Electronic Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Supporting Information

Enantioselective Synthesis of Pyranonaphthoquinone Antibiotics using a CBS Reduction/ Cross-metathesis/ oxa-Michael Strategy†

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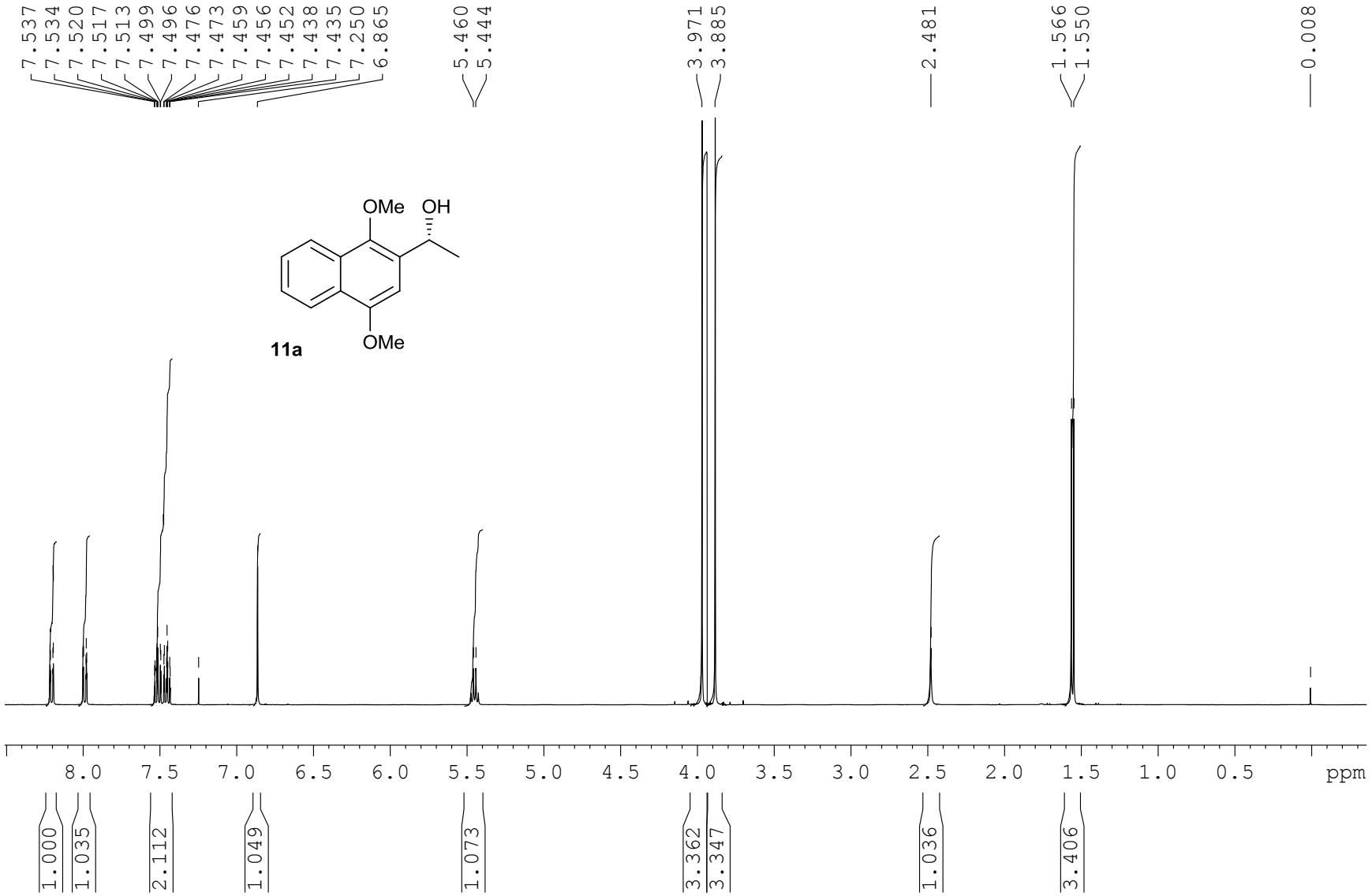
(±)-2-(1-(*tert*-Butyldimethylsilyloxy)ethyl)-1,4-dimethoxynaphthalene (11b). To a solution of alcohol **11a** (1.14 g, 4.9 mmol) in dry DMF (15 mL) was added TBDMSCl (1.11 g, 7.3 mmol), imidazole (0.67 g, 9.8 mmol), and DMAP (0.12 g, 0.98 mmol). The reaction mixture was stirred under nitrogen at room temperature for 24 hours. The solution was quenched by the addition of sat. aq. $NaHCO_3$ (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 5:1) gave TBDMS ether **11b** (1.7 g, 100%) as a colourless solid: mp 53-57 ºC; IR (film) ν_{max}/cm^{-1} 3071, 2953, 2928, 2857, 1629, 1592, 1452, 1369, 1247, 1212, 1127, 1085, 999, 896, 828, 764; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (1 H, d, *J* = 7.7 Hz, 5-H or 8-H), 8.05 (1 H, d, *J* = 8.4 Hz, 5-H or 8-H), 7.57-7.46 (2 H, m, 6-H and 7-H), 7.07 (1 H, s, 3-H), 5.47 (1 H, q, *J* = 6.3 Hz, CHOSi), 4.03 (3 H, s OCH_3), 3.94 (3 H, s, OCH_3), 1.53 (3 H, d, *J* = 6.3 Hz, CH_3), 0.96 (9 H, s, ^{t}Bu), 0.14 (3 H, s, $SiCH_3$), 0.01 (3 H, s, $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1 (C-Ar), 144.3 (C-Ar), 134.9 (C-Ar), 128.2 (C-Ar), 126.4 (CH-Ar), 125.9 (C-Ar), 125.0 (CH-Ar), 122.4 (CH-Ar), 121.9 (CH-Ar), 101.8 (CH-Ar), 65.3 (CHOSi), 62.1 (OCH_3), 55.6 (OCH_3), 26.6 (CH_3), 25.9 (3 × CH_3), 18.3 ($\underline{C}(CH_3)_3$), -4.8 ($SiCH_3$), -4.8 ($SiCH_3$); MS (ESI) *m/z* 369 ($[M\text{-}Na]^+$, 12%), 299 (10), 215 (100), 186 (58); HRMS (ESI) *m/z* for $C_{20}H_{30}NaO_3Si^+$ $[M\text{-}Na]^+$ calcd 369.1856, found 369.1844.

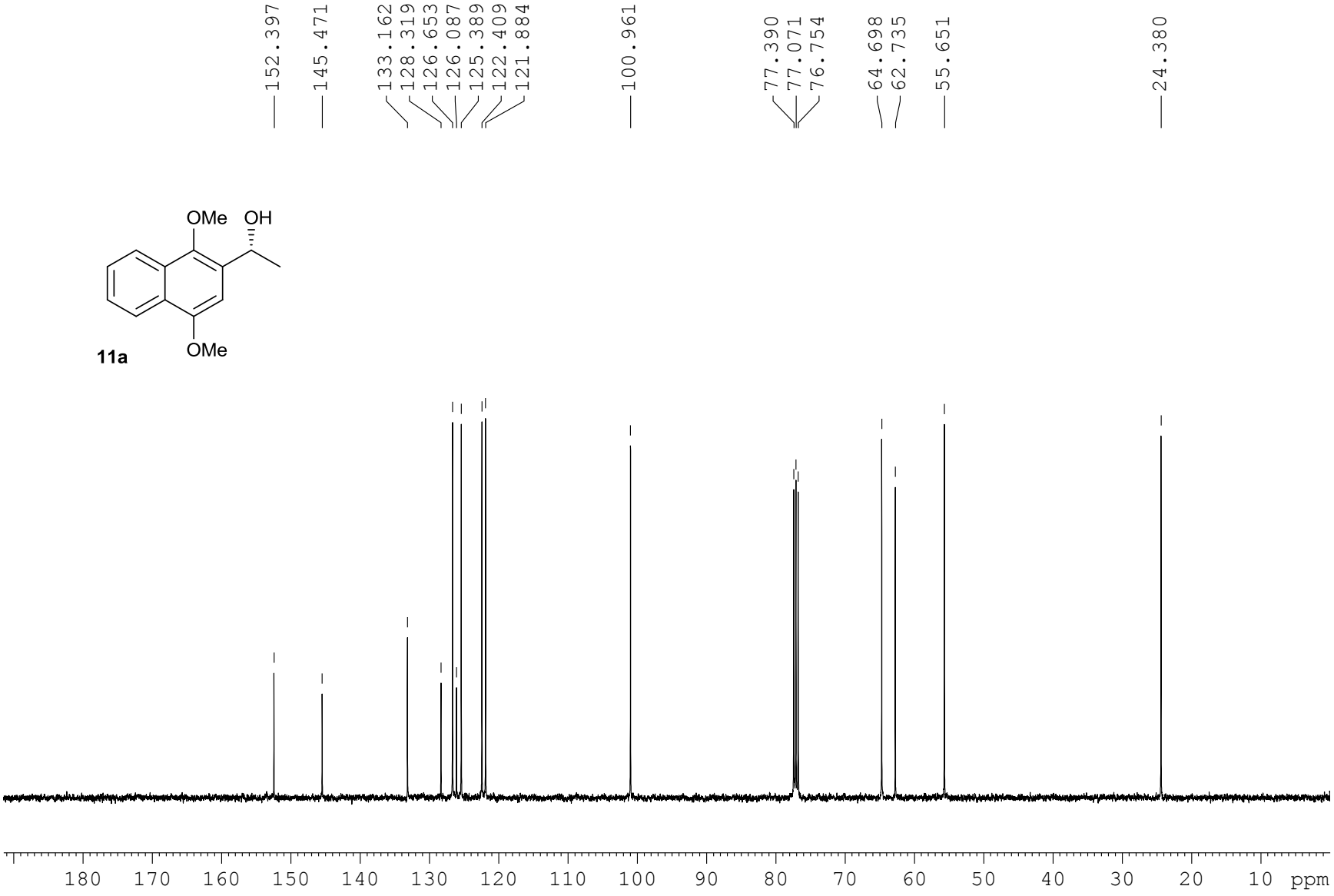
(±)-2-(1-(*tert*-Butyldimethylsilyloxy)ethyl)-1,4-naphthoquinone (9b). To a stirred solution of TBDMS ether **11b** (0.2 g, 0.6 mmol) in acetonitrile (5 mL) was added a solution of CAN (0.63 g, 1.2 mmol) in water (1 mL). The solution was stirred at room temperature for 5 minutes and then diluted with water (30 mL). The reaction mixture was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 30:1) gave naphthoquinone **9b** (0.14 g, 75%) as a yellow oil: IR (film) ν_{max}/cm^{-1} 2956, 2930, 2857, 1662, 1620, 1596, 1298, 1249, 1112, 893, 830, 776; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02-7.99 (2 H, m, 5-H and 8-H), 7.68-7.65 (2 H,

m, 6-H and 7-H), 7.05 (1 H, s, 3-H), 4.99 (1 H, q, *J* = 6.4 Hz, CHOSi), 1.35 (3 H, d, *J* = 6.4 Hz, CH_3), 0.87 (9 H, s, ^{t}Bu), 0.06 (3 H, s, $SiCH_3$), 0.01 (3 H, s, $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3 (C=O), 184.7 (C=O), 155.0 (C-Ar), 133.7 (CH-Ar), 133.5 (CH-Ar), 132.9 (CH-Ar), 132.2 (C-Ar), 132.0 (C-Ar), 126.2 (CH-Ar), 126.0 (CH-Ar), 64.7 (CHOSi), 25.7 (3 × CH_3), 24.8 (CH_3), 18.1 ($\underline{C}(CH_3)_3$), -5.0 ($SiCH_3$), -5.1 ($SiCH_3$); MS (ESI) *m/z* 339 ($[M\text{-}Na]^+$, 50%), 317 ($[M\text{-}H]^+$, 58), 185 (100); HRMS (ESI) *m/z* for $C_{18}H_{25}O_3Si^+$ $[M\text{-}H]^+$ calcd 317.1567, found 317.1567.

(±)-2-(1-(Ethoxymethoxy)ethyl)-1,4-dimethoxynaphthalene (11c). To a solution of alcohol **11a** (0.5 g, 2.2 mmol) and DIPEA (1.5 mL, 8.6 mmol) in CH_2Cl_2 (21 mL) was added ethoxymethyl chloride (0.4 mL, 4.3 mmol) and DMAP (50 mg, 4.3 mmol). The solution was stirred under nitrogen at room temperature for 2 days. The solution was quenched with sat. aq. NH_4Cl (50 mL). The layers were separated and the aqueous phase extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 5:1) gave EOM ether **11c** (0.56 g, 90%) as a colourless oil: IR (film) ν_{max}/cm^{-1} 2975, 2934, 1596, 1459, 1365, 1213, 1088, 997, 846, 768; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31-8.29 (1 H, d, *J* = 8.4 Hz, 5-H or 8-H), 8.09 (1 H, d, *J* = 7.8 Hz, 5-H or 8-H), 7.57-7.47 (2 H, m, 6-H and 7-H), 6.92 (1 H, s, 3-H), 5.50 (1 H, q, *J* = 6.8 Hz, CHOEOM), 4.73 (1 H, d, *J* = 6.6 Hz, OCH_2O), 4.66 (1 H, d, *J* = 6.6 Hz, OCH_2O), 4.01 (3 H, s, OCH_3), 3.96 (3 H,s, OCH_3), 3.83-3.74 (1 H, m, OCH_2CH_3), 3.61-3.53 (1 H, m, OCH_2CH_3), 1.60 (3 H, d, *J* = 6.8 Hz,CH_3), 1.23 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2 (C-Ar), 146.4 (C-Ar), 130.9 (C-Ar), 128.2 (C-Ar), 126.4 (CH-Ar), 126.1 (C-Ar) 125.2 (CH-Ar), 122.2 (CH-Ar), 121.8 (CH-Ar) 101.0 (3-C), 92.6 (OCH_2O), 67.3 (CHOEOM), 63.1 ($O\underline{C}H_2CH_3$), 62.3 (OCH_3), 55.4 (OCH_3), 23.0 (CH_3), 15.0 ($OCH_2\underline{C}H_3$); MS (ESI) *m/z* 313 ($[M\text{-}Na]^+$, 35%), 215 (100), 186 (40); HRMS (ESI) *m/z* for $C_{17}H_{22}NaO_4^+$ $[M\text{-}Na]^+$ calcd 313.1410, found 313.1413.

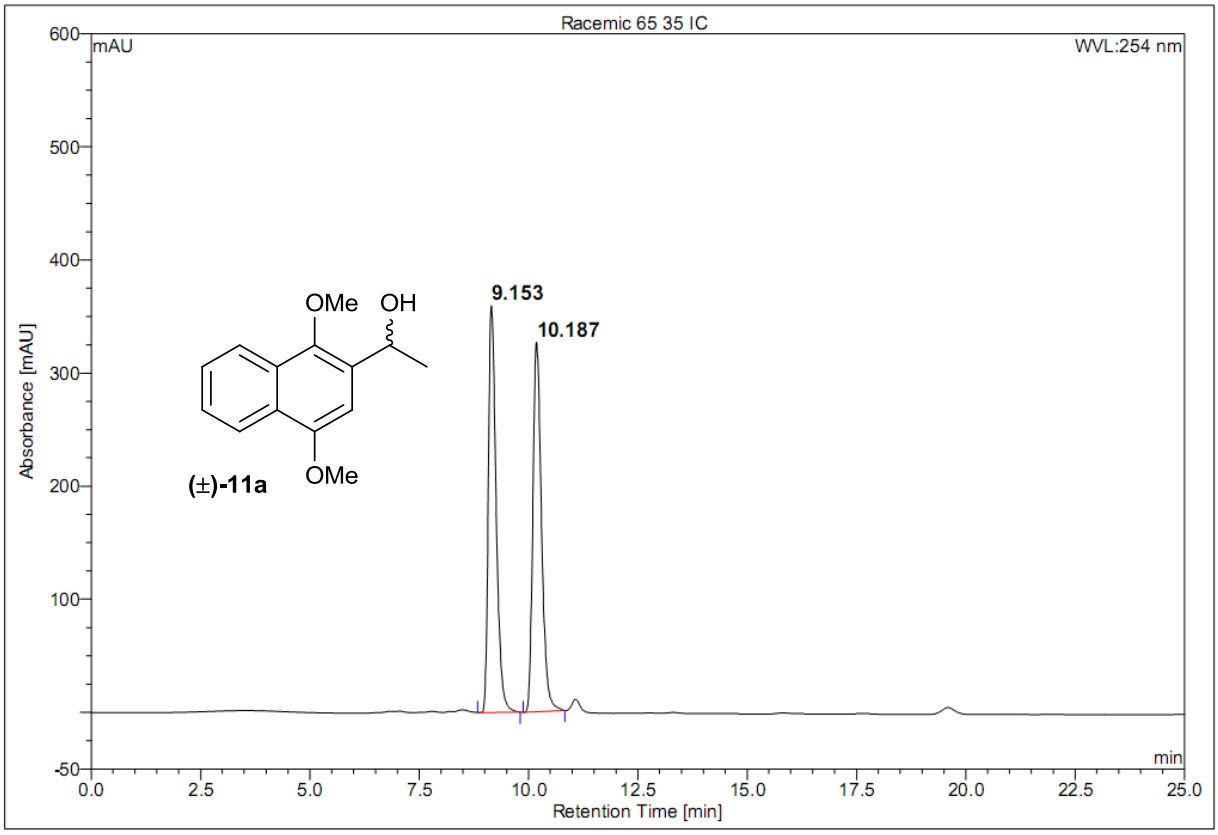
(±)-2-(1-(Ethoxymethoxy)ethyl)-1,4-naphthoquinone (9c). To a stirred solution of EOM ether **11c** (0.48 g, 1.6 mmol) in acetonitrile (4.2 mL) was added a solution of CAN (1.8 g, 3.3 mmol) in water (4.2 mL). The solution was stirred at room temperature for 15 minutes then diluted with water (25 mL). The reaction mixture was extracted with EtOAc (3 × 25 mL). The combined organic extracts were washed with brine (25 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 7:1) gave quinone **9c** (0.37 g, 86%) as a yellow oil: IR (film) ν_{max}/cm^{-1} 2931, 2856, 1722, 1653, 1355,1260, 1082, 1014, 969, 826; ^1H NMR (400 MHz, $CDCl_3$): δ 8.04-7.99 (2 H, m, 5-H and 8-H), 7.74-7.70 (2 H, m, 6-H and 7-H), 7.03 (1 H, s, 3-H), 5.01 (1 H, q, *J* = 6.5 Hz, C*H*OEOM), 4.79 (1 H, d, *J* = 6.9 Hz, OCH_2O), 4.71 (1 H, d, *J* = 6.9 Hz, OCH_2O), 3.73-3.55 (2 H, m, OCH_2CH_3), 1.46 (3 H, d, *J* = 6.5 Hz, $ArCHCH_3$), 1.19 (3 H, t, *J* = 7.1 Hz, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.6 (C=O), 184.0 (C=O), 152.1 (2-C), 133.3 (CH-Ar), 133.2 (CH-Ar), 132.6 (3-C), 131.8 (C-Ar), 131.5 (C-Ar), 125.9 (CH-Ar), 125.6 (CH-Ar), 93.3 (OCH_2O), 67.9 (CHOEOM), 63.2 ($O\underline{C}H_2CH_3$), 21.4 (CH_3), 14.7 ($OCH_2\underline{C}H_3$); MS (ESI) *m/z* 283 ($[M-Na]^+$,100%), 185 (20); HRMS (ESI) *m/z* for $C_{15}H_{16}NaO_4^+$ $[M-Na]^+$ calcd. 283.0941, found 283.0935.





