Electronic Supplementary Material (ESI) for Chemical Communications

Morpholine Catalyzed Direct C3 Alkenylation of Indoles with α,β-Unsaturated Aldehydes

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Supporting Information

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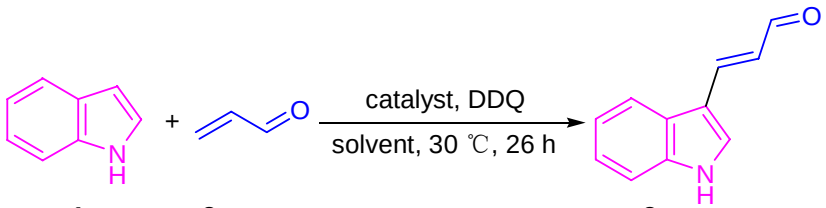
General Remarks

General: All manipulations were conducted with Schlenk tube. 1H-NMR spectra were recorded on Bruker AVIII-400 spectrometers. Chemical shifts are reported in ppm referenced to the internal solvent peaks of methanol-d4 and DMSO-d6, at 3.30 ppm and 2.49 ppm for 1H NMR and 49.0 ppm and 39.5 ppm for 13C NMR, respectively. Mass spectra were obtained using electrospray ionization (ESI) mass spectrometer. Unless otherwise noted, materials and solvents obtained from commercial suppliers were used without further purification. Morpholine·TFA was prepared with morpholine and trifluoroacetic acid in Et_2O.

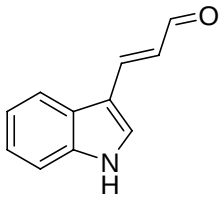


1a **2a** **3aa**

entry	catalyst (mol%)	solvent	yield (%)[b]
1	**morpholine•TFA (20)**	**THF**	**95**
2	morpholine•TFA (20)	CH_2Cl_2	15
3	morpholine•TFA (20)	DCE	trace
4	morpholine•TFA (20)	toluene	ND
5	morpholine•TFA (20)	MeCN	80
6	morpholine•TFA (20)	$MeNO_2$	29
7	morpholine•TFA (20)	dioxane	90

Experimental Section

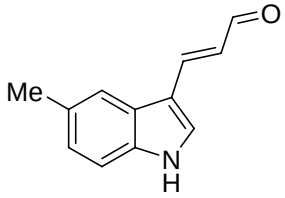
(*E*)-3-(1H-Indol-3-yl)acrylaldehyde **(3aa)**



Morpholine•TFA (16.1 mg, 0.08 mmol), indole **1a** (46.8 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 30 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 65.0 mg (95% yield) of ***E*-3aa**. IR:(KBr) ν_{max} 3278, 1649, 1604, 1505, 1117 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.44 (d, *J* = 8.0 Hz, 1H), 7.83-7.78 (m, 2H), 7.74 (s, 1H), 7.45-7.42 (m, 1H), 7.25-7.16 (m, 2H), 6.68 (dd, *J* = 15.4 Hz, 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.6, 150.8, 139.4, 133.8, 126.5, 124.3, 123.9, 122.7, 121.1, 114.4, 113.4;

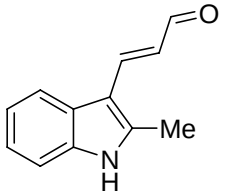
HRMS m/z (ESI): Calcd. for $C_{11}H_{10}NO$ $[M+H]^+$ 172.0757, Found: 172.0757.

(*E*)-3-(5-Methyl-1H-indol-3-yl)acrylaldehyde **(3ba)**



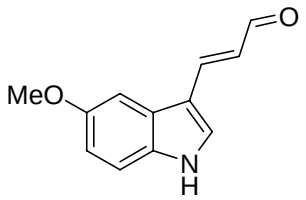
Morpholine•TFA (16.1 mg, 0.08 mmol), 5-methyl-indole **1b** (52.4 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 30 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 69.8 mg (94% yield) of *E* **-3ba**. IR:(KBr) ν_{max} 3269, 1647, 1603, 1579, 1508, 1417, 1124 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.44 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 15.6 Hz, 1H), 7.72 (s, 1H), 7.62 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.68 (dd, *J* = 15.6 Hz, 8.4 Hz, 1H), 2.44 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.6, 151.0, 137.7, 133.9, 132.3, 126.8, 125.8, 123.7, 120.9, 114.1, 113.0, 21.7; HRMS m/z (ESI): Calcd. for $C_{12}H_{12}NO$ $[M+H]^+$ 186.0913, Found: 186.0912.

(*E*)-3-(2-Methyl-1H-indol-3-yl)acrylaldehyde **(3ca)**



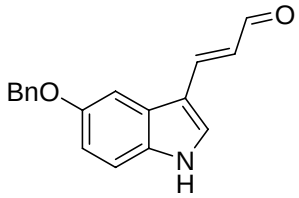
Morpholine•TFA (16.1 mg, 0.08 mmol), 2-methyl-indole **1c** (52.4 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 0 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 52.1 mg (70% yield) of *E* **-3ca**. IR:(KBr) ν_{max} 3244, 1649, 1598, 1573, 1458, 1422, 1142 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.42 (d, *J* = 7.2 Hz, 1H), 7.82 (d, *J* = 14.8 Hz, 1H), 7.74-7.70 (m, 1H), 7.33-7.30 (m, 1H), 7.17-7.12 (m, 2H), 6.62 (dd, *J* = 15.6 Hz, 8.0 Hz, 1H), 2.52 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.6, 149.8, 145.6, 138.0, 127.4, 123.6, 122.7, 120.7, 112.5, 110.9, 11.9; HRMS m/z (ESI): Calcd. for $C_{12}H_{12}NO$ $[M+H]^+$ 186.0913, Found: 186.0911.

(*E*)-3-(5-Methoxy-1H-indol-3-yl)acrylaldehyde **(3da)**



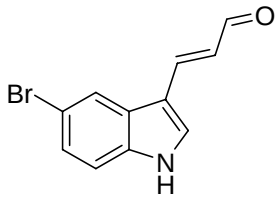
Morpholine•TFA (16.1 mg, 0.08 mmol), 5-methoxy-indole **1d** (58.6 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 10 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 250/100/3 as the eluent to afford 68.2 mg (85% yield) of ***E*-3da**. IR:(KBr) ν_{max} 3161, 1641, 1601, 1508, 1479, 1439, 1119 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.44 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 15.2 Hz, 1H), 7.73 (s, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 7.27 (d, *J* = 2.4 Hz, 1H), 6.88 (dd, *J* = 9.0 Hz, 2.4 Hz, 1H), 6.62 (dd, *J* = 15.6 Hz, 8.0 Hz, 1H), 3.83 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.5, 157.2, 150.9, 134.2, 134.0, 127.3, 123.3, 114.3, 114.1, 114.0, 103.3, 56.2; HRMS m/z (ESI): Calcd. for $C_{12}H_{12}NO_2$ $[M+H]^+$ 202.0863, Found: 202.0860.

(*E*)-3-(5-(Benzyloxy)-1H-indol-3-yl)acrylaldehyde **(3ea)**



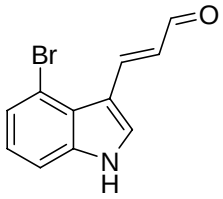
Morpholine•TFA (16.1 mg, 0.08 mmol), 5-benzyloxy-indole **1e** (83.6 mg, 0.37 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 30 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 250/100/3 as the eluent to afford 63.8 mg (61% yield) of ***E*-3ea**. IR:(KBr) ν_{max} 3279, 1651, 1606, 1510, 1479, 1431, 1125 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.44 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 15.6 Hz, 1H), 7.73 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.36-7.33 (m, 4H), 7.29 (d, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.60 (dd, *J* = 15.6 Hz, 8.0 Hz, 1H), 5.10 (s, 2H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.5, 156.2, 150.8, 139.1, 134.4, 134.1, 129.5, 128.8, 128.7, 127.2, 123.5, 114.8, 114.4, 114.1, 105.1, 71.9; HRMS m/z (ESI): Calcd. for $C_{18}H_{16}NO_2$ $[M+H]^+$ 278.1176, Found: 278.1170.

(*E*)-3-(5-Bromo-1H-indol-3-yl)acrylaldehyde **(3fa)**



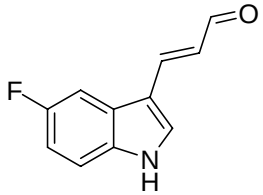
Morpholine•TFA (16.1 mg, 0.08 mmol), 5-bromo-indole **1f** (78.4 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 40 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 81.4 mg (81% yield) of *E* **-3fa**. IR:(KBr) ν_{max} 3145, 1644, 1604, 1507, 1475, 1429, 1119 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.47 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 1.6 Hz, 1H), 7.82-7.77 (m, 2H), 7.36-7.29 (m, 2H), 6.60 (dd, *J* = 15.6 Hz, 7.6 Hz, 1H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.4, 149.5, 137.9, 134.1, 128.3, 127.0, 124.5, 123.5, 115.9, 115.0, 113.8; HRMS m/z (ESI): Calcd. for $C_{11}H_9BrNO$ $[M+H]^+$ 249.9862, Found: 249.9856.

(*E*)-3-(4-Bromo-1H-indol-3-yl)acrylaldehyde **(3ga)**



Morpholine•TFA (16.1 mg, 0.08 mmol), 4-bromo-indole **1g** (78.4 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 48 h at 40 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 48.7 mg (49% yield) of *E* **-3ga**. IR:(KBr) ν_{max} 3107, 1652, 1603, 1506, 1312, 1155 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d6, ppm) δ 9.57 (d, *J* = 7.6 Hz, 1H), 8.58 (d, *J* = 15.6 Hz, 1H), 8.37 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 6.8 Hz, 1H), 7.12-7.07 (m, 1H), 6.73 (dd, *J* = 15.0 Hz, 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d6, ppm) δ 193.5, 146.4, 138.1, 129.7, 125.4, 124.0, 123.7, 123.5, 112.7, 112.3, 112.2; HRMS m/z (ESI): Calcd. for $C_{11}H_9BrNO$ $[M+H]^+$ 249.9862, Found: 249.9859.

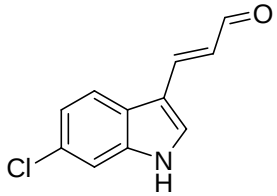
(*E*)-3-(5-Fluoro-1H-indol-3-yl)acrylaldehyde **(3ha)**



Morpholine•TFA (16.1 mg, 0.08 mmol), 5-fluoro-indole **1h** (54.0 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The Acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 30 ℃, then DDQ (118.0 mg, 0.52mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 64.0 mg (85% yield) of *E* **-3ha**. IR:(KBr) ν_{max} 3261, 1650, 1606, 1511, 1470, 1424, 1116 cm^{-1}; ^{1}H-NMR (400

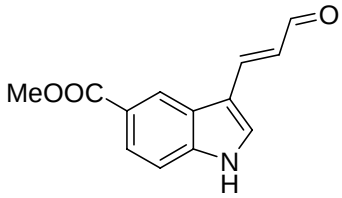
MHz, CD_3OD, ppm) δ 9.47 (d, *J* = 8.4 Hz, 1H), 7.85-7.80 (m, 2H), 7.53-7.49 (m, 1H), 7.43-7.39 (m, 1H), 7.03-6.97 (m, 1H), 6.62 (dd, *J* = 15.8 Hz, 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.5, 160.4 (*J* = 235.3 Hz), 150.2, 135.8, 134.9, 127.2, 124.1, 114.4 (*J* = 5.7 Hz), 114.3, 112.3 (*J* = 25.6 Hz), 106.1 (*J* = 24.4 Hz); HRMS m/z (ESI): Calcd. for $C_{11}H_9FNO$ $[M+H]^+$ 190.0663, Found: 190.0658.

(*E*)-3-(6-Chloro-1H-indol-3-yl)acrylaldehyde **(3ia)**



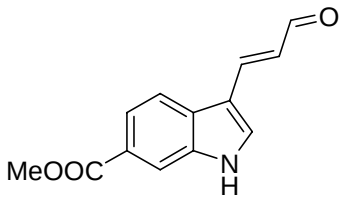
Morpholine•TFA (16.1 mg, 0.08 mmol), 6-chloro-indole **1i** (64.0 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 30 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 73.9 mg (90% yield) of *E* **-3ia**. IR:(KBr) ν_{max} 3272, 1657, 1607, 1510, 1117 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.48 (d, *J* = 8.0 Hz, 1H), 7.82-7.75 (m, 3H), 7.43 (d, *J* = 1.6 Hz, 1H), 7.18-7.14 (m, 1H), 6.66 (dd, *J* = 16.0 Hz, 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.5, 149.7, 139.7, 134.1, 130.0, 125.2, 124.7, 123.0, 122.0, 114.4, 113.2; HRMS m/z (ESI): Calcd. for $C_{11}H_9ClNO$ $[M+H]^+$ 206.0367, Found: 206.0361.

(*E*)-Methyl 3-(3-oxoprop-1-enyl)-1H-indole-5-carboxylate **(3ja)**



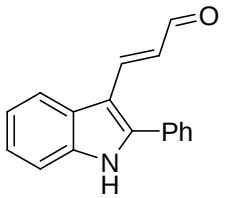
Morpholine•TFA (8.0 mg, 0.04 mmol), methyl 1H-indole-5-carboxylate **1j** (35.0 mg, 0.2 mmol), were mixtured in 2.0 mL THF. The acrolein **2a** (33.6 mg, 0.6 mmol) was added to the reaction mixture. The reaction was stirred for 48 h at 40 ℃, then DDQ (59.0 mg, 0.26 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 200/100/3 as the eluent to afford 27.8 mg (61% yield) of *E* **-3ja**. IR:(KBr) ν_{max} 3143, 1712, 1647, 1607, 1442, 1283, 1237, 1114, 764 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d6, ppm) δ 9.59 (d, *J* = 7.6 Hz, 1H), 8.51 (s, 1H), 8.19 (s, 1H), 7.99 (d, *J* = 16.4 Hz, 1H), 7.85 (dd, *J* = 8.8 Hz, 1.2 Hz, 1H), 7.58 (d, 1H), 6.67 (dd, *J* = 16.0 Hz, 8.4 Hz, 1H), 3.87 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d6, ppm) δ 193.8, 166.9, 146.6, 139.8, 133.1, 124.8, 124.1, 123.6, 122.6, 121.6, 113.0, 112.6, 51.9; HRMS m/z (ESI): Calcd. for $C_{13}H_{12}NO_3$ $[M+H]^+$ 230.0812, Found: 230.0806.

(E)-Methyl 3-(3-oxoprop-1-enyl)-1H-indole-6-carboxylate **(3ka)**



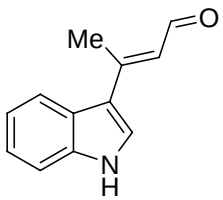
Morpholine•TFA (16.1 mg, 0.08 mmol), methyl 1H-indole-6-carboxylate **1k** (70.0 mg, 0.2 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 48 h at 40 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 200/100/3 as the eluent to afford 45.8 mg (50% yield) of ***E*-3ka**. IR:(KBr) ν_{max} 3232, 1709, 1650, 1608, 1497, 1454, 1425, 1287, 1213, 1143, 1086, 764, 739 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d6, ppm) δ 9.56 (d, *J* = 8.0 Hz, 1H), 8.25 (s, 1H), 8.11 (s, 1H), 8.00 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 16.0 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 6.72 (dd, *J* = 15.2 Hz, 7.6 Hz, 1H), 3.86 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d6, ppm) δ 193.8, 166.8, 146.8, 136.6, 134.9, 128.6, 124.0, 123.8, 121.8, 119.7, 114.2, 112.3, 52.0; HRMS m/z (ESI): Calcd. for $C_{13}H_{12}NO_3$ $[M+H]^+$ 230.0812, Found: 230.0806.

(*E*)-3-(2-Phenyl-1H-indol-3-yl)acrylaldehyde **(3la)**



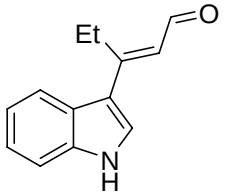
Morpholine•TFA (16.1 mg, 0.08 mmol), 2-phenyl-indole **1l** (77.2 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 30 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 82.2 mg (83% yield) of ***E*-3la**. IR:(KBr) ν_{max} 3255, 1639, 1598, 1574, 1452, 1423, 1138 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.41 (d, *J* = 7.6 Hz, 1H), 7.92-7.82 (m, 2H), 7.64-7.46 (m, 6H), 7.30-7.22 (m, 2H), 6.81 (dd, *J* = 16.0 Hz, 7.6 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d6, ppm) δ 194.1, 147.1, 144.3, 136.8, 130.7, 129.7, 129.4, 129.1, 125.7, 124.0, 123.3, 121.8, 120.5, 112.3, 108.7; HRMS m/z (ESI): Calcd. for $C_{17}H_{14}NO$ $[M+H]^+$ 248.1070, Found: 248.1066.

3-(1H-Indol-3-yl)but-2-enal **(3ab)**



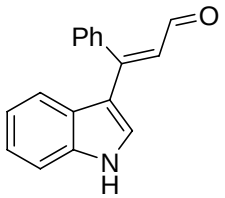
Morpholine•TFA (16.1 mg, 0.08 mmol), indole **1a** (46.8 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The Crotonaldehyde **2b** (84.0 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 10 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 42.3 mg (57% yield, *E*/*Z* = 96:4) of **3ab**. IR: (KBr) ν_{max} 3164, 1626, 1586, 1567, 1513, 1489, 1429, 1384, 1172, 738 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm): *E*-**3ab** δ 10.03 (d, *J* = 8.8 Hz, 1H), 7.87-7.84 (m, 1H), 7.80 (s, 1H), 7.44-7.41 (m, 1H), 7.21-7.12 (m, 2H), 6.67-6.64 (m, 1H), 2.57 (d, *J* = 0.8 Hz, 3H), *Z*-**3ab** δ 9.57 (d, *J* = 8.0 Hz, 1H), 6.05 (m, 1H), 2.40 (d, *J* = 1.2 Hz, 3H); HRMS m/z (ESI): Calcd. for $C_{12}H_{12}NO$ $[M+H]^+$ 186.0913, Found: 186.0909.

3-(1H-Indol-3-yl)pent-2-enal **(3ac)**



Morpholine•TFA (16.1 mg, 0.08 mmol), indole **1a** (46.8 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The (*E*)-pent-2-enal **2c** (100.8 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 48 h at 30 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 40.3 mg (51% yield, *E*/*Z* = 82:18) of **3ac**. IR:(KBr) ν_{max} 3214, 1626, 1584, 1569, 1508, 1430, 1171, 1126, 741 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm): *E*-**3ac** δ 10.06 (d, *J* = 8.4 Hz, 1H), 7.87-7.85 (m, 2H), 7.46-7.43 (m, 1H), 7.21-7.16 (m, 2H), 6.59 (d, *J* = 8.0 Hz, 1H), 3.12 (q, *J* = 7.3 Hz, 2H), 1.32 (t, *J* = 5.1 Hz, 3H), *Z*-**3ac** δ 9.55 (d, *J* = 8.0 Hz, 1H), 6.10 (d, *J* = 8.0 Hz, 1H), 3.12 (m, 2H), 1.10 (t, *J* = 7.2 Hz, 3H); HRMS m/z (ESI): Calcd. for $C_{13}H_{14}NO$ $[M+H]^+$ 200.1070, Found: 200.1067.

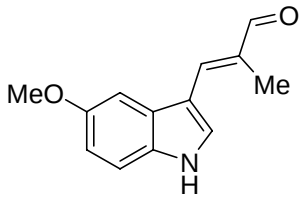
3-(1H-Indol-3-yl)-3-phenylacrylaldehyde **(3ad)**



Morpholine•TFA (16.1 mg, 0.08 mmol), indole **1a** (46.8 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The *trans*-Cinnamaldehyde **2d** (79.2 mg, 0.6 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 60 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 40.3 mg (41% yield,

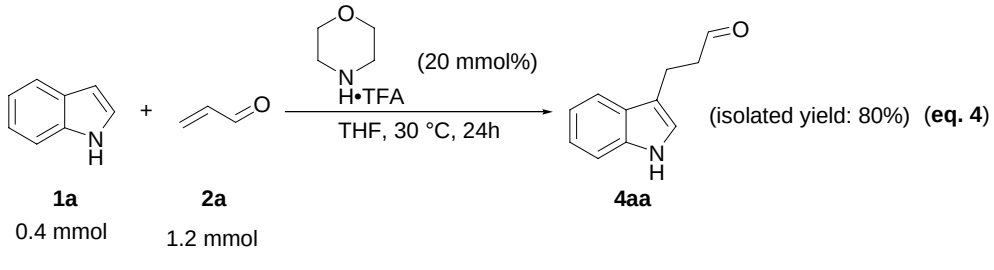
major/minor = 89:11) of **3ad**. IR:(KBr) ν_{max} 3242, 1630, 1559, 1496, 1357, 1167, 1135, 747, 729 cm^{-1}; Major product: ^{1}H-NMR (400 MHz, CD_3OD, ppm): major product: δ 9.29 (d, *J* = 8.0 Hz, 1H), 7.66-7.63 (m, 1H), 7.52-7.42 (m, 6H), 7.25-7.14 (m, 3H), 6.80-6.76 (m, 1H), minor product: δ 9.62 (d, *J* = 7.6 Hz, 1H), 6.43 (m, 1H); HRMS m/z (ESI): Calcd. for $C_{17}H_{14}NO$ $[M+H]^+$ 248.1070, Found: 248.1068.

