Supplementary Information

Aerobic oxidative C–C bond formation through C–H bond activation catalysed by flavin and iodine

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1. General

Melting points (M.p.) were determined on a SANSYO SMP-300 (SANSYO, Tokyo, Japan) and are uncorrected. The IR spectra were recorded on a JASCO FT/IR-660plus spectrophotometer (JASCO, Tokyo, Japan). The NMR spectra were measured using a JEOL JNM ECX-500 spectrometer (JEOL, Akishima, Japan) operating at 500 MHz for ^{1}H and 126 MHz for ^{13}C using tetramethylsilane (TMS) or a solvent residual peak as the internal standard. The electrospray ionization mass (ESI-MS) spectra were recorded on a Bruker microTOFII mass spectrometer (Bruker, Billerica, MA) using the positive or negative mode ESI-TOF method for acetonitrile solutions and sodium formate as the reference.

2. Materials

Riboflavin tetraacetate (**10b**),[S1] 5-ethyl-10-(2-hydroxylethyl)-3,7,8-trimethylisoalloxazinium triflate (**11a•TfO**),[S2] 5-ethyl-10-(2-hydroxylethyl)-7,8-dimethylisoalloxazinium triflate (**11b•TfO**),[S2] 5-ethyl-1,3,7,8-tetramethylalloxazinium triflate (**12a•TfO**),[S2] 5-ethyl-1,3-dimethylalloxazinium triflate (**12b•TfO**),[S2] 5-ethyl-1,3-dimethyl-8-trifluoromethylalloxazinium triflate (**12c•TfO**),[S2] 1,10-ethylene-3,7,8-trimethylisoalloxazinium chloride (**13a•Cl**),[S3] 1,10-ethylene-7,8-dimethylisoalloxazinium chloride (**13b•Cl**),[S4] 1,10-ethylene-3-methylisoalloxazinium chloride (**13c•Cl**),[S5] 1,10-ethylene-3-methyl-7-trifluoromethylalloxazinium chloride (**13d•Cl**),[S6] and 1,10-ethylene-3,7,8-trimethylisoalloxazinium triflate (**13a•TfO**)[S2] were synthesized according to the previously reported methods. Tetrahydroisoquinolines **1a-c**,[S7] **f**[S7], **d**,[S8] **e**,[S8] **h**[S9] and tetrahydroisoquinolinylacetate **6**[S10] were synthesized according to the previously reported method (Chart S1). Other starting materials including dimethylmalonate **2**s were purchased from Aldrich (Milwaukee, WI), FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan), Nacalai tesque (Kyoto, Japan), and Tokyo Kasei (TCI, Tokyo, Japan) and were used as received.

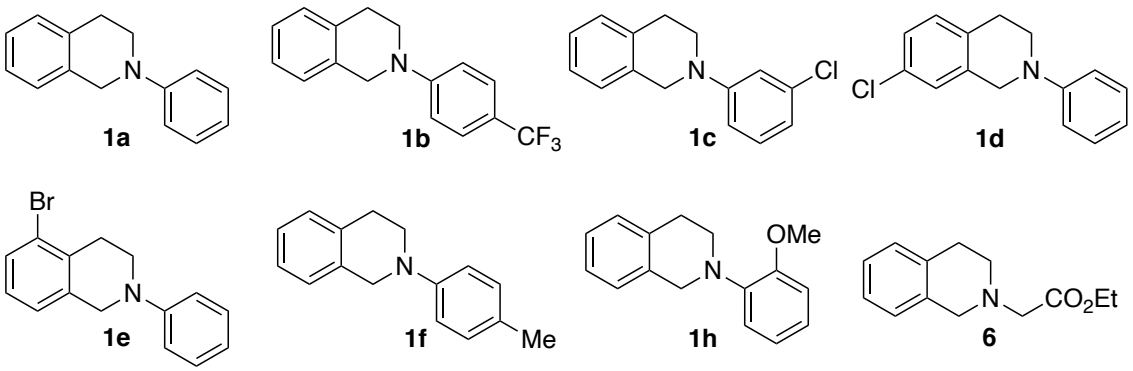
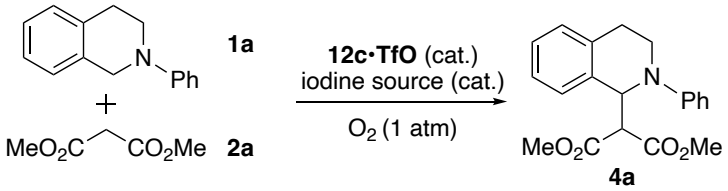


Chart S1. Structures of tetrahydroisoquinolines **1**s and tetrahydroisoquinolinylacetate **6**.

3. Experimental Procedures

Optimization of the reaction condition for the aerobic CDC between 1a and 2a. The effect of solvents, temperature, iodine sources, catalyst quantity, and reaction time on the aerobic CDC of **1a** and **2a** was investigated as shown in Table S1.

Table S1. Effect of solvents, temperature, iodine sources, catalyst quantity, and reaction time[a]

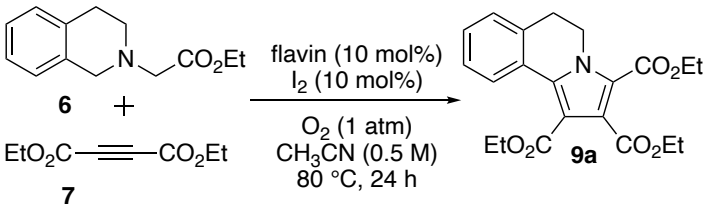


Entry	**2a** (eq.)	Solvent	Iodine	Flavin (mol%)	Temperature (°C)	Time (h)	Yield (%)
1	3	CH_3CN (0.5)	I_2 (5 mol%)	5	40	18	60
2	3	DMF (0.5)	I_2 (5 mol%)	5	40	18	19
3	3	pyridine (0.5)	I_2 (5 mol%)	5	40	18	20
4	3	$CHCl_3$ (0.5)	I_2 (5 mol%)	5	40	18	61
5	3	AcOEt (0.5)	I_2 (5 mol%)	5	40	18	44
6	3	dioxane (0.5)	I_2 (5 mol%)	5	40	18	58
7	3	MeOH (0.5)	I_2 (5 mol%)	5	40	18	33
8	3	*t*-BuOH (0.5)	I_2 (5 mol%)	5	40	18	55
9	3	-	I_2 (5 mol%)	5	40	18	68
10	8.7	-	I_2 (5 mol%)	5	40	18	73
11	8.7	-	I_2 (5 mol%)	5	25	18	52
12	8.7	-	I_2 (5 mol%)	5	60	18	80
13	8.7	-	KI (10 mol%)	5	40	18	19
14	8.7	-	NH_4I (10 mol%)	5	40	18	46
15	8.7	-	HI (10 mol%)	5	40	18	68
16	8.7	-	I_2 (5 mol%)	2	40	18	58
17	8.7	-	I_2 (5 mol%)	5	40	24	74
18	8.7	-	I_2 (5 mol%)	5	40	32	75
19	8.7	-	I_2 (5 mol%)	5	40	48	78
20	8.7	-	I_2 (5 mol%)	5	40	48	79[b]

[a]Conditions: **1a** (0.3 mmol), **2a**, **12c•TfO**, iodine source, and solvent under O_2 (1 atm). Yield was determined by ^{1}H NMR using 1,3,5-trioxane as an internal standard. [b]Under air (1 atm, balloon).

Effects of catalyst on the catalytic activity of the reaction of 6 with 7. We examined the catalytic activity of the flavin catalysts for the reaction of **6** with **7** (Table S2). Among the seven flavins, **13a•TfO** showed the most efficient catalytic activity.

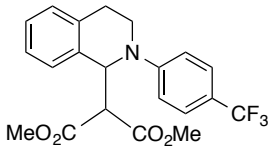
Table S2. Comparison with the catalytic activity of flavins for the reaction of **6** with **7**[a]



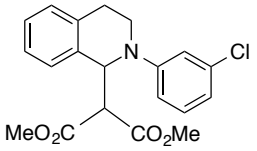
Entry	Flavin (mol%)	E_1[b] (V vs Fc/Fc$^+$)	Yield (%)
1	**11a•TfO**	-0.136	8
2	**11b•TfO**	-0.118	9
3	**12a•TfO**	-0.425	8
4	**12c•TfO**	-0.168	29
5	**13a•TfO**	-0.650	36
6	**13a•Cl**	-0.650[c]	27
7	**13b•Cl**	-0.608[c]	13
8	**13d•Cl**	-0.426[c]	22

[a]Conditions: **6** (0.3 mmol), **7** (1.5 eq.), flavin (10 mol%), and I_2 (10 mol%) under O_2 (1 atm) at 80 °C for 24 h. Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b]From refs. S2, S11, and S12. [c]The TfO salts were used for electrochemical measurements.

Spectroscopic data of products

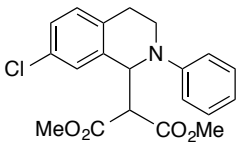


Spectroscopic data of 2-(2-(4-trifluoromethyl)-1,2,3,4-tetrahydroisoquinoline-1-yl)-malonic acid dimethyl ester (**4b**):[S11] The yield was determined to be 87% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate/triethylamine = 94/1/5, v/v) afforded the desired product (111 mg, 90%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.44 (d, J = 10.9 Hz, 2H), 7.24-7.12 (m, 4H), 7.01 (d, J = 11.1 Hz, 2H), 5.81 (d, J = 11.8 Hz, 1H), 3.90 (d, J = 11.7 Hz, 1H), 3.76-3.70 (m, 1H), 3.68 (s, 3H), 3.62-3.55 (m, 1H), 3.50 (s, 3H), 3.11-2.99 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 25 °C, δ): 168.2, 167.3, 150.8, 135.6, 134.6, 128.9, 128.2, 127.1, 126.5, 126.0, 119.6 (q, J = 133 Hz), 113.3, 59.0, 57.6, 52.8, 42.6, 26.6.

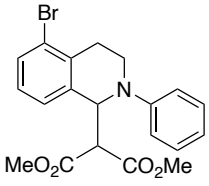
Spectroscopic data of 2-(2-(3-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline-1-yl)-malonic acid dimethyl ester (**4c**):[S11] 

The yield was determined to be 94% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate = 30/1) afforded the desired product (92.4 mg, 82%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.22-7.19 (m, 2H), 7.16-7.11 (m, 3H), 6.92 (t, J = 2.2 Hz, 1H), 6.88 (dd, J = 8.4, 2.3 Hz, 1H), 6.73-6.71 (m, 1H), 5.67 (d, J = 9.5 Hz, 1H), 3.91 (d, J = 9.5 Hz, 1H), 3.70-3.65 (m, 4H), 3.58-3.53 (m, 4H), 3.11-3.05 (m, 1H), 2.94 (dt, J = 16.4, 5.7 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 25 °C, δ): 168.2, 167.3, 149.8, 135.5, 135.1, 134.7, 130.2, 129.0, 128.0, 127.2, 126.4, 118.3, 114.5, 113.0, 59.1, 58.0, 52.8, 42.5, 26.3.

Spectroscopic data of 2-(7-chloro-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-yl)-malonic acid dimethyl ester (**4d**): The yield was determined to be 81% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate = 30/1 to 10/1, v/v) afforded the desired product (70.7 mg, 63%) as a colorless oil. IR (neat, cm^{-1}): 2952, 2922, 1734, 1594, 1488, 1434, 1268, 945, 753. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.25-7.20 (m, 3H), 7.15 (dd, J = 8.2, 2.2 Hz, 1H), 7.04 (d, J = 8.2 Hz, 1H), 6.96 (d, J = 8.0 Hz, 2H), 6.79 (t, J = 7.3 Hz, 1H), 5.63 (d, J = 9.5 Hz, 1H), 3.93 (d, J = 9.5 Hz, 1H), 3.70 (s, 3H), 3.66 (dd, J = 8.1, 4.8 Hz, 2H), 3.57 (s, 3H), 3.04-2.97 (m, 1H), 2.78 (dt, J = 16.7, 4.7 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 25 °C, δ): 168.2, 167.2, 148.7, 137.3, 133.3, 131.6, 130.5, 129.3, 127.9, 127.2, 119.3, 115.7, 59.0, 58.0, 52.8, 52.7, 42.0, 25.4. Anal. Calcd for $C_{20}H_{20}ClNO_4$: C, 64.26; H, 5.39; N, 3.75. Found: C, 64.07; H, 5.26; N, 3.94.

