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A new oxidation system for the oxidation of Hantzsch-1,4-dihydropyridines and polyhydroquinoline derivatives under mild conditions

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1. Experimental section

General: All solvents and chemicals are used directly from commercial sources without further purification. Analytical Thin Layer Chromatography was carried out on precoated plates (silica gel 60), visualized with UV light. NMR spectra was performed on a Bruker DPX-400 spectrometer operating at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR). All spectra were recorded in $CDCl_3$ and the chemical shifts (δ) are reported in ppm relative to tetramethylsilane referenced to the residual solvent peaks. High-resolution mass spectral analyses (HRMS) were measured using ESI ionization.

General procedure for the aromatization of Hantzsch 1,4-dihydropyridines (1,4-DHPs) and polyhydroquinoline derivatives (PHQs)

To a mixture of Hantzsch 1,4-dihydropyridines or polyhydroquinoline derivatives (0.2 mmol), $Na_2S_2O_4$ (69 mg, 0.4 mmol) and ethyl acetate (5 mL), *tert*-butyl hydroperoxide (104 mg, 0.8 mmol, 70% in water) was added dropwise and the mixture stirred at room temperature. After completion of the reaction, the reaction mixture was treated with saturated aqueous $NaHCO_3$ and H_2O, extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered, and evaporated. The residue was separated on a silica gel column by using petroleum ether and ethyl acetate as eluent.

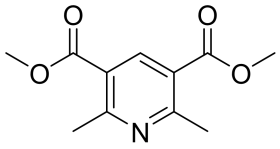
2. Table S1. Optimization of reaction conditions

Entry[a]	$Na_2S_2O_4$/TBHP/Sub[b]	Solvent	Time (h)	Yield (%)[c]
1	1 / 1 / 1	EtOAc	3	52
2	1 / 2 / 1	EtOAc	3	61
3	2 / 3 / 1	EtOAc	3	80
4	**2 / 4 / 1**	**EtOAc**	**3**	**96**
5	2 / 5 / 1	EtOAc	3	93
6	2 / 0 / 1	EtOAc	3	NR[d]
7	0 / 4 / 1	EtOAc	3	NR
8	2 / 4 / 1	CH_2Cl_2	3	64
9	2 / 4 / 1	$CHCl_3$	4	70
10	2 / 4 / 1	CH_3CN	4	67
11	2 / 4 / 1	C_2H_5OH	5	20
12	2 / 4 / 1	$PhCH_3$	5	76
13	2 / 4 / 1	THF	4	75
14	2 / 4 / 1	cyclohexane	5	NR
15	2 / 4 / 1	dioxane	4	73
16	2 / 4 / 1	H_2O	5	15

[a] Reaction conditions: **1** (0.2 mmol) and $Na_2S_2O_4$ (0.4 mmol) in solvent (5 mL) were stirred at room temperature.

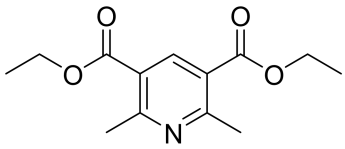
[b] TBHP = *tert*-butylhydroperoxide, 70% in water. [c] Isolated yield. [d] No recation.

3. Analytical data for compounds



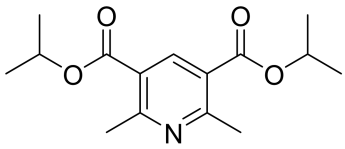
Dimethyl 2,6-dimethylpyridine-3,5-dicarboxylate (2a)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 3.93 (s, 6H), 2.85 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.19, 162.61, 141.03, 122.59, 52.28, 24.93.



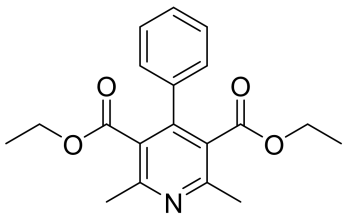
Diethyl 2,6-dimethylpyridine-3,5-dicarboxylate (2b)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 4.40 (dd, J = 14.28, 7.16 Hz, 4H), 2.85 (s, 6H), 1.42 (t, J = 7.14 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.92, 162.18, 140.85, 123.04, 61.36, 24.93, 14.26.



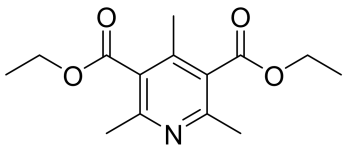
Diisopropyl 2,6-dimethylpyridine-3,5-dicarboxylate (2c)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 5.30-5.24 (m, 2H), 2.83 (s, 6H), 1.40 (d, J = 6.29 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.63, 161.74, 140.76, 123.56, 69.08, 24.94, 21.88.



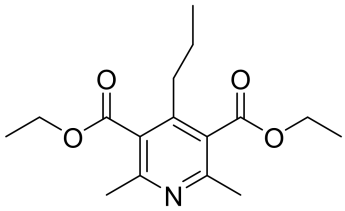
Diethyl 2,6-dimethyl-4-phenylpyridine-3,5-dicarboxylate (2d)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.33 (m, 2H), 7.24-7.23 (m, 2H), 3.98 (dd, J = 14.24, 7.12 Hz, 4H), 2.58 (s, 6H), 0.88 (t, J = 7.13 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.80, 155.37, 146.08, 136.57, 128.35, 128.10, 128.00, 126.90, 61.25, 22.85, 13.49; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}NO_4$ 328.1543; Found 328.1540.



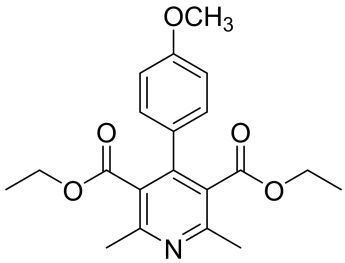
Diethyl 2,4,6-trimethylpyridine-3,5-dicarboxylate (2e)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (dd, *J* = 14.24, 7.08 Hz, 4H), 2.52 (s, 6H), 2.27 (s, 3H), 1.39 (t, *J* = 7.14 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.32, 154.88, 141.98, 127.53, 61.48, 22.87, 16.86, 14.11.



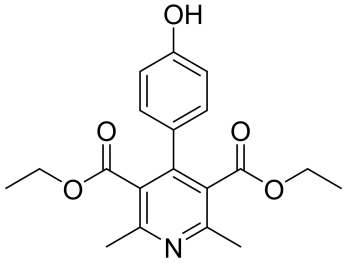
Diethyl 2,6-dimethyl-4-propylpyridine-3,5-dicarboxylate (2f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (dd, *J* = 14.28, 7.12 Hz, 4H), 2.58 – 2.53 (m, 2H), 2.51 (s, 6H), 1.61 – 1.55 (m, 2H), 1.39 (t, *J* = 7.14 Hz, 6H), 0.93 (t, *J* = 7.35 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.53, 155.04, 146.34, 127.23, 61.53, 33.43, 24.19, 22.93, 14.41, 14.14.



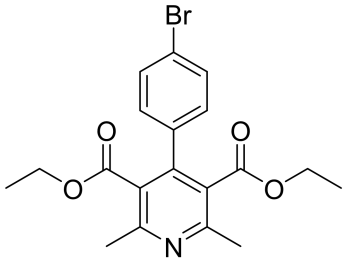
Diethyl 4-(4-methoxyphenyl)-2,6-dimethylpyridine-3,5-dicarboxylate (2g)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.62 Hz, 2H), 6.89 (d, *J* = 8.62 Hz, 2H), 4.05 (q, *J* = 7.13 Hz, 4H), 3.82 (s, 3H), 2.59 (s, 6H), 0.99 (t, *J* = 7.13 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.00, 159.80, 155.11, 145.68, 129.42, 128.69, 127.21, 113.52, 61.24, 55.24, 22.79, 13.67.



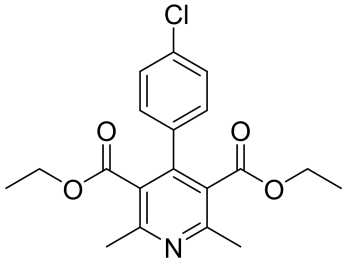
Diethyl 4-(4-hydroxyphenyl)-2,6-dimethylpyridine-3,5-dicarboxylate (2h)[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.12 (d, *J* = 8.51 Hz, 2H), 6.78 (d, *J* = 8.52 Hz, 2H), 4.08 (q, *J* = 7.12 Hz, 4H), 2.60 (s, 6H), 1.01 (d, *J* = 7.13 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.17, 156.95, 156.90, 155.08, 146.36, 129.50, 127.58, 115.26, 61.61, 22.44, 13.72.



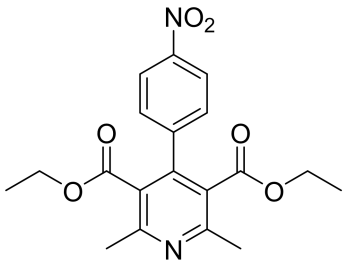
Diethyl 4-(4-bromophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate (2i)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.22 Hz, 2H), 7.14 (d, *J* = 8.26 Hz, 2H), 4.05 (dd, *J* = 14.24, 7.12 Hz, 4H), 2.60 (s, 6H), 0.98 (d, *J* = 7.10 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.59, 155.63, 144.82, 135.45, 131.27, 129.85, 126.70, 122.84, 61.50, 22.94, 13.65.



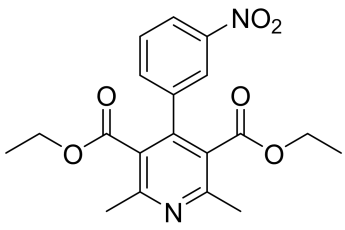
Diethyl 4-(4-chlorophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate (2j)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.43 Hz, 2H), 7.21 (d, *J* = 8.42 Hz, 2H), 4.05 (d, *J* = 7.14 Hz, 4H), 2.60 (s, 6H), 0.98 (d, *J* = 7.14 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.59, 155.58, 144.79, 134.94, 134.69, 129.57, 128.30, 126.77, 61.47, 22.94, 13.65.



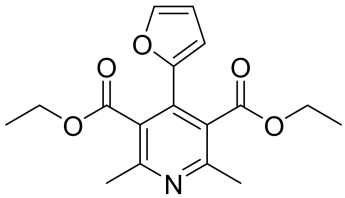
Diethyl 2,6-dimethyl-4-(4-nitrophenyl)pyridine-3,5-dicarboxylate (2k)[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.71 Hz, 2H), 7.46 (d, *J* = 8.73 Hz, 2H), 4.04 (dd, *J* = 14.28, 7.16 Hz, 4H), 2.63 (s, 6H), 0.98 (d, *J* = 7.14 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.09, 156.12, 147.83, 143.89, 143.27, 129.41, 126.19, 123.14, 61.60, 23.05, 13.66.



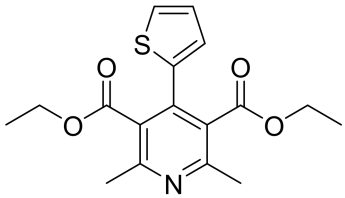
Diethyl 2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate (2l)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.25 (m, 1H), 8.19 (s, 1H), 7.63 – 7.57 (m, 2H), 4.06 (d, *J* = 7.13 Hz, 4H), 2.64 (s, 6H), 1.00 (d, *J* = 7.14 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.16, 156.07, 147.81, 143.48, 138.12, 134.37, 129.21, 126.55, 123.34, 61.64, 23.09, 13.71.



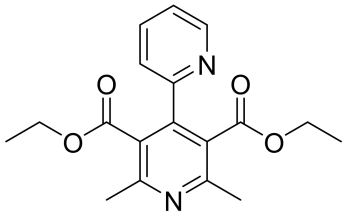
Diethyl 4-(furan-2-yl)-2,6-dimethylpyridine-3,5-dicarboxylate (2m)[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 6.62 (d, *J* = 3.40 Hz, 1H), 6.49-6.48 (m, 1H), 4.28 (dd, *J* = 14.24, 7.12 Hz, 4H), 2.58 (s, 6H), 1.23 (t, *J* = 7.14 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.16, 155.70, 148.03, 143.89, 133.76, 124.78, 111.92, 111.79, 61.77, 22.78, 13.99.



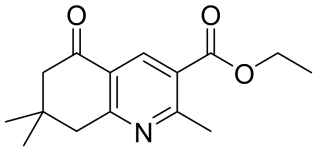
Diethyl 2,6-dimethyl-4-(thiophen-2-yl)pyridine-3,5-dicarboxylate (2n)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 4.70 Hz, 1H), 7.04 (t, *J* = 2.32 Hz, 2H), 4.12 (dd, *J* = 14.28, 7.12 Hz, 4H), 2.59 (s, 6H), 1.07 (d, *J* = 7.14 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.68, 155.34, 138.80, 135.89 , 128.58, 127.61, 127.38, 127.05, 61.57, 22.86, 13.71.



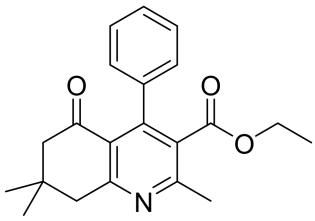
Diethyl 2',6'-dimethyl-[2,4'-bipyridine]-3',5'-dicarboxylate (2o)[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 4.63 Hz, 1H), 7.76 – 7.72 (m, 1H), 7.39 (d, *J* = 7.84 Hz, 1H), 7.31 (dd, *J* = 7.40, 5.00 Hz, 1H), 4.06 (dd, *J* = 14.20, 7.08 Hz, 2H), 2.65 (s, 3H), 0.97 (d, *J* = 7.14 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.85, 156.63, 155.82, 149.47, 145.66, 136.24, 126.31, 123.41, 123.09, 61.41, 23.19, 13.80.



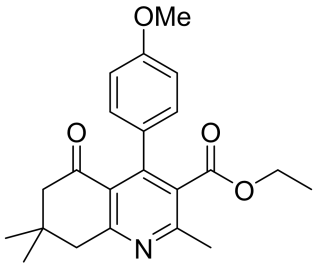
Ethyl 2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (4a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 4.39 (dd, *J* = 13.84, 6.84 Hz, 2H), 3.03 (s, 2H), 2.88 (s, 3H), 2.56 (s, 2H), 1.41 (d, *J* = 6.91 Hz, 3H), 1.12 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.17, 165.83, 164.66, 164.30, 137.01, 124.90, 124.55, 61.46, 51.94, 46.51, 32.91, 28.29, 25.20, 14.28.



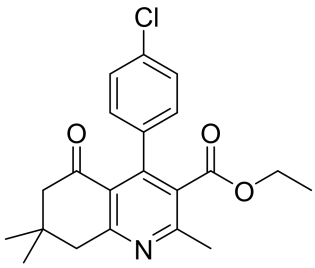
Ethyl 2,7,7-trimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylate (4b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.35 (m, 3H), 7.14 – 7.12 (m, 2H), 3.96 (dd, *J* = 14.24, 7.12 Hz, 2H), 3.09 (s, 2H), 2.61 (s, 3H), 2.47 (s, 2H), 1.11 (s, 6H), 0.92 (t, *J* = 7.13 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.98, 167.52, 163.10, 158.29, 148.52, 137.38, 130.14, 127.66, 127.54, 122.94, 61.40, 53.66, 47.53, 32.39, 28.15, 23.21, 13.57 (s); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{23}NO_3$ 338.1751; Found 338.1747.



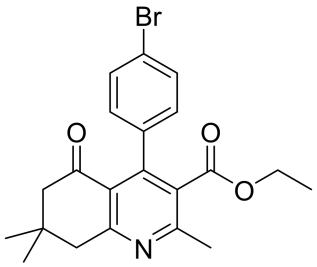
Ethyl 4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (4c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 8.67 Hz, 2H), 6.88 (d, *J* = 8.69 Hz, 2H), 4.00 (dd, *J* = 14.24, 7.12 Hz, 2H), 3.81 (s, 3H), 3.06 (s, 2H), 2.58 (s, 3H), 2.45 (s, 2H), 1.10 (s, 6H), 0.98 (t, *J* = 7.14 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.23, 167.75, 163.09, 159.28, 158.13, 148.39, 130.53, 129.48, 128.93, 123.21, 113.27, 61.42, 55.20, 53.81, 47.58, 32.41, 28.17, 23.20, 13.74 (s)

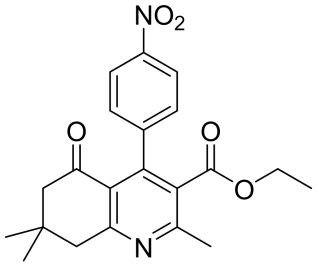


Ethyl4-(4-chlorophenyl)-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate(4d)

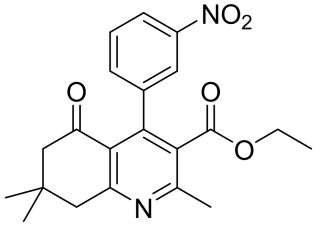
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.31 (m, 2H), 7.06 – 7.04 (m, 2H), 3.98 (dd, *J* = 14.28, 7.12 Hz, 2H), 3.07 (s, 2H), 2.58 (s, 3H), 2.44 (s, 2H), 1.09 (s, 6H), 0.97 (t, *J* = 7.14 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.00, 167.27, 163.26, 158.54, 147.20, 135.85, 133.80, 130.03, 129.05, 127.94, 122.78, 61.55, 53.62, 47.50, 32.40, 28.13, 23.25, 13.65 (s); HRMS (ESI) m/z: $[M+H]^+$ Calcud for $C_{21}H_{22}NO_3Cl$ 372.1361; Found 372.1359.



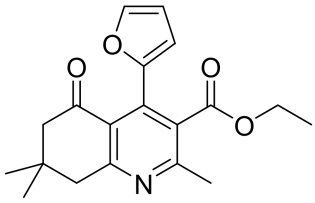
Ethyl4-(4-bromophenyl)-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate(4e)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.47 (m, 2H), 7.01 – 6.98 (m, 2H), 4.00 (dd, *J* = 14.28, 7.12 Hz, 2H), 3.08 (s, 2H), 2.59 (s, 3H), 2.46 (s, 2H), 1.10 (s, 6H), 0.98 (d, *J* = 7.14 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.05, 167.28, 163.29, 158.59, 147.20, 136.35, 130.90, 129.95, 129.33, 122.72, 121.97, 61.59, 53.63, 47.51, 32.42, 28.14, 23.27, 13.66 (s).



Ethyl 2,7,7-trimethyl-4-(4-nitrophenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (4f)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.78 Hz, 2H), 7.29 (d, *J* = 8.78 Hz, 2H), 3.99 (dd, *J* = 14.28, 7.12 Hz, 2H), 3.11 (s, 2H), 2.62 (s, 3H), 2.47 (s, 2H), 1.12 (s, 6H), 0.97 (d, *J* = 7.12 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.99, 166.81, 163.60, 159.13, 147.34, 146.06, 144.65, 129.32, 128.72, 122.97, 122.31, 61.75, 53.40, 47.42, 32.47, 28.11, 23.38, 13.70 (s); HRMS (ESI) m/z: $[M+H]^+$ Calcud for $C_{21}H_{22}N_2O_5$ 383.1601; Found 383.1604.

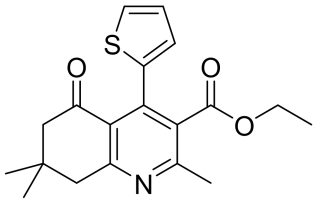


Ethyl 2,7,7-trimethyl-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (4g)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.15 Hz, 1H), 8.03 (s, 1H), 7.56 (d, *J* = 7.92 Hz, 1H), 7.47 (d, *J* = 7.64 Hz, 1H), 4.00 (dd, *J* = 14.24, 7.12 Hz, 2H), 3.12 (s, 2H), 2.63 (s, 3H), 2.48 (d, *J* = 4.02 Hz, 2H), 1.13 (d, *J* = 6.72 Hz, 6H), 0.97 (d, *J* = 7.12 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.00, 166.84, 163.59, 159.08, 147.75, 145.64, 139.12, 133.88, 129.78, 128.63, 122.89, 122.64, 122.43, 61.69, 53.47, 47.45, 32.45, 28.20, 28.02, 23.35, 13.67 (s).



Ethyl 4-(furan-2-yl)-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (4h)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 6.49 (s, 2H), 4.20 (dd, *J* = 14.28, 7.16 Hz, 2H), 3.07 (s, 2H), 2.61 (s, 3H), 2.55 (s, 2H), 1.18 (t, *J* = 7.13 Hz, 3H), 1.12 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.51, 167.58, 163.16, 158.91, 148.22, 143.33, 136.21, 129.49, 123.30, 111.16, 110.57, 61.77, 53.49, 47.37, 32.65, 28.18, 23.21, 13.95 (s); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}NO_4$ 328.1543; Found 328.1548.