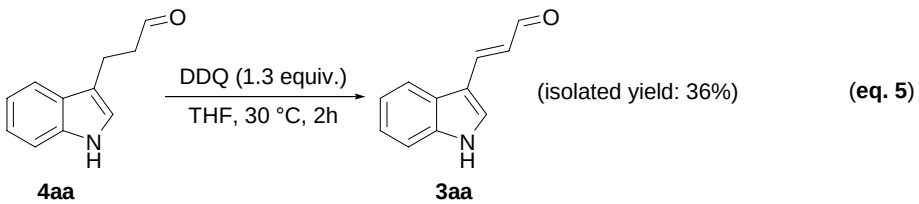
(*E*)-3-(5-Methoxy-1H-indol-3-yl)-2-methylacrylaldehyde **(3de)**



Morpholine•TFA (16.1 mg, 0.08 mmol), 5-methoxy-indole **1d** (58.8 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The methacrylaldehyde **2e** (84.0 mg, 1.2 mmol) was added to the reaction mixture. The reaction was stirred for 24 h at 70 ℃, then DDQ (118.0 mg, 0.52 mmol) was added and the reaction continues for another 2 h. The crude reaction mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 250/100/3 as the eluent to afford 45.8 mg (53% yield) of *E*-**3de**. IR:(KBr) ν_{max} 3166, 1644, 1603, 1508, 1488, 1445, 1247 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD, ppm) δ 9.47 (s, 1H), 7.76 (s, 1H), 7.74 (s, 1H), 7.35-7.31 (m, 2H), 6.87 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 3.86 (s, 3H), 2.03 (d, J_1 = 0.8 Hz, 3H); ^{13}C-NMR (100 MHz, CD_3OD, ppm) δ 196.4, 156.7, 144.9, 132.8, 132.6, 130.1, 129.7, 114.2, 113.8, 113.6, 101.2, 56.2, 11.4; HRMS m/z (ESI): Calcd. for $C_{13}H_{14}NO_2$ $[M+H]^+$ 216.1019, Found: 216.1014.

Mechanistic experiments

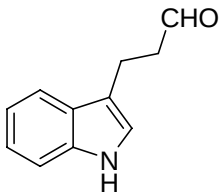




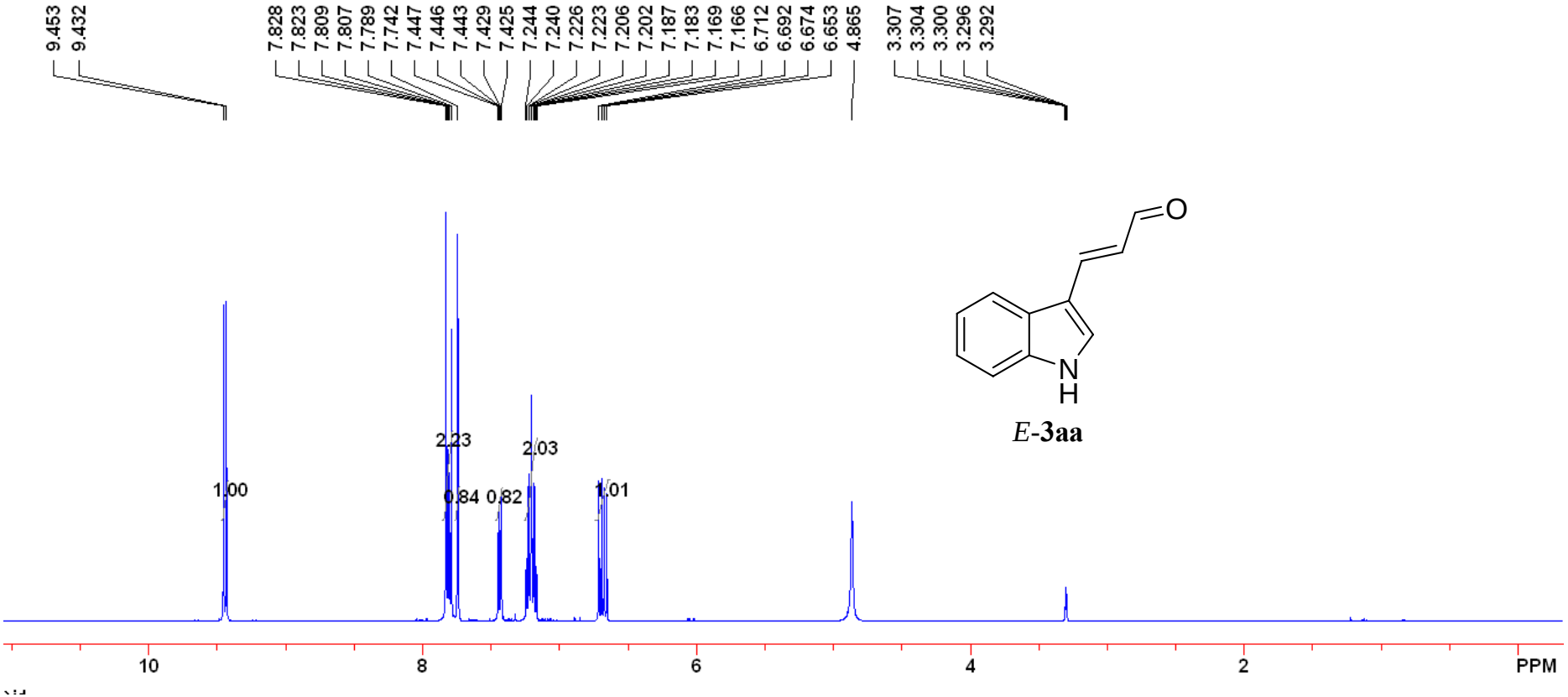
Morpholine•TFA (16.1 mg, 0.08 mmol), indole **1a** (46.8 mg, 0.4 mmol), were mixtured in 3.0 mL THF. The acrolein **2a** (67.2 mg, 1.2 mmol) was added to the reaction mixture. After the reaction was stirred for 24 h at 30 ℃, the crude mixture was directly purified by flash chromatography column using hexane/ ethyl acetate = 5/1 as the eluent to afford 55.6 mg (80% yield) of **4aa**. The generated **4aa** (55.6 mg)

was dissolved in 3.0 mL THF, then DDQ (73.0 mg) was added to the mixture. After the reaction was stirred for 2 h at 30 ℃, the mixture was directly purified by flash chromatography column using hexane/acetone/Et_3N = 300/100/3 as the eluent to afford 20.0 mg (36% yield) of **3aa**.

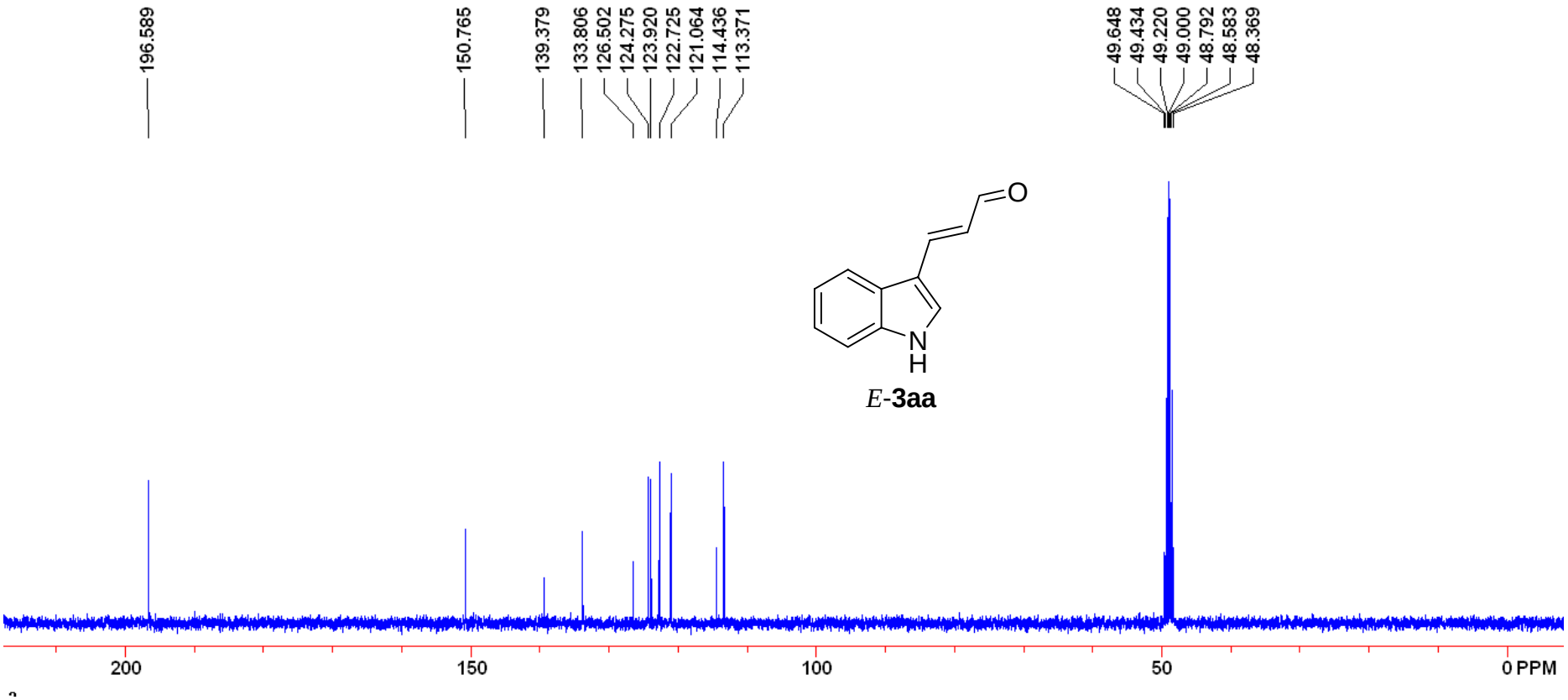
3-(1H-indol-3-yl)propanal (**4aa**)



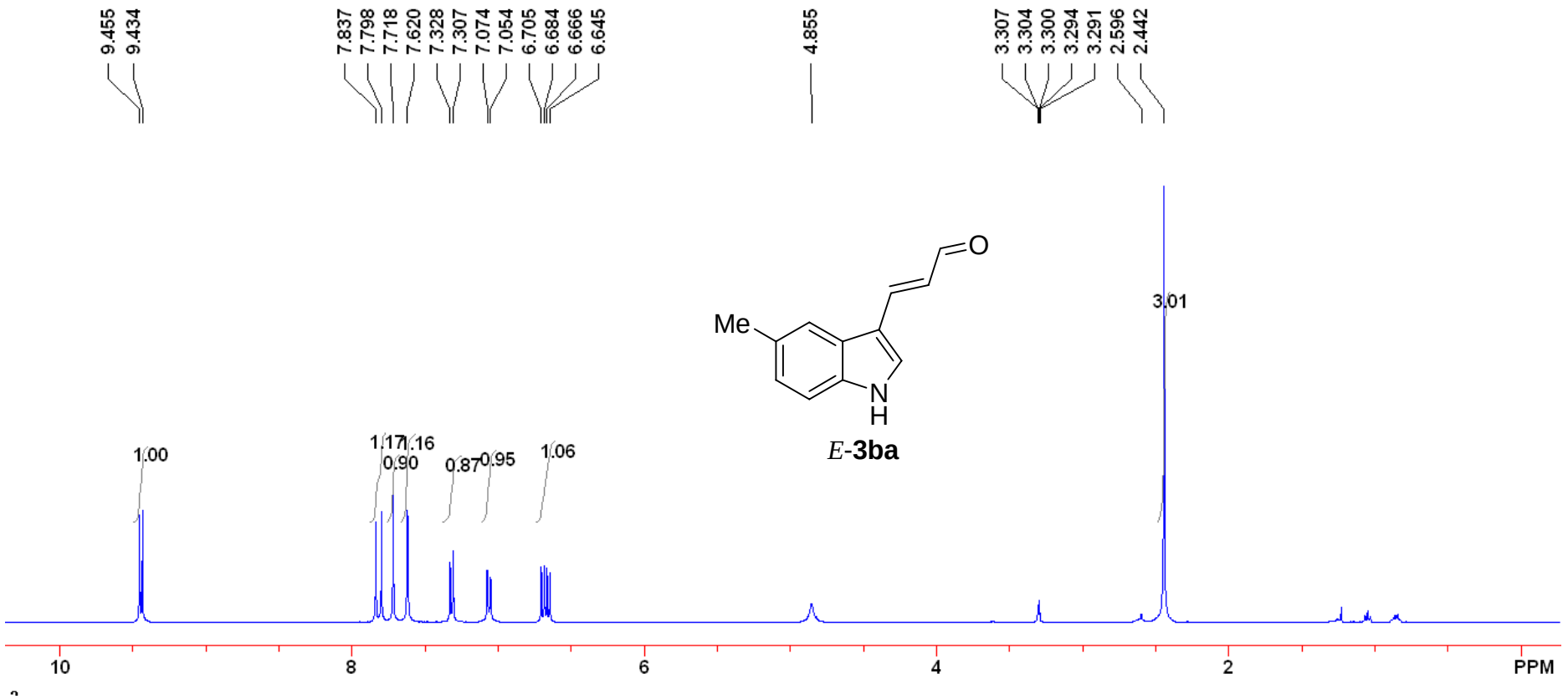
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 9.79 (t, *J* = 1.6 Hz, 1H), 7.98 (br, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.21-7.16 (m, 1H), 7.14-7.09 (m,1H), 6.91-6.89 (m,1H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.80 (td, *J* = 7.2, 1.2 Hz, 2H); ^{13}CNMR (100 MHz, $CDCl_3$): 202.7, 136.3, 127.0, 122.1, 121.5, 119.3, 118.5, 114.5, 111.2, 43.9, 17.8; MS (70 eV): m/z (%): 130.1 (100), 173.1(46).

