Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Asymmetric Synthesis of Poly-Substituted Spirocyclohexane Oxindoles via Squaramide Catalyzed cascade Michael-Michael-Aldol Sequence

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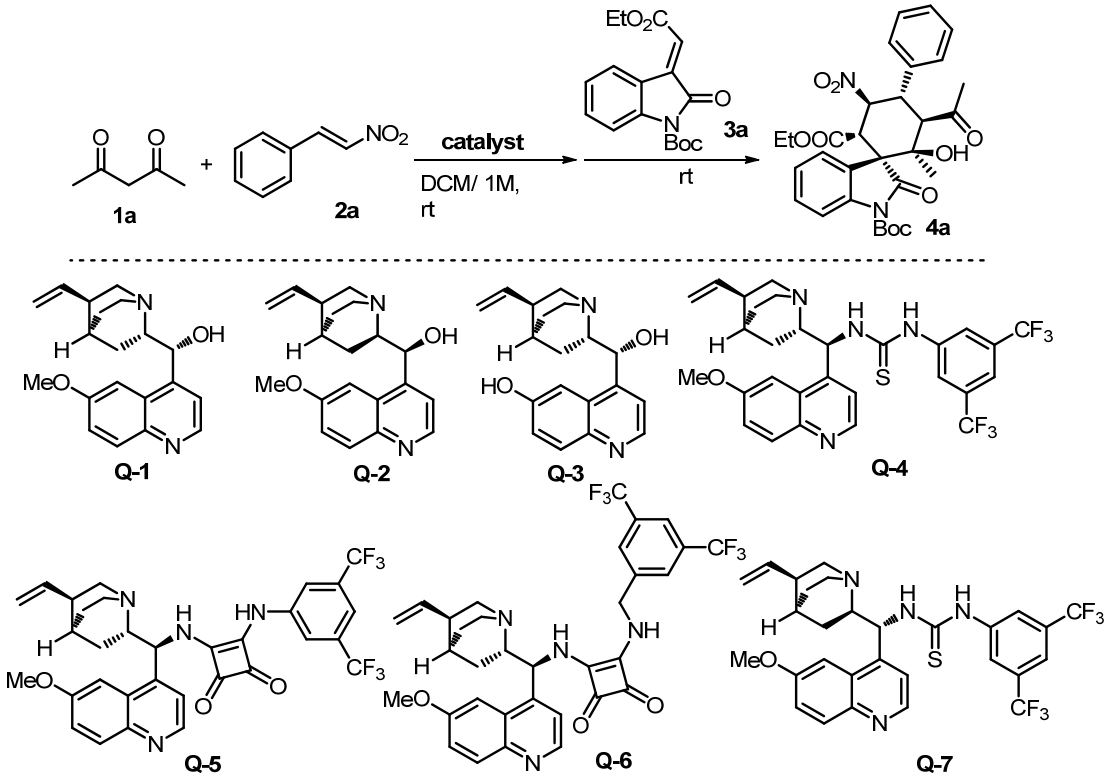
General experiment methods:

NMR spectra were all recorded on ECA (400 MHz) spectrometer. Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR and chloroform-d (δ 77.0) for ^{13}C NMR. HRMS was measured on Brucker micrOTOF II serial 10257. Optical rotations were measured in $CHCl_3$ on a Rudolph research analytical, Auto pol® IV, automatic parameter. HPLC was performed on an Agilent 1100 series instrument or a Jasco uv-2075 plus intelligent uv/vis detector by using Daicel Chiracel AD-H column or PC-2 column. Flash column chromatography was performed using silica gel (300–400 mesh). Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 300–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Commercial reagents and solvents were used as received. Dichloromethane was fractionally distilled.

Screening of other catalysts and achiral bases:

Table 1 Screening of other catalysts [a]

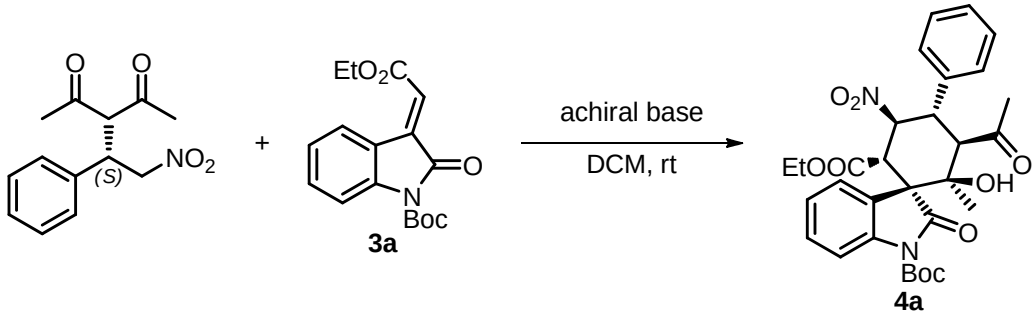


Entry	Catalyst/(X mol%)	Time/h	Yield[b]	dr[c]	ee[d]
1	**Q-1** (10)	3+48	27%	1:1.4	-
2	**Q-2** (10)	3+48	25%	1:1.3	-
3	**Q-3** (10)	3+48	19%	2.2:1	-
4	**Q-4** (10)	3+21	55%	> 20:1	95%
5	**Q-5** (5)	1+21	65%	> 20:1	> 99%
6	**Q-6** (5)	1+21	85%	> 20:1	> 99%
7[e]	**Q-7** (10)	3+21	64%	> 20:1	-98%

[a] The reaction was performed using 0.22 mmol of **1a**, 0.20 mmol of **2a**, X mol% of catalyst, followed adding 0.3 mmol of **3a** in DCM (1.0 M) at room temperature. [b] Isolated yield after

column chromatography. [c] dr was detected by ^{1}H NMR. [d] ee value of the major product was determined by HPLC analysis on a chiral stationary phase. [e] opposite enantiomer.

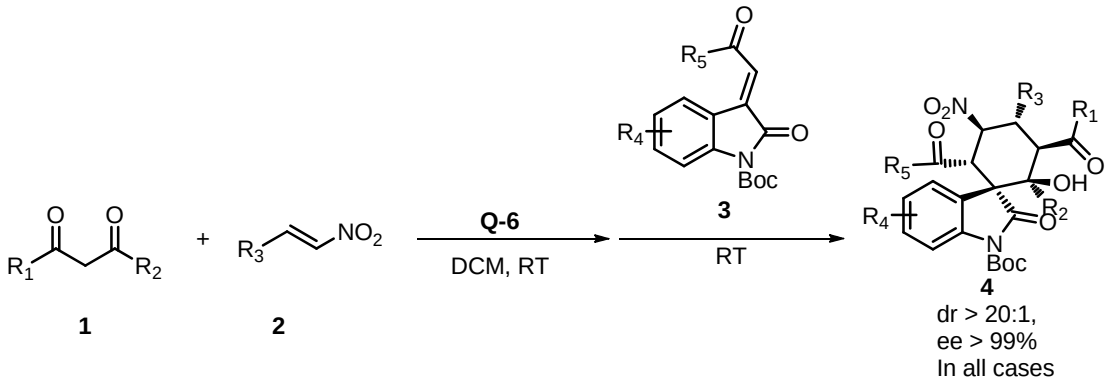
Table 2 Screening of achiral bases[a]



Entry	Catalyst/(X mol%)	Time/h	Yield[b]	dr[c]	ee[d]
1	**TEA**(100)	24	36%	1:1	>99%
2	**TBD**(100)	24	59%	2.7(desired):1	>99%
3	**DABCO**(100)	24	41%	2(desired):1	>99%

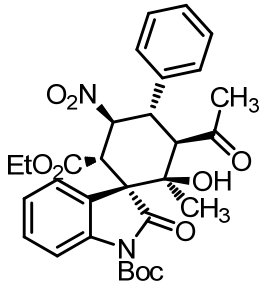
[a] The reaction was performed using 0.20 mmol (*S*)-Michael adduct of acac and nitroalkene, 0.2 mmol achiral base, 0.3 mmol of **3a** in DCM (1.0 M) at room temperature. [b] Isolated yield after column chromatography. [c] dr was detected by ^{1}H NMR. [d] ee value of the major product was determined by HPLC analysis on a chiral stationary phase.

General procedure for synthesis of spirocyclic oxindoles 4a-4p



A solution of β-dicarbonyl compounds **1** (0.22 mmol), nitroalkene **2** (0.20 mmol) and catalyst **Q-6** (5 mol%) in CH_2Cl_2 (0.20 mL) was stirred for 1 hour until all the nitroalkene consumed, then **3** (0.3 mmol) was added. After the reaction completed, the solution was concentrated and purified using column chromatography (Petroleum ether: ethyl acetate: DCM = 10: 1: 1, R_f(P) = 0.4) to afford the desired product.

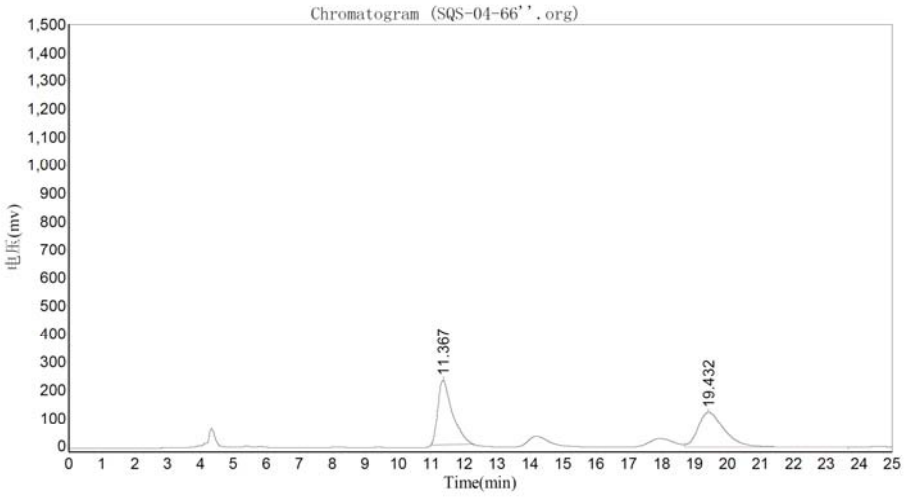
All racemic reactions were catalyzed by achiral base TEA.



4a was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 85% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak PC-2 column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 19.22 min., τ_{minor} = 11.36 min. $[\alpha]_{20}^{D}$ = 11.788 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{30}H_{34}N_2O_9Na]^+$ $(M+Na)^+$: 589.2162, found: 589.2149.

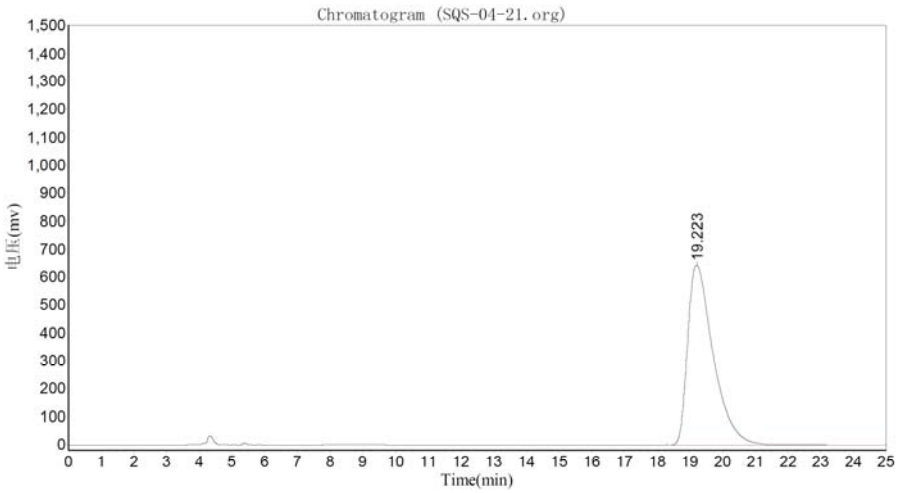
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (s, 3H), 0.86 (t, *J* = 6.8 Hz, 3H), 1.63 (s, 1H), 1.71 (s, 9H), 3.83-3.88 (m, 2H), 3.95 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.22 (d, *J* = 12.0 Hz, 1H), 4.32 (d, *J* = 12.0 Hz, 1H), 5.35 (s, 1H), 5.96 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.18-7.37 (m, 7H), 7.64-7.66 (m, 1H), 7.72 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.39, 175.20, 168.44, 148.50, 140.24, 135.98, 129.51, 129.36, 128.69, 126.68, 125.63, 124.68, 114.44, 87.22, 85.29, 73.20, 61.88, 57.46, 55.01, 50.19, 46.08, 34.66, 28.17, 22.72, 13.42.



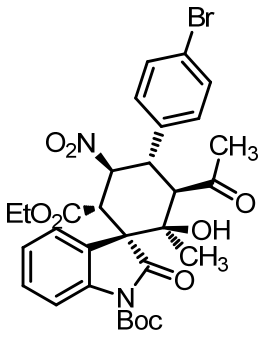
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		11.367	230144.266	7057787.000	50.0328
2		19.432	125606.414	7048541.000	49.9672
Total			355750.680	14106328.000	100.0000



Results

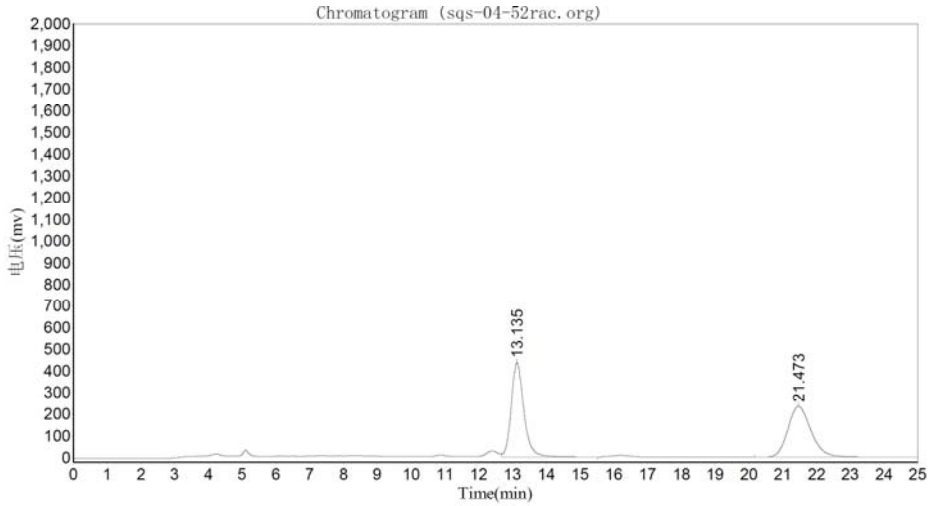
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.223	645553.375	35441856.000	100.0000
Total			645553.375	35441856.000	100.0000



4b was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 80% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 13.03 min., τ_{minor} = 21.47 min. $[\alpha]_{20}^{D}$ = 7.989 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{30}H_{33}BrN_2O_9Na]^+$ $(M+Na)^+$: 667.1267, found: 667.1244.

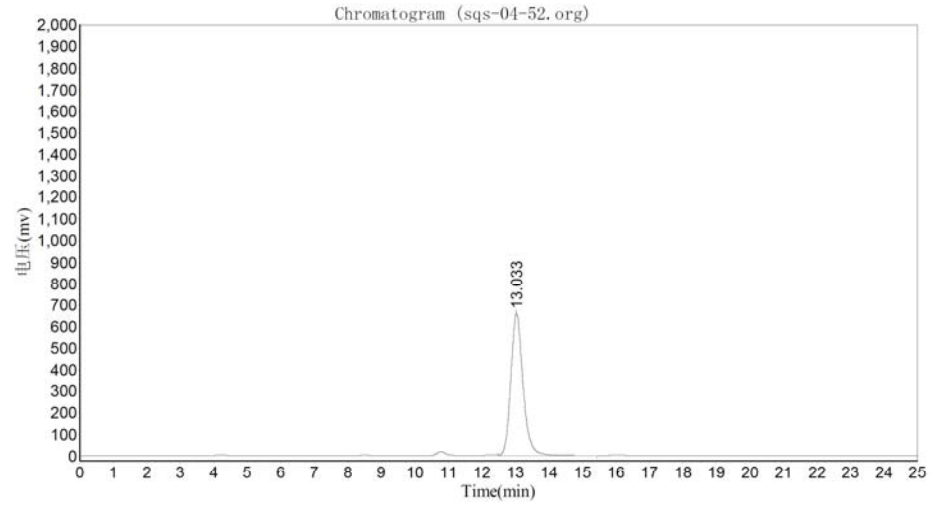
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (s, 3H), 0.86 (t, *J* = 6.8 Hz, 3H), 1.62 (s, 1H), 1.75 (s, 9H), 3.78-3.84 (m, 2H), 3.92 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.22 (d, *J* = 12.0 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.73 (s, 1H), 5.99 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.22-7.75 (m, 6H), 7.67 (m, 1H), 7.72 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 214.85, 175.20, 168.28, 148.43, 135.18, 132.57, 129.58, 126.65, 125.49, 124.73, 122.82, 114.48, 87.06, 85.39, 73.15, 61.94, 57.43, 54.89, 50.07, 45.46, 34.88, 28.17, 22.72, 13.41.



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.135	433661.563	11299696.000	50.4726
2		21.473	231076.844	11088107.000	49.5274
Total			664738.406	22387803.000	100.0000



Results

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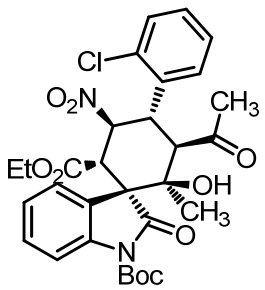
Total			659692.438	16935784.000	100.0000

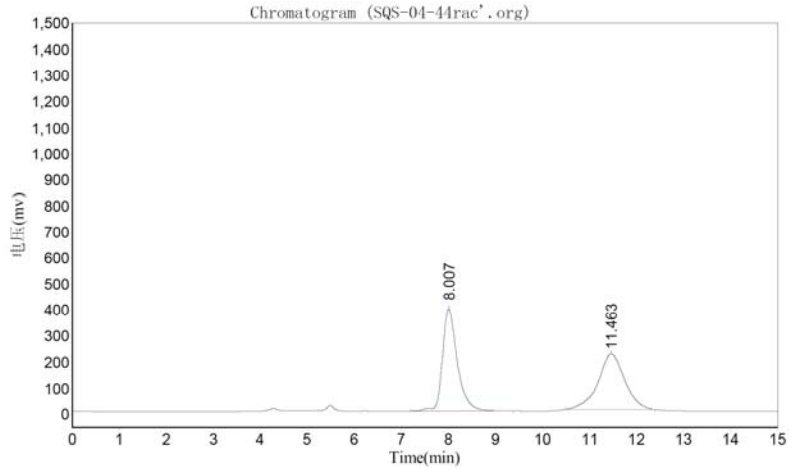


4c was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 79% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 8.32 min., τ_{minor} = 12.08 min. $[\alpha]_{20}^{D}$ = 11.189 (c = 1.0,

$CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{30}H_{33}ClN_2O_9Na]^+$ $(M+Na)^+$: 623.1772, found: 623.1738.

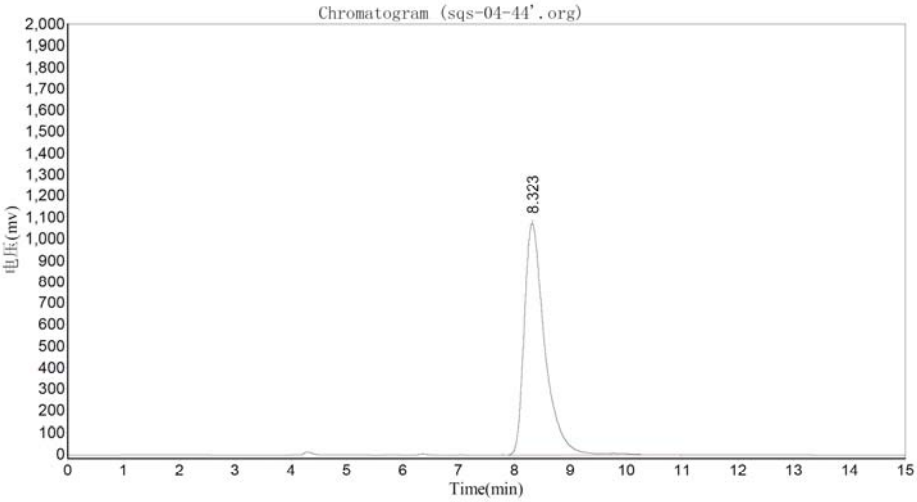
^1H NMR (400 MHz, $CDCl_3$): δ 0.86 (s, 3H), 0.86 (t, *J* = 6.8 Hz, 3H), 1.75 (s, 12H), 3.82-3.88 (m, 2H), 3.96 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.22 (d, *J* = 12.0 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.64 (s, 1H), 5.99 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.22-7.42 (m, 6H), 7.69(m, 1H), 7.75 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 214.89, 175.23, 168.31, 148.44, 140.21, 134.64, 129.61, 126.64, 125.49, 124.73, 114.49, 87.13, 85.40, 73.16, 61.94, 57.43, 54.94, 50.07, 45.39, 34.87, 28.17, 22.72, 13.41.



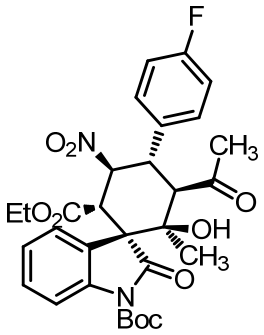
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		8.007	389757.156	8590370.000	50.2686
2		11.463	212585.781	8498571.000	49.7314
Total			602342.938	17088941.000	100.0000



Results

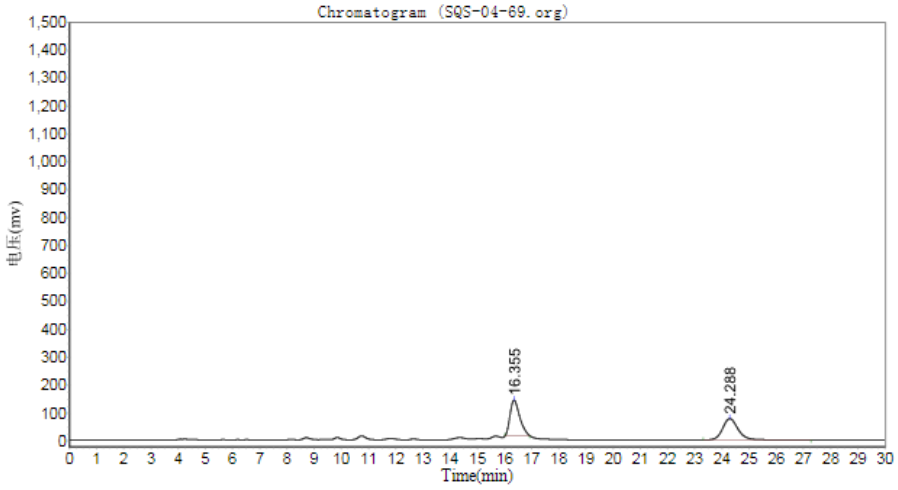
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		8.323	1072532.250	27116426.000	100.0000
Total			1072532.250	27116426.000	100.0000



4d was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 68% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 16.47 min., τ_{minor} = 24.28 min. $[\alpha]_{20}^{D}$ = 6.793 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{30}H_{33}FN_2O_9Na]^+$ $(M+Na)^+$: 607.2068, found: 607.2023.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (s, 3H), 0.86 (t, *J* = 7.2 Hz, 3H), 1.73 (s, 3H), 1.75 (s, 9H), 3.82-3.88 (m, 2H), 3.97 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.24 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.66 (s, 1H), 5.99 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.09-7.42 (m, 6H), 7.69(m, 1H), 7.76 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.05, 175.22, 168.34, 163.90, 161.43, 148.45, 140.22, 131.84, 129.56, 126.64, 125.52, 124.72, 116.32 (d, 1C, *J* = 1.2Hz), 114.48, 87.31, 85.36, 73.17, 61.92, 57.44, 55.08, 50.10, 45.28, 34.76, 28.17, 22.73, 13.41.



Results

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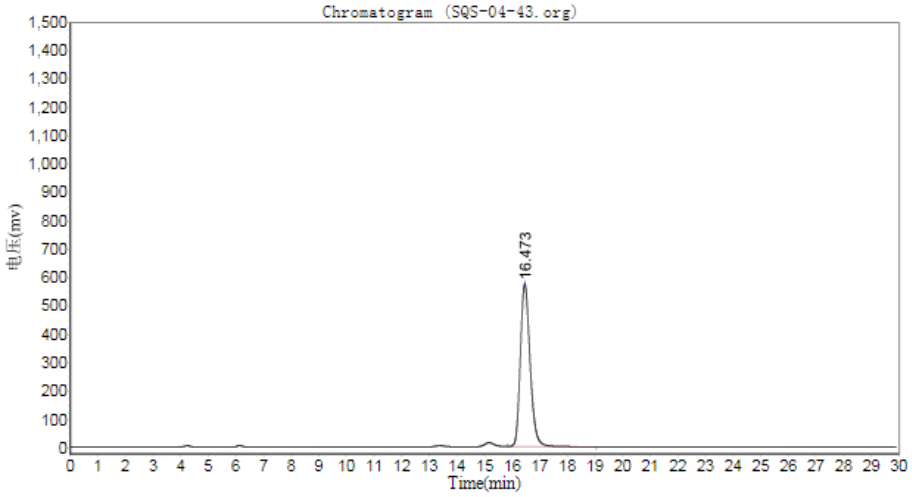
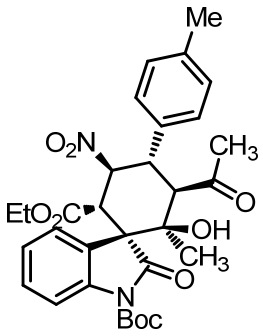
1		16.355	127354.016	3132911.750	51.0075
2		24.288	76144.156	3009144.000	48.9925
Total			203498.172	6142055.750	100.0000



Results

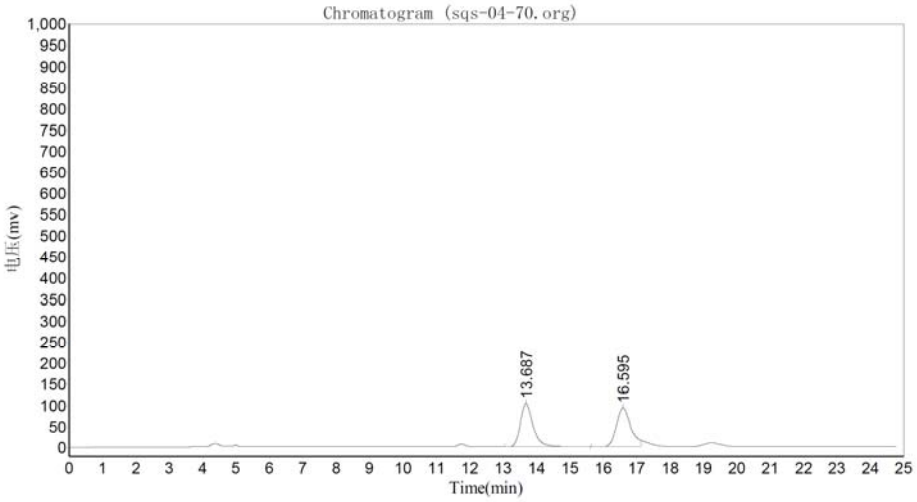
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.473	573197.188	14134037.000	100.0000
Total			573197.188	14134037.000	100.0000



4e was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 72% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 13.88 min., τ_{minor} = 16.59 min. $[\alpha]_{20}^{D}$ = 12.388 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{31}H_{36}N_2O_9Na]^+$ $(M+Na)^+$: 603.2319, found: 603.2298.

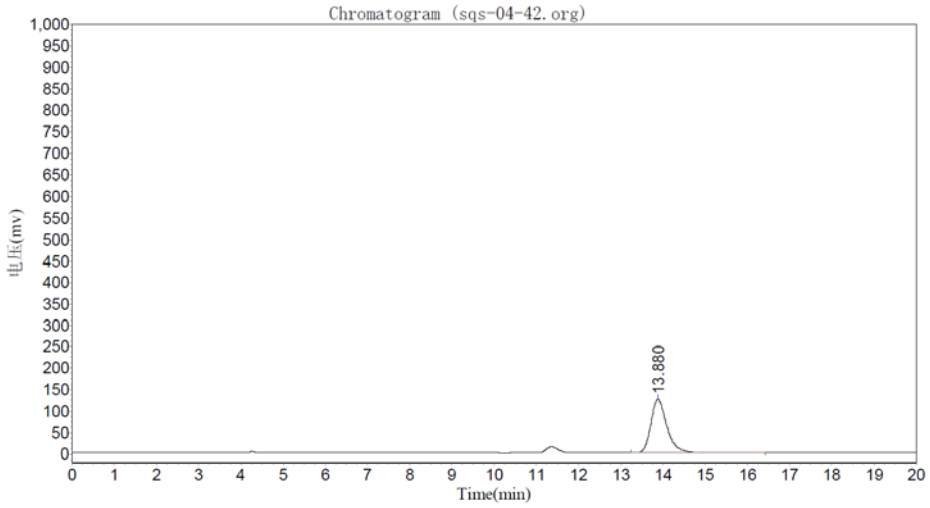
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (s, 3H), 0.86 (t, *J* = 7.2 Hz, 3H), 1.69 (s, 3H), 1.75 (s, 9H), 2.36 (s, 3H), 3.82-3.88 (m, 2H), 3.95 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.24 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.79 (s, 1H), 5.99 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.17-7.42 (m, 6H), 7.69(m, 1H), 7.76 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.51, 175.22, 168.47, 148.50, 140.23, 138.44, 132.80, 130.02, 129.47, 126.69, 125.69, 124.66, 114.42, 87.35, 85.26, 73.21, 61.84, 57.46, 54.99, 50.21, 45.73, 34.75, 28.18, 22.73, 21.15, 13.42.



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.687	102792.250	2704530.000	49.7972
2		16.595	92130.219	2726556.250	50.2028
Total			194922.469	5431086.250	100.0000



Results

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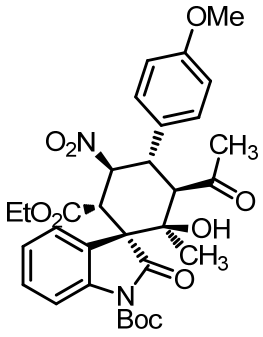
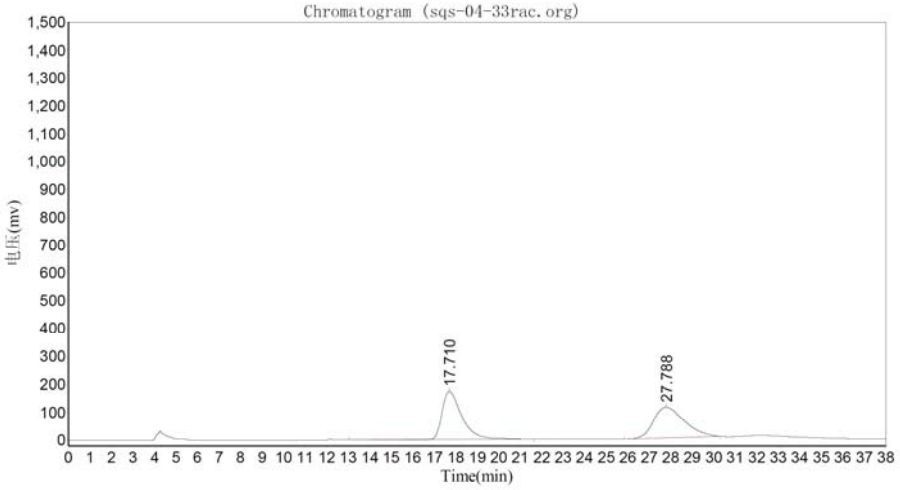
1		13.880	124894.852	3319747.750	100.0000
Total			124894.852	3319747.750	100.0000



4f was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 71% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 27.56 min., τ_{minor} = 17.71 min. $[\alpha]_{20}^{D}$ = 7.793 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{31}H_{36}N_2O_{10}Na]^+$ $(M+Na)^+$: 619.2268, found: 619.2212.

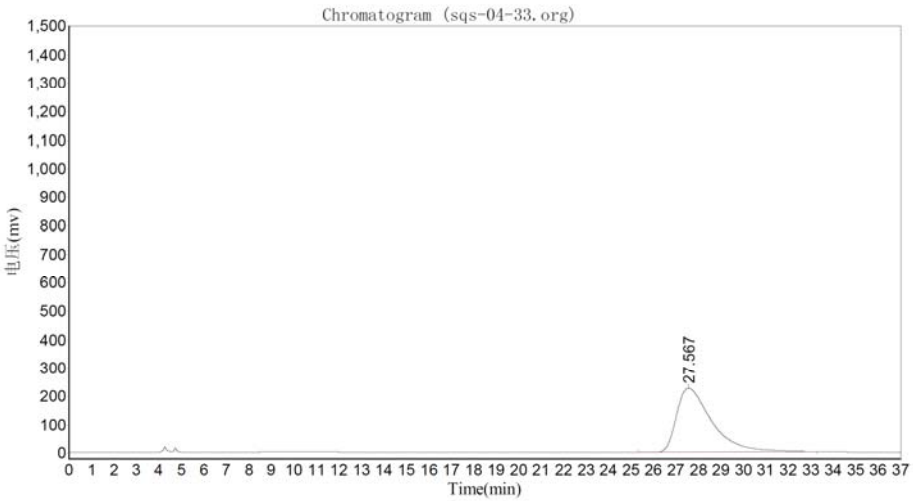
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (s, 3H), 0.86 (t, *J* = 7.2 Hz, 3H), 1.72 (s, 3H), 1.74 (s, 9H), 3.83 (s, 3H), 3.82-3.88 (m, 2H), 3.94 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.23 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.77 (s, 1H), 5.99 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 6.92-7.44 (m, 6H), 7.70(m, 1H), 7.76 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.53, 175.17, 168.45, 159.66, 148.51, 140.24, 129.46, 127.72, 126.67, 125.68, 124.65, 114.42, 87.44, 85.24, 73.21, 61.83, 57.45, 55.24, 55.07, 50.21, 45.34, 34.73, 28.17, 22.72, 13.41.



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.710	172161.938	11016949.000	50.0078
2		27.788	110738.055	11013500.000	49.9922
Total			282899.992	22030449.000	100.0000



Results

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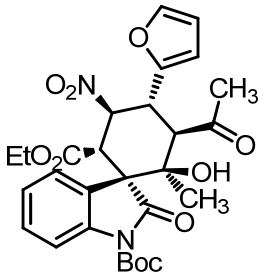
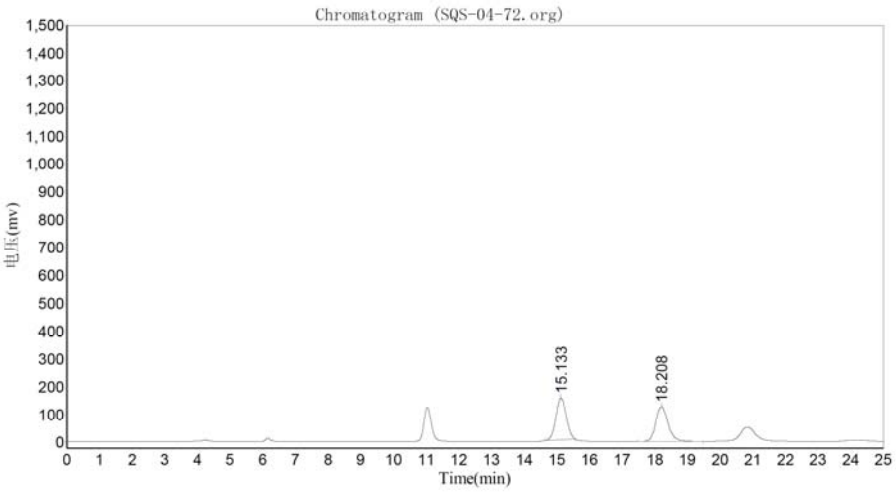
1		27.567	224634.297	24382386.000	100.0000
Total			224634.297	24382386.000	100.0000



4g was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 87% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 18.20 min., τ_{minor} = 15.13 min. $[\alpha]_{20}^{D}$ = -4.995 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{28}H_{32}N_2O_{10}Na]^+$ $(M+Na)^+$: 579.1955, found: 579.1938.