1 Racemic 65 35 IC

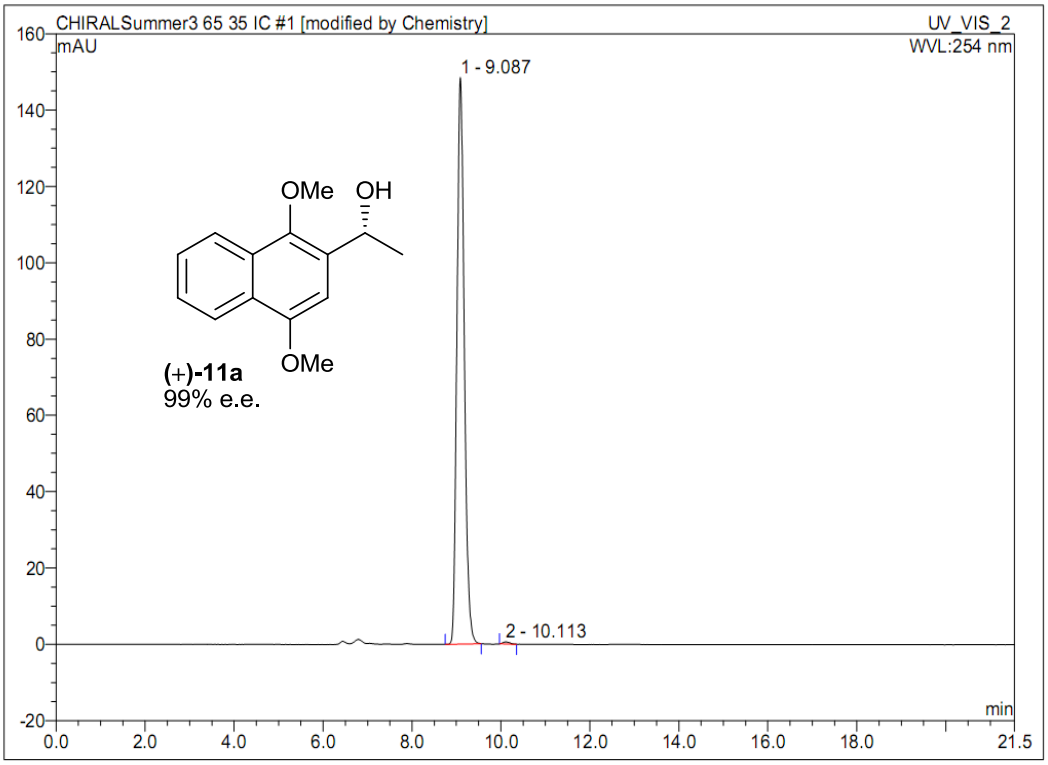
Sample Name:	**Racemic 65 35 IC**	*Injection Volume:*	**20.0**
Vial Number:	**2**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**254**
Control Program:	**ZEW085 65_35**	*Bandwidth:*	**n.a.**
Quantif. Method:	**default**	*Dilution Factor:*	**1.0000**
Recording Time:	**2/12/2010 10:57**	*Sample Weight:*	**1.0000**
Run Time (min):	**38.50**	*Sample Amount:*	**1.0000**



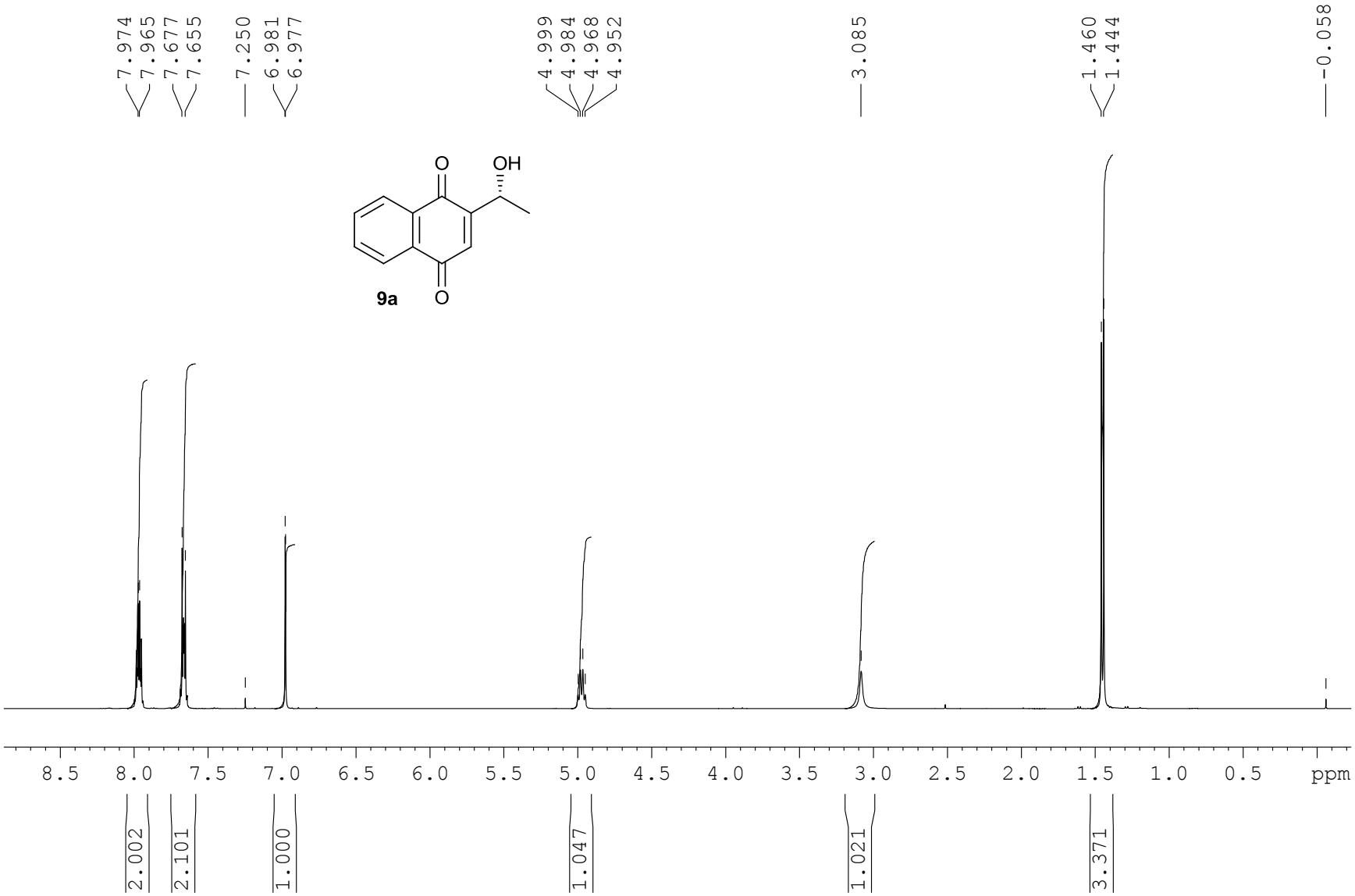
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.15	n.a.	359.864	74.678	49.92	n.a.	BMB*
2	10.19	n.a.	326.938	74.929	50.08	n.a.	BMB*
Total:			686.802	149.607	100.00	0.000	

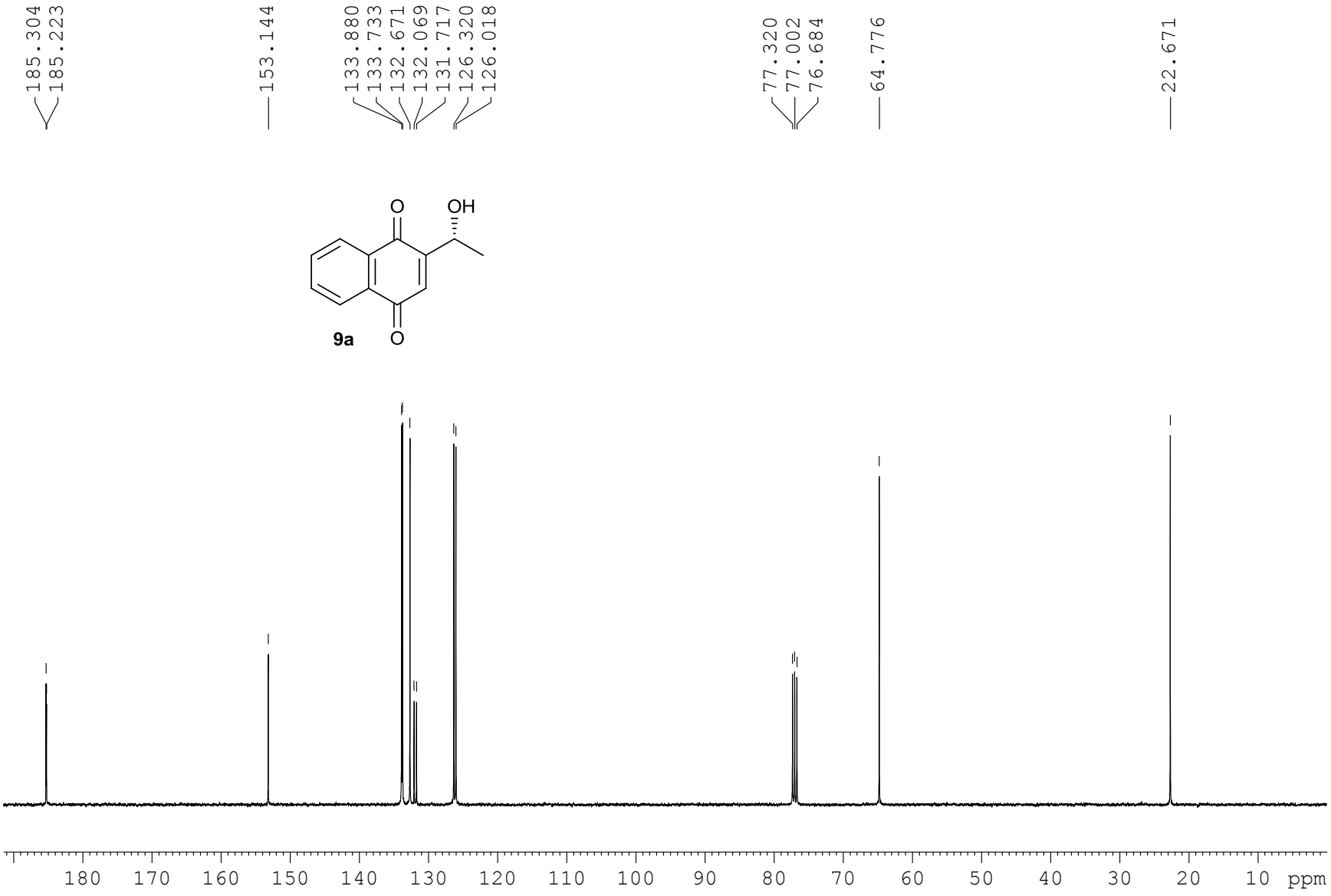
1 ChiralSummer3 IC 65 35

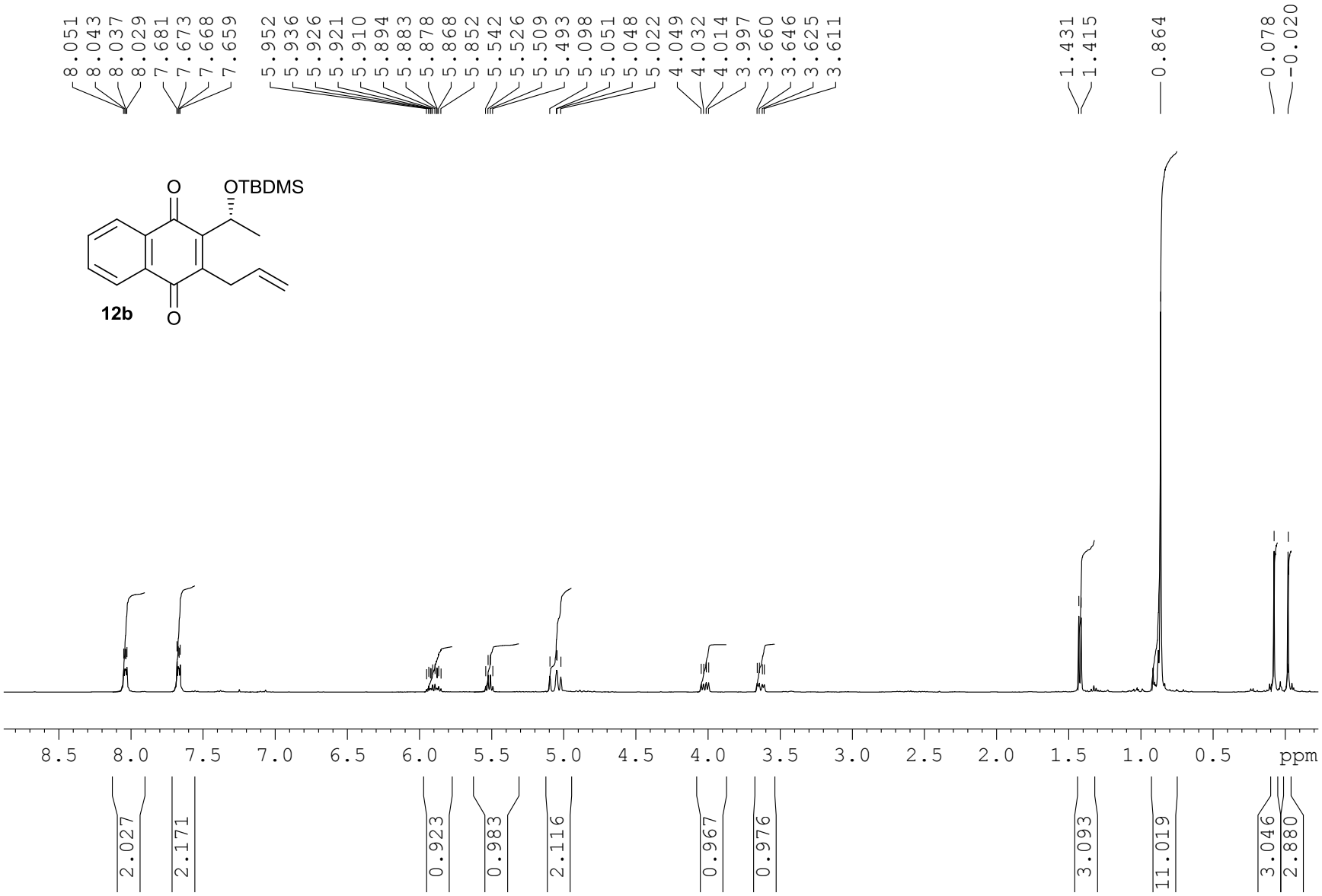
Sample Name:	**ChiralSummer3 IC 65 35**	*Injection Volume:*	**20.0**
Vial Number:	**2**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**254**
Control Program:	**alcohol 65_35**	*Bandwidth:*	**n.a.**
Quantif. Method:	**default**	*Dilution Factor:*	**1.0000**
Recording Time:	**12/1/2010 14:16**	*Sample Weight:*	**1.0000**
Run Time (min):	**21.55**	*Sample Amount:*	**1.0000**