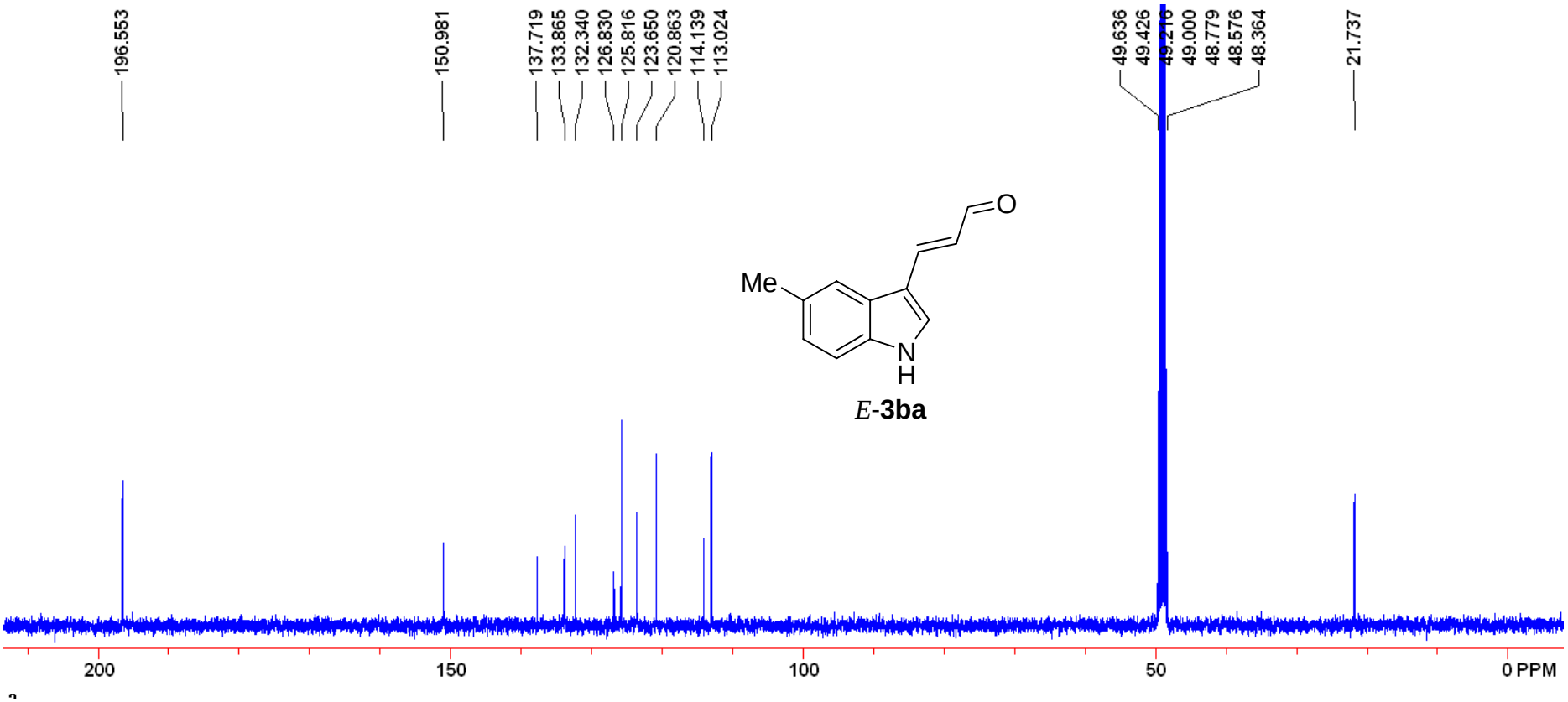


E-**3aa**

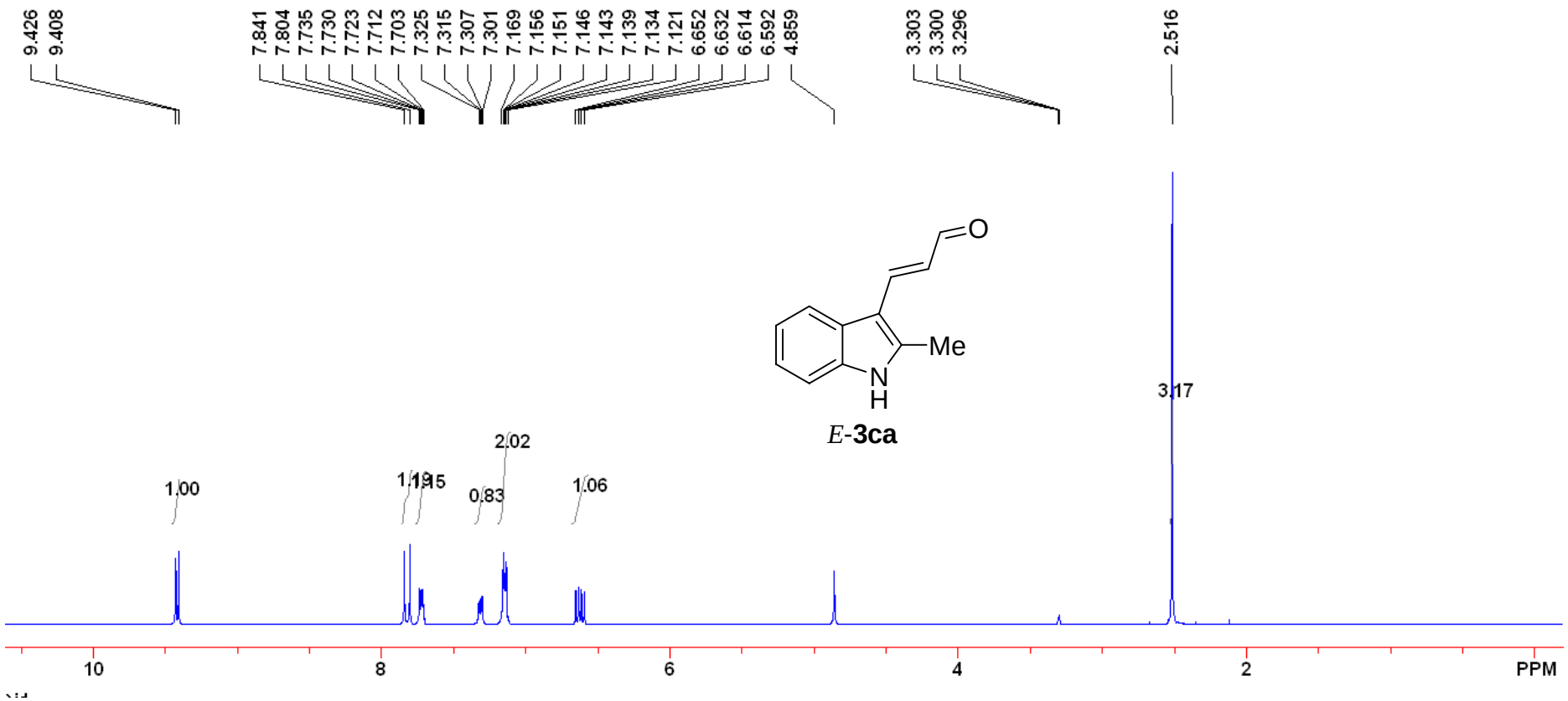


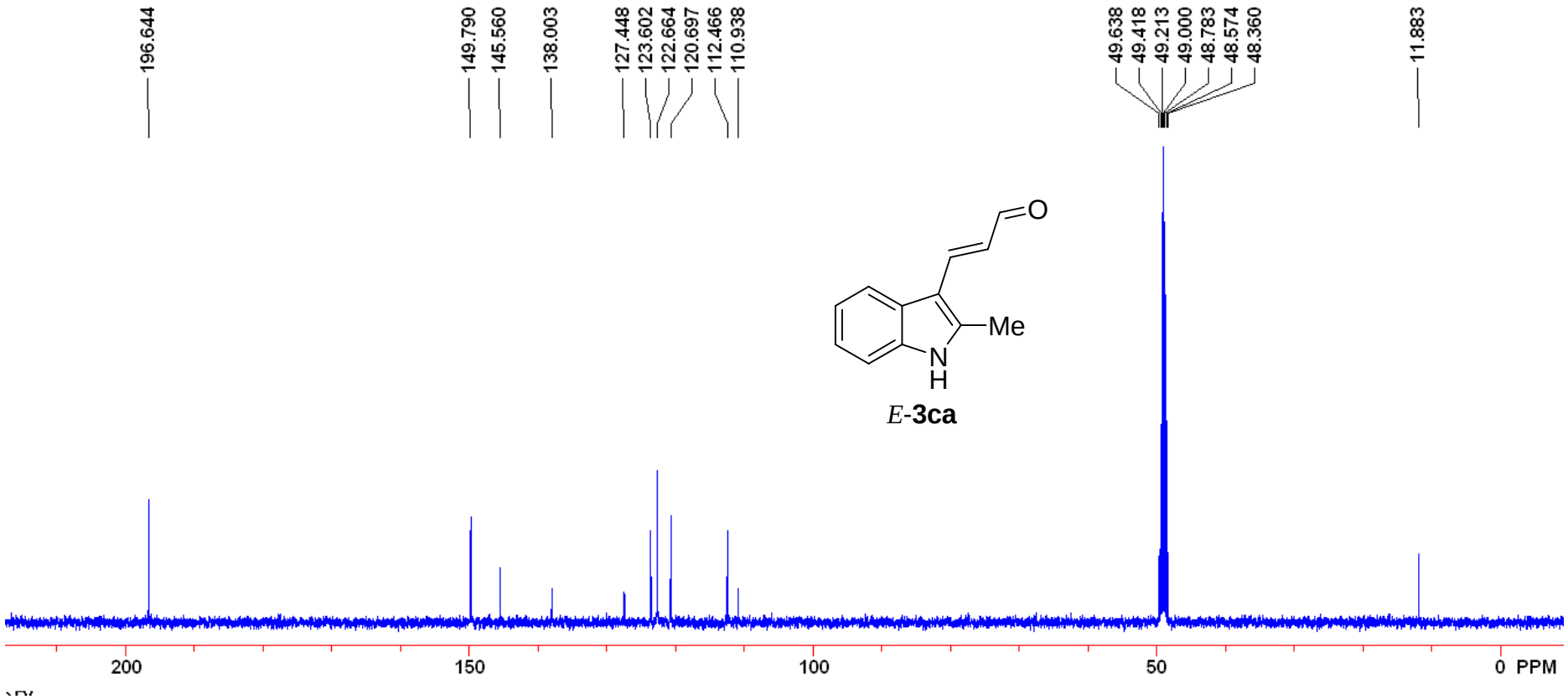
E-**3aa**





E-**3ba**





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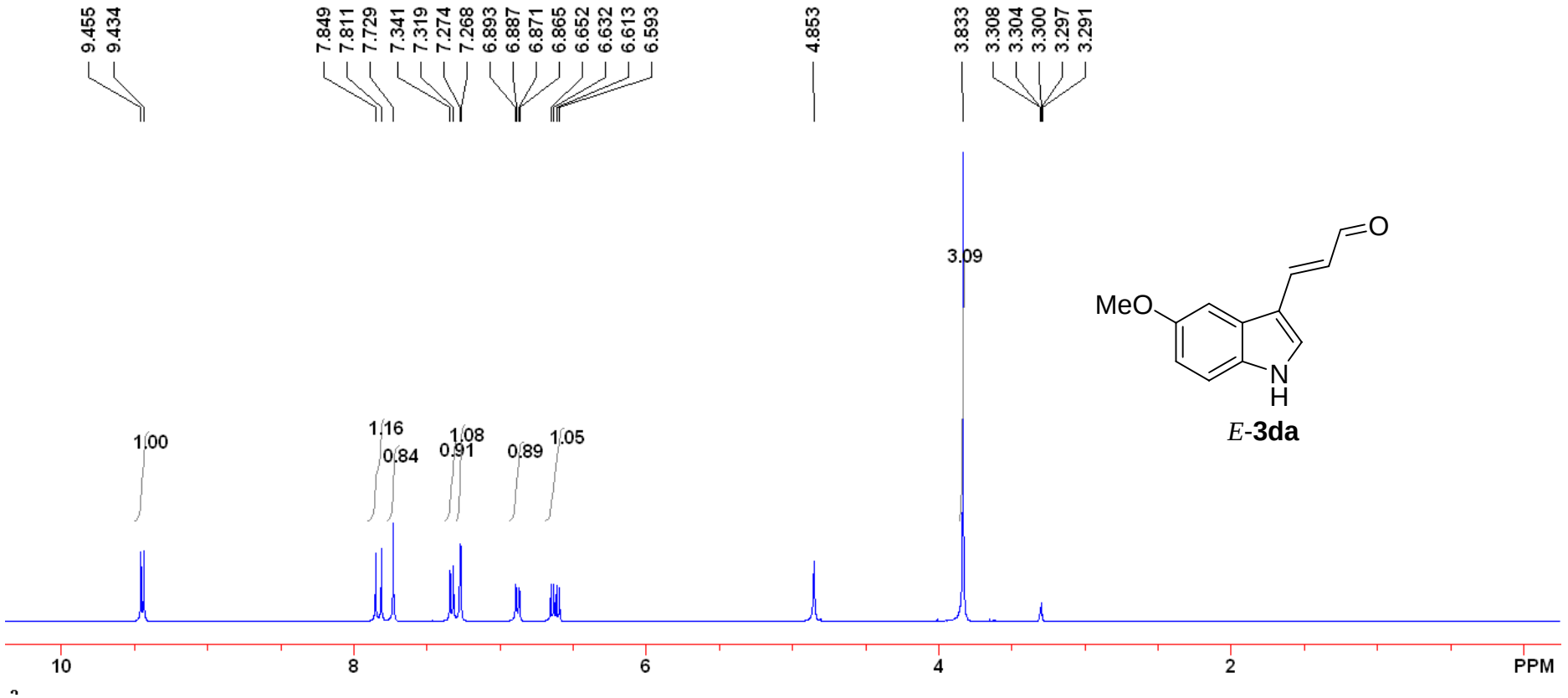
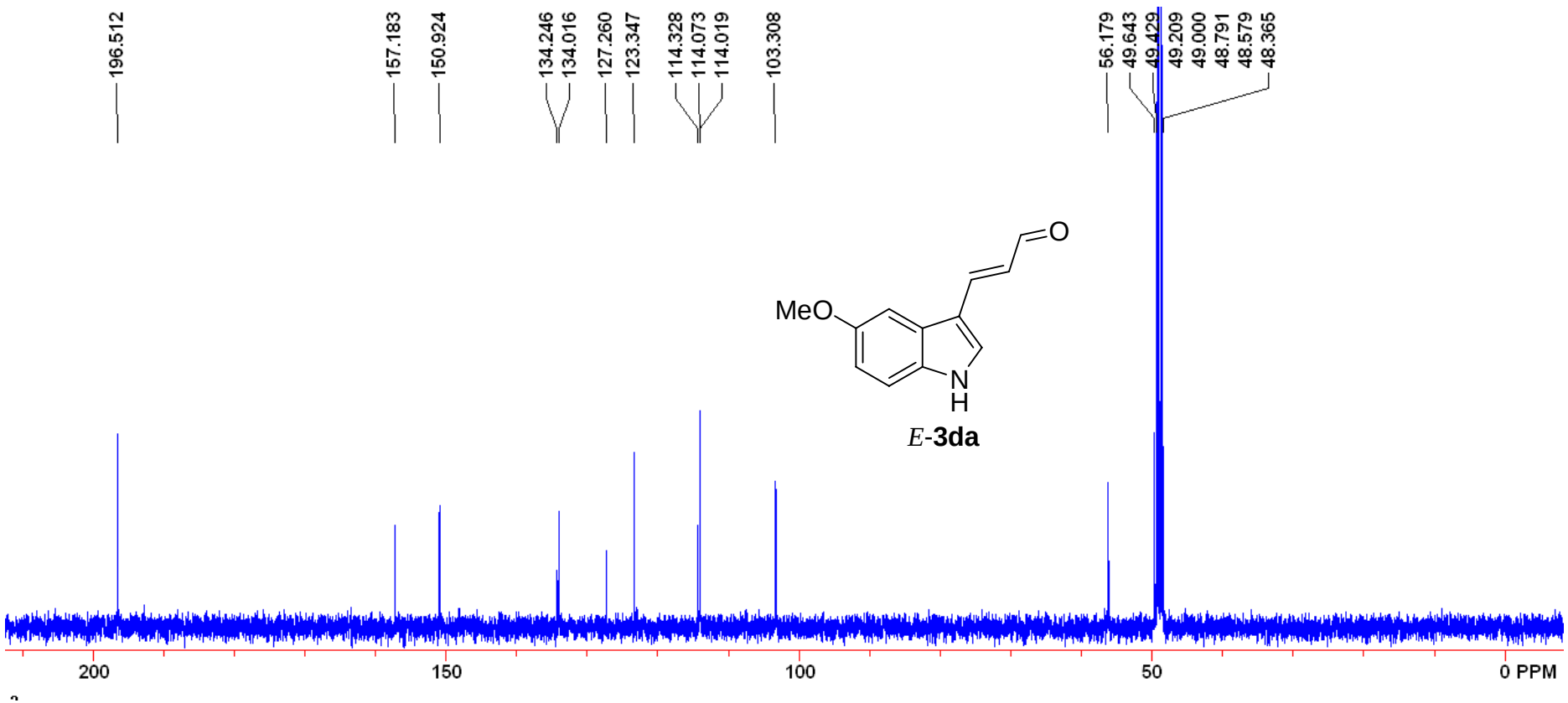


E-**3da**



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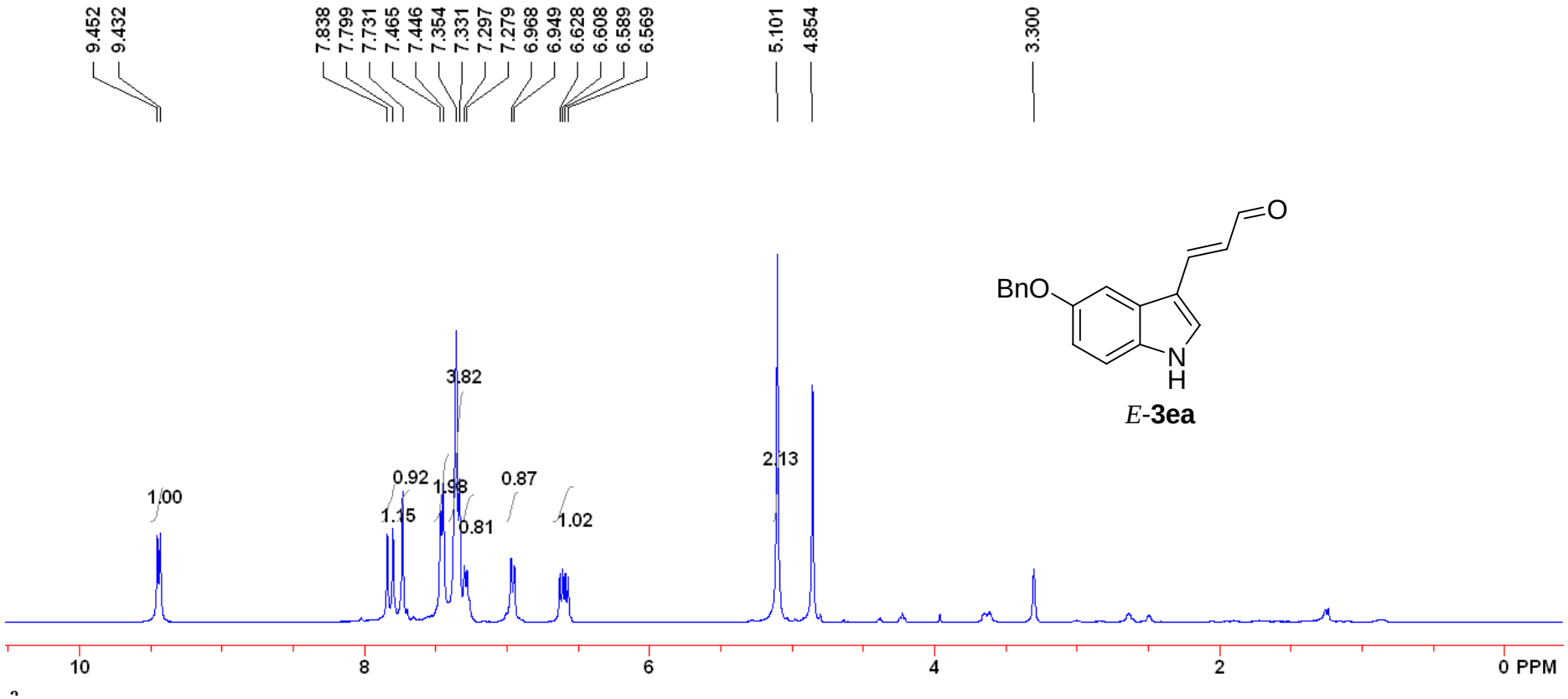

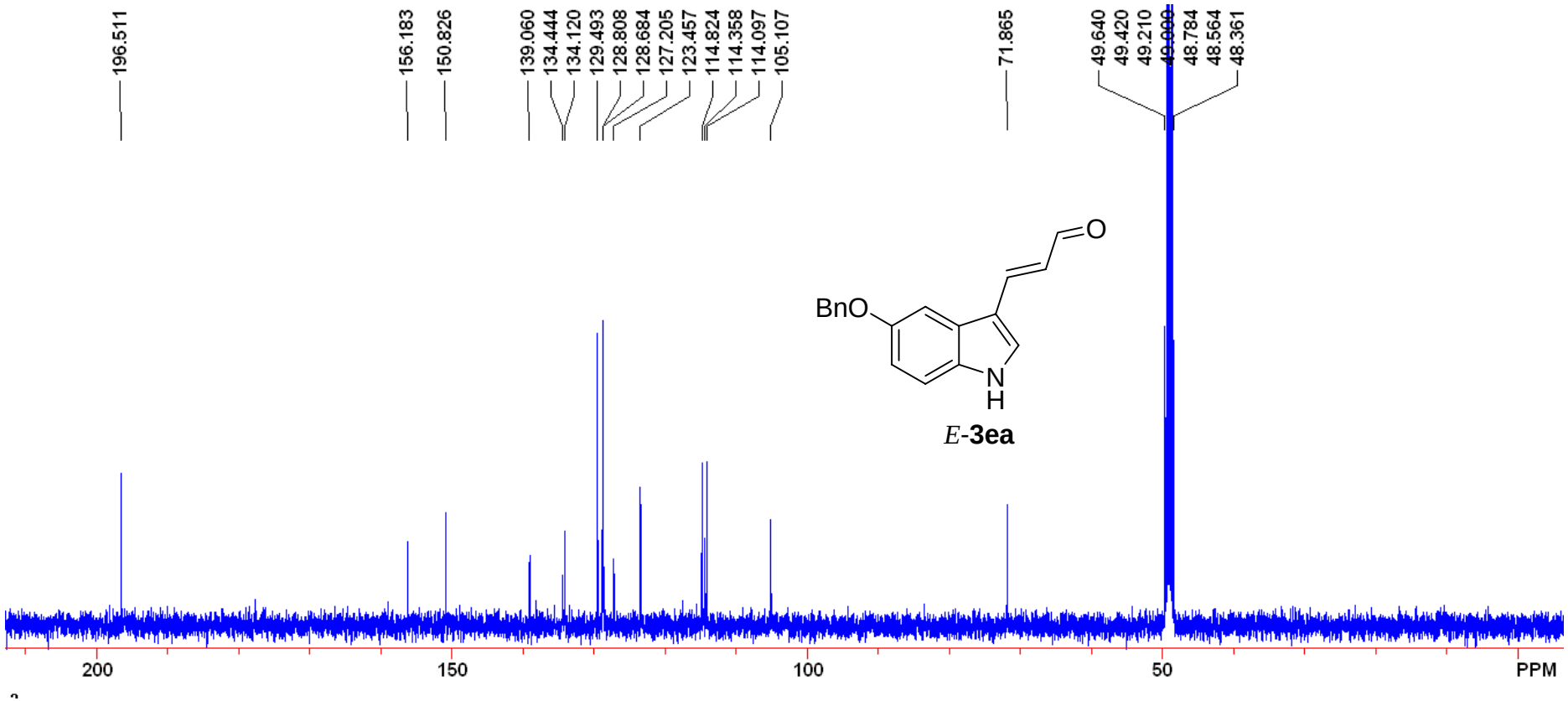

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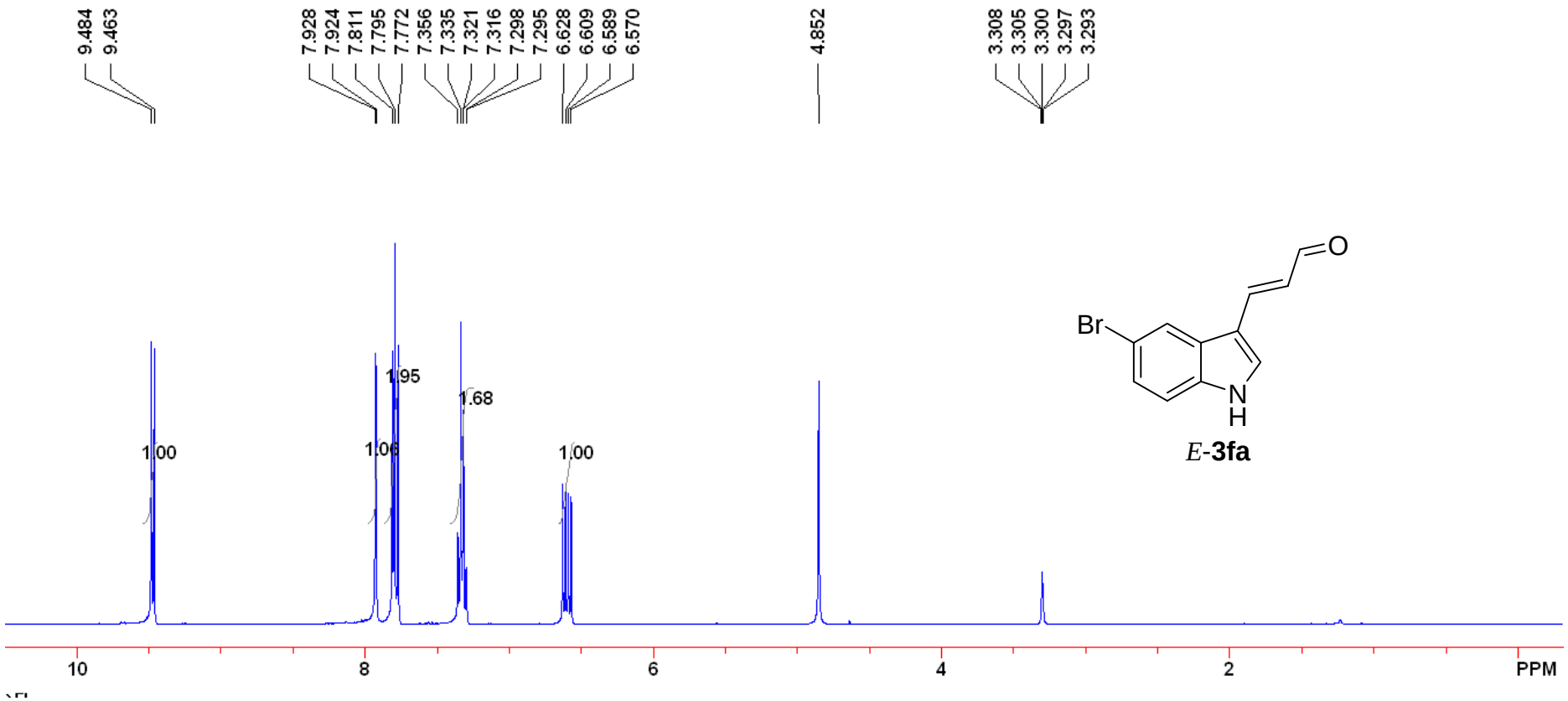

