Chiral Aryliodine-Mediated Enantioselective Organocatalytic Spirocyclization: Synthesis of Spirofurooxindoles via Cascade Oxidative C–O and C–C Bond Formation

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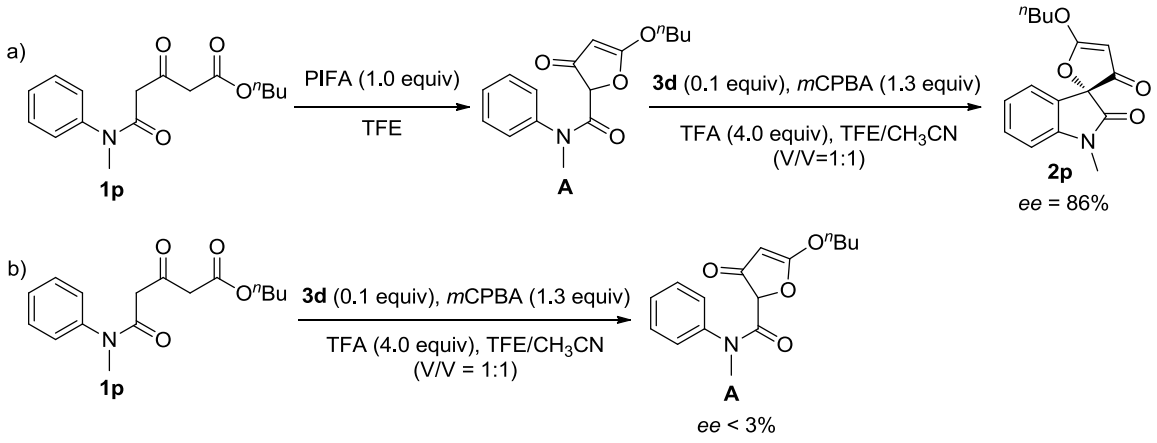
Supporting Information

I. General Information

All reactions were carried out at room temperature under air unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded on 600 MHz or 400 MHz spectrometer at 25 ^{o}C. Chemical shifts values are given in ppm and referred as the internal standard to TMS: 0.00 ppm. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; m, multiplet and dd, doublet of doublets, brs, broad singlet. The coupling constants *J*, are reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer. Melting points were determined with a Micromelting point apparatus without corrections. Infrared spectra were measured on a FT/IR instrument. HPLC analysis was conducted using Ultimate 3000 and chiral column of Daicel CHIRALCEL AD-H (4.6 mm × 25 cm), OJ-H (4.6 mm × 25 cm) and OD-H (4.6 mm × 25 cm). Organic solutions were concentrated by rotary evaporation below 40 °C in vacuum. TLC plates were visualized by exposure to ultraviolet light. Reagents and solvents were purchased as reagent grade and were used without further purification. All reactions were performed in standard glassware, heated at 70 ^{o}C for 3 h before use. Flash column chromatography was performed over silica gel 200-300 m and the eluent was a mixture of ethyl acetate (EA) and petroleum ether (PE).

II. Mechanistic Studies



a. Preparation of intermediate A

To a solution of substrate **1p** (1.0 mmol) in TFE (10 mL) was slowly added PIFA (1.0 equiv) with stirring. The resulting mixture was maintained at room temperature, and the process of the reaction was monitored by TLC. Upon completion, the reaction solvent was removed under vacuum and the residue was purified by silica gel chromatography, using a mixture of PE/EA (30% EA/PE) to afford the intermediate **A** (89%, 257mg).

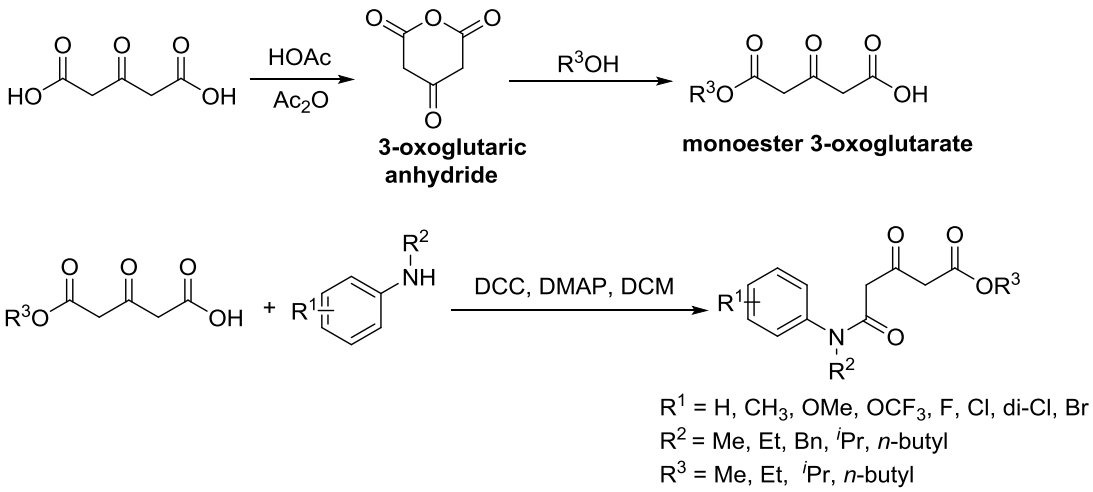
b. Preparation of the optically active spirofurooxindoles 2p

To a reaction tube filled with the intermediate **A** (0.2 mmol), chiral organoiodine **3d** (10 mol%), *m*CPBA (1.3 equiv) and TFE/CH_3CN (4.0 mL) was added CF_3CO_2H (4.0 equiv). The resulting mixture was allowed to be stirred at room temperature for 8 h. The mixture was filtered, washed with CH_3CN (2 mL × 2), the combined organic phase was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: petroleum ether/EtOAc = 3/1) to afford optically active spirofurooxindoles **2p** as a white solid (75%, 43 mg).

c. Preparation of the optically active intermediate A

To a reaction tube filled with substrate **1p** (1.0 mmol), chiral organoiodine **3d** (10 mol%), *m*CPBA (1.3 equiv) and TFE/CH_3CN (4.0 mL) was added CF_3CO_2H (4.0 equiv). The resulting mixture was allowed to be stirred at room temperature for 8 h. Then, the mixture was filtered, washed with CH_3CN (2 mL × 2), the combined organic phase was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: petroleum ether/EtOAc = 3/1) to afford intermediate **A** as a white solid (81%, 234 mg).

III. Preparation of Substrate 1.[1]



a. Preparation of 3-oxoglutaric anhydride

3-Oxoglutaric acid (100 g, 0.68 mol) was added by portions to a solution of acetic acid (150 mL) and acetic anhydride (100 mL) at 5 °C and stirred below 10 °C. The acid dissolved slowly and a pale yellow solid precipitated over 3 h. The product was filtered, washed with acetic acid (100 mL), and followed by methylbenzene (100 mL × 3). The resultant white powder was dried at high vacuum to afford 76 g (86.7%) of the desired 3-oxoglutairc anhydride, which was used directly in the following step.

b. Preparation of monoester 3-oxoglutarate

To 3-oxoglutairc anhydride (2 g, 16 mmol) was add cold dry alcohol (12 mL). The mixture was stirred at room temperature for 2 h and the solvent was evaporated to give a brown liquid product with quantitative yield, which was used directly for the next step without further purification.

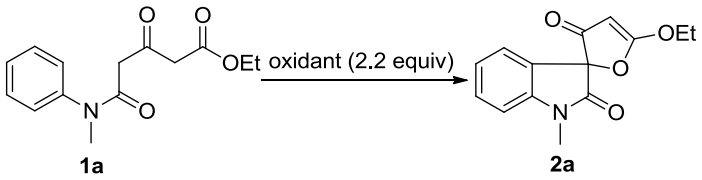
c. General procedure for the preparation of ethyl 3-oxopentanioate monoamide derivatives

Aniline derivatives (12.0 mmol), DMAP (1.0 mmol) and monoester 3-oxoglutarate (10.0 mmol) was mixed in CH_2Cl_2 (20 mL) with an ice bath. Then DCC (12.0 mmol) was added by portions. After addition, the ice bath was removed and the reaction was maintained at room temperature for 12 hours. The mixture was filtered, washed with minimum amount of CH_2Cl_2 for several times (10 mL × 3). The combined organic phase was washed with 10% HCl solution and saturated brine, dried over Na_2SO_4 and

evaporation of the solvent under reduced pressure and purification of the crude residue by flash column chromatography on silica gel (EA/PE) afforded the desired amides.

IV. Preparation of the Optically Inactive Spirofurooxindoles 2

a. Optimization of the reaction conditions.[a]



Entry	Oxidant	Additive (equiv）	Solvent	*t* (°C)	Yield (%)[b]
1	PIDA	$BF_3{\cdot}Et_2O$ (0.1)	DCE	rt	25
2	PIDA	none	DCE	75	46
3	PIFA	none	DCE	rt	32
4	PIFA	none	DCE	75	50
5	PIFA	none	C_2H_5O	rt	0[c]
6	PIFA	none	CH_3CN	rt	81
7	PIFA	none	HFIP	rt	33
8	PIFA	none	CH_3NO_2	rt	78
9	PIFA	none	TFE	rt	85
10	PIFA	DBU (4)	TFE	rt	0[c]
11	PIFA	Et_3N (4)	TFE	rt	0[c]
12	PIFA	Na_2CO_3 (2)	TFE	rt	0[c]
13	PIFA	$NaHCO_3$ (4)	TFE	rt	81

[a] Reaction conditions: **1a** (0.5 mmol) and oxidant (2.2 mmol), in solvent (5 mL). [b] Isolated yield.

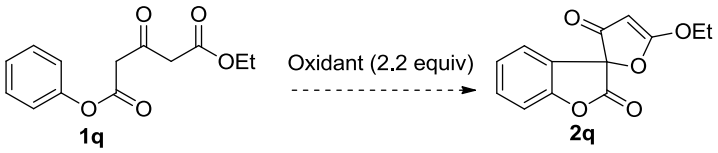
[c] Decomposition

b. General procedure for the synthesis of the optically inactive spirofurooxindoles 2

To a solution of substrate **1** (0.5 mmol) in TFE (5 mL) was slowly added PIFA (2.2 equiv) with stirring. The resulting mixture was maintained at room temperature, and the process of the reaction was monitored by TLC. Upon completion, the reaction solvent was removed under vacuum and the residue was purified by silica gel

chromatography, using a mixture of PE/EA to afford the desired product **2**.

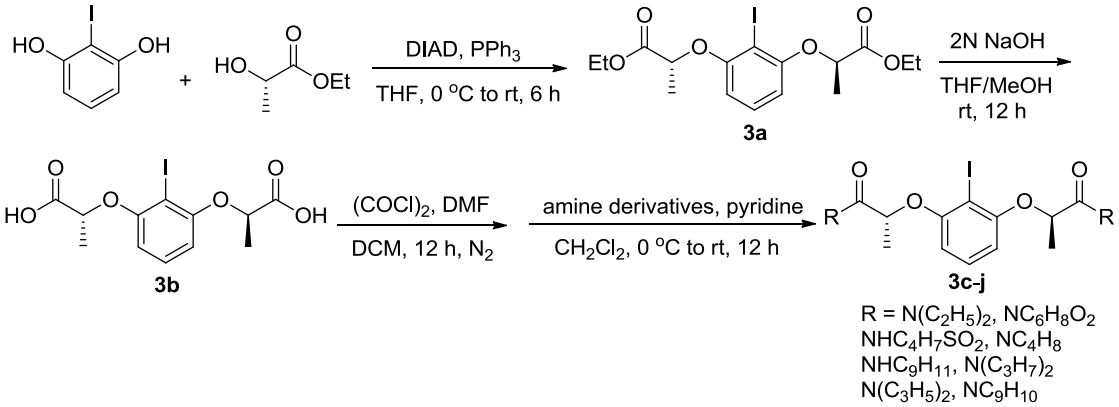
c. Investigation of a substrate of an ester[a]



Entry	Oxidant	Solvent	*t* (°C)	Yield (%)[b]
1	PIDA	DCE	rt	0[c]
2	PIDA	DCE	-10	0[c]
3	PIDA	DCE	-20	0[c]
4	PIFA	DCE	rt	0[c]
5	PIFA	C_2H_5O	rt	0[c]
6	PIFA	CH_3CN	rt	0[c]
7	PIFA	HFIP	rt	0[c]
8	PIFA	TFE	rt	0[c]
9	PIFA	TFE	-20	0[c]
10	PIFA	CH_3NO_2	rt	0[c]

[a] Reaction conditions: **1q** (0.5 mmol) and oxidant (2.2 mmol), in solvent (5 mL). [b] Isolated yield. [c] Decomposition

V. Preparation of chiral iodobenzene 3[2-5]



(2*R*,2'*R*)-Diethyl 2,2'-(2-iodo-1,3-phenylene)bis(oxy)dipropanoate (3a): To a solution of 2-iodoresorcinol (2.36 g, 10.0 mmol), PPh_3 (6.56 g, 25.0 mmol) and (–)-lactic acid ethylester (2.80 mL, 25.0 mmol) in THF (50 mL) was added slowly

diisopropyl azodicarboxylate (DIAD, 1.9 M in toluene, 25.0 mmol, 13.2 mL) at 0°C. The reaction mixture was allowed to warm to room temperature. After stirring for 6 h, the resulting mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane–EtOAc = 15:1) to give (3.93 g, 9.0 mmol) in 90% yield. Colorless oil; TLC, R_f = 0.33 (hexane–EtOAc = 4:1).

(2*R*,2'*R*)-2,2'-(2-Iodo-1,3-phenylene)bis(oxy)dipropanoic acid (3b): To a solution of **3a** (3.93 g, 9.0 mmol) in THF (25.0 mL) and MeOH (25.0 mL) was added 2N NaOH (25 mL) and stirred overnight at room temperature. The reaction mixture was cooled to 0 °C, quenched with 1N HCl and extracted with EtOAc (30 mL × 3). The organic layers were dried over anhydrous $MgSO_4$ and the solvents were removed *in vacuo* to give analytically pure **3b** (3.42 g, 9.0 mmol) in >99% yield. White solid; TLC, R_f = 0.15 (hexane–EtOAc–$CHCl_3$ = 1:2:1 with a few drops of AcOH).

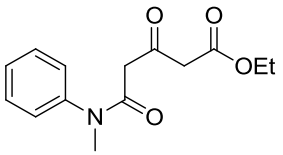
General procedure for preparation of 3c-j: To a solution of (*2R,2'R*)-2,2'-((2-iodo-1,3-phenylene)bis(oxy))dipropanoic acid (0.87 g, 2.29 mmol) in CH_2Cl_2 (10 mL) and DMF (1 drop) was added oxalyl chloride (1.57 mL, 18.32 mmol) and the mixture was stirred overnight under N_2. The resulting mixture was concentrated under vacuum. The residue was dissolved in CH_2Cl_2 (6 mL) at 0 °C and amine derivative (4.17 mmol) was added. After 0.5 h, Et_3N (1.16 mL, 8.34 mmol) was added. After stirring overnight, the reaction mixture was poured into aqueous HCl (1 M, 20 mL) and extracted with brine and CH_2Cl_2 (10 mL × 2). The organic layers were dried with $MgSO_4$, filtered and the solvent was removed under vacuum to give the product as a white solid.

VI. Preparation of the Optically Active Spirofurooxindoles 2

To a reaction tube filled with ethyl 5-(methyl(phenyl)amino)-3,5-dioxopentanoate **1a** (0.2 mmol), chiral organoiodine **3d** (20 mol%), *m*CPBA (2.5 equiv) and TFE/CH_3CN (4.0 mL) was added CF_3CO_2H (4.0 equiv). The resulting mixture was allowed to be stirred at room temperature for 8 h. The mixture was filtered, washed with CH_3CN (2 mL × 2), the combined organic phase was removed *in vacuo*. The

residue was purified by flash column chromatography on silica gel (eluent: petroleum ether/EtOAc = 3/1) to afford (*R*)-5-ethoxy-1'-methyl-3H-spiro[furan-2,3'-indoline] -2',3- dione **2a** as a white solid.

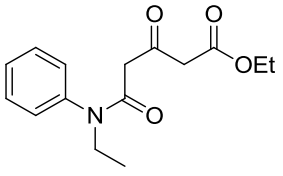
Ethyl 5-(methyl(phenyl)amino)-3,5-dioxopentanoate (1a)



1a

Following the general procedure, **1a** was purified by silica gel chromatography (20% EA/PE). Yield: 71% (1.87 g), colorless oil. IR (KBr) 2934, 1740, 1649, 1594, 1469, 1384, 775, 702 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (600 MHz, $CDCl_3$) δ 14.37 (s, 0.28), 12.07 (s, 0.01H), 7.43 (t, *J* = 6.3 Hz, 2H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 2H), 5.01 (s, 0.04H), 4.82 (s, 0.34H), 4.20 – 4.09 (m, 2H), 3.51 (s, 1H), 3.44 (s, 1H), 3.30 (d, *J* = 8.6 Hz, 3H), 3.06 (s, 0.8H), 1.29 ‒ 1.18 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.20, 172.4, 171.6, 171.4, 168.6, 168.4, 167.0, 166.3, 143.3, 143.0, 130.0, 129.9, 129.7, 128.4, 127.9, 127.3, 127.2, 91.8, 90.9, 61.4, 61.2, 60.2, 49.2, 48.9, 41.6, 40.5, 37.6, 37.3, 36.5, 14.2, 14.1. HRMS (ESI) calcd for $C_{14}H_{17}NNaO_4^+$ [M + Na^+] 286.1050, found 286.1052.

Ethyl 5-(ethyl(phenyl)amino)-3,5-dioxopentanoate (1b)

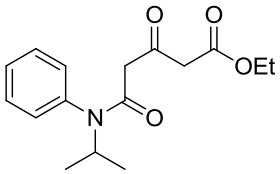


1b

Following the general procedure, **1b** was purified by silica gel chromatography (20% EA/PE). Yield: 63% (1.75 g), colorless oil. IR (KBr) 2980, 1741, 1650, 1593, 1495, 1369, 771, 702 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (600 MHz, $CDCl_3$) δ 14.46 (s, 0.23H), 12.06 (s, 0.02H), 7.44 (t, *J* = 7.1 Hz, 2H), 7.39 (d, *J* = 6.5 Hz, 1H), 7.18 (d, *J* = 7.4 Hz, 2H), 5.00 (s, 0.04H), 4.69 (s, 0.33H), 4.16 – 4.08 (m, 2H), 3.77 (d, *J* = 6.9 Hz, 2H), 3.50 (s, 1H), 3.38 (s, 1H), 3.04 (s, 0.8H), 1.25 – 1.20

(m, 3H), 1.14 (t, J = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.3, 172.4, 171.8, 171.0, 168.6, 168.5, 167.0, 166.6, 165.8, 141.6, 141.4, 129.9, 129.8, 129.7, 128.6, 128.5, 128.3, 128.0, 91.8, 91.2, 61.3, 61.2, 49.3, 49.2, 44.2, 43.5, 41.6, 40.9, 14.1, 13.1, 12.9. HRMS (ESI) calcd for $C_{15}H_{19}NNaO_4^+$ [M + Na^+] 300.1206, found 300.1205.

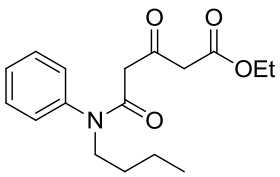
Ethyl 5-(isopropyl(phenyl)amino)-3,5-dioxopentanoate (1c)



1c

Following the general procedure, **1c** was purified by silica gel chromatography (20% EA/PE). Yield: 56% (1.63 g), colorless oil. IR (KBr) 2979, 1742, 1645, 1590, 1494, 1317, 772, 705 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.54 (s, 0.31H), 12.03 (s, 0.03H), 7.46 – 7.38 (m, 3H), 7.15 – 7.08 (m, 2H), 4.98 (dt, J = 13.5, 6.8 Hz, 1H), 4.46 (s, 0.31H), 4.21 – 4.05 (m, 2H), 3.45 (s, 1.33H), 3.27 (s, 1.34H), 3.00 (s, 0.66H), 2.89 (s, 0.09H), 1.27 – 1.16 (m, 3H), 1.07 (t, J = 6.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 171.9, 171.0, 168.5, 168.4, 167.0, 166.5, 165.8, 137.9, 137.6, 130.5, 130.4, 130.2, 129.5, 129.4, 129.3, 128.8, 128.4, 91.8, 61.3, 61.1, 60.1, 49.9, 49.2, 46.4, 45.6, 41.5, 21.0, 20.9, 14.2, 14.1. HRMS (ESI) calcd for $C_{16}H_{21}NNaO_4^+$ [M + Na^+] 314.1363, found 314.1361.

Ethyl 5-(butyl(phenyl)amino)-3,5-dioxopentanoate (1d)

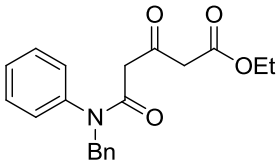


1d

Following the general procedure, **1d** was purified by silica gel chromatography (20% EA/PE). Yield: 61% (1.86 g), colorless oil. IR (KBr) 2960, 1742, 1650, 1593, 1495, 1369, 774, 702 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz,

$CDCl_3$) δ 14.47 (s, 0.31H), 12.05 (s, 0.02H), 7.46 – 7.41 (m, 2H), 7.38 – 7.36 (m, 1H), 7.20 – 7.16 (m, 2H), 5.00 (s, 0.03H), 4.70 (s, 0.33H), 4.19 – 4.06 (m, 2H), 3.72 (dd, *J* = 14.3, 6.7 Hz, 2H), 3.50 (s, 1.66H), 3.37 (s, 1.66H), 3.04 (s, 0.66H), 3.00 (s, 0.10H), 1.57 – 1.45 (m, 2H), 1.38 – 1.28 (m, 2H), 1.28 – 1.16 (m, 3H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 171.2, 168.6, 168.5, 167.0, 166.0, 141.9, 141.6, 129.9, 129.8, 129.7, 128.4, 128.4, 128.2, 128.0, 91.8, 91.1, 61.3, 61.2, 60.1, 50.3, 49.3, 49.3, 49.2, 49.1, 48.4, 41.6, 40.9, 29.9, 29.7, 20.0, 20.0, 14.1, 13.8. HRMS (ESI) calcd for $C_{17}H_{23}NNaO_4^+$ [M + Na^+] 328.1519, found 328.1516.

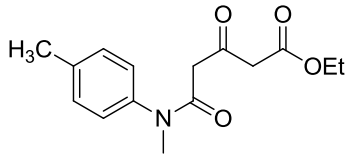
Ethyl 5-(benzyl(phenyl)amino)-3,5-dioxopentanoate (1e)



1e

Following the general procedure, **1e** was purified by silica gel chromatography (20% EA/PE). Yield: 67% (2.27 g), a light yellow solid, mp. 63 – 66 ^{o}C. IR (KBr) 2982, 1737, 1647, 1594, 1495, 1329, 763, 703 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (600 MHz, $CDCl_3$) δ 14.40 (s, 0.28H), 12.07 (s, 0.05H), 7.32 (s, 3H), 7.27 – 7.23 (m, 3H), 7.21 (d, *J* = 6.6 Hz, 2H), 7.05 – 6.98 (m, 2H), 4.91 (d, *J* = 11.6 Hz, 2H), 4.76 (s, 0.33H), 4.15 – 4.09 (m, 2H), 3.49 (s, 1.13H), 3.45 (s, 1H), 3.06 (s, 0.8H), 1.31 – 1.16 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.2, 171.3, 169.1, 168.5, 166.9, 166.4, 141.5, 141.5, 137.1, 136.8, 129.8, 129.6, 128.9, 128.8, 128.6, 128.6, 128.5, 128.4, 128.4, 128.1, 127.6, 127.5, 92.0, 91.1, 61.4, 61.3, 60.2, 53.4, 53.1, 52.3, 49.2, 49.1, 41.6, 40.8, 14.3, 14.1. HRMS (ESI) calcd for $C_{20}H_{21}NNaO_4^+$ [M + Na^+] 362.1363, found 362.1365.

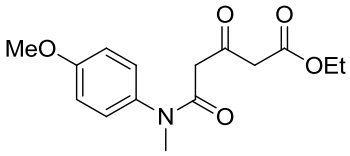
Ethyl 5-(methyl(p-tolyl)amino)-3,5-dioxopentanoate (1f)



1f

Following the general procedure, **1f** was purified by silica gel chromatography (20% EA/PE). Yield: 73% (2.02 g), colorless oil. IR (KBr) 2981, 1742, 1651, 1514, 1466, 1327, 783, 722 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.37 (s, 0.21H), 12.06 (s, 0.01H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 5.01 (s, 0.04H), 4.82 (s, 0.34H), 4.18 – 4.11 (m, 2H), 3.51 (s, 1.11H), 3.43 (s, 1.17H), 3.27 (s, 3H), 3.05 (s, 0.77H), 2.38 (s, 3H), 1.29 – 1.21 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 172.4, 171.8, 171.5, 168.4 167.3, 167.0, 166.4, 141.0, 140.7, 140.5, 138.4, 137.8, 130.6, 130.5, 130.3, 127.1, 126.9, 91.8, 90.9, 61.3, 61.2, 60.1, 49.2, 48.9, 41.5, 40.4, 37.6, 37.3, 36.5, 21.1, 14.2, 14.0. HRMS (ESI) calcd for $C_{15}H_{19}NNaO_4^+$ [M + Na^+] 300.1206, found 300.1203.

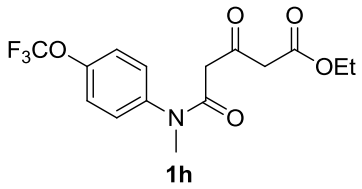
Ethyl 5-((4-methoxyphenyl)(methyl)amino)-3,5-dioxopentanoate (1g)



1g

Following the general procedure, **1g** was purified by silica gel chromatography (20% EA/PE). Yield: 76% (2.23 g), colorless oil. IR (KBr) 2980, 1741, 1650, 1512, 1467, 1369, 840, 783 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (600 MHz, $CDCl_3$) δ 14.39 (s, 0.31H), 12.05 (s, 0.08H), 7.12 (dd, *J* = 9.0, 3.0 Hz, 2H), 6.92 (dd, *J* = 8.9, 2.4 Hz, 2H), 5.01 (s, 0.03H), 4.80 (s, 0.32H), 4.13 (dt, *J* = 12.8, 6.6 Hz, 2H), 3.83 (d, *J* = 5.0 Hz, 3H), 3.51 (s, 1.22H), 3.42 (s, 1.20H), 3.26 (d, *J* = 8.8 Hz, 3H), 3.05 (s, .0.77H), 1.23 (dt, *J* = 20.9, 7.1 Hz, 3H). ^{13}C NMR (150MHz, $CDCl_3$) δ 197.3, 171.7, 168.5, 168.4, 167.0, 166.7, 159.3, 159.0, 136.1, 135.8, 128.4, 128.3, 115.1, 115.0, 114.9, 91.7, 90.9, 61.3, 61.2, 55.5, 49.2, 48.9, 41.6, 37.5, 36.6, 14.0. HRMS (ESI) calcd for $C_{15}H_{19}NNaO_5^+$ [M + Na^+] 316.1155, found 316.1156.

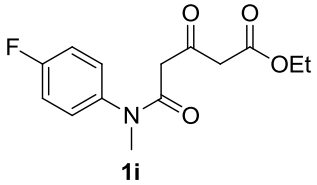
Ethyl 5-(methyl(4-(trifluoromethoxy)phenyl)amino)-3,5-dioxopentanoate (1h)



1h

Following the general procedure, **1h** was purified by silica gel chromatography (20% EA/PE). Yield: 53% (1.84 g), colorless oil. IR (KBr) 2985, 1742, 1659, 1507, 1370, 1260, 788, 740 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.29 (s, 0.40H), 12.08 (s, 0.04H), 7.33 – 7.20 (m, 4H), 5.00 (s, 0.05H), 4.81 (s, 0.37H), 4.23 – 4.09 (m, 2H), 3.53 (s, 1.10H), 3.45 (s, 1.11H), 3.30 (d, *J* = 7.5 Hz, 3H), 3.09 (s, 0.70H), 3.07 (s, 0.16H), 1.41 (td, *J* = 7.1, 2.4 Hz, 0.26H), 1.28 – 1.18 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 174.2, 172.3, 171.4, 171.1, 169.2, 168.3, 166.9, 166.14 (s), 164.1, 162.3, 148.7, 148.2, 141.8, 141.5, 128.9, 124.2, 122.4, 122.2, 121.6, 119.1, 116.5, 92.0, 90.5, 82.1, 77.7, 65.1, 64.9, 61.4, 61.2, 60.2, 49.1, 48.8, 41.5, 40.5, 37.6, 37.4, 36.5, 14.2, 14.1, 14.0. HRMS (ESI) calcd for $C_{15}H_{16}F_3NNaO_5^+$ [M + Na^+] 370.0873, found 370.0871.

Ethyl 5-((4-fluorophenyl)(methyl)amino)-3,5-dioxopentanoate (1i)

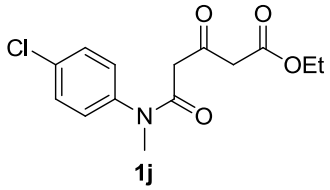


1i

Following the general procedure, **1i** was purified by silica gel chromatography (20% EA/PE). Yield: 57% (1.60 g), colorless oil. IR (KBr) 2983, 1741, 1651, 1510, 1469, 1370, 847, 727 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.31 (s, 0.32H), 12.07 (s, 0.03H), 7.22 (tt, *J* = 11.4, 5.7 Hz, 2H), 7.12 (dt, *J* = 8.7, 2.6 Hz, 2H), 5.00 (s, 0.05H), 4.78 (s, 0.34H), 4.23 – 4.04 (m, 2H), 3.52 (s, 1H), 3.43 (s, 1.12H), 3.28 (d, *J* = 5.8 Hz, 3H), 3.07 (s, 0.6H), 3.04 (s, 0.2H), 1.29 – 1.17 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 172.3, 171.5, 171.3, 168.9, 168.4, 167.2, 166.9, 166.3, 163.2, 163.0, 160.8, 160.5, 139.3, 139.0, 129.2, 129.1, 117.0, 116.8, 116.6, 93.1, 91.9, 90.7, 61.4, 61.2, 60.2, 49.1, 48.9, 41.5, 40.5, 38.9, 37.7, 37.5,

36.6, 14.2, 14.0. HRMS (ESI) calcd for $C_{14}H_{16}FNNaO_4^+$ [M + Na^+] 304.0956, found 304.0958.

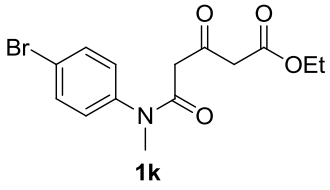
Ethyl 5-((4-chlorophenyl)(methyl)amino)-3,5-dioxopentanoate (1j)



1j

Following the general procedure, **1j** was purified by silica gel chromatography (20% EA/PE). Yield: 65% (1.93 g), colorless oil. IR (KBr) 2982, 1740, 1656, 1544, 1491, 1369, 841, 724 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.26 (s, 0.36H), 12.07 (s, 0.04H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.24 – 7.13 (m, 2H), 5.01 (s, 0.05H), 4.80 (s, 0.36H), 4.20 – 4.07 (m, 2H), 3.53 (s, 1H), 3.45 (s, 1H), 3.28 (d, *J* = 6.9 Hz, 3H)., 3.08 (s, 0.66H), 3.05 (s, 0.15H), 1.30 – 1.17 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 172.3, 171.4, 171.2, 169.1, 168.4, 166.9, 166.2, 141.8, 141.6, 134.3, 133.6, 130.2, 130.0, 128.7, 92.0, 90.7, 61.5, 61.3, 60.3, 49.2, 48.9, 42.0, 41.5, 40.5, 37.7, 37.4, 36.5, 14.2, 14.1. HRMS (ESI) calcd for $C_{14}H_{16}{}^{35}ClNNaO_4^+$ [M + Na^+] 320.0660, found 320.0664.

Ethyl 5-((4-bromophenyl)(methyl)amino)-3,5-dioxopentanoate (1k)

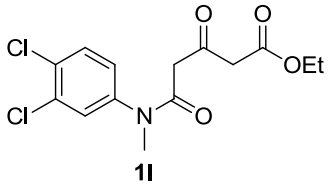


1k

Following the general procedure, **1k** was purified by silica gel chromatography (20% EA/PE). Yield: 70% (2.39 g), colorless oil. IR (KBr) 2982, 1740, 1565, 1587, 1475, 1369, 791, 698 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.25 (s, 0.43H), 12.08 (s, 0.03H), 7.51 (t, *J* = 9.0 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.35 – 7.26 (m, 1H), 7.18 (t, *J* = 6.5 Hz, 1H), 5.01 (s, 0.05H), 4.83 (s, 0.39H), 4.18 – 4.10 (m, 2H), 3.54 (s, 1H), 3.45 (s, 1H), 3.28 (d, *J* = 6.7 Hz, 3H)., 3.10 (s, 1H), 1.24 (dt, *J* = 10.3, 7.1 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 197.0, 171.3, 169.3, 168.3, 166.9, 166.1, 144.5, 144.3, 131.6, 131.3, 131.0, 131.0, 130.6, 130.5, 126.2,

126.1, 123.2, 122.9, 92.0, 90.6, 61.5, 61.4, 60.3, 49.2, 48.8, 41.6, 37.4, 36.5, 14.1. HRMS (ESI) calcd for $C_{14}H_{16}{}^{79}BrNNaO_4^+$ [M + Na^+] 364.0155, found 364.0152.

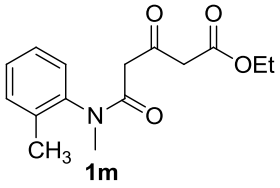
Ethyl 5-((3,4-dichlorophenyl)(methyl)amino)-3,5-dioxopentanoate (1l)



1l

Following the general procedure, **1l** was purified by silica gel chromatography (20% EA/PE). Yield: 61% (2.02 g), colorless oil. IR (KBr) 2982, 1740, 1658, 1588, 1473, 1368, 711, 679 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.19 (s, 0.43H), 12.09 (s, 0.03H), 7.51 (dd, *J* = 8.5, 2.8 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.15 – 7.08 (m, 1H), 5.01 (s, 0.06H), 4.85 (s, 0.38H), 4.15 (qd, *J* = 7.1, 1.9 Hz, 2H), 3.54 (s, 1H), 3.47 (s, 1H), 3.28 (d, *J* = 7.7 Hz, 3H), 3.11 (s, 1H), 1.27 – 1.21 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 172.3, 171.3, 170.8, 169.7, 168.2, 166.9, 166.0, 142.6, 142.4, 133.8, 133.5, 132.8, 131.6, 131.4, 129.4, 126.8, 92.1, 90.5, 61.5, 61.3, 60.3, 49.1, 48.8, 41.5, 37.4, 36.5, 14.2, 14.1. HRMS (ESI) calcd for $C_{14}H_{15}{}^{35}Cl_2NNaO_4^+$ [M + Na^+] 354.0270, found 354.0267.

Ethyl 5-(methyl(*o*-tolyl)amino)-3,5-dioxopentanoate (1m)

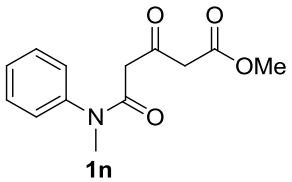


1m

Following the general procedure, **1m** was purified by silica gel chromatography (20% EA/PE). Yield: 51% (1.41 g), colorless oil. IR (KBr) 2982, 1741, 1651, 1579, 1493, 1370, 733, 728 cm^{-1}. Mixture of enol and keto form: ^{1}H NMR (600 MHz, $CDCl_3$) δ 14.40 (s, 0.24H), 12.03 (s, 0.02H), 7.32 – 7.24 (m, 3H), 7.16 – 7.12 (m, 1H), 4.98 (s, 0.04H), 4.61 (s, 0.38H), 4.20 – 4.02 (m, 2H), 3.51 (s, 1H), 3.37 – 3.26 (m, 1.22H), 3.22 (d, J = 7.1 Hz, 3H), 3.04 (s, 0.79H), 2.23 (d, *J* = 20.1 Hz, 3H), 1.21 (d, *J* = 27.4 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 197.1, 171.5, 168.8, 168.4, 167.0, 166.6, 141.7, 141.5, 135.8, 135.4, 131.7, 131.6, 131.4, 129.0, 128.6, 128.1, 128.1,

127.7, 127.5, 92.0, 90.5, 61.4, 61.2, 60.2, 49.3, 48.5, 41.5, 40.2, 36.2, 36.0, 35.2, 17.4, 17.3, 14.2, 14.1. HRMS (ESI) calcd for $C_{15}H_{19}NNaO_4^+$ [M + Na^+] 300.1206, found 300.1207.

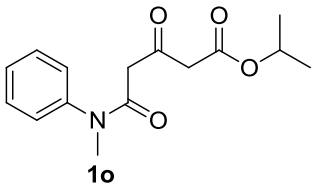
Methyl 5-(methyl(phenyl)amino)-3,5-dioxopentanoate (1n)



1n

Following the general procedure, **1n** was purified by silica gel chromatography (20% EA/PE). Yield: 75% (1.87 g), colorless oil. IR (KBr) 2953, 1745, 1649, 1593, 1496, 1385, 755, 702 cm^{-1}. Mixture of enol and keto form: ^1H NMR (400 MHz, $CDCl_3$) δ 14.38 (s, 0.31H), 11.98 (s, 0.01H), 7.47 – 7.40 (m, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 2H), 5.03 (s, 0.04H), 4.82 (s, 0.36H), 3.72 – 3.66 (m, 3H), 3.53 (s, 1.12H), 3.43 (s, 1.14H), 3.30 (d, J = 6.9 Hz, 3H), 3.07 (s, 0.78H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 171.7, 171.4, 168.9, 168.3, 167.4, 167.1, 166.3, 143.3, 143.0, 130.0, 129.9, 129.8, 128.4, 128.3, 127.9, 127.3, 127.2, 91.5, 91.1, 52.3, 52.3, 51.3, 48.9, 41.3, 40.5, 37.6, 37.3, 36.5. HRMS (ESI) calcd for $C_{13}H_{15}NNaO_4^+$ [M + Na^+] 272.0893, found 272.0890.

Isopropyl 5-(methyl(phenyl)amino)-3,5-dioxopentanoate (1o)

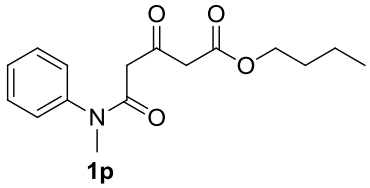


1o

Following the general procedure, **1o** was purified by silica gel chromatography (20% EA/PE). Yield: 55% (1.52 g), colorless oil. IR (KBr) 2982, 1735, 1651, 1593, 1496, 1376, 774, 701 cm^{-1}. Mixture of enol and keto form: ^1H NMR (400 MHz, $CDCl_3$) δ 14.38 (s, 0.22H), 12.13 (s, 0.04H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.37 (d, *J* = 6.8 Hz, 1H), 7.23 – 7.17 (m, 2H), 5.02 – 4.93 (m, 1H), 4.81 (s, 0.31), 3.47 (s, 1H), 3.43 (s, 1.10H), 3.30 (s, 3H), 3.05 (s, 0.77H), 1.22 (dt, *J* = 17.0, 8.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 172.0, 171.5, 171.4, 168.9, 167.9, 167.2, 166.5, 166.3, 143.3,

143.1, 130.0, 129.9, 129.7, 128.4, 127.8, 127.3, 127.2, 92.2, 90.6, 69.0, 68.7, 67.6, 49.5, 48.9, 41.8, 40.4, 37.3, 36.5, 21.9, 21.6. HRMS (ESI) calcd for $C_{15}H_{19}NNaO_4^+$ [M + Na^+] 300.1206, found 300.1202.

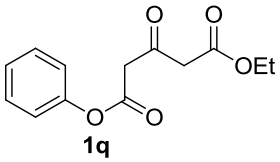
Butyl 5-(methyl(phenyl)amino)-3,5-dioxopentanoate (1p)



1p

Following the general procedure, **1p** was purified by silica gel chromatography (20% EA/PE). Yield: 58% (1.52 g), colorless oil. IR (KBr) 2961, 1741, 1650, 1593, 1496, 1383, 774, 701 cm^{-1}. Mixture of enol and keto form: ^1H NMR (400 MHz, $CDCl_3$) δ 14.36 (s, 0.29H), 12.07 (s, 0.01H), 7.47 – 7.41 (m, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 7.7 Hz, 2H), 5.02 (s, 0.05H), 4.82 (s, 0.33H), 4.18 – 3.94 (m, 2H), 3.51 (s, 1.14H), 3.43 (s, 1.15H), 3.30 (d, *J* = 6.6 Hz, 3H)., 3.06 (s, 0.82H), 1.67 – 1.49 (m, 2H), 1.43 – 1.25 (m, 2H), 0.92 (td, *J* = 7.4, 5.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 172.5, 171.6, 171.4, 168.6, 168.5, 167.0, 166.3, 143.3, 143.0, 130.0, 129.9, 129.7, 128.4, 127.8, 127.3, 127.2, 91.8, 90.9, 65.2, 65.1, 64.0, 49.2, 48.9, 41.6, 40.5, 37.6, 37.3, 36.5, 30.6, 30.4, 19.1, 19.0, 13.7. HRMS (ESI) calcd for $C_{16}H_{21}NNaO_4^+$ [M+Na^+] 314.1363, found 314.1366.

1-Ethyl 5-phenyl 3-oxopentanedioate (1q)

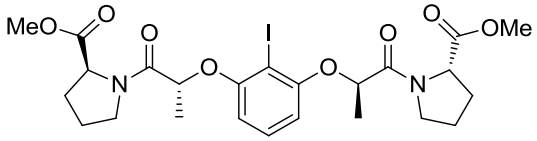


1q

Following the general procedure, **1q** was purified by silica gel chromatography (20% EA/PE). Yield: 51% (1.27 g), colorless oil. IR (KBr) 2984, 1743, 1661, 1593, 1492, 1369, 753, 691 cm^{-1}. Mixture of enol and keto form: ^1H NMR (400 MHz, $CDCl_3$) δ 12.19 (s, 0.10H), 11.83 (s, 0.14H), 7.39 (t, *J* = 7.3 Hz, 2H), 7.29 – 7.20 (m, 1H), 7.12 (dt, *J* = 8.7, 1.6 Hz, 2H), 5.40 (s, 0.16H), 5.23 (s, 0.11H). 4.22 (m, 2H), 3.86 (d, *J* = 1.2 Hz, 1.47H), 3.67 (s, *J* = 1.1 Hz, 1.55H), 3.60 (d, *J* = 0.9 Hz, 0.24H), 3.46 (s,

0.23H), 3.31 (s, 0.30H), 1.37 – 1.18 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.1, 172.3, 171.9, 169.2, 167.8, 166.7, 165.5, 150.5, 150.0, 129.6, 129.5, 126.3, 126.2, 121.6, 121.4, 115.3, 92.4, 91.6, 61.8, 61.7, 60.5, 49.1, 49.0, 48.9, 41.2, 41.0, 14.1. HRMS (ESI) calcd for $C_{13}H_{14}NaO_5^+$ [M+Na^+] 273.0733, found 273.0735.

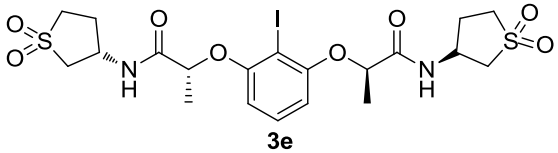
(2*S*,2'*S*)-Dimethyl1,1'-((2*R*,2'*R*)-2,2'-((2-iodo-1,3-phenylene)bis(oxy))bis(propanoyl))bis(pyrrolidine-2-carboxylate) (3d)



3d

Following the general procedure, **3d** was purified by silica gel chromatography (PE/EA = 3/1 to 1/1). Yield: 85% (1.17 g), white solid, mp. 179 – 181 ^{o}C.[4] IR (KBr) 2983, 2956, 2892, 1743, 1655, 1462, 1421, 1254, 1141, 1096, 775 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (td, *J* = 8.3, 5.7 Hz, 1H), 6.48 (d, *J* = 8.3 Hz, 2H), 4.82 (q, *J* = 6.8 Hz, 2H), 4.46 (dd, *J* = 8.0, 3.1 Hz, 2H), 3.91 (td, *J* = 6.9, 3.6 Hz, 2H), 3.73 (s, 6H), 3.48 (dt, *J* = 10.5, 7.8 Hz, 2H), 3.31 (s, 1H), 2.07 – 1.88 (m, 8H), 1.72 (dd, *J* = 6.8, 3.7 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.0, 157.5, 130.4, 106.2, 76.3, 59.6, 52.2, 46.9, 28.1, 25.2, 17.3. HRMS (ESI) calcd for $C_{24}H_{31}IN_2NaO_8^+$ [M + Na^+] 625.1017, found 625.1010. $[\alpha]_D^{25}$ = -181.4 (c = 0.54, $CHCl_3$).

(*R*)-*N*-((*R*)-1,1-Dioxidotetrahydrothiophen-3-yl)-2-(3-(((*R*)-1-(((*S*)-1,1-dioxidotetrahydrothiophen-3-yl)amino)-1-oxopropan-2-yl)oxy)-2-iodophenoxy) propanamide (3e)

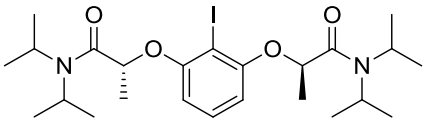


3e

Following the general procedure, **3e** was purified by silica gel chromatography (PE/EA = 3/1 to 1/1). Yield: 81% (1.14 g), white solid, mp. 88 – 90 ^{o}C. IR (KBr) 3378, 2986, 2937, 1663, 1585, 1553, 1459, 1305, 1250, 1116, 767 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.1 Hz, 2H), 7.34 – 7.23 (m, 1H), 6.52 (d, *J* = 8.3

Hz, 2H), 4.87 – 4.72 (m, 4H), 3.50 (dd, *J* = 13.6, 7.5 Hz, 2H), 3.16 (dtd, *J* = 26.3, 13.5, 6.3 Hz, 6H), 2.57 (td, *J* = 13.5, 6.7 Hz, 2H), 2.27 (td, *J* = 14.6, 7.5 Hz, 2H), 1.64 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 156.7, 130.6, 107.1, 81.0, 75.8, 55.9, 50.3, 46.0, 29.3, 18.2. HRMS (ESI) calcd for $C_{20}H_{28}IN_2O_8S_2^+$ [M + H^+] 615.0326, found 615.0324. $[\alpha]_D^{25}$ = -57.9 (c = 0.14, $CHCl_3$).

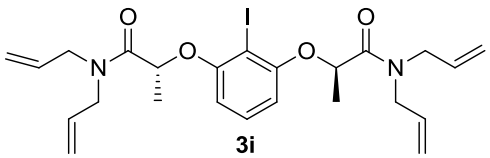
(2*R*,2'*R*)-2,2'-((2-Iodo-1,3-phenylene)bis(oxy))bis(*N*,*N*-diisopropylpropanamide) (3 h)



3h

Following the general procedure, **3h** was purified by silica gel chromatography (PE/EA = 3/1 to 1/1). Yield: 77% (962 mg), white solid, mp. 127 – 130 ^{o}C.[5] IR (KBr) 2967, 2936, 1743, 1643, 1623, 1585, 1460, 1376, 1345, 1237, 1106, 770 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (t, *J* = 8.0 Hz, 1H), 6.53 (d, *J* = 8.2 Hz, 2H), 4.85 (q, *J* = 6.5 Hz, 2H), 4.55 (dt, *J* = 12.5, 6.1 Hz, 2H), 3.31 (dt, *J* = 13.1, 6.4 Hz, 2H), 1.68 (d, *J* = 6.0 Hz, 6H), 1.42 (d, *J* = 6.6 Hz, 6H), 1.30 (d, *J* = 6.6 Hz, 6H), 1.20 (d, *J* = 6.3 Hz, 6H), 0.91 (t, *J* = 5.7 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 157.6, 129.9, 106.1, 106.0, 78.5, 77.9, 47.6, 46.5, 20.9, 20.6, 20.6, 19.9, 18.0. HRMS (ESI) calcd for $C_{24}H_{40}IN_2O_4^+$ [M+H^+] 547.2027, found 547.2023. $[\alpha]_D^{25}$ = -157.1 (c = 0.14, $CHCl_3$).

(2*R*,2'*R*)-2,2'-((2-Iodo-1,3-phenylene)bis(oxy))bis(*N*,*N*-diallylpropanamide) (3i)

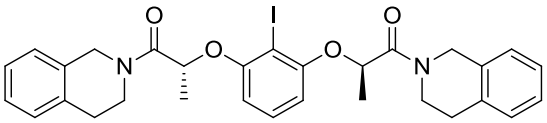


3i

Following the general procedure, **3h** was purified by silica gel chromatography (PE/EA = 3/1 to 1/1). Yield: 82% (1.01 g), white solid, mp. 110 – 112 ^{o}C. IR (KBr) 3080, 2983, 2945, 2921, 1743, 1658, 1639, 1588, 1461, 1379, 1365, 1256, 1135, 858, 781 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 8.3 Hz, 1H), 6.51 (d, *J* = 8.3 Hz,

2H), 5.82 – 5.51 (m, 4H), 5.26 – 4.90 (m, 10H), 4.18 – 4.03 (m, 4H), 3.95 (qd, *J* = 15.3, 5.7 Hz, 4H), 1.69 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 157.7, 133.1, 132.3, 130.0, 117.7, 117.3, 106.8, 79.8, 76.0, 48.7, 47.7, 18.1. HRMS (ESI) calcd for $C_{24}H_{32}IN_2O_4^+$ [M + H^+] 539.1401, found 539.1405. $[\alpha]_D^{25}$ = -142.9 (c = 0.28, $CHCl_3$).

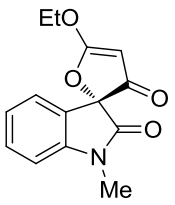
(2*R*,2'*R*)-2,2'-((2-Iodo-1,3-phenylene)bis(oxy))bis(1-(3,4-dihydroisoquinolin-2(1*H*)-yl)propan-1-one) (3j)



3j

Following the general procedure, **3j** was purified by silica gel chromatography (PE/EA = 3/1 to 1/1). Yield: 72% (969 mg), white solid, mp. 95 – 98 °C. IR (KBr) 2985, 2933, 1657, 1585, 1460, 1373, 1283, 1251, 1136, 1095, 751 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 – 7.03 (m, 9H), 6.48 (dd, *J* = 18.7, 8.5 Hz, 2H), 5.14 – 4.94 (m, 3H), 4.78 (d, *J* = 17.5 Hz, 1H), 4.62 (dd, *J* = 16.8, 9.8 Hz, 2H), 4.25 – 3.89 (m, 2H), 3.84 – 3.44 (m, 2H), 2.98 – 2.71 (m, 3H), 2.70 – 2.47 (m, 1H), 1.86 – 1.59 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 169.5, 157.5, 157.3, 134.5, 133.9, 132.7, 132.6, 130.6, 130.5, 128.8, 128.4, 126.9, 126.6, 126.5, 126.5, 126.3, 126.1, 106.2, 106.1, 78.5, 47.0, 45.1, 42.7, 41.1, 40.3, 29.7, 28.2, 18.1, 18.0. HRMS (ESI) calcd for $C_{30}H_{32}IN_2O_4^+$ [M + H^+] 611.1401, found 611.1405. $[\alpha]_D^{25}$ = -181.8 (c = 0.22, $CHCl_3$).

(*R*)-5-Ethoxy-1'-methyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2a)

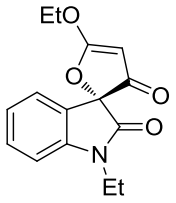


2a

Following the general procedure, **2a** was purified by silica gel chromatography

(30% EA/PE). Yield: 63% (33 mg), white solid, mp. 135 – 138 ^{o}C. IR (KBr) 3112, 2933, 1735, 1702, 1583, 1352, 1002, 879, 771 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.4 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 4.96 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.24 (s, 3H), 1.52 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 186.4, 168.8, 145.3, 131.5, 124.1, 123.5, 122.7, 109.2, 89.2, 79.9, 68.9, 26.9, 14.3. HRMS (ESI) calcd for $C_{14}H_{13}NNaO_4^+$ [M + Na^+] 282.0737, found 282.0735. $[\alpha]_D^{25}$ = -48.4 (c = 0.12, $CHCl_3$). Enantiomeric excess: 87%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 15.29 min (major), t_R = 18.19 min (minor). The absolute configuration was tentatively assigned by analogy.

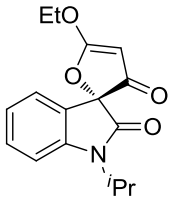
(*R*)-5-Ethoxy-1'-ethyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2b)



2b

Following the general procedure, **2b** was purified by silica gel chromatograohy (30% EA/PE). Yield: 71% (39 mg), white solid, mp. 151 – 153 ^{o}C. IR (KBr) 3108, 2986, 1731, 1698, 1580, 1347, 1010, 881, 766 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.6 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.08 (t, *J* = 7.3 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 4.95 (s, 1H), 4.41 (dd, *J* = 13.1, 6.3 Hz, 2H), 3.80 (td, *J* = 13.7, 6.9 Hz, 1H), 3.73 (td, *J* = 13.6, 6.7 Hz, 1H), 1.52 (t, *J* = 6.3 Hz, 3H), 1.30 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.6, 186.4, 168.4, 144.4, 131.4, 124.3, 123.3, 123.0, 109.3, 89.2, 79.8, 68.9, 35.5, 14.3, 12.5. HRMS (ESI) calcd for $C_{15}H_{15}NNaO_4^+$ [M + Na^+] 296.0893, found 296.0891. $[\alpha]_D^{25}$ = -34.1 (c = 0.15, $CHCl_3$). Enantiomeric excess: 87%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 15.40 min (major), t_R = 19.34 min (minor). The absolute configuration was determined by X-ray crystallography analysis.

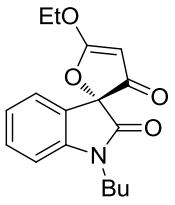
(*R*)-5-Ethoxy-1'-isopropyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (1c)



2c

Following the general procedure, **2c** was purified by silica gel chromatography (30% EA/PE). Yield: 65% (37 mg), white solid, mp. 118 – 121 ^{o}C. IR (KBr) 3087, 2961, 1732, 1708, 1582, 1344, 1030, 884, 753 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (td, *J* = 7.9, 1.1 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 1H), 7.05 (dd, *J* = 14.6, 7.7 Hz, 2H), 4.94 (s, 1H), 4.51 (dt, *J* = 14.0, 7.0 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.51 (dd, *J* = 9.5, 3.9 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 186.4, 168.4, 144.2, 131.2, 124.4, 123.2, 122.9, 110.6, 89.3, 79.7, 68.9, 45.1, 19.5, 19.1, 14.2. HRMS (ESI) calcd for $C_{16}H_{17}NNaO_4^+$ [M + Na^+] 310.1050, found 310.1046. $[\alpha]_D^{25}$ = -21.4 (c = 0.15, $CHCl_3$). Enantiomeric excess: 82%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 10.46 min (major), t_R = 16.06 min (minor). The absolute configuration was tentatively assigned by analogy.

(*R*)-1'-Butyl-5-ethoxy-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (1d)

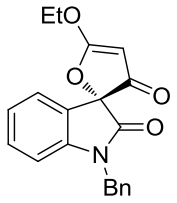


2d

Following the general procedure, **2d** was purified by silica gel chromatography (30% EA/PE). Yield: 57% (34 mg), white solid, mp. 97 – 100 ^{o}C. IR (KBr) 3115, 2960, 1732, 1698, 1579, 1348, 1039, 885, 766 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (td, *J* = 7.8, 1.1 Hz, 1H), 7.20 (d, *J* = 7.4 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 4.95 (s, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.71 (td, *J* = 7.4, 2.2 Hz, 2H), 1.67 (ddd, *J* = 10.4, 7.0, 3.8 Hz, 2H), 1.52 (t, *J* = 7.1 Hz, 3H), 1.41 (dd, *J* = 14.8,

7.4 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 186.4, 168.7, 144.8, 131.4, 124.3, 123.2, 122.9, 109.5, 89.2, 79.8, 68.9, 40.4, 29.3, 20.0, 14.3, 13.7. HRMS (ESI) calcd for $C_{17}H_{19}NNaO_4^+$ [M + Na^+] 324.1206, found 324.1206. $[\alpha]_D^{25}$ = -57.1 (c = 0.11, $CHCl_3$). Enantiomeric excess: 86%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^oC, 254 nm): t_R = 16.62 min (major), t_R = 21.57 min (minor). The absolute configuration was tentatively assigned by analogy.

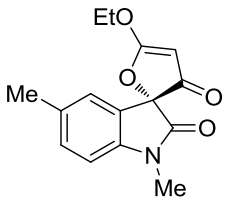
(*R*)-1'-Benzyl-5-ethoxy-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2e)



2e

Following the general procedure, **2e** was purified by silica gel chromatograohy (30% EA/PE). Yield: 77% (52 mg), white solid, mp. 109 – 112 ^oC. IR (KBr) 3117, 2927, 1743, 1579, 1488, 1345, 1106, 882, 751 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 3.5 Hz, 4H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.21 (d, *J* = 7.4 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 4.98 (t, *J* = 7.9 Hz, 2H), 4.86 (d, *J* = 15.9 Hz, 1H), 4.42 (q, *J* = 6.8 Hz, 2H), 1.52 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.6, 186.5, 169.0, 144.3, 134.6, 131.4, 129.0, 127.8, 127.1, 124.2, 123.5, 122.8, 110.3, 89.3, 79.7, 69.1, 44.3, 14.3. HRMS (ESI) calcd for $C_{20}H_{17}NNaO_4^+$ [M+Na^+] 358.1050, found 358.1053. $[\alpha]_D^{25}$ = -44.1 (c = 0.21, $CHCl_3$). Enantiomeric excess: 90%, determined by HPLC (Chiracel-OJ, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^oC, 254 nm): t_R = 25.88 min (major), t_R = 35.09 min (minor). The absolute configuration was tentatively assigned by analogy.

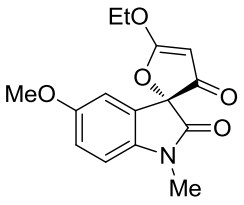
(*R*)-5-Ethoxy-1',5'-dimethyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2f)



2f

Following the general procedure, **2e** was purified by silica gel chromatography (30% EA/PE). Yield: 58% (32 mg), white solid, mp. 132 – 135 ^{o}C. IR (KBr) 3120, 2960, 1735, 1707, 1586, 1379, 1003, 888, 767 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, *J* = 7.8 Hz, 1H), 7.03 (s, 1H), 6.78 (d, *J* = 7.9 Hz, 1H), 4.95 (s, 1H), 4.41 (q, *J* = 6.9 Hz, 2H), 3.21 (s, 3H), 2.31 (s, 3H), 1.52 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.8, 186.4, 168.7, 142.9, 133.2, 131.8, 124.9, 122.7, 109.0, 89.3, 79.9, 68.9, 26.9, 21.0, 14.3. HRMS (ESI) calcd for $C_{15}H_{15}NNaO_4^+$ [M + Na^+] 296.0893, found 296.0891. $[\alpha]_D^{25}$ = -25.3 (c = 0.20, $CHCl_3$). Enantiomeric excess: 86%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 14.17 min (major), t_R = 18.91 min (minor). The absolute configuration was tentatively assigned by analogy.

(*R*)-5-Ethoxy-5'-methoxy-1'-methyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2g)

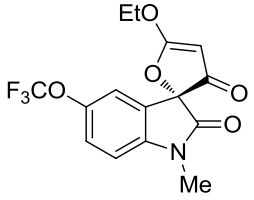


2g

Following the general procedure, **2g** was purified by silica gel chromatography (30% EA/PE). Yield: 55% (32 mg), white solid, mp. 150 – 153 ^{o}C. IR (KBr) 3117, 2944, 1730, 1704, 1584, 1496, 1344, 1029, 881, 804, 765 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.92 (d, *J* = 8.0 Hz, 1H), 6.80 (d, *J* = 8.9 Hz, 2H), 4.96 (s, 1H), 4.41 (dd, *J* = 12.8, 6.1 Hz, 2H), 3.76 (s, 3H), 3.20 (s, 3H), 1.51 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.6, 186.5, 168.5, 156.5, 138.5, 123.7, 116.22, 111.0, 109.8, 89.4, 79.8, 69.0, 55.9, 27.0, 14.3. HRMS (ESI) calcd for $C_{15}H_{15}NNaO_5^+$ [M + Na^+]

312.0842, found 312.0844. $[\alpha]_D^{25}$ = -80.9 (c = 0.27, $CHCl_3$). Enantiomeric excess: 90%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^oC, 254 nm): t_R = 18.80 min (major), t_R = 29.53 min (minor). The absolute configuration was tentatively assigned by analogy.

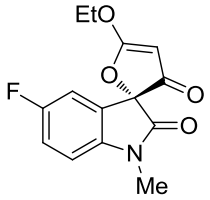
(*R*)-5-Ethoxy-1'-methyl-5'-(trifluoromethoxy)-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2h)



2h

Following the general procedure, **2h** was purified by silica gel chromatography (30% EA/PE). Yield: 62% (43 mg), white solid, mp. 108 – 111 ^oC. IR (KBr) 3117, 2990, 1740, 1716, 1586, 1472, 1348, 1104, 881, 861, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 1H), 7.10 (d, *J* = 1.6 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 4.96 (s, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.24 (s, 3H), 1.54 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 186.5, 168.6, 145.07 (d, J_{C-F}= 2.0 Hz), 143.9, 124.6, 124.03 (s), 123.0 (d, J_{C-F}= 257.4 Hz), 120.4 (d, J_{C-F}= 257.4 Hz), 118.1, 117.9 (d, J_{C-F}= 257.3 Hz), 109.9, 88.6, 79.6, 69.3, 27.1, 14.2. HRMS (ESI) calcd for $C_{15}H_{12}F_3NNaO_5^+$ [M + Na^+] 366.0560, found 366.0564. $[\alpha]_D^{25}$ = -40.8 (c = 0.18, $CHCl_3$). Enantiomeric excess: 89%, determined by HPLC (Chiracel-OD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^oC, 254 nm): t_R = 19.01 min (minor), t_R = 23.01 min (major). The absolute configuration was tentatively assigned by analogy.

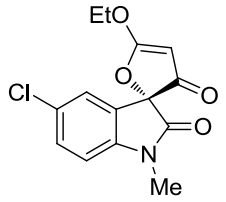
(*R*)-5-Ethoxy-5'-fluoro-1'-methyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2i)



2i

Following the general procedure, **2i** was purified by silica gel chromatography (30% EA/PE). Yield: 74% (41 mg), white solid, mp. 126 – 128 ^{o}C. IR (KBr) 3122, 2949, 1733, 1699, 1579, 1494, 1349, 1005, 878, 765 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 6.0 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 4.95 (s, 1H), 4.42 (d, *J* = 6.6 Hz, 2H), 3.22 (s, 3H), 1.52 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.9, 186.5, 168.5, 159.4 (d, J_{C-F}= 243.1 Hz), 141.3, 124.0 (d, J_{C-F} = 8.4 Hz), 117.8 (d, J_{C-F} = 23.5 Hz), 112.4 (d, J_{C-F} = 25.5 Hz), 109.9 (d, J_{C-F} = 8.0 Hz), 88.8, 79.7, 69.2, 27.0, 14.2. HRMS (ESI) calcd for $C_{14}H_{12}FNNaO_4^+$ [M + Na^+] 300.0643, found 300.0640. $[\alpha]_D^{25}$ = -39.7 (c = 0.23, $CHCl_3$). Enantiomeric excess: 89%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 14.74 min (major), t_R = 18.15 min (minor). The absolute configuration was tentatively assigned by analogy.