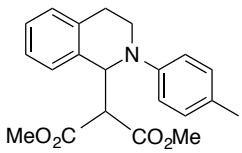


Spectroscopic data of 2-(5-bromo-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-yl)-malonic acid dimethyl ester (**4e**): The yield was determined to be 88% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate = 20/1) afforded the desired product (33.6 mg, 54%) as a colorless oil. IR (neat, cm^{-1}): 3025, 2952, 1732, 1596, 1436, 1267, 1146, 1030, 752. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.28 (s, 1H) 7.26-7.20 (m, 3H), 7.12 (d, J = 8.3 Hz, 1H), 6.95 (d, J = 8.0 Hz,

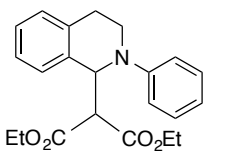


2H), 6.79 (t, J = 7.3 Hz, 1H), 5.63 (d, J = 9.4 Hz, 1H), 3.92 (d, J = 9.3 Hz, 1H), 3.66-3.64 (m, 5H), 3.56 (s, 3H), 3.07-3.00 (m, 1H), 2.82 (dt, J = 16.7, 4.8 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 168.3, 167.3, 148.7, 137.3, 134.7, 132.0, 129.32, 129.28, 129.0, 121.6, 119.3, 115.7, 59.0, 57.9, 52.8, 41.9, 25.9. Anal. Calcd for $C_{20}H_{20}BrNO_4$: C, 57.43; H, 4.82; N, 3.35. Found: C, 57.05; H, 4.43; N, 3.54.

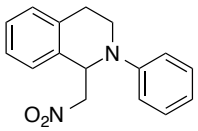
Spectroscopic data of 2-(2-*p*-tolyl-1,2,3,4-tetrahydroisoquinoline-1-yl)-malonic acid dimethyl ester (**4f**):[S13] The yield was determined to be 90% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate = 30/1, v/v) afforded the desired product (71.2 mg, 67%) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.20-7.14 (m, 2H), 7.10-7.07 (m, 2H), 7.01 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 5.61 (d, J = 9.5 Hz, 1H), 3.96 (d, J = 9.4 Hz, 1H), 3.69-3.59 (m, 5H), 3.57 (s, 3H), 3.07-3.01 (m, 1H), 2.79 (dt, J = 16.5, 4.7 Hz, 1H), 2.22 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 168.4, 167.6, 146.8, 135.6, 134.9, 129.7, 129.2, 128.3, 127.6, 127.2, 126.0, 116.0, 59.2, 58.7, 52.64, 52.59, 42.4, 25.8, 20.4.



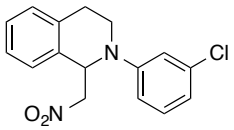
Spectroscopic data of 2-(2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-yl)-malonic acid diethyl ester (**4g**):[S9] The yield was determined to be 82% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate = 30/1 to 20/1, v/v) afforded the desired product (64.1 mg, 58%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.26-7.09 (m, 6H), 6.98 (d, J = 8.0 Hz, 2H), 6.74 (t, J = 7.2 Hz, 1H), 5.72 (d, J = 9.2 Hz, 1H), 4.18-3.94 (m, 4H), 3.90 (d, J = 9.2 Hz, 1H), 3.73-3.61 (m, 2H), 3.10-3.03 (m, 1H), 2.88 (dt, J = 16.4, 5.1 Hz, 1H), 1.16 (t, J = 7.2 Hz, 3H), 1.08 (t, J = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 168.1, 167.3, 149.0, 136.1, 134.9, 129.2, 129.0, 127.6, 127.3, 126.1, 118.6, 115.2, 61.7, 59.7, 58.0, 42.4, 26.2, 14.04, 13.99.



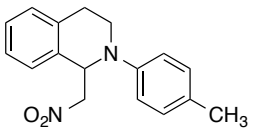
Spectroscopic data of 1-(nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**5a**):[S9] The yield was determined to be 85% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate=15/1, v/v) afforded the desired product (58.6 mg, 73%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.28-7.16 (m,



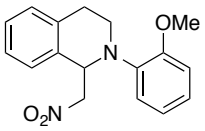
5H), 7.11 (d, J = 7.4 Hz, 1H), 6.97 (d, J = 8.2 Hz, 2H), 6.84 (t, J = 7.3 Hz, 1H), 5.54 (t, J = 7.2 Hz, 1H), 4.85 (dd, J = 11.8, 7.9 Hz, 1H), 4.54 (dd, J = 11.8, 6.6 Hz, 1H), 3.67-3.57 (m, 2H), 3.10-3.04 (m, 1H), 2.77 (dt, J = 16.3, 4.9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 148.5, 135.4, 133.0, 129.6, 129.3, 128.2, 127.1, 126.8, 119.5, 115.2, 78.9, 58.3, 42.1, 26.5.



Spectroscopic data of 2-(3-chlorophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**5c**):[S14] The yield was determined to be 69% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/diethyl ether=30/1 to 5/1, v/v) afforded the desired product (57.3 mg, 64%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.27-7.12 (m, 5H), 6.92 (t, J = 2.2 Hz, 1H), 6.85 (dd, J = 8.4, 2.5 Hz, 1H), 6.79 (dd, J = 8.0, 1.8 Hz, 1H), 5.51 (t, J = 7.3 Hz, 1H), 4.84 (dd, J = 12.0, 8.0 Hz, 1H), 4.56 (dd, J = 12.1, 6.7 Hz, 1H), 3.66-3.57 (m, 2H), 3.11-3.05 (m, 1H), 2.80 (dt, J = 16.4, 5.1 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 149.6, 135.4, 135.1, 132.5, 130.6, 129.3, 128.4, 127.1, 127.0, 119.3, 114.8, 112.9, 78.7, 58.1, 42.1, 26.4



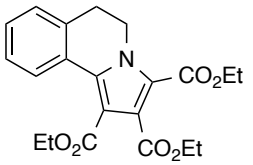
Spectroscopic data of 1-(nitromethyl)-2-*p*-tolyl-1,2,3,4-tetrahydroisoquinoline (**5f**):[S14] The yield was determined to be 88% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2,hexane/ethyl acetate=10/1, v/v) afforded the desired product (72.0 mg, 85%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.24-7.15 (m, 3H), 7.11 (d, J = 7.3 Hz, 1H), 7.06 (d, J = 8.4 Hz, 2H), 6.87 (dt, J = 8.6, 2.5 Hz, 2H), 5.48 (t, J = 7.3 Hz, 1H), 4.83 (dd, J = 11.9, 8.2 Hz, 1H), 4.53 (dd, J = 11.9, 6.3 Hz, 1H), 3.65-3.53 (m, 2H), 3.07-3.01 (m, 1H), 2.73 (dt, J = 16.4, 4.5 Hz, 1H), 2.25 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 146.5, 135.5, 133.0, 130.1, 129.4, 129.2, 128.1, 127.1, 126.7, 116.0, 78.9, 58.5, 42.4, 26.3, 20.5.



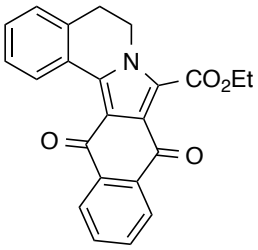
Spectroscopic data of 2-(2-methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**5h**):[S9] The yield was determined to be 71% by ^{1}H NMR measurement of the reaction mixture. Column chromatography (SiO_2, hexane/ethyl acetate=10/1, v/v) afforded the desired product (56.5 mg, 63%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.25-

7.20 (m, 2H), 7.16-7.14 (m, 2H), 7.02 (td, J = 7.7, 1.8 Hz, 1H), 6.89-6.82 (m, 3H), 5.50 (dd, J = 8.3, 5.0 Hz, 1H), 4.82 (dd, J = 12.0, 8.4 Hz, 1H), 4.53 (dd, J = 12.1, 5.0 Hz, 1H), 3.62-3.58 (m, 1H), 3.51-3.45 (m, 1H), 3.02-2.95 (m, 1H), 2.71 (ddd, J = 16.5, 4.0, 2.3 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 153.2, 139.0, 135.5, 133.8, 129.7, 127.7, 127.0, 126.6, 124.2, 122.1, 121.1, 112.6, 79.3, 58.3, 55.9, 43.1, 27.0

Spectroscopic data of triethyl 5,6-dihydropyrro[1,2-*a*]isoquinoline-1,2,3-tricarboxylate (**9a**):[S15] Column chromatography (SiO_2, hexane/CH_2Cl_2 = 1:1 to 2:8,v/v) afforded the desired product (60.7 mg, 52%) as an orange solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 8.20-8.16 (m, 1H), 7.34-7.29 (m, 2H), 7.26-7.24 (m, 1H), 4.54 (t, 2H), 4.38 (q, J = 7.2 Hz, 2H), 4.34-4.29 (m, 4H), 3.00 (t, J = 6.5 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H), 1.36-1.32 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 166.2, 163.5, 160.0, 136.8, 134.4, 129.3, 128.6, 127.4, 127.0, 126.5, 119.1, 110.8, 61.6, 61.1, 60.8, 42.6, 29.4, 14.21, 14.17, 14.1.



Spectroscopic data of ethyl 9,14-dioxo-5,6,9,14-tetrahydrobenzo[5,6]isoindolo[1,2-*a*]isoquinoline-8-carboxylate (**9b**):[S15] Column chromatography (SiO_2, hexane/ethyl acetate/triethylamine = 99/1/0.2, v/v) afforded the desired product (61.9 mg, 56%) as an orange solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 8.99 (dd, J = 8.0, 0.8 Hz, 1H), 8.31-8.27 (m, 1H), 8.23-8.19 (m, 1H), 7.74-7.68 (m, 2H), 7.45 (td, J = 7.6, 1.1 Hz, 1H), 7.37 (td, J = 7.4, 1.3 Hz, 1H), 7.27 (d, J = 7.0 Hz, 1H, overlapped with $CHCl_3$), 4.55 (q, J = 7.2 Hz, 2H), 4.29 (t, J = 6.6 Hz, 2H), 3.10 (t, J = 6.6 Hz, 2H), 1.50 (t, J = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$, 25 °C, δ): 179.9, 179.6, 161.6, 135.8, 134.8, 133.8, 133.4, 133.1, 130.2, 129.0, 127.6, 127.3, 126.7, 126.5,126.2, 123.3, 117.6, 62.6, 43.3, 29.2, 14.1.



ESI-MS Analysis of 14a. The reaction intermediate **14a** was confirmed by ESI-TOF-MS measurement of the reaction mixture obtained after stirring for 12 h under the standard condition (Scheme 3C, Figure S1).