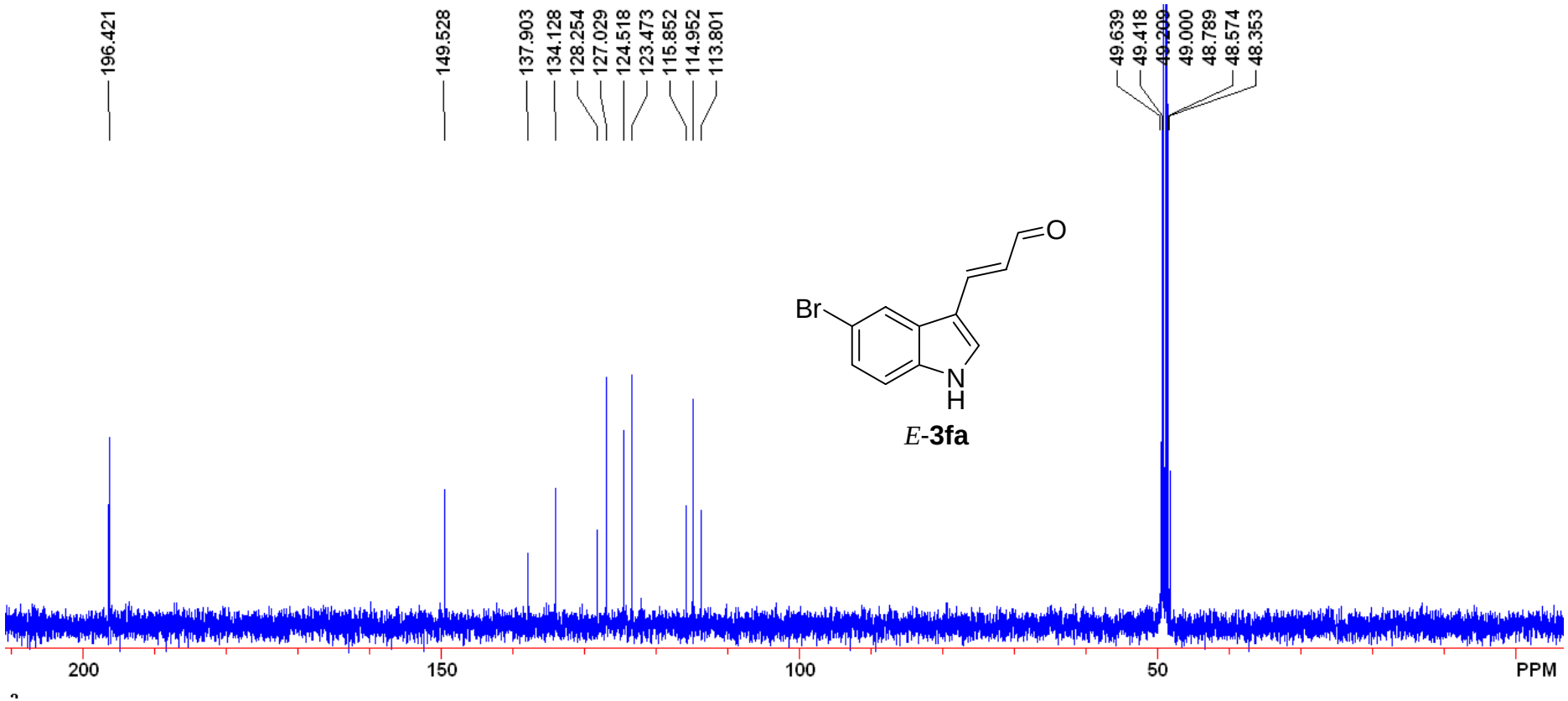

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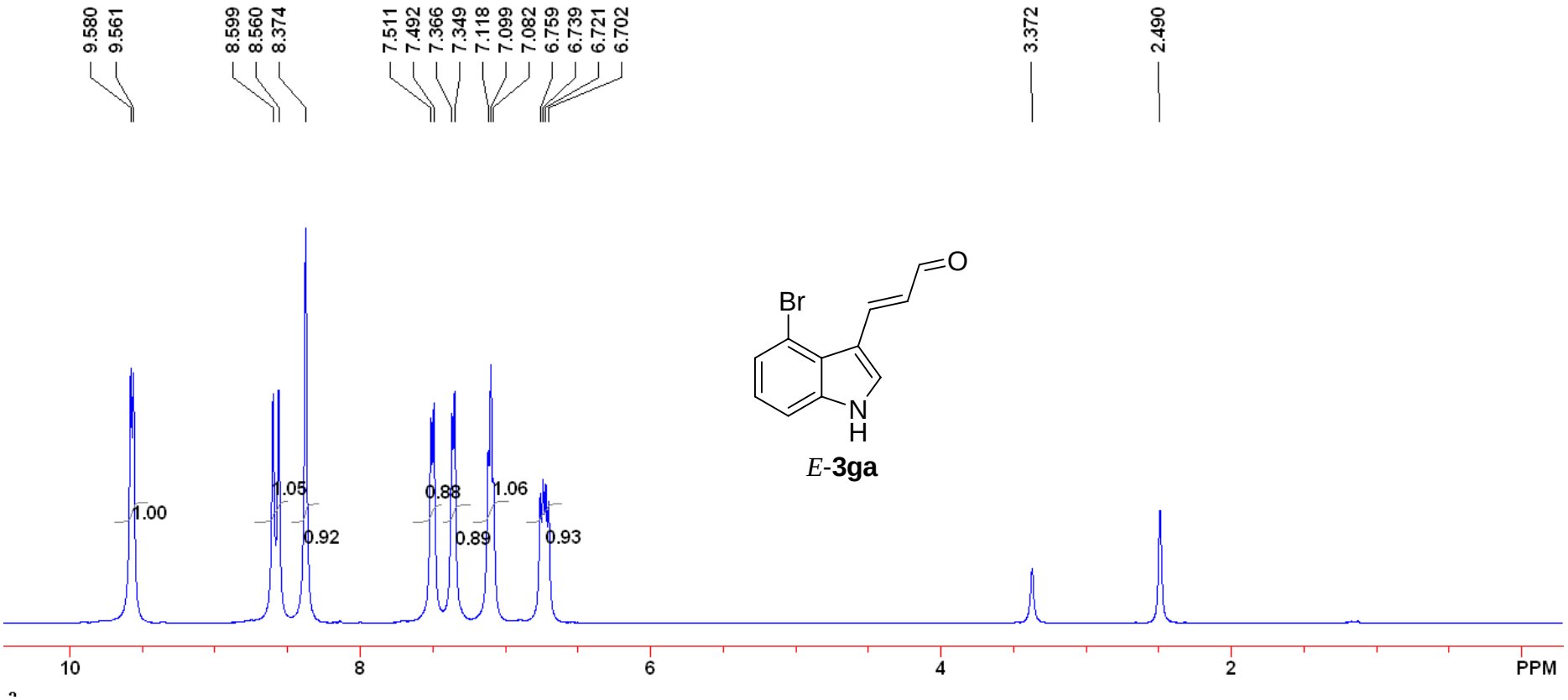

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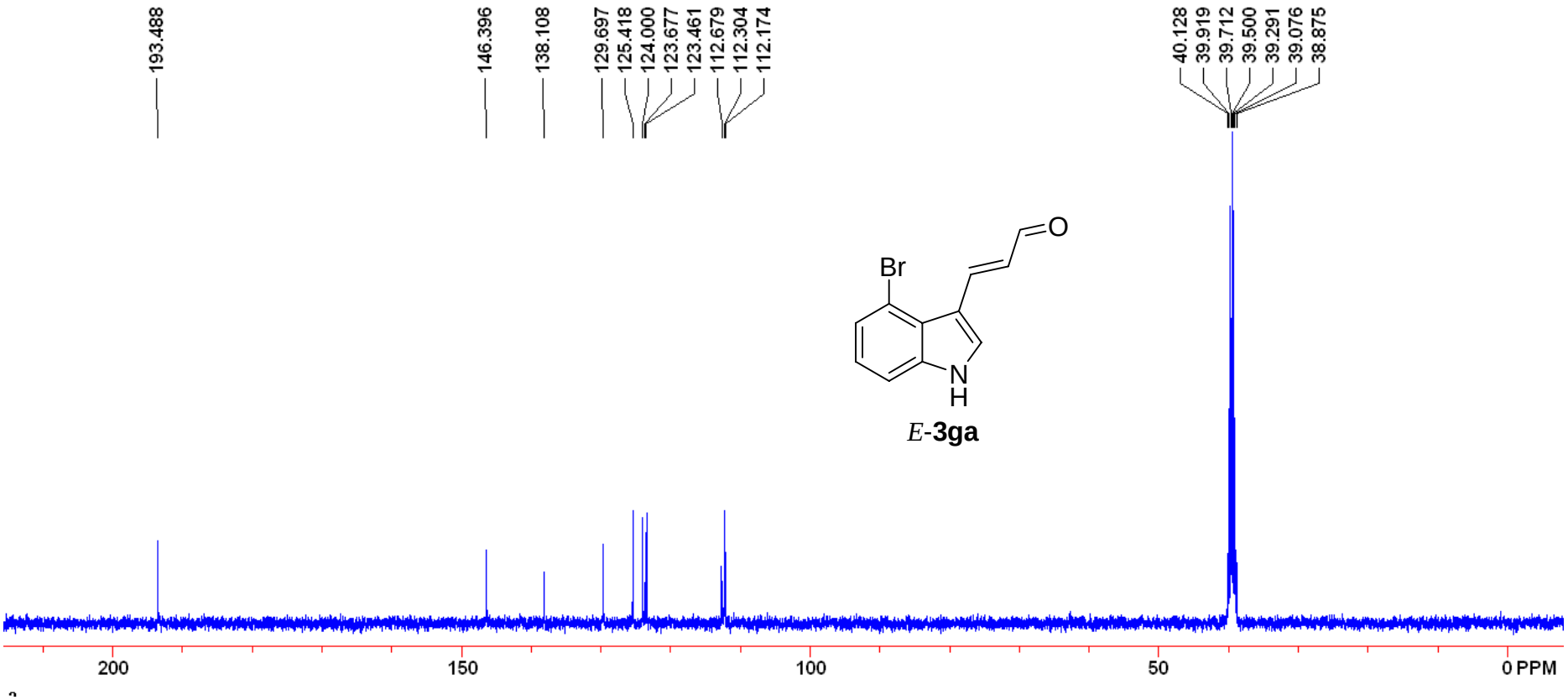

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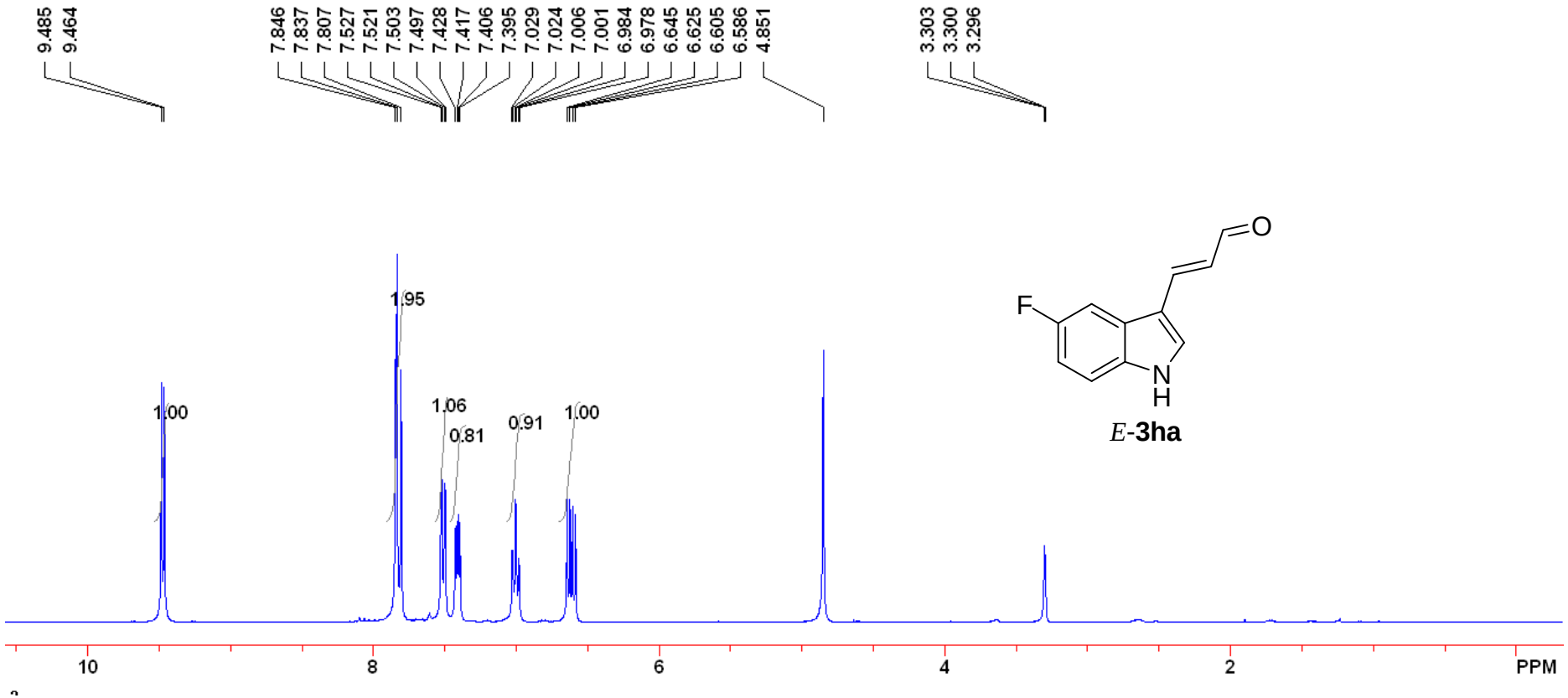

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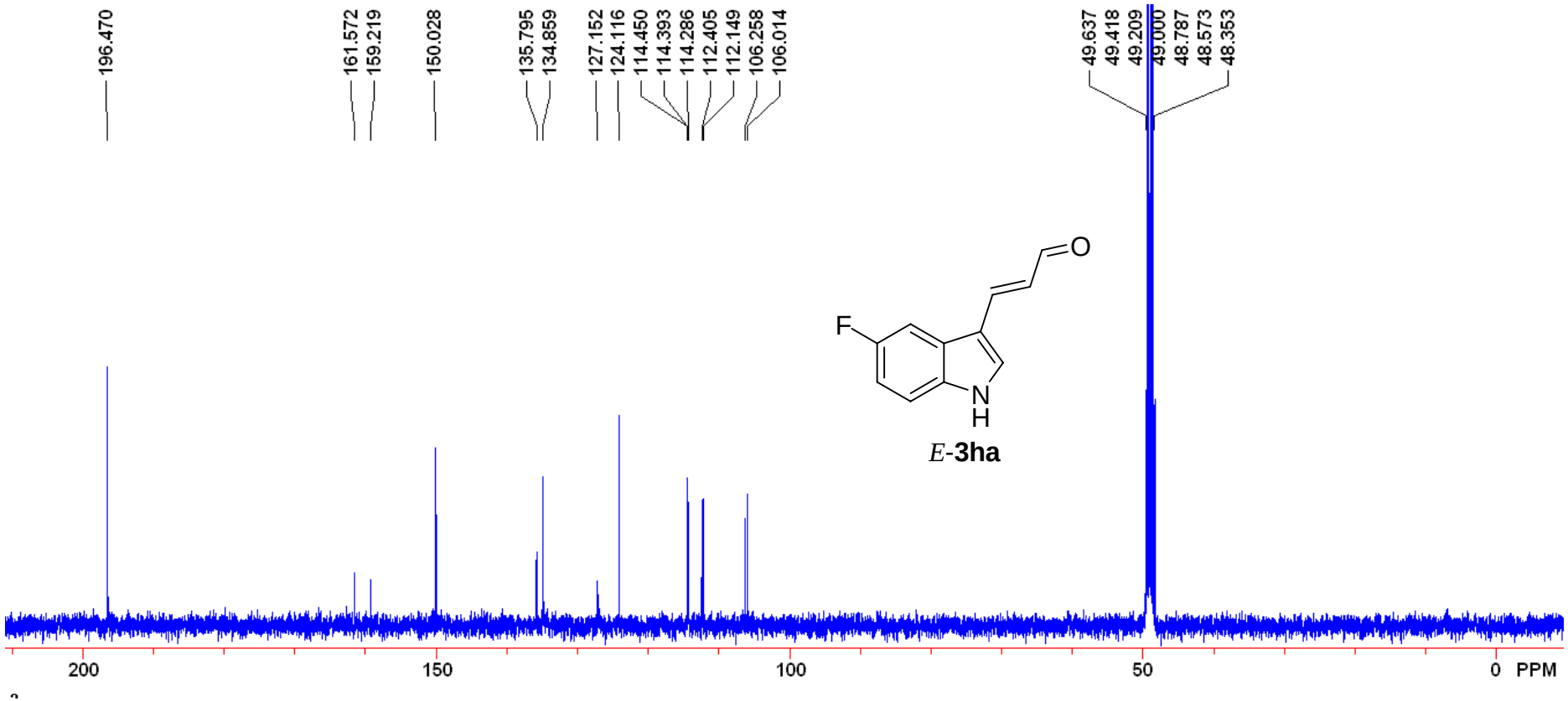

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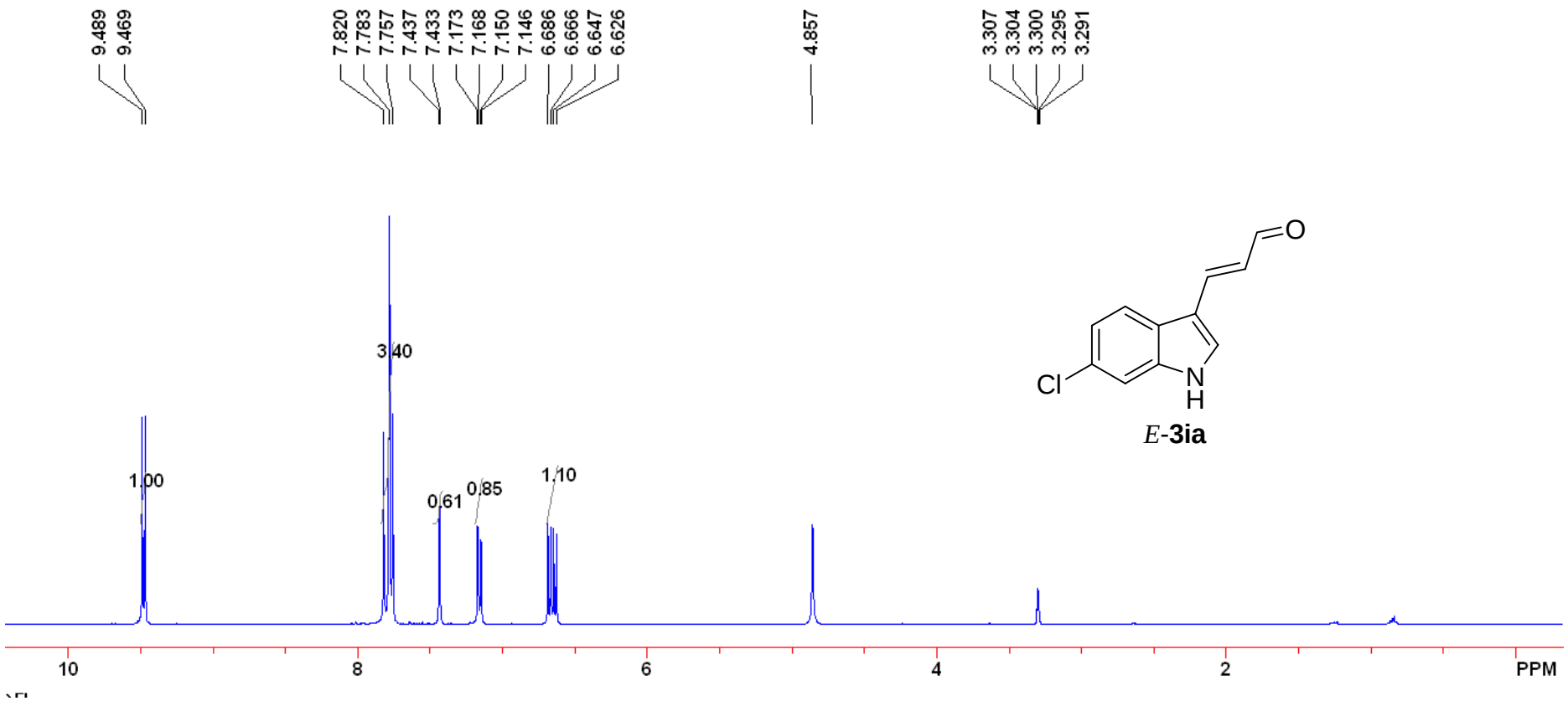
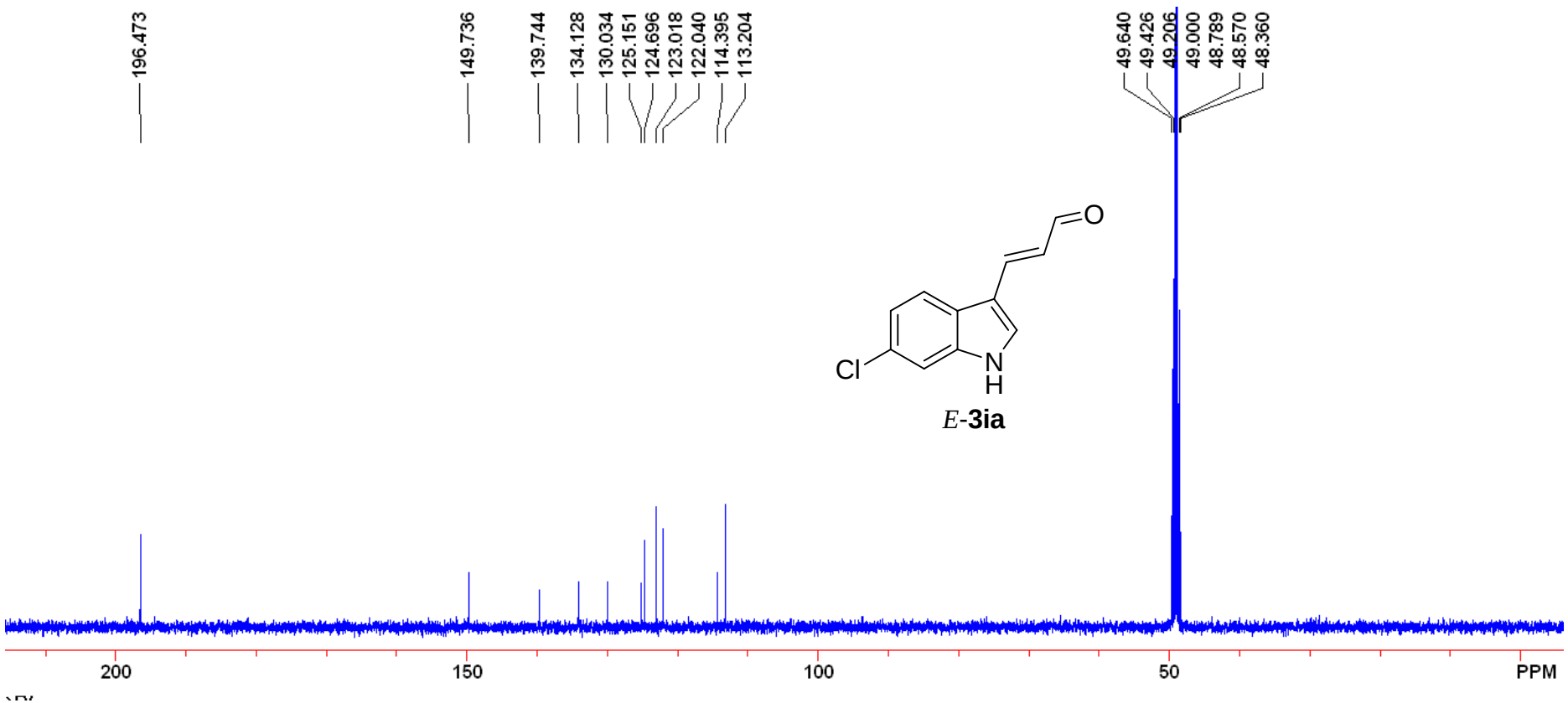