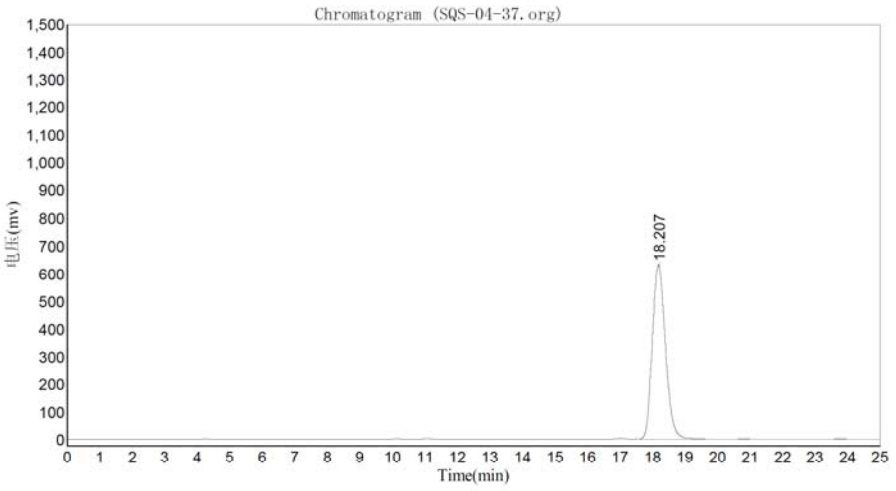
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (s, 3H), 0.86 (t, *J* = 7.2 Hz, 3H), 1.73 (s, 9H), 1.87 (s, 3H), 3.82-3.88 (m, 2H), 4.17 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.31 (d, *J* = 12.0 Hz, 1H), 4.39 (d, *J* = 12.0 Hz, 1H), 4.67 (s, 1H), 6.01 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 6.26 (d, *J* = 3.2 Hz, 1H), 6.35 (dd, *J*1 = 3.2 Hz, *J*2 = 1.6 Hz, 1H), 7.21-7.25 (m, 1H), 7.37-7.41 (m, 1H), 7.49(d, *J* = 1.6 Hz, 1H), 7.69 (m, 1H), 7.78 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.04, 174.42, 168.15, 151.08, 148.69, 143.34, 140.32, 129.50, 126.74, 125.54, 124.55, 114.39, 110.85, 109.76, 85.18, 73.17, 61.88, 57.26, 52.49, 50.03, 39.85, 33.42, 28.16, 22.42, 13.38.



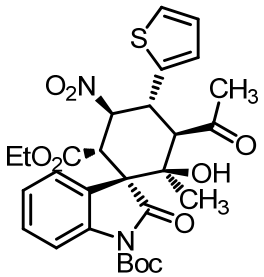
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.133	151190.813	3337171.000	50.1297
2		18.208	125682.258	3319904.000	49.8703
Total			276873.070	6657075.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.207	629709.125	17820950.000	100.0000
Total			629709.125	17820950.000	100.0000

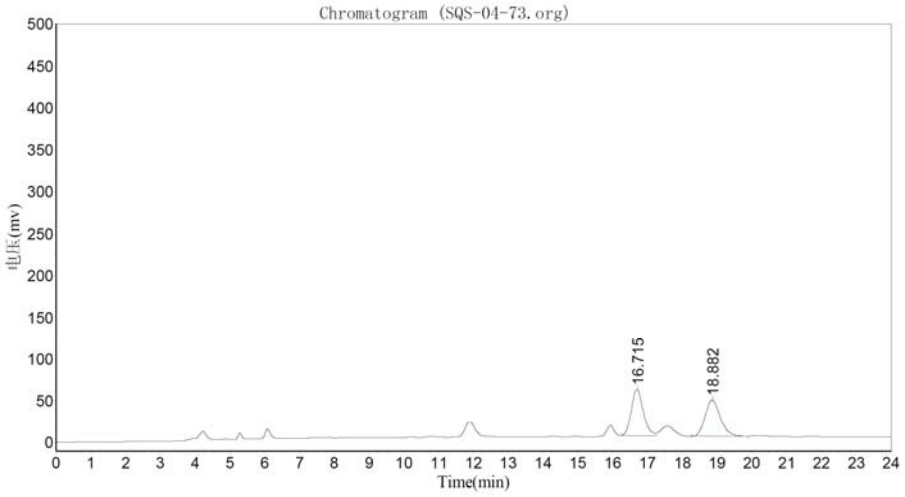


4h was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 77% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 18.65 min., τ_{minor} = 16.71 min. $[\alpha]_{20}^{D}$ = 6.794 (c = 1.0,

$CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{28}H_{32}N_2O_9SNa]^+$ $(M+Na)^+$: 595.1726, found: 595.1680.

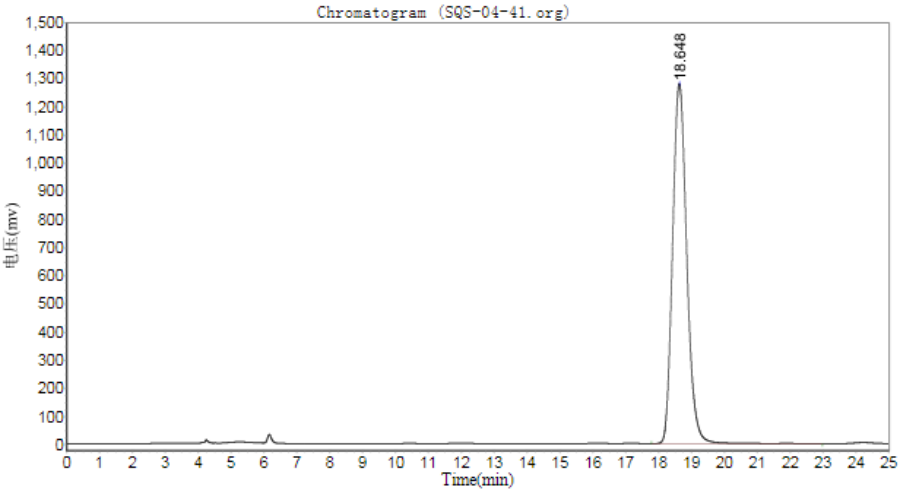
^1H NMR (400 MHz, $CDCl_3$): δ 0.85 (s, 3H), 0.87 (t, *J* = 7.2 Hz, 3H), 1.74 (s, 9H), 1.87 (s, 3H), 3.82-3.89 (m, 2H), 4.25-4.38 (m, 3H), 4.66 (s, 1H), 5.94 (dd, *J*1 = 12.8 Hz, *J*2 = 12.8 Hz, 1H), 7.00 (dd, *J*1 = 5.2 Hz, *J*2 = 3.6 Hz, 1H), 7.08 (d, *J* = 2.4 Hz, 1H), 7.22-7.26 (m, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.38-7.42 (m, 1H), 7.68 (m, 1H), 7.76 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.09, 168.14, 163.41, 140.29, 138.40, 129.55, 127.56, 127.32, 126.64, 126.13, 125.51, 124.66, 114.46, 88.12, 85.28, 73.27, 61.96, 57.27, 55.81, 50.39, 41.45, 34.62, 28.17, 22.62, 13.40.



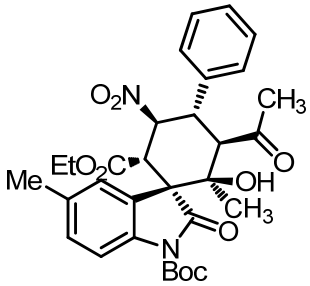
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.715	57203.418	1432345.375	50.3162
2		18.882	44700.711	1414341.250	49.6838
Total			101904.129	2846686.625	100.0000



Results

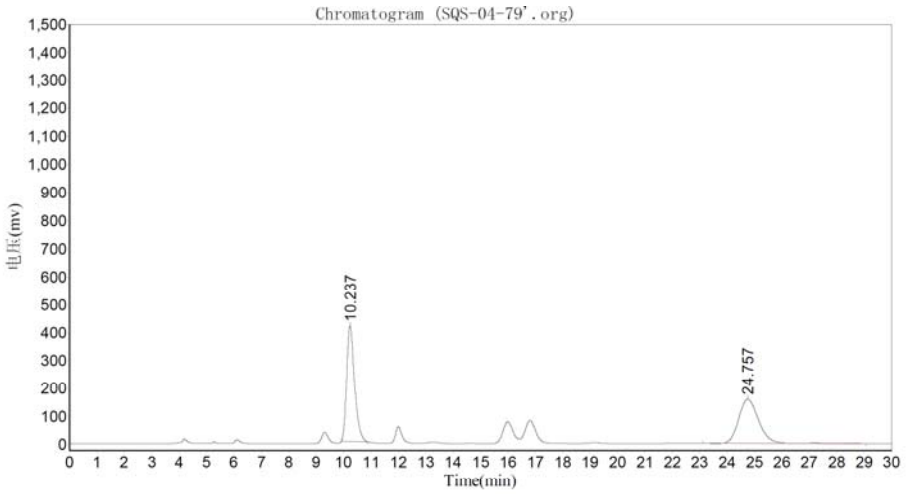
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.648	1278089.125	38255328.000	100.0000
Total			1278089.125	38255328.000	100.0000



4i was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 65% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 10.08 min., τ_{minor} = 24.75 min. $[\alpha]_{20}^{D}$ = -1.699 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{31}H_{36}N_2O_9Na]^+$ $(M+Na)^+$: 603.2319, found: 603.2303.

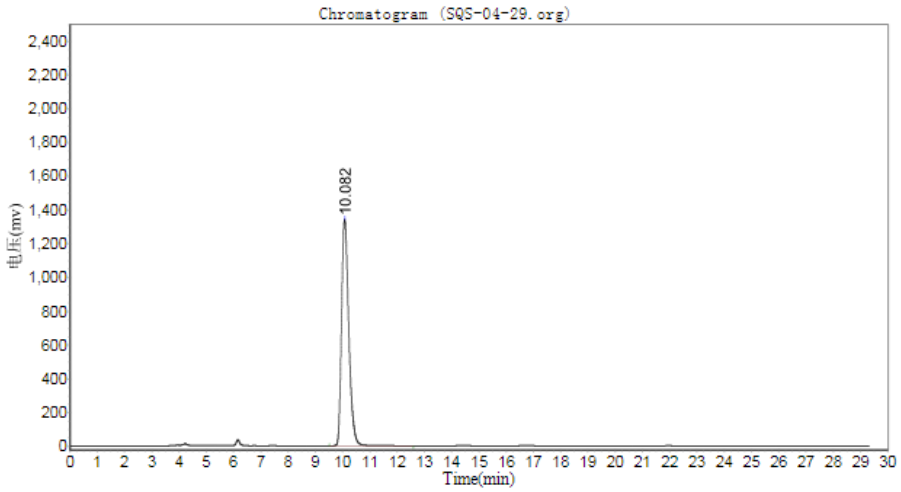
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (s, 3H), 0.87 (t, *J* = 7.2 Hz, 3H), 1.67 (s, 3H), 1.74 (s, 9H), 2.41 (s, 3H), 3.84-3.89 (q, 2H), 3.95 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.27 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.77 (s, 1H), 6.02 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.18-7.51 (m, 7H), 7.63 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.39, 175.32, 168.37, 148.56, 137.87, 136.04, 134.36, 129.97, 129.33, 128.66, 127.17, 125.53, 114.20, 87.30, 85.05, 73.19, 61.78, 57.53, 55.06, 50.22, 46.11, 34.62, 28.18, 22.74, 21.16, 13.39.



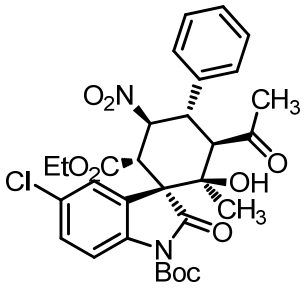
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		10.237	410704.000	8191423.000	50.7545
2		24.757	156324.578	7947874.500	49.2455
Total			567028.578	16139297.500	100.0000



Results

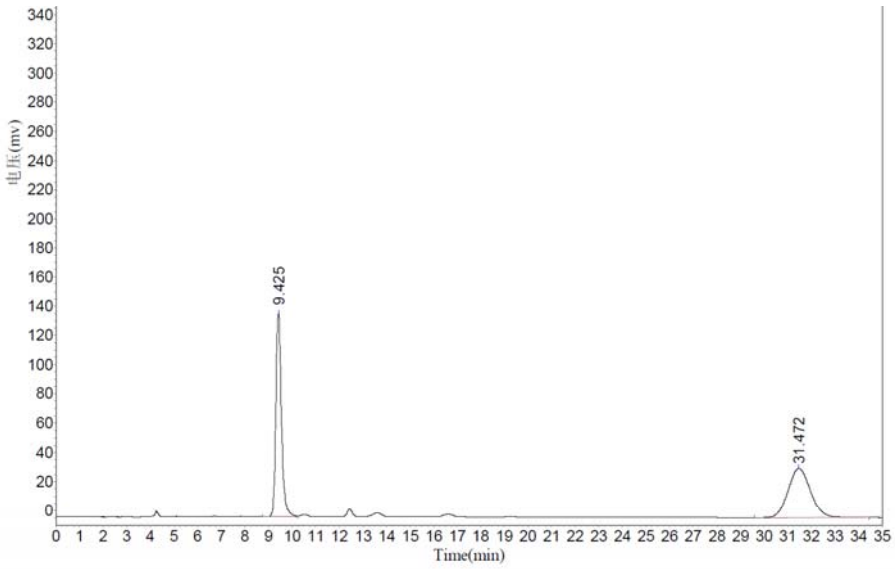
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		10.082	1340083.375	24650558.000	100.0000
Total			1340083.375	24650558.000	100.0000



4j was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 77% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 9.42 min., τ_{minor} = 31.47 min. $[\alpha]_{20}^{D}$ = -1.798 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{30}H_{33}ClN_2O_9Na]^+$ $(M+Na)^+$: 623.1772, found: 623.1742.

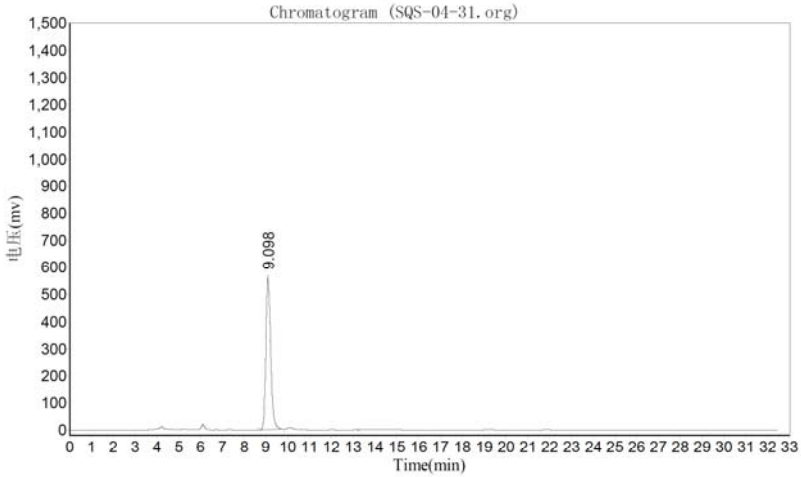
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (s, 3H), 0.91 (t, *J* = 7.2 Hz, 3H), 1.67 (s, 3H), 1.74 (s, 9H), 3.86-3.91 (q, 2H), 3.94 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.21 (d, *J* = 12.0 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.81 (s, 1H), 5.99 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.33-7.46 (m, 6H), 7.71(d, *J* = 2.4 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.13, 174.43, 168.36, 150.38, 148.31, 138.88, 135.79, 130.21, 129.51, 129.39, 128.76, 128.56, 127.50, 126.89, 115.66, 87.05, 85.62, 73.12, 62.06, 57.56, 54.94, 50.09, 46.10, 34.62, 28.15, 22.74, 13.42.



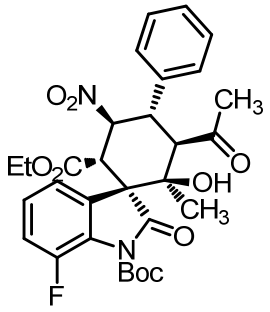
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.425	139106.422	2310805.750	50.5819
2		31.472	33952.355	2257639.750	49.4181
Total			173058.777	4568445.500	100.0000



Results

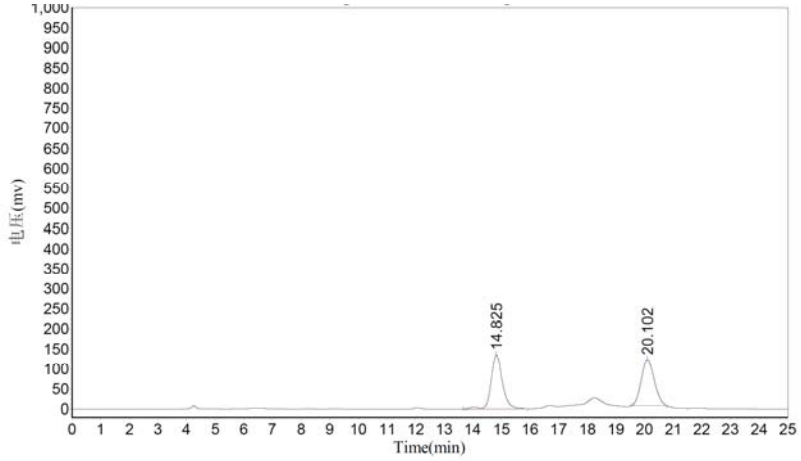
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.098	557453.063	8776667.000	100.0000
Total			557453.063	8776667.000	100.0000



4k was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 79% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 21.48 min., τ_{minor} = 15.82 min. $[\alpha]_{20}^{D}$ = 14.985 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{30}H_{33}FN_2O_9Na]^+$ $(M+Na)^+$: 607.2068, found: 607.2035.

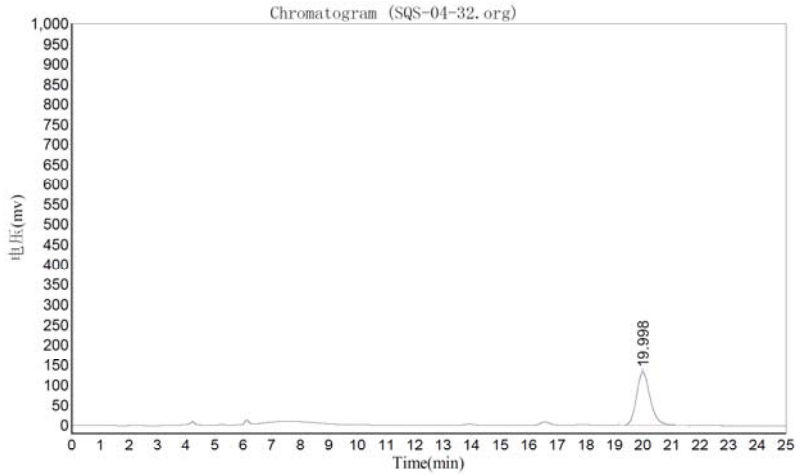
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (s, 3H), 0.88 (t, *J* = 7.2 Hz, 3H), 1.67 (s, 3H), 1.68 (s, 9H), 3.84-3.99 (m, 3H), 4.24 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 12.0 H, 1H,), 4.80(s, 1H), 6.00 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.13-7.40 (m, 6H), 7.50(d, *J* = 1.2 Hz, 1H), 7.52 (d, *J* = 1.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.24, 174.35, 168.26, 149.43, 146.93 (d, 1C, *J* = 5.1Hz), 135.81, 129.37, 128.93, 128.74, 125.45, 124.20, 122.57, 117.75, 117.55, 87.01, 86.51, 85.55, 73.12, 62.05, 58.23, 54.89, 50.04, 46.05, 34.62, 27.67, 22.67, 13.40.



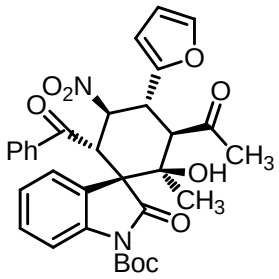
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.825	134987.266	3664578.500	50.1018
2		20.102	115954.211	3649687.000	49.8982
Total			250941.477	7314265.500	100.0000



Results

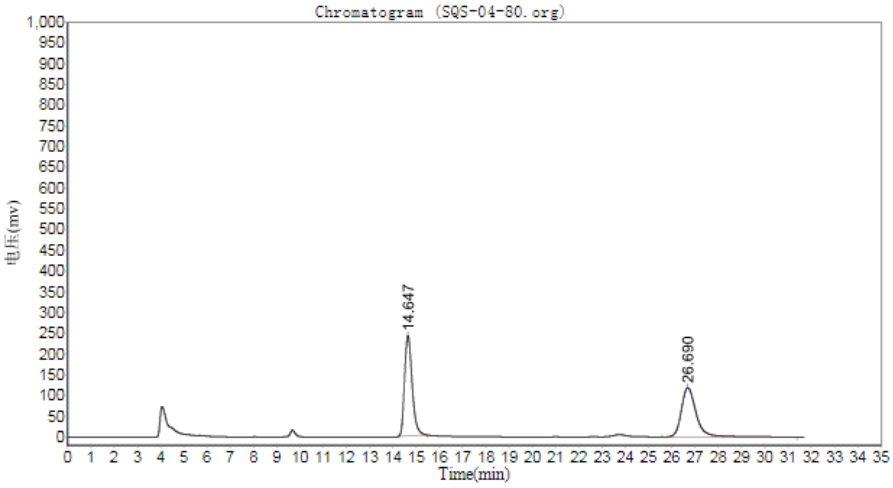
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.998	133029.734	4415189.500	100.0000
Total			133029.734	4415189.500	100.0000



4l was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 32% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 14.76 min., τ_{minor} = 26.71 min. $[\alpha]_{20}^{D}$ = 51.149 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{32}H_{32}N_2O_9Na]^+$ $(M+Na)^+$: 611.2006, found: 611.1982.

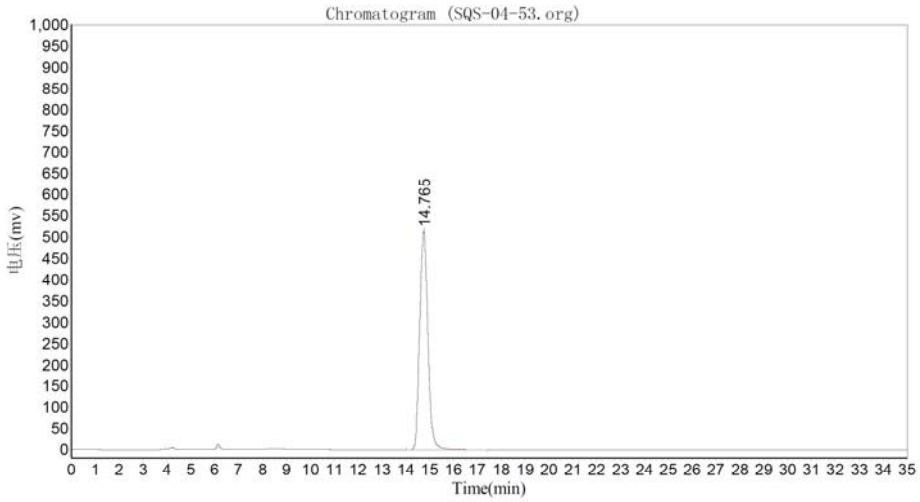
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (s, 3H), 1.76 (s, 9H), 1.90 (s, 3H), 4.26 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 H, 1H,), 4.87 (s, 1H), 5.48 (d, *J* = 12.0 Hz, 1H), 6.28 (dd, *J*1 = 2.4 Hz, *J*2 = 0.4 Hz, 1H), 6.35 (dd, *J*1 = 3.2 Hz, *J*2 = 2.4 Hz, 1H), 6.91 (m, 1H), 7.32 (m, 2H), 7.50 (m, 2H), 7.66 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.51, 197.06, 174.28, 148.70, 148.64, 143.38, 140.03, 136.54, 133.76, 129.41, 128.36, 128.22, 126.83, 124.87, 124.18, 114.53, 110.84, 109.71, 85.93, 85.07, 73.70, 57.75, 52.78, 49.58, 40.37, 33.56, 28.20, 22.44.



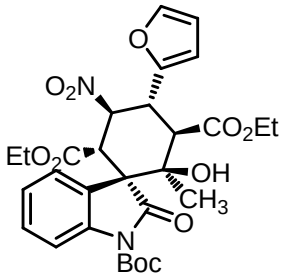
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.647	240920.906	5459471.500	50.6469
2		26.690	118747.156	5320004.500	49.3531
Total			359668.063	10779476.000	100.0000



Results

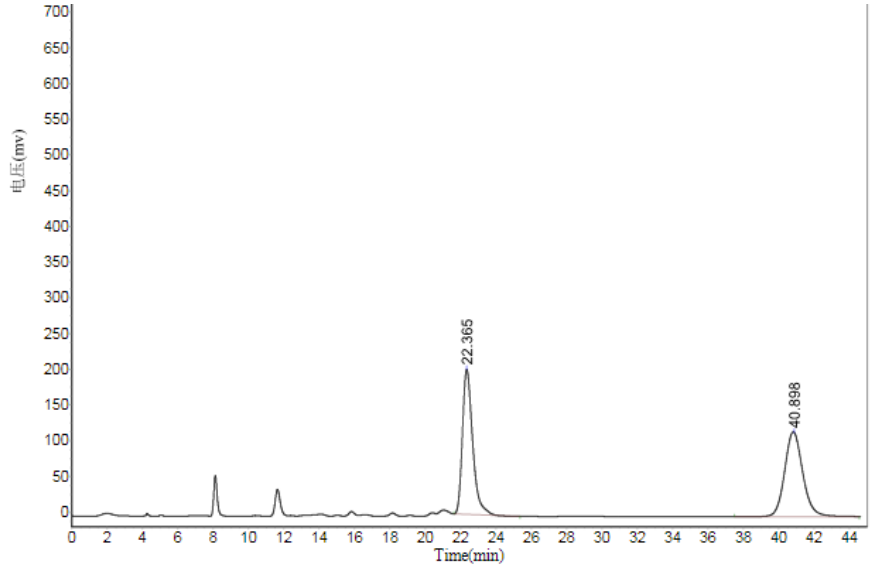
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.765	513609.344	12280146.000	100.0000
Total			513609.344	12280146.000	100.0000



4m was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 70% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 48.80 min., τ_{minor} = 22.35 min. $[\alpha]_{20}^{D}$ = 4.396 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{29}H3_4N_2O_{11}Na]^+$ $(M+Na)^+$: 609.2060, found: 609.2021.

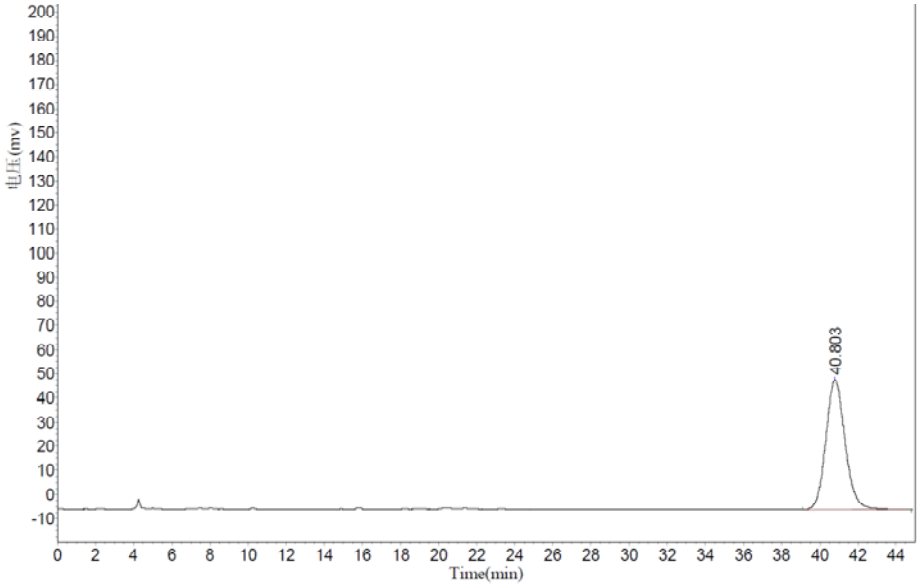
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (t, *J* = 7.2 Hz, 3H), 0.89 (s, 3H), 1.01 (t, *J* = 7.2 Hz, 3H), 1.57 (s, 3H), 1.67 (s, 9H), 3.82-3.88 (q, 2H), 4.04 (dd, *J*1 = 7.6 Hz, *J*2 = 7.2 Hz, 1H), 4.09 (d, *J* = 12.0 Hz, 1H), 4.24 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.32 (d, *J* = 12.0 Hz, 1H), 4.41 (s, 1H), 5.99 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 6.29 (d, *J* = 3.2 Hz, 1H), 6.32 (dd, *J*1 = 3.2 Hz, *J*2 = 1.6 Hz, 1H), 7.21-7.25 (m, 1H), 7.38-7.42 (m, 1H), 7.46(d, *J* = 1.6 Hz, 1H), 7.70 (m, 1H), 7.82 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 174.21, 157.17, 149.09, 148.74, 143.25, 129.52, 126.64, 124.50, 114.45, 110.29, 109.23, 85.16, 72.46, 61.89, 61.59, 56.92, 50.04, 49.48, 39.59, 28.16, 22.63, 13.76, 13.39.



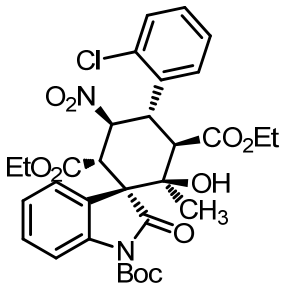
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.365	205666.594	8657572.000	50.5855
2		40.898	118452.391	8457153.000	49.4145
Total			324118.984	17114725.000	100.0000



Results

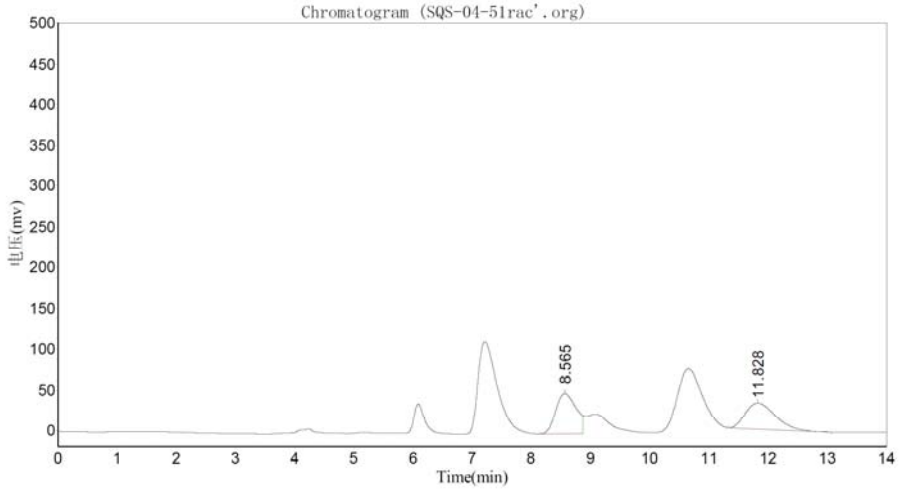
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		40.803	53600.082	3775297.000	100.0000
Total			53600.082	3775297.000	100.0000



4n was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 79% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak PC-2 column: hexane/i-PrOH 80:20, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 8.34 min., τ_{minor} = 11.82 min. $[\alpha]_{20}^{D}$ = 4.596 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{31}H_{35}ClN_2O_{10}Na]^+$ $(M+Na)^+$: 653.1878, found: 653.1845.

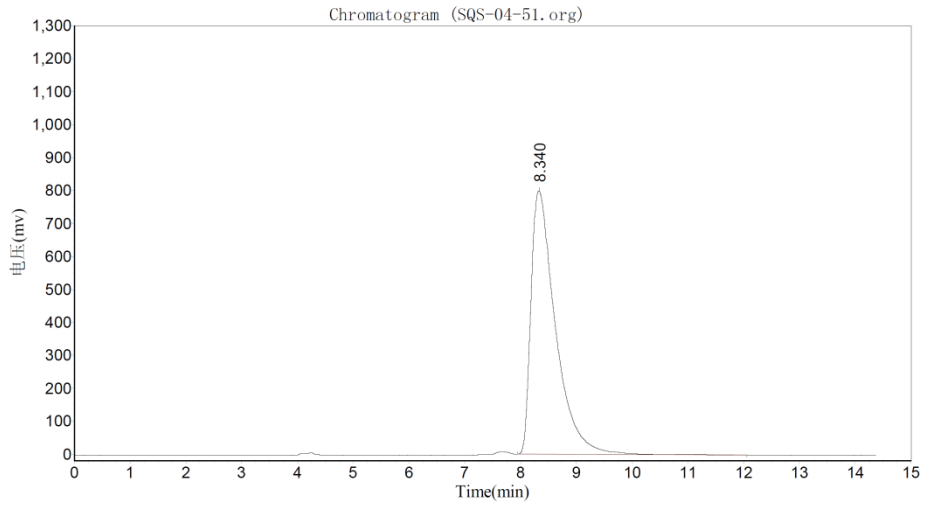
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, *J* = 7.2 Hz, 3H), 0.85 (t, *J* = 7.2 Hz, 3H), 0.90 (s, 3H), 1.74 (s, 9H), 3.82-3.90 (m, 4H), 3.98 (d, *J*1 = 12.0 Hz, 1H), 4.07 (q, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.34 (s, 1H), 5.93 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.23-7.43 (m, 6H), 7.69(m, 1H), 7.79 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 174.76, 174.00, 168.20, 148.55, 140.30, 134.50, 134.42, 129.90, 129.58, 129.09, 126.57, 125.68, 124.64, 114.52, 87.21, 85.23, 72.50, 61.92, 61.46, 57.07, 51.20, 50.14, 45.11, 28.17, 22.78, 13.56, 13.40.