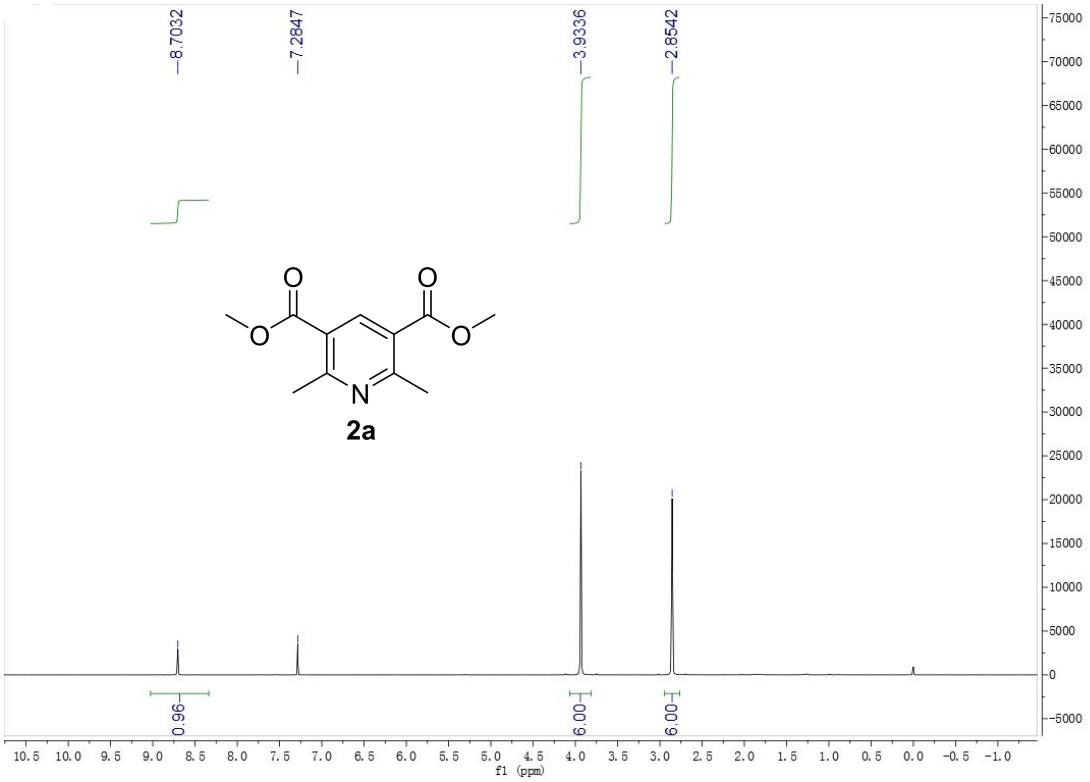
Ethyl 2,7,7-trimethyl-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylate (4i)

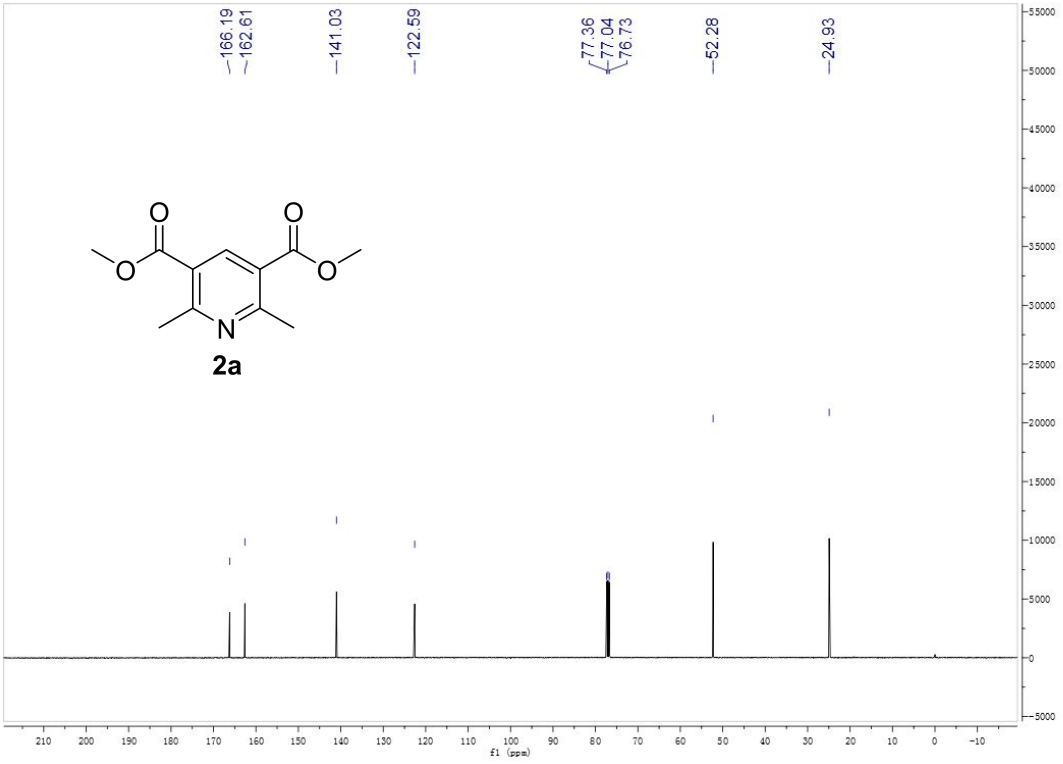
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 4.97 Hz, 1H), 7.04 (t, *J* = 4.26 Hz, 1H), 6.91 (d, *J* = 3.24 Hz, 1H), 4.08 (dd, *J* = 14.24, 7.12 Hz, 2H), 3.08 (s, 2H), 2.60 (s, 3H), 2.50 (s, 2H), 1.08 (s, 6H), 1.06 (d, *J* = 7.14 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.65, 167.33, 163.06, 158.33, 141.22, 137.24, 131.21, 126.99, 126.76, 126.46, 123.89, 61.63, 53.71, 47.49, 32.45, 28.14, 23.20, 13.75 (s); HRMS (ESI) m/z: $[M+H]^+$ Calcud for $C_{19}H_{21}NO_3S$ 344.1315; Found 344.1317.

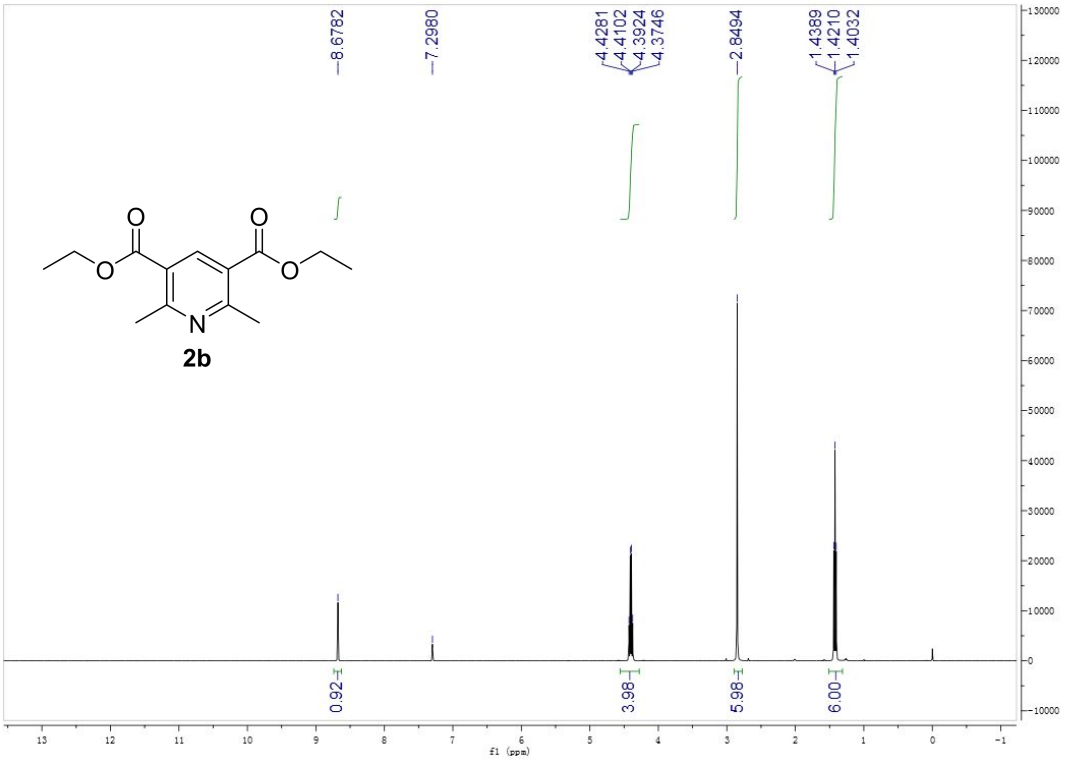
References for known compounds

1. Abdel-Mohsen, H. T., Conrad, J., Beifuss, U. *Green Chem.*, **2012**, 14, 2686.
2. Saikh, F., De, R., Ghosh, S. *Tetrahedron Lett.* **2014**, 55, 6171.
3. Nakamichi, N., Kawashita, Y., Hayashi, M. *Org. Lett*., **2002**, 4, 3955.
4. Jia, X.-D., Yu, L.-L., Huo, C.-D, Wang, Y.-X, Liu, J., Wang, X.-C. *Tetrahedron Lett.* **2014**, 55, 264.

4. ^{1}H and ^{13}C NMR spectra



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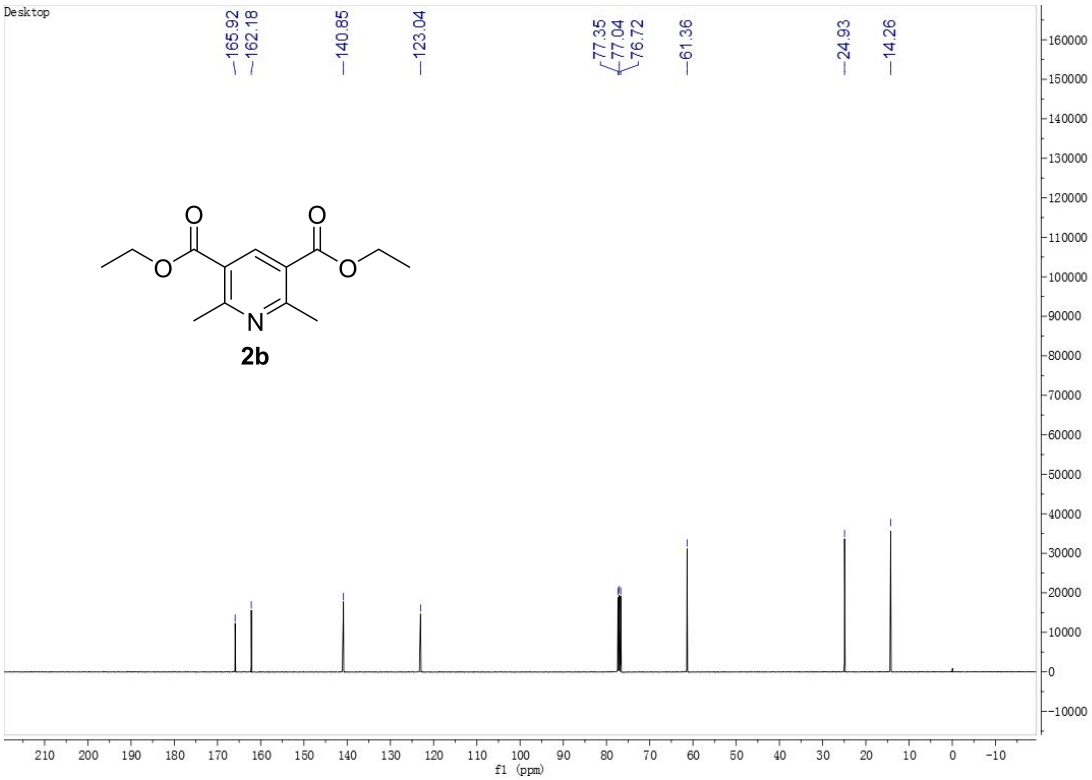
3.98
5.98
6.00
f1 (ppm)
2b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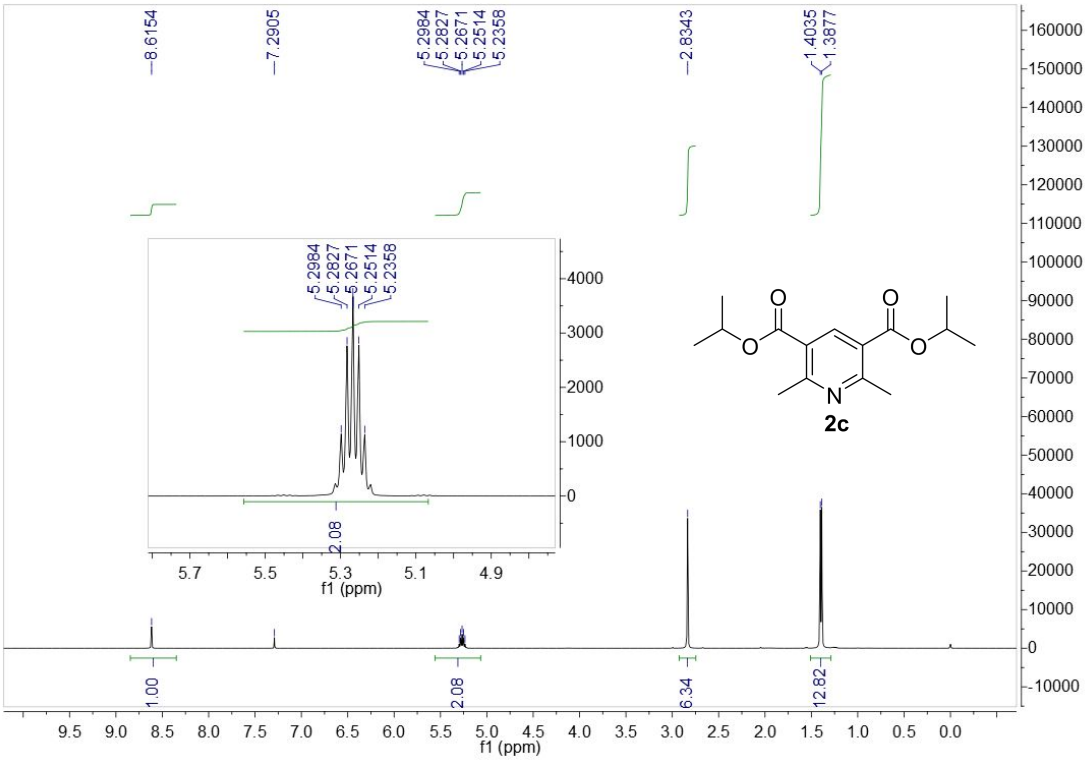
2b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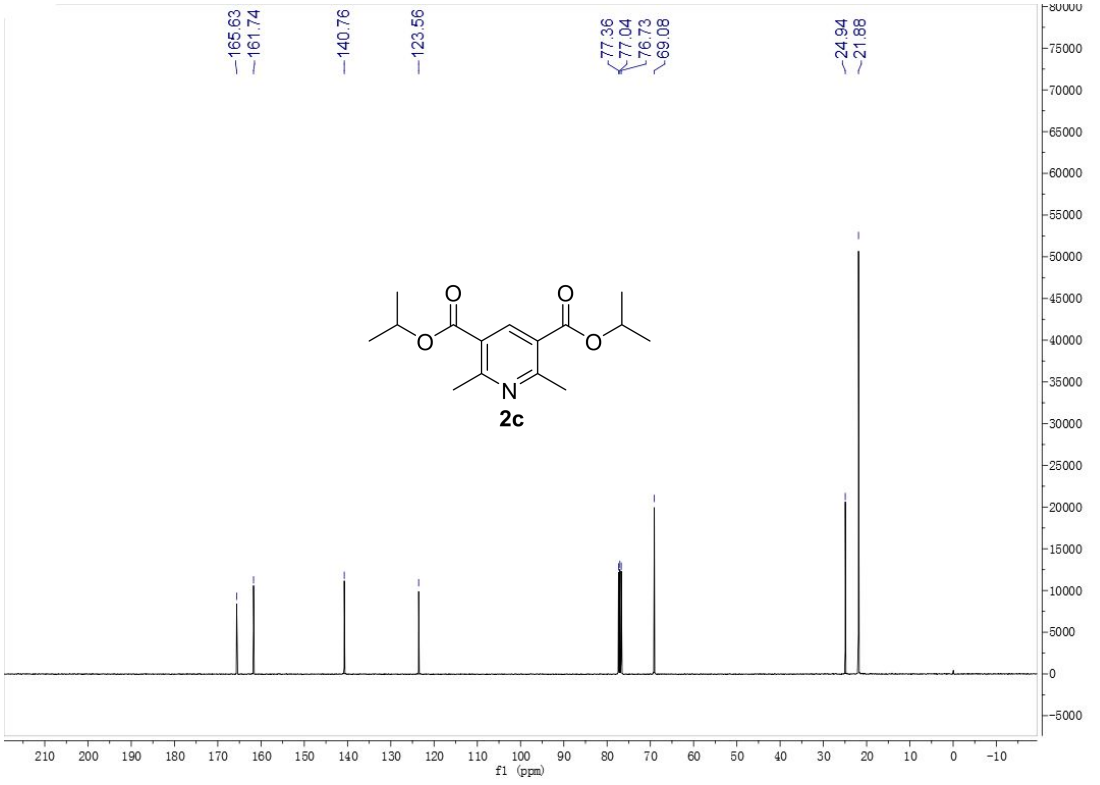
2c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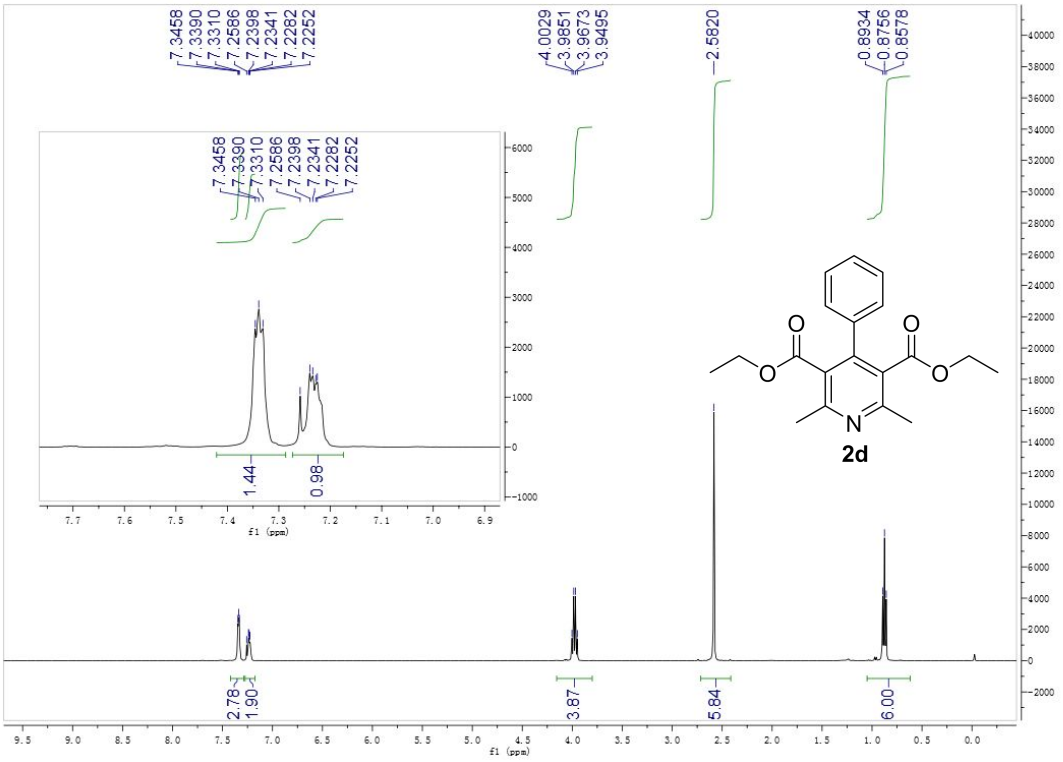
2c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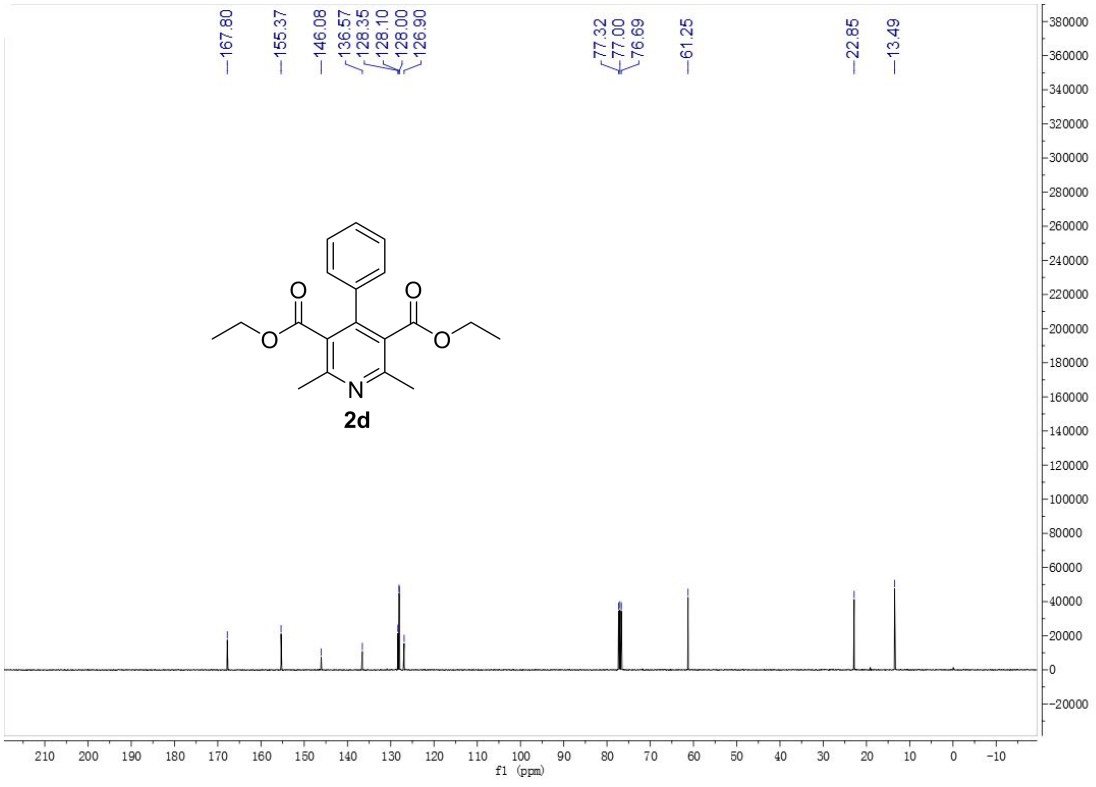
f1 (ppm)
2d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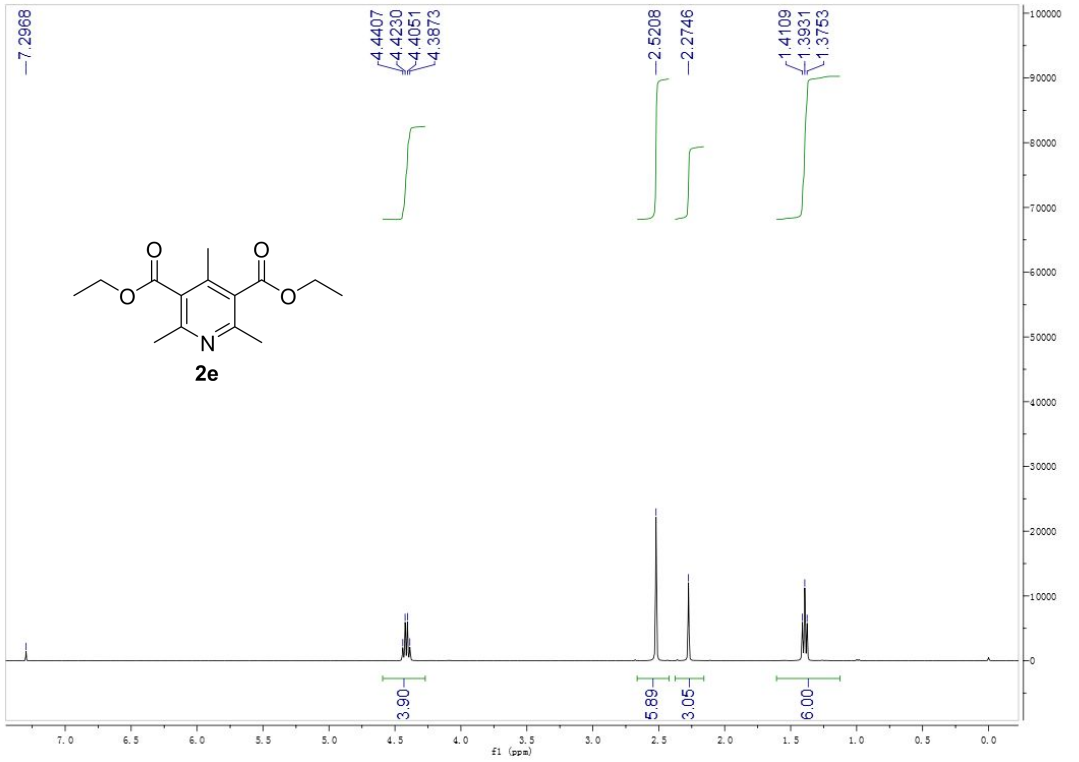
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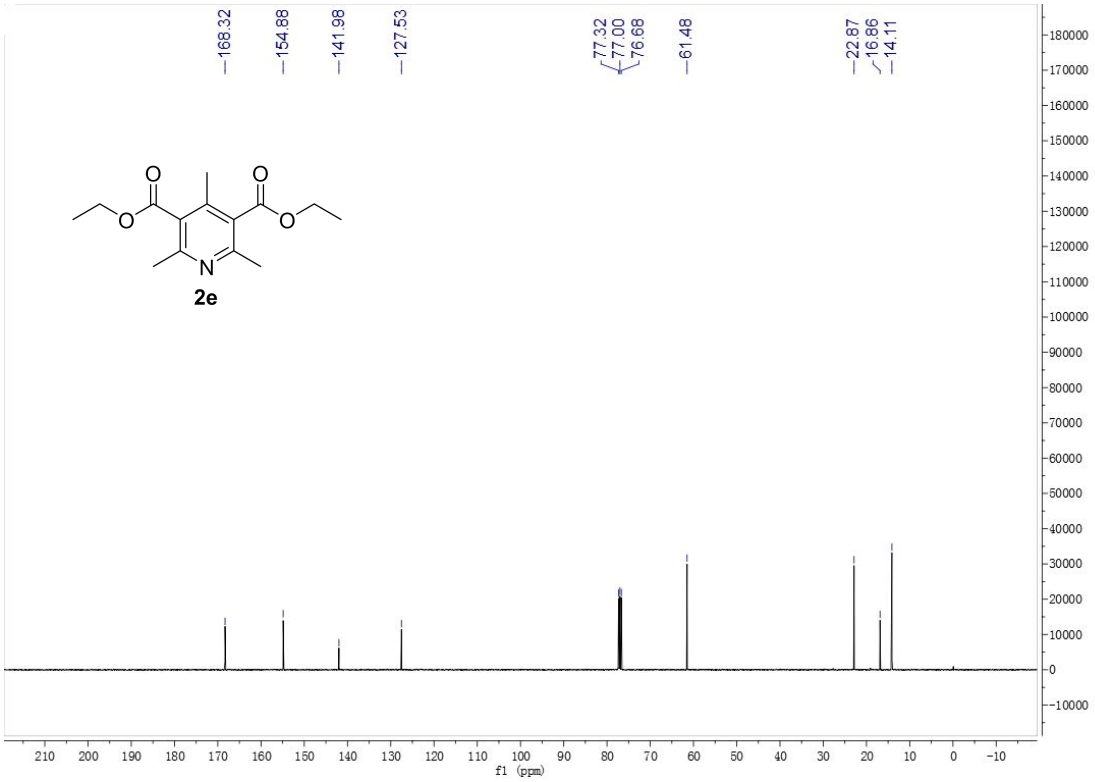
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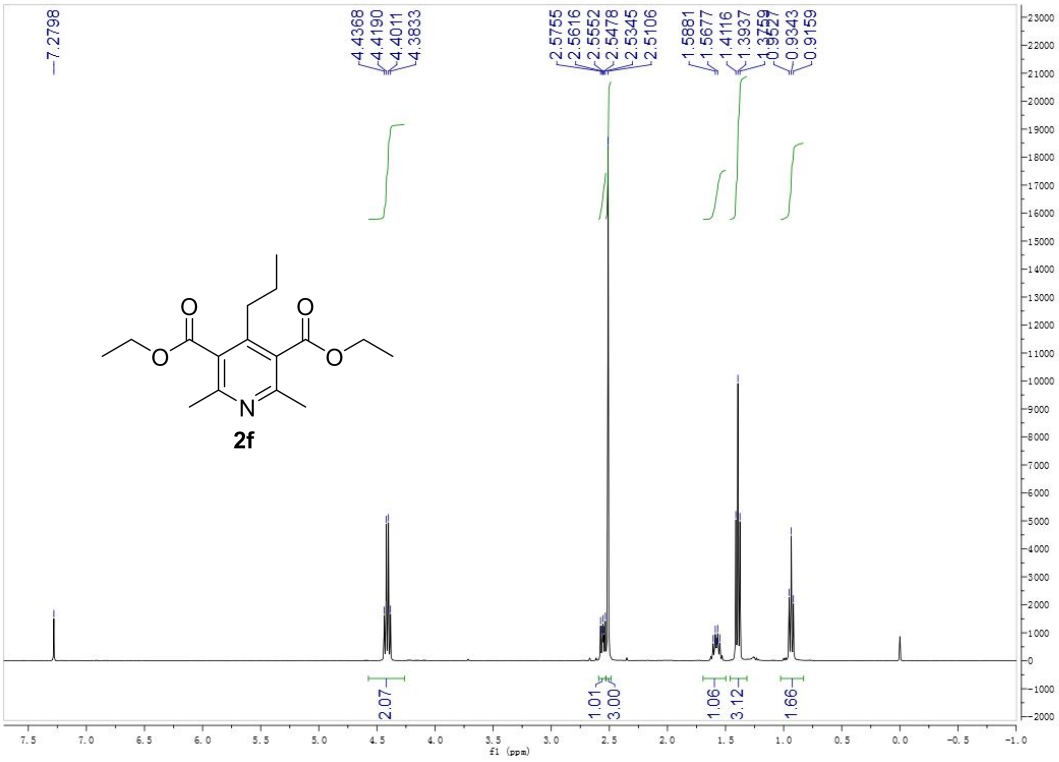
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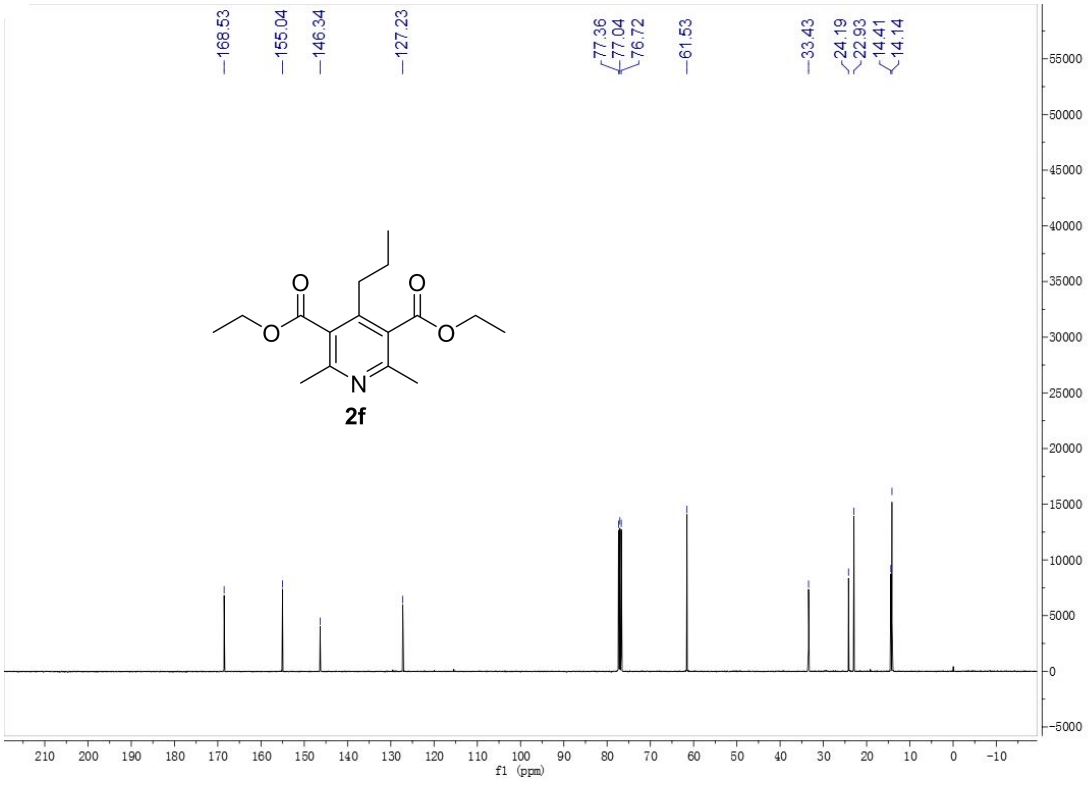
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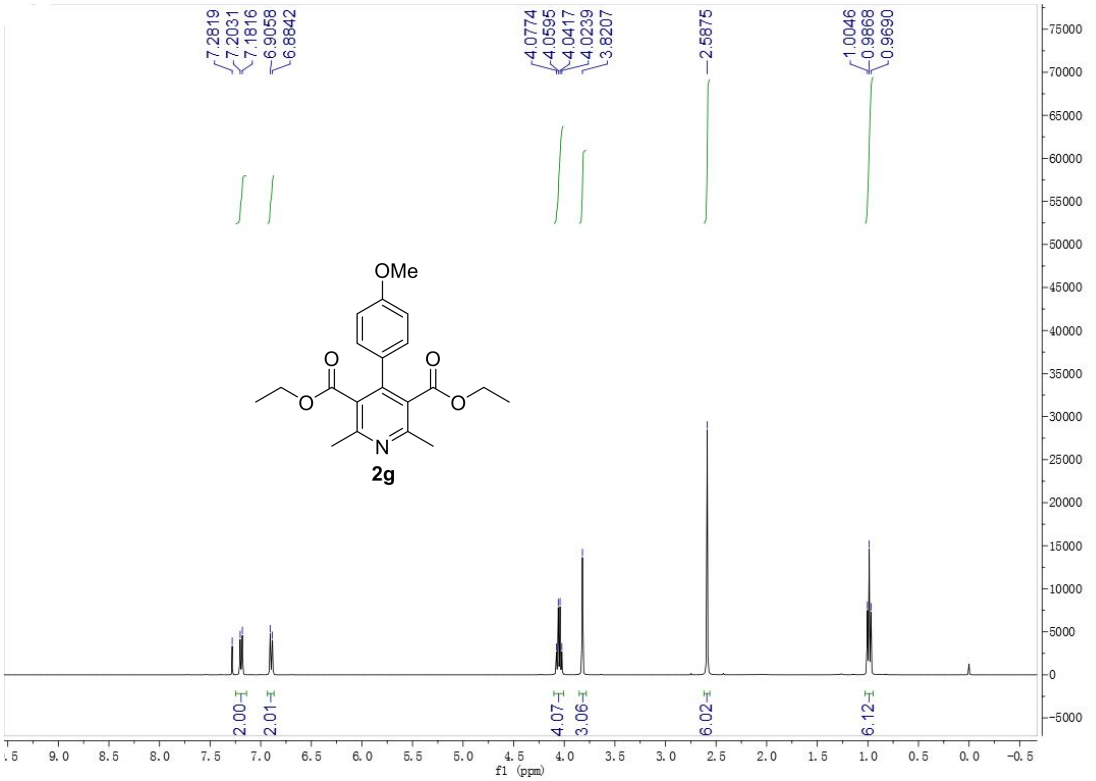
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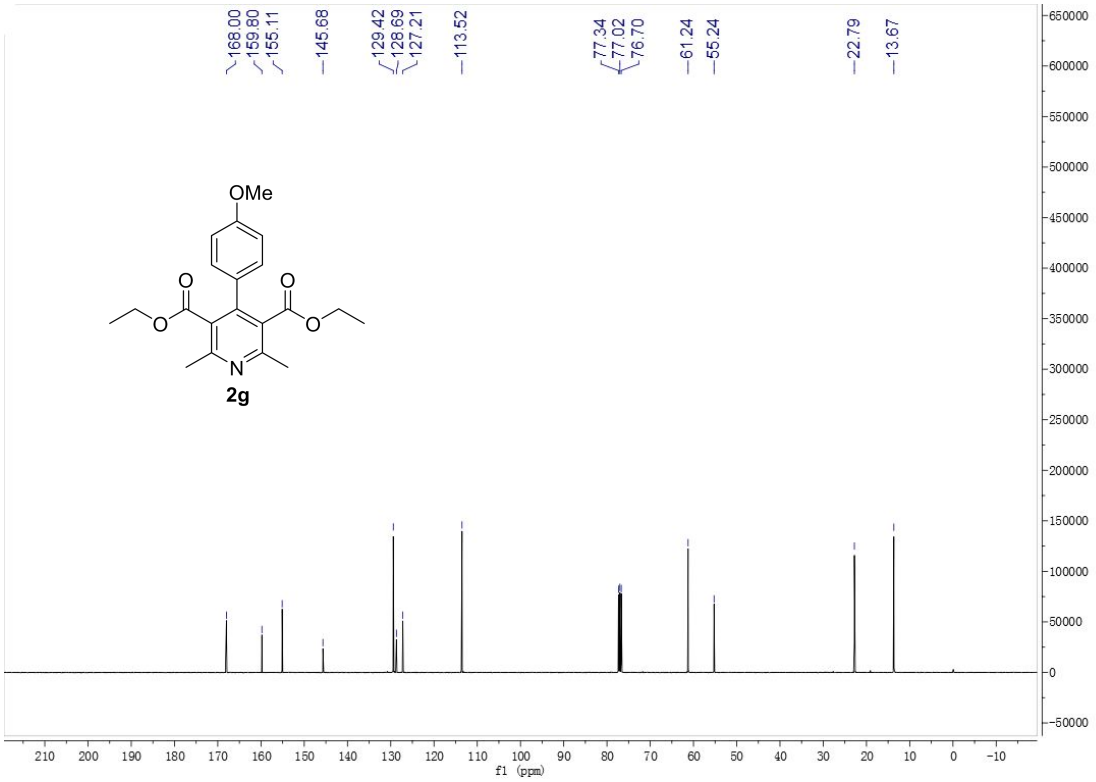
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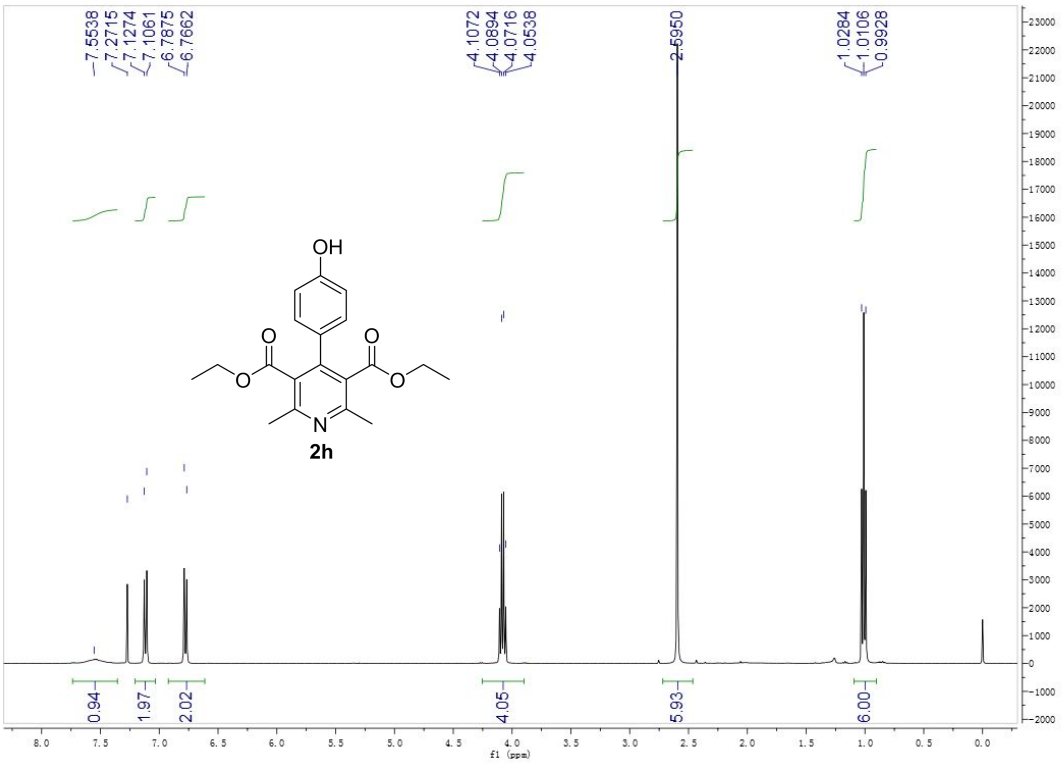
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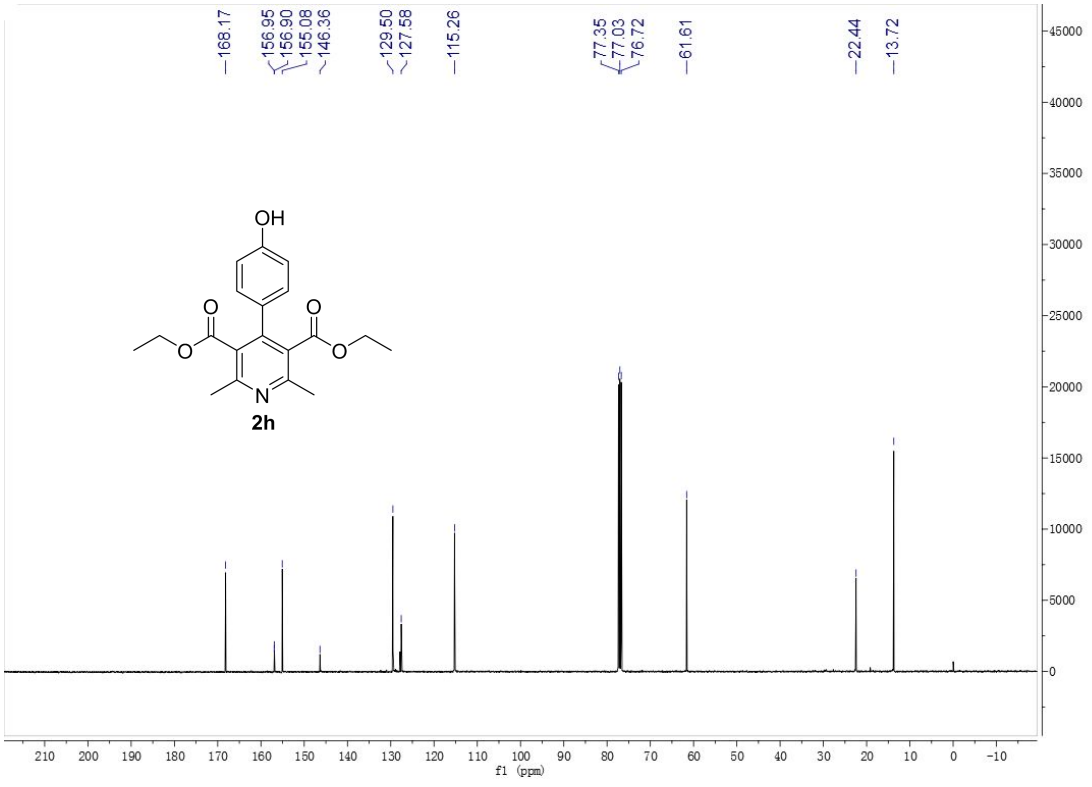
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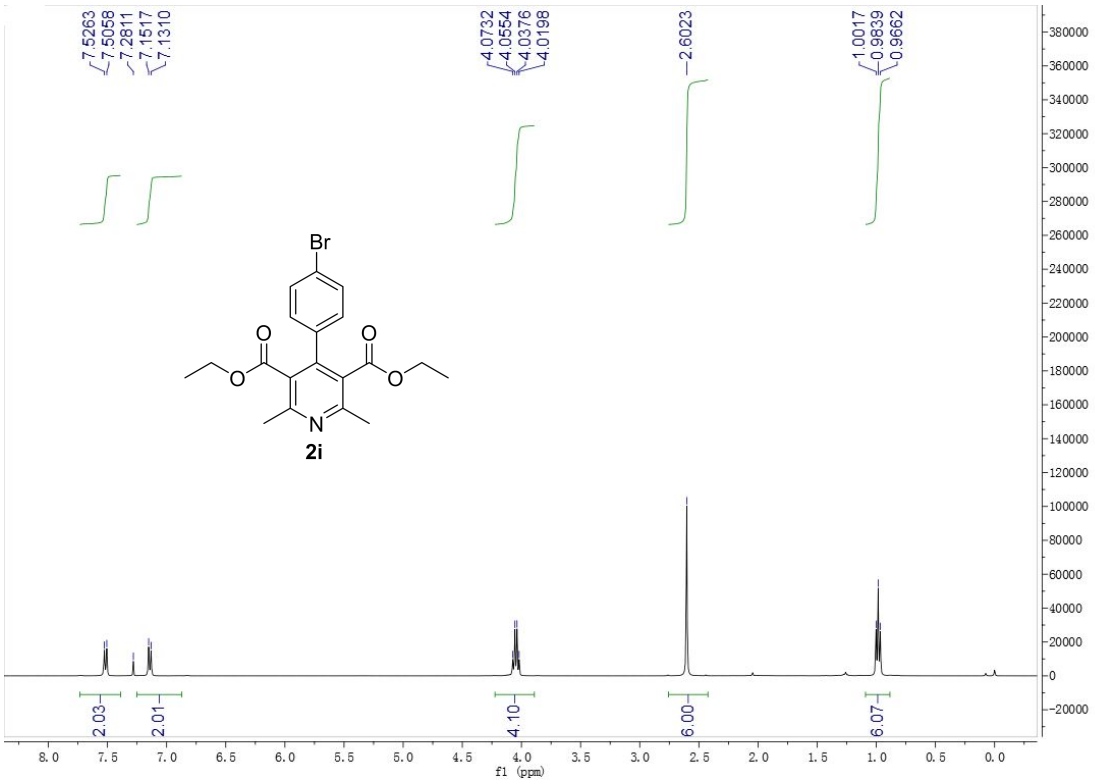
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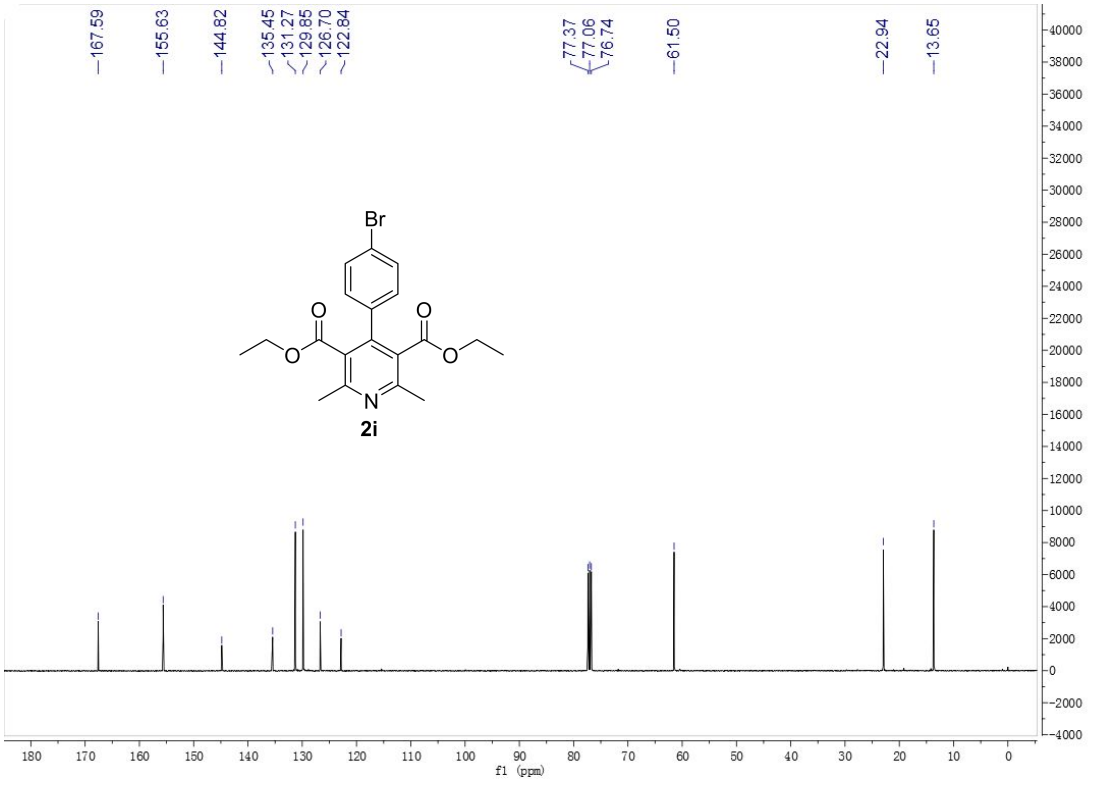
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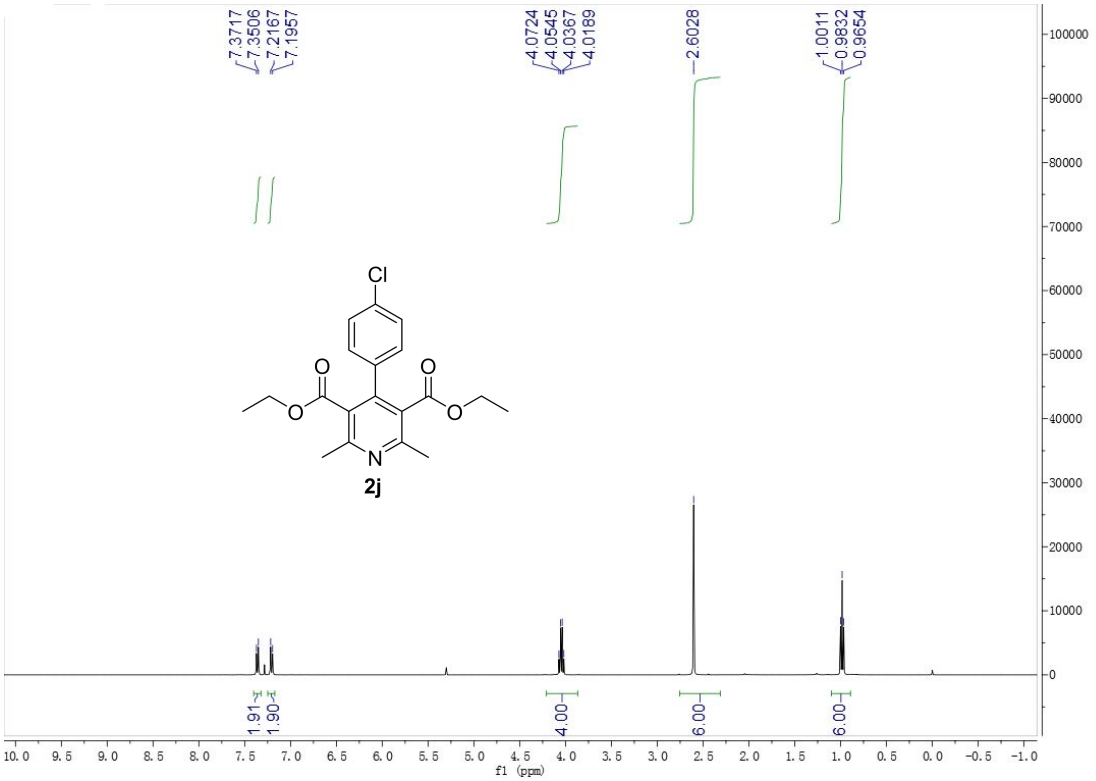
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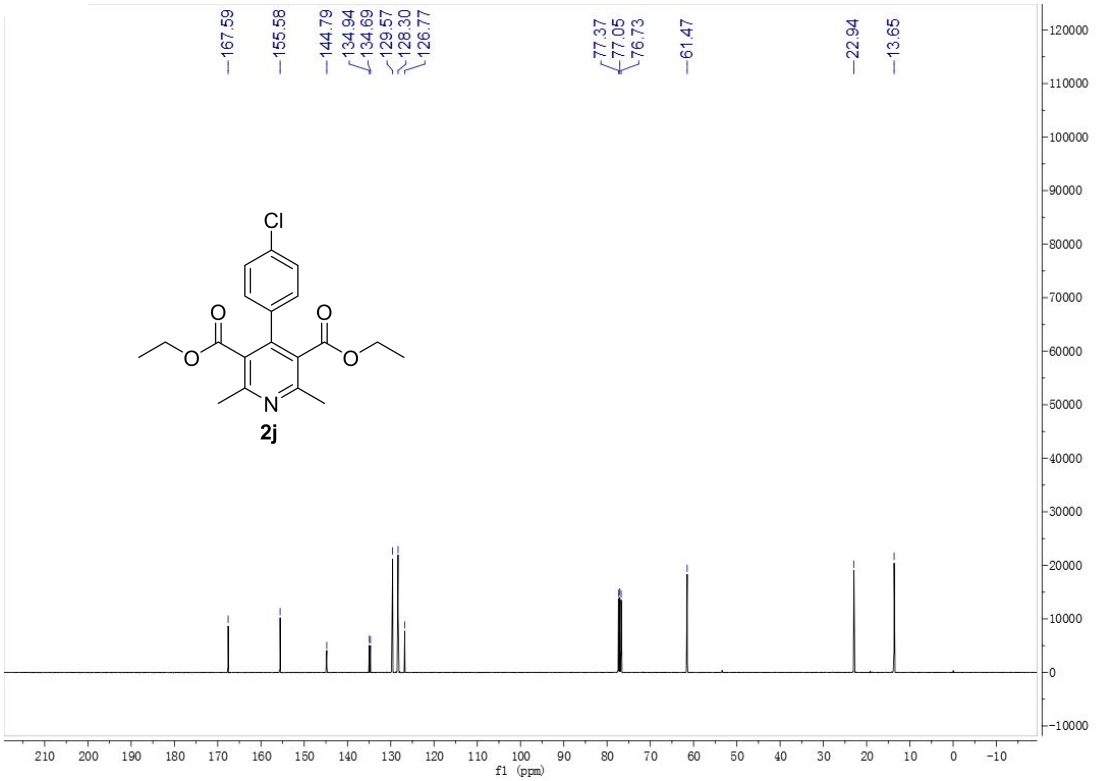
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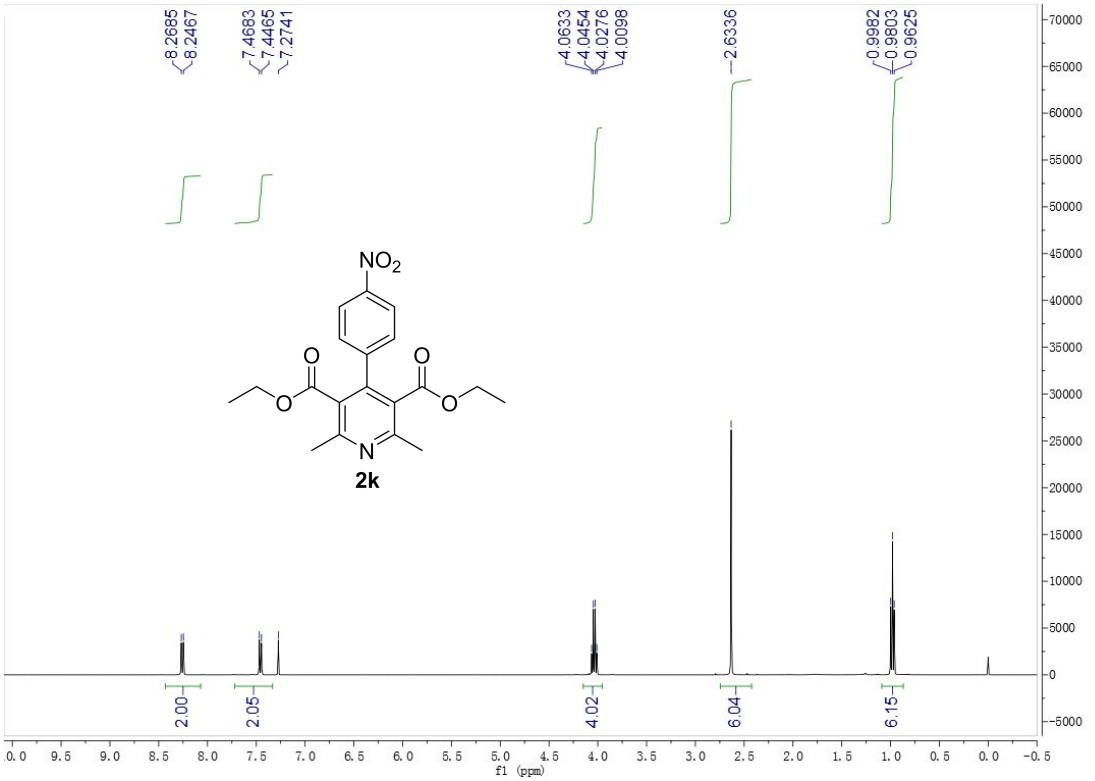
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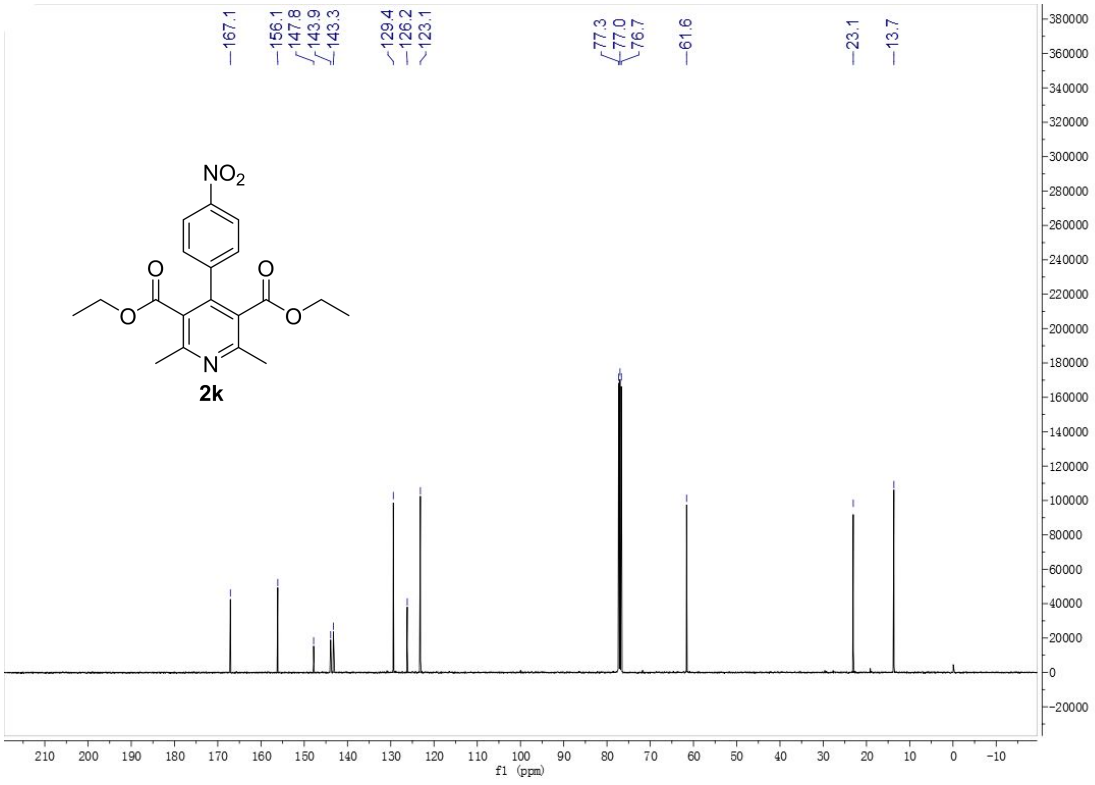
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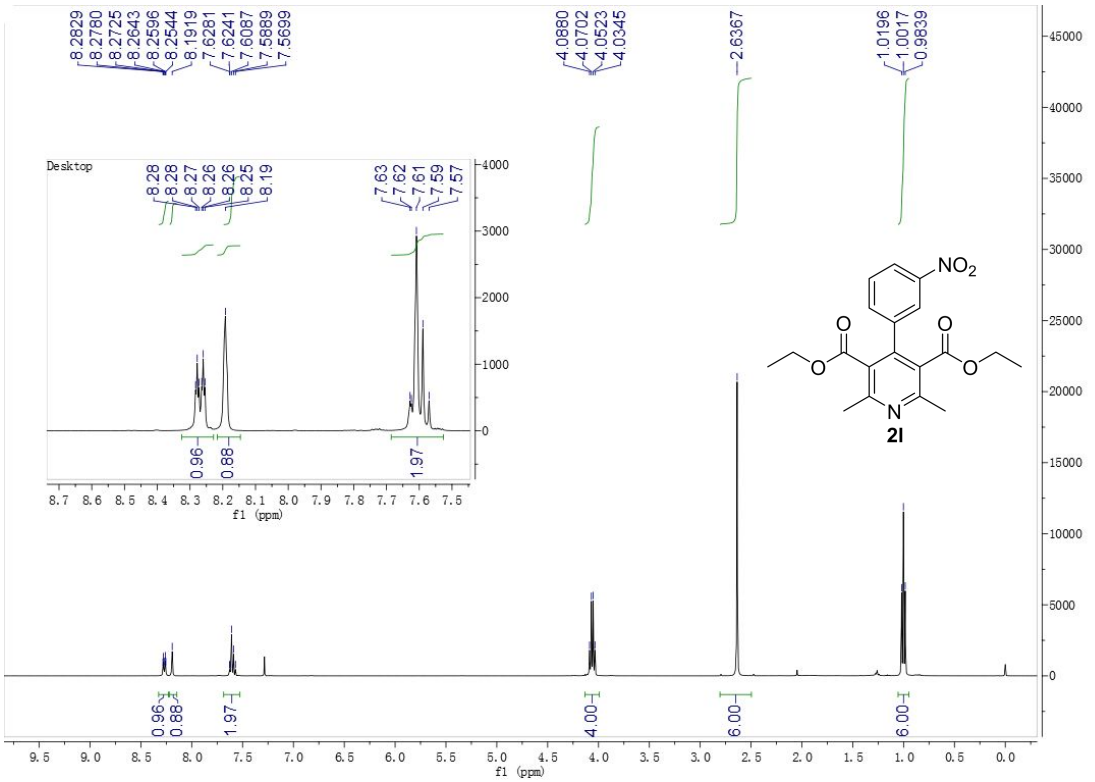
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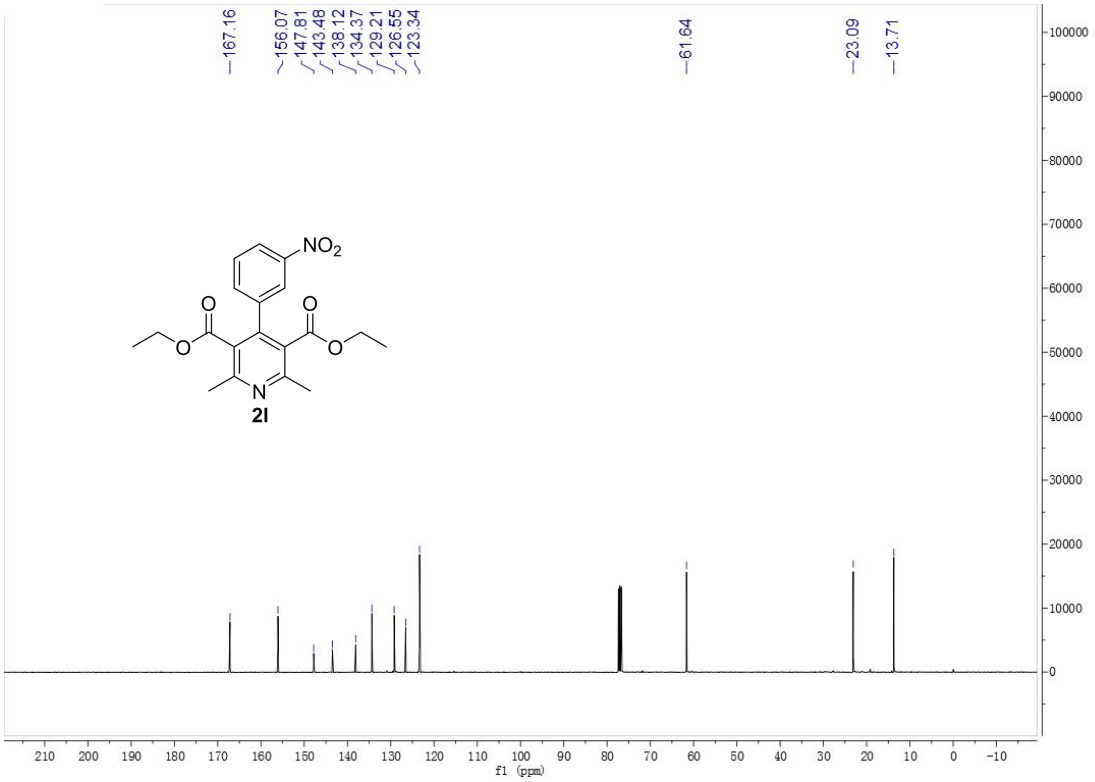
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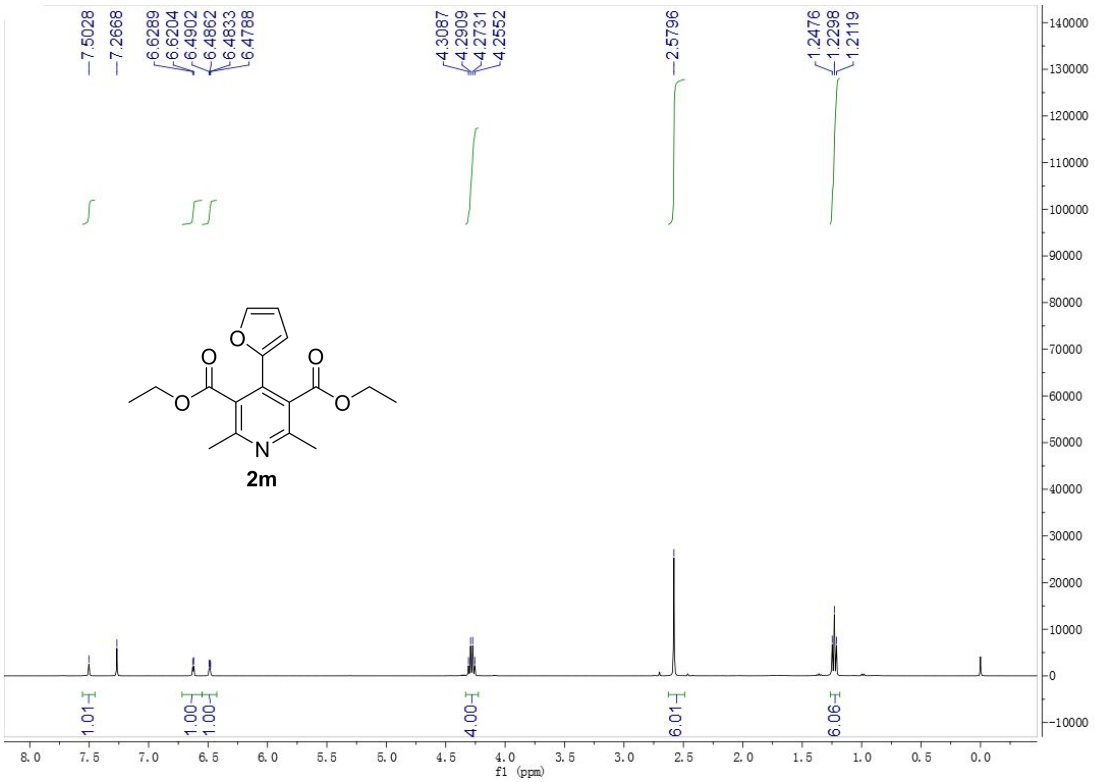
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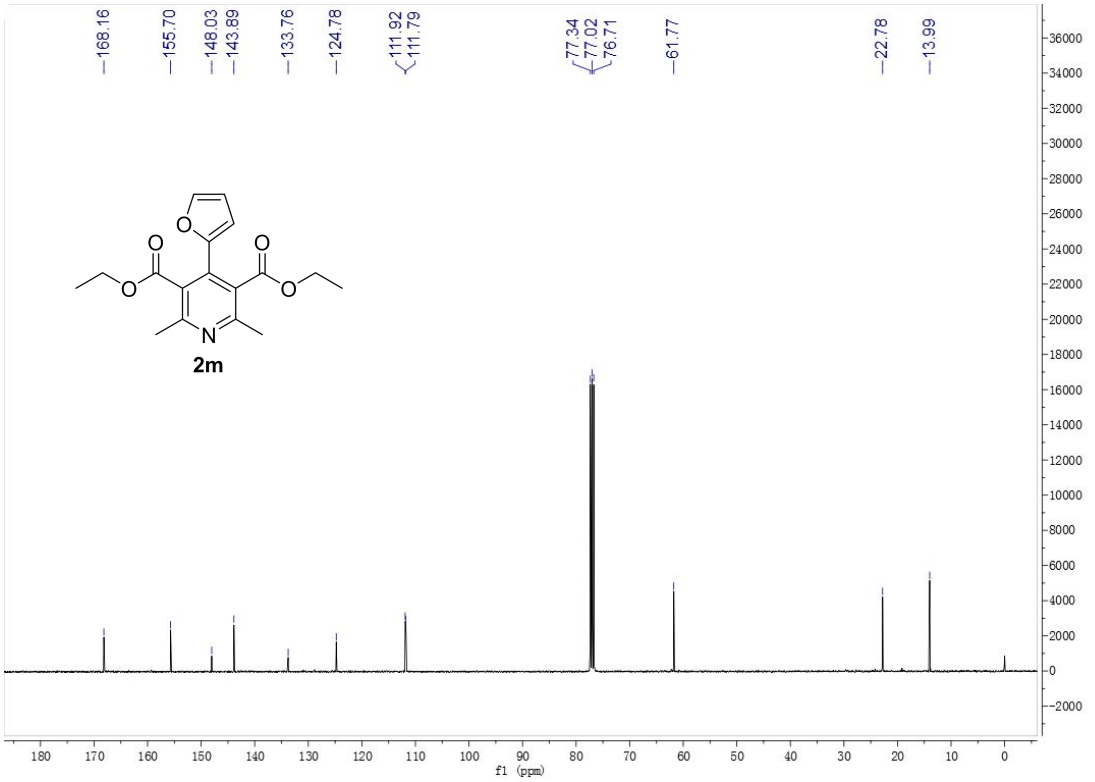
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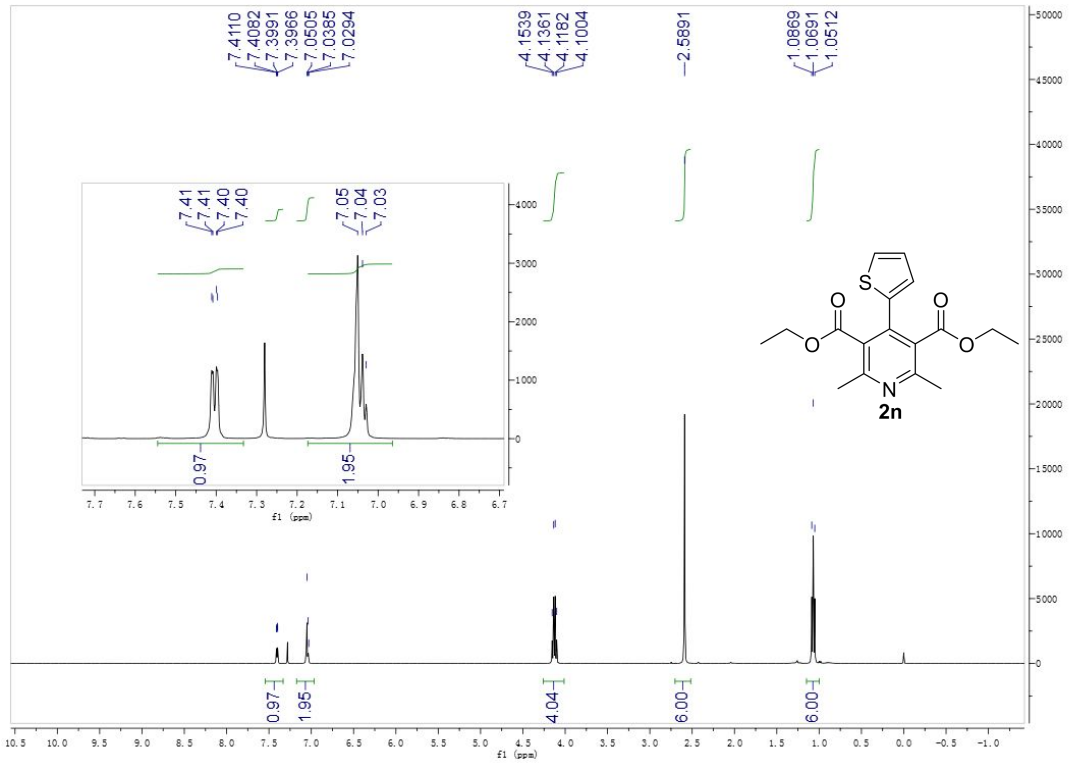
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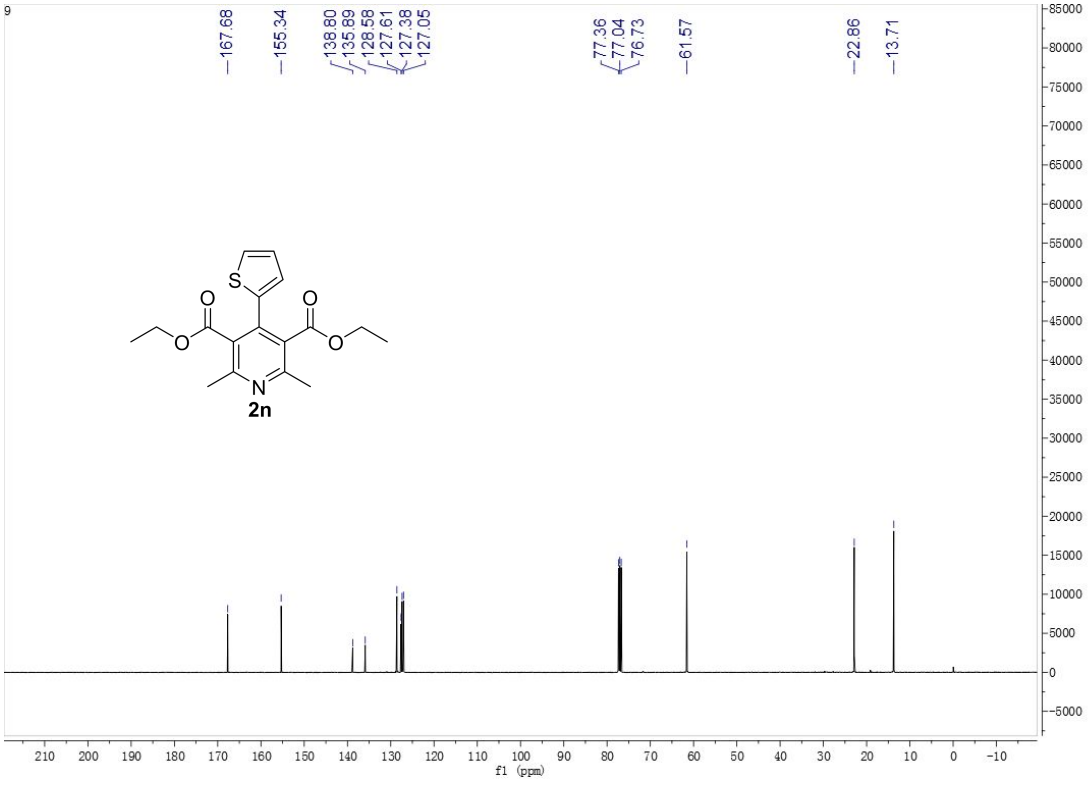
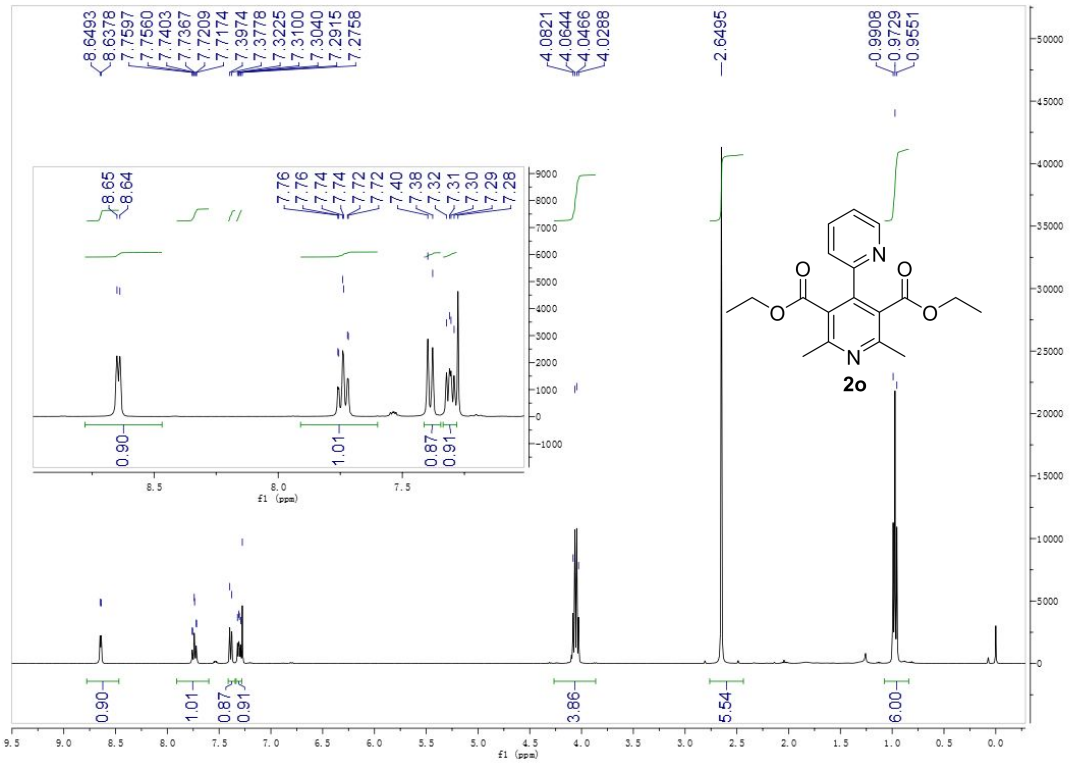
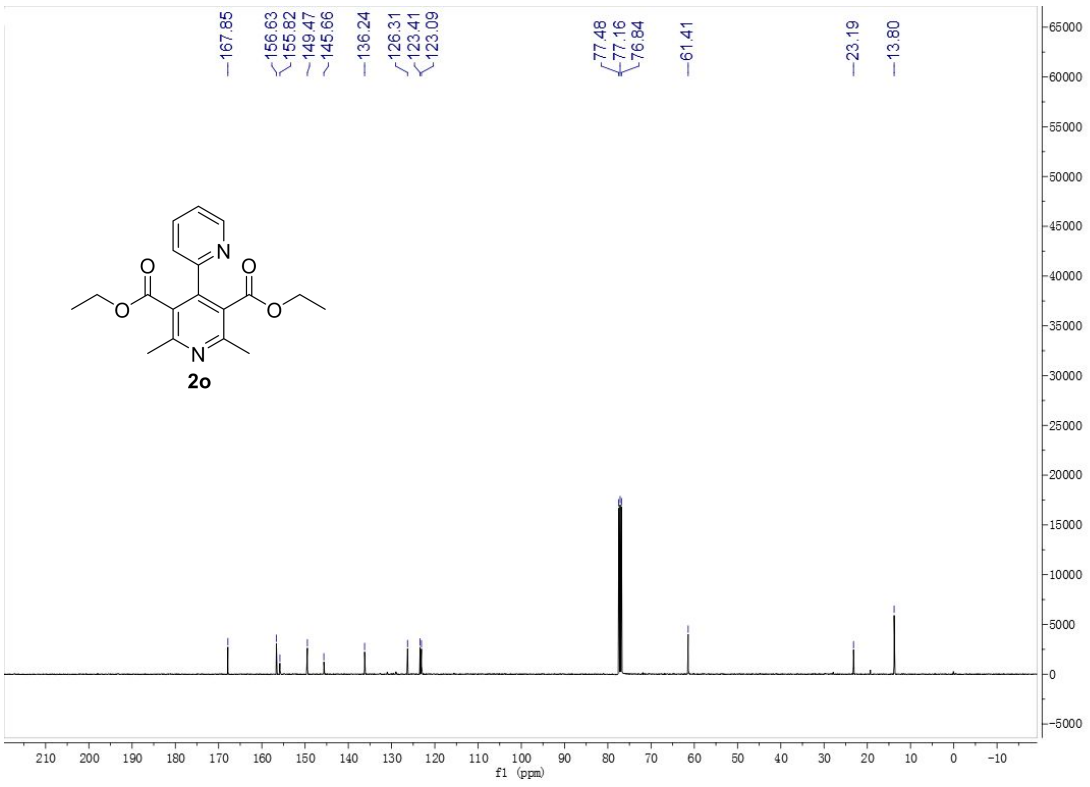
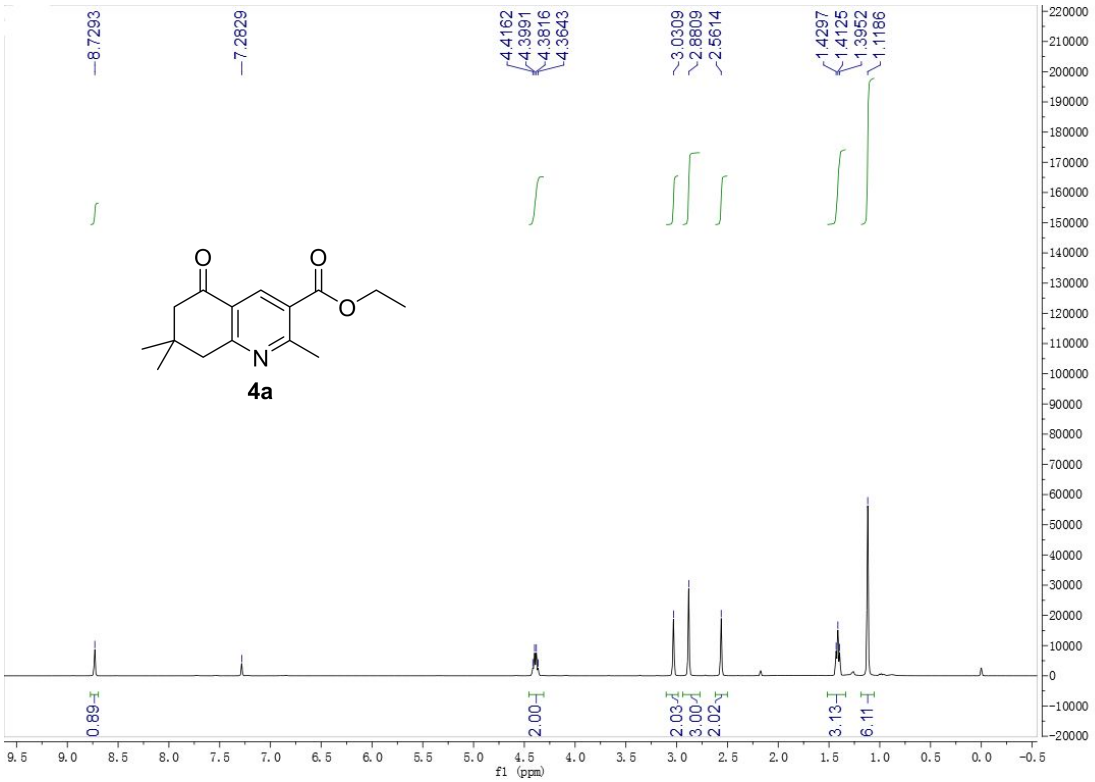
7.4082
7.3991
7.3966
7.0505
7.0385
7.0294
4.1539
4.1361
4.1182
4.1004
2.5891
1.0869
1.0691
1.0512
7.41
7.41
7.40
7.40
7.05
7.04
7.03
0.97
1.95
2n
0.97
1.95
4.04
6.00
6.00
f1 (ppm)

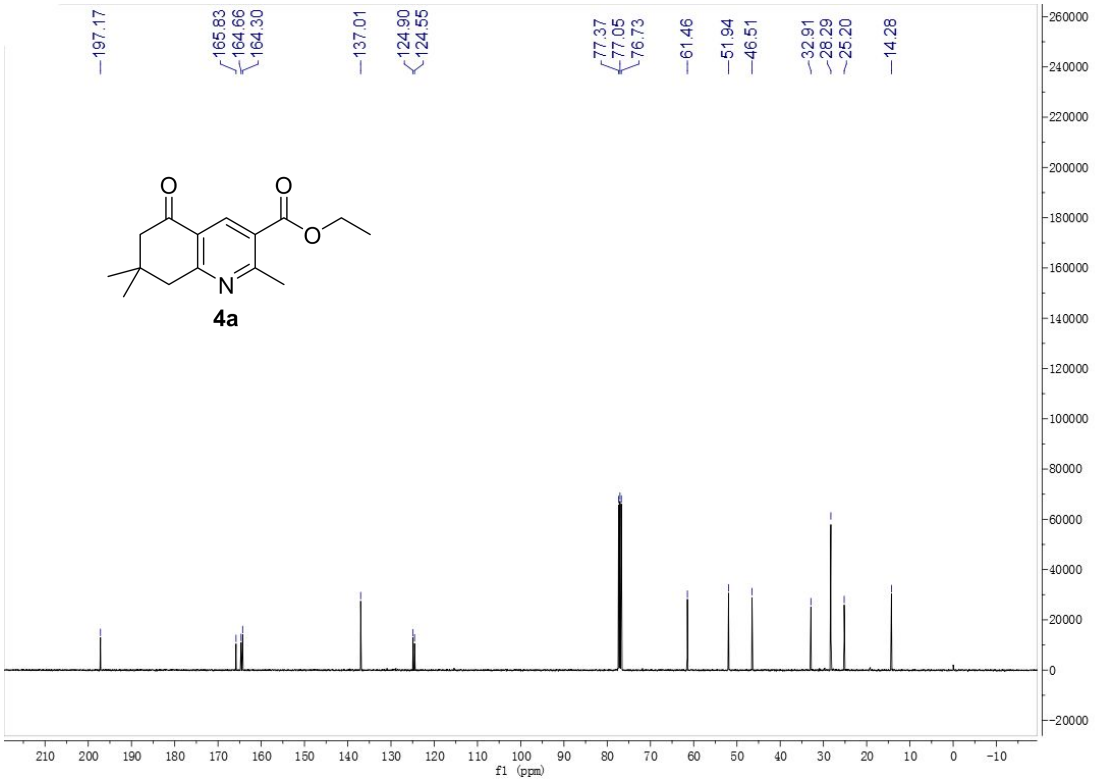

167.68
155.34
138.80
135.89
128.58
127.61
127.38
127.05
77.36
77.04
76.73
61.57
22.86
13.71
2n
f1 (ppm)


8.6493
8.6378
7.7597
7.7560
7.7403
7.7367
7.7209
7.7174
7.3974
7.3778
7.3225
7.3100
7.3040
7.2915
7.2758
4.0821
4.0644
4.0466
4.0288
2.6495
0.9908
0.9729
0.9551
8.65
8.64
7.76
7.76
7.74
7.74
7.72
7.72
7.40
7.38
7.32
7.31
7.30
7.29
7.28
0.90
1.01
0.87
0.91
3.86
5.54
6.00
f1 (ppm)
2o

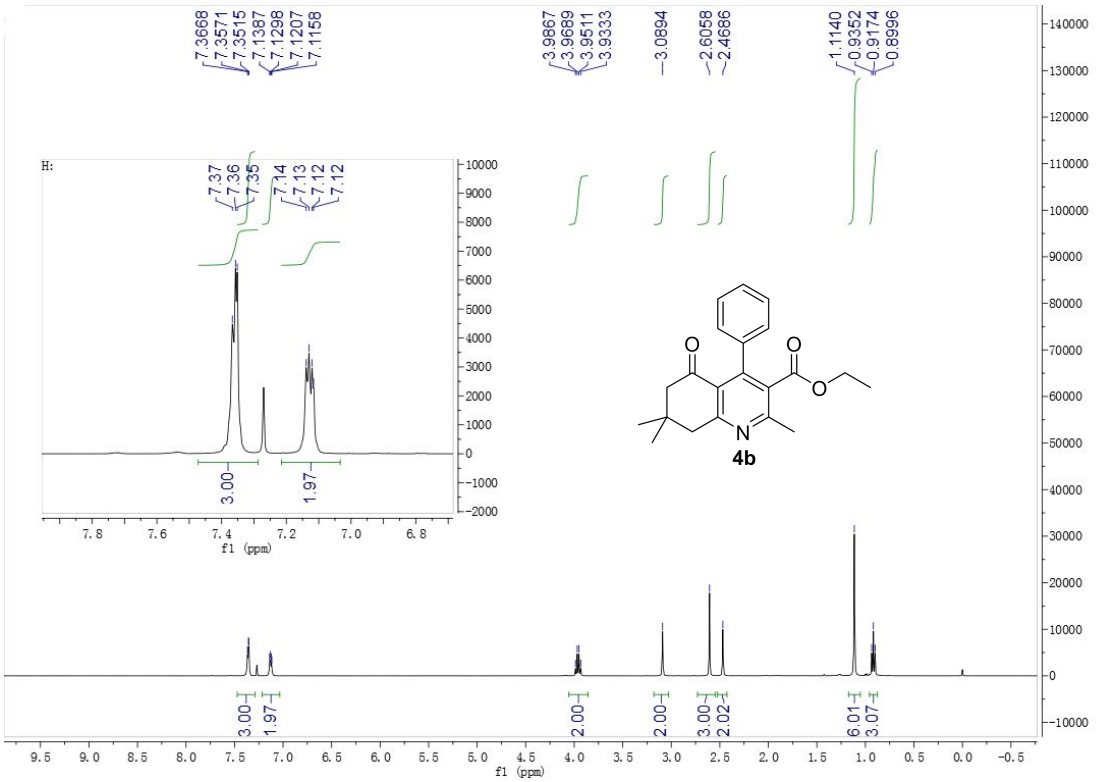

167.85
156.63
155.82
149.47
145.66
136.24
126.31
123.41
123.09
77.48
77.16
76.84
61.41
23.19
13.80
f1 (ppm)
2o

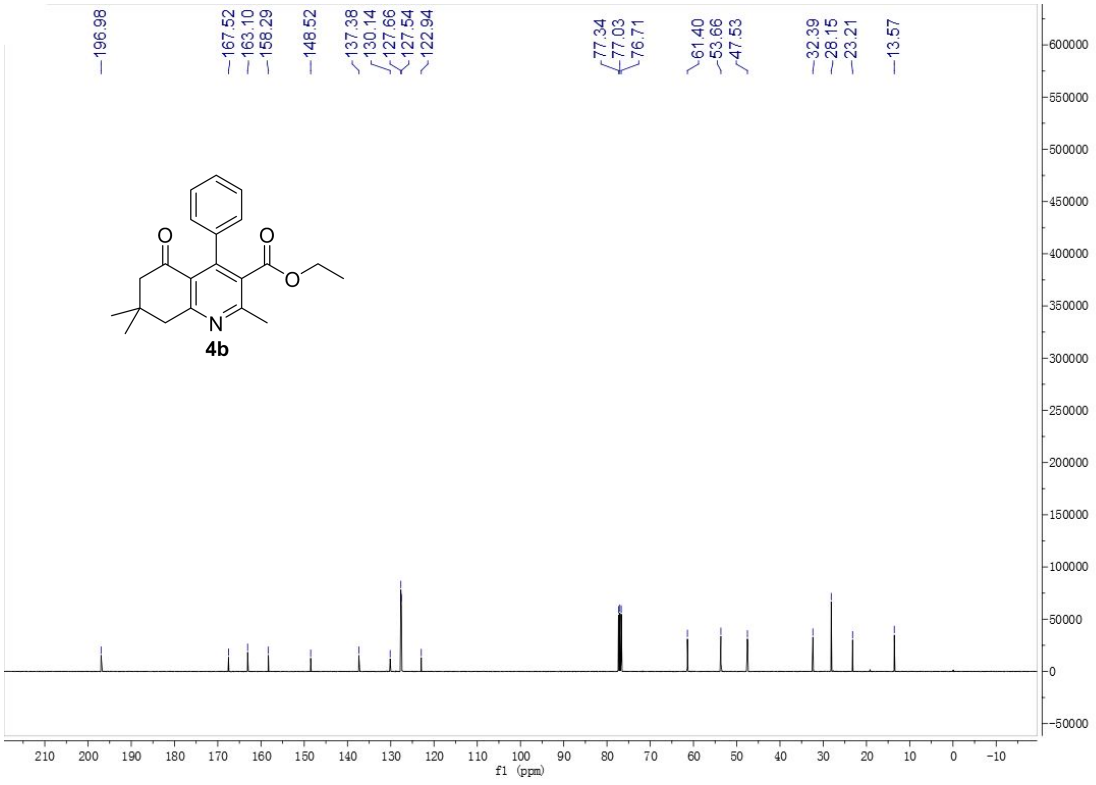

8.7293
7.2829
4.4162
4.3991
4.3816
4.3643
3.0309
2.8809
2.5614
1.4297
1.4125
1.3952
1.1186
0.89
2.00
2.03
3.00
2.02
3.13
6.11
f1 (ppm)

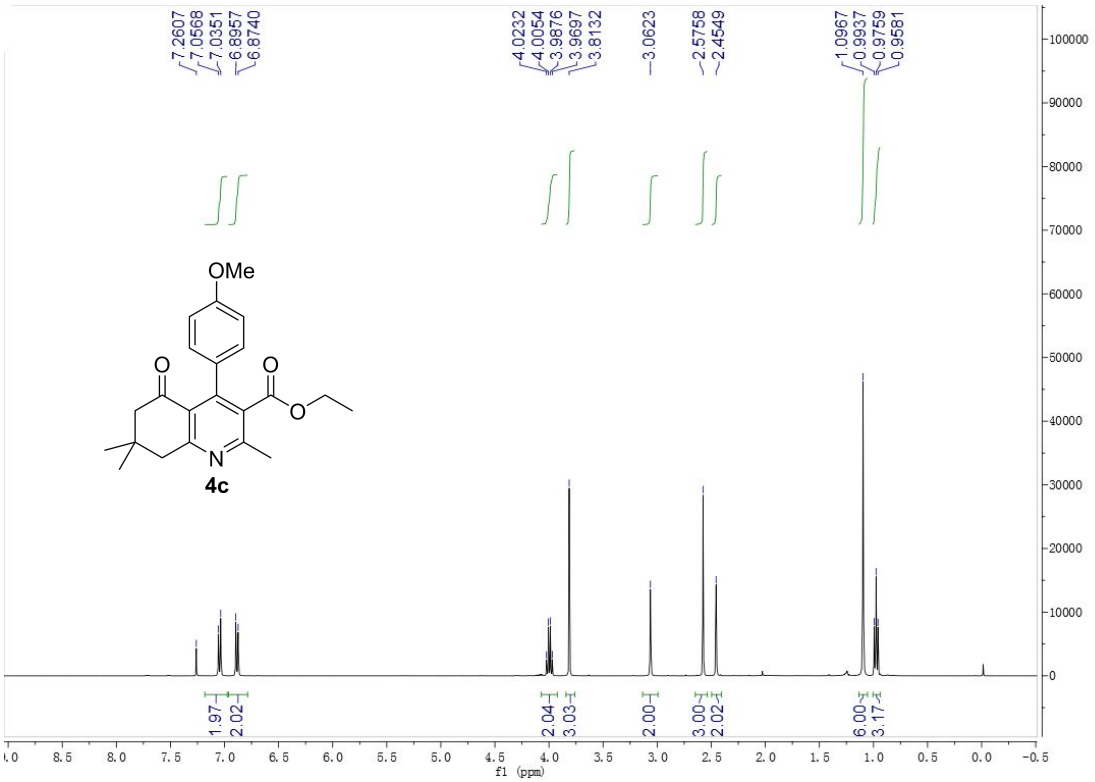
4a

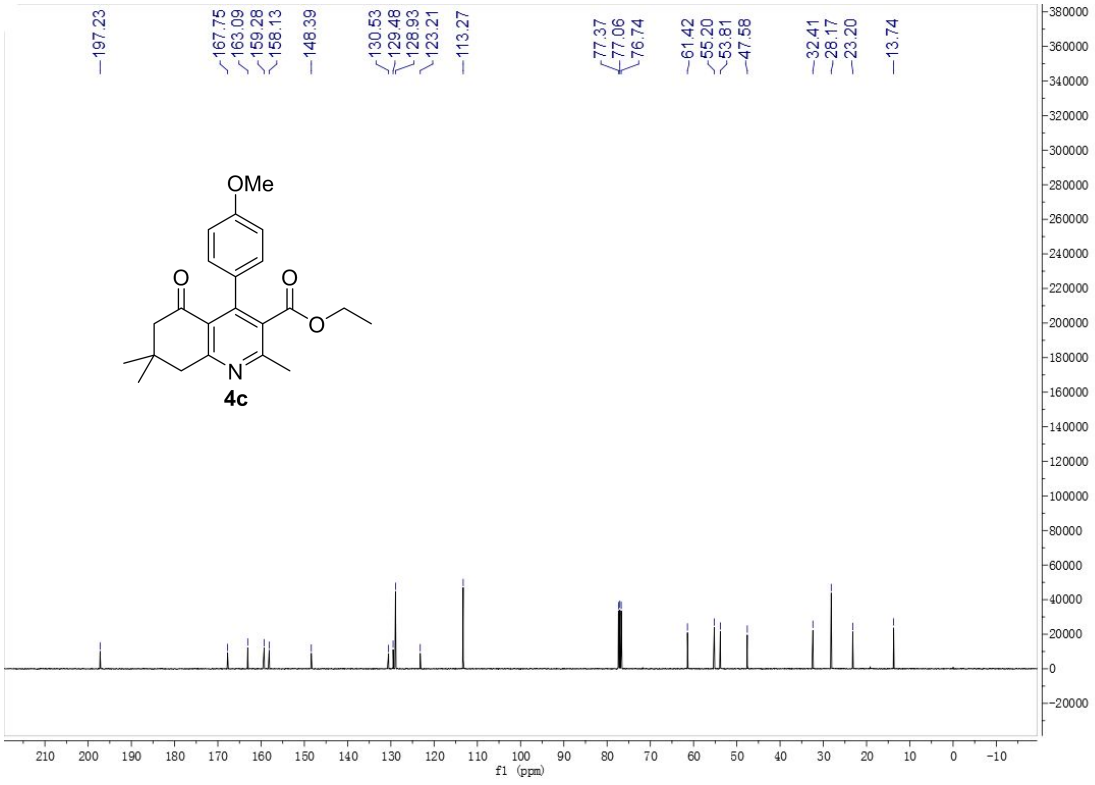

197.17
165.83
164.66
164.30
137.01
124.90
124.55
77.37
77.05
76.73
61.46
51.94
46.51
32.91
28.29
25.20
14.28
f1 (ppm)

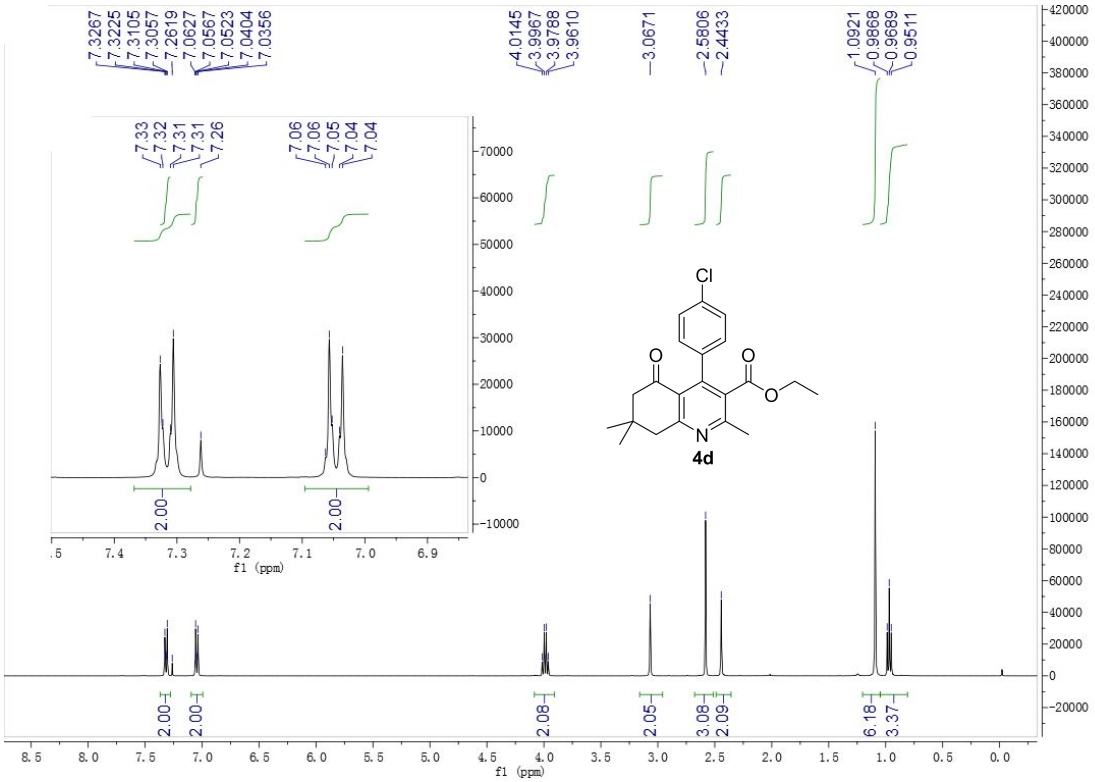
4a

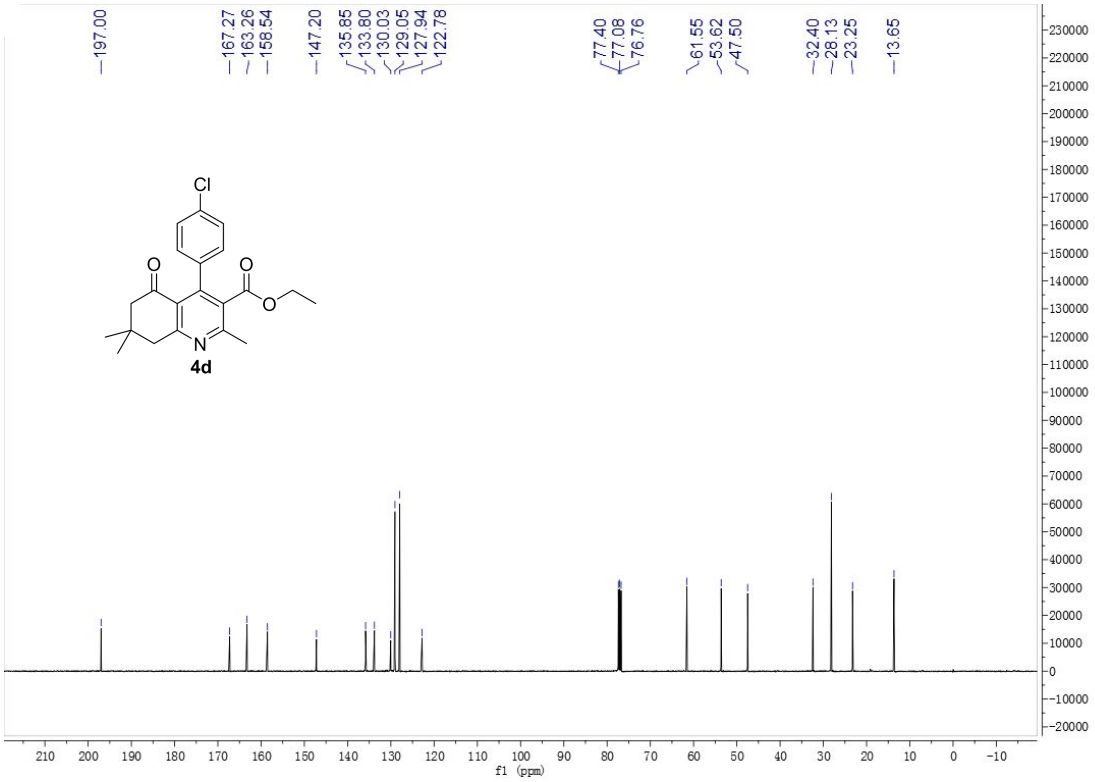

7.3668
7.3571
7.3515
7.1387
7.1298
7.1207
7.1158
3.9867
3.9689
3.9511
3.9333
3.0894
2.6058
2.4686
1.1140
0.9352
0.9174
0.8996
7.37
7.36
7.35
7.14
7.13
7.12
7.12
3.00
1.97
4b
3.00
1.97
2.00
2.00
3.00
2.02
6.01
3.07
f1 (ppm)

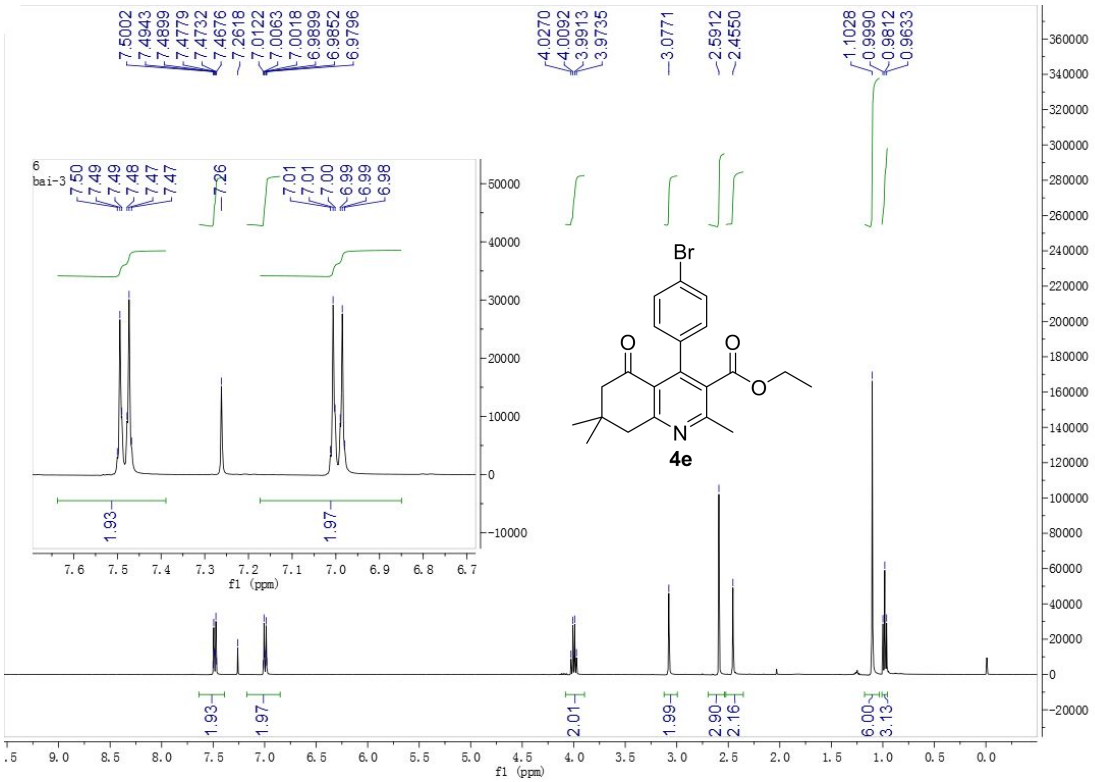

196.98
167.52
163.10
158.29
148.52
137.38
130.14
127.66
127.54
122.94
77.34
77.03
76.71
61.40
53.66
47.53
32.39
28.15
23.21
13.57
4b
f1 (ppm)

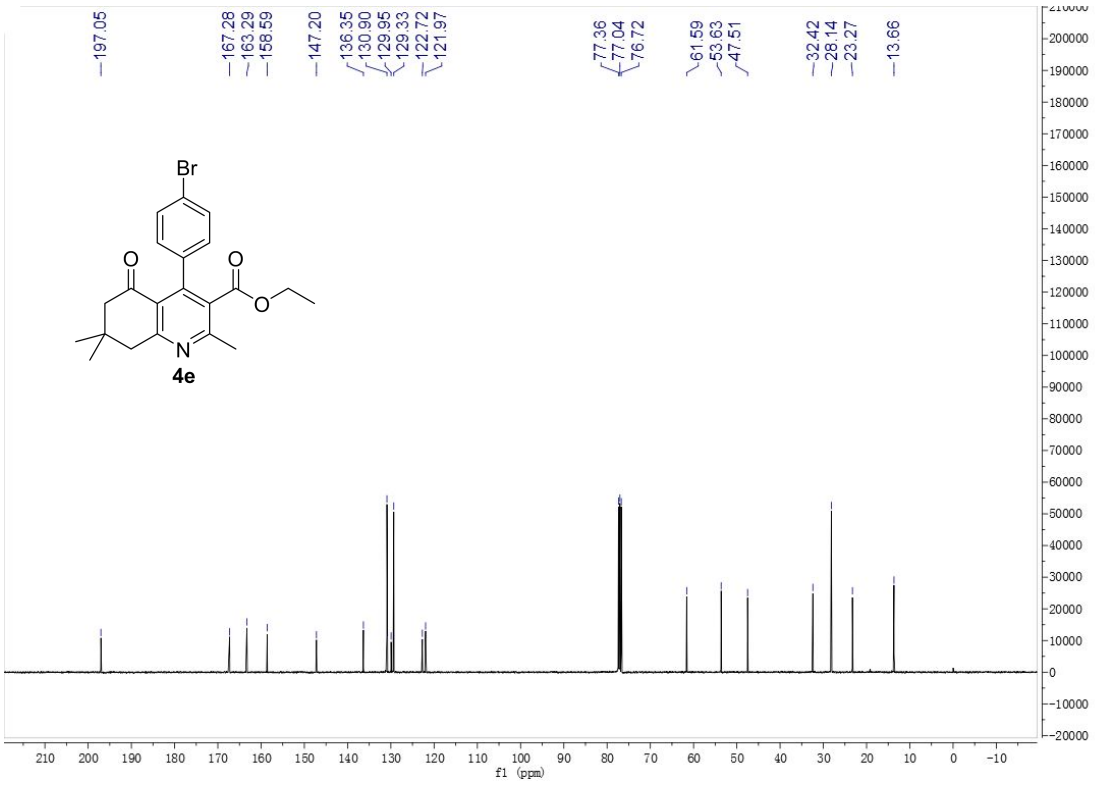

7.2607
7.0568
7.0351
6.8957
6.8740
4.0232
4.0054
3.9876
3.9697
3.8132
3.0623
2.5758
2.4549
1.0967
0.9937
0.9759
0.9581
OMe
O
O
O
N
4c
1.97
2.02
2.04
3.03
2.00
3.00
2.02
6.00
3.17
f1 (ppm)

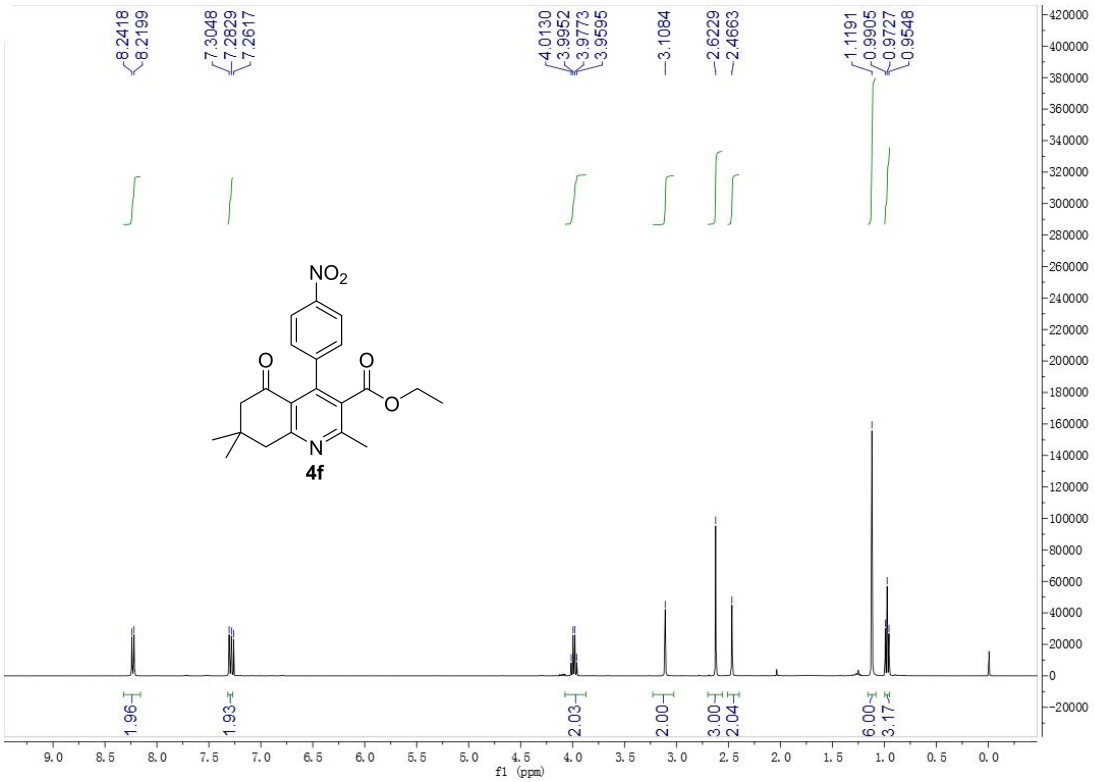

197.23
167.75
163.09
159.28
158.13
148.39
130.53
129.48
128.93
123.21
113.27
77.37
77.06
76.74
61.42
55.20
53.81
47.58
32.41
28.17
23.20
13.74
OMe
O
O
O
N
4c
f1 (ppm)

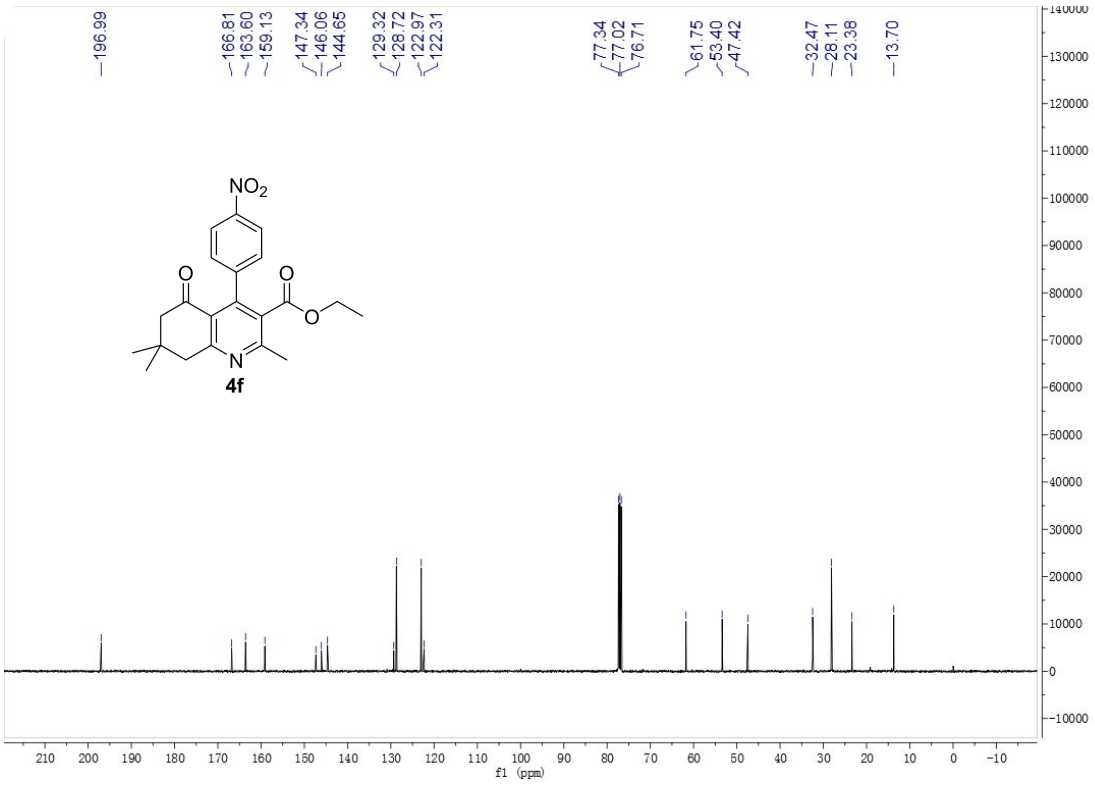

7.3267
7.3225
7.3105
7.3057
7.2619
7.0627
7.0567
7.0523
7.0404
7.0356
4.0145
3.9967
3.9788
3.9610
3.0671
2.5806
2.4433
1.0921
0.9868
0.9689
0.9511
7.33
7.32
7.31
7.31
7.26
7.06
7.06
7.05
7.04
7.04
Cl
O
O
O
N
4d
2.00
2.00
2.00
2.00
2.08
2.05
3.08
2.09
6.18
3.37
f1 (ppm)

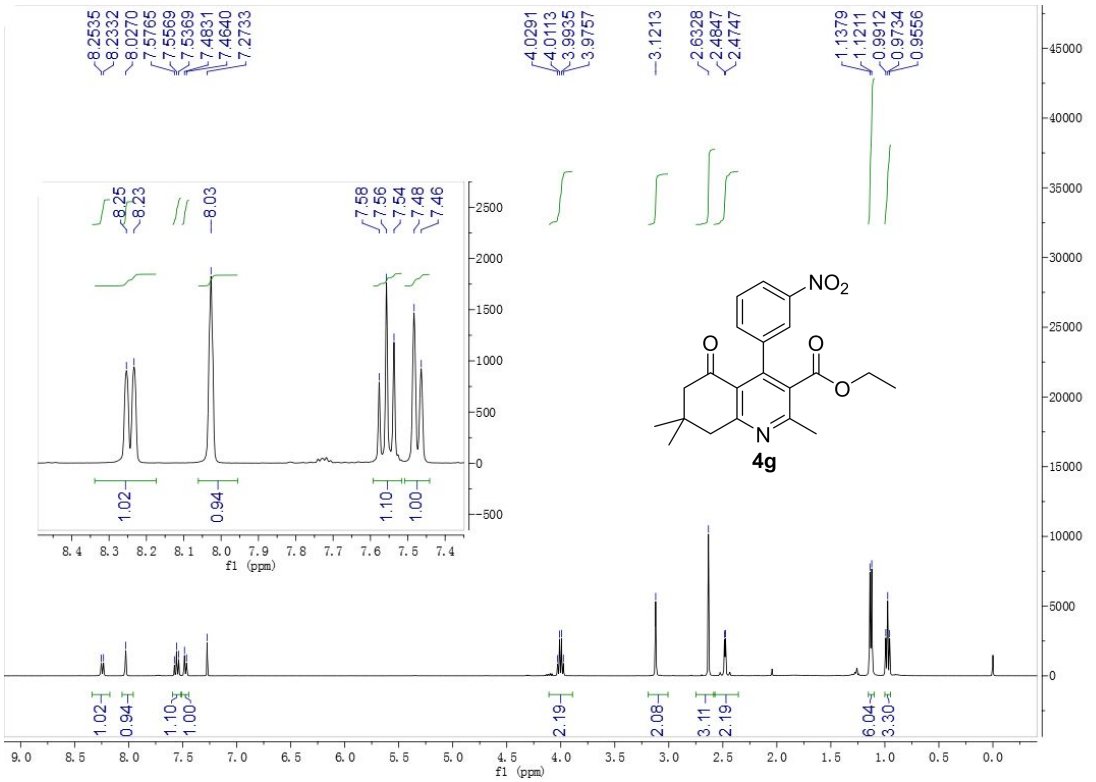

197.00
167.27
163.26
158.54
147.20
135.85
133.80
130.03
129.05
127.94
122.78
77.40
77.08
76.76
61.55
53.62
47.50
32.40
28.13
23.25
13.65
Cl
O
O
O
N
4d
f1 (ppm)

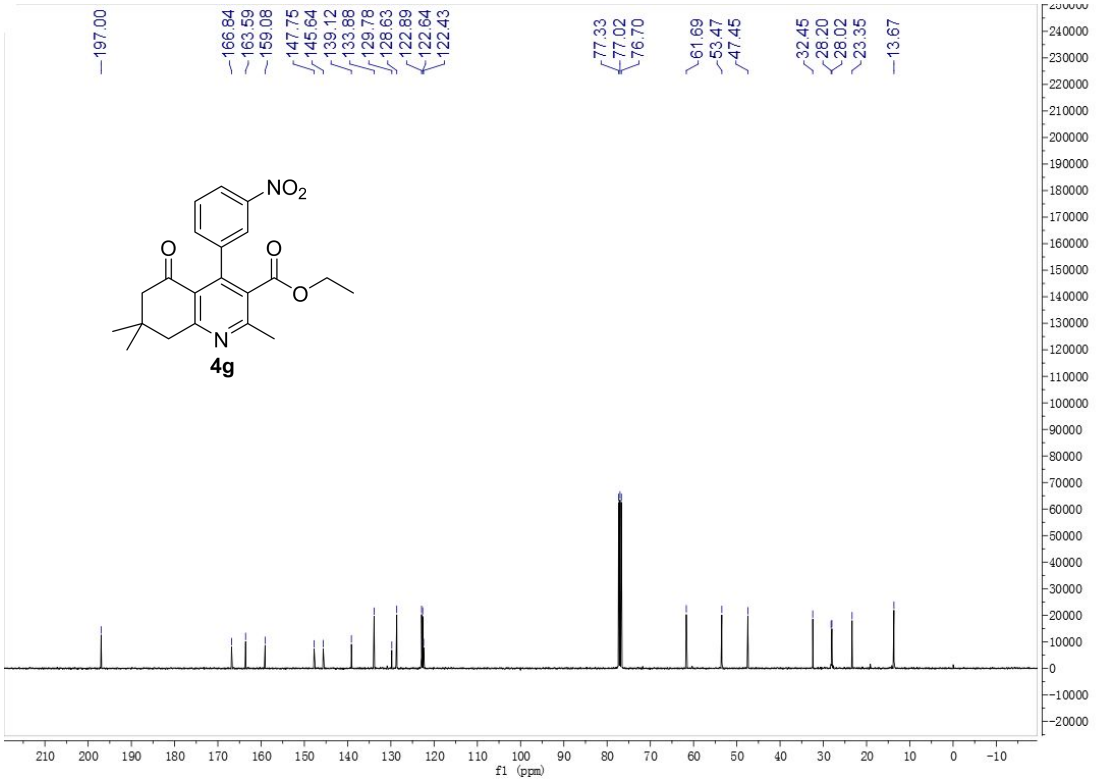

7.5002
7.4943
7.4899
7.4779
7.4732
7.4676
7.2618
7.0122
7.0063
7.0018
6.9899
6.9852
6.9796
4.0270
4.0092
3.9913
3.9735
3.0771
2.5912
2.4550
1.1028
0.9990
0.9812
0.9633
6
bai-3
7.50
7.49
7.49
7.48
7.47
7.47
7.26
7.01
7.01
7.00
6.99
6.99
6.98
1.93
1.97
f1 (ppm)
Br
O
O
O
N
4e
1.93
1.97
2.01
1.99
2.90
2.16
6.00
3.13
f1 (ppm)

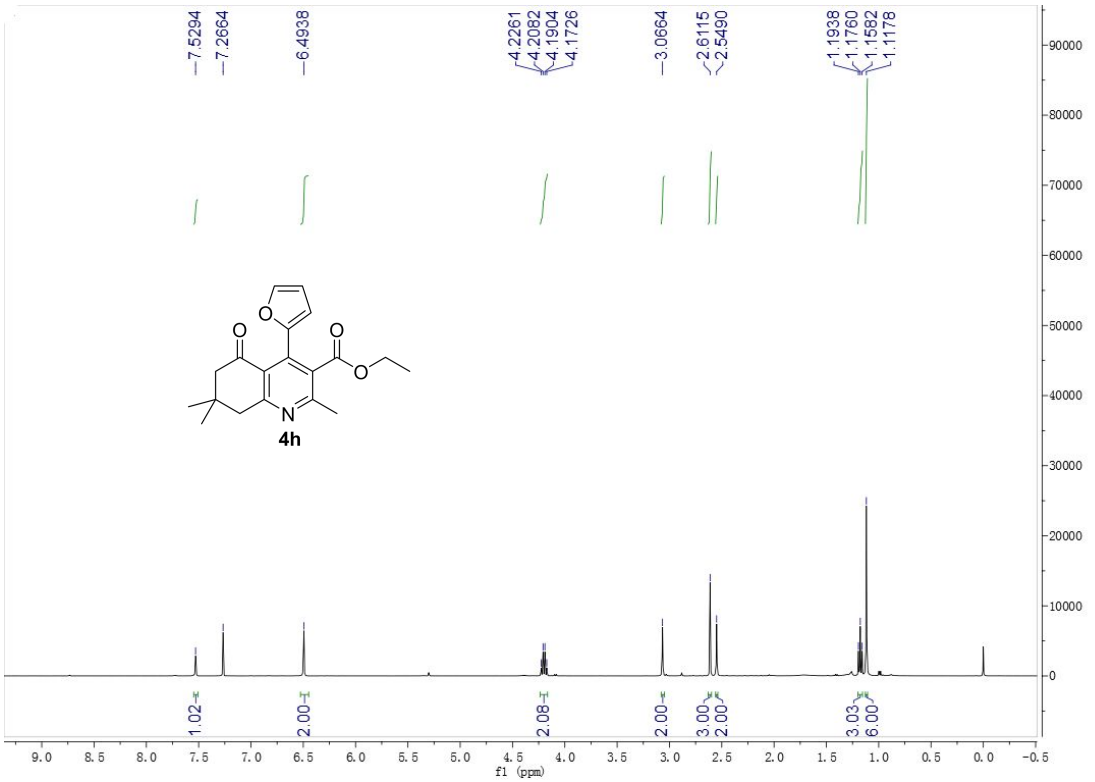

197.05
167.28
163.29
158.59
147.20
136.35
130.90
129.95
129.33
122.72
121.97
77.36
77.04
76.72
61.59
53.63
47.51
32.42
28.14
23.27
13.66
Br
O
O
O
N
4e
f1 (ppm)

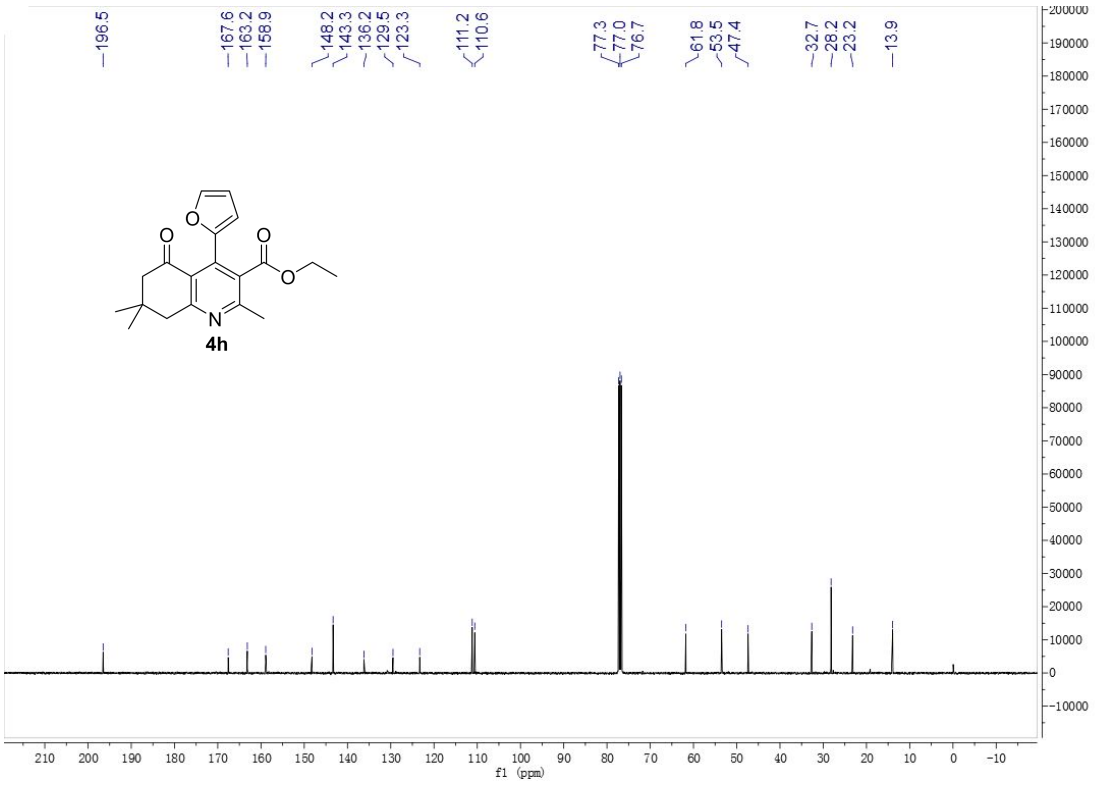

8.2418
8.2199
7.3048
7.2829
7.2617
4.0130
3.9952
3.9773
3.9595
3.1084
2.6229
2.4663
1.1191
0.9905
0.9727
0.9548
NO2
O
O
O
N
4f
1.96
1.93
2.03
2.00
3.00
2.04
6.00
3.17
f1 (ppm)

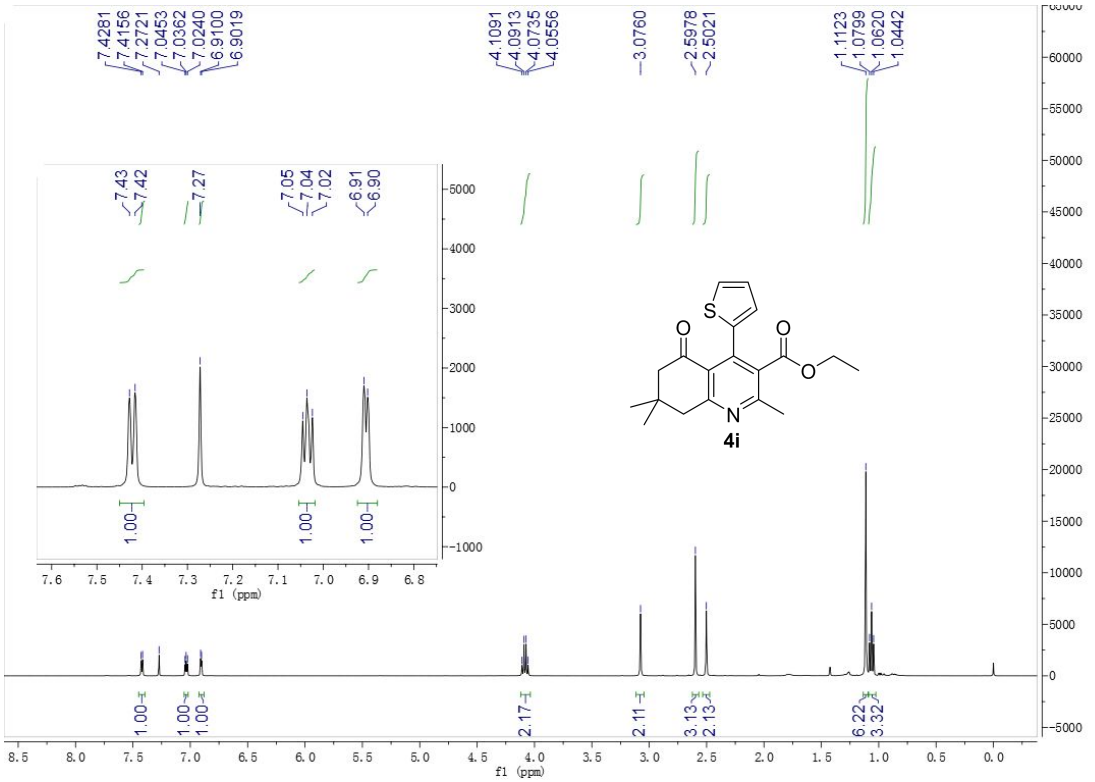

196.99
166.81
163.60
159.13
147.34
146.06
144.65
129.32
128.72
122.97
122.31
77.34
77.02
76.71
61.75
53.40
47.42
32.47
28.11
23.38
13.70
NO2
O
O
O
N
4f
f1 (ppm)

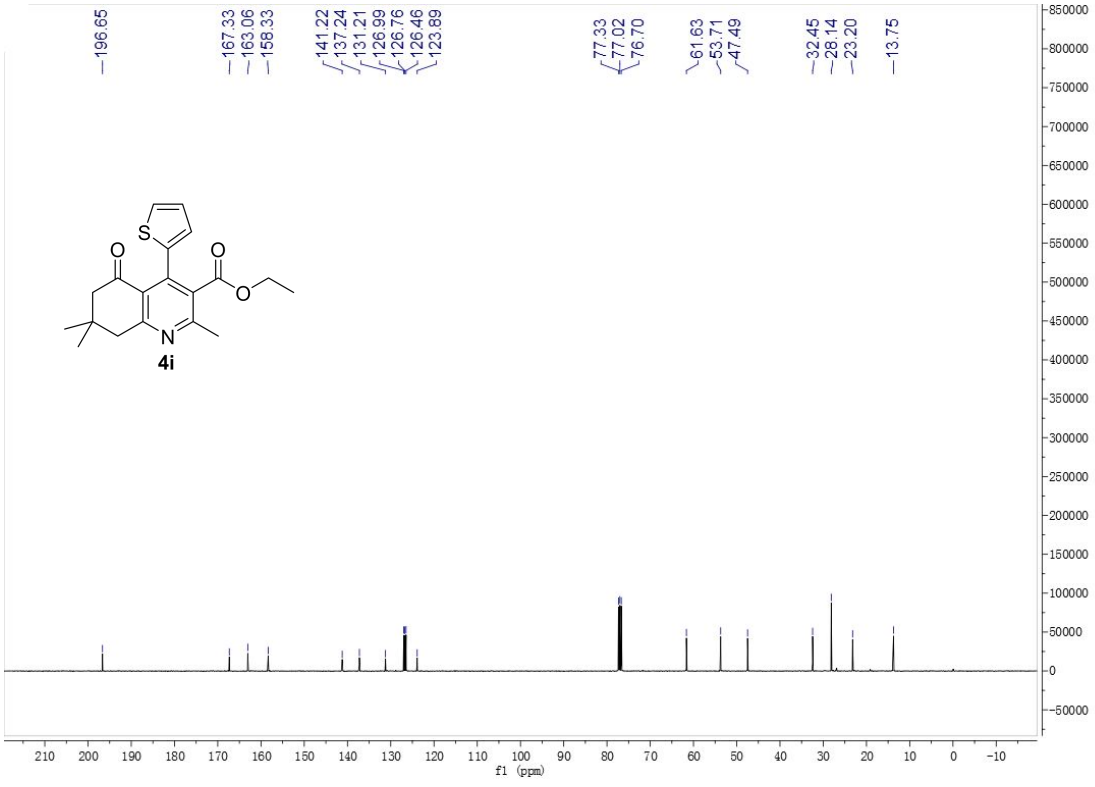

8.2535
8.2332
8.0270
7.5765
7.5569
7.5369
7.4831
7.4640
7.2733
4.0291
4.0113
3.9935
3.9757
3.1213
2.6328
2.4847
2.4747
1.1379
1.1211
0.9912
0.9734
0.9556
8.25
8.23
8.03
7.58
7.56
7.54
7.48
7.46
1.02
0.94
1.10
1.00
2.19
2.08
3.11
2.19
6.04
3.30
NO2
O
O
O
N
4g
f1 (ppm)


197.00
166.84
163.59
159.08
147.75
145.64
139.12
133.88
129.78
128.63
122.89
122.64
122.43
77.33
77.02
76.70
61.69
53.47
47.45
32.45
28.20
28.02
23.35
13.67
NO2
O
O
O
N
4g
f1 (ppm)

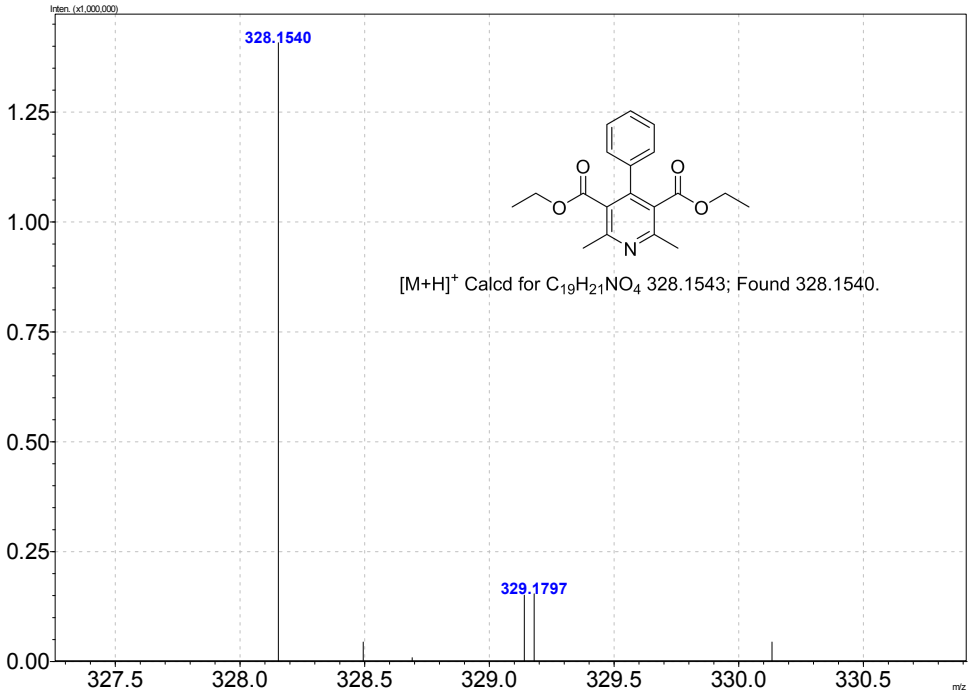

7.5294
7.2664
6.4938
4.2261
4.2082
4.1904
4.1726
3.0664
2.6115
2.5490
1.1938
1.1760
1.1582
1.1178
4h
1.02
2.00
2.08
2.00
3.00
2.00
3.03
6.00
f1 (ppm)

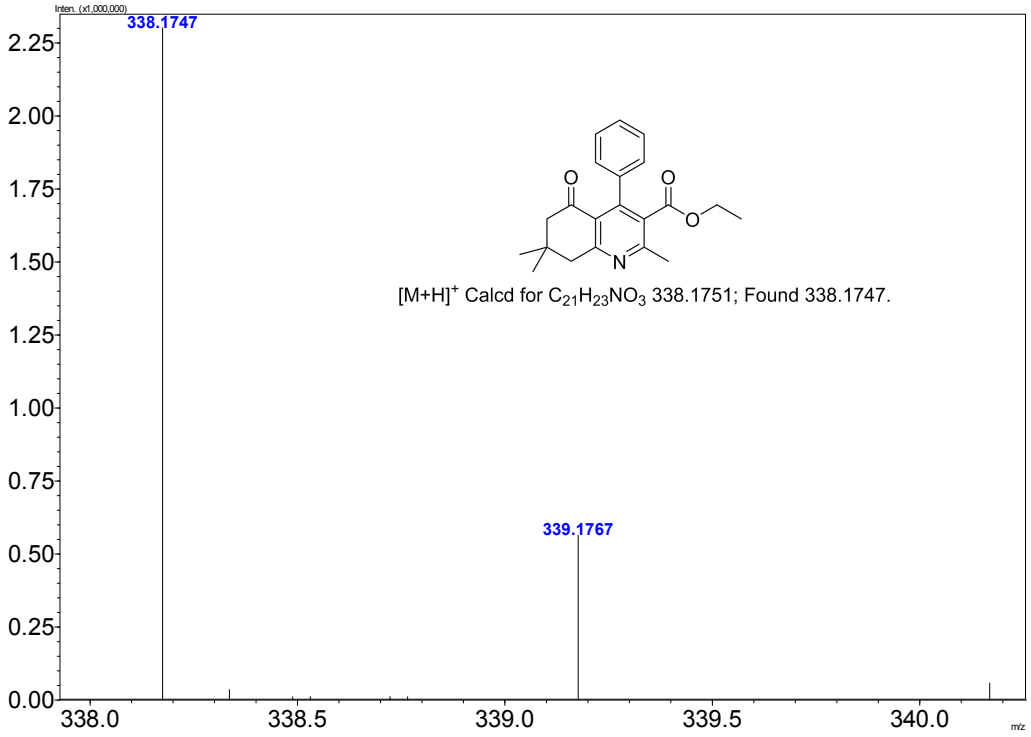

196.5
167.6
163.2
158.9
148.2
143.3
136.2
129.5
123.3
111.2
110.6
77.3
77.0
76.7
61.8
53.5
47.4
32.7
28.2
23.2
13.9
4h
f1 (ppm)

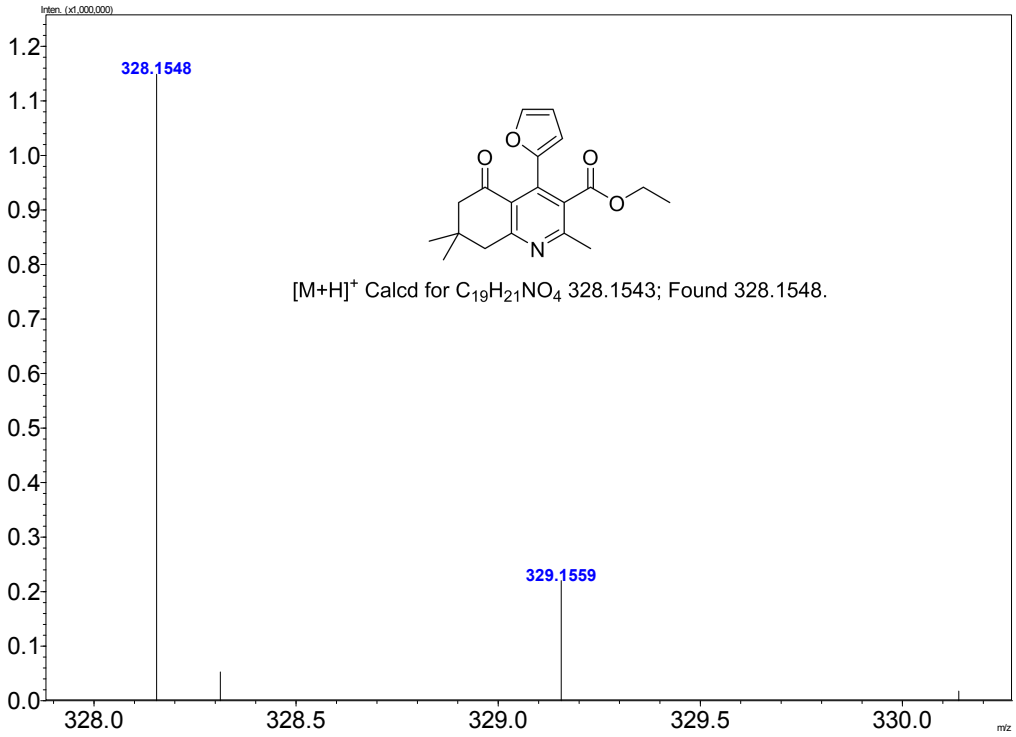

7.4281
7.4156
7.2721
7.0453
7.0362
7.0240
6.9100
6.9019
4.1091
4.0913
4.0735
4.0556
3.0760
2.5978
2.5021
1.1123
1.0799
1.0620
1.0442
7.43
7.42
7.27
7.05
7.04
7.02
6.91
6.90
1.00
1.00
1.00
f1 (ppm)
S
O
O
O
N
4i
1.00
1.00
1.00
2.17
2.11
3.13
2.13
6.22
3.32
f1 (ppm)


196.65
167.33
163.06
158.33
141.22
137.24
131.21
126.99
126.76
126.46
123.89
77.33
77.02
76.70
61.63
53.71
47.49
32.45
28.14
23.20
13.75
S
O
O
O
N
4i
f1 (ppm)

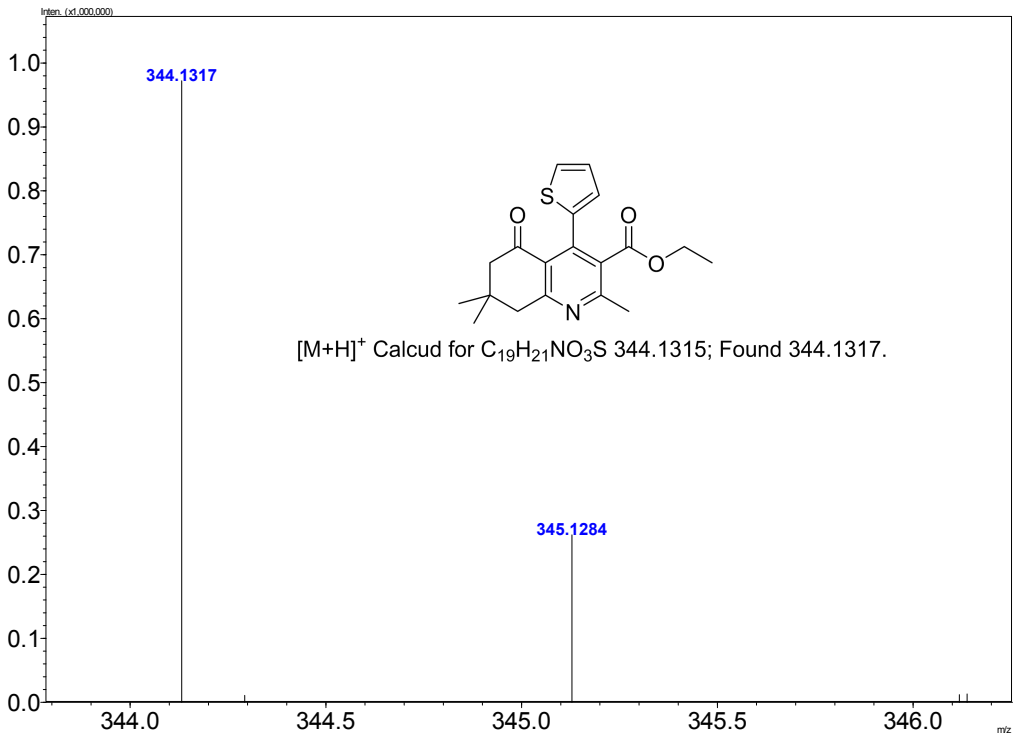
5. HRMS spectra



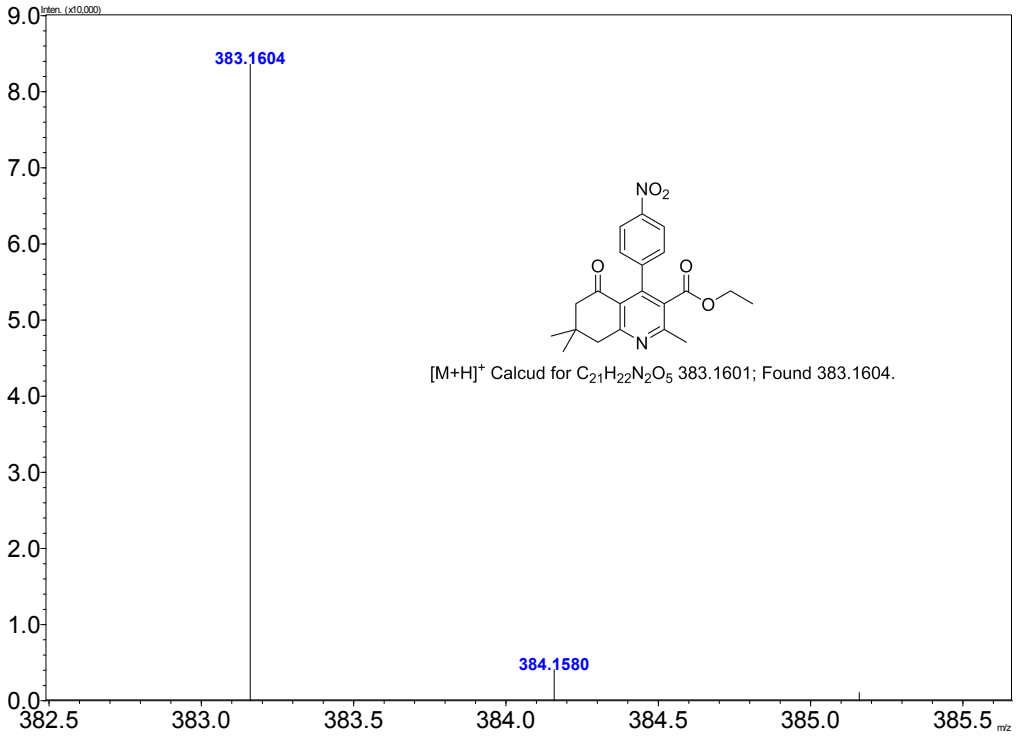




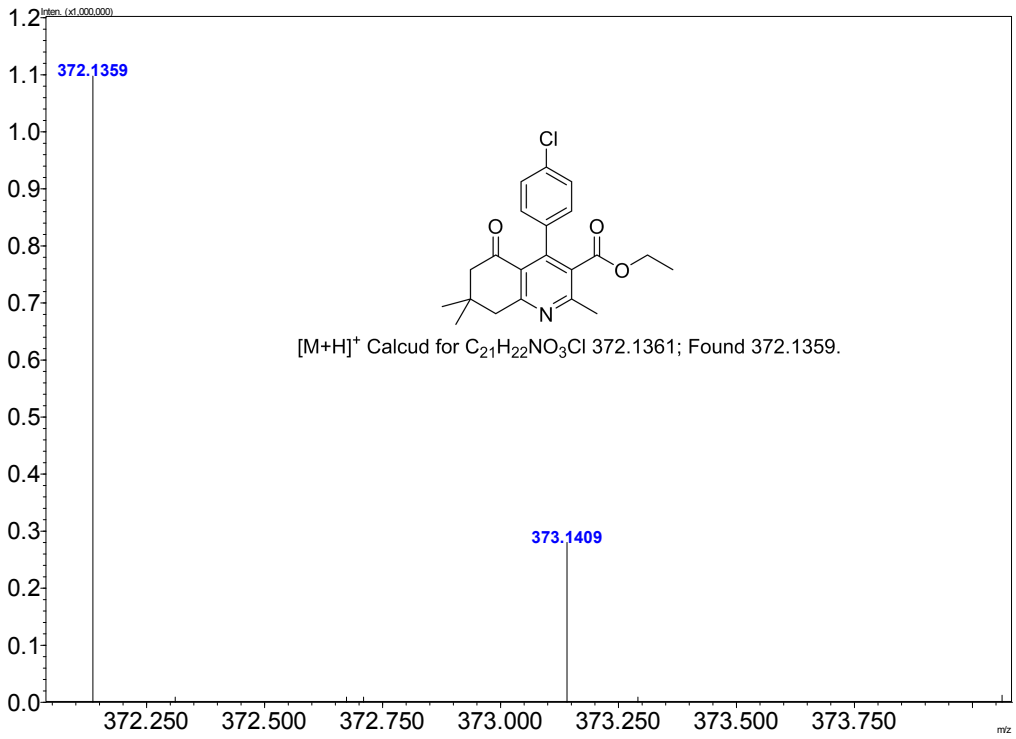
$[M+H]^+$ Calcd for $C_{19}H_{21}NO_4$ 328.1543; Found 328.1548.



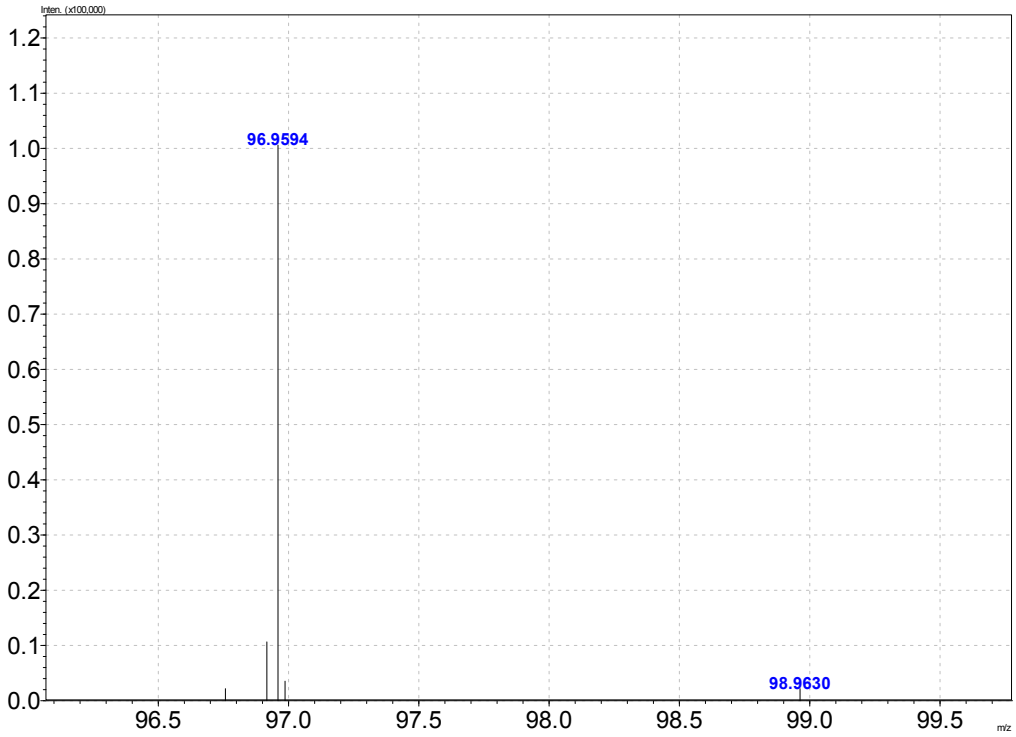
$[M+H]^+$ Calcud for $C_{19}H_{21}NO_3S$ 344.1315; Found 344.1317.



$[M+H]^+$ Calcud for $C_{21}H_{22}N_2O_5$ 383.1601; Found 383.1604.



$[M+H]^+$ Calcud for $C_{21}H_{22}NO_3Cl$ 372.1361; Found 372.1359.



A signal at m/z=96.9594 was observed in the reaction (Table S1). That was assigned to $[SO_4^{2-}+H]^-$ (calculated: 96.9596) species.