E-**3ia**



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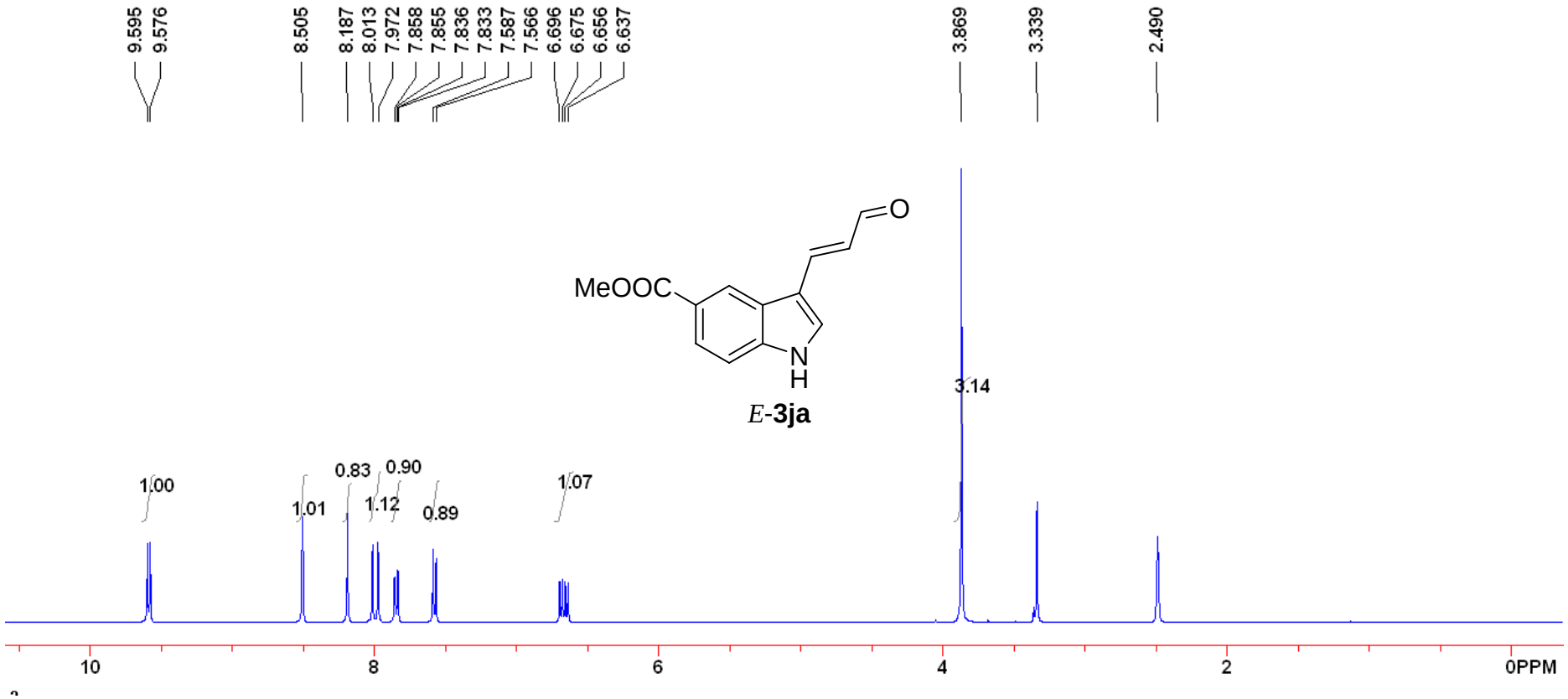

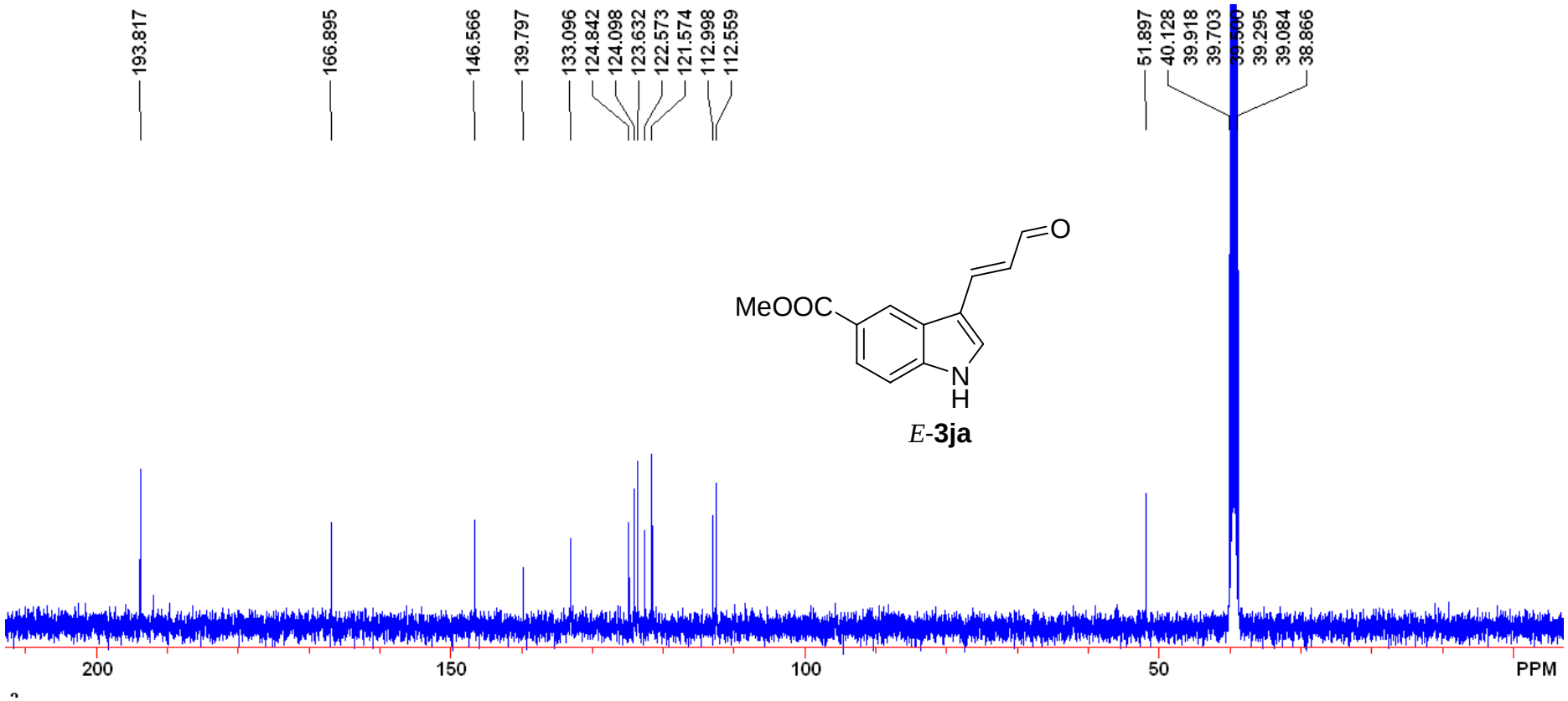

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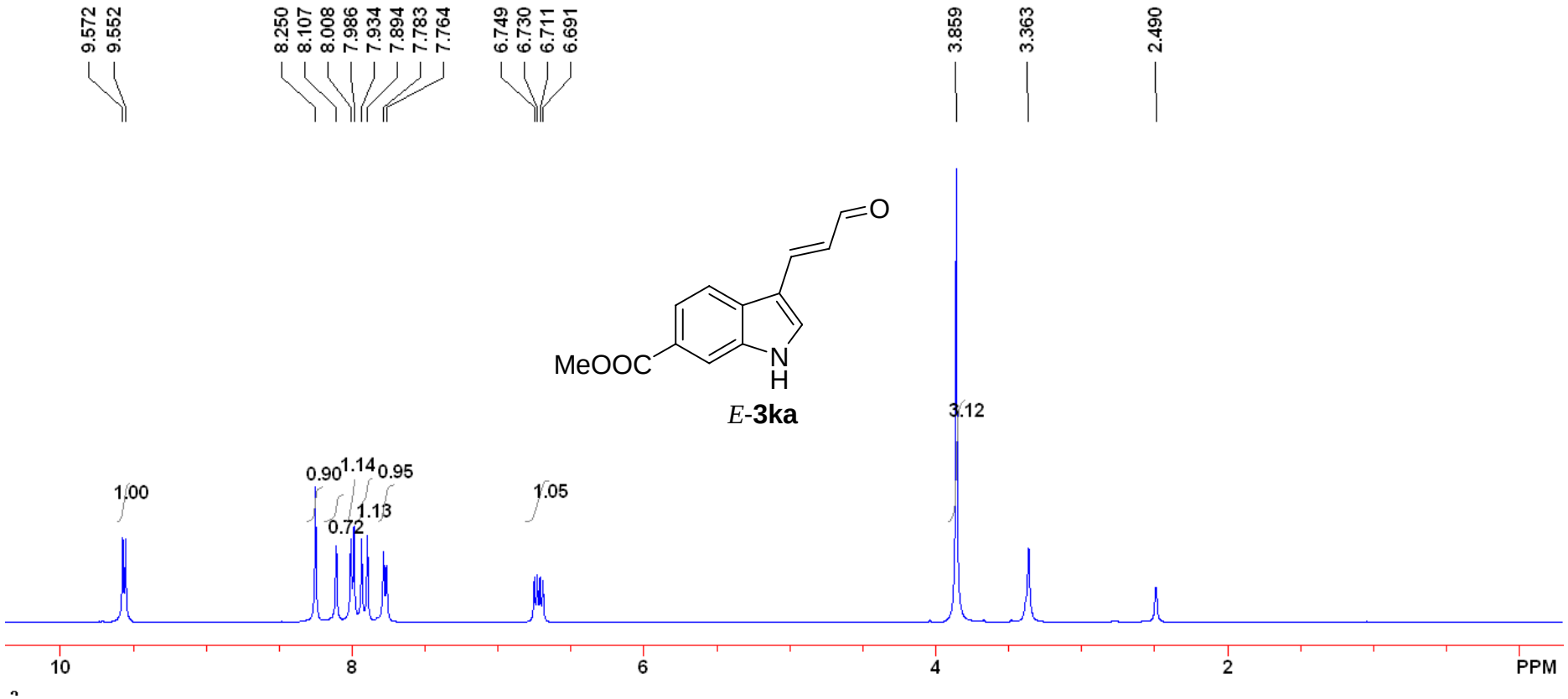

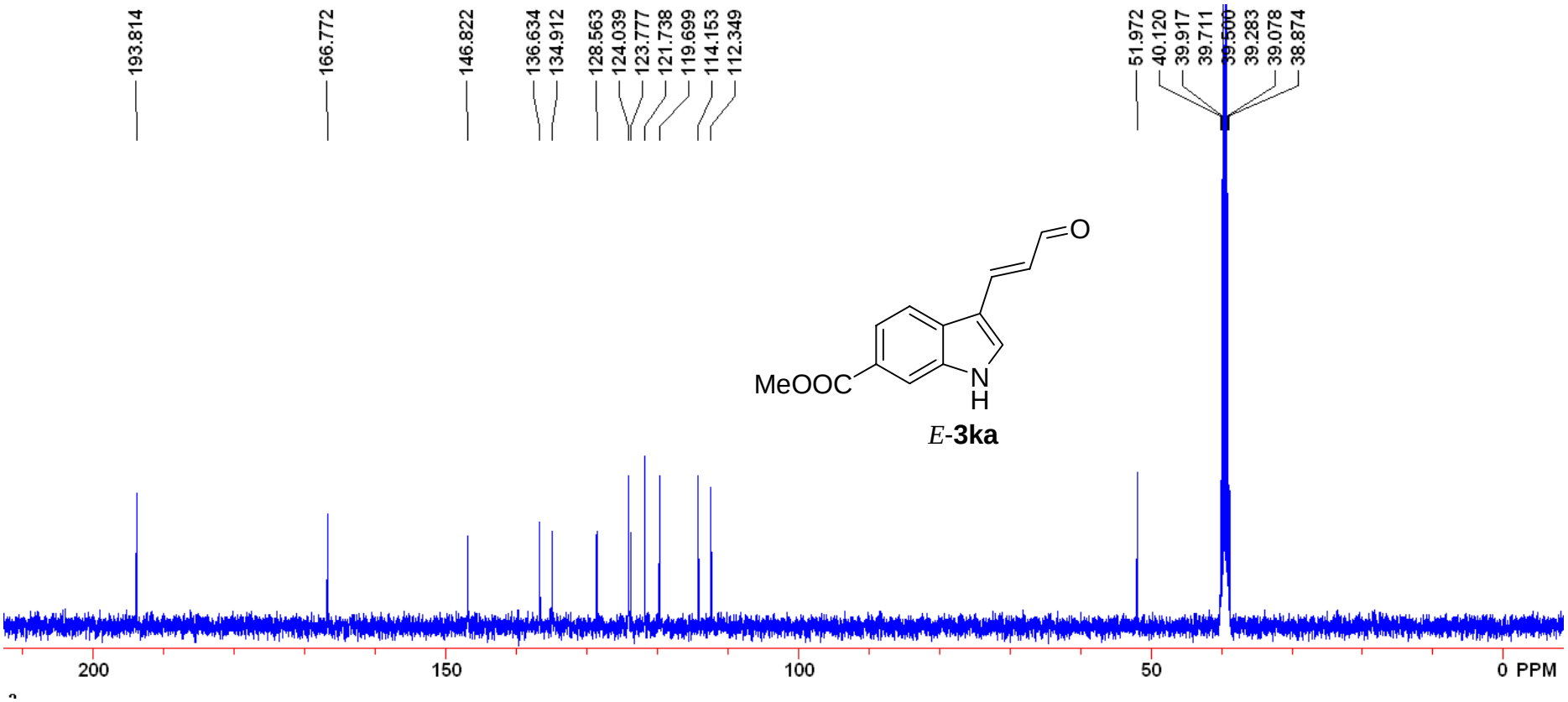

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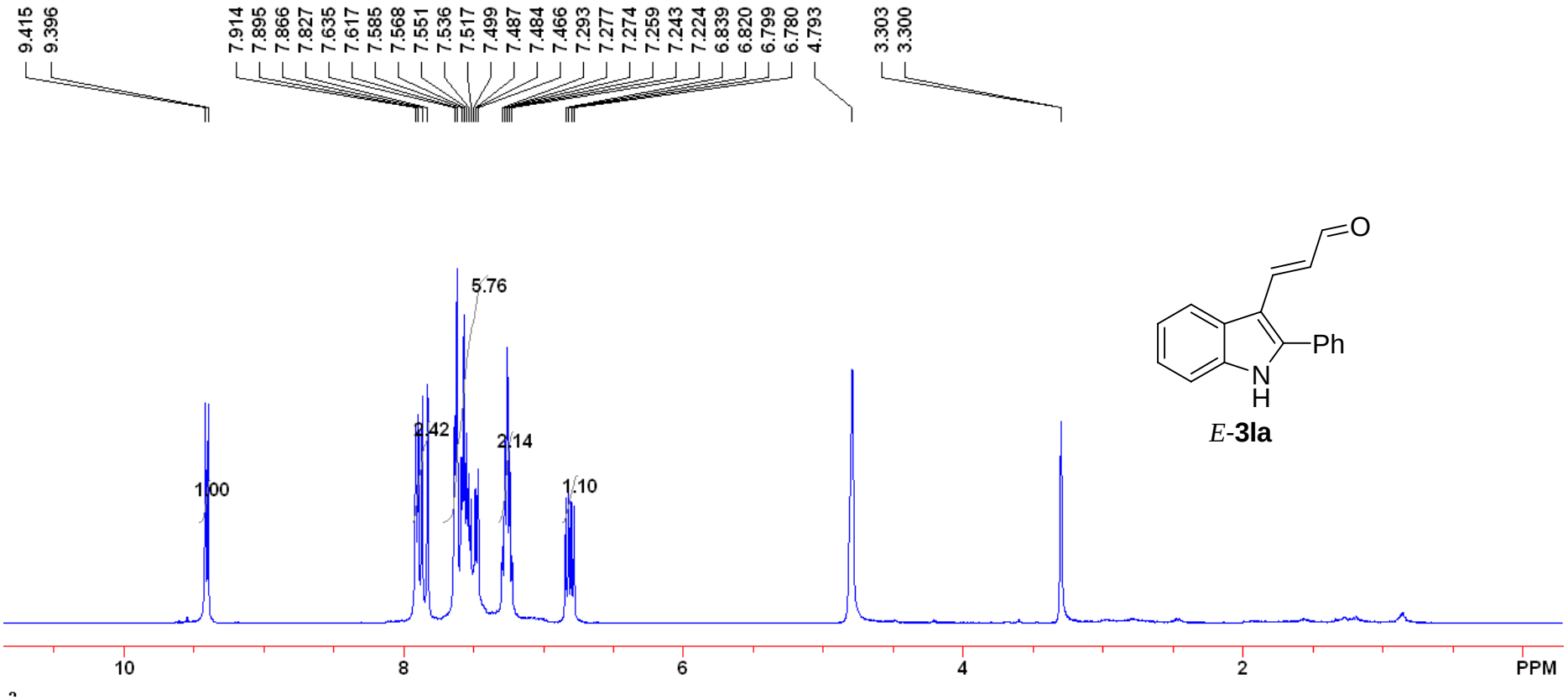

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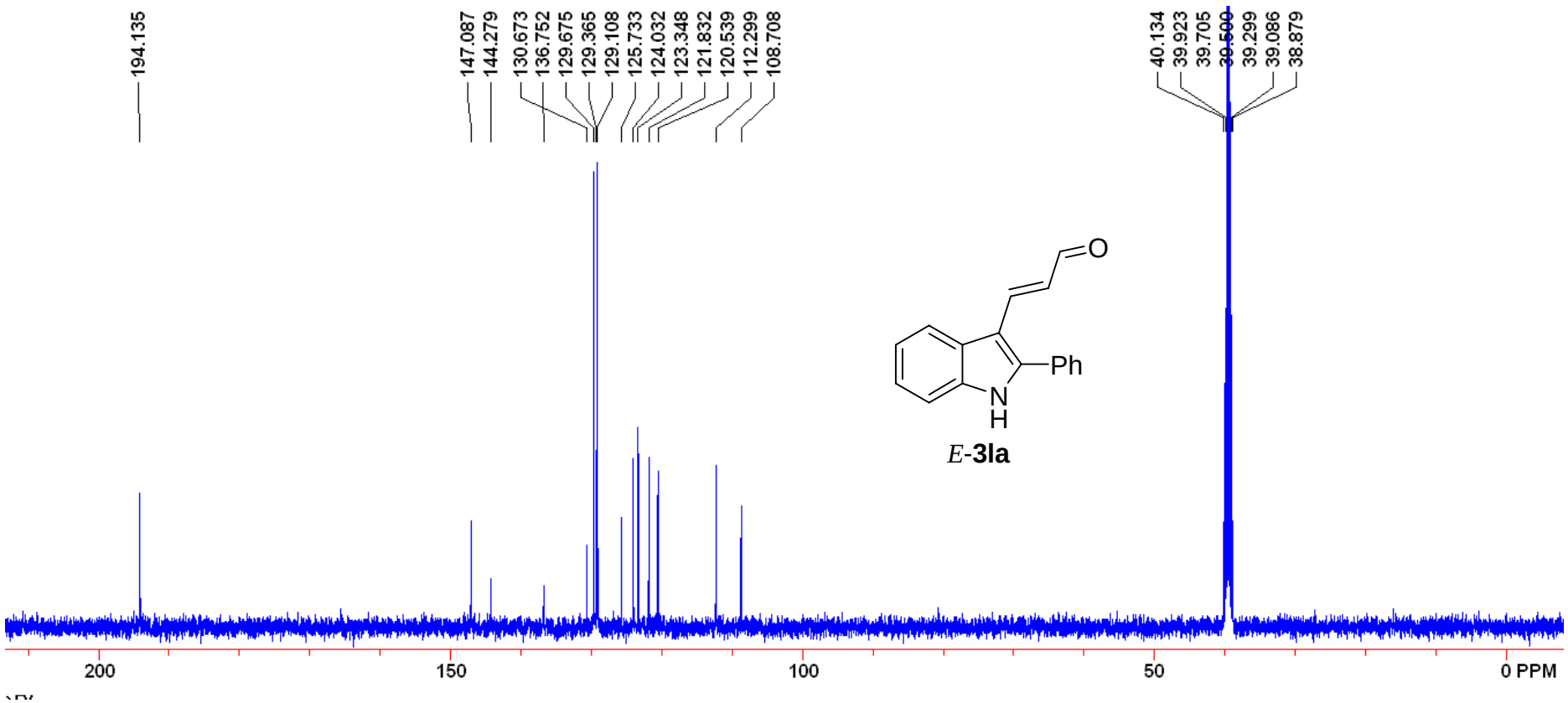