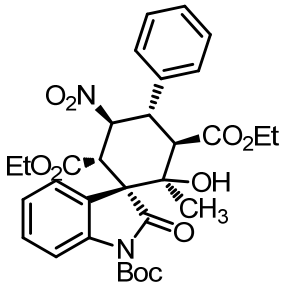
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		8.565	50485.660	1209014.375	51.4611
2		11.828	32712.617	1140361.000	48.5389
Total			83198.277	2349375.375	100.0000



Results

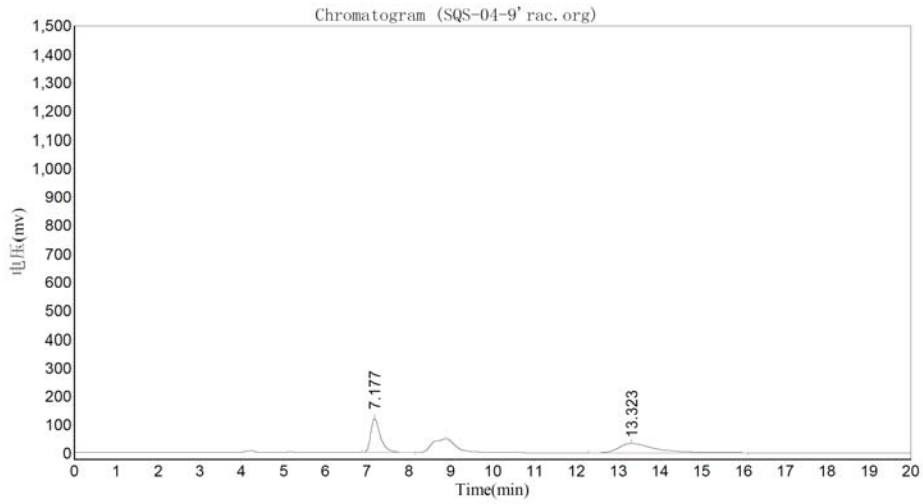
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		8.340	801711.813	24794072.000	100.0000
Total			801711.813	24794072.000	100.0000



4o was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 48% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 12.69 min., τ_{minor} = 7.17 min. $[\alpha]_{20}^{D}$ = 5.993 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{31}H_{36}N_2O_{10}Na]^+$ $(M+Na)^+$: 619.2268, found: 619.2238

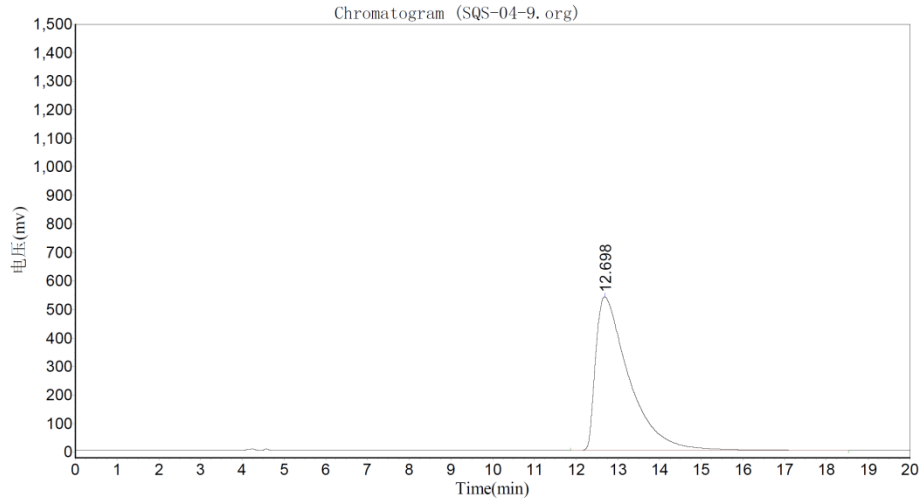
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.73 (t, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H), 0.93 (s, 3H), 1.73 (s, 9H), 3.76-3.90 (m, 4H), 3.97 (d, *J*1 = 12.0 Hz, 1H), 4.07 (q, 1H), 4.34 (d, *J* = 12.0 Hz, 1H), 4.45 (s, 1H), 5.98 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.21-7.43 (m, 7H), 7.71(m, 1H), 7.80 (d, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 174.70, 174.24, 168.33, 148.63, 140.31, 135.82, 129.51, 128.84, 128.45, 126.60, 125.80, 124.59, 114.48, 87.33, 85.12, 77.38, 77.07, 76.75, 72.50, 61.85, 61.27, 57.09, 51.33, 50.27, 45.76, 28.17, 22.81, 13.44, 13.40.



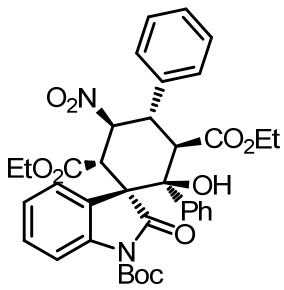
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		7.177	115862.844	1862437.750	50.9346
2		13.323	31866.393	1794088.125	49.0654
Total			147729.236	3656525.875	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		12.698	537923.063	29979000.000	100.0000
Total			537923.063	29979000.000	100.0000

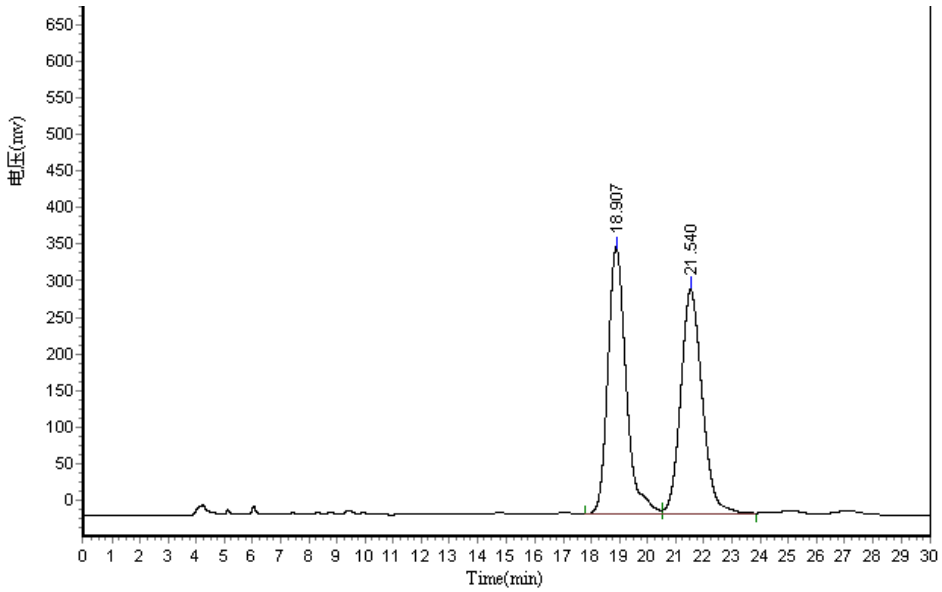


4p was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 18% yield with >20:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 95:5, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 18.88 min., τ_{minor} = 21.54 min. $[\alpha]_{20}^{D}$ = 20.778 (c = 1.0,

$CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{36}H_{38}N_2O_{10}Na]^+$ $(M+Na)^+$: 681.2424, found: 681.2395

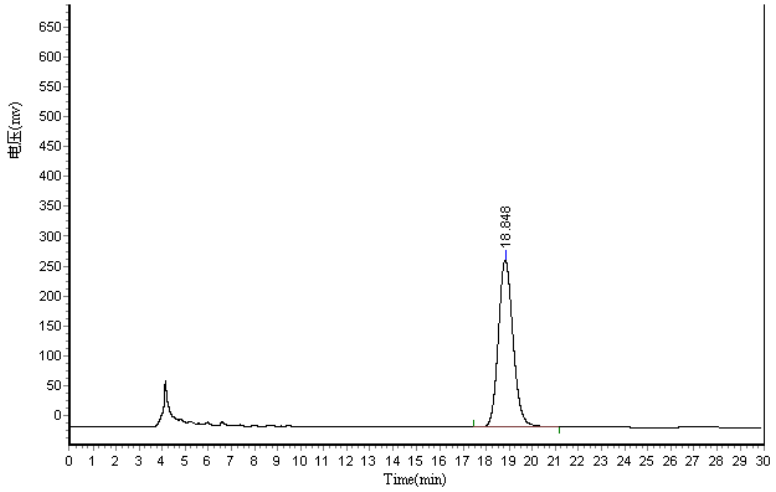
^1H NMR (400 MHz, $CDCl_3$): δ 0.49 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H), 1.61 (s, 9H), 3.51-3.56 (m, 2H), 3.80-3.93 (m, 2H), 4.30 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 5.03 (s, 1H), 6.23 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 6.96-7.54 (m, 13H), 7.80 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 174.67, 173.88, 168.46, 148.00, 139.80, 138.25, 135.78, 129.17, 128.92, 128.55, 128.12, 127.34, 126.14, 125.40, 123.94, 114.13, 87.31, 84.29, 76.08, 61.93, 61.03, 58.21, 50.08, 49.59, 46.11, 28.09, 13.38, 13.13.



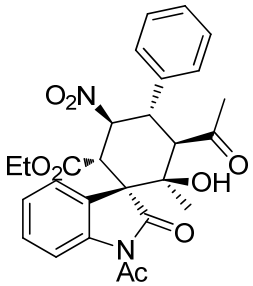
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.907	364761.438	16647207.000	50.1037
2		21.540	306541.781	16578283.000	49.8963
Total			671303.219	33225490.000	100.0000



Results

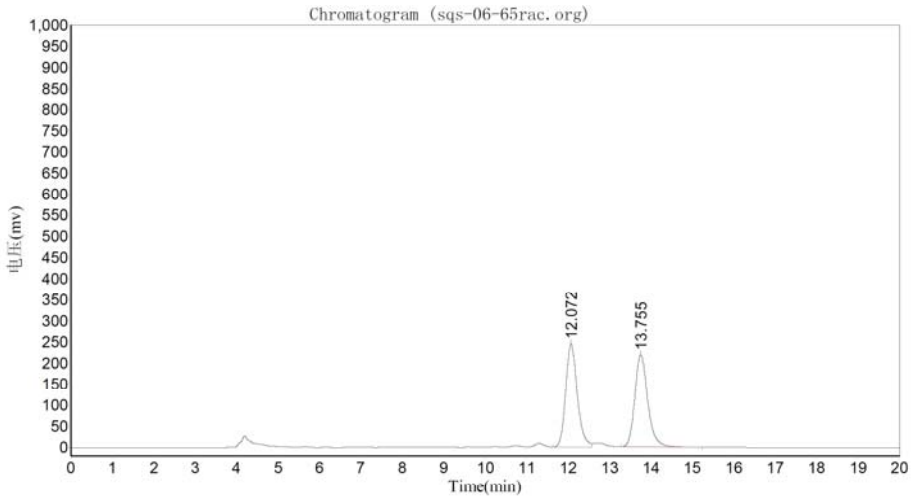
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.848	280418.125	12507439.000	100.0000
Total			280418.125	12507439.000	100.0000



4q was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =10/1/1) in 15% yield with 1:1 dr and >99% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 90:10, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 12.07 min., τ_{minor} = 13.81 min. $[\alpha]_{20}^{D}$ = 0.999 (c = 0.4, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{36}H_{38}N_2O_{10}H]^+$ $(M+H)^+$: 509.1924, found: 509.1915.

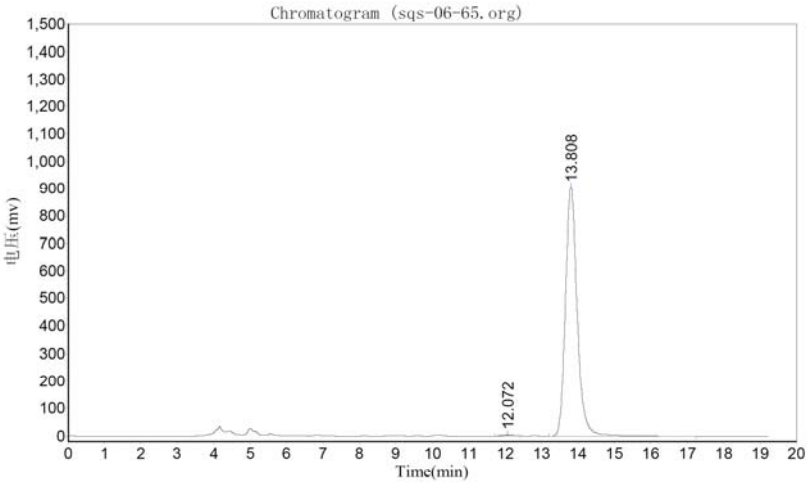
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80 (t, *J* = 7.2 Hz, 3H), 0.84 (s, 3H), 1.66 (s, 3H), 2.78 (s, 3H), 3.73-3.79 (m, 2H), 3.92 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 4.14 (d, *J* = 12.0 Hz, 1H), 4.29 (d, *J* = 12.0 Hz, 1H), 4.74 (s, 1H), 5.87 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 7.21-7.39 (m, 7H), 7.67-7.69 (m, 1H), 8.17-8.20(m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.12, 177.32, 170.86, 169.10, 140.83, 135.99, 129.88, 129.59, 128.93, 126.69, 125.86, 125.45, 116.04, 87.37, 73.33, 62.14, 57.83, 55.42, 50.71, 46.01, 34.76, 27.12, 22.92, 13.52.



Results

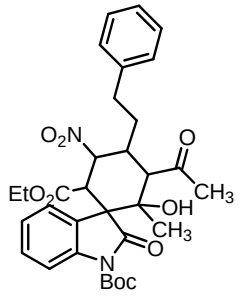
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		12.072	244632.406	4754877.000	50.0936
2		13.755	218626.859	4737103.000	49.9064
Total			463259.266	9491980.000	100.0000



Results

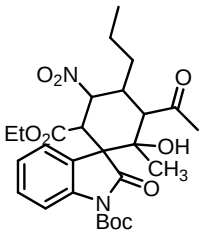
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		12.072	3777.002	71899.250	0.3560
2		13.808	906497.250	20126010.000	99.6440
Total			910274.252	20197909.250	100.0000

Results of other Michael acceptors:



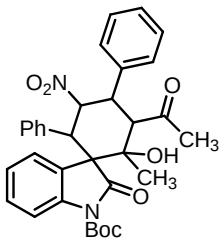
4r

yield = 59% dr = 1.08:1



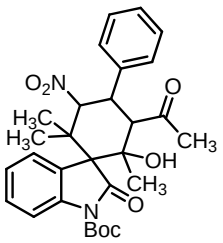
4s

yield = 78%, dr = 2:1



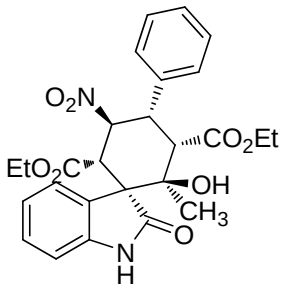
4t

yield = 0%



4u

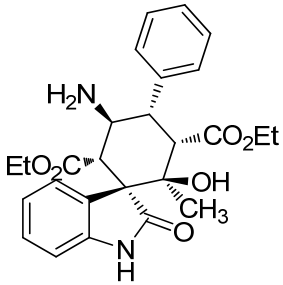
yield = 0%



To a solution of **4o** (59 mg, 0.1 mmol) in DCM (2 mL) was added TFA (2 mL). After 10 minutes, the reaction mixture was cooled to 0 ^{o}C and diluted by 20 mL DCM. Then the mixture was quenched by 1M NaOH aq. and adjusted pH = 11.0. The mixture was extracted by DCM (3×20 mL). The organic layer was combined, dried by Na_2SO_4, and concertrated in *vacuo.* Purification on flash column chromatography (petroleum/ethyl acetate =2/1) obtained **6o** in quatitative yield. $[\alpha]_{20}^{D}$ = 3.525 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{26}H_{28}N_2O_8Na]^+$ $(M+Na)^+$: 519.1743, found: 519.1721

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74 (t, *J* = 7.2 Hz, 3H), 0.77 (t, *J* = 7.2 Hz, 3H), 1.00 (s, 3H), 3.75-3.92 (m, 4H), 4.01-4.10 (m, 2H), 4.39-4.42 (m, 2H), 6.11 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 7.10-7.14 (m, 1H), 7.28-7.38 (m, 4H), 7.43 (br, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 8.40 (s, 1H).

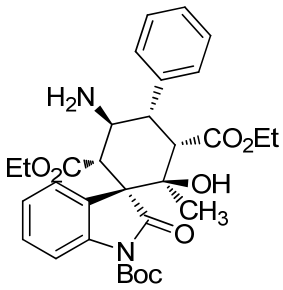
^{13}C NMR (100 MHz, $CDCl_3$): 177.46, 174.26, 169.20, 141.32, 136.03, 129.33, 128.83, 128.41, 127.41, 127.24, 122.76, 109.73, 87.13, 72.25, 61.64, 61.17, 57.44, 51.46, 49.71, 45.74, 22.73, 13.49, 13.36.



To a solution of **6o** (52 mg, 0.1 mmol) in MeOH (2 mL) was added Zn powder (50 mg) and 2 mL 0.1 N HCl aq.. After 10 minutes, the reaction mixture was cooled to 0 ^{o}C and diluted by 20 mL ethyl acetate. Then the mixture was quenched by 1M NaOH aq. and adjusted pH = 11.0. The mixture was extracted by ethyl acetate (3×20 mL). The organic layer was combined, dried by Na_2SO_4, and concertrated in *vacuo.* **7o** was obtained in 75% yield. $[\alpha]_{20}^{D}$ = -17.985 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{26}H_{31}N_2O_6H]^+$ $(M+H)^+$: 467.2182, found: 467.2217

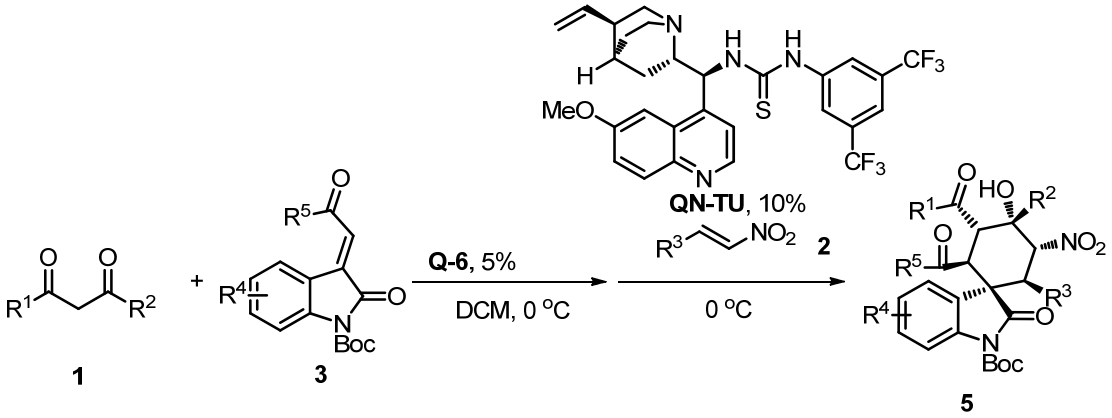
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.69 (t, *J* = 7.2 Hz, 3H), 0.73 (t, *J* = 7.2 Hz, 3H), 0.96 (s, 3H), 3.17 (dd, *J*1 = 12.0 Hz, *J*2 = 12.0 Hz, 1H), 3.70 (d, *J* = 12.0 Hz, 1H), 3.73-3.94 (m, 4H), 4.04 (d, *J* = 12.0 Hz, 1H), 4.30 (dd, *J* = 12.0 Hz, 1H), 4.38 (br, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 7.07-7.112 (m, 1H), 7.24-7.38 (m, 6H), 7.67 (d, *J* = 8.0 Hz, 1H), 8.07 (br, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 178.72, 175.57, 172.19, 141.28, 138.75, 128.67, 127.61, 127.34, 122.35, 109.38, 72.42, 60.63, 60.53, 59.95, 57.57, 52.00, 48.97, 43.23, 23.14, 13.52.

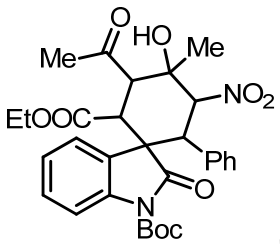


To a solution of **4o** (59 mg, 0.1 mmol) in MeOH (2 mL) was added Zn powder (50 mg) and 2 mL 0.1 N HCl aq.. After 10 minutes, the reaction mixture was cooled to 0 ^{o}C and diluted by 20 mL ethyl acetate. Then the mixture was quenched by 1M NaOH aq. and adjusted pH = 11.0. The mixture was extracted by ethyl acetate (3×20 mL). The organic layer was combined, dried by Na_2SO_4, and concertrated in *vacuo.* **8o** was obtained in 77% yield. $[\alpha]_{20}^{D}$ = -9.987 (c = 1.0, $CHCl_3$). HRMS: (ESI+, m/z) calculated for [$C_{31}H_{39}N_2O_8$+H] $(M+H)^+$: 567.2706, found: 567.2692.
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.73 (t, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H), 0.93 (s, 3H), 1.73 (s, 9H), 3.75-3.93 (m, 5H), 4.15-4.19 (m, 2H), 4.52 (s, 1H), 7.21-7.25 (m, 1H), 7.33-7.39 (br, 6H), 7.74-7.78 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): 175.51, 174.83, 171.22, 148.84, 139.99, 137.23, 135.41, 129.70, 128.95, 128.57, 127.60, 126.97, 124.44, 114.16, 84.68, 72.77, 60.94, 60.79, 60.56, 57.13, 51.95, 49.85, 38.79, 28.19, 23.08, 13.53, 13.45.

General procedure for synthesis of spirocyclic oxindoles **5**:



A solution of β-dicarbonyl compounds **1** (0.2 mmol), oxindoles derivatives **3** (0.3 mmol) and catalyst **Q-6** (5 mol%) in CH_2Cl_2 (0.20 mL) was stirred under 0 ^{o}C until all the β-dicarbonyl compounds consumed, then 10 mol% of **QN-TU** and nitroalkenes **2** (0.22 mmol) was added. After the reaction completed, the solution was concentrated and purified using column chromatography (Petroleum ether: ethyl acetate: DCM = 5: 1: 1, R_f(**5**)= 0.3) to afford the desired product.

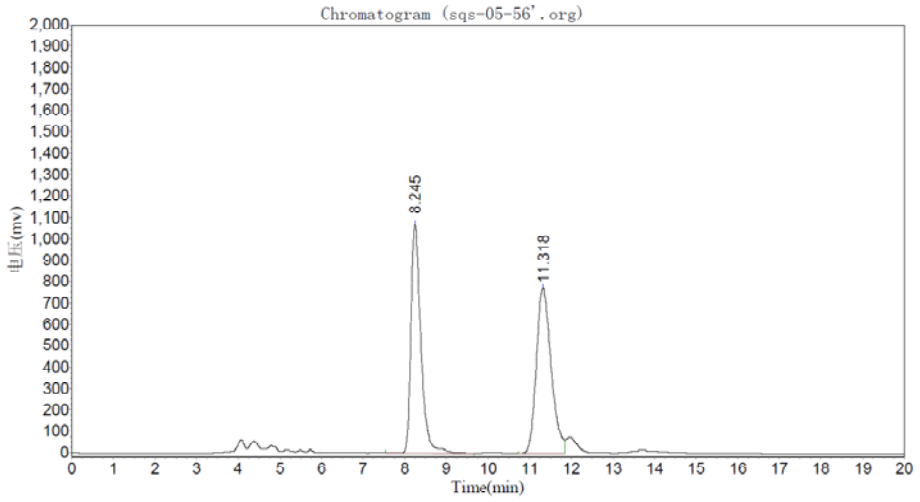


5a

The title compound **5a** was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =5/1/1) in 43% yield with 2.5:1 dr and 96% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 80:20, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 10.83 min., τ_{minor} = 8.08 min. $[\alpha]_{20}^{D}$ = -2.597 (c = 1, $CHCl_3$). HRMS: (ESI+, m/z) calculated for $[C_{30}H_{34}N_2O_9+Na]$ $(M+Na)^+$: 589.2162, found: 589.2138.

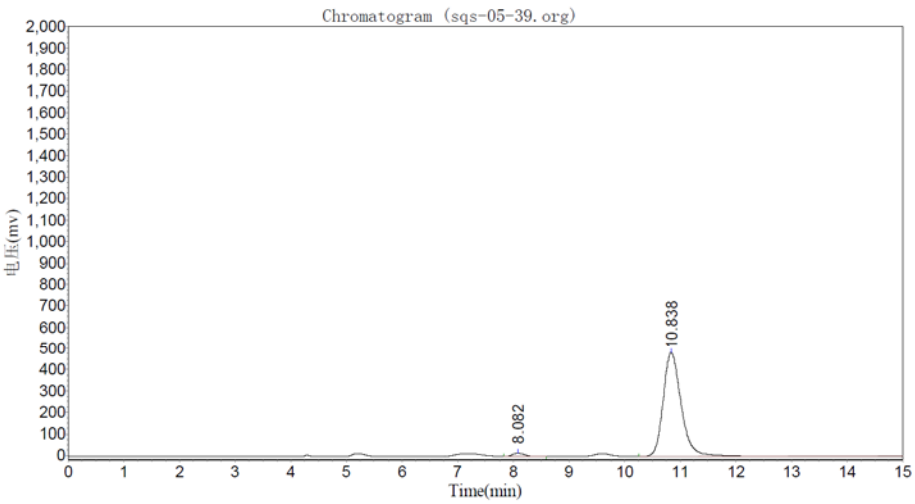
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, *J* = 7.2 Hz, 3H), 1.49 (s, 3H), 1.55 (s, 9H), 2.36 (s, 3H), 3.69-3.86 (m, 2H), 3.93 (d, J = 12.0 Hz, 1H), 4.12(d, J = 12.0 Hz, 1H), 4.13 (s, 1H), 4.21(d, J = 2.4 Hz, 1H), 4.24 (d, J = 2.4 Hz, 1H), 5.35 (s, 1H), 5.86 (d, J = 12.0 Hz), 6.44-7.19 (m, 7H), 7.38 (m, 1H), 7.45 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 211.69, 175.45, 169.91, 148.17, 139.48, 132.11, 129.08, 128.21, 127.91, 124.52, 122.39, 114.74, 89.74, 84.34, 70.98, 61.70, 52.55, 48.77, 48.42, 33.91, 28.07, 25.31, 13.29.



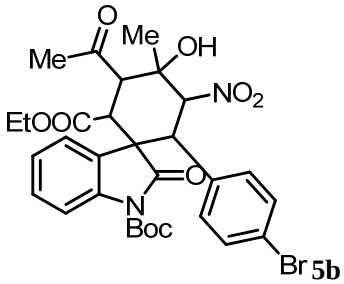
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		8.245	1070426.750	17691554.000	48.1757
2		11.318	771053.313	19031460.000	51.8243
Total			1841480.063	36723014.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		8.082	16431.469	280644.031	2.4975
2		10.838	481880.656	10956487.000	97.5025
Total			498312.125	11237131.031	100.0000

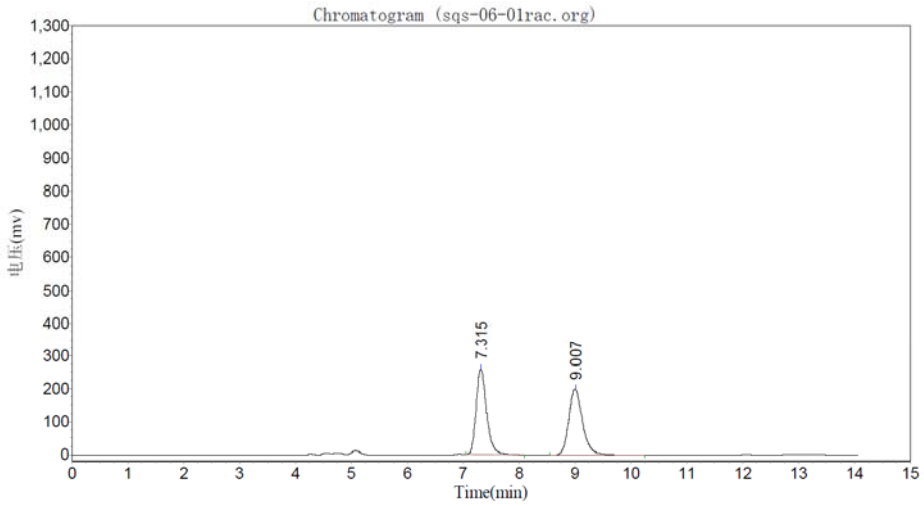


5b

The title compound **5b** was isolated as single diasteroisomer by flash column chromatography (petroleum/ethyl acetate/dichloromethane =5/1/1) in 52% yield with 4:1 dr and 92% ee. The ee was determined by HPLC analysis on a Daicel Chiralpak AD-H column: hexane/i-PrOH 80:20, flow rate 0.70 mL/min, λ = 214 nm: τ_{major} = 9.29 min., τ_{minor} = 7.31 min. $[\alpha]_{20}^{D}$ = 20.575 (c = 1, $CHCl_3$). HRMS: (ESI+, m/z) calculated for [$C_{30}H_{33}BrN_2O_9$+Na] (M+ Na)$^+$: 667.1267, found: 667.1237.

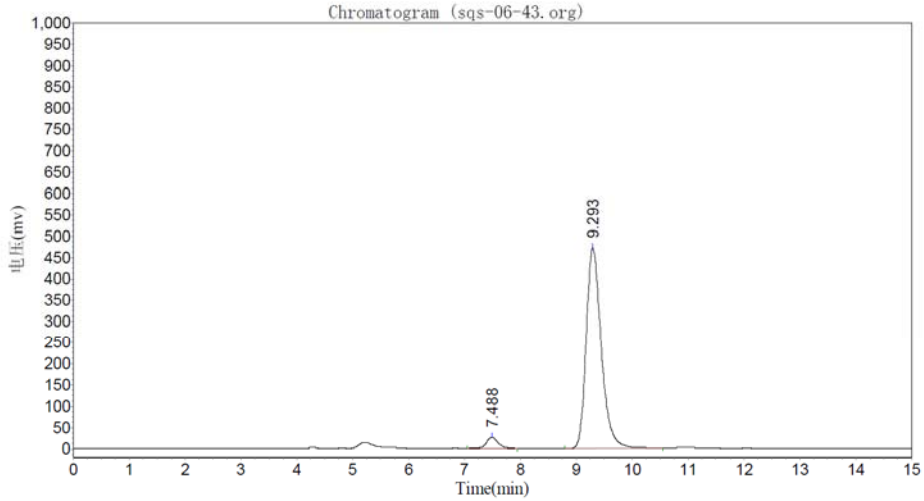
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, *J* = 7.2 Hz, 3H), 1.49 (s, 3H), 1.57 (s, 9H), 2.36 (s, 3H), 3.70-3.85 (m, 2H), 3.91 (d, *J* = 12.0 Hz, 1H), 4.13 (s, 1H), 4.19 (d, *J* = 5.2 Hz, 1H), 4.22 (d, *J* = 5.2 Hz, 1H), 5.80 (d, *J* = 12.0 Hz, 1H), 6.31-7.02 (br, 4H), 7.19-7.23 (m, 2H), 7.38-7.44 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): 211.68, 175.42, 169.77, 147.92, 139.43, 131.38, 131.13, 129.36, 127.65, 124.68, 122.48, 122.34, 114.96, 89.54, 84.69, 70.98, 61.80, 52.43, 48.76, 47.82, 33.97, 28.05, 25.26, 13.31.



Results

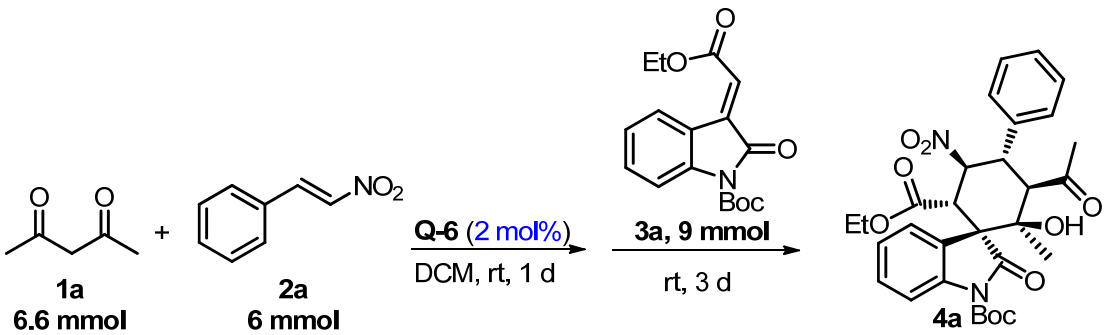
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		7.315	260576.641	3430902.000	50.0682
2		9.007	199189.266	3421556.500	49.9318
Total			459765.906	6852458.500	100.0000

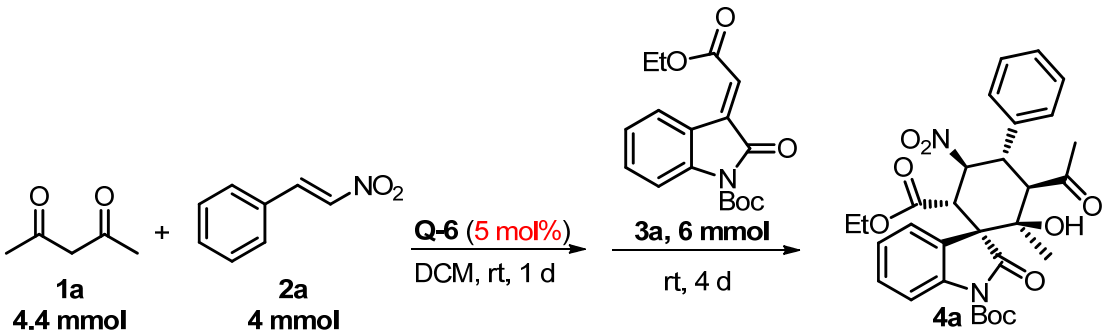


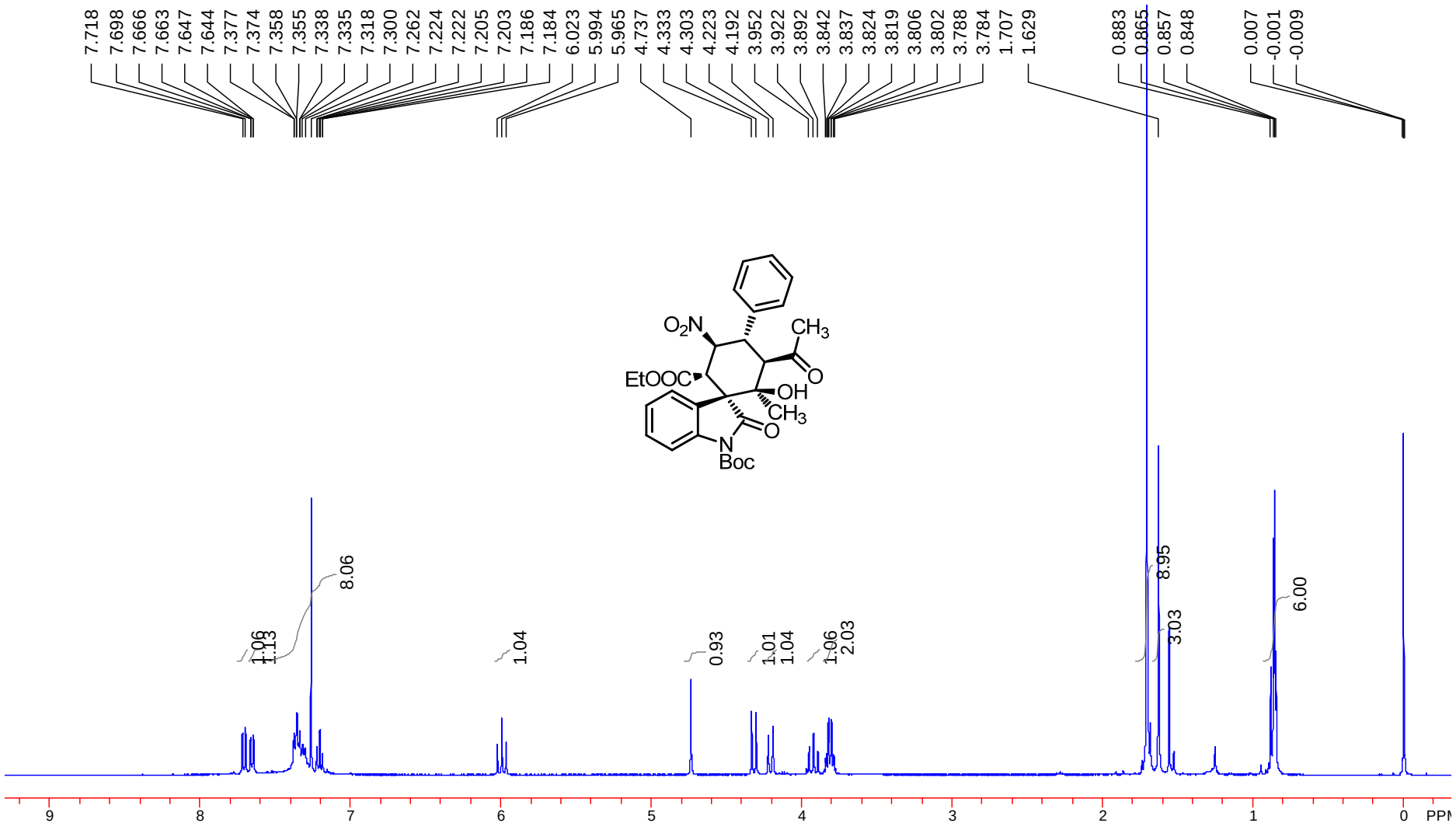
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		7.488	25747.566	361981.906	3.9418
2		9.293	471531.781	8821191.000	96.0582
Total			497279.348	9183172.906	100.0000