(*R*)-5'-Chloro-5-ethoxy-1'-methyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2j)

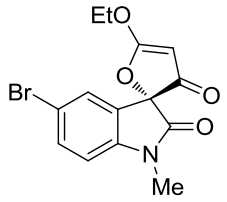


2j

Following the general procedure, **2j** was purified by silica gel chromatography (30% EA/PE). Yield: 67% (39 mg), white solid, mp. 158 – 161 ^{o}C. IR (KBr) 3129, 2934, 1739, 1712, 1585, 1489, 1378, 1044, 884, 731 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 6.9 Hz, 1H), 7.19 (s, 1H), 6.83 (d, *J* = 8.3 Hz, 1H), 4.96 (s, 1H), 4.77 – 4.21 (m, 2H), 3.22 (d, *J* = 6.4 Hz, 3H), 1.52 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.9, 186.5, 168.4, 143.8, 131.4, 128.8, 124.6, 124.2,

110.3, 88.6, 79.7, 69.3, 27.0, 14.2. HRMS (ESI) calcd for $C_{14}H_{12}{}^{35}ClNNaO_4{}^+$ [M + Na^+] 316.0347, found 316.0343. $[\alpha]_D{}^{25}$ = -28.6 (c = 0.14, $CHCl_3$). Enantiomeric excess: 88%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^oC, 254 nm): t_R = 13.86 min (major), t_R = 15.88 min (minor). The absolute configuration was tentatively assigned by analogy.

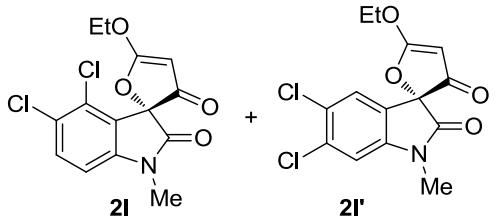
(*R*)-5'-Bromo-5-ethoxy-1'-methyl-3*H*-spiro[furan-2,3'-indoline]-2',3-dione (2k)



2k

Following the general procedure, **2k** was purified by silica gel chromatography (30% EA/PE). Yield: 69% (46 mg), white solid, mp. 158 – 161 ^oC. IR (KBr) 3127, 2987, 1740, 1711, 1585, 1487, 1377, 1043, 885, 738 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 6.7 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 4.96 (d, *J* = 7.8 Hz, 1H), 4.63 – 4.22 (m, 2H), 3.22 (d, *J* = 7.9 Hz, 3H), 1.54 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (150MHz, $CDCl_3$) δ 191.8, 186.5, 168.3, 144.3, 134.2, 127.3, 124.6, 116.0, 110.7, 88.5, 79.7, 69.2, 27.0, 14.3. HRMS (ESI) calcd for $C_{14}H_{12}{}^{79}BrNNaO_4{}^+$ [M + Na^+] 359.9842, found 359.9843. $[\alpha]_D{}^{25}$ = -23.1 (c = 0.13, $CHCl_3$). Enantiomeric excess: 90%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^oC, 254 nm): t_R = 16.02 min (major), t_R = 17.99 min (minor). The absolute configuration was tentatively assigned by analogy.

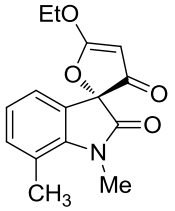
(*R*)-4',5'-Dichloro-5-ethoxy-1'-methyl-3H-spiro[furan-2,3'-indoline]-2',3-dione (2l) and (*R*)-5',6'-dichloro-5-ethoxy-1'-methyl-3H-spiro[furan-2,3'-indoline] -2',3- dione (2l')



2l **2l'**

Following the general procedure, **2l** and **2l'** were isolated and purified as a mixture by silica gel chromatography (30% EA/PE). Yield: 58% (38 mg), white solid, mp. 134 – 137 ^{o}C. IR (KBr) 3097, 2987, 1741, 1703, 1580, 1460, 1347, 1043, 875, 747 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.4 Hz, 1.21H), 7.28 (d, *J* = 1.1 Hz, 1.20H), 7.00 (s, 0.96H), 6.77 (d, *J* = 8.4 Hz, 1.21H), 5.08 (s, 1.19H), 4.96 (s, 1H), 4.43 (p, *J* = 7.2 Hz, 4.48H), 3.21 (s, 6.63H), 1.53 (td, *J* = 7.1, 2.0 Hz, 6.62H). ^{13}C NMR (100MHz, $CDCl_3$) δ 191.6, 190.9, 186.5, 186.1, 168.2, 167.8, 145.3, 144.6, 135.6, 132.9, 130.4, 127.5, 127.1, 126.0, 122.3, 121.8, 111.4, 108.3, 88.4, 88.0, 81.2, 79.7, 69.5, 69.2, 27.1, 14.3, 14.2. HRMS (ESI) calcd for $C_{14}H_{11}{}^{35}C_{l2}NNaO_4^+$ [M + Na^+] 349.9957, found 349.9961. $[\alpha]_D^{25}$ = -26.3 (c = 0.19, $CHCl_3$). Enantiomeric excess: **2l**: 91%, **2l':** 86%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 90/10, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): **2l**: t_R = 42.30 min (minor), t_R = 52.63 min (major). **2l'**: t_R = 32.28 min (minor), t_R = 38.22 min (major).The absolute configuration was tentatively assigned by analogy.

(*R*)-5-Ethoxy-1',7'-dimethyl-3H-spiro[furan-2,3'-indoline]-2',3-dione (2m)

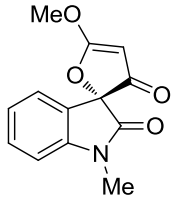


2m

Following the general procedure, **2m** were purified by silica gel chromatography (30% EA/PE). Yield: 46% (25 mg), white solid, mp. 107 – 110 ^{o}C. IR (KBr) 3095, 2933, 1730, 1699, 1576, 1456, 1379, 1076, 860, 749 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 4.94 (s, 1H), 4.41 (q, *J* = 7.0 Hz, 2H), 3.49 (s, 3H), 2.56 (s, 3H), 1.51 (t, *J* = 7.0 Hz,

3H). ^{13}C NMR (150MHz, $CDCl_3$) δ 192.8, 186.4, 169.5, 142.9, 135.3, 123.4, 123.3, 122.0, 121.0, 89.1, 79.8, 68.9, 30.2, 18.9, 14.3. HRMS (ESI) calcd for $C_{15}H_{15}NNaO_4^+$ [M + Na^+] 296.0893, found 296.0891. $[\alpha]_D^{25}$ = -33.3 (c = 0.12, $CHCl_3$). Enantiomeric excess: 74%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 14.70 min (major), t_R = 25.36 min (minor). The absolute configuration was tentatively assigned by analogy.

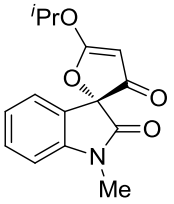
(*R*)-5-Methoxy-1'-methyl-3H-spiro[furan-2,3'-indoline]-2',3-dione (2n)



2n

Following the general procedure, **2n** were purified by silica gel chromatography (30% EA/PE). Yield: 51% (25 mg), white solid, mp. 164 – 167 ^{o}C. IR (KBr) 3122, 2956, 1731, 1702, 1586, 1494, 1363, 987, 928, 767 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 1H), 7.24 – 7.16 (m, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 4.99 (s, 1H), 4.11 (d, *J* = 0.9 Hz, 3H), 3.23 (d, *J* = 0.8 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 192.5, 187.3, 168.7, 145.3, 131.6, 124.2, 123.5, 122.6, 109.2, 89.5, 79.7, 58.9, 26.9. HRMS (ESI) calcd for $C_{13}H_{11}NNaO_4^+$ [M + Na^+] 268.0580, found 268.0583. $[\alpha]_D^{25}$ = -37.0 (c = 0.13, $CHCl_3$). Enantiomeric excess: 88%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 17.85 min (major), t_R = 19.31 min (minor). The absolute configuration was tentatively assigned by analogy.

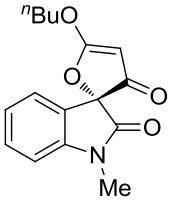
(*R*)-5-Isopropoxy-1'-methyl-3H-spiro[furan-2,3'-indoline]-2',3-dione (2o)



2o

Following the general procedure, **2o** were purified by silica gel chromatography (30% EA/PE). Yield: 55% (30 mg), white solid, mp. 124 – 127 ^{o}C. IR (KBr) 3098, 2941, 1745, 1693, 1566, 1490, 1346, 1089, 976, 906, 800 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (td, *J* = 7.8, 1.1 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 4.93 (s, 1H), 4.89 (dt, *J* = 12.3, 6.2 Hz, 1H), 3.23 (s, 3H), 1.50 (d, *J* = 2.7 Hz, 3H), 1.49 (d, *J* = 2.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 185.7, 168.9, 145.3, 131.5, 124.1, 123.5, 122.9, 109.2, 89.0, 80.3, 77.9, 26.9, 21.9, 21.8. HRMS (ESI) calcd for $C_{15}H_{15}NNaO_4^+$ [M + Na^+] 296.0893, found 296.0891. $[\alpha]_D^{25}$ = -35.6 (c = 0.45, $CHCl_3$). Enantiomeric excess: 89%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 ^{o}C, 254 nm): t_R = 12.26 min (major), t_R = 15.30 min (minor). The absolute configuration was tentatively assigned by analogy.

(*R*)-5-Butoxy-1'-methyl-3H-spiro[furan-2,3'-indoline]-2',3-dione (2p)

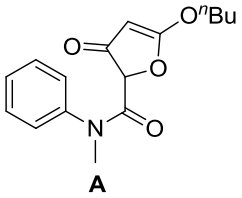


2p

Following the general procedure, **2p** were purified by silica gel chromatography (30% EA/PE). Yield: 59% (34 mg), white solid, mp. 132 – 134 ^{o}C. IR (KBr) 3130, 2946, 1730, 1698, 1575, 1492, 1354, 1044, 847, 778, 769 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 11.3, 4.3 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 4.95 (s, 1H), 4.34 (t, *J* = 6.5 Hz, 2H), 3.23 (s, 3H), 1.94 – 1.78 (m, 2H), 1.68 – 1.38 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR

(100MHz, $CDCl_3$) δ 192.6, 186.6, 168.8, 145.3, 131.5, 124.1, 123.5, 122.8, 109.2, 89.2, 79.8, 72.7, 30.6, 26.9, 18.8, 13.6. HRMS (ESI) calcd for $C_{16}H_{17}NNaO_4^+$ [M + Na^+] 310.1050, found 310.1052. $[\alpha]_D^{25}$ = -29.4 (c = 0.17, $CHCl_3$). Enantiomeric excess: 88%, determined by HPLC (Chiracel-AD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 °C, 254 nm): t_R = 13.29 min (major), t_R = 17.88 min (minor). The absolute configuration was tentatively assigned by analogy.

5-Butoxy-*N*-methyl-3-oxo-*N*-phenyl-2,3-dihydrofuran-2-carboxamide (A)



A were purified by silica gel chromatography (30% EA/PE). Yield: 81% (234 mg), white solid, mp. 65– 67 °C. IR (KBr) 2966, 2876, 1697, 1665, 1601, 1471, 1392, 981, 701 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (t, *J* = 7.7 Hz, 4H), 7.39 (d, *J* = 8.6 Hz, 1H), 5.17 (s, 1H), 4.76 (s, 1H), 4.20 (qd, *J* = 7.8, 3.3 Hz, 2H), 3.36 (s, 3H), 1.82 – 1.70 (m, 2H), 1.45 (dd, *J* = 15.1, 7.5 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 186.4, 163.0, 142.0, 130.0, 128.6, 127.7, 80.1, 80.0, 72.3, 38.1, 30.5, 18.7, 13.6. HRMS (ESI) calcd for $C_{16}H_{19}NNaO_4^+$ [M + Na^+] 312.1206, found 312.1203. $[\alpha]_D^{25}$ = 0 (c = 0.23, $CHCl_3$). Enantiomeric excess: < 3%, determined by HPLC (Chiracel-OD, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 25 °C, 254 nm): t_R = 11.69 min, t_R = 14.40 min.

VII. References

1. Li, W.; Ma, X.; Fan, W.; Tao, X.; Li, X.; Xie, Z.; Zhang, Z. *Org. Lett.* **2011**, *13*, 3876.

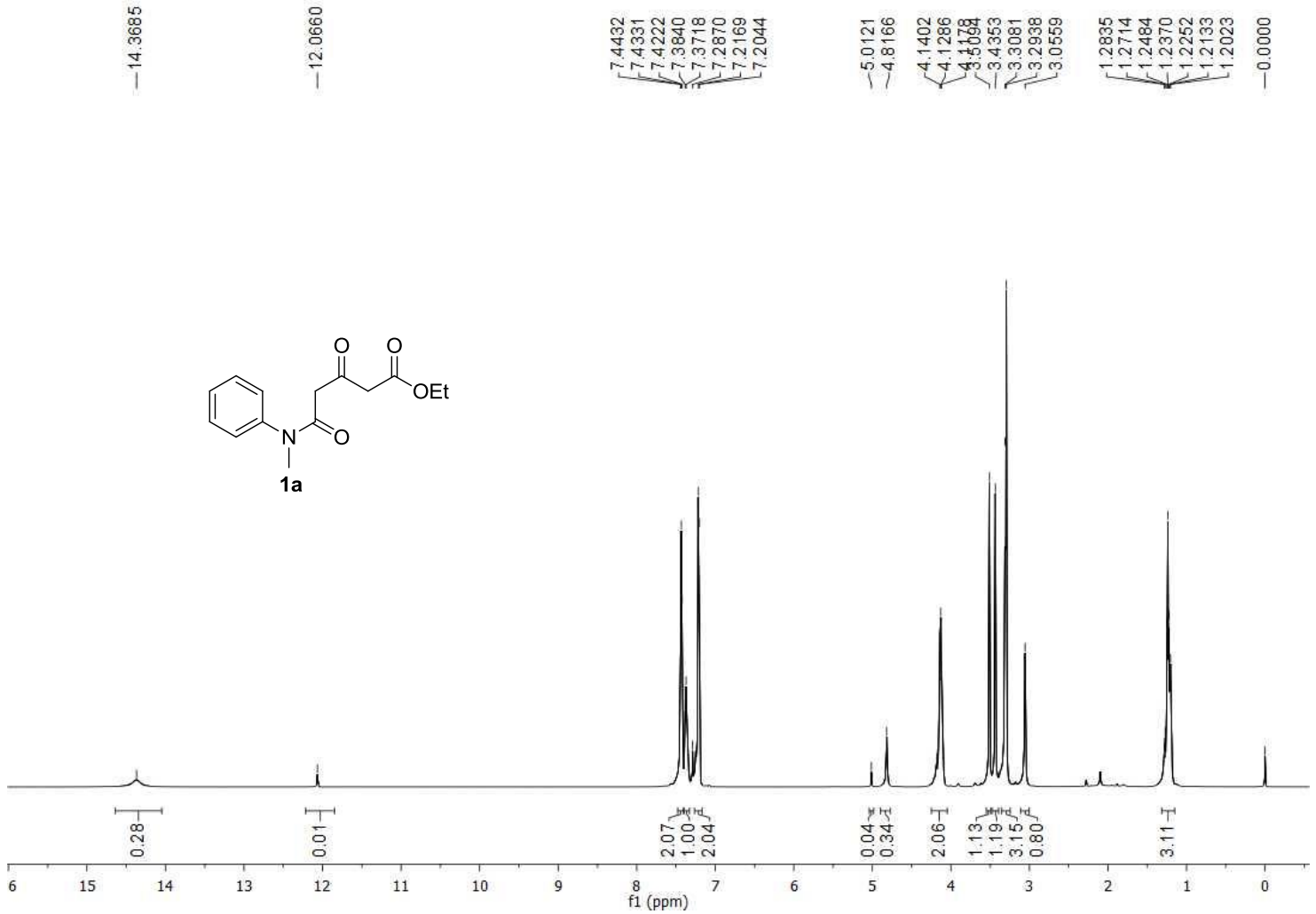
2. Dohi, T.; Maruyama, A.; Takenaga, N.; Senami, K.; MinamitsuJi, Y.; FuJioka, H.; Caemmerer, S. B.; Kita, Y. *Angew. Chem., Int. Ed*. **2008**, *47*, 3787.