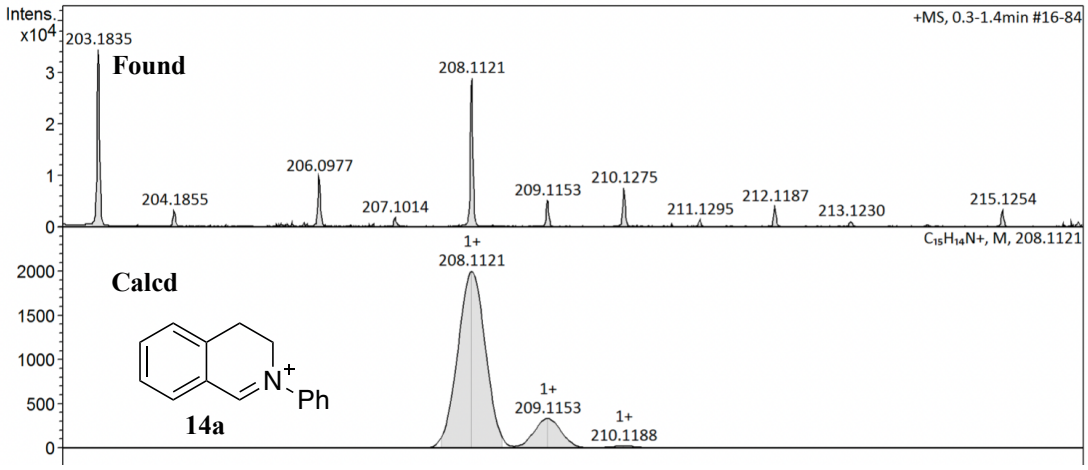
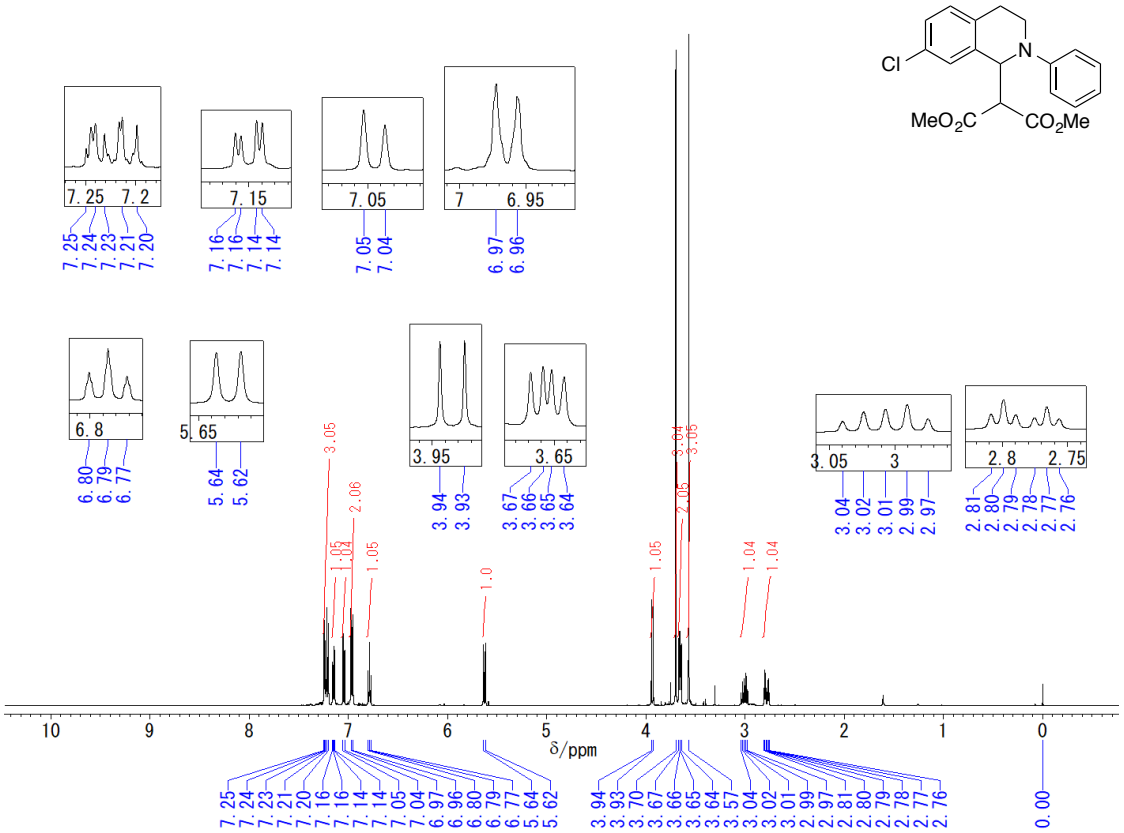
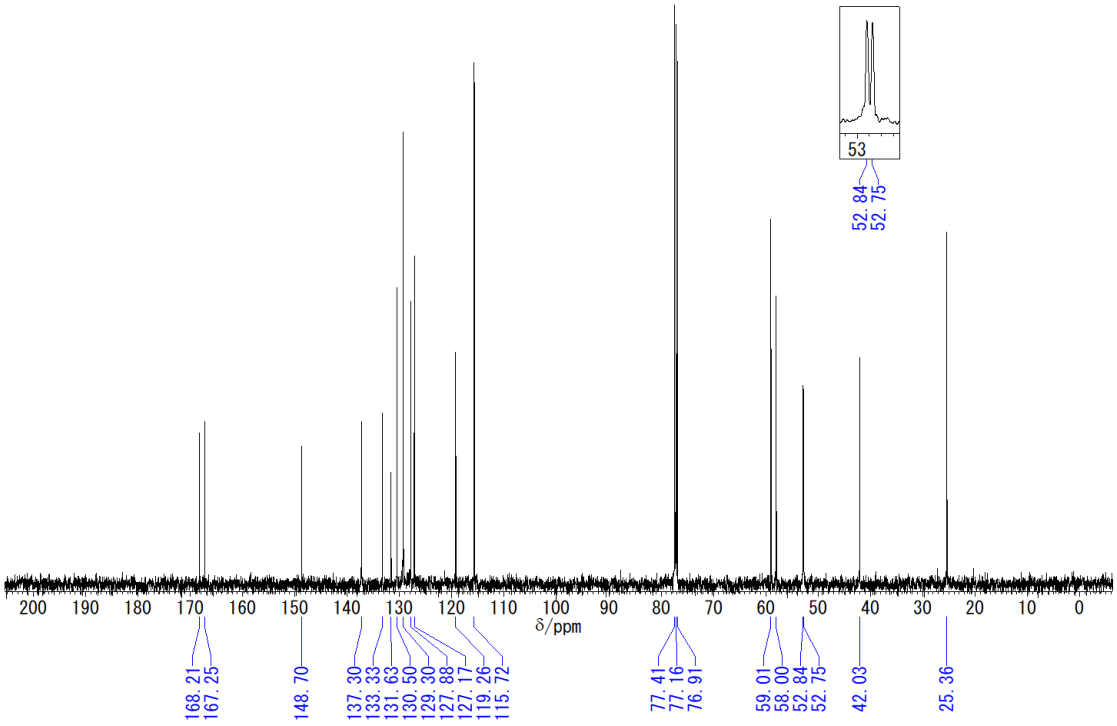


Figure S1. ESI-TOF mass spectrum of the reaction mixture.

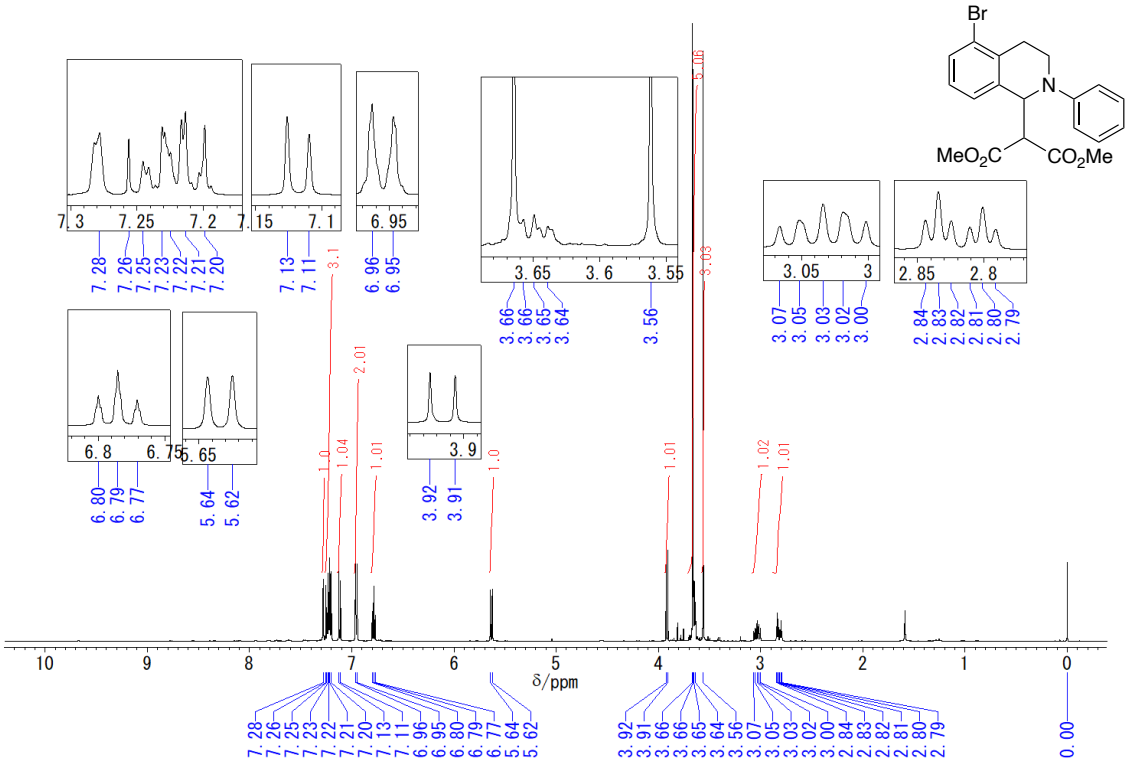
4. ^{1}H and $^{13}C\{^{1}H\}$ NMR Spectra of Novel Compounds



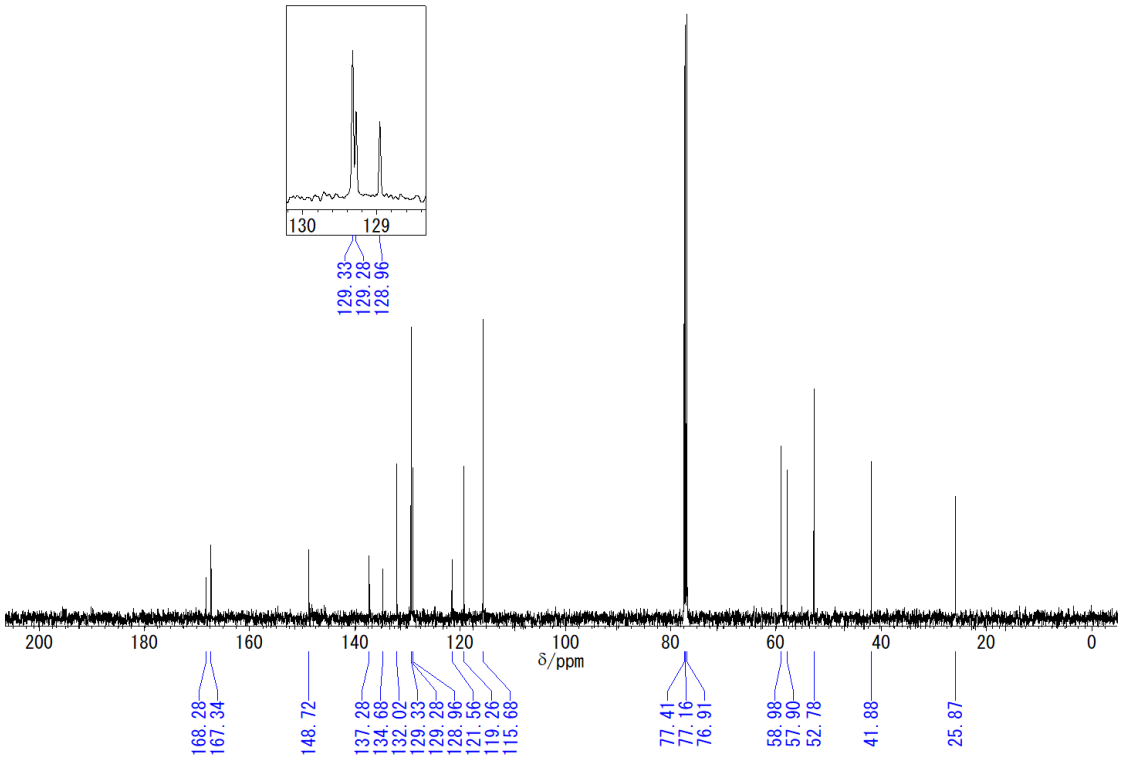
Spectrum S1. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **4d**.



Spectrum S2. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **4d**.

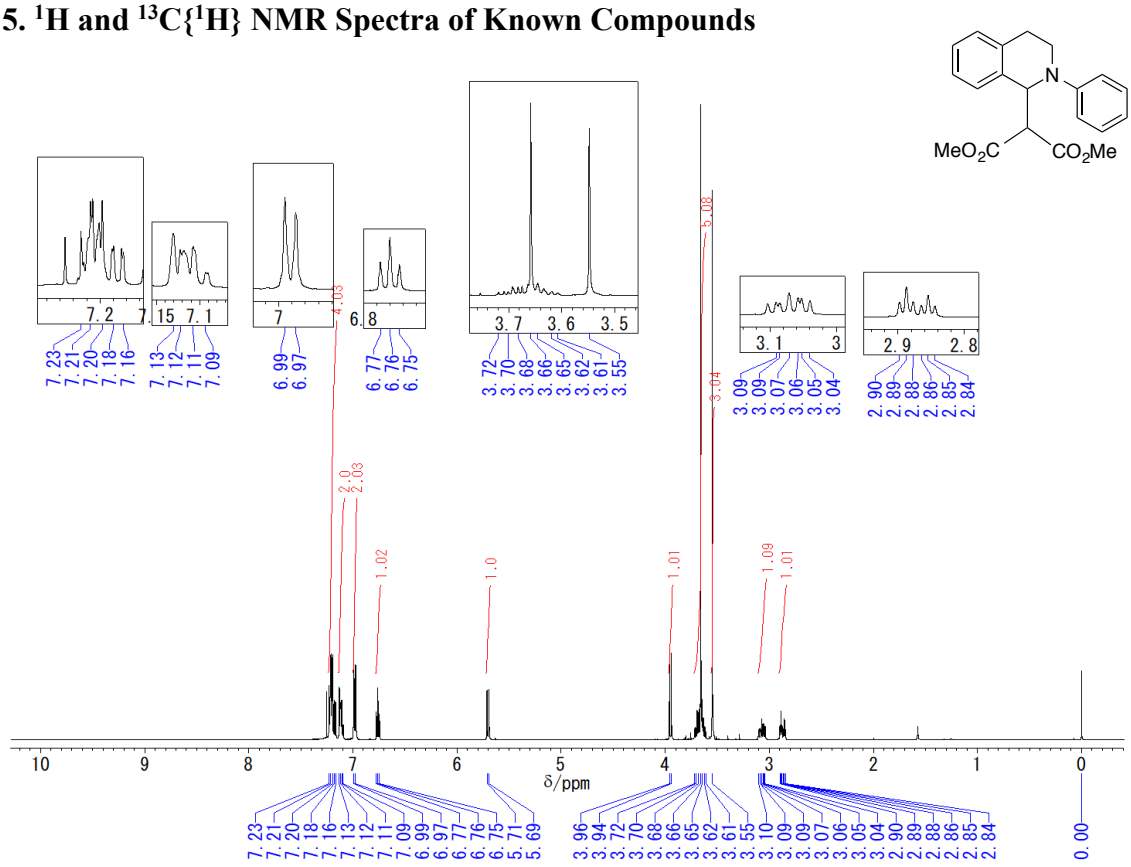


Spectrum S3. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **4e**.