Gram-scale cascade reactions:



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7.338
7.335
7.318
7.300
7.262
7.224
7.222
7.205
7.203
7.186
7.184
6.023
5.994
5.965
4.737
4.333
4.303
4.223
4.192
3.952
3.922
3.892
3.842
3.837
3.824
3.819
3.806
3.802
3.788
3.784
1.707
1.629
0.883
0.865
0.857
0.848
0.007
-0.001
-0.009
O2N
CH3
EtOOC
O
OH
CH3
O
N
Boc
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1.13
8.06
1.04
0.93
1.01
1.04
1.06
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8.95
3.03
6.00
9
8
7
6
5
4
3
2
1
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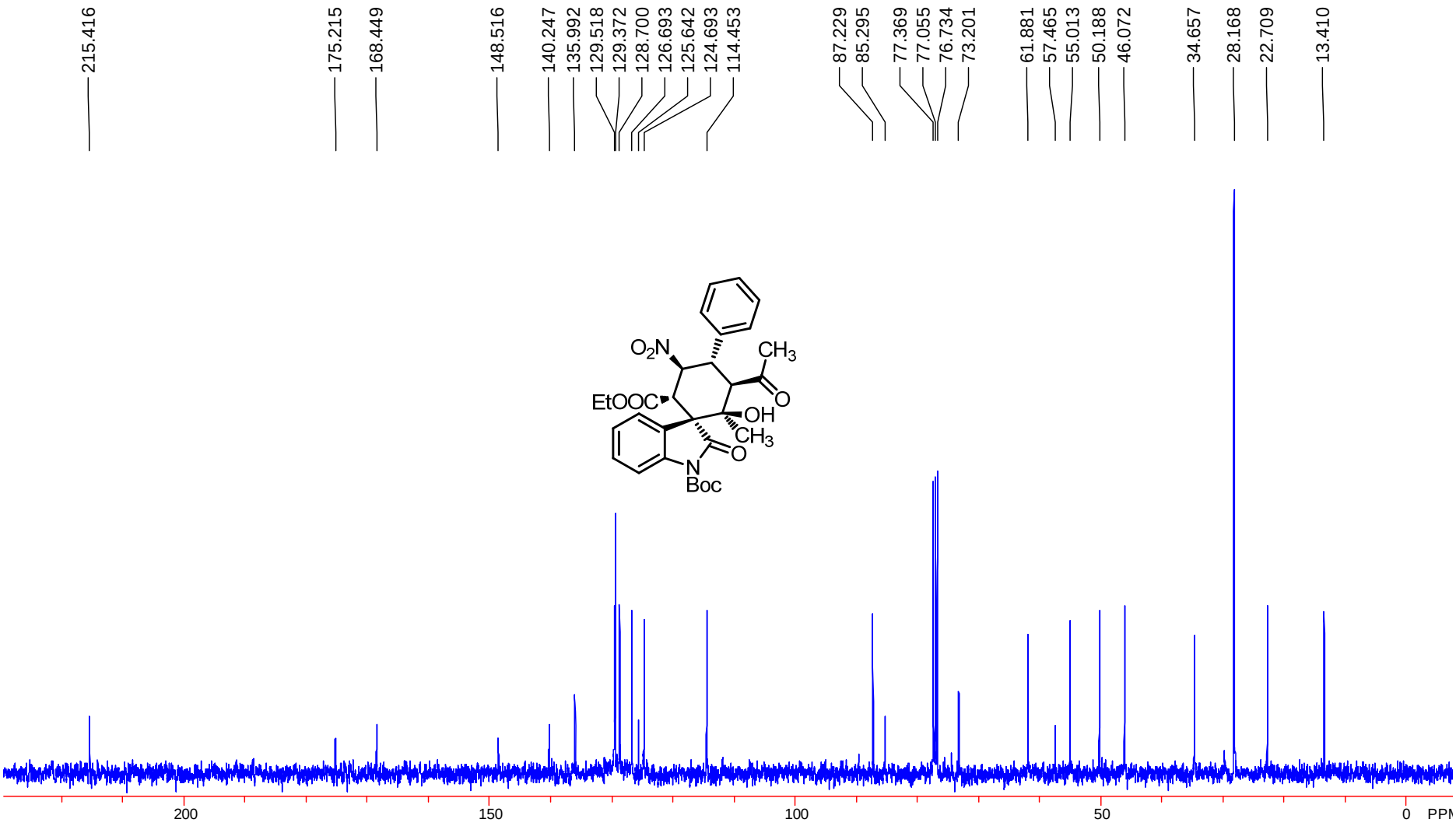
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129.372
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126.693
125.642
124.693
114.453
87.229
85.295
77.369
77.055
76.734
73.201
61.881
57.465
55.013
50.188
46.072
34.657
28.168
22.709
13.410
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CH3
EtOOC
O
OH
CH3
O
N
Boc
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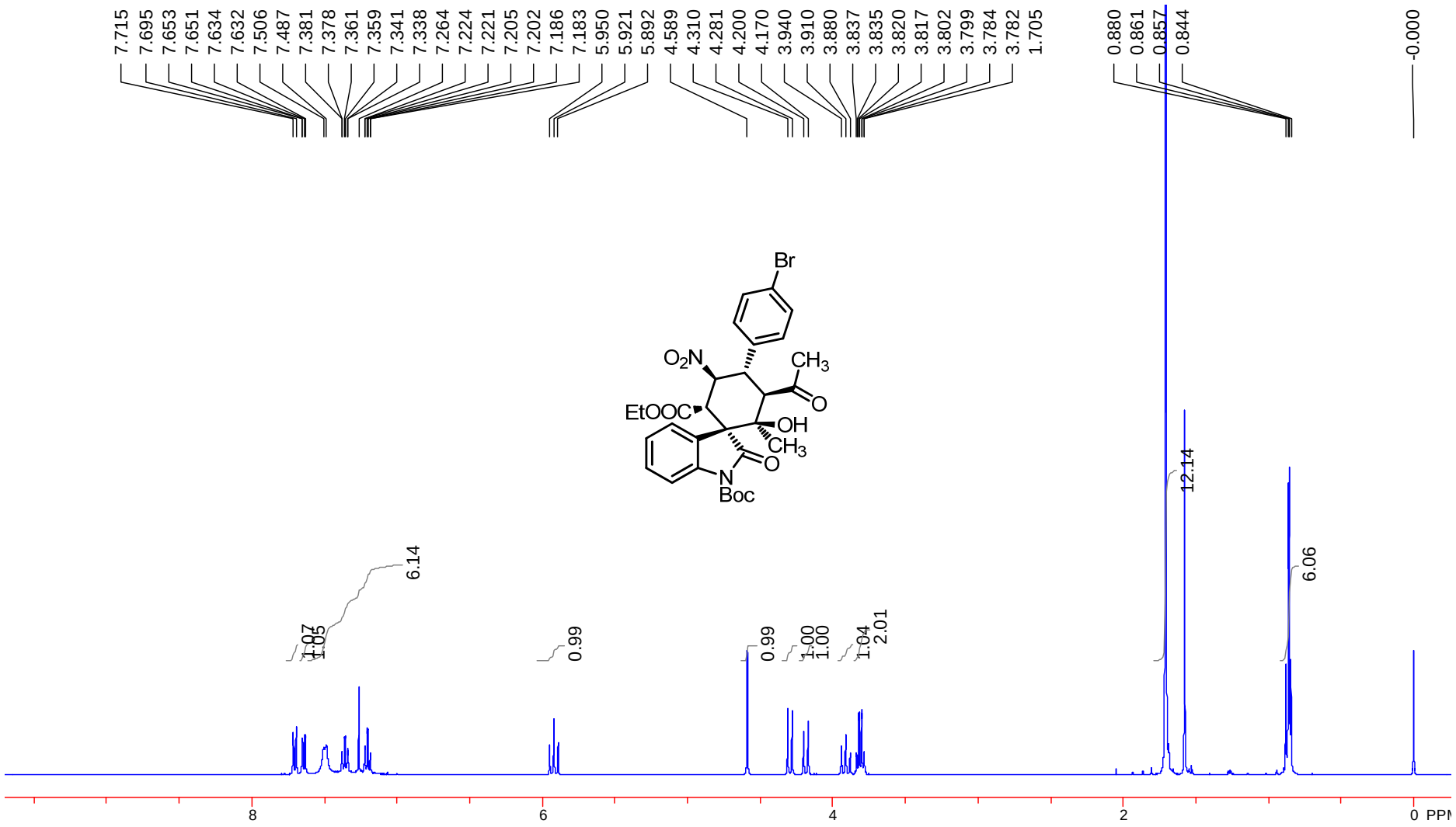
150
100
50
0
PPM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7.506
7.487
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7.378
7.361
7.359
7.341
7.338
7.264
7.224
7.221
7.205
7.202
7.186
7.183
5.950
5.921
5.892
4.589
4.310
4.281
4.200
4.170
3.940
3.910
3.880
3.837
3.835
3.820
3.817
3.802
3.799
3.784
3.782
1.705
0.880
0.861
0.857
0.844
-0.000
Br
O2N
CH3
O
EtOOC
OH
CH3
O
N
Boc
6.14
1.07
1.05
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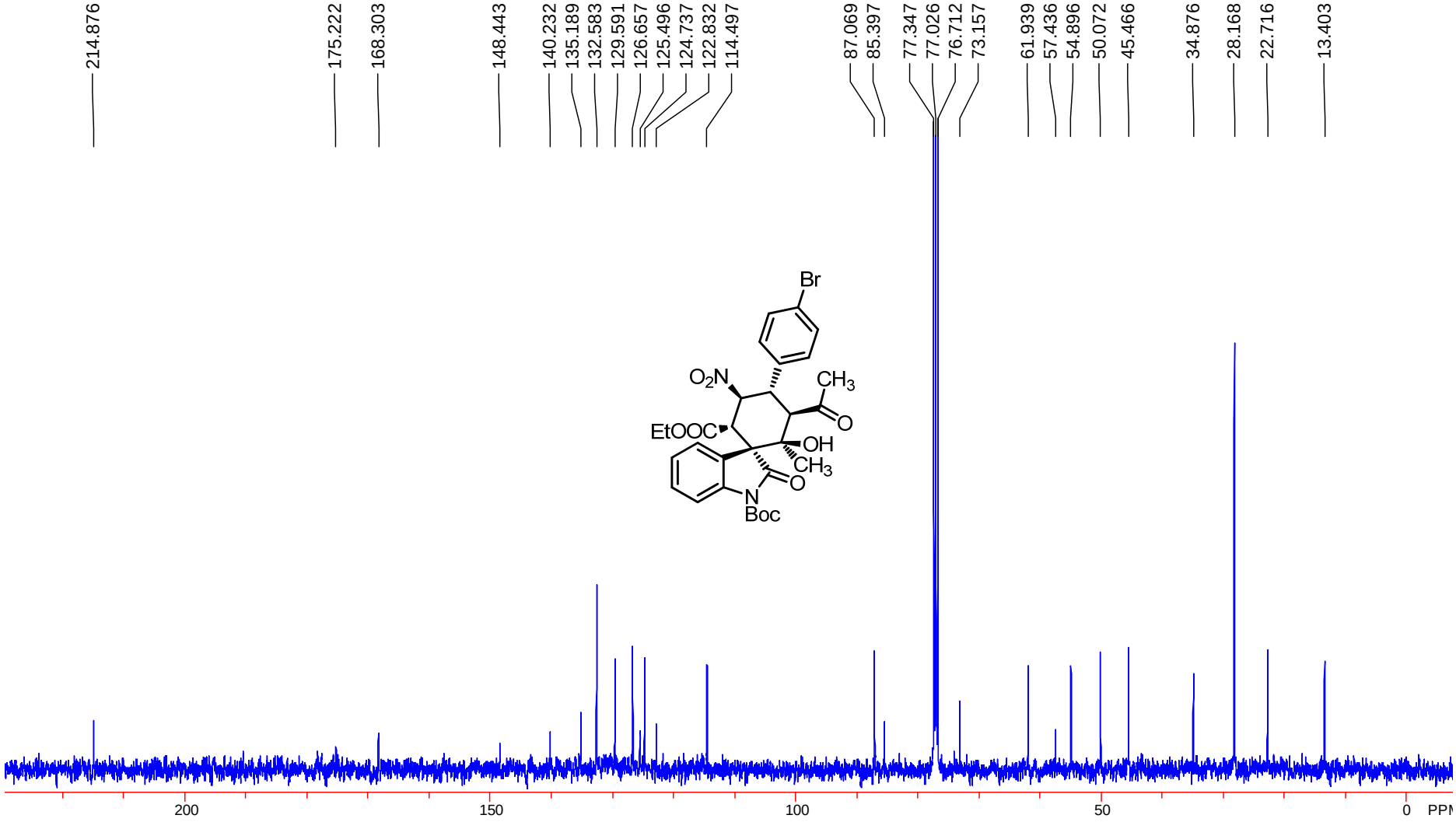
1.00
1.00
1.04
2.01
12.14
6.06
8
6
4
2
0 PPM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124.737
122.832
114.497
87.069
85.397
77.347
77.026
76.712
73.157
61.939
57.436
54.896
50.072
45.466
34.876
28.168
22.716
13.403
Br
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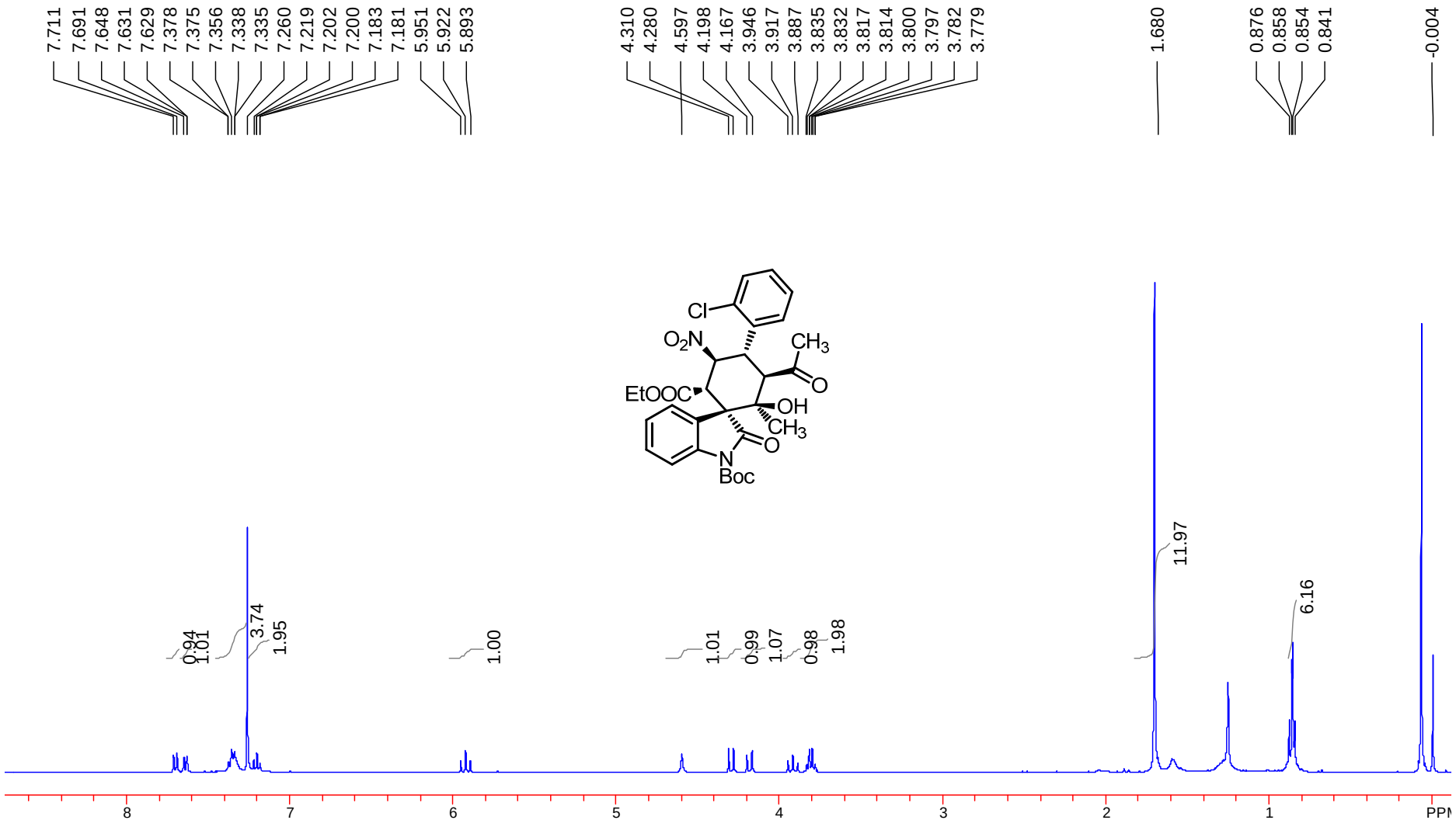
CH3
EtOOC
O
OH
CH3
O
N
Boc
200
150
100
50
0
PPM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7.335
7.260
7.219
7.202
7.200
7.183
7.181
5.951
5.922
5.893
4.310
4.280
4.597
4.198
4.167
3.946
3.917
3.887
3.835
3.832
3.817
3.814
3.800
3.797
3.782
3.779
1.680
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0.854
0.841
-0.004
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CH3
O
EtOOC
OH
CH3
O
N
Boc
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1.01
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1.00
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0.98
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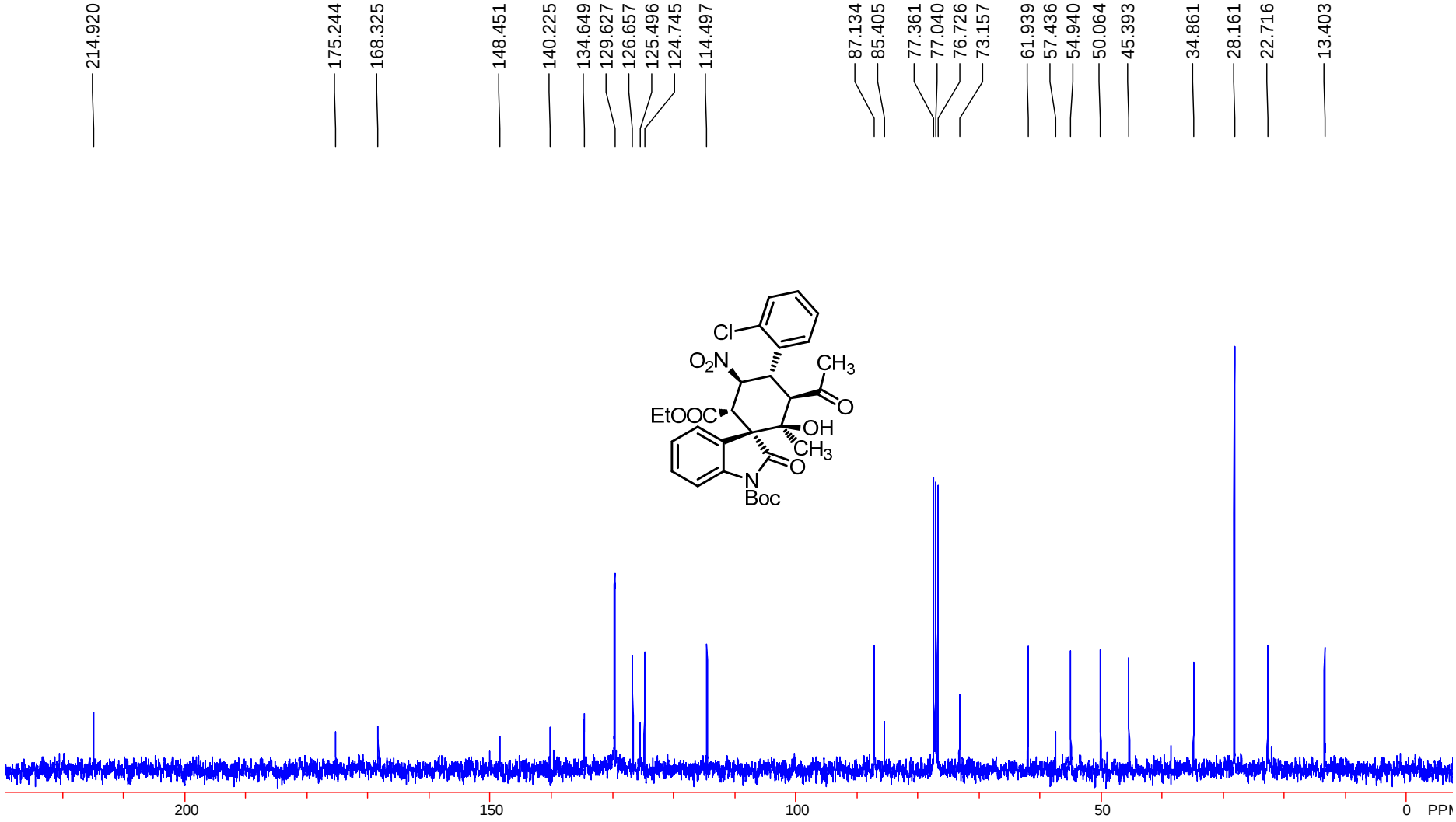
7
6
5
4
3
2
1
PPM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124.745
114.497
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85.405
77.361
77.040
76.726
73.157
61.939
57.436
54.940
50.064
45.393
34.861
28.161
22.716
13.403
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CH3
O
EtOOC
OH
CH3
O
N
Boc
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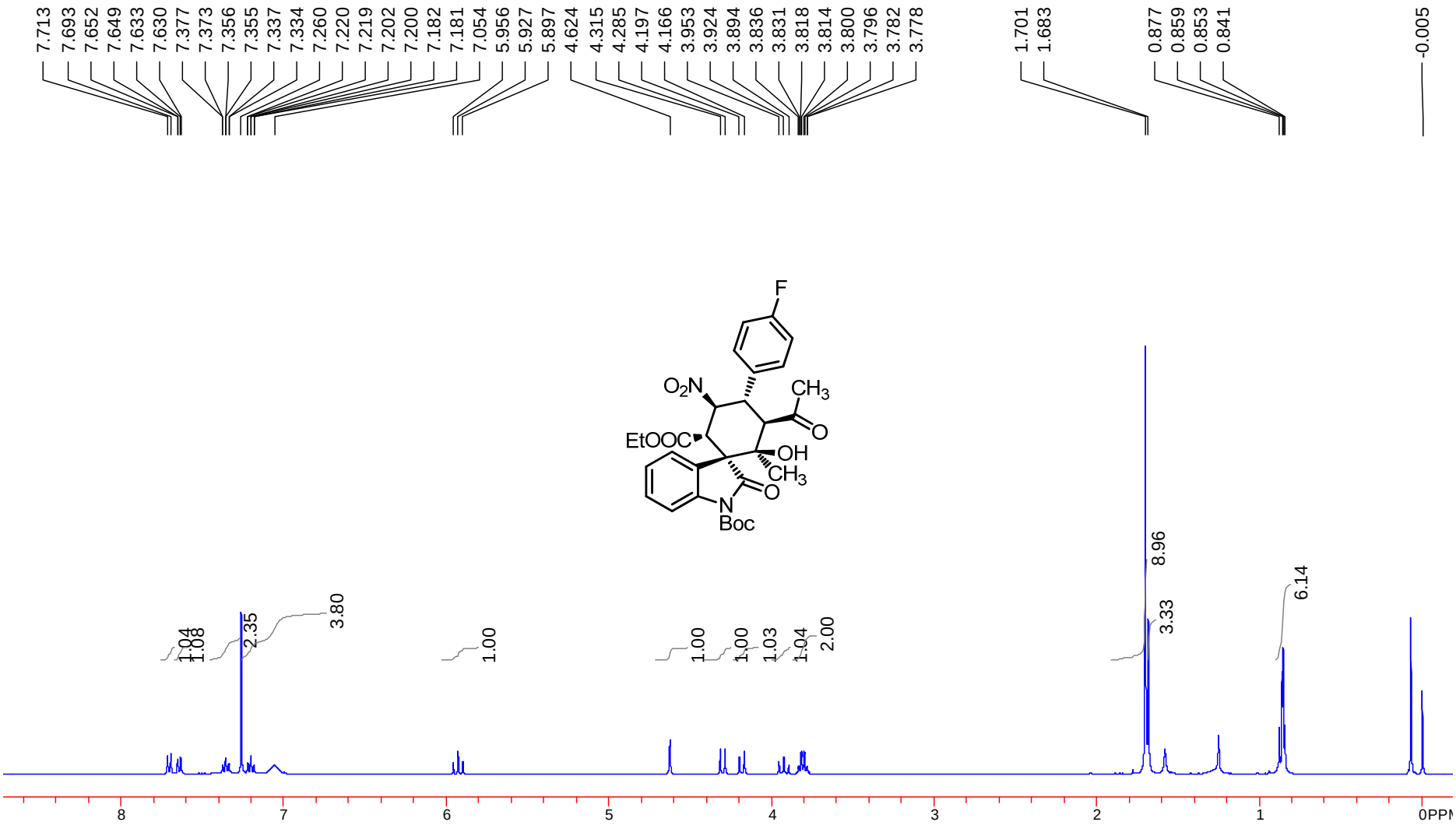
100
50
0
PPM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7.260
7.220
7.219
7.202
7.200