3. Uyanik, M.; Yasui, T.; Ishihara, K. *Angew. Chem., Int. Ed*. **2010**, *49*, 2175.

4. Wu, H.; He, Y.-P.; Xu, L.; Zhang, D.-Y.; Gong, L.-Z. *Angew. Chem., Int. Ed*. **2014**, *53*, 3466.

5. Alhalib, A.; Kamouka, S.; Moran, W. J. *Org. Lett.* **2015**, *17*, 1453.

VIII. ^{1}H-NMR, ^{13}C-NMR Spectra and HPLC Data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4.1402
4.1286
4.1178
3.5094
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3.3081
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1.2023
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O
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N
O
1a
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0.01
2.07
1.00
2.04
0.04
0.34
2.06
1.13
1.19
3.15
0.80
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9
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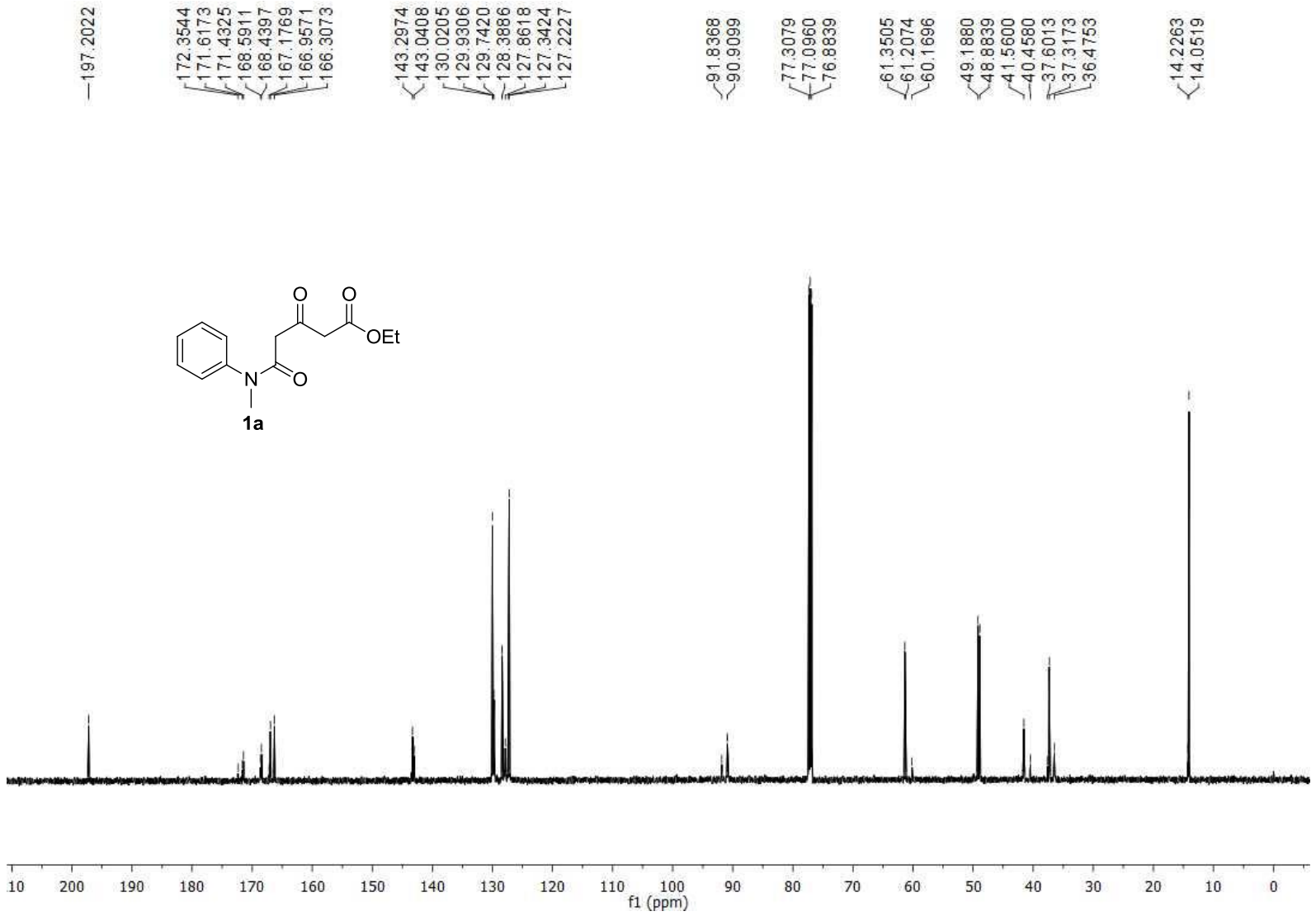
f1 (ppm)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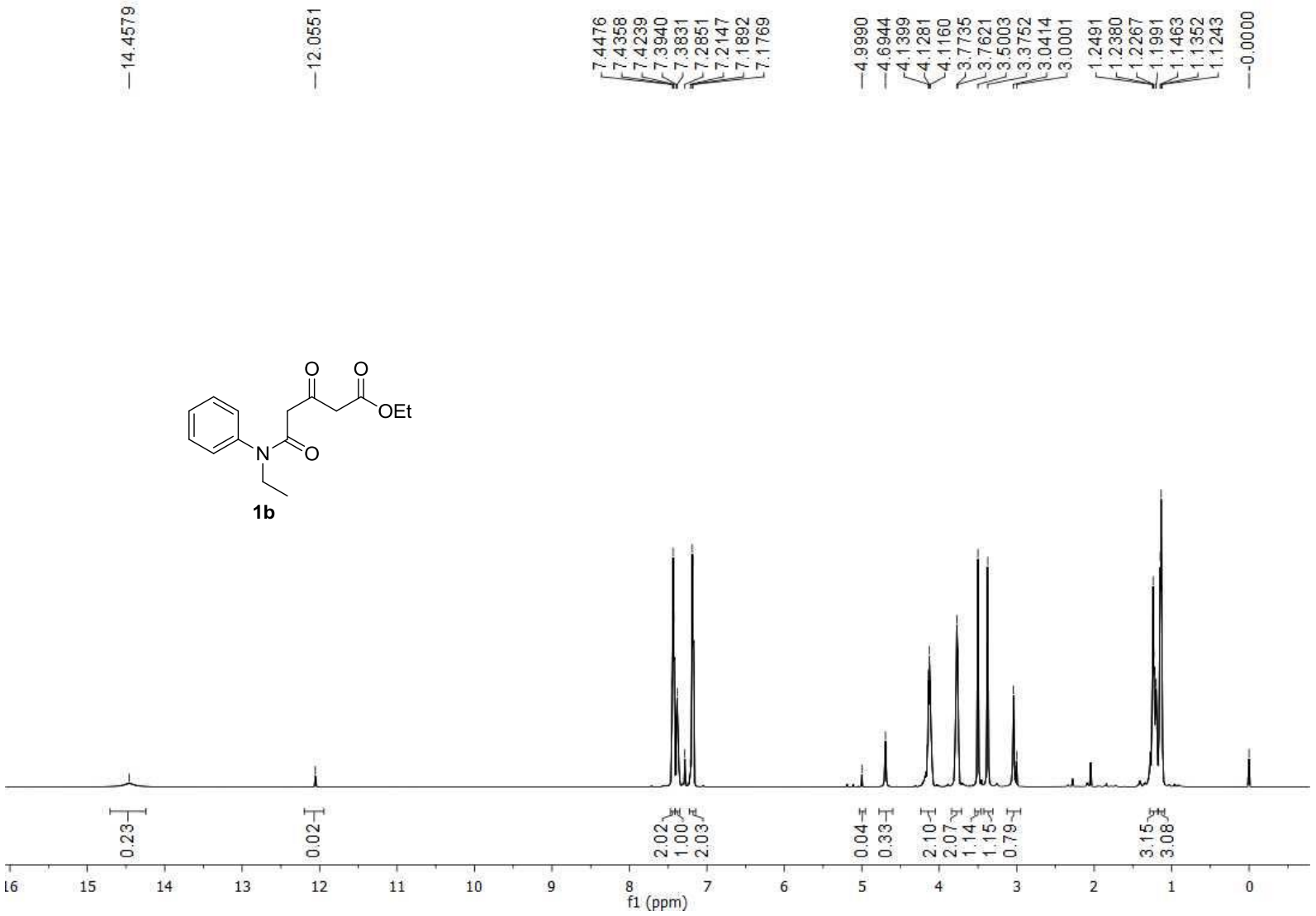
f1 (ppm)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3.0414
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0.04
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2.10
2.07
1.14
1.15
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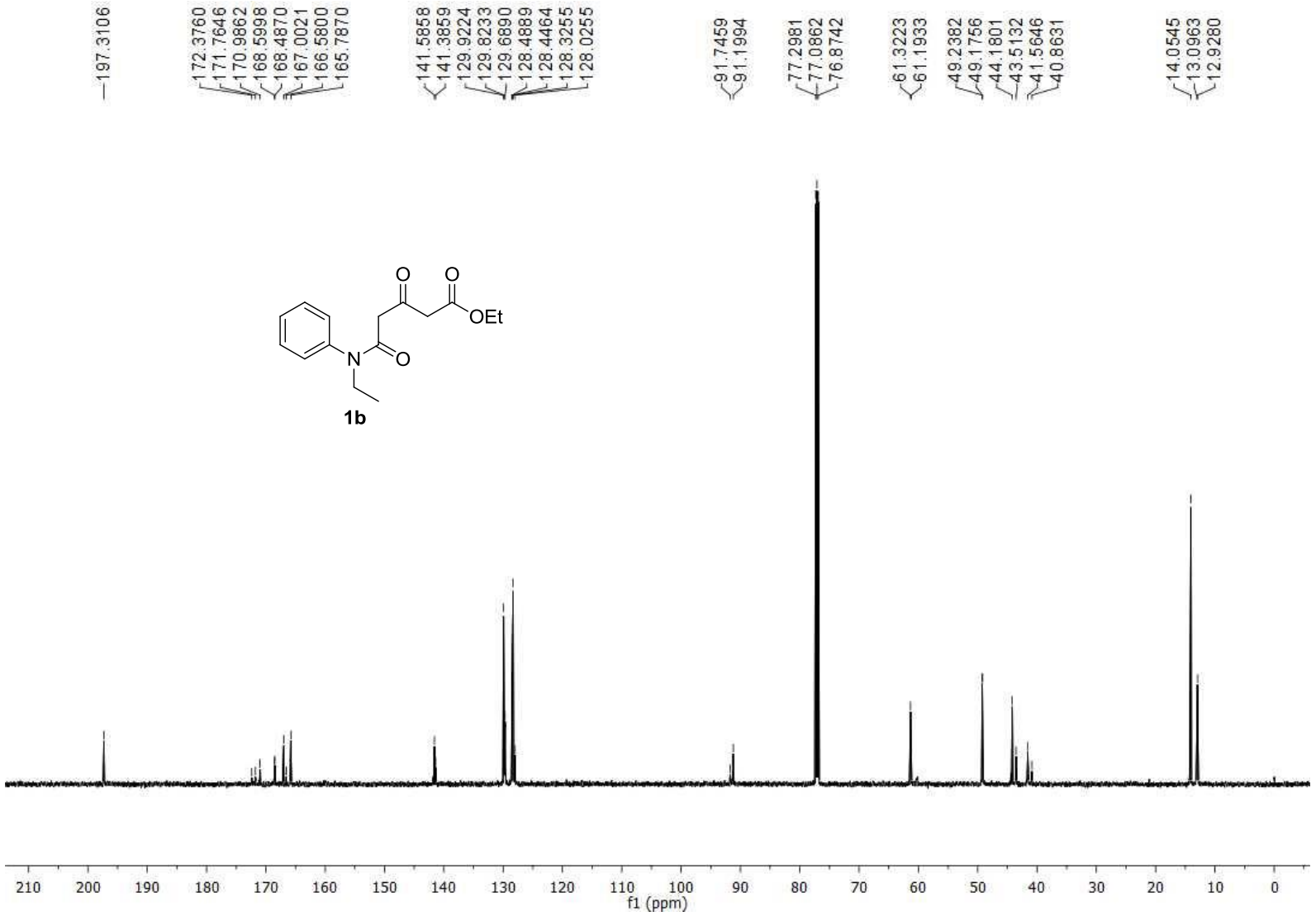
f1 (ppm)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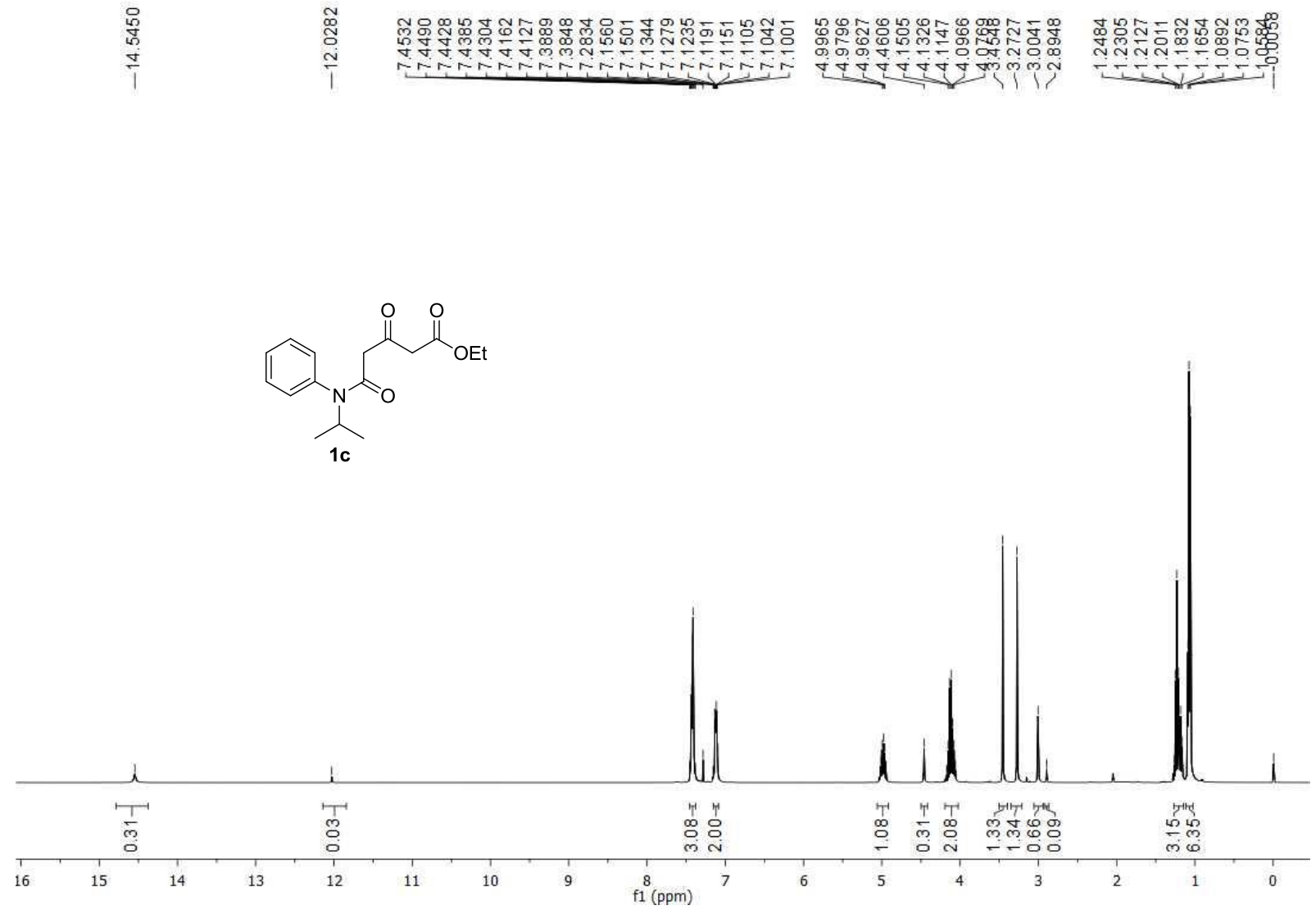
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1.33
1.34
0.66
0.09
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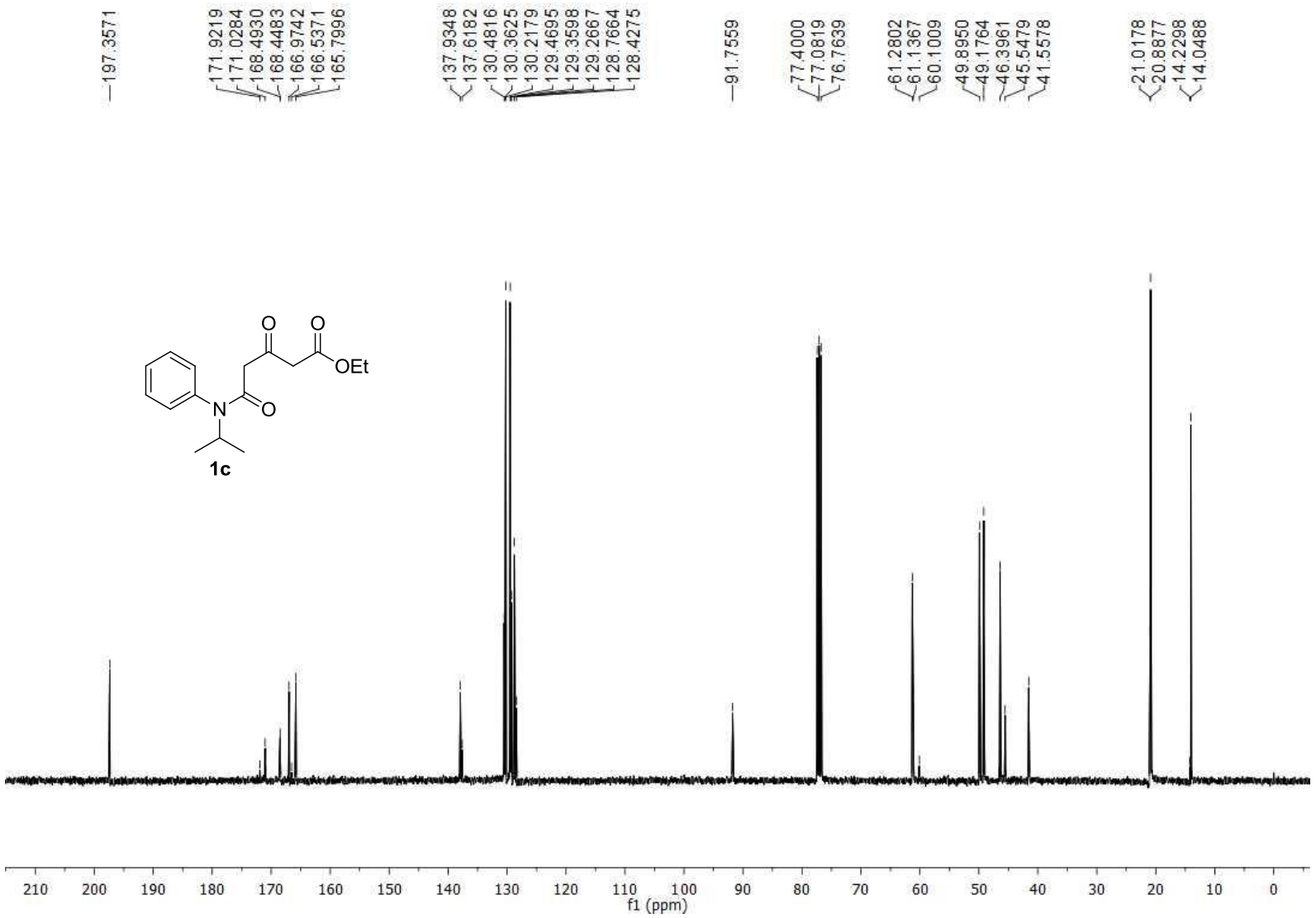
f1 (ppm)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180
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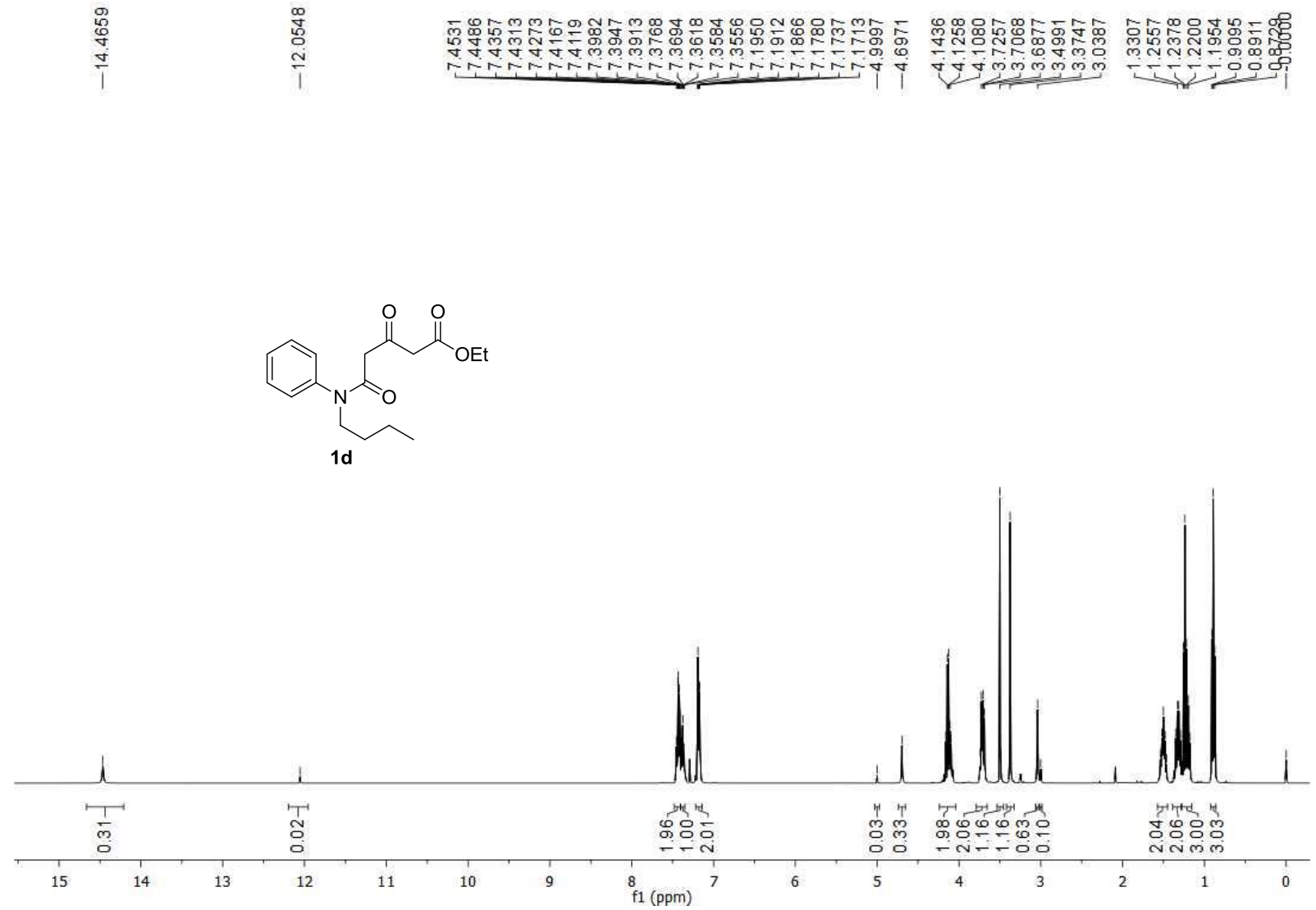
f1 (ppm)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7.3618
7.3584
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N
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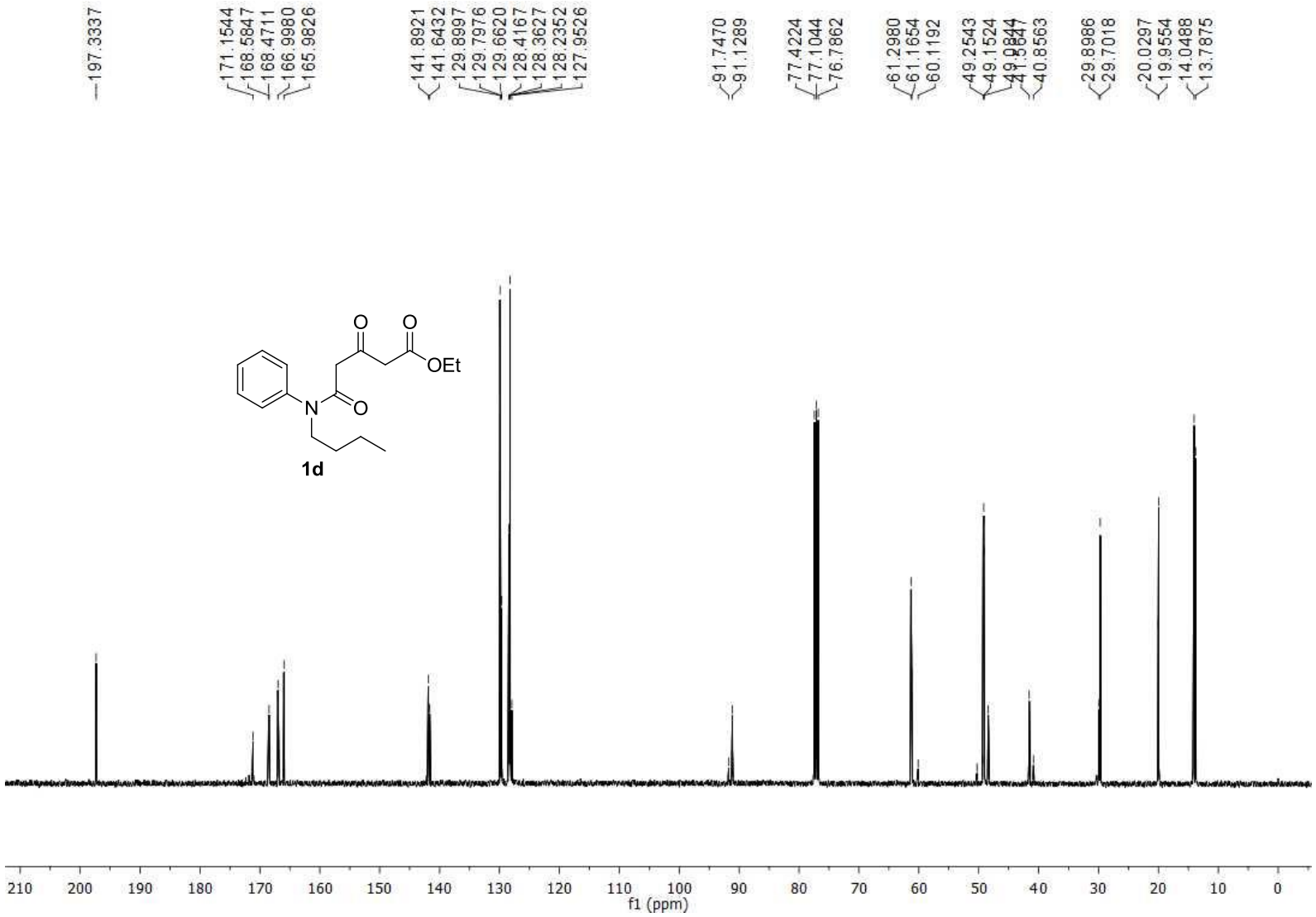
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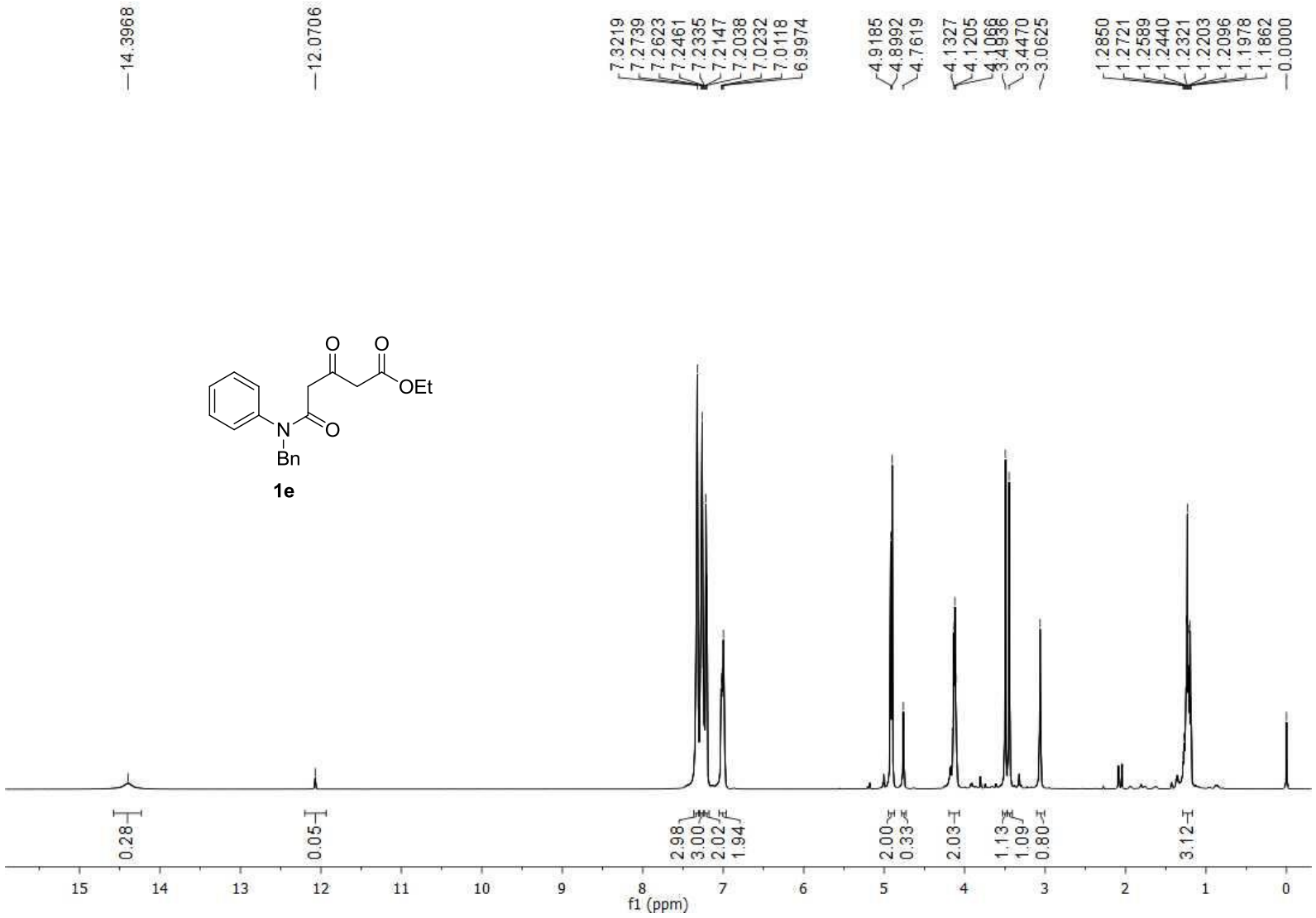
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N
O
Bn
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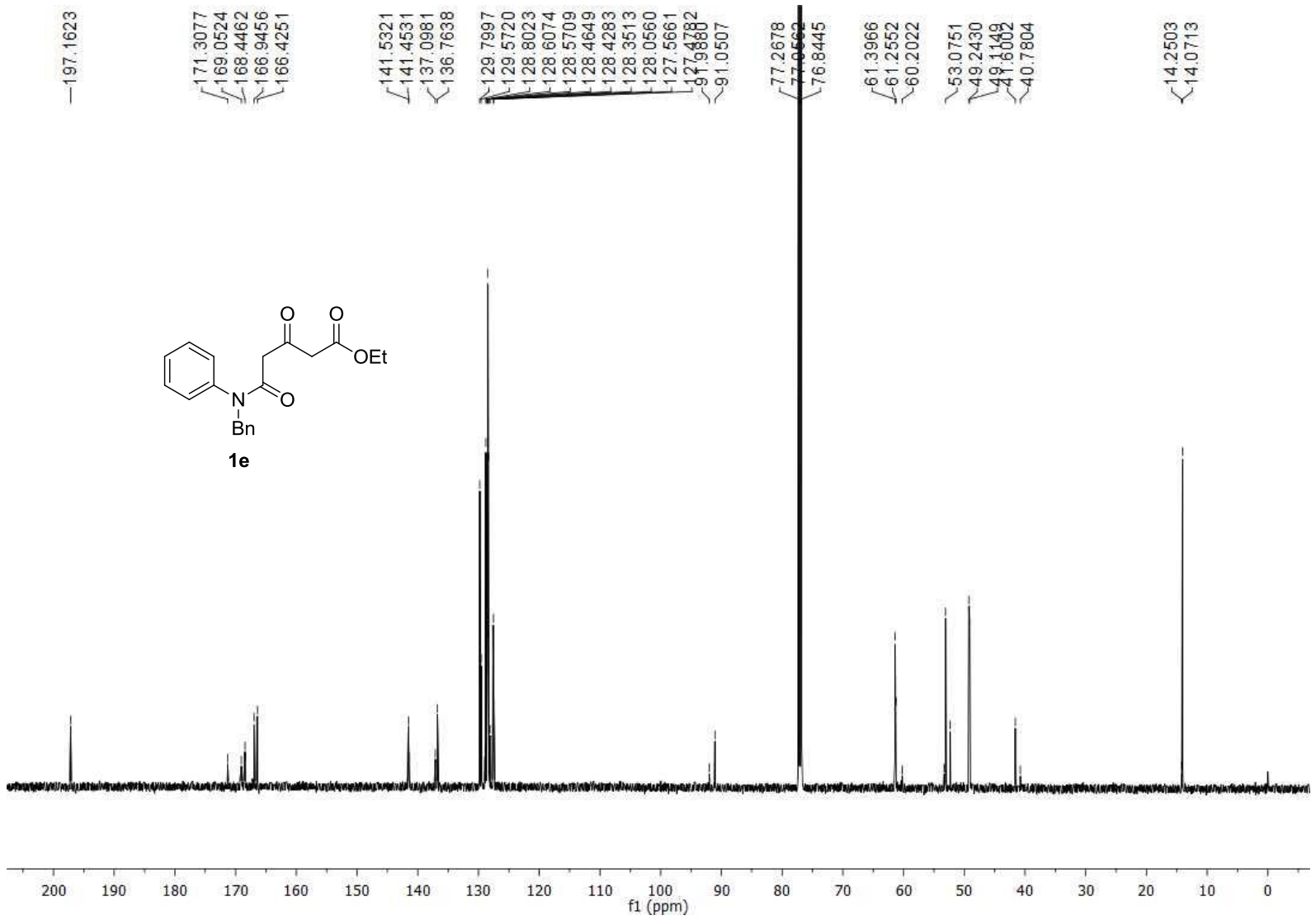
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O
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N
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Bn
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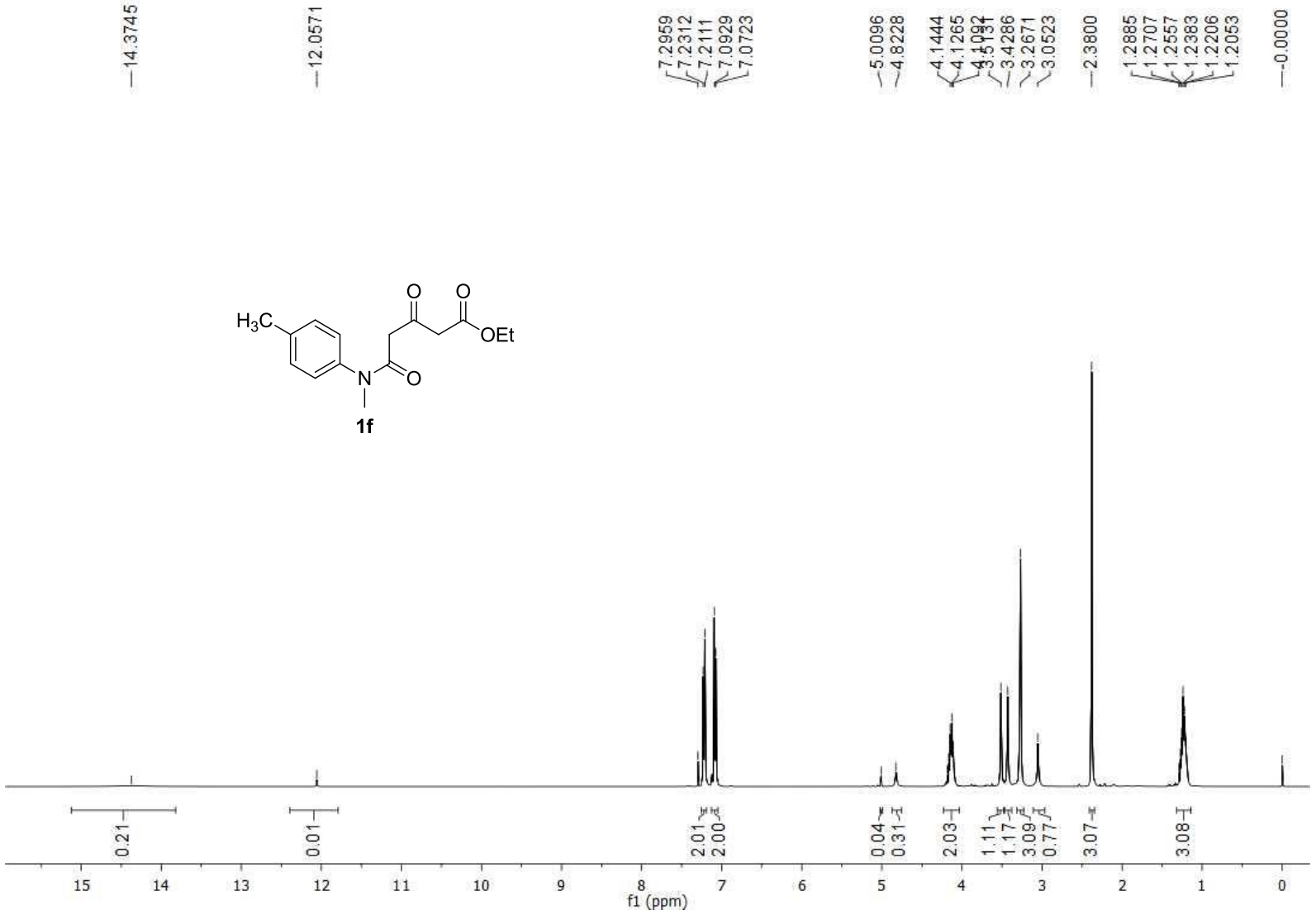
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N
O
1f
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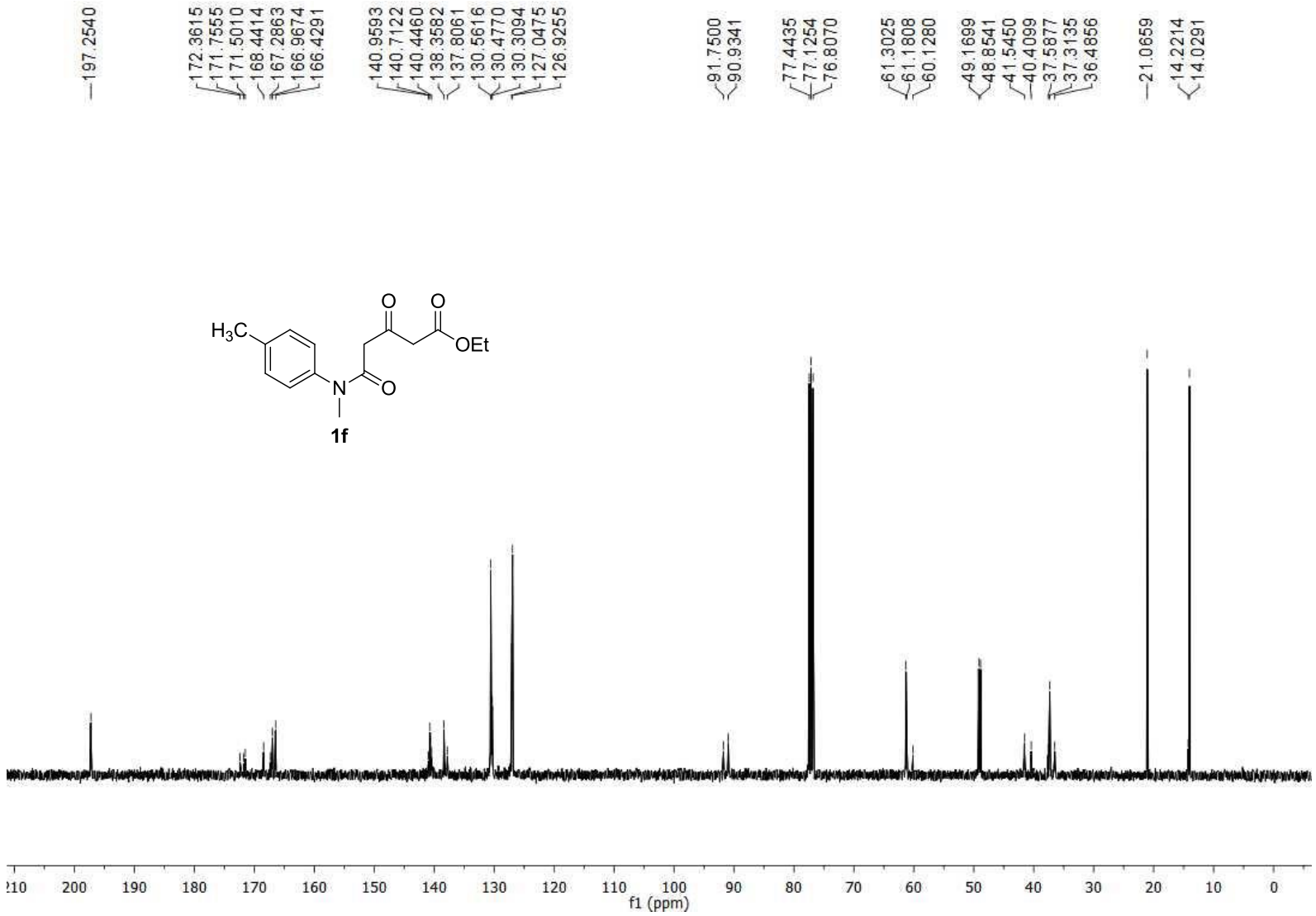
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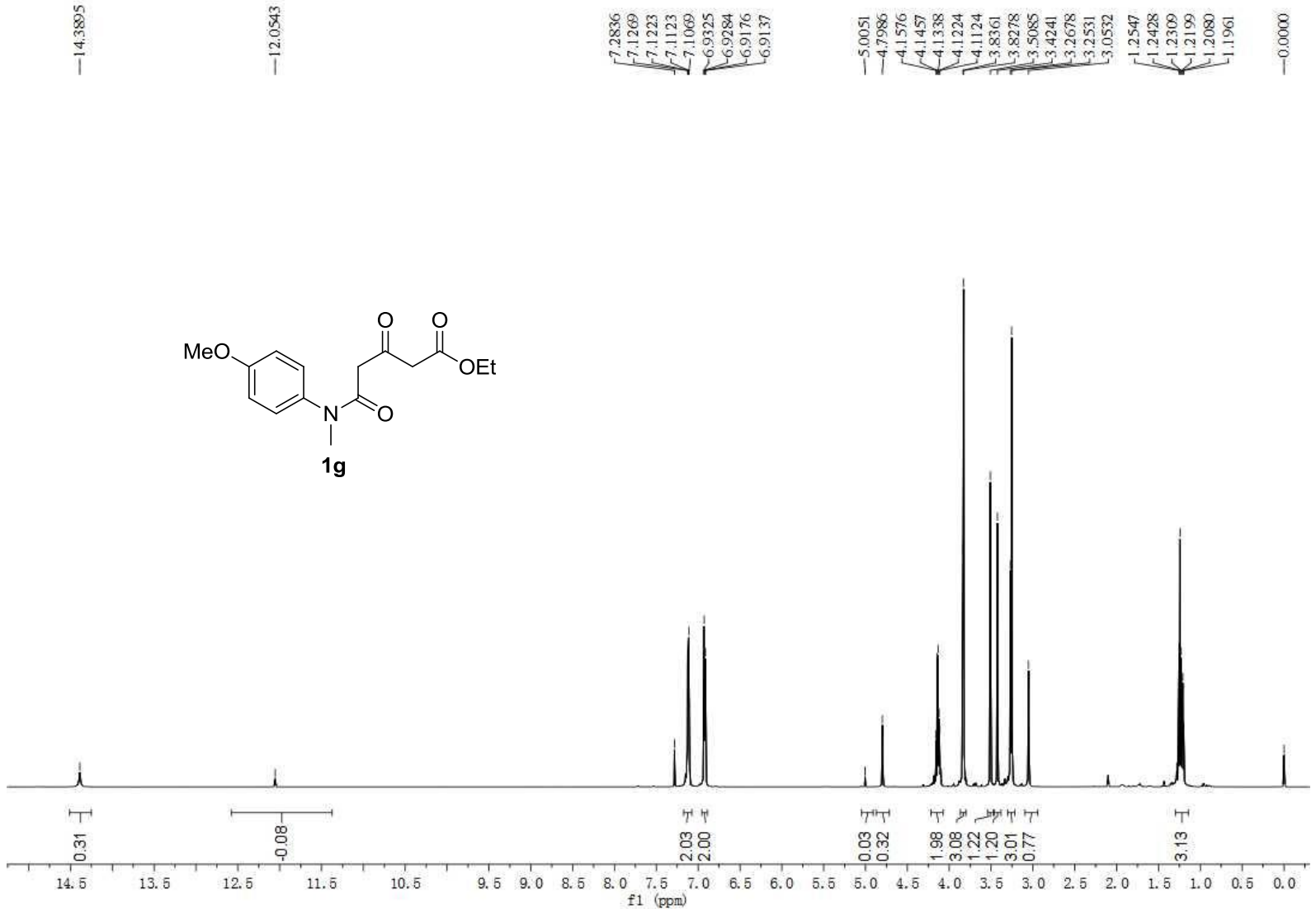
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O
OEt
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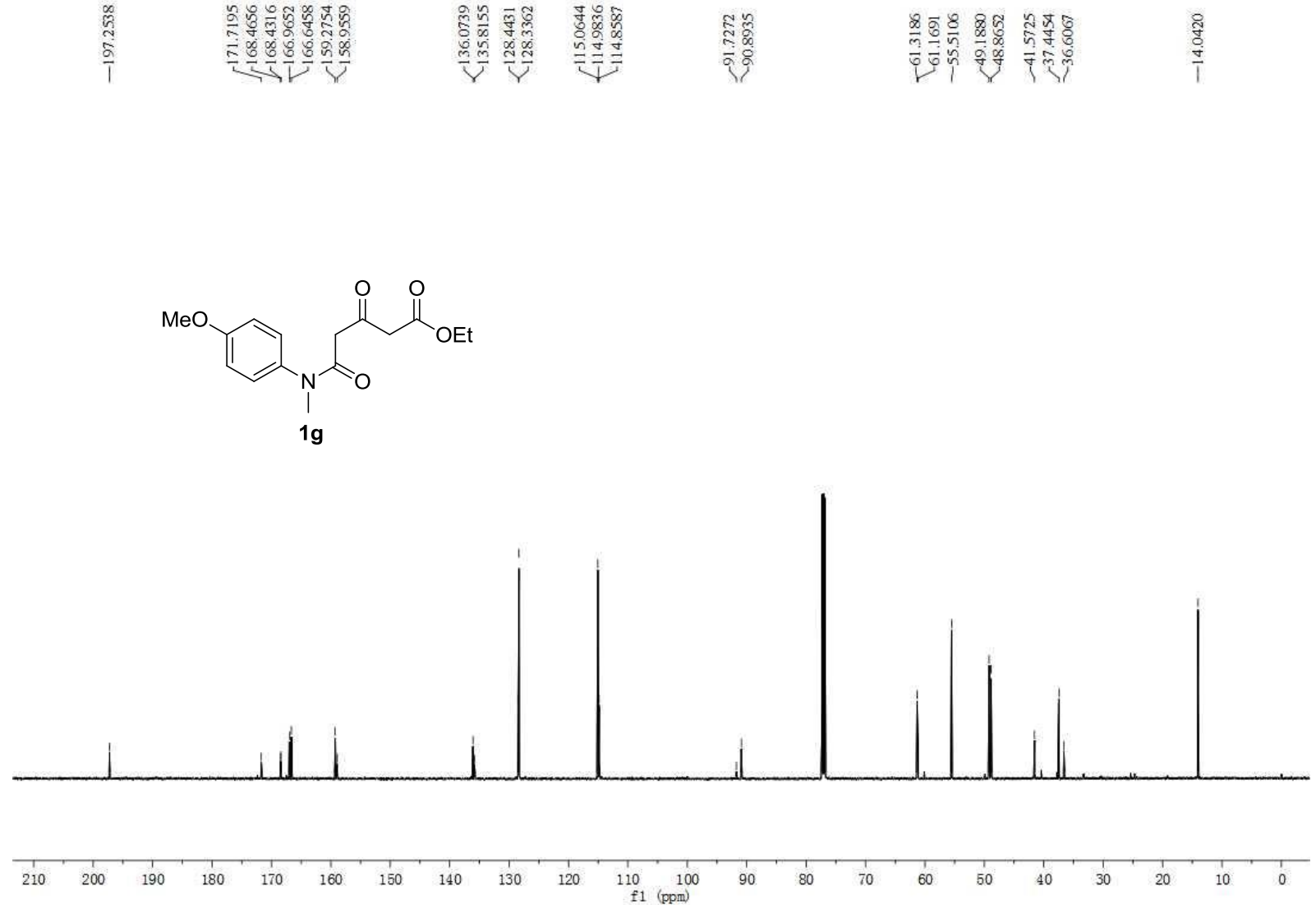
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O
O
OEt
N
O
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200
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180
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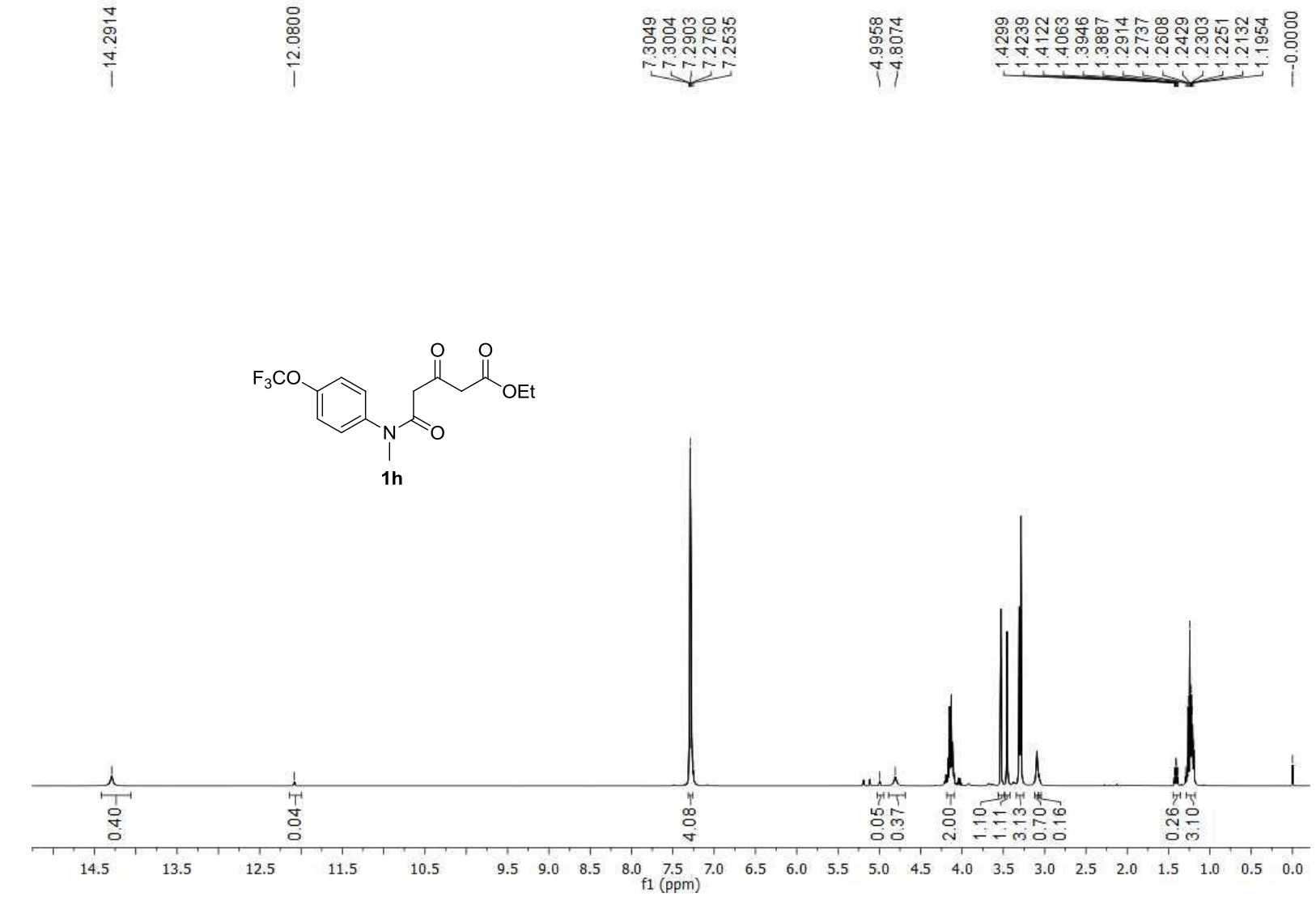
f1 (ppm)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OEt
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1.11
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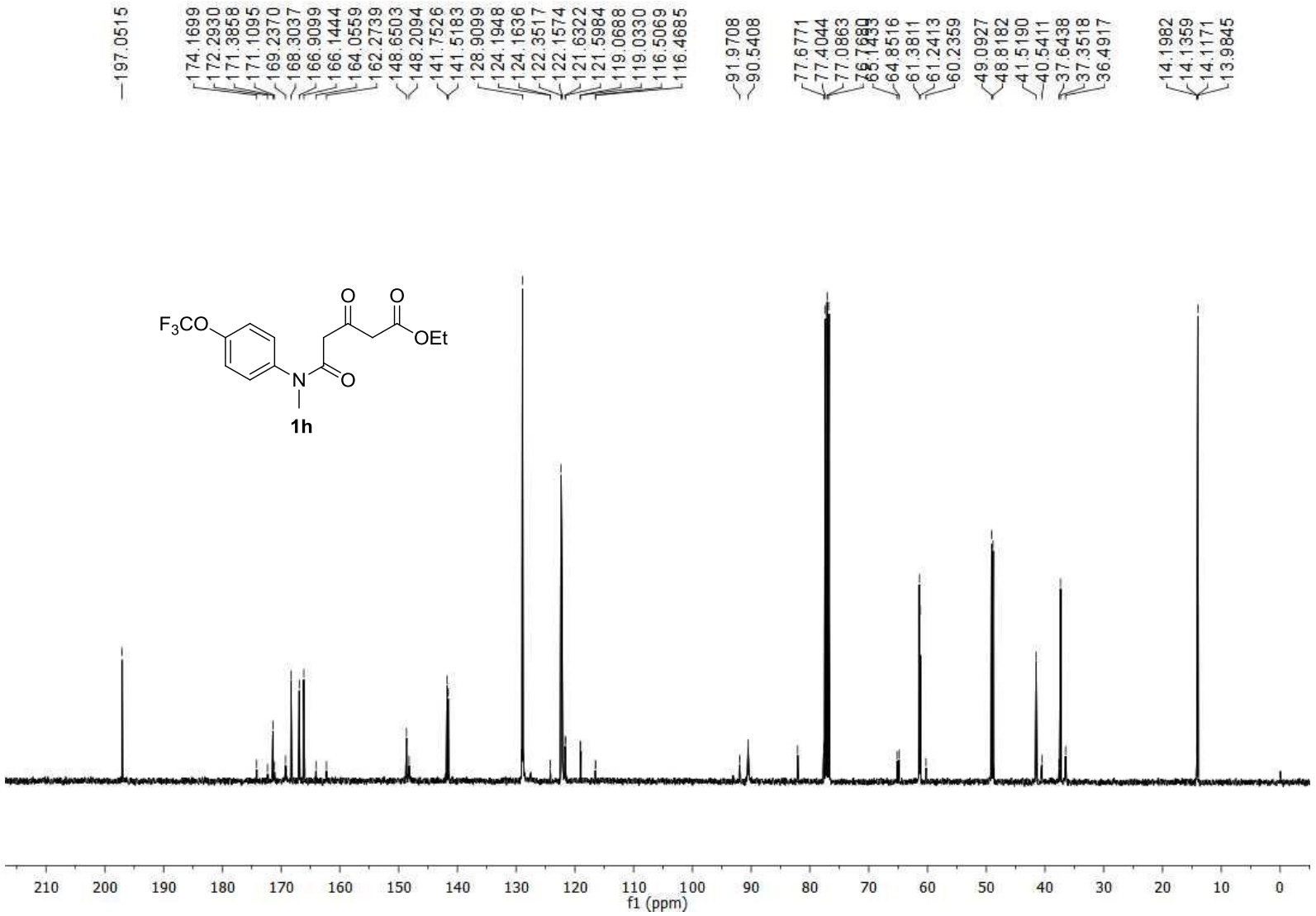
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14.1171
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F3CO
O
O
OEt
N
O
1h
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180
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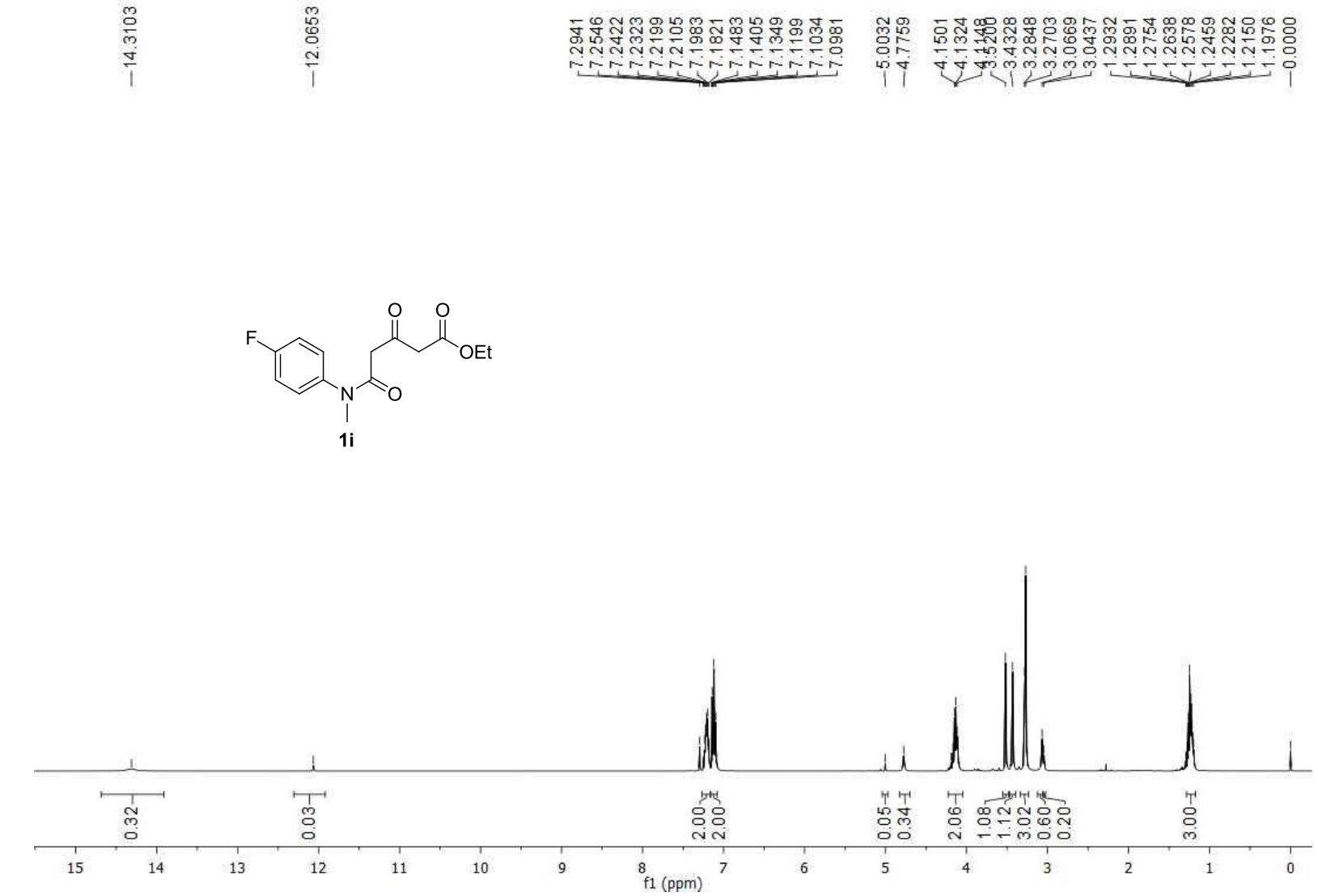
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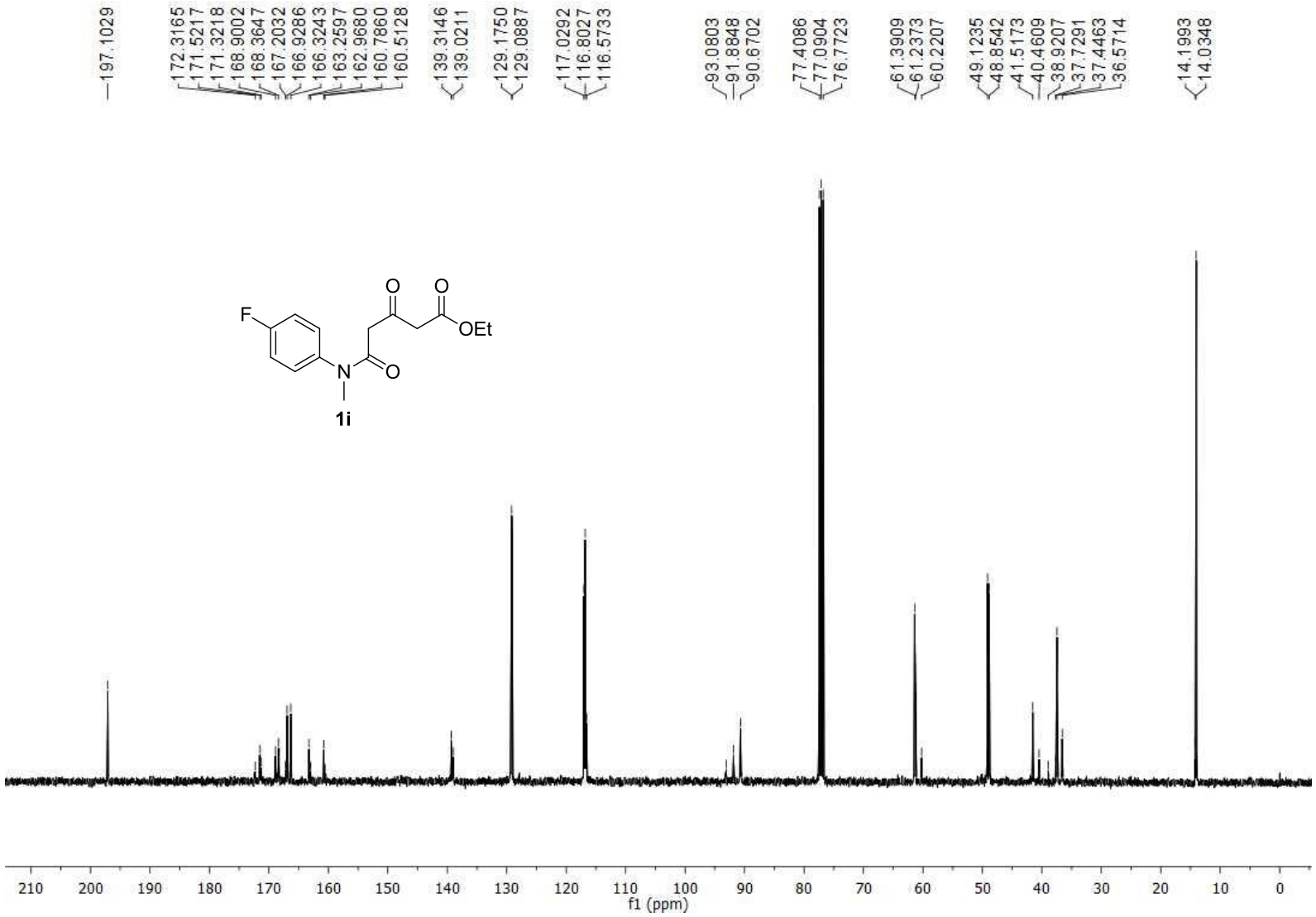
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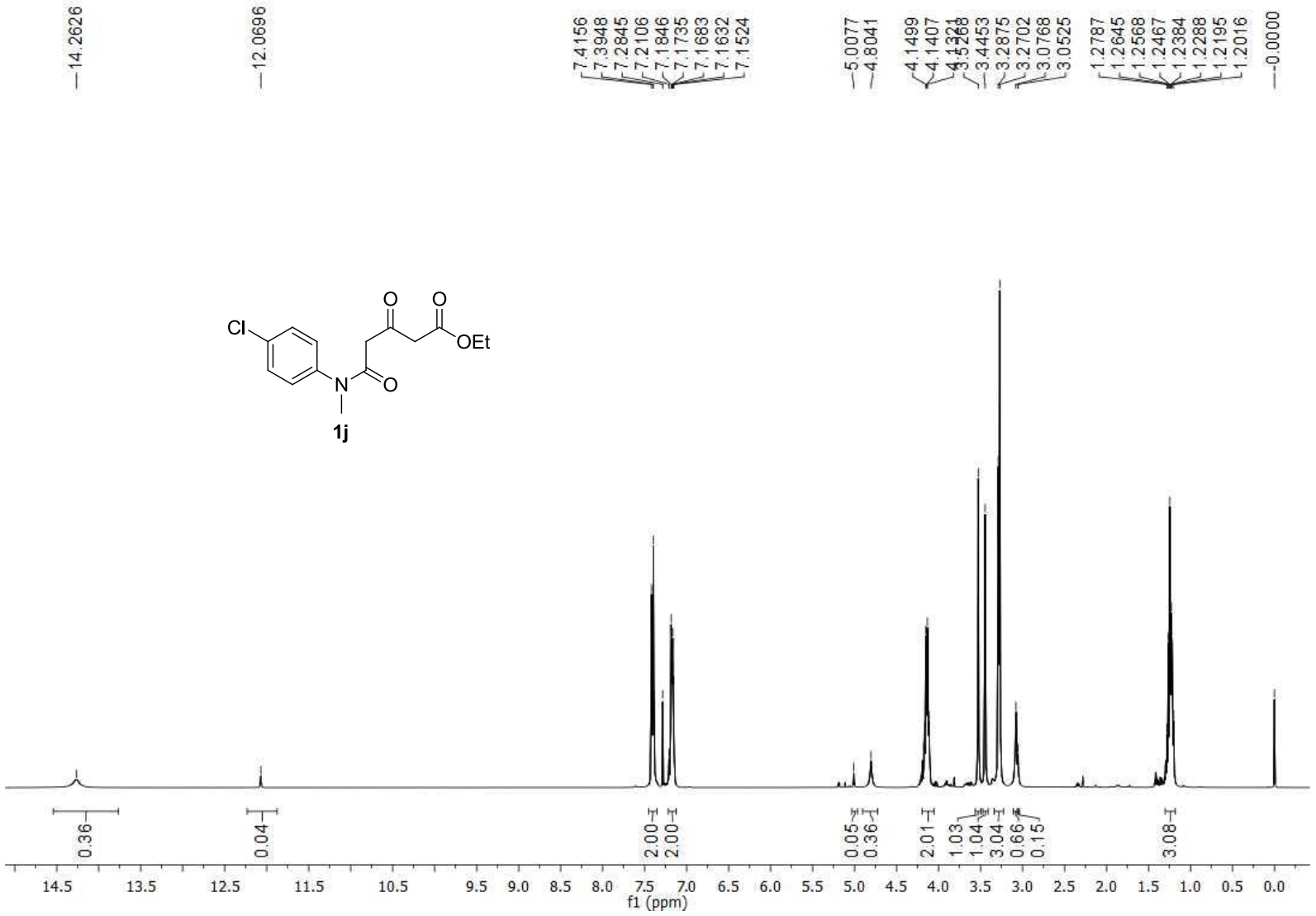
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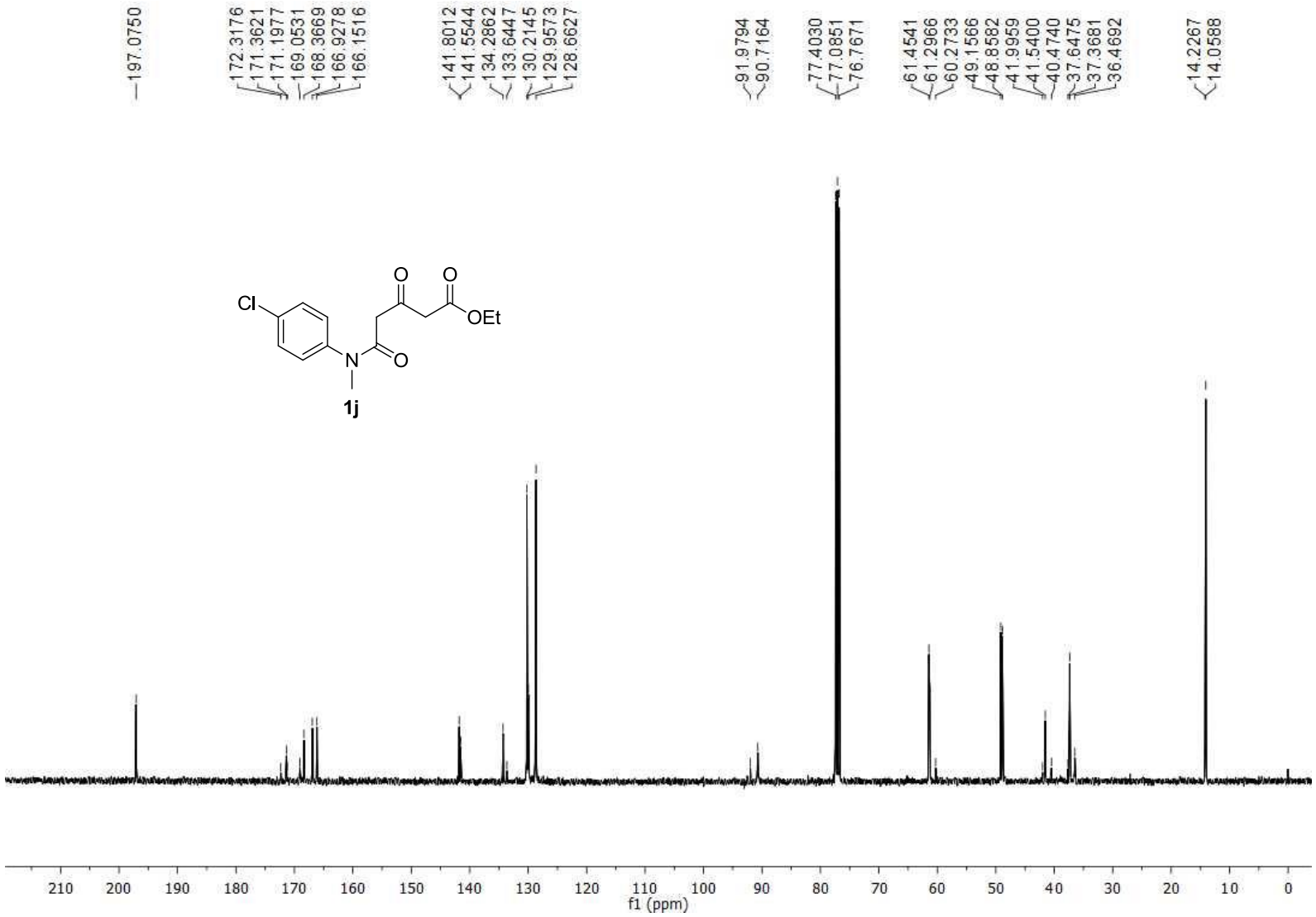
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Cl
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O
OEt
N
O
1j
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200
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180
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120
110
100
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70
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50
40
30
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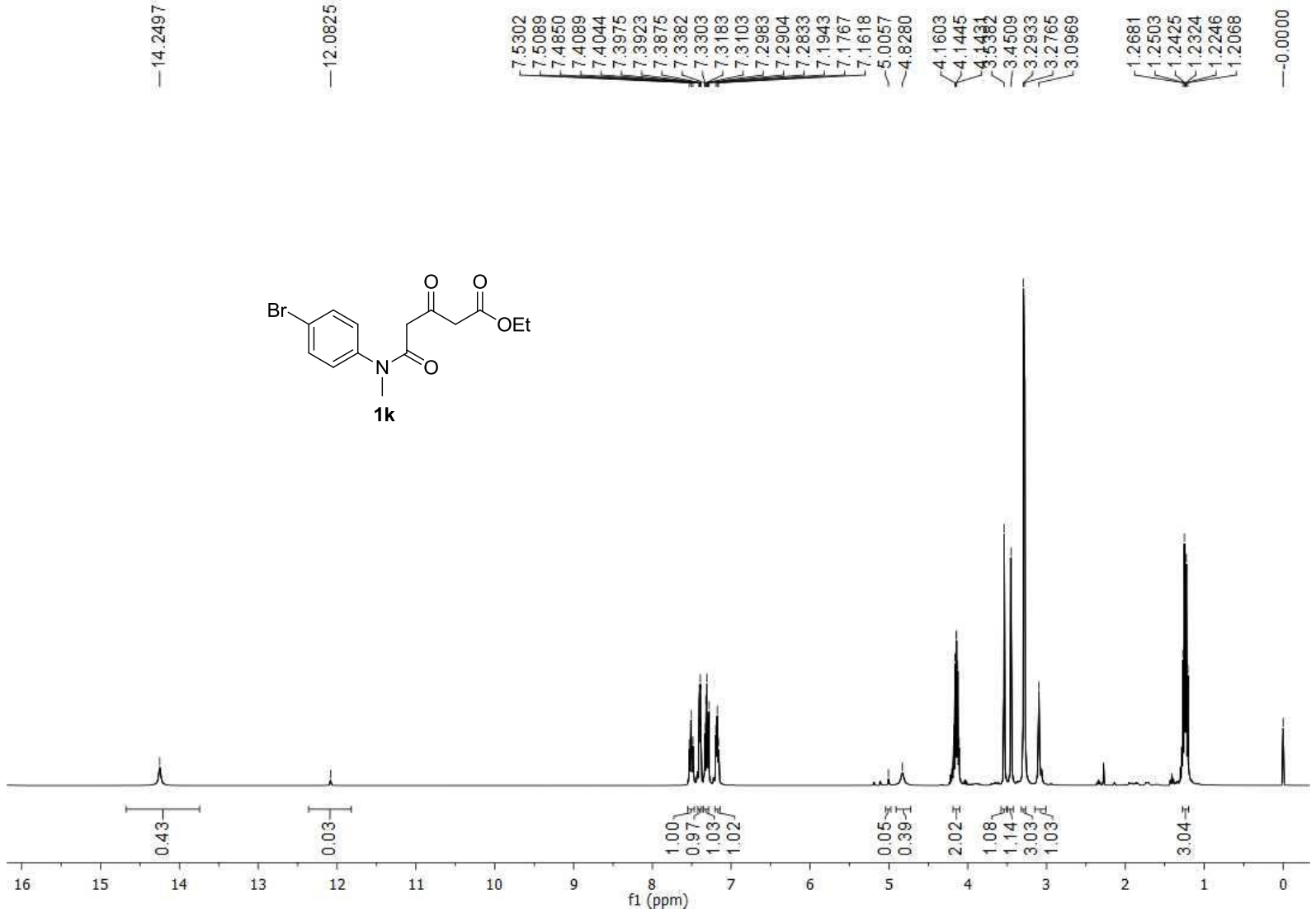
f1 (ppm)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Br
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O
OEt
N
O
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1.00
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1.02
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0.39
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1.08
1.14
3.03
1.03
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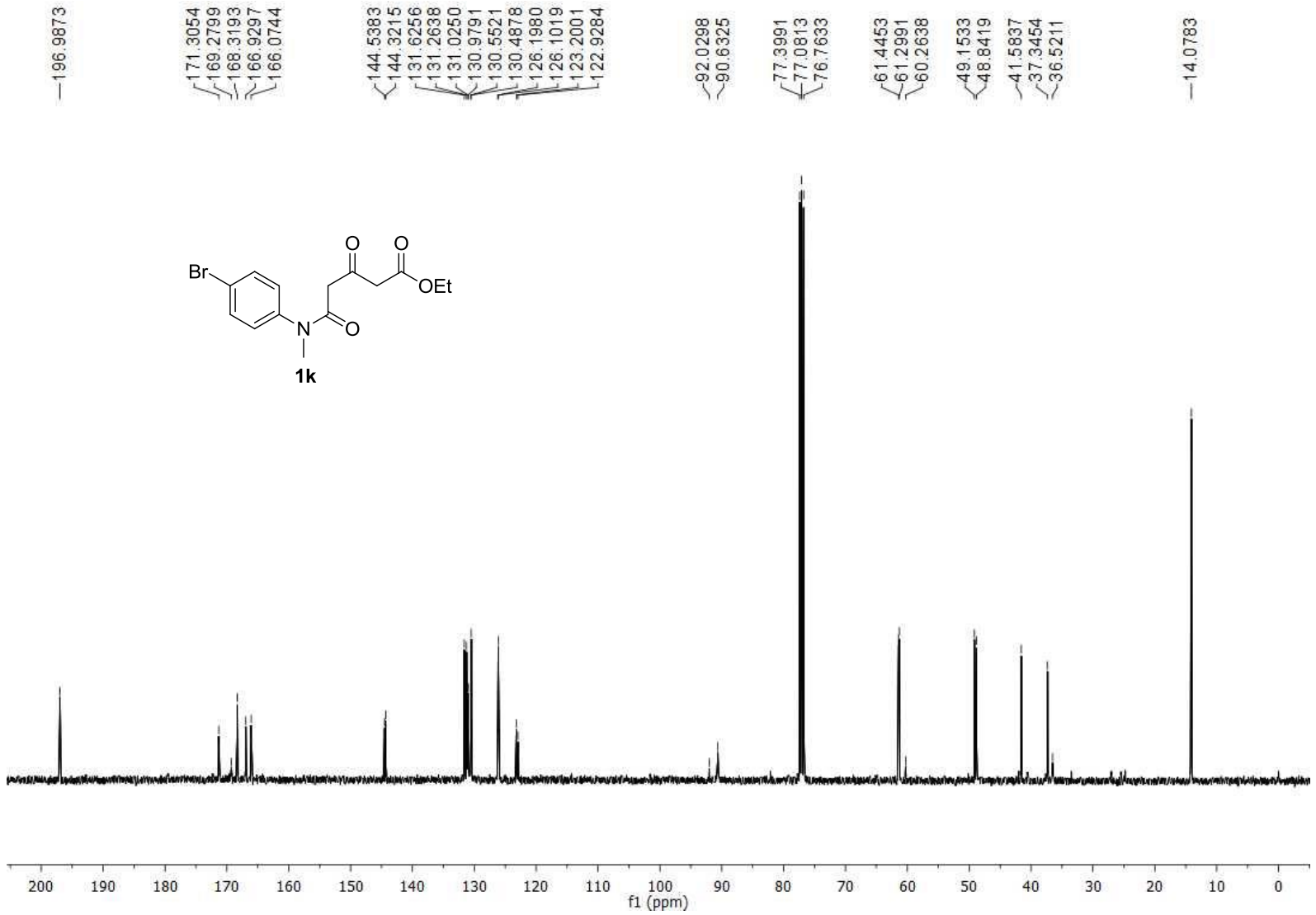
f1 (ppm)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Br
O
O
OEt
N
O
1k
200
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180
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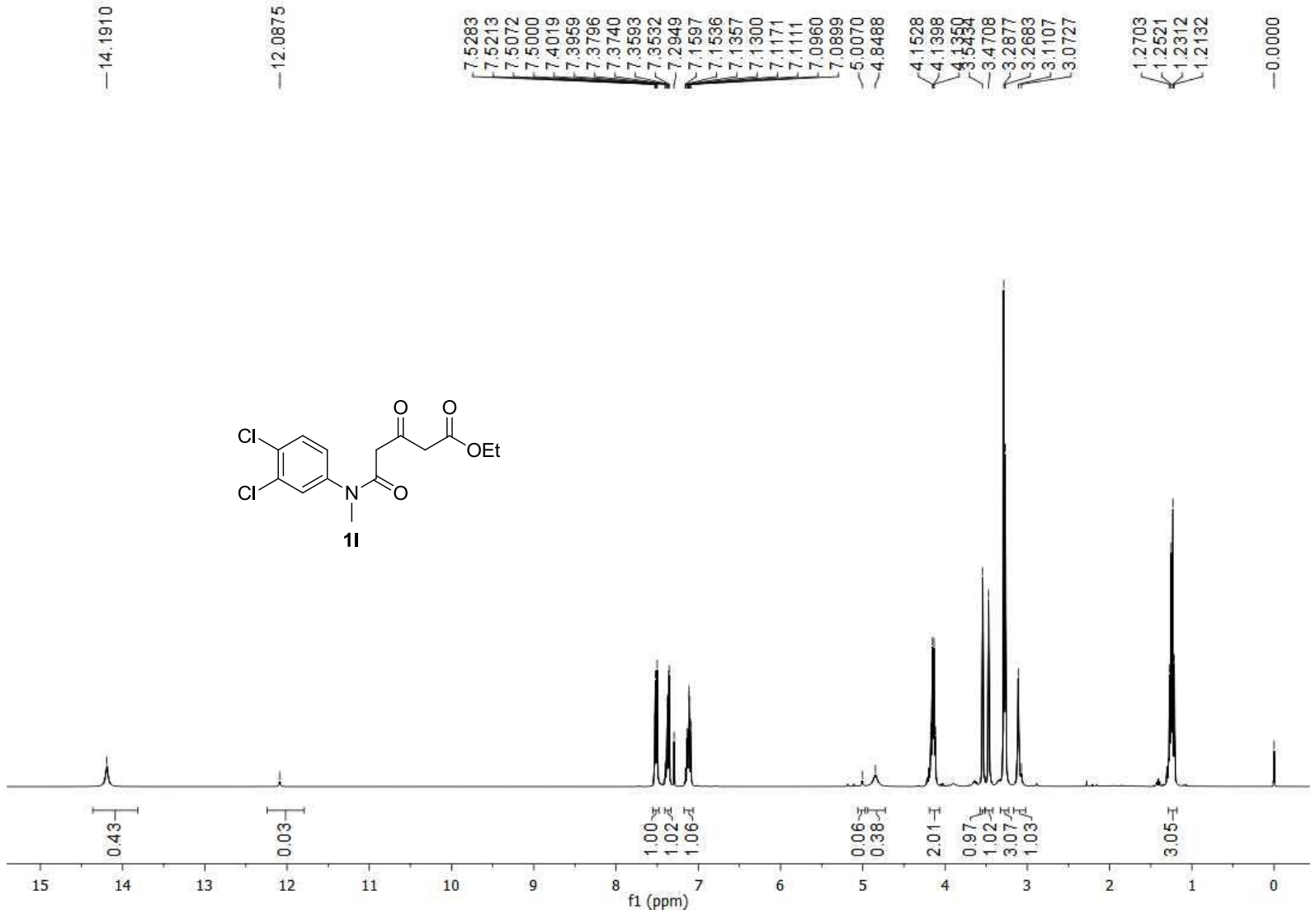
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Cl
Cl
O
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OEt
N
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0.03
1.00
1.02
1.06
0.06
0.38
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3.07
1.03
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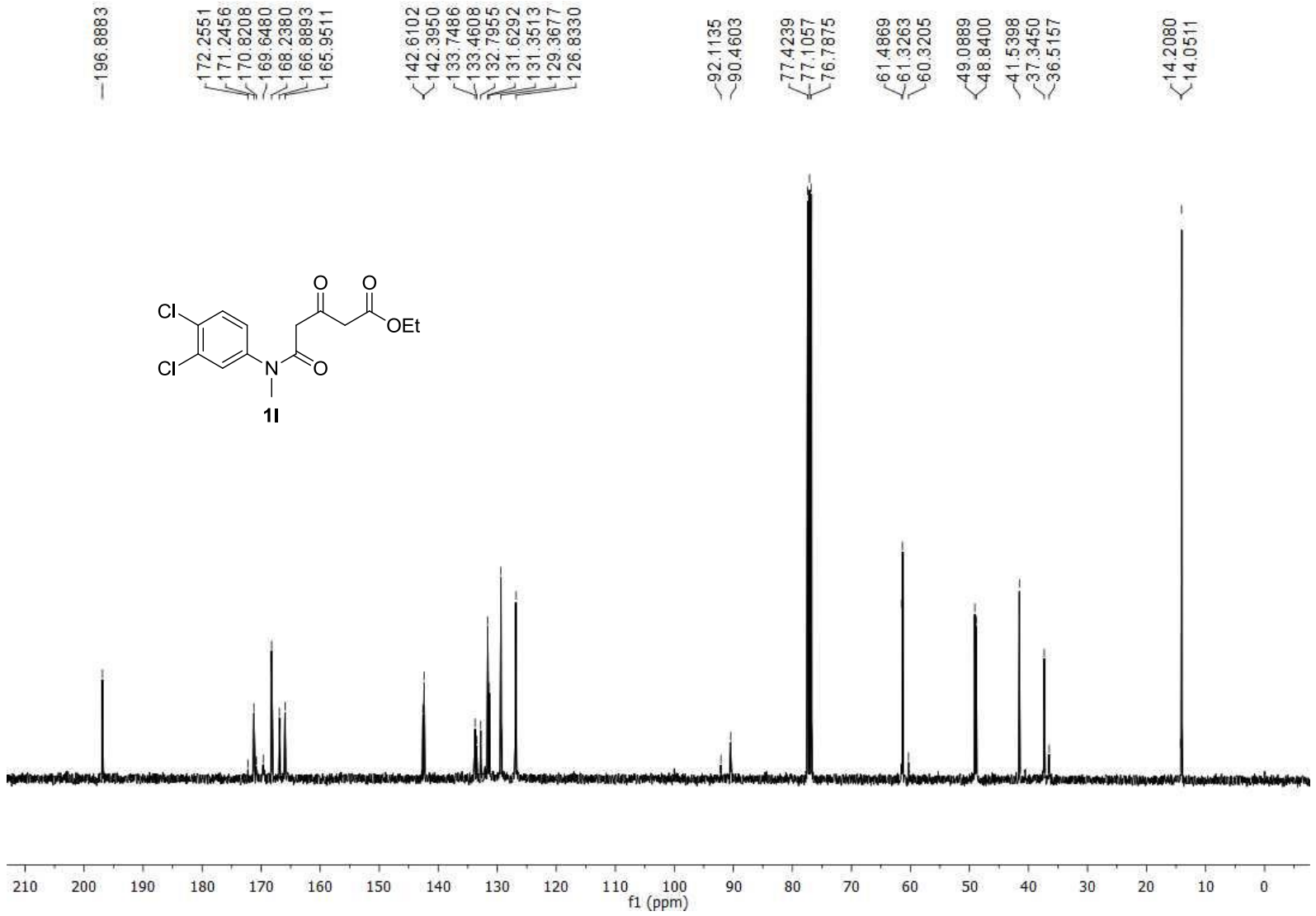
f1 (ppm)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Cl
Cl
O
O
OEt
N
O
1l
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200
190
180
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50
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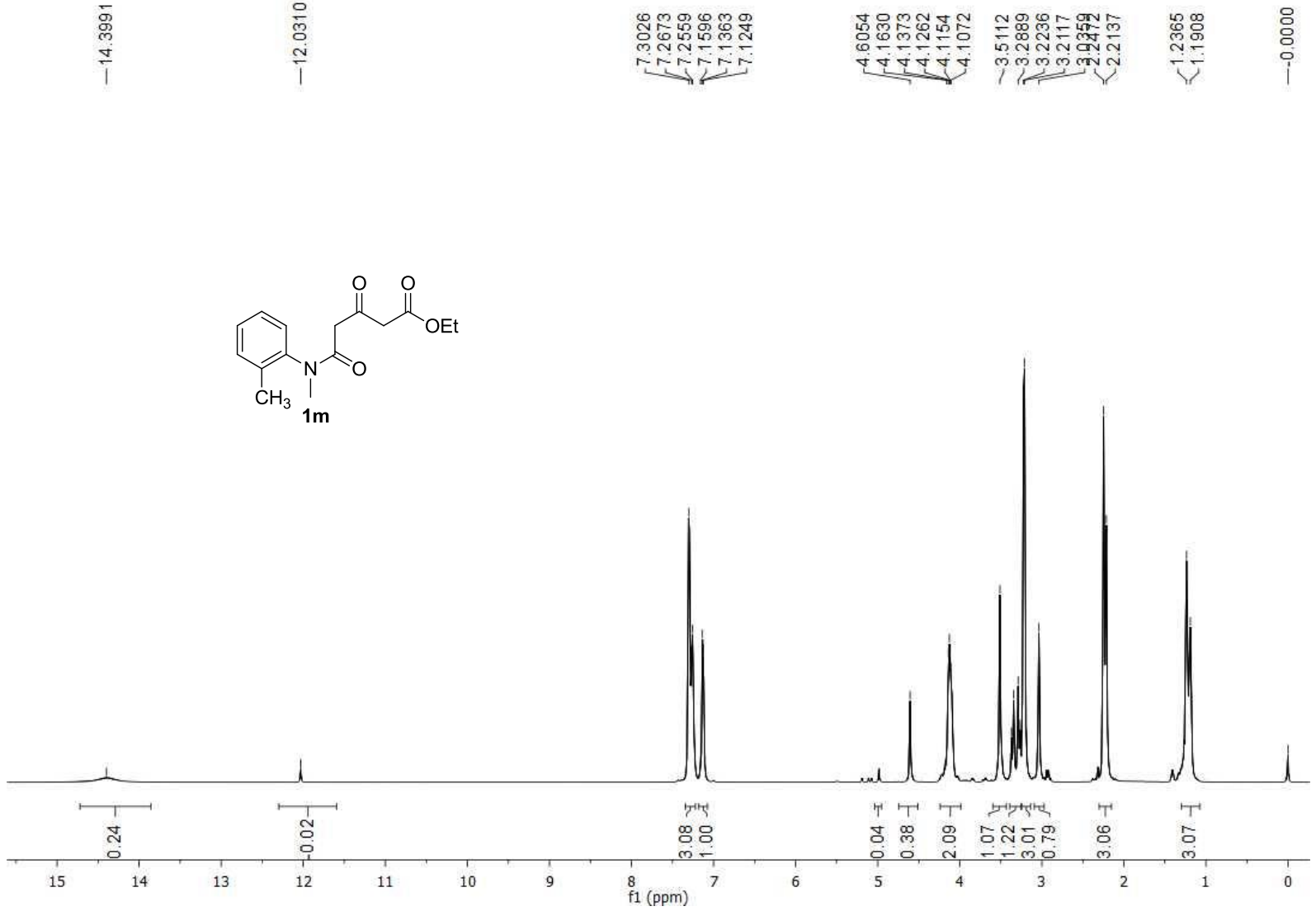
f1 (ppm)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CH3
1m
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1.22
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0.79
3.06
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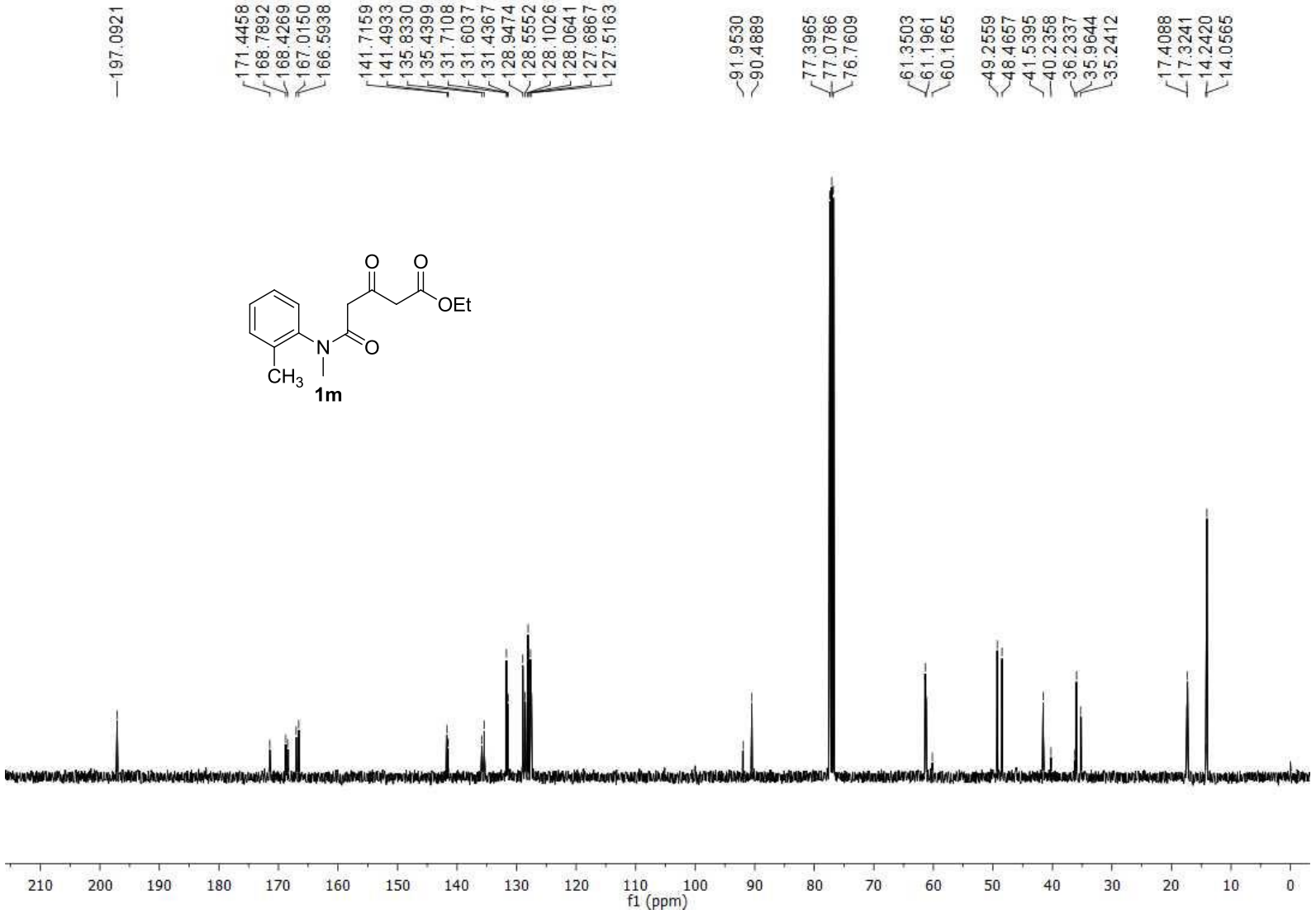
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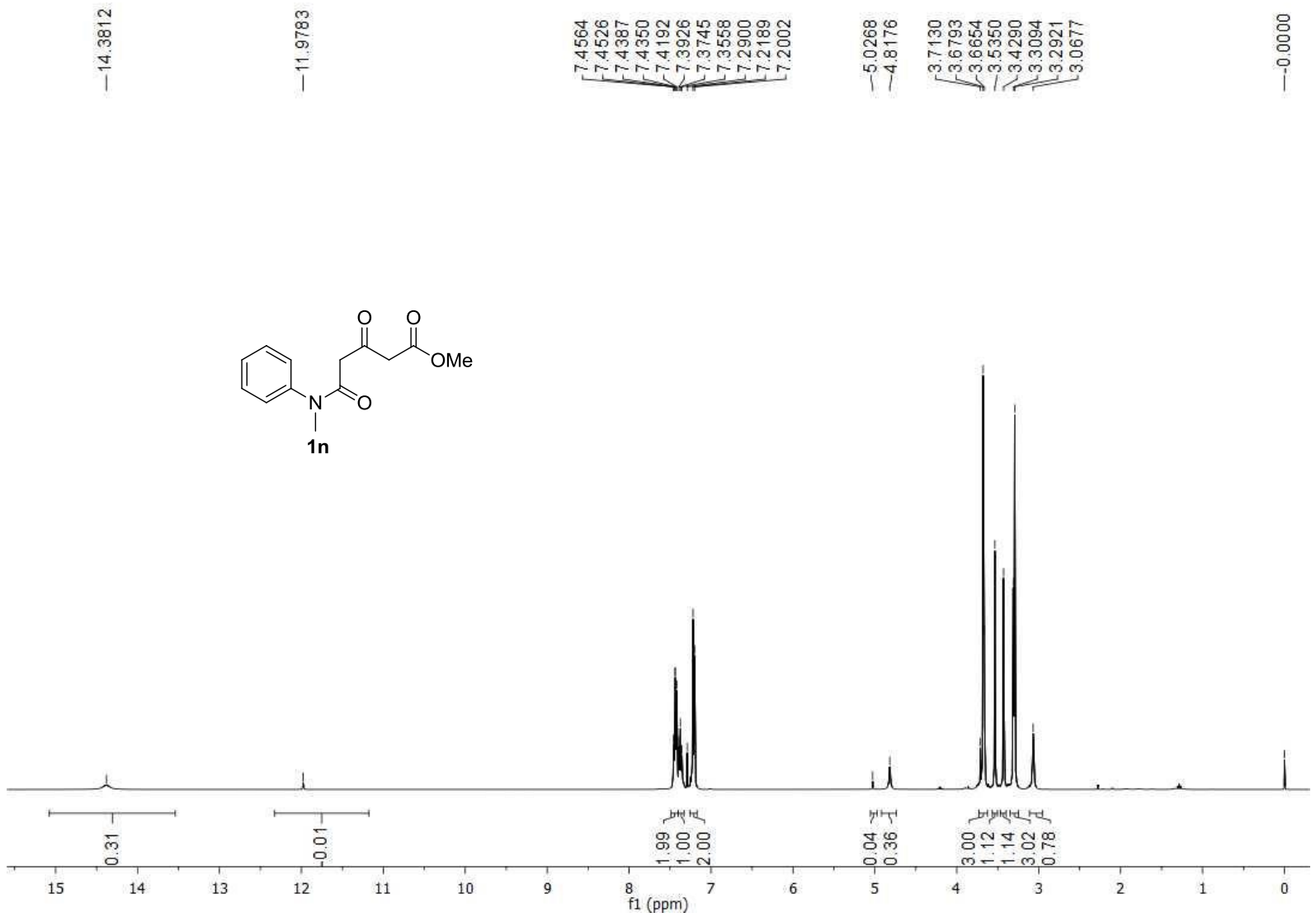
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O
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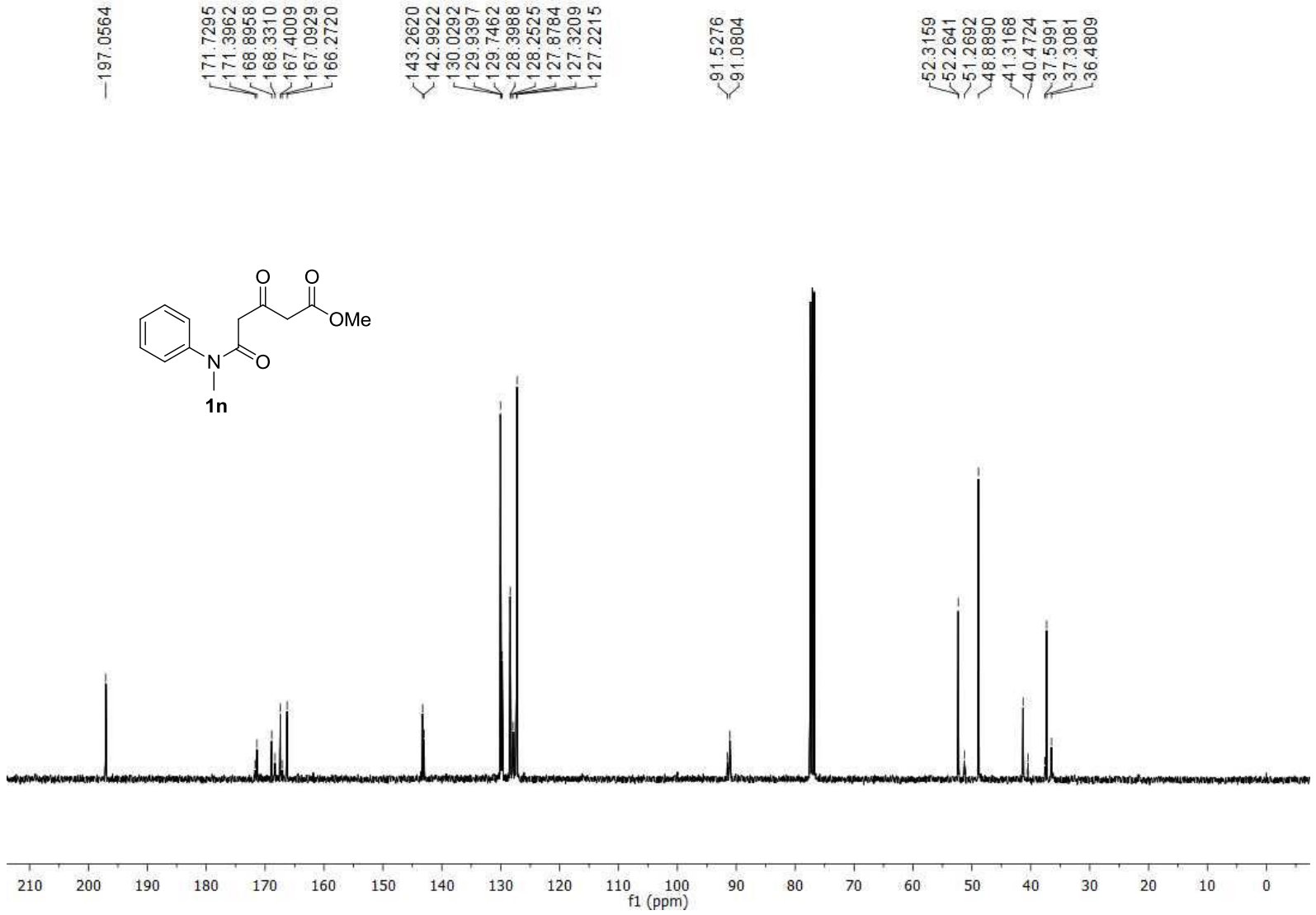
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O
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N
O
1n
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200
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180
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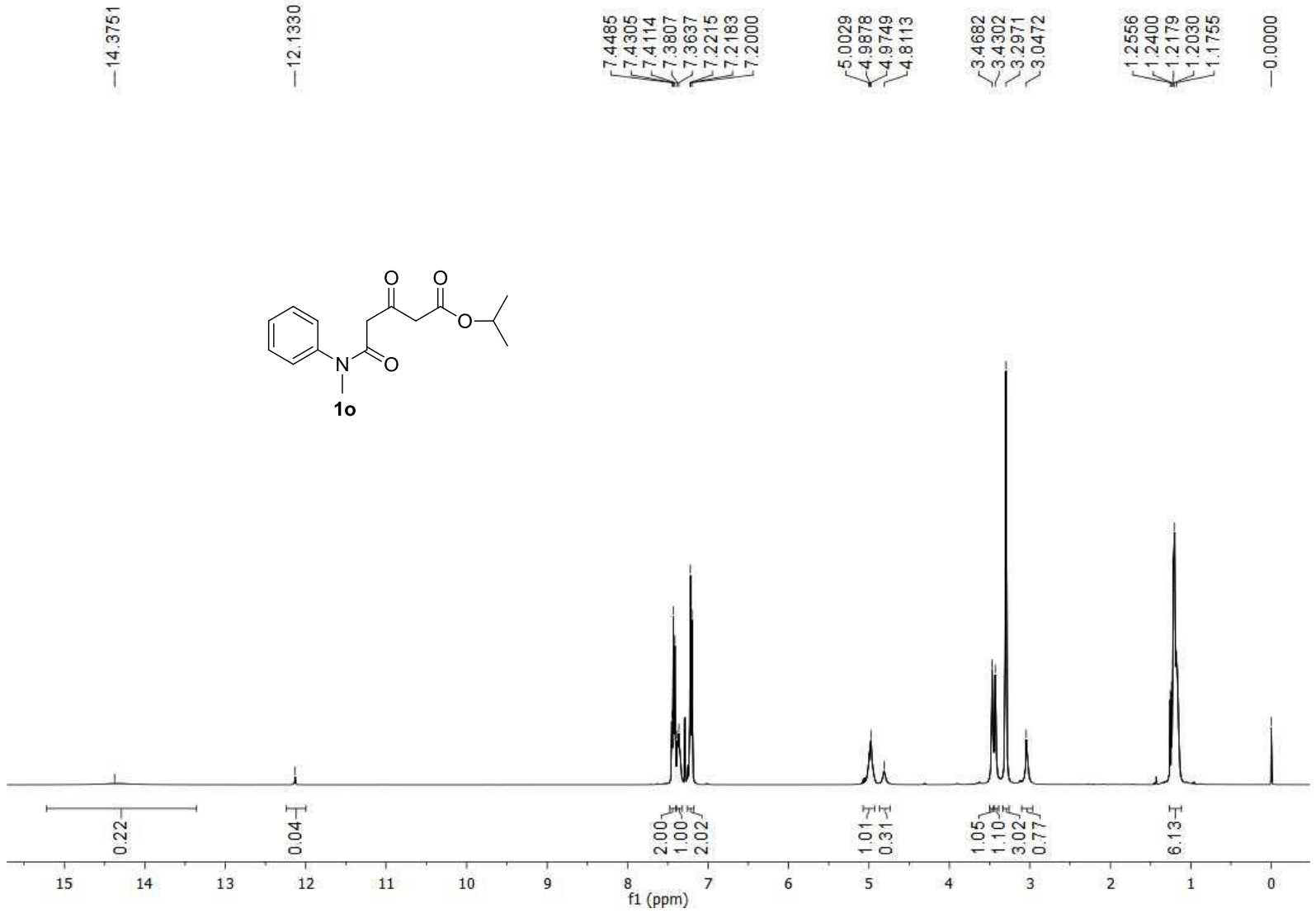
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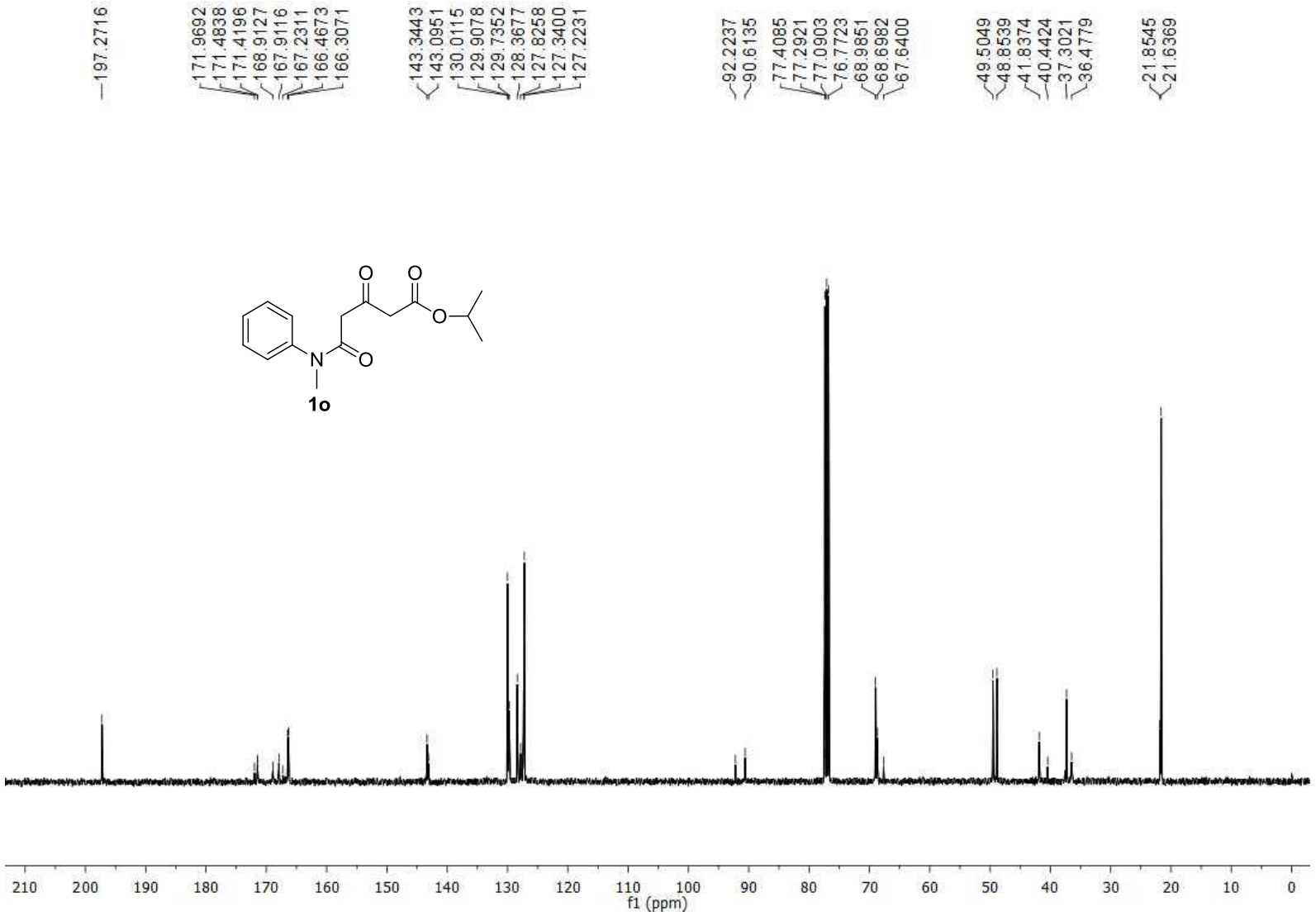
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O
O
N
O
1o
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200
190
180
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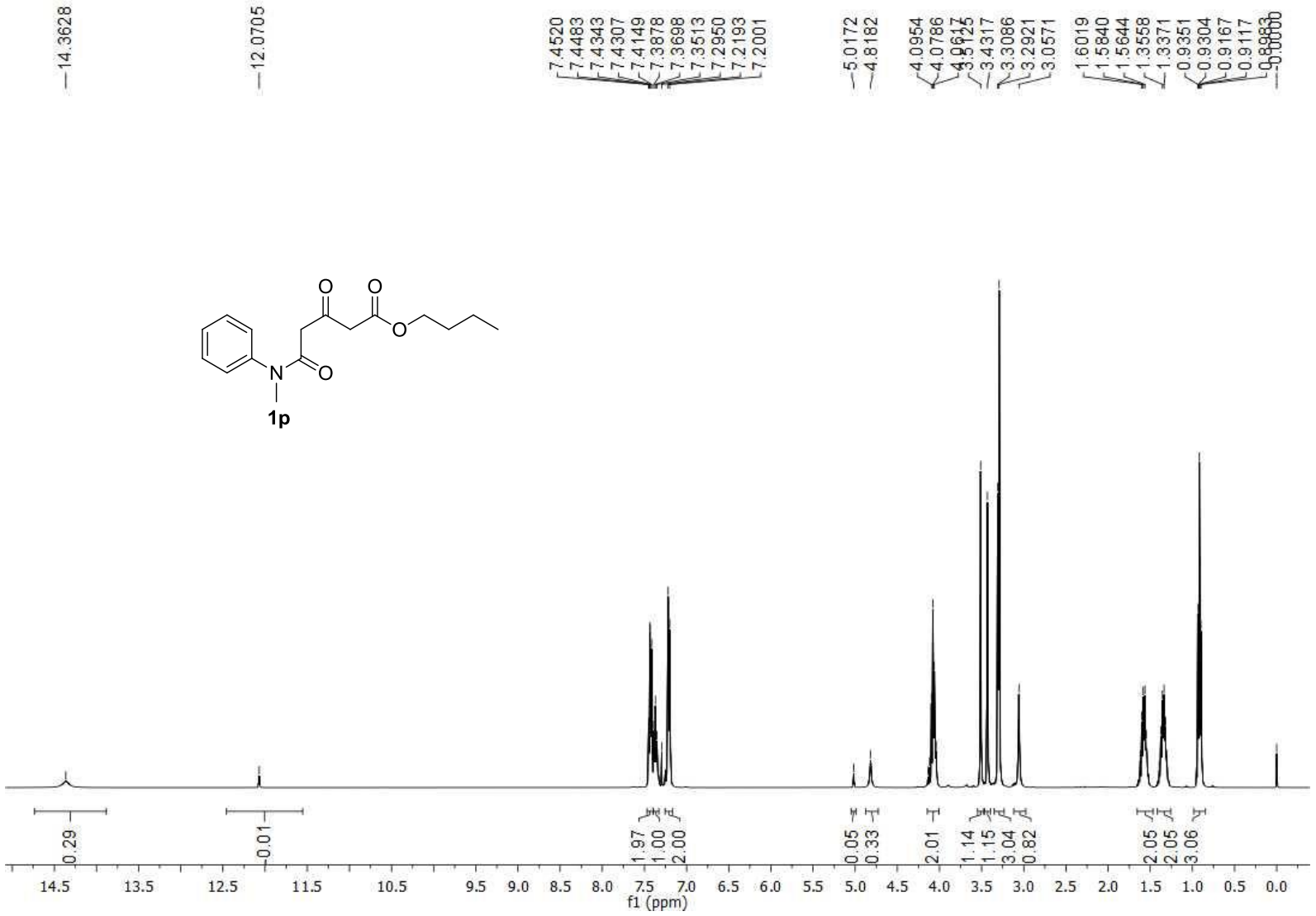
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O
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N
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1.97
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2.00
0.05
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2.01
1.14
1.15
3.04
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2.05
2.05
3.06
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12.5
11.5
10.5
9.5
9.0
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8.0
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6.5
6.0
5.5
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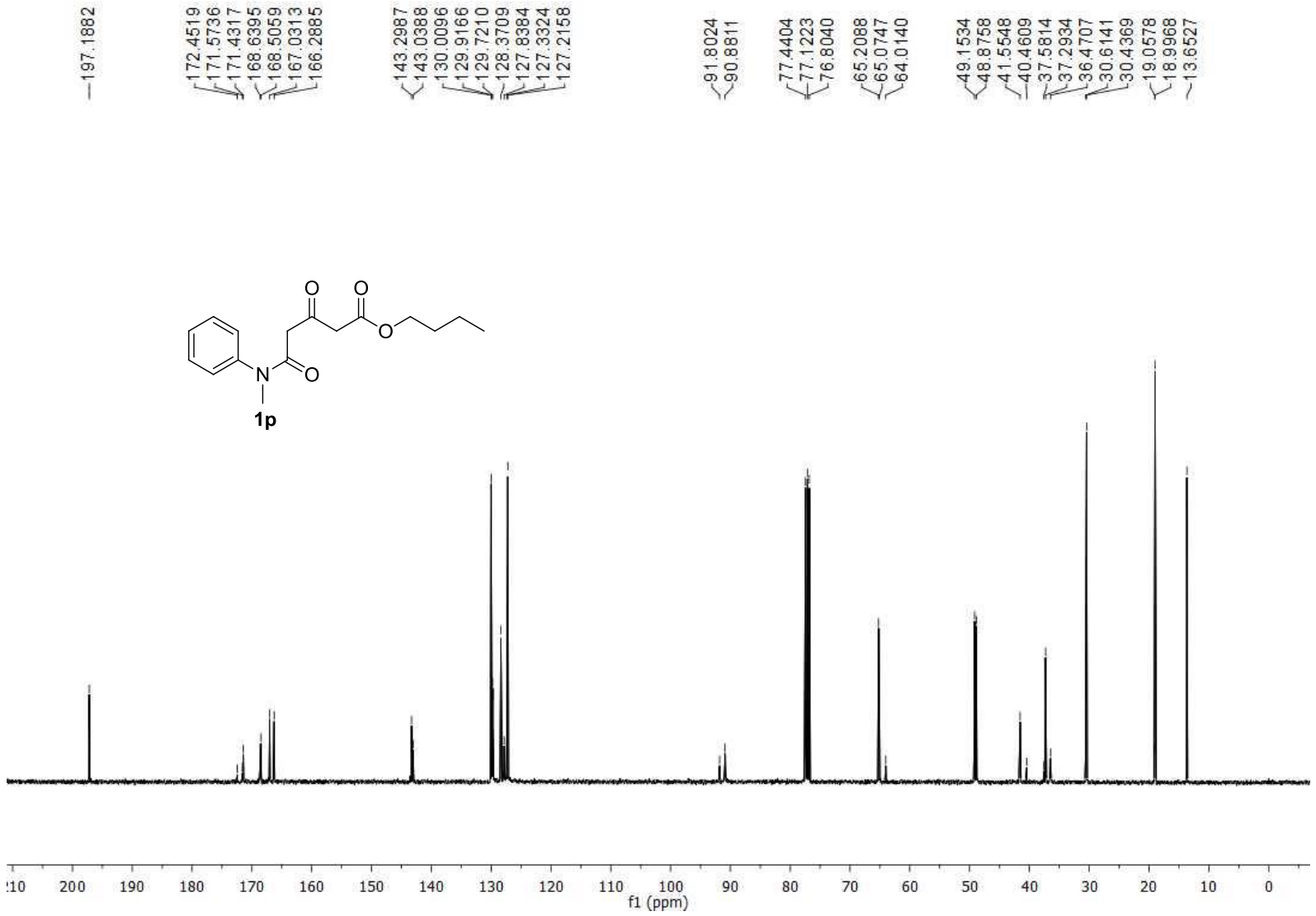
0.0
f1 (ppm)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O
O
N
O
1p
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180
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110
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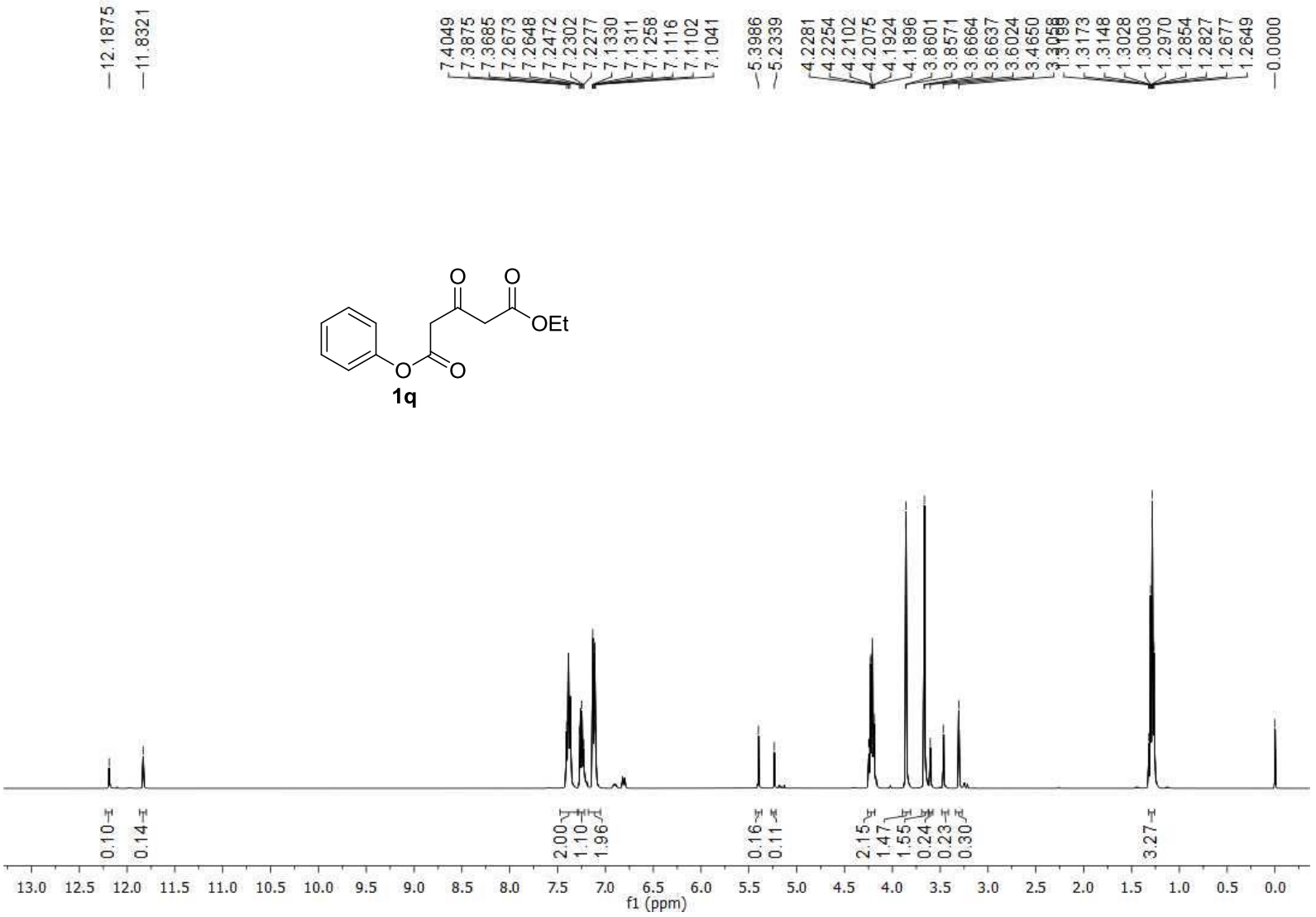
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7.1258
7.1116
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7.1041
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4.2102
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3.8571
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3.6637
3.6024
3.4650
1.3173
1.3148
1.3028
1.3003
1.2970
1.2854
1.2827
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1.2649
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O
OEt
O
O
1q
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0.14
2.00
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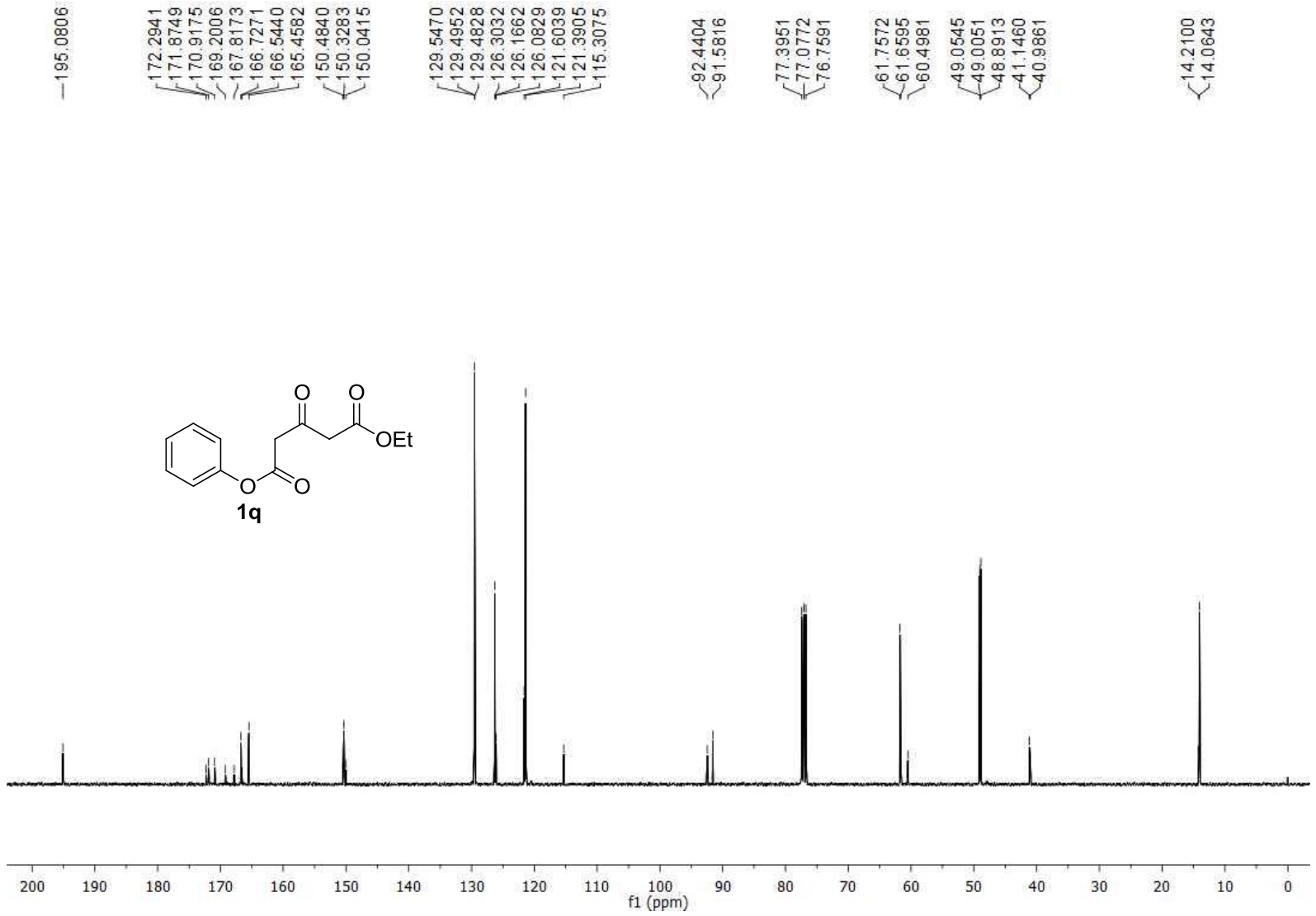
f1 (ppm)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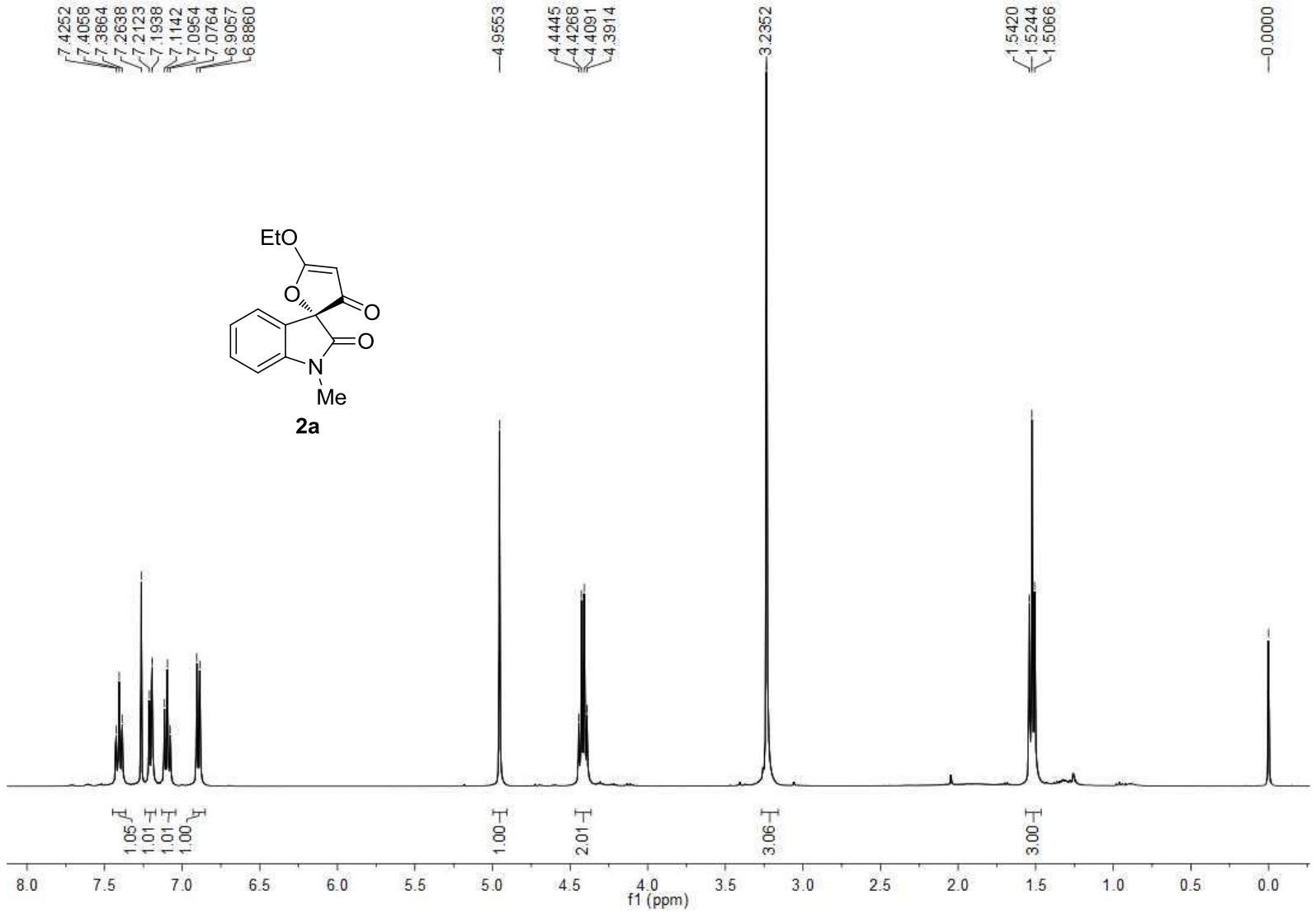
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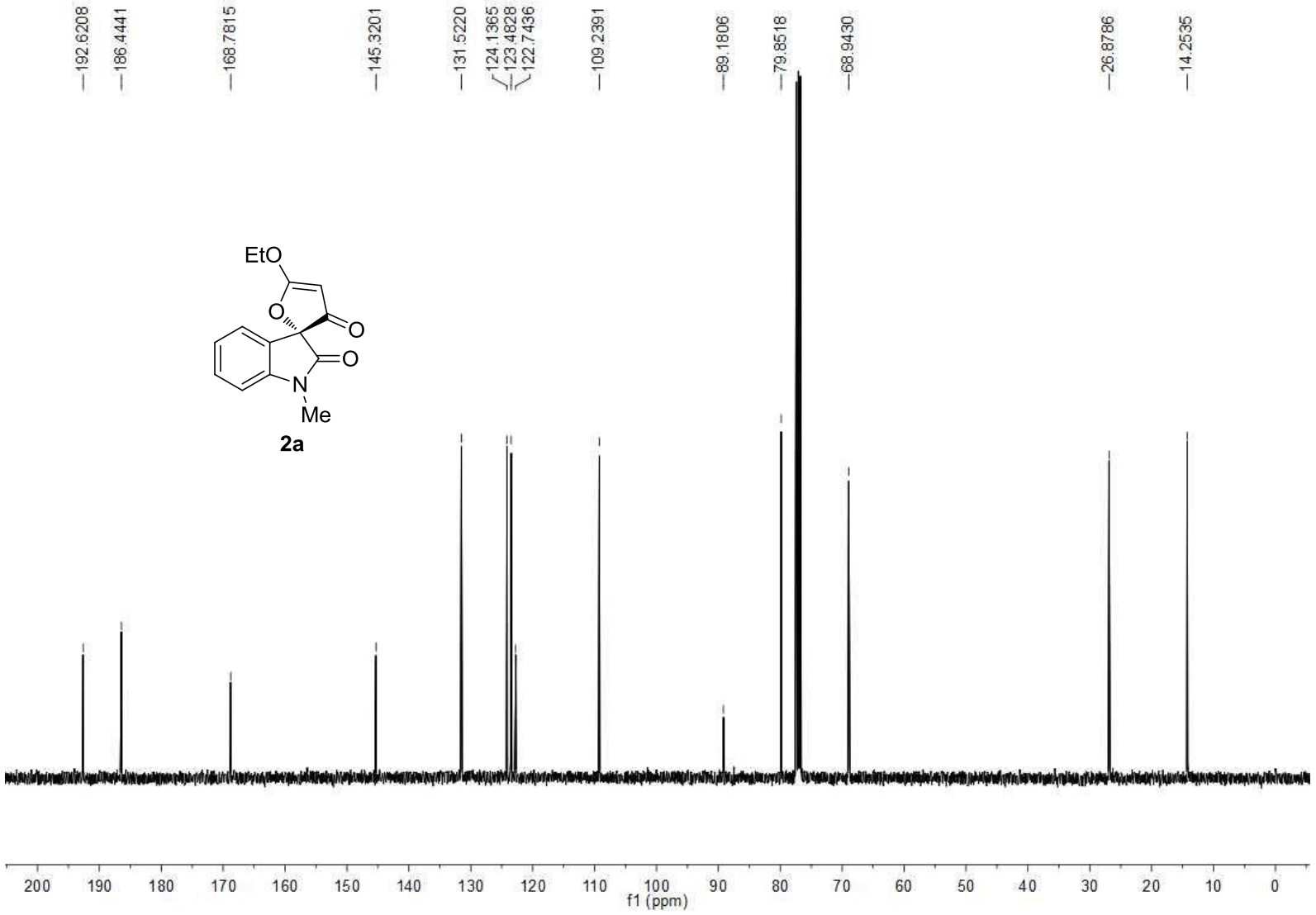
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EtO
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O
O
N
Me
2a
200
190
180
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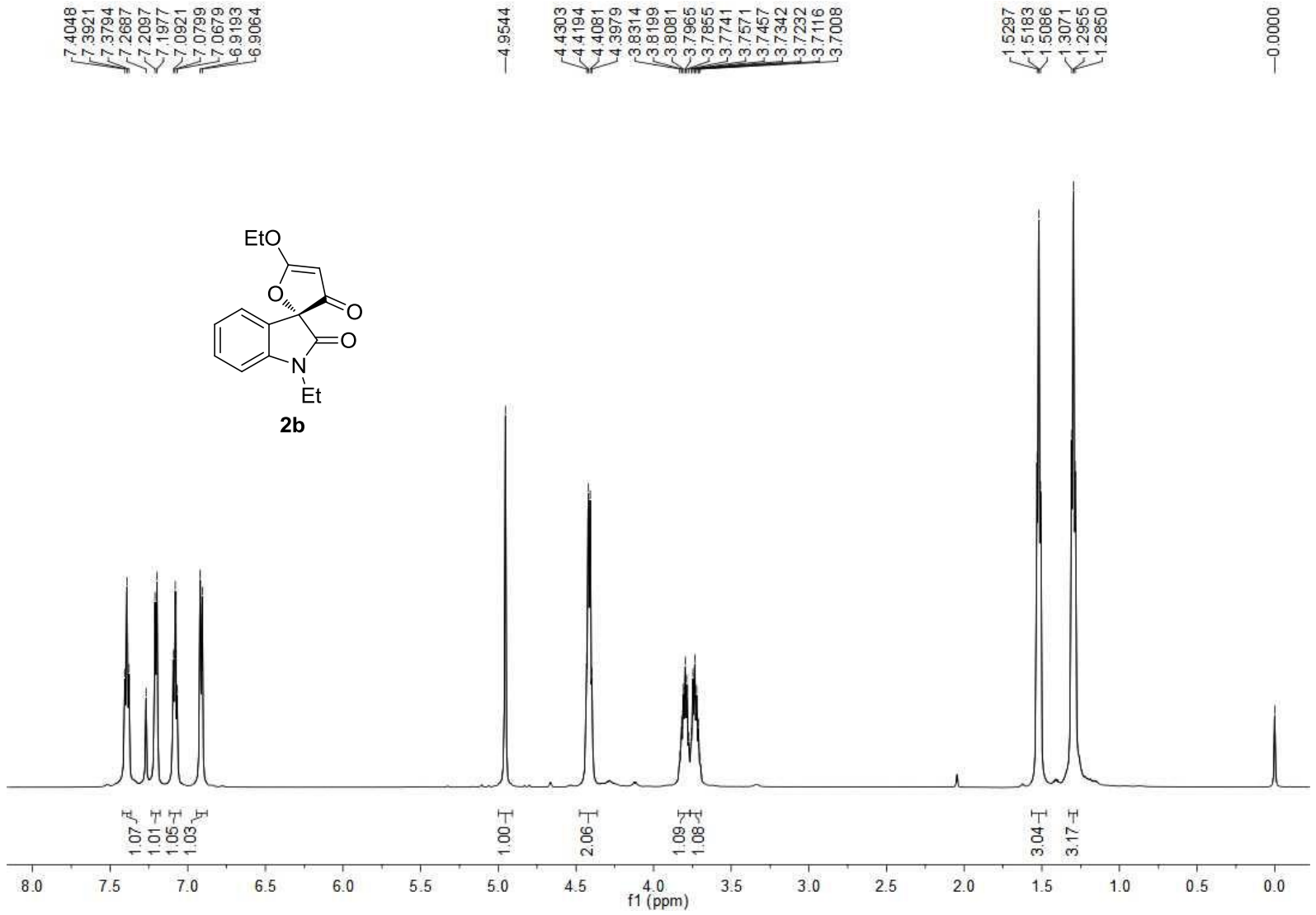
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O
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Et
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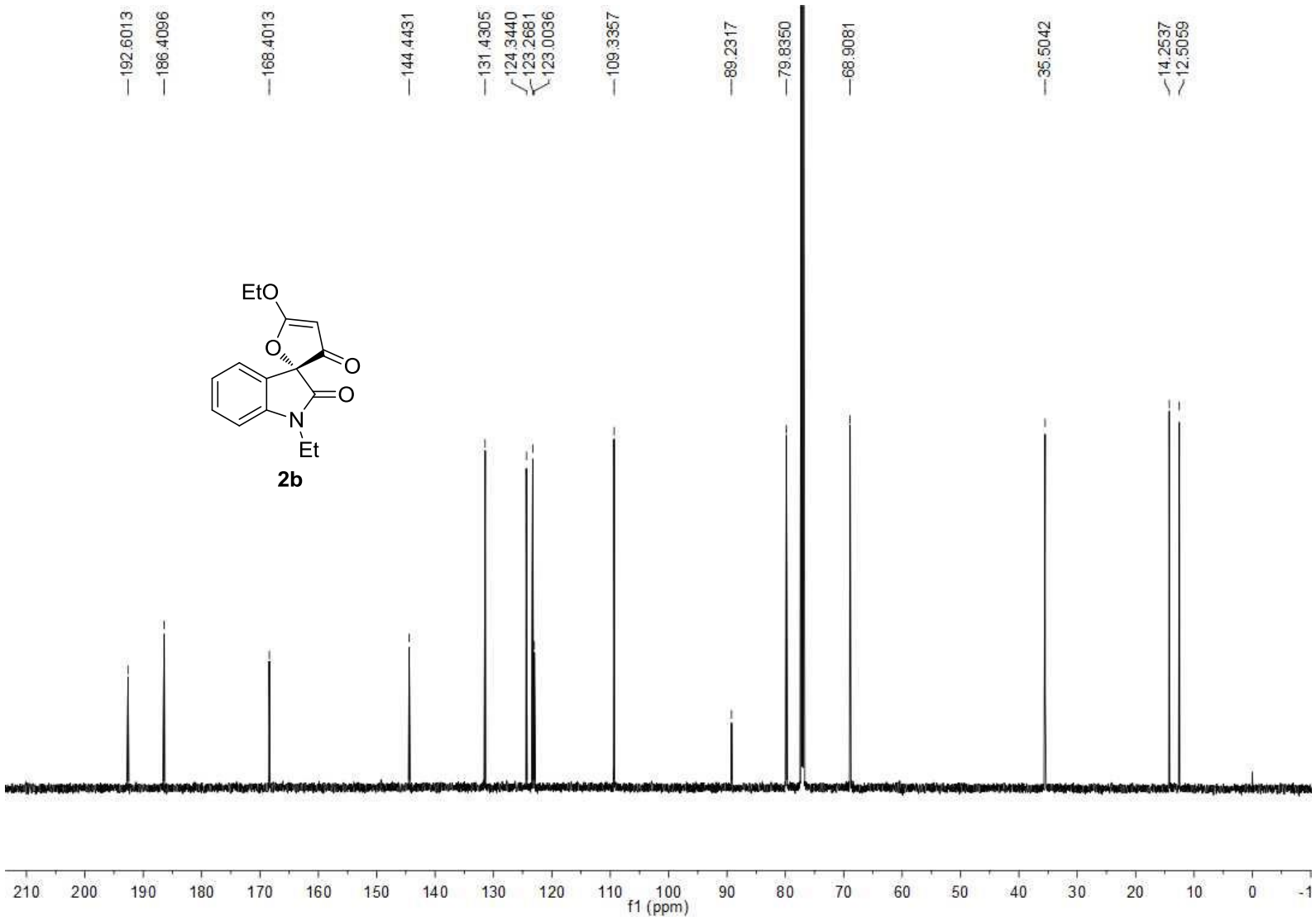
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O
O
O
N
Et
2b
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200
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180
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100
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80
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30
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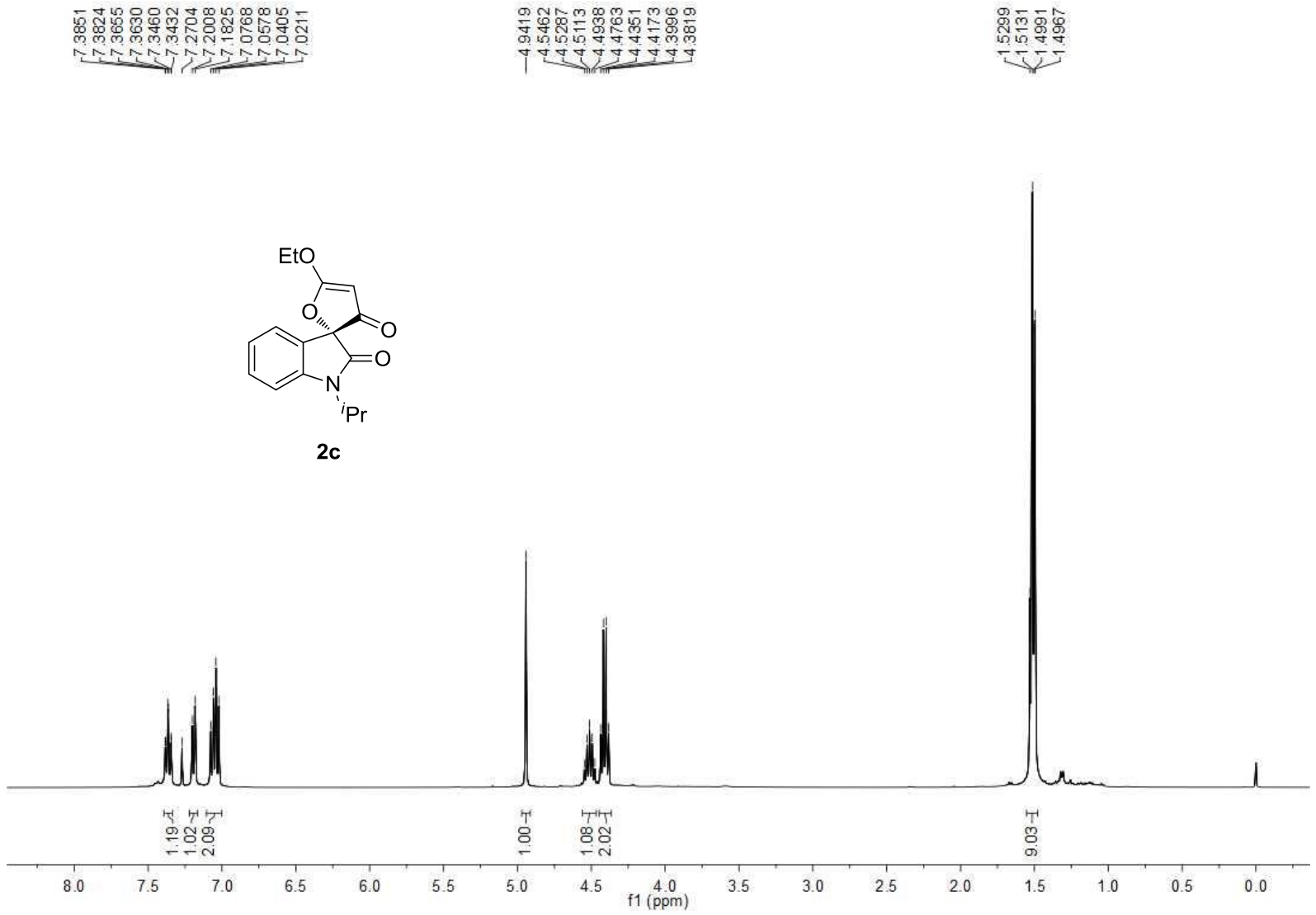
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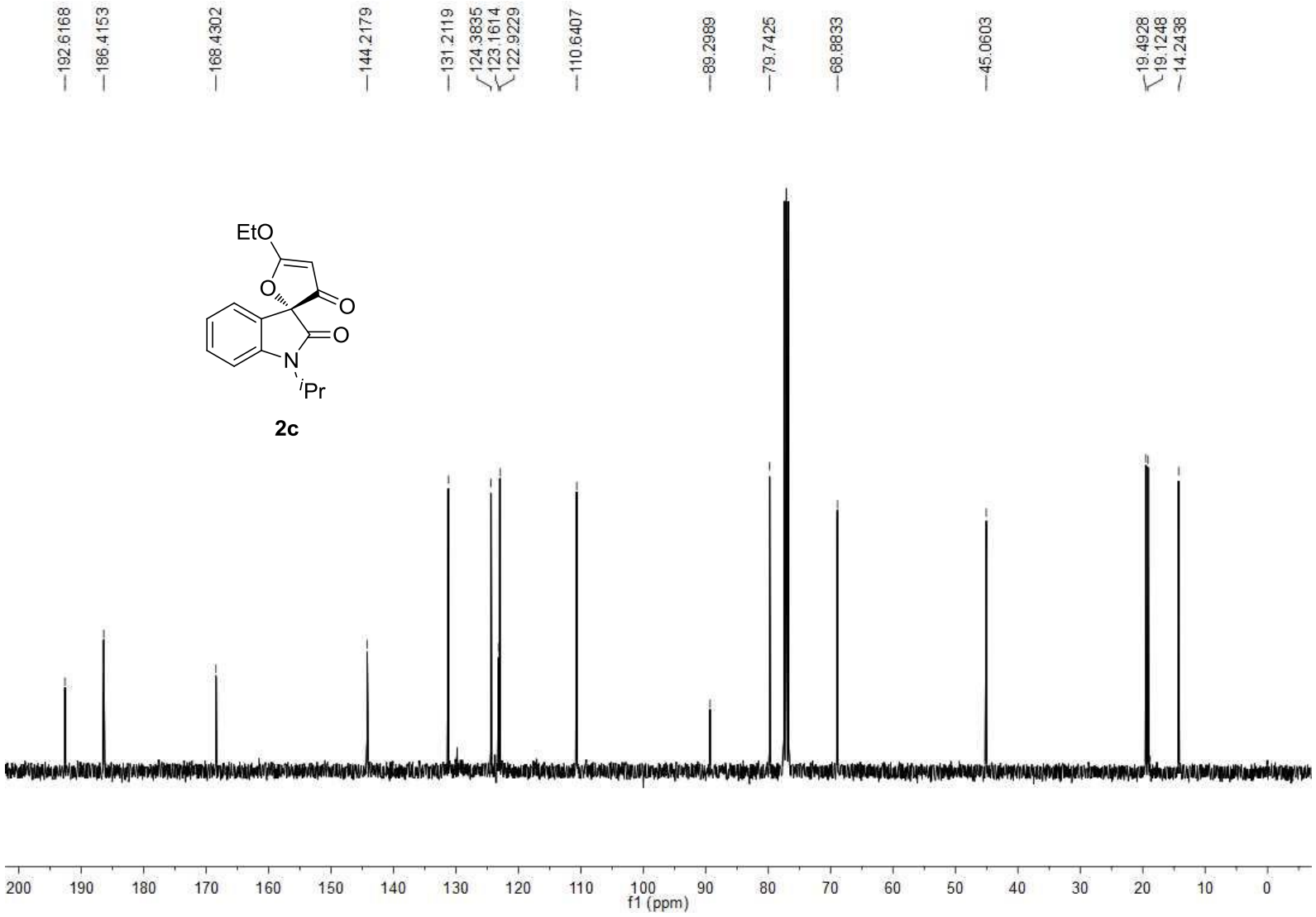
2c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O
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N
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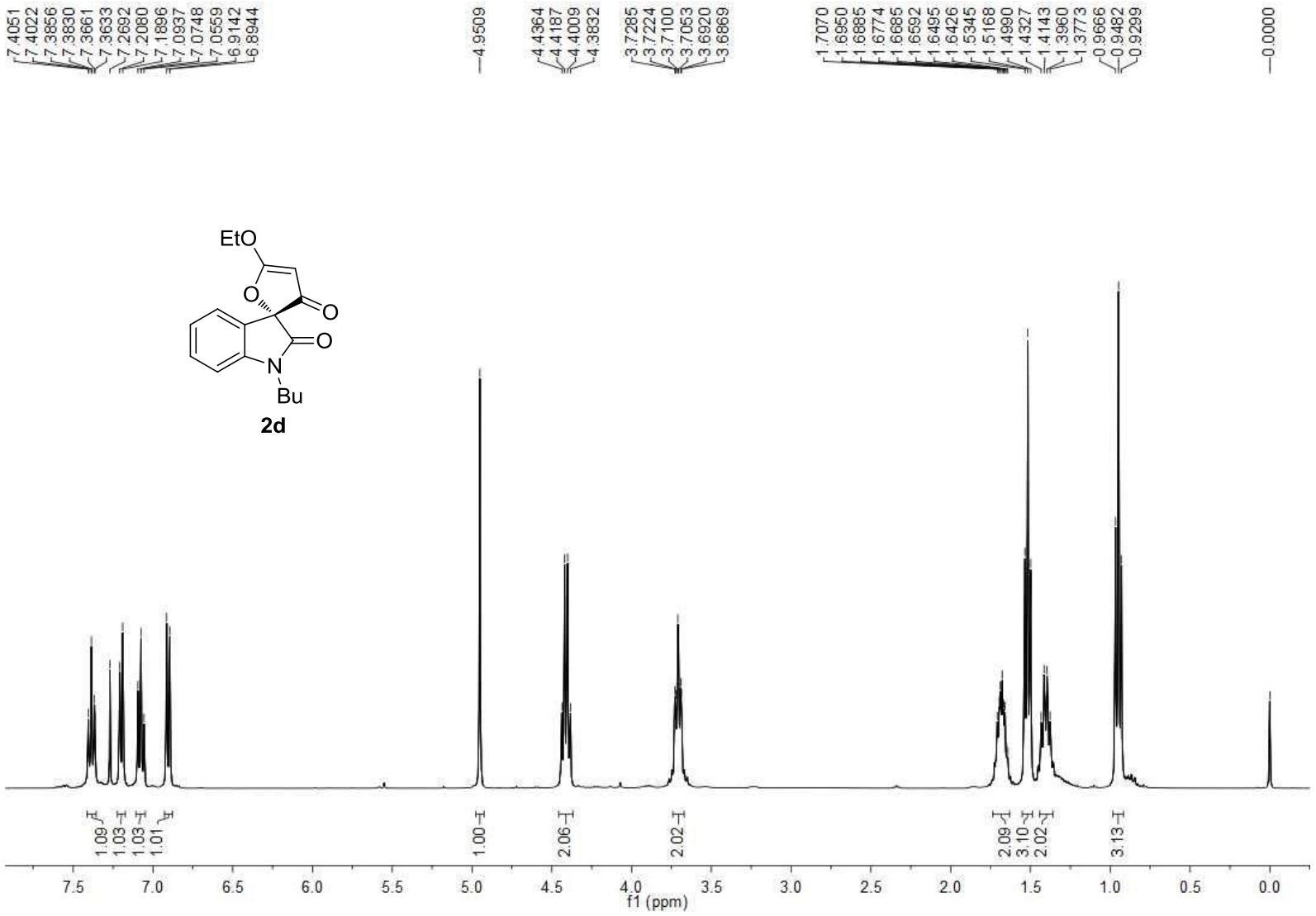
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Bu
2d
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1.00
2.06
2.02
2.09
3.10
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6.5
6.0
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0.0
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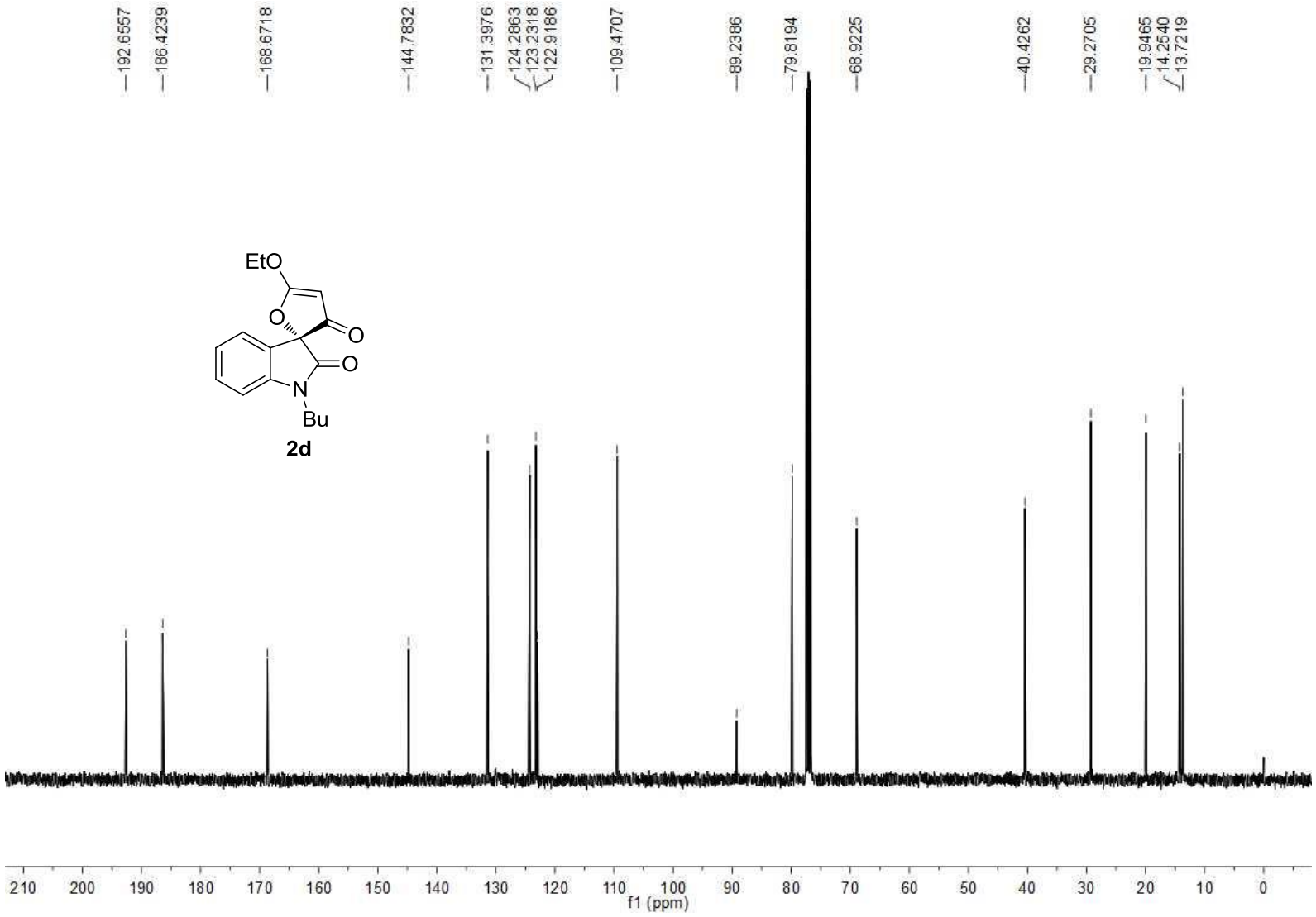
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EtO
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O
O
N
Bu
2d
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180
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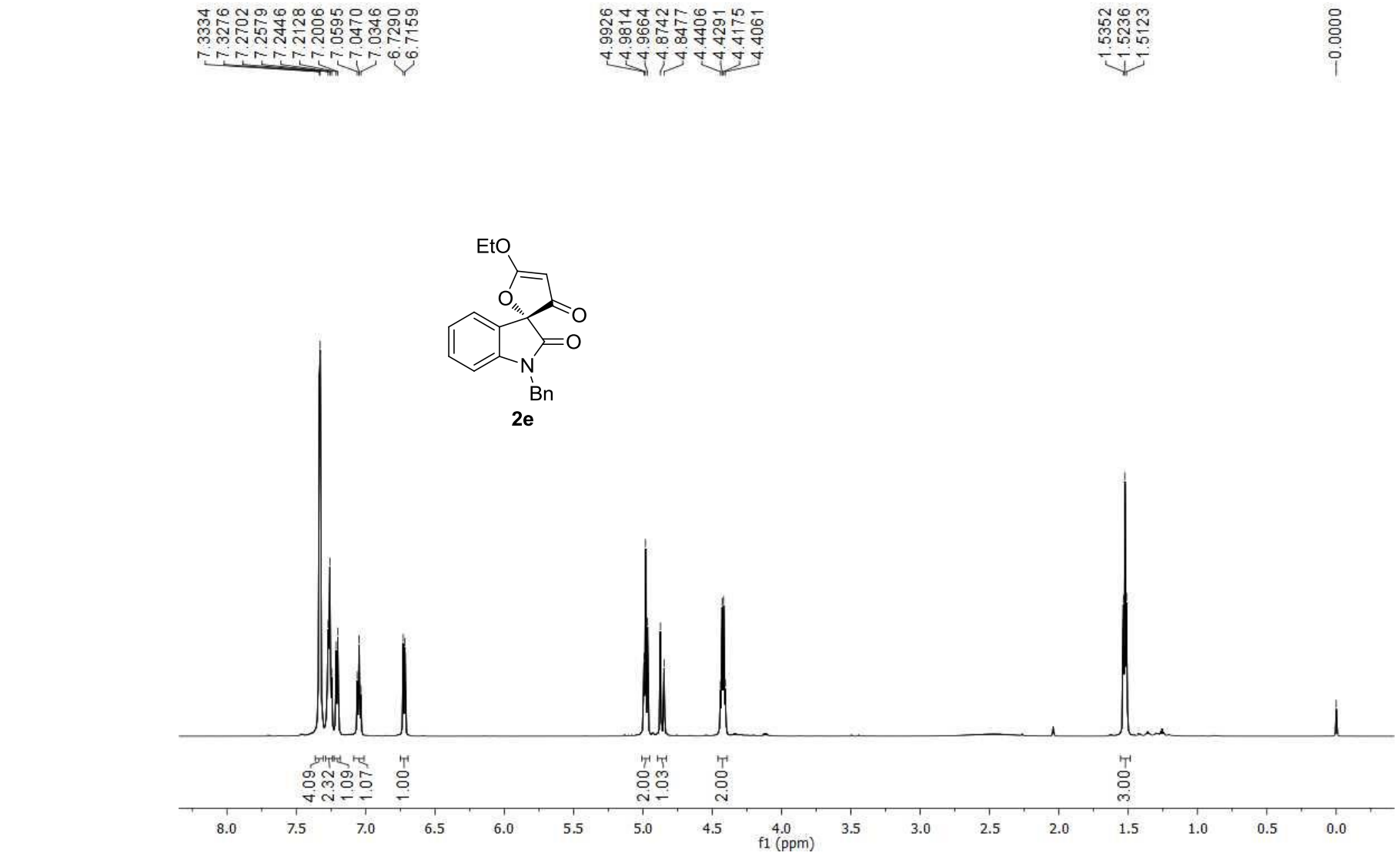
f1 (ppm)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Bn
2e
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6.0
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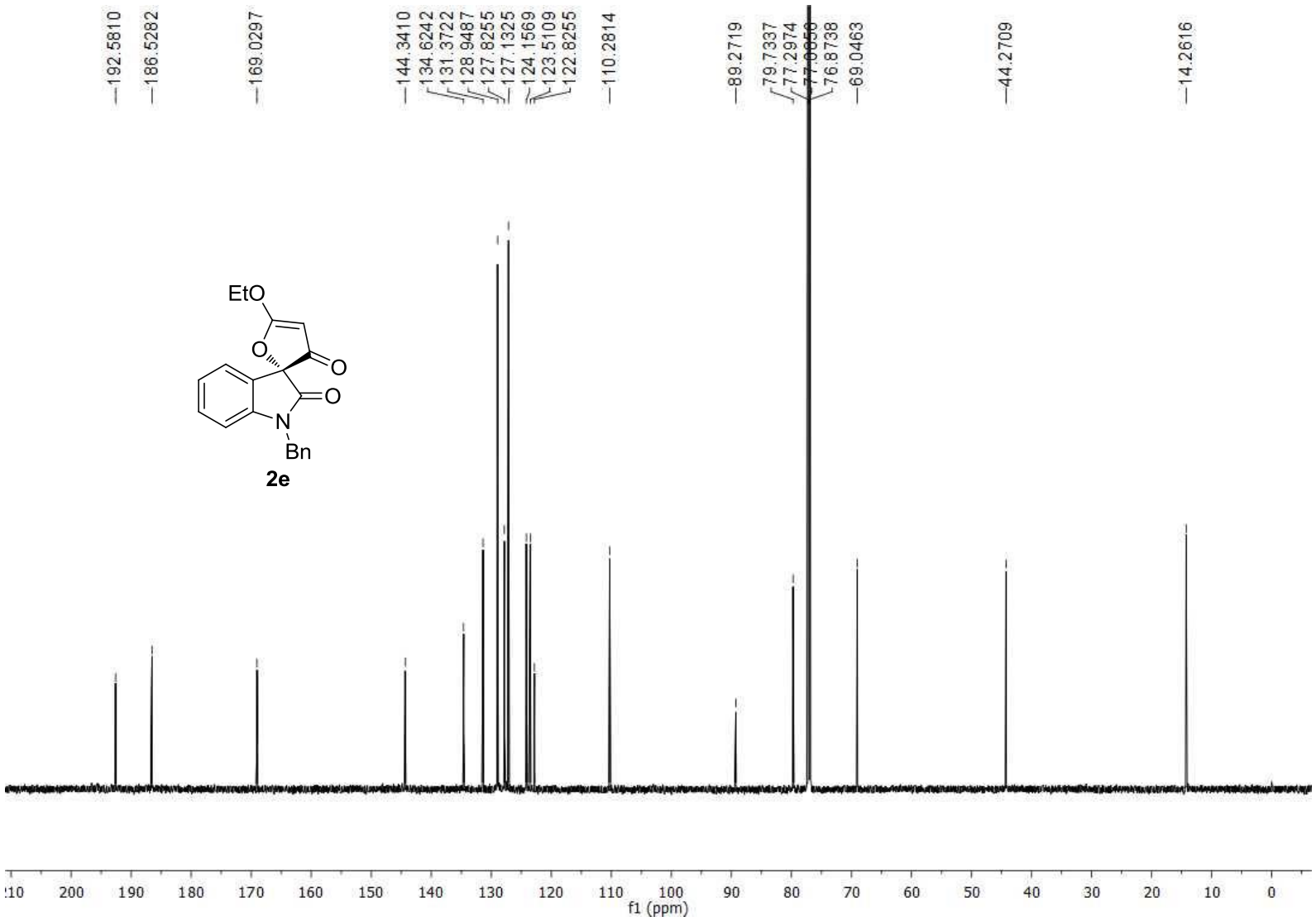
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EtO
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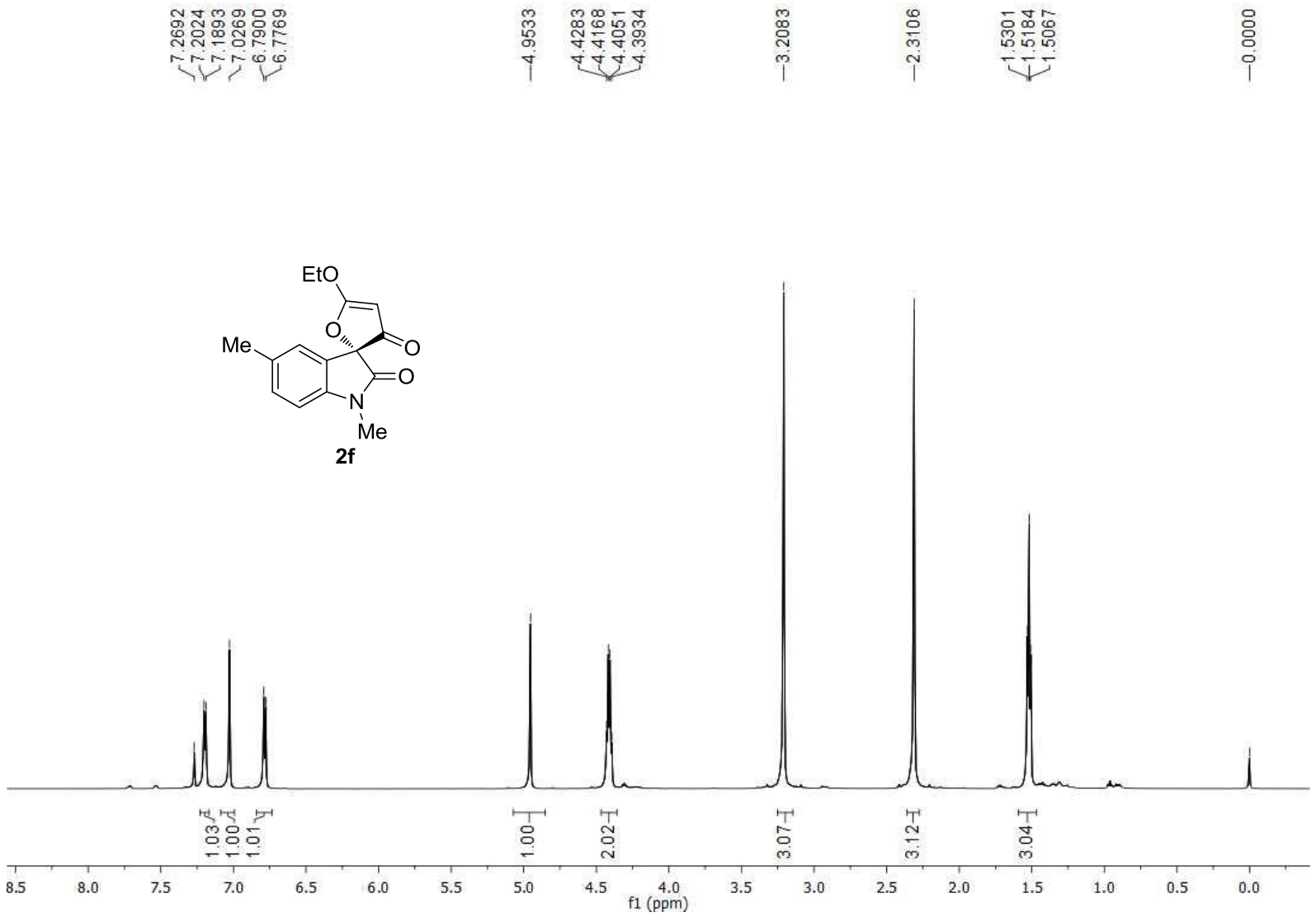
Bn
2e
f1 (ppm)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1.5067
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EtO
O
O
O
Me
N
Me
2f
1.03
1.00
1.01
1.00
2.02
3.07
3.12
3.04
8.5
8.0
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7.0
6.5
6.0
5.5
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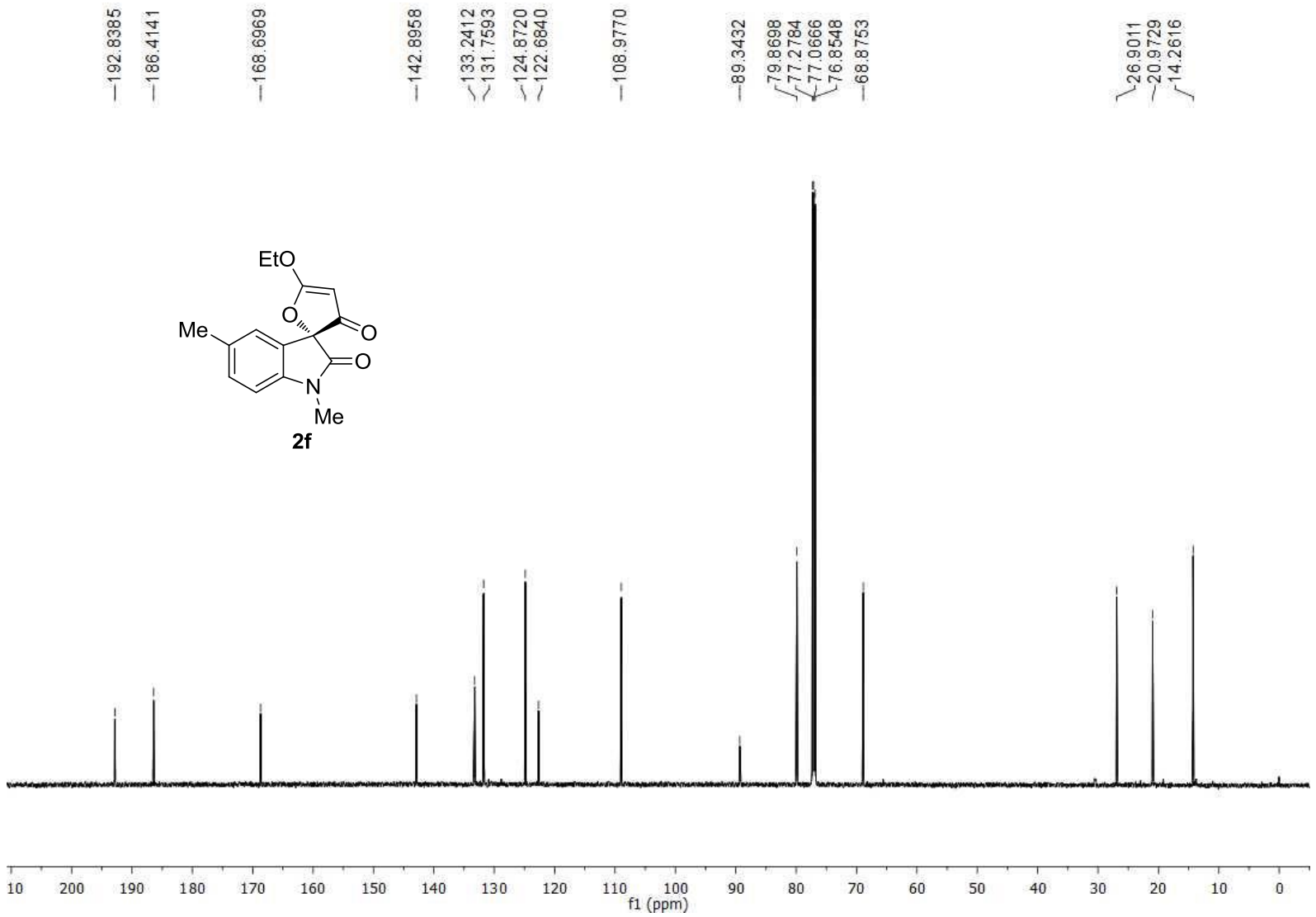
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77.0666
76.8548
68.8753
26.9011
20.9729
14.2616
EtO
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O
O
Me
N
Me
2f
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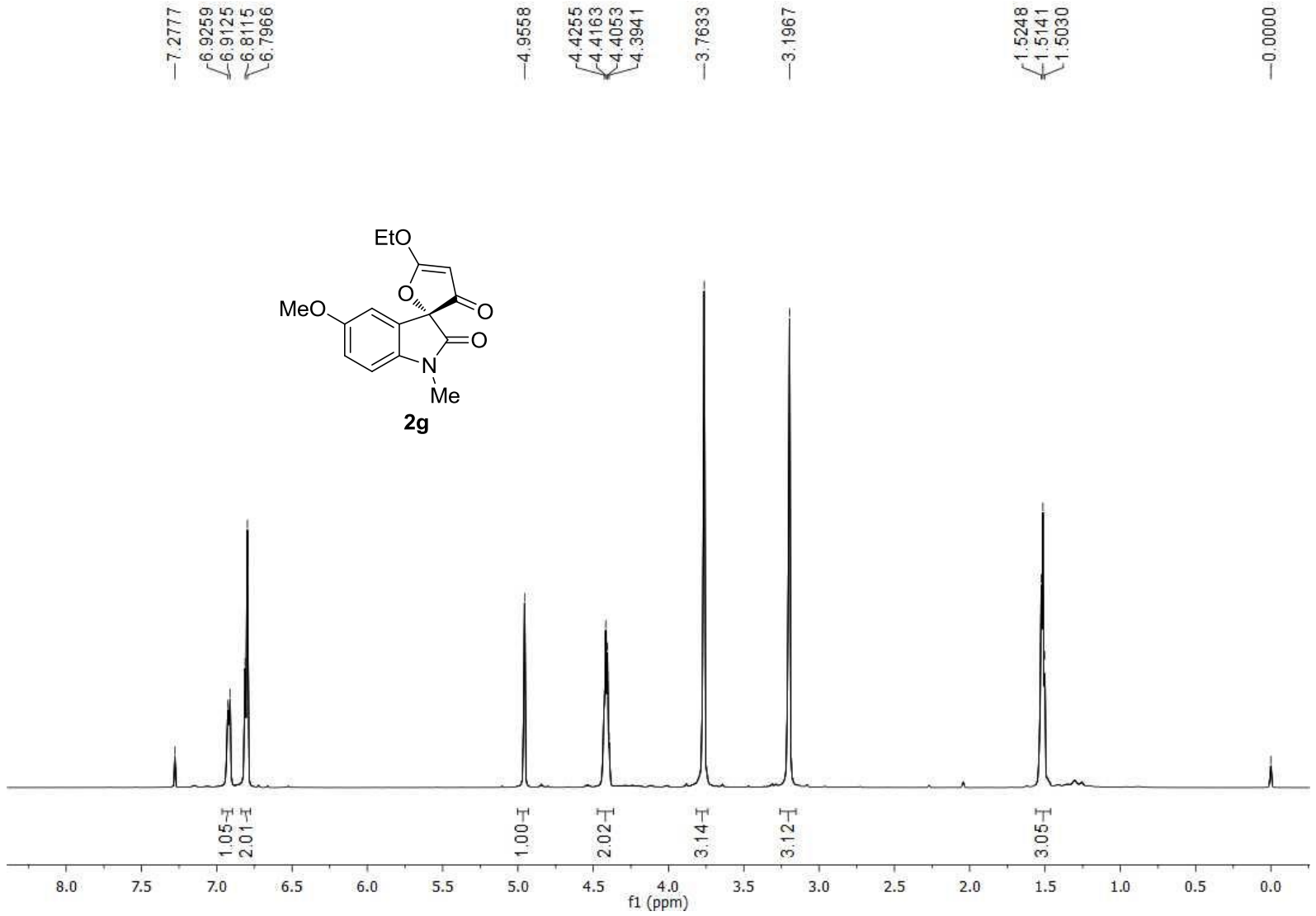
f1 (ppm)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3.7633
3.1967
1.5248
1.5141
1.5030
0.0000
EtO
MeO
O
O
O
N
Me
2g
1.05
2.01
1.00
2.02
3.14
3.12
3.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
1.5
1.0
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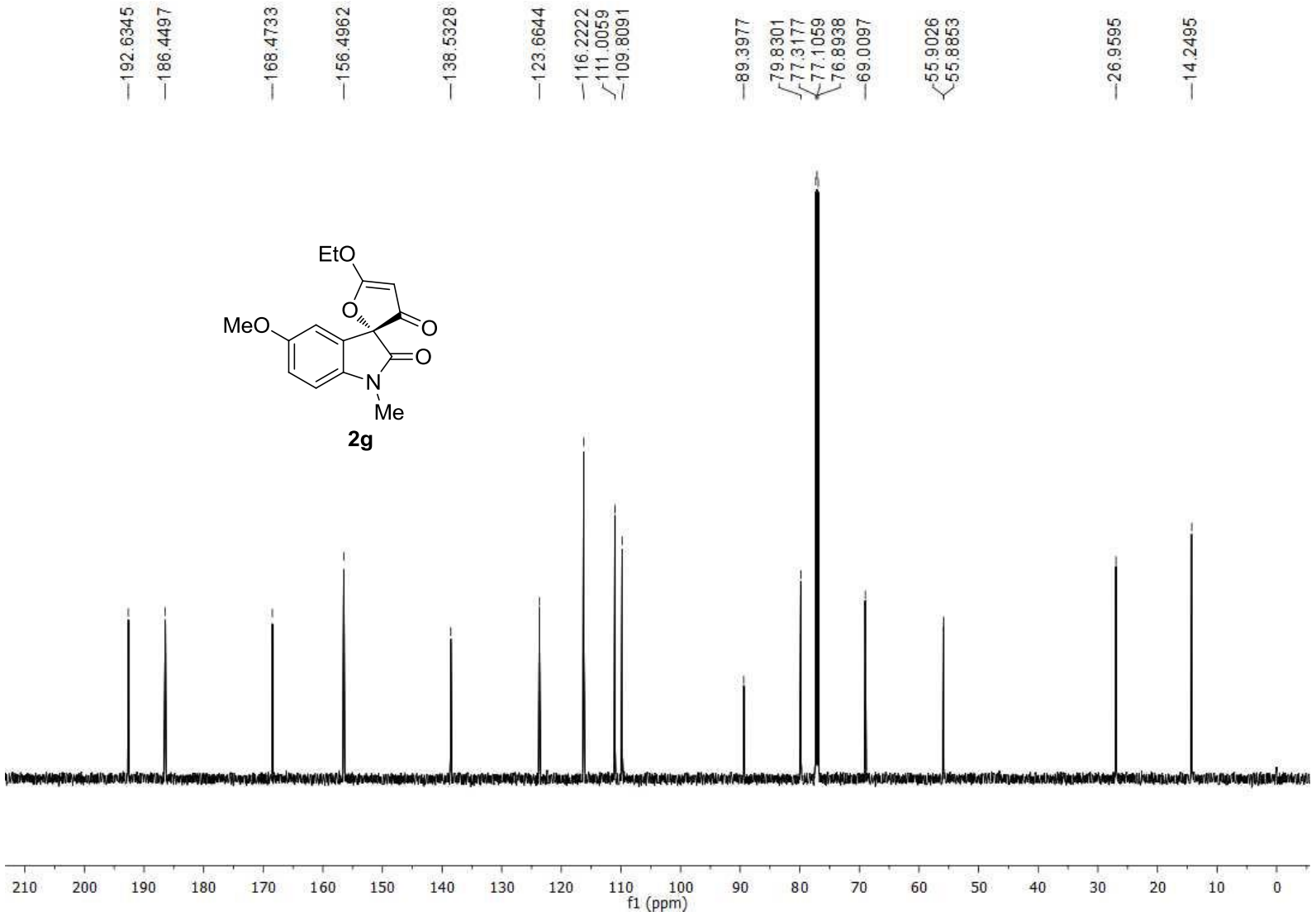
0.0
f1 (ppm)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77.3177
77.1059
76.8938
69.0097
55.9026
55.8853
26.9595
14.2495
EtO
MeO
O
O
O
N
Me
2g
210
200
190
180
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130
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110
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90
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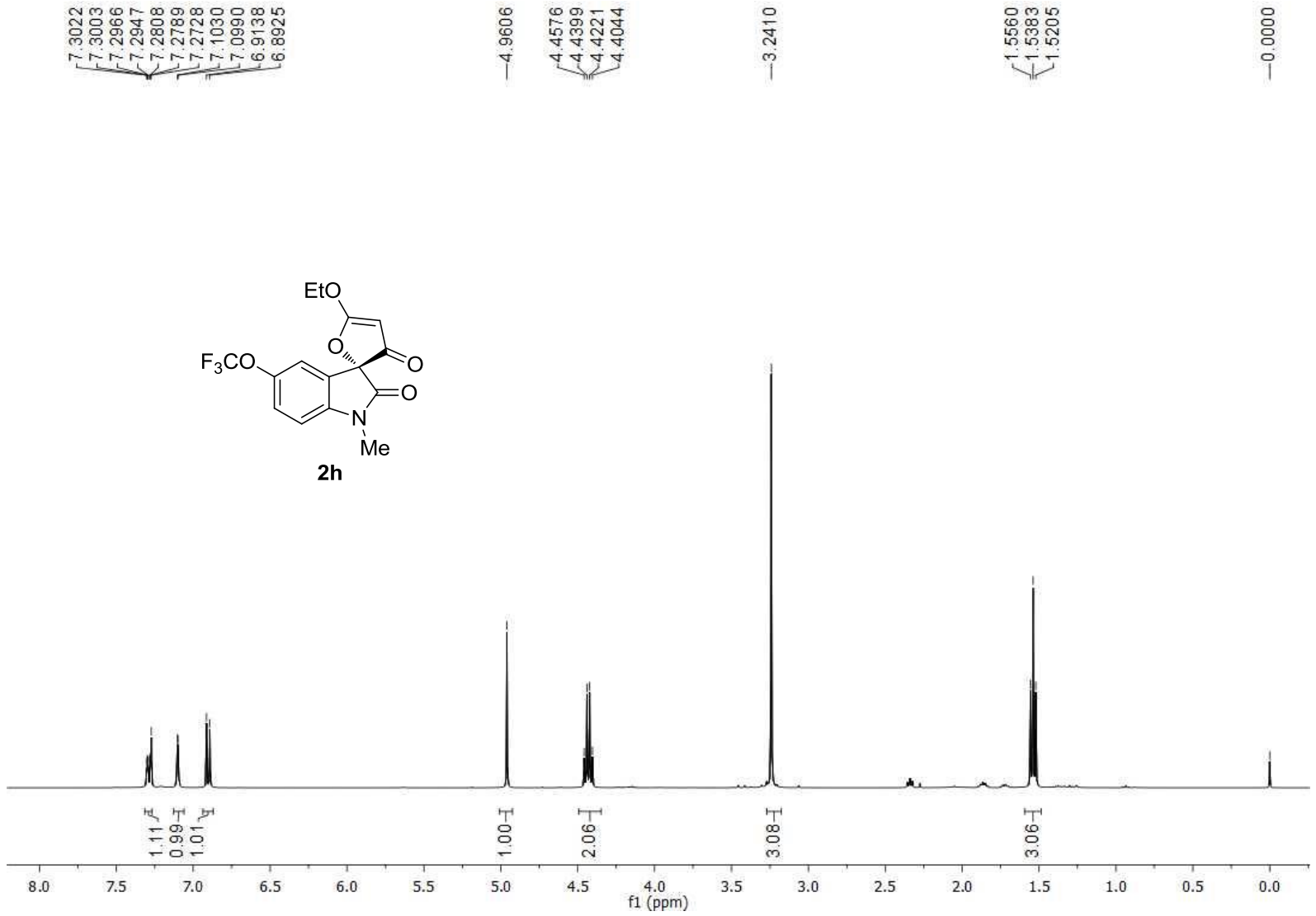
f1 (ppm)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6.8925
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4.4399
4.4221
4.4044
3.2410
1.5560
1.5383
1.5205
0.0000
EtO
O
O
F3CO
O
N
Me
2h
1.11
0.99
1.01
1.00
2.06
3.08
3.06
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
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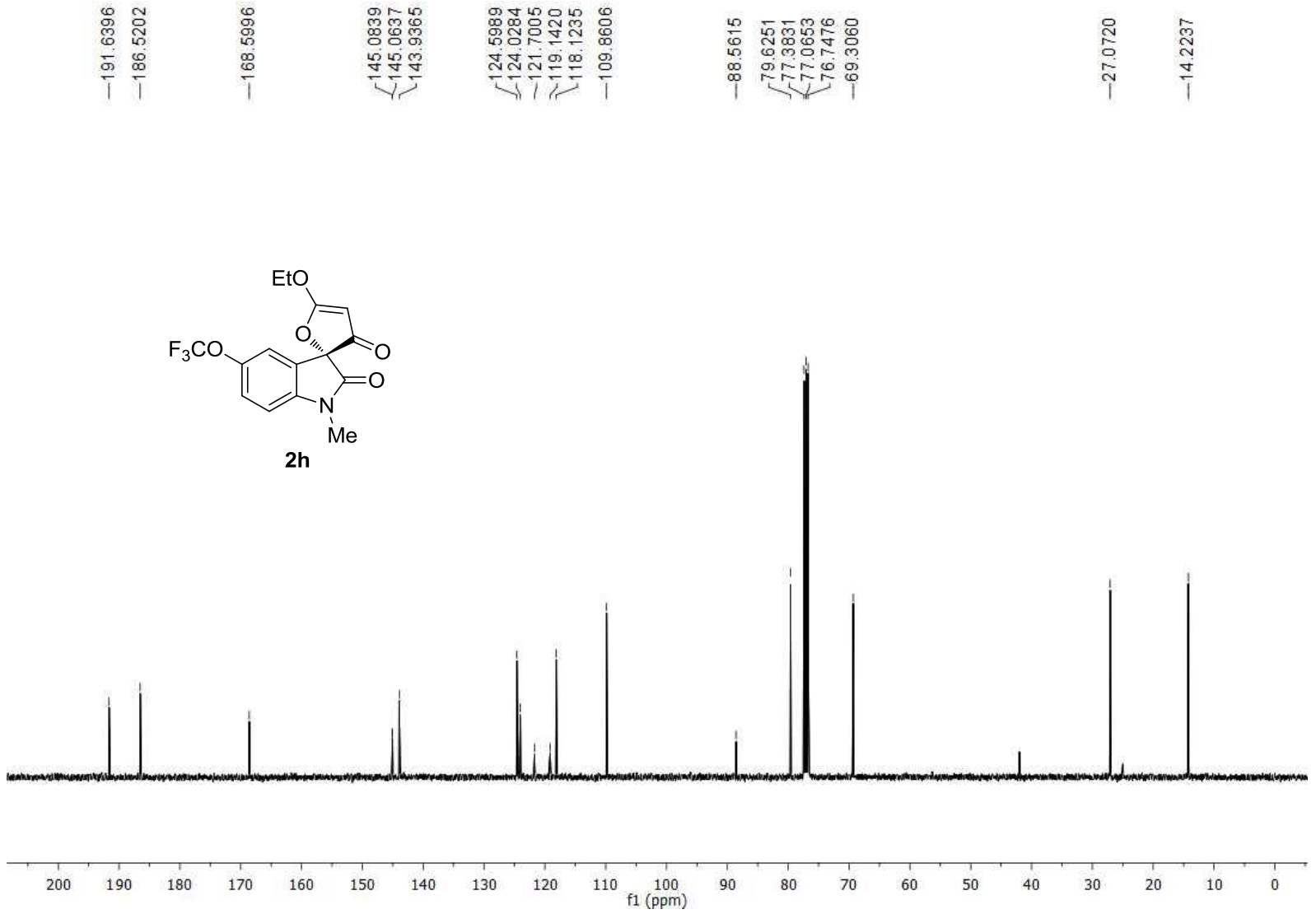
f1 (ppm)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88.5615
79.6251
77.3831
77.0653
76.7476
69.3060
27.0720
14.2237
EtO
O
O
F3CO
O
N
Me
2h
200
190
180
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130
120
110
100
90
80
70
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50
40
30
20
10
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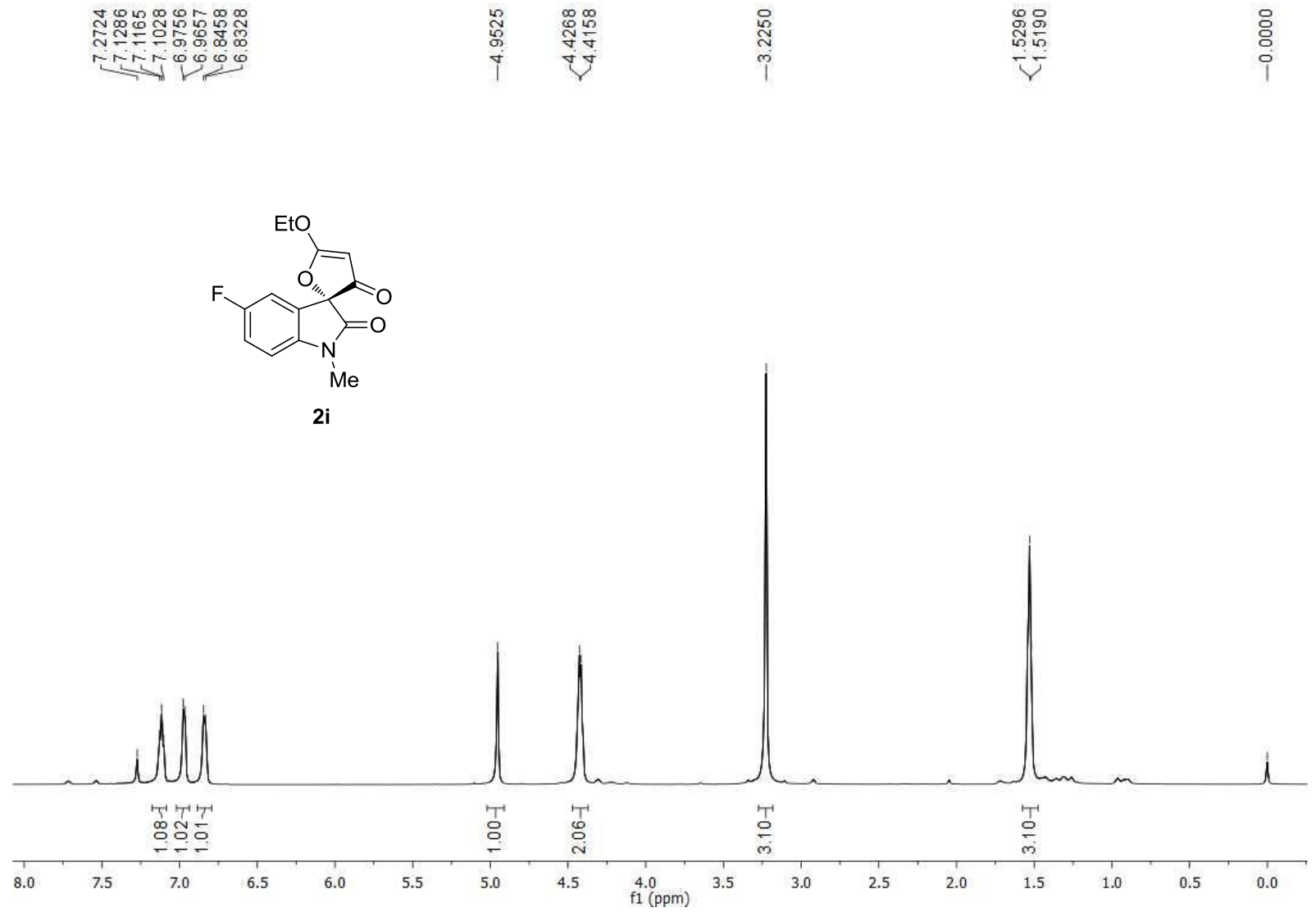
f1 (ppm)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4.4158
3.2250
1.5296
1.5190
0.0000
EtO
O
O
F
O
N
Me
1.08
1.02
1.01
1.00
2.06
3.10
3.10
8.0
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7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
1.5
1.0
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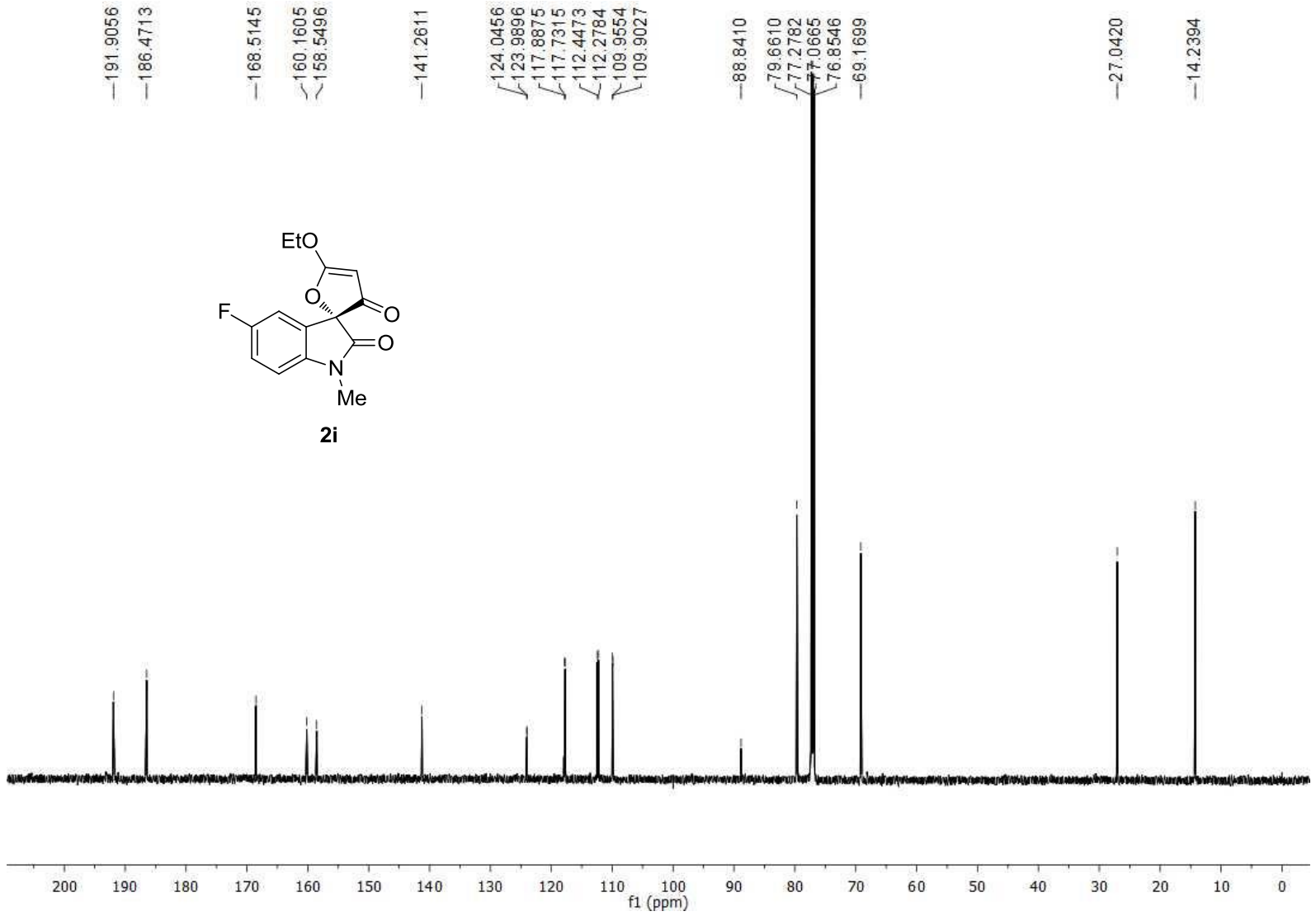
0.0
f1 (ppm)