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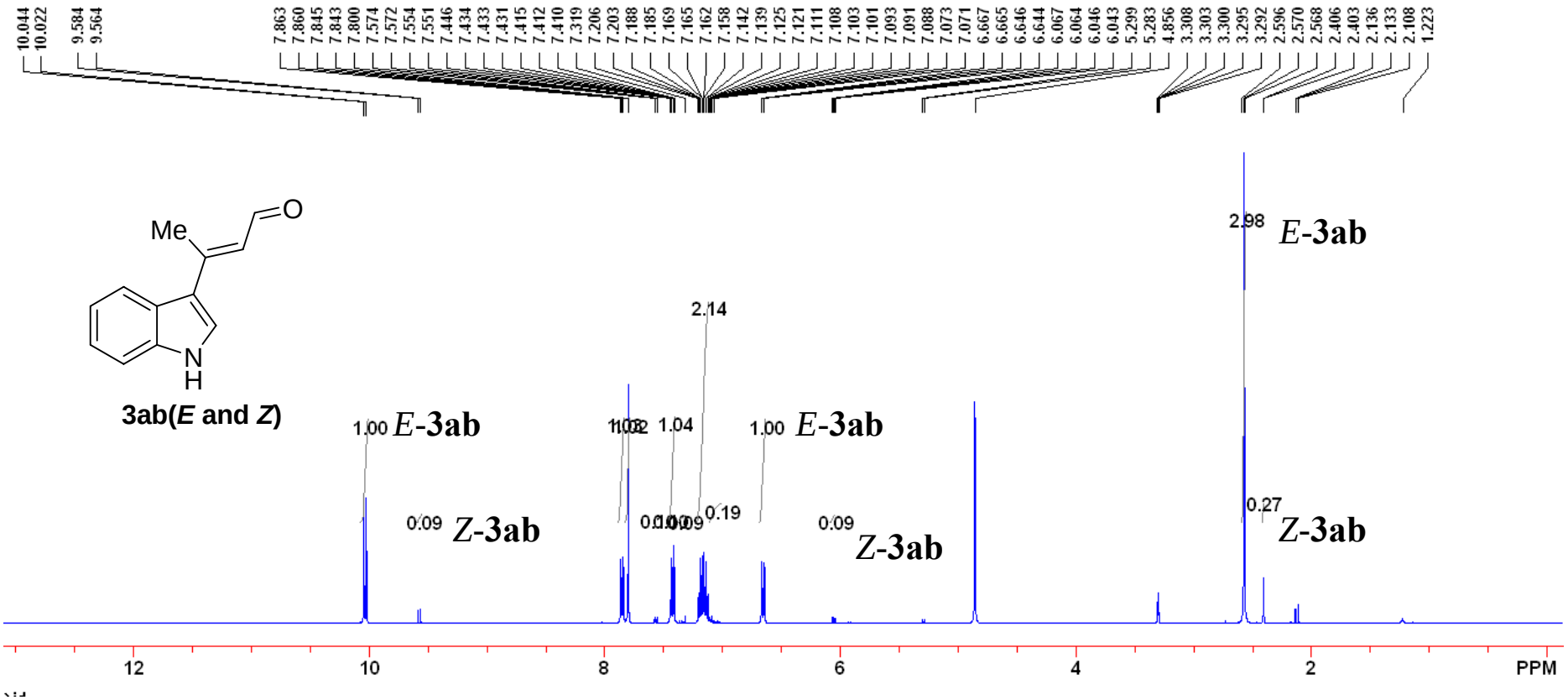

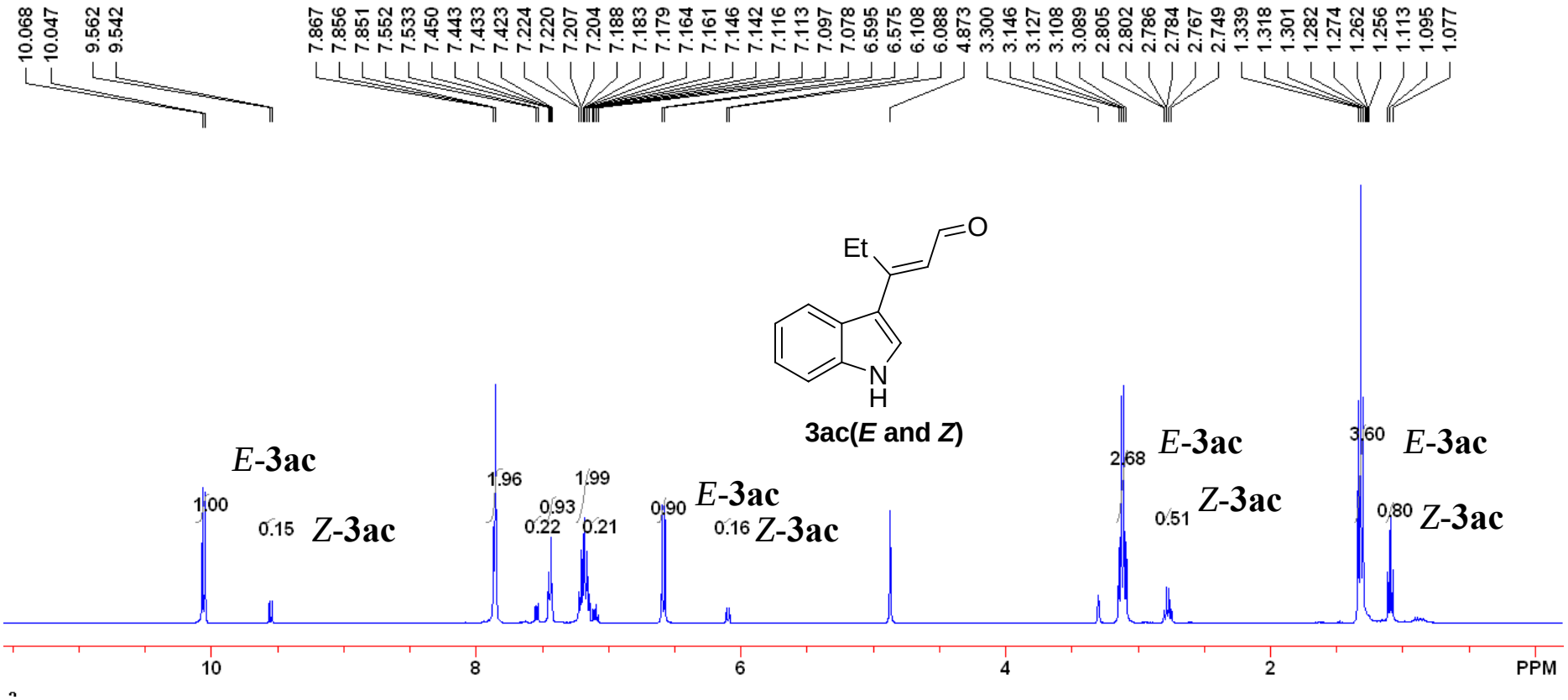

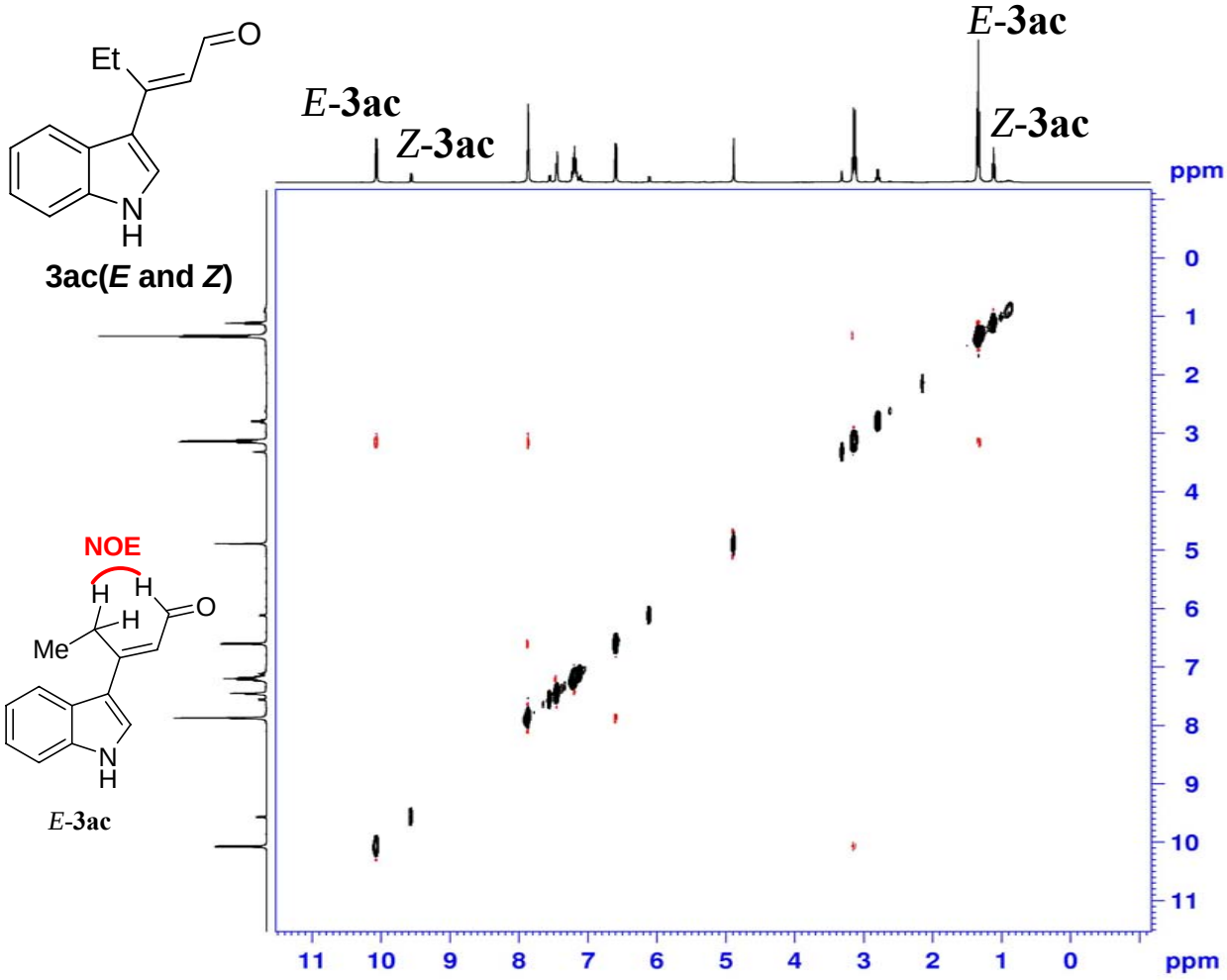

BRUKER

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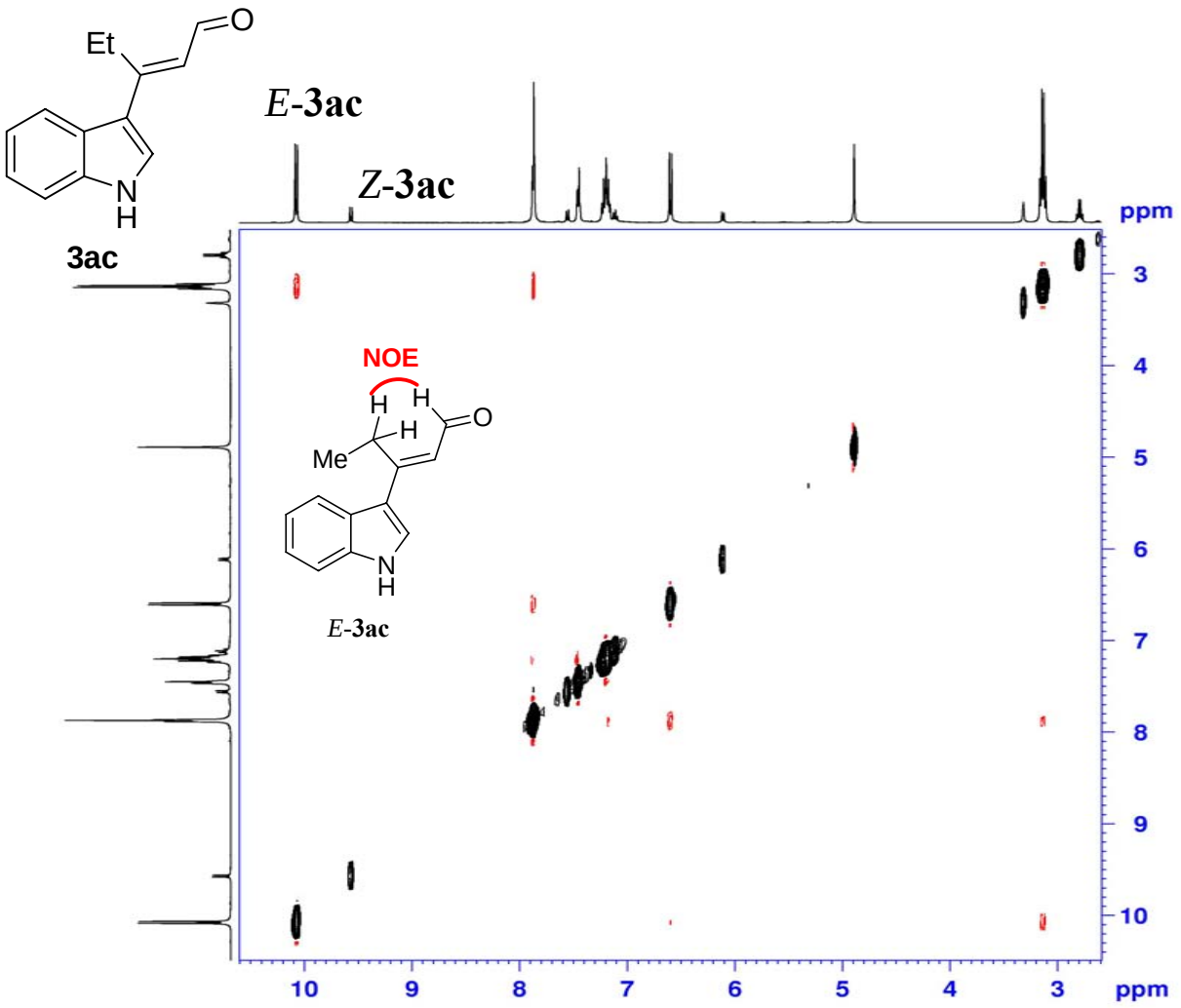
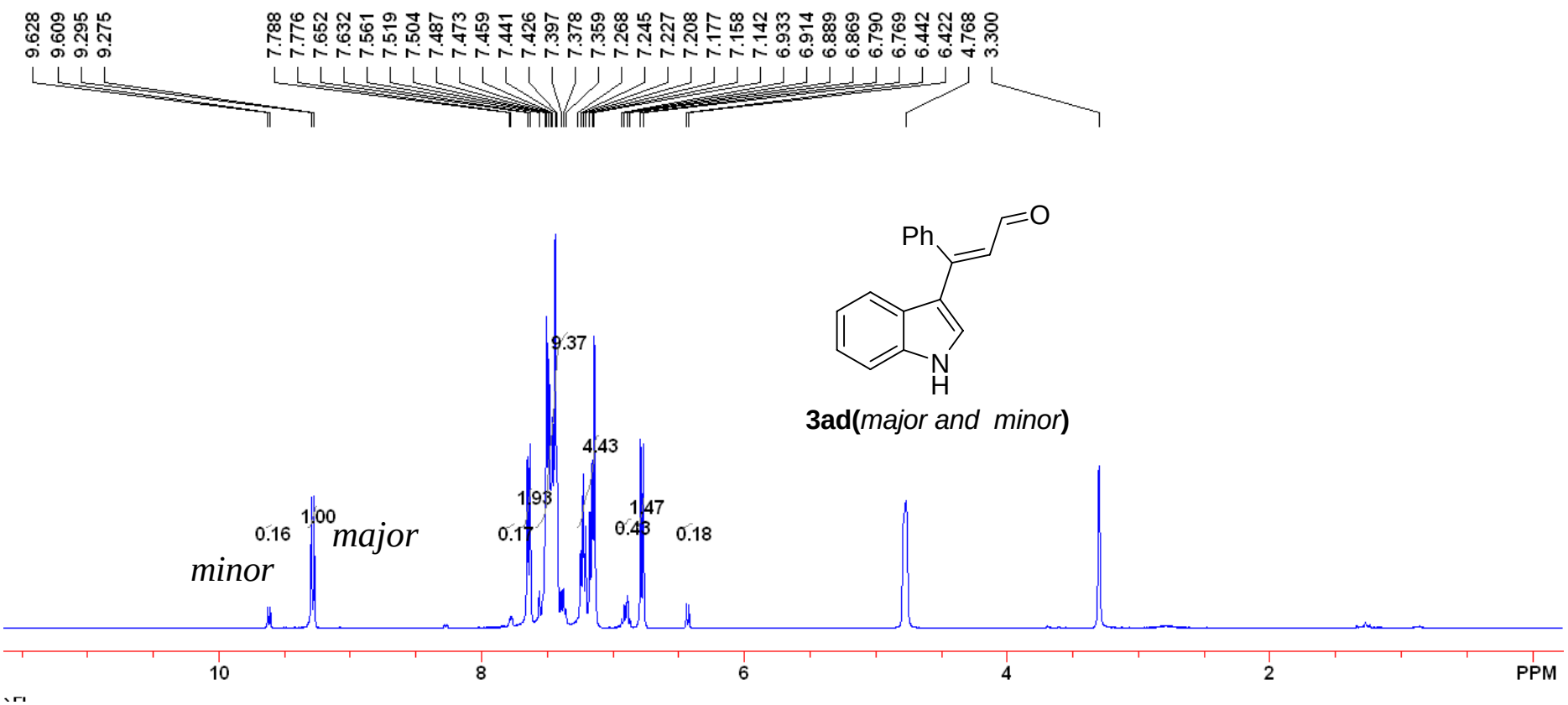
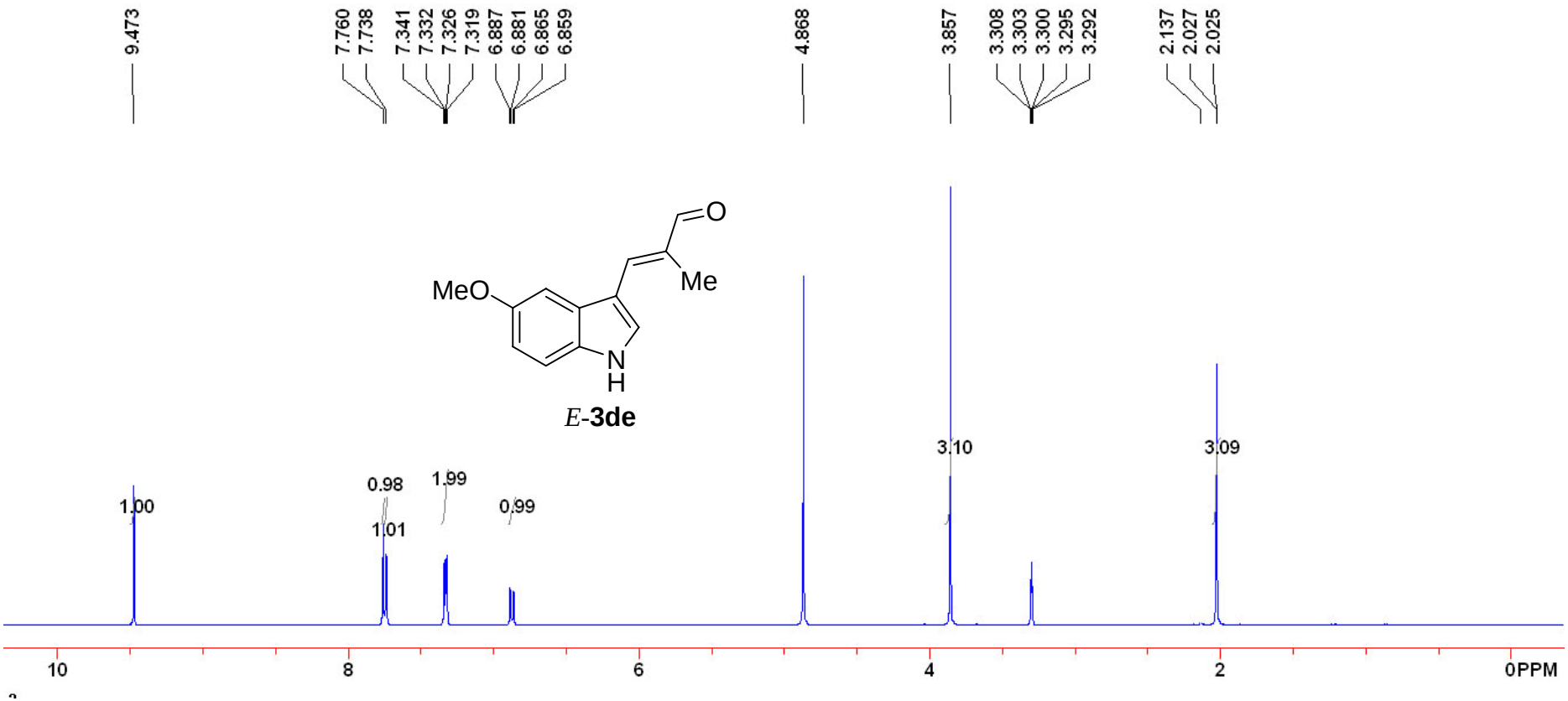
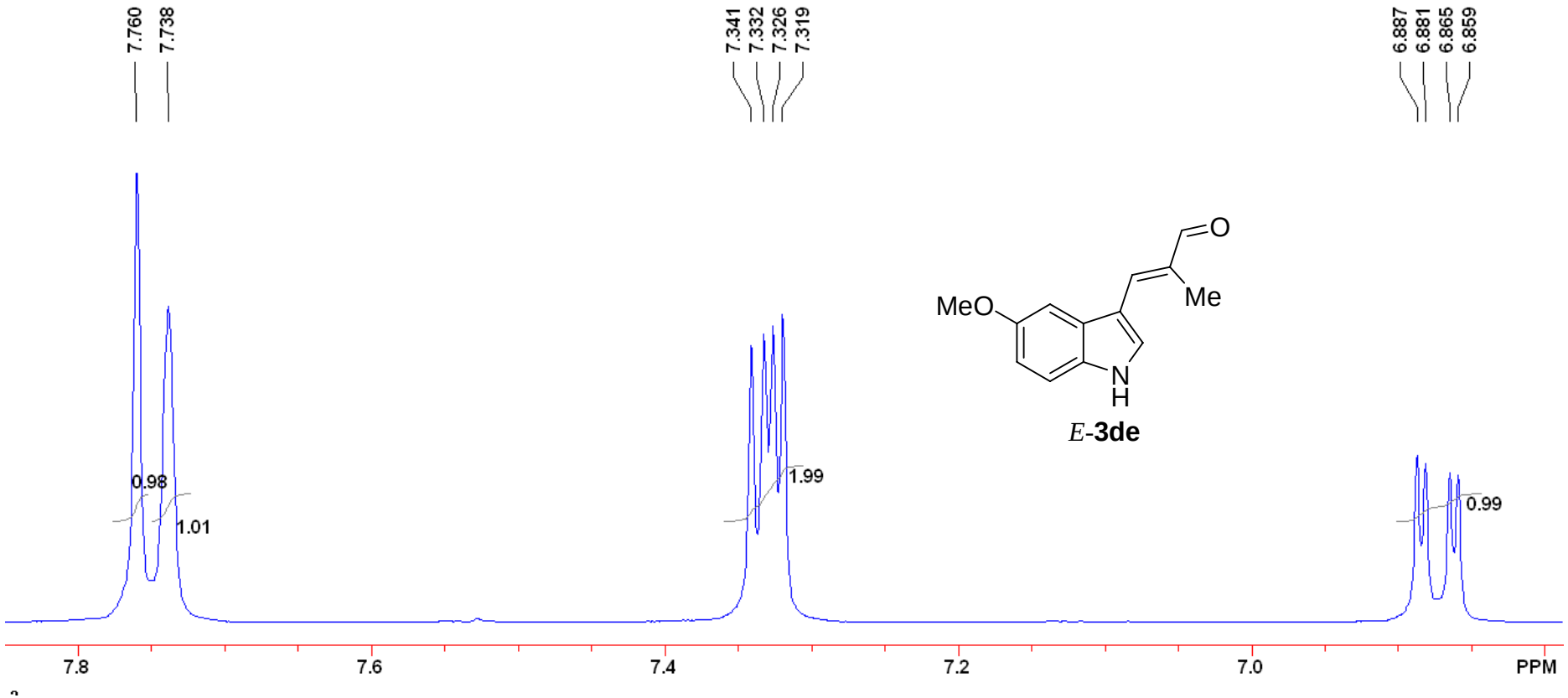
GB	0	
PC	1.00	
SI	1024	
MC2	States-TPPI	
SF	400.1500000	MHz
WDW	QSINE	
SSB	2	
LB	0.00	Hz
GB	0	