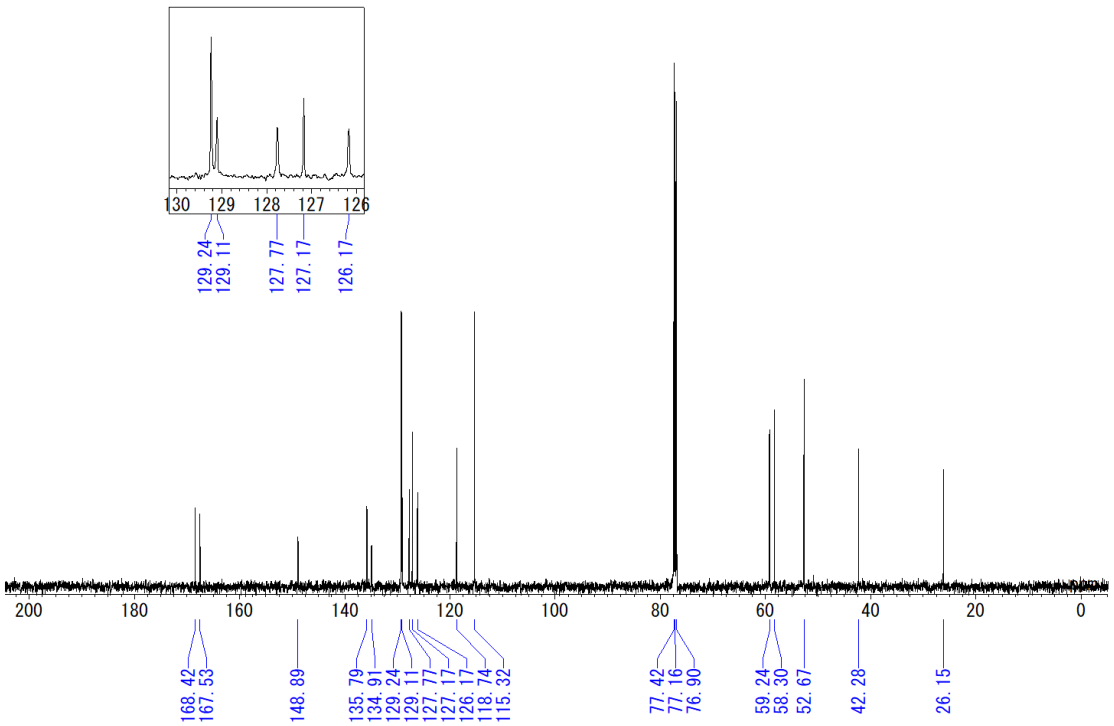


Spectrum S4. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **4e**.

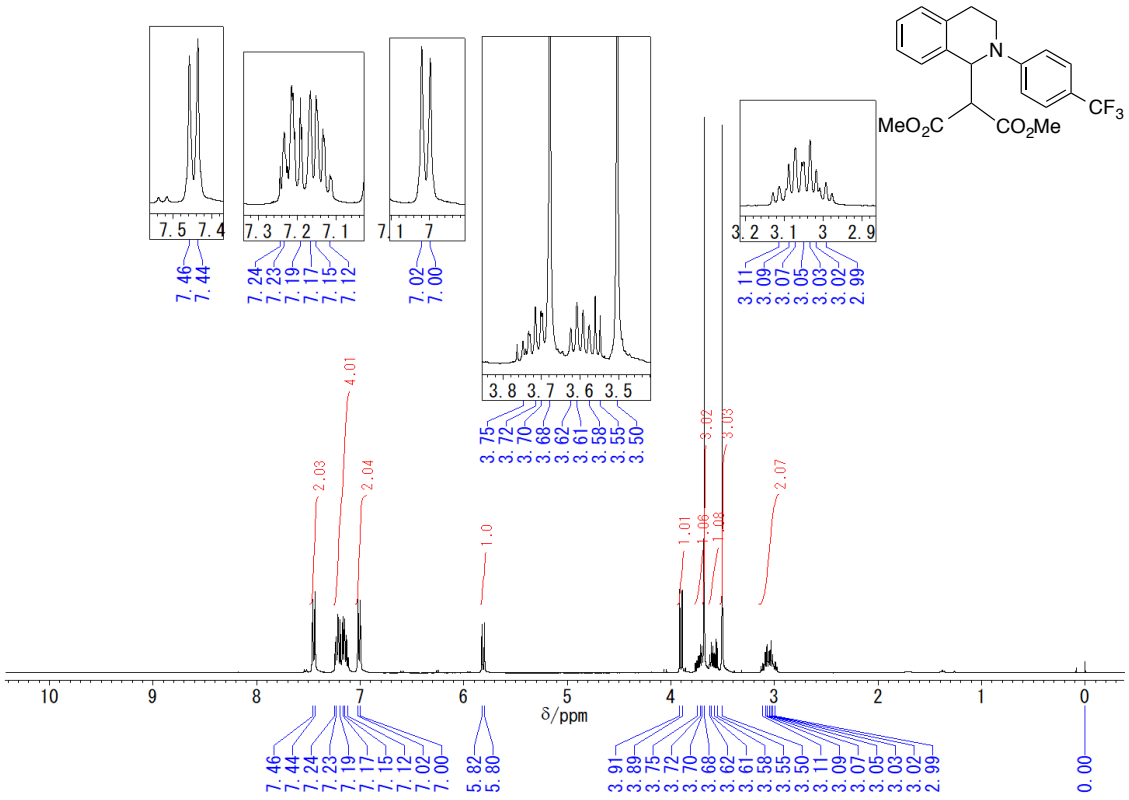
5. ^{1}H and $^{13}C\{^{1}H\}$ NMR Spectra of Known Compounds



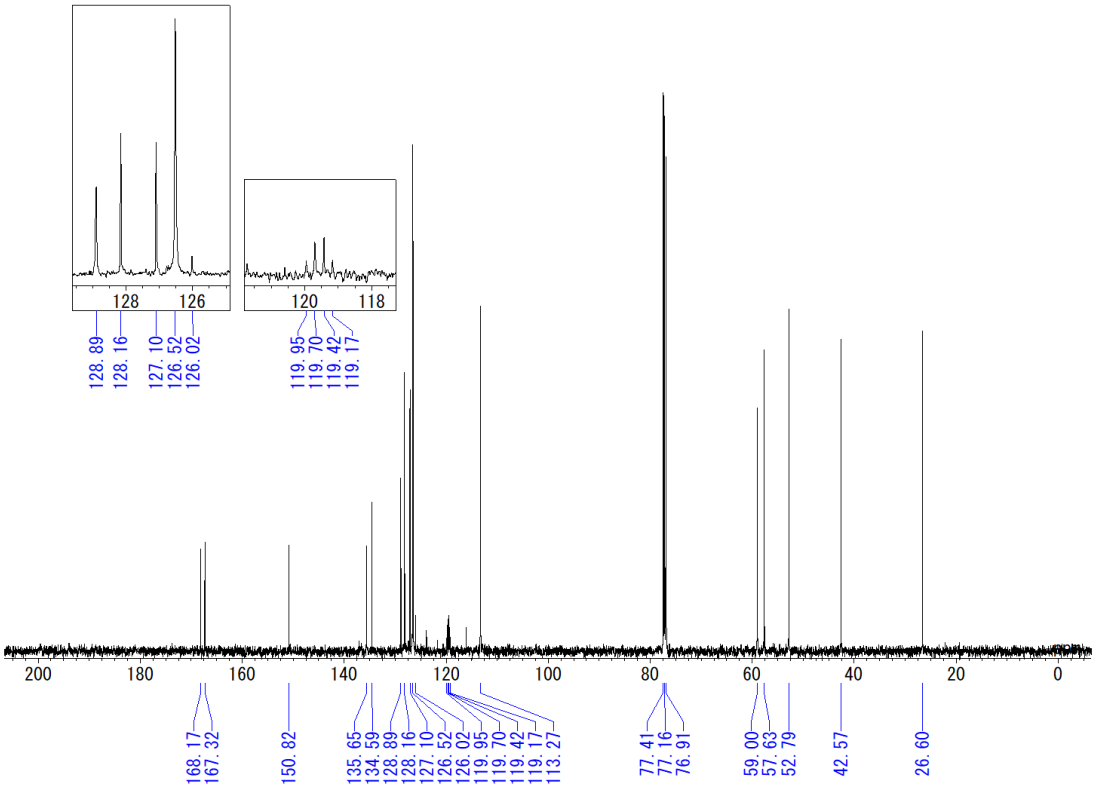
Spectrum S5. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **4a**.



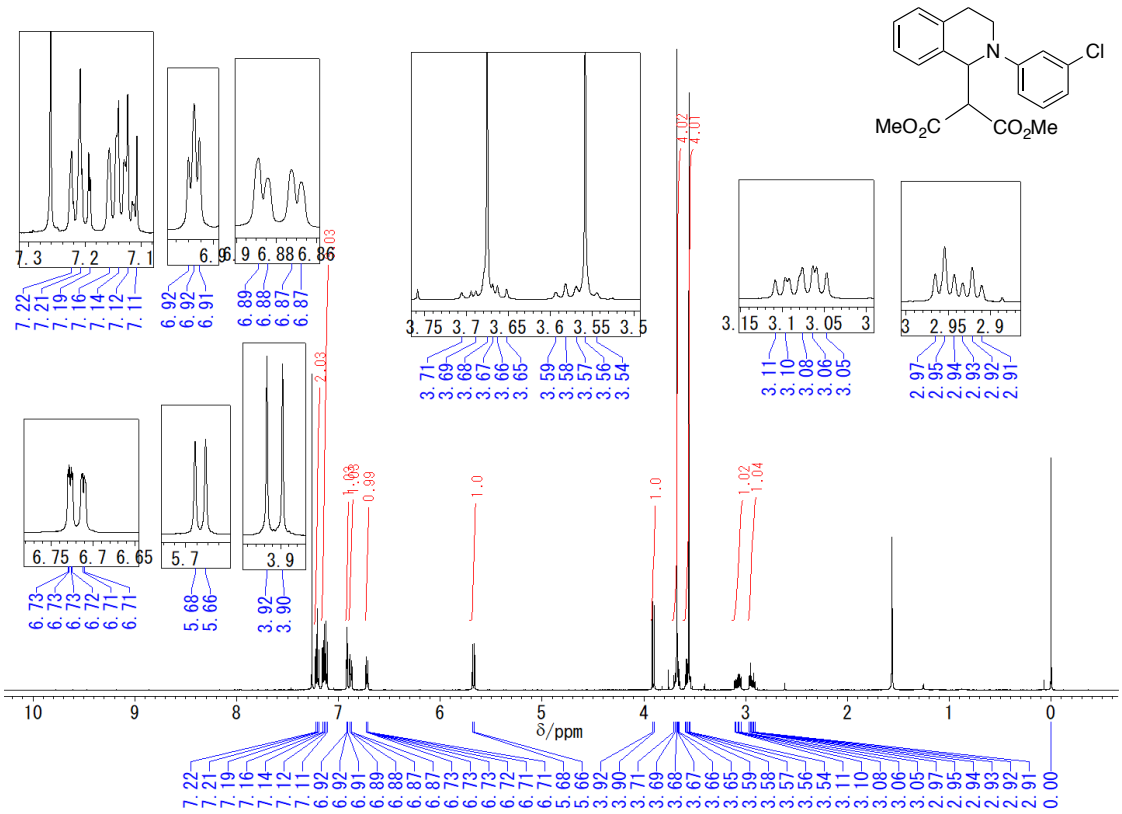
Spectrum S6. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **4a**.



