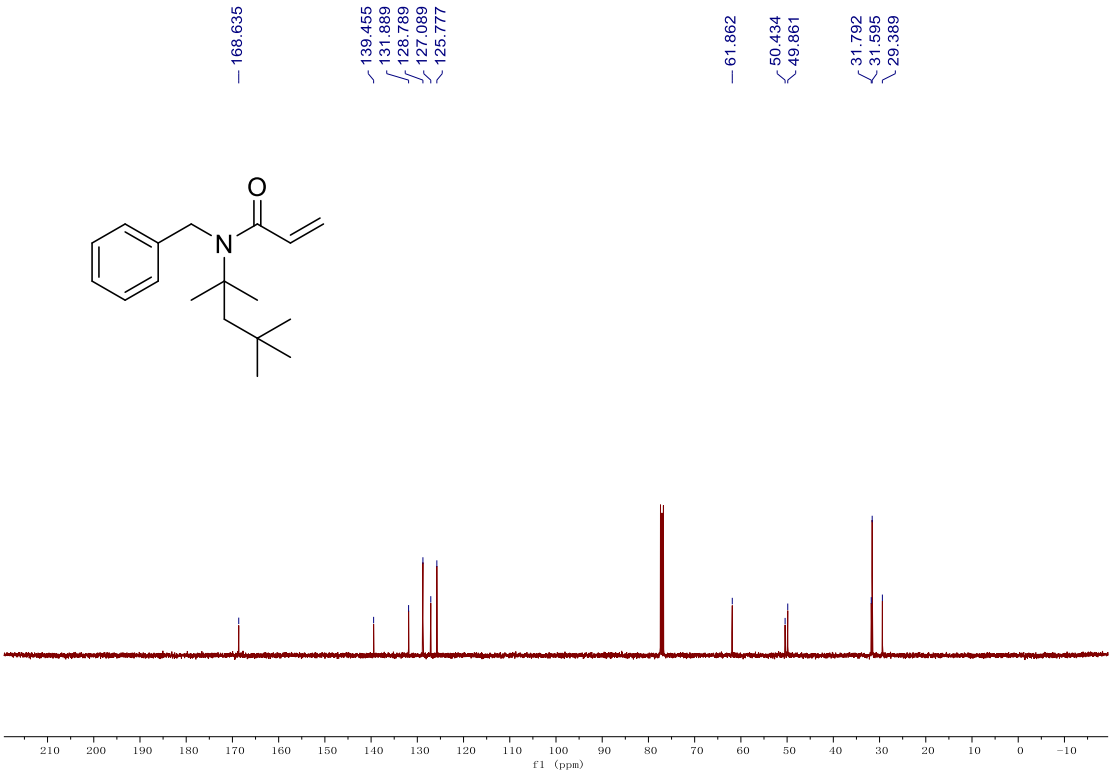
^{1}H NMR spectrum of **3a** ($CDCl_3$, 500MHz)



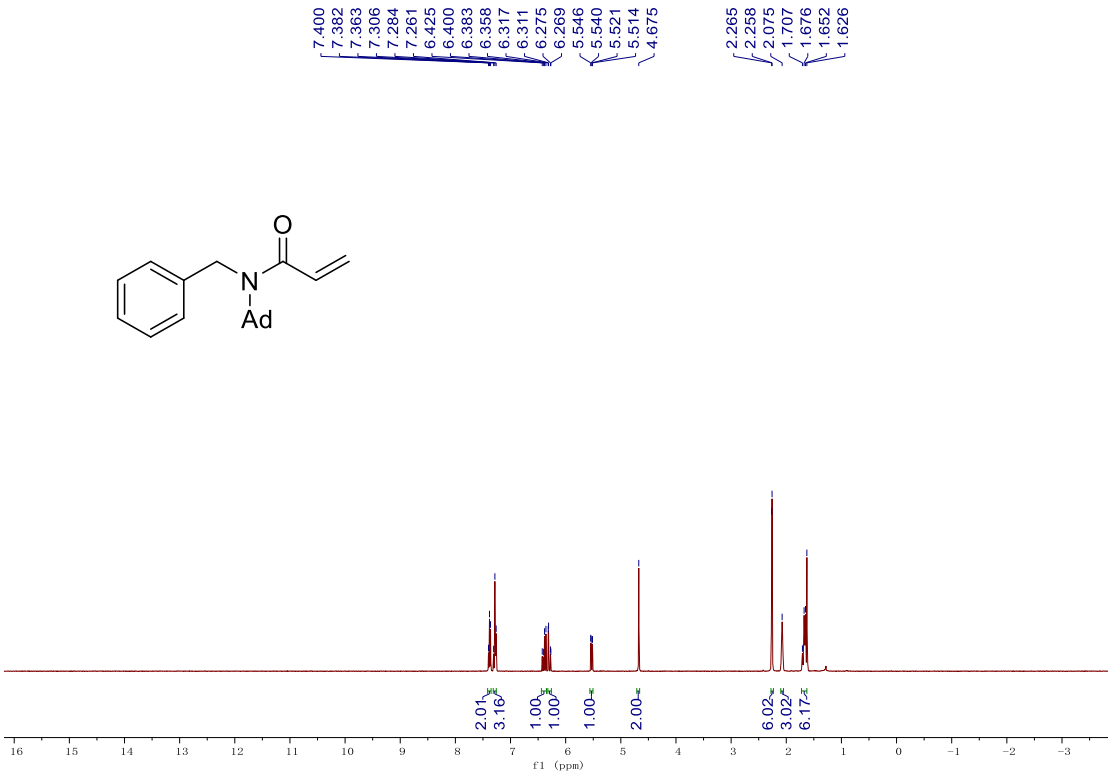
^{13}C NMR spectrum of **3a** ($CDCl_3$, 101MHz)



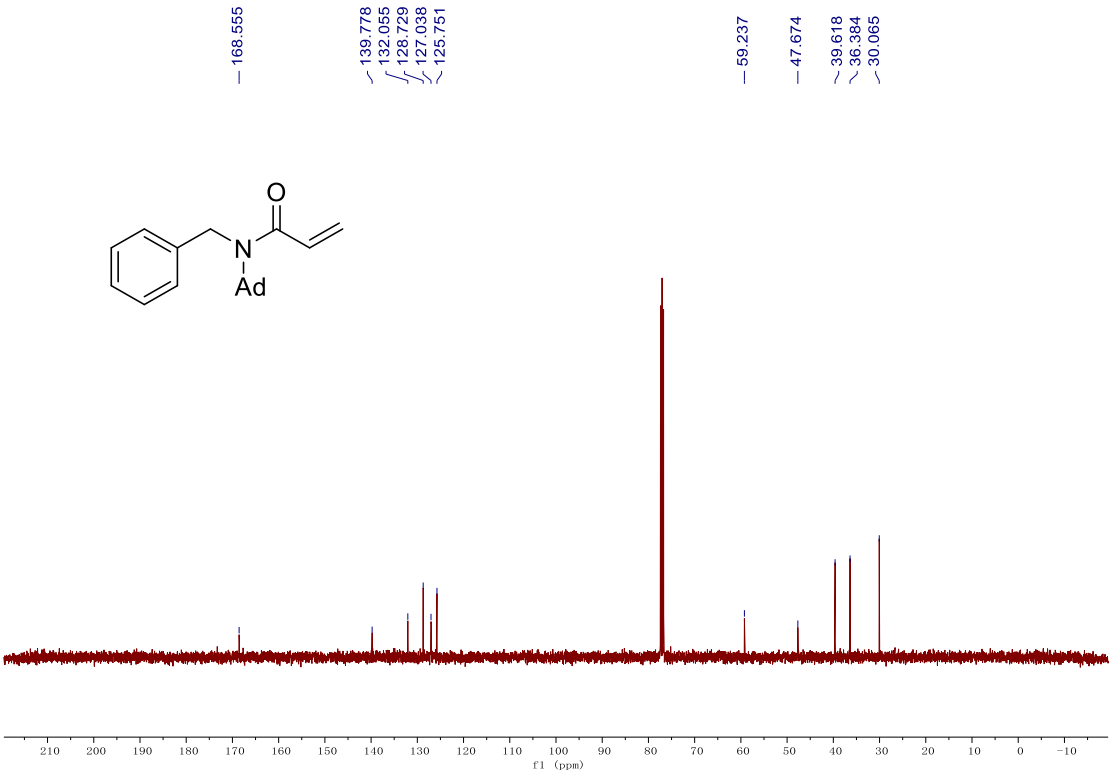
^{1}H NMR spectrum of **3ab** ($CDCl_3$, 400MHz)



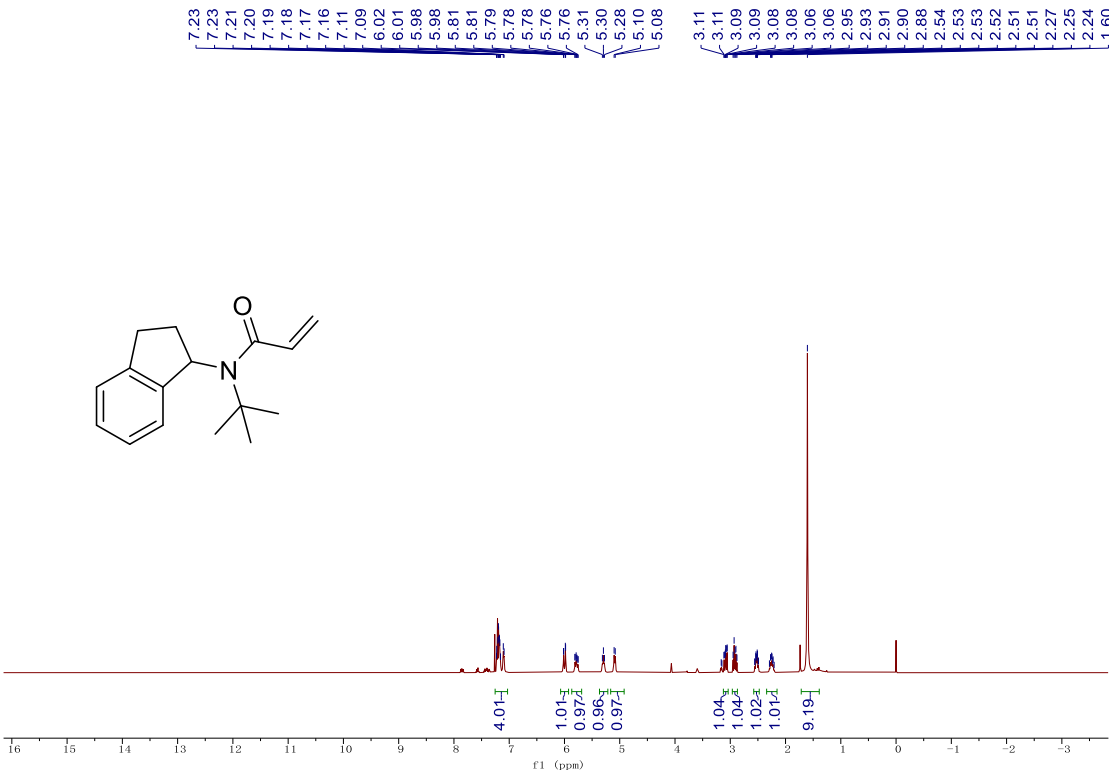
^{13}C NMR spectrum of **3ab** ($CDCl_3$, 101MHz)



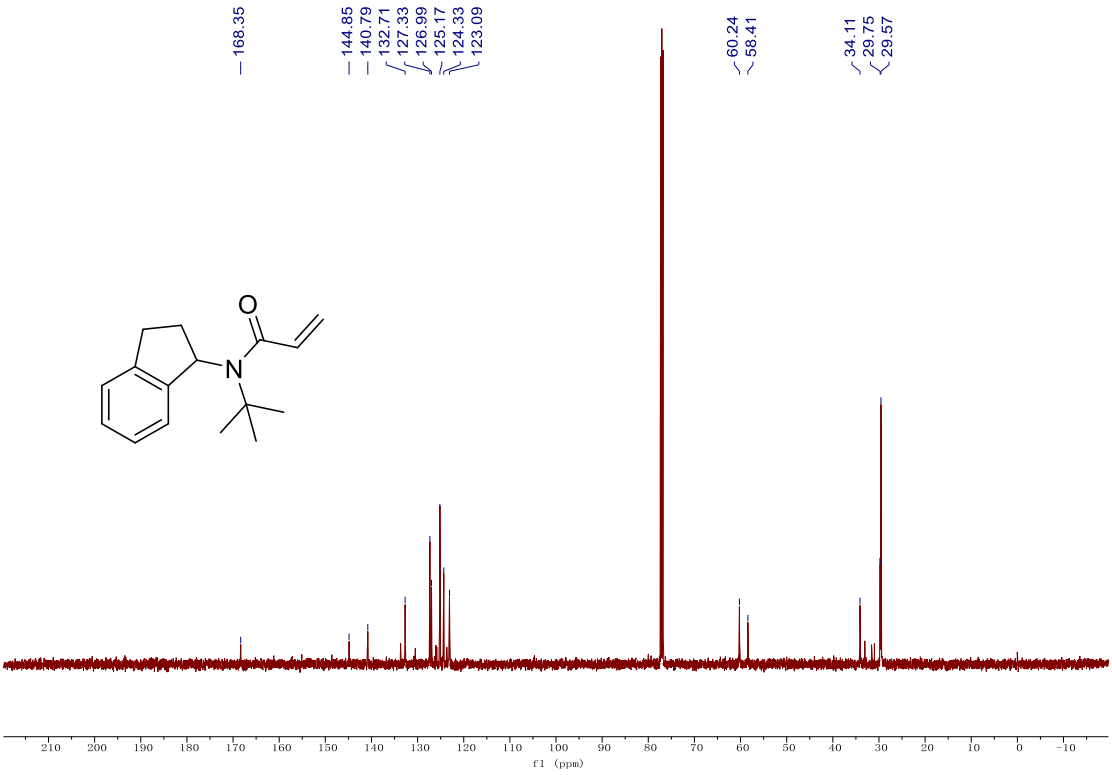
^{1}H NMR spectrum of **3ac** ($CDCl_3$, 400MHz)



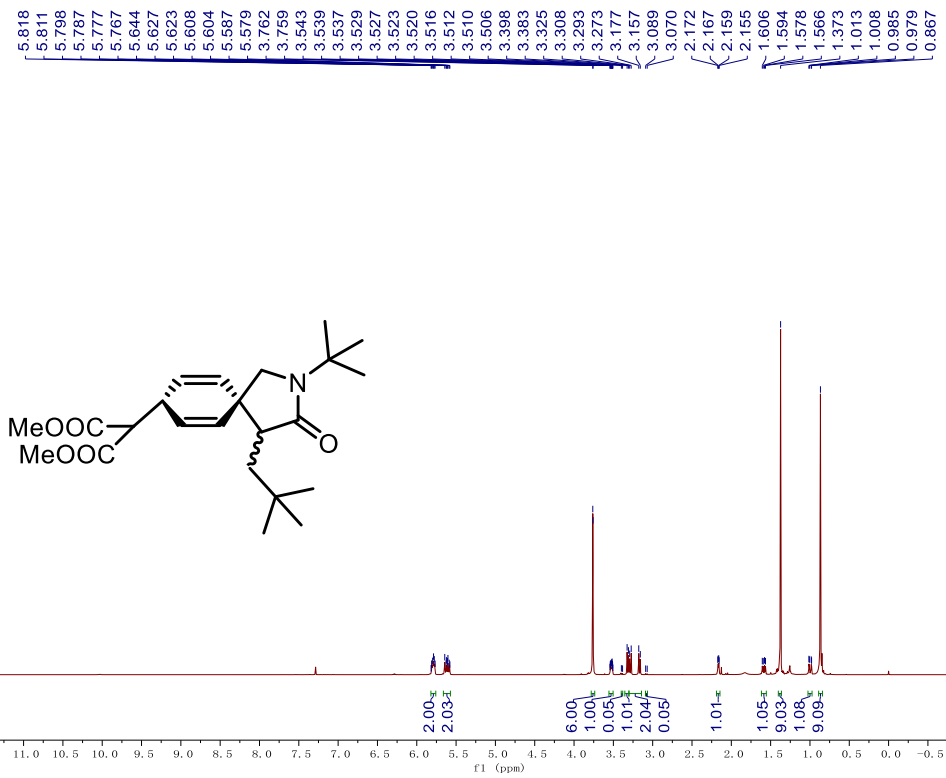
^{13}C NMR spectrum of **3ac** ($CDCl_3$, 101MHz)



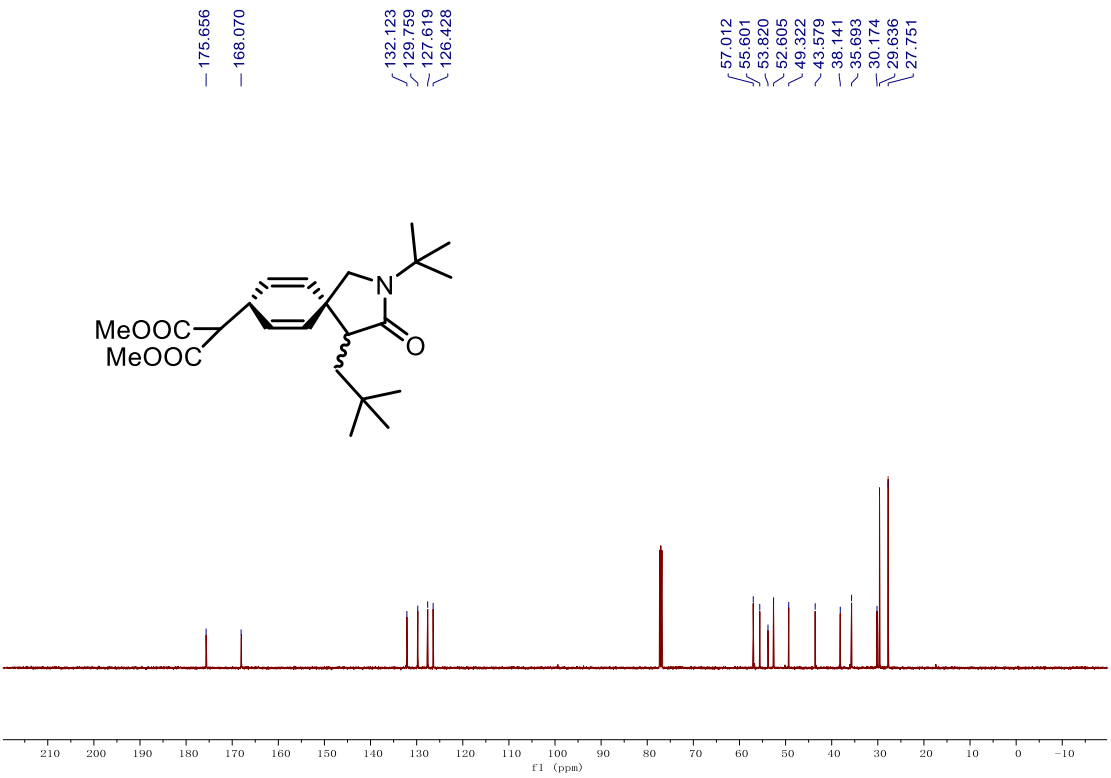
^{1}H NMR spectrum of **3ae** ($CDCl_3$, 500MHz)