2i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117.7315
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112.2784
109.9554
109.9027
88.8410
79.6610
77.2782
77.0665
76.8546
69.1699
27.0420
14.2394
EtO
O
F
O
O
N
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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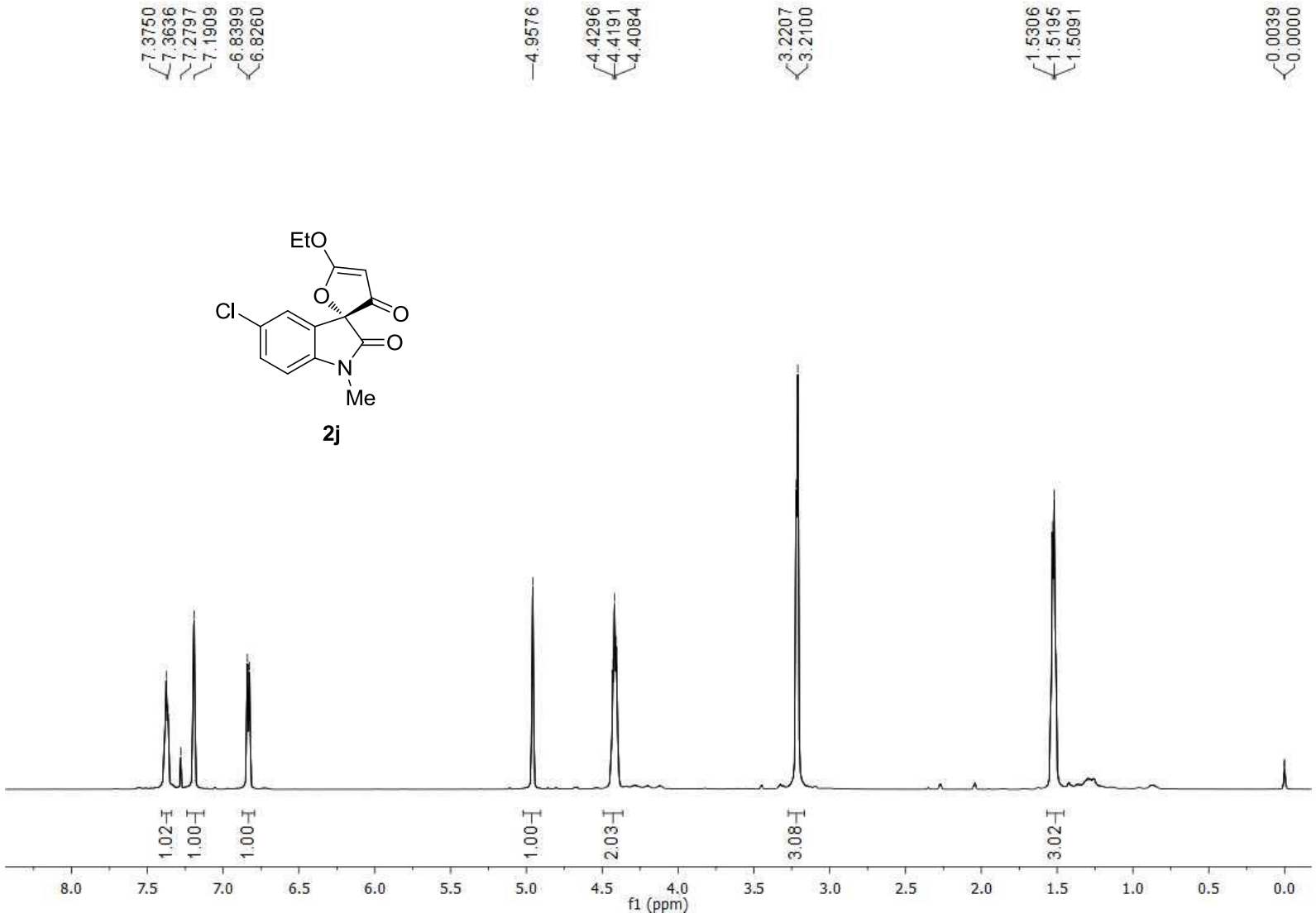
50
40
30
20
10
0
f1 (ppm)