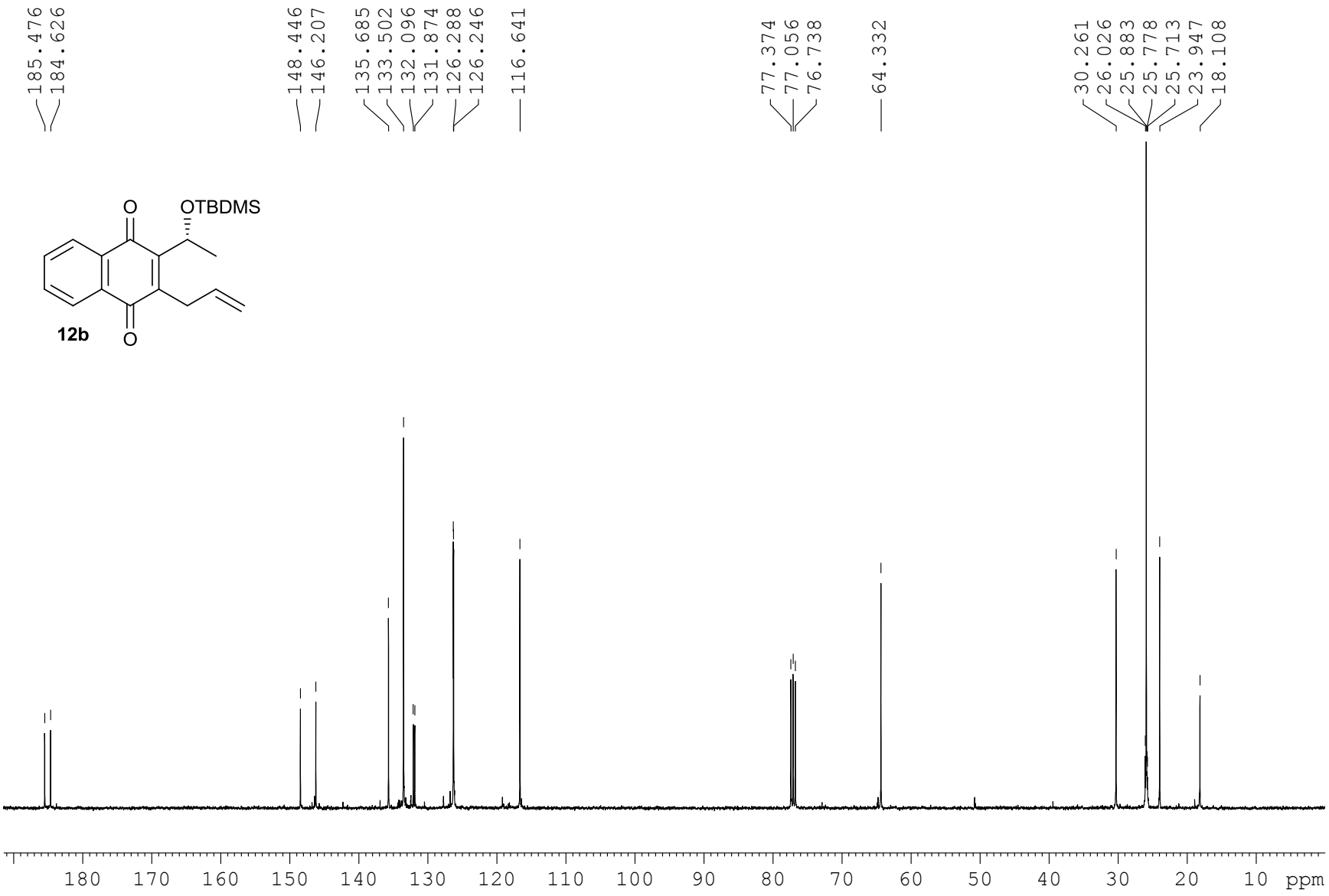


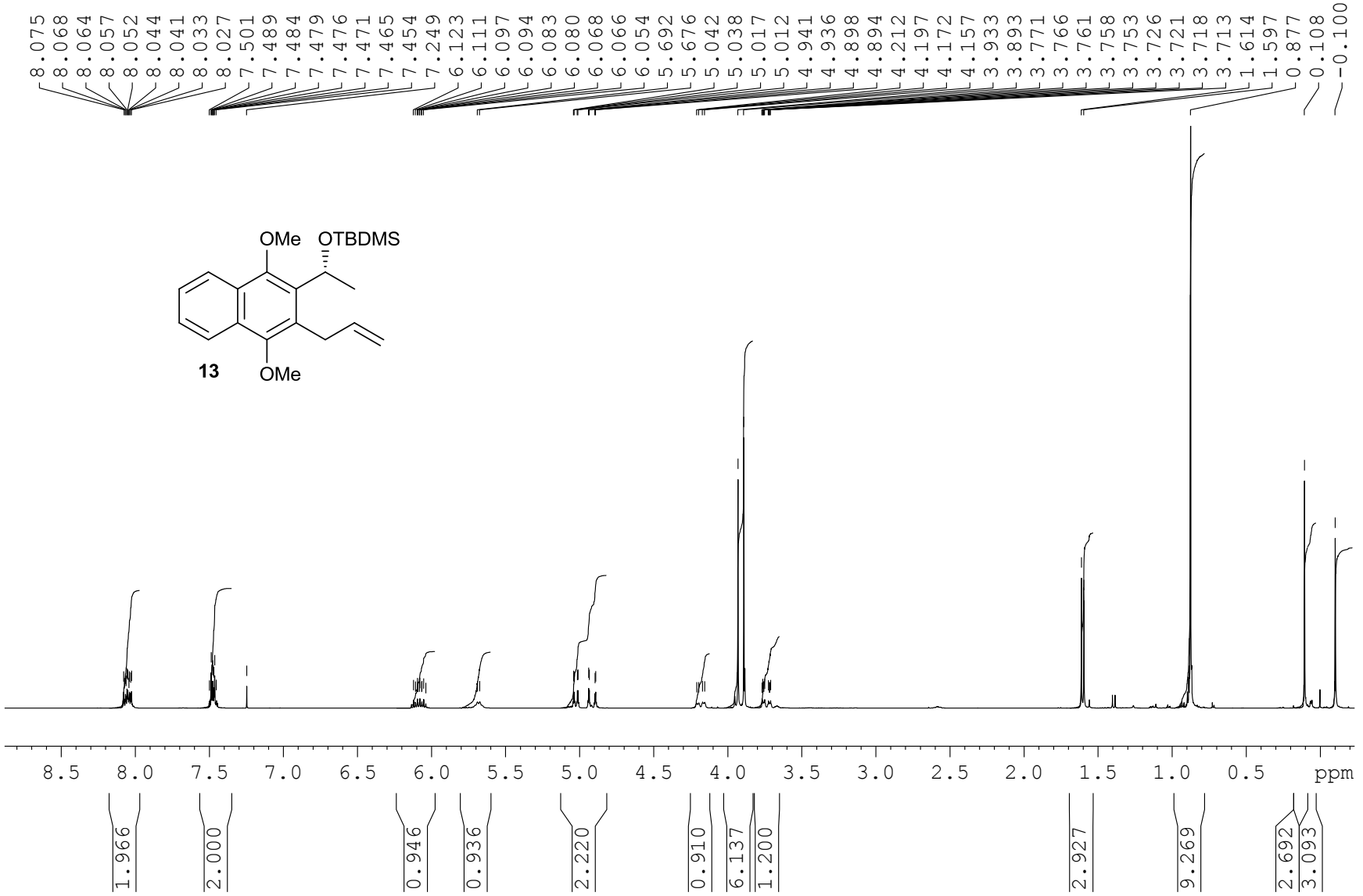
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.09	n.a.	148.492	28.446	99.65	n.a.	BMB*
2	10.11	n.a.	0.570	0.100	0.35	n.a.	BMB*
Total:			149.061	28.545	100.00	0.000	