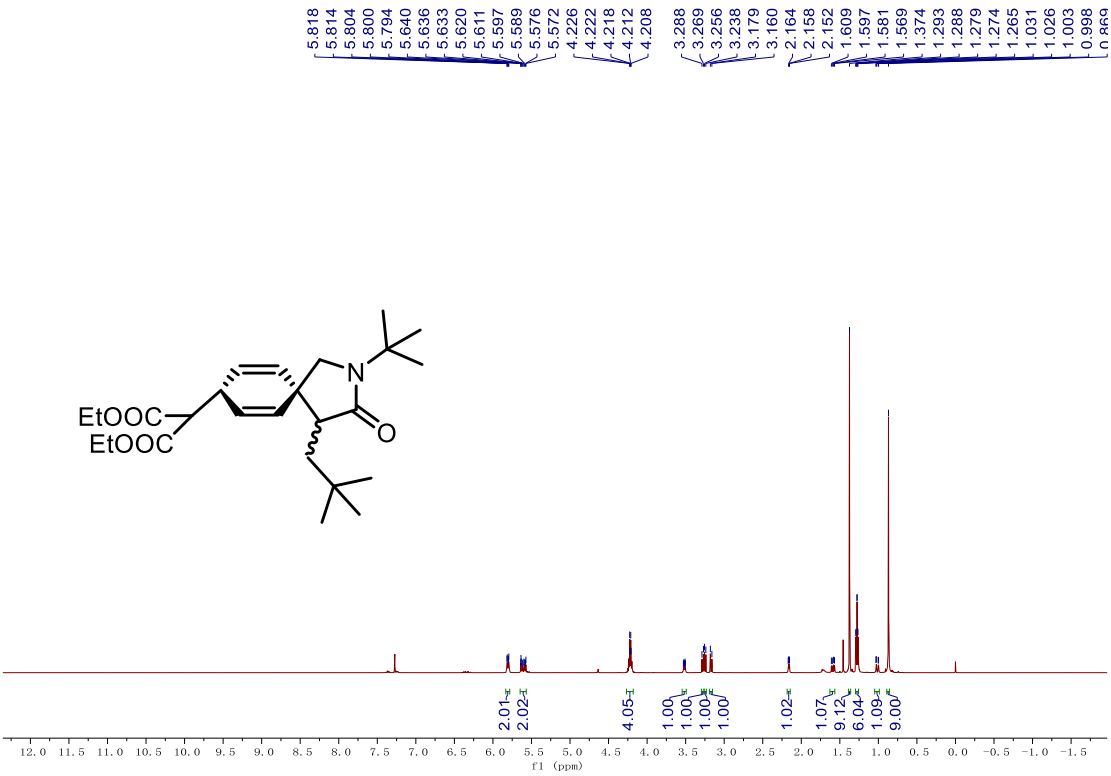
^{13}C NMR spectrum of **3ae** ($CDCl_3$, 126MHz)



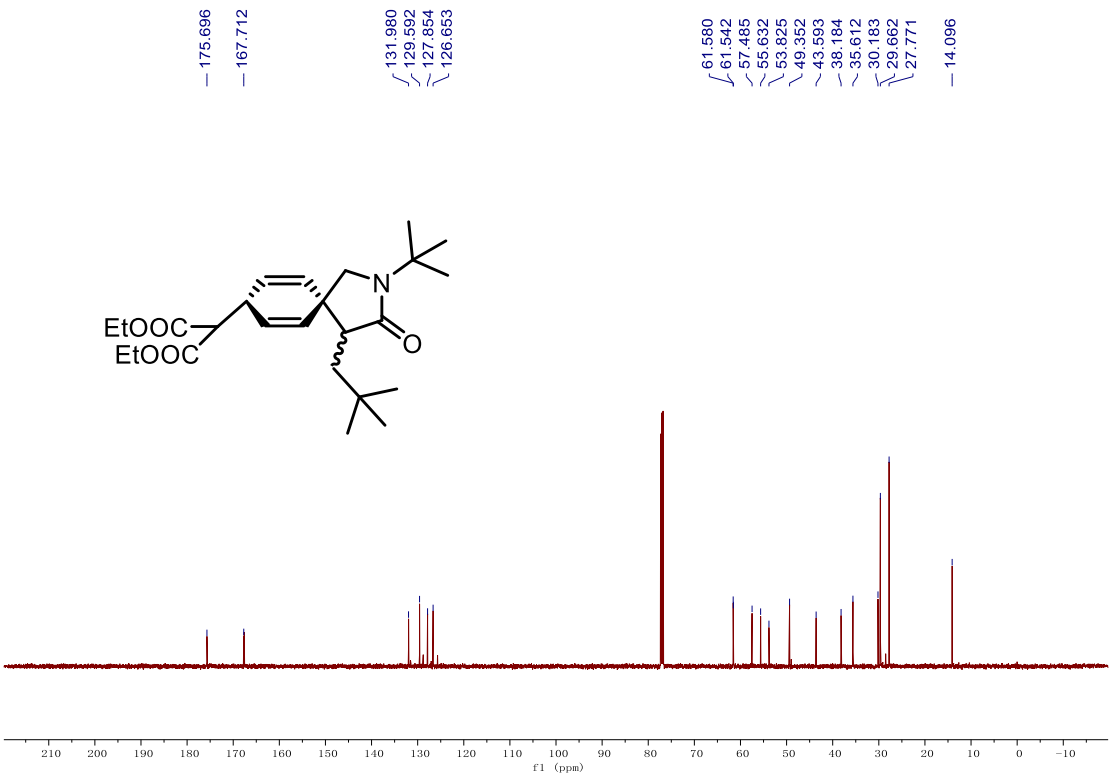
^{1}H NMR spectrum of **4a** ($CDCl_3$, 500MHz)



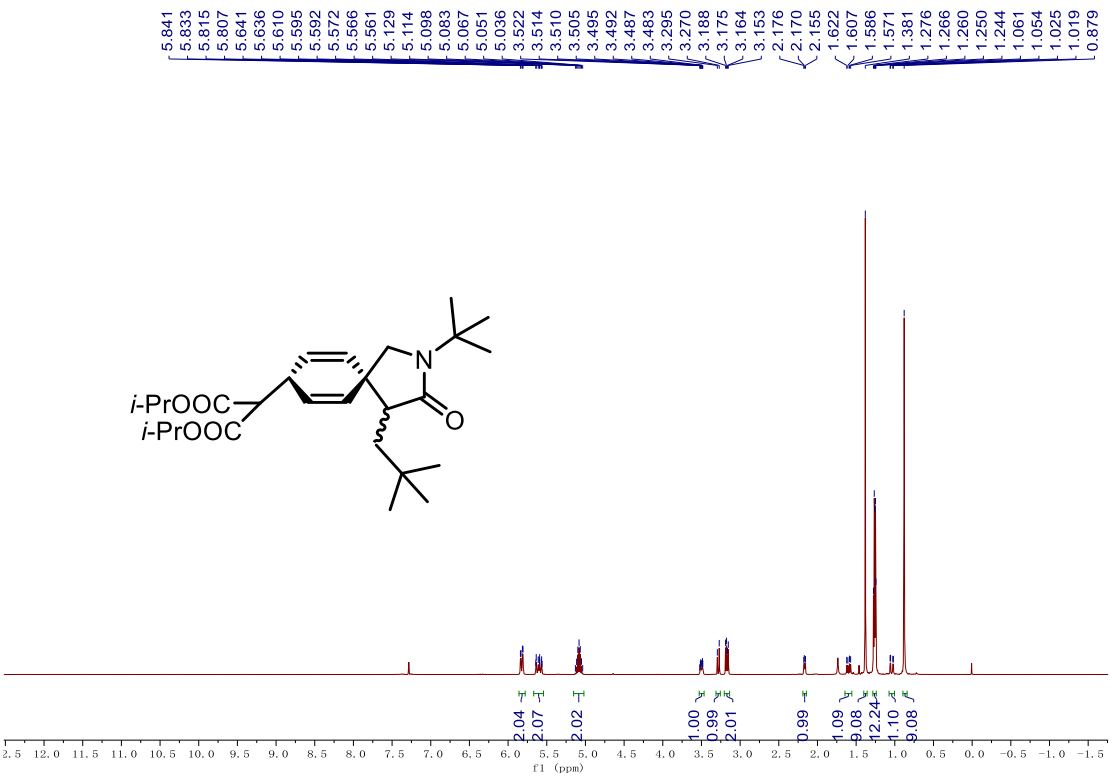
^{13}C NMR spectrum of **4a** ($CDCl_3$, 126MHz)



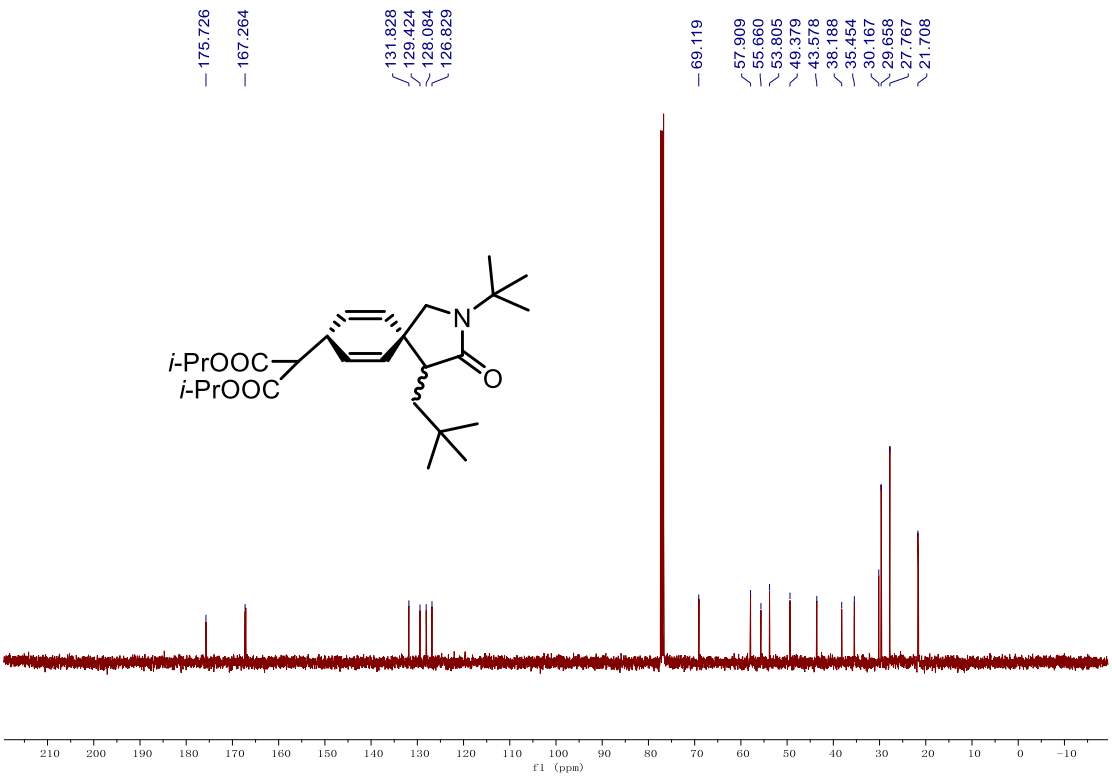
^{1}H NMR spectrum of **4b** ($CDCl_3$, 500MHz)



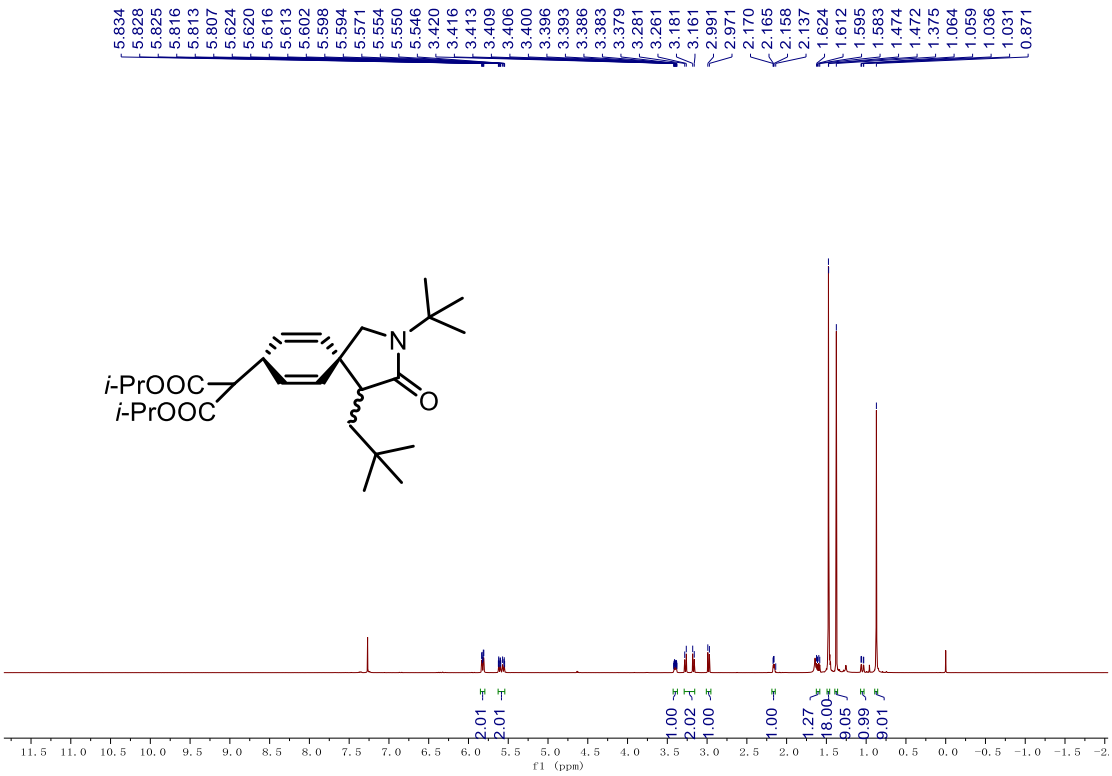
^{13}C NMR spectrum of **4b** ($CDCl_3$, 126MHz)



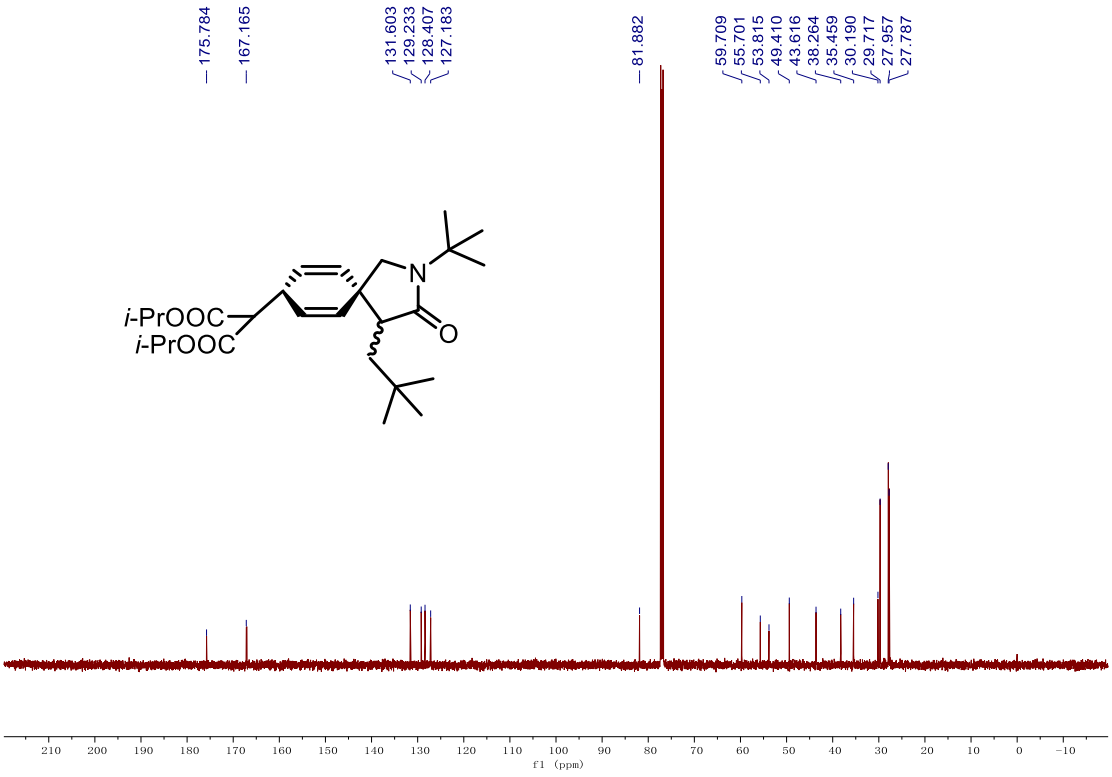
^{1}H NMR spectrum of **4c** ($CDCl_3$, 400MHz)



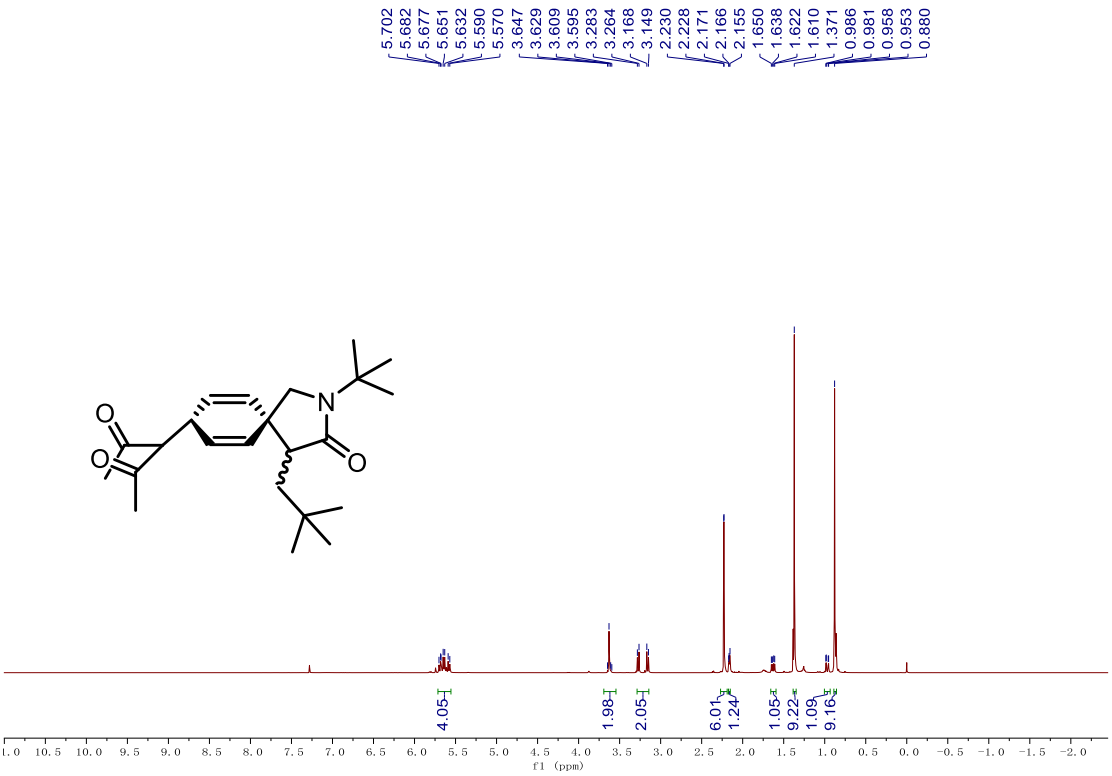
^{13}C NMR spectrum of **4c** ($CDCl_3$, 101MHz)