7.182
7.181
7.054
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5.927
5.897
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4.285
4.197
4.166
3.953
3.924
3.894
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3.831
3.818
3.814
3.800
3.796
3.782
3.778
1.701
1.683
0.877
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0.853
0.841
-0.005
F
O2N
CH3
O
EtOOC
OH
CH3
O
N
Boc
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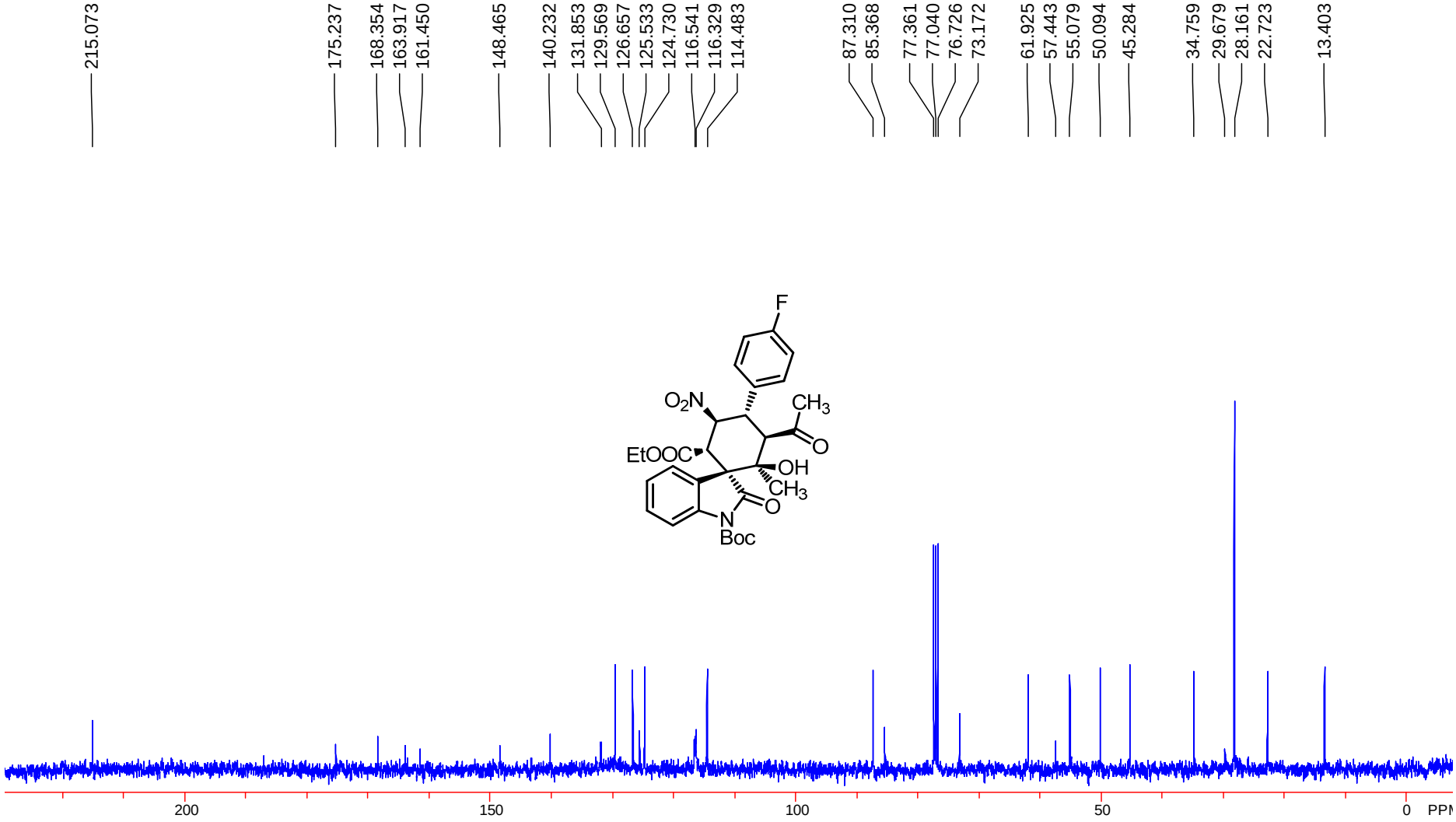
1.08
2.35
3.80
1.00
1.00
1.00
1.03
1.04
2.00
8.96
3.33
6.14
8
7
6
5
4
3
2
1
0PPM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85.368
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77.040
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73.172
61.925
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55.079
50.094
45.284
34.759
29.679
28.161
22.723
13.403
F
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CH3
O
EtOOC
OH
CH3
O
N
Boc
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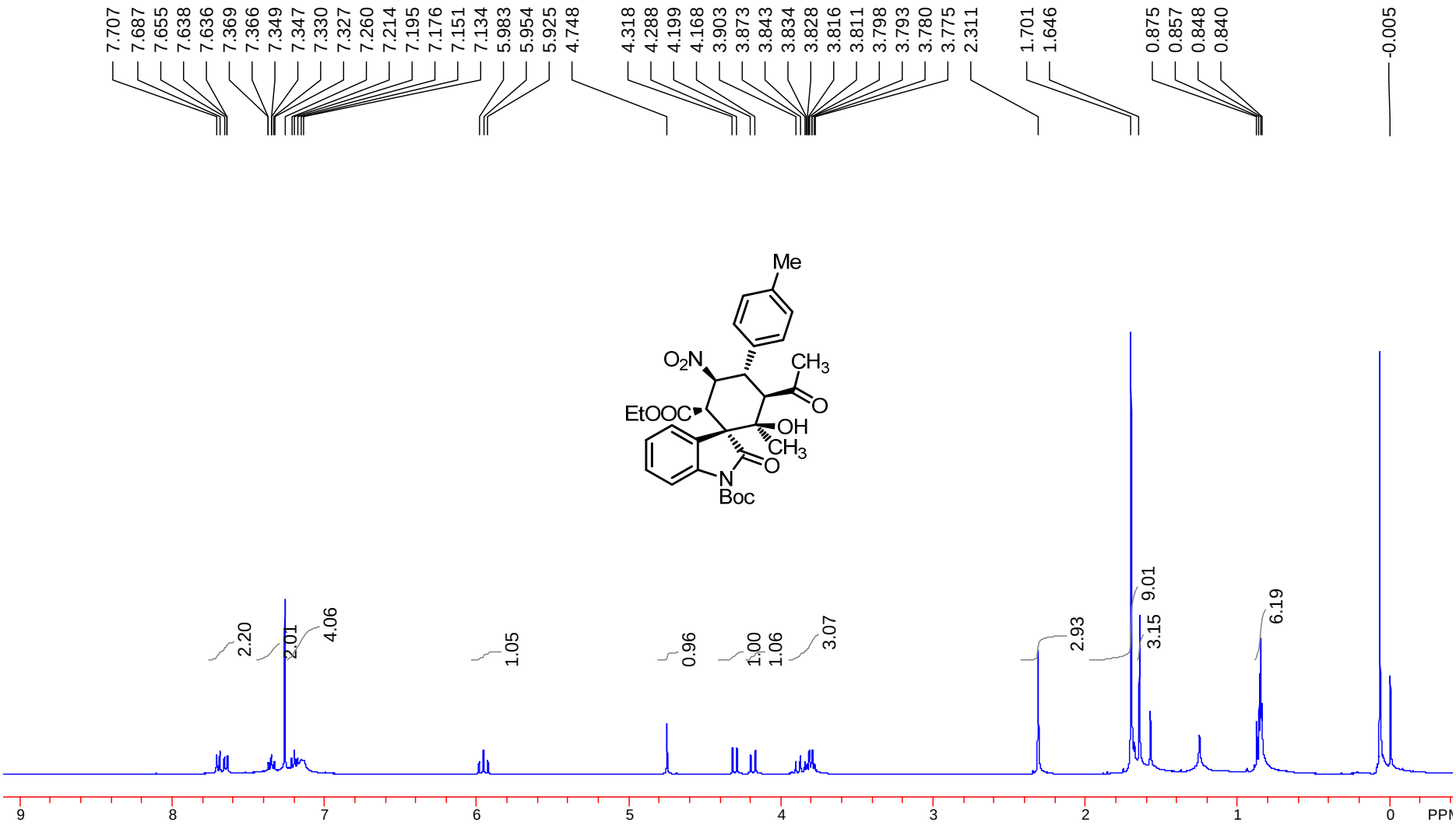
100
50
0
PPM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7.330
7.327
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7.214
7.195
7.176
7.151
7.134
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5.954
5.925
4.748
4.318
4.288
4.199
4.168
3.903
3.873
3.843
3.834
3.828
3.816
3.811
3.798
3.793
3.780
3.775
2.311
1.701
1.646
0.875
0.857
0.848
0.840
-0.005
Me
O2N
CH3
O
EtOOC
OH
CH3
O
N
Boc
2.20
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4.06
1.05
0.96
1.00
1.06
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3.15
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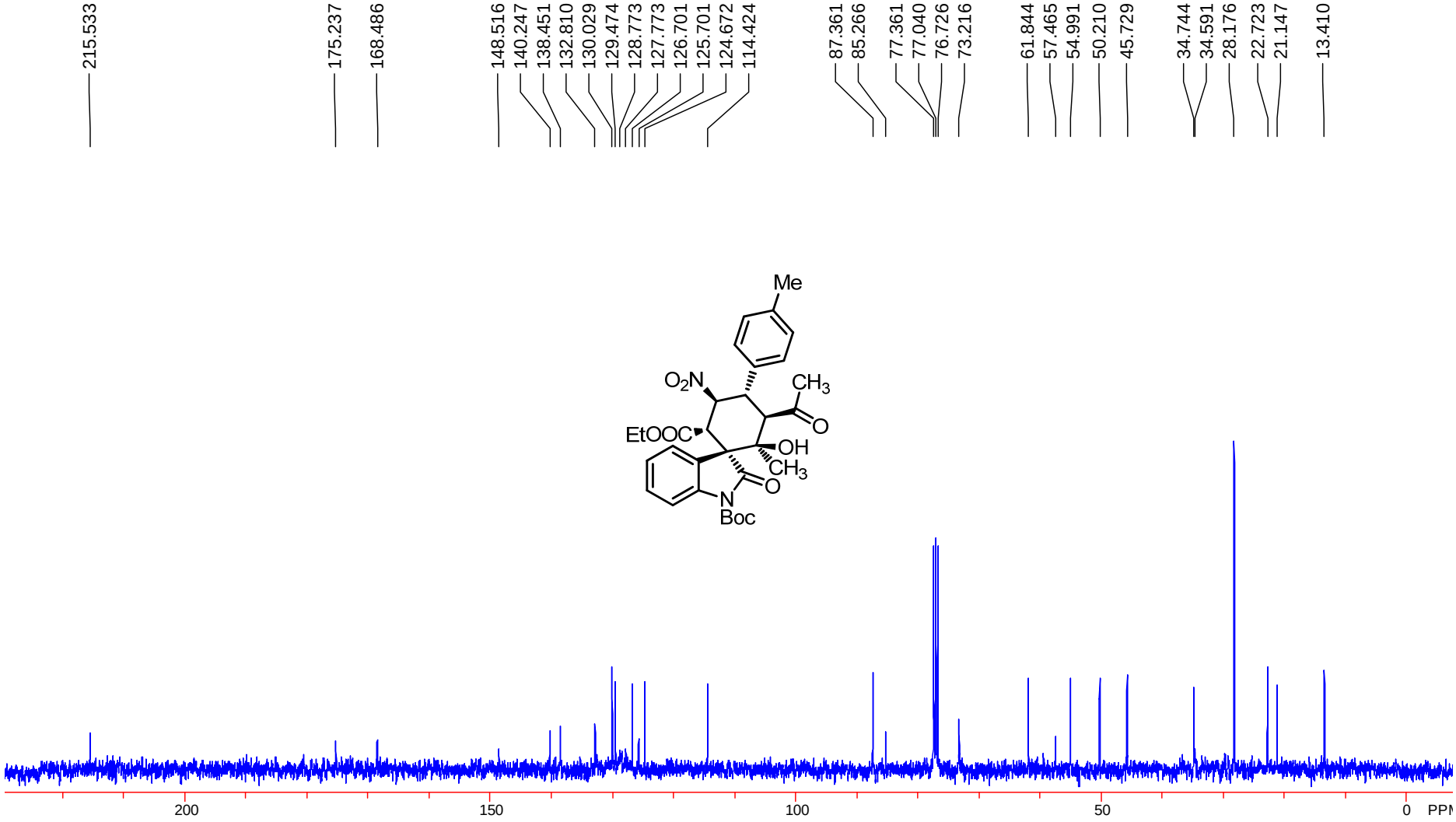
7
6
5
4
3
2
1
0
PPM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114.424
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77.040
76.726
73.216
61.844
57.465
54.991
50.210
45.729
34.744
34.591
28.176
22.723
21.147
13.410
Me
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CH3
O
EtOOC
OH
CH3
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N
Boc
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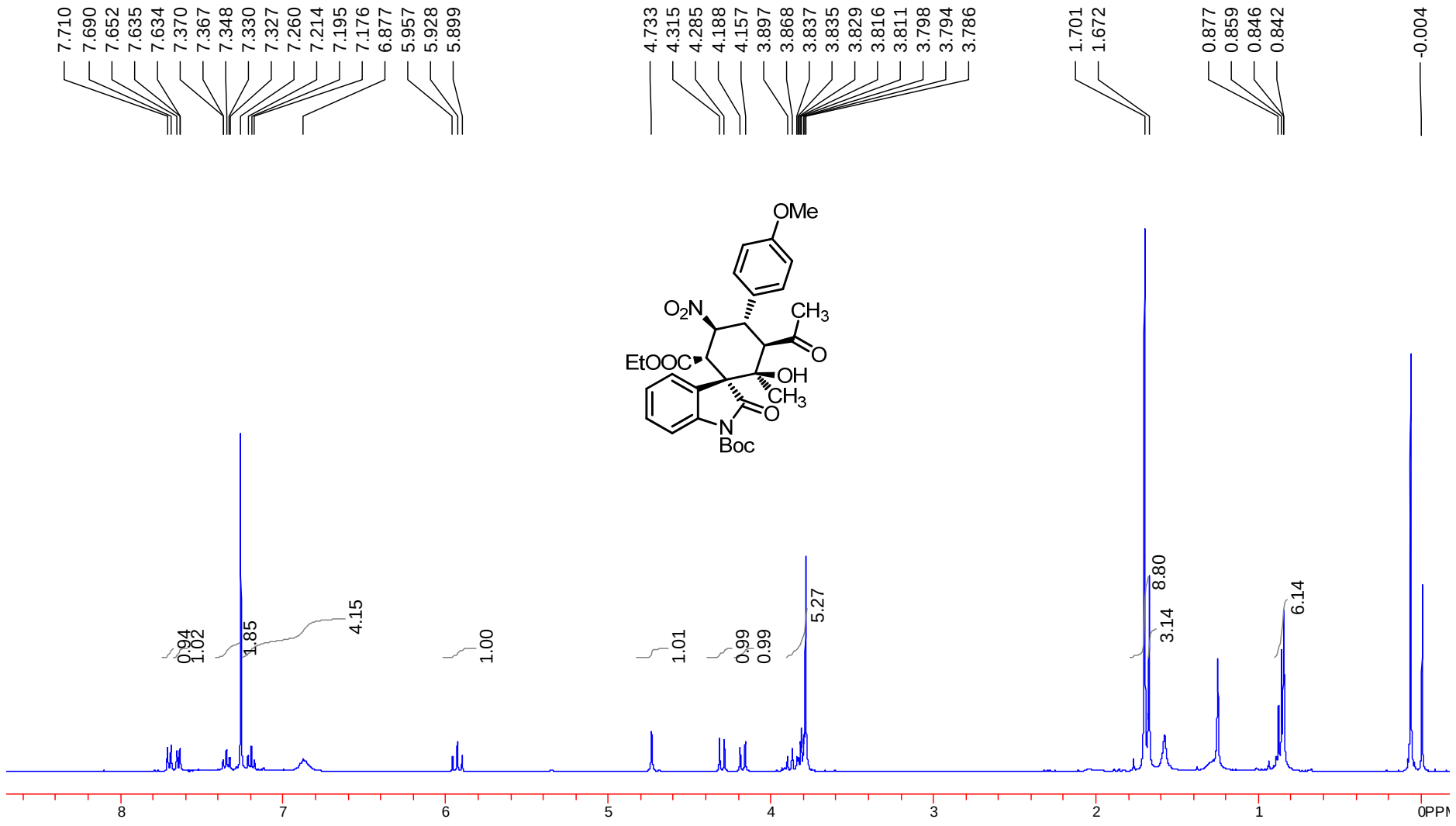
100
50
0
PPM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7.260
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7.195
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6.877
5.957
5.928
5.899
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4.315
4.285
4.188
4.157
3.897
3.868
3.837
3.835
3.829
3.816
3.811
3.798
3.794
3.786
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1.672
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0.842
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OMe
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CH3
O
EtOOC
OH
CH3
O
N
Boc
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1.01
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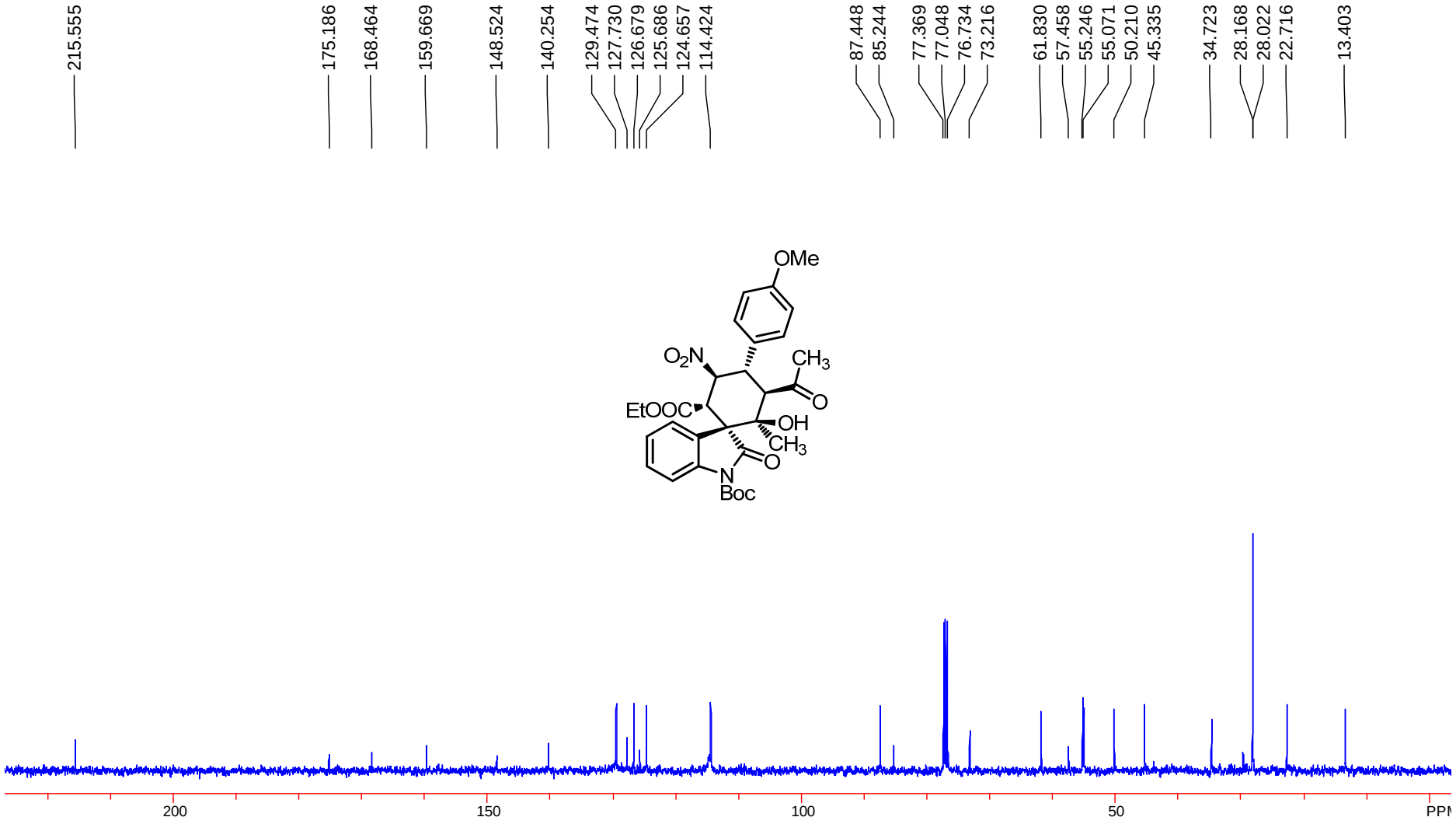
0PPM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77.369
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76.734
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61.830