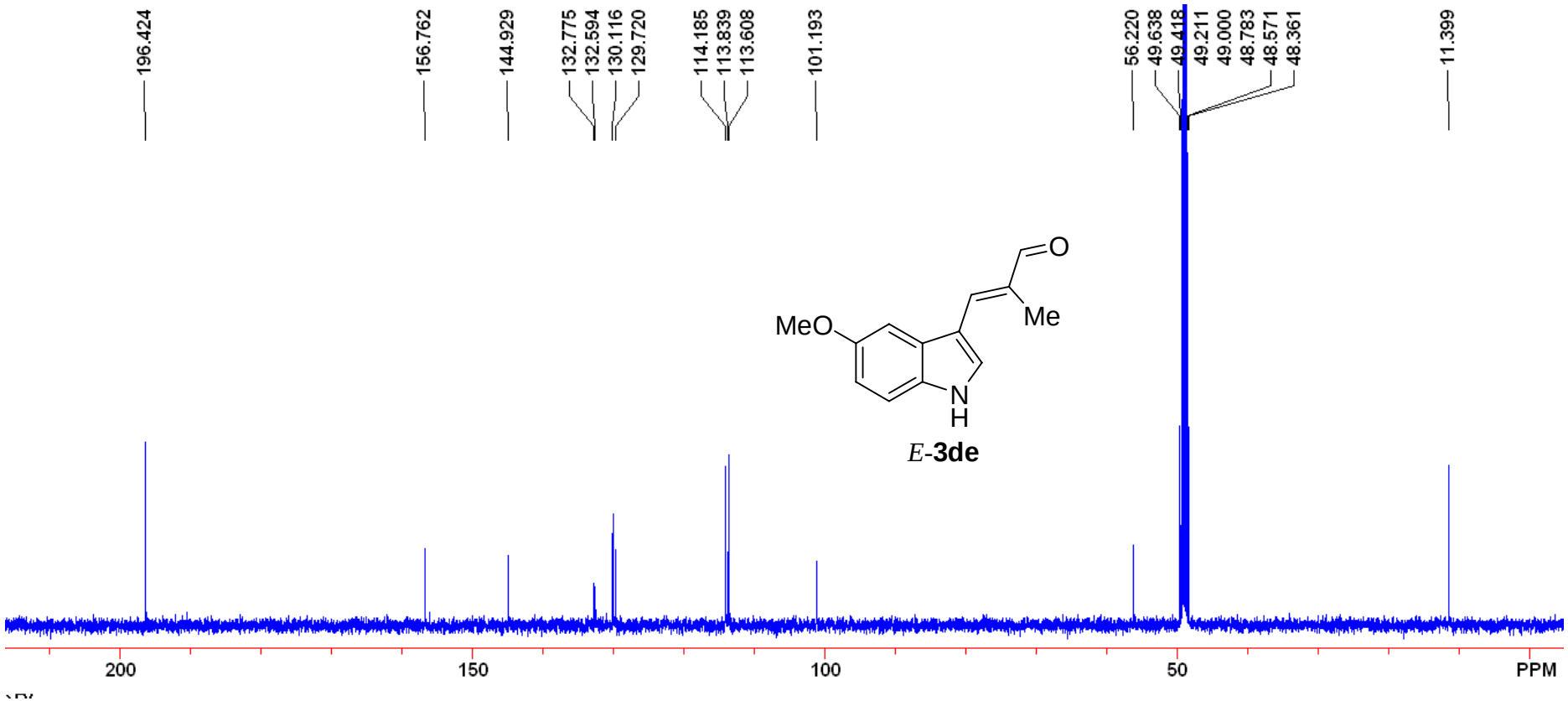

```
NAME                xsk10-26-3
EXPNO                        5
PROCNO                       1
Date_                 20101019
Time                     23.02
INSTRUM                  spect
PROBHD    5 mm PADUL 13C
PULPROG                noesyph
TD                        2048
SOLVENT                   MeOD
NS                          96
DS                          16
SWH                   5081.301 Hz
FIDRES                2.481104 Hz
AQ                    0.2015732 sec
RG                          228
DW                     98.400 usec
DE                      6.50 usec
TE                      280.8 K
D0                 0.00008036 sec
D1                 1.50000000 sec
D8                 0.69999999 sec
IN0                0.00019680 sec

======== CHANNEL f1 ========
NUC1                        1H
P1                      14.16 usec
PL1                      0.00 dB
PL1W                9.46981144 W
SFO1               400.1520730 MHz
ND0                         1
TD                        128
SFO1                 400.1521 MHz
FIDRES               39.702587 Hz
SW                      12.700 ppm
FnMODE           States-TPPI
SI                        1024
SF                 400.1500000 MHz
WDW                     QSINE
SSB                         2
LB                       0.00 Hz
GB                          0
PC                       1.00
SI                        1024
MC2              States-TPPI
SF                 400.1500000 MHz
WDW                     QSINE
SSB                         2
LB                       0.00 Hz
GB                          0
```



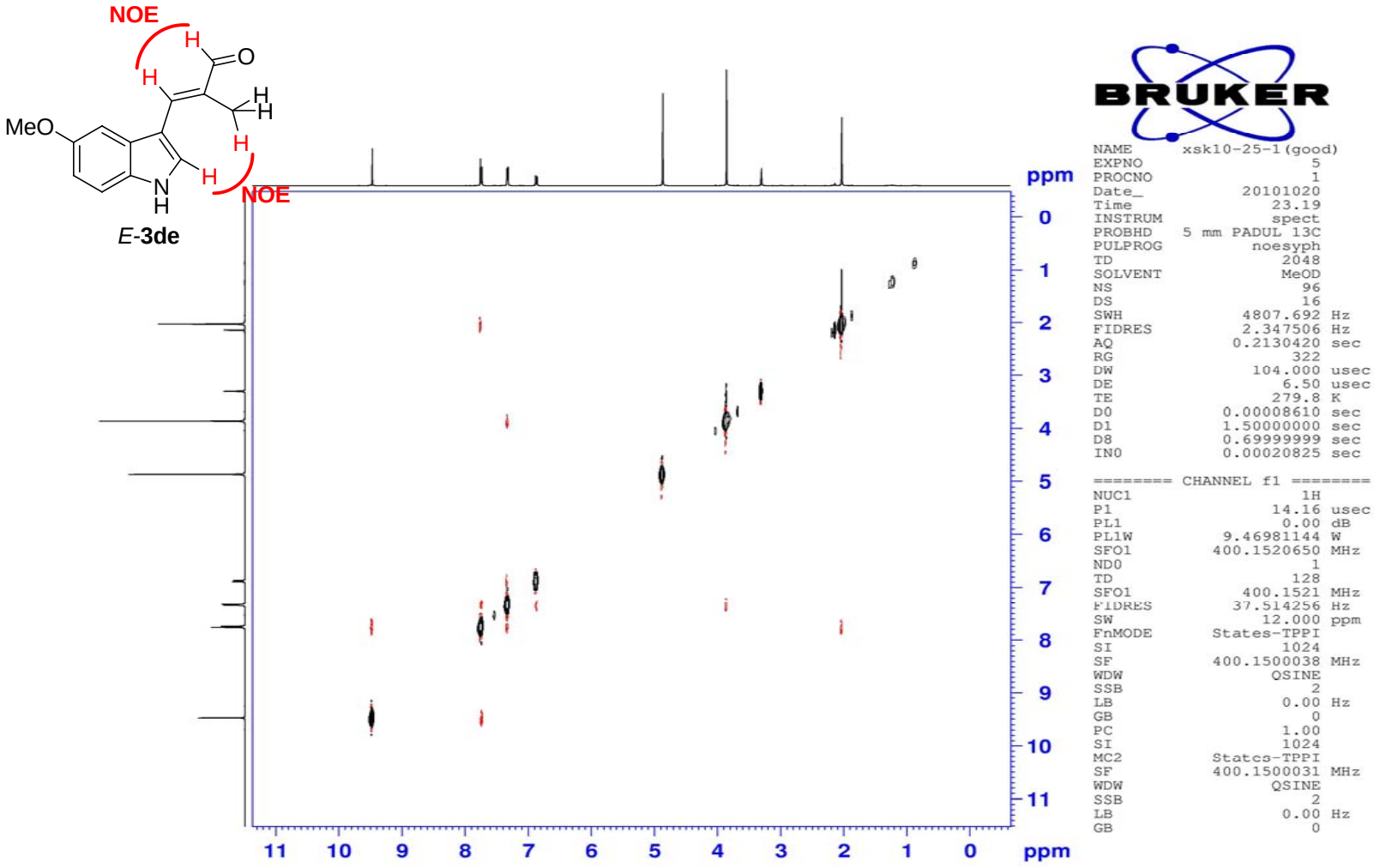




E-**3de**

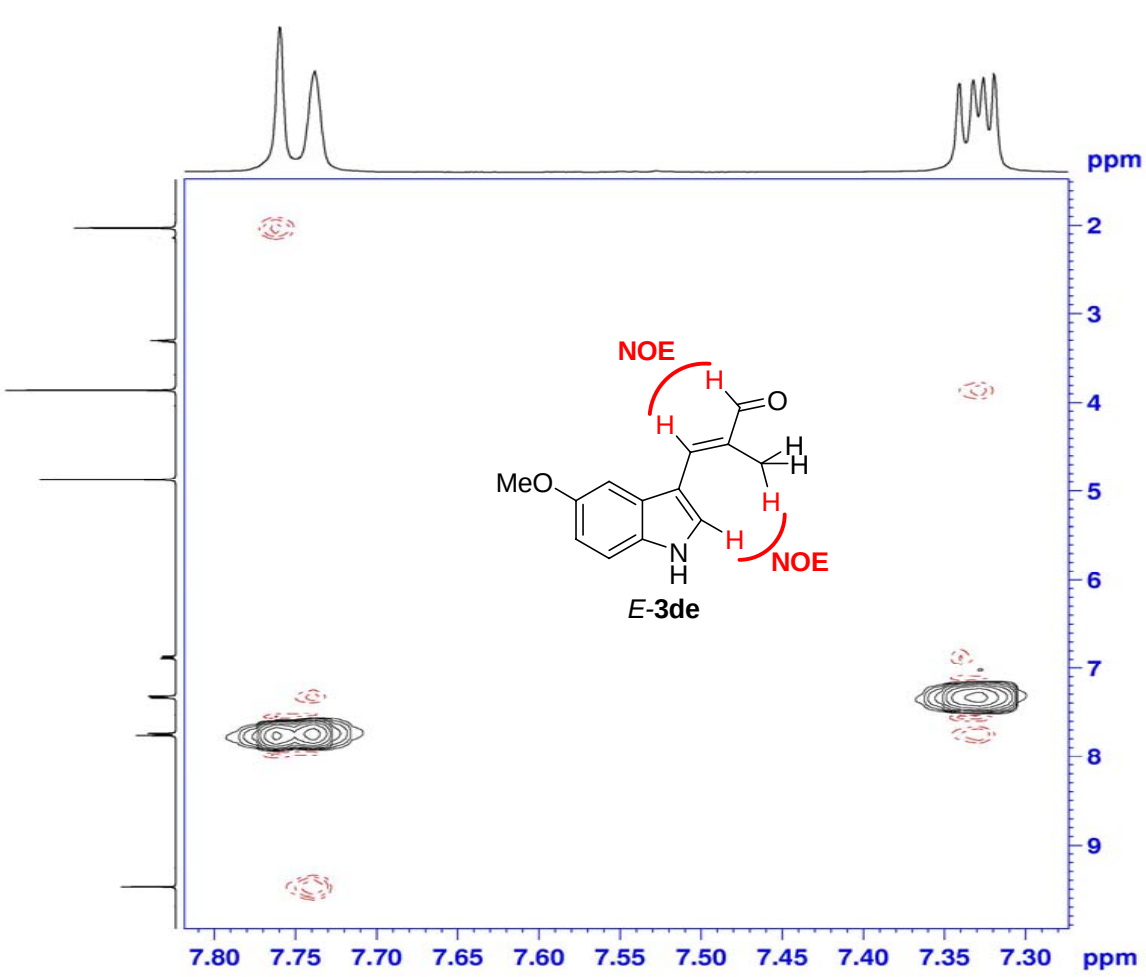


E-**3de**



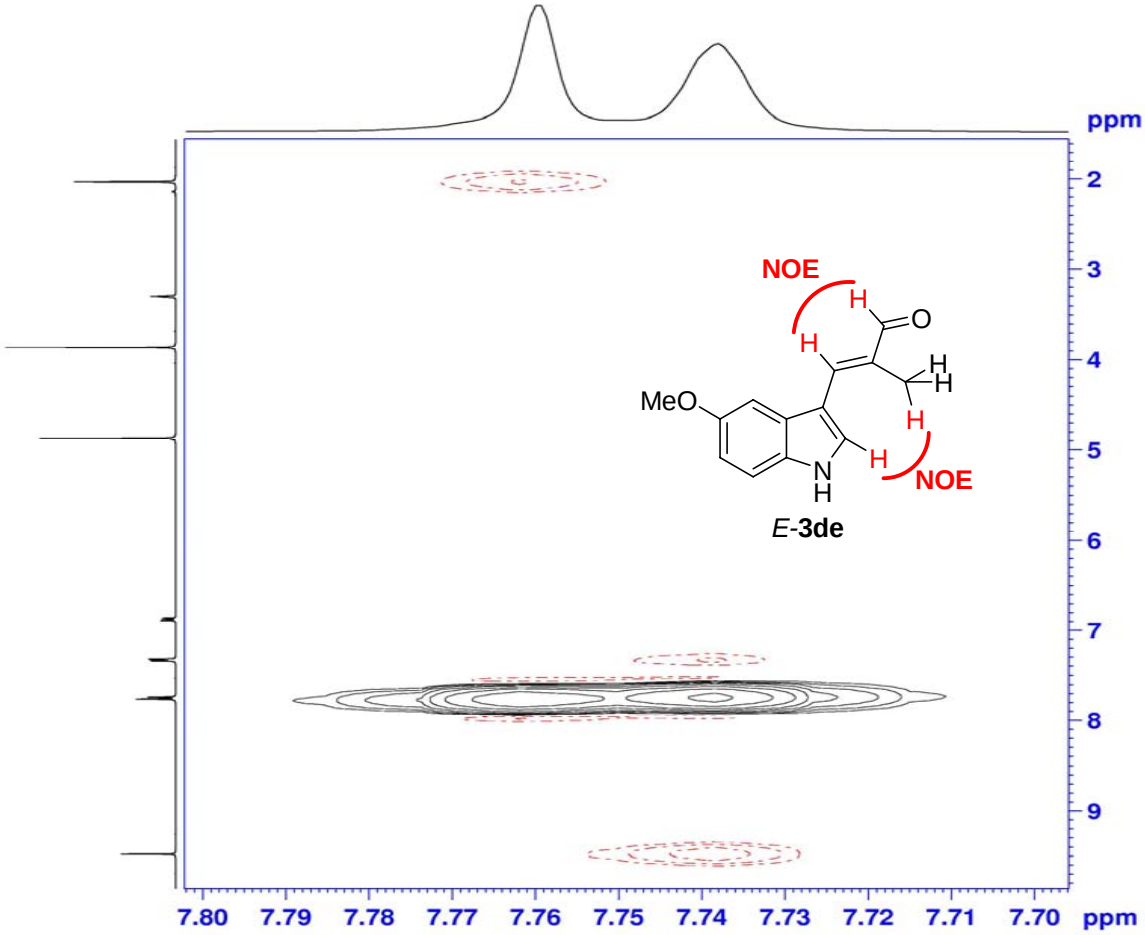
BRUKER

```
NAME          xsk10-25-1(good)
EXPNO                        5
PROCNO                       1
Date_                 20101020
Time                     23.19
INSTRUM                  spect
PROBHD    5 mm PADUL 13C
PULPROG               noesyph
TD                        2048
SOLVENT                   MeOD
NS                          96
DS                          16
SWH                   4807.692 Hz
FIDRES                2.347506 Hz
AQ                    0.2130420 sec
RG                          322
DW                    104.000 usec
DE                      6.50 usec
TE                      279.8 K
D0                 0.00008610 sec
D1                 1.50000000 sec
D8                 0.69999999 sec
IN0                0.00020825 sec

======== CHANNEL f1 ========
NUC1                        1H
P1                      14.16 usec
PL1                      0.00 dB
PL1W                9.46981144 W
SFO1               400.1520650 MHz
ND0                          1
TD                         128
SFO1                  400.1521 MHz
FIDRES                37.514256 Hz
SW                       12.000 ppm
FnMODE             States-TPPI
SI                         1024
SF                 400.1500038 MHz
WDW                      QSINE
SSB                          2
LB                       0.00 Hz
GB                           0
PC                       1.00
SI                         1024
MC2                States-TPPI
SF                 400.1500031 MHz
WDW                      QSINE
SSB                          2
LB                       0.00 Hz
GB                           0
```



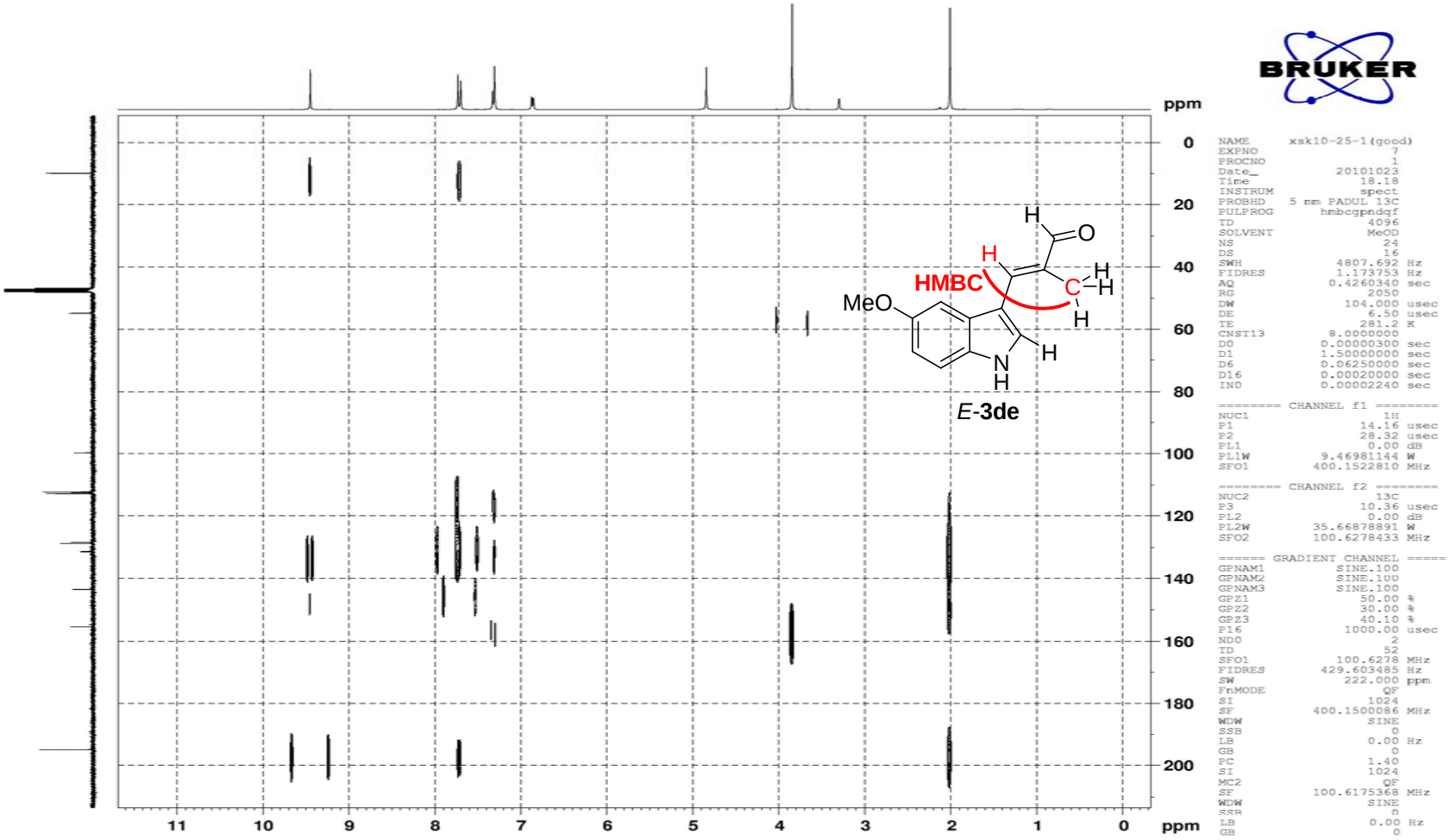
BRUKER

```
NAME        xsk10-25-1(good)
EXPNO                     5
PROCNO                    1
Date_              20101020
Time                 23.19
INSTRUM              spect
PROBHD    5 mm PADUL 13C
PULPROG           noesyph
TD                     2048
SOLVENT                MeOD
NS                       96
DS                       16
SWH                4807.692 Hz
FIDRES             2.347506 Hz
AQ                 0.2130420 sec
RG                       322
DW                 104.000 usec
DE                   6.50 usec
TE                   279.8 K
D0                 0.00008610 sec
D1                 1.50000000 sec
D8                 0.69999999 sec
IN0                0.00020825 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                   14.16 usec
PL1                   0.00 dB
PL1W               9.46981144 W
SFO1             400.1520650 MHz
ND0                      1
TD                     128
SFO1               400.1521 MHz
FIDRES            37.514256 Hz
SW                   12.000 ppm
FnMODE          States-TPPI
SI                    1024
SF               400.1500038 MHz
WDW                   QSINE
SSB                      2
LB                    0.00 Hz
GB                       0
PC                    1.00
SI                    1024
MC2             States-TPPI
SF               400.1500031 MHz
WDW                   QSINE
SSB                      2
LB                    0.00 Hz
GB                       0
```