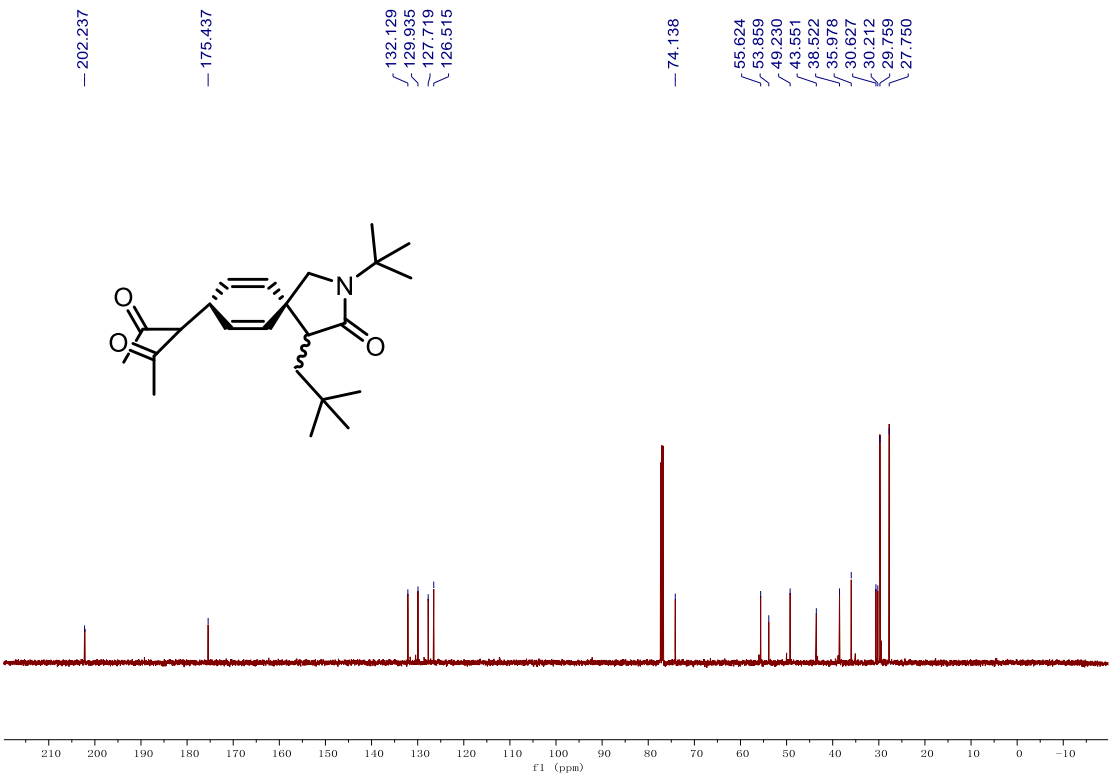
^{1}H NMR spectrum of **4d** ($CDCl_3$, 500MHz)



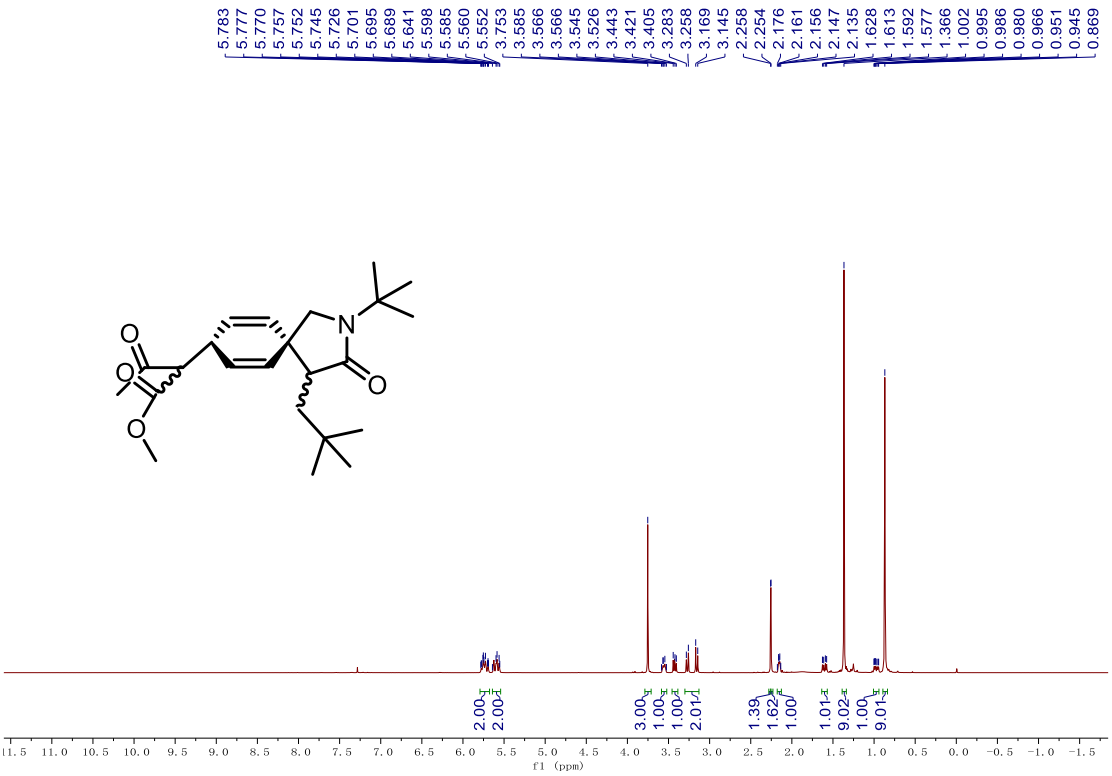
^{13}C NMR spectrum of **4d** ($CDCl_3$, 126MHz)



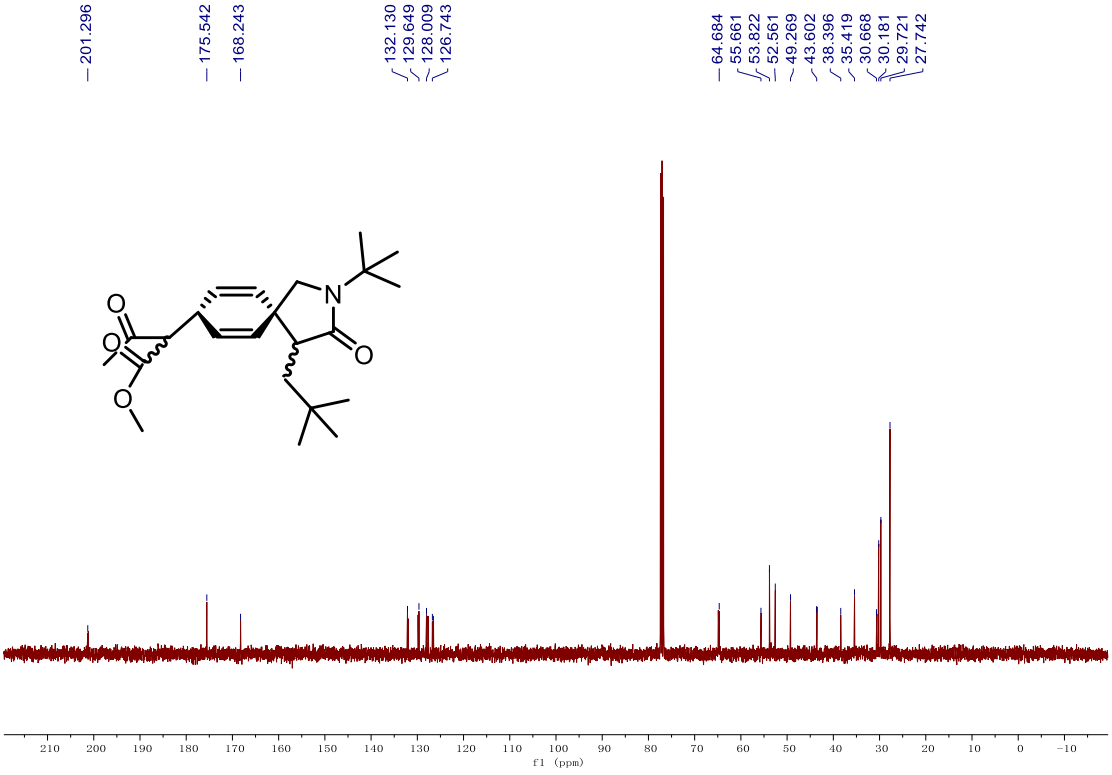
^{1}H NMR spectrum of **4e** ($CDCl_3$, 500MHz)



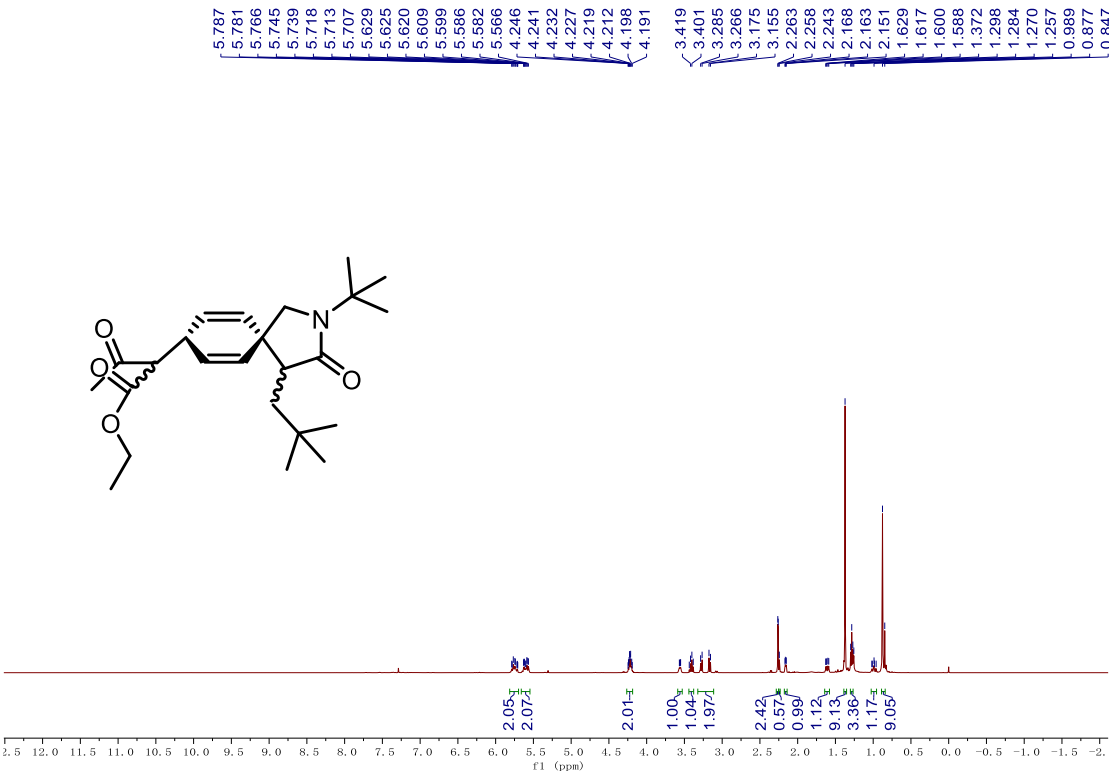
^{13}C NMR spectrum of **4e** ($CDCl_3$, 126MHz)



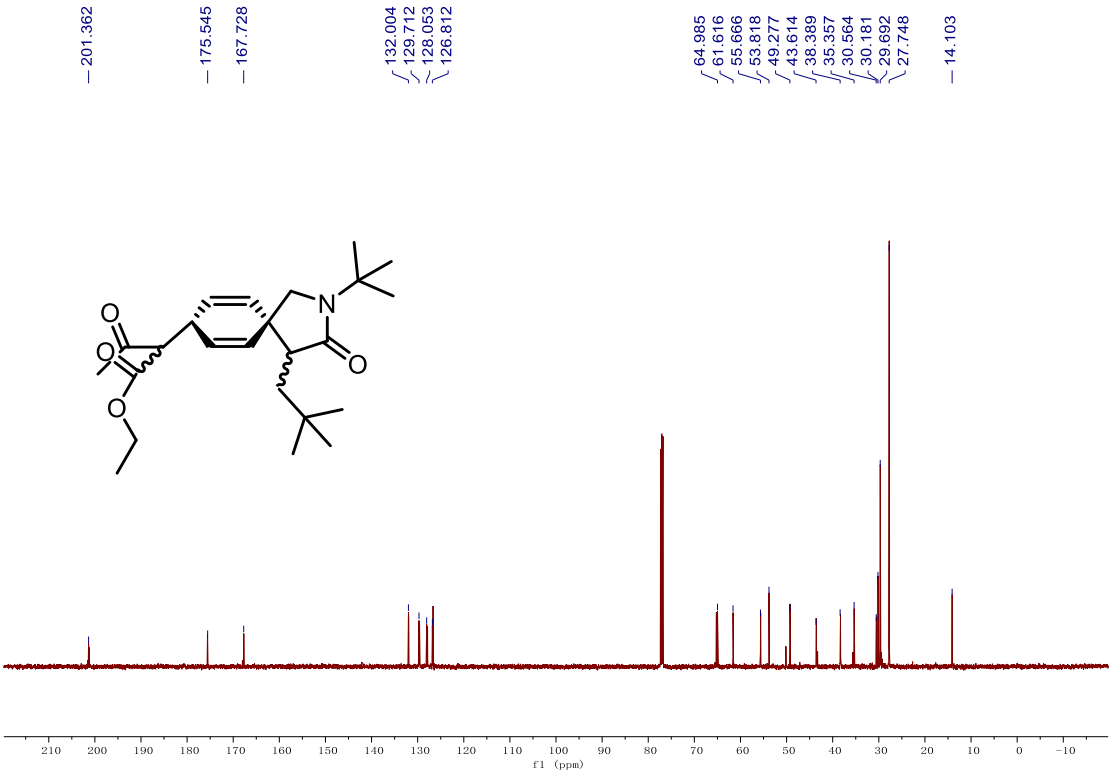
^{1}H NMR spectrum of **4f** ($CDCl_3$, 400MHz)



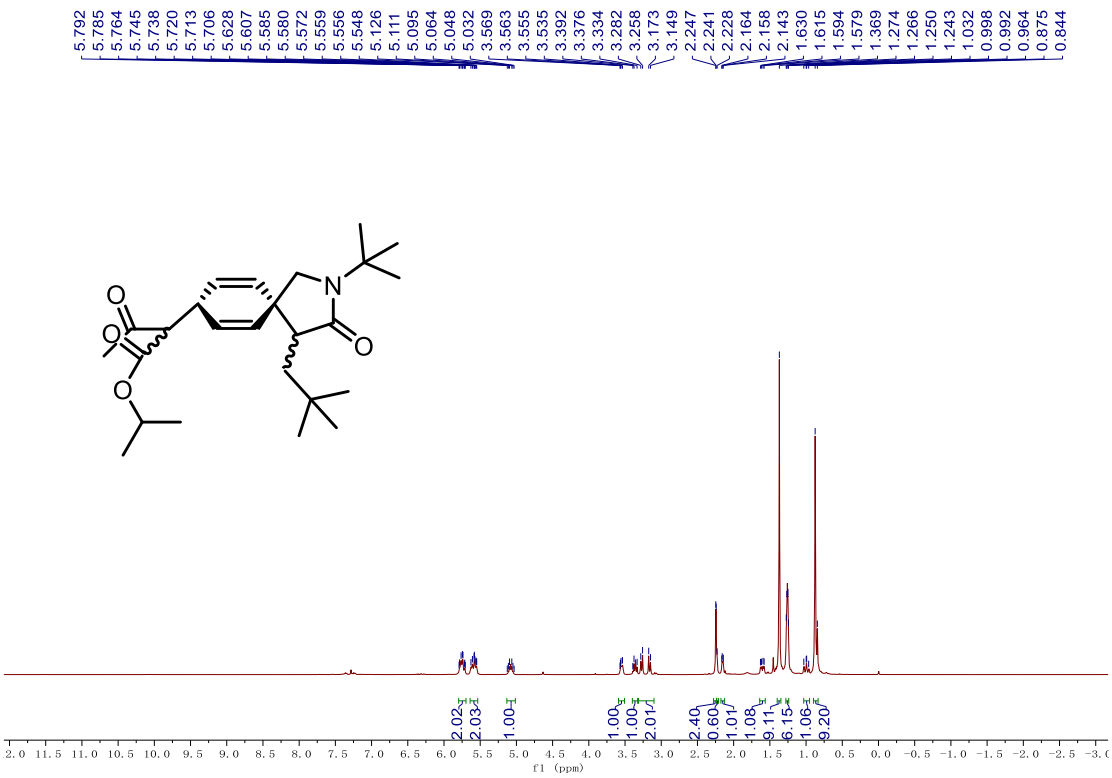
^{13}C NMR spectrum of **4f** ($CDCl_3$, 101MHz)