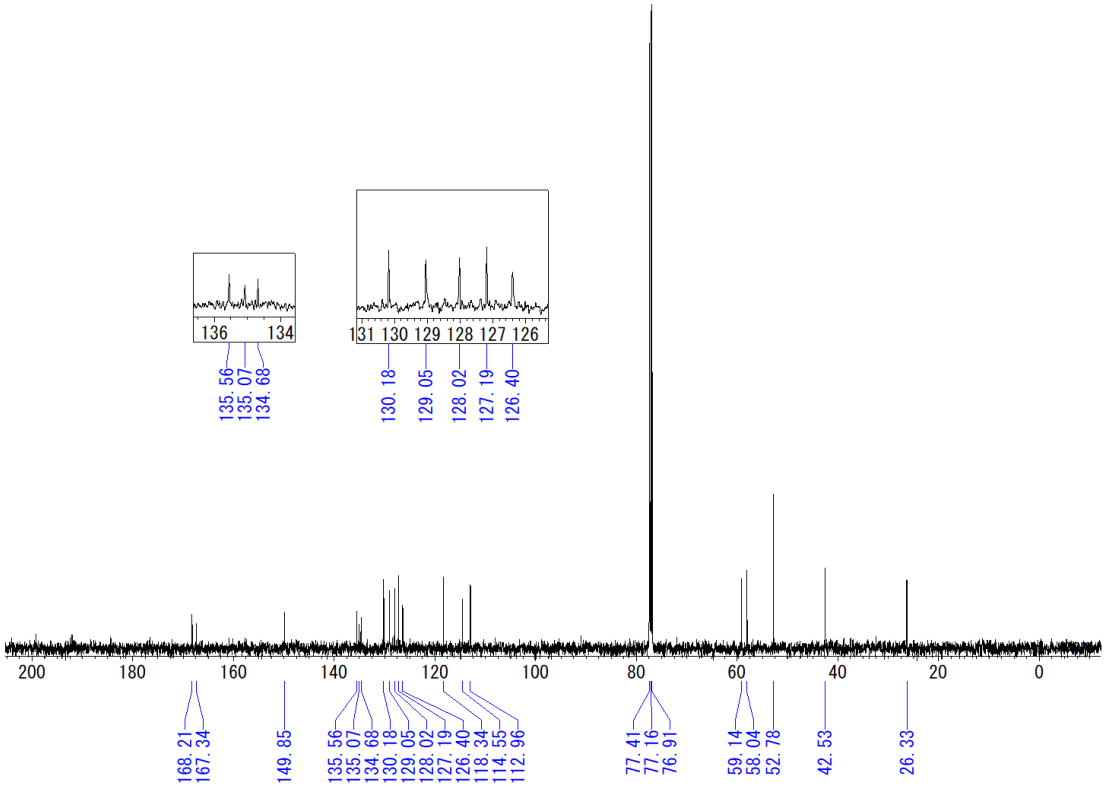
Spectrum S7. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **4b**.



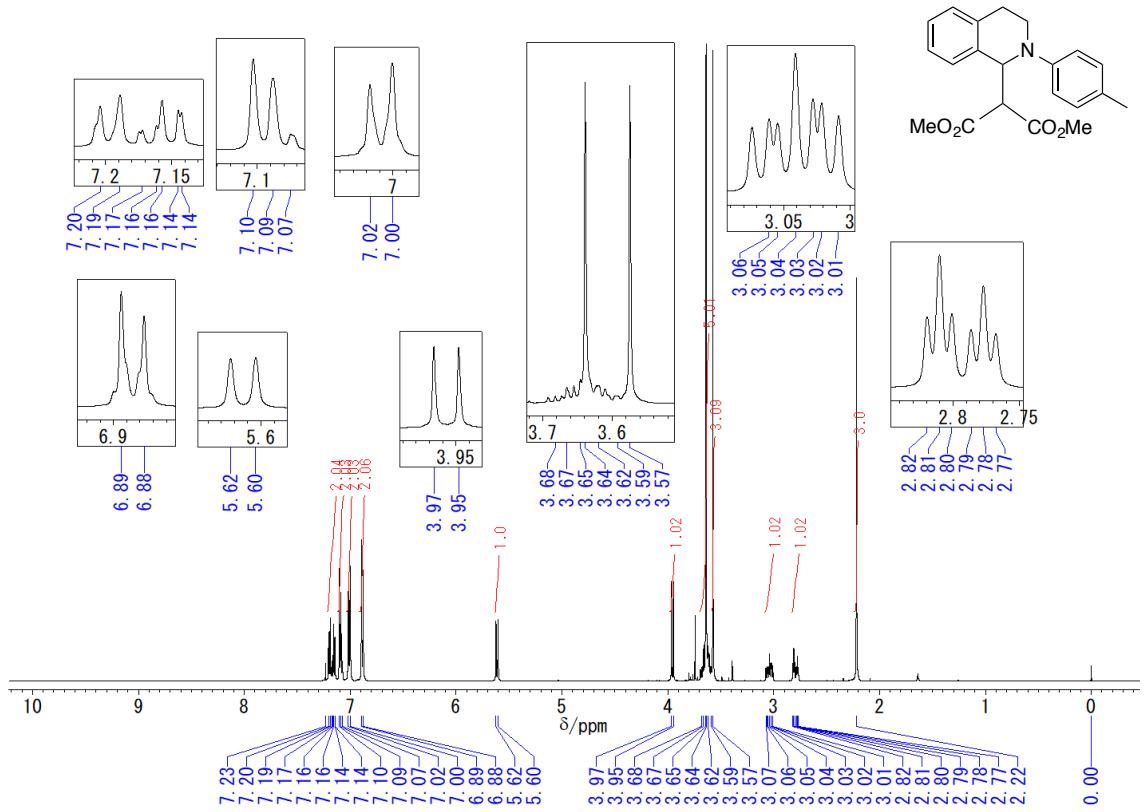
Spectrum S8. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **4b**.



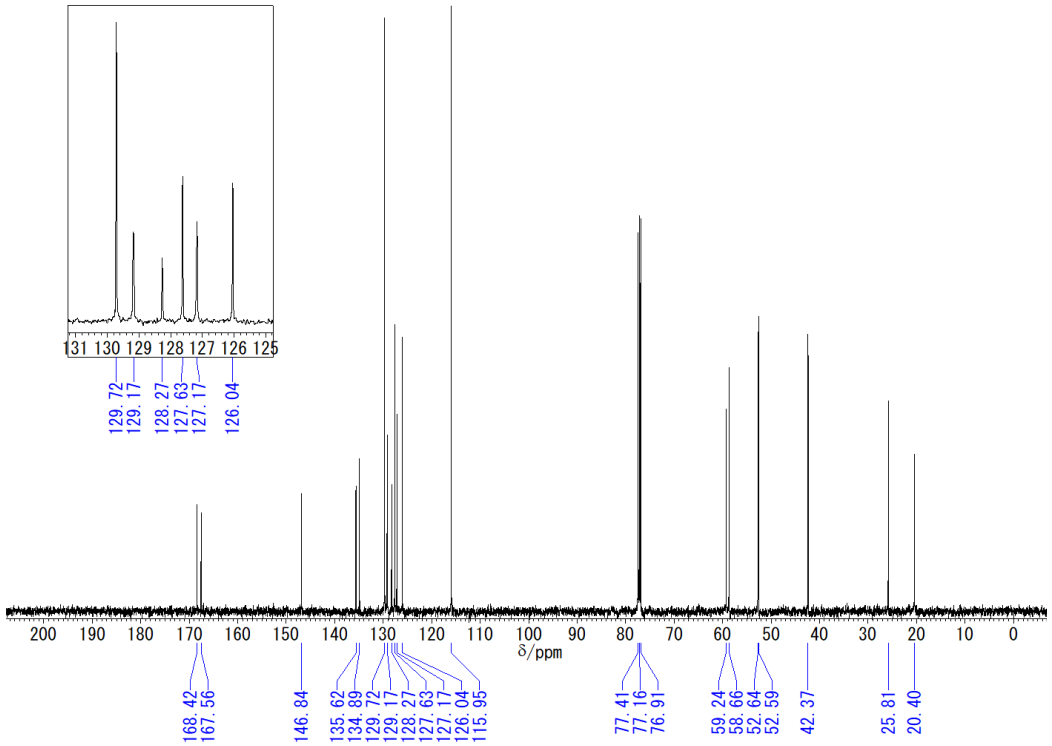
Spectrum S9. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **4c**.



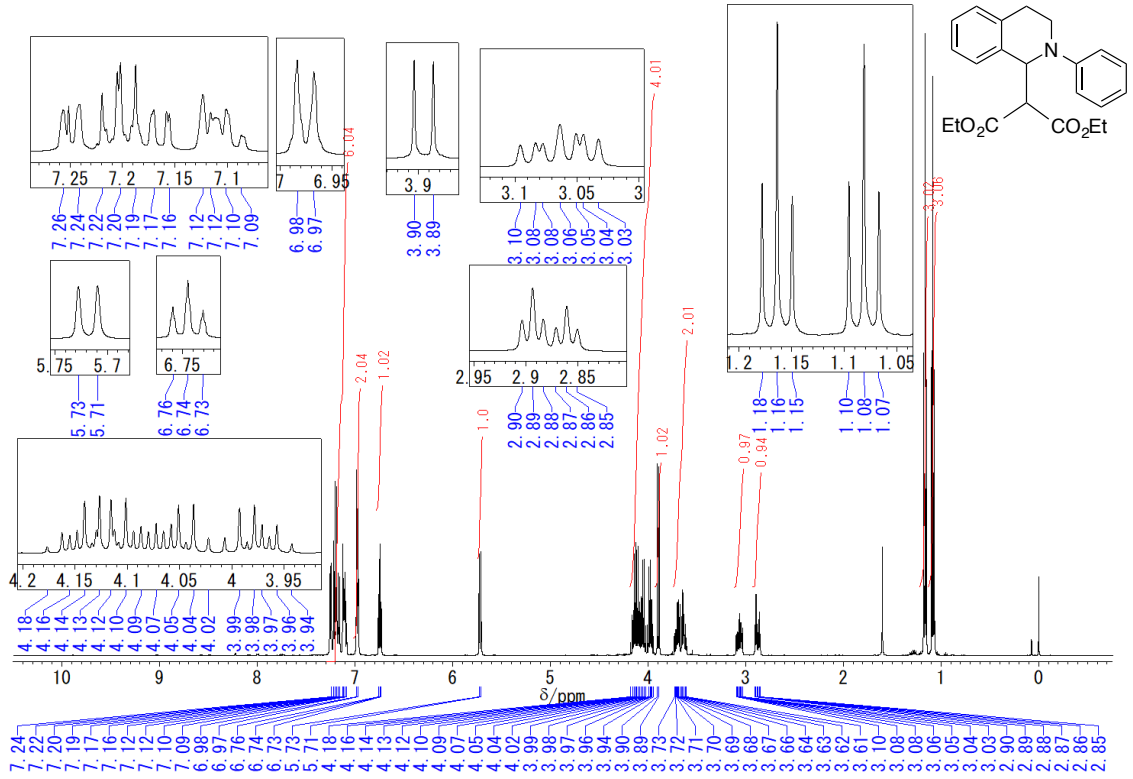
Spectrum S10. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **4c**.



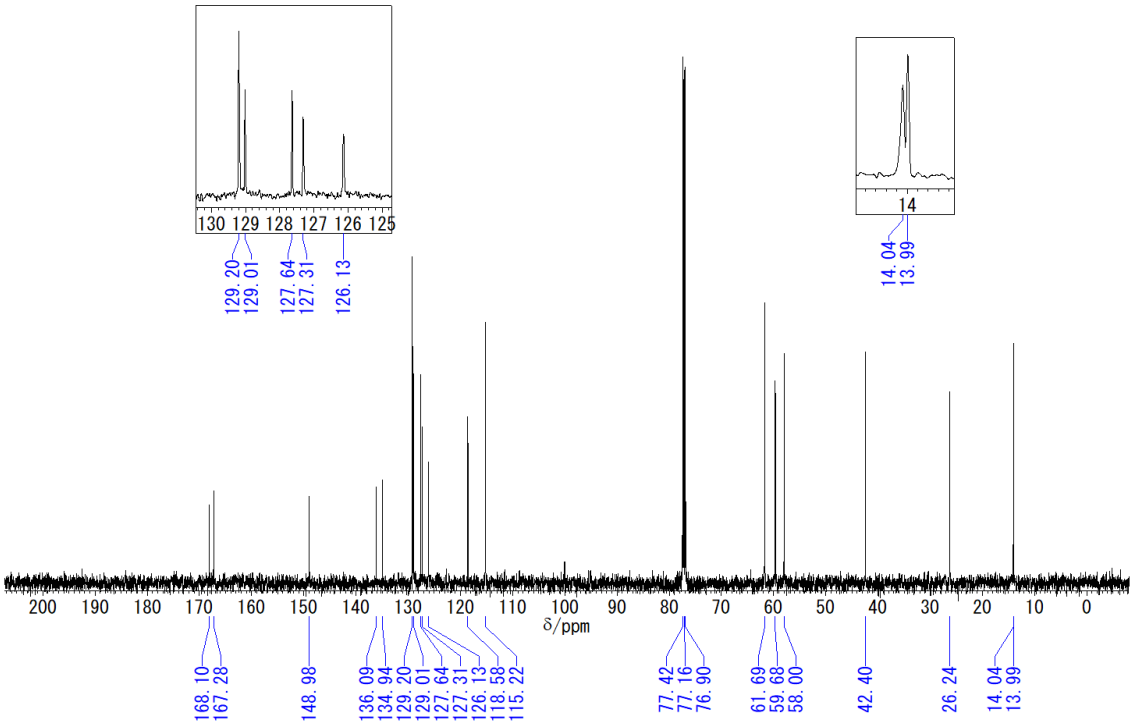
Spectrum S11. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **4f**.