2i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6.8399
6.8260
4.9576
4.4296
4.4191
4.4084
3.2207
3.2100
1.5306
1.5195
1.5091
0.0039
0.0000
EtO
O
Cl
O
O
N
Me
2j
1.02
1.00
1.00
1.00
2.03
3.08
3.02
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
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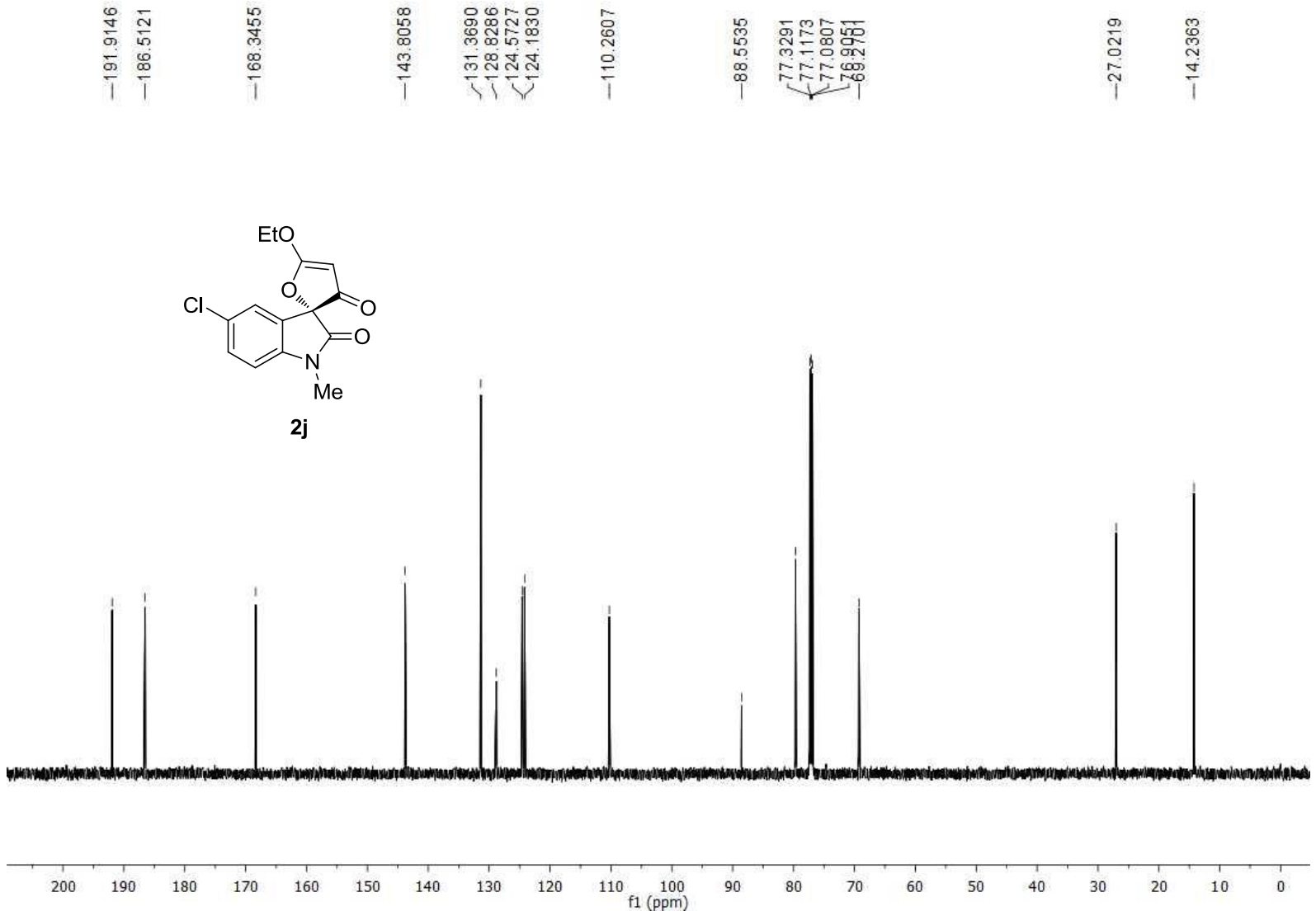
0.0
f1 (ppm)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124.5727
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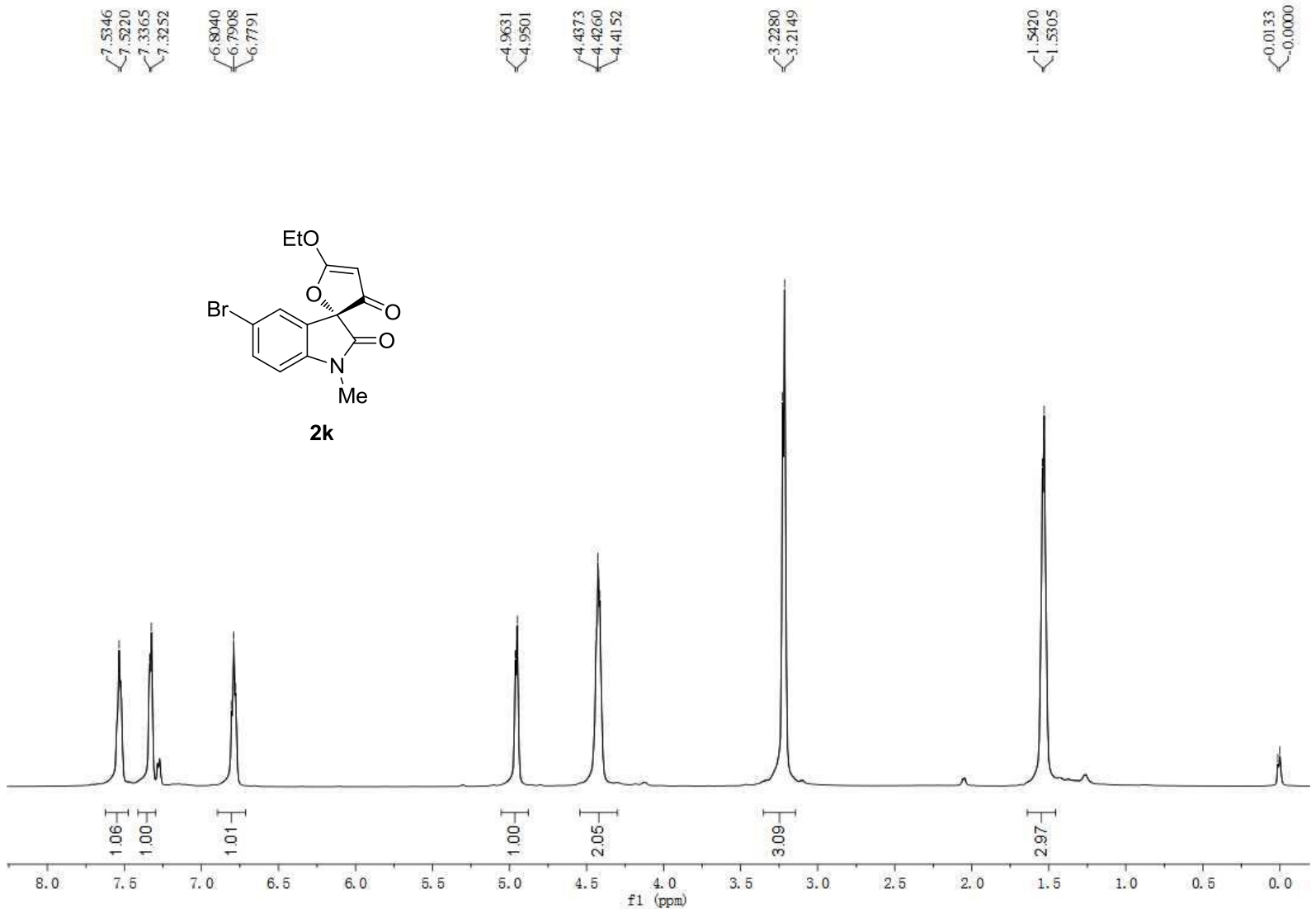
77.1173
77.0807
76.9051
69.2701
27.0219
14.2363
EtO
O
O
Cl
O
N
Me
2j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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6.7791
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4.4373
4.4260
4.4152
3.2280
3.2149
1.5420
1.5305
0.0133
-0.0000
EtO
O
O
Br
O
N
Me
1.06
1.00
1.01
1.00
2.05
3.09
2.97
8.0
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
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2.0
1.5
1.0
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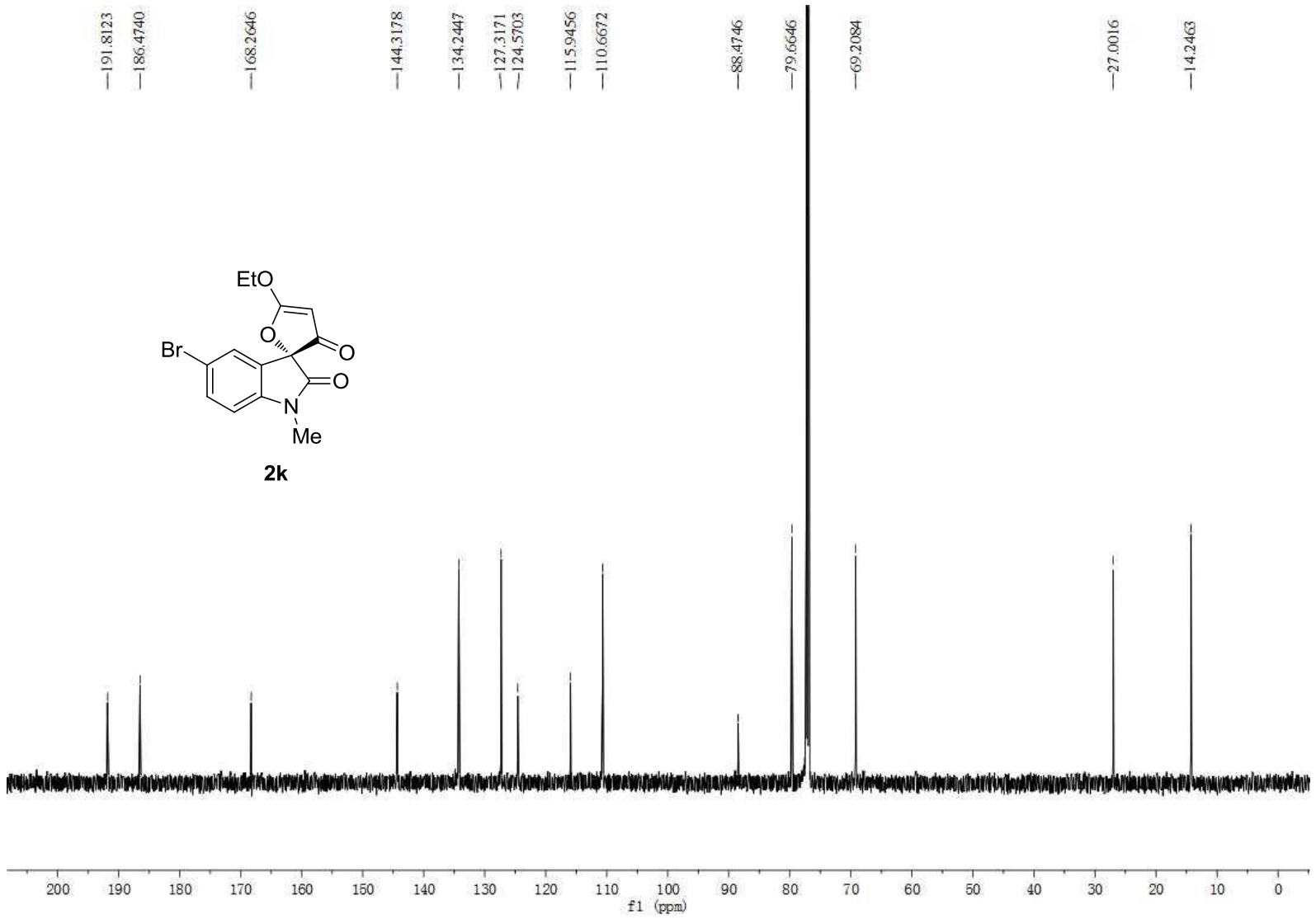
0.0
f1 (ppm)