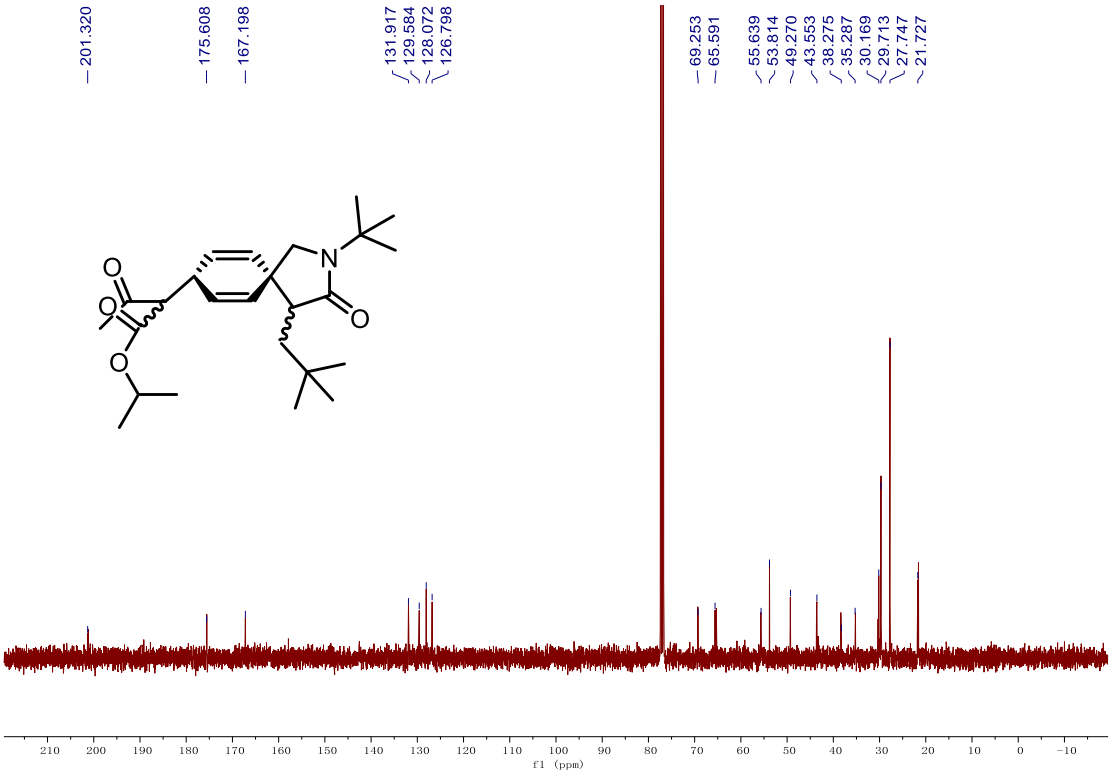
^{1}H NMR spectrum of **4g** ($CDCl_3$, 500MHz)



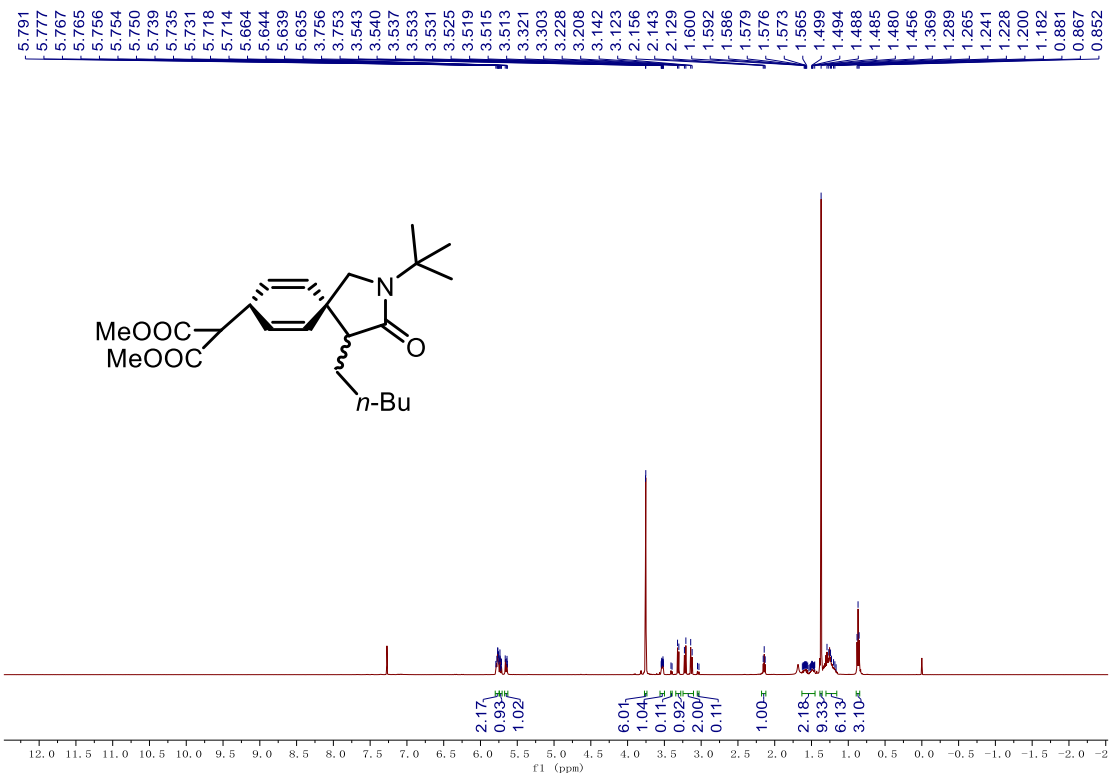
^{13}C NMR spectrum of **4g** ($CDCl_3$, 126MHz)



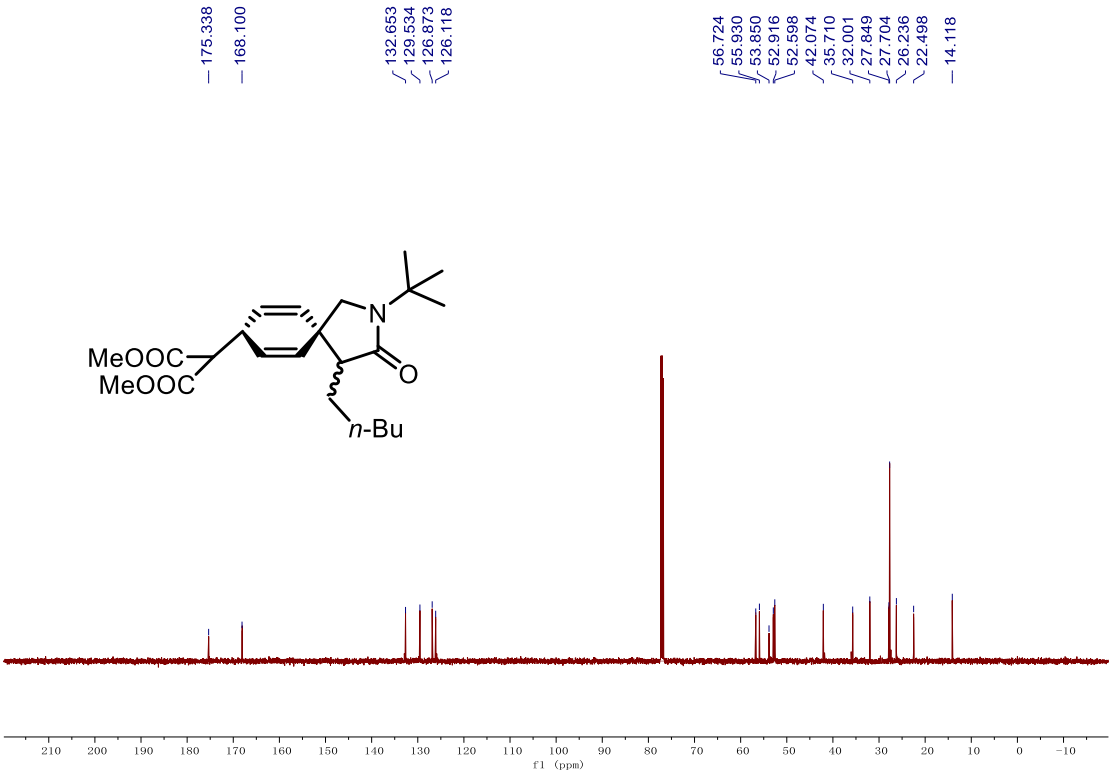
^{1}H NMR spectrum of **4h** ($CDCl_3$, 400MHz)



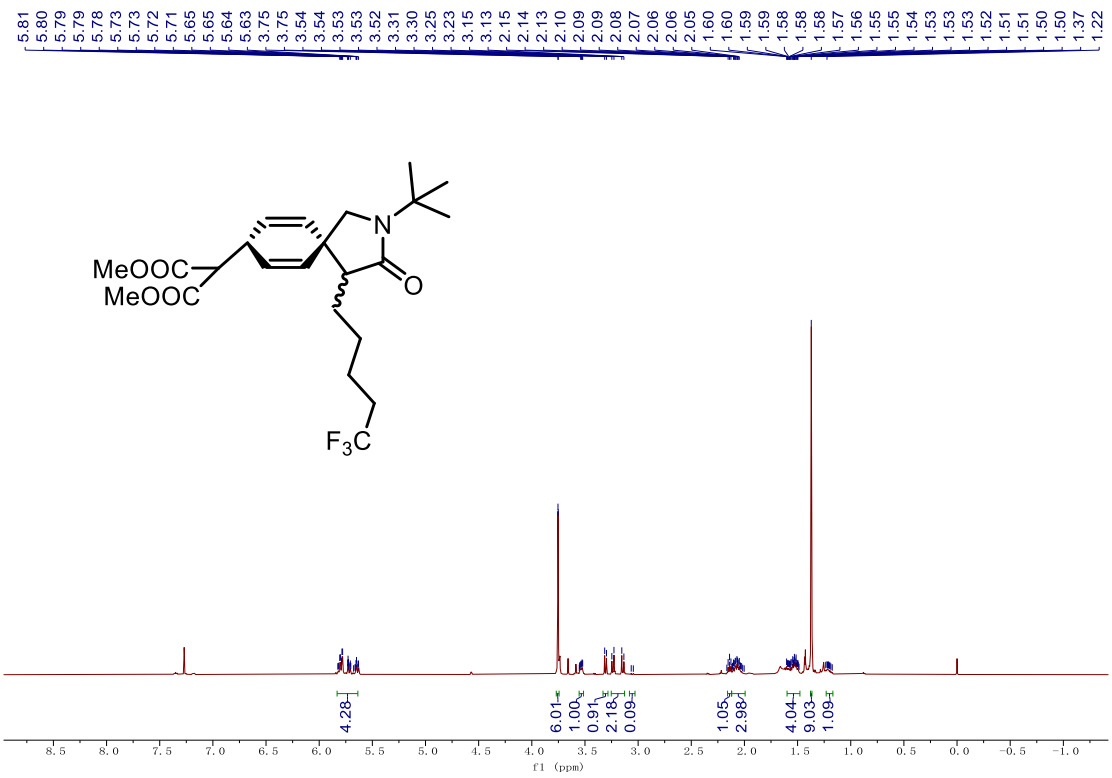
^{13}C NMR spectrum of **4h** ($CDCl_3$, 101MHz)



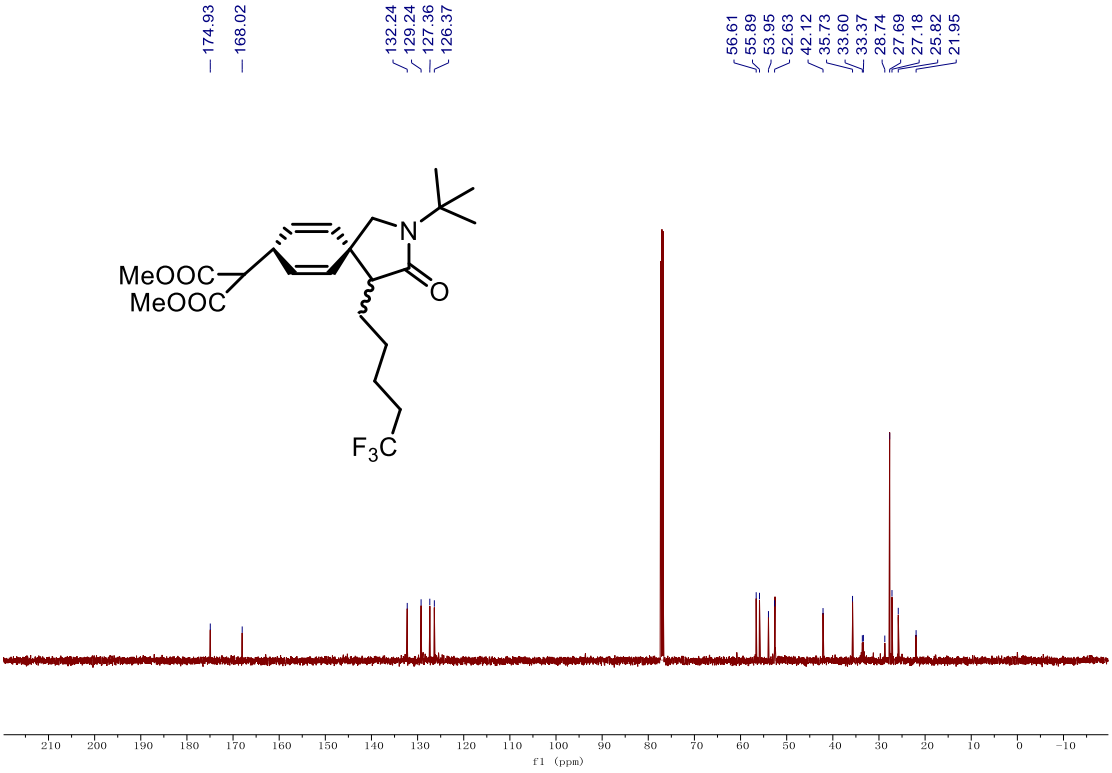
^{1}H NMR spectrum of **4p** ($CDCl_3$, 500MHz)



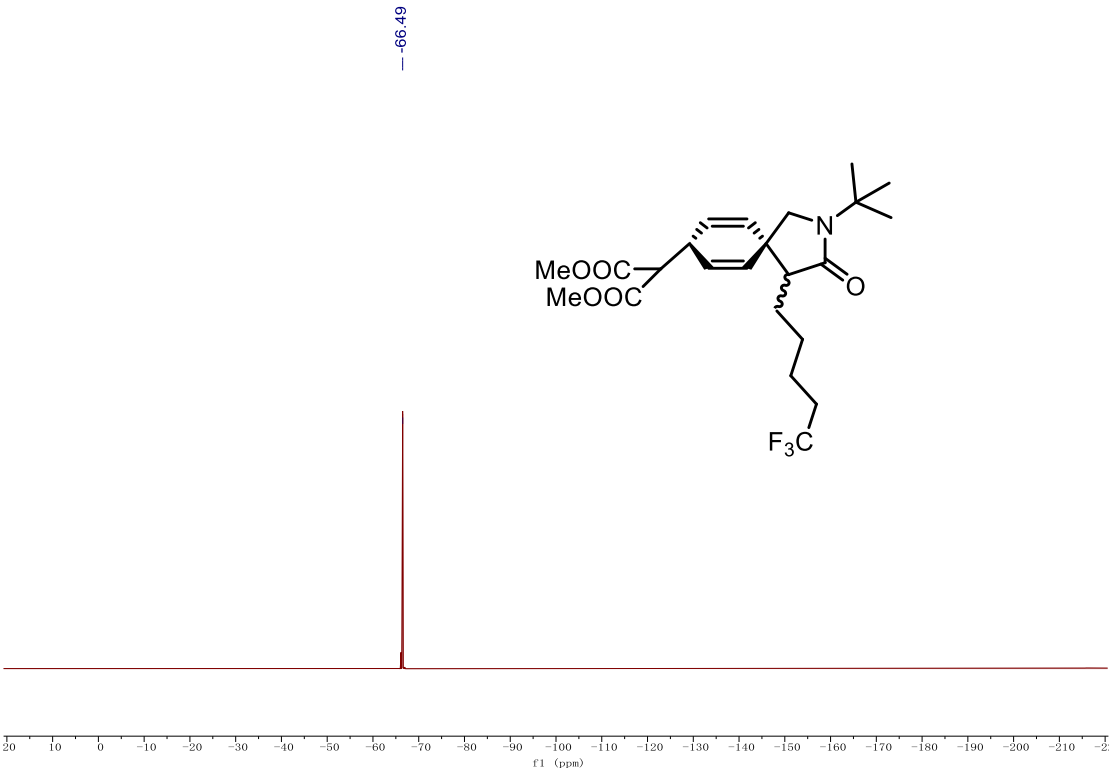
^{13}C NMR spectrum of **4p** ($CDCl_3$, 126MHz)



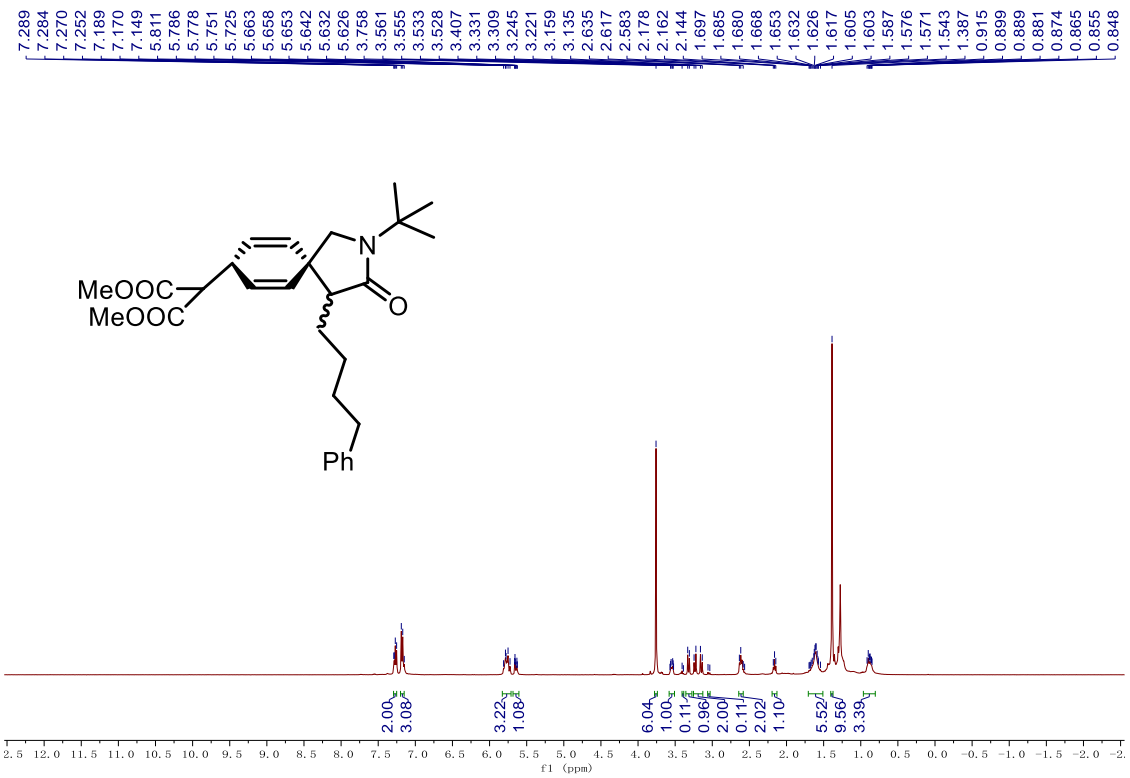
^{1}H NMR spectrum of **4q** ($CDCl_3$, 500MHz)