57.458
55.246
55.071
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45.335
34.723
28.168
28.022
22.716
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CH3
O
EtOOC
OH
CH3
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N
Boc
200
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50
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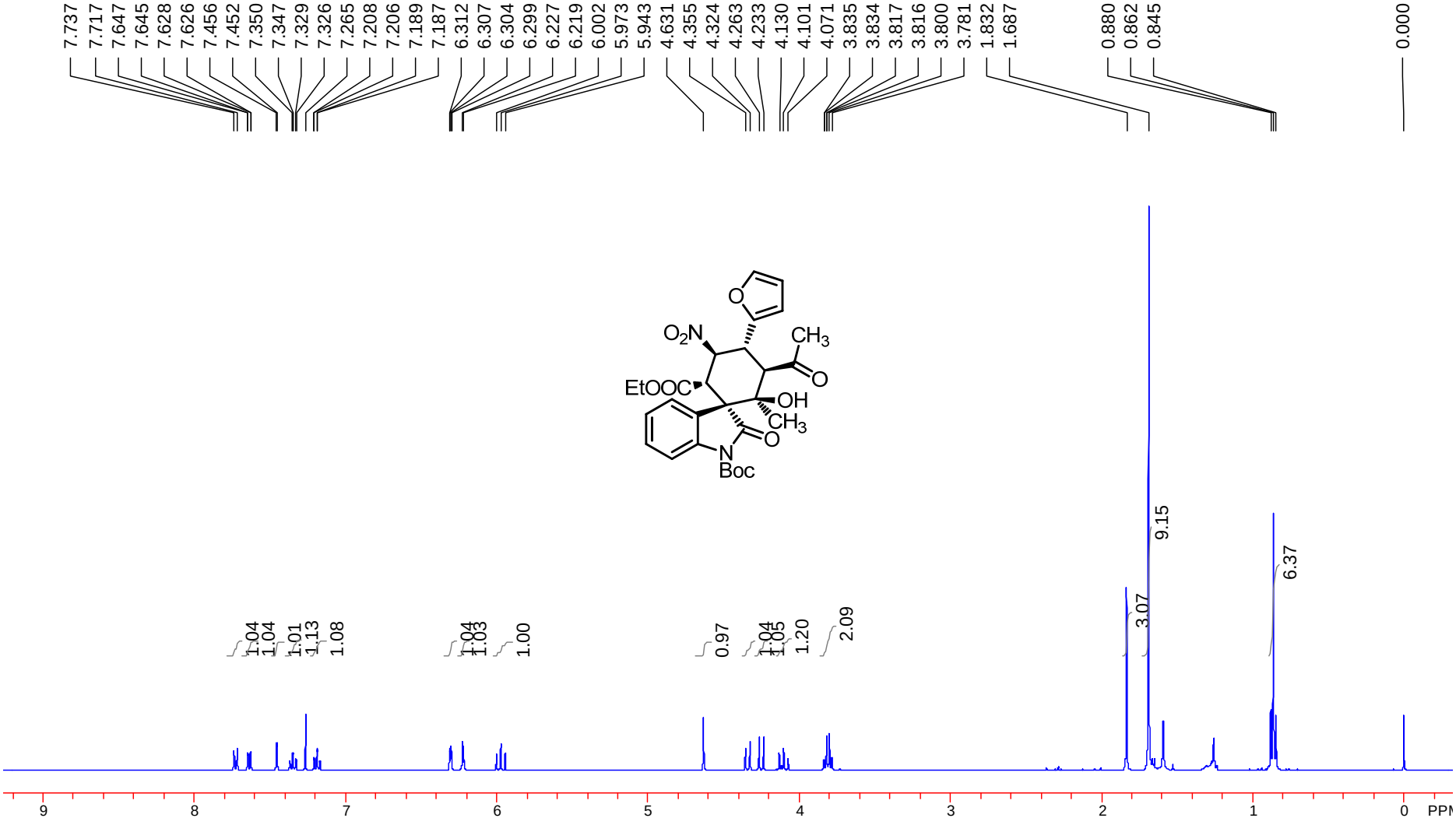
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7.187
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6.304
6.299
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4.233
4.130
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3.835
3.834
3.817
3.816
3.800
3.781
1.832
1.687
0.880
0.862
0.845
0.000
O
O2N
CH3
O
EtOOC
OH
CH3
O
N
Boc
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1.04
1.01
1.13
1.08
1.04
1.03
1.00
0.97
1.04
1.05
1.20
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3.07
9.15
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9
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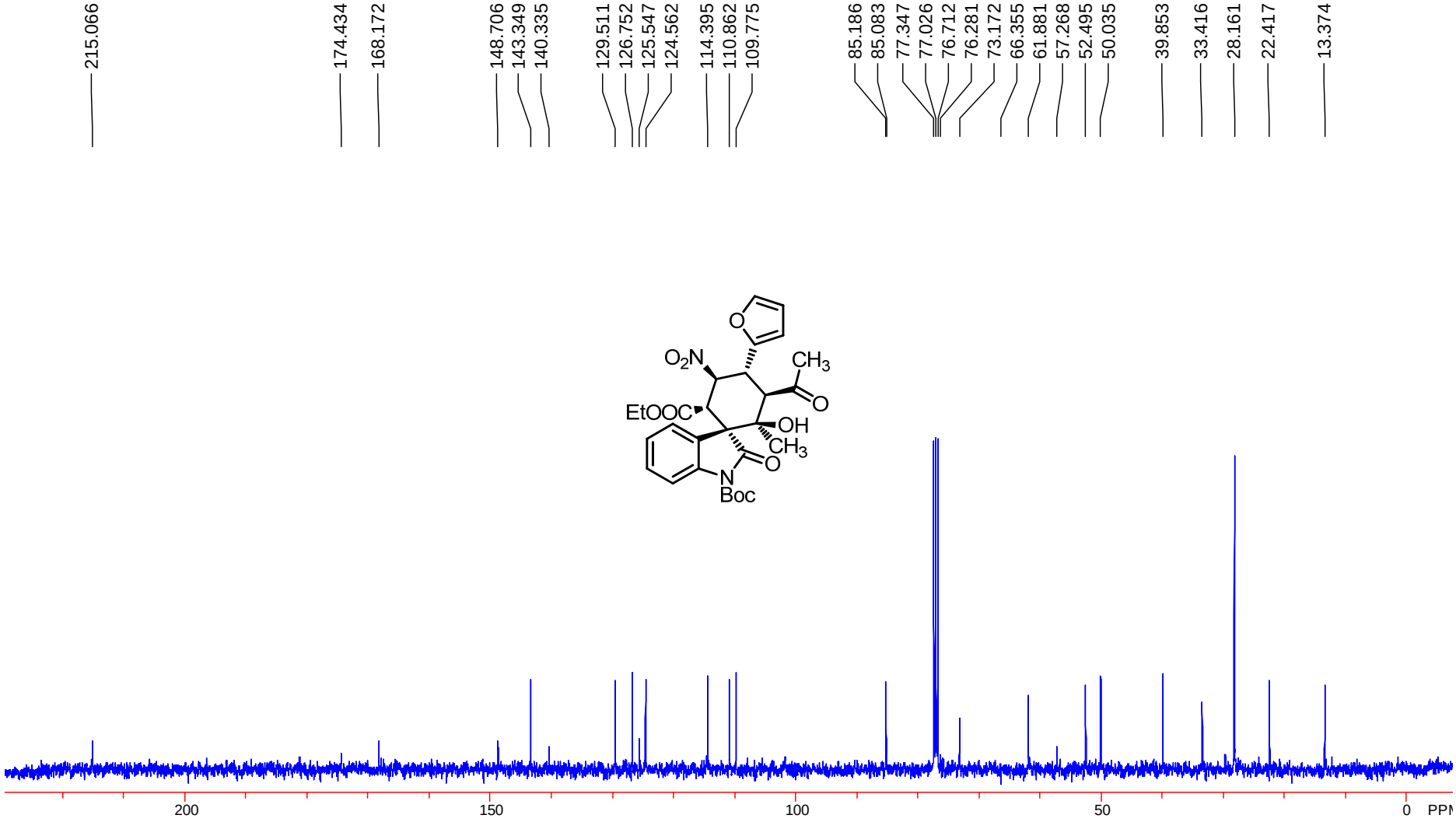
6
5
4
3
2
1
0
PPM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77.026
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76.281
73.172
66.355
61.881
57.268
52.495
50.035
39.853
33.416
28.161
22.417
13.374
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CH3
O
EtOOC
OH
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Boc
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100
50
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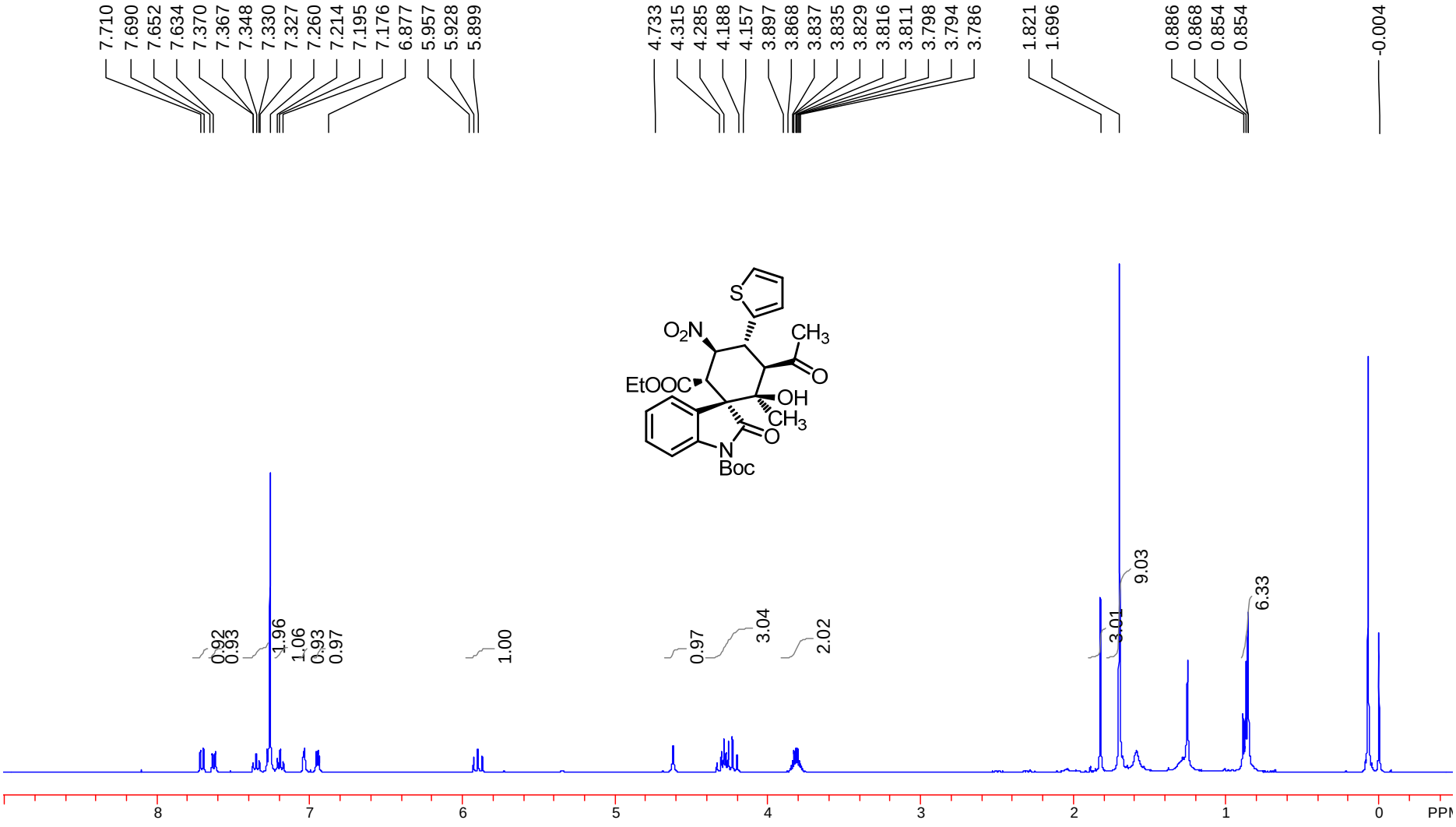
PPM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5.957
5.928
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4.733
4.315
4.285
4.188
4.157
3.897
3.868
3.837
3.835
3.829
3.816
3.811
3.798
3.794
3.786
1.821
1.696
0.886
0.868
0.854
0.854
-0.004
S
O2N
CH3
O
EtOOC
OH
CH3
O
N
Boc
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0.93
1.96
1.06
0.93
0.97
1.00
0.97
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3.01
9.03
6.33
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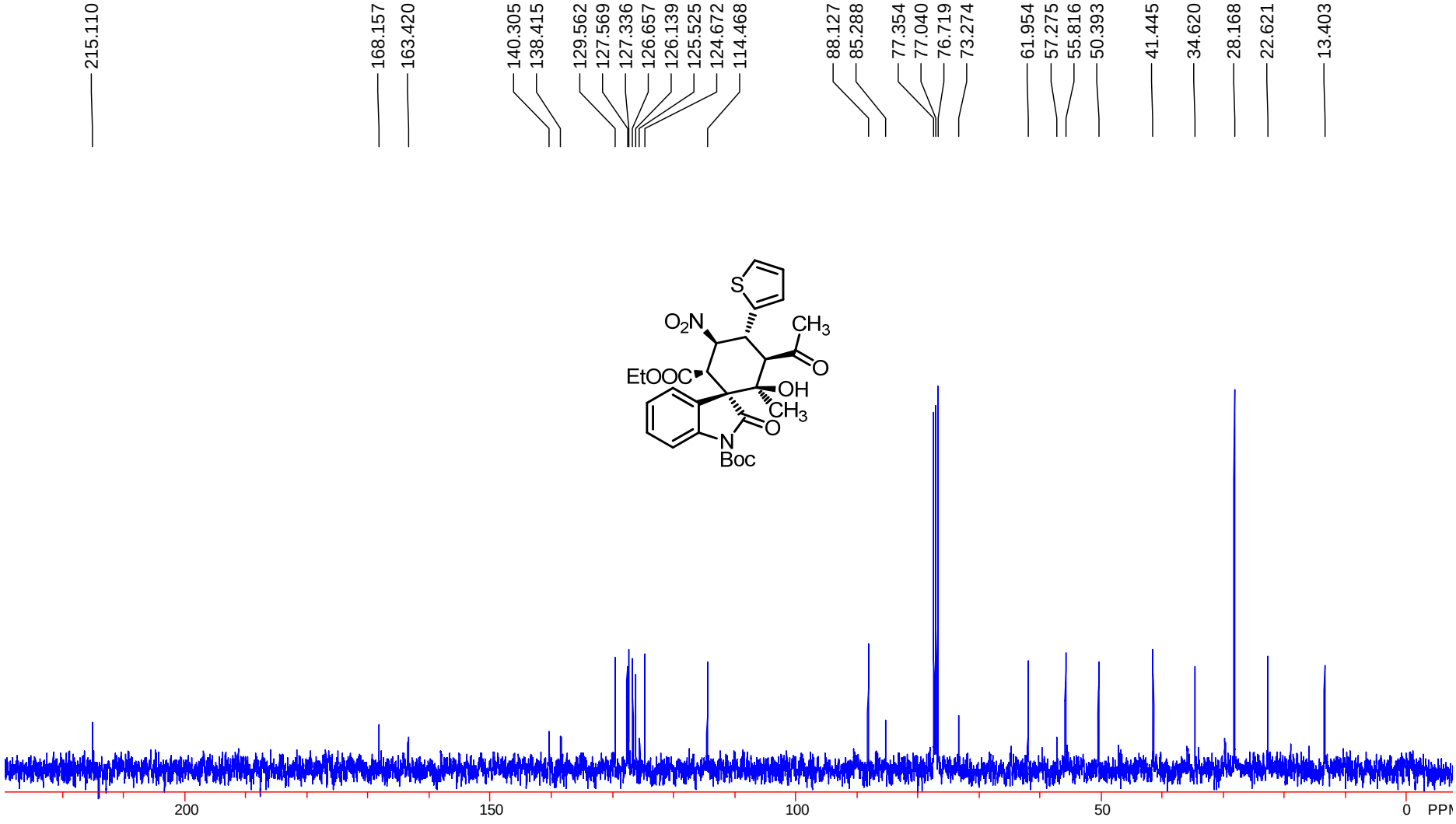
6
5
4
3
2
1
0
PPM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57.275
55.816
50.393
41.445
34.620
28.168
22.621
13.403
S
O2N
CH3
O
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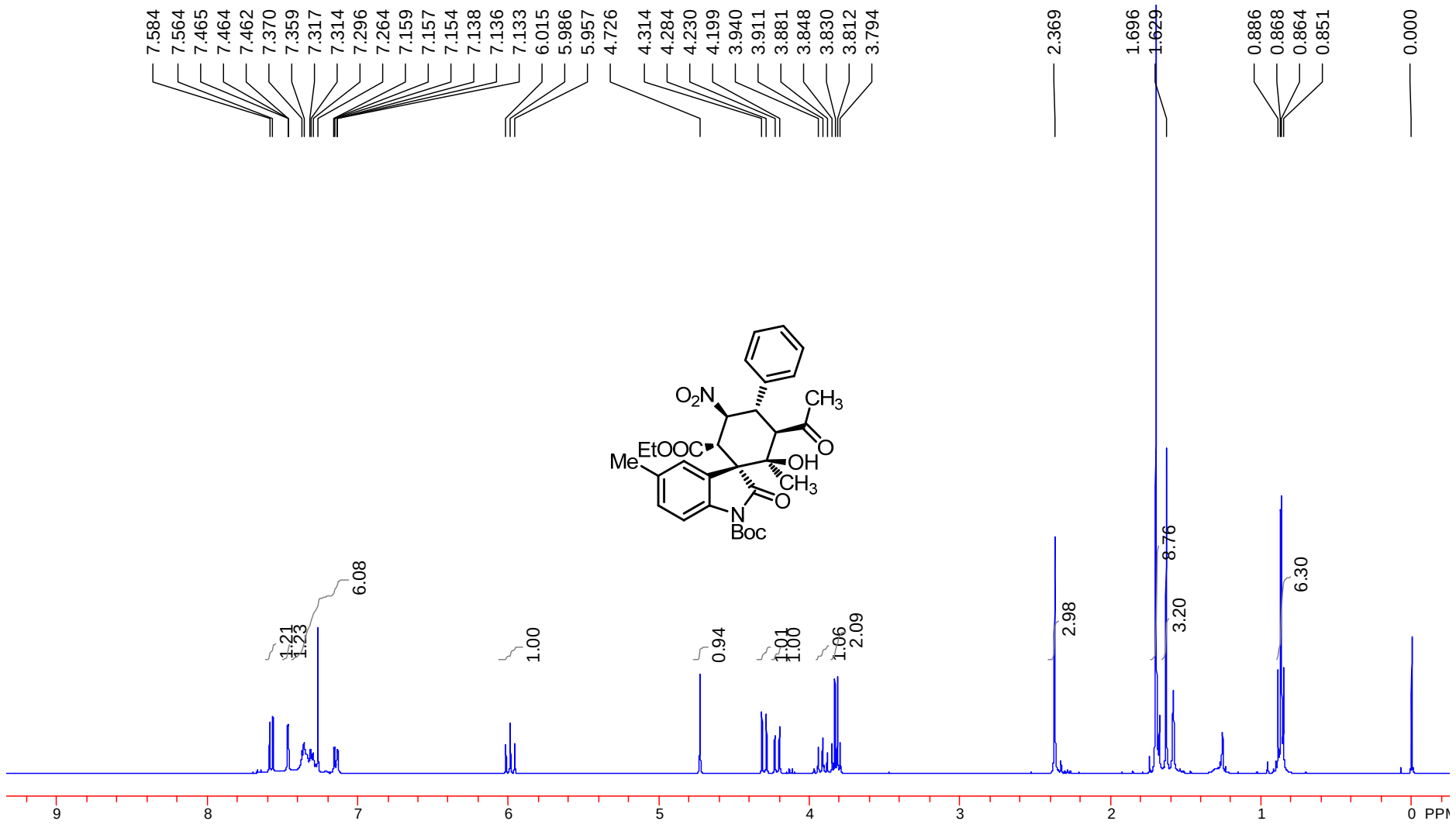
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Boc
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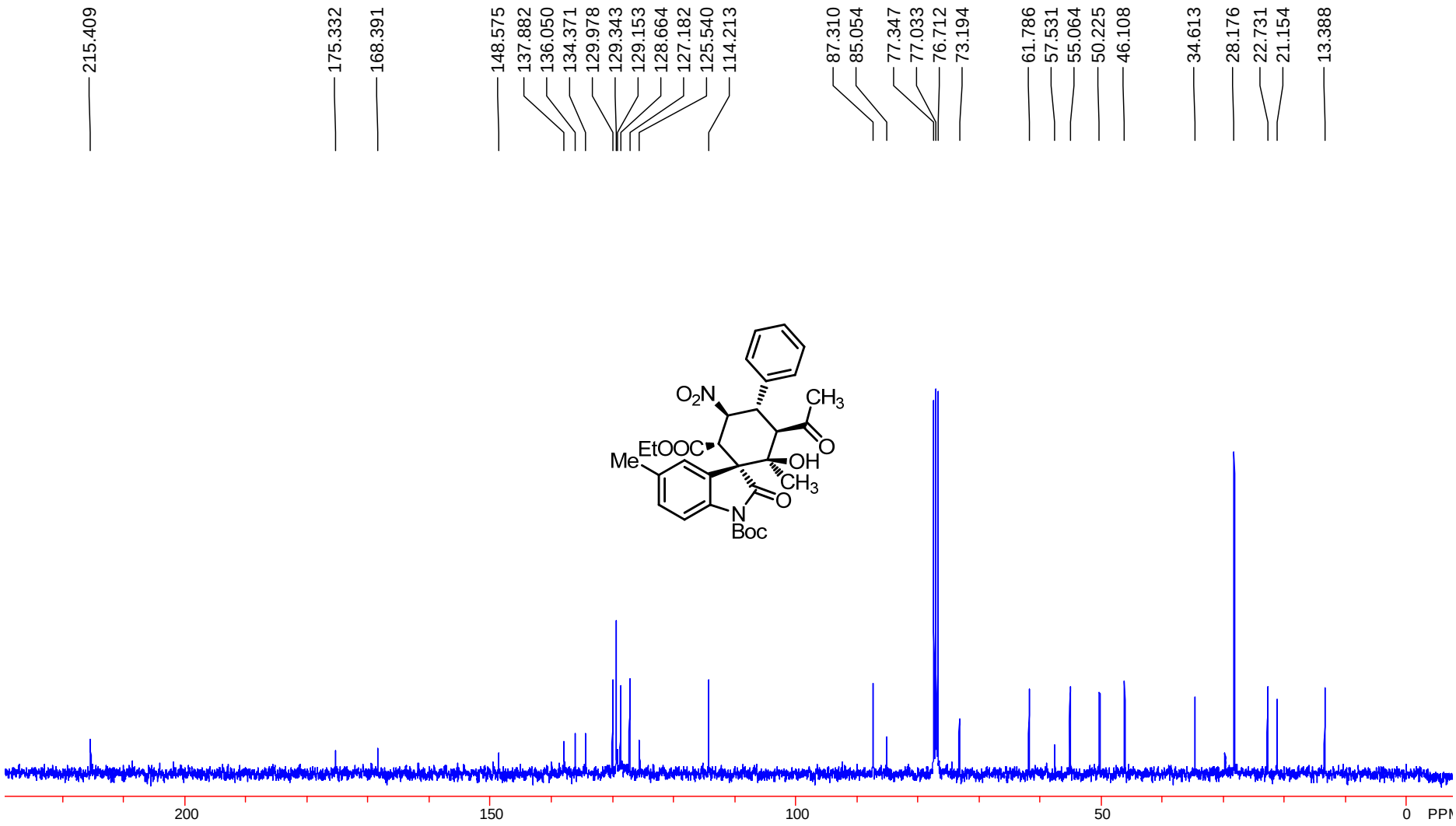
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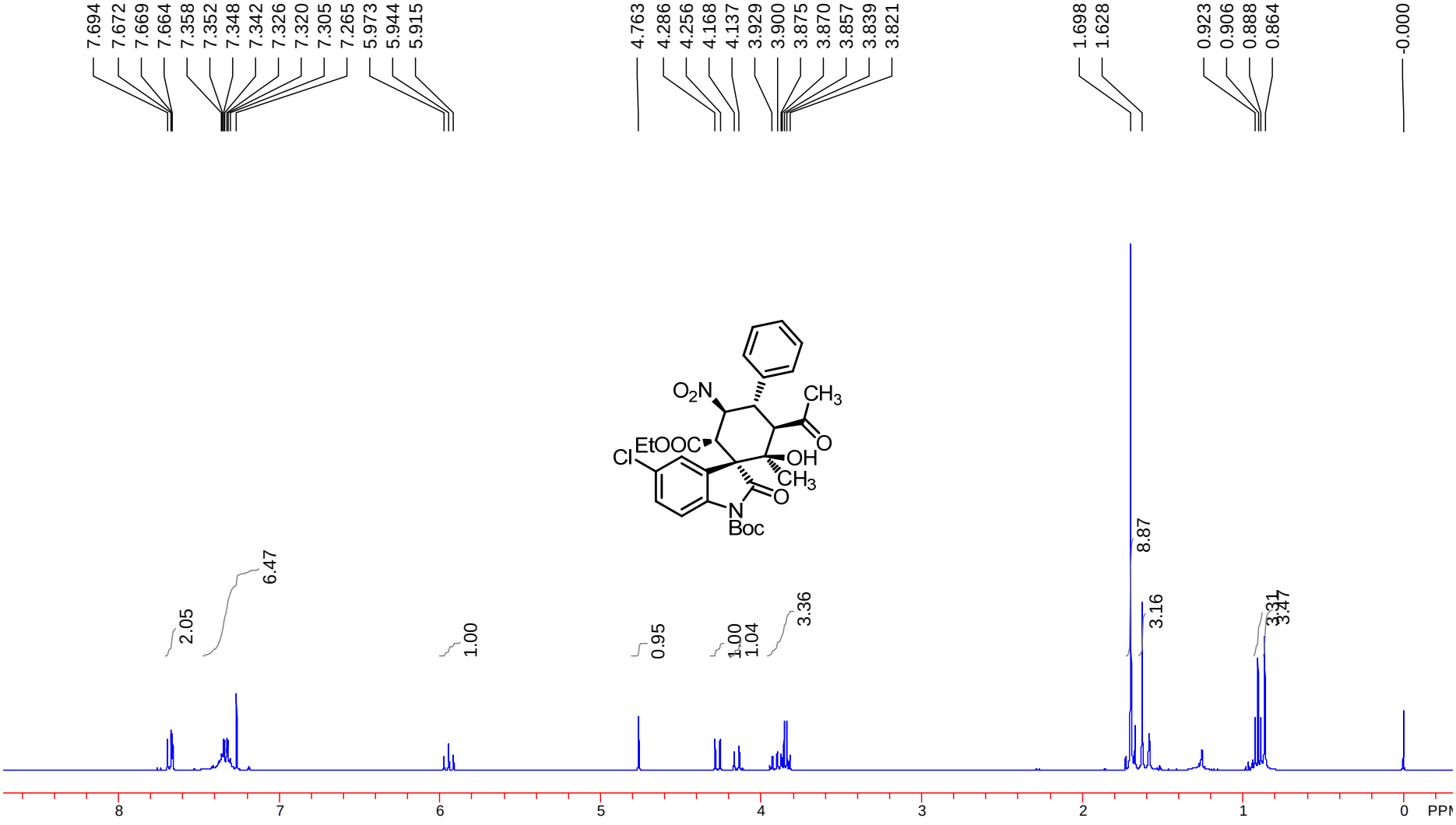
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Boc
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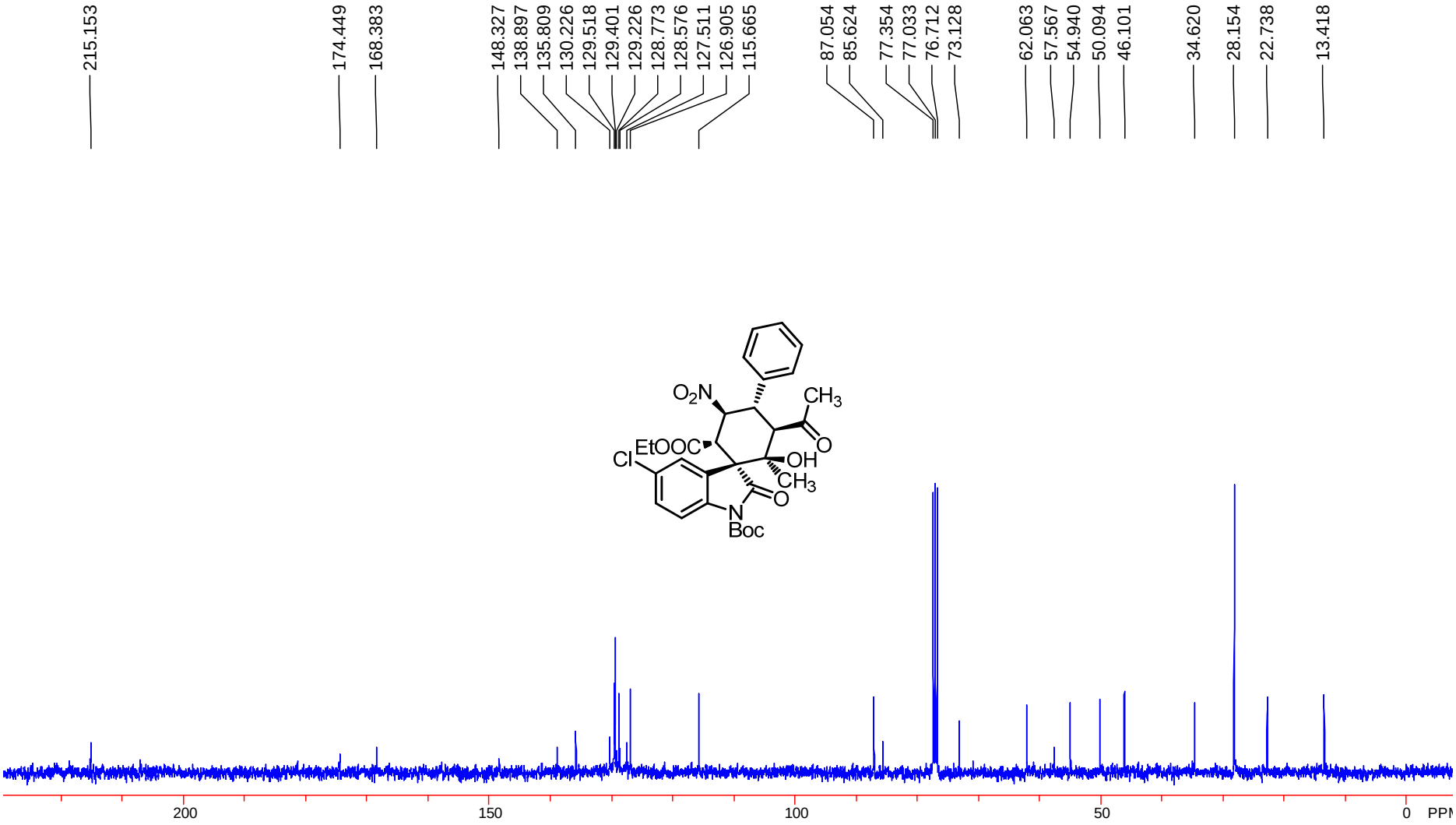
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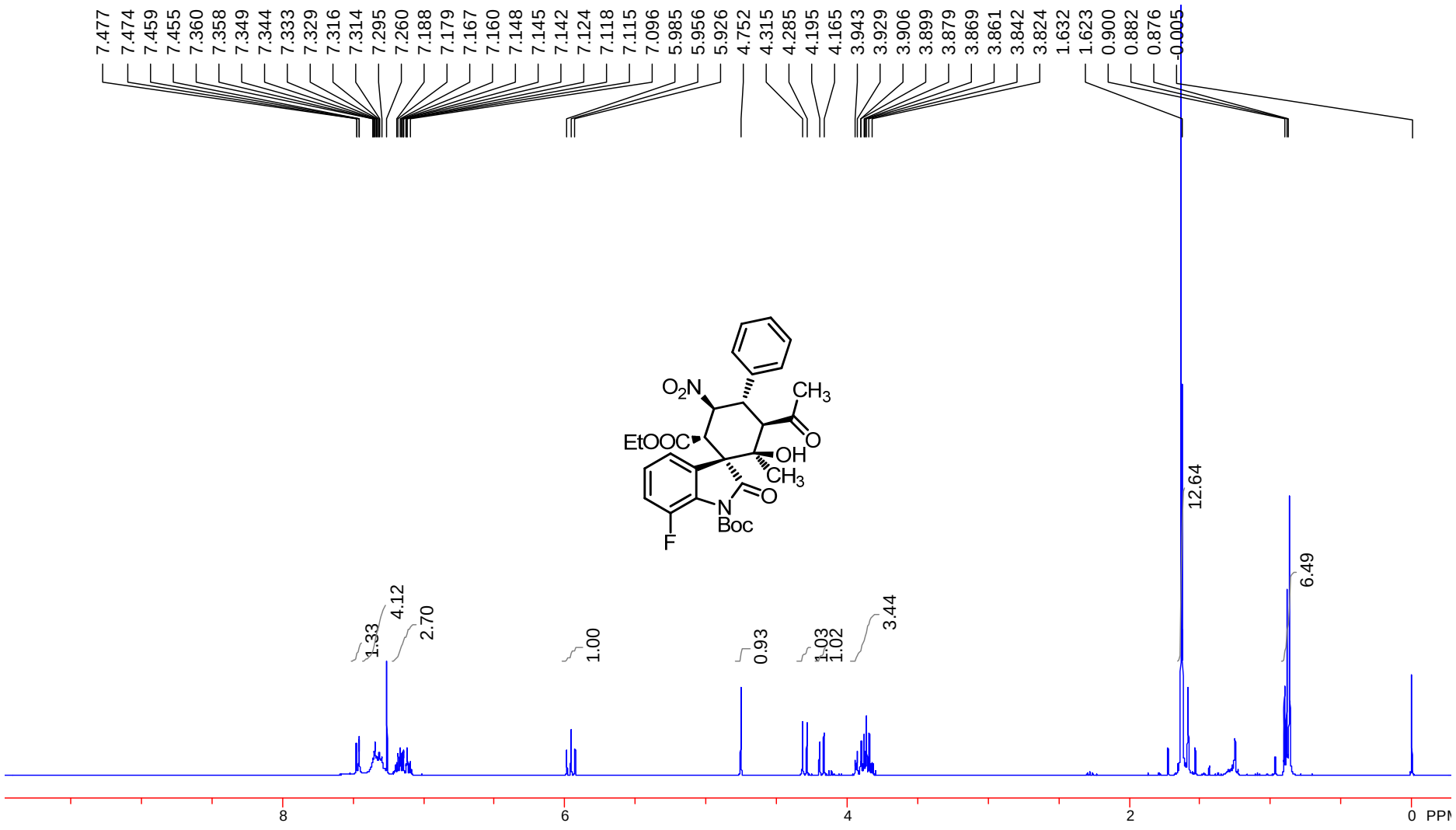
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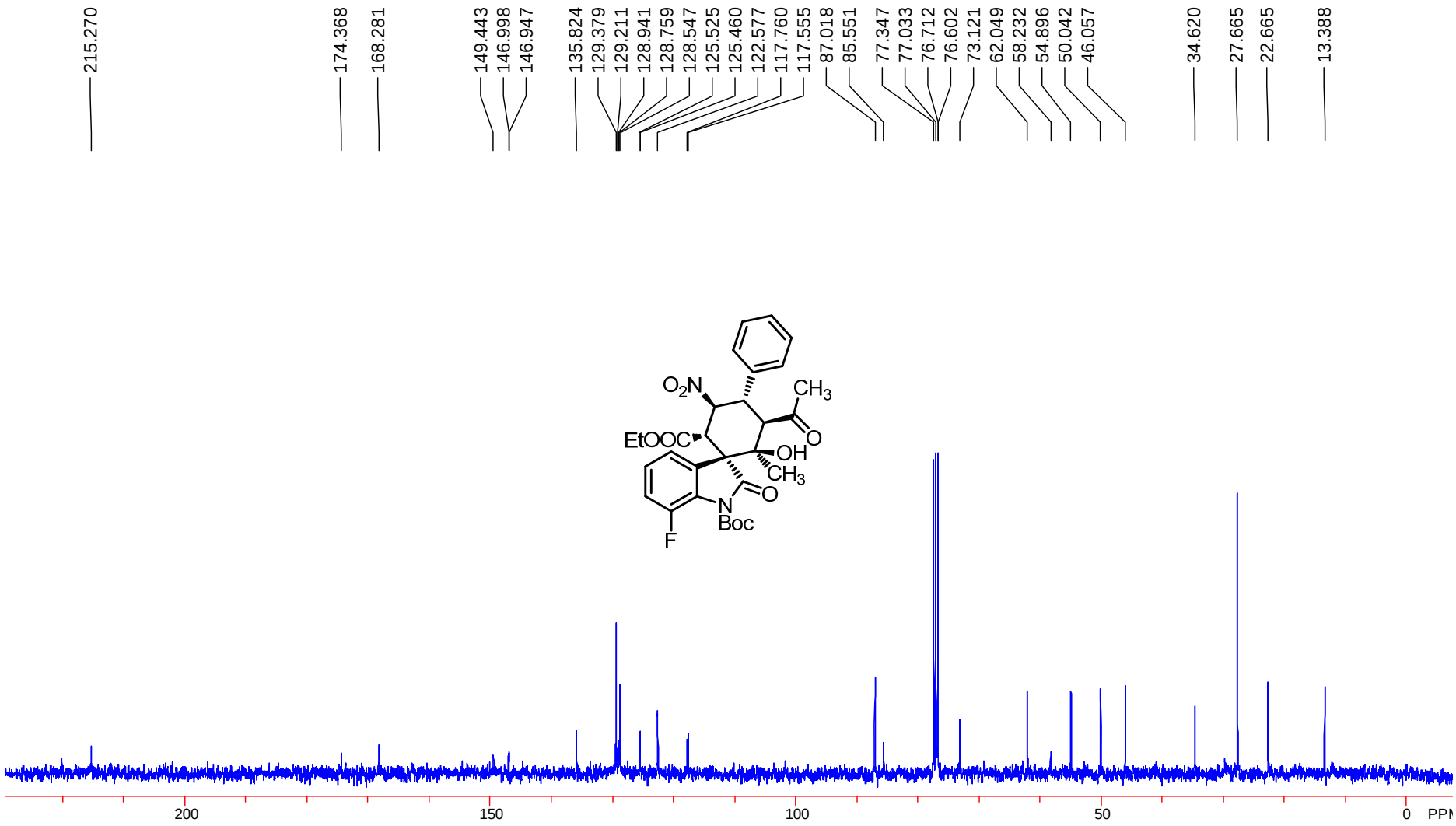
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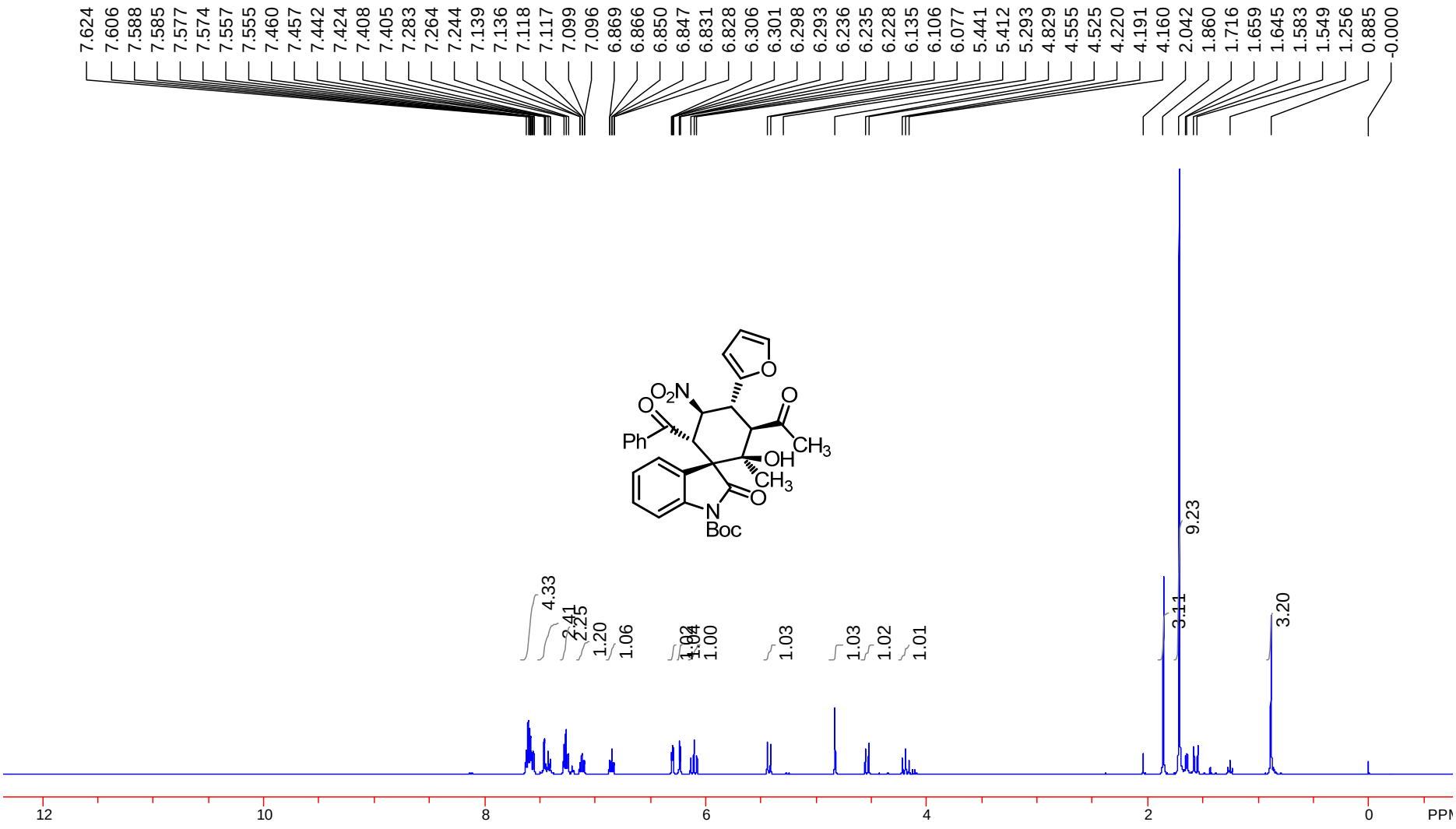
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Boc