BRUKER

```
NAME        xsk10-25-1(good)
EXPNO                     5
PROCNO                    1
Date_              20101020
Time                 23.19
INSTRUM              spect
PROBHD    5 mm PADUL 13C
PULPROG           noesyph
TD                   2048
SOLVENT              MeOD
NS                     96
DS                     16
SWH               4807.692 Hz
FIDRES            2.347506 Hz
AQ               0.2130420 sec
RG                     322
DW                 104.000 usec
DE                   6.50 usec
TE                  279.8 K
D0               0.00008610 sec
D1               1.50000000 sec
D8               0.69999999 sec
IN0              0.00020825 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  14.16 usec
PL1                  0.00 dB
PL1W            9.46981144 W
SFO1          400.1520650 MHz
ND0                    1
TD                   128
SFO1             400.1521 MHz
FIDRES          37.514256 Hz
SW                 12.000 ppm
FnMODE       States-TPPI
SI                  1024
SF            400.1500038 MHz
WDW                 QSINE
SSB                    2
LB                  0.00 Hz
GB                     0
PC                  1.00
SI                  1024
MC2          States-TPPI
SF            400.1500031 MHz
WDW                 QSINE
SSB                    2
LB                  0.00 Hz
GB                     0
```

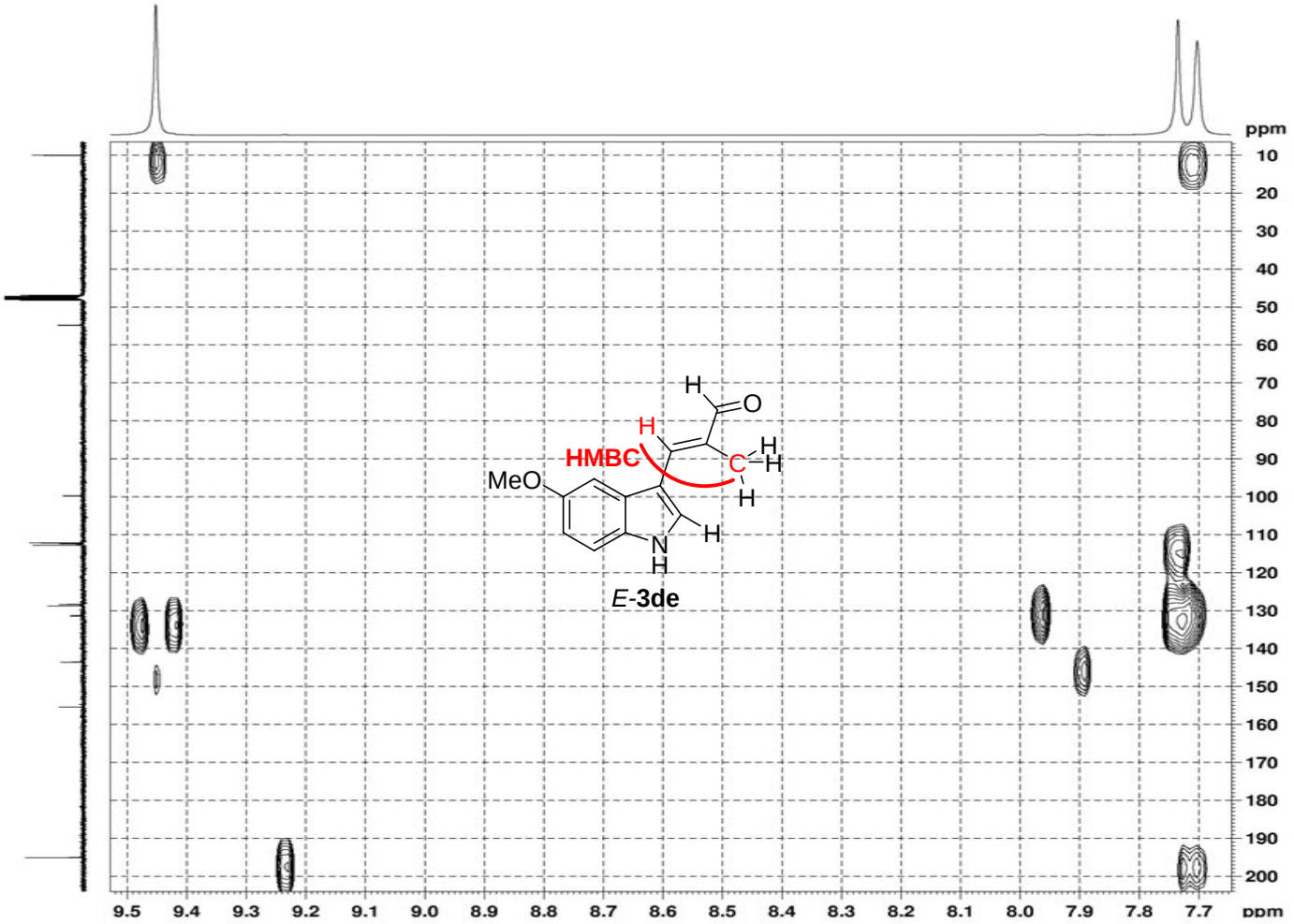


NAME xsk10-25-1(good)
EXPNO 7
PROCNO 1
Date_ 20101023
Time 18.18
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG hmbcgpndqf
TD 4096
SOLVENT MeOD
NS 24
DS 16
SWH 4807.692 Hz
FIDRES 1.173753 Hz
AQ 0.4260340 sec
RG 2050
DW 104.000 usec
DE 6.50 usec
TE 281.2 K
CNST13 8.0000000
D0 0.00000300 sec
D1 1.50000000 sec
D6 0.06250000 sec
D16 0.00020000 sec
IN0 0.00002240 sec

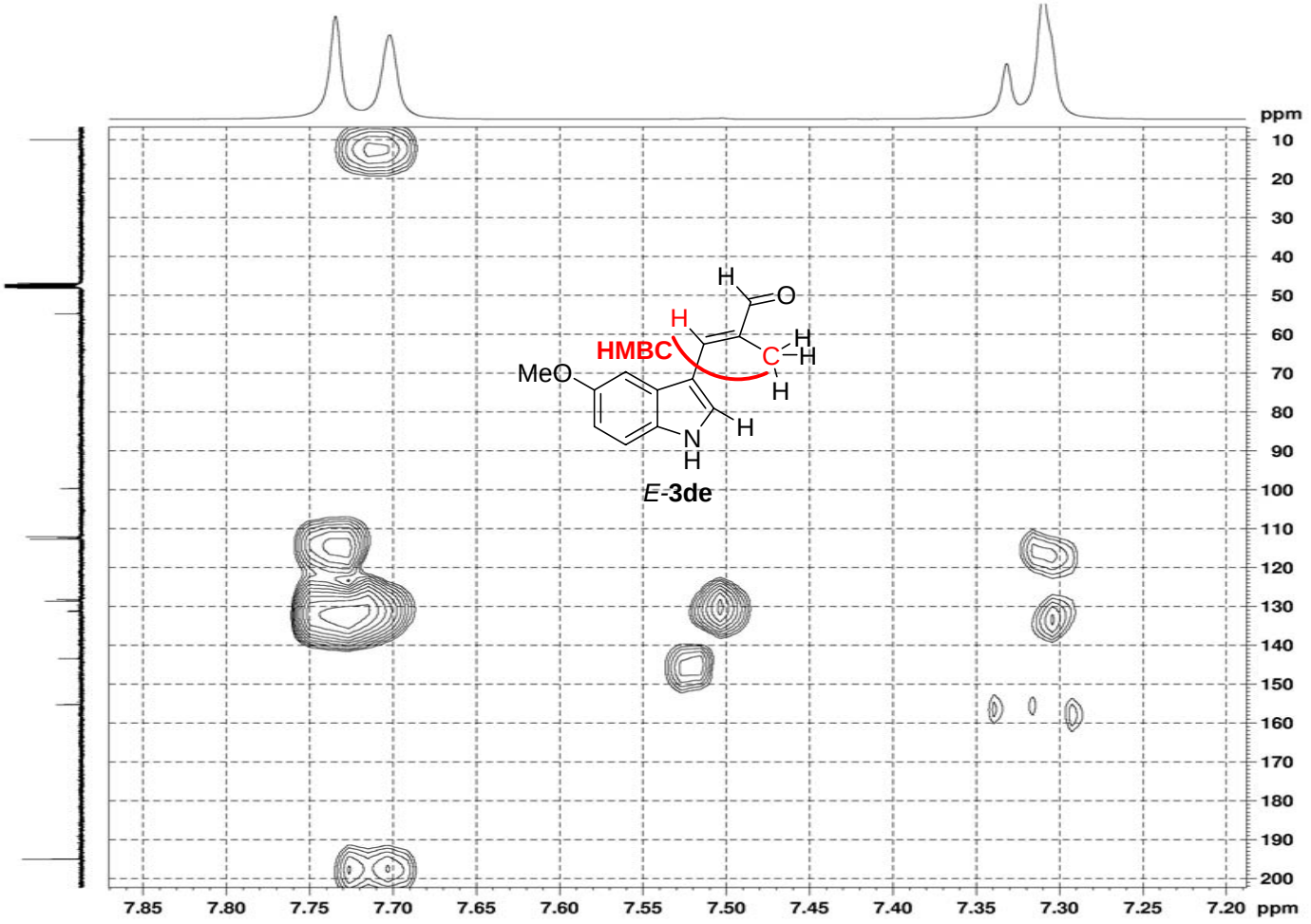
======== CHANNEL f1 ========
NUC1 1H
P1 14.16 usec
P2 28.32 usec
PL1 0.00 dB
PL1W 9.46981144 W
SFO1 400.1522810 MHz

======== CHANNEL f2 ========
NUC2 13C
P3 10.36 usec
PL2 0.00 dB
PL2W 35.66878891 W
SFO2 100.6278433 MHz

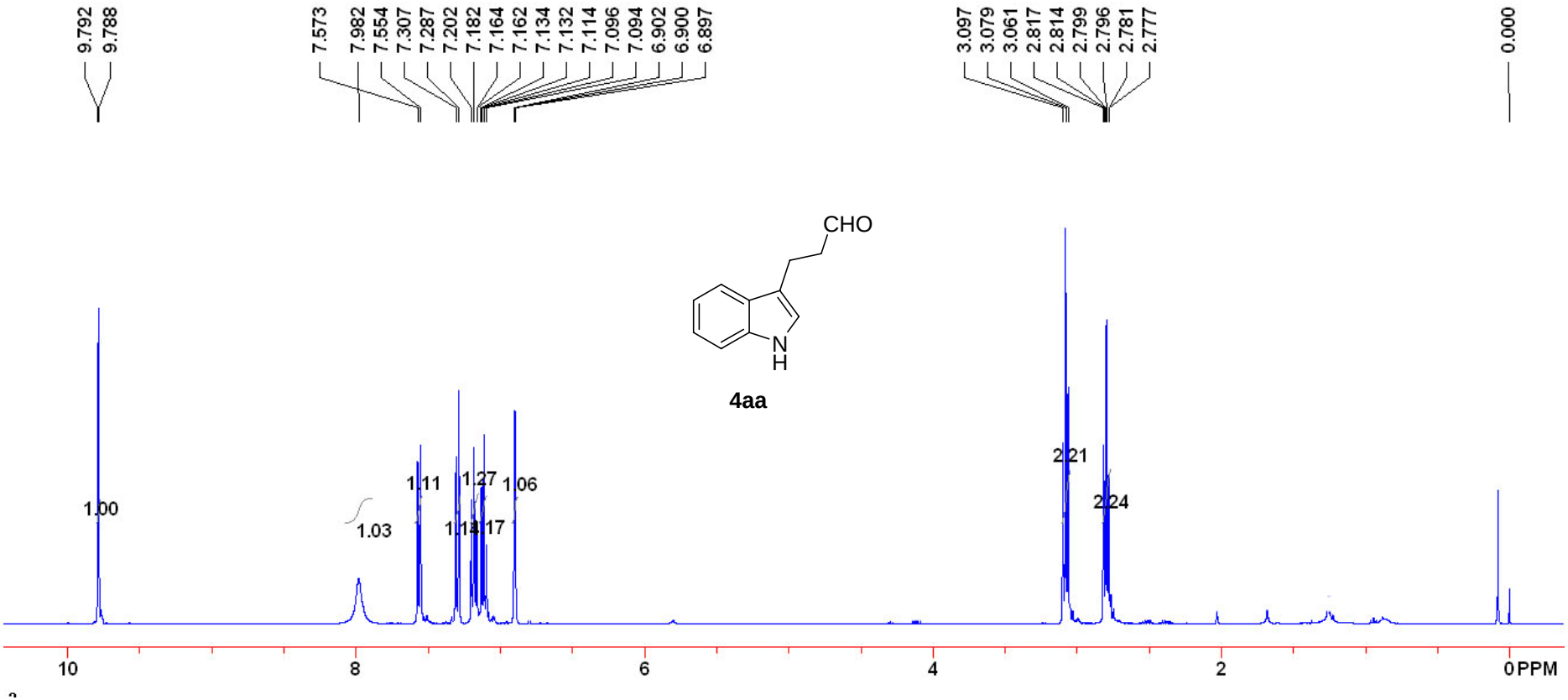
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec
ND0 2
TD 52
SFO1 100.6278 MHz
FIDRES 429.603485 Hz
SW 222.000 ppm
FnMODE QF
SI 1024
SF 400.1500086 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 100.6175368 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

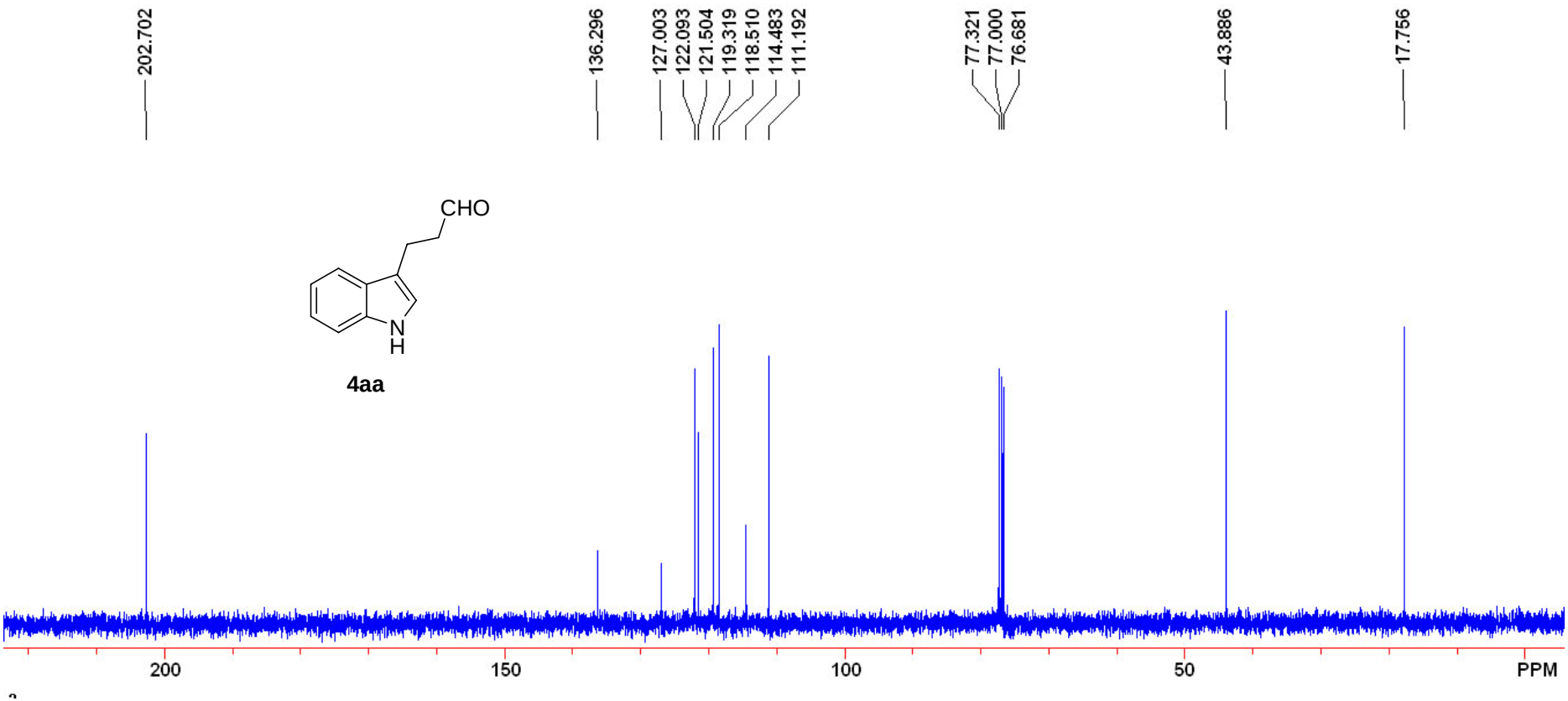



```
NAME            xsk10-25-1(good)
EXPNO                         7
PROCNO                        1
Date_                  20101023
Time                      18.18
INSTRUM                   spect
PROBHD    5 mm PADUL 13C
PULPROG          hmbcgpndqf
TD                         4096
SOLVENT                   MeOD
NS                          24
DS                          16
SWH                   4807.692 Hz
FIDRES                1.173753 Hz
AQ                    0.4260340 sec
RG                         2050
DW                      104.000 usec
DE                        6.50 usec
TE                      281.2 K
CNST13                8.0000000
D0                    0.00000300 sec
D1                    1.50000000 sec
D6                    0.06250000 sec
D16                   0.00020000 sec
IN0                   0.00002240 sec

======== CHANNEL f1 ========
NUC1                         1H
P1                        14.16 usec
P2                        28.32 usec
PL1                        0.00 dB
PL1W                  9.46981144 W
SFO1                400.1522810 MHz

======== CHANNEL f2 ========
NUC2                        13C
P3                        10.36 usec
PL2                        0.00 dB
PL2W                 35.66878891 W
SFO2                100.6278433 MHz

====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPNAM2                SINE.100
GPNAM3                SINE.100
GPZ1                      50.00 %
GPZ2                      30.00 %
GPZ3                      40.10 %
P16                     1000.00 usec
ND0                          2
TD                          52
SFO1                100.6278 MHz
FIDRES               429.603485 Hz
SW                      222.000 ppm
FnMODE                       QF
SI                         1024
SF                  400.1500086 MHz
WDW                        SINE
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.40
SI                         1024
MC2                          QF
SF                  100.6175368 MHz
WDW                        SINE
SSB                           0
LB                         0.00 Hz
GB                            0
```



NAME	xsk10-25-1(good)
EXPNO	7
PROCNO	1
Date_	20101023
Time	18.18
INSTRUM	spect
PROBHD	5 mm PADUL 13C
PULPROG	hmbcgpndqf
TD	4096
SOLVENT	MeOD
NS	24
DS	16
SWH	4807.692 Hz
FIDRES	1.173753 Hz
AQ	0.4260340 sec
RG	2050
DW	104.000 usec
DE	6.50 usec
TE	281.2 K
CNST13	8.0000000
D0	0.00000300 sec
D1	1.50000000 sec
D6	0.06250000 sec
D16	0.00020000 sec
IN0	0.00002240 sec
========	CHANNEL f1 ========
NUC1	1H
P1	14.16 usec
P2	28.32 usec
PL1	0.00 dB
PL1W	9.46981144 W
SFO1	400.1522810 MHz
========	CHANNEL f2 ========
NUC2	13C
P3	10.36 usec
PL2	0.00 dB
PL2W	35.66878891 W
SFO2	100.6278433 MHz
======	GRADIENT CHANNEL =====
GPNAM1	SINE.100
GPNAM2	SINE.100
GPNAM3	SINE.100
GPZ1	50.00 %
GPZ2	30.00 %
GPZ3	40.10 %
P16	1000.00 usec
ND0	2
TD	52
SFO1	100.6278 MHz
FIDRES	429.603485 Hz
SW	222.000 ppm
FnMODE	QF
SI	1024
SF	400.1500086 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.40
SI	1024
MC2	QF
SF	100.6175368 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0





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