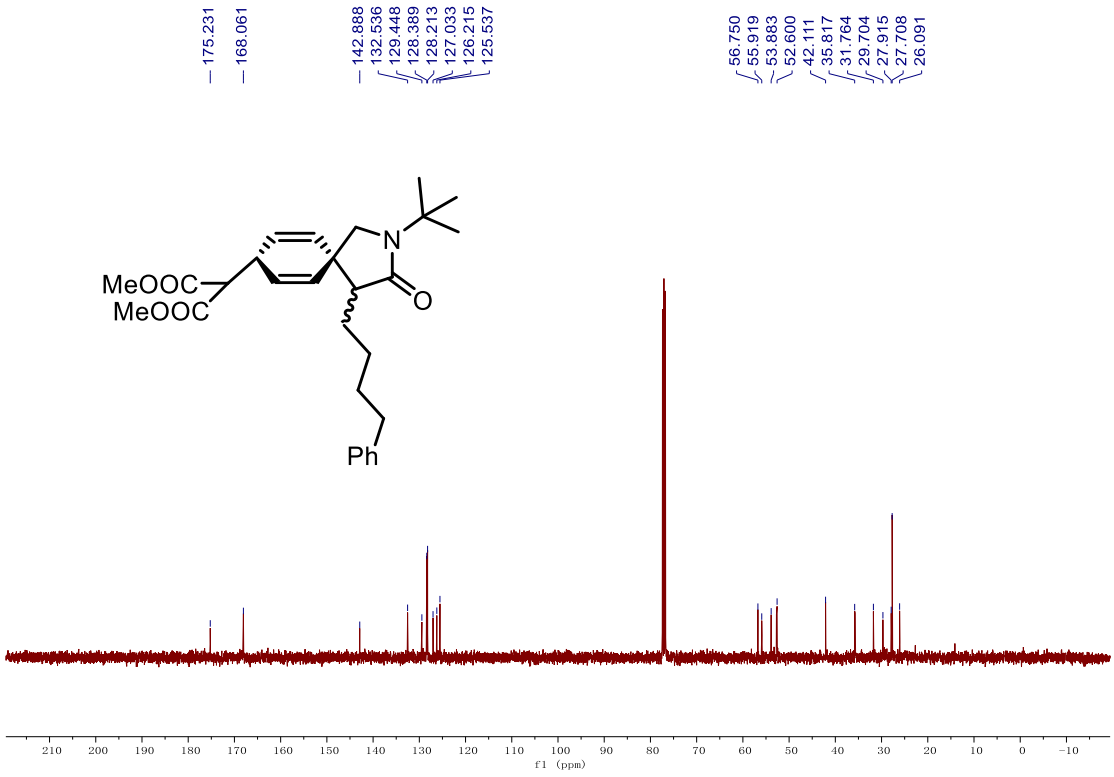
^{13}C NMR spectrum of **4q** ($CDCl_3$, 126MHz)



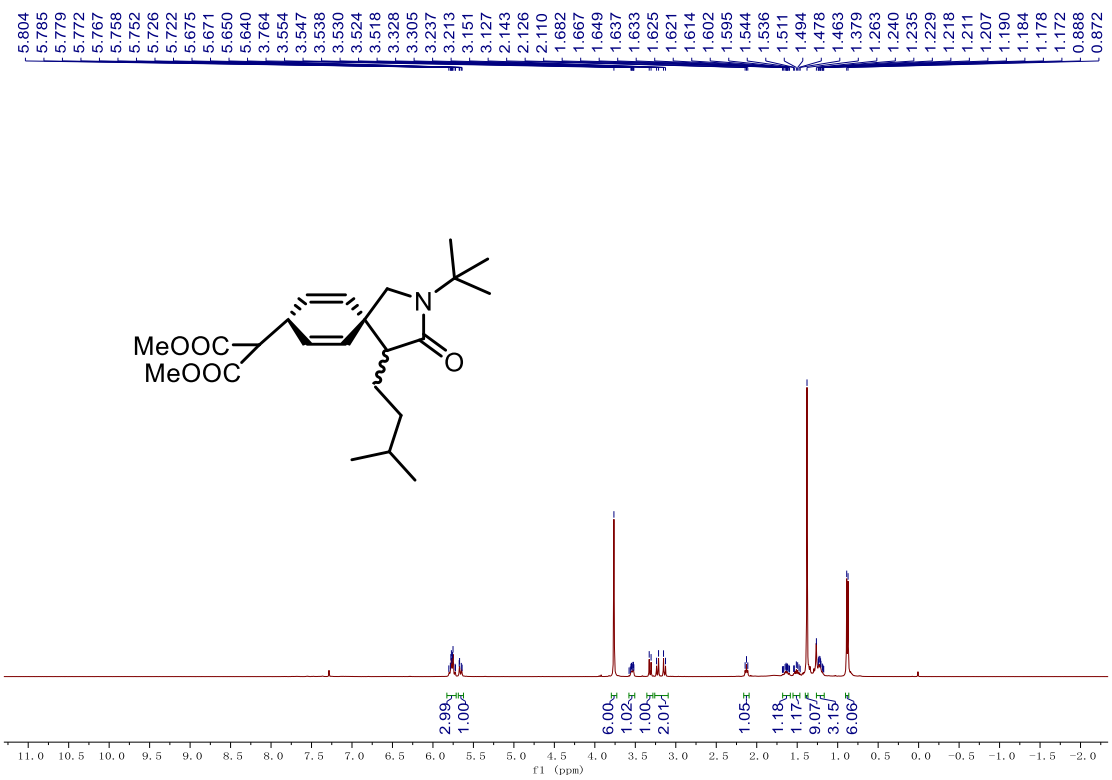
^{19}F NMR spectrum of **4q** ($CDCl_3$, 471 MHz)



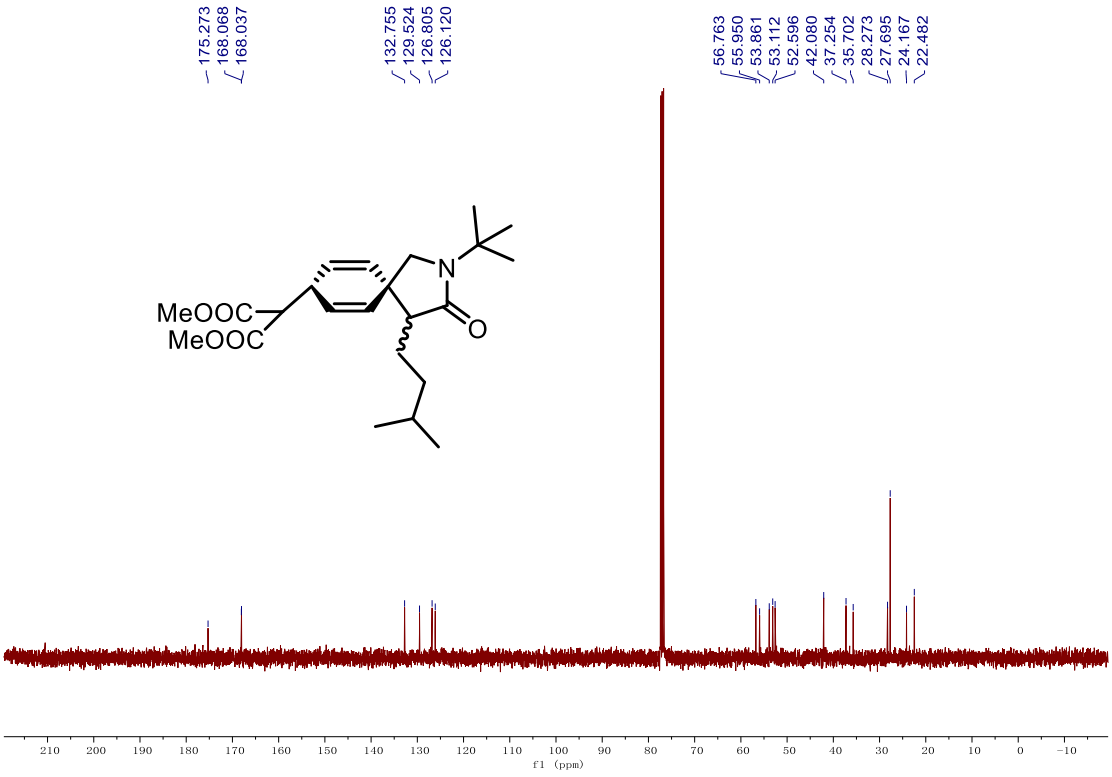
^{1}H NMR spectrum of **4r** ($CDCl_3$, 400MHz)



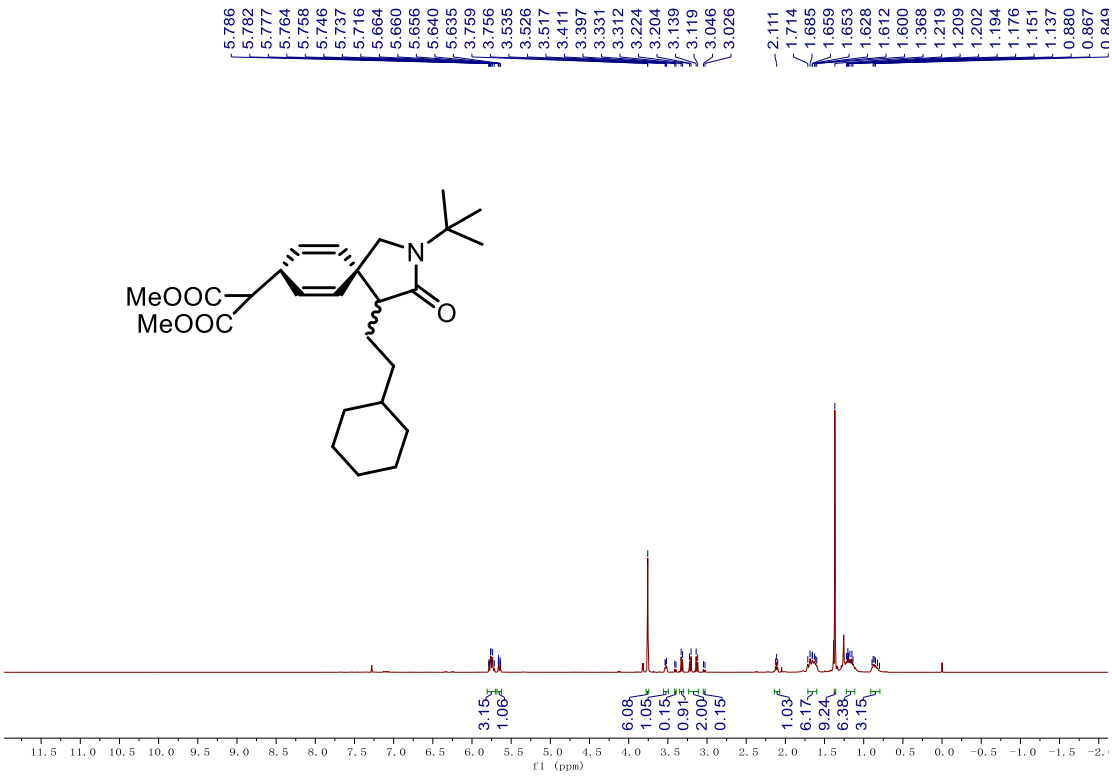
^{13}C NMR spectrum of **4r** ($CDCl_3$, 101MHz)



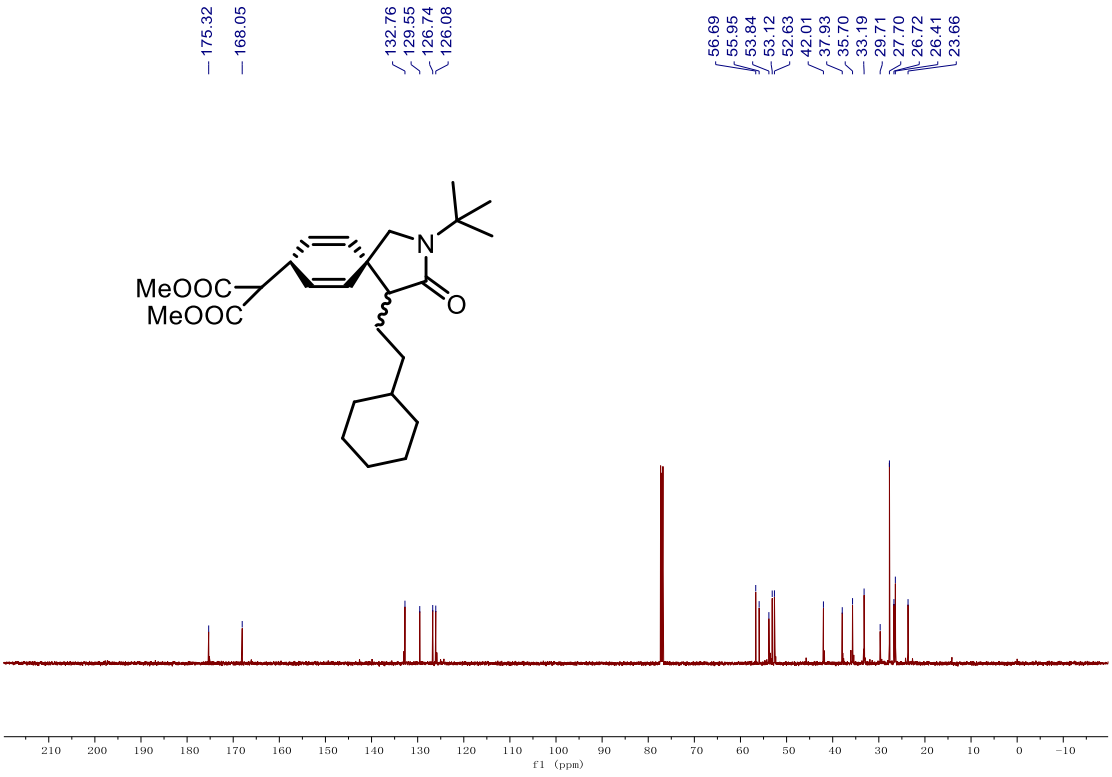
^{1}H NMR spectrum of **4s** ($CDCl_3$, 400MHz)



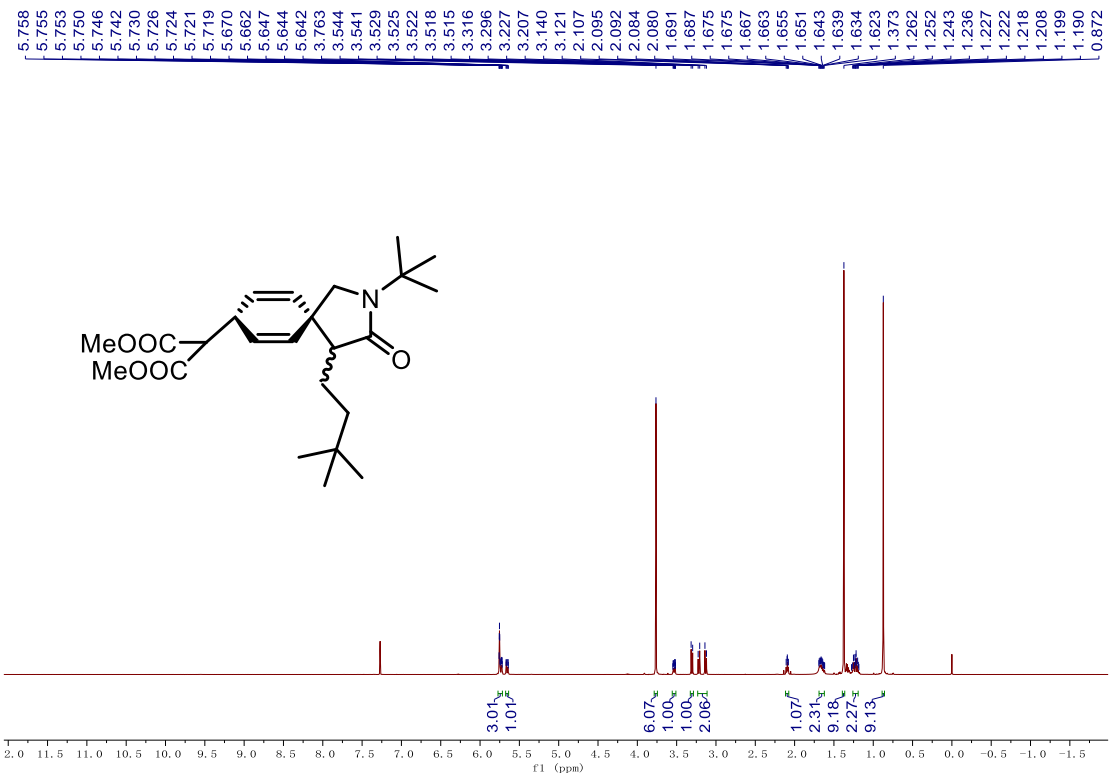
^{13}C NMR spectrum of **4s** ($CDCl_3$, 101MHz)



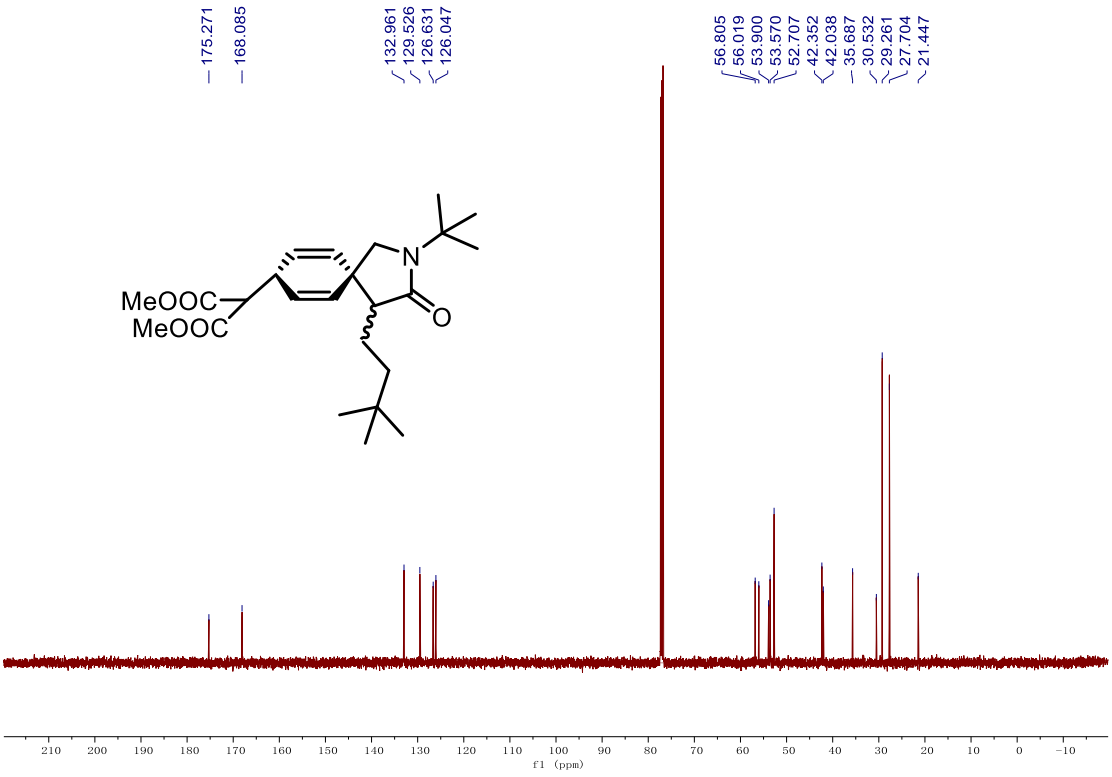
^{1}H NMR spectrum of **4t** ($CDCl_3$, 500MHz)