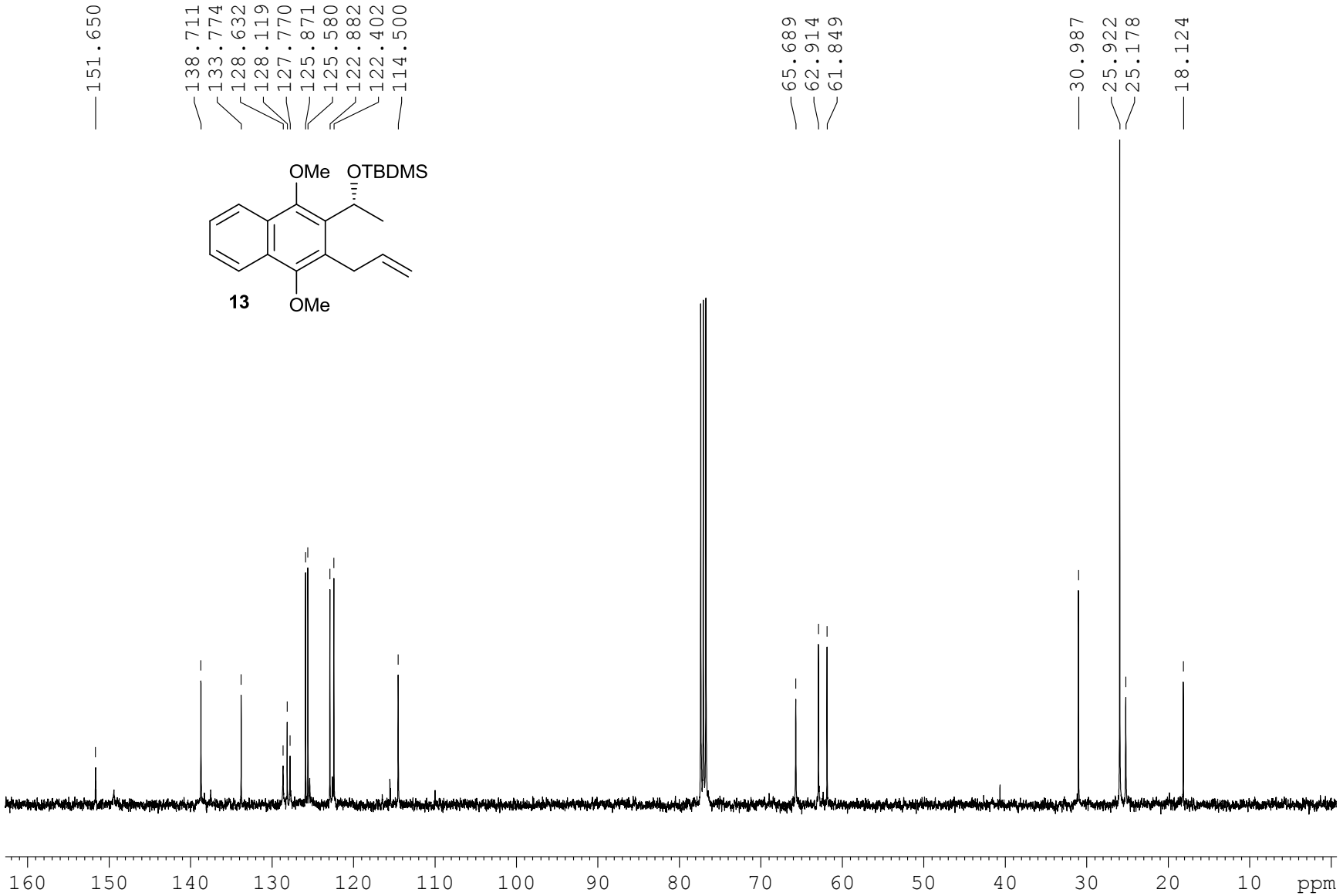


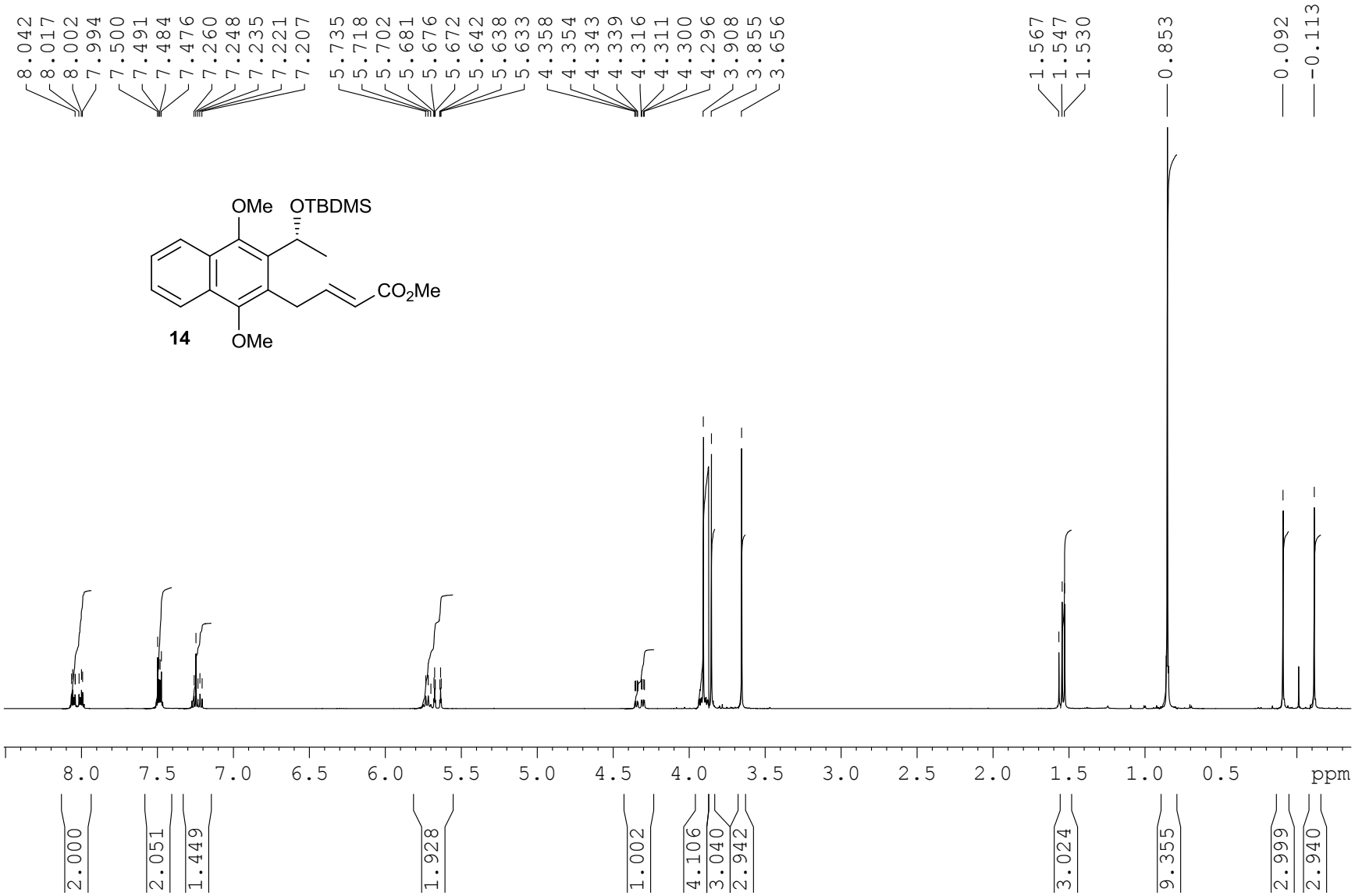


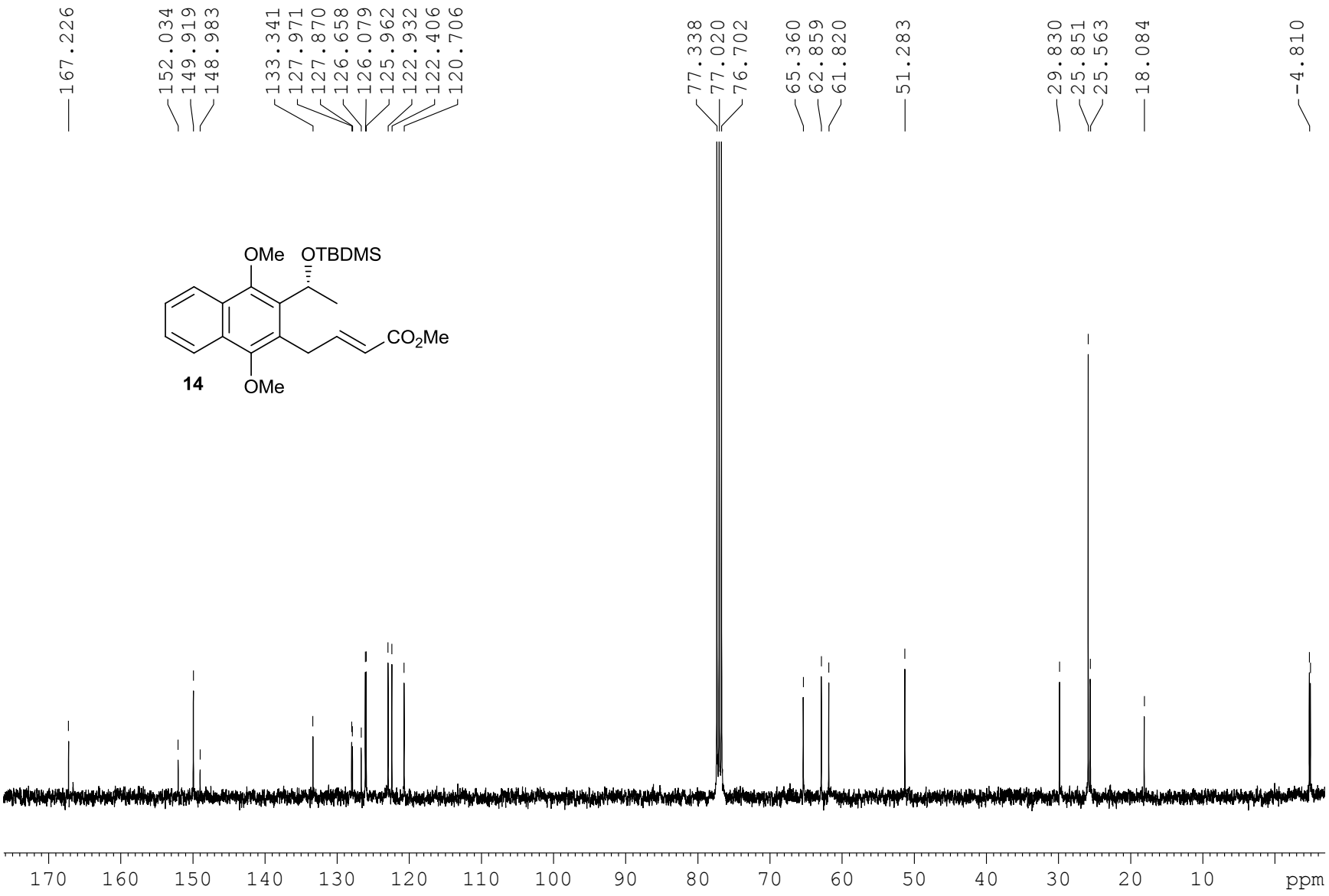


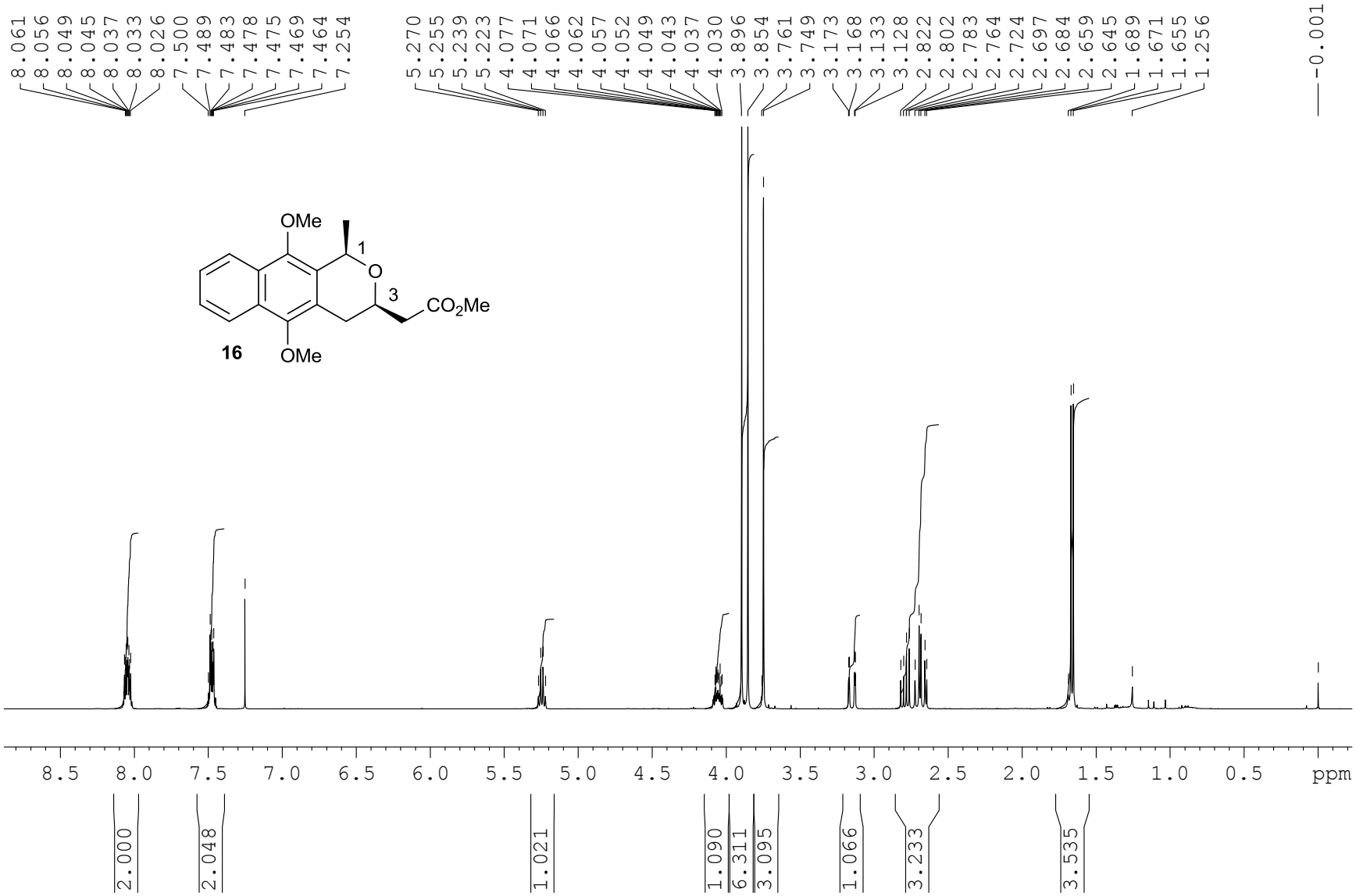


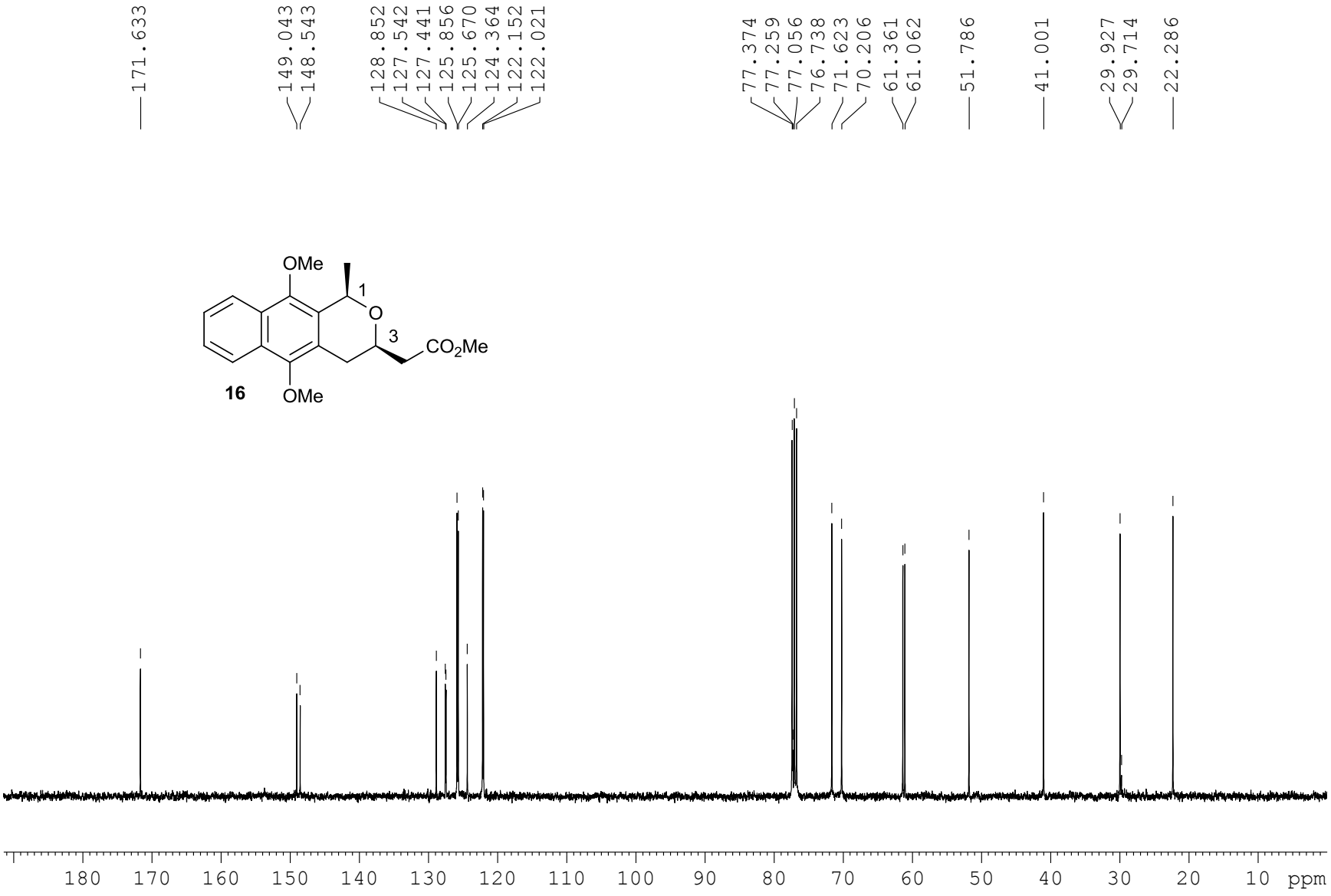


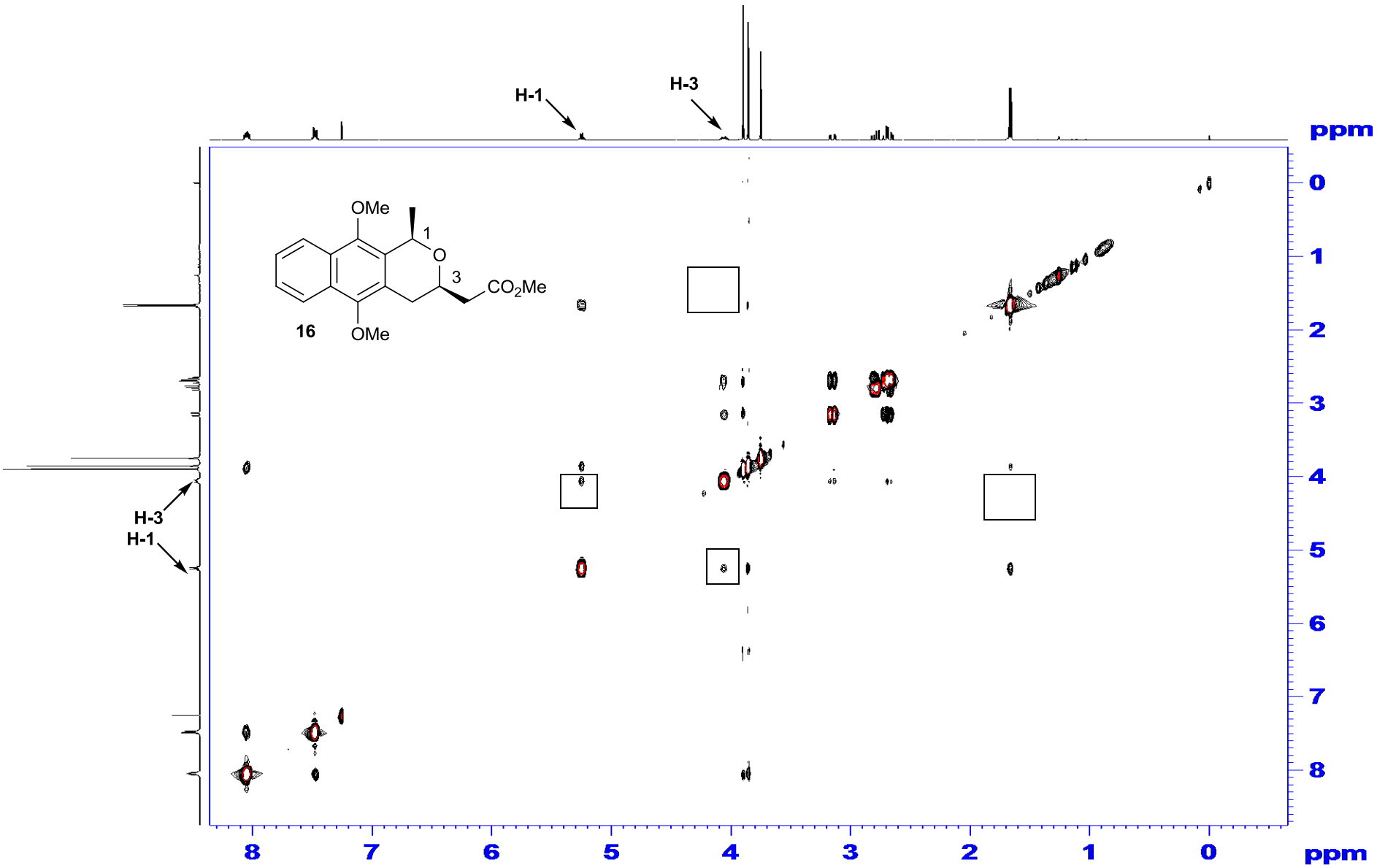


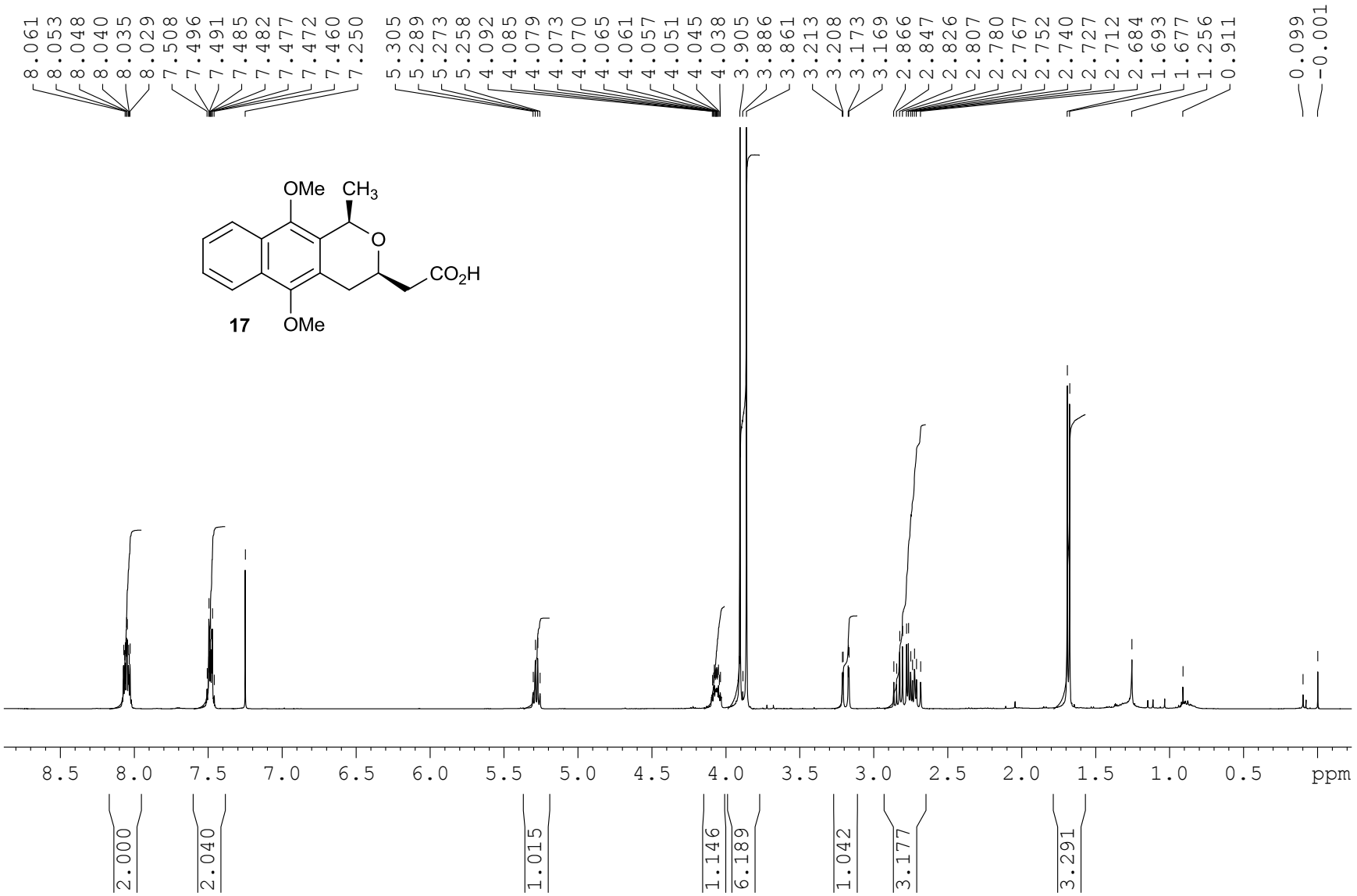


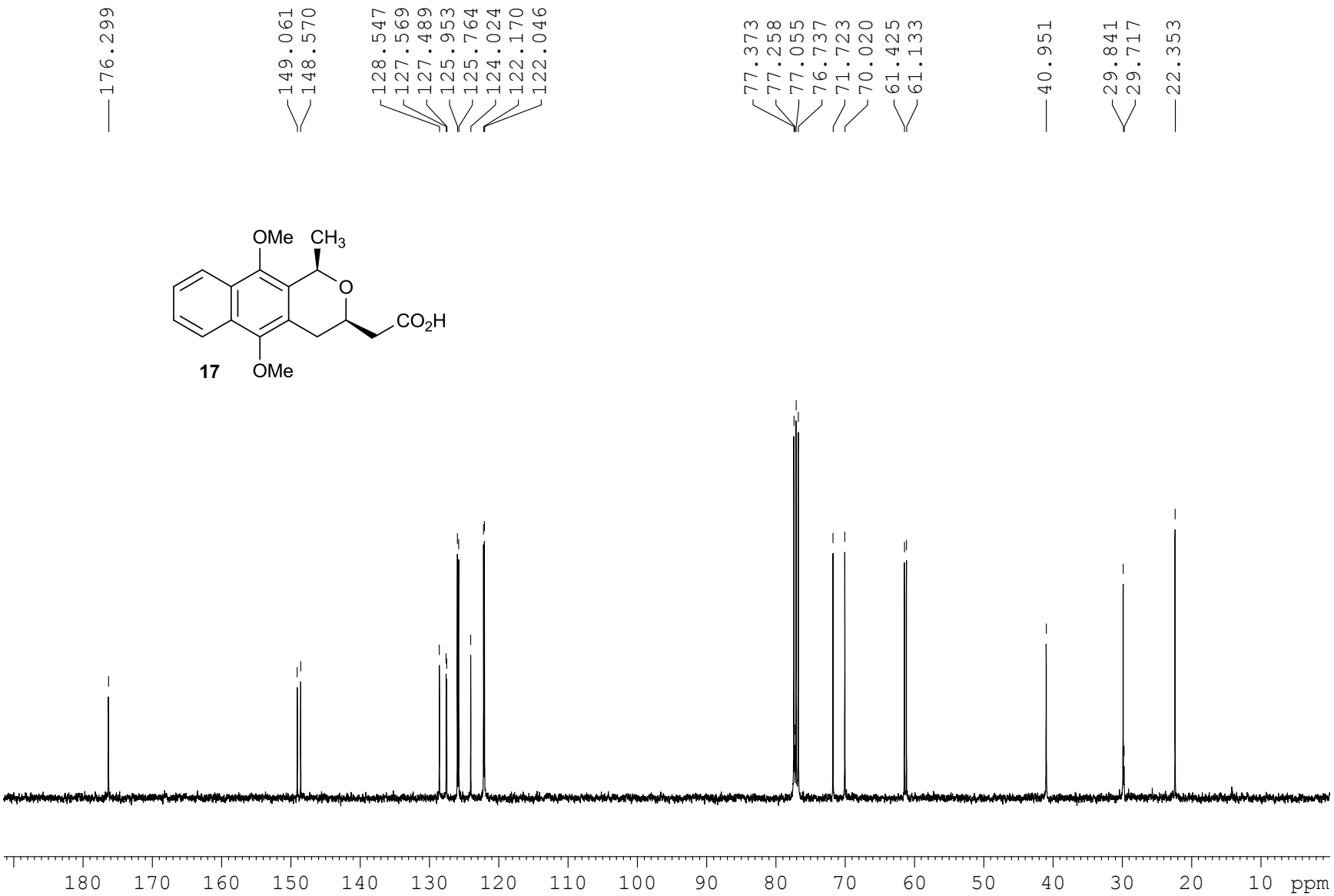












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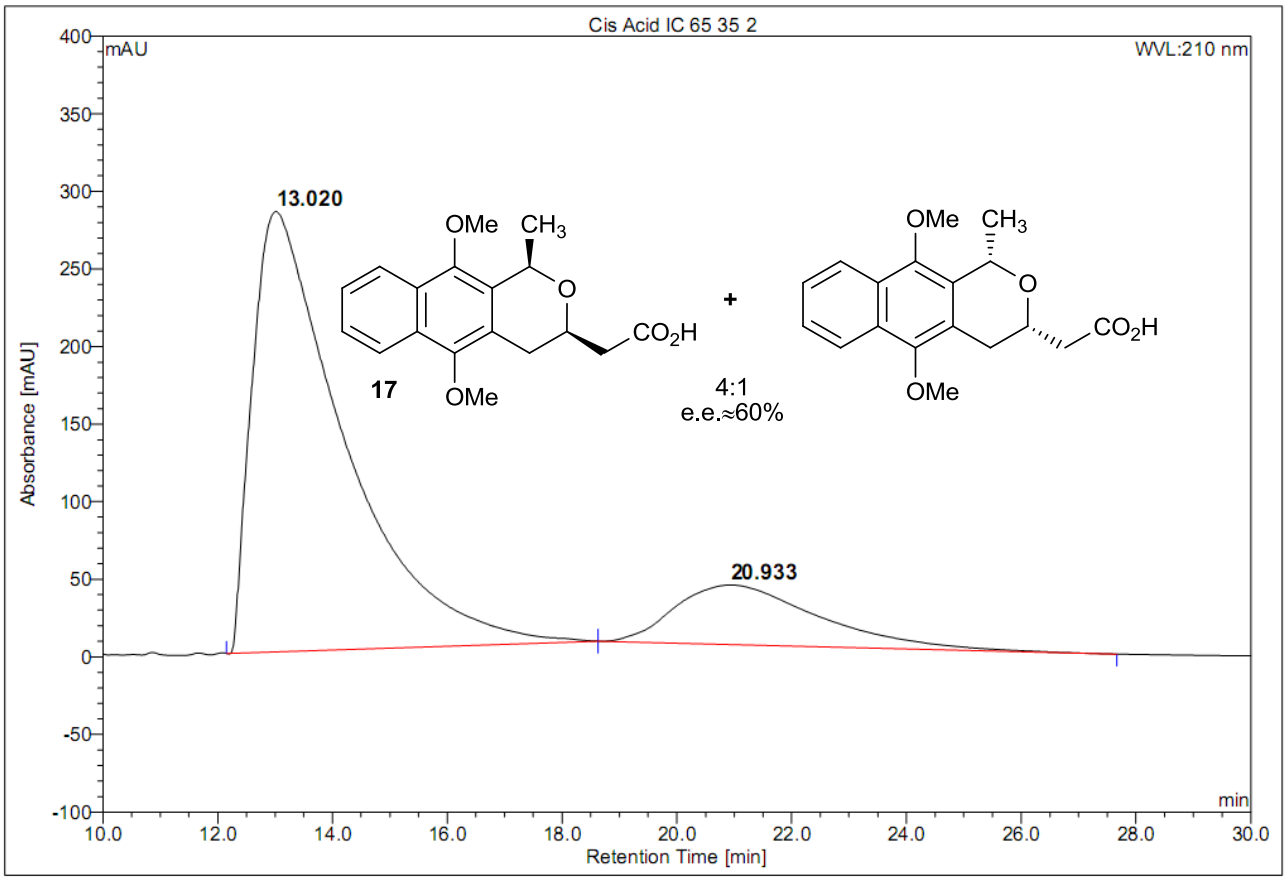
1 Cis Acid IC 65 35 2