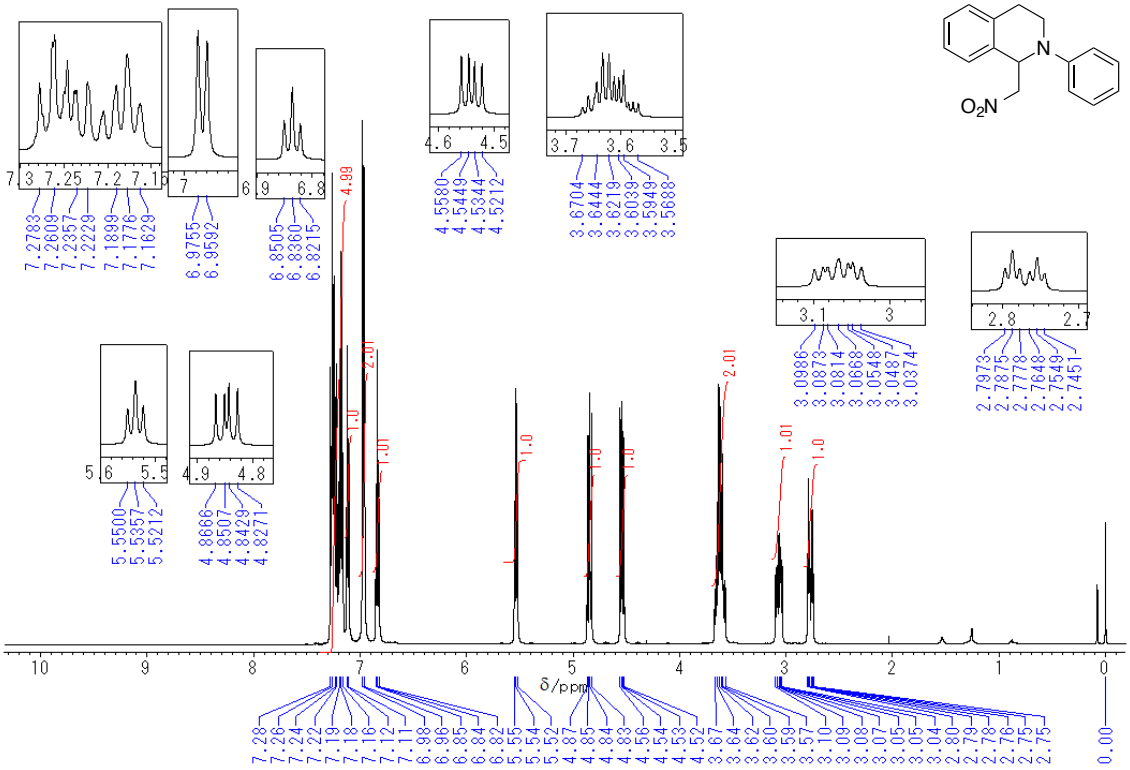
Spectrum S12. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **4f**.



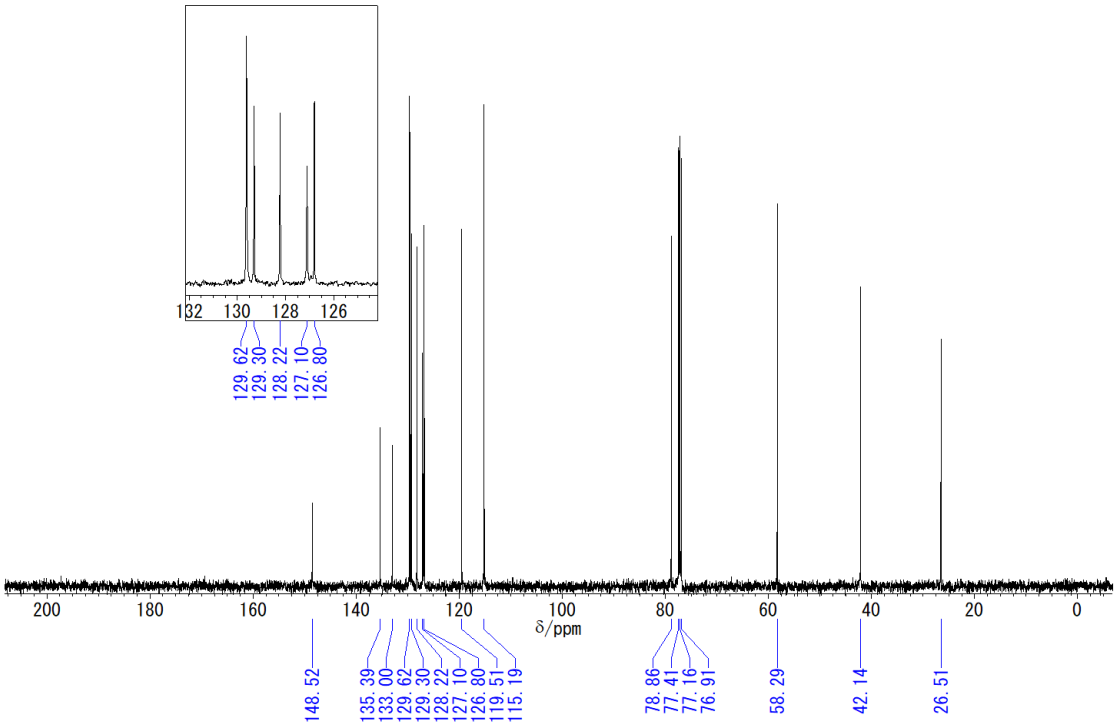
Spectrum S13. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **4g**.



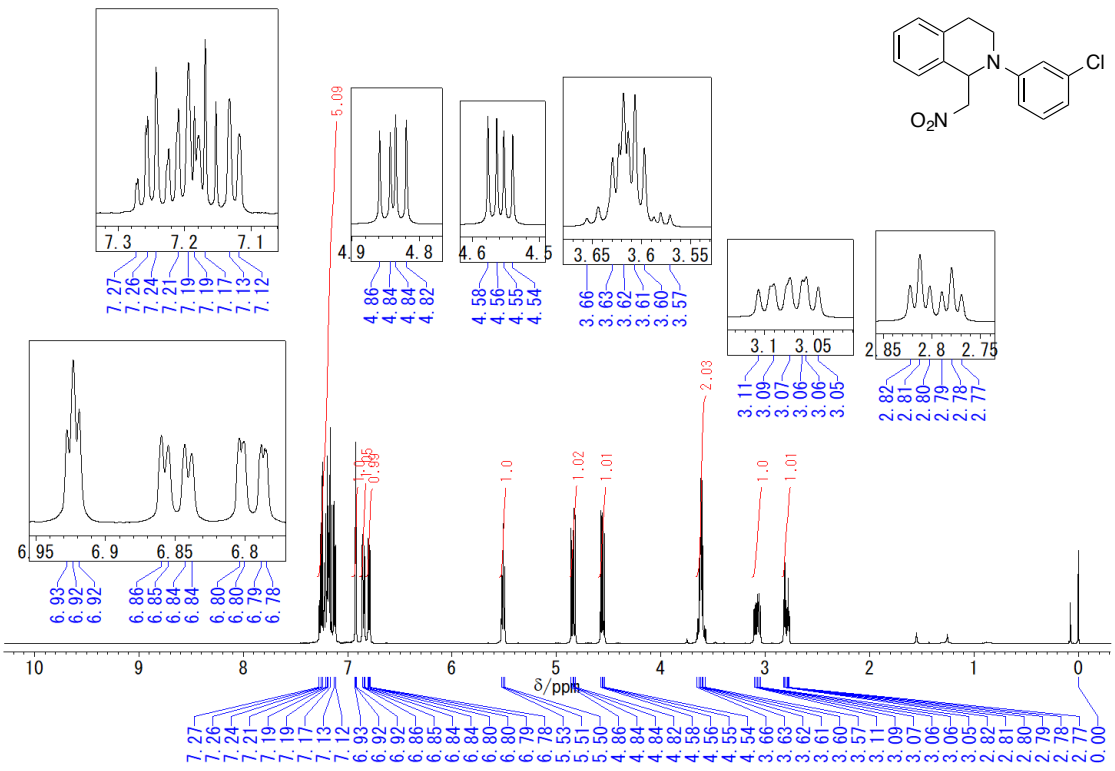
Spectrum S14. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **4g**.



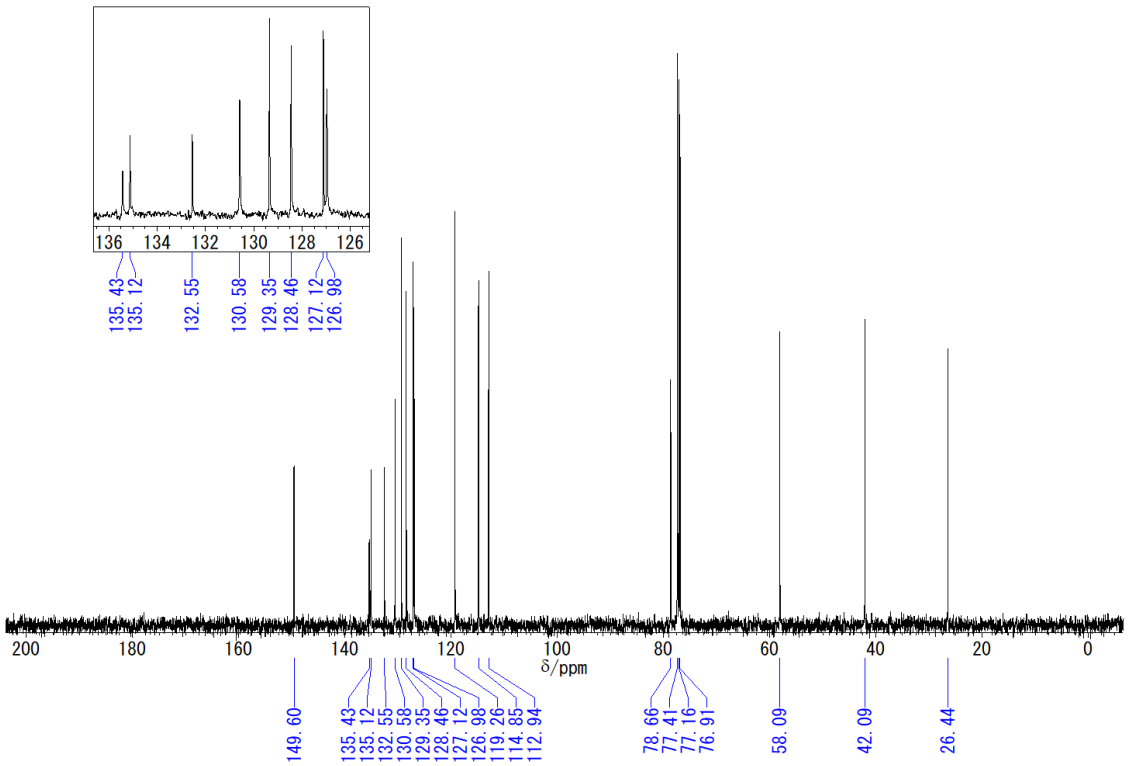
Spectrum S15. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **5a**.



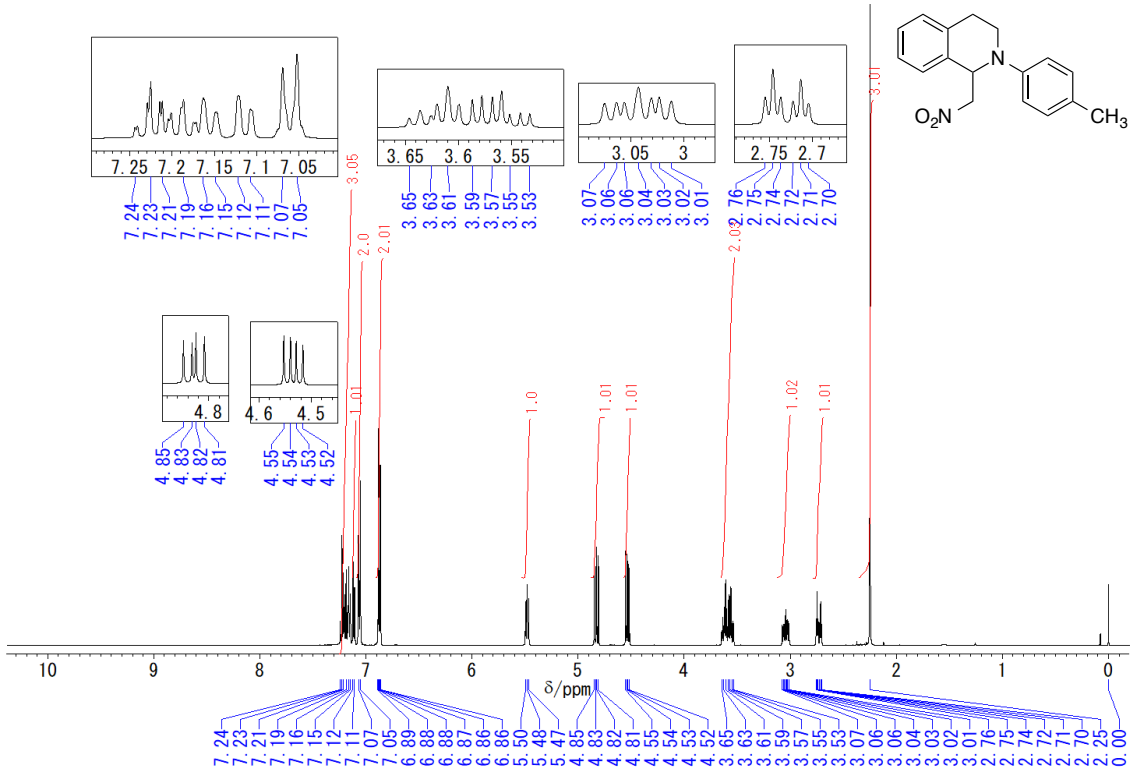
Spectrum S16. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **5a**.