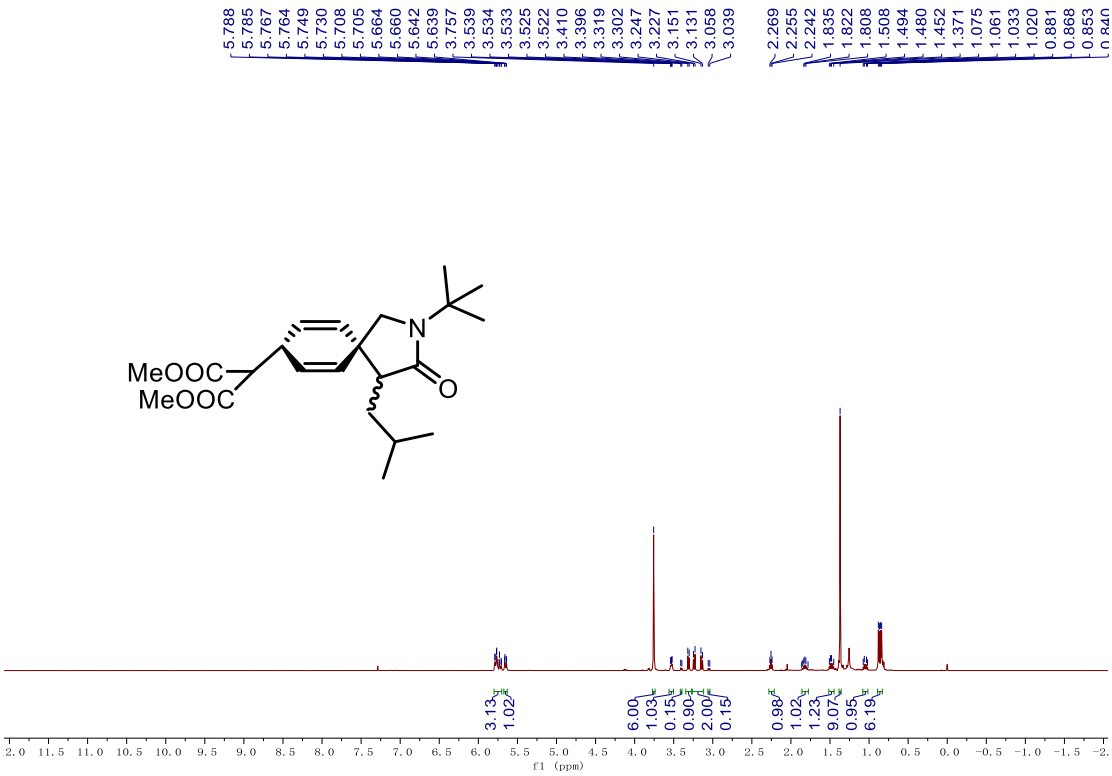
^{13}C NMR spectrum of **4t** ($CDCl_3$, 126MHz)



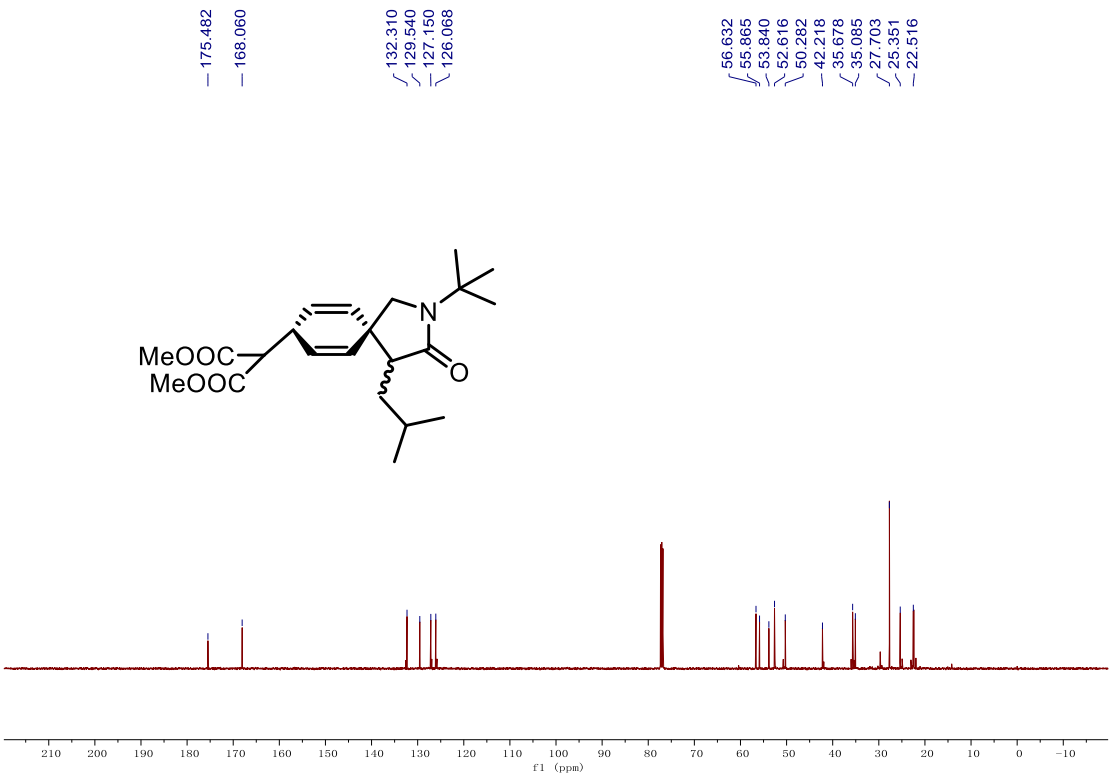
^{1}H NMR spectrum of **4u** ($CDCl_3$, 500MHz)



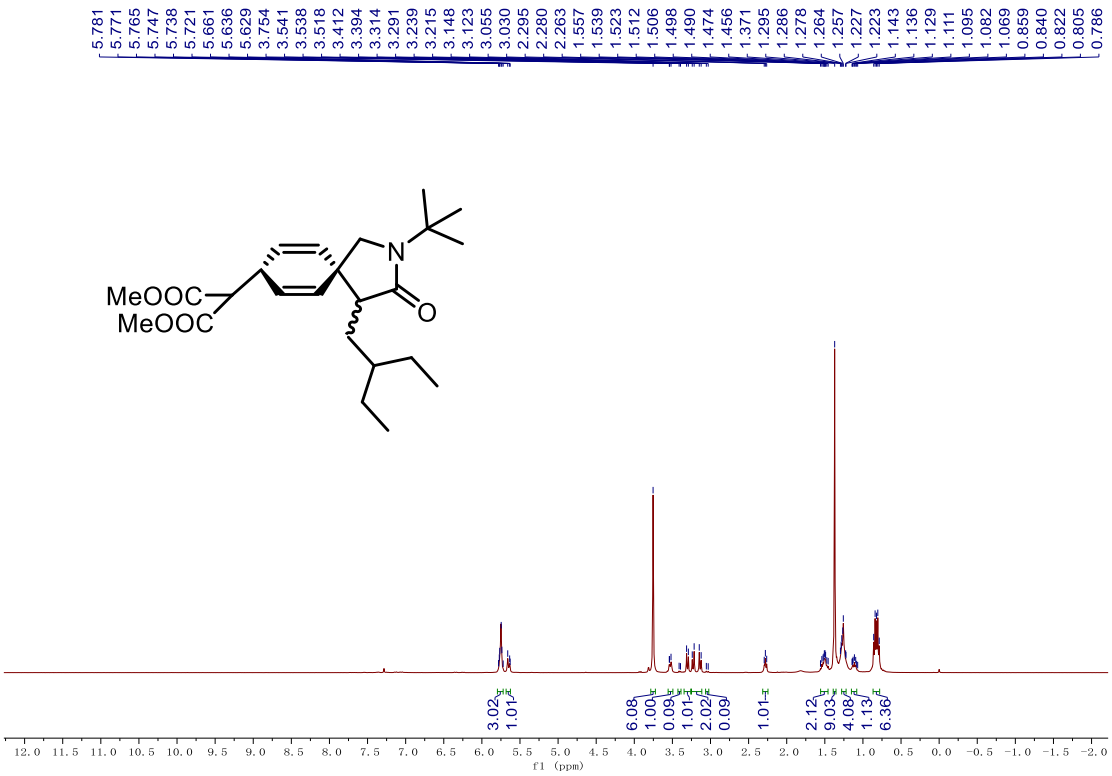
^{13}C NMR spectrum of **4u** ($CDCl_3$, 126MHz)



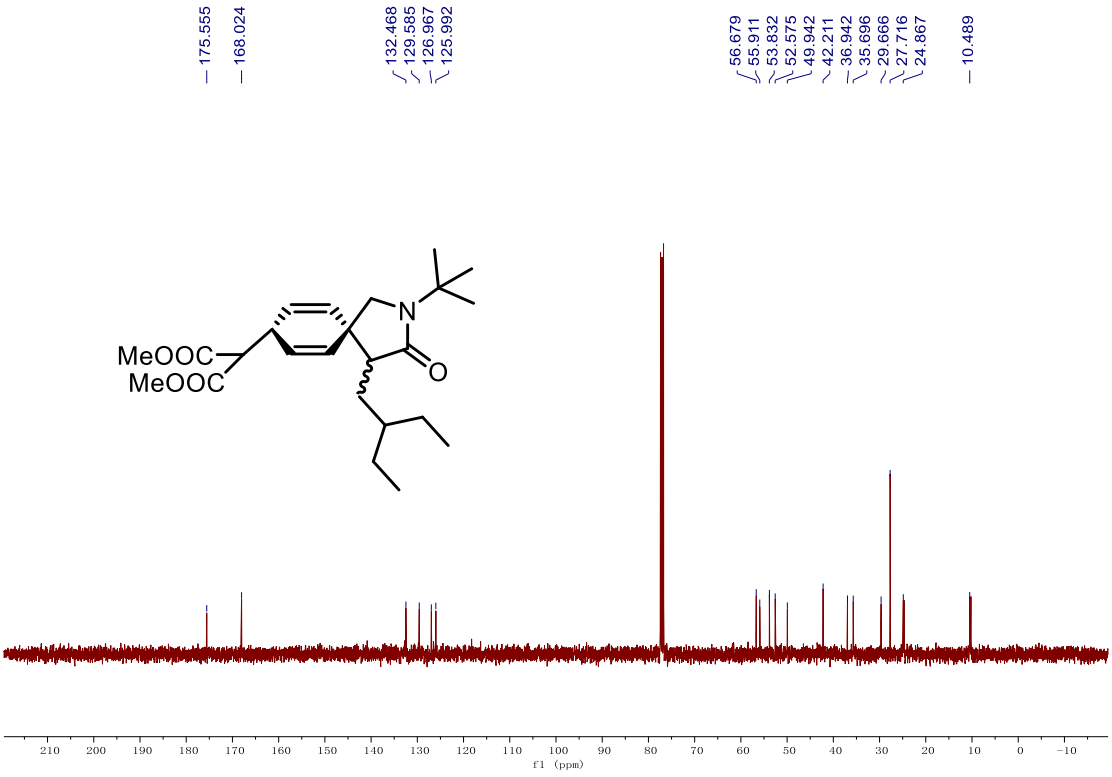
^{1}H NMR spectrum of **4v** ($CDCl_3$, 500MHz)



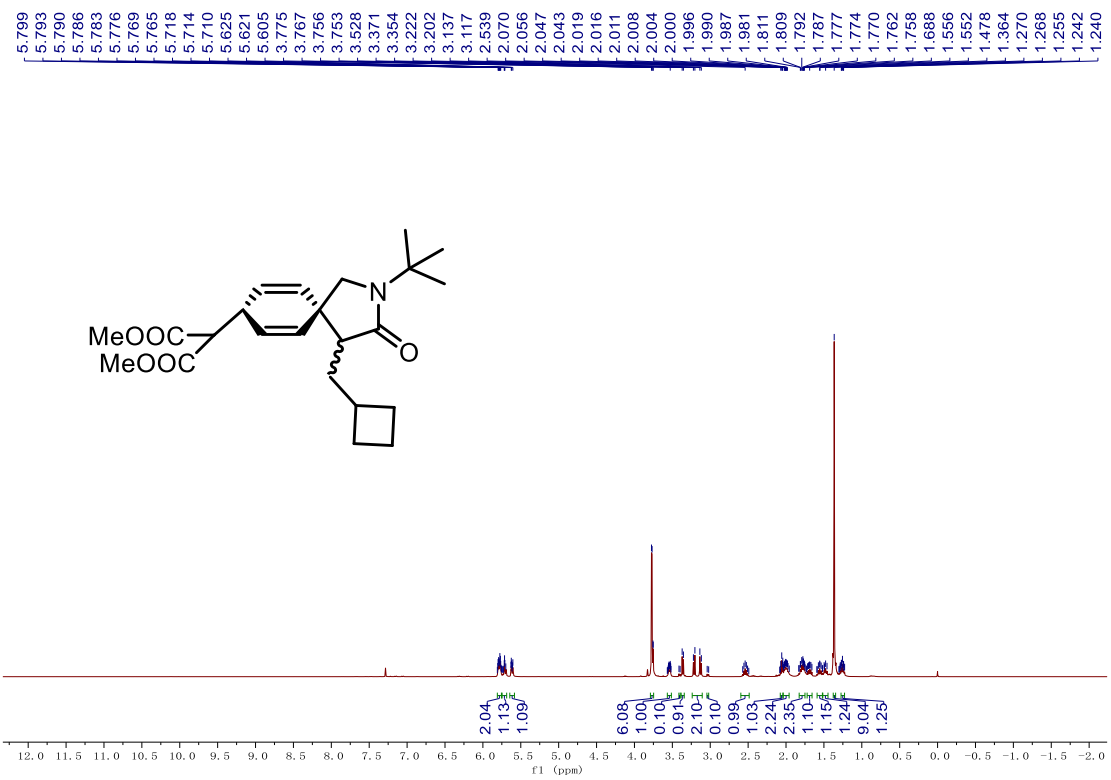
^{13}C NMR spectrum of **4v** ($CDCl_3$, 126MHz)



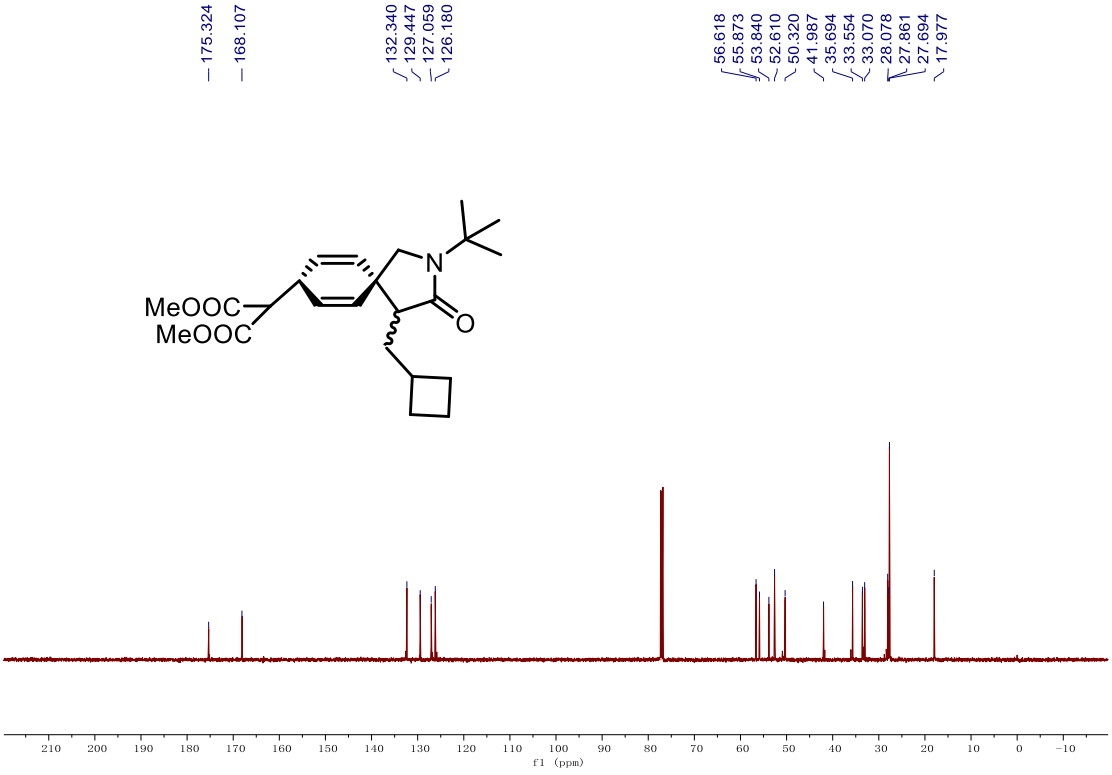
^{1}H NMR spectrum of **4w** ($CDCl_3$, 400MHz)



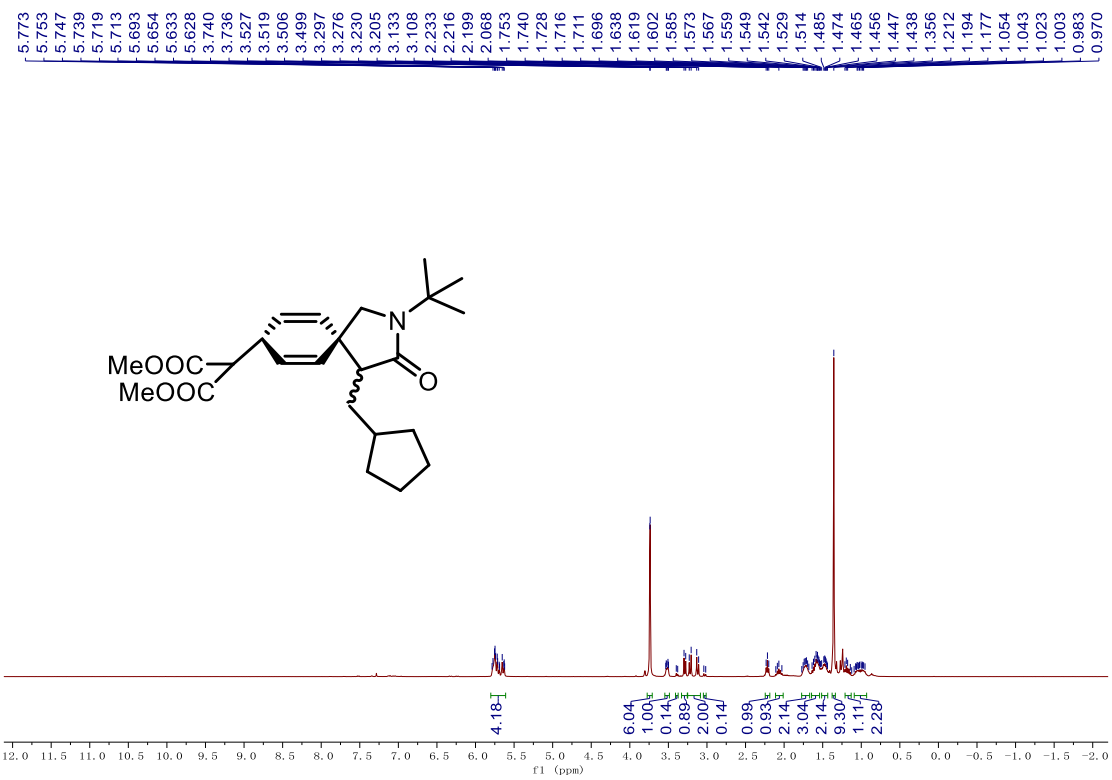
^{13}C NMR spectrum of **4w** ($CDCl_3$, 101MHz)