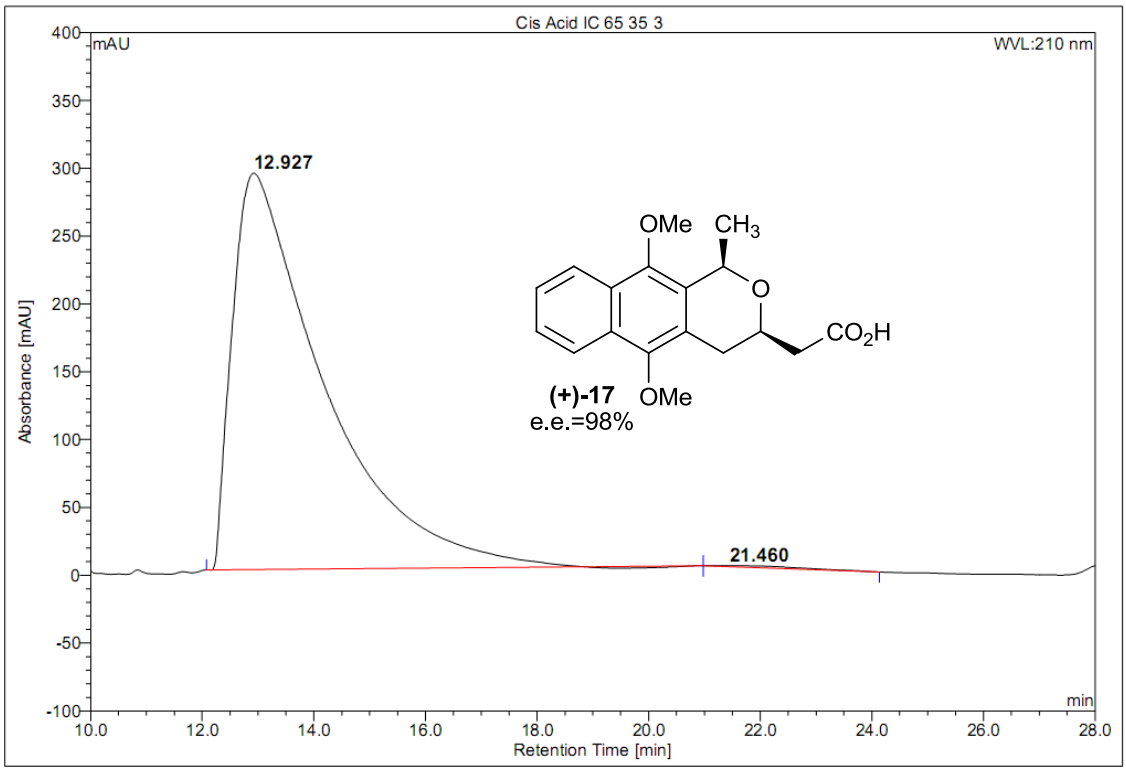
Sample Name:	**Cis Acid IC 65 35 2**	*Injection Volume:*	**20.0**
Vial Number:	**2**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**210**
Control Program:	**alcohol 65_35**	*Bandwidth:*	**n.a.**
Quantif. Method:	**default**	*Dilution Factor:*	**1.0000**
Recording Time:	**2/4/2011 12:20**	*Sample Weight:*	**1.0000**
Run Time (min):	**30.07**	*Sample Amount:*	**1.0000**



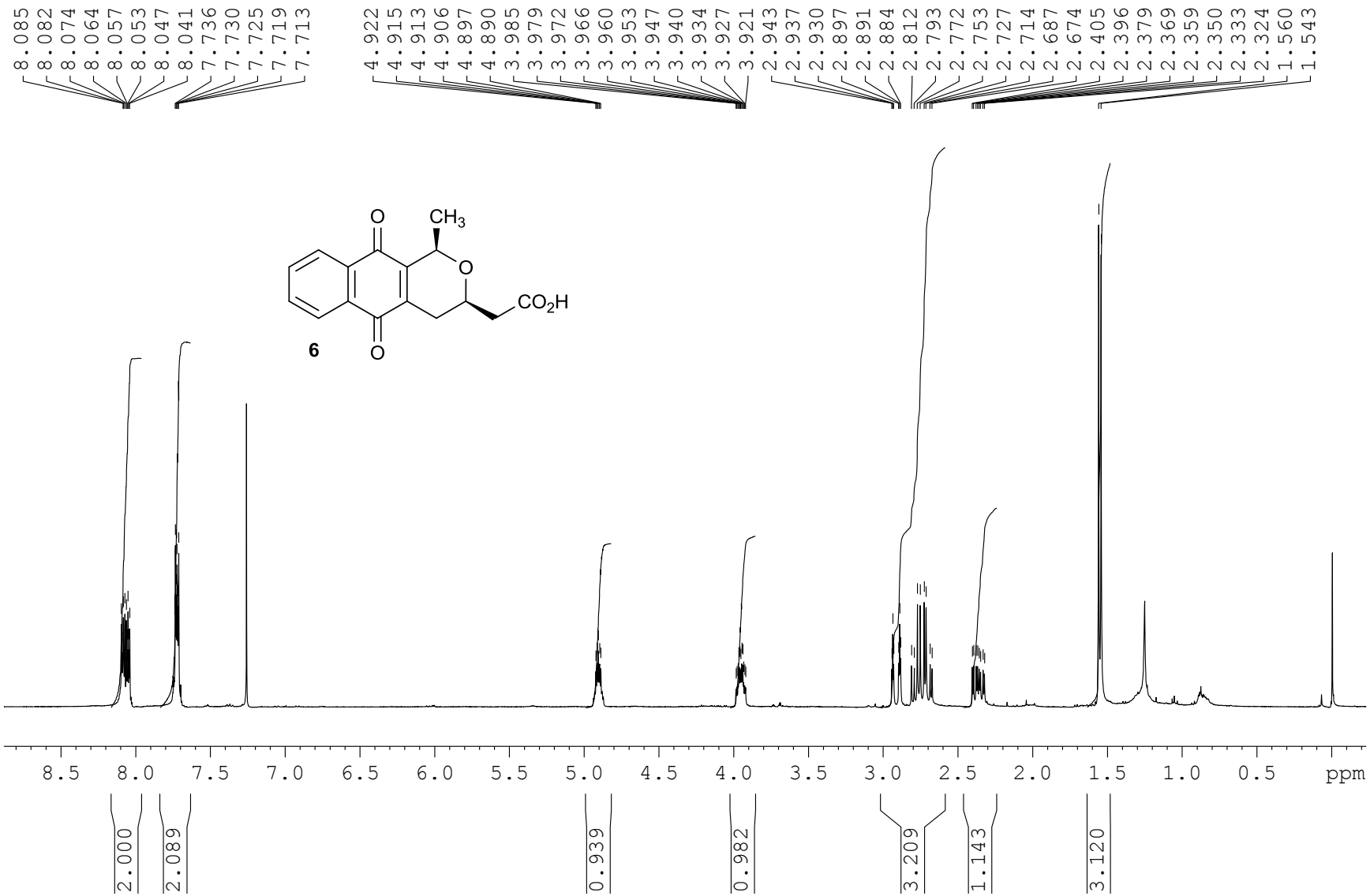
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13.02	n.a.	283.761	529.741	82.64	n.a.	BMb*
2	20.93	n.a.	38.272	111.280	17.36	n.a.	bMB*
Total:			322.033	641.021	100.00	0.000	

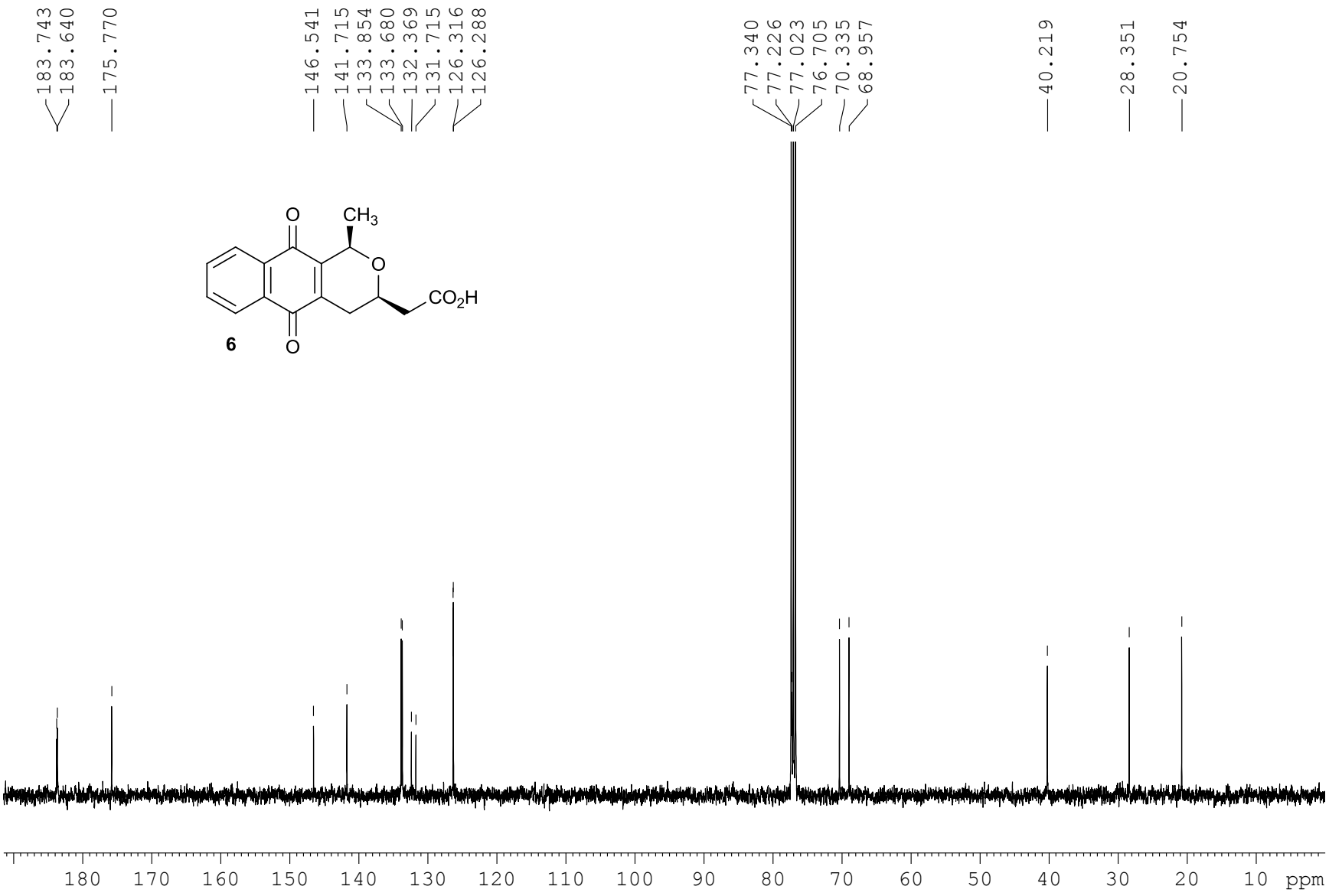
1 Cis Acid IC 65 35 3

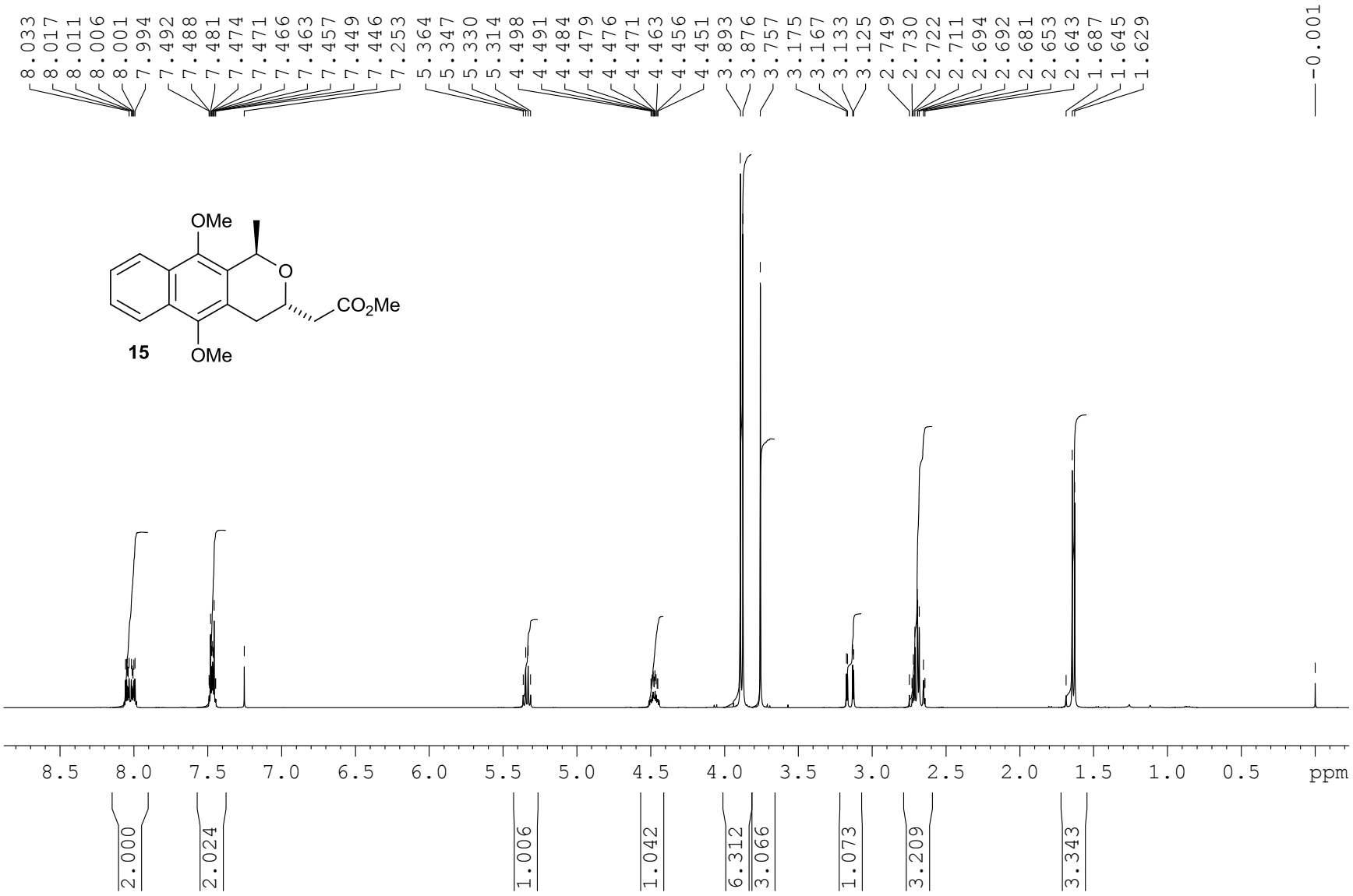
Sample Name:	**Cis Acid IC 65 35 3**	*Injection Volume:*	**20.0**
Vial Number:	**2**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**210**
Control Program:	**alcohol 65_35**	*Bandwidth:*	**n.a.**
Quantif. Method:	**default**	*Dilution Factor:*	**1.0000**
Recording Time:	**2/4/2011 12:55**	*Sample Weight:*	**1.0000**
Run Time (min):	**31.00**	*Sample Amount:*	**1.0000**

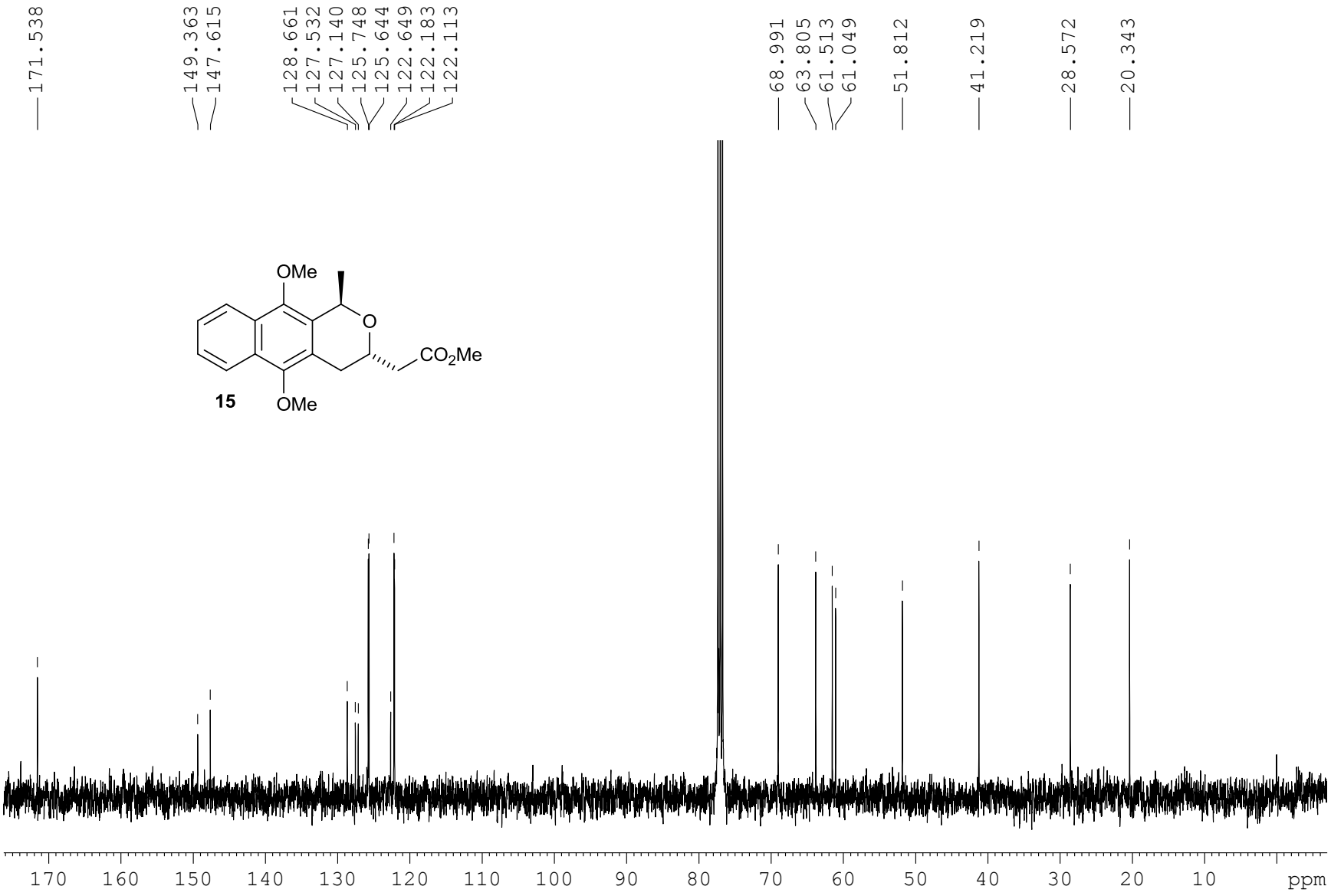


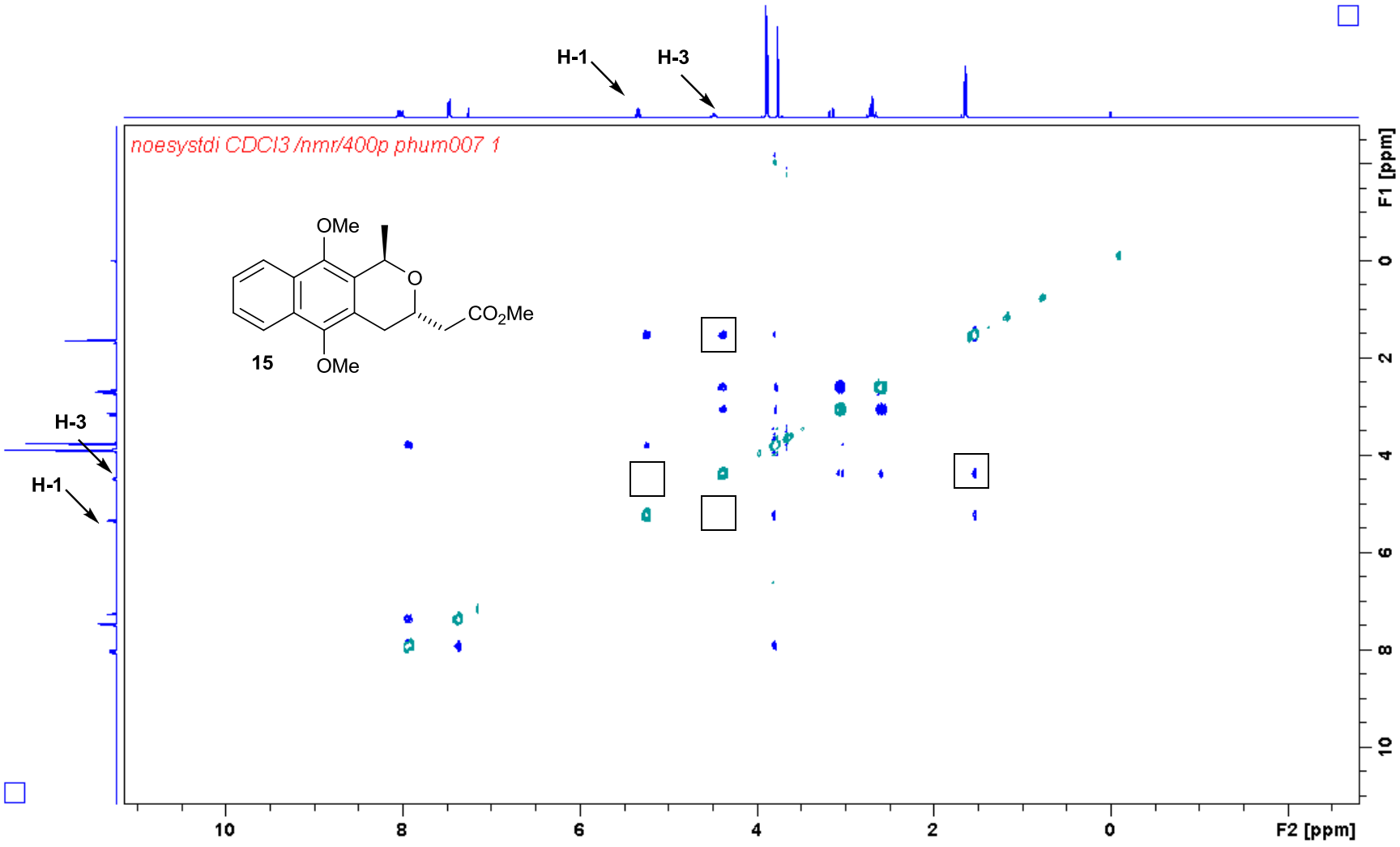
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12.93	n.a.	292.266	552.464	99.61	n.a.	BMb*
2	21.46	n.a.	0.822	2.186	0.39	n.a.	bMB*
Total:			293.088	554.650	100.00	0.000	

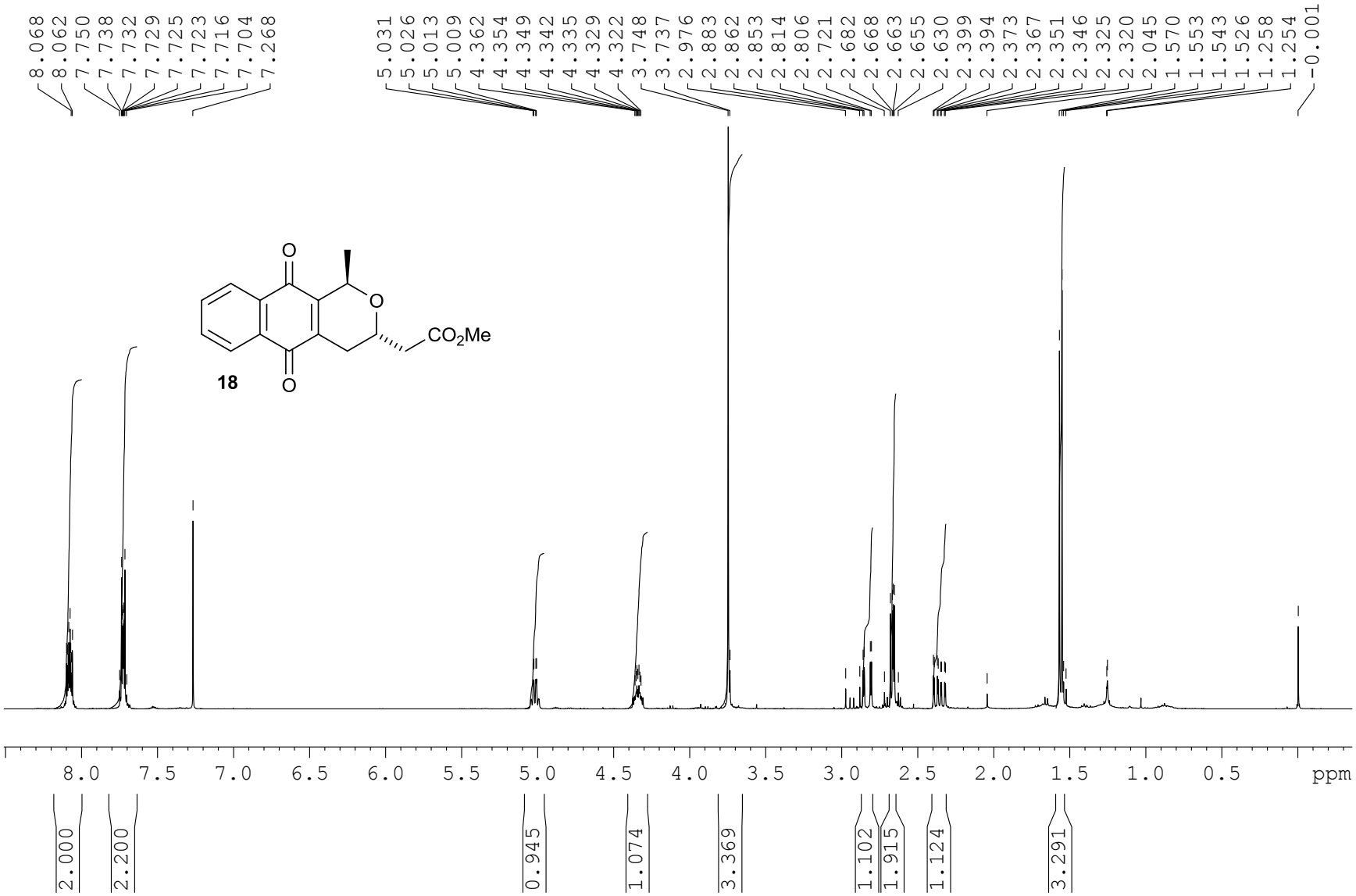


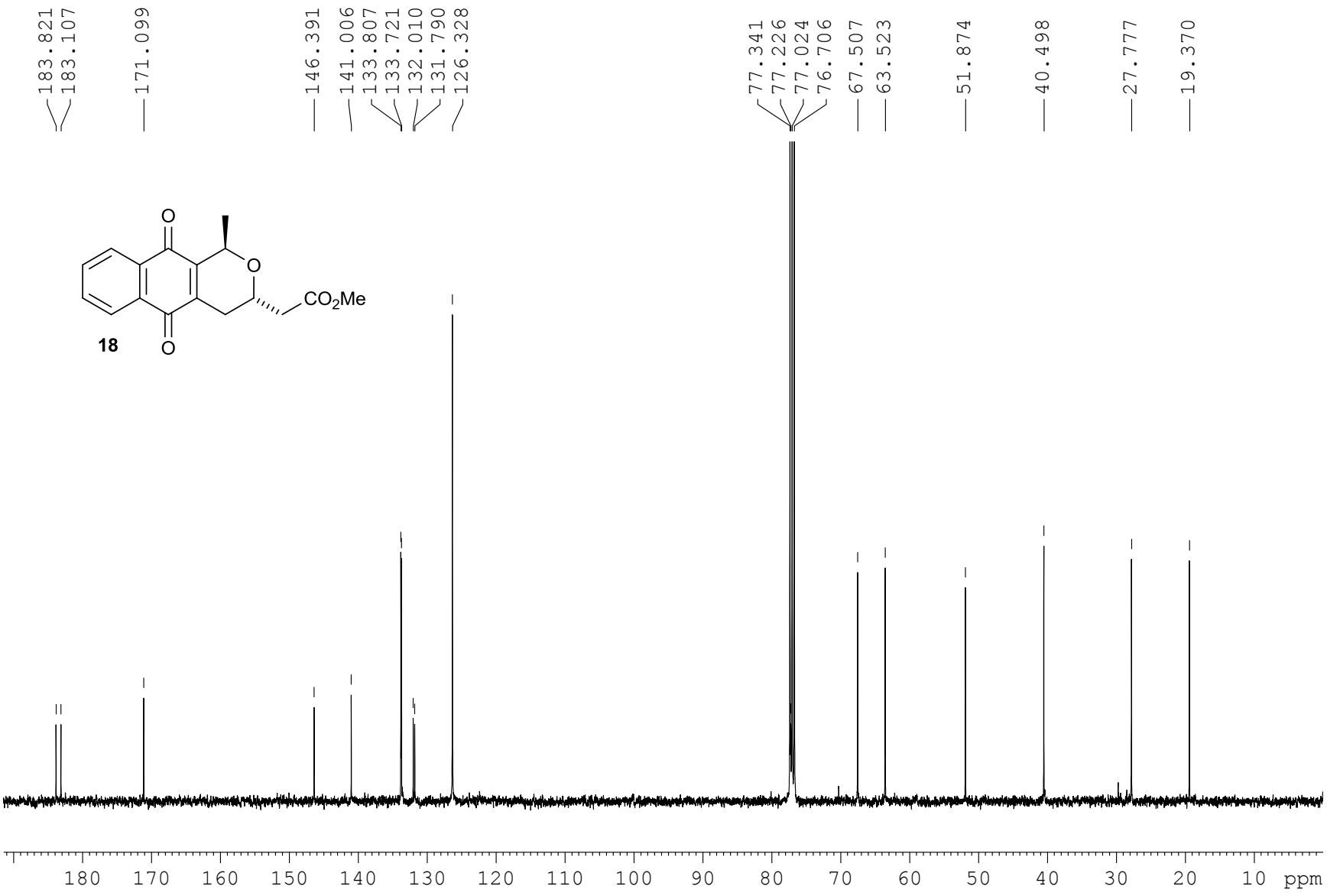


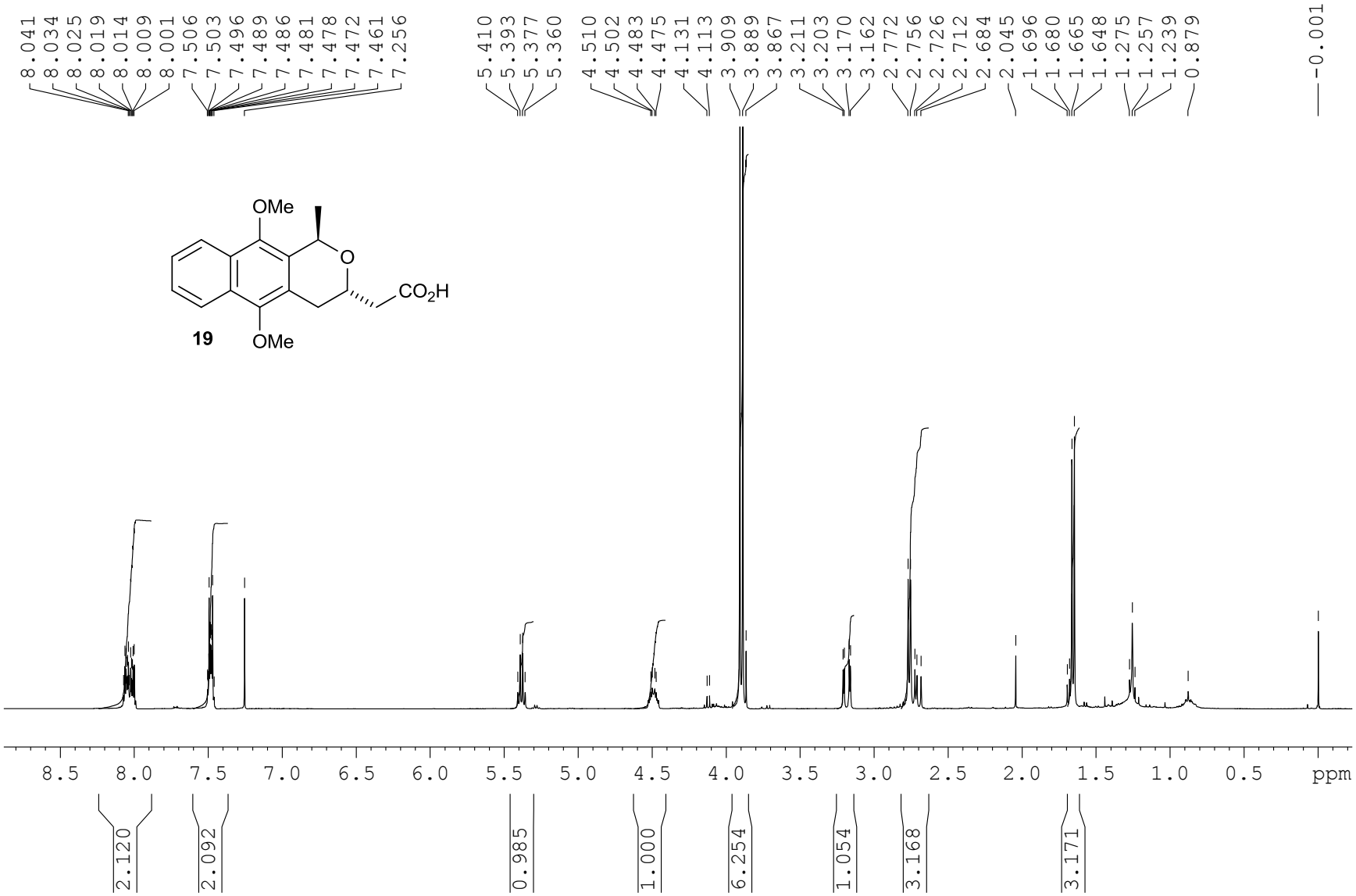


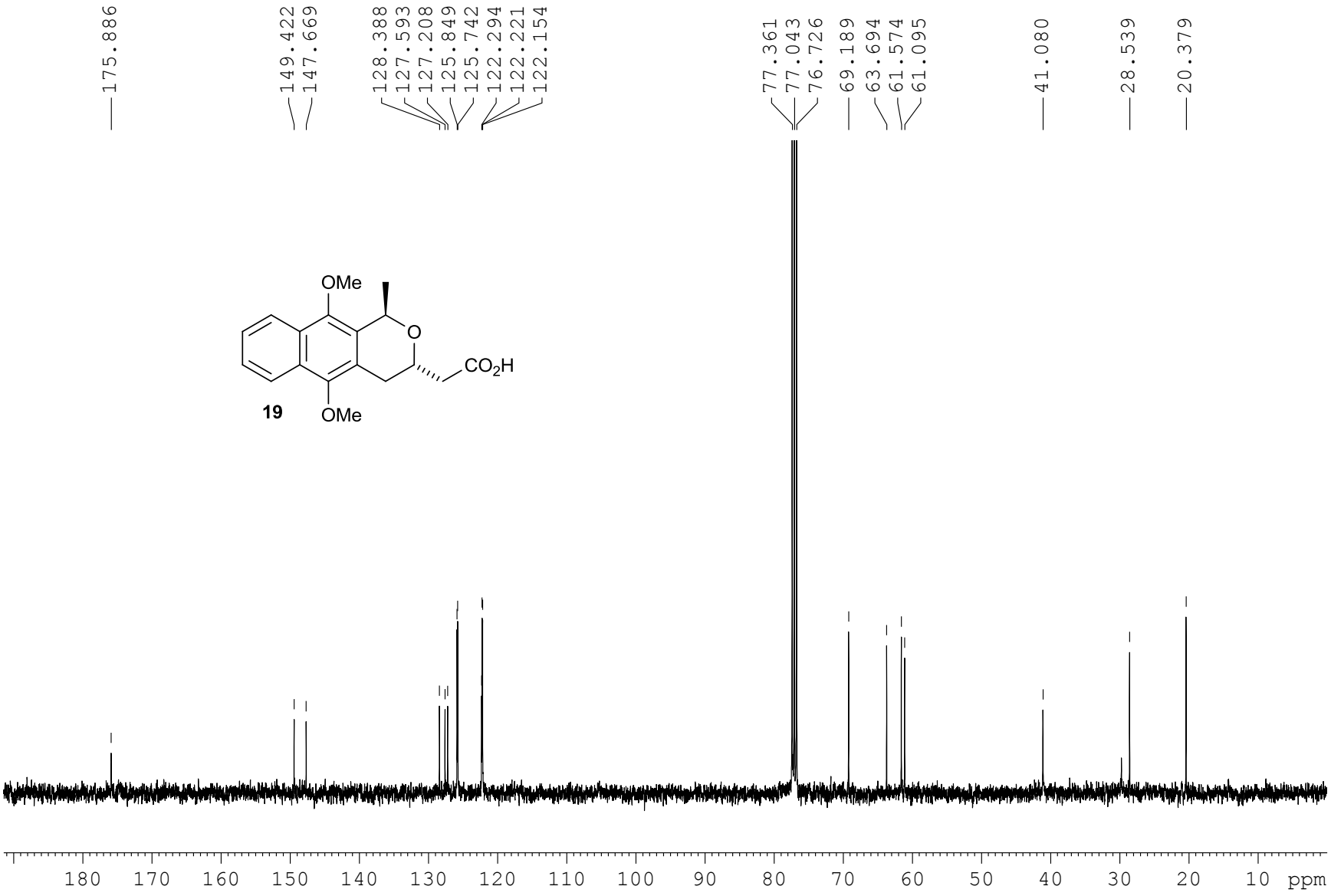


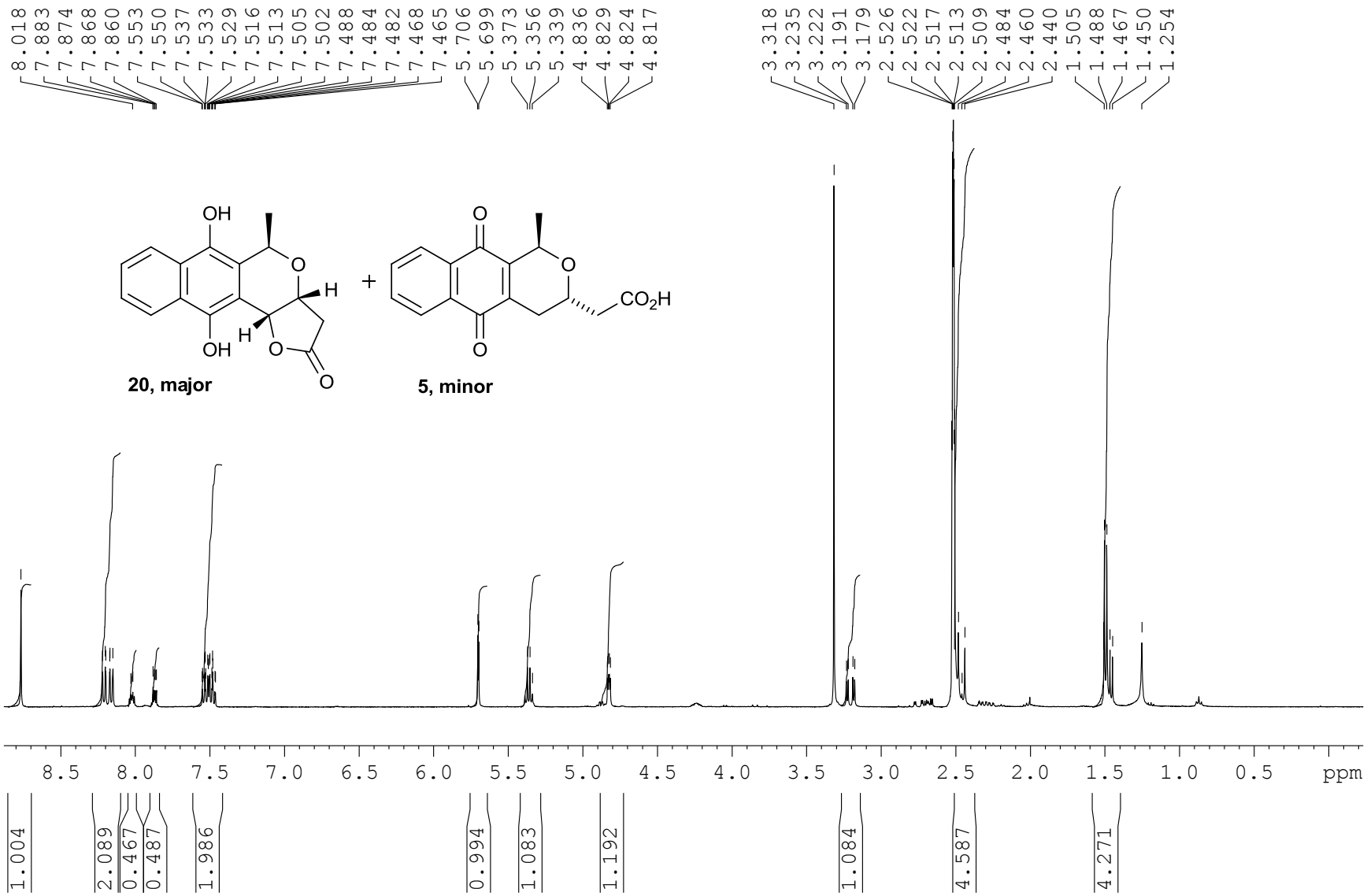


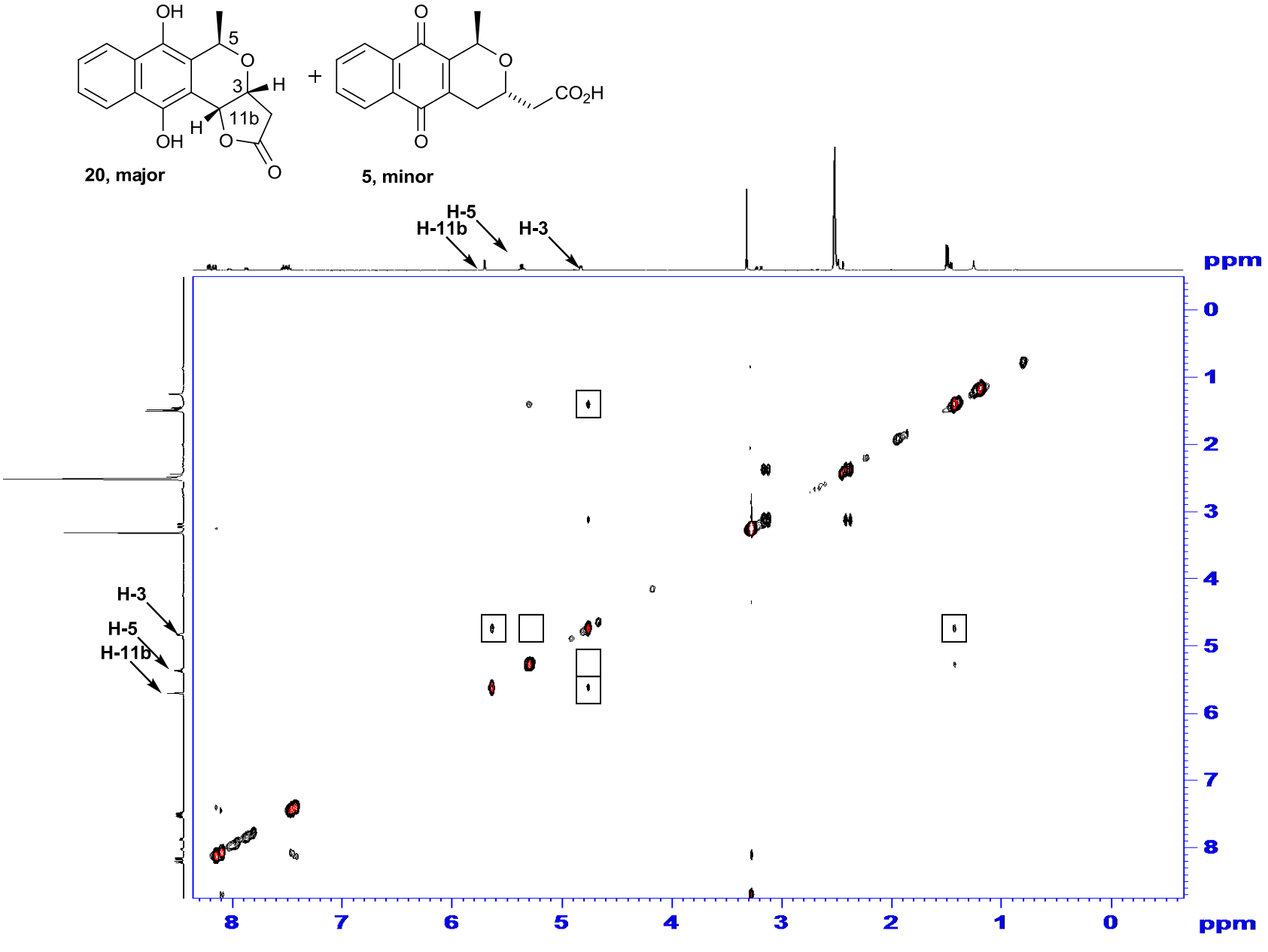


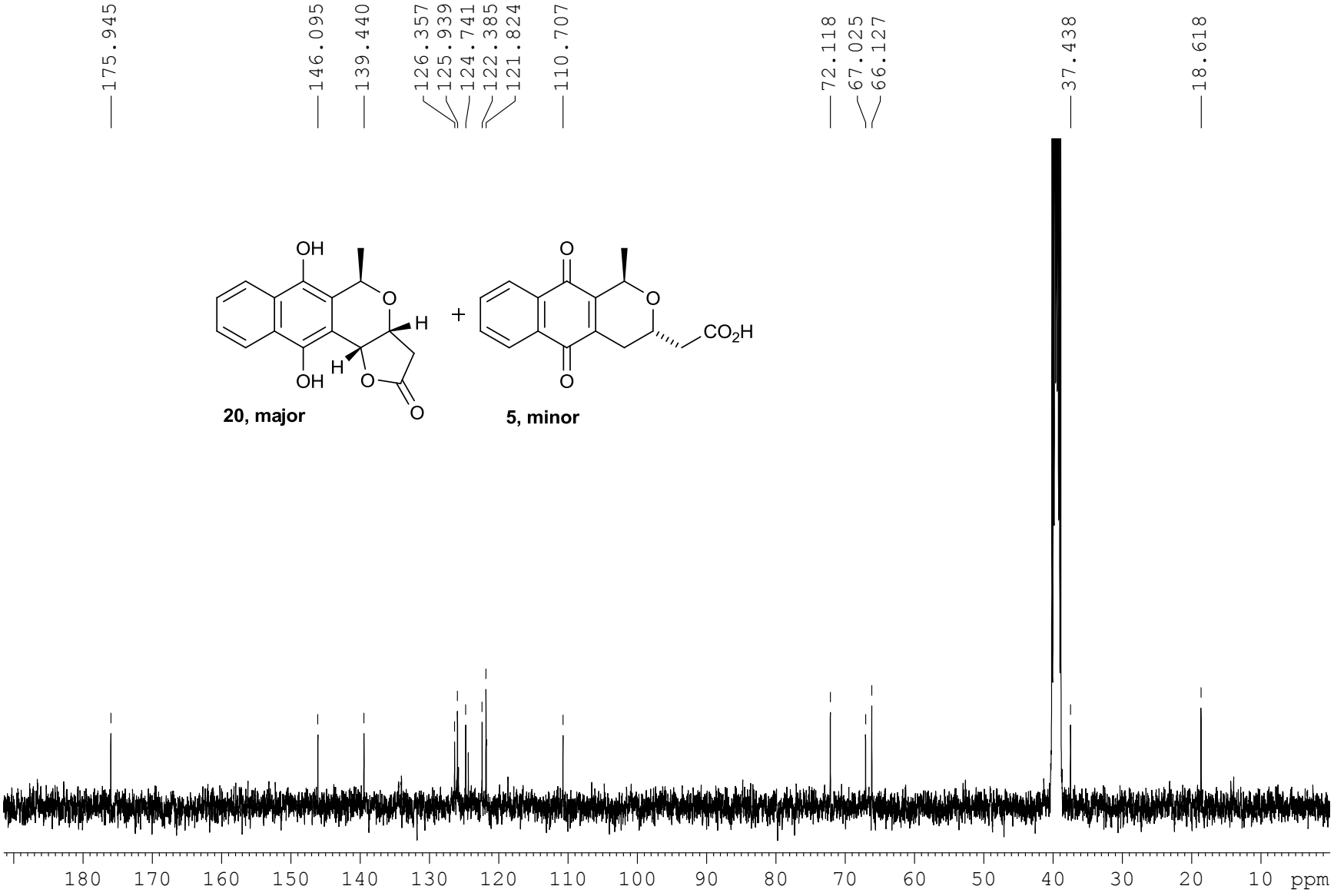


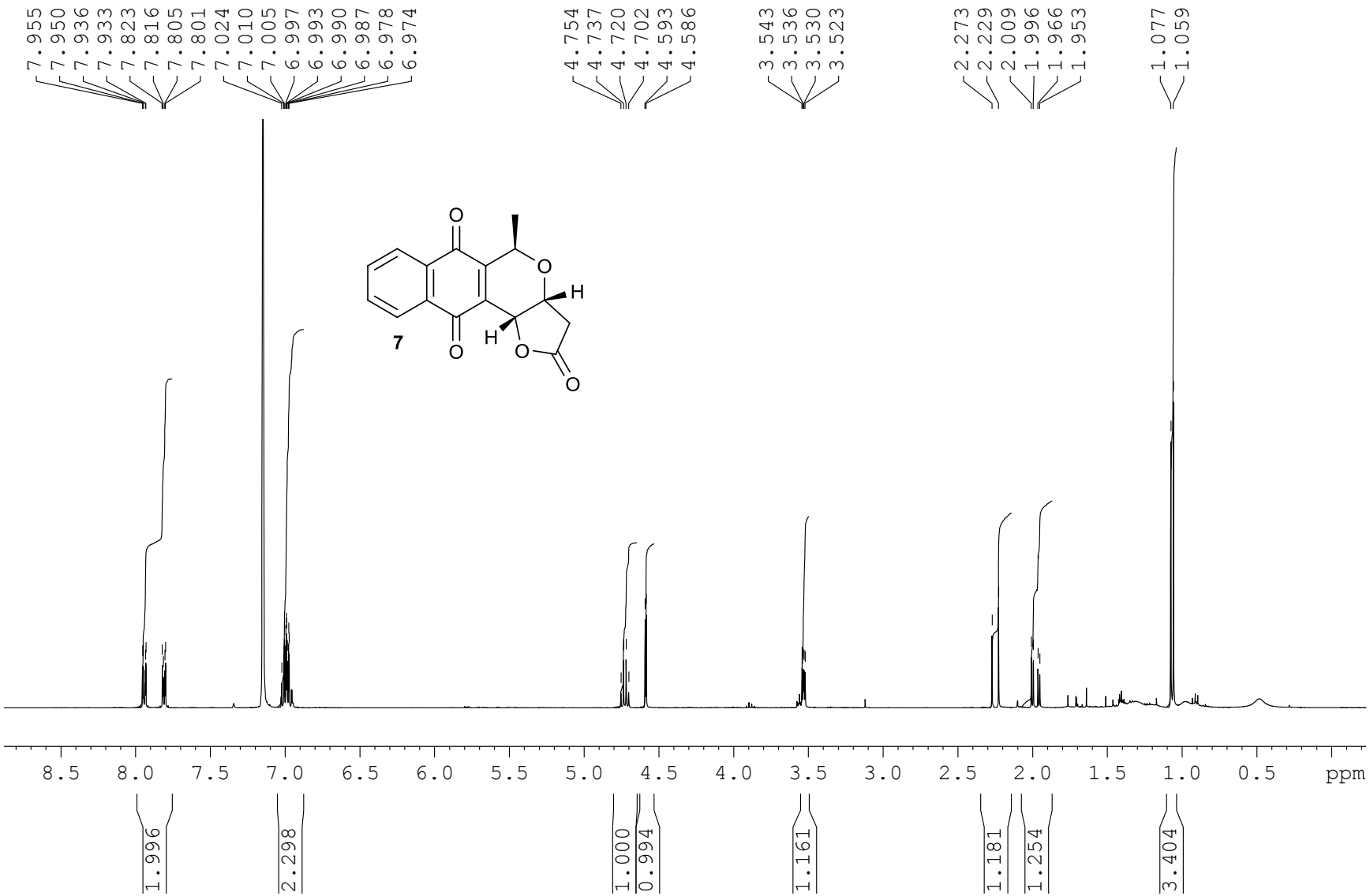


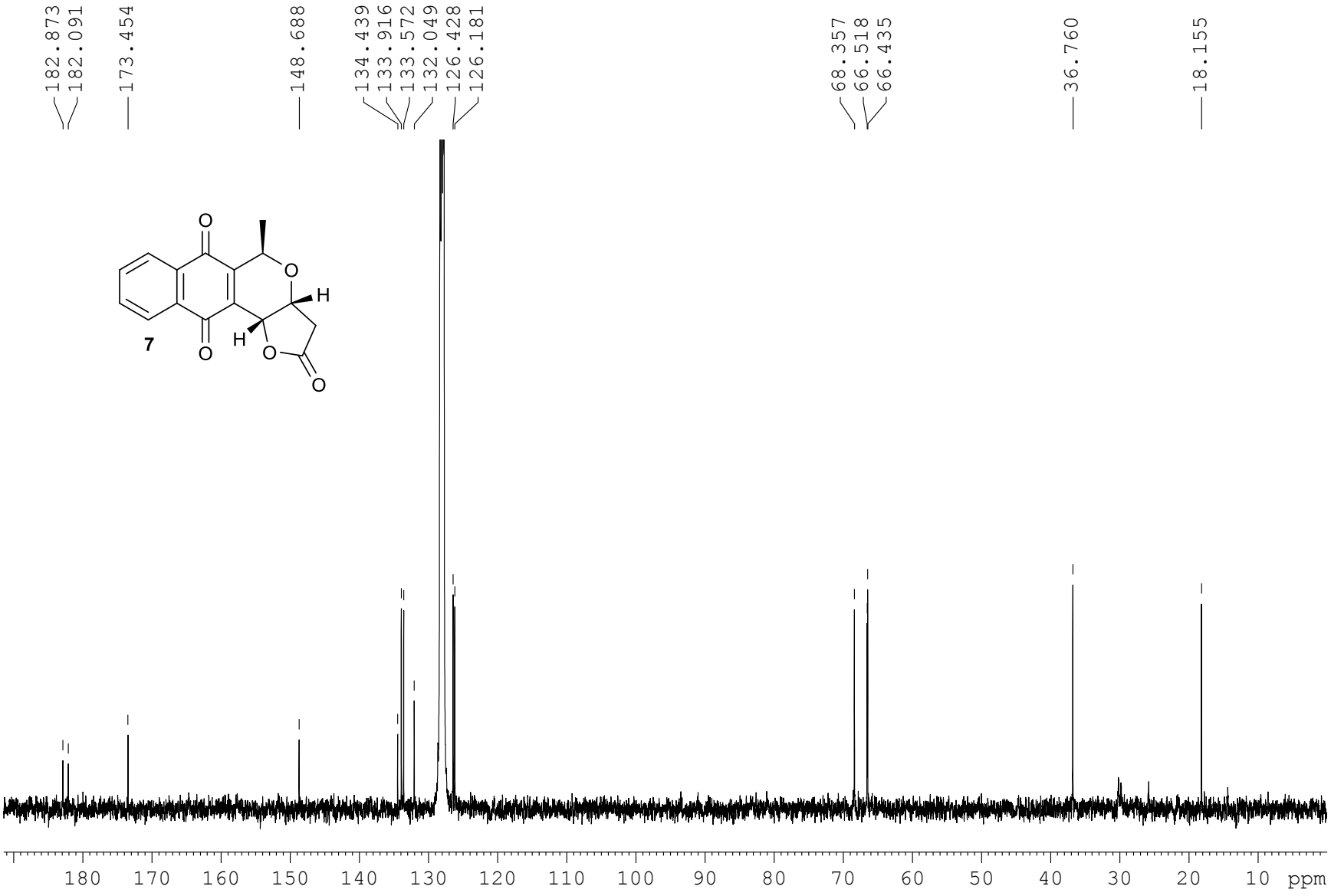


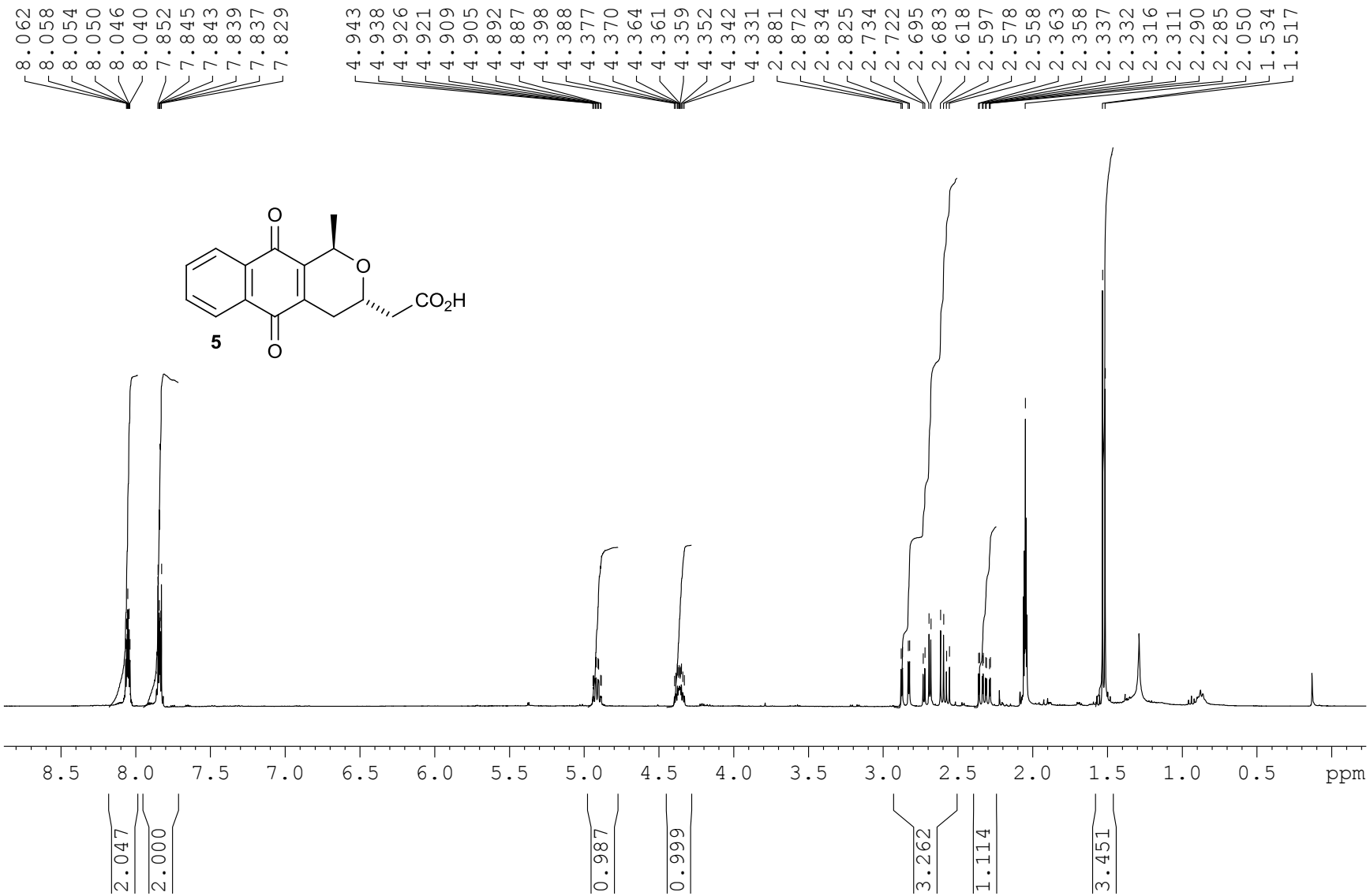


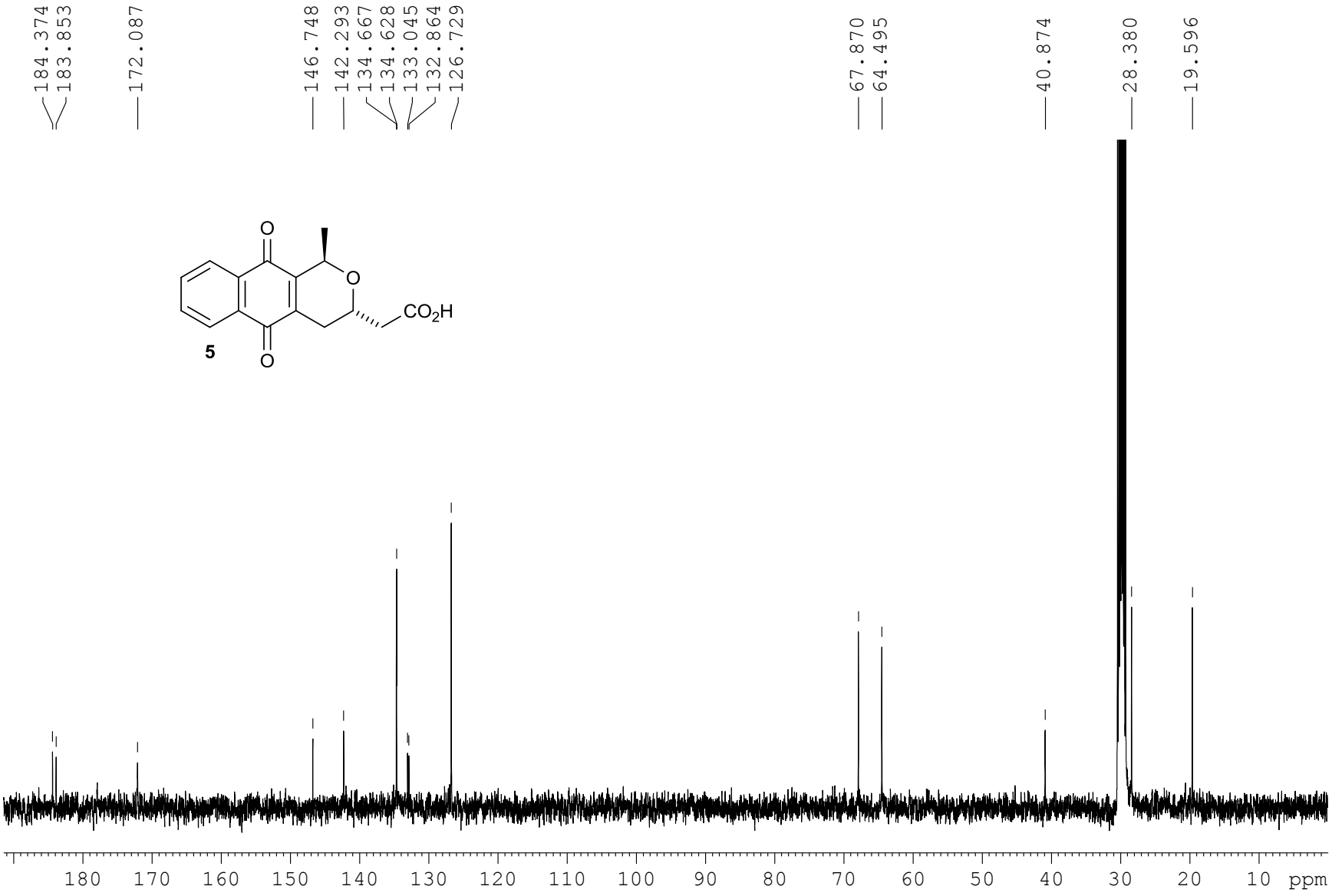


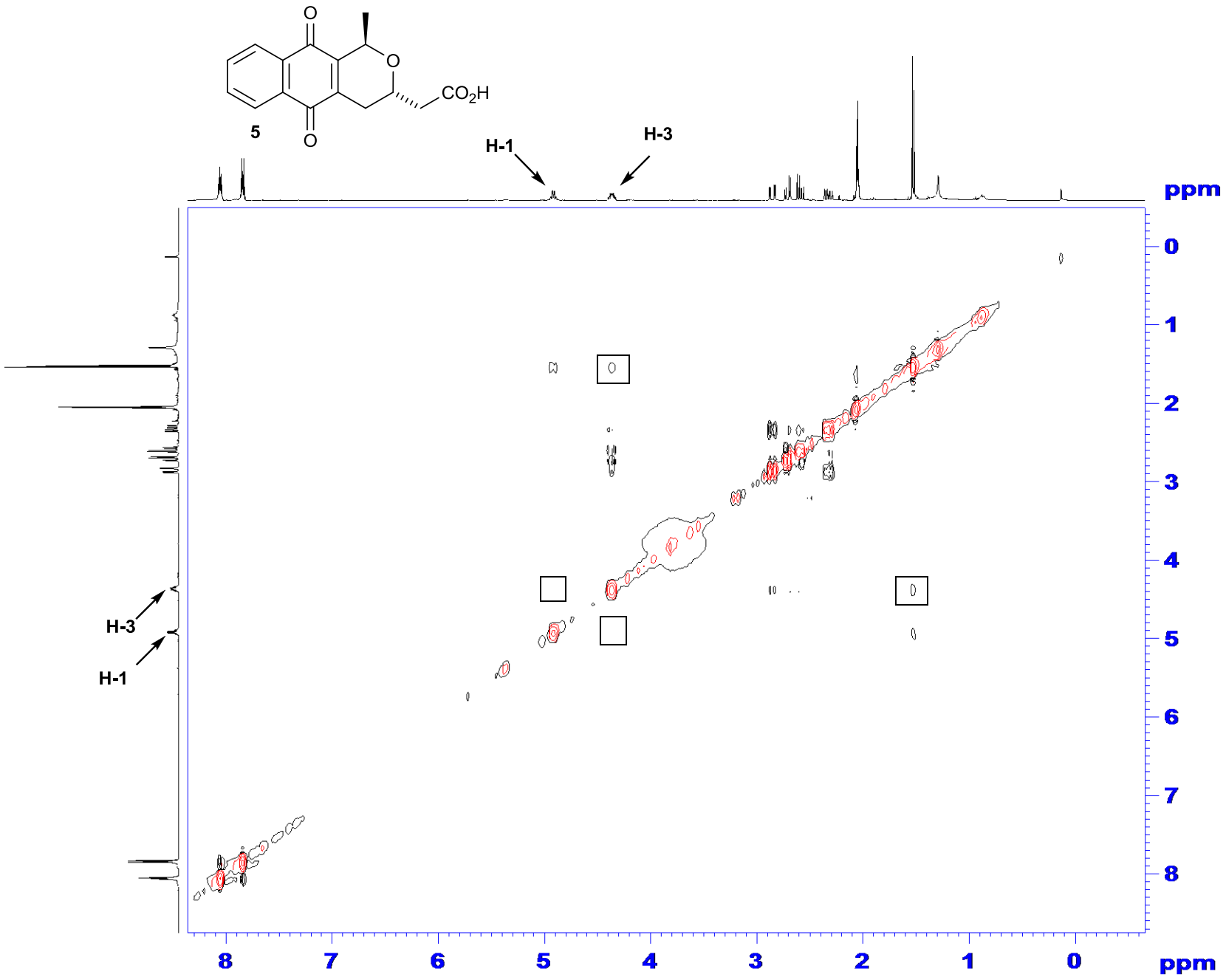






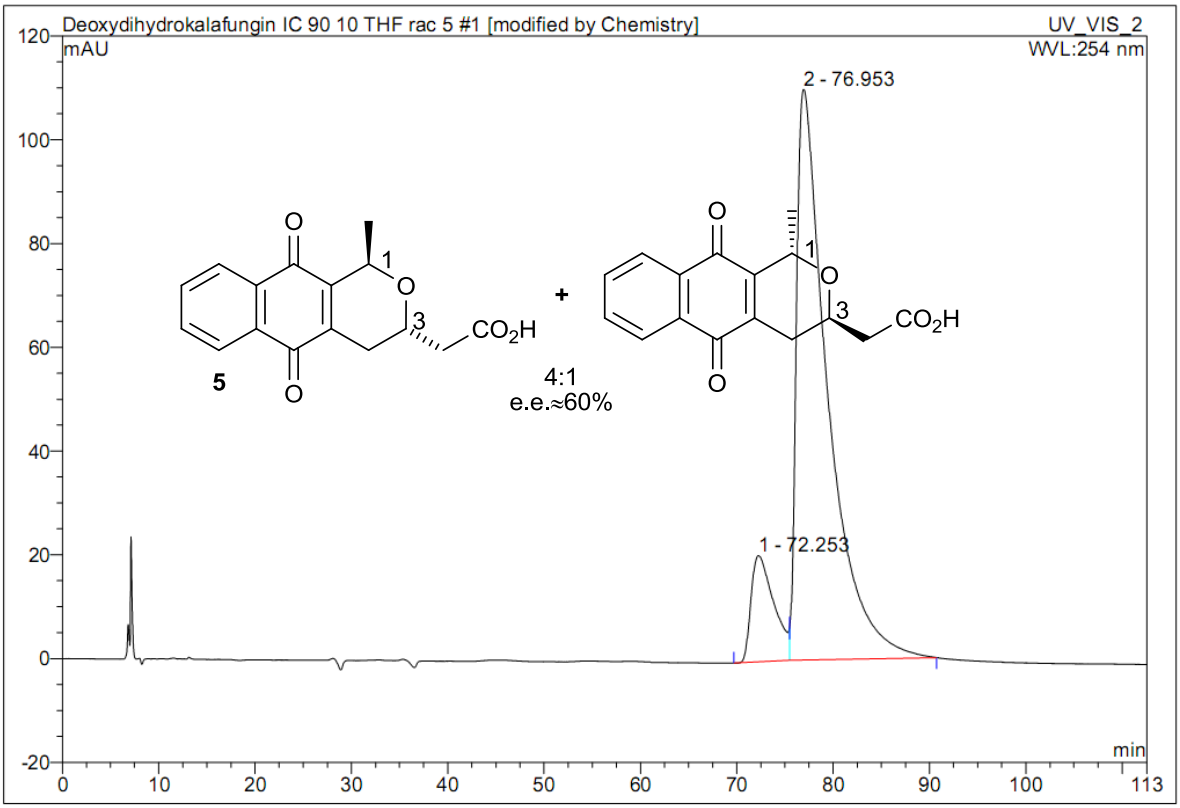






1 Deoxydihydrokalafungin IC 90 10 THF rac 5

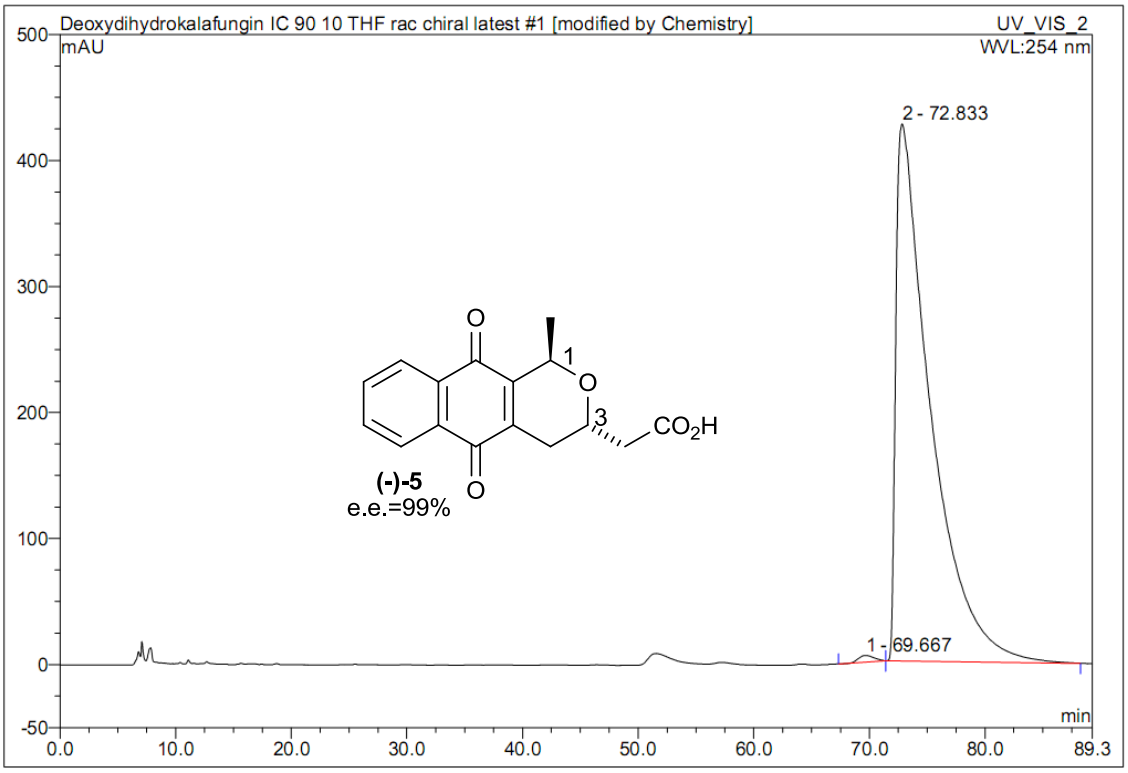
Sample Name:	**Deoxydihydrokalafungin IC 90 10 THF rac 5**	*Injection Volume:*	**20.0**
Vial Number:	**2**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**254**
Control Program:	**alcohol 65_35**	*Bandwidth:*	**n.a.**
Quantif. Method:	**default**	*Dilution Factor:*	**1.0000**
Recording Time:	**3/31/2011 11:01**	*Sample Weight:*	**1.0000**
Run Time (min):	**112.54**	*Sample Amount:*	**1.0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	72.25	n.a.	20.470	56.335	12.00	n.a.	BM *
2	76.95	n.a.	109.956	413.018	88.00	n.a.	MB*
Total:			130.426	469.353	100.00	0.000	

1 Deoxydihydrokalafungin IC 90 10 THF rac chiral latest

Sample Name:	**Deoxydihydrokalafungin IC 90 10 THF rac c**	*Injection Volume:*	**20.0**
Vial Number:	**2**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**254**
Control Program:	**alcohol 65_35**	*Bandwidth:*	**n.a.**
Quantif. Method:	**default**	*Dilution Factor:*	**1.0000**
Recording Time:	**3/31/2011 14:35**	*Sample Weight:*	**1.0000**
Run Time (min):	**89.28**	*Sample Amount:*	**1.0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	69.67	n.a.	5.266	8.214	0.55	n.a.	BMb*
2	72.83	n.a.	426.188	1478.830	99.45	n.a.	bMB*
Total:			431.454	1487.044	100.00	0.000	