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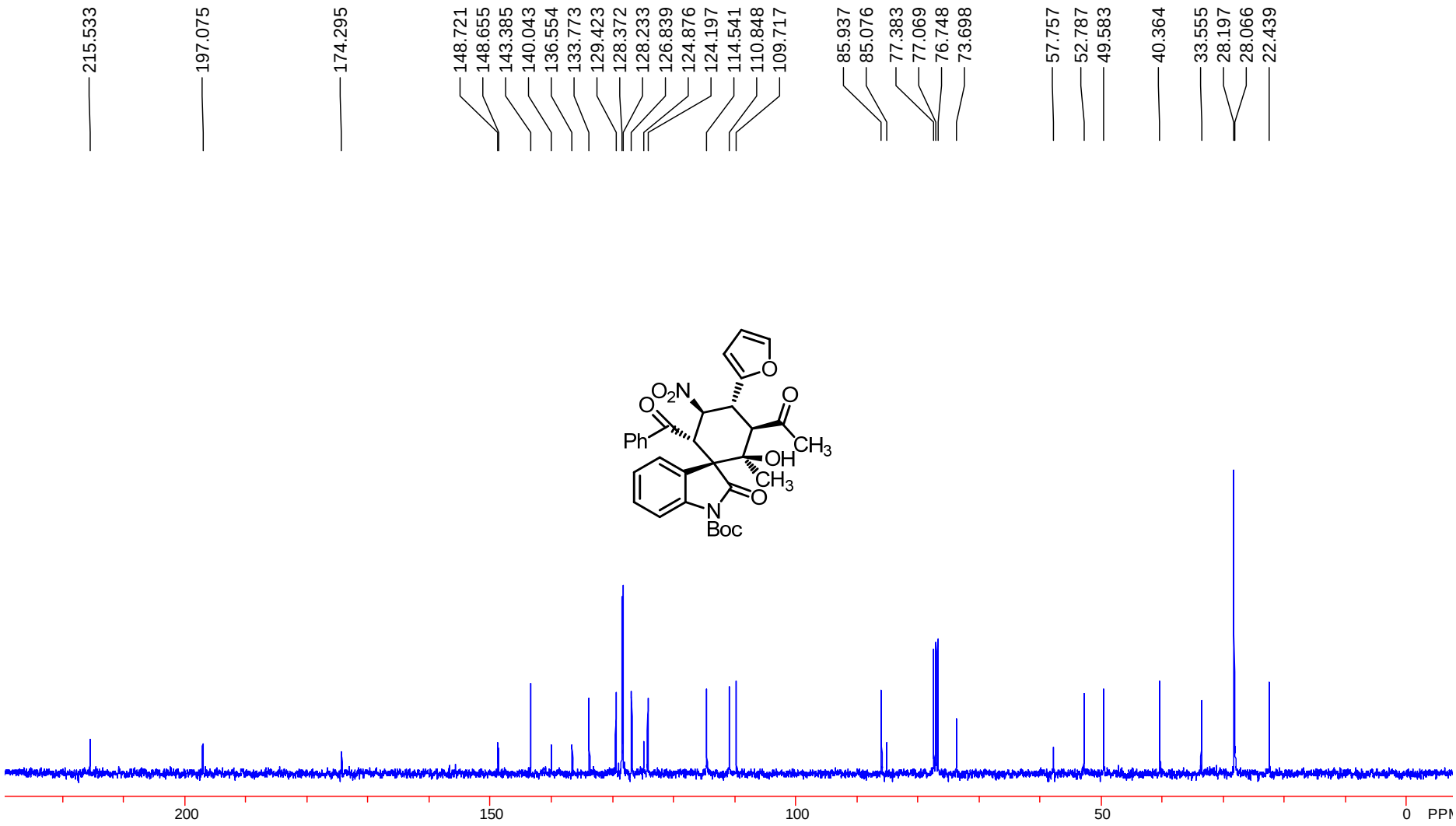
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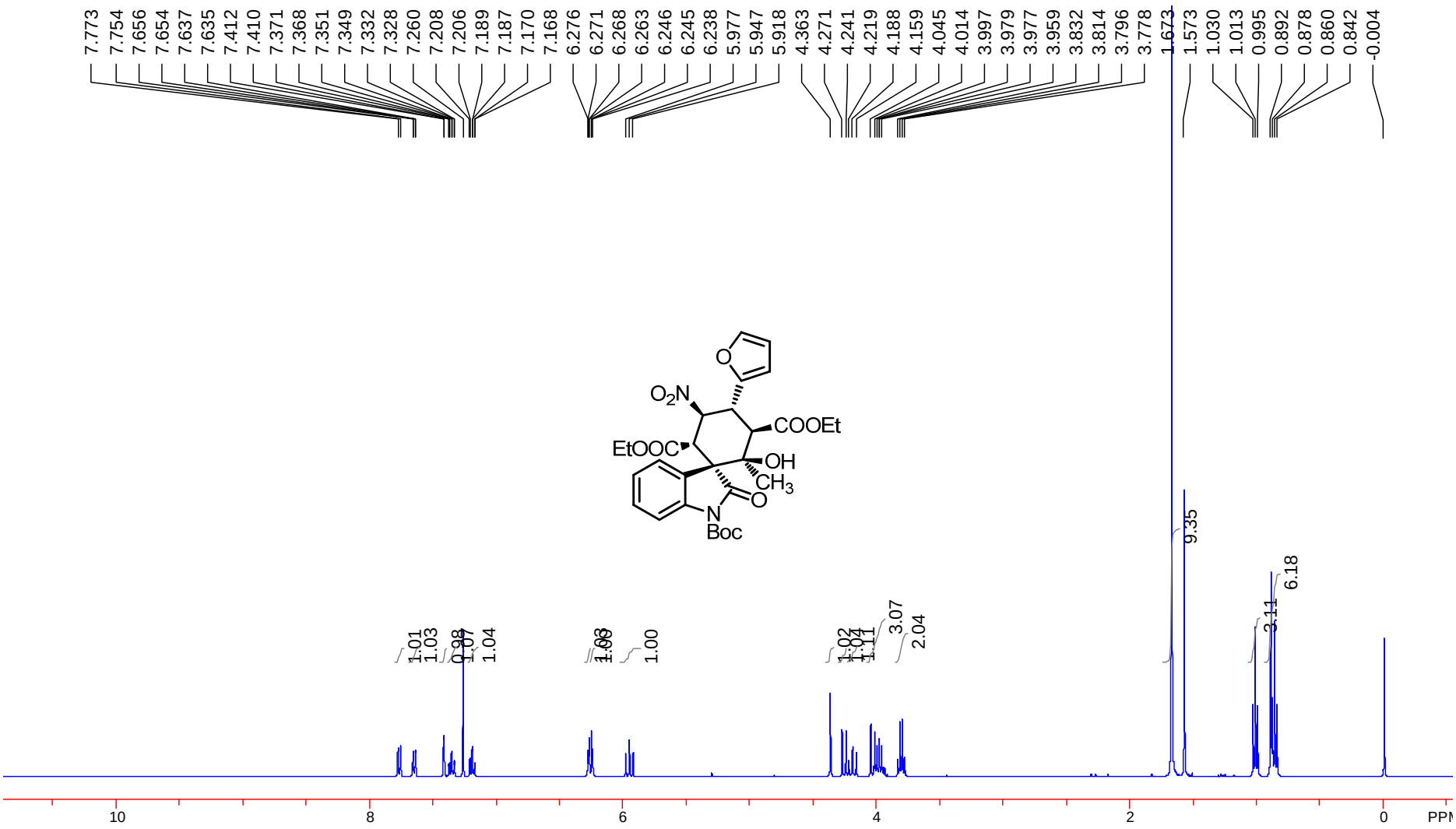
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Boc
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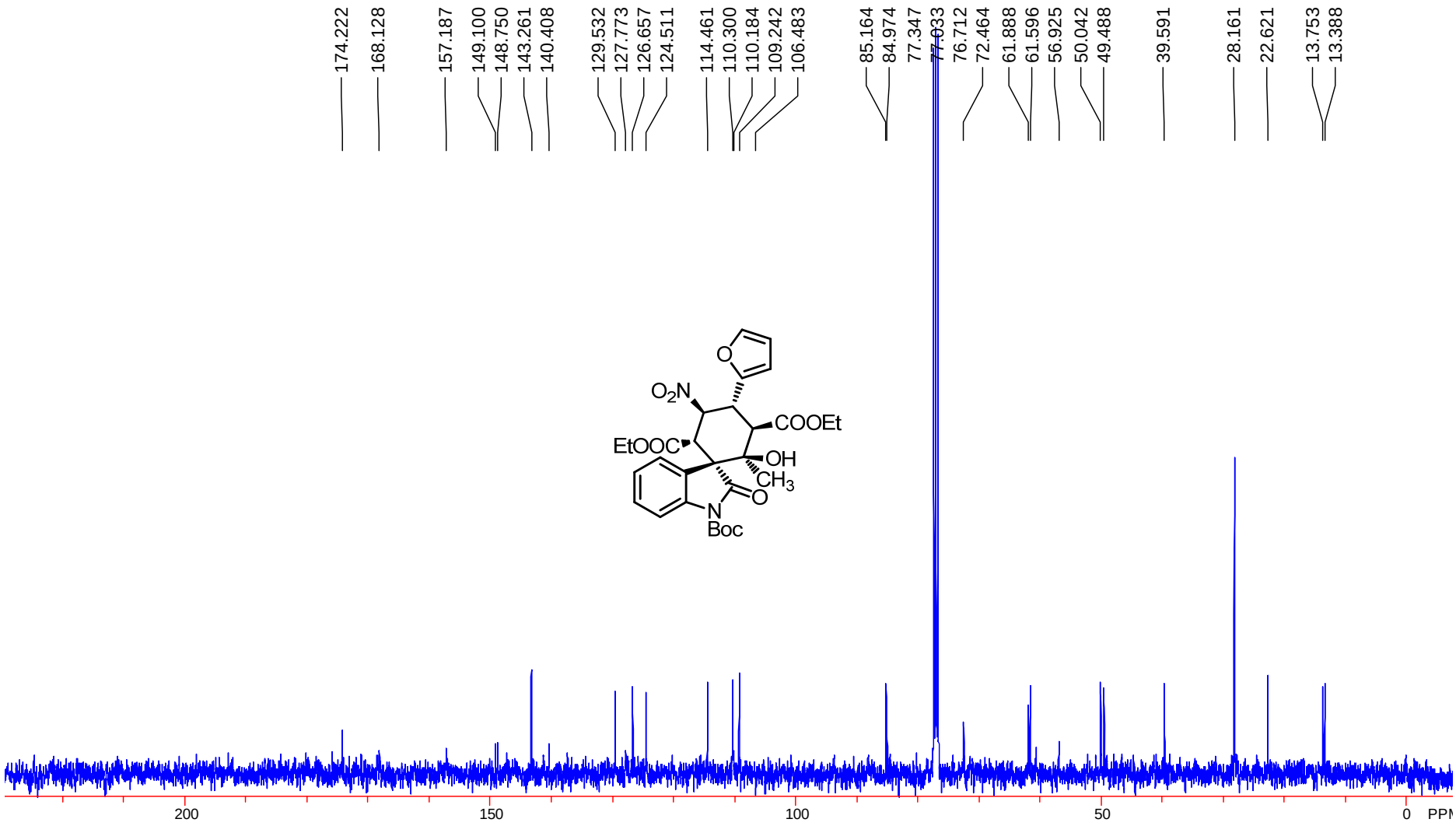
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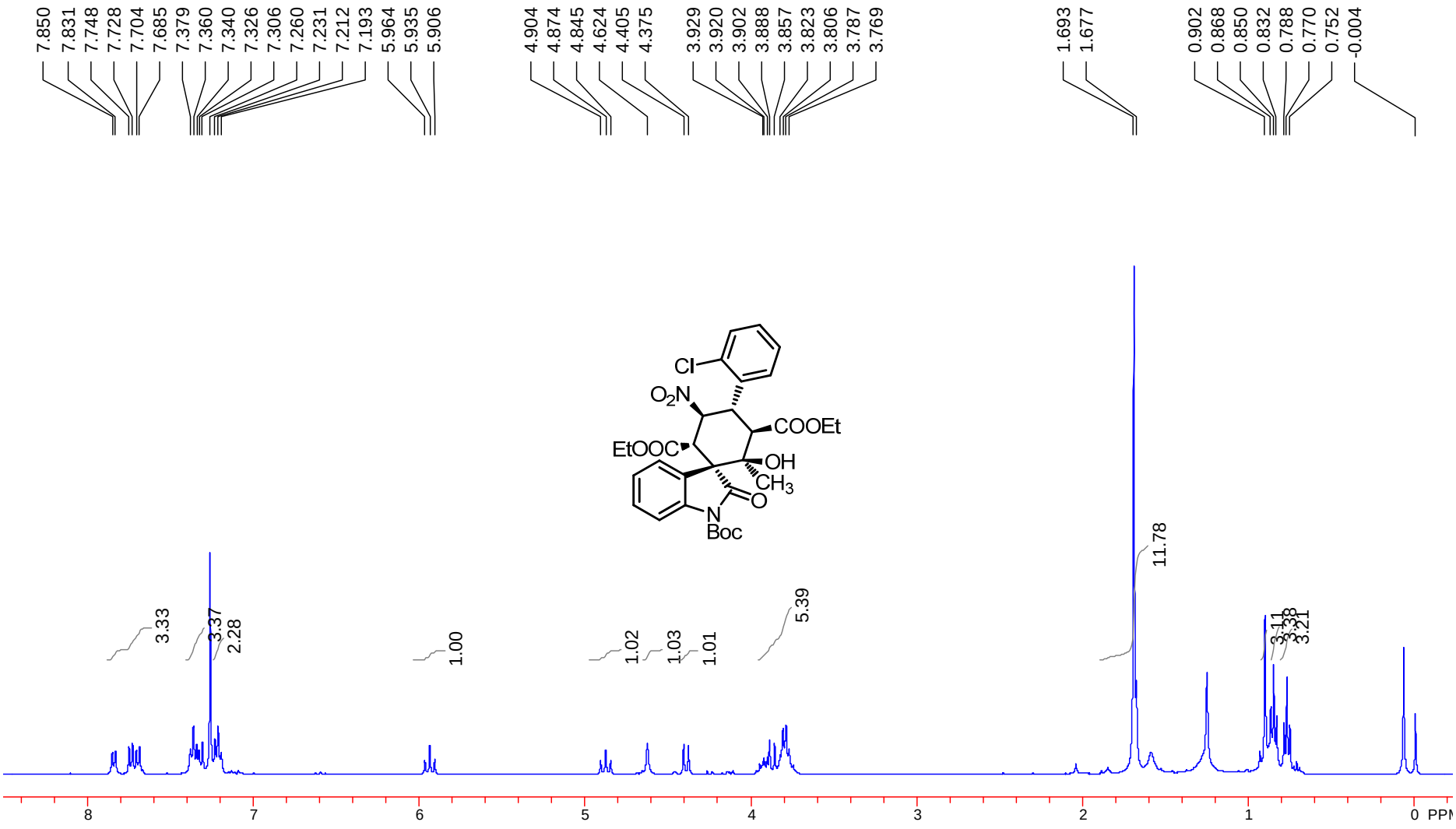
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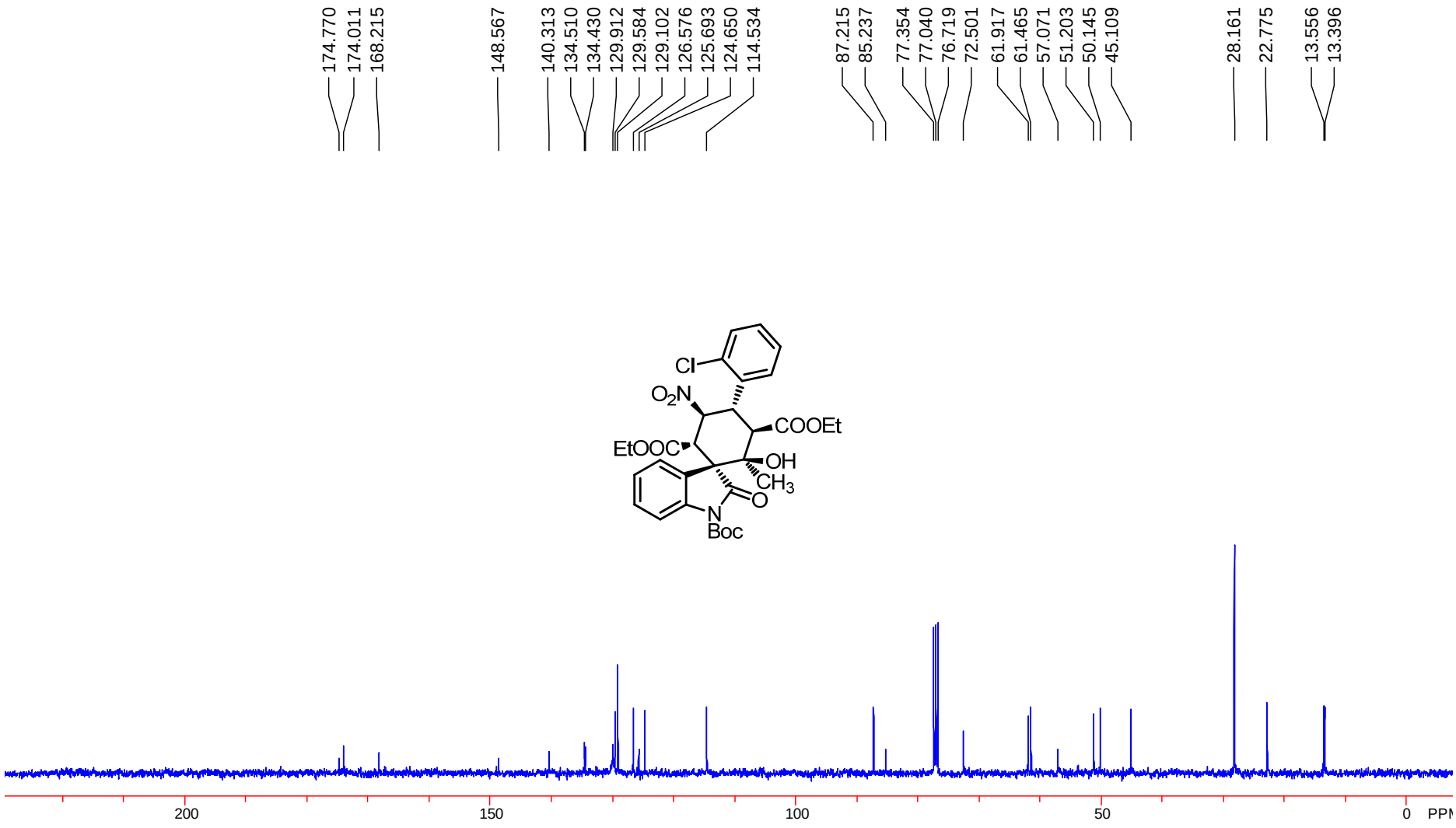
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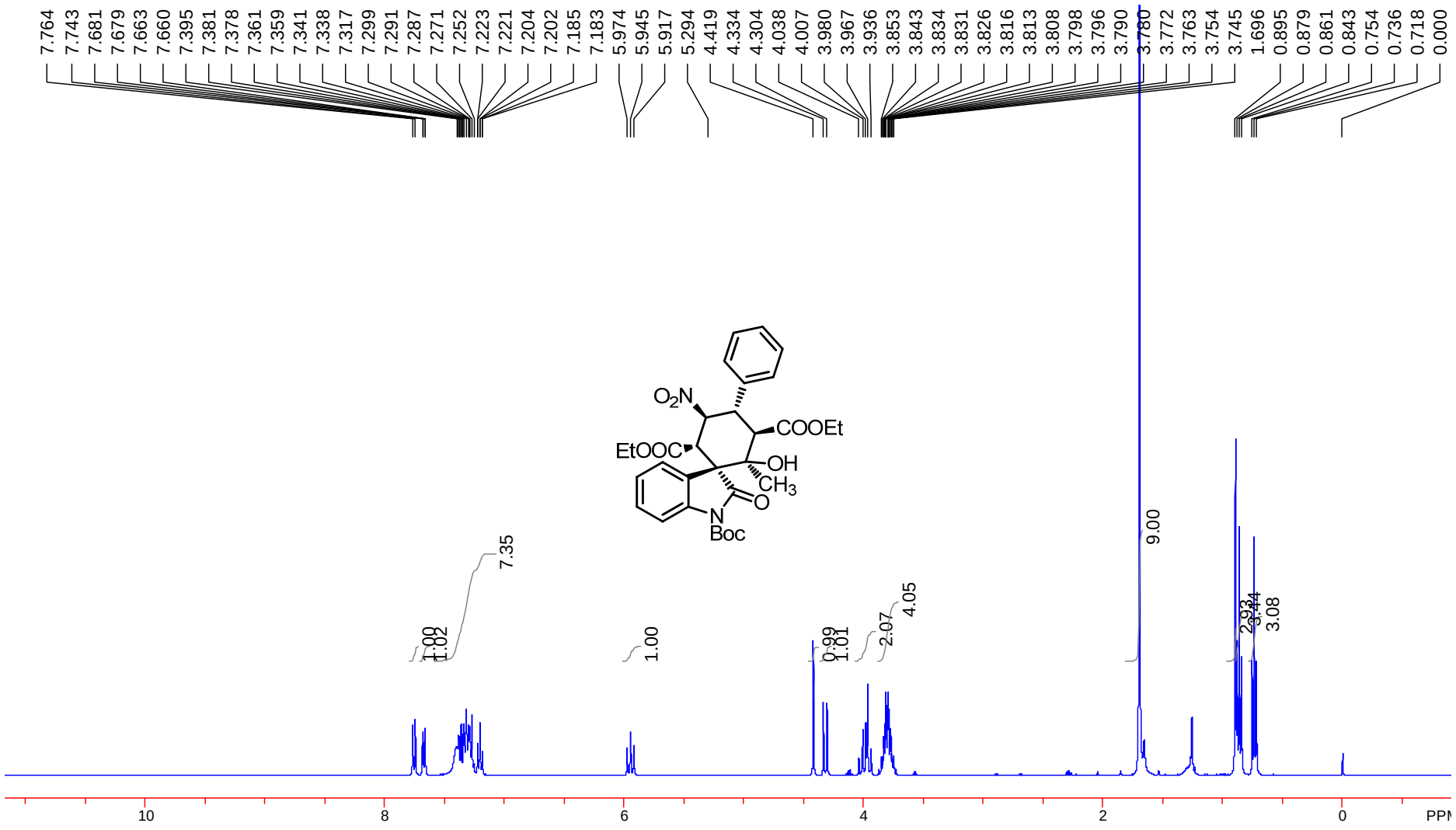
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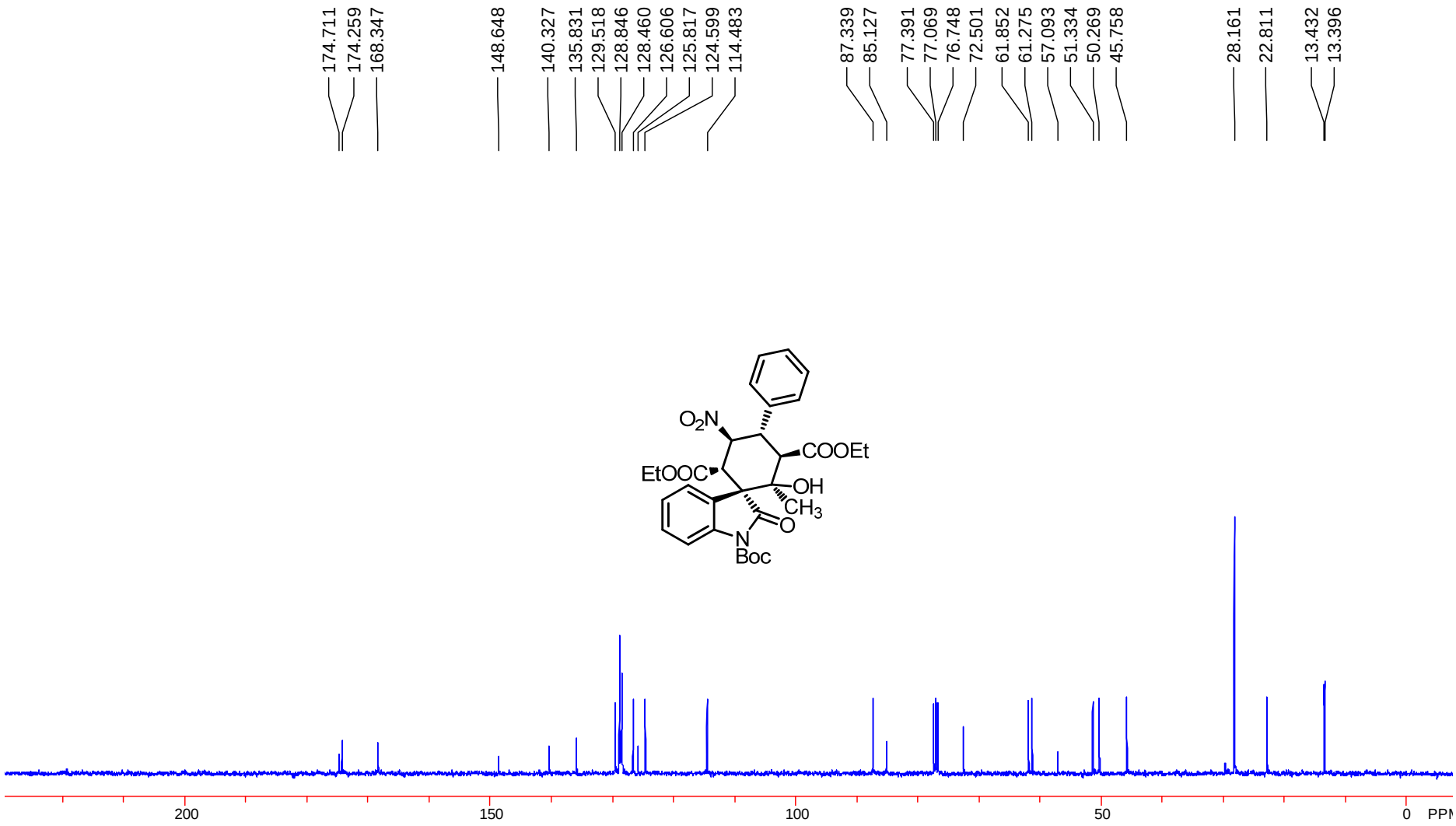
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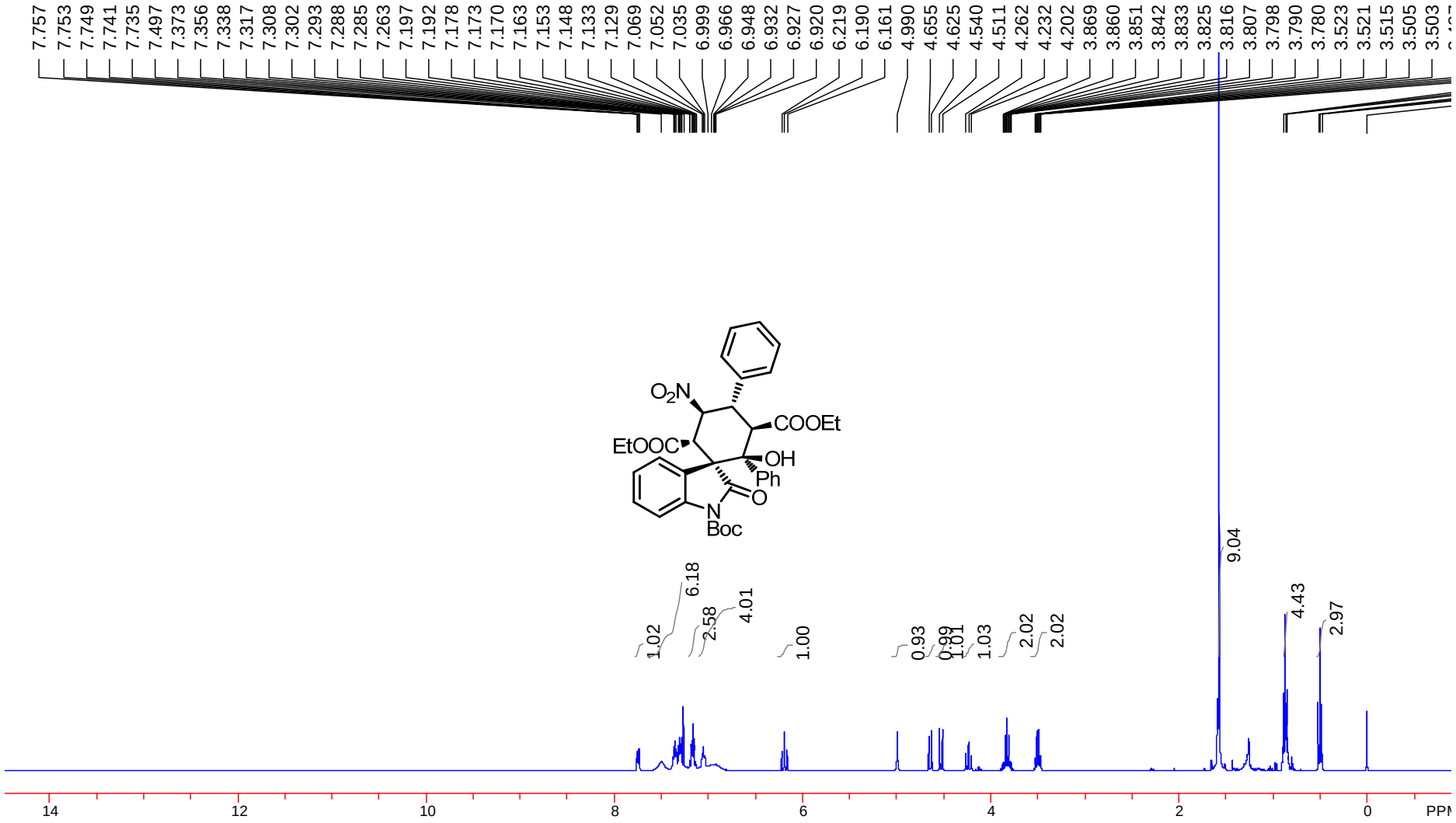
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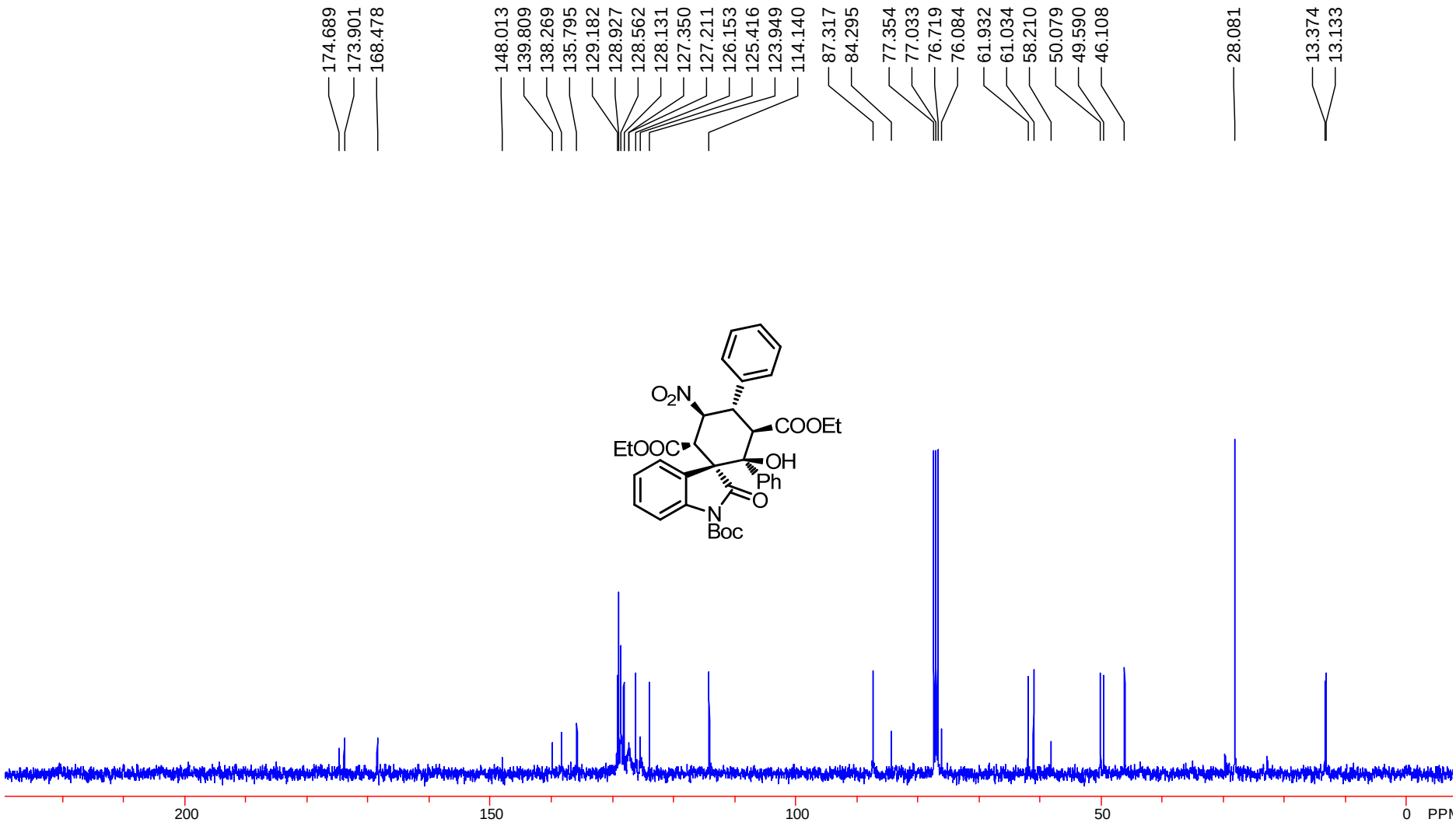
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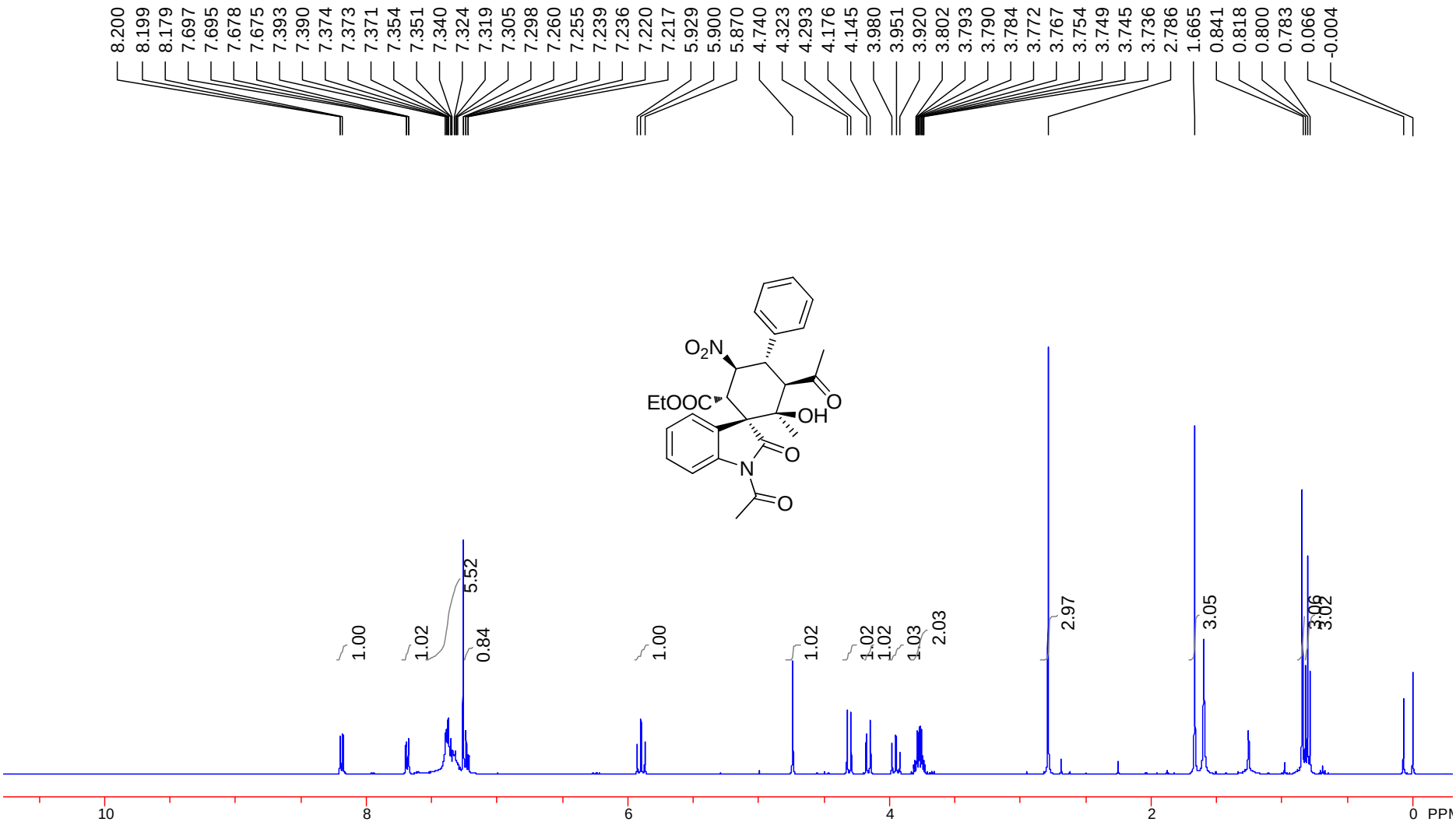
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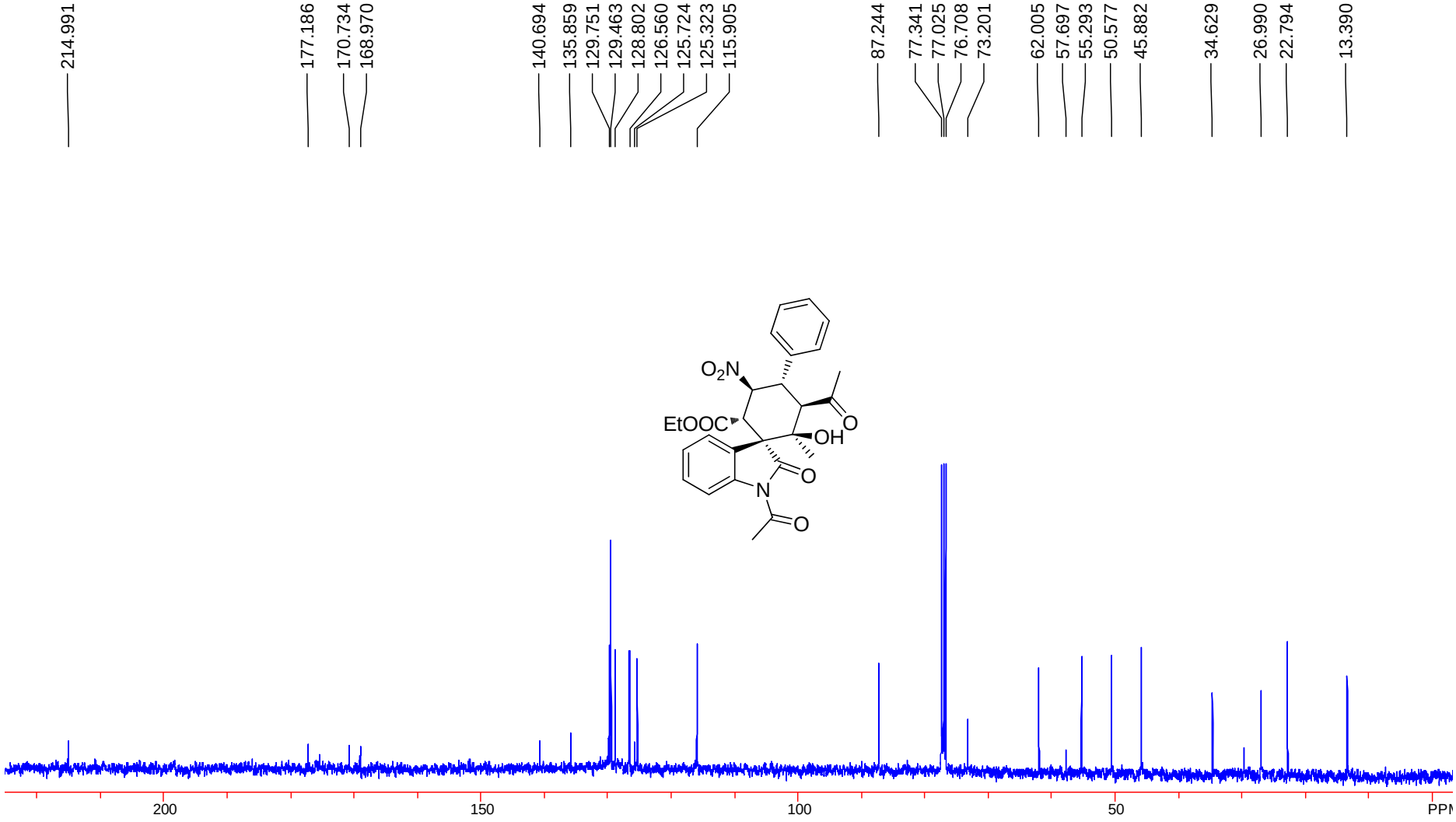
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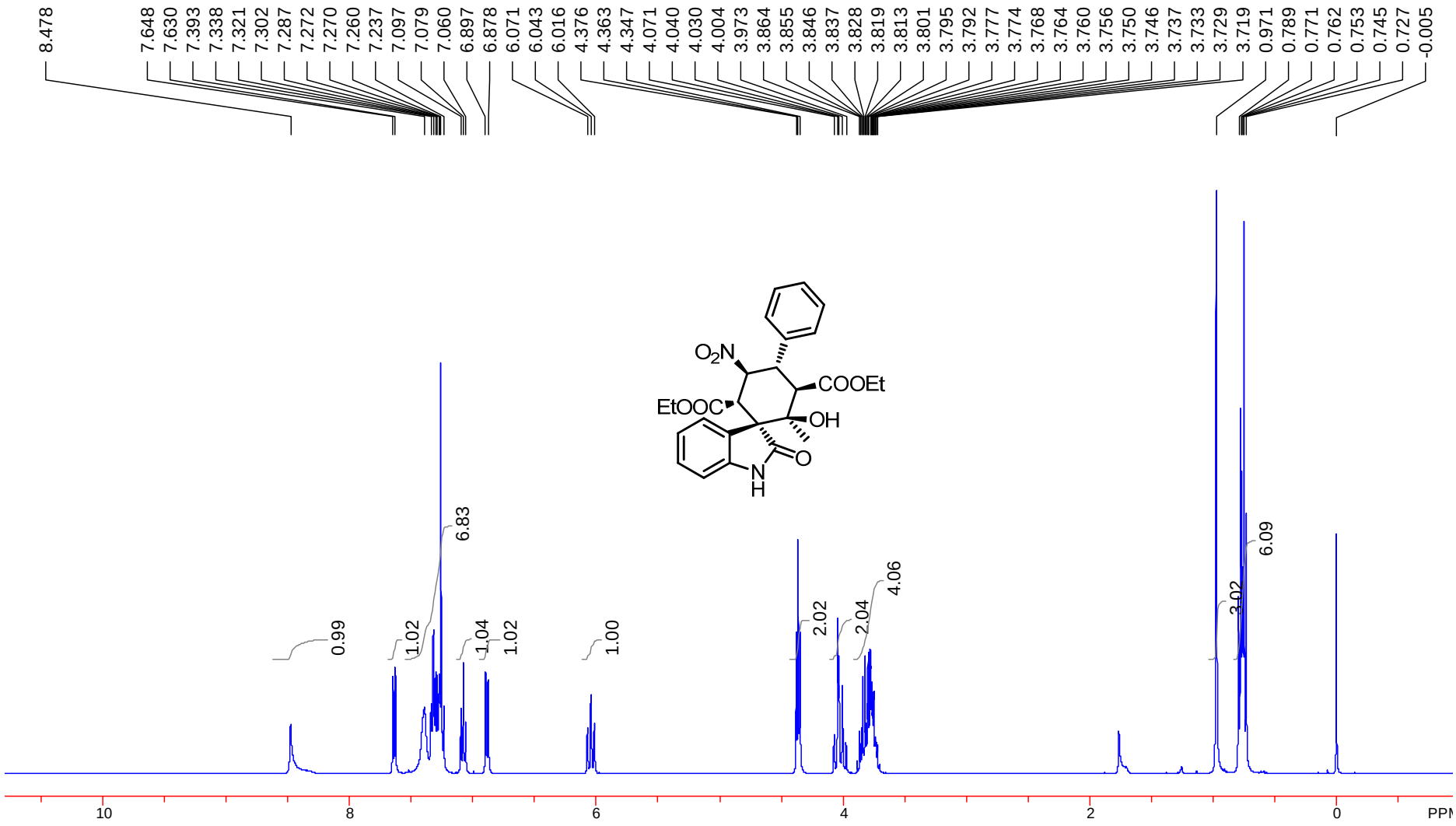
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EtOOC
OH
O
N
H
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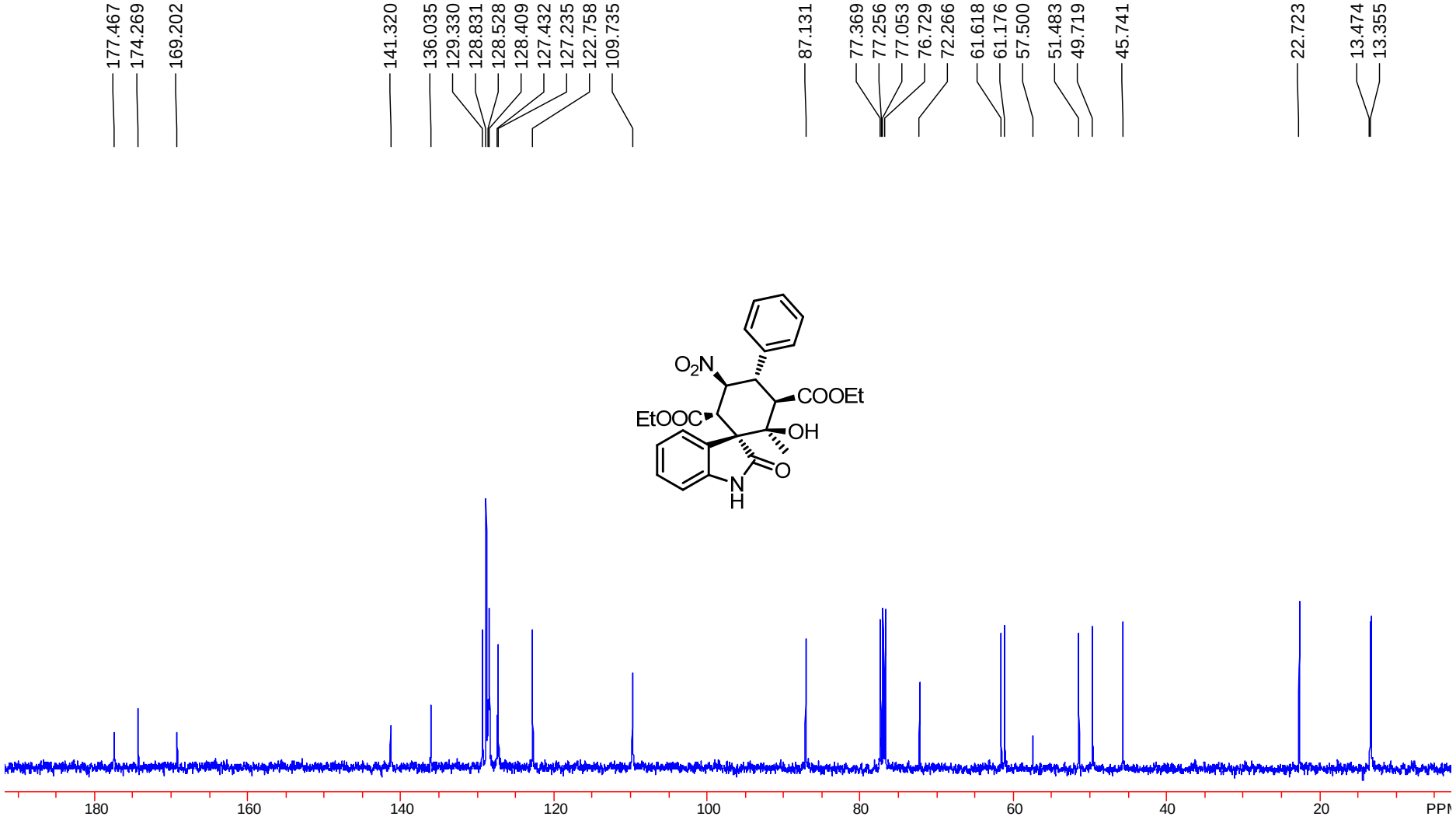
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45.741
22.723
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EtOOC
OH
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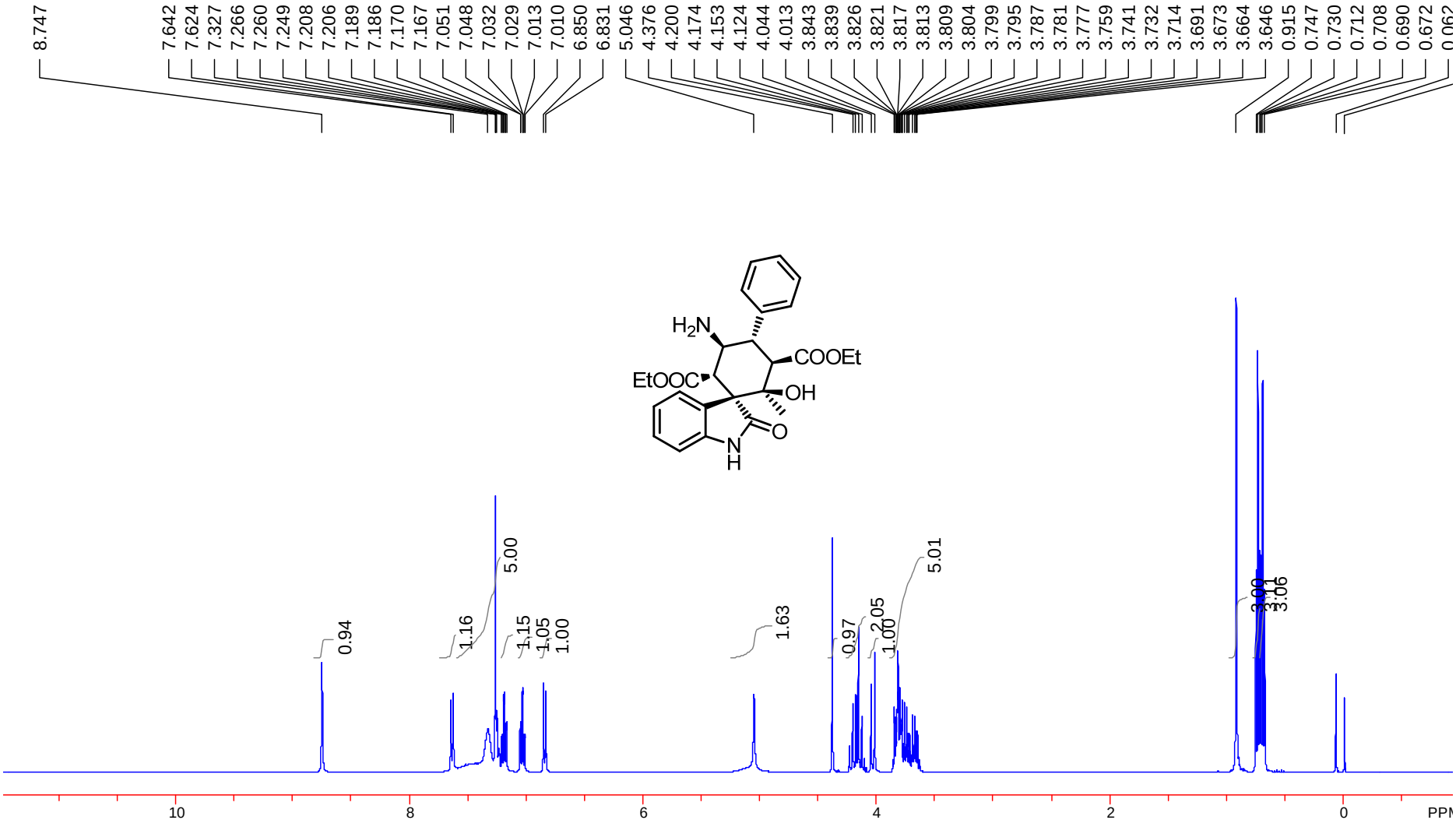
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7.029
7.013
7.010
6.850
6.831
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4.200
4.174
4.153
4.124
4.044
4.013
3.843
3.839
3.826
3.821
3.817
3.813
3.809
3.804
3.799
3.795
3.787
3.781
3.777
3.759
3.741
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3.646
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0.747
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0.708
0.690
0.672
H2N
COOEt
EtOOC
OH
O
N
H
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1.16
5.00
1.15
1.05
1.00
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1.00
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3.00
3.01
3.06
10
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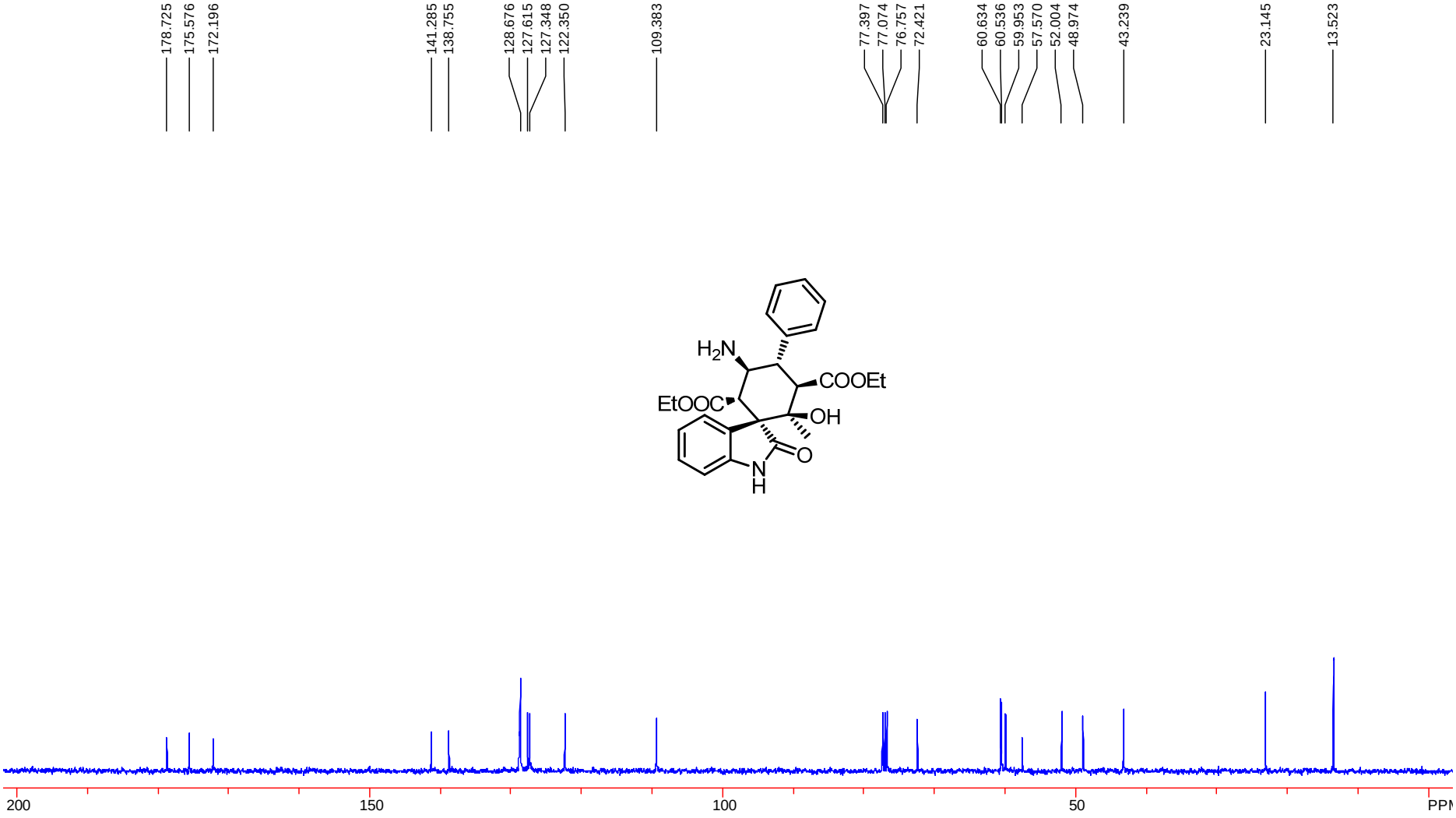
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59.953
57.570
52.004
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H2N
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EtOOC
OH
O
N
H
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50
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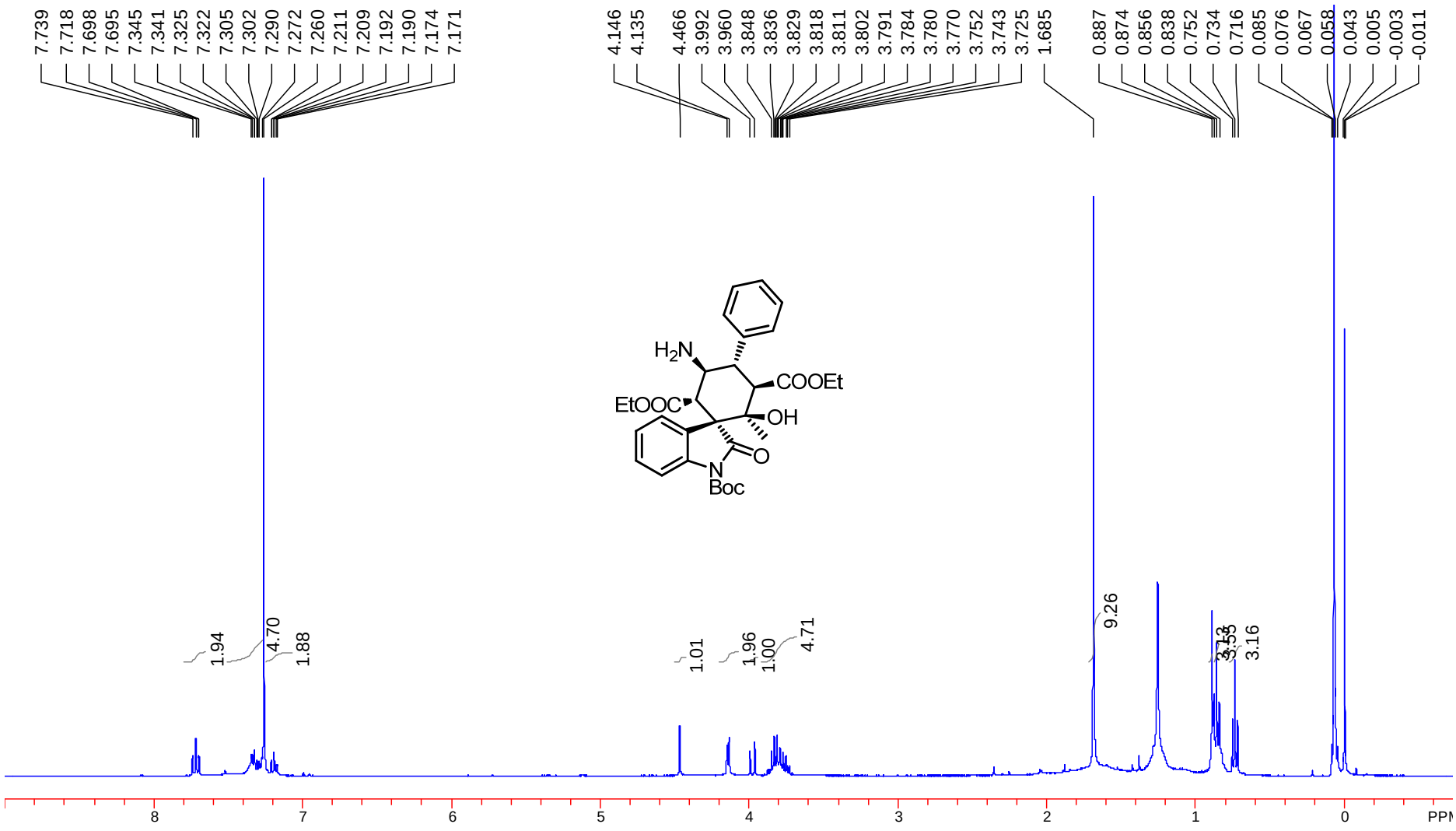
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7.211
7.209
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7.190
7.174
7.171
4.146
4.135
4.466
3.992
3.960
3.848
3.836
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3.818
3.811
3.802
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3.743
3.725
1.685