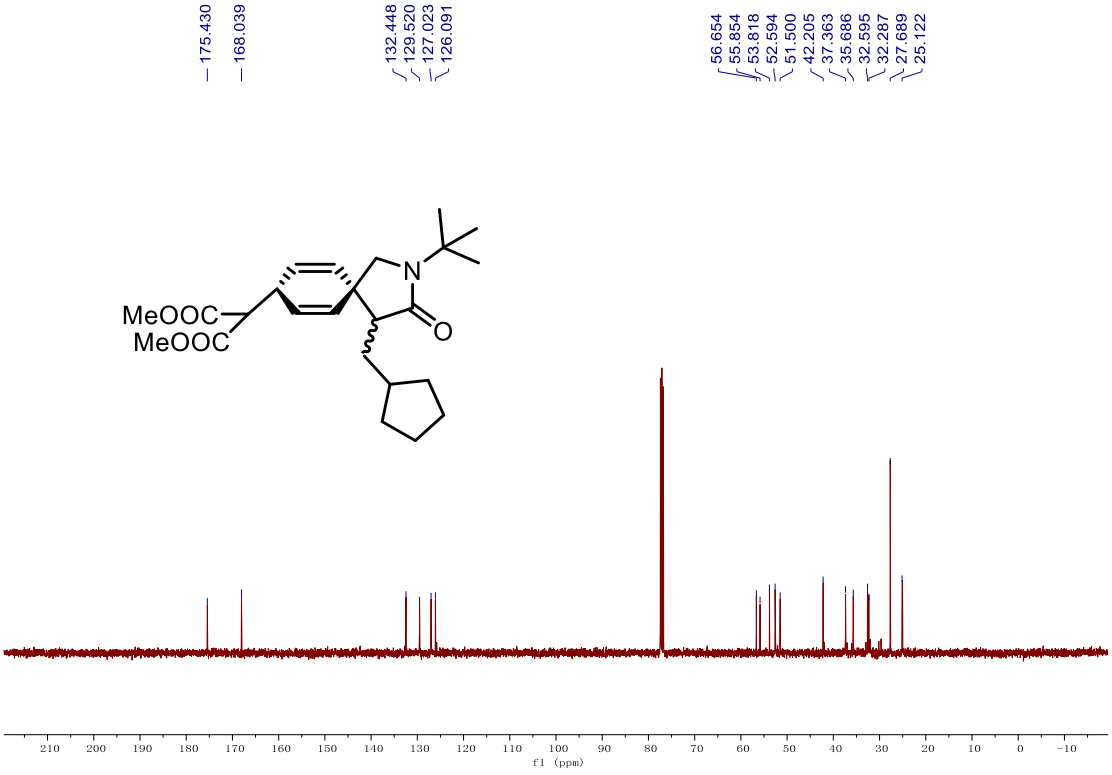
^{1}H NMR spectrum of **4x** ($CDCl_3$, 500MHz)



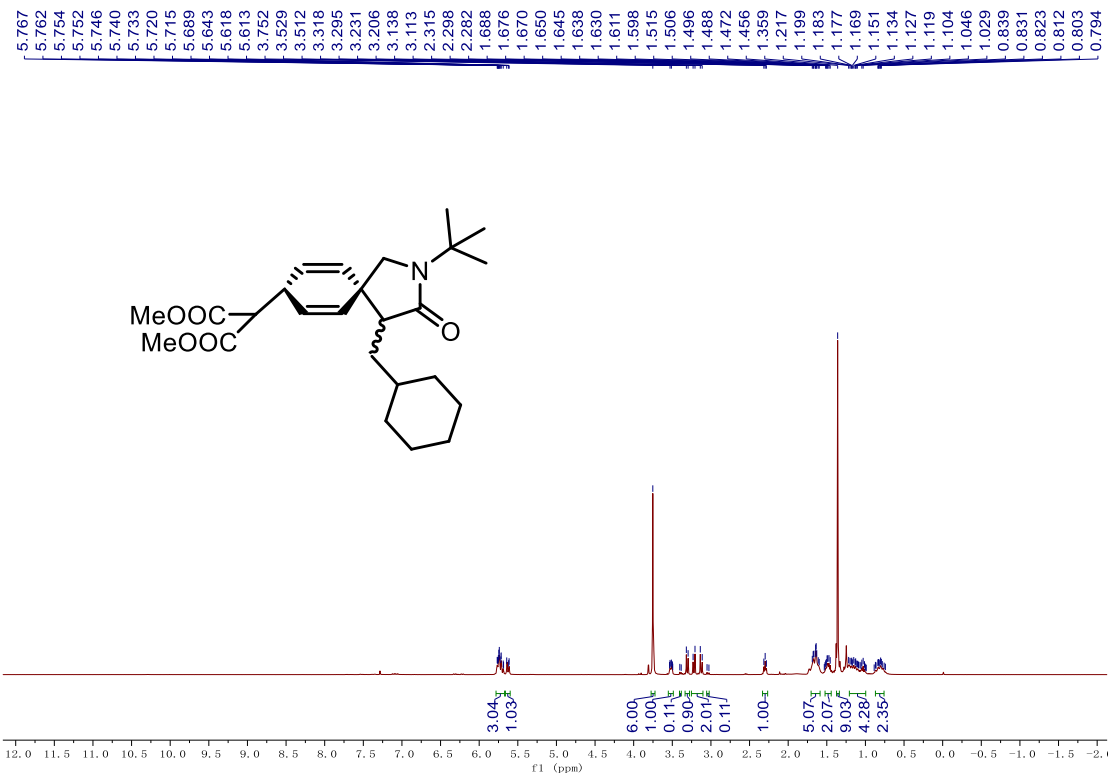
^{13}C NMR spectrum of **4x** ($CDCl_3$, 126MHz)



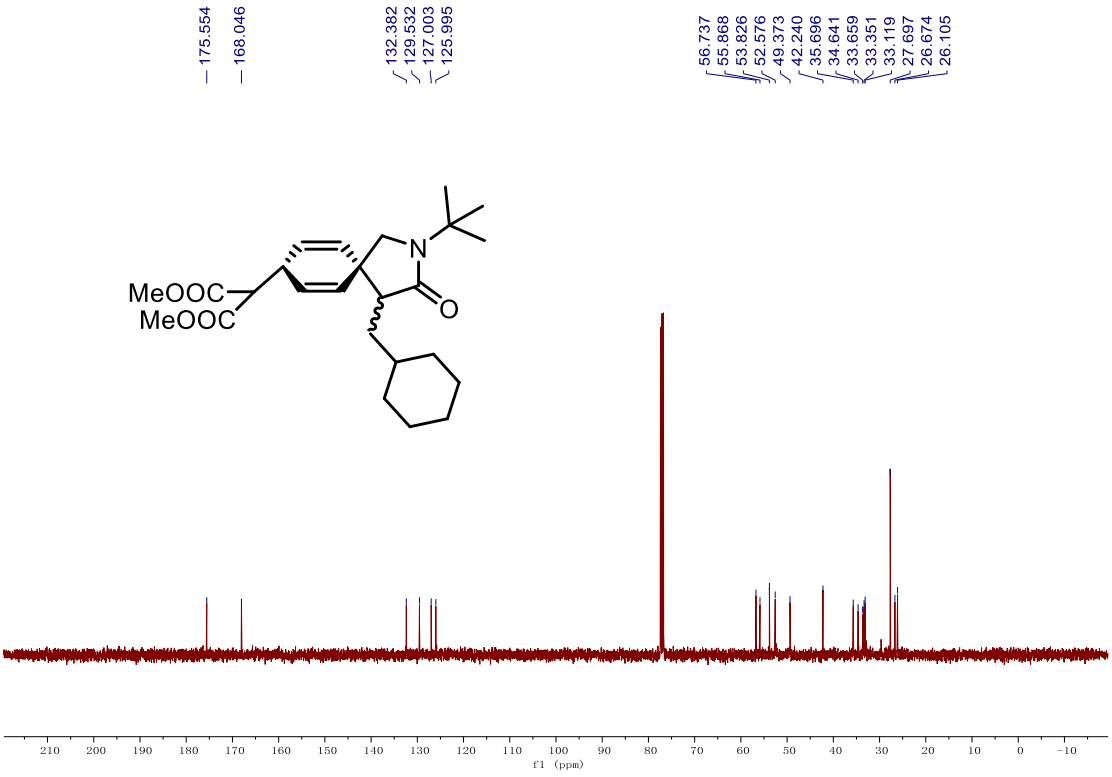
^{1}H NMR spectrum of **4y** ($CDCl_3$, 400MHz)



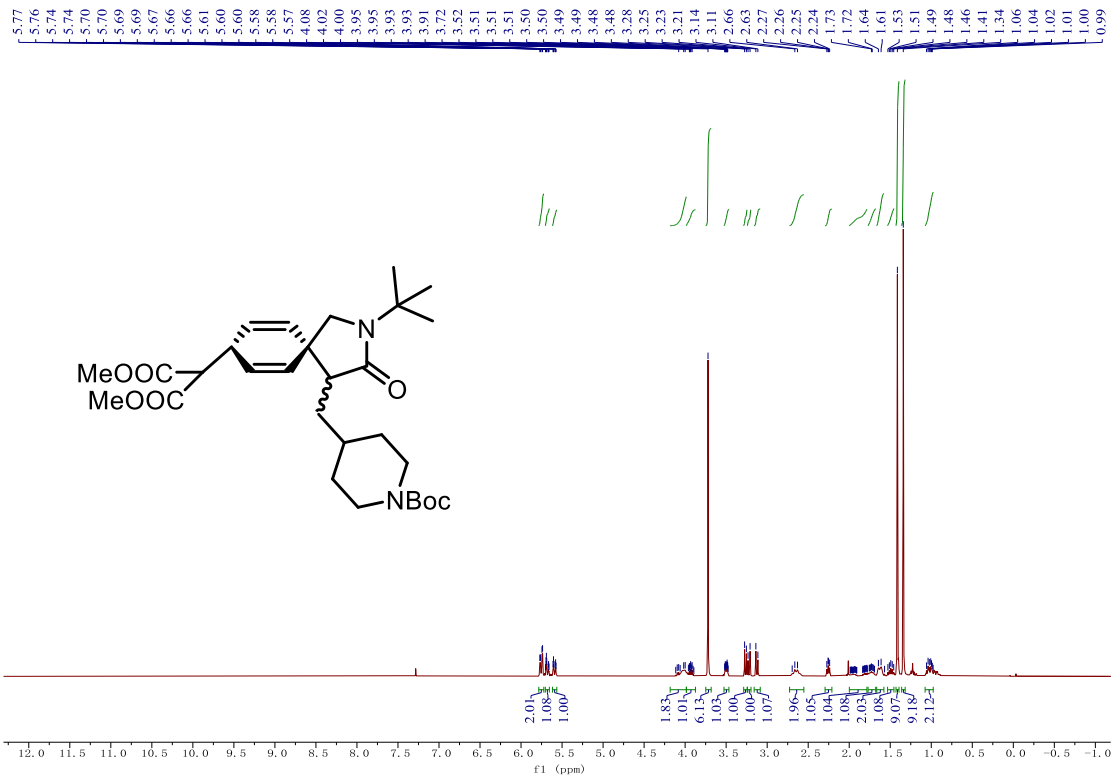
^{13}C NMR spectrum of **4y** ($CDCl_3$, 101MHz)



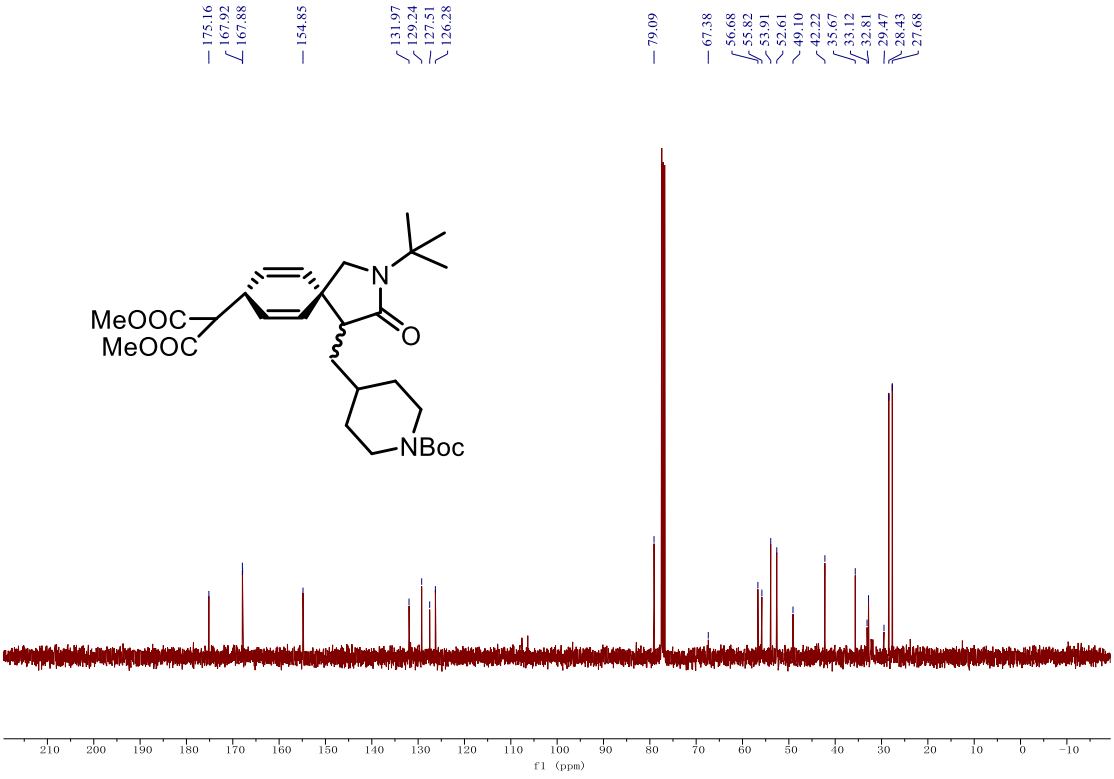
^{1}H NMR spectrum of **4z** ($CDCl_3$, 400MHz)



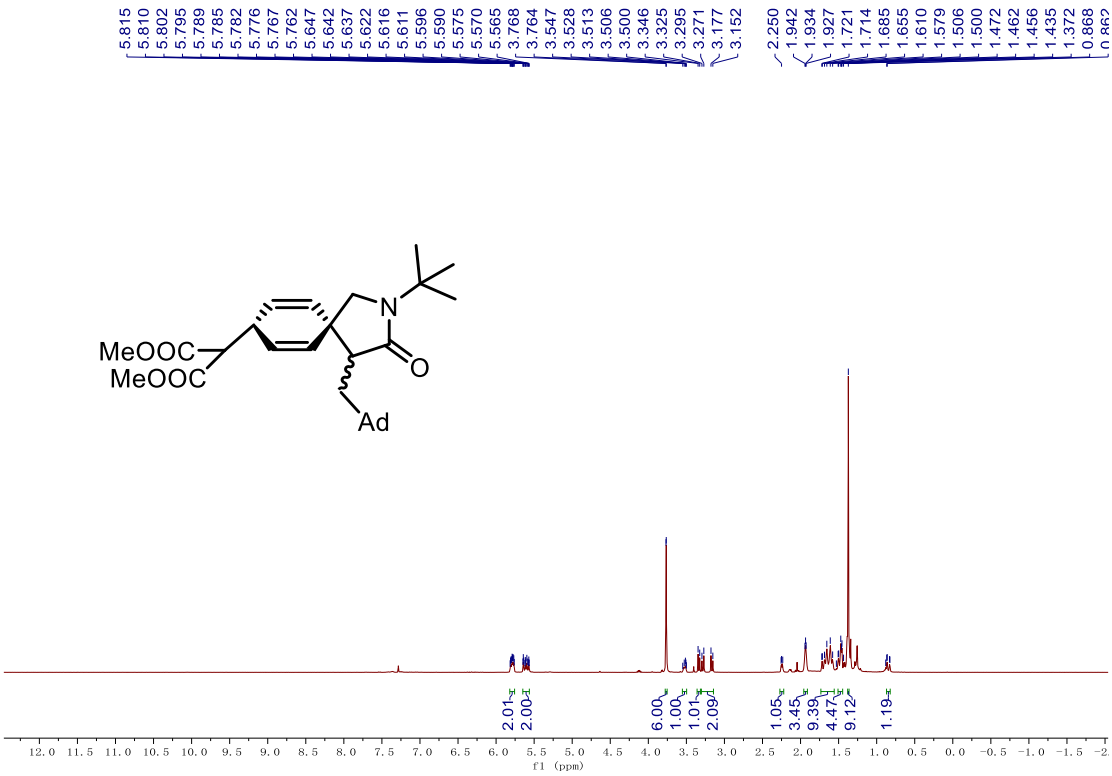
^{13}C NMR spectrum of **4z** ($CDCl_3$, 101MHz)