2k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124.5703
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88.4746
79.6646
69.2084
27.0016
14.2463
EtO
O
O
Br
O
N
Me
2k
200
190
180
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150
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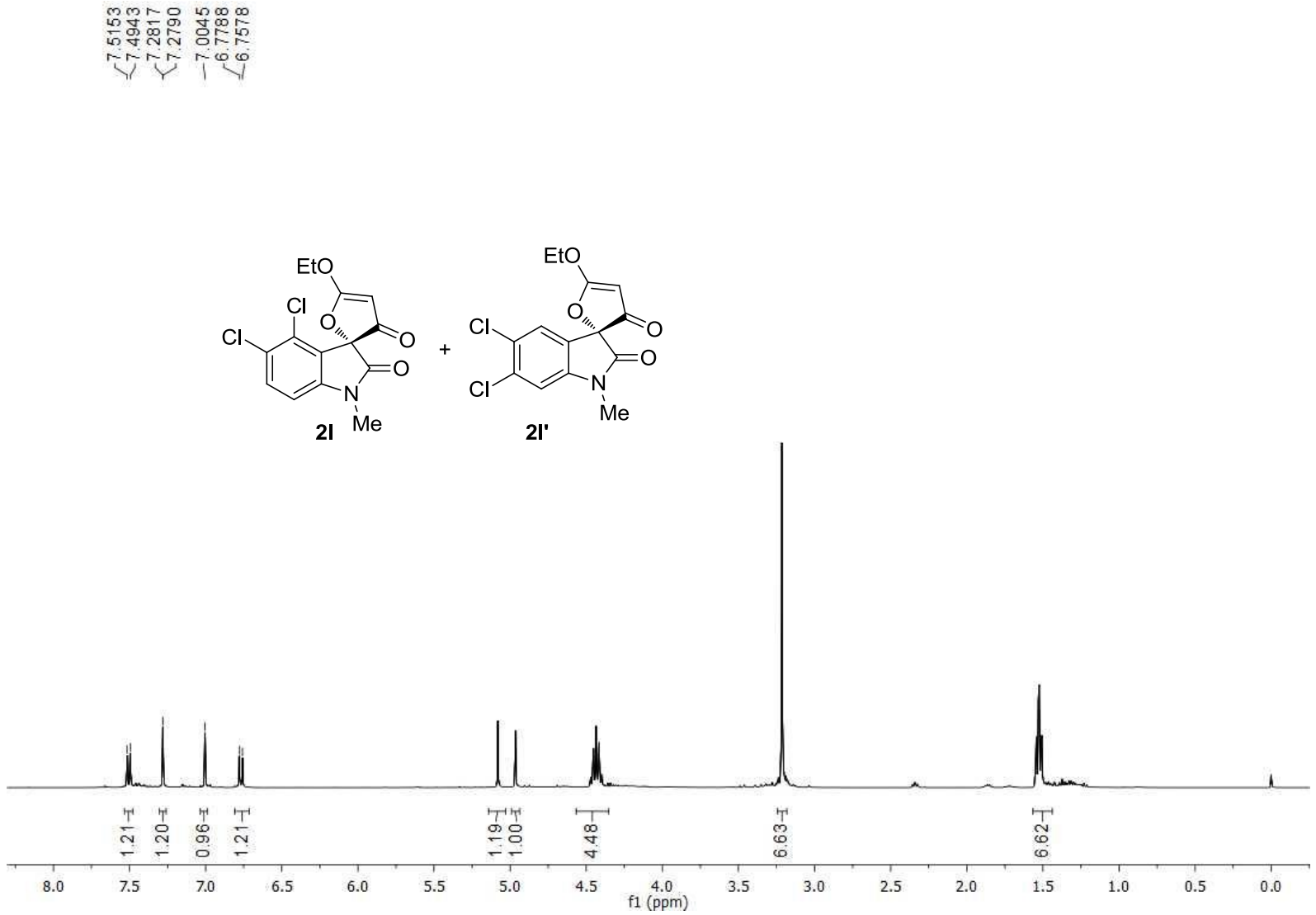
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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Cl
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N
Me
2l
+
EtO
Cl
Cl
O
O
O
N
Me
2l'
1.21
1.20
0.96
1.21
1.19
1.00
4.48
6.63
6.62
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
3.0
2.5
2.0
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1.0
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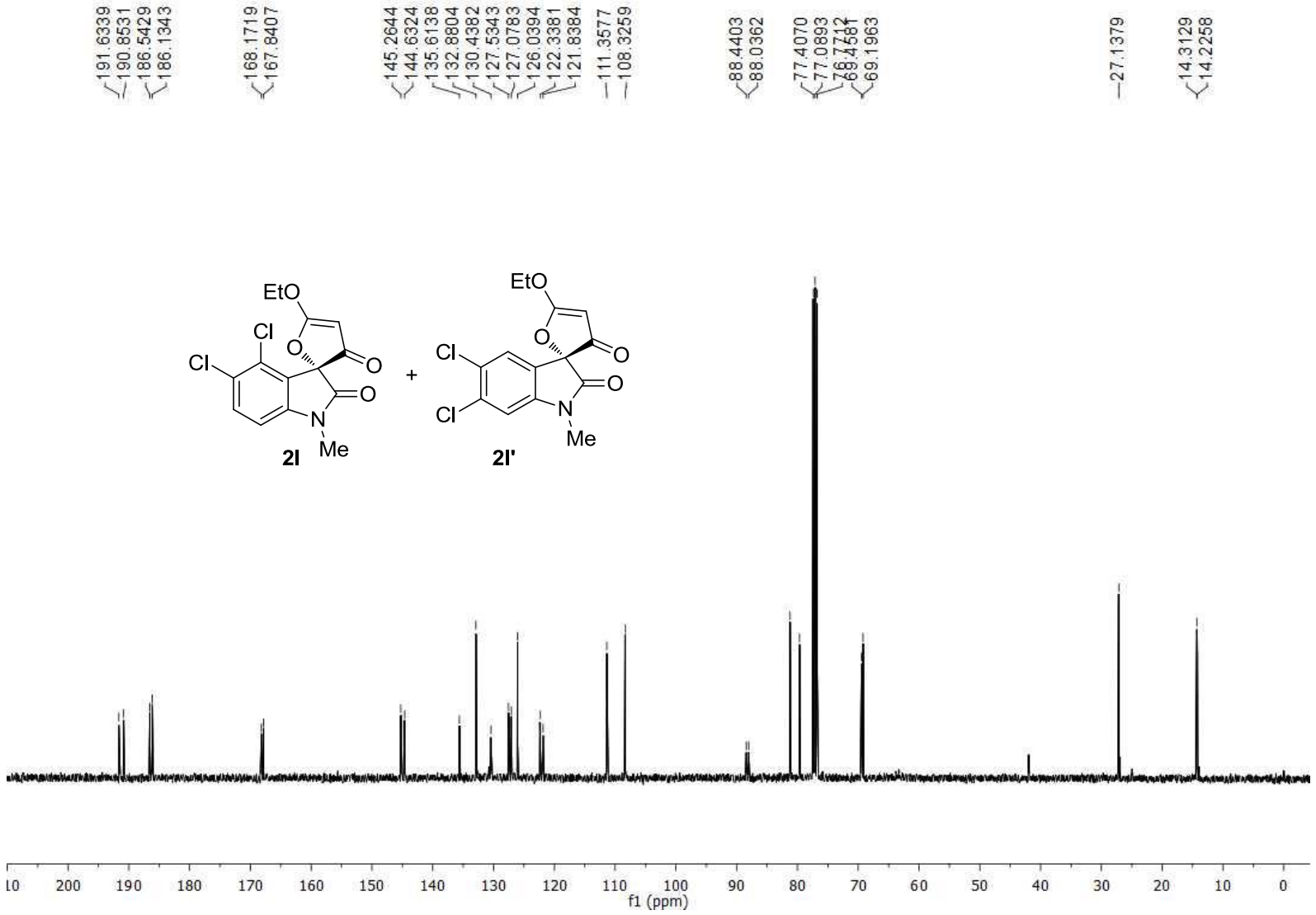
0.0
f1 (ppm)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127.5343
127.0783
126.0394
122.3381
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111.3577
108.3259
88.4403
88.0362
77.4070
77.0893
76.7712
69.4581
69.1963
27.1379
14.3129
14.2258
EtO
Cl
Cl
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N
Me
2l
+
EtO
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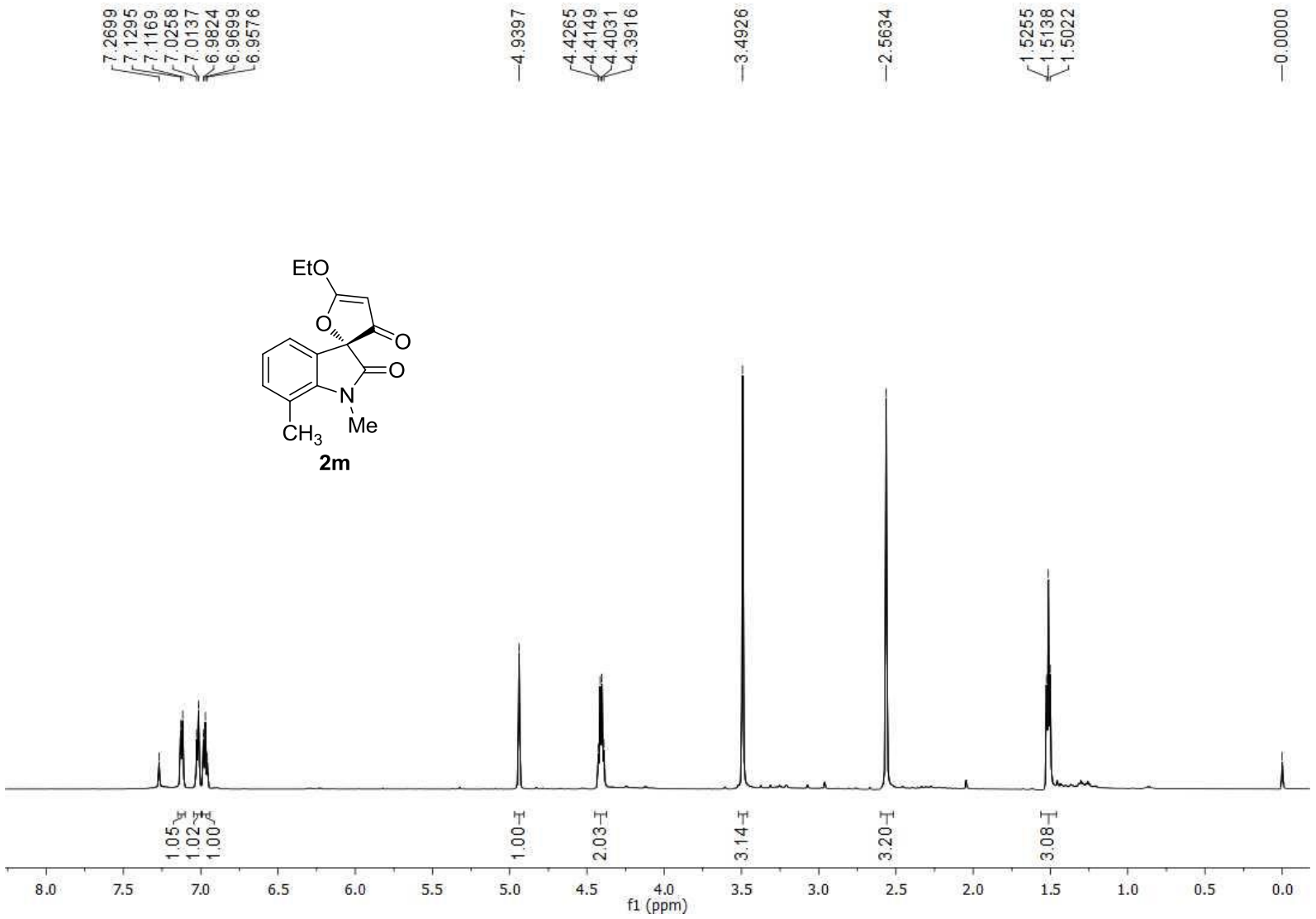
Cl
O
O
O
N
Me
2l'
f1 (ppm)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4.3916
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O
O
N
Me
CH3
2m
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1.02
1.00
1.00
2.03
3.14
3.20
3.08
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
3.0
2.5
2.0
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1.0
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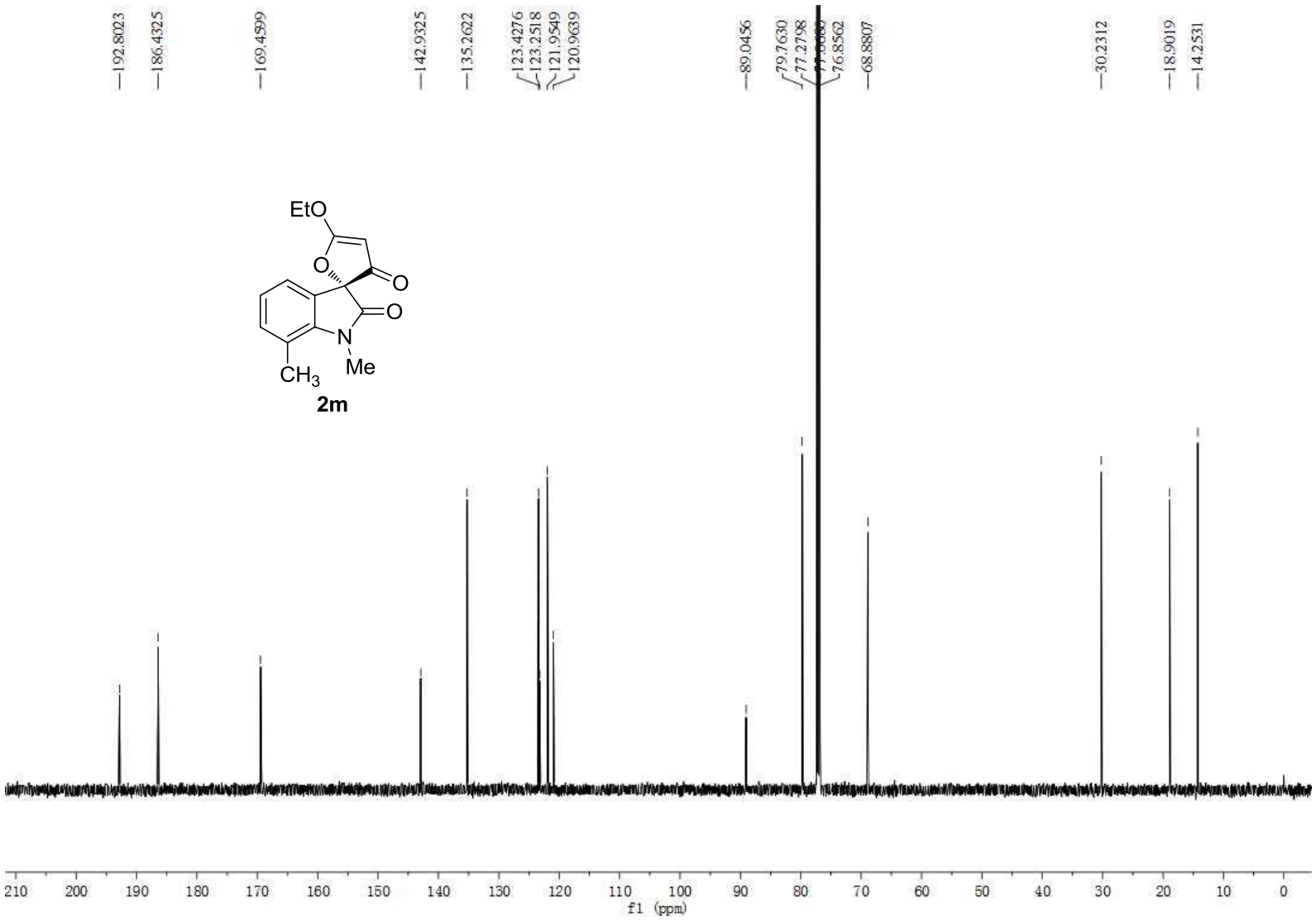
f1 (ppm)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77.2798
76.8562
68.8807
30.2312
18.9019
14.2531
EtO
O
O
O
N
Me
CH3
2m
210
200
190
180
170
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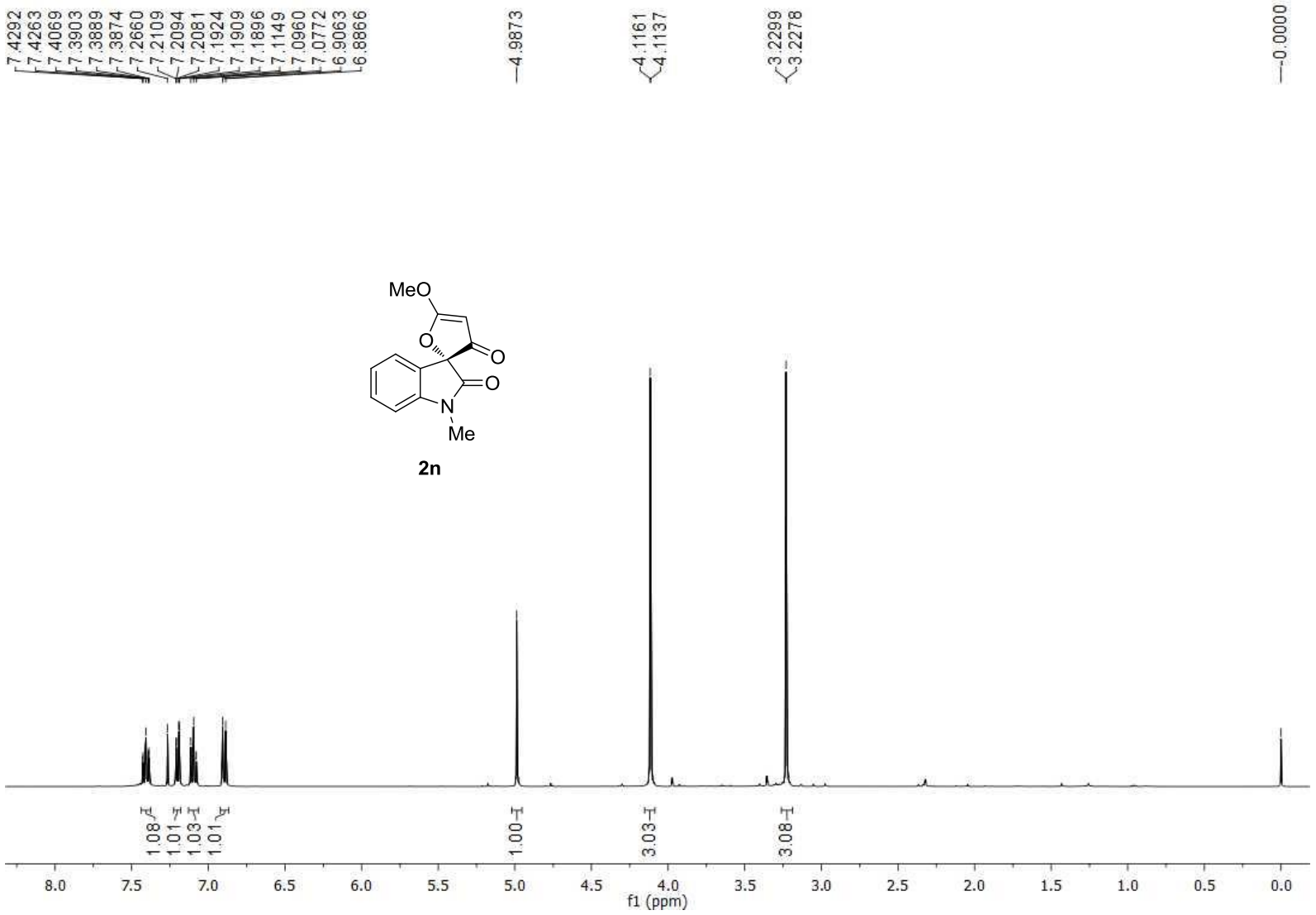
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.1909
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7.1149
7.0960
7.0772
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6.8866
4.9873
4.1161
4.1137
3.2299
3.2278
0.0000
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O
O
O
N
Me
2n
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1.01
1.03
1.01
1.00
3.03
3.08
8.0
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7.0
6.5
6.0
5.5
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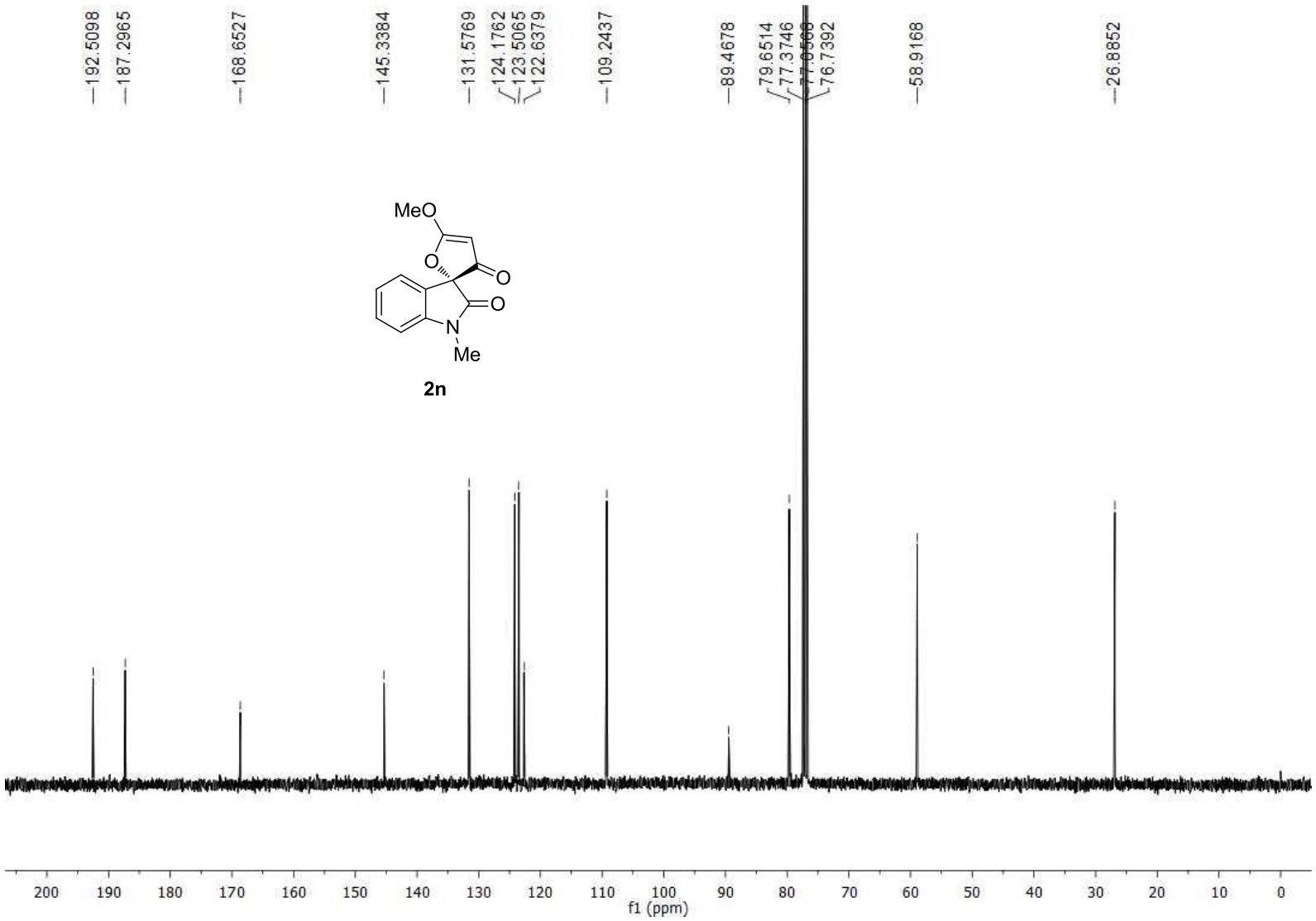
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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77.3746
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MeO
O
O
O
N
Me
2n
200
190
180
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130
120
110
100
90
80
70
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50
40
30
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10
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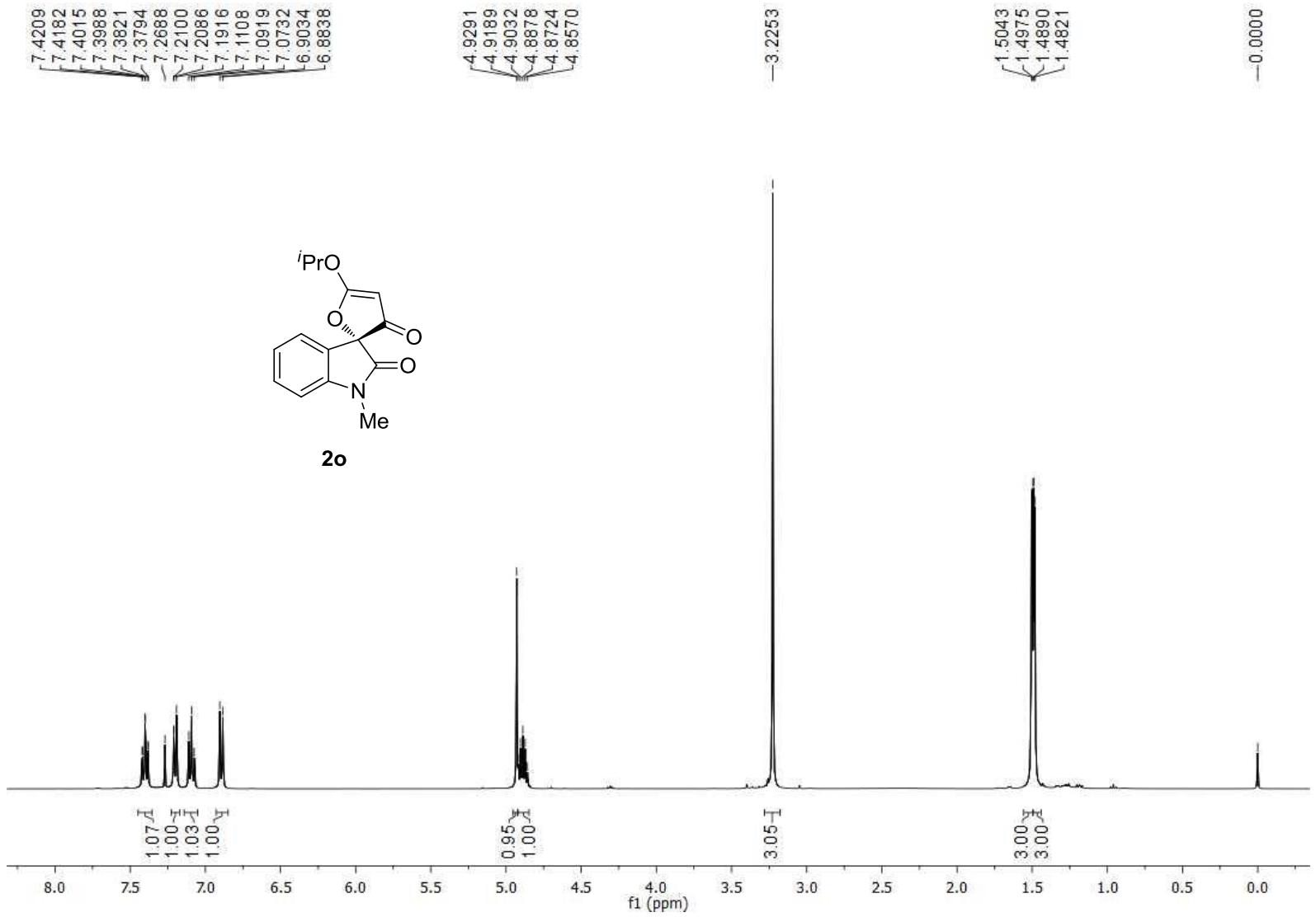
f1 (ppm)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4.8878
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1.4890
1.4821
0.0000
iPrO
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O
O
N
Me
2o
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1.00
1.03
1.00
0.95
1.00
3.05
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3.00
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7.0
6.5
6.0
5.5
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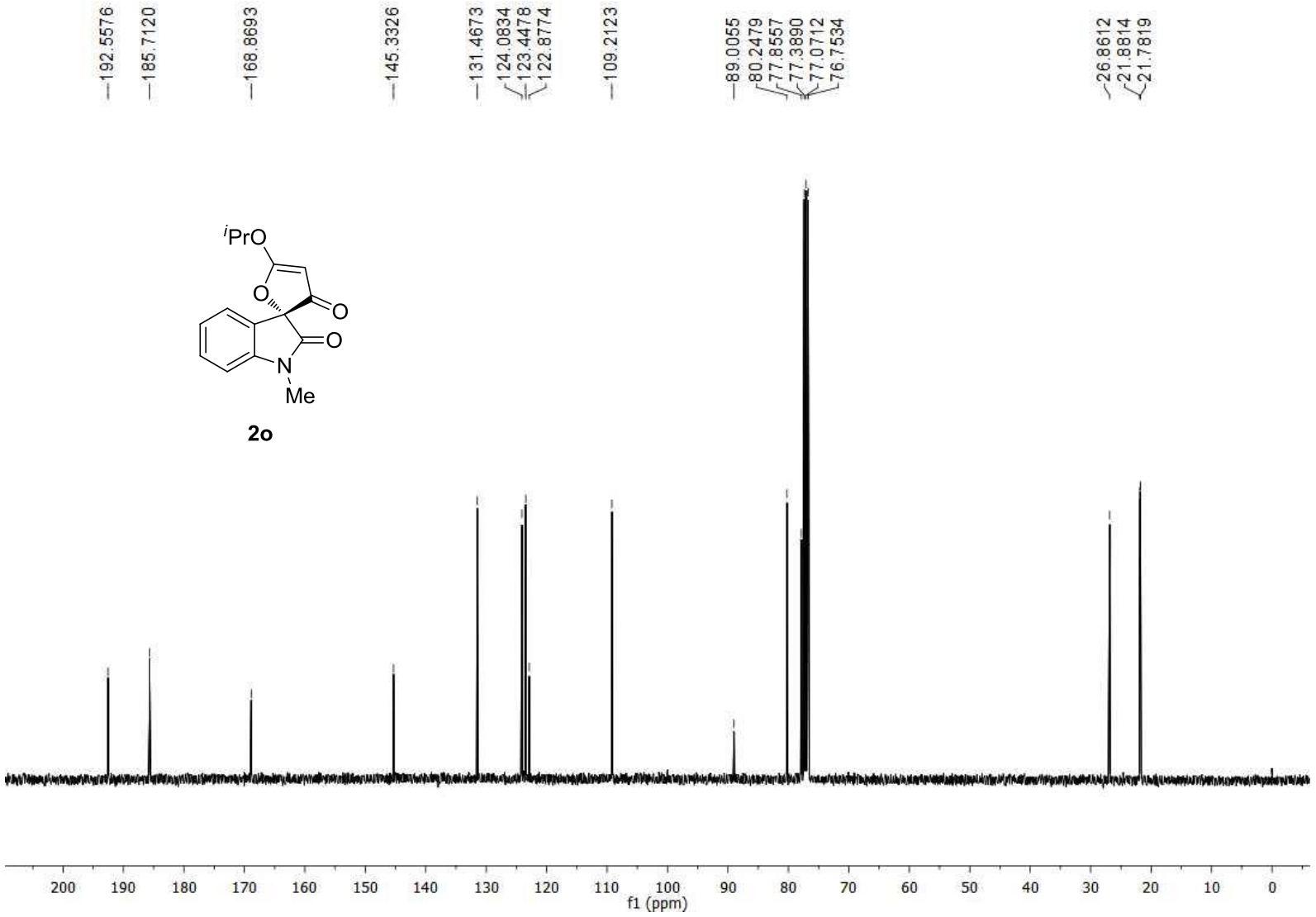
f1 (ppm)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76.7534
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21.8814
21.7819
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O
O
O
N
Me
2o
200
190
180
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110
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90
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50
40
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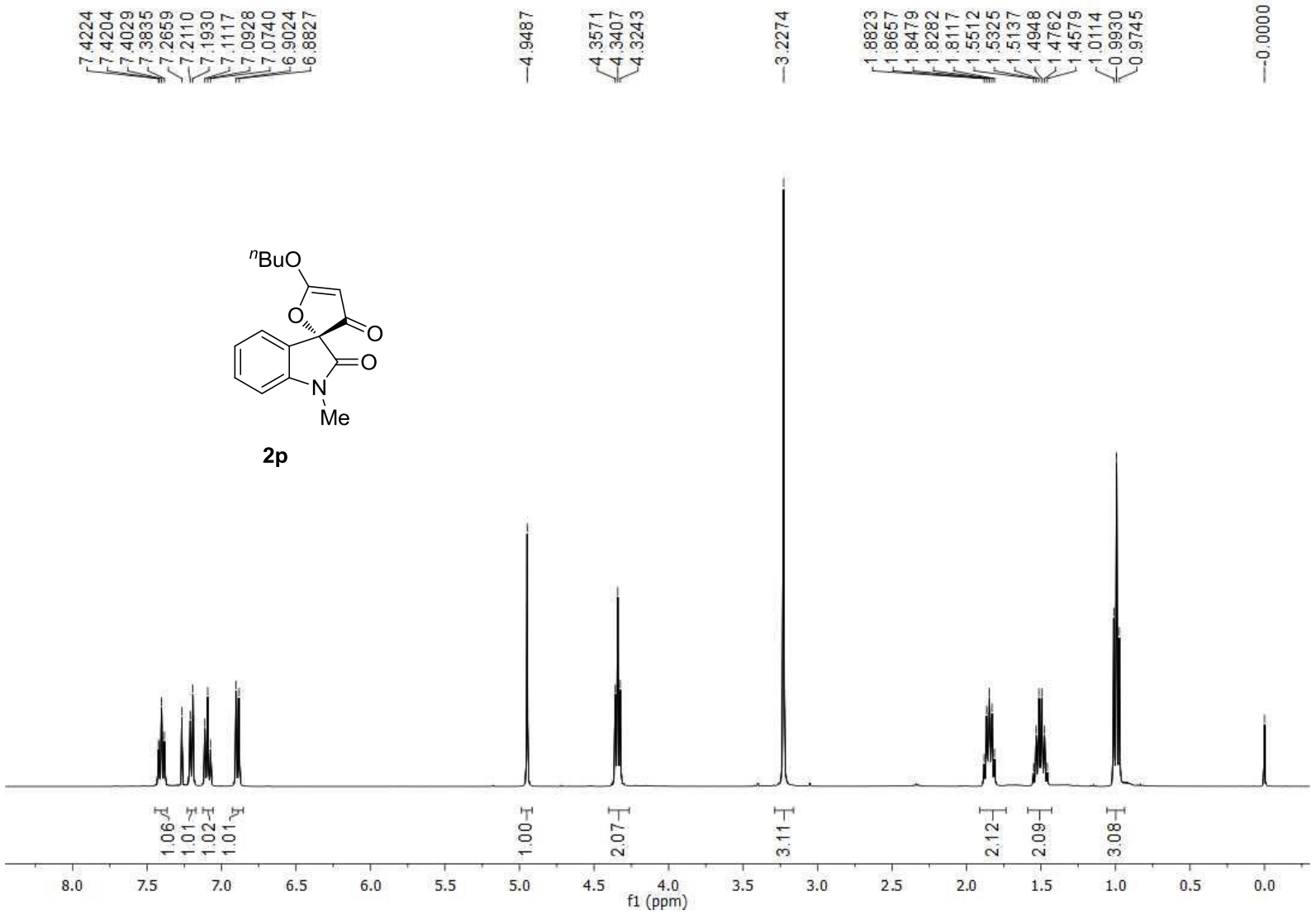
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1.8282
1.8117
1.5512
1.5325
1.5137
1.4948
1.4762
1.4579
1.0114
0.9930
0.9745
0.0000
nBuO
O
O
O
N
Me
2p
1.06
1.01
1.02
1.01
1.00
2.07
3.11
2.12
2.09
3.08
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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3.5
3.0
2.5
2.0
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1.0
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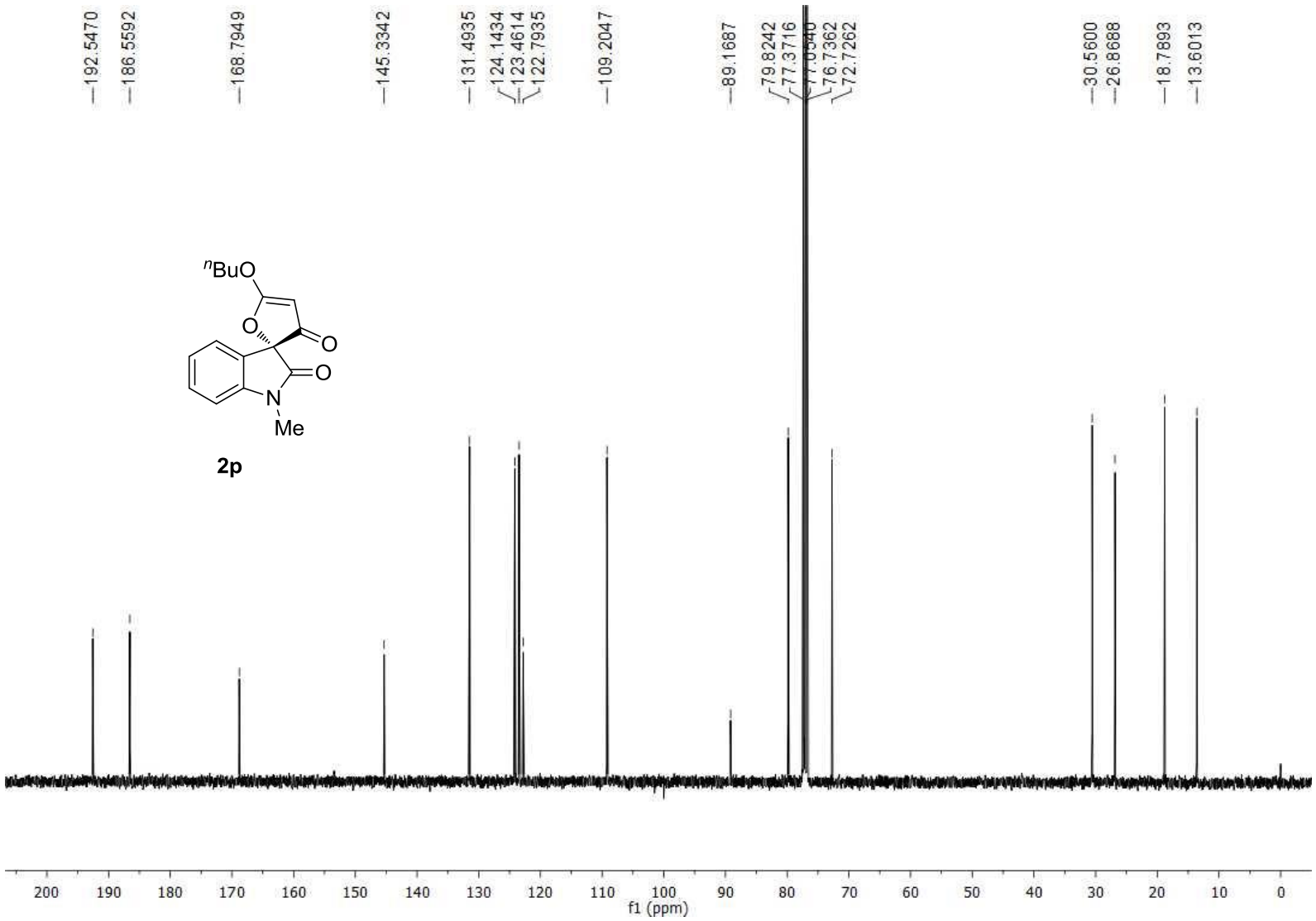
0.0
f1 (ppm)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77.3716
76.7362
72.7262
30.5600
26.8688
18.7893
13.6013
nBuO
O
O
O
N
Me
2p
200
190
180
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90
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70
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50
40
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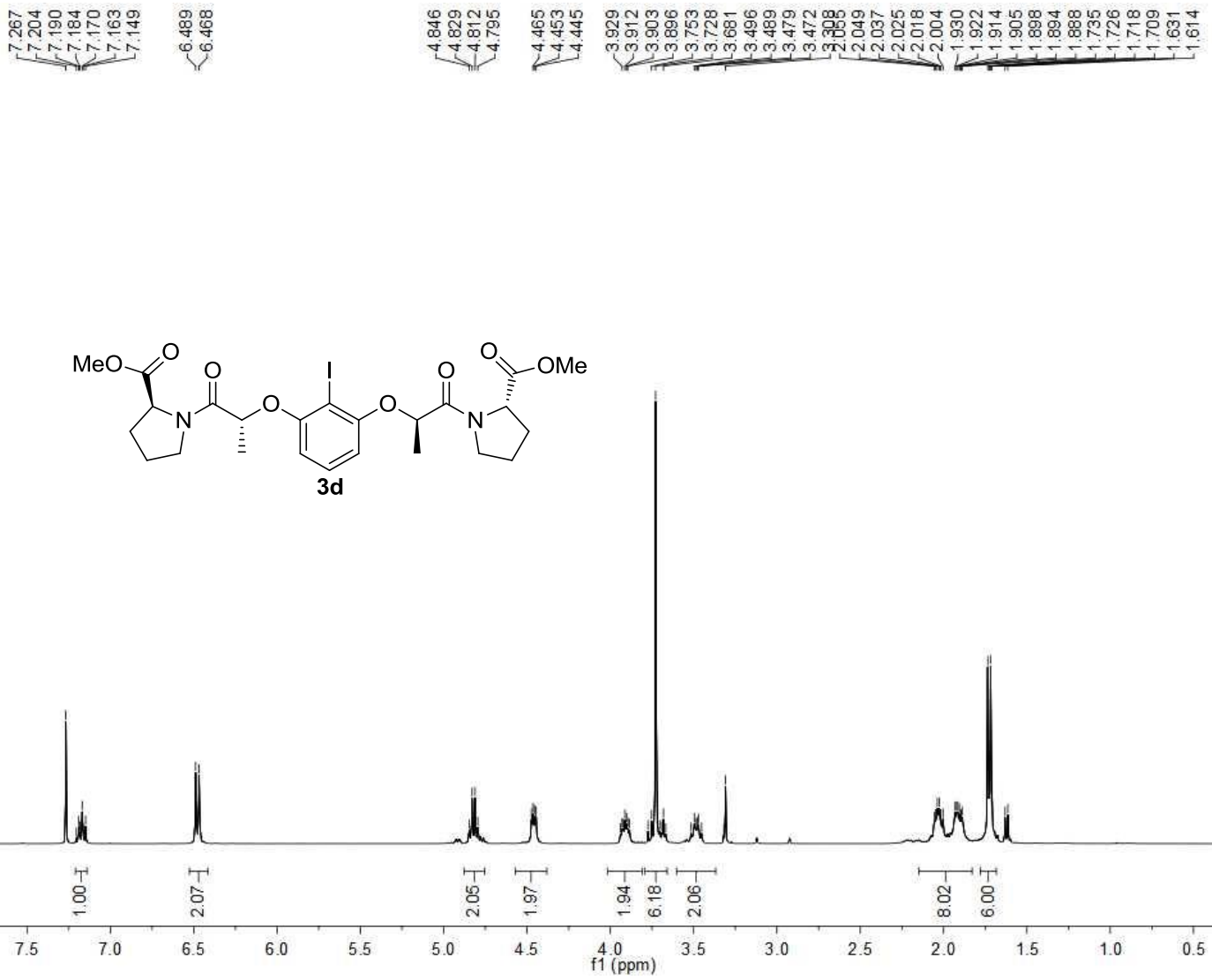
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N
O
OMe
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2.06
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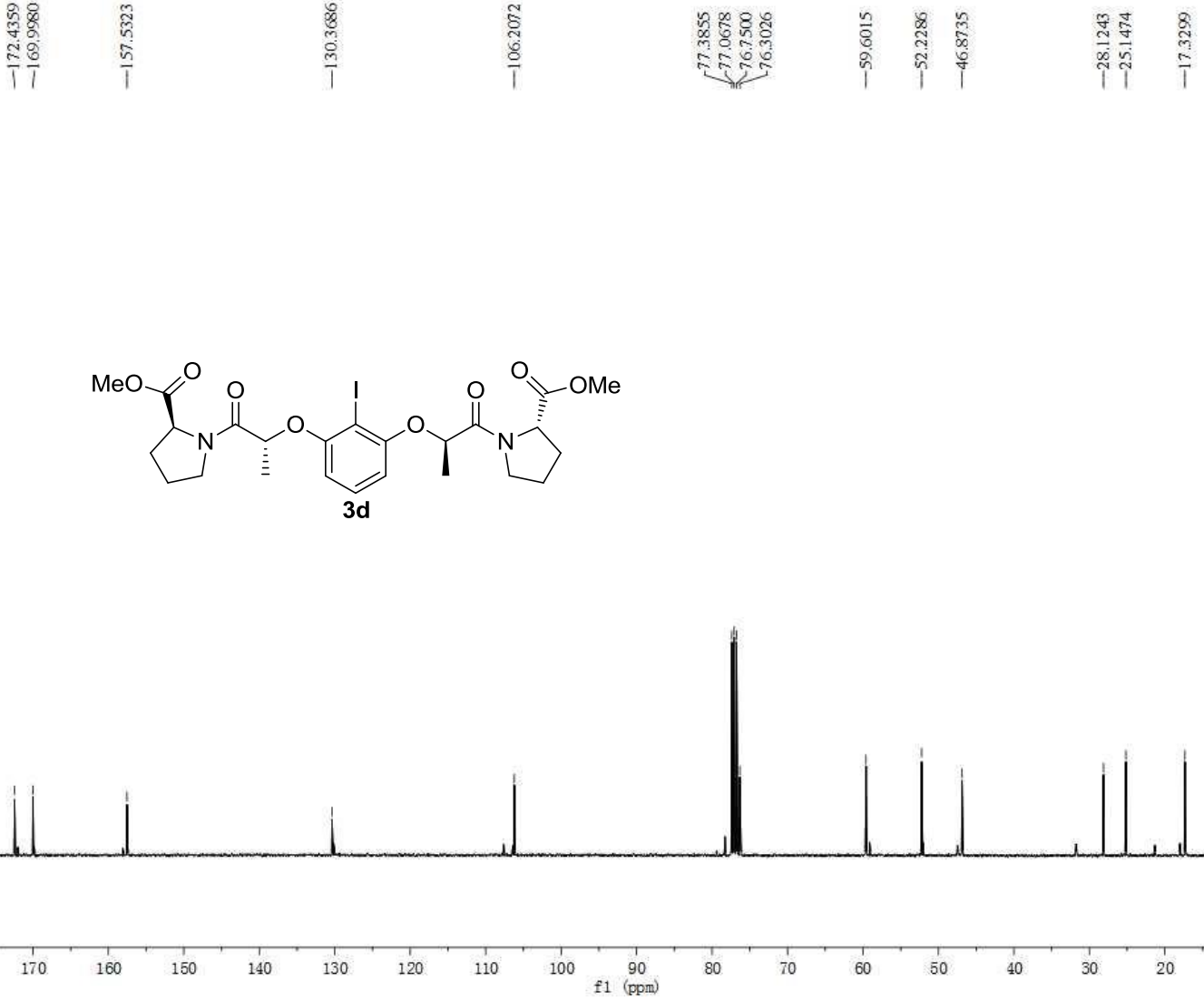
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3d
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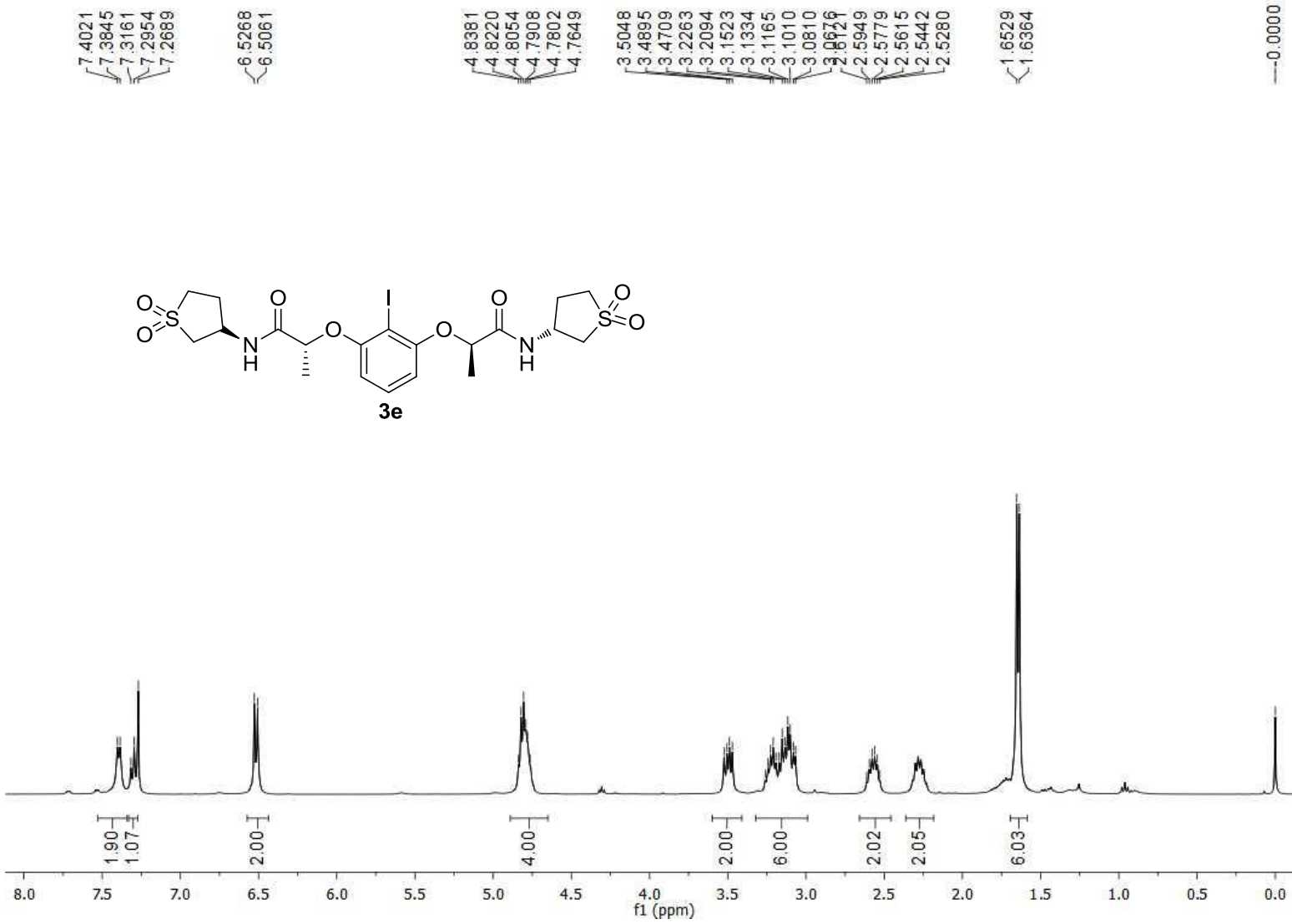
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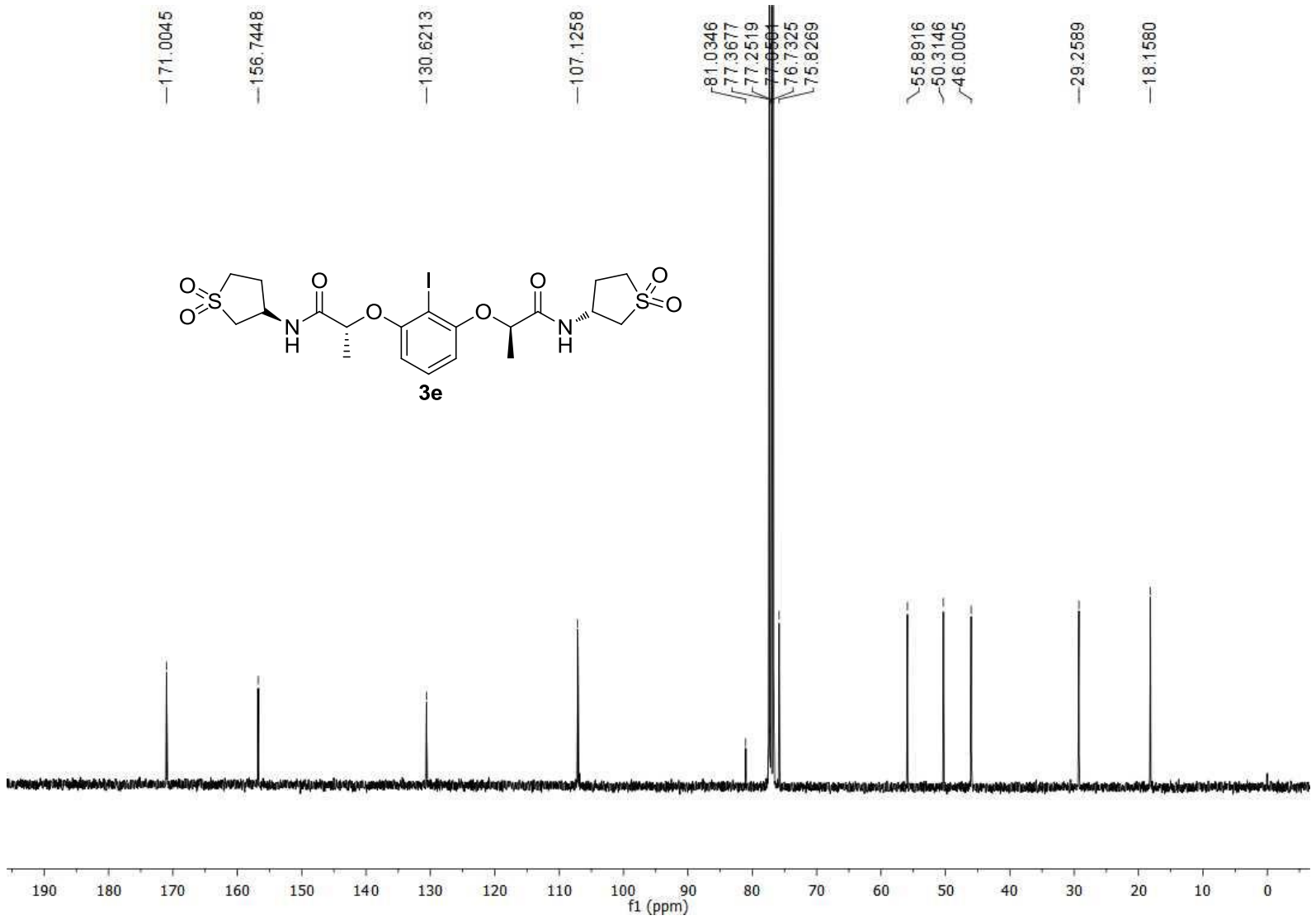
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3e
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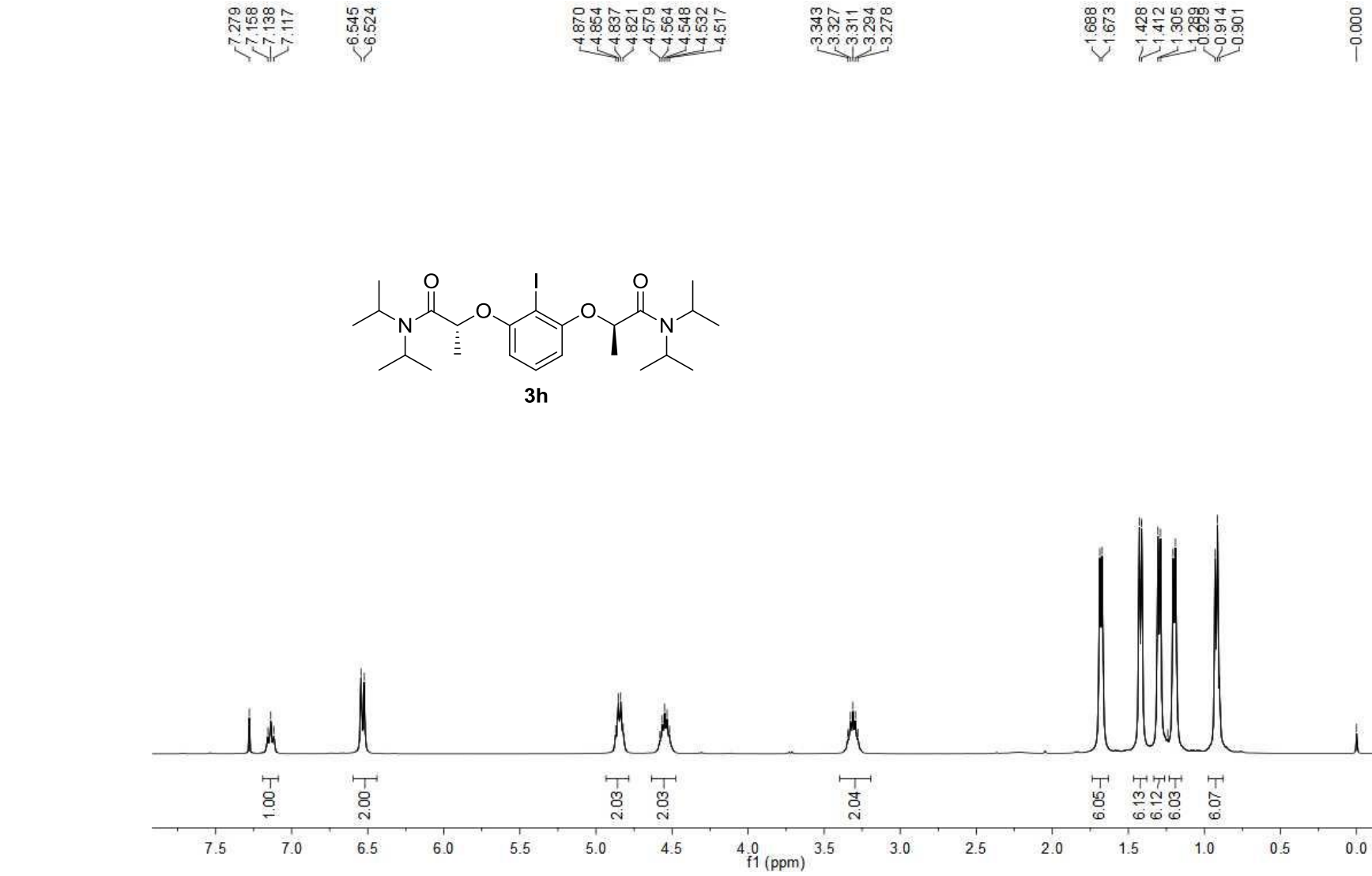
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2.03
2.04
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6.13
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6.07
7.5
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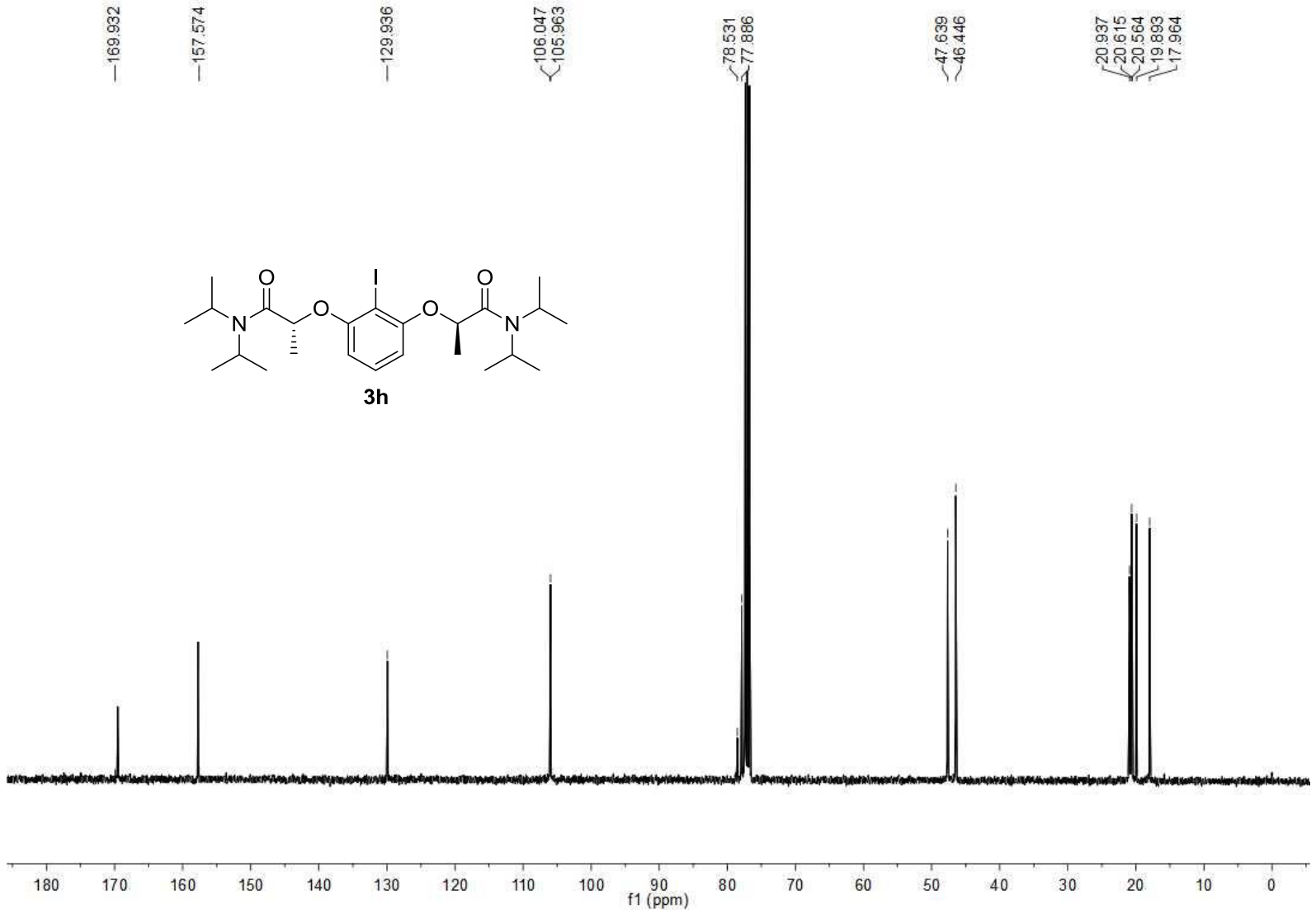
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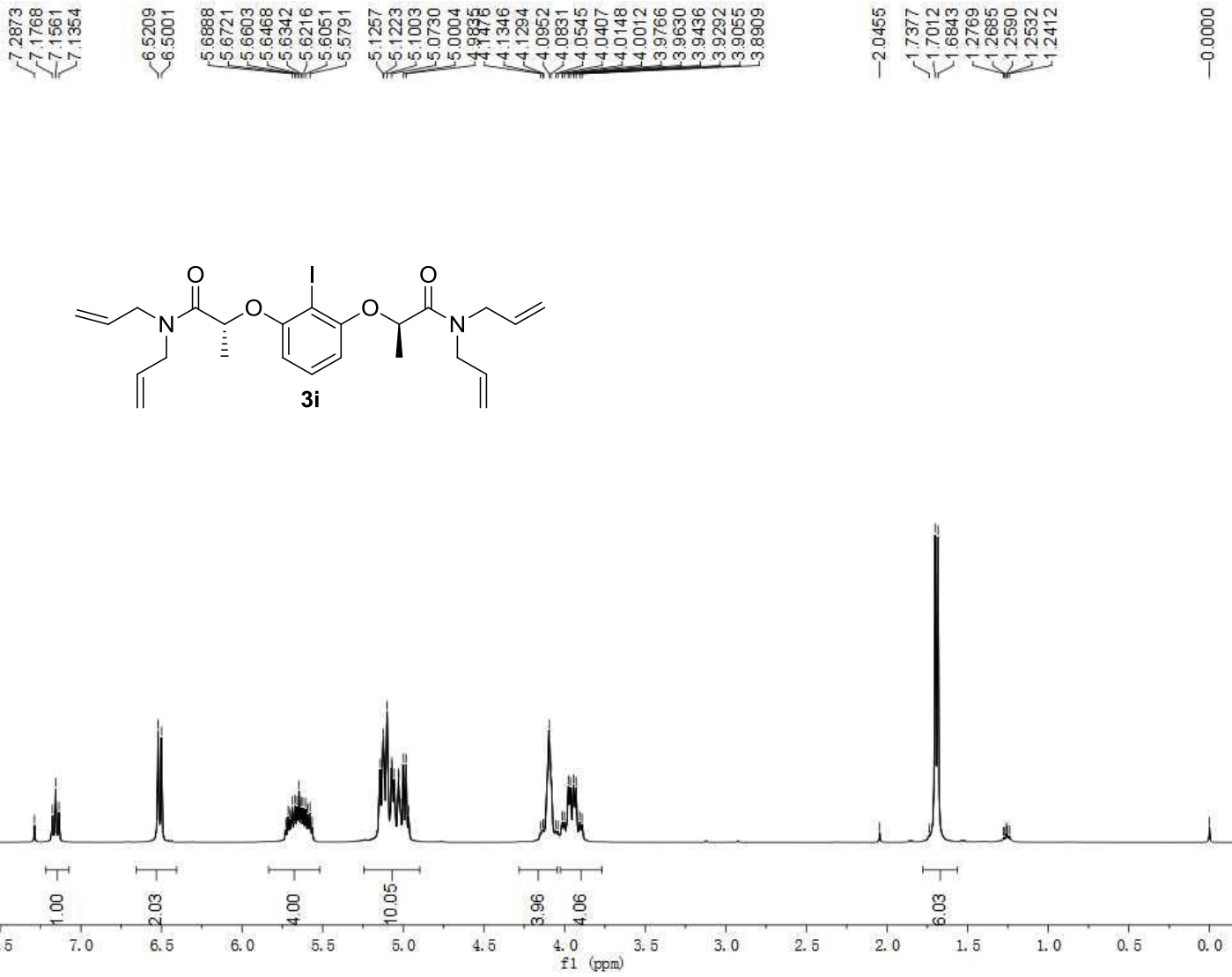
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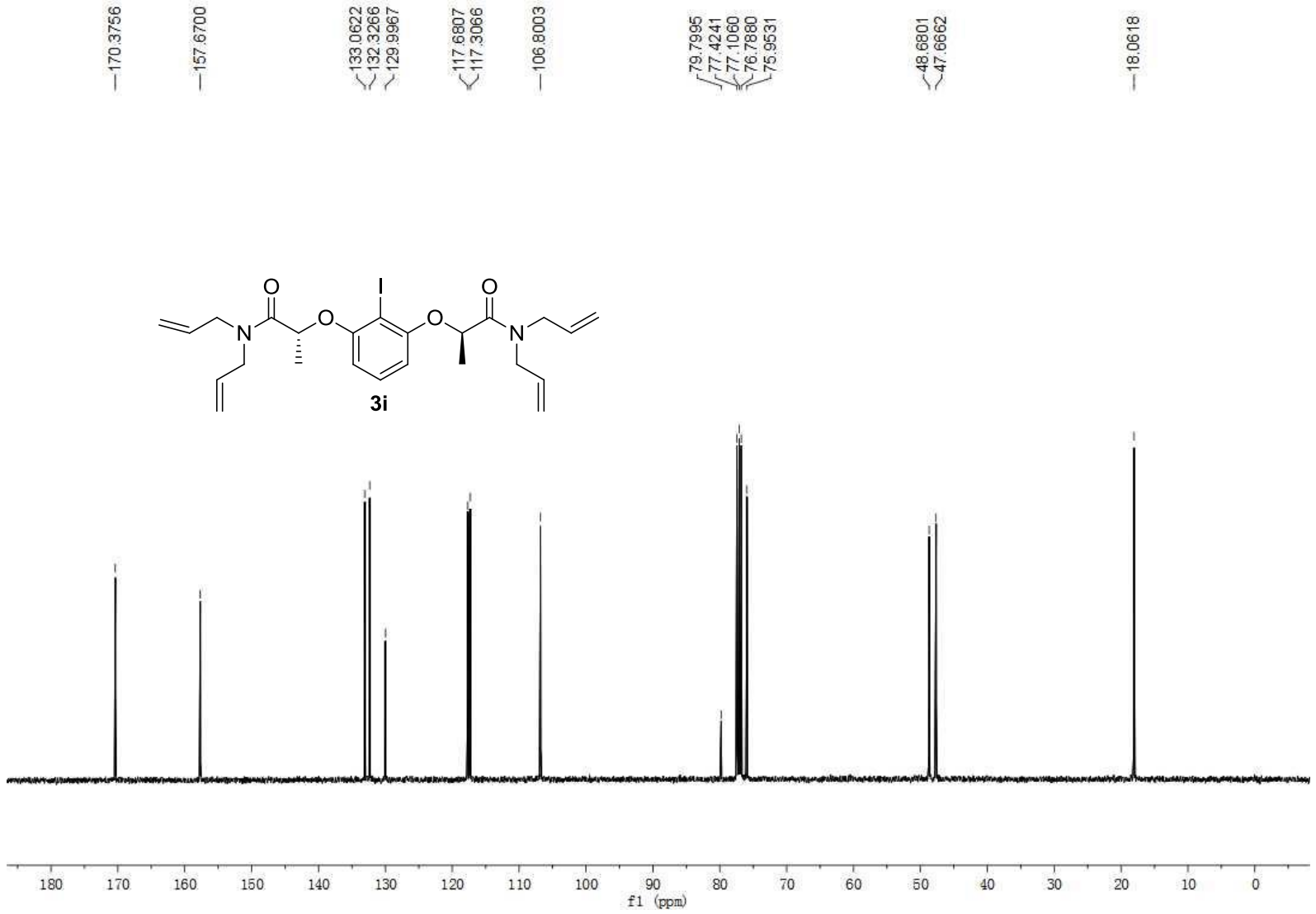
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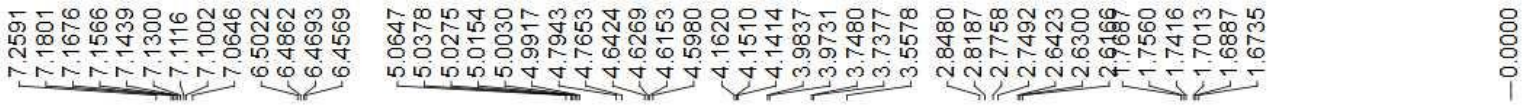
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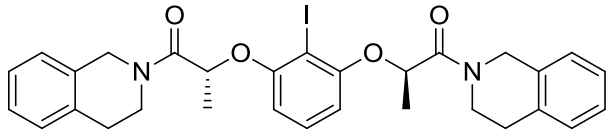

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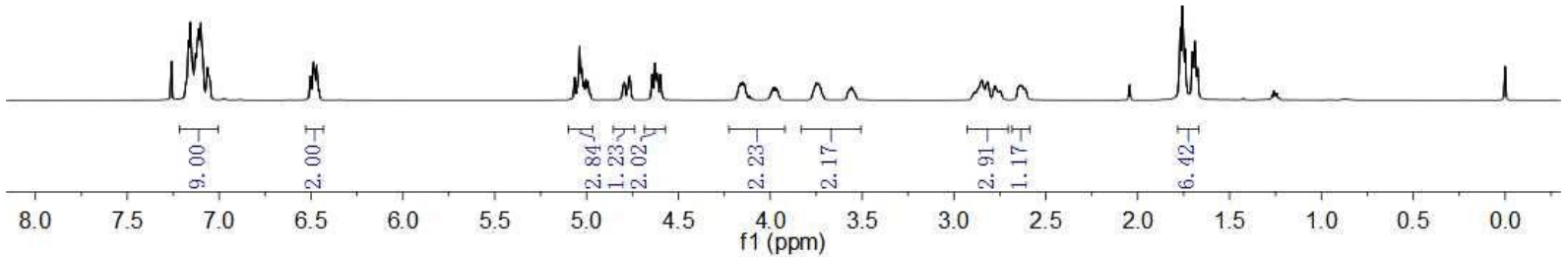
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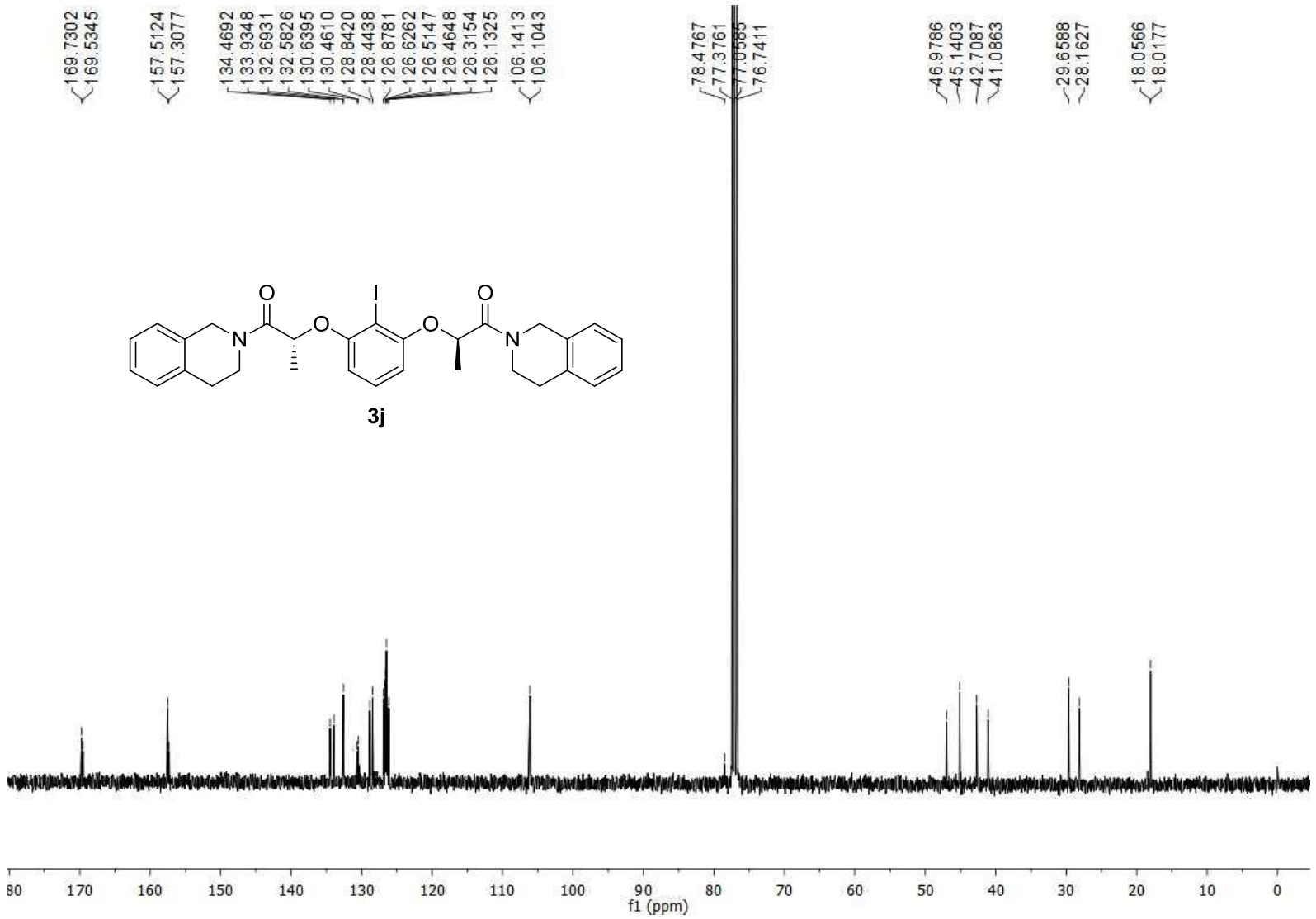
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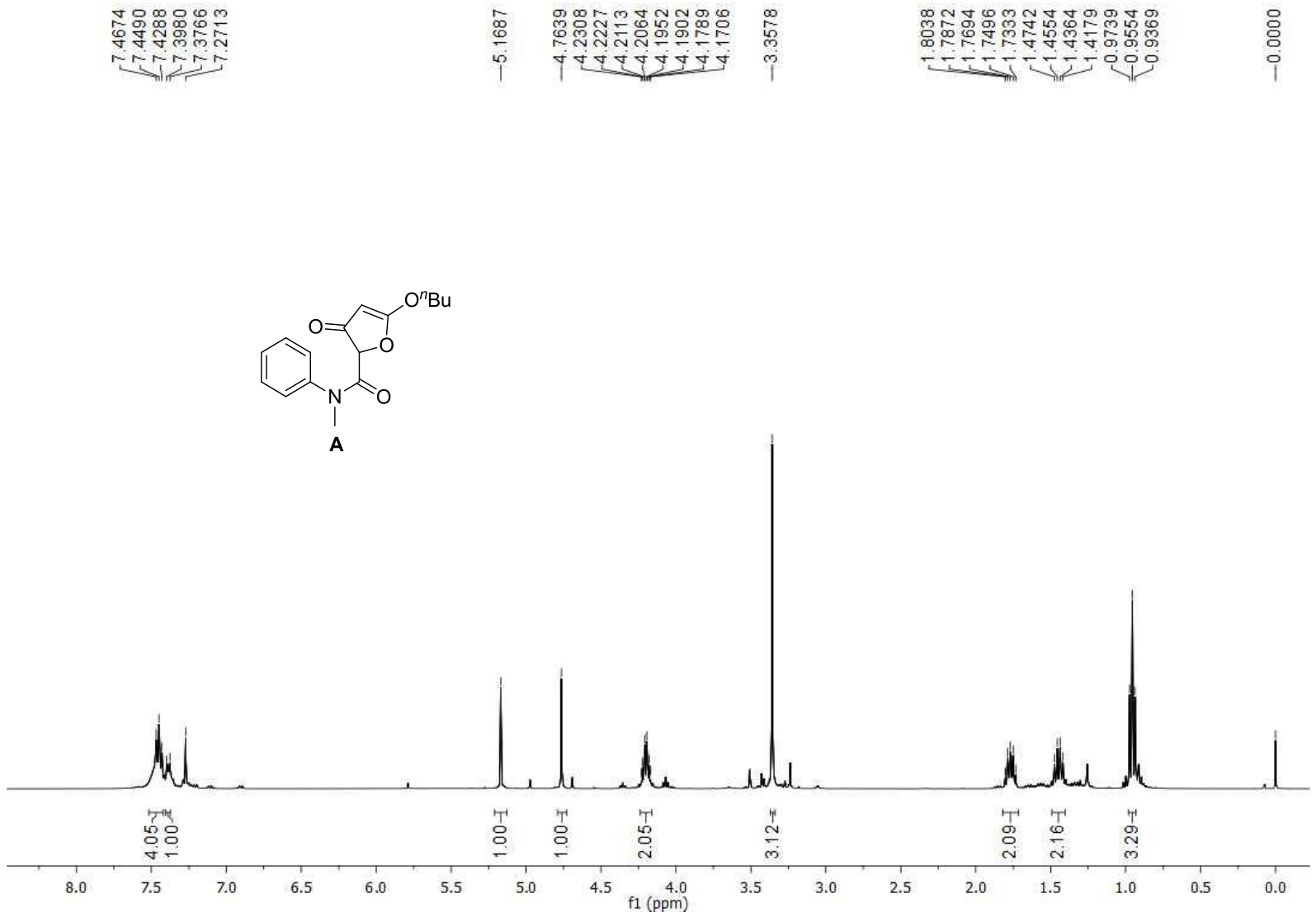
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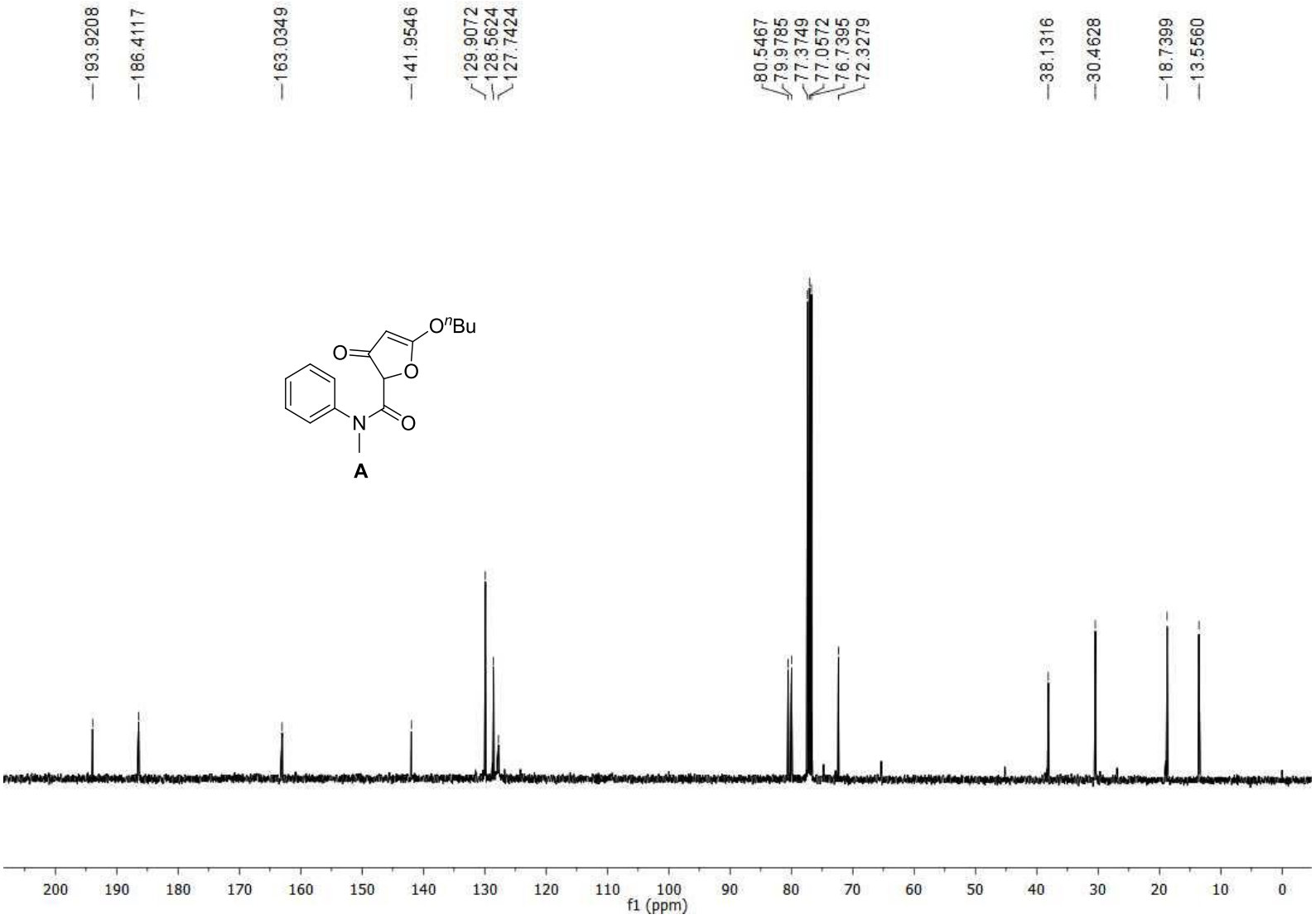
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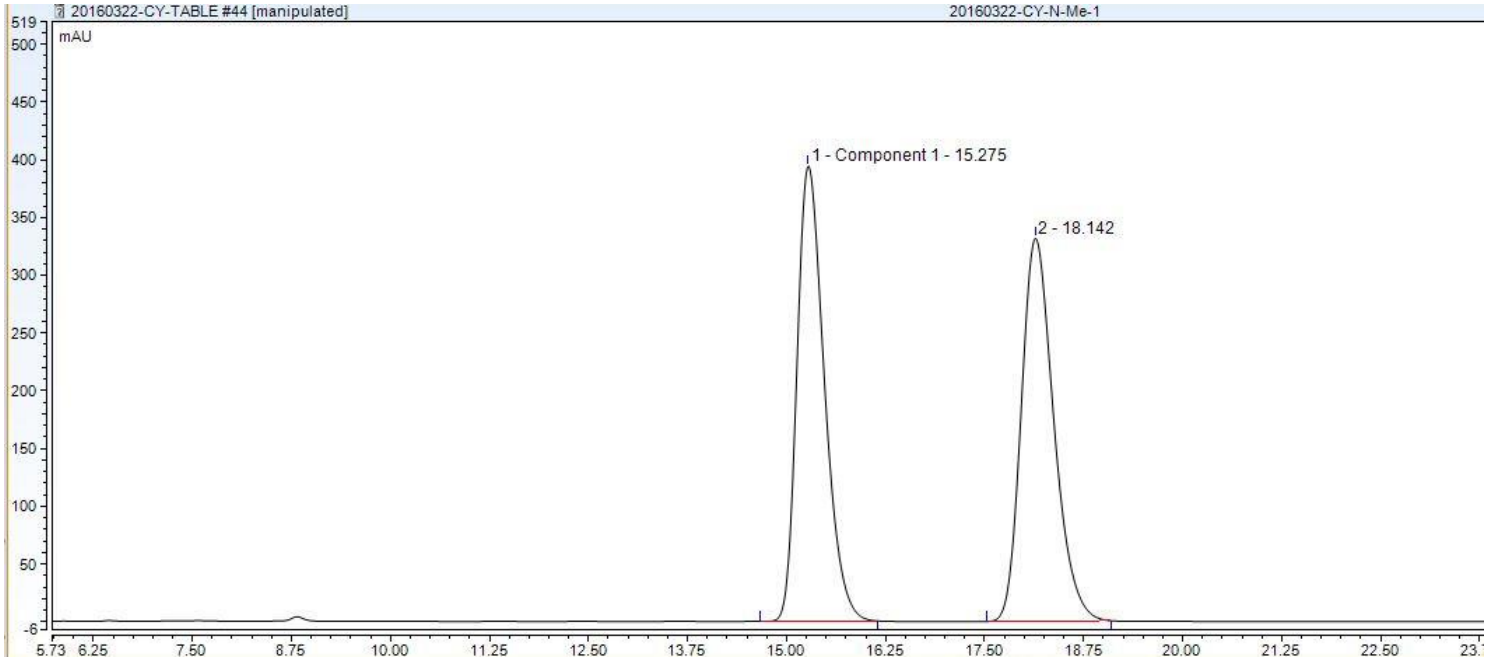
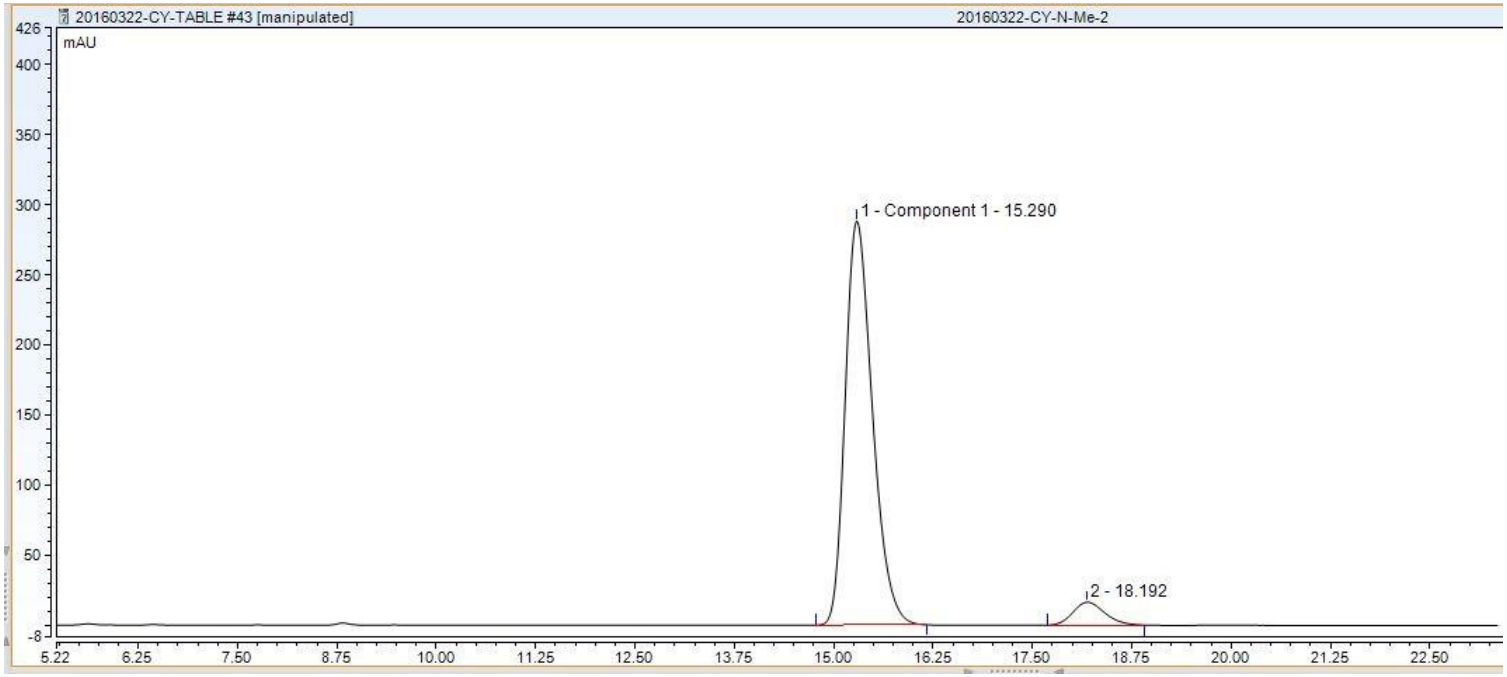
2a



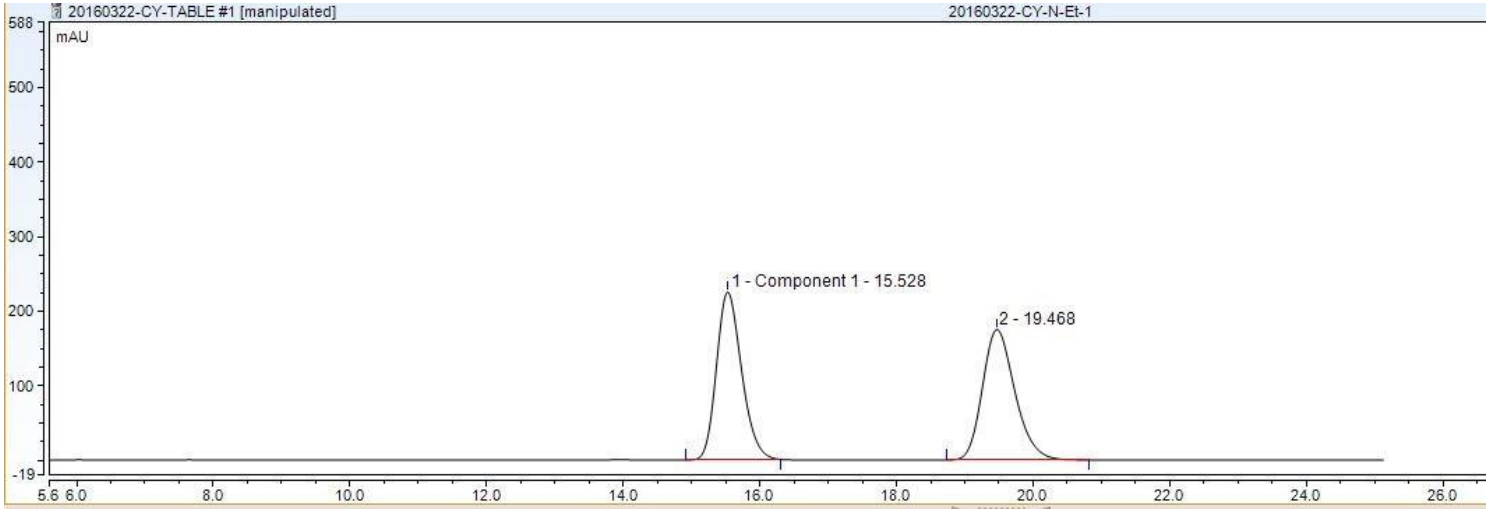
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	15.28	BMB*	0.369	157.6620	394.12	50.07
2	18.42	BMB*	0.435	157.2273	331.57	49.93

2a



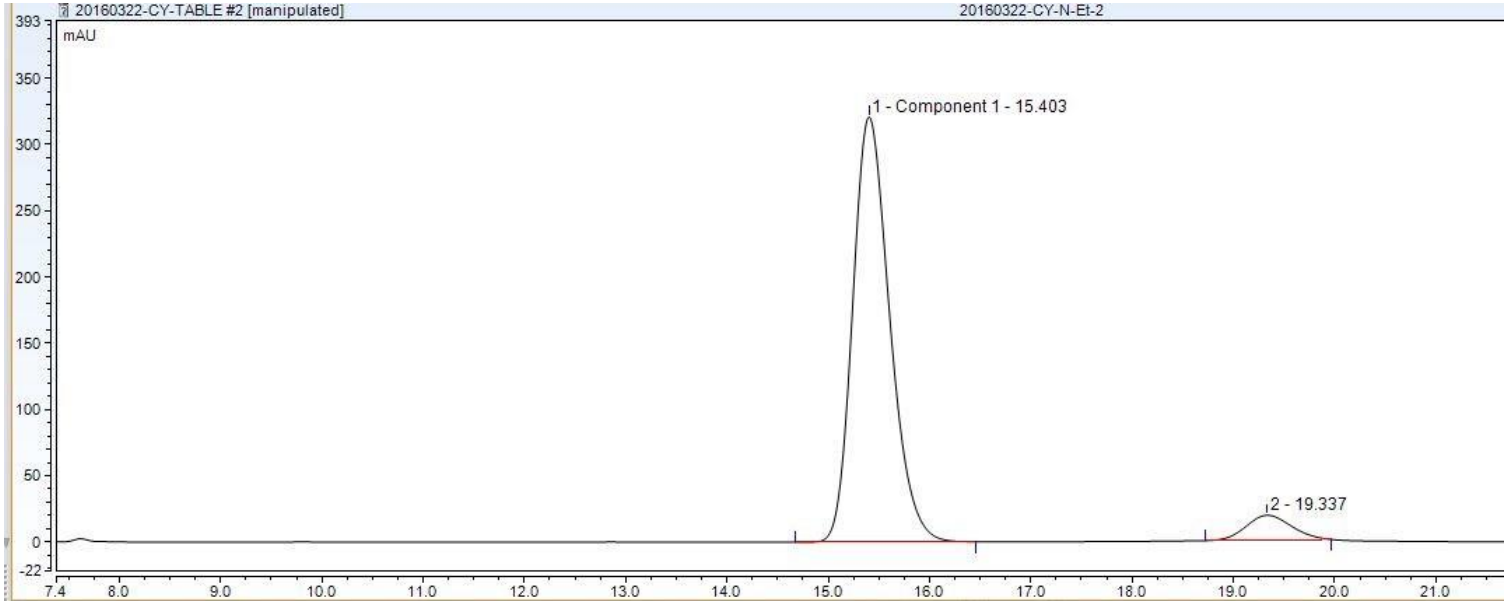
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	15.29	BMB*	0.365	114.5106	288.59	93.78
2	18.19	BMB*	0.430	7.5977	16.41	6.22