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0.874
0.856
0.838
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0.734
0.716
0.085
0.076
0.067
0.058
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0.005
-0.003
-0.011
H2N
COOEt
EtOOC
OH
O
N
Boc
1.94
4.70
1.88
1.01
1.96
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3.16
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7
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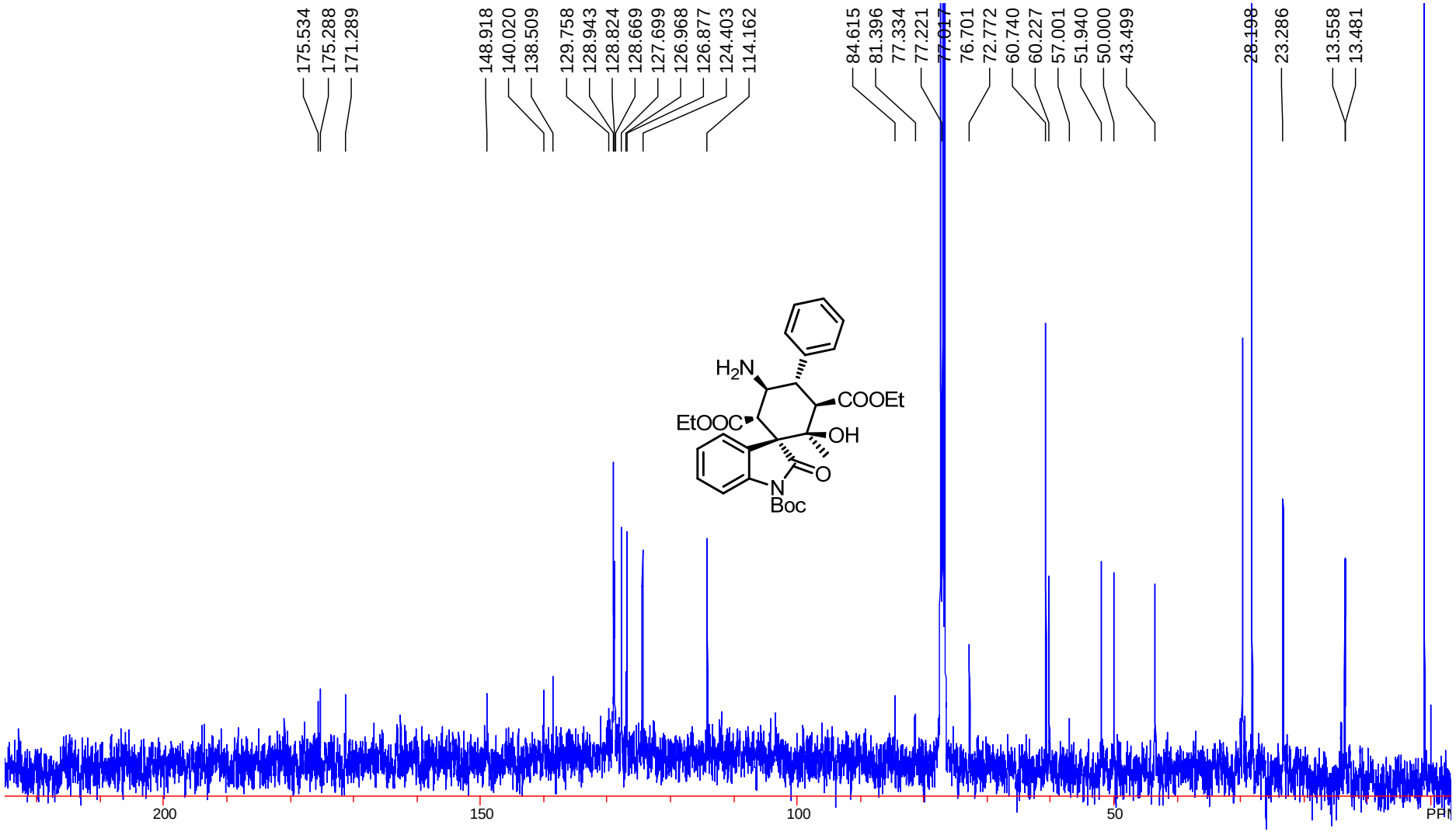
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EtOOC
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Boc
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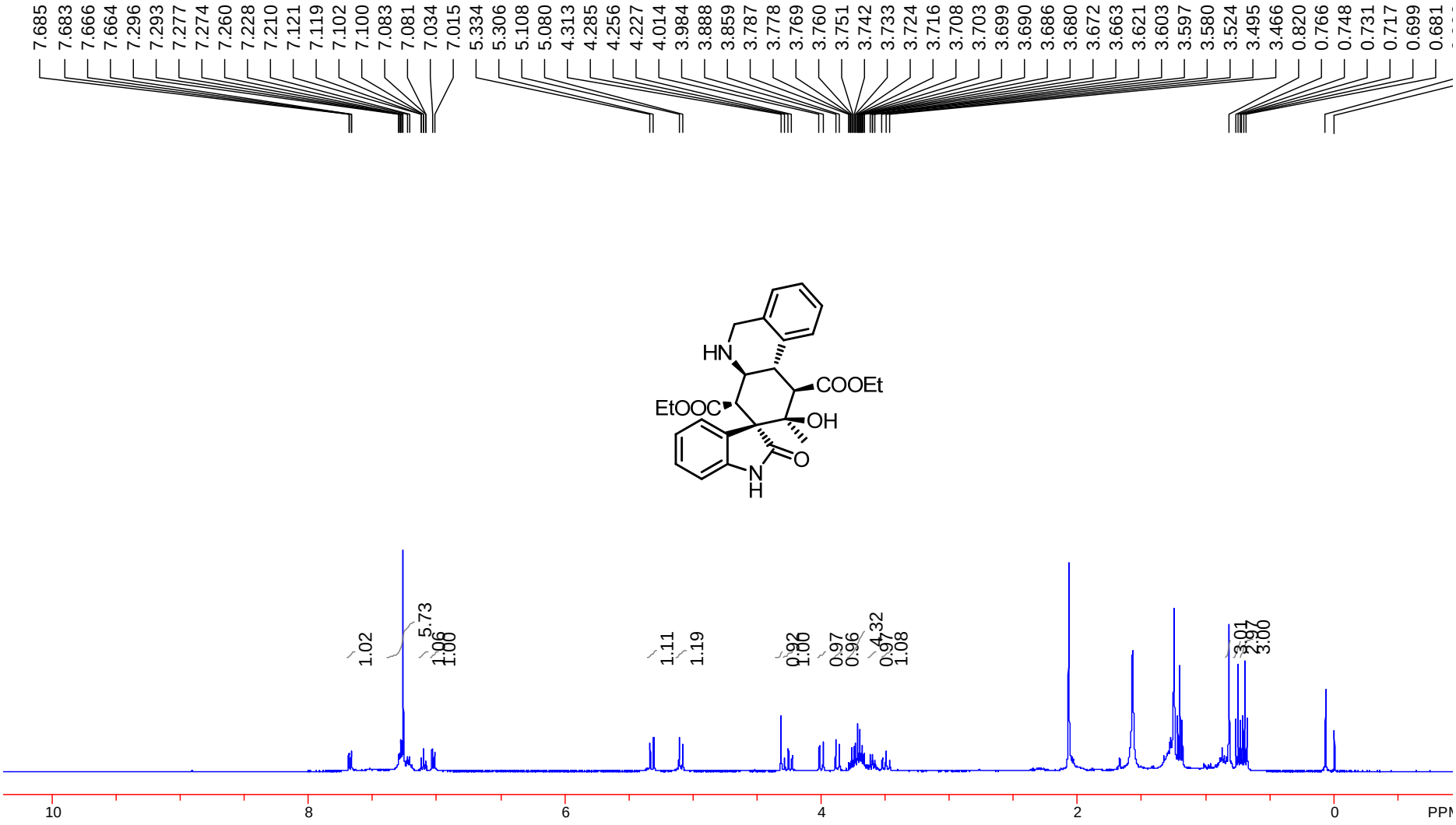
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7.100
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7.081
7.034
7.015
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5.306
5.108
5.080
4.313
4.285
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4.227
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3.859
3.787
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3.699
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3.672
3.663
3.621
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0.748
0.731
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0.699
0.681
HN
COOEt
EtOOC
OH
O
N
H
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5.73
1.06
1.00
1.11
1.19
0.92
1.00
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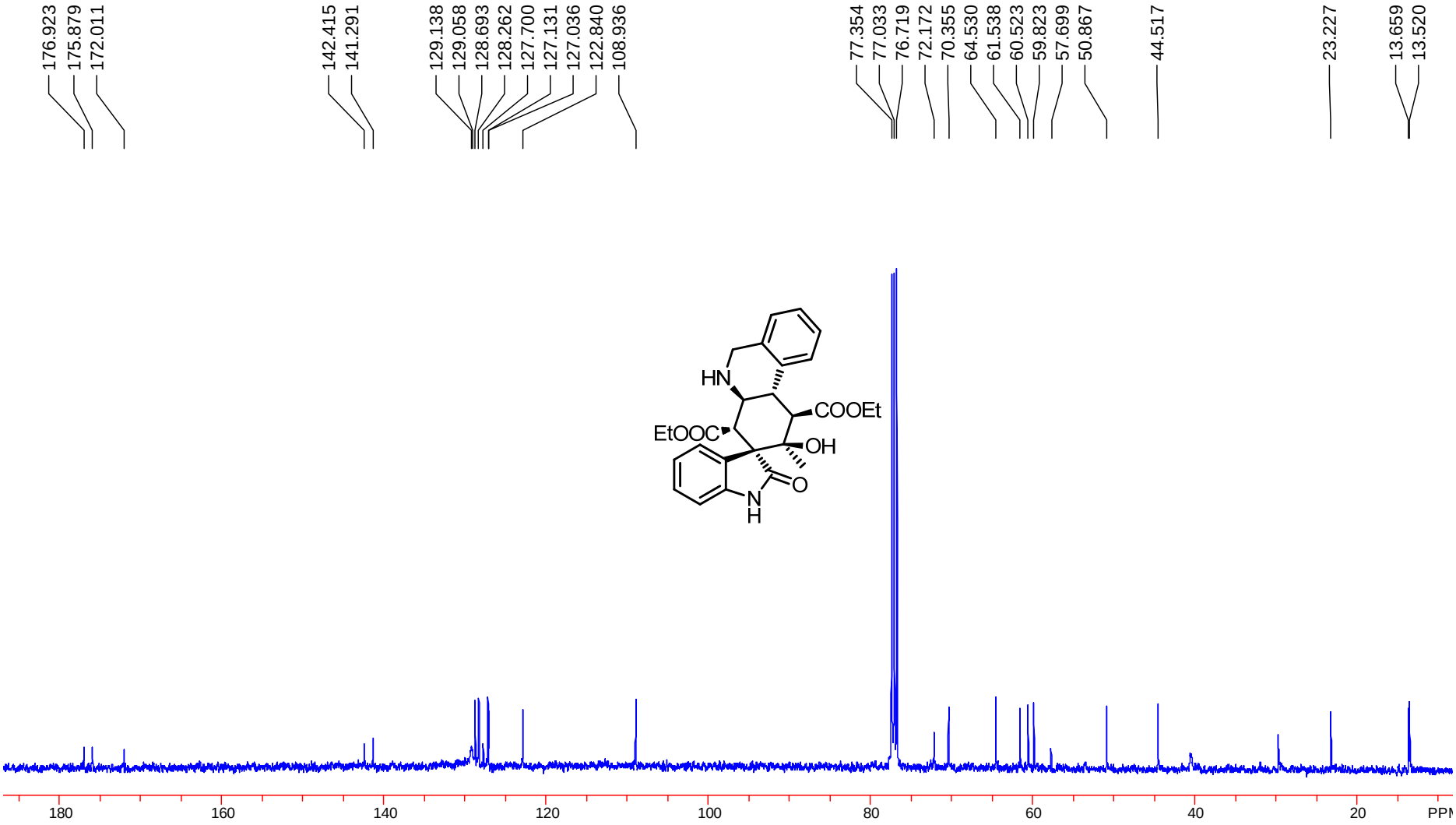
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77.033
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57.699
50.867
44.517
23.227
13.659
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HN
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EtOOC
OH
O
N
H
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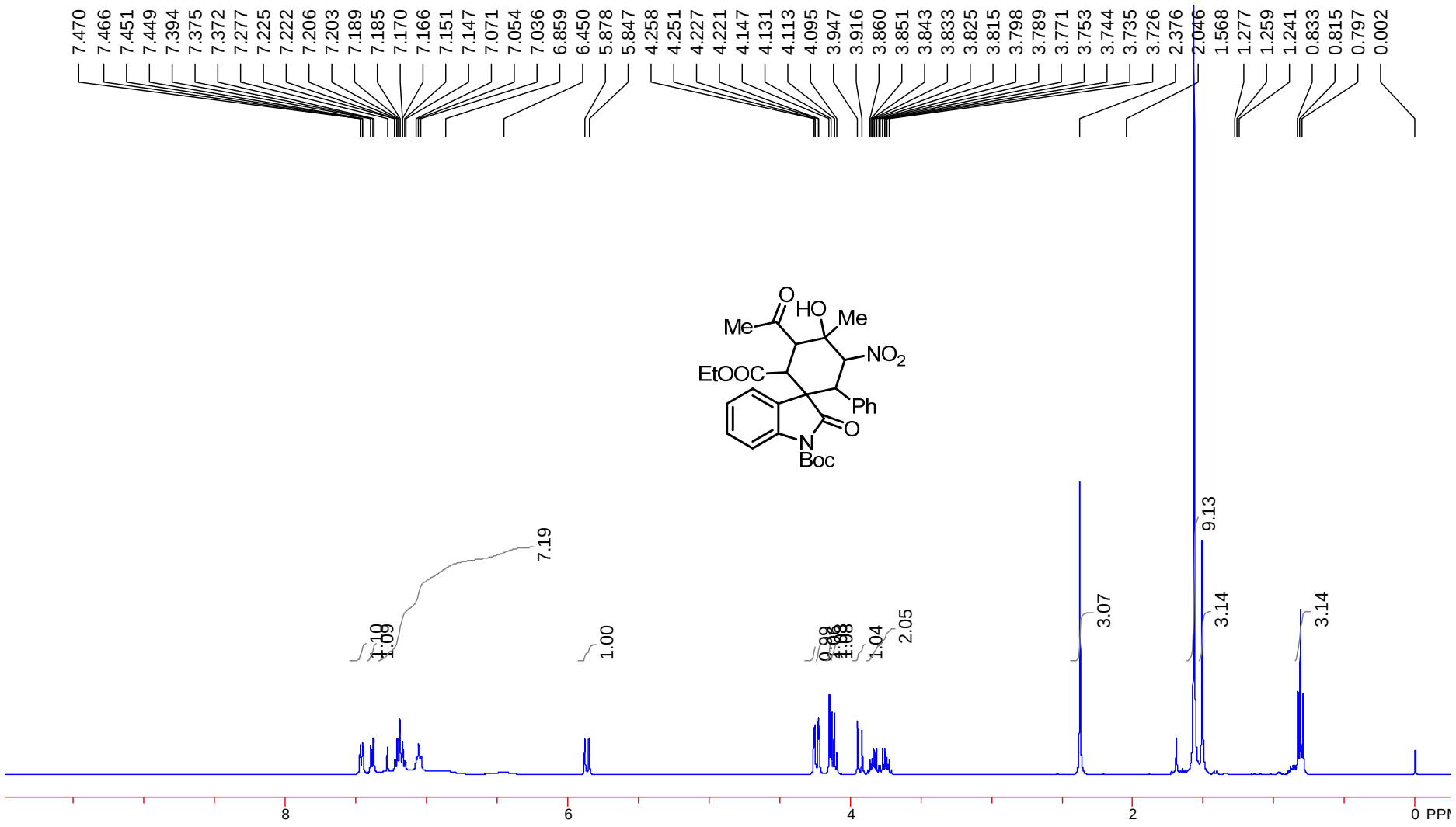
140
120
100
80
60
40
20
PPM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1.259
1.241
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O
HO
Me
Me
NO2
EtOOC
Ph
O
N
Boc
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1.04
3.07
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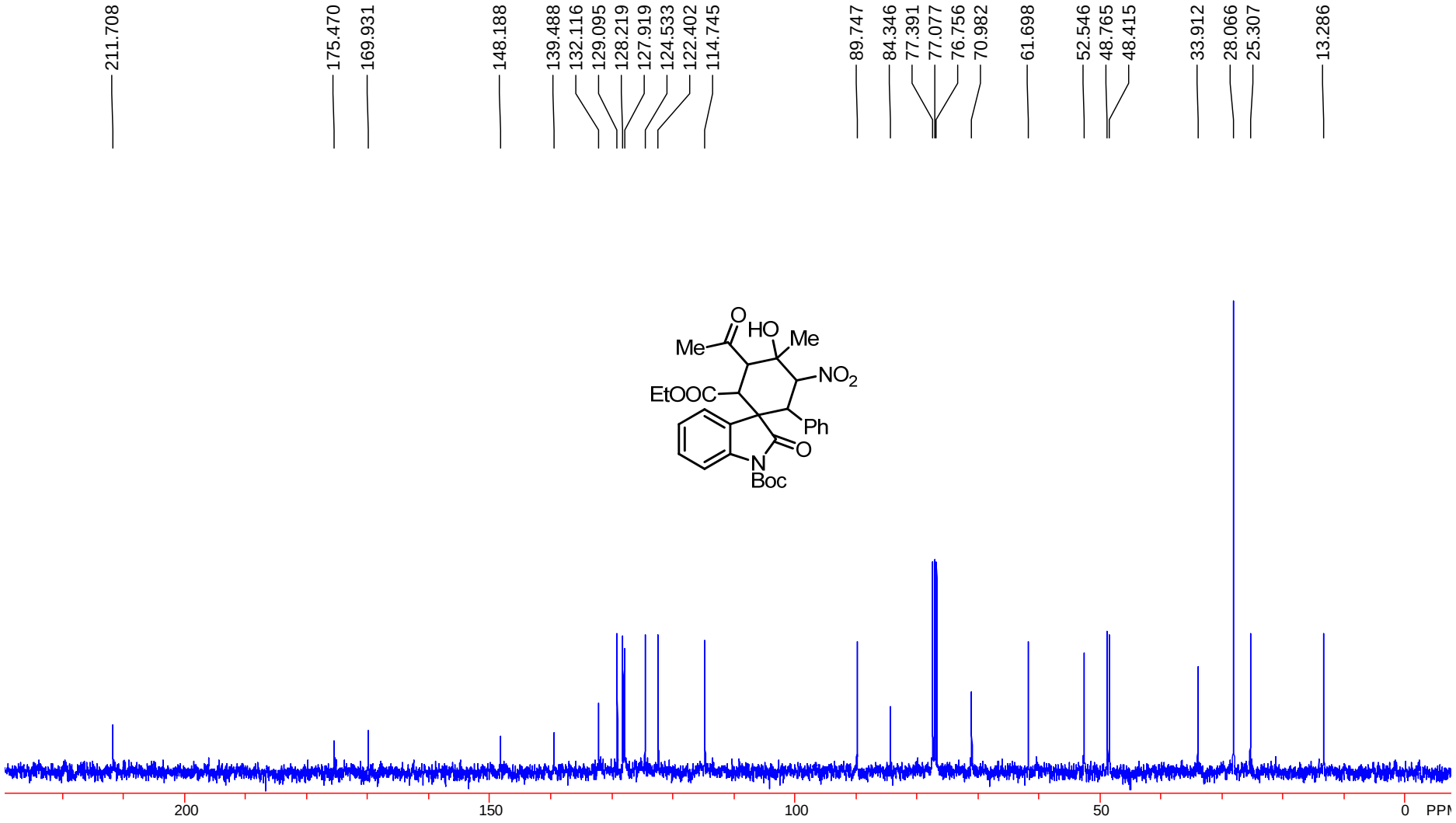
3.14
8
6
4
2
0 PPM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28.066
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Me
Me
NO2
EtOOC
Ph
O
N
Boc
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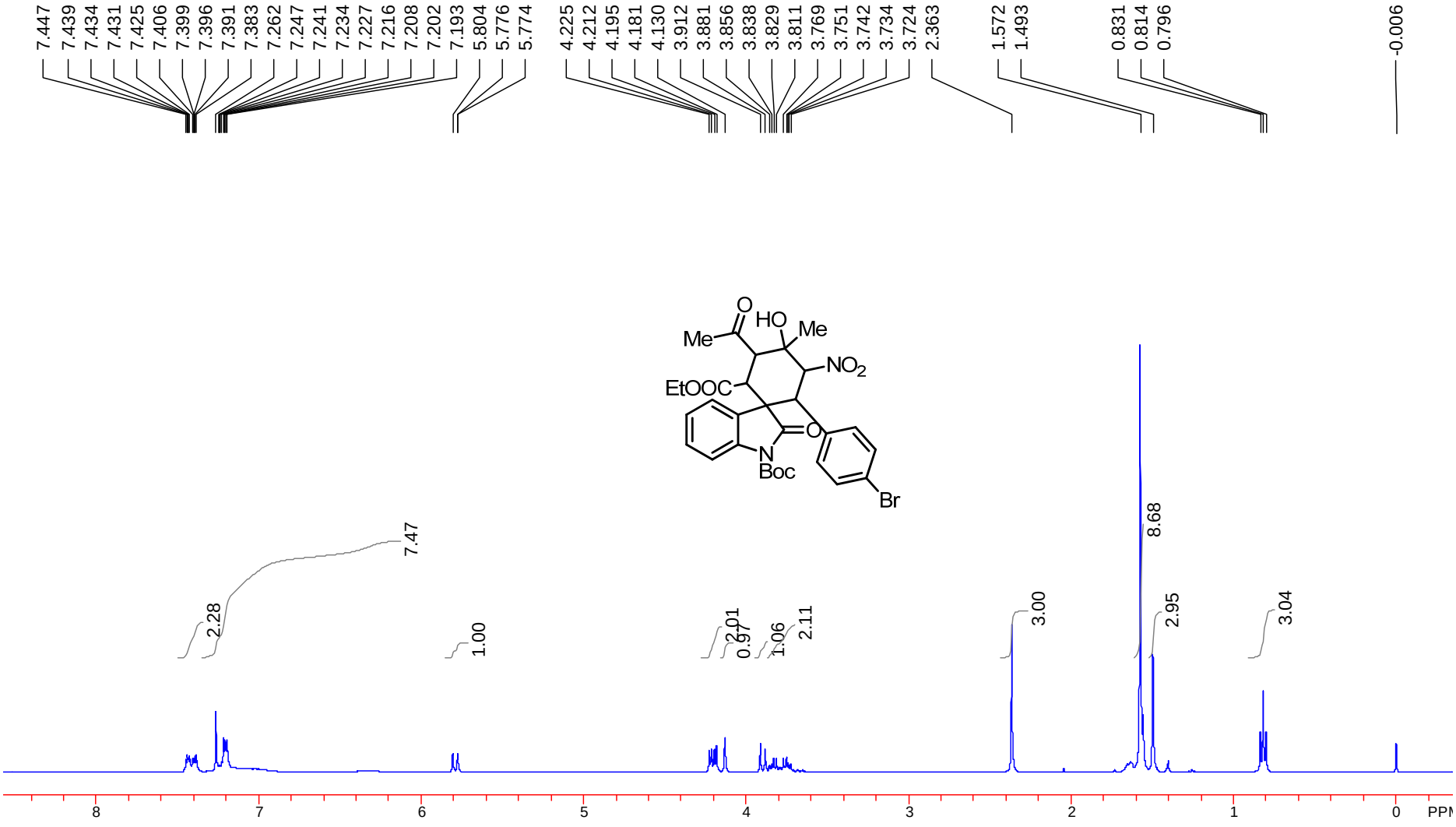
PPM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5.774
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4.195
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3.856
3.838
3.829
3.811
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HO
Me
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O
N
Boc
Br
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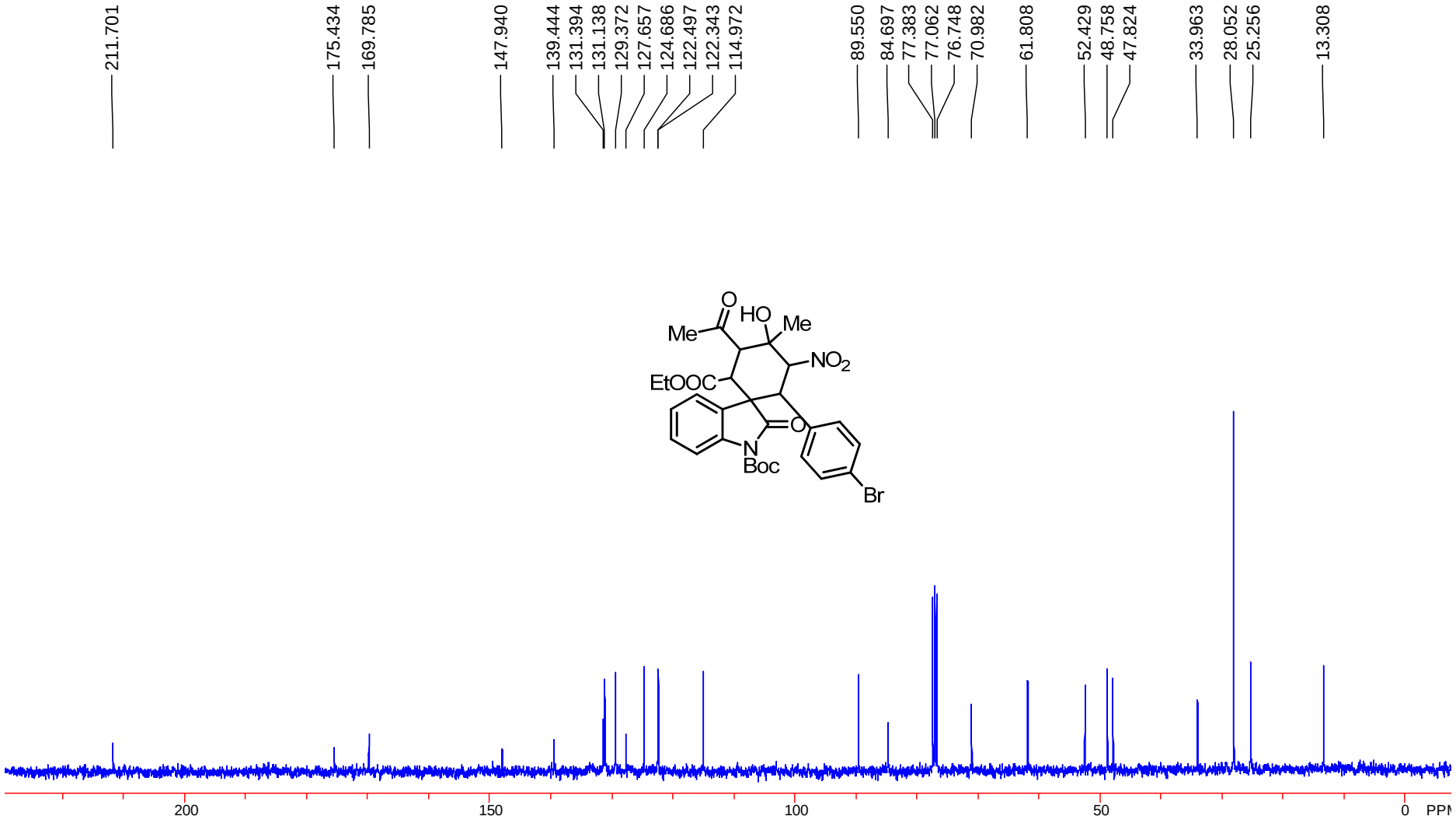
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13.308
O
HO
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Me
NO2
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O
N
Boc
Br
200
150
100
50
0
PPM