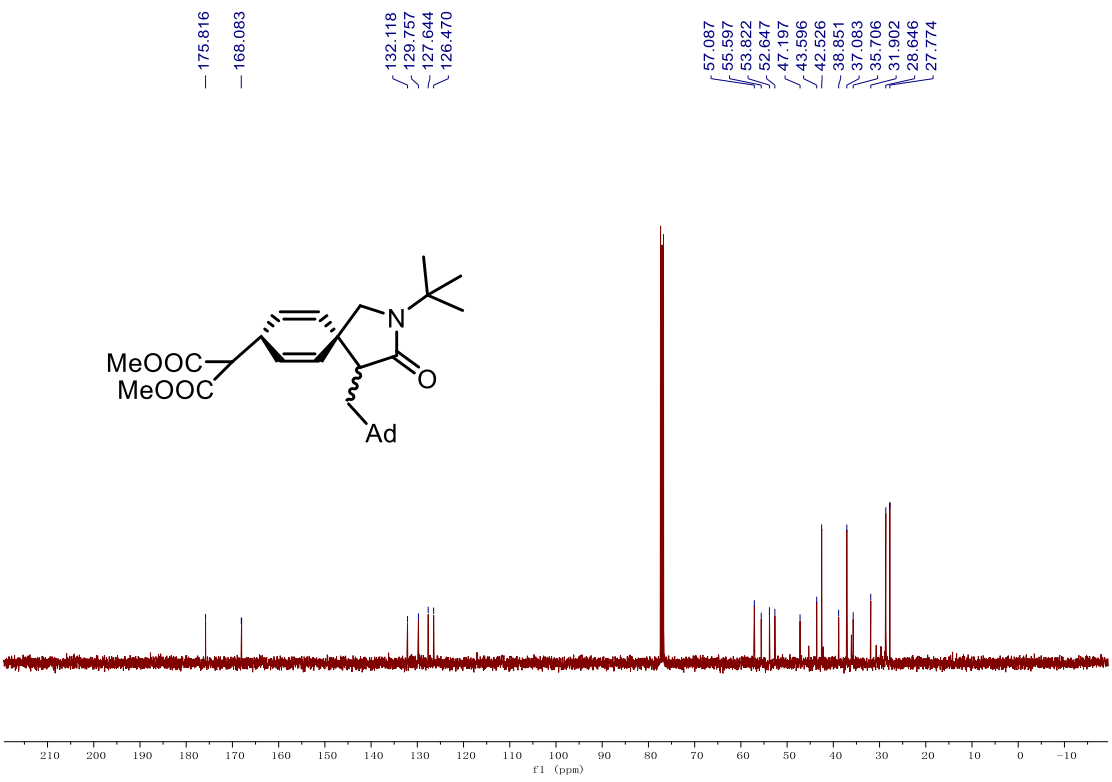
^{1}H NMR spectrum of **4aa** ($CDCl_3$, 400MHz)



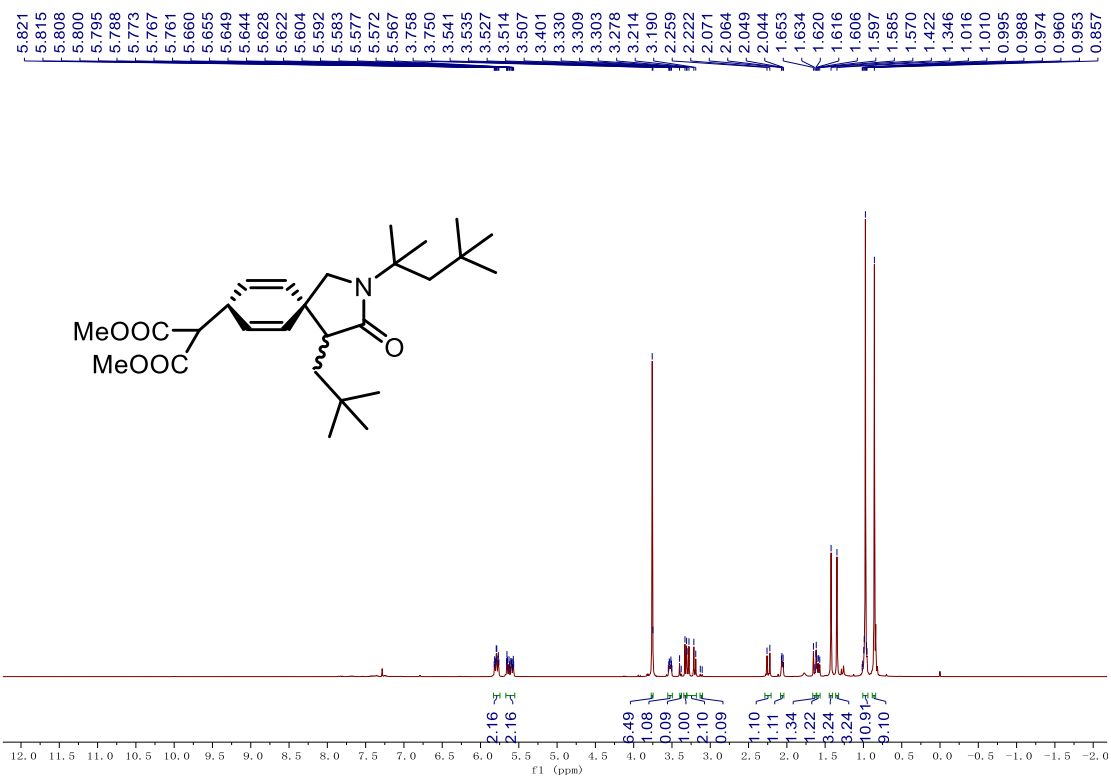
^{13}C NMR spectrum of **4aa** ($CDCl_3$, 101MHz)



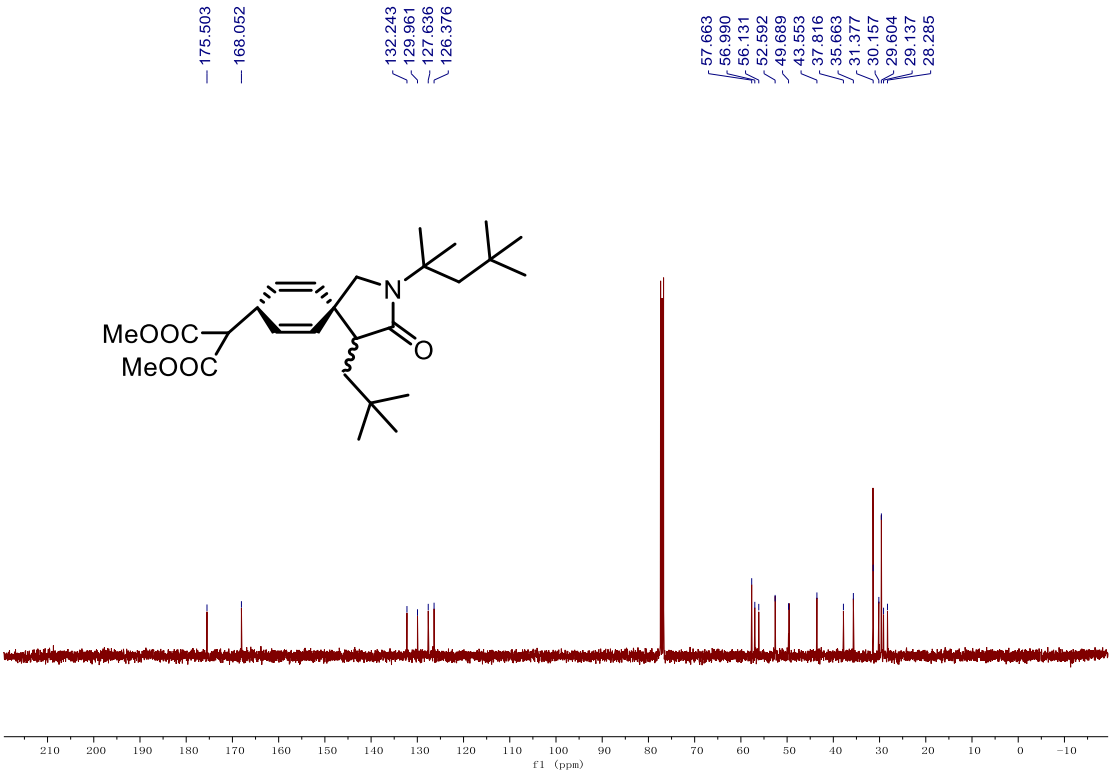
^{1}H NMR spectrum of **4ab** ($CDCl_3$, 400MHz)



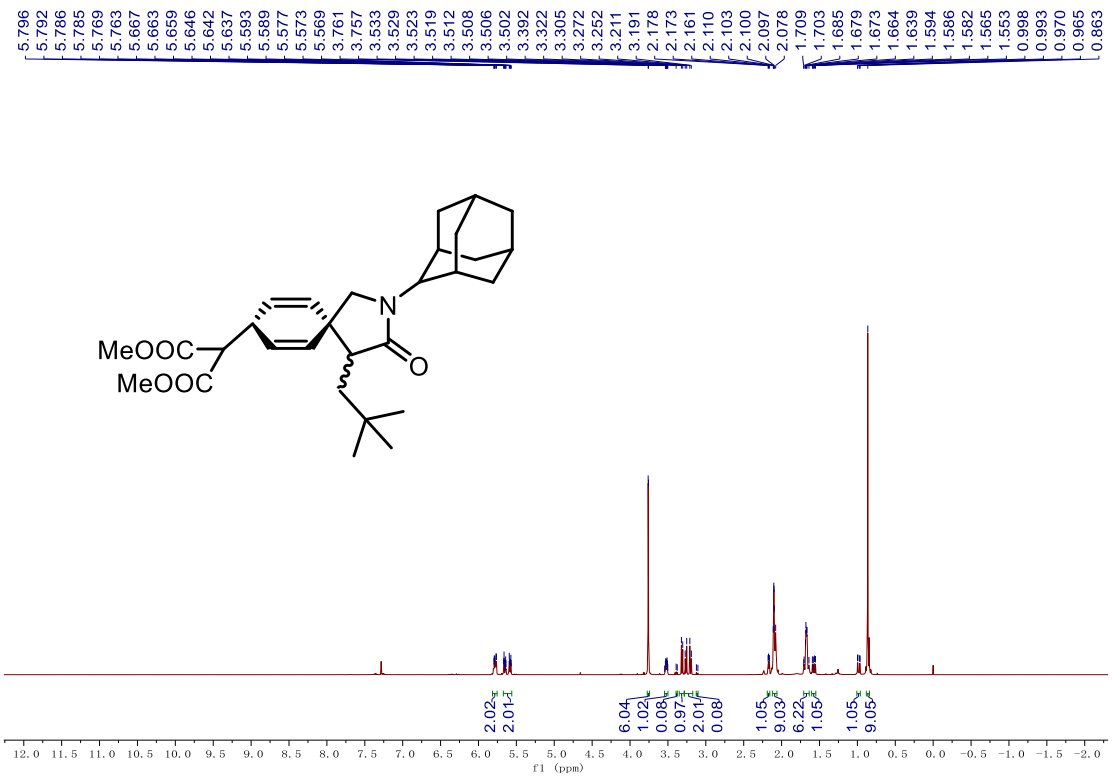
^{13}C NMR spectrum of **4ab** ($CDCl_3$, 101MHz)



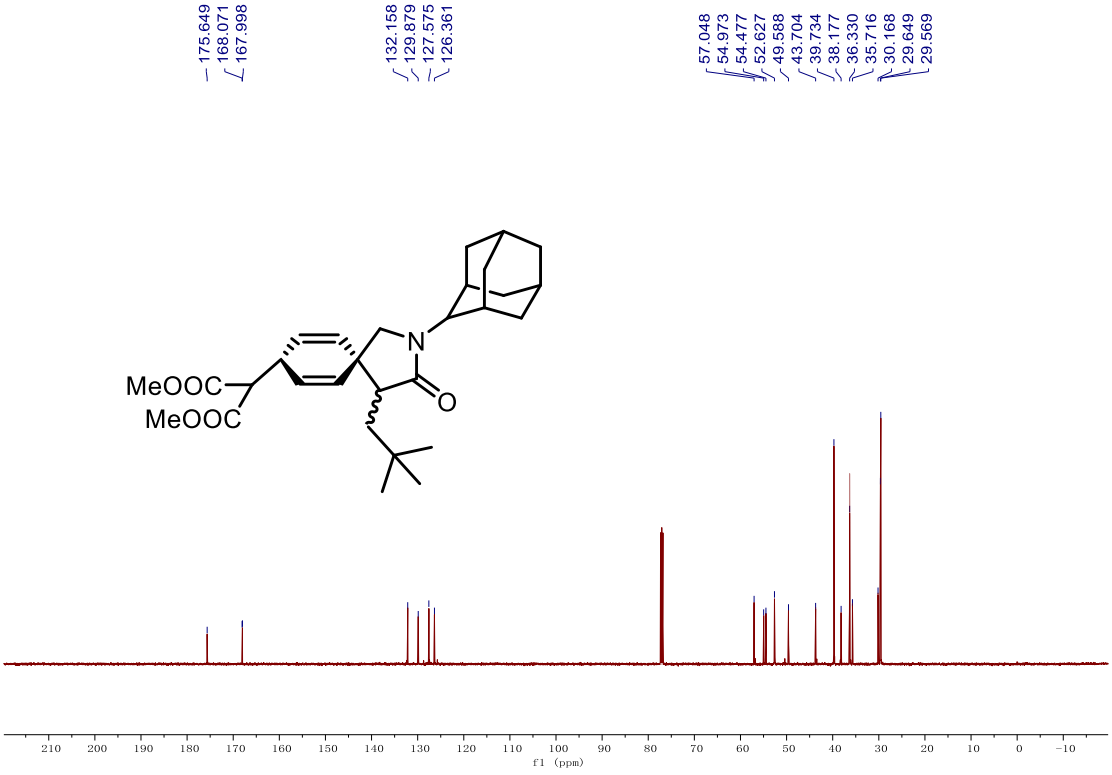
^{1}H NMR spectrum of **4ac** ($CDCl_3$, 400MHz)



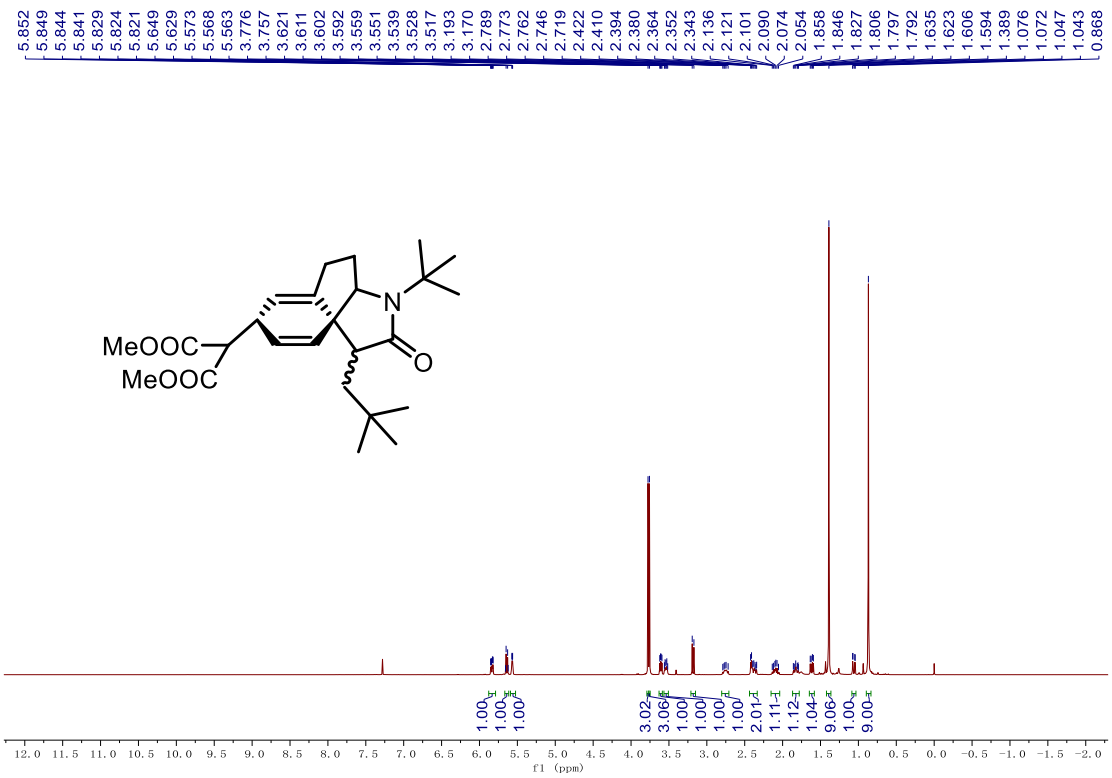
^{13}C NMR spectrum of **4ac** ($CDCl_3$, 101MHz)



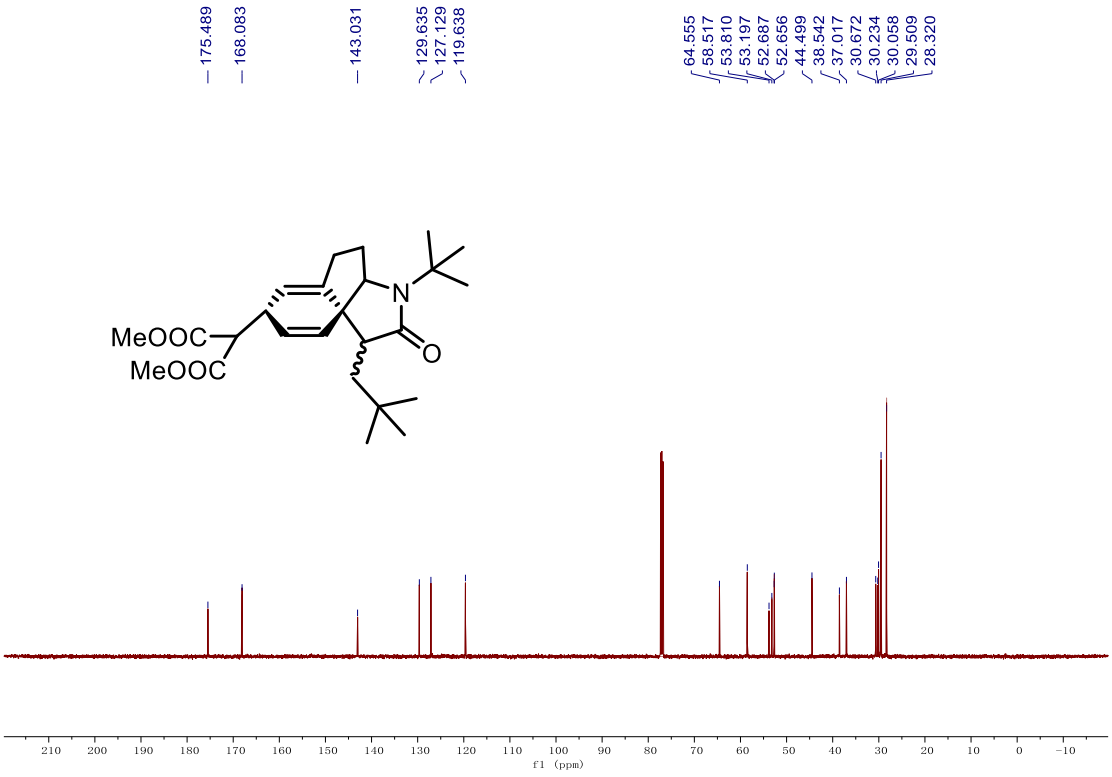
^{1}H NMR spectrum of **4ad** ($CDCl_3$, 500MHz)



^{13}C NMR spectrum of **4ad** ($CDCl_3$, 126MHz)



^{1}H NMR spectrum of **4ae** ($CDCl_3$, 500MHz)



^{13}C NMR spectrum of **4ae** ($CDCl_3$, 126MHz)