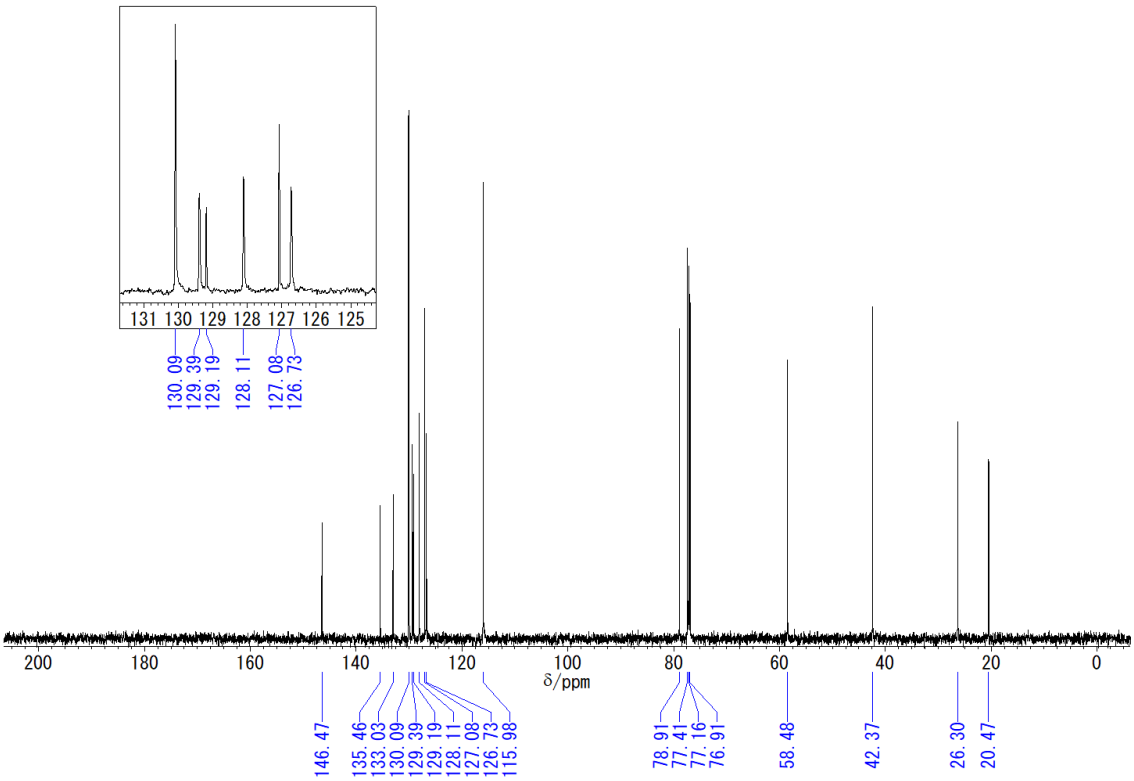
Spectrum S17. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **5c**.



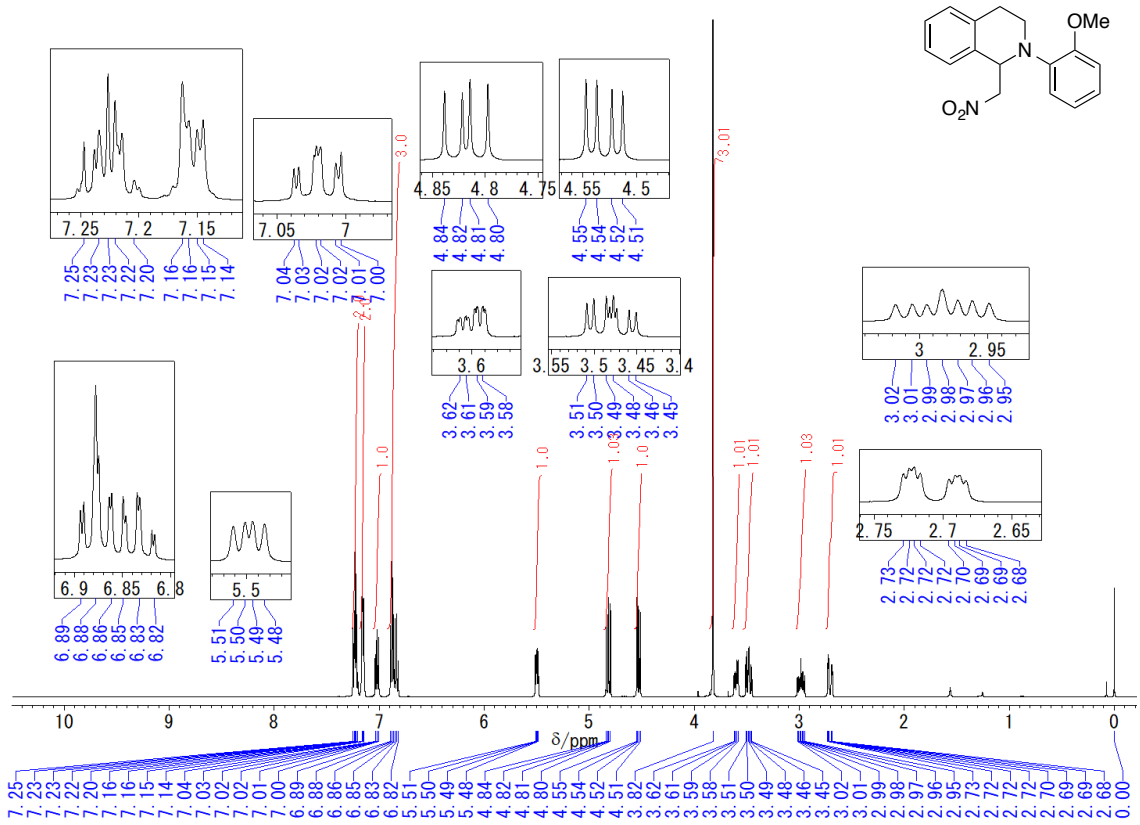
Spectrum S18. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **5c**.



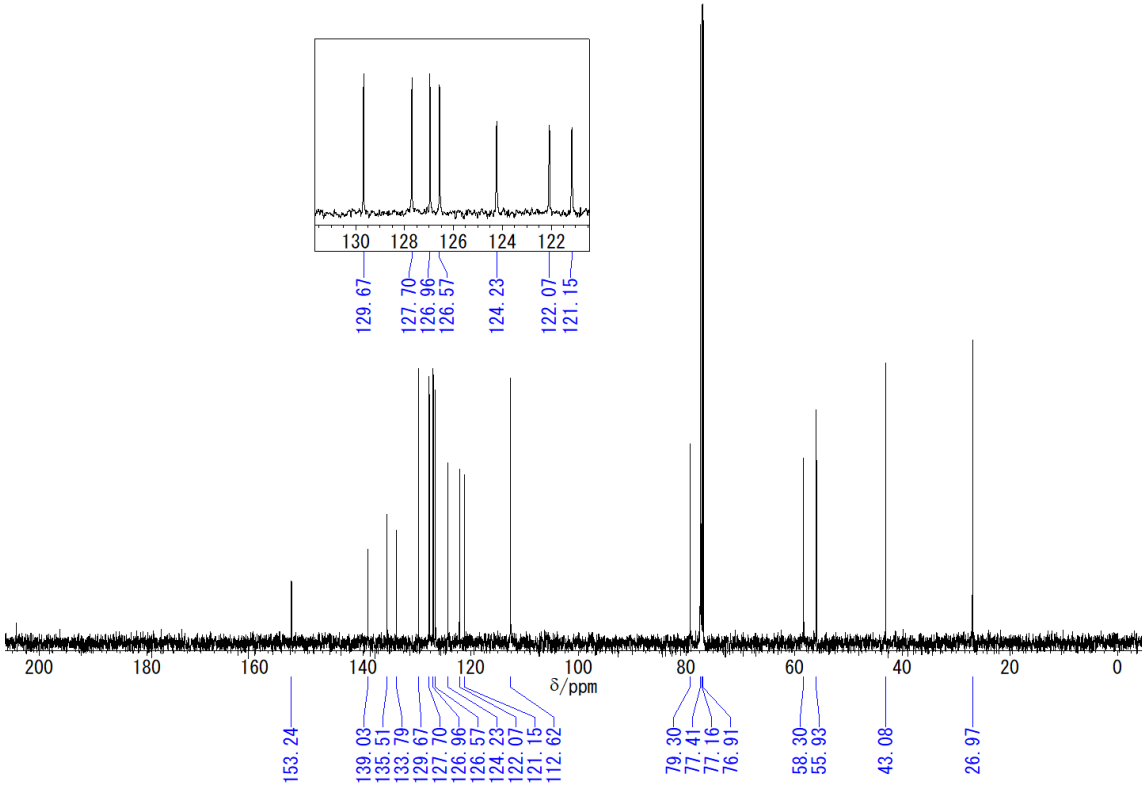
Spectrum S19. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **5f**.



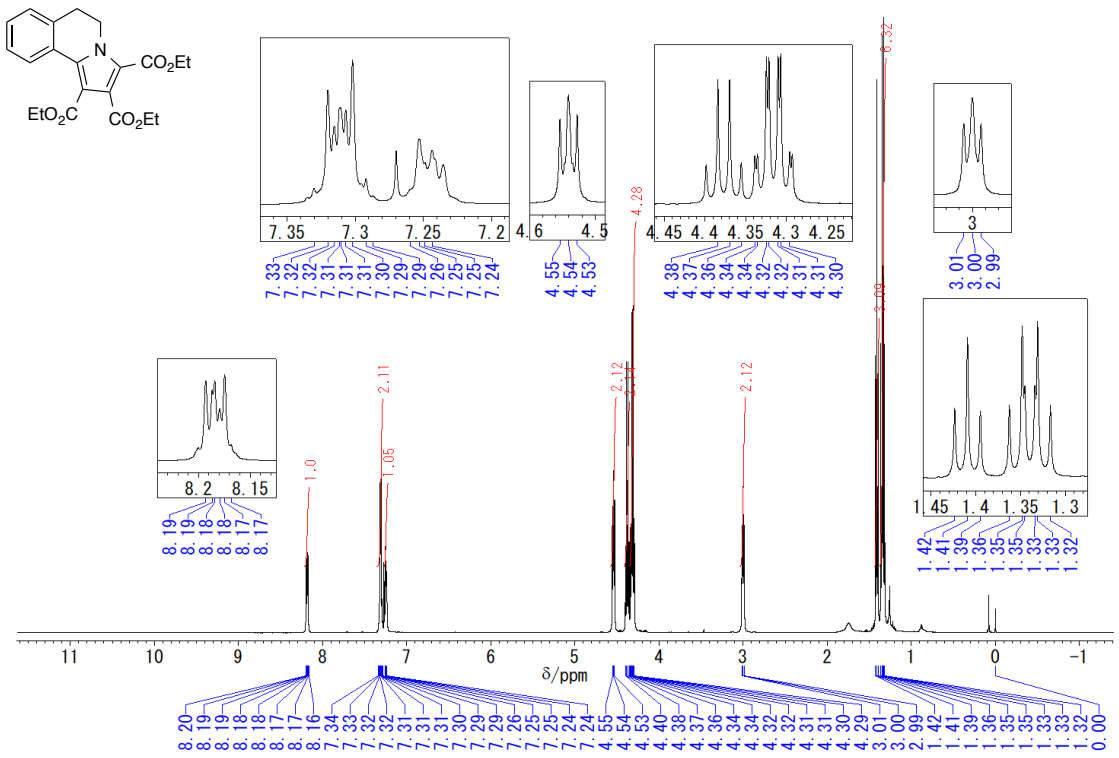
Spectrum S20. ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz) spectrum of compound **5f**.



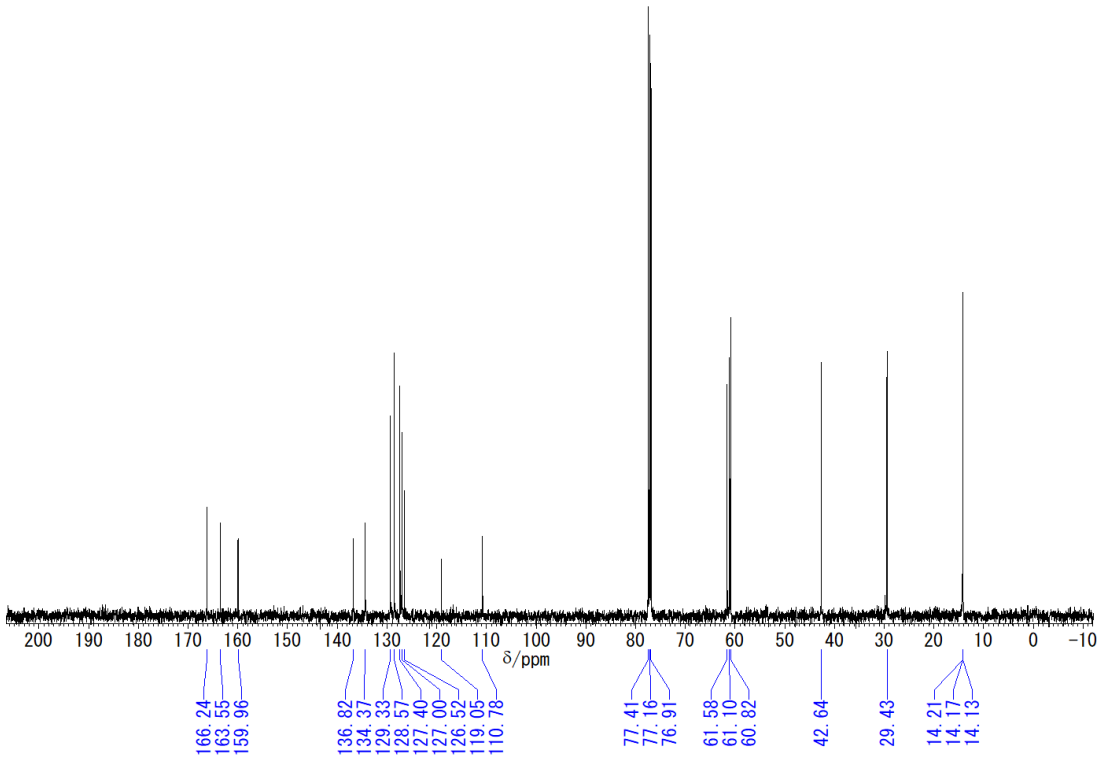
Spectrum S21. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **5h**.



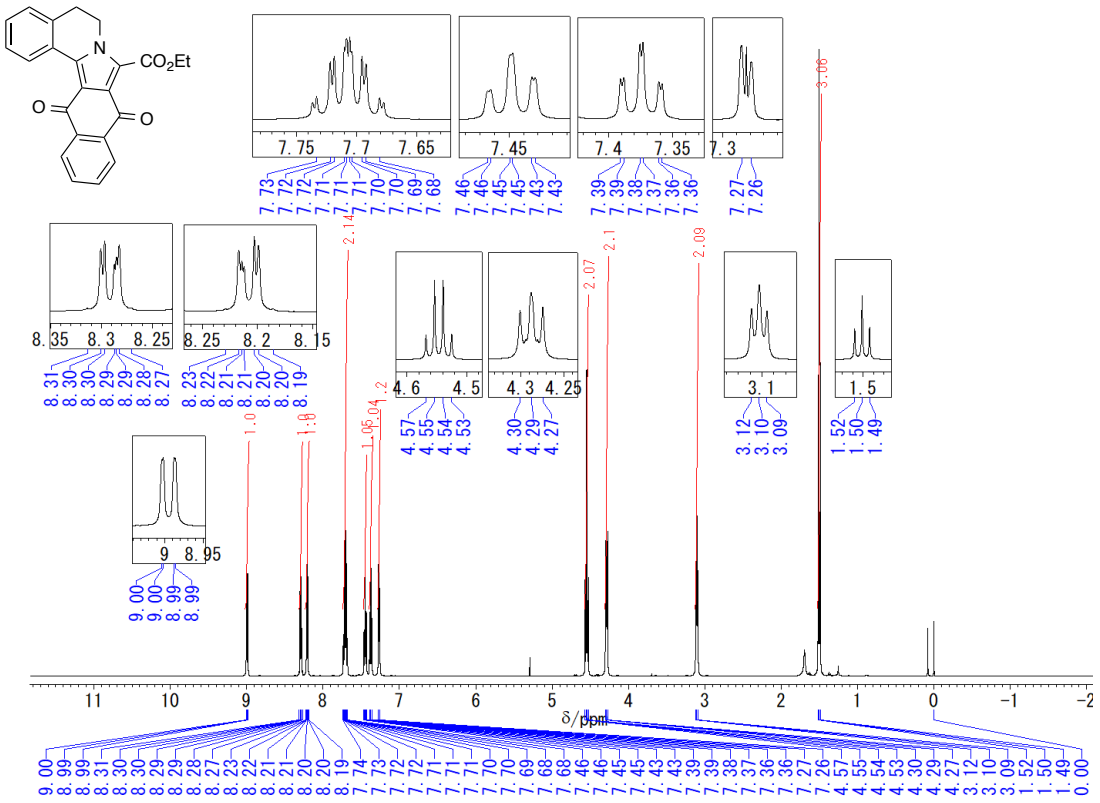
Spectrum S22. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **5h**.



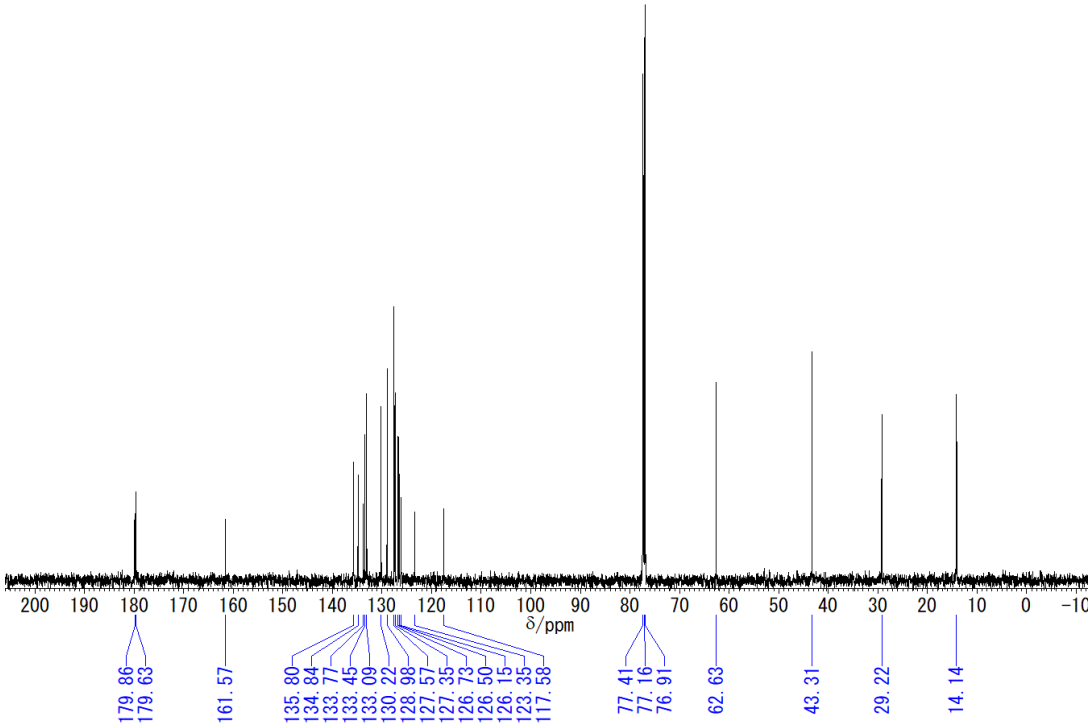
Spectrum S23. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **9a**.



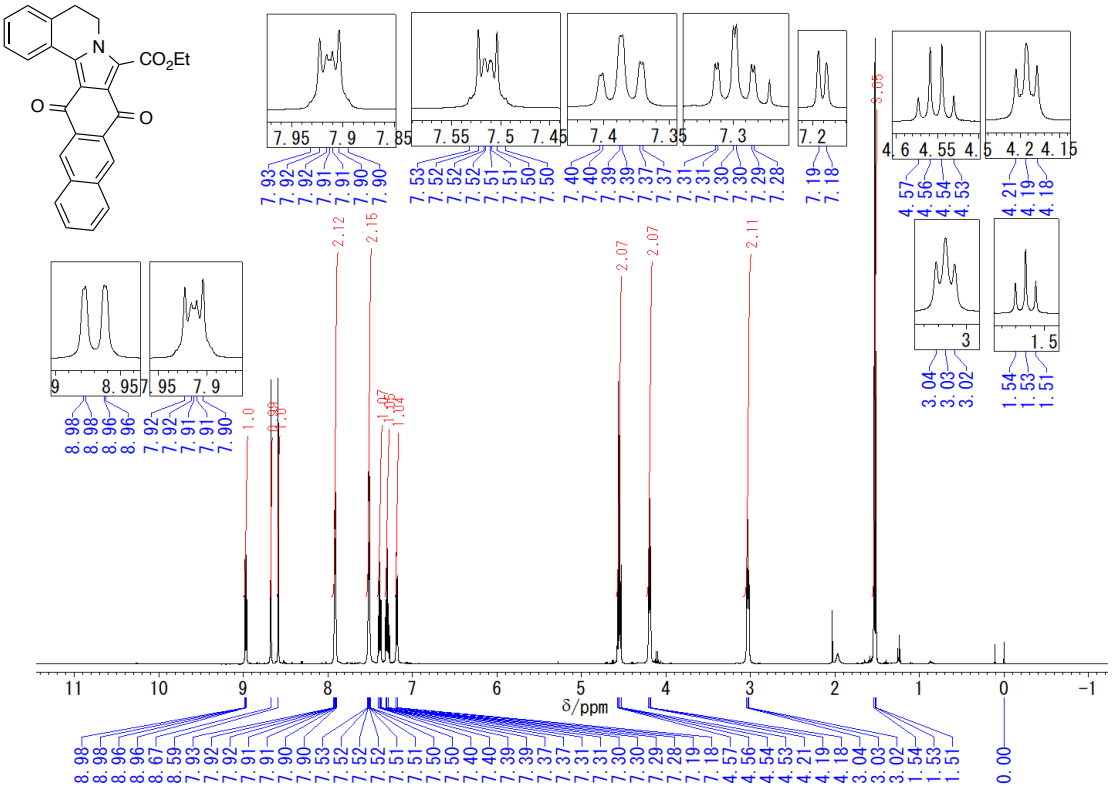
Spectrum S24. ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz) spectrum of compound **9a**.



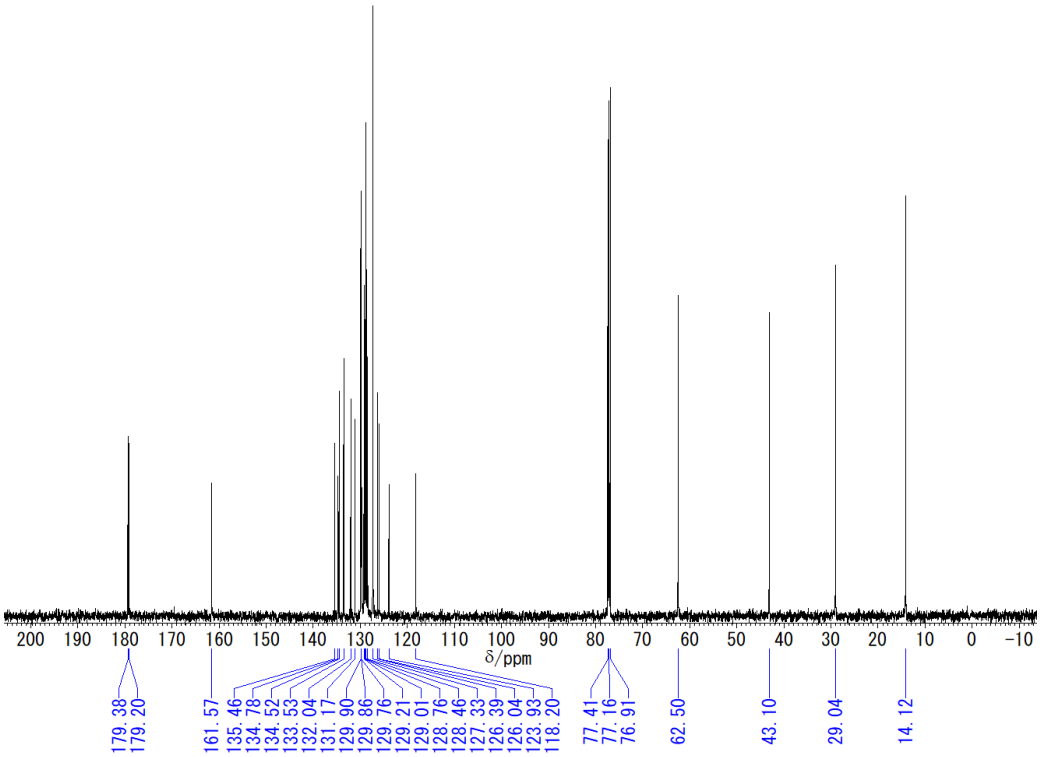
Spectrum S25. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **9b**.



Spectrum S26. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **9b**.



Spectrum S27. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **9c**.



Spectrum S28. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz) spectrum of compound **9c**.

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