2b



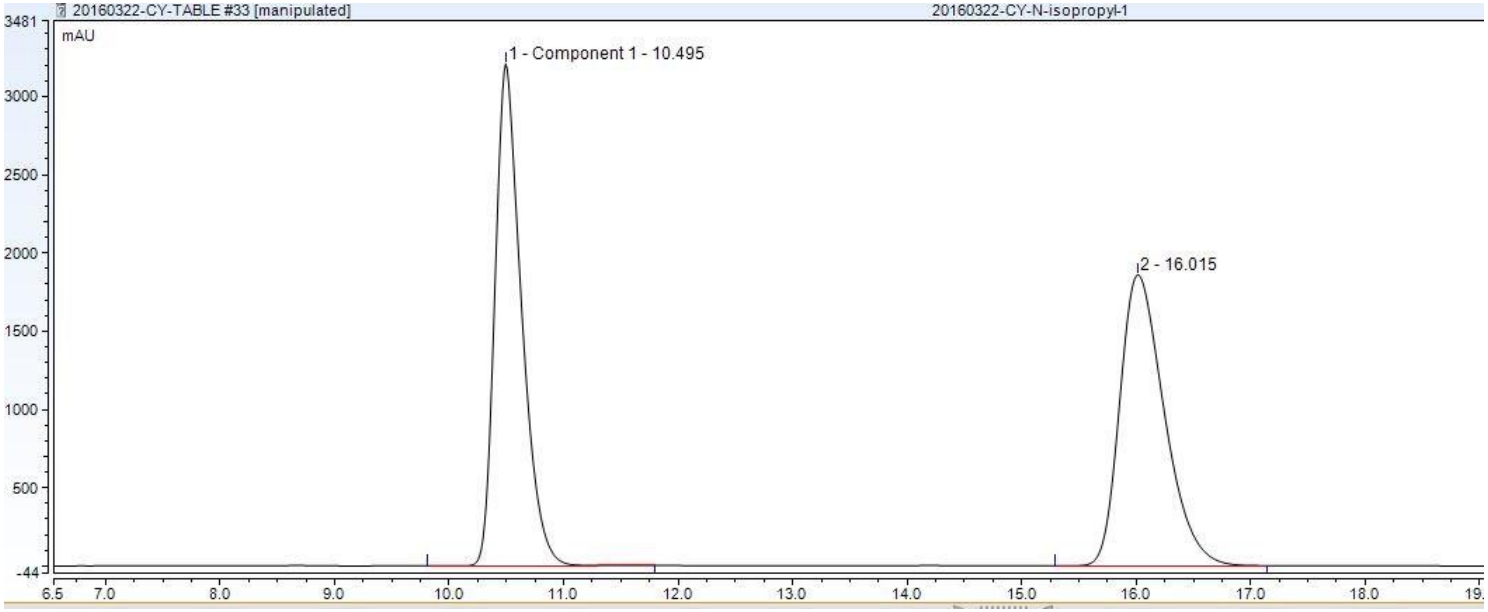
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	15.53	BMB*	0.394	95.9105	225.18	49.86
2	19.47	BMB*	0.505	96.4636	175.23	50.14

2b



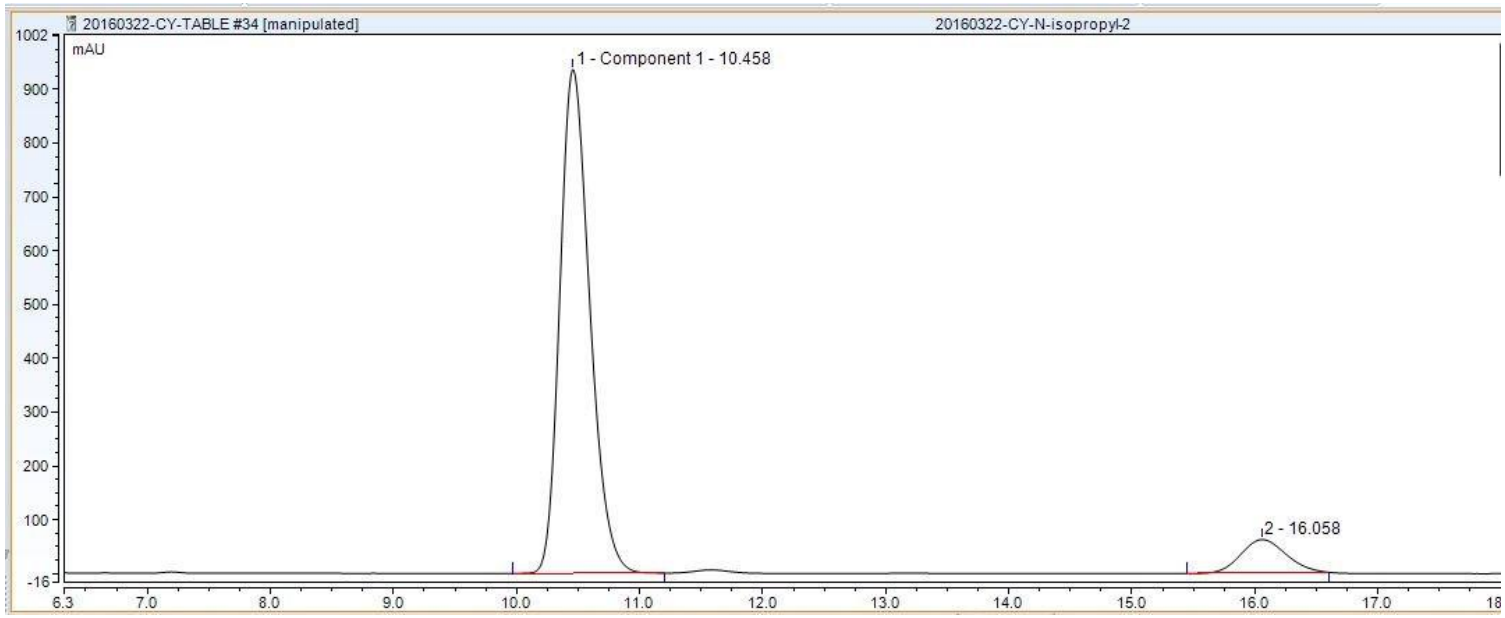
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	15.40	BMB*	0.389	135.5745	320.87	93.32
2	19.34	BMB*	0.488	9.7012	18.75	6.68

2c



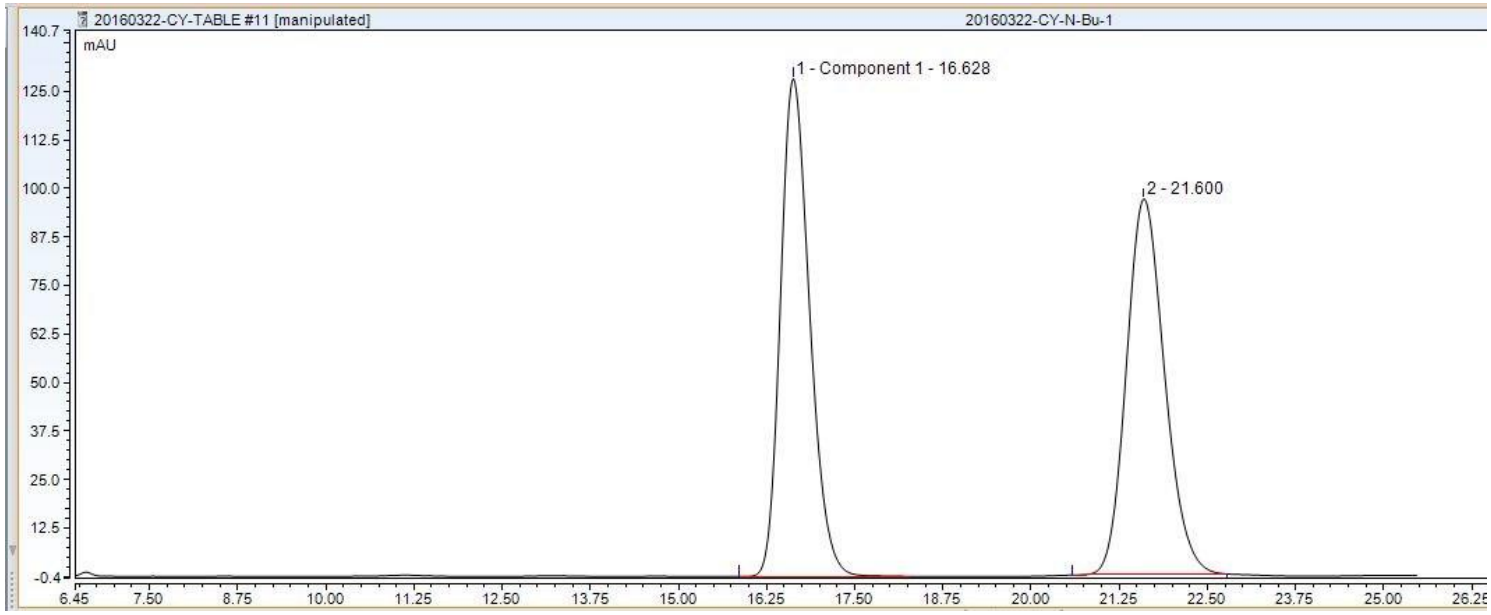
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	10.50	BMB*	0.245	858.0904	3206.08	50.66
2	16.02	BMB*	0.415	853.7206	1859.07	49.34

2c



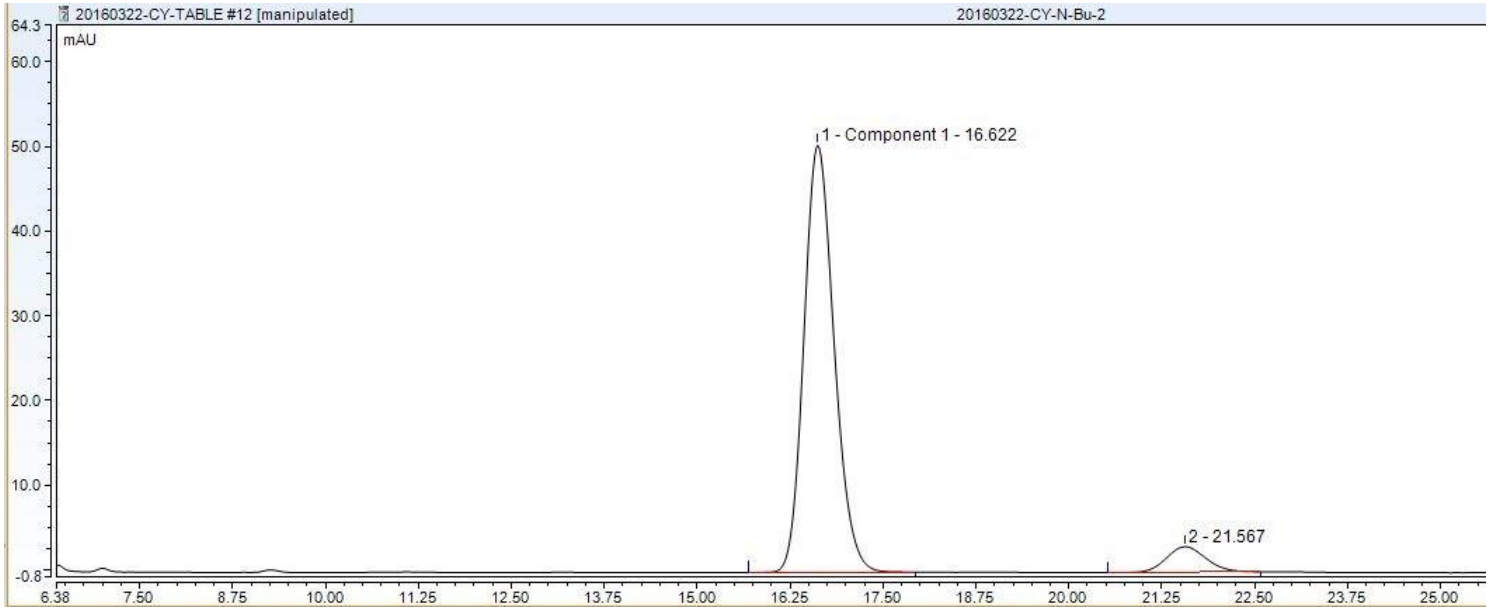
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	10.46	BMB*	0.260	263.8111	937.31	90.89
2	16.06	BMB*	0.400	26.4302	62.07	9.11

2d



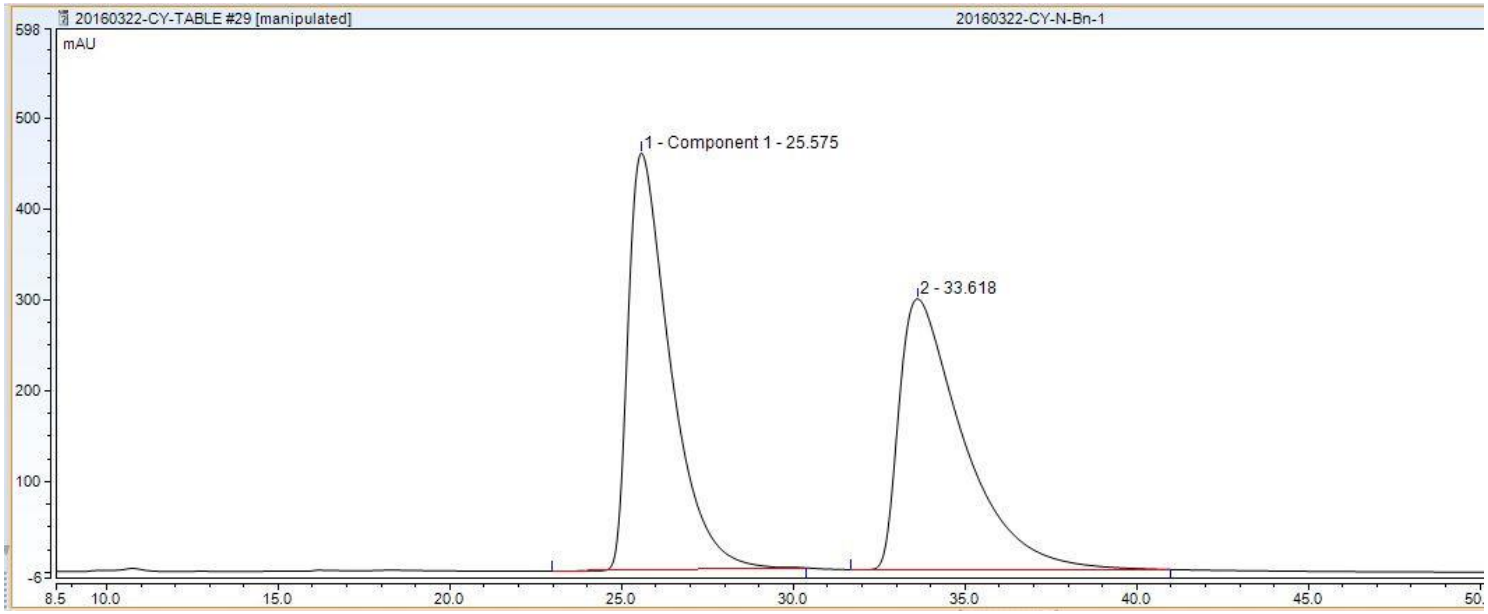
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	16.63	BMB*	0.442	61.4744	128.30	50.29
2	21.60	BMB*	0.580	60.7541	96.82	49.71

2d



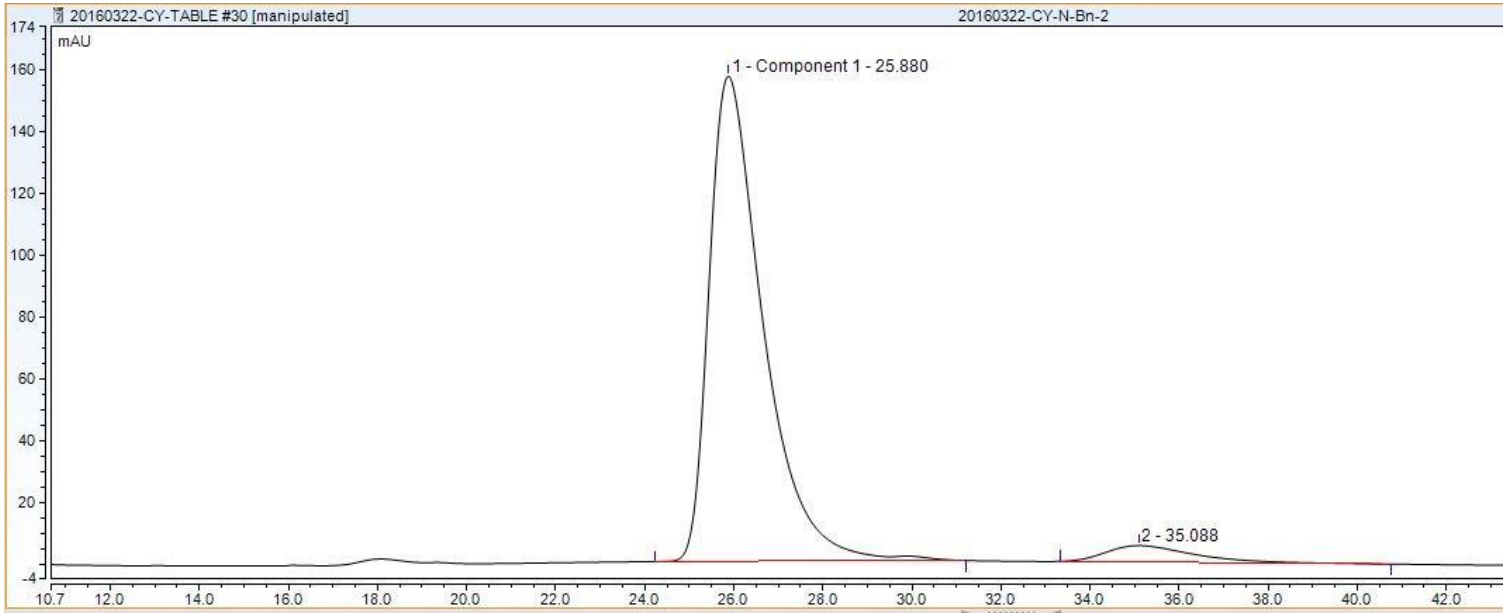
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	16.62	BMB*	0.435	23.7391	50.43	92.80
2	21.57	BMB*	0.571	1.8412	3.01	7.20

2e



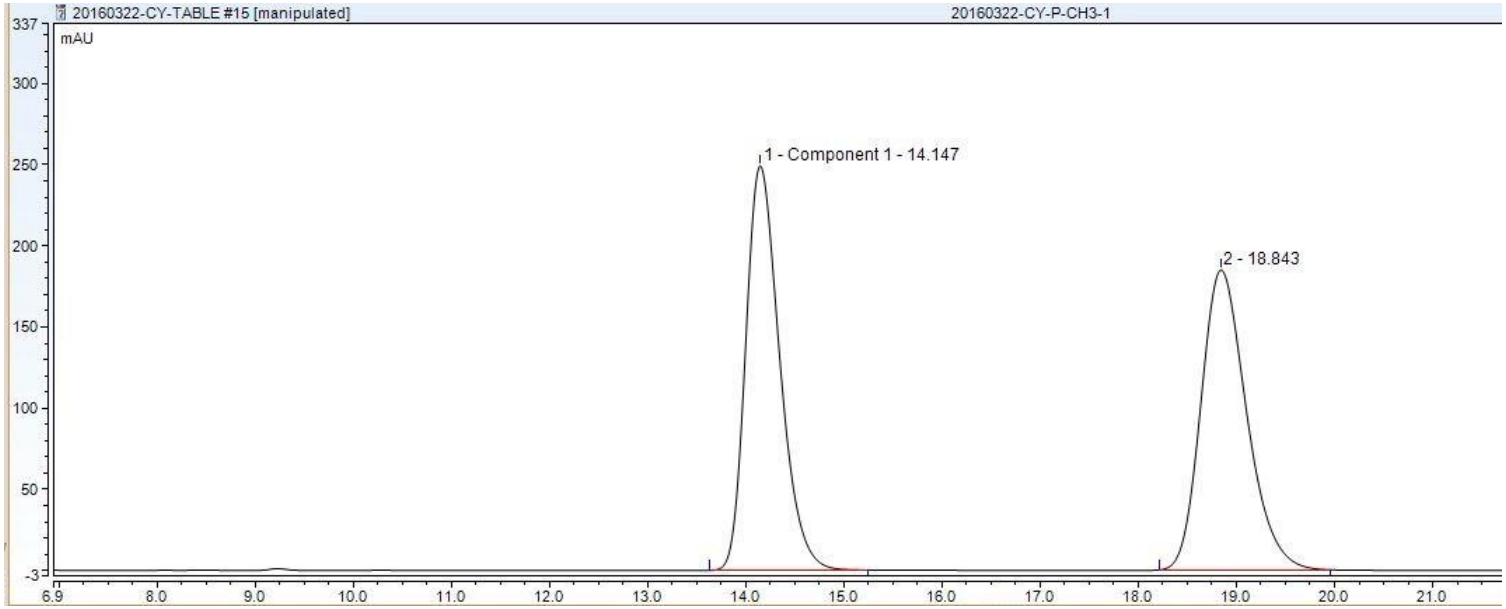
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	25.58	BMB*	1.268	651.6989	459.21	50.22
2	33.62	BMB*	1.903	646.0428	298.24	49.78

2e



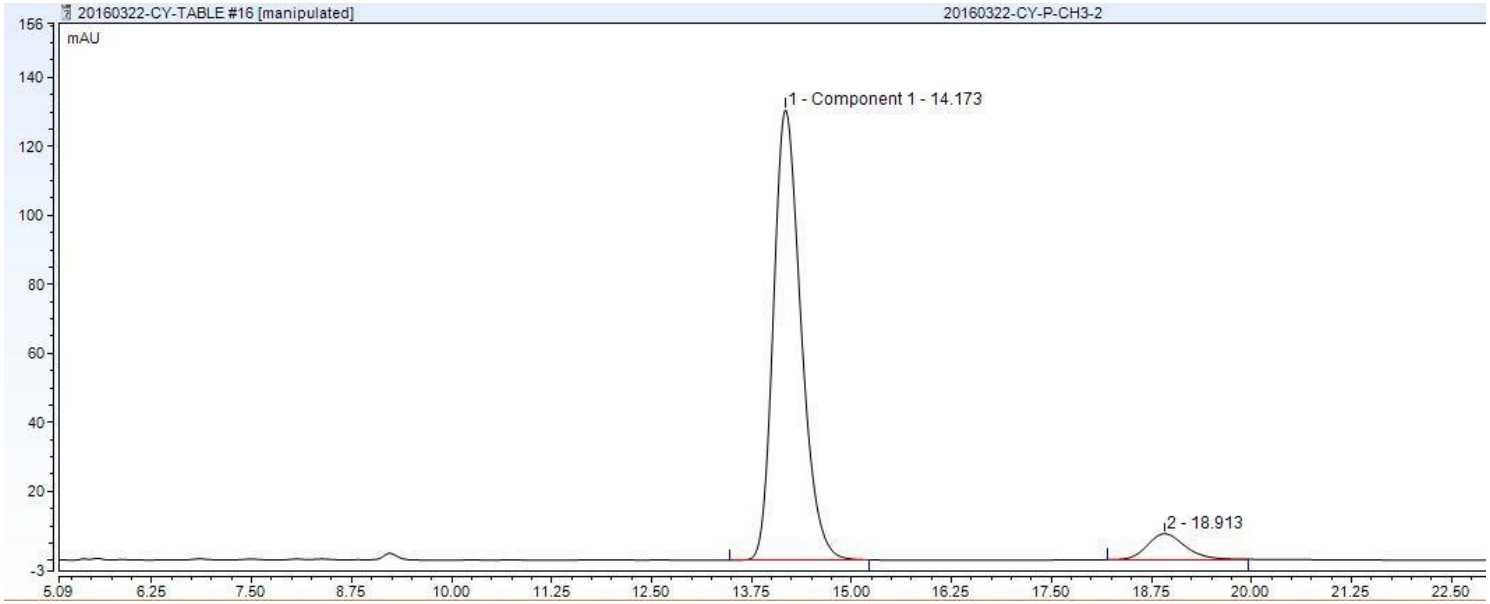
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	25.89	BMB*	1.241	220.7252	156.73	94.75
2	35.09	BMB*	2.053	12.2295	5.30	5.25

2f



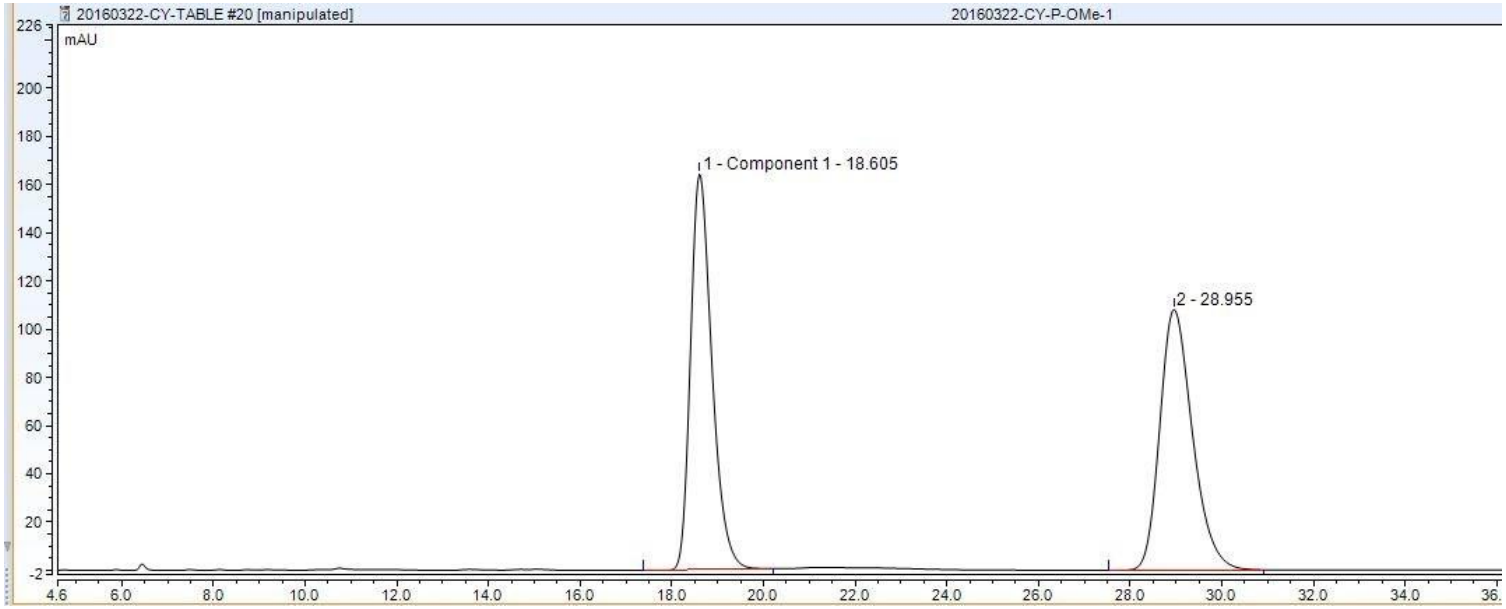
Peak #	RetTime [min]	Type	Width [min]	Area mAu *s	Height [mAu]	Area %
1	14.15	BMB*	0.368	99.7924	249.31	50.13
2	18.84	BMB*	0.494	99.2606	184.88	49.87

2f



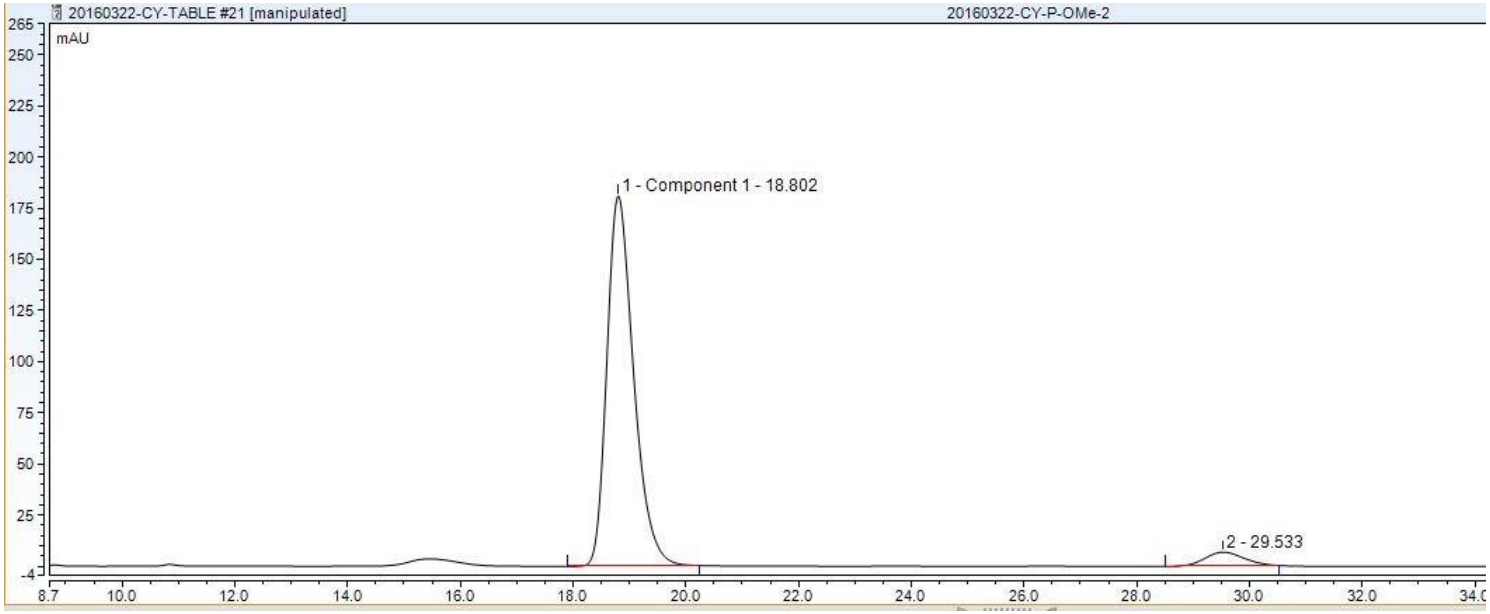
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.17	BMB*	0.365	51.9919	130.51	92.70
2	18.91	BMB*	0.499	4.0969	7.50	7.30

2g



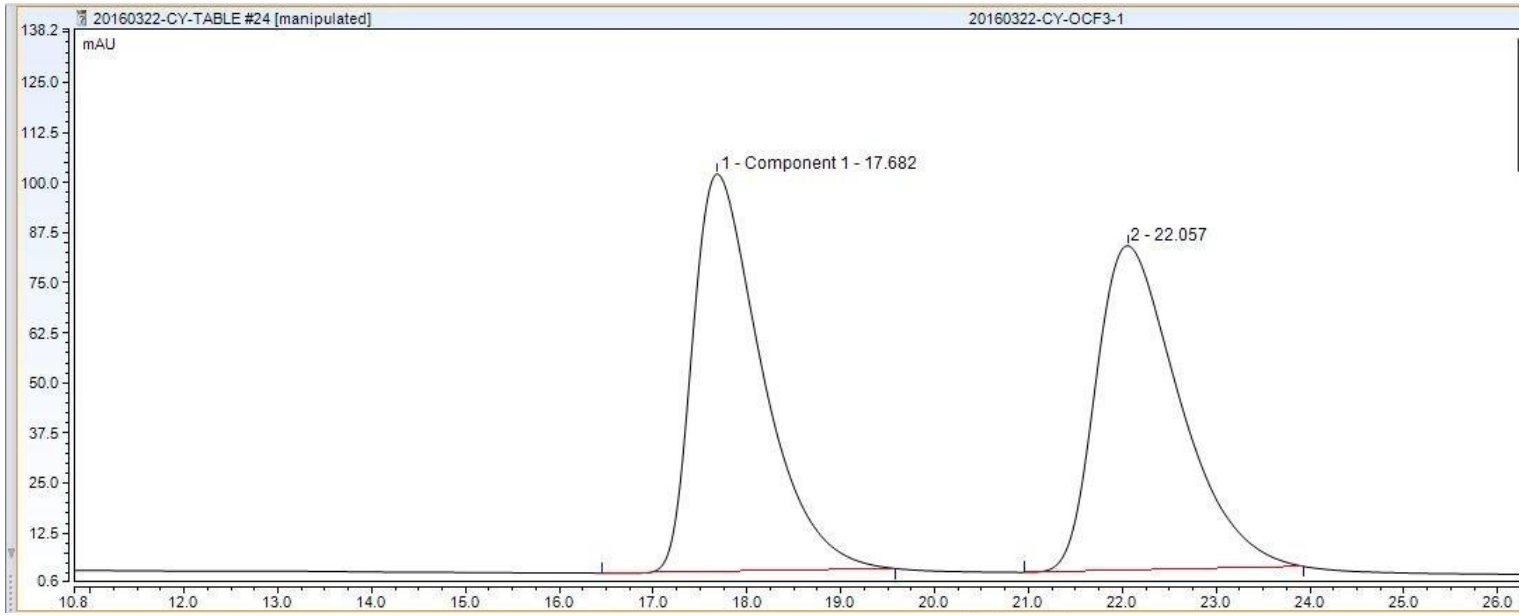
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	18.61	BMB*	0.492	88.6177	164.27	49.83
2	28.96	BMB*	0.754	89.2242	108.20	50.17

2g



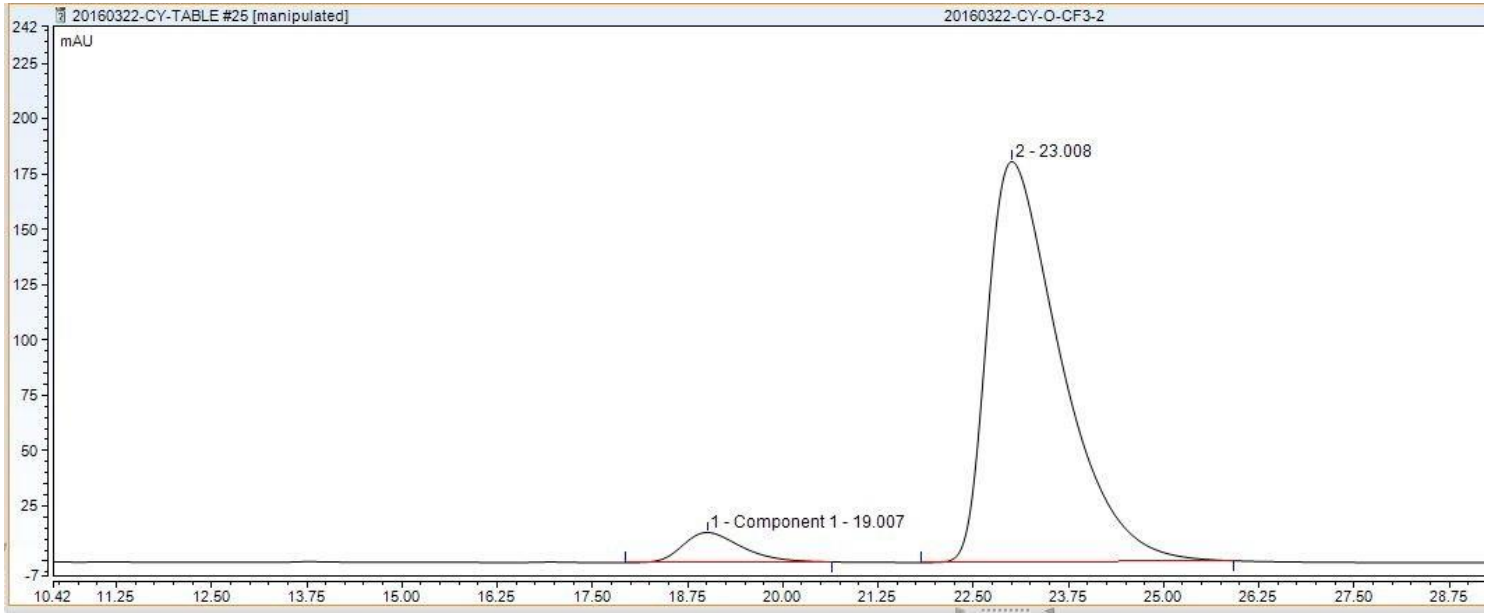
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	18.80	BMB*	0.499	99.2181	180.90	94.86
2	29.53	BMB*	0.755	5.3753	6.72	5.14

2h



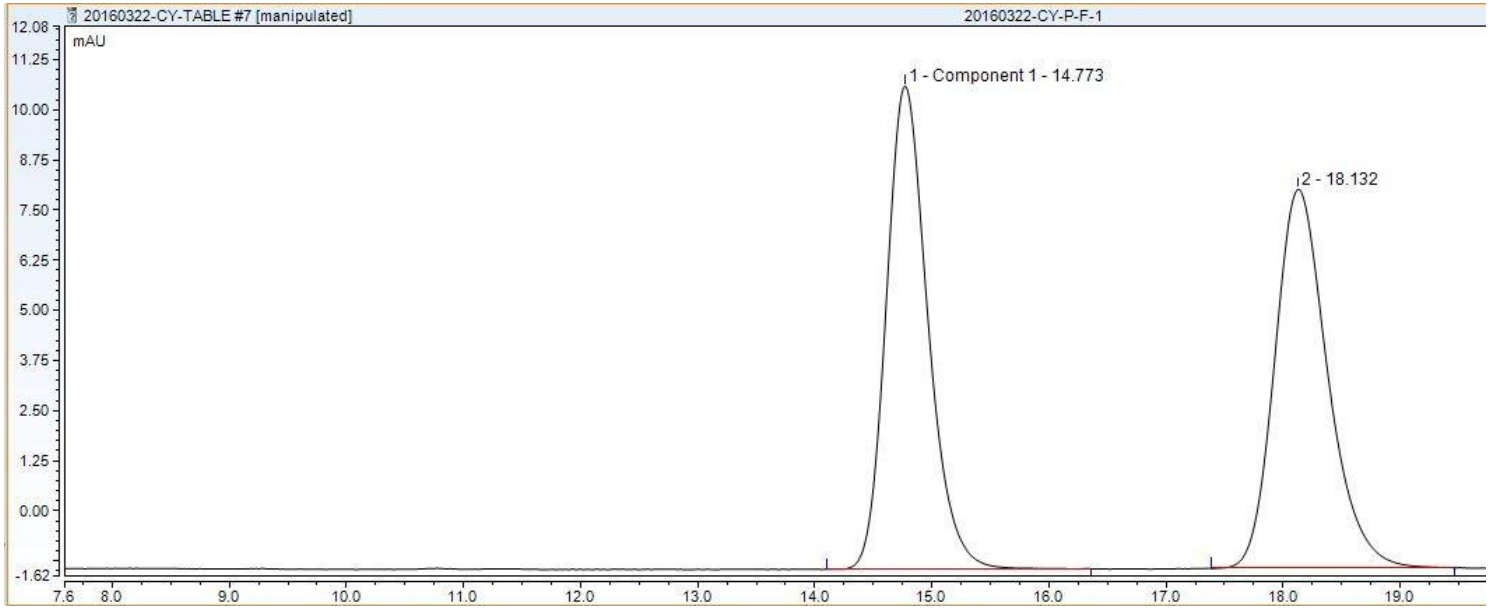
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	17.68	BMB*	0.776	84.5080	99.14	50.29
2	22.06	BMB*	0.995	83.5449	80.94	49.71

2h



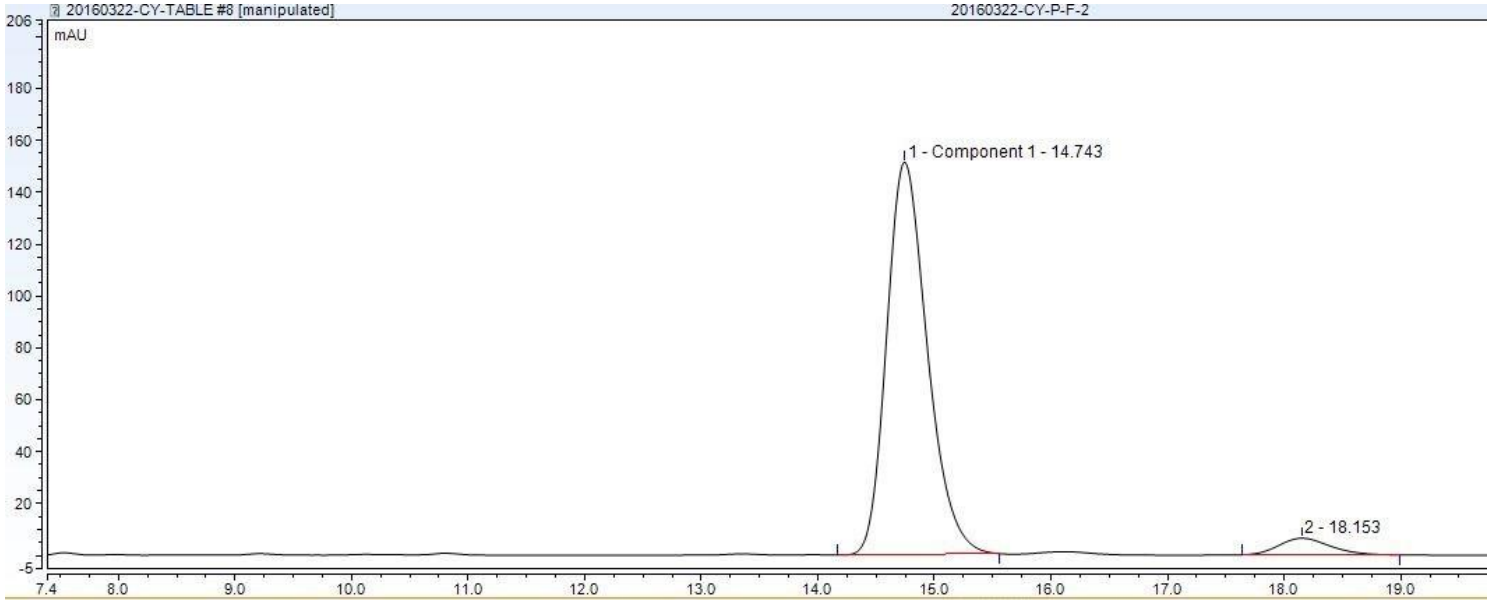
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	19.01	BMB*	0.822	12.0799	13.47	5.65
2	23.01	BMB*	1.016	201.8550	180.90	94.35

2i



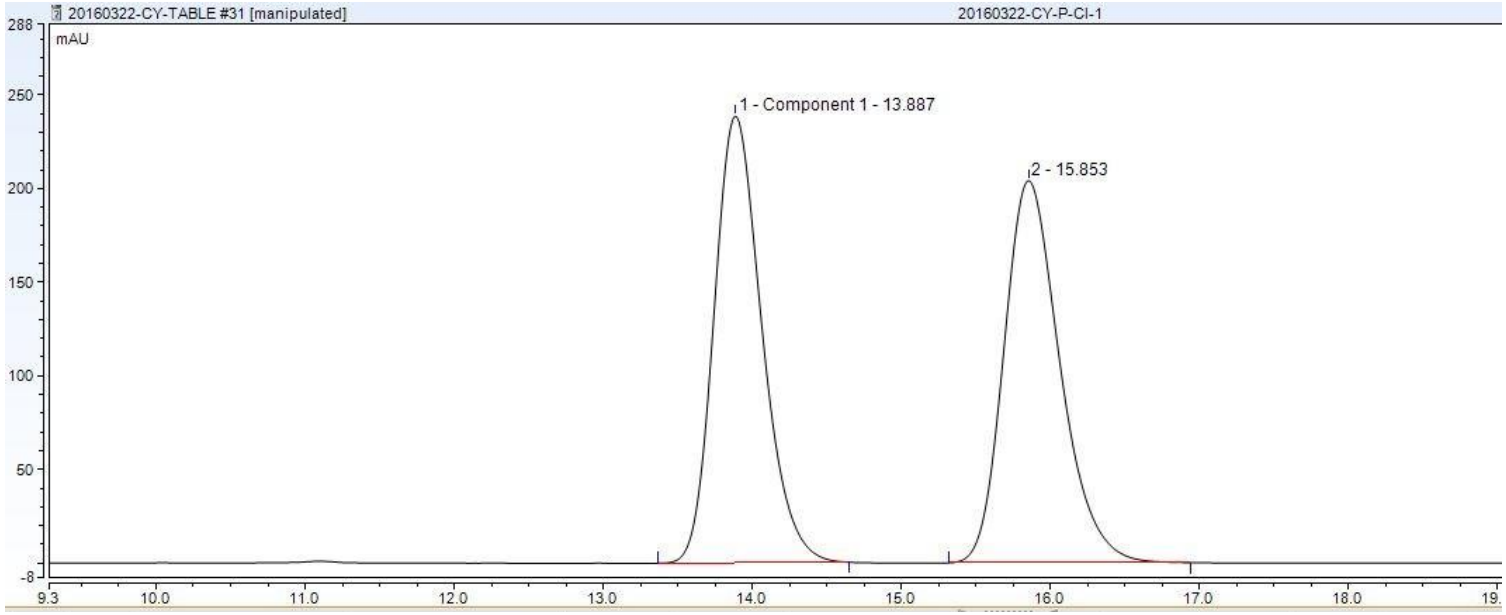
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.77	BMB*	0.374	4.9480	12.05	50.06
2	18.13	BMB*	0.475	4.9352	9.46	49.94

2i



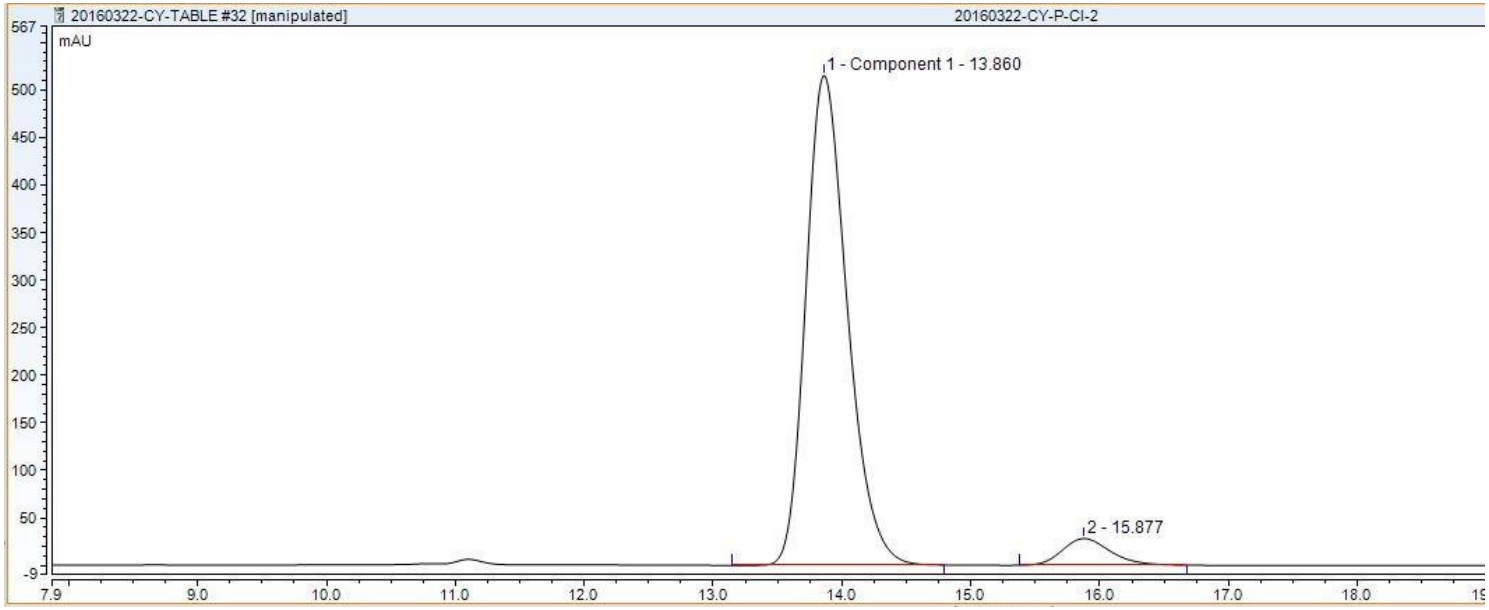
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.74	BMB*	0.371	61.1405	151.32	94.90
2	18.15	BMB*	0.474	3.2840	6.43	5.10

2j



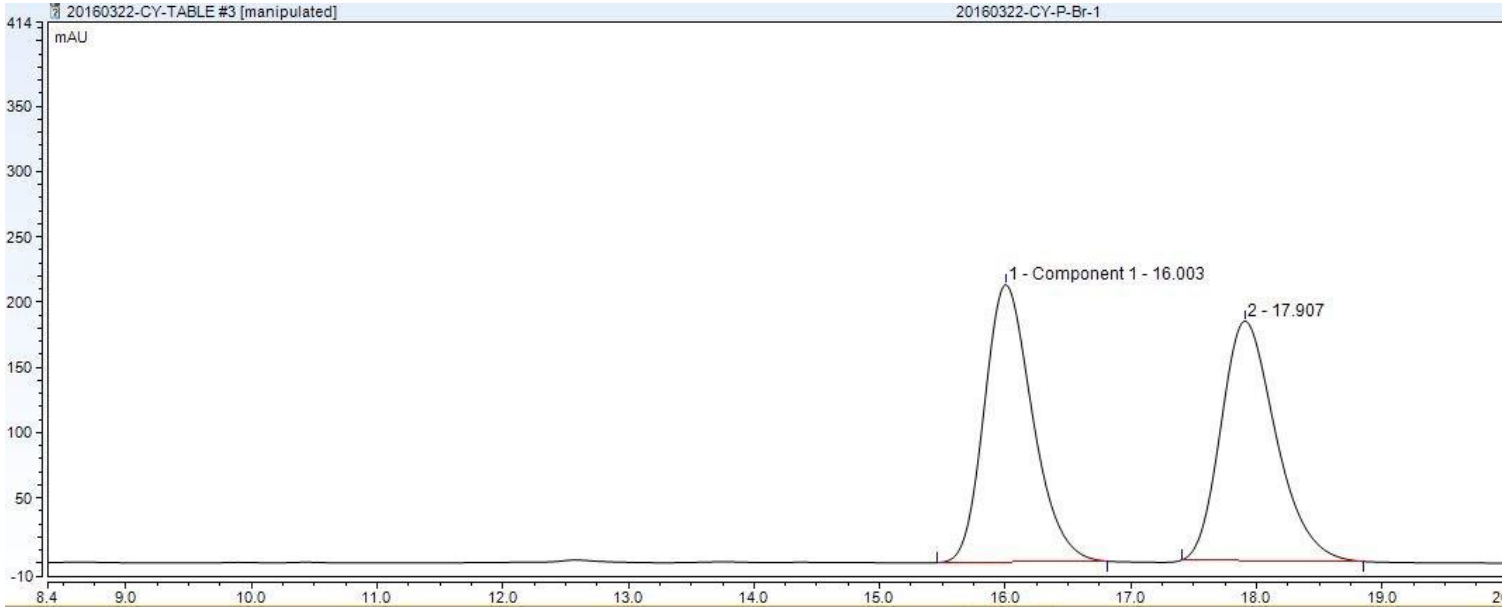
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	13.89	BMB*	0.342	88.6503	238.57	49.99
2	15.85	BMB*	0.398	88.7015	204.09	50.01

2j



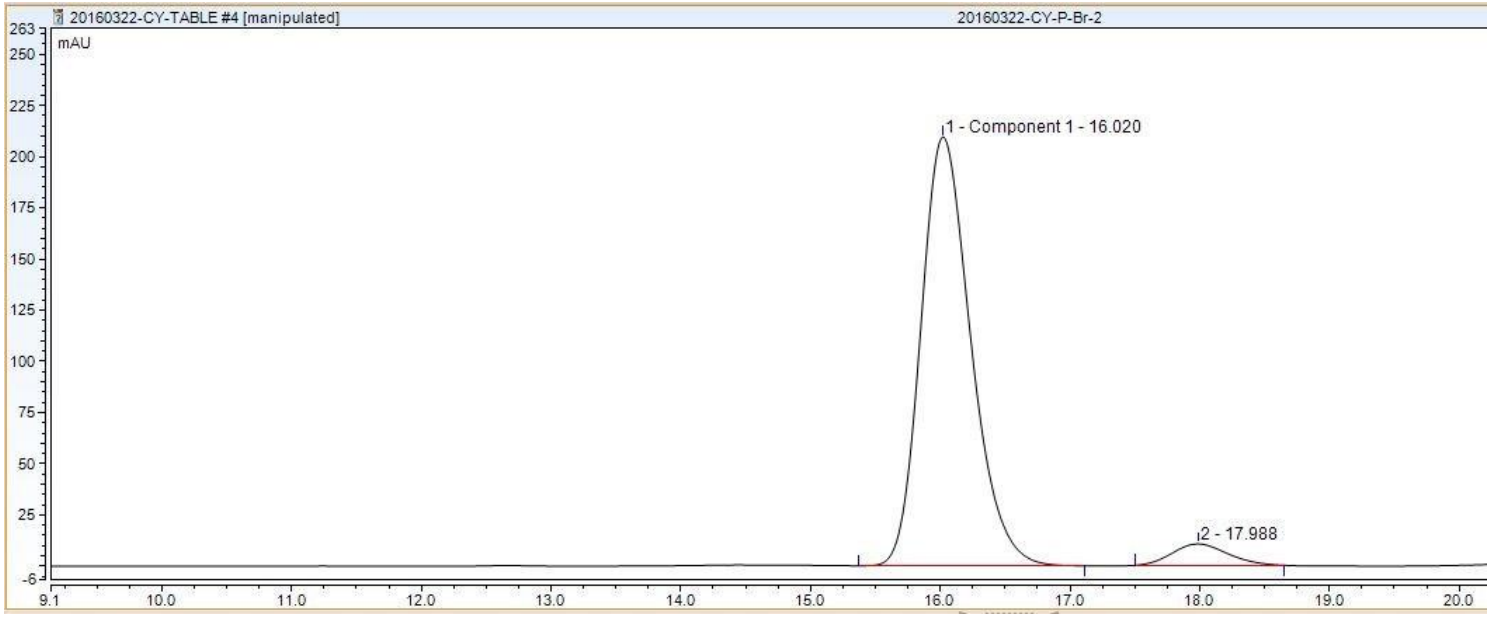
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	13.89	BMB*	0.342	192.0053	515.47	94.05
2	15.85	BMB*	0.396	12.1561	28.09	5.95

2k



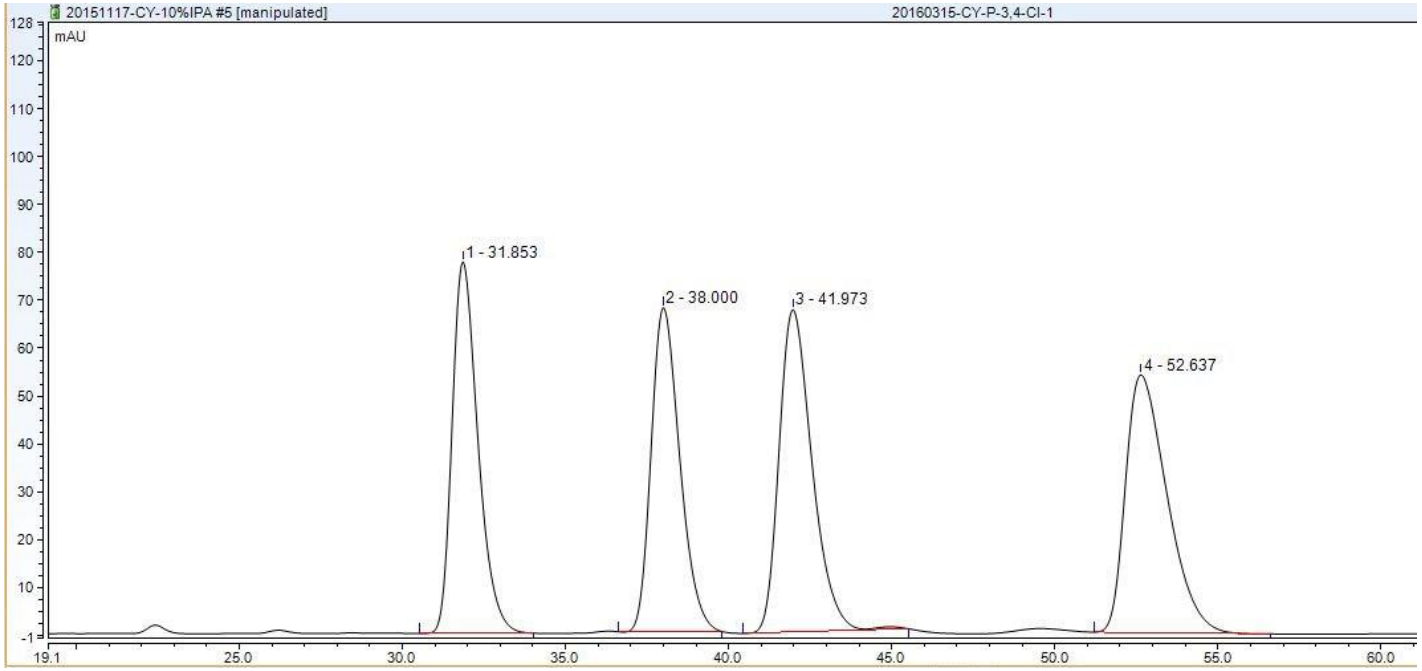
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	16.00	BMB*	0.409	94.1555	212.36	50.39
2	17.91	BMB*	0.466	92.7144	183.41	49.61

2k



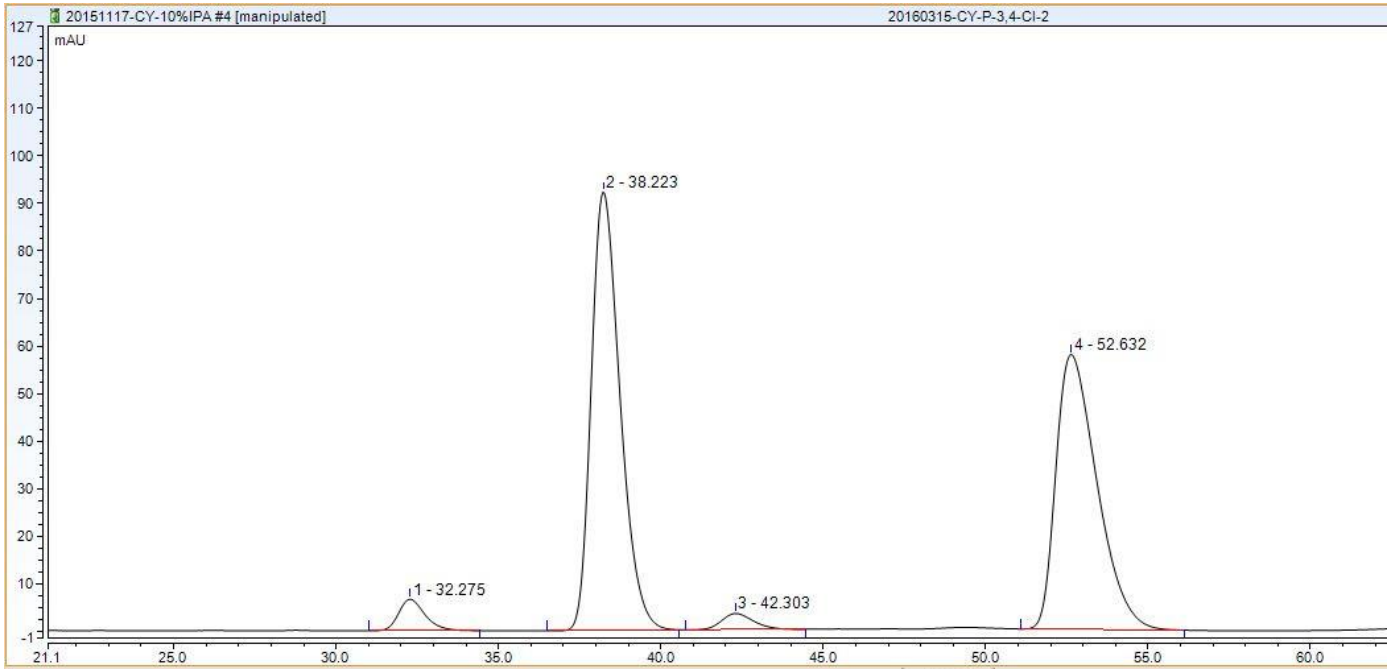
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	16.02	BMB*	0.409	93.4072	209.47	94.78
2	17.99	BMB*	0.465	5.1473	10.44	5.22

2l + 2l’



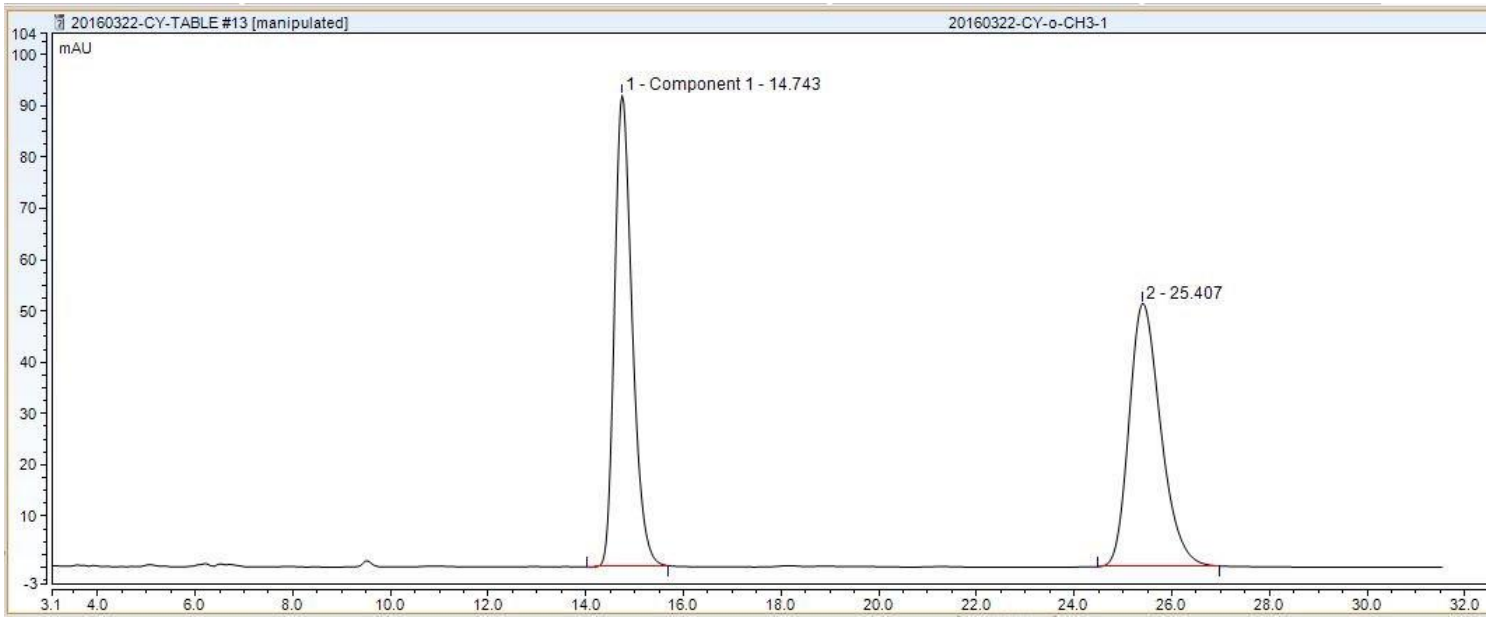
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	31.85	BMB*	0.837	71.1203	77.60	23.85
2	38.00	BMB*	0.943	68.8646	67.69	23.10
3	41.97	BMB*	1.072	78.9083	67.34	26.47
4	52.64	BMB*	1.374	79.2540	58.85	26.58

2l + 2l’



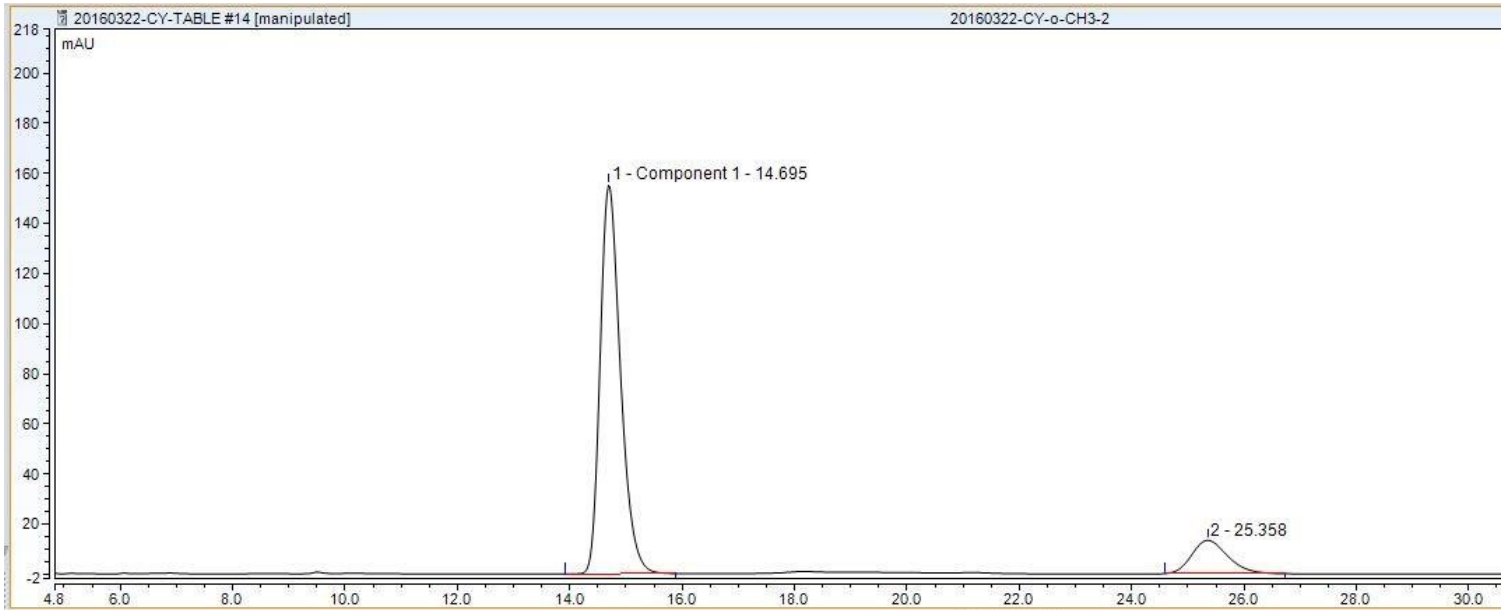
Peak #	RetTime [min]	Type	Width [min]	Area mAu ⋆s	Height [mAu]	Area %
1	32.28	BMB⋆	0.847	6.1198	6.59	3.24
2	38.22	BMB⋆	0.948	94.7447	92.18	50.10
3	42.30	BMB⋆	1.032	3.7100	3.35	1.96
4	52.63	BMB⋆	1.366	84.5221	57.74	44.70

2m



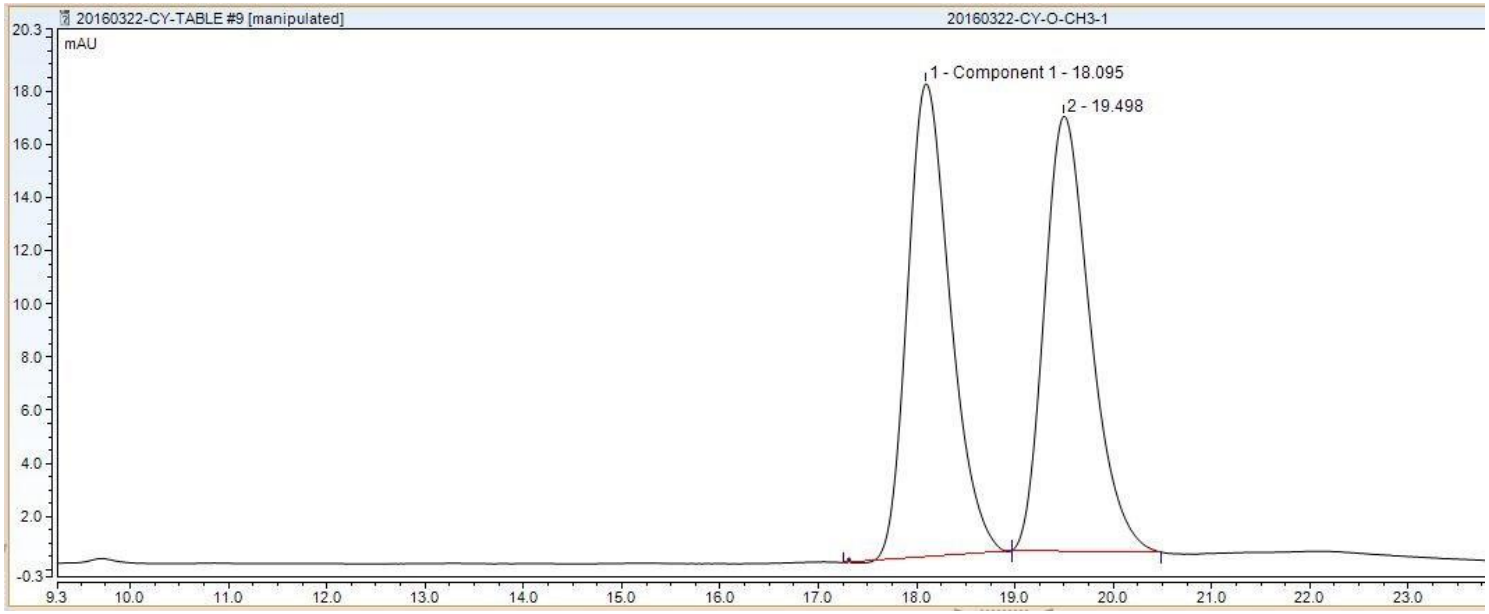
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.74	BMB*	0.384	38.5650	91.88	50.05
2	25.41	BMB*	0.688	38.4804	51.38	49.95

2m



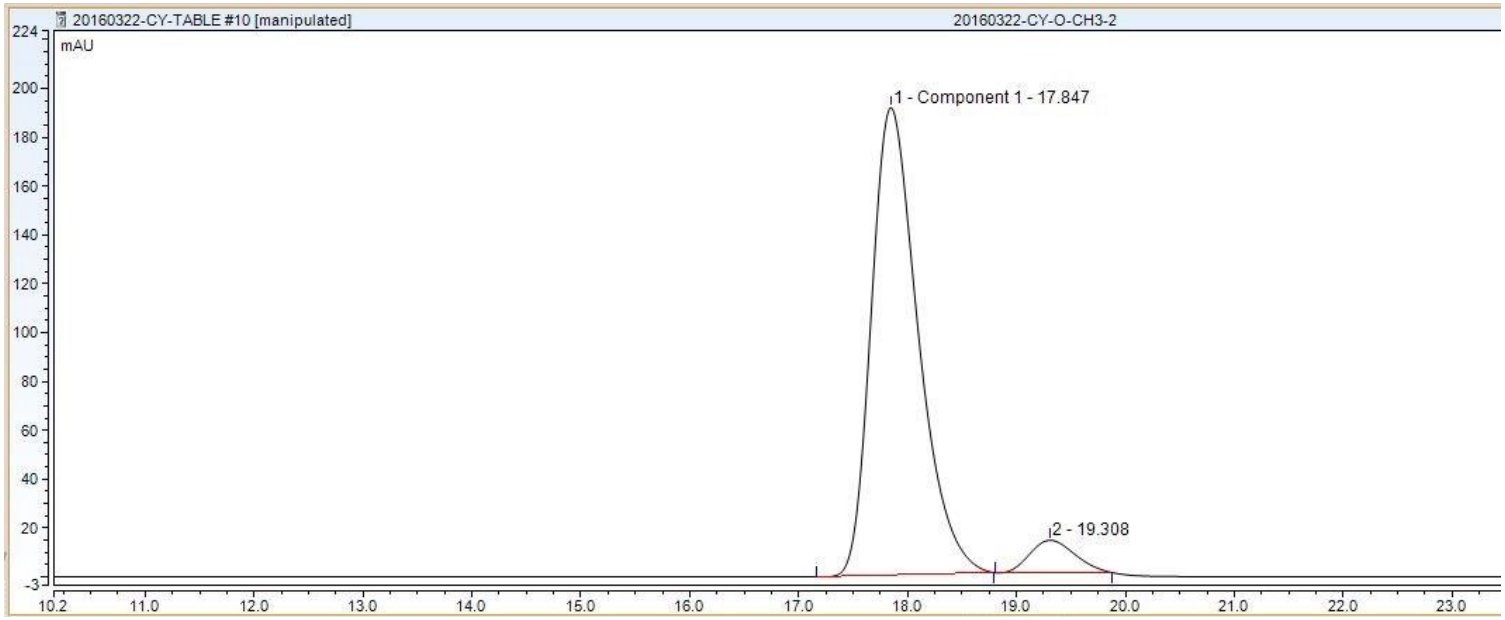
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.70	BMB*	0.382	64.9926	155.32	86.82
2	25.36	BMB*	0.684	9.8652	13.30	13.18

2n



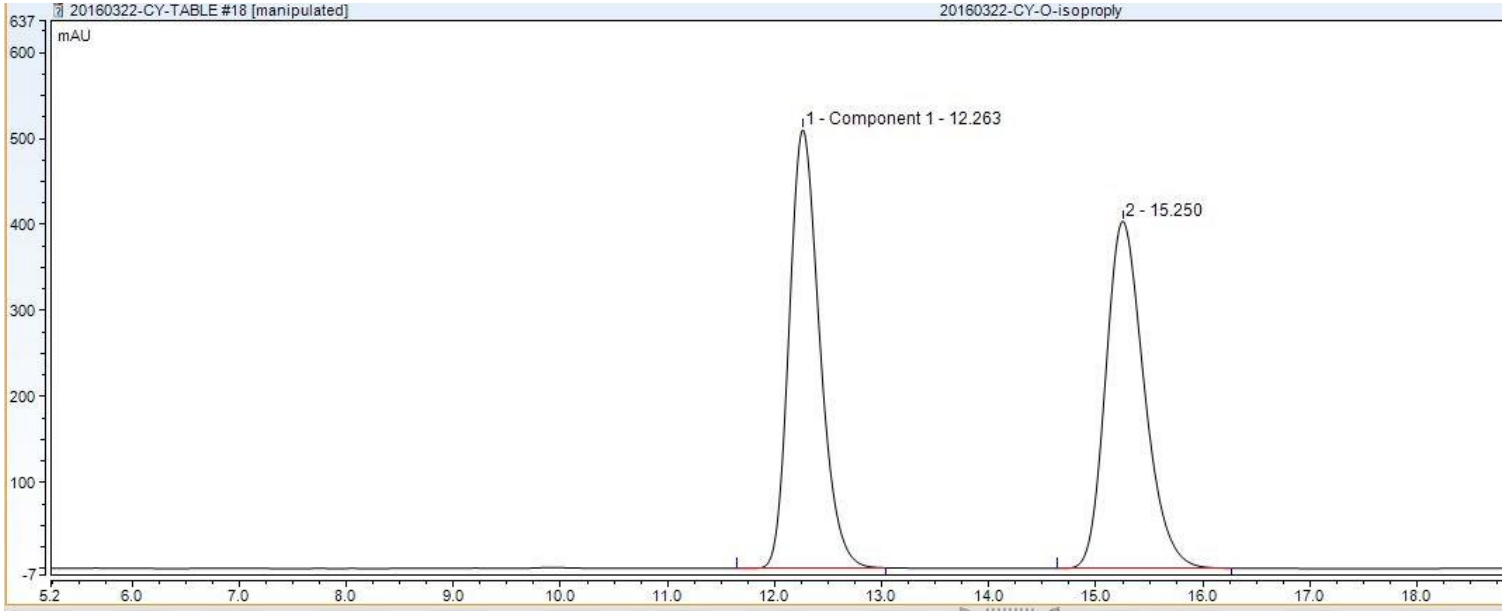
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	18.10	BMB*	0.465	8.9133	17.78	50.15
2	19.50	BMB*	0.499	8.8605	16.35	49.85

2n



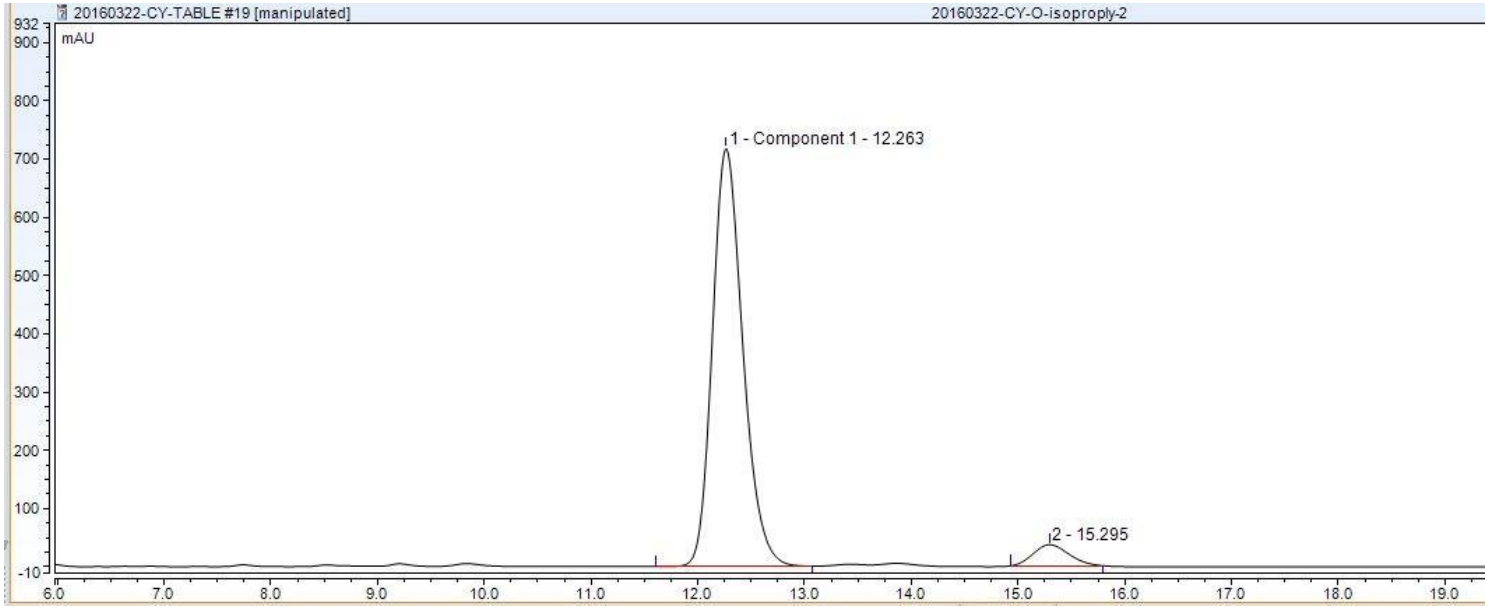
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	17.85	BMB*	0.456	95.1504	191.41	93.78
2	19.31	BMB*	0.460	6.3148	13.25	6.22

2o



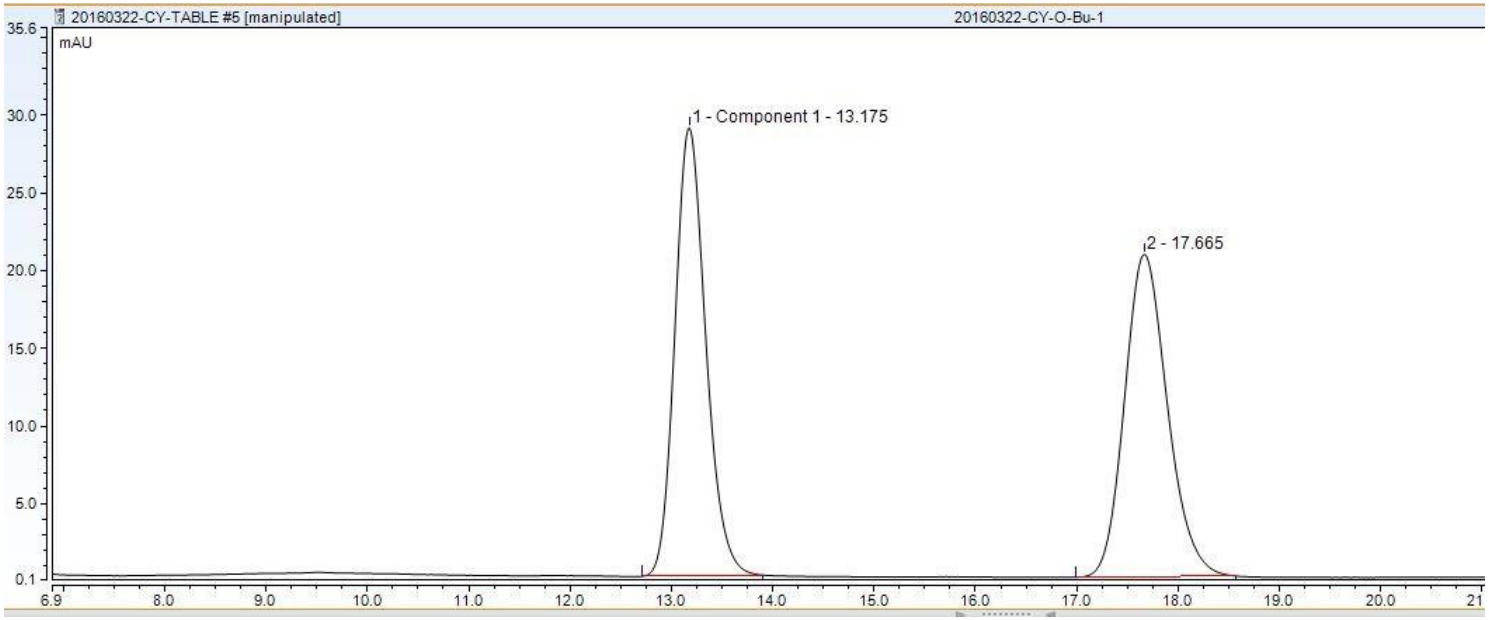
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	12.26	BMB*	0.302	167.6284	509.84	49.97
2	15.25	BMB*	0.382	167.8541	403.71	50.03

2o



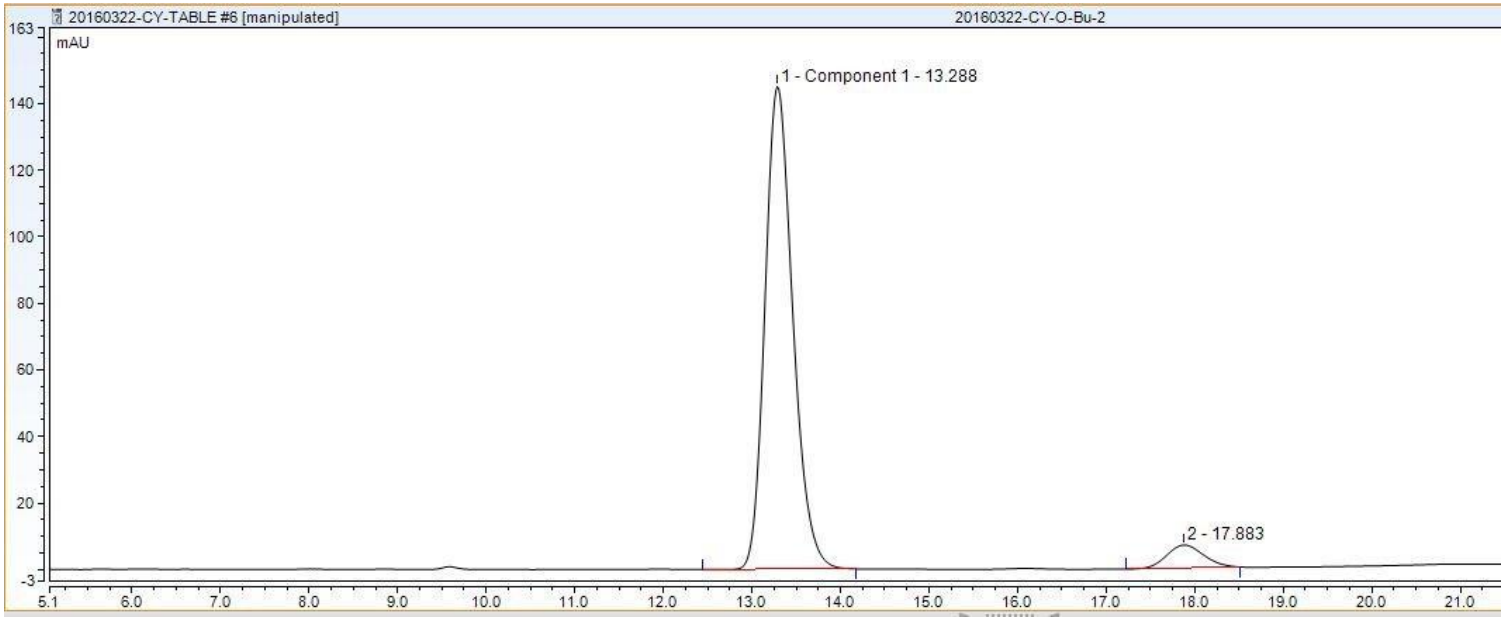
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	12.26	BMB*	0.302	236.7526	717.13	94.42
2	15.30	BMB*	0.367	13.9937	36.22	5.58

2p



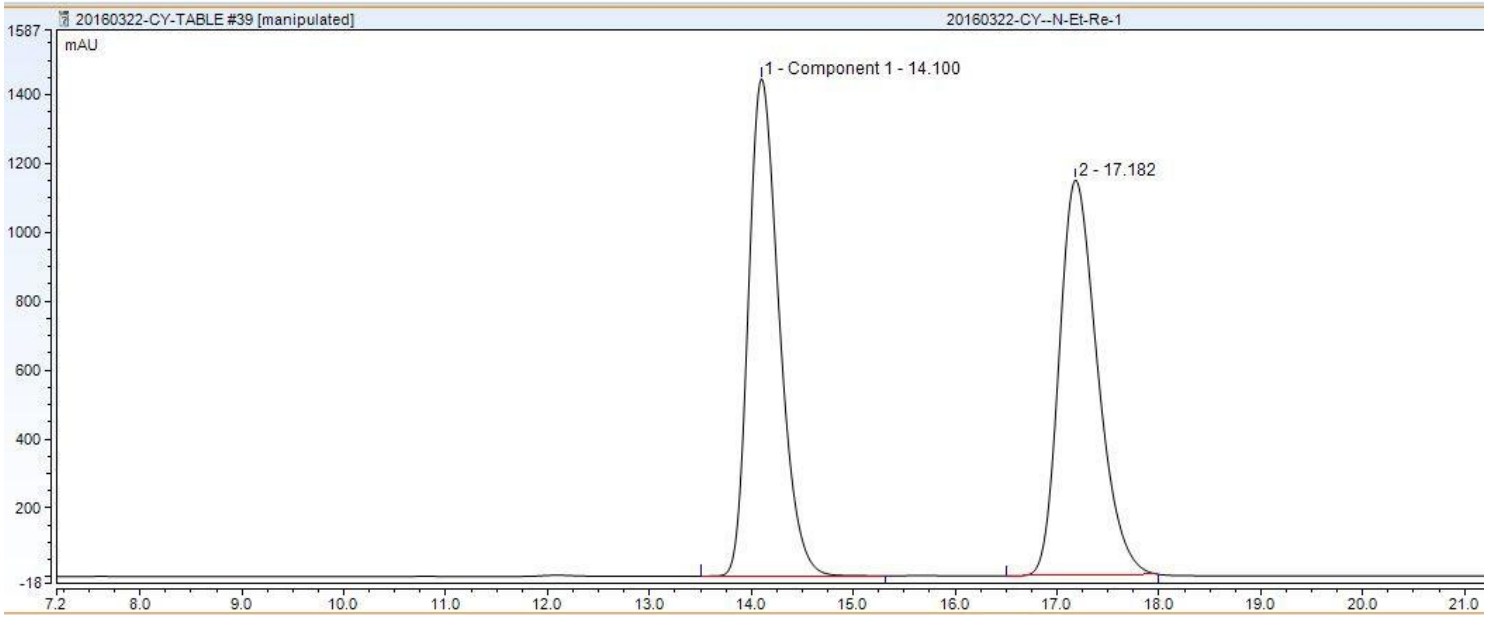
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	13.18	BMB*	0.323	10.1563	28.83	50.00
2	17.67	BMB*	0.451	10.1550	20.74	50.00

2p



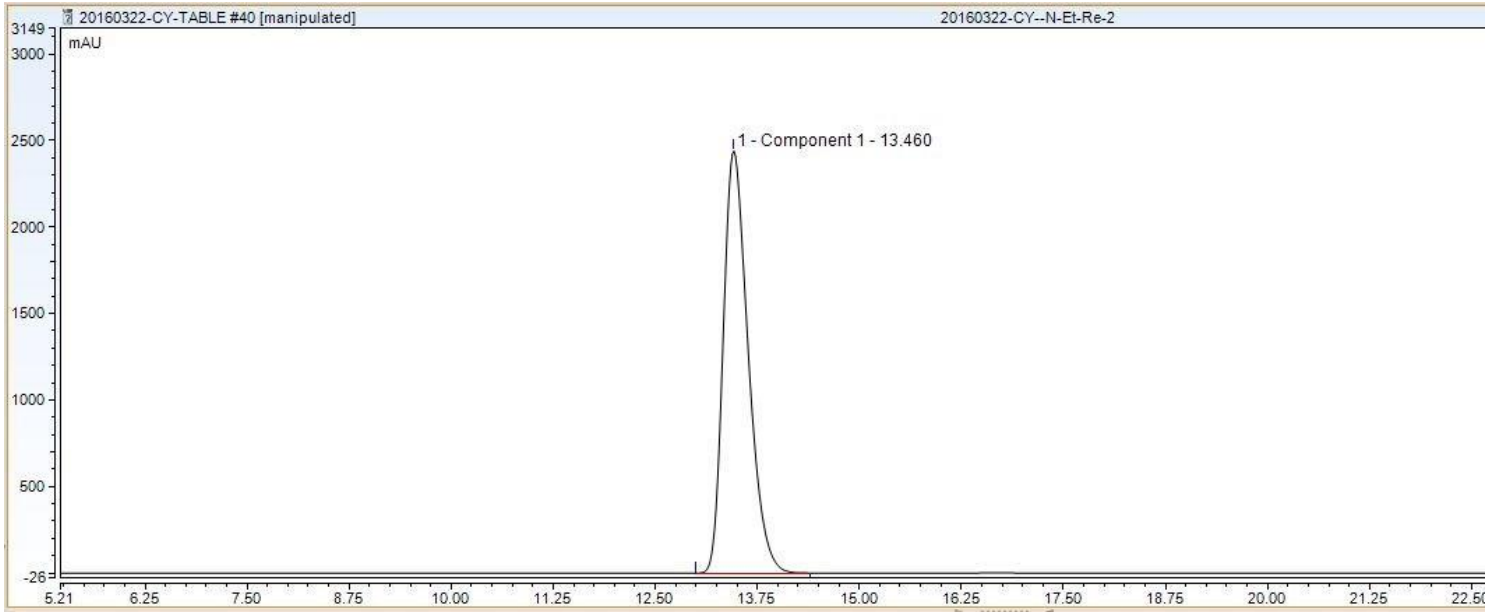
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	13.29	BMB*	0.334	52.8272	145.12	94.05
2	17.88	BMB*	0.454	3.3446	6.92	5.95

2b (after recrystallization)



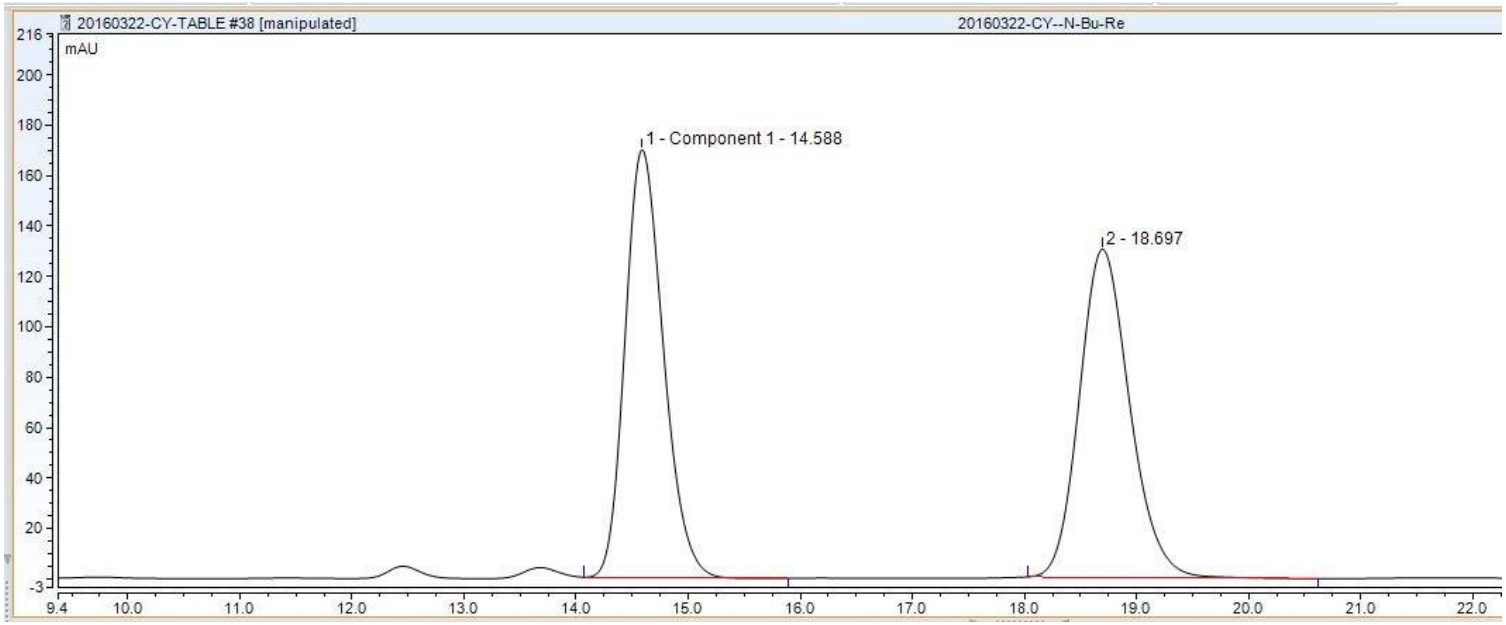
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.10	BMB*	0.334	52.8272	145.12	94.05
2	17.18	BMB*	0.454	3.3446	6.92	5.95

2b (after recrystallization)



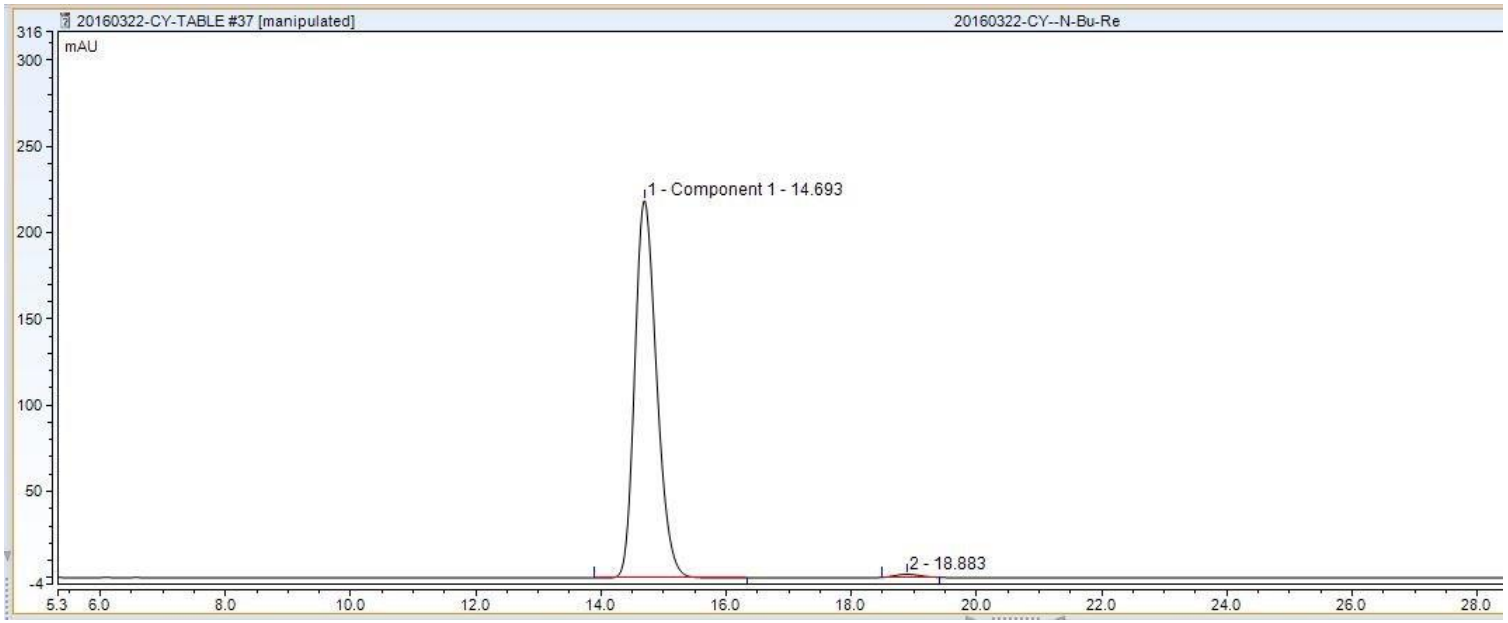
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	13.46	BMB*	0.326	862.0079	2441.53	100.00

2d (after recrystallization)



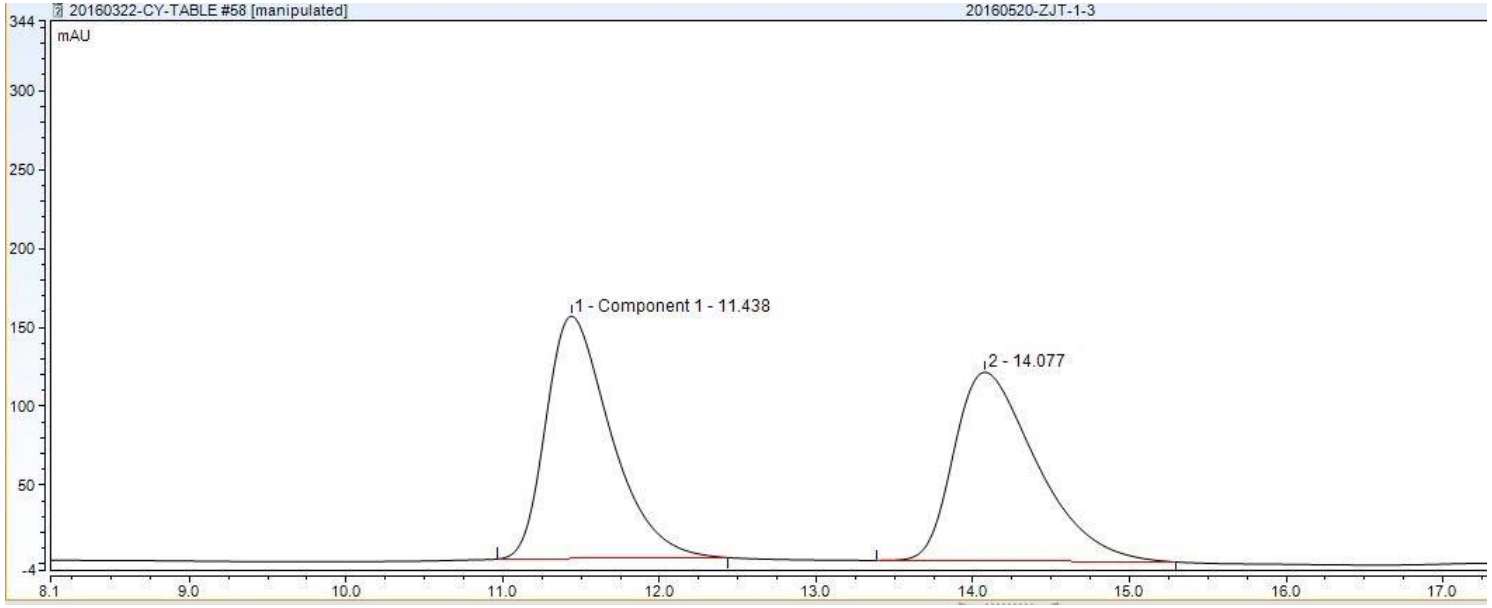
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.59	BMB*	0.367	67.2341	169.88	49.87
2	18.70	BMB*	0.477	67.5776	130.27	50.13

2d (after recrystallization)



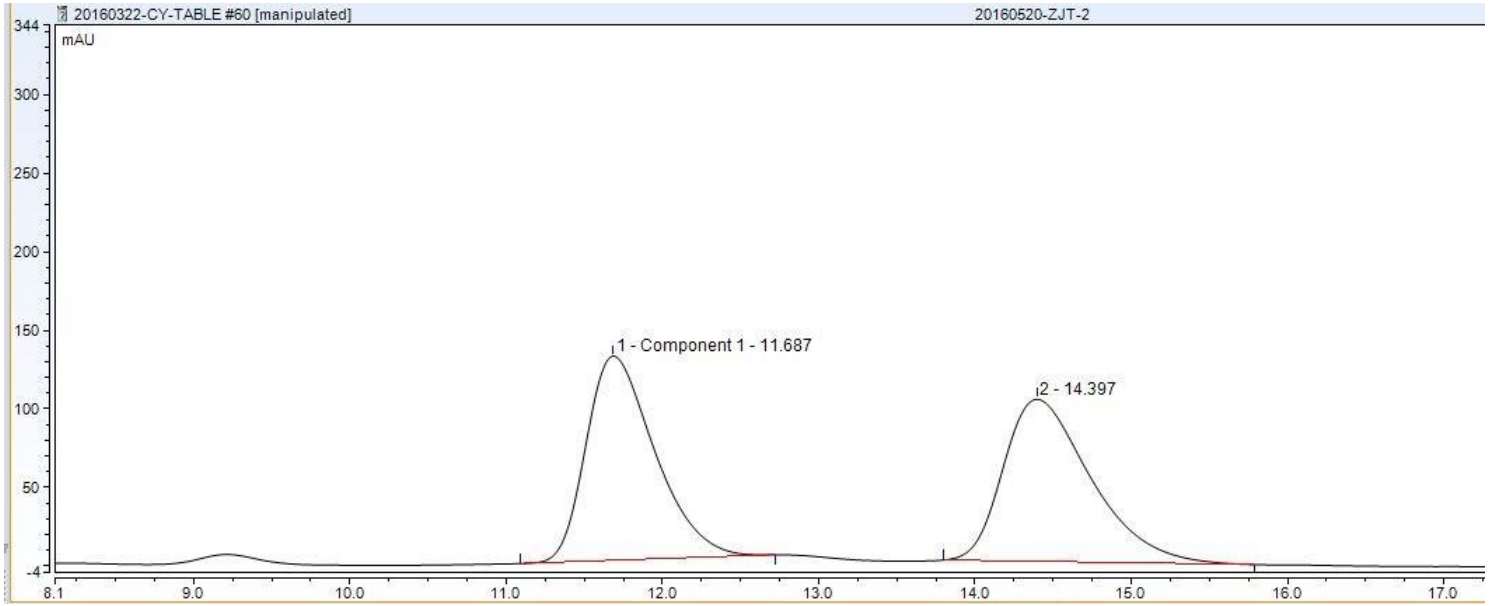
Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	14.69	BMB*	0.373	88.3537	218.94	99.04
2	18.88	BMB*	0.451	0.8557	1.85	0.96

Intermediate A



Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	11.44	BMB*	0.438	73.7198	153.64	50.13
2	14.08	BMB*	0.564	73.3414	119.60	49.87

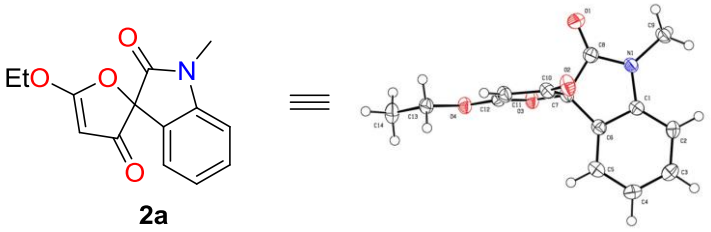
Intermediate A



Peak #	RetTime [min]	Type	Width [min]	Area mAu * s	Height [mAu]	Area %
1	11.69	BMB*	0.471	66.2338	130.03	49.74
2	14.40	BMB*	0.595	66.9163	103.17	50.26

IX. X-Ray Structure and Data of 2a and (*R*)-2b

1. X-ray and Data Structure of Compound **2a**



2a

Data of Compound **2a**

Table 1. Crystal data and structure refinement for 2a

Identification code	**2a**
Empirical formula	$C_{14}H_{13}NO_4$
Formula weight	259.25
Temperature	113(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 9.625(3) A alpha = 90 deg.
	b = 16.950(5) A beta = 114.355(6) deg.
	c = 8.295(3) A gamma = 90 deg.
Volume	1232.8(7) A^3
Z, Calculated density	4, 1.397 Mg/m^3
Absorption coefficient	0.103 mm^-1
F(000)	544
Crystal size	0.20 x 0.18 x 0.12 mm
Theta range for data collection	3.34 to 25.02 deg.
Limiting indices	-9<=h<=11, -20<=k<=20, -9<=l<=9
Reflections collected / unique	10260 / 2160 [R(int) = 0.0523]
Completeness to theta = 25.02	99.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9877 and 0.9796
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	2160 / 0 / 174
Goodness-of-fit on F^2	1.050
Final R indices [I>2sigma(I)]	R1 = 0.0631, wR2 = 0.2530
R indices (all data)	R1 = 0.0757, wR2 = 0.2627
Largest diff. peak and hole	0.340 and -0.280 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for 2a

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(4)	10293(3)	1374(2)	1972(4)	26(1)
O(3)	9266(3)	679(2)	3440(4)	26(1)
O(1)	9006(4)	1280(2)	6697(4)	40(1)
O(2)	5690(4)	1531(2)	2685(4)	36(1)
N(1)	7475(4)	180(2)	6168(4)	24(1)
C(1)	6813(4)	-365(2)	4768(5)	23(1)
C(2)	6021(5)	-1049(2)	4751(5)	27(1)
C(3)	5530(5)	-1504(2)	3217(6)	31(1)
C(4)	5812(5)	-1284(3)	1771(6)	30(1)
C(5)	6582(5)	-582(2)	1805(5)	29(1)
C(6)	7091(5)	-130(2)	3323(5)	24(1)
C(7)	7900(5)	647(2)	3762(5)	24(1)
C(8)	8253(5)	751(2)	5744(5)	27(1)
C(9)	7450(5)	115(2)	7899(5)	28(1)
C(10)	6934(5)	1366(2)	2714(5)	26(1)
C(11)	7817(5)	1729(2)	1913(5)	27(1)
C(12)	9116(5)	1305(2)	2374(5)	23(1)
C(13)	10217(5)	2041(2)	794(5)	27(1)

C(14)	11635(5)	2022(3)	468(6)	35(1)

Table 3. Bond lengths [A] and angles [deg] for 2a.

O(4)-C(12)	1.310(5)
O(4)-C(13)	1.477(5)
O(3)-C(12)	1.350(5)
O(3)-C(7)	1.447(5)
O(1)-C(8)	1.218(5)
O(2)-C(10)	1.221(5)
N(1)-C(8)	1.356(5)
N(1)-C(1)	1.413(5)
N(1)-C(9)	1.450(5)
C(1)-C(2)	1.385(6)
C(1)-C(6)	1.390(5)
C(2)-C(3)	1.394(6)
C(2)-H(2)	0.9500
C(3)-C(4)	1.386(6)
C(3)-H(3)	0.9500
C(4)-C(5)	1.396(6)
C(4)-H(4)	0.9500
C(5)-C(6)	1.379(6)
C(5)-H(5)	0.9500
C(6)-C(7)	1.497(6)
C(7)-C(8)	1.545(5)
C(7)-C(10)	1.561(5)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800

C(10)-C(11)	1.417(6)
C(11)-C(12)	1.354(6)
C(11)-H(11)	0.9500
C(13)-C(14)	1.496(6)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800

C(12)-O(4)-C(13)	115.1(3)
C(12)-O(3)-C(7)	106.9(3)
C(8)-N(1)-C(1)	111.3(3)
C(8)-N(1)-C(9)	123.2(3)
C(1)-N(1)-C(9)	125.3(3)
C(2)-C(1)-C(6)	122.1(4)
C(2)-C(1)-N(1)	128.0(3)
C(6)-C(1)-N(1)	109.9(3)
C(1)-C(2)-C(3)	116.8(4)
C(1)-C(2)-H(2)	121.6
C(3)-C(2)-H(2)	121.6
C(4)-C(3)-C(2)	121.8(4)
C(4)-C(3)-H(3)	119.1
C(2)-C(3)-H(3)	119.1
C(3)-C(4)-C(5)	120.3(4)
C(3)-C(4)-H(4)	119.9
C(5)-C(4)-H(4)	119.9
C(6)-C(5)-C(4)	118.5(4)
C(6)-C(5)-H(5)	120.7

C(4)-C(5)-H(5)	120.7
C(5)-C(6)-C(1)	120.4(4)
C(5)-C(6)-C(7)	131.6(4)
C(1)-C(6)-C(7)	107.9(3)
O(3)-C(7)-C(6)	114.1(3)
O(3)-C(7)-C(8)	112.0(3)
C(6)-C(7)-C(8)	102.9(3)
O(3)-C(7)-C(10)	104.2(3)
C(6)-C(7)-C(10)	114.9(3)
C(8)-C(7)-C(10)	108.8(3)
O(1)-C(8)-N(1)	127.0(4)
O(1)-C(8)-C(7)	125.9(4)
N(1)-C(8)-C(7)	107.0(3)
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
O(2)-C(10)-C(11)	131.7(4)
O(2)-C(10)-C(7)	122.9(4)
C(11)-C(10)-C(7)	105.4(3)
C(12)-C(11)-C(10)	107.4(4)
C(12)-C(11)-H(11)	126.3
C(10)-C(11)-H(11)	126.3
O(4)-C(12)-O(3)	111.5(3)
O(4)-C(12)-C(11)	132.5(4)
O(3)-C(12)-C(11)	116.0(3)
O(4)-C(13)-C(14)	107.6(3)

O(4)-C(13)-H(13A)	110.2
C(14)-C(13)-H(13A)	110.2
O(4)-C(13)-H(13B)	110.2
C(14)-C(13)-H(13B)	110.2
H(13A)-C(13)-H(13B)	108.5
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for 2a.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(4)	30(2)	24(2)	28(2)	5(1)	15(1)	1(1)
O(3)	29(2)	24(2)	28(2)	6(1)	14(1)	1(1)
O(1)	57(2)	31(2)	32(2)	-6(1)	19(2)	-13(2)
O(2)	40(2)	35(2)	43(2)	11(1)	27(2)	10(1)
N(1)	32(2)	23(2)	21(2)	1(1)	14(1)	1(1)
C(1)	25(2)	21(2)	22(2)	2(2)	10(2)	4(2)
C(2)	27(2)	25(2)	30(2)	6(2)	14(2)	2(2)
C(3)	29(2)	24(2)	36(2)	0(2)	10(2)	-1(2)
C(4)	30(2)	28(2)	30(2)	-7(2)	10(2)	-1(2)

C(5)	31(2)	32(2)	24(2)	0(2)	13(2)	3(2)
C(6)	27(2)	23(2)	23(2)	3(2)	11(2)	3(2)
C(7)	27(2)	24(2)	26(2)	1(2)	15(2)	2(2)
C(8)	35(2)	21(2)	26(2)	3(2)	13(2)	2(2)
C(9)	39(2)	26(2)	22(2)	2(2)	16(2)	3(2)
C(10)	35(2)	22(2)	25(2)	3(2)	16(2)	6(2)
C(11)	34(2)	25(2)	26(2)	4(2)	16(2)	2(2)
C(12)	31(2)	19(2)	20(2)	-1(1)	12(2)	-2(2)
C(13)	33(2)	22(2)	26(2)	4(2)	14(2)	0(2)
C(14)	35(2)	36(2)	37(2)	10(2)	18(2)	-3(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters(A^2 x 10^3) for 2a.

	x	y	z	U(eq)
H(2)	5821	-1200	5738	32
H(3)	4987	-1979	3161	37
H(4)	5481	-1612	753	36
H(5)	6752	-419	805	34
H(9A)	8327	-197	8680	42
H(9B)	6505	-146	7786	42
H(9C)	7500	643	8401	42
H(11)	7547	2186	1186	33
H(13A)	10152	2546	1358	32
H(13B)	9305	1992	-338	32
H(14A)	12531	2028	1603	53
H(14B)	11658	2484	-230	53
H(14C)	11644	1540	-182	53

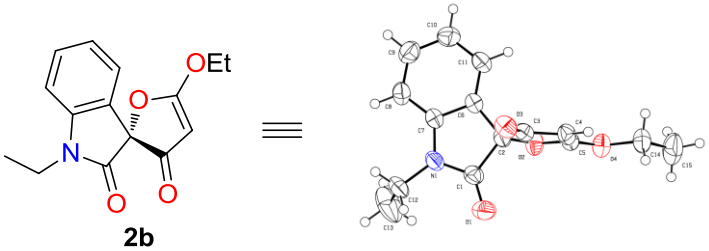
Table 6. Torsion angles [deg] for 2a.

C(8)-N(1)-C(1)-C(2)	175.7(4)
C(9)-N(1)-C(1)-C(2)	0.4(6)
C(8)-N(1)-C(1)-C(6)	-3.0(5)
C(9)-N(1)-C(1)-C(6)	-178.3(4)
C(6)-C(1)-C(2)-C(3)	1.0(6)
N(1)-C(1)-C(2)-C(3)	-177.5(4)
C(1)-C(2)-C(3)-C(4)	-0.3(6)
C(2)-C(3)-C(4)-C(5)	-1.2(7)
C(3)-C(4)-C(5)-C(6)	2.0(6)
C(4)-C(5)-C(6)-C(1)	-1.3(6)
C(4)-C(5)-C(6)-C(7)	-178.1(4)
C(2)-C(1)-C(6)-C(5)	-0.3(6)
N(1)-C(1)-C(6)-C(5)	178.5(4)
C(2)-C(1)-C(6)-C(7)	177.3(3)
N(1)-C(1)-C(6)-C(7)	-4.0(4)
C(12)-O(3)-C(7)-C(6)	125.7(3)
C(12)-O(3)-C(7)-C(8)	-118.0(3)
C(12)-O(3)-C(7)-C(10)	-0.5(4)
C(5)-C(6)-C(7)-O(3)	-53.0(6)
C(1)-C(6)-C(7)-O(3)	129.9(3)
C(5)-C(6)-C(7)-C(8)	-174.5(4)
C(1)-C(6)-C(7)-C(8)	8.4(4)
C(5)-C(6)-C(7)-C(10)	67.4(6)
C(1)-C(6)-C(7)-C(10)	-109.8(4)
C(1)-N(1)-C(8)-O(1)	-176.1(4)
C(9)-N(1)-C(8)-O(1)	-0.8(7)
C(1)-N(1)-C(8)-C(7)	8.4(4)

C(9)-N(1)-C(8)-C(7)	-176.2(3)
O(3)-C(7)-C(8)-O(1)	51.3(5)
C(6)-C(7)-C(8)-O(1)	174.3(4)
C(10)-C(7)-C(8)-O(1)	-63.4(5)
O(3)-C(7)-C(8)-N(1)	-133.1(3)
C(6)-C(7)-C(8)-N(1)	-10.1(4)
C(10)-C(7)-C(8)-N(1)	112.2(4)
O(3)-C(7)-C(10)-O(2)	-179.6(4)
C(6)-C(7)-C(10)-O(2)	54.7(5)
C(8)-C(7)-C(10)-O(2)	-60.0(5)
O(3)-C(7)-C(10)-C(11)	0.1(4)
C(6)-C(7)-C(10)-C(11)	-125.6(4)
C(8)-C(7)-C(10)-C(11)	119.7(4)
O(2)-C(10)-C(11)-C(12)	-180.0(5)
C(7)-C(10)-C(11)-C(12)	0.4(4)
C(13)-O(4)-C(12)-O(3)	179.5(3)
C(13)-O(4)-C(12)-C(11)	0.3(6)
C(7)-O(3)-C(12)-O(4)	-178.6(3)
C(7)-O(3)-C(12)-C(11)	0.8(4)
C(10)-C(11)-C(12)-O(4)	178.5(4)
C(10)-C(11)-C(12)-O(3)	-0.7(5)
C(12)-O(4)-C(13)-C(14)	-179.4(3)

Symmetry transformations used to generate equivalent atoms:

2. X-ray and Data Structure of Compound **(*R*)-2b**



Data of Compound **(*R*)-2b**

Table 1. Crystal data and structure refinement for (*R*)-2b

Identification code	p20160406a
Empirical formula	C15 H15 N O4
Formula weight	273.28
Temperature	293(2) K
Wavelength	1.54184 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 8.56310(8) A alpha = 90 deg.
	b = 11.52249(11) A beta = 90 deg.
	c = 13.97167(11) A gamma = 90 deg.
Volume	1378.56(2) A^3
Z, Calculated density	4, 1.317 Mg/m^3
Absorption coefficient	0.797 mm^-1
F(000)	576
Crystal size	0.240 x 0.180 x 0.160 mm
Theta range for data collection	4.975 to 79.088 deg.
Limiting indices	-10<=h<=10, -14<=k<=14, -11<=l<=17
Reflections collected / unique	11908 / 2942 [R(int) = 0.0187]
Completeness to theta = 67.684	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.80907
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2942 / 0 / 184
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0293, wR2 = 0.0834
R indices (all data)	R1 = 0.0298, wR2 = 0.0839
Absolute structure parameter	0.08(7)

Extinction coefficient	0.0140(12)
Largest diff. peak and hole	0.140 and -0.153 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for (*R*)-2b.

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	9162(2)	7298(1)	2201(1)	64(1)
O(2)	5851(2)	6585(1)	2422(1)	46(1)
O(3)	6875(1)	9048(1)	3788(1)	51(1)
O(4)	3999(2)	7068(1)	1421(1)	51(1)
N(1)	9254(2)	6470(1)	3701(1)	44(1)
C(1)	8543(2)	6972(1)	2931(1)	43(1)
C(2)	6788(2)	7076(1)	3177(1)	39(1)
C(3)	6296(2)	8361(1)	3227(1)	39(1)
C(4)	5100(2)	8487(1)	2528(1)	43(1)
C(5)	4916(2)	7440(1)	2099(1)	40(1)
C(6)	6657(2)	6437(1)	4104(1)	38(1)
C(7)	8151(2)	6116(1)	4392(1)	40(1)
C(8)	8399(2)	5532(2)	5240(1)	49(1)
C(9)	7099(2)	5286(2)	5799(1)	56(1)
C(10)	5611(2)	5610(2)	5527(1)	54(1)
C(11)	5379(2)	6205(2)	4671(1)	47(1)
C(12)	10940(2)	6273(2)	3753(1)	52(1)
C(13)	11397(3)	5146(3)	3325(3)	103(1)
C(14)	2857(2)	7891(2)	1048(1)	59(1)
C(15)	1989(3)	7307(3)	263(2)	84(1)

Table 3. Bond lengths [A] and angles [deg] for (*R*)-2b.

O(1)-C(1)	1.210(2)
O(2)-C(5)	1.3479(18)
O(2)-C(2)	1.4413(18)
O(3)-C(3)	1.2190(19)
O(4)-C(5)	1.3030(19)
O(4)-C(14)	1.459(2)
N(1)-C(1)	1.364(2)
N(1)-C(7)	1.411(2)
N(1)-C(12)	1.464(2)
C(1)-C(2)	1.546(2)
C(2)-C(6)	1.493(2)
C(2)-C(3)	1.542(2)
C(3)-C(4)	1.422(2)
C(4)-C(5)	1.356(2)
C(4)-H(4)	0.9300
C(6)-C(11)	1.378(2)
C(6)-C(7)	1.391(2)
C(7)-C(8)	1.378(2)
C(8)-C(9)	1.389(3)
C(8)-H(8)	0.9300
C(9)-C(10)	1.381(3)
C(9)-H(9)	0.9300
C(10)-C(11)	1.393(3)
C(10)-H(10)	0.9300
C(11)-H(11)	0.9300
C(12)-C(13)	1.483(3)
C(12)-H(12A)	0.9700

C(12)-H(12B)	0.9700
C(13)-H(13A)	0.9600
C(13)-H(13B)	0.9600
C(13)-H(13C)	0.9600
C(14)-C(15)	1.486(3)
C(14)-H(14A)	0.9700
C(14)-H(14B)	0.9700
C(15)-H(15A)	0.9600
C(15)-H(15B)	0.9600
C(15)-H(15C)	0.9600

C(5)-O(2)-C(2)	106.79(11)
C(5)-O(4)-C(14)	116.69(14)
C(1)-N(1)-C(7)	111.33(13)
C(1)-N(1)-C(12)	123.05(15)
C(7)-N(1)-C(12)	125.52(14)
O(1)-C(1)-N(1)	126.96(16)
O(1)-C(1)-C(2)	126.10(15)
N(1)-C(1)-C(2)	106.93(13)
O(2)-C(2)-C(6)	113.58(12)
O(2)-C(2)-C(3)	104.95(11)
C(6)-C(2)-C(3)	114.40(12)
O(2)-C(2)-C(1)	110.38(12)
C(6)-C(2)-C(1)	103.14(12)
C(3)-C(2)-C(1)	110.50(12)
O(3)-C(3)-C(4)	131.94(15)
O(3)-C(3)-C(2)	122.78(14)
C(4)-C(3)-C(2)	105.27(12)
C(5)-C(4)-C(3)	107.29(13)

C(5)-C(4)-H(4)	126.4
C(3)-C(4)-H(4)	126.4
O(4)-C(5)-O(2)	111.11(13)
O(4)-C(5)-C(4)	133.23(15)
O(2)-C(5)-C(4)	115.66(14)
C(11)-C(6)-C(7)	120.79(14)
C(11)-C(6)-C(2)	130.84(14)
C(7)-C(6)-C(2)	108.28(13)
C(8)-C(7)-C(6)	121.40(15)
C(8)-C(7)-N(1)	128.74(14)
C(6)-C(7)-N(1)	109.85(13)
C(7)-C(8)-C(9)	117.31(15)
C(7)-C(8)-H(8)	121.3
C(9)-C(8)-H(8)	121.3
C(10)-C(9)-C(8)	122.01(16)
C(10)-C(9)-H(9)	119.0
C(8)-C(9)-H(9)	119.0
C(9)-C(10)-C(11)	120.01(16)
C(9)-C(10)-H(10)	120.0
C(11)-C(10)-H(10)	120.0
C(6)-C(11)-C(10)	118.45(15)
C(6)-C(11)-H(11)	120.8
C(10)-C(11)-H(11)	120.8
N(1)-C(12)-C(13)	112.12(18)
N(1)-C(12)-H(12A)	109.2
C(13)-C(12)-H(12A)	109.2
N(1)-C(12)-H(12B)	109.2
C(13)-C(12)-H(12B)	109.2
H(12A)-C(12)-H(12B)	107.9

C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
O(4)-C(14)-C(15)	107.72(19)
O(4)-C(14)-H(14A)	110.2
C(15)-C(14)-H(14A)	110.2
O(4)-C(14)-H(14B)	110.2
C(15)-C(14)-H(14B)	110.2
H(14A)-C(14)-H(14B)	108.5
C(14)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(14)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for (*R*)-2b.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1)	57(1)	77(1)	58(1)	13(1)	18(1)	15(1)
O(2)	50(1)	40(1)	48(1)	-5(1)	-12(1)	9(1)
O(3)	45(1)	47(1)	60(1)	-10(1)	0(1)	-3(1)

O(4)	50(1)	54(1)	49(1)	1(1)	-13(1)	1(1)
N(1)	31(1)	51(1)	50(1)	-1(1)	1(1)	5(1)
C(1)	40(1)	44(1)	46(1)	-1(1)	5(1)	7(1)
C(2)	34(1)	42(1)	42(1)	-2(1)	-3(1)	5(1)
C(3)	32(1)	39(1)	44(1)	0(1)	4(1)	2(1)
C(4)	40(1)	39(1)	51(1)	4(1)	-2(1)	8(1)
C(5)	36(1)	44(1)	40(1)	4(1)	-1(1)	4(1)
C(6)	32(1)	38(1)	45(1)	-1(1)	-3(1)	2(1)
C(7)	33(1)	40(1)	46(1)	-2(1)	-3(1)	0(1)
C(8)	42(1)	52(1)	52(1)	4(1)	-11(1)	1(1)
C(9)	61(1)	57(1)	49(1)	10(1)	-4(1)	-4(1)
C(10)	51(1)	56(1)	54(1)	6(1)	7(1)	-8(1)
C(11)	33(1)	50(1)	58(1)	1(1)	1(1)	1(1)
C(12)	31(1)	63(1)	63(1)	-9(1)	1(1)	7(1)
C(13)	70(2)	105(2)	135(3)	-55(2)	-20(2)	44(2)
C(14)	48(1)	70(1)	58(1)	10(1)	-14(1)	6(1)
C(15)	76(1)	95(2)	82(2)	10(1)	-39(1)	-8(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for (*R*)-2b.

	x	y	z	U(eq)
H(4)	4547	9162	2391	52
H(8)	9397	5311	5429	59
H(9)	7235	4891	6373	67
H(10)	4763	5431	5916	64
H(11)	4384	6440	4487	56
H(12A)	11266	6290	4418	63

H(12B)	11476	6895	3421	63
H(13A)	11096	5131	2663	155
H(13B)	10884	4526	3659	155
H(13C)	12508	5050	3374	155
H(14A)	3380	8578	807	71
H(14B)	2142	8124	1551	71
H(15A)	2685	7156	-260	126
H(15B)	1154	7800	50	126
H(15C)	1565	6588	493	126

Table 6. Torsion angles [deg] for (*R*)-2b.

C(7)-N(1)-C(1)-O(1)	-175.19(17)
C(12)-N(1)-C(1)-O(1)	1.3(3)
C(7)-N(1)-C(1)-C(2)	6.14(17)
C(12)-N(1)-C(1)-C(2)	-177.33(15)
C(5)-O(2)-C(2)-C(6)	123.96(13)
C(5)-O(2)-C(2)-C(3)	-1.71(15)
C(5)-O(2)-C(2)-C(1)	-120.78(14)
O(1)-C(1)-C(2)-O(2)	52.9(2)
N(1)-C(1)-C(2)-O(2)	-128.47(13)
O(1)-C(1)-C(2)-C(6)	174.51(17)
N(1)-C(1)-C(2)-C(6)	-6.80(16)
O(1)-C(1)-C(2)-C(3)	-62.8(2)
N(1)-C(1)-C(2)-C(3)	115.89(14)
O(2)-C(2)-C(3)-O(3)	-179.09(14)
C(6)-C(2)-C(3)-O(3)	55.75(19)
C(1)-C(2)-C(3)-O(3)	-60.10(19)
O(2)-C(2)-C(3)-C(4)	1.83(16)

C(6)-C(2)-C(3)-C(4)	-123.33(14)
C(1)-C(2)-C(3)-C(4)	120.82(14)
O(3)-C(3)-C(4)-C(5)	179.78(16)
C(2)-C(3)-C(4)-C(5)	-1.26(18)
C(14)-O(4)-C(5)-O(2)	176.33(14)
C(14)-O(4)-C(5)-C(4)	-3.5(3)
C(2)-O(2)-C(5)-O(4)	-178.83(13)
C(2)-O(2)-C(5)-C(4)	1.03(19)
C(3)-C(4)-C(5)-O(4)	-179.97(16)
C(3)-C(4)-C(5)-O(2)	0.2(2)
O(2)-C(2)-C(6)-C(11)	-58.8(2)
C(3)-C(2)-C(6)-C(11)	61.6(2)
C(1)-C(2)-C(6)-C(11)	-178.31(17)
O(2)-C(2)-C(6)-C(7)	124.61(13)
C(3)-C(2)-C(6)-C(7)	-114.92(14)
C(1)-C(2)-C(6)-C(7)	5.13(15)
C(11)-C(6)-C(7)-C(8)	1.6(2)
C(2)-C(6)-C(7)-C(8)	178.60(14)
C(11)-C(6)-C(7)-N(1)	-178.77(15)
C(2)-C(6)-C(7)-N(1)	-1.80(17)
C(1)-N(1)-C(7)-C(8)	176.64(16)
C(12)-N(1)-C(7)-C(8)	0.2(3)
C(1)-N(1)-C(7)-C(6)	-2.92(18)
C(12)-N(1)-C(7)-C(6)	-179.35(15)
C(6)-C(7)-C(8)-C(9)	-0.6(2)
N(1)-C(7)-C(8)-C(9)	179.91(17)
C(7)-C(8)-C(9)-C(10)	-0.1(3)
C(8)-C(9)-C(10)-C(11)	-0.2(3)
C(7)-C(6)-C(11)-C(10)	-1.9(3)

C(2)-C(6)-C(11)-C(10)	-178.09(15)
C(9)-C(10)-C(11)-C(6)	1.2(3)
C(1)-N(1)-C(12)-C(13)	-87.4(3)
C(7)-N(1)-C(12)-C(13)	88.6(3)
C(5)-O(4)-C(14)-C(15)	177.74(18)

Symmetry transformations used to generate equivalent atoms: