Asymmetric Total Synthesis of (-)-Plicatic Acid via a Highly Enantioselective and Diastereoselective Nucleophilic Epoxidation of Acyclic Trisubstitued Olefins

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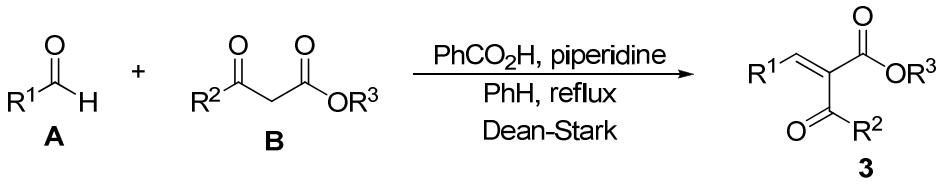
Supporting Information

Contents

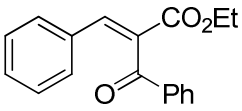
General Information. ^{1}H NMR spectra were recorded on a Varian Inova 400 (400 MHz) or Varian Inova 500 (500 MHz) spectrometers. Chemical shifts are reported in ppm down field from TMS, using TMS (0.00 ppm) or residual $CDCl_3$ (7.26 ppm) as an internal standard. Data are reported as: (b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant in Hz, integration). ^{13}C NMR spectra were recorded on a Varian Inova 400 (100 MHz) or Varian Inova 500 (125 MHz) spectrometers, using proton decoupling unless otherwise noted. Chemical shifts are reported in ppm down field from TMS, using the central resonance of $CDCl_3$ (77.00 ppm) or CD_3OD (49.00 ppm) as the internal standard. Infrared spectra were recorded on a Perkin Elmer FT-IR spectrometer and are reported in frequency of absorption. Mass spectrometry was performed by Mass Spectrometry Laboratory, University of Illinois at Urbana-Champaign. Optical rotations were measured on a Jasco Digital Polarimeter with a sodium lamp. CD spectra were recorded on Jasco J-810 circular dichroism spectrometer.

Materials. Unless otherwise noted, reagents and solvents were commercially available and used without further purification. Anhydrous DMF was obtained by distillation from calcium hydride. Anhydrous THF was obtained by distillation from sodium metal (benzophenone indicator).

General Procedure for the Preparation of 3 [1]



The mixture of aldehyde **A** (11.0 mmol equiv.), 1,3-dicarbonyl compound **B** (10.0 mmol), benzoic acid (1.0 mmol), and piperidine (1.0 mmol) in benzene (50.0 mL) was heated at reflux in a round bottom flask connected to a Dean-Stark apparatus until the starting materials were consumed as indicated by TLC analysis. After being cooled down to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford (*E*)-**3** in 40-60% yield. The stereochemistry of **3c-g** was assigned based on the $^{3}J_{C\text{-}H}$ coupling constants of C_{ketone}-H and C_{ester}-H.[2]



(*E*)-Ethyl 2-benzoyl-3-phenylacrylate (3b) [3]

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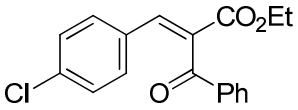
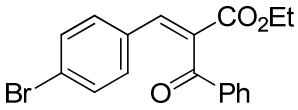
[1] Allen, C. F. H.; Spangler, F. W. *Org. Syn.* **1955**, *Coll. Vol. 3*, 377.
[2] Kingsbury, C. A.; Draney, D.; Sopchik, A.; Rissler, W.; Durham, D. *J. Org. Chem.* **1978**, *41*, 3863.
[3] Li, Z.; Li, H.; Guo, X.; Cao, L.; Yu, R.; Li, H.; Pan, S. *Org. Lett.* **2008**, *10*, 803.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 6.8 Hz, 2H), 7.56-7.20 (m, 9H), 4.20 (q, *J* = 7.2 Hz, 2H), 1.15 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.66, 164.99, 142.60, 136.09, 133.87, 132.78, 131.24, 130.35, 130.17, 129.12, 128.80, 128.76, 61.54, 14.00; **IR** (thin film) 3061, 2980, 1720, 1702, 1674, 1624, 1597, 1449, 1253, 1231, 1198, 1092 cm^{-1}; **LRMS (ESI)**: 303 (M + Na^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{16}O_3Na$ (M + Na), 303.0997. Found 303.0997.



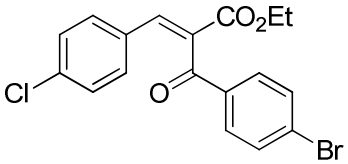
(*E*)-Ethyl 2-benzoyl-3-(4-chlorophenyl)acrylate (3c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94-7.90 (m, 2H), 7.59-7.20 (m, 7H), 4.22 (q, *J* = 7.2 Hz, 2H), 1.17 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.38, 164.76, 141.04, 136.44, 135.90, 134.09, 131.84, 131.30, 129.09, 128.90, 61.68, 14.00; **IR** (thin film) 3061, 2981, 1720, 1673, 1624, 1592, 1492, 1252, 1093, 1013 cm^{-1}; **LRMS (ESI)**: 315 (M + H^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{16}ClO_3$ (M + H), 315.0788. Found 315.0794. $^3J_{C\text{-}H}$ = 9.9 Hz for C_{ketone}-H, $^3J_{C\text{-}H}$ = 7.6 Hz for C_{ester}-H.



(*E*)-Ethyl 2-benzoyl-3-(4-bromophenyl)acrylate (3d)

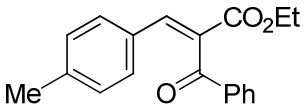
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.2 Hz, 2H), 7.88 (s, 1H), 7.58-7.41 (m, 3H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.21 (d, *J* = 7.6 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.24, 164.65, 140.99, 135.78, 134.03, 131.95, 131.92, 131.62, 131.38, 128.99, 128.82, 124.81, 61.59, 13.91; **IR** (thin film) 2978, 2366, 2346, 1720, 1707, 1702, 1672, 1250, 1230, 1196, 1073, 1010, 818 cm^{-1}; **LRMS (ESI)**: 359, 361 (M + H^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{16}BrO_3$ (M + H), 359.0283. Found 359.0280. $^3J_{C\text{-}H}$ = 9.9 Hz for C_{ketone}-H, $^3J_{C\text{-}H}$ = 7.6 Hz for C_{ester}-H.



(*E*)-Ethyl 2-(4-bromobenzoyl)-3-(4-chlorophenyl)acrylate (3e)

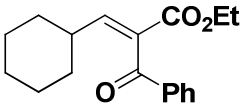
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.17, 164.34, 141.21, 136.48, 134.51, 132.15, 131.14, 131.11, 130.94, 130.97, 129.36,

129.02, 61.63, 13.90; **IR** (thin film) 2980, 2361, 2345, 1720, 1702, 1672, 1584, 1252, 1195, 1011 cm^{-1}; **LRMS (ESI)**: 393 (M + H^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{15}ClBrO_3$ (M + H), 392.9893. Found 392.9898. $^3J_{C\text{-}H}$ = 9.9 Hz for C_{ketone}-H, $^3J_{C\text{-}H}$ = 7.7 Hz for C_{ester}-H.



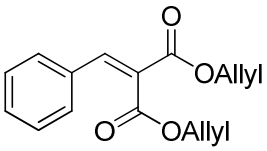
(*E*)-Ethyl 2-benzoyl-3-p-tolylacrylate (3f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 2.25 (s, 3H), 1.15 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.16, 165.36, 142.82, 141.19, 136.42, 134.06, 130.53, 130.35, 130.24, 129.78, 129.35, 129.04, 61.64, 21.60, 14.26; **IR** (thin film) 2961, 2930, 2870, 2362, 2345, 1719, 1702, 1676, 1253, 1230, 1200, 1183, 1085 cm^{-1}; **LRMS (ESI)**: 295 (M + H^+); **HRMS (ESI)**: Exact mass calcd for $C_{19}H_{19}O_3$ (M + H), 295.1334. Found 295.1324. $^3J_{C\text{-}H}$ = 9.8 Hz for C_{ketone}-H, $^3J_{C\text{-}H}$ = 7.6 Hz for C_{ester}-H.



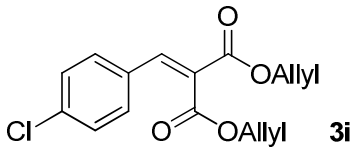
(*E*)-Ethyl 2-benzoyl-3-cyclohexylacrylate (3g)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 2H), 7.61-7.44 (m, 3H), 6.90 (d, *J* = 10.8 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.12 (m, 1H), 1.67-1.01 (m, 13H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.49, 164.79, 152.80, 136.91, 133.54, 131.72, 128.98, 128.59, 61.03, 38.55, 31.60 (2), 25.47, 24.90 (2), 13.90; **IR** (thin film) 2929, 2853, 1724, 1675, 1639, 1597, 1449, 1252, 1233, 1221 cm^{-1}; **LRMS (ESI)**: 287 (M + H^+, 100); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{23}O_3$ (M +H), 287.1647. Found 287.1635. $^3J_{C\text{-}H}$ = 9.8 Hz for C_{ketone}-H, $^3J_{C\text{-}H}$ = 7.6 Hz for C_{ester}-H.



Diallyl 2-benzylidenemalonate (3h)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.47-7.35 (m, 5H), 6.01-5.86 (m, 2H), 5.39-5.24 (m, 4H), 4.78-4.74 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.21, 163.28, 142.96, 132.69, 131.55, 131.15, 130.69, 129.53, 128.80, 125.60, 119.33, 118.43, 66.28, 66.04; **IR** (thin film) 2980, 2962, 2363, 1730, 1629, 1257, 1198 cm^{-1}; **LRMS (ESI)**: 295 (M + Na^+, 100); **HRMS (ESI)**: Exact mass calcd for $C_{16}H_{16}O_4Na$ (M + Na), 295.0946. Found 295.0944.



3i

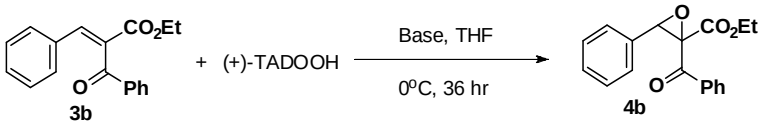
Diallyl 2-(4-chlorobenzylidene)malonate (3i)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.41-7.34 (m, 4H), 6.00-5.86 (m, 2H), 5.39-5.26 (m, 4H), 4.78-4.75 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.91, 163.43, 141.41, 136.76, 131.42, 131.12, 131.00, 130.73, 129.10, 126.10, 119.55, 118.53, 66.36, 66.12; **IR** (thin film) 3086, 3021, 2947, 1734, 1648, 1630, 1591, 1492, 1385, 1254, 1197, 1093, 1060 cm^{-1}; **LRMS (ESI)**: 329 ($M + Na^+$); **HRMS (ESI)**: Exact mass calcd for $C_{16}H_{15}ClO_4Na$ (M + Na), 329.0557. Found 329.0550.

General Procedure for Base Screening

The base (0.010 mmol) was added to a stirring mixture of (+)-(*S, S*)-TADOOH (0.12 mmol) and **3b** (0.10 mmol) in THF (0.50 mL) via a syringe at 0 ^oC under air. After 36 hours, the reaction mixture was allowed to pass rapidly through a plug (20 mm) of silica gel. The silica gel plug was washed with ethyl acetate (10 mL). The filtrate was concentrated under reduced pressure. The residue was subjected to ^{1}H NMR and HPLC analysis to determine the conversion. The ee of **4b** was determined by HPLC analysis [Chiralcel AD-H column, Hexanes/*i*-PrOH = 98/2, 1.0 mL/min, 254 nm, 15 ^oC, t_R (1) ≈ 22 min, t_R (2) ≈ 33 min]. The results were listed in Table 1.

Table 1. Base Screening



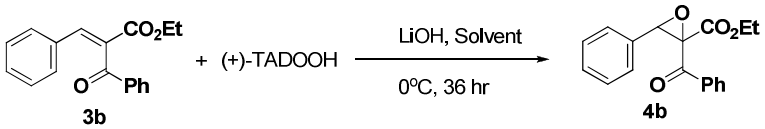
3b **4b**

Entry	Base (10 mol %)	conv. (%, HPLC)	ee (%)	Major peak
1	LiOH (5.0 M, aq.)	99	92	t_R (2)
2	Li_2CO_3 (5.0 M, aq.)	trace	/	/
3	NaOH (5.0 M, aq.)	12	44	t_R (1)
4	Na_2CO_3 (5.0 M, aq.)	trace	/	/
5	KOH (5.0 M, aq.) (indissolvable)	trace	/	/
6	K_2CO_3 (5.0 M, aq.)	21	73	t_R (2)
7	CsOH (5.0 M, aq.)	94	24	t_R (1)
8	Cs_2CO_3 (5.0 M, aq.)	92	30	t_R (1)
9	DBU	35	42	t_R (2)
10	DABCO	4	/	/
11	Et_3N	4	/	/

General Procedure for Solvent Screening

An aqueous solution of LiOH (0.010 mmol, 2.0 μL, 5.0 M) was added via a syringe at 0 ^{o}C to a stirring solution of (+)-TADOOH (0.12 mmol) and **3b** (0.10 mmol) in a solvent (0.50 mL) specified in Table 2 under air. The resulting reaction mixture was stirred for 36 hr, after which the reaction mixture was allowed to pass rapidly through a plug (20 mm) of silica gel. The silica gel was washed with ethyl acetate (10 mL). The filtrate was concentrated under reduced pressure. The residue was subjected to ^{1}H NMR and HPLC analysis to determine the conversion. The ee of **4b** was determined by HPLC analysis [Chiralcel AD-H column, Hexanes/*i*-PrOH = 98/2, 1.0 mL/min, 254 nm, 15 ^{o}C, t_R (1) ≈ 22 min, t_R (2) ≈ 33 min]. The results were listed in Table 2.

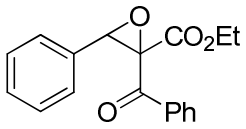
Table 2. Solvent Screening



Entry	Solvent (0.20 M)	conv. (%, HPLC)	ee (%)	Major peak
1	THF	99	92	t_R (2)
2	Et_2O	77	80	t_R (2)
3	DCM	12	45	t_R (1)
4	Toluene (slurry)	35	39	t_R (2)
5	EtOH	4	/	t_R (1)
6	EtOAc	50	93	t_R (2)
7	DMF (slurry)	43	32	t_R (2)

General Procedure for the Asymmetric Epoxidation of 3

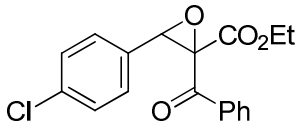
An aqueous solution of LiOH (0.010 mmol, 2.0 μL, 5.0 M) was added via a syringe to a solution of (+)-TADOOH (0.12 mmol) and **3** (0.10 mmol) in THF (0.50 mL) at 0 ^{o}C (or indicated temperature), under air. The reaction mixture was stirred vigorously at this temperature for indicated time. After the reaction was complete as indicated by TLC analysis, the reaction mixture was allowed to pass rapidly through a plug (20 mm) of silica gel. The silica gel was washed with ethyl acetate (10 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography or preparative TLC to give pure epoxide **4**.



(-)-Ethyl 2-benzoyl-3-phenyloxirane-2-carboxylate (4b)

0 °C, 1.5 days, 98% yield, 92% ee.

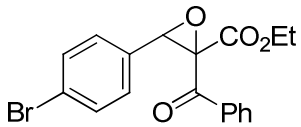
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.19 (s, 5H), 4.73 (s, 1H), 4.24 (q, *J* = 6.8 Hz, 2H), 1.17 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.81, 166.40, 135.15, 133.81, 132.04, 128.87, 128.70, 128.45, 128.27, 126.21, 65.80, 62.97, 62.74, 13.73; **IR** (thin film) 2925, 2853, 2360, 2342, 1748, 1730, 1693, 1450, 1256, 1235, 696 cm^{-1}; **LRMS (ESI)**: 319 (M + Na^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{16}O_4Na$ (M + Na), 319.0946. Found 319.0933; $[\alpha]_D^{25}$ = -15.3° (*c* 1.0, $CHCl_3$, 92% ee), 92% ee was determined by HPLC analysis [Chiralcel OD-H column, Hexanes/*i*-PrOH = 96/4, 1.0 mL/min, 220 nm, 20 °C, t_R (1) = 11.3 min (major), t_R (2) = 20.6 min (minor)].



(+)-Ethyl 2-benzoyl-3-(4-chlorophenyl)oxirane-2-carboxylate (4c)

0 °C, 2 days, 99% yield, 94% ee.

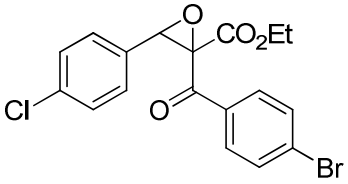
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 2H), 4.70 (s, 1H), 4.26 (q, *J* = 6.8 Hz, 2H), 1.18 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.62, 166.24, 135.05, 134.91, 134.11, 130.73, 128.79, 128.67, 128.65, 127.66, 65.80, 62.96, 62.36, 13.80; **IR** (thin film) 2360, 2334, 1748, 1733, 1691, 1256, 1234 cm^{-1}; **LRMS (ESI)**: 353 (M + Na^+, 100); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{15}ClO_4Na$ (M + Na), 353.0557. Found 353.0554; $[\alpha]_D^{25}$ = +0.8° (*c* 1.0, $CHCl_3$, 94% ee), 94% ee was determined by HPLC analysis [Chiralcel OD-H column, Hexanes/*i*-PrOH = 90/10, 1.0 mL/min, 220 nm, 20 °C, t_R (1) = 9.5 min (major), t_R (2) = 15.7 min (minor)].



(+)-Ethyl 2-benzoyl-3-(4-bromophenyl)oxirane-2-carboxylate (4d)

0 °C, 2 days, 83% yield, 93% ee.

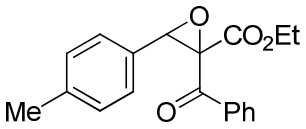
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 7.6 Hz, 2H), 4.68 (s, 1H), 4.26 (q, *J* = 7.6 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.61, 166.21, 135.02, 134.13, 131.59, 131.23, 128.78, 128.65, 127.92, 123.16, 65.75, 62.97, 62.40, 13.80; **IR** (thin film) 2982, 1748, 1734, 1690, 1596, 1490, 1256, 1233 cm^{-1}; **LRMS (ESI)**: 397, 399 (M + Na^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{15}BrO_4Na$ (M + Na), 397.0051. Found 397.0056; $[\alpha]_D^{25}$ = +5.4^o (*c* 1.0, $CHCl_3$, 93% ee), 93% ee was determined by HPLC analysis [Chiralcel OD-H column, Hexanes/*i*-PrOH = 90/10, 0.8 mL/min, 220 nm, 20 ^{o}C, t_R (1) = 11.2 min (major), t_R (2) = 18.6 min (minor)].



(+)-Ethyl 2-(4-bromobenzoyl)-3-(4-chlorophenyl)oxirane-2-carboxylate (4e)

0 ^{o}C, 2 days, 99% yield, 93% ee.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.57 (t, *J* = 8.4 Hz, 1H), 7.21 (t, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 4.68 (s, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 188.79, 166.00, 135.09, 133.77, 132.09, 130.51, 130.23, 129.61, 128.79, 127.56, 65.62, 63.12, 62.37, 13.87; **IR** (thin film) 2984, 2933, 2360, 2341, 1749, 1734, 1691, 1584, 1494, 1398, 1257, 1236, 1012, 832 cm^{-1}; **LRMS (ESI)**: 431, 433 (M + Na^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{14}ClBrO_4Na$ (M + Na), 430.9662. Found 430.9670; $[\alpha]_D^{25}$ = +25.0^o (*c* 1.0, $CHCl_3$, 93% ee), 93% ee was determined by HPLC analysis [Chiralcel OD-H column, Hexanes/*i*-PrOH = 96/4, 0.8 mL/min, 220 nm, 20 ^{o}C, t_R (1) = 19.2 min (major), t_R (2) = 42.7 min (minor)].

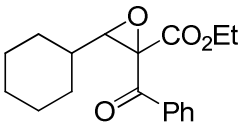


(+)-Ethyl 2-benzoyl-3-p-tolyloxirane-2-carboxylate (4f)

0 ^{o}C, 2 days, 60% yield, 96% ee.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 4.69 (s, 1H), 4.24 (q, *J* = 7.6 Hz, 2H), 2.22 (s, 3H), 1.17 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.99, 166.51, 138.80, 135.26, 133.80, 129.04, 129.02, 128.76, 128.48, 126.18, 65.86, 63.16, 62.72, 21.10, 13.76; **IR** (thin film) 2983, 1746, 1730, 1601, 1450, 1256, 1233, 1177 cm^{-1}; **LRMS (ESI)**: 311 (M + H^+); **HRMS (ESI)**: Exact mass calcd for $C_{19}H_{19}O_4$

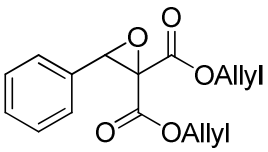
(M + H), 311.1283. Found 311.1278; $[\alpha]_D^{25}$ = +0.7° (*c* 1.0, $CHCl_3$, 96% ee), 96% ee was determined by HPLC analysis [Chiralcel OD-H column, Hexanes/*i*-PrOH = 90/10, 0.8 mL/min, 220 nm, 20 °C, t_R (1) = 10.0 min (major), t_R (2) = 12.9 min (minor)].



(+)-Ethyl 2-benzoyl-3-cyclohexyloxirane-2-carboxylate (4g)

-40 °C, 3 days, 86% yield, 86% ee.

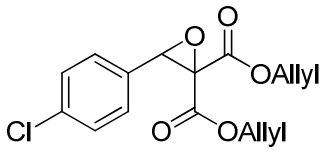
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.34 (d, *J* = 8.8 Hz, 1H), 1.87 (d, *J* = 7.6 Hz, 2H), 1.69-0.97 (m, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 190.94, 167.50, 135.06, 134.02, 129.23, 128.62, 67.06, 63.69, 62.55, 38.04, 30.16, 28.00, 25.93, 25.03, 24.97, 13.81; **IR** (thin film) 2976, 2931, 2854, 2360, 2338, 1749, 1730, 1691, 1450, 1285, 1256, 1233, 698 cm^{-1}; **LRMS (ESI)**: 303 (M + H^+); **HRMS (ESI)**: Exact mass calcd for $C_{18}H_{23}O_4$ (M + H), 303.1596. Found 303.1585; $[\alpha]_D^{25}$ = +7.4° (*c* 1.0, $CHCl_3$, 86% ee), 86% ee was determined by HPLC analysis [Chiralcel As-H + Chialpak AD + Chiralcel AD-H column, Hexanes/*i*-PrOH = 99/1, 0.8 mL/min, 254 nm, 20 °C, t_R (1) = 50.2 min (major), t_R (2) = 54.65 min (minor)].



(-)-Diallyl 3-phenyloxirane-2,2-dicarboxylate (4h)

0°C, 3 days, 90% yield, 92% ee.

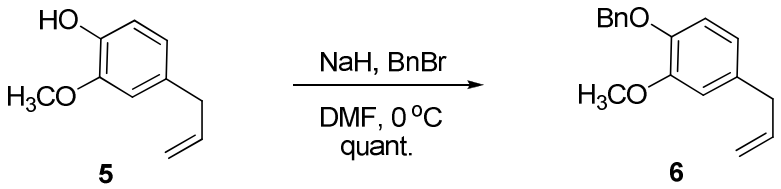
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 5H), 5.98-5.88 (m, 1H), 5.60-5.50 (m, 1H), 5.38 (dd, *J* = 16.8, 1.2 Hz, 1H), 5.30 (d, *J* = 10.4 Hz, 1H), 5.08 (dd, *J* = 14.8, 2.8 Hz, 2H), 4.76-4.74 (m, 2H), 4.59 (s, 1H), 4.45 (d, *J* = 5.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.04, 163.13, 131.83, 130.69, 129.11, 128.38, 126.18, 119.41, 119.05, 67.10, 66.24, 63.12, 62.21; **IR** (thin film) 3028, 2918, 1753, 1750, 1650, 1455, 1264, 1227, 1122, 1045, 936, 754 cm^{-1}; **LRMS (ESI)**: 311 (M + Na^+); **HRMS (ESI)**: Exact mass calcd for $C_{16}H_{16}O_5Na$ (M + Na), 311.0895. Found 311.0894; $[\alpha]_D^{25}$ = -57.2° (*c* 1.0, $CHCl_3$, 92% ee), 92% ee was determined by HPLC analysis [Chiralcel OD-H column, Hexanes/*i*-PrOH = 96/4, 1 mL/min, 254 nm, 20 °C, t_R (1) = 11.2 min (minor), t_R (2) = 12.3 min (major)].



(-)-Diallyl 3-(4-chlorophenyl)oxirane-2,2-dicarboxylate (4i)

-20 °C, 3 days, 70% yield, 84% ee.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.98-5.88 (m, 1H), 5.65-5.55 (m, 1H), 5.39 (d, *J* = 17.2 Hz, 1H), 5.30 (d, *J* = 10.4 Hz, 1H), 5.13 (d, *J* = 11.6 Hz, 2H), 4.80-4.71 (m, 2H); 4.56 (s, 1H), 4.48 (d, *J* = 6.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.78, 162.92, 135.16, 130.63, 130.57, 130.40, 128.67, 127.65, 119.53, 119.35, 67.19, 66.39, 63.03, 61.54; **IR** (thin film) 2362, 2338, 1751, 1270, 1225 cm^{-1}; **LRMS (ESI)**: 345 $(M + Na)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{16}H_{15}ClO_5Na$ (M + Na), 345.0506. Found 345.0497; $[\alpha]_D^{25}$ = -62.7° (*c* 1.0, $CHCl_3$, 84% ee.), 84% ee was determined by HPLC analysis [Chiralcel OD-H column, Hexanes/*i*-PrOH = 99/1, 0.8 mL/min, 254 nm, 20 °C, t_R (1) = 13.5 min (major), t_R (2) = 16.8 min (minor).



5 **6**

To a suspension of NaH (55% assay, 1.05 g, 24.0 mmol) in anhydrous DMF (20.0 mL) at 0 °C was added dropwise a solution of eugenol (**5**) (3.28 g, 20.0 mmol) in anhydrous DMF (10.0 mL) via syringe over 15 min. The resulting deep green mixture was stirred at 0 °C for 15 min, and then to this solution was added dropwise a solution of benzylbromide (2.85 mL, 24.0 mmol) in anhydrous DMF (10.0 mL) via syringe over 2 min. The resulting mixture was stirred at 0 °C for 1 hr. Then the reaction was quenched by a slow addition of saturated aqueous NH_4Cl (50 mL) and then ethyl acetate (50 mL). The organic layer was collected, and the aqueous layer was extracted with ethyl acetate (3×50 mL). The combined extracts were washed with water (4×50 mL), brine (40 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was subjected to silica gel chromatography (petroleum ether/EtOAc = 8/1) to give **6** (5.07 g, quant.) as a coloress oil.

^{1}H NMR (400MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.28 (t, *J* = 7.2 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.72 (s, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 5.93 (m, 1H), 5.12 (s, 2H), 5.07 (d, *J* = 11.6 Hz, 1H), 5.04 (d, *J* = 2.8 Hz, 1H), 3.86 (s, 3H), 3.31 (d, *J* = 7.2 Hz, 2H);

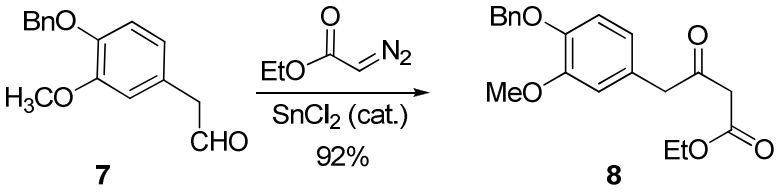
IR (thin film) 3064, 3034, 3003, 2976, 2935, 2907, 2874, 2833, 1638, 1606, 1591, 1514, 1506, 1464, 1454, 1418, 1335, 1260, 1230, 1156, 1140, 1034, 914, 850, 806, 739, 697, 654, 597 cm^{-1}; **LRMS (ESI)**: 277.1 $(M + Na)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{17}H_{18}O_2Na$ (M + Na), 277.1204. Found 277.1196.

6 **7**

To a solution of **6** (508 mg, 2.0 mmol) in *t*-BuOH/H_2O/THF (2/1/4) (7.0 mL) was added a solution of OsO_4 in *t*-BuOH (0.20 M, 0.50 mL, 0.010 mmol, 5 mol %) at 10 ^oC. To the resulting mixture, *N*-methylmorpholine *N*-oxide (NMO) (357 mg, 3.0 mmol) was added in one portion. The resulting reaction mixture was stirred at 10 ^oC for 15 min and then warmed to room temperature. The stirring was continued for another 1 hr before the reaction was quenched with addition of sat. $NaHSO_3$. The resulting mixture was stirred at room temperature overnight. The mixture was diluted with ethyl acetate (30 mL), and then washed with sat. $NaHSO_3$(15 mL). The aqueous layer was extracted with ethyl acetate (2×20 mL). The organic phase was collected and washed with brine (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (5.0 mL), and the resulting solution was added into a solution of $NaIO_4$ (630 mg, 3.0 mmol) in water (5.0 mL) at 0 ^oC. The resulting light yellow mixture was stirred at 0 ^oC for 40 min and then quenched with saturated aqueous $NaHSO_3$. The resulting mixture was stirred at room temperature for 30 min, and then extracted with ethyl acetate (3×20 mL). The organic phase was collected, washed with brine (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was subjected silica gel chromatography (petroleum ether/EtOAc = 4/1) to give aldehyde **7** (507 mg, quant.) as a coloress oil.

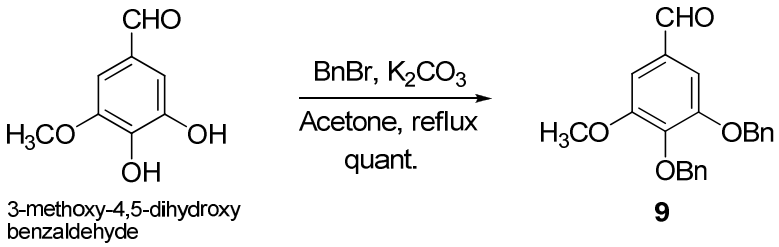
^{1}H NMR (400MHz, $CDCl_3$) δ 9.68 (t, *J* = 2.4 Hz, 1H), 7.41 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.72 (s, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.12 (s, 2H), 3.85 (s, 3H), 3.57 (d, *J* = 2.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.418, 149.965, 147.506, 136.987, 128.479, 127.796, 127.181, 124.669, 121.740, 114.401, 1 13.118, 71.012, 55.947, 50.073; **IR** (thin film) 3063, 3034, 3007, 2937, 2876, 2833, 2728, 1723, 1682, 1591, 1514, 1464, 1454, 1383, 1332, 1231, 1261, 1141, 1034, 854, 810, 741, 698 cm^{-1};

LRMS (ESI): 279.1 $(M + Na)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{16}H_{16}O_3Na$ (M + Na), 279.0997. Found 279.0990.



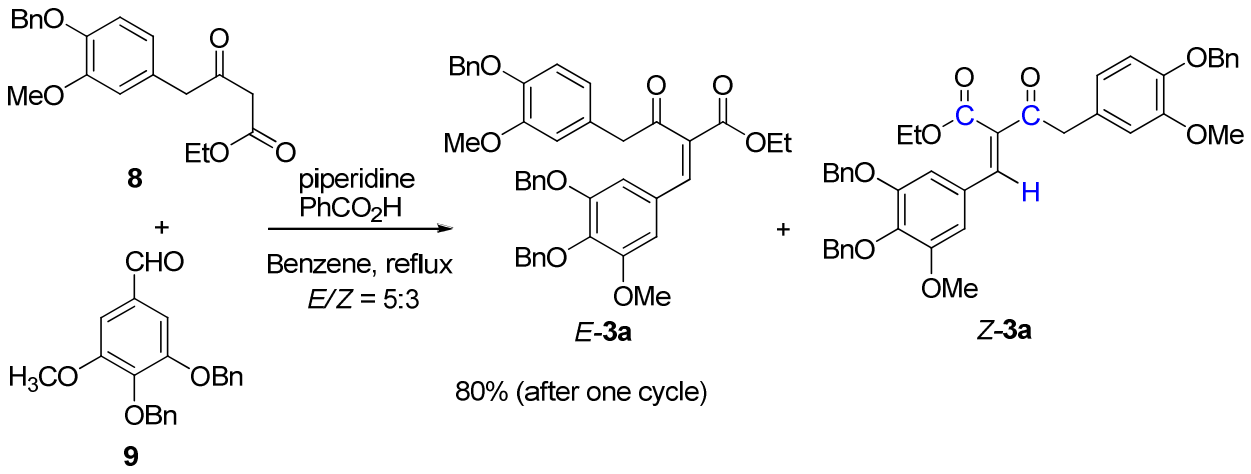
$SnCl_2 \cdot 2H_2O$ (45 mg, 2.0 mmol, 10 mol %) was suspended in anhydrous CH_2Cl_2 (3.0 mL) at -72 ^oC. To this suspension, ethyl diazoacetate (0.23 mL, 2.2 mmol) was added dropwise via syringe. The resulting yellow mixture was stirred at this temperature for 10 min and warmed up to room temperature for another 15 min. The mixture was recooled to -72 ^oC and a solution of **7** (507 mg, 2.0 mmol) in CH_2Cl_2 (5.0 mL) was introduced via syringe over 5 min. The resulting mixture was stirred while warming up to room temperature over 1 hr and stirred at room temperature overnight. The reaction was quenched with addition of aq. HCl (1.0 N, 2.0 mL) and extracted with ethyl acetate (3×25 mL). The combined extracted were washed with 5% aq. $NaHCO_3$ (3×15 mL), brine (20 mL), dried over Na_2SO_4 and concentrated at reduced pressure. The residue was subjected to silica gel chromatography (petroleum ether/EtOAc = 8/1→4/1) to give β-keto ester **8** (640 mg, 92% yield) as a white solid.

^{1}H NMR (400MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.2 Hz, 2H), 7.33 (dd, *J* = 7.6 Hz, 7.2 Hz, 2H), 7.27 (d, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 8.6 Hz, 1H), 6.71 (s, 1H), 6.65 (d, *J* = 8.6 Hz), 5.11 (s, 2H), 4.14 (q, *J* = 7.4 Hz, 2H), 3.85 (s, 3H), 3.71 (s, 2H), 3.41 (s, 2H), 1.22 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100MHz, $CDCl_3$) δ 200.722, 167.029, 149.654, 147.324, 136.910, 128.394, 127.696, 127.088, 126.056, 121.593, 113.980, 112.834, 70.821, 61.220, 55.815, 49.470, 47.914, 13.940; **IR** (thin film) 3064, 3033, 2982, 2938, 1745, 1716, 1606, 1591, 1515, 1464, 1454, 1421, 1385, 1368, 1317, 1262, 1232, 1142, 1032, 855, 805, 741, 698 cm^{-1}; **LRMS (ESI)**: 343.2 $(M + H)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{20}H_{23}O_5$ (M + H), 343.1545. Found 343.1541.



To a brown mixture slurry of 3-methoxy-4,5-dihydroxy-benzaldehyde (1.00 g, 6.0 mmol) and K_2CO_3 (3.00 g, 21.7 mmol, 3.5 eq.) in acetone (20 mL) was added benzyl bromide (1.78 mL, 15.0 mmol, 2.5 eq.) at 0 ^oC. The corresponding yellow mixture was refluxed for 7 hr. The resulting green mixture was cooled down to 0 ^oC and quenched carefully with aq. HCl (1N, 35.0 mL). The mixture was diluted with ethyl acetate, washed with water (3×20 mL), saturated $NaHCO_3$ (3×10 mL), brine (25 mL) and dried over Na_2SO_4. After concentration at reduced pressure, the residue was subjected to silica gel chromatography (petroleum ether/EtOAc = 4/1) to give aldehyde **9** (2.1 g, quant.) as an orange oil.

^{1}H NMR (400MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.43-7.27 (m, 10H), 7.15 (s, 1H), 7.12 (s, 1H), 5.14 (s, 4H), 3.89 (s, 3H); **^{13}C NMR** (100MHz, $CDCl_3$) δ 191.014, 154.125, 152.926, 142.929, 137.138, 136.295, 131.741, 128.538, 128.386, 128.159, 128.060, 127.999, 127.415, 108.750, 106.534, 75.019, 71.110, 56.181; **IR** (thin film) 3063, 3032, 2939, 2841, 1693, 1587, 1498, 1454, 1428, 1386, 1327, 1232, 1141, 1120, 979, 833, 737, 697 cm^{-1}; **LRMS (ESI)**: 349.1 $(M + H)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{22}H_{21}O_4$ (M + H), 349.1440. Found 349.1441.

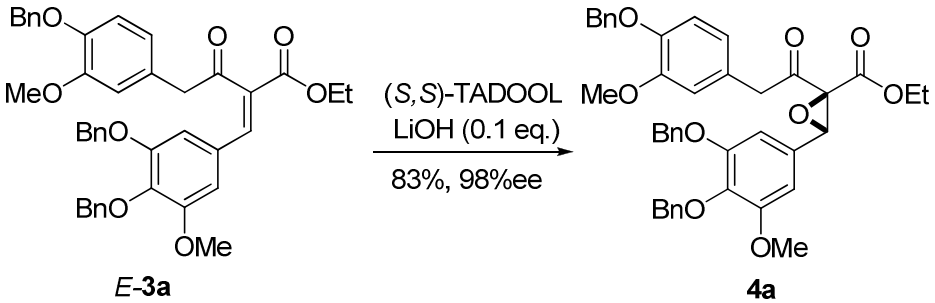


A mixture of β-keto ester **8** (172 mg, 0.50 mmol), aldehyde **9** (174 mg, 0.50 mmol), piperidine (distilled, 8.5 mg, 0.10 mmol) and benzoic acid (9.2 mg, 0.075 mmol) in benzene (20 mL) in a round bottom flask (50 mL) connected to a Dean-Stark apparatus was heated to reflux. After 2.5 hr, the reaction mixture was cooled to room temperature and concentrated at reduced pressure. The residue was subjected to silica gel chromatography (petroleum ether/diethyl ether = 3/1→1/1) to give *E*-**3a** (199 mg, 59% yield) as a light yellow oil and *Z*-**3a** (66 mg, 20% yield) as a white solid. Ketoester **8** and aldehyde **9** were recovered (ca. 23 mg for each) in 13% yield.

Isomerization of Z-isomer: A solution of *Z*-**3a** (66 mg, 0.10 mmol) and pyridine (1 drop) in benzene (5 mL) was refluxed for 5 hr. The solution was cooled to room temperature and diluted with ether. The mixture was concentrated at reduced pressure and the residue was subjected to silica gel chromatography (petroleum ether/EtOAc = 2/1) to give *E*-**3a** (38 mg, 58%yield) and *Z*-**3a** (25 mg, 38%yield), respectively.

E-**3a**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.42-7.24 (m, 15H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.01 (br, 1H), 6.59 (br, 1H), 6.55 (br, 1H), 6.46 (dd, *J* = 8.4 Hz, 0.8 Hz, 1H), 5.06 (s, 2H), 5.04 (s, 2H), 4.92 (s, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 3.70 (s, 2H), 3.69 (s, 3H),1.28 (t, 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 203.447, 164.380, 153.632, 152.531, 149.389, 147.256, 141.138, 139.476, 137.366, 137.055, 136.432, 132.675, 128.500, 128.462, 128.402, 128.143, 127.984, 127.931, 127.749, 127.438, 127.172, 126.064, 121.897, 113.676, 113.418, 108.705, 107.301, 75.004, 70.890, 70.875, 61.501, 56.013, 55.785, 49.956, 14.145; **IR** (thin film) 3063, 3032, 2937, 2873, 1722, 1580, 1513, 1504, 1462, 1454, 1423, 1377, 1333, 1259, 1232, 1158, 1122, 1027, 912, 855, 736, 697 cm^{-1}; **LRMS (ESI)**: 673.3 $(M + H)^+$; **HRMS (ESI)** Exact mass calcd for $C_{42}H_{41}O_8$ (M + H), 673.2801. Found 673.2812.

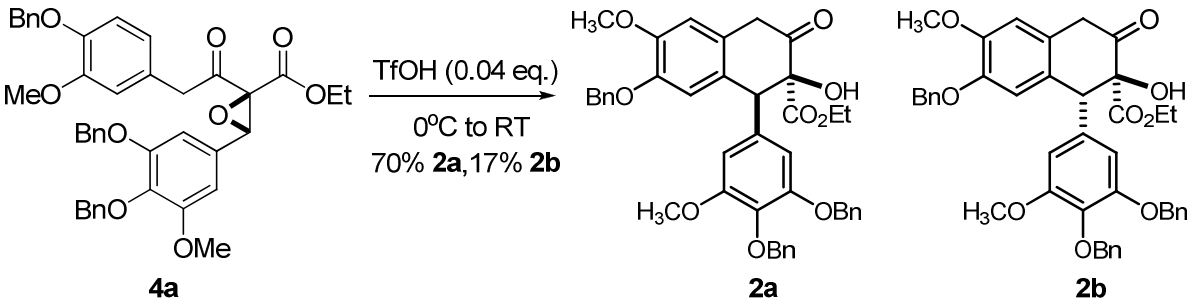
Z-**3a**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.42-7.24 (m, 15H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.75 (s, 1H), 6.74 (s, 1H), 6.70 (s, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.13 (s, 2H), 5.08 (s, 2H), 5.05 (s, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.95 (s, 2H), 3.86 (s, 3H), 3.80 (s, 3H), 1.19 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, C-H coupling) δ 194.02 (td, *J* = 6.8, 6.1 Hz, C=O), 168.07 (dt, *J* = 12.2 Hz, 3.0 Hz, COOEt), 153.65, 152.61, 149.58, 147.21, 141.65, 137.27, 137.08, 136.42, 132.71, 128.51, 128.46, 128.40, 128.29, 128.12, 128.00, 127.92, 127.73, 127.41, 127.34, 127.14, 126.47, 121.63, 113.90, 113.02, 109.05, 107.17, 77.21, 75.03, 71.10, 70.91, 61.71, 56.04, 55.89, 45.15, 13.85. $^3J_{C\text{-}H}$ = 6.1 Hz for C_{ketone}-H, $^3J_{C\text{-}H}$ = 12.2 Hz for C_{ester}-H.



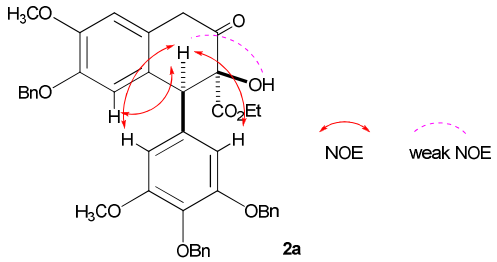
E-**3a** **4a**

To a solution of *E*-**3a** (17.0 mg, 0.0250 mmol) and (+)-TADOOL (13.3mg, 0.0275 mmol) in THF (0.15 mL) at 0 ^{o}C was added a solution of LiOH (5.0 M, 0.5 μL, 0.50 mmol) via syringe. The resulting mixture was stirred at 0 ^{o}C for 6 hr, and then warmed up to RT over night. The mixture was subjected to silica gel chromatography (petroleum ether/EtOAc = 10/1→2/1) to give the desired epoxide **4a** (14.5 mg, 83% yield) as a light yellow oil. The 98% ee of **4a** was determined by converting **4a** into **2a** and then an ee analysis of **2a**. TADDOL was recycled as a white solid in > 90 % yield.

$[\alpha]^{23}_{D}$ = - 61^{o} (*c* 0.96, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43-7.25 (m, 15H), 6.66 (d, *J* = 8.0Hz, 1H), 6.51 (s, 1H), 6.45 (s, 1H), 6.41 (s, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 5.05 (s, 2H), 5.04 (d, *J* = 11.6 Hz, 1H), 5.01 (s, 2H), 4.96 (d, *J* = 11.6 Hz, 1H), 4.45 (s, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 3H), 3.69 (d, *J* = 16.8 Hz, 1H), 3.41 (d, *J* = 16.8 Hz, 1H), 1.29 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.974, 165.943, 153.905, 152.744, 149.381, 147.233, 138.003, 137.548 137.047, 136.554, 128.470, 128.432, 128.356, 128.113, 127.916, 127.832, 127.711, 127.415, 127.180, 124.728, 121.768, 113.623, 113.183, 105.099, 103.596, 74.935, 70.958, 70.799, 66.662, 62.859, 62.799, 56.066, 55.846, 47.906, 13.947; **IR** (thin film) 3063, 3032, 2938, 1748, 1726, 1592, 1513, 1454, 1430, 1374, 1262, 1235, 1121, 1026, 850, 736, 697 cm^{-1}; **LRMS (ESI)**: 689.3 $(M + H)^{+}$; **HRMS (ESI)**: Exact mass calcd for $C_{42}H_{41}O_9$ (M + H), 689.2751. Found 689.2744.



4a **2a** **2b**



2a

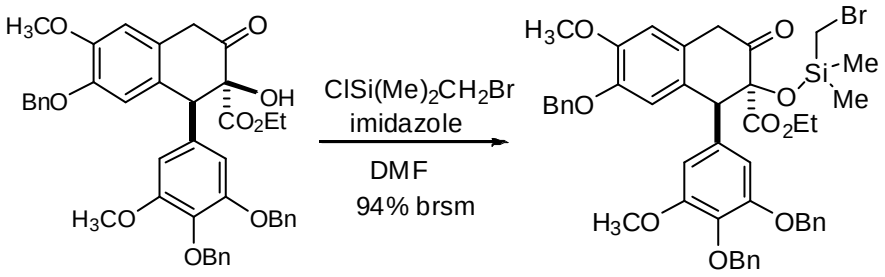
To a solution of epoxide **4a** (344 mg, 0.500 mmol) in CH_2Cl_2 (35 mL) at -10 ^oC was added dropwise a freshly prepared solution of TfOH in Et_2O (0.50 M, 40 μL, 0.020 mmol) via syringe with vigorous stirring. After stirring at this temperature for 15 min, a TLC test indicated the starting material **4a** was completely consumed. The reaction was quenched with addition of Et_3N (3 μL). The reaction mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography (petroleum ether/EtOAc = 5/1→3/1) to give light blue **2a** (240 mg, 70% yield) and its distereoisomer **2b** (58 mg, 17% yield), respectively. **2a** was determined to be > 98% ee by HPLC analysis [Chiralpak AD, Hexanes/*i*-PrOH = 65:35, 1 mL/min, 220 nm, 20 ^oC, t_R (1) = 25 min, t_R (2) = 33 min].

2a: $[\alpha]_D^{20}$ = + 66 (*c* 0.43, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23-7.45 (m, 15H), 6.64 (s, 1H), 6.62 (s, 1H), 6.37 (d, *J* = 2.0 Hz, 1H), 6.08 (d, *J* = 1.2 Hz, 1H), 5.02 (s, 2H), 5.00 (s, 2H), 4.93 (AB, *J* = 12 Hz, 2H), 4.63 (s, 1H, H-7′), 4.13 (s, 1H, C8′-OH), 4.04 (q, *J* = 6.8 Hz, 2H), 3.91 (s, 3H), 3.88 (d, *J* = 22 Hz, H-7α), 3.77 (s, 3H), 3.48 (d, *J* = 22 Hz, H-7β), 1.02 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 204.61, 168.78, 153.11, 151.87, 149.40, 147.60, 137.78, 137.07, 136.93, 136.50, 131.97, 128.45, 128.35, 128.06, 127.90, 127.69, 127.65, 127.42, 127.03, 124.68, 114.58, 111.00, 108.46, 107.51, 82.13, 74.92, 70.82, 70.76, 62.02, 56.07, 55.96, 52.75, 40.99, 13.72; **IR** (thin film) 3436, 2936, 1724, 1589, 1514, 1504, 1454, 1372, 1328, 1298, 1246, 1115, 1014, 736, 697 cm^{-1}; **LRMS (ESI)**: 689.3 $(M + H)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{42}H_{41}O_9$ $(M + H)^+$, 689.2751. Found 689.2753.

2b: **^{1}H NMR** (400 MHz, $CDCl_3$): see spectrum; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 203.76, 168.43, 153.44, 152.40, 148.92, 146.77, 137.89, 136.92, 136.75, 133.00, 128.46, 128.44, 128.39, 128.15, 127.86, 127.84, 127.79, 127.38, 127.23, 125.27, 114.13, 110.74, 109.19, 107.71, 83.23, 75.01, 70.92, 70.89, 62.24, 58.12, 56.06, 56.03, 42.24, 13.73.

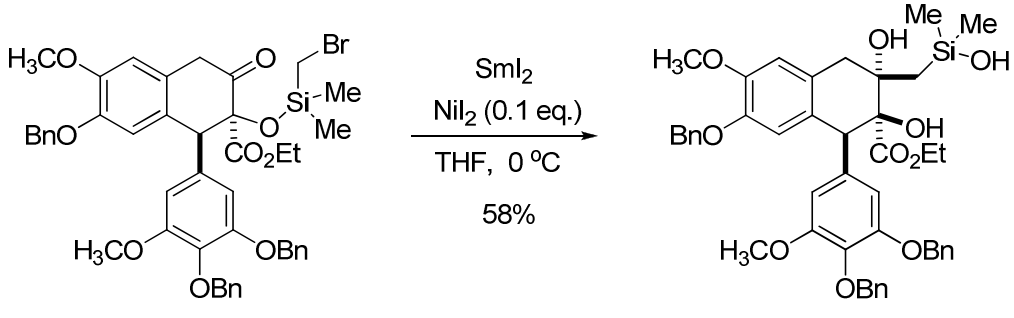
NOTE: Various Lewis acids were screened for their ability to effect the intramolecular epoxide ring opening Friedel-Crafts cyclization with **4a** to form the 2,7'-cyclolignane skeleton with concomitant installation of the C7' stereocenter. Although both $SnCl_4$[4a-c] and $BF_3{\cdot}Et_2O$[4d] have been documented for promoting Friedel-Crafts reaction with epoxides, only the latter promoted the desired cyclization when employed in large excess (six equivalents). However, the yield of the BF_3-promoted Friedel-Crafts reaction was found to be inconsistent at a scale of greater than 100 mg.

[4] (a) Nicolaou, K. C.; Wu, T. R.; Kang, Q.; Chen, D. Y.-K. *Angew. Chem. Int. Ed.* **2009**, *48*, 3440. (b) Kraus, G. A.; Kim, I. *Org. Lett.***2003**, *5*, 1991. (c) Amupitan, J.; Sutherland, J. K. *J. Chem. Soc., Chem. Commun.* **1978**, 852. (d) Ono, M.; Suzuki, K.; Akia, H. *Tetrahedron Lett.* **1999**, *40*, 8223.

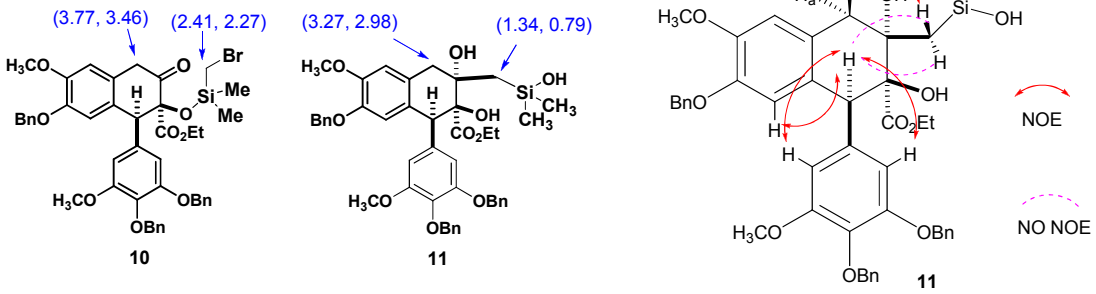


2a **10**

To a solution of hydroxyketone **2a** (180 mg, 0.26 mmol) in anhydrous DMF (1.0 mL) at RT was added $ClSi(Me)_2CH_2Br$ (113 μL, 0.83 mmol), followed by imidazole (54 mg, 0.78 mmol). The resulting mixture was stirred at this temperature for 1 hr and then subjected to silica gel chromatography directly eluted with petroleum ether/EtOAc = 10/1→3/1 to give silyl ether **10** (165 mg, 94%yield brsm) as light green foam, and the starting material (37 mg, 20% recovery). $[\alpha]_D^{20}$ = +42.4 (*c* 1.34, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50~7.15 (m, 15H), 6.59 (s, 2H), 6.36 (s, 1H), 6.03 (s, 1H), 5.00(s, 2H), 4.99 (s, 2H), 4.93 (AB, *J* = 12.4 Hz, 2H), 4.53 (s, 1H), 4.02 (m, 2H), 3.89 (s, 3H), 3.77 (A of AB, *J* = 22.0 Hz, 1H), 3.77 (s, 3H), 3.46 (B of AB, *J* = 22.0 Hz, 1H), 2.41 (A of AB, *J* = 12.7 Hz, 1H), 2.27 (B of AB, *J* = 12.7 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H), 0.13 (s, 3H), 0.06 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 204.16, 168.90, 153.01, 151.97, 149.35, 147. 49, 137.67, 137.06, 137.03, 136.53, 132.78, 128.45, 128.42, 128.40, 128.09, 127.86, 127.75, 127.68, 127.39, 127.22, 126.99, 124.76, 114.50, 110.76, 108.57, 107.94, 85.71, 75.06, 71.01, 70.75, 61.92, 56.11, 55.95, 54.87, 42.08, 18.63, 13.72, -1.01, -1.10; **IR** (thin film) 3088, 3064, 3032, 2936, 1731, 1590, 1514, 1454, 1248, 1114, 1028 cm^{-1}; **LRMS (ESI)**: 841.2, 839.2 $(M + H)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{45}H_{48}O_9BrSi$ (M + H), 839.2251.Found 839.2239.

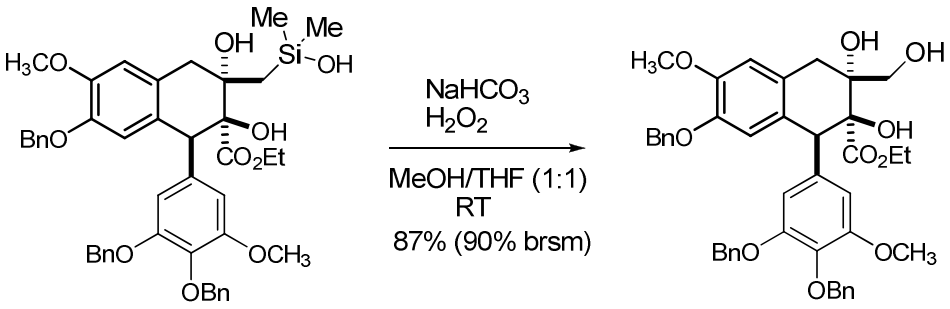


10 **11**



To a solution of bromide **10** (120 mg, 0.143 mmol) in anhydrous THF (10 mL) under N_2 at 0 ^oC was added SmI_2 (0.10M THF soln, containing 1 mol % NiI_2, 5.0 mL, 0.50 mmol) dropwise. The resulting mixture was stirred at 0 ^oC for 1 hr and then let warm to RT. The solvent was evaporated and the residue was taken up in EtOAc, rinsed with aq. $NaHCO_3$ (sat.) and brine successively. The organic layer was dried over anhydrous Na_2SO_4. After the solvent was removed by rotavap, the residue was subjected to purification on silica gel eluted with petroleum ether/EtOAc = 3/1→ 2/1 to give silanol **11** (65 mg, 58% yield) as dense colorless liquid. Splitting and broadening peaks are observed in both the ^1H NMR and ^{13}C NMR spectra due to the existence of atropisomers arising from hindered rotation along C1'-C7' bond.

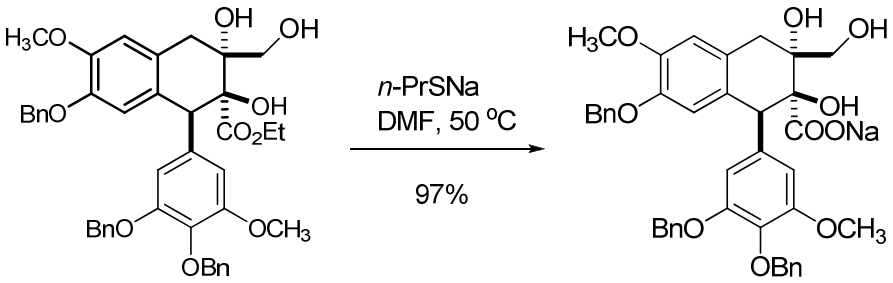
$[\alpha]_D^{20}$ = -2.98 (*c* 1.17, $CHCl_3$); **^1H NMR** (400 MHz, $CDCl_3$) δ 7.50~7.18 (m, 15H), 6.65 (s, 1H), 6.44 (br, 0.4H), 6.38 (br, 0.6H), 6.29 (br, 0.6H), 6.25 (br, 1.4H), 5.09 (br, 1H), 5.08 (s, 2H), 4.89~4.78 (m, 2H), 4.81 (s, 1H), 4.57 (s, 1H), 4.10 (m, 1.2H), 3.98 (m, 0.8H), 3.89 (s, 3H), 3.82 (s, 1.8H), 3.67 (s, 1.2H), 3.55 (br, 1H), 3.27 (A of AB, *J* = 16.9 Hz), 2.98 (B of AB, J = 16.9 Hz), 2.86 (br, 1H), 1.34 (A of AB, *J* = 14.6 Hz), 1.11 (t, *J* = 6.8 Hz), 0.79 (B of AB, *J* = 14.6 Hz), 0.30 (s, 3H), 0.22 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.71, 153.80 (br), 153.19 (br), 152.34 (br), 152.04 (br), 148.40, 146.19, 137.78, 137.15, 136.86 (br), 134.66, 128.46 (br), 128.39, 128.30, 128.11, 128.07 (br), 127.78, 127.61, 127.28, 127.14, 127.06 (br), 126.66, 114.94, 111.77, 110.36 (br), 108.52 , 107.02 (br), 81.53, 75.54, 74.93, 71.16 (br), 70.90 (br), 70.33 (br), 62.35, 56.07 (br), 55.90, 50.39 (br), 39.00, 27.82 (br), 14.09, 2.29, 2.14; **IR** (thin film) 3505, 3063, 3031, 2936, 1712, 1589, 1514, 1454, 1373, 1330, 1252, 1213, 1119, 1028cm^{-1}; **LRMS (ESI)**: 801.3 $(M + Na)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{45}H_{50}O_{10}NaSi$ (M + Na), 801.3071. Found 801.3062.



11 **12**

To a solution of silanol **11** (65 mg, 0.084 mmol) in a mixed solvent of MeOH/THF (1:1, 6.0 mL) at RT was added $NaHCO_3$ (45 mg, 0.54 mmol) in one portion and H_2O_2 (35%, 150 μL, ca. 1.5 mmol) successively. The resulting mixture was stirred at this temperature over night. The solvent was evaporated at reduced pressure and the residue was subjected to silica gel chromatography eluted with petroleum ether/EtOAc = 3/1→ 1/1 to give triol **12** (50 mg, 87% yield, 90% yield brsm) as dense colorless liquid, along with recovered substrate (3mg). Splitting and broadening peaks are observed in both the ^{1}H NMR and ^{13}C NMR spectra due to the existence of atropisomers arising from hindered rotation along C1'-C7' bond.

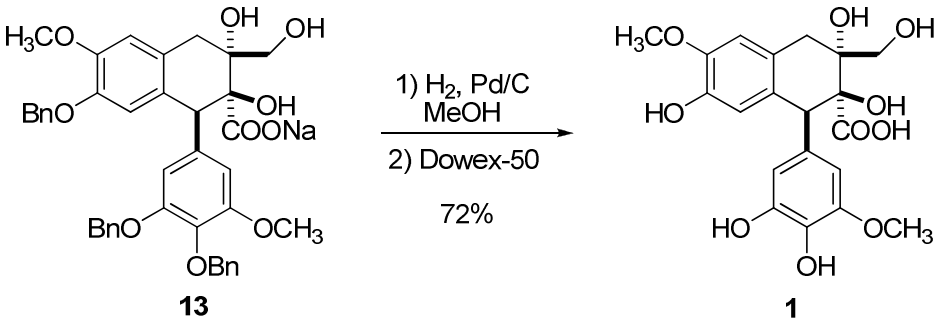
$[\alpha]_D^{20}$ = +5.31 (*c* 0.833, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49~7.16 (m, 15H), 6.65 (s, 1H), 6.39 (br, 2H), 6.23 (s, 1H), 5.08 (s, 2H), 5.05 (m, 1H), 4.89~4.79(3H), 4.58 (s, 1H), 4.08 (br, 2H), 3.88 (s, 3H), 3.82 (br, 1.4H), 3.74 (br, 1.6H), 3.55~3.53(br, 2H), 3.25 (br, 1H), 3.14 (A of AB, *J* = 17.2 Hz, 1H), 2.68 (B of AB, *J* = 17.2 Hz, 1H), 1.89 (br, 1H), 1.17 (br, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.90, 153.64-153.04 (br), 152.29-151.94 (br), 148.33, 146.27, 137.83, 137.13, 136.92 (br), 134.20, 128.40, 128.31, 128.27, 128.10, 127.76, 127.67, 127.62, 127.28, 127.15, 125.52, 114.92, 111.80, 110.89 (br), 108.88 (br), 107.40 (br), 77.76, 74.91, 74.83, 71.14 (br), 70.86, 70.37 (br), 66.11, 62.50, 56.06 (br), 55.94, 49.94, 34.95, 29.66, 14.03; **IR** (thin film) 3506, 3064, 3031, 2936, 1712, 1589, 1514, 1453, 1373, 1330, 1252, 1213, 1119, 1028 cm^{-1}; **LRMS (ESI)**: 721.3 $(M + H)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{43}H_{45}O_{10}$ (M + H), 721.3013. Found 721.3010.



12 **13**

Triol **12** (50 mg, 0.069 mmol) was placed in a dry flask under N_2 and a freshly prepared solution of *n*-PrSNa in anhydrous DMF (0.15 M, 0.60 mL, 0.090 mmol) was introduced. The resulting mixture was stirred at 50 ^oC for 24 hr. DMF was then evaporated at reduced pressure and the residue was subjected to silica gel chromatography eluted with CH_2Cl_2/CH_3OH = 5/1→ 0/1 to give sodium carboxylate **13** (48 mg, 97% yield) as white amorphous powder. Splitting and broadening peaks are observed in both the ^1H NMR and ^{13}C NMR spectra due to the existence of atropisomers arising from hindered rotation along C1'-C7' bond.

$[\alpha]_D^{20}$ = +62.5 (*c* 0.233, $CHCl_3$); **^{1}H NMR** (400 MHz, CD_3OD) δ 7.42~7.13 (m, 15H), 6.73 (s, 1H), 6.69-6.62 (split br, 1H), 6.46-6.36 (split br, 1H), 6.23 (s, 1H), 5.10~4.70 (6H), 4.64 (s, 1H), 3.82 (s, 3H), 3.77-3.51 (split br, 3H), 3.68 (A of AB, *J* = 11.2 Hz, 1H), 3.60 (B of AB, *J* = 11.2 Hz, 1H), 3.13 (A of AB, *J* = 17.0 Hz, 1H), 2.75(A of AB, *J* = 17.0 Hz, 1H); **^{13}C NMR** (125 MHz, CD_3OD) δ 179.94 (br), 154.05 (br), 152.96 (br), 149.48, 147.24, 139.31, 138.74, 137.90, 137.25, 131.40, 129.67, 129.36, 129.13, 129.02, 128.87, 128.72, 28.47, 116.87, 113.66, 112.59 (br), 111.02 (br), 110.78 (br), 109.43 (br), 78.82 (br), 76.14, 75.87, 72.02 (br), 71.45 (br), 67.86, 56.57, 51.19, 35.61, 30.75 (br); **IR** (thin film) 3439, 3089, 3063, 3031, 2922, 2852, 1651, 1598, 1514, 1504, 1454, 1378, 1327, 1255, 1218, 1119, 1100, 1027cm^{-1}; **LRMS (ESI)**: 715.3 $(M + H)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{41}H_{40}O_{10}Na$ (M + H), 715.2519. Found 715.2507.



13 **1**

To a solution of sodium carboxylate **13** (47 mg, 0.066 mmol) in MeOH (25 mL) was added Pd/C (15%, 20 mg). A balloon filled with H_2 was connected to the flask. The reaction mixture was flushed with H_2 by 3 cycles of vacuuming/refilling and then kept stirring at RT for 4 hr. The mixture was then filtered through a Dowex-50 column, which was further eluted with MeOH. The filtrate was collected and concentrated at reduced pressure to give a light brown solid (28 mg, 100% crude yield). The crude product was further purified on preparative TLC plate developing with CH_2Cl_2/CH_3OH (4:1) to give a light tan amorphous solid (20 mg, 72% yield). Splitting and broadening peaks are observed in both the ^{1}H NMR and ^{13}C NMR spectra due to the existence of atropisomers arising from hindered rotation along C1'-C7' bond.

Synthetic Sample

$[\alpha]_D^{20}$ = -40 (*c* 0.040, water), -130 (*c* 0.017, water); **^{1}H NMR** (400 MHz, CD_3OD, 21 ^{o}C) δ 6.67 (s, 1H), 6.51 (br, 1H), 6.36 (br, 1H), 6.22 (s, 1H), 4.59 (m, 1H), 3.81 (s, 3H), 3.747-3.66 (4H), 3.51 (br, 1H), 3.11 (A of AB, *J* = 16.2 Hz, 1H), 2.65 (B of AB, *J* = 16.2 Hz, 1H); **^{1}H NMR** (400 MHz, CD_3OD, 70 ^{o}C) δ 6.67 (s, 1H), 6.47 (br, 2H), 6.25 (s, 1H), 4.57 (s, 1H), 3.82 (s, 3H), 3.73 (br, 4H), 3.53 (br, 1H), 3.15 (A of AB, *J* = 17.2 Hz, 1H), 2.64 (B of AB, *J* = 17.2 Hz, 1H); **^{13}C NMR** (125 MHz, CD_3OD, 21 ^{o}C) δ 181.20 (br), 149.25 (br), 148.58 (br), 147.50, 146.00 (br), 145.32 (br), 145.25, 134.02 (br), 132.65(br), 132.18 (br), 126.11 (br), 117.30, 114.43 (br), 113.03, 112.62, 109.38 (br), 107.37 (br), 78.82 (br), 76.09 (br), 67.41 (br), 56.66 (br), 56.48, 50.52 (br), 36.03; **IR** (thin film) 3392 (br, strong), 2954, 1611 (split), 1515, 1350 (br), 1236 (br, multiple), 1104, 870 (weak) cm^{-1}; **LRMS (ESI)**: 445.1 $(M + Na)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{20}H_{22}O_{10}Na$ (M + Na), 445.1111. Found 445.1112.

Authentic Sample

$[\alpha]_D^{21}$ = -9.99 (water) [5]; $[\alpha]_D^{20}$ = -18 (*c* 0.040, water); **^{1}H NMR** (400 MHz, CD_3OD, 21 ^{o}C) δ 6.68 (s, 1H), 6.50 (br, 1H), 6.33 (br, 1H), 6.24 (s, 1H), 4.54 (m, 1H), 3.81 (s, 3H), 3.81-3.67 (4H), 3.58 (br, 1H), 3.12 (A of AB, *J* = 16.6Hz, 1H), 2.79 (B of AB, *J* = 16.6Hz, 1H); **^{1}H NMR** (400 MHz, CD_3OD, 70 ^{o}C) δ 6.67 (s, 1H), 6.45 (s, 2H), 6.27 (s, 1H), 4.55 (m, 1H), 3.82 (s, 3H), 3.77 (br, 3H), 3.68 (A of AB, *J* = 11.2 Hz, 1H), 3.61 (B of AB, *J* = 11.2 Hz, 1H), 3.17 (A of AB, *J* = 16.6 Hz, 1H), 2.75 (B of AB, *J* = 16.6 Hz, 1H); **^{13}C NMR** (125 MHz, CD_3OD, 21 ^{o}C) δ 180.52, 149.14, 148.67, 147.42, 145.80, 145.38, 145.06, 133.91, 132.72, 132.12, 126.78, 117.23, 114.17, 113.00, 112.68, 109.12, 107.50, 79.04, 75.72, 68.38, 56.63, 56.44, 50.67, 35.19; **IR** (thin film)

[5] Gradner, J. A. F.; Barton, G. M.; MacLean, H. *Can. J. Chem.* **1959**, *37*, 1703.

3391 (br, strong), 2957, 1610 (split), 1515, 1361 (br), 1236 (br), 1097, 868 (weak) cm^{-1}; **LRMS (ESI)**: 445.1 $(M + Na)^+$; **HRMS (ESI)**: Exact mass calcd for $C_{20}H_{22}O_{10}Na$ (M + Na), 445.1111. Found 445.1111.

Mixture Sample* [prepared by mixing the Authentic Sample (~10 mg) and Synthetic Sample (~10mg)]

^{1}H NMR (400 MHz, CD_3OD, 21 ^oC) δ 6.65 (s, 1H), 6.48 (br, 1H), 6.32 (br, 1H), 6.21 (s, 1H), 4.54 (m, 1H), 3.79 (s, 3H), 3.79-3.64 (4H), 3.57 (br, 1H), 3.11 (A of AB, *J* = 16.6 Hz, 1H), 2.72 (B of AB, *J* = 16.6 Hz, 1H); **^{1}H NMR** (400 MHz, CD_3OD, 70 ^oC) δ 6.67 (s, 1H), 6.46 (s, 2H), 6.26 (s, 1H), 4.56 (m, 1H), 3.83 (s, 3H), 3.75 (br, 3H), 3.66 (br, 1H), 3.62 (br, 1H), 3.16 (A of AB, *J* = 16.6 Hz, 1H), 2.70 (B of AB, *J* = 16.6 Hz, 1H); **^{13}C NMR** (125 MHz, CD_3OD, 21 ^oC) δ 180.77, 149.16, 148.60, 147.44, 145.85, 145.29, 145.12, 133.96, 132.69, 132.13, 126.47, 117.26, 114.27, 113.00, 112.65, 109.24, 107.41, 78.95, 75.86, 67.96, 56.63, 56.45, 50.59, 35.53;

Comparison of ^{13}C NMR

	AUTHENTIC	SYNTHETIC	MIXTURE*
1	180.52	181.20	180.77
2 [a]	149.14	149.25	149.16
3 [a]	148.67	148.58	148.60
4	147.42	147.50	147.44
5 [b]	145.80	146.00	145.85
6 [b]	145.38	145.32	145.29
7	145.06	145.25	145.12
8	133.91	134.02	133.96
9	132.72	132.65	132.69
10	132.12	132.18	132.13
11	126.78	126.11	126.47
12	117.23	117.30	117.26
13[c]	114.17	114.43	114.27
14	113.00	113.03	113.00
15[c]	112.68	112.62	112.65
16[d]	109.12	109.38	109.24
17[d]	107.50	107.37	107.41
18	79.04	78.82	78.95
19	75.72	76.09	75.86
20	68.38	67.41	67.96
21	56.63	56.66	56.63
22	56.44	56.48	56.45
23	50.67	50.52	50.59
24	35.19	36.03	35.53

* Mixture Sample was prepared by mixing the Authentic Sample (~10 mg) and Synthetic Sample (~10mg).

[a] probably splitting from one carbon due to existence of the rotamers.

[b] probably splitting from one carbon due to existence of the rotamers.

[c] probably splitting from one carbon due to existence of the rotamers.

[d] probably splitting from one carbon due to existence of the rotamers.

Characterization of synthetic plicatic acid by spiking experiments and CD spectrometry

The ^{1}H and ^{13}C NMR spectra of natural plicatic acid were not reported. Perhaps due to numerous possible patterns of intra or inter molecular hydrogen bonding interactions between various functionalities, the ^{1}H and ^{13} C NMR spectra were found to vary with either the synthetic or the authentic sample. The identity of the synthetic (-)-plicatic acid was established by spiking experiments. A sample of an approximately 1:1 mixture of synthetic and authentic plicatic acids was prepared. Spectroscopic and chromatographic studies of this mixture, including ^{1}H NMR, ^{13}C NMR as well as HPLC chromatograms obtained with two different columns, showed that the mixture was homogeneous. The exact mass of both the synthetic and natural plicatic acid was determined to be consistent with the molecular formula of plicatic acid by HRMS analysis. The absolute configuration of the synthetic sample was determined to be the same as the natural plicatic acid through a comparison of their respective CD spectrum.

1. ^{1}H NMR and ^{13}C NMR (see page S73-S99)

First, NMR (^{1}H NMR and ^{13}C NMR) spectra of Synthetic Sample and Authentic Sample were recorded respectively; they were found to be slightly different. Then, NMR (^{1}H NMR and ^{13}C NMR) spectra of Mixture Sample comprising Synthetic Sample and Authentic Sample in approximately 1:1 ratio were recorded; only one set of peaks was observed in the NMR spectra, which indicated that the mixture sample was homogeneous. It's worth mentioning that both ^{1}H NMR and ^{13}C NMR spectra of these samples show splitting and broadening peaks probably due to atropisomerism (retarded rotation along C1'-C7' bond) and extensive hydrogen bonding interactions as well. Similar splitting and broadening patterns are present in the ^{1}H NMR and ^{13}C NMR spectra of **11**, **12**, and **13.**

2. VT-^{1}H NMR (see page S100)

VT-^{1}H NMR experiments were performed on Authentic Sample, Synthetic Sample, Mixture Sample, respectively, at 21, 30, 40, 50, 60, and 70 ^{o}C in stages. Similar patterns and trends in the NMR spectra were observed for all three samples.

Take Mixture Sample for instance. Two separate peaks (1H for each by integration) at δ 6.48 and δ 6.32 at 21 ^{o}C gradually merge into one at δ 6.46 (2H by integration) as the temperature steadily rises to 70 ^{o}C; C**H**$_3$O (on pending ring C) gives split peaks at δ 3.79 and δ 3.64 (3H combined, by integration) at 21 ^{o}C which gradually unite at δ 3.75 (3H by integration) as the temperature steadily rises to 70 ^{o}C.

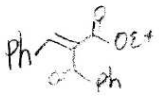
3. HPLC (see page S106)

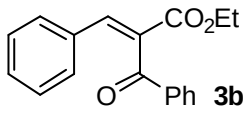
HPLC analysis was performed using two different columns, Zorbax Rx C8 and Symmetry® C18, for Synthetic Sample, Authentic Sample and Mixture Sample, respectively. On Zorbax Rx C8 column (100% water, 0.25 mL/min, 254 nm), the retention time for Synthetic, Authentic, Mixture Sample are 7.91, 7.91, 8.05 min. On Symmetry® C18 column (100% water, 0.20 mL/min, 254 nm), the retention time for Synthetic, Authentic, Mixture Sample are 9.19, 8.97, 9.09 min, respectively. Thus, only one peak was shown by HPLC analysis of Mixture Sample.

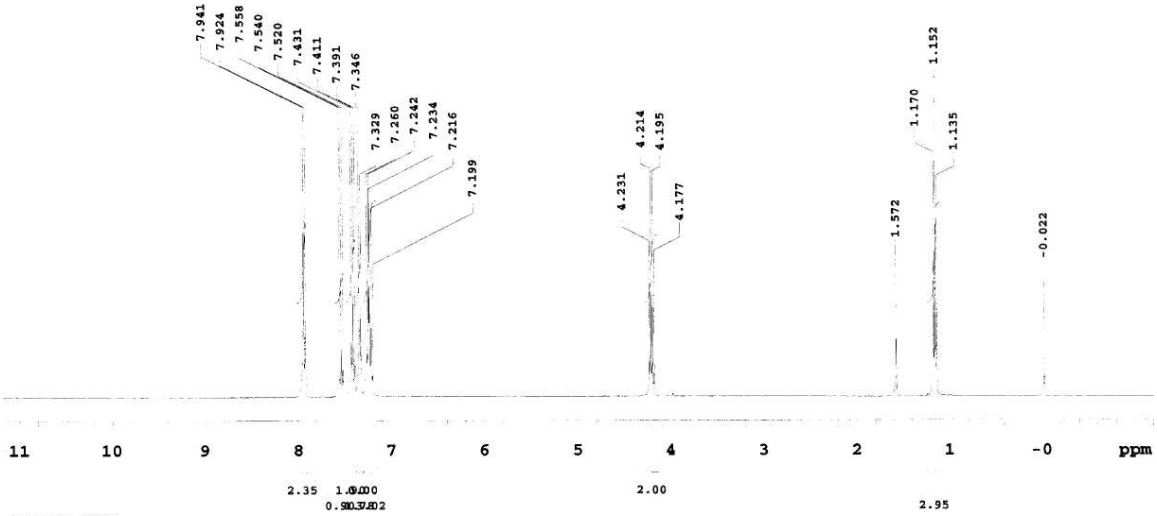
4. CD (see page S106)

A comparison of CD spectrum of Synthetic Sample and Authentic Sample indicates they are of the sample absolute configuration.

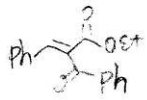
```
Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: kyb-1-34-2-pure
INOVA-500  "gamble"

 Pulse 46.1 degrees
 Acq. time 1.638 sec
 Width 5000.0 Hz
 16 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 52 sec
```

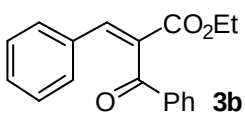


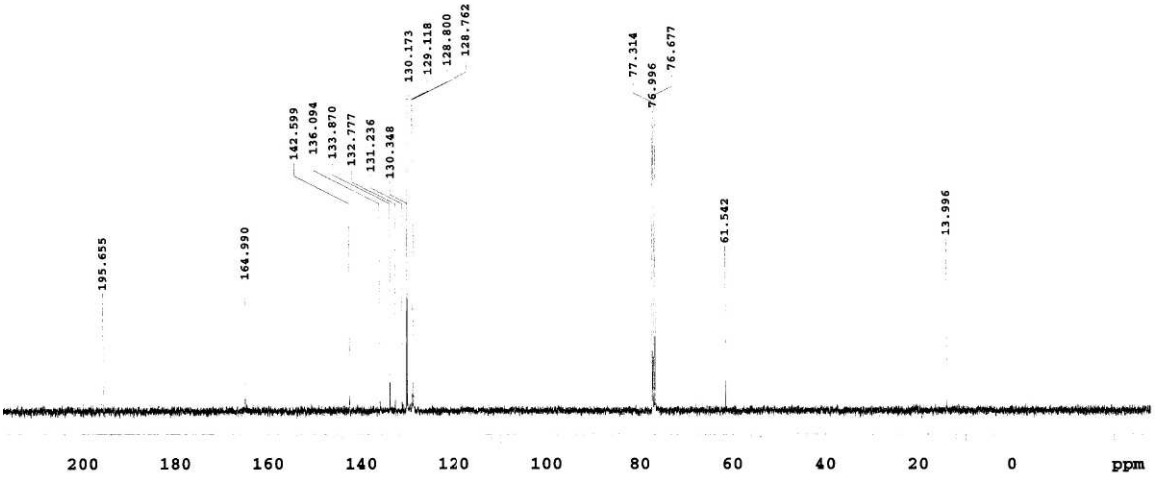


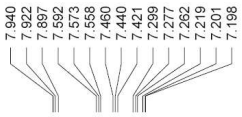


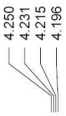

```
 Solvent: CDCl3
 Ambient temperature
File: kyb-1-34-c
INOVA-500  "gamble"

 Pulse 53.1 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 772 repetitions
OBSERVE C13, 100.5180359 MHz
DECOUPLE H1, 399.7552490 MHz
 Power 37 dB
 on during acquisition
 off during delay
 GARP-1 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 336168 hr, 19 min, 12 sec
```

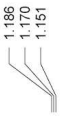


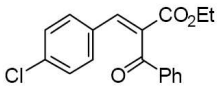


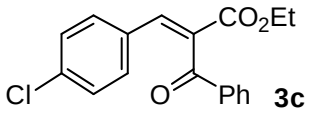




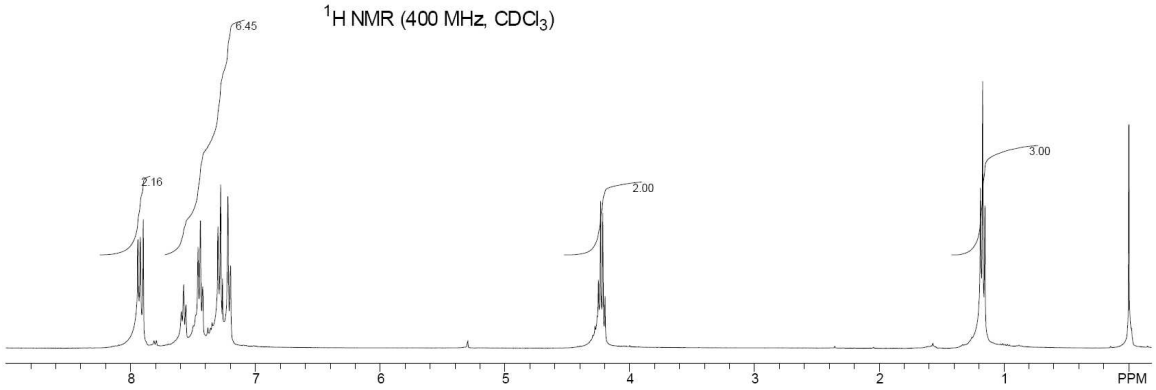




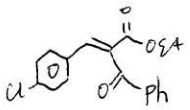


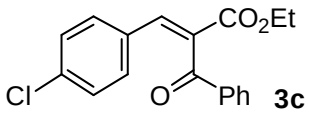


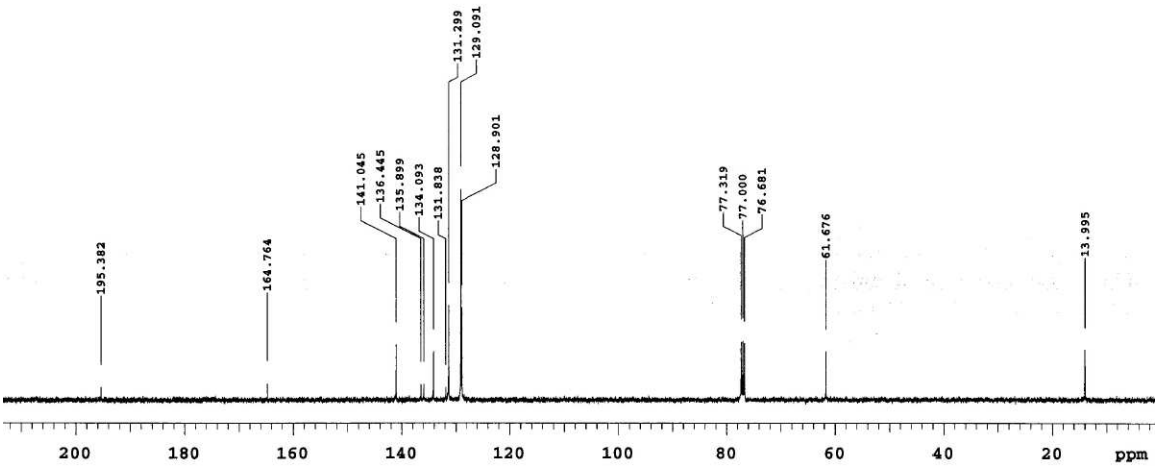
^{1}H NMR (400 MHz, $CDCl_3$)




```
Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
INOVA-400  "fid"

 Pulse 53.1 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 808 repetitions
OBSERVE  C13, 100.5180342 MHz
DECOUPLE  H1, 399.7552472 MHz
 Power 37 dB
 on during acquisition
 off during delay
 GARP-1 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 335612 hr, 45 min, 52 sec
```

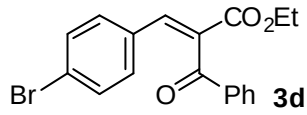




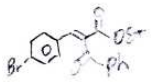


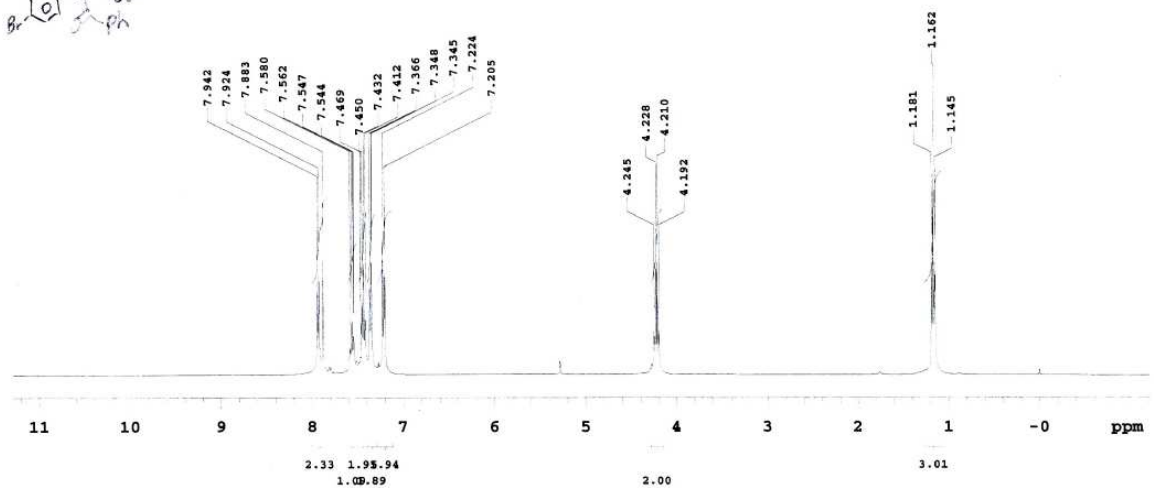
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-50HH
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
54 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 1 min, 29 sec



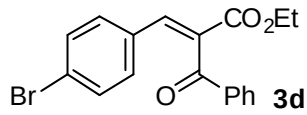
3d



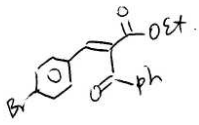


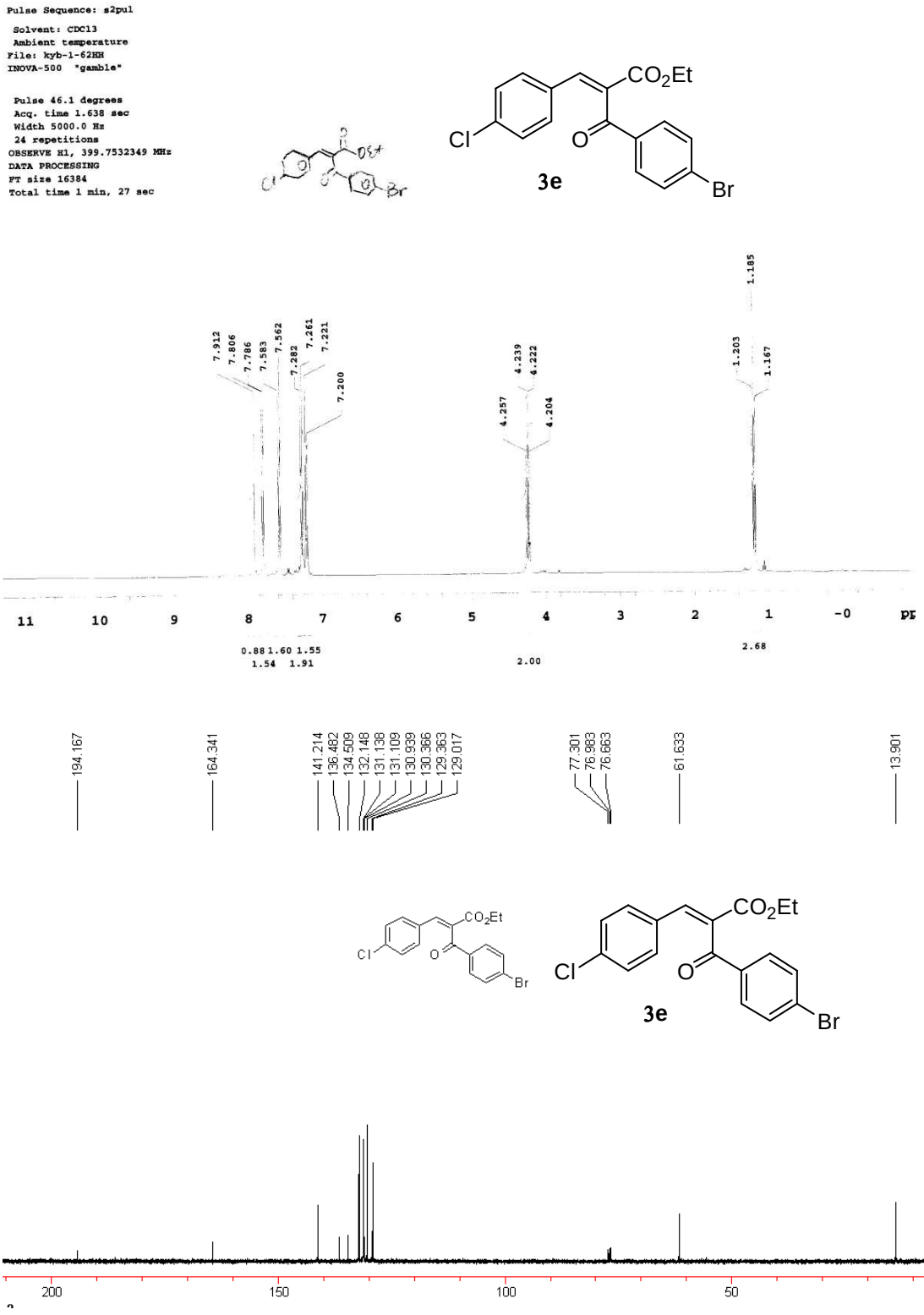
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"

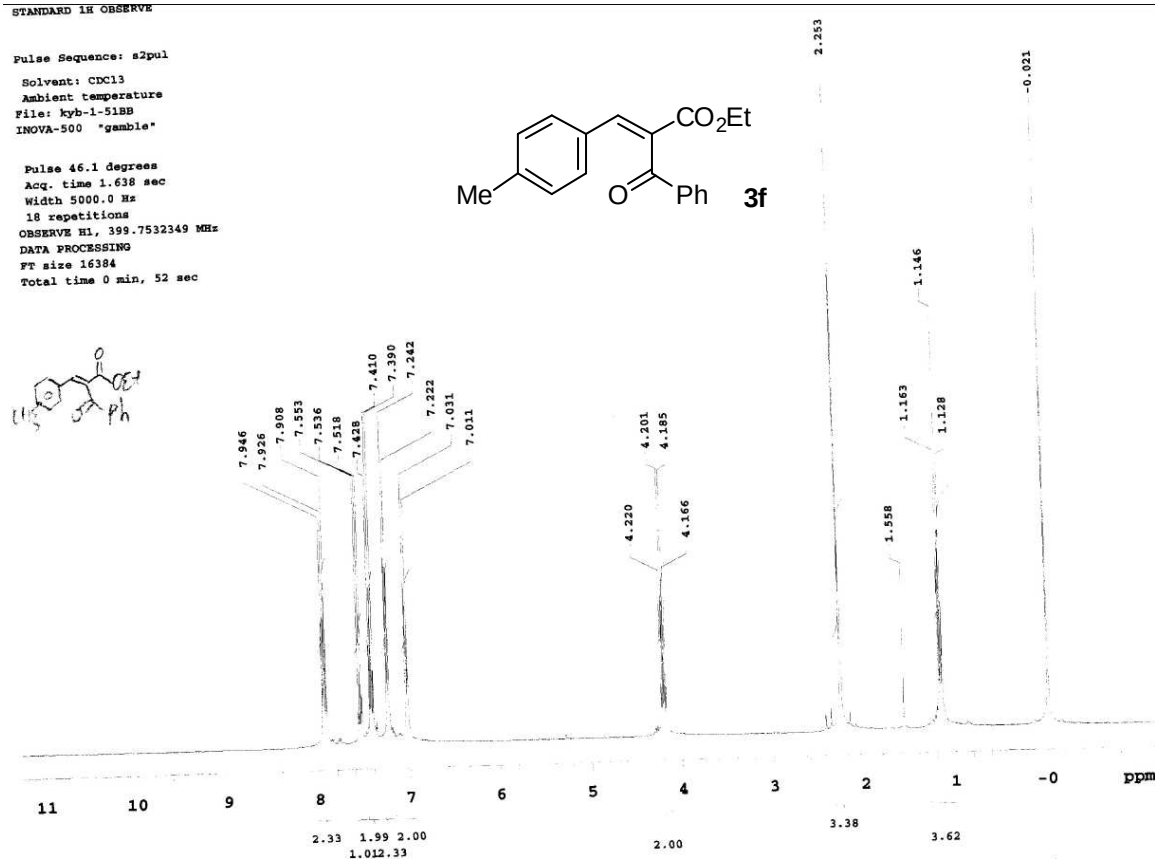
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
258 repetitions
OBSERVE C13, 100.5180426 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
FT size 65536
Total time 335612 hr, 45 min, 52 sec

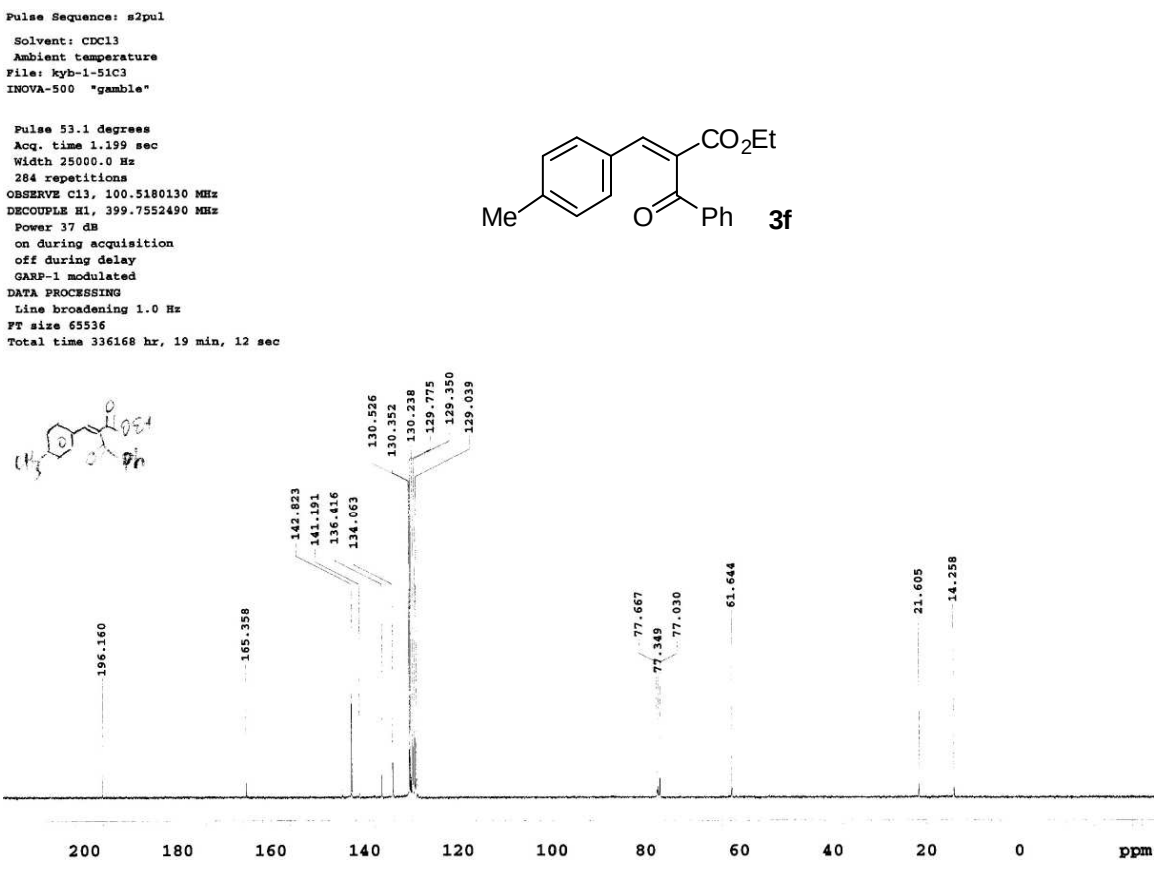


3d



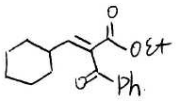

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-62HH
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
24 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 1 min, 27 sec
CO2Et
Cl
O
Br
3e
7.912
7.806
7.786
7.583
7.562
7.282
7.261
7.221
7.200
4.257
4.239
4.222
4.204
1.203
1.185
1.167
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
0.88 1.60 1.55
1.54 1.91
2.00
2.68
194.167
164.341
141.214
136.482
134.509
132.148
131.138
131.109
130.939
130.366
129.363
129.017
77.301
76.983
76.663
61.633
13.901
200
150
100
50
PPM

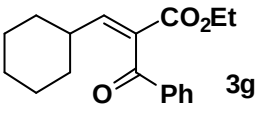

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-51BB
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
18 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 52 sec
CO2Et
Me
O
Ph
3f
2.253
-0.021
1.146
1.163
1.128
1.558
4.220
4.201
4.185
4.166
7.946
7.926
7.908
7.553
7.536
7.518
7.428
7.410
7.390
7.242
7.222
7.031
7.011
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
2.33
1.99
2.00
1.012.33
2.00
3.38
3.62


Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-51C3
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
284 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 336168 hr, 19 min, 12 sec
CO2Et
Me
O
Ph
3f
196.160
165.358
142.823
141.191
136.416
134.063
130.526
130.352
130.238
129.775
129.350
129.039
77.667
77.349
77.030
61.644
21.605
14.258
200
180
160
140
120
100
80
60
40
20
0
ppm

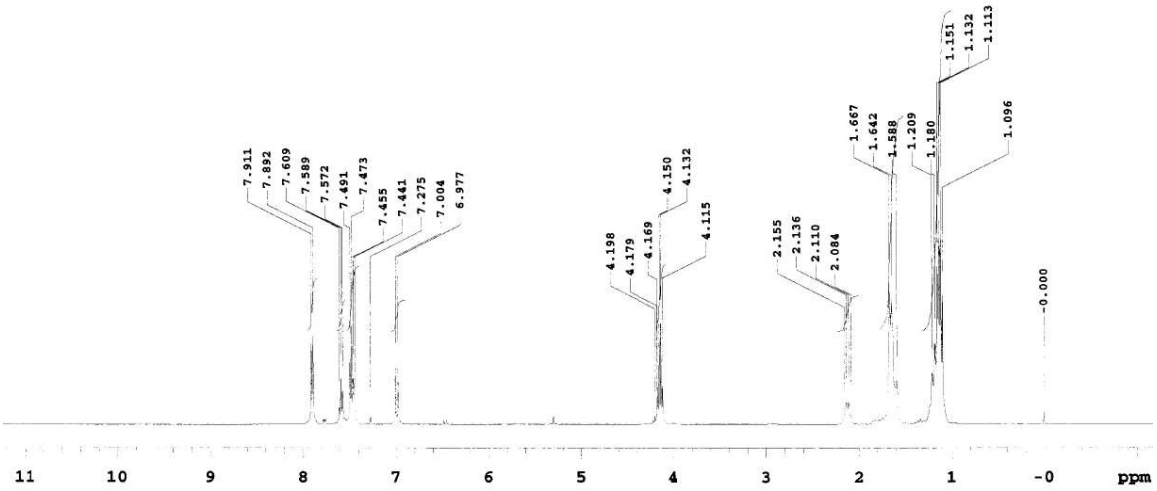
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-127B-better
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
20 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 2 min, 28 sec



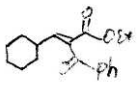


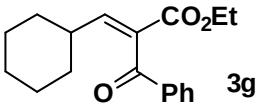
3g



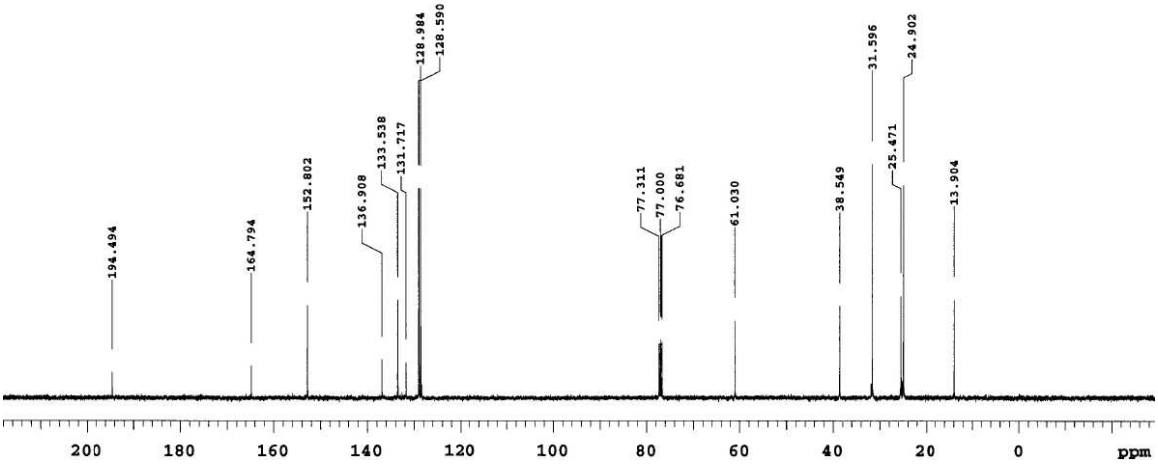
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"

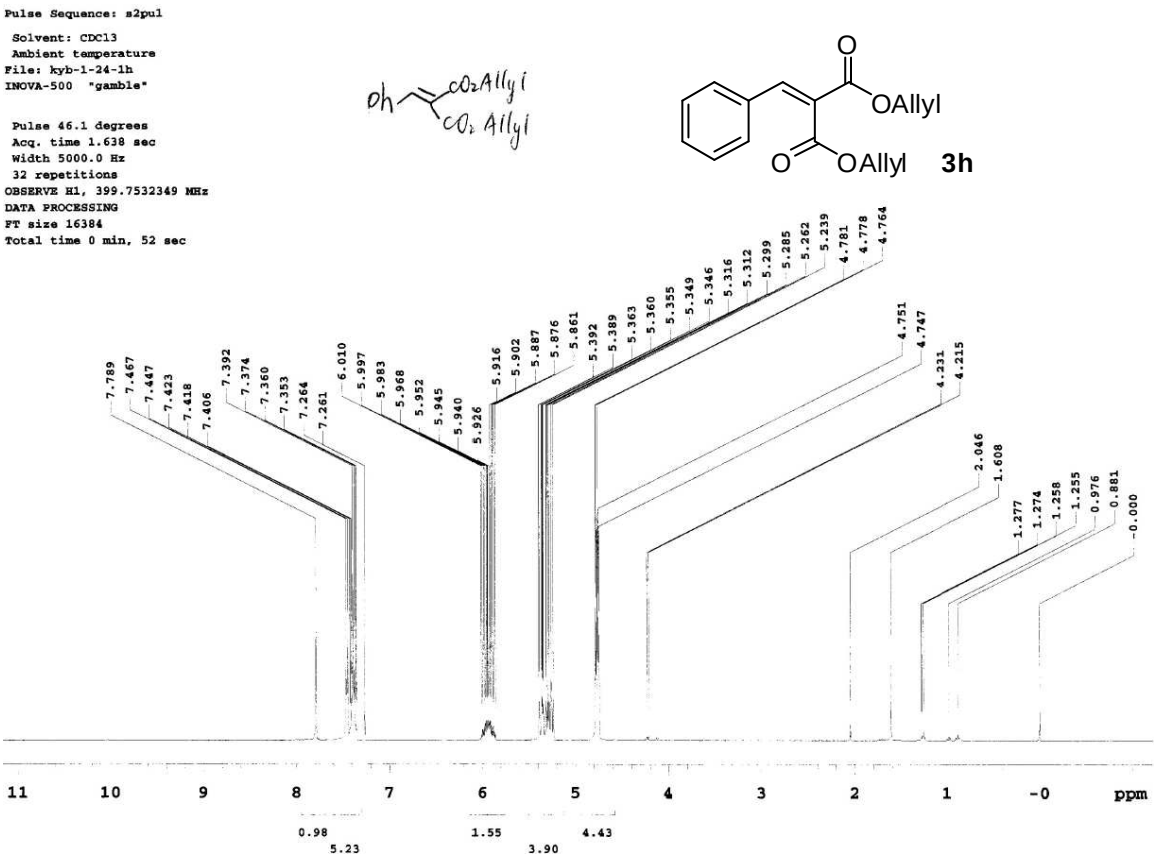
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
368 repetitions
OBSERVE C13, 100.5180373 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 33 hr, 33 min, 39 sec

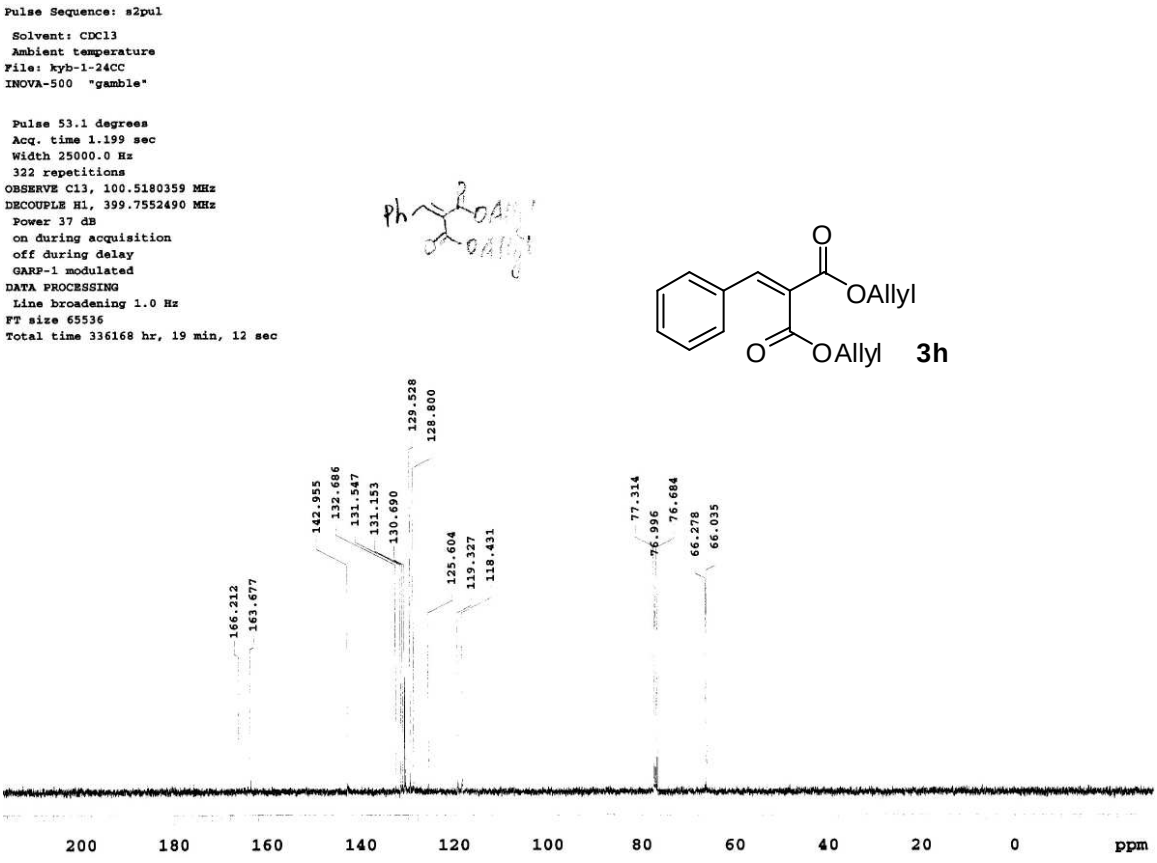


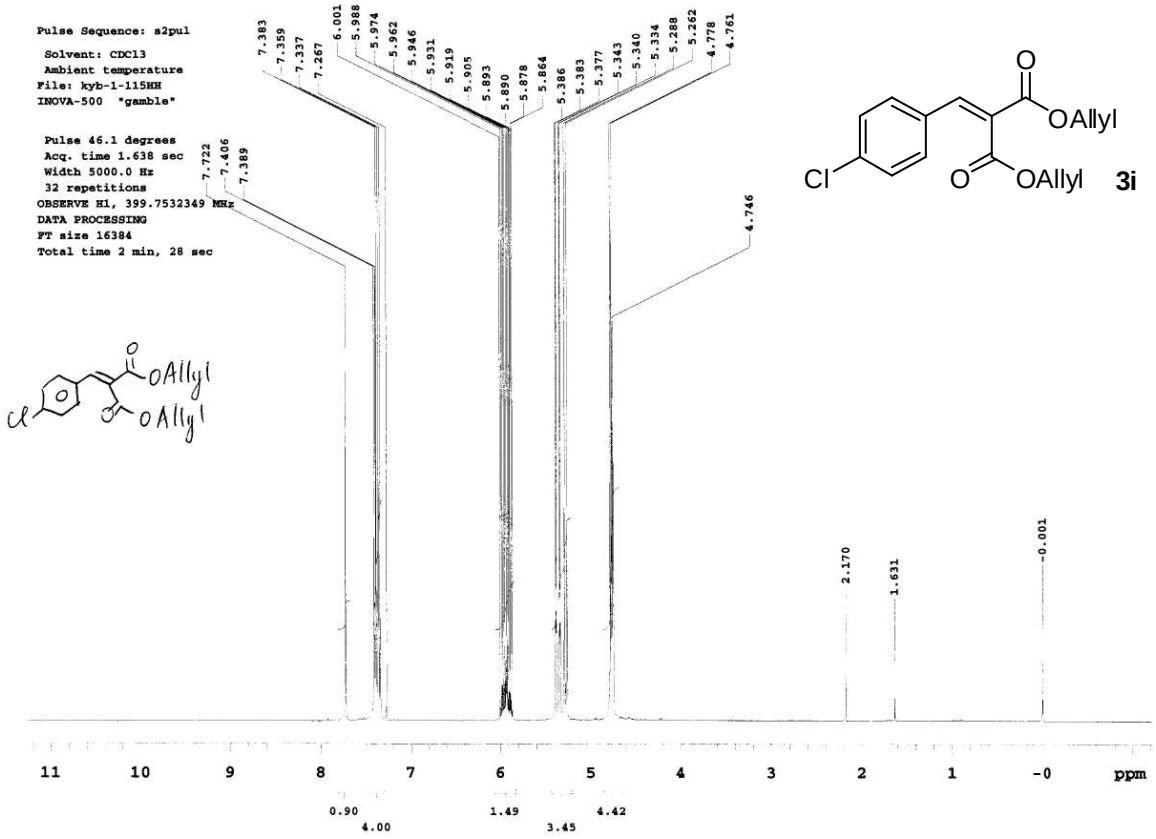


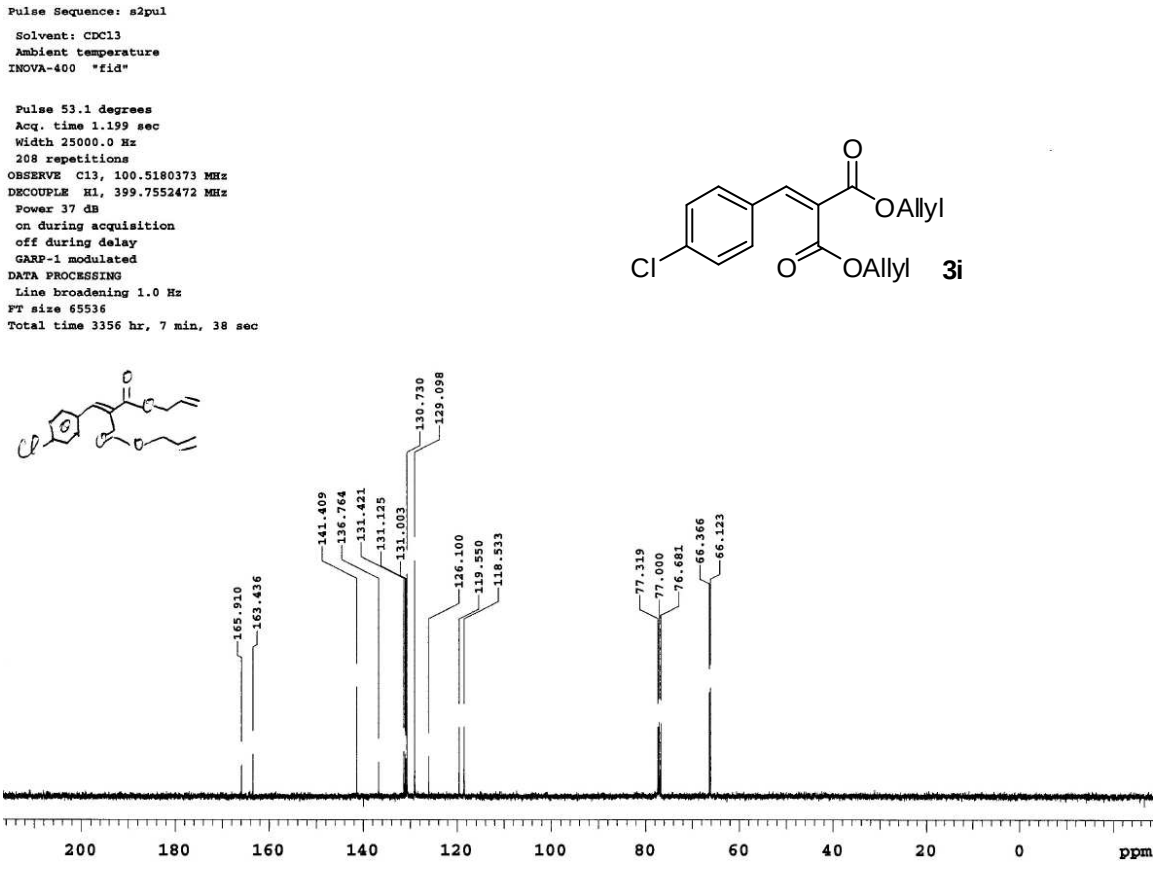
3g

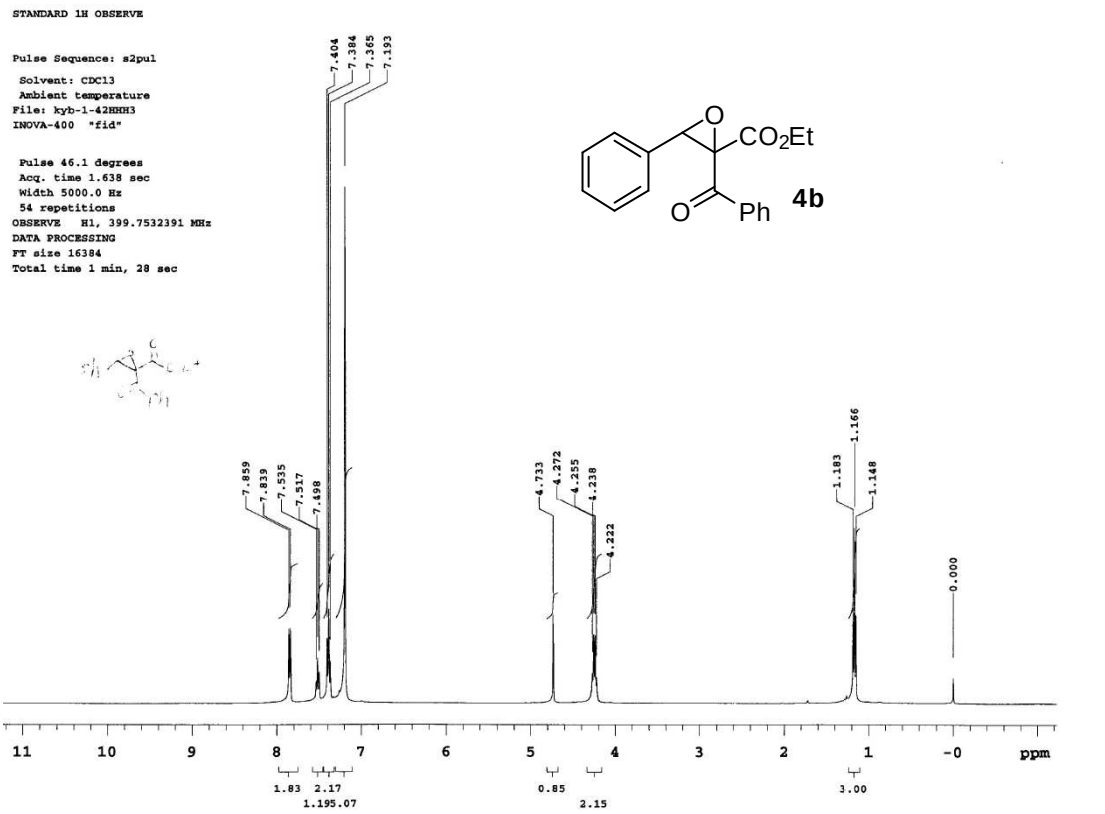


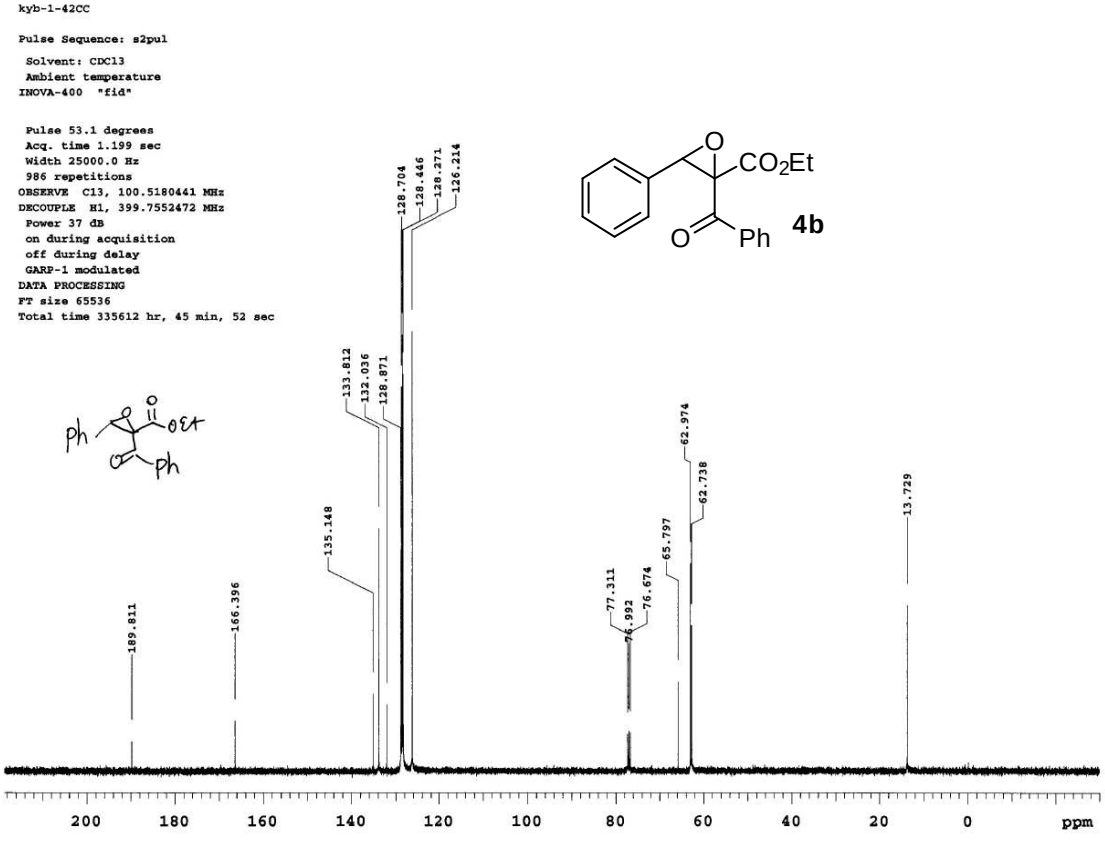

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-24-1h
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
32 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 52 sec
OAllyl
OAllyl
3h
ppm
0.98
5.23
1.55
3.90
4.43

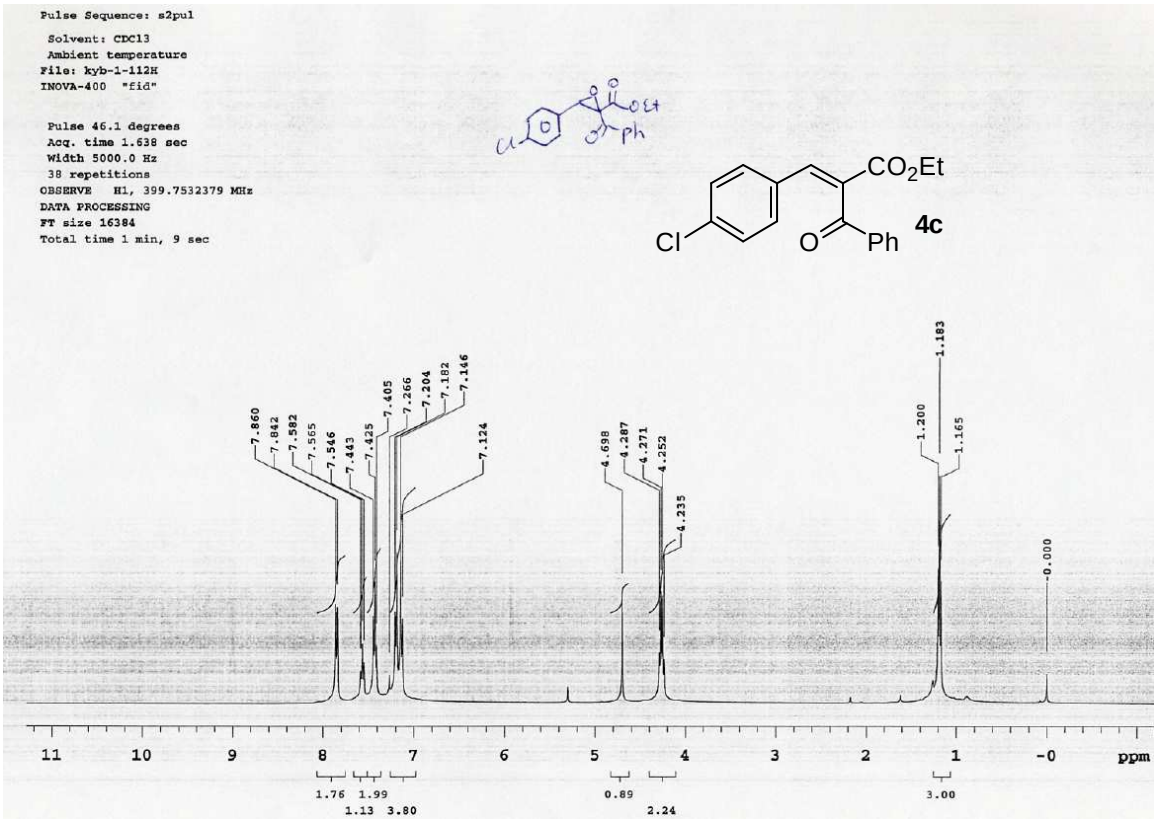

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-24CC
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
322 repetitions
OBSERVE C13, 100.5180359 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 336168 hr, 19 min, 12 sec
OAllyl
OAllyl
3h
ppm

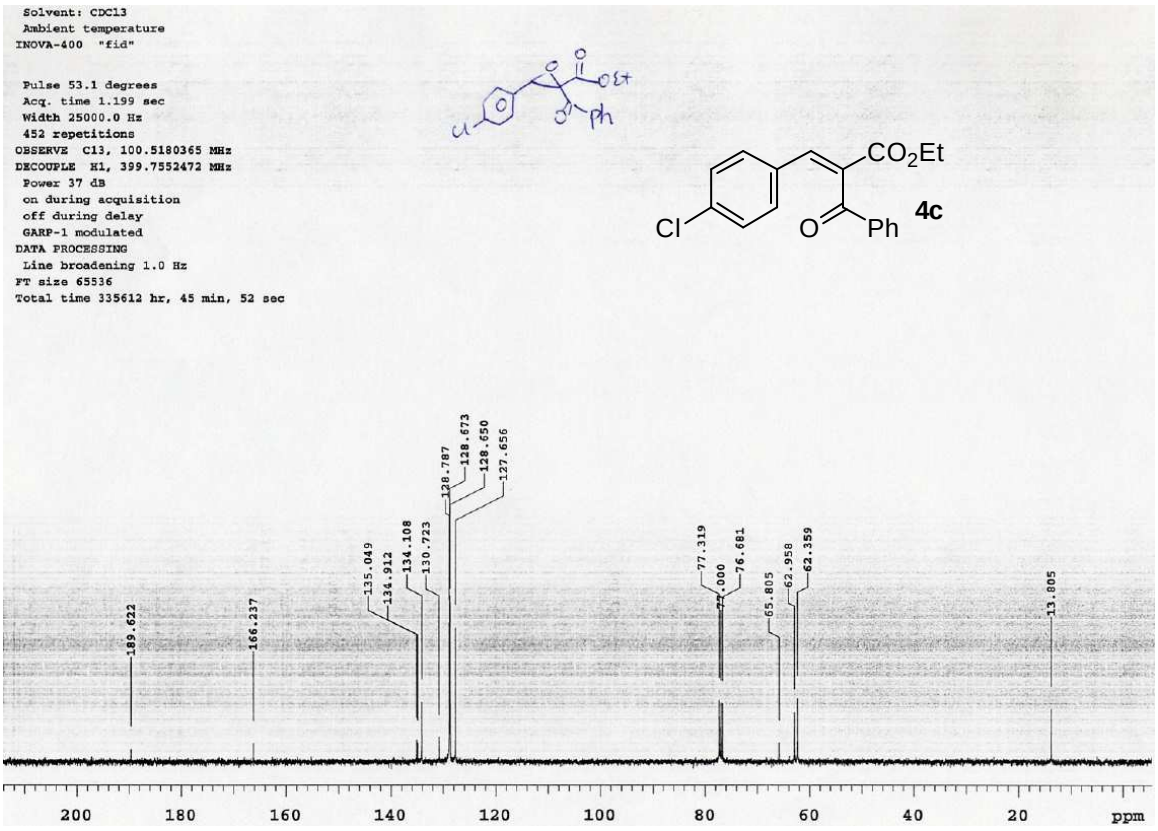

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-115HH
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
32 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 2 min, 28 sec
7.383
7.359
7.337
7.267
6.001
5.988
5.974
5.962
5.946
5.931
5.919
5.905
5.893
5.890
5.878
5.864
5.386
5.383
5.377
5.343
5.340
5.334
5.288
5.262
4.778
4.761
7.722
7.406
7.389
4.746
2.170
1.631
-0.001
OAllyl
OAllyl
Cl
3i
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
0.90
4.00
1.49
3.45
4.42

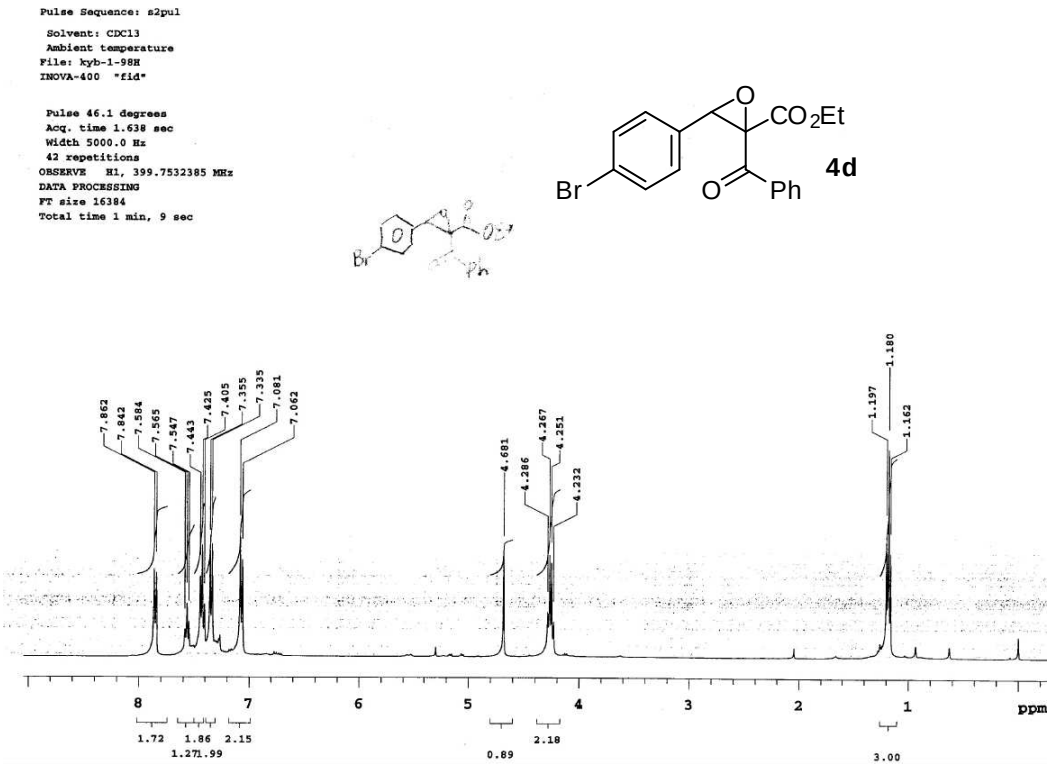

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
208 repetitions
OBSERVE C13, 100.5180373 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3356 hr, 7 min, 38 sec
OAllyl
OAllyl
Cl
3i
165.910
163.436
141.409
136.764
131.421
131.125
131.003
130.730
129.098
126.100
119.550
118.533
77.319
77.000
76.681
66.366
66.123
200
180
160
140
120
100
80
60
40
20
0
ppm

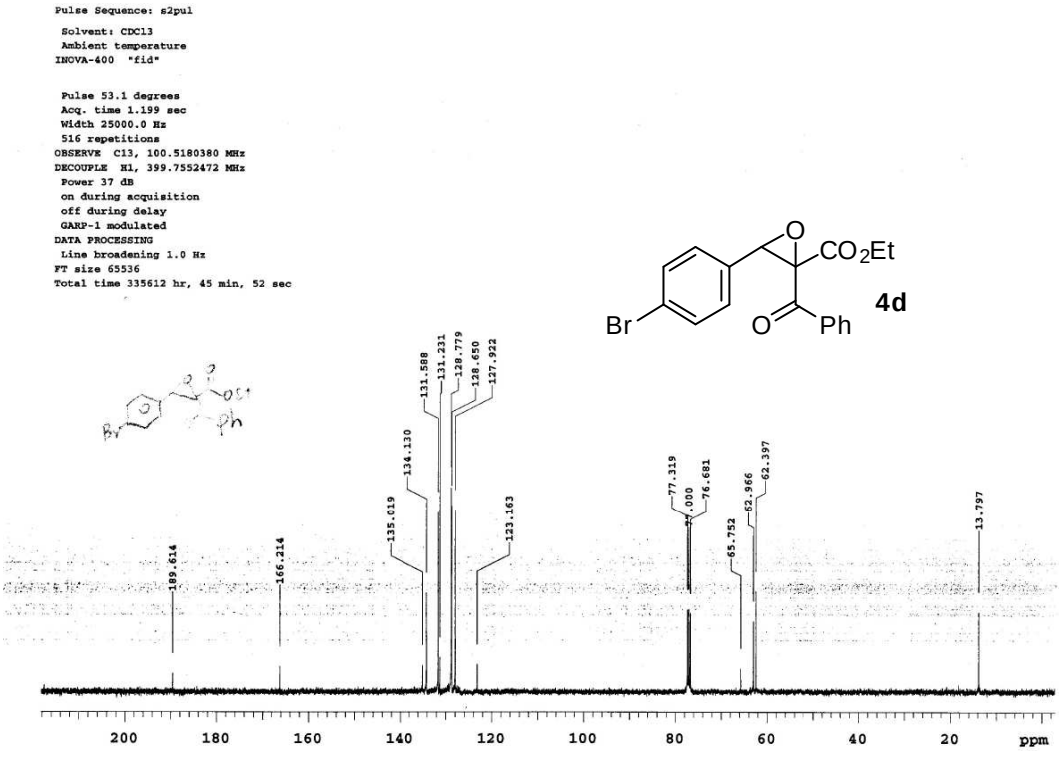

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-42HHH3
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
54 repetitions
OBSERVE H1, 399.7532391 MHz
DATA PROCESSING
FT size 16384
Total time 1 min, 28 sec
7.404
7.384
7.365
7.193
7.859
7.839
7.535
7.517
7.498
4.733
4.272
4.255
4.238
4.222
1.183
1.166
1.148
0.000
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
1.83
2.17
1.195.07
0.85
2.15
3.00
O
CO2Et
O
Ph
4b


kyb-1-42CC
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
986 repetitions
OBSERVE C13, 100.5180441 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
FT size 65536
Total time 335612 hr, 45 min, 52 sec
128.704
128.446
128.271
126.214
133.812
132.036
128.871
135.148
189.811
166.396
77.311
76.992
76.674
65.797
62.974
62.738
13.729
200
180
160
140
120
100
80
60
40
20
0
ppm
O
CO2Et
O
Ph
4b

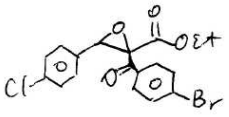

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-112H
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
38 repetitions
OBSERVE H1, 399.7532379 MHz
DATA PROCESSING
FT size 16384
Total time 1 min, 9 sec
CO2Et
Cl
O
Ph
4c
7.860
7.842
7.582
7.565
7.546
7.443
7.425
7.405
7.266
7.204
7.182
7.146
7.124
4.698
4.287
4.271
4.252
4.235
1.200
1.183
1.165
0.000
11 10 9 8 7 6 5 4 3 2 1 -0 ppm
1.76 1.99 1.13 3.80
0.89 2.24
3.00

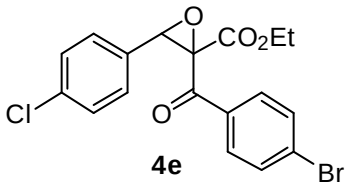

Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
452 repetitions
OBSERVE C13, 100.5180365 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 335612 hr, 45 min, 52 sec
CO2Et
Cl
O
Ph
4c
189.622
166.237
135.049
134.912
134.108
130.723
128.787
128.673
128.650
127.656
77.319
77.000
76.681
65.805
62.958
62.359
13.805
200 180 160 140 120 100 80 60 40 20 ppm


Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-98H
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
42 repetitions
OBSERVE H1, 399.7532385 MHz
DATA PROCESSING
FT size 16384
Total time 1 min, 9 sec
Br
O
CO2Et
O
Ph
4d
7.862
7.842
7.584
7.565
7.547
7.443
7.425
7.405
7.355
7.335
7.081
7.062
4.681
4.286
4.267
4.251
4.232
1.197
1.180
1.162
8
7
6
5
4
3
2
1
ppm
1.72
1.86
2.15
1.27
1.99
0.89
2.18
3.00

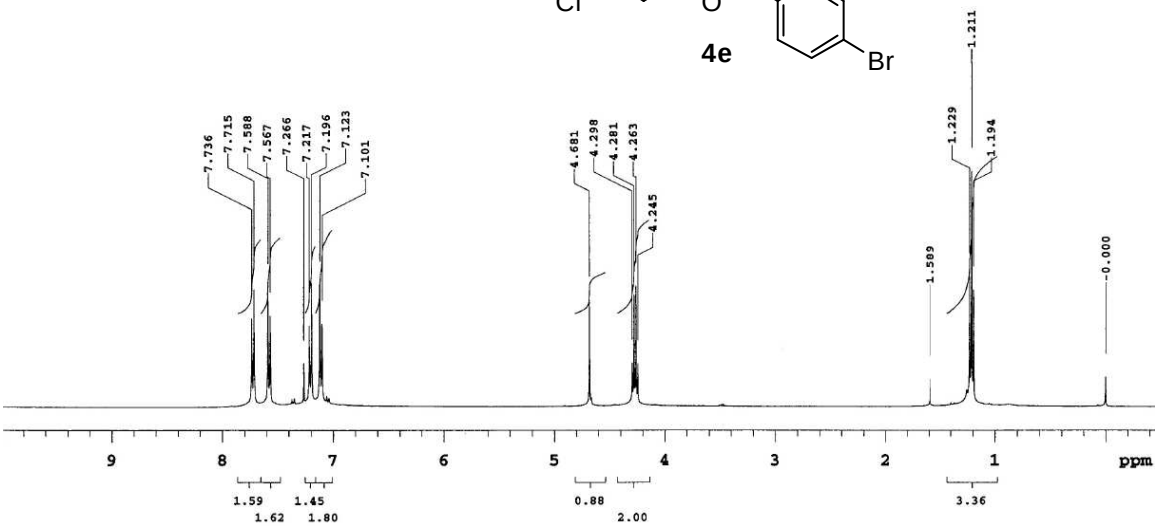

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
516 repetitions
OBSERVE C13, 100.5180380 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 335612 hr, 45 min, 52 sec
Br
O
CO2Et
O
Ph
4d
189.614
166.214
135.619
134.130
131.588
131.231
128.779
128.650
127.922
123.163
77.319
77.000
76.681
65.752
62.966
62.397
13.797
200
180
160
140
120
100
80
60
40
20
ppm

```
Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
INOVA-400  "fid"

 Pulse 46.1 degrees
 Acq. time 1.638 sec
 Width 5000.0 Hz
 42 repetitions
OBSERVE   H1, 399.7532379 MHz
DATA PROCESSING
FT size 16384
Total time 1 min, 9 sec
```

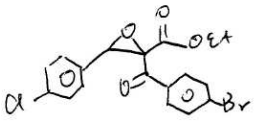


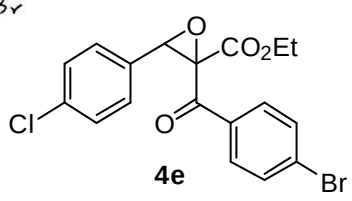


4e

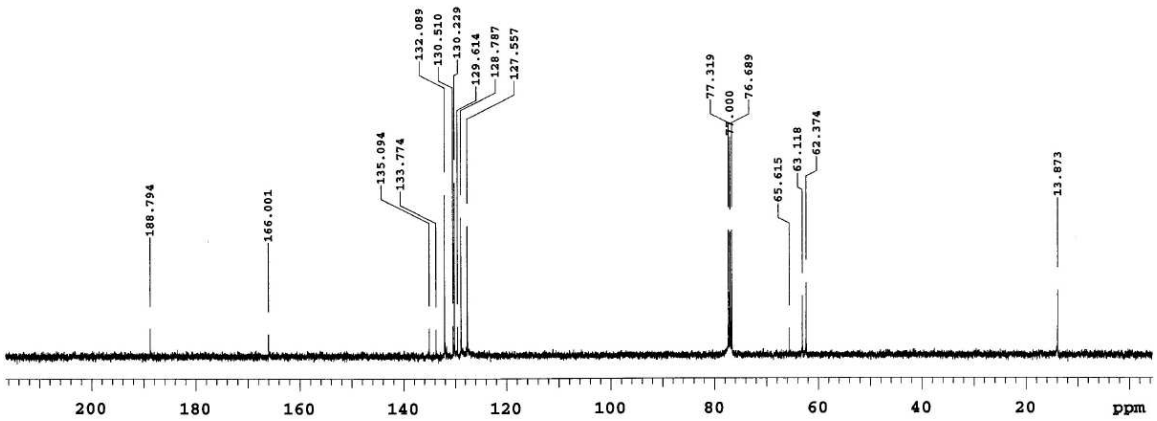


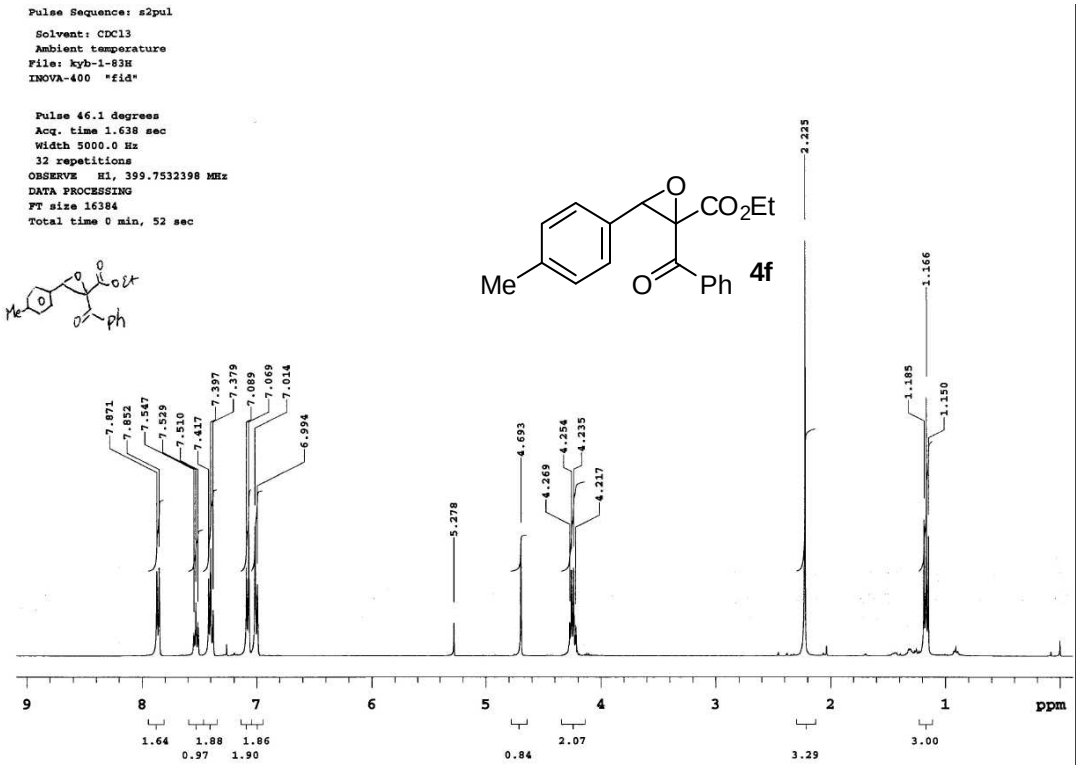

```
Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
INOVA-400  "fid"

 Pulse 53.1 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 974 repetitions
OBSERVE   C13, 100.5180350 MHz
DECOUPLE  H1, 399.7552472 MHz
 Power 37 dB
 on during acquisition
 off during delay
 GARP-1 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 335612 hr, 45 min, 52 sec
```

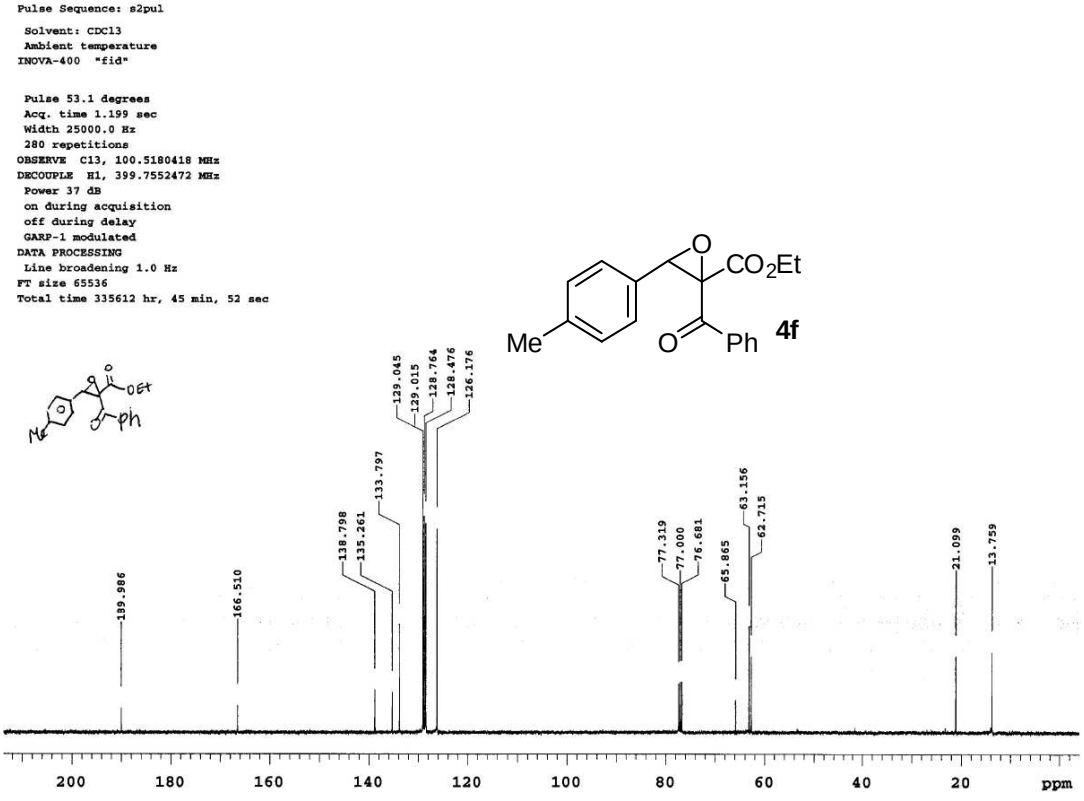


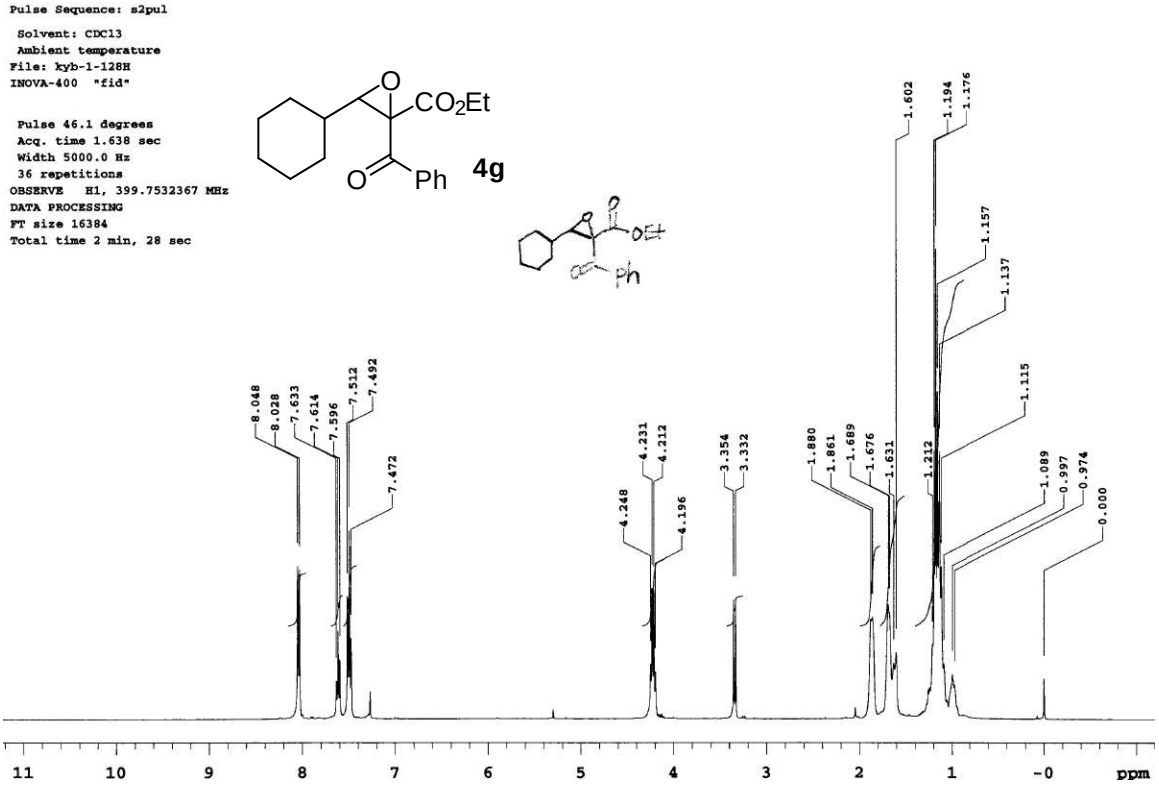


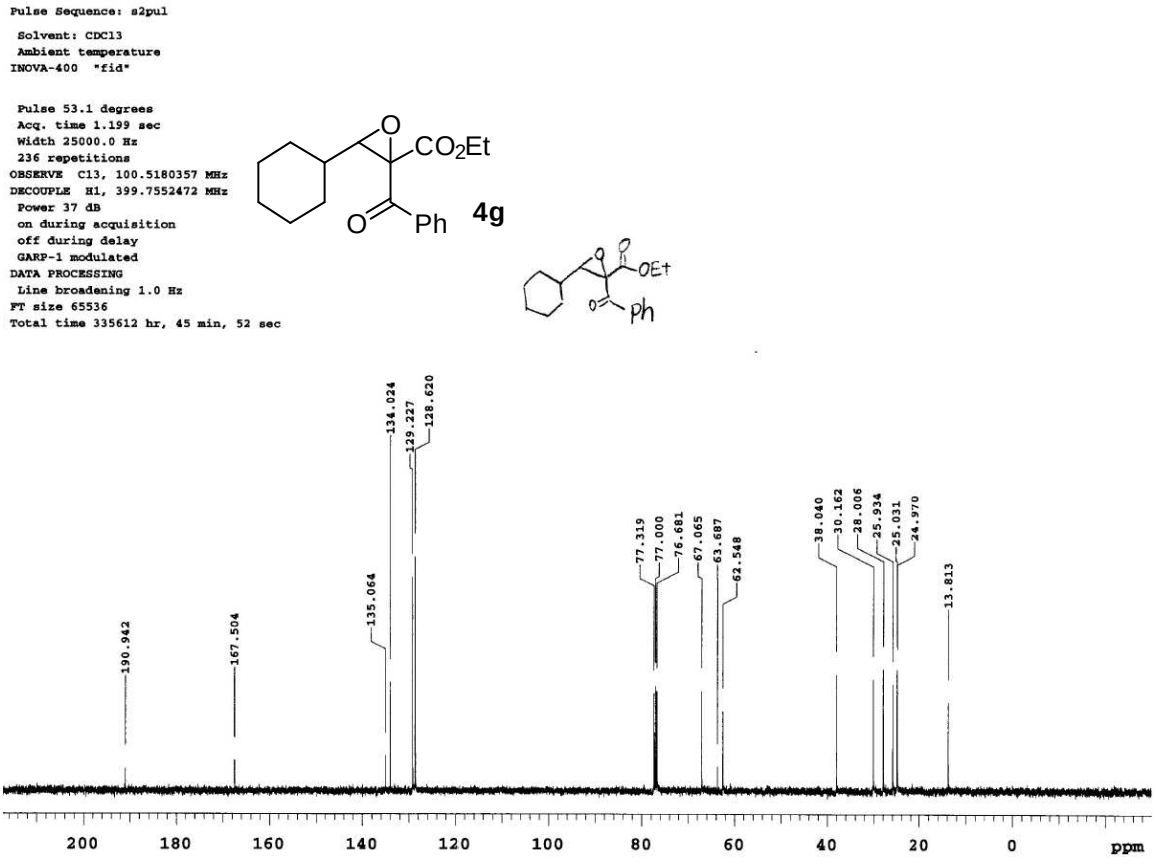
4e

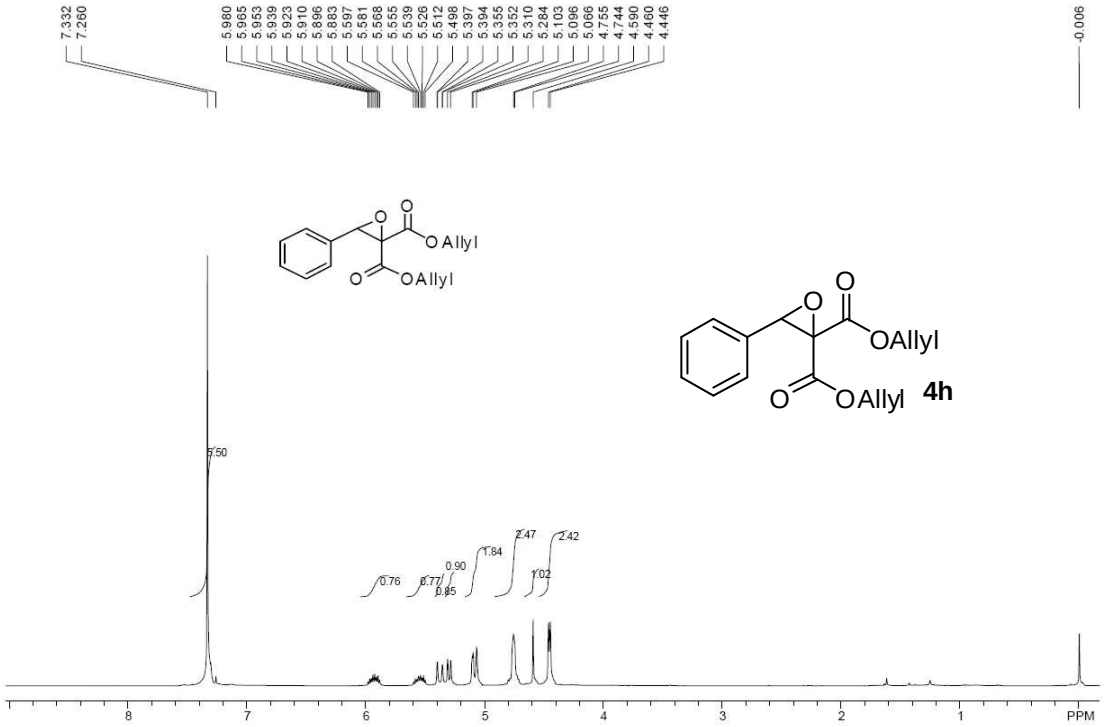



Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-83H
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
32 repetitions
OBSERVE H1, 399.7532398 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 52 sec
CO2Et
Me
O
Ph
4f
7.871
7.852
7.547
7.529
7.510
7.417
7.397
7.379
7.089
7.069
7.014
6.994
5.278
4.693
4.269
4.254
4.235
4.217
2.225
1.185
1.166
1.150
ppm
1.64
1.88
1.86
0.97
1.90
0.84
2.07
3.29
3.00

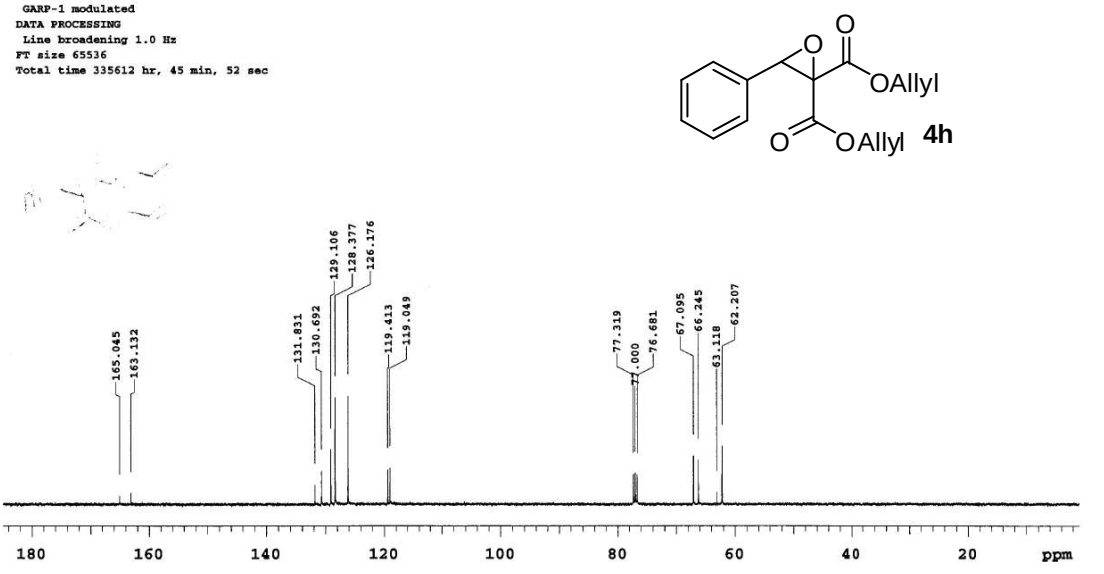

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
280 repetitions
OBSERVE C13, 100.5180418 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 335612 hr, 45 min, 52 sec
CO2Et
Me
O
Ph
4f
189.986
166.510
139.045
138.798
135.261
133.797
129.015
128.764
128.476
126.176
77.319
77.000
76.681
65.865
63.156
62.715
21.099
13.759
ppm

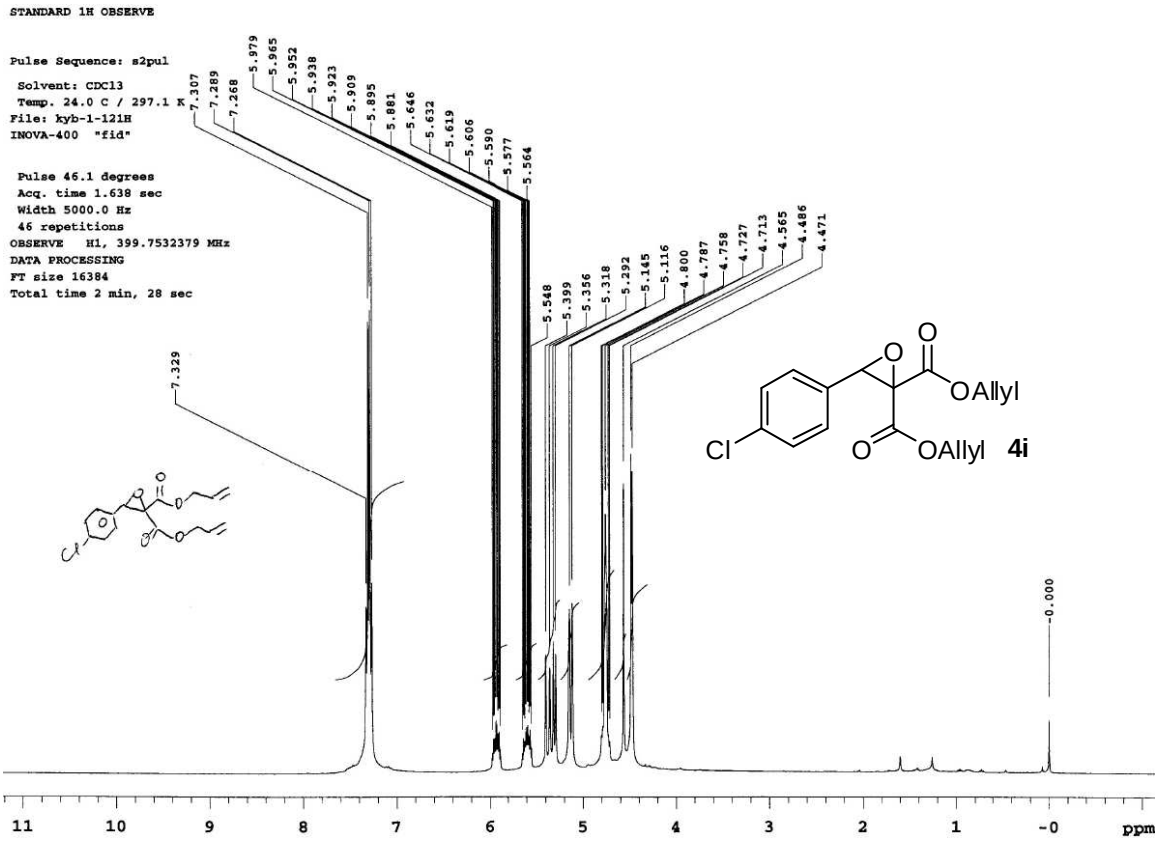

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: kyb-1-128H
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
36 repetitions
OBSERVE H1, 399.7532367 MHz
DATA PROCESSING
FT size 16384
Total time 2 min, 28 sec
CO2Et
Ph
4g
8.048
8.028
7.633
7.614
7.596
7.512
7.492
7.472
4.248
4.231
4.212
4.196
3.354
3.332
1.880
1.861
1.689
1.676
1.631
1.602
1.212
1.194
1.176
1.157
1.137
1.115
1.089
0.997
0.974
0.000
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

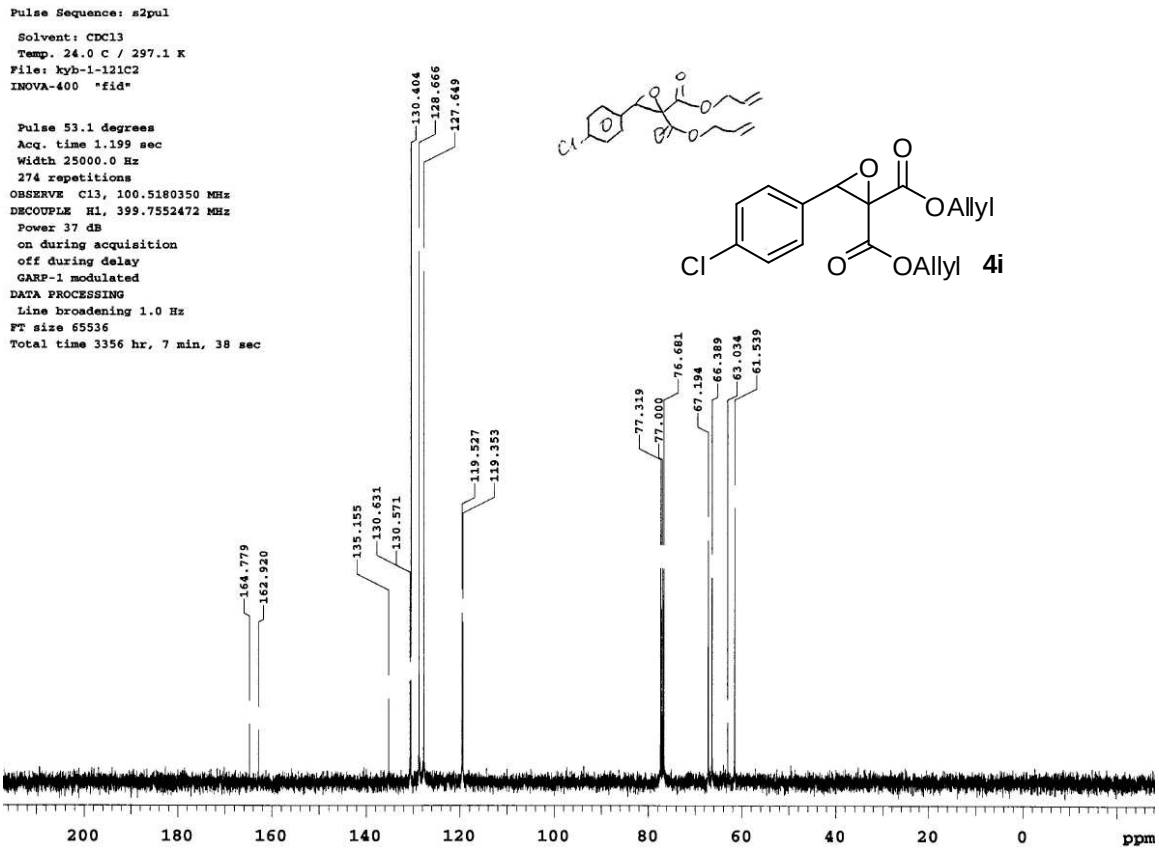

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
236 repetitions
OBSERVE C13, 100.5180357 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 335612 hr, 45 min, 52 sec
CO2Et
Ph
4g
190.942
167.504
135.064
134.024
129.227
128.620
77.319
77.000
76.681
67.065
63.687
62.548
38.040
30.162
28.006
25.934
25.031
24.970
13.813
200
180
160
140
120
100
80
60
40
20
0
ppm



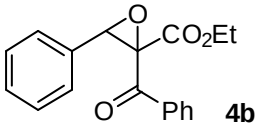

```
Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
INOVA-400  "fid"

 Pulse 53.1 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 298 repetitions
OBSERVE  C13, 100.5180365 MHz
DECOUPLE  H1, 399.7552472 MHz
 Power 37 dB
 on during acquisition
 off during delay
 GARP-1 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 335612 hr, 45 min, 52 sec
```



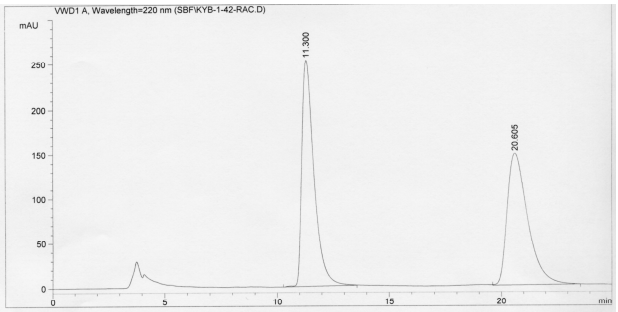

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
File: kyb-1-121H
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
46 repetitions
OBSERVE H1, 399.7532379 MHz
DATA PROCESSING
FT size 16384
Total time 2 min, 28 sec
7.307
7.289
7.268
7.329
5.979
5.965
5.952
5.938
5.923
5.909
5.895
5.881
5.646
5.632
5.619
5.606
5.590
5.577
5.564
5.548
5.399
5.356
5.318
5.292
5.145
5.116
4.800
4.787
4.758
4.727
4.713
4.565
4.486
4.471
-0.000
OAllyl
Cl
OAllyl
4i
11
10
9
8
7
6
5
4
3
2
1
-0
ppm


Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
File: kyb-1-121C2
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
274 repetitions
OBSERVE C13, 100.5180350 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3356 hr, 7 min, 38 sec
164.779
162.920
135.155
130.631
130.571
130.404
128.666
127.649
119.527
119.353
77.319
77.000
76.681
67.194
66.389
63.034
61.539
OAllyl
Cl
OAllyl
4i
200
180
160
140
120
100
80
60
40
20
0
ppm

HPLC Spectra for 4b-i



4b



Area Percent Report

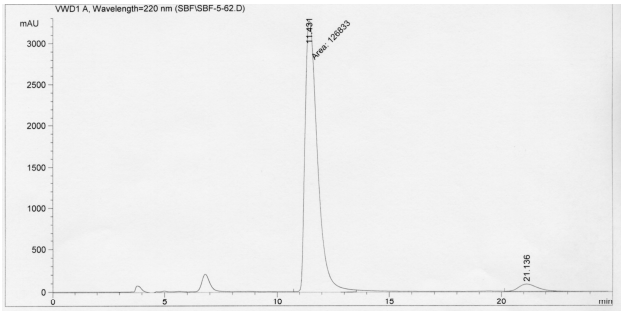
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.300	BB	0.5769	9596.76465	251.96046	50.3129
2	20.605	BB	0.9817	9477.41504	147.38446	49.6871

Totals : 1.90742e4 399.34492

*** End of Report ***



Area Percent Report

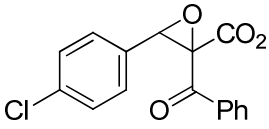
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

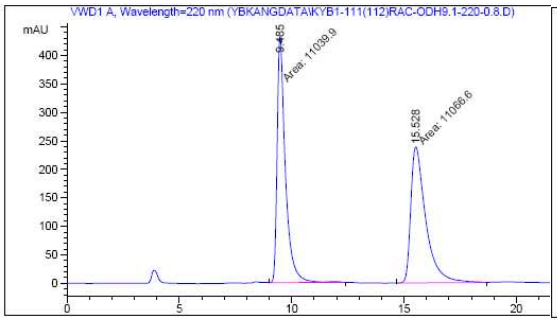
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.431	MM	0.6458	1.26833e5	3273.21777	96.1816
2	21.136	VB	0.9090	5035.32178	84.35349	3.8184

Totals : 1.31869e5 3357.57126

*** End of Report ***



4c

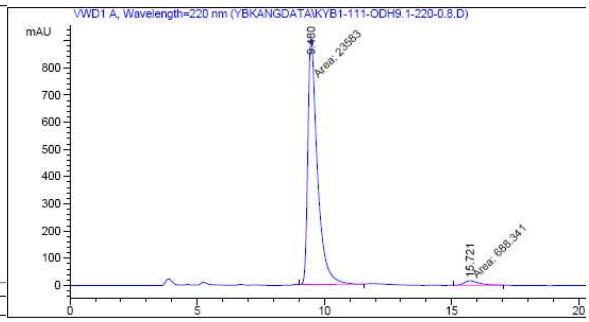


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.485	MM	0.4256	1.10399e4	432.37308	49.9397
2	15.528	MM	0.7726	1.10666e4	238.73206	50.0603

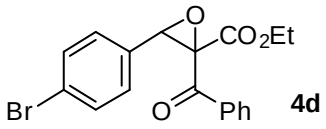


Area Percent Report

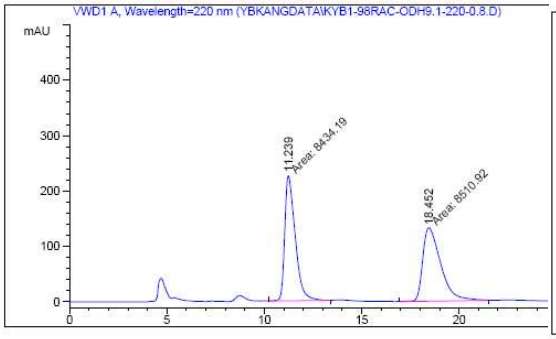
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

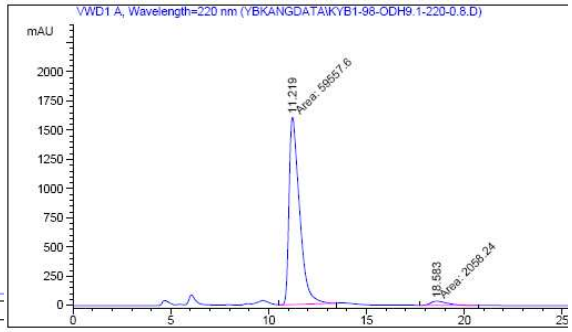
Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.480	MM	0.4343	2.35830e4	905.00415	97.1640
2	15.721	MM	0.6867	688.34058	16.70532	2.8360



4d





Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

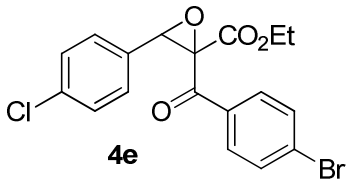
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.239	MM	0.6217	8434.19336	226.11493	49.7736
2	18.452	MM	1.0698	8510.92188	132.58762	50.2264

Area Percent Report

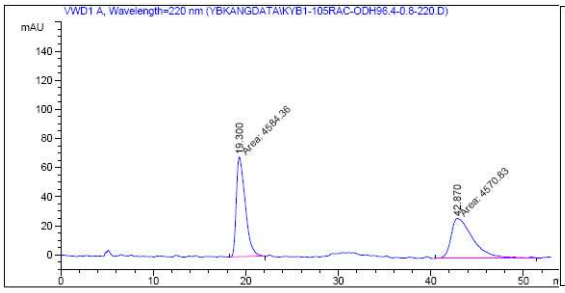
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

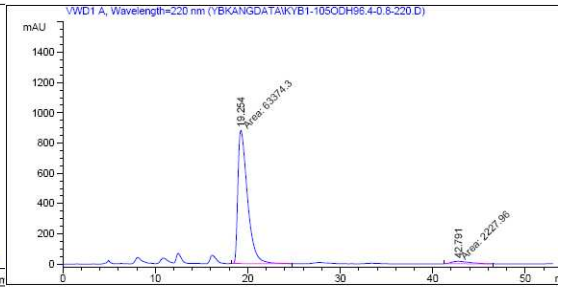
Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.219	MM	0.6177	5.95576e4	1607.08411	96.6596
2	18.583	MM	0.9654	2058.24268	35.53381	3.3404



4e





Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

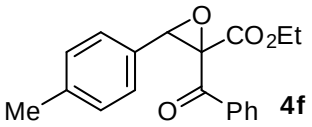
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.300	MM	1.1136	4584.35693	68.61414	50.0739
2	42.870	MM	2.7815	4570.82715	27.38843	49.9261

Area Percent Report

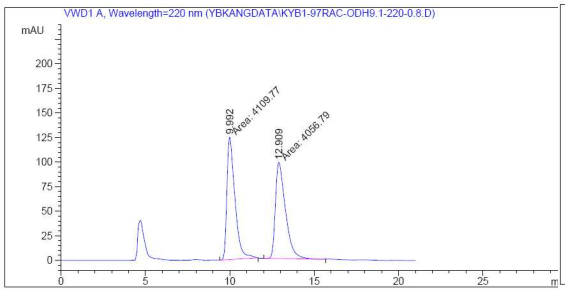
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

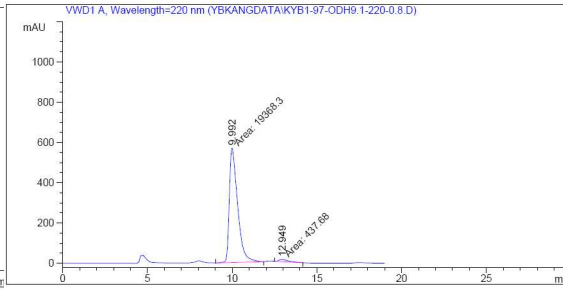
Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.254	MM	1.1991	6.33743e4	880.87677	96.6038
2	42.791	MM	2.2990	2227.96313	16.15156	3.3962



4f





Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

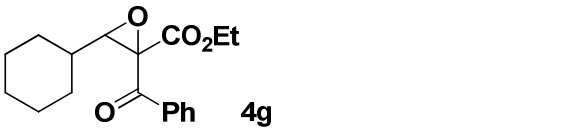
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.992	MM	0.5487	4109.76953	124.84371	50.3244
2	12.909	MM	0.6898	4056.78760	98.02475	49.6756

Area Percent Report

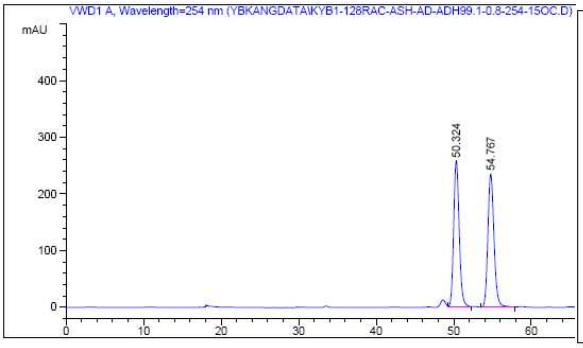
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

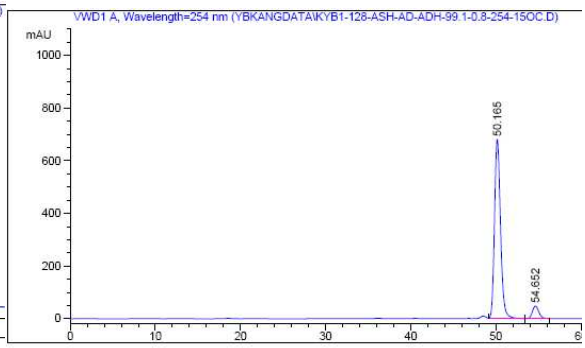
Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.992	MM	0.5667	1.93683e4	569.64313	97.7902
2	12.949	MM	0.6366	437.67972	11.45819	2.2098



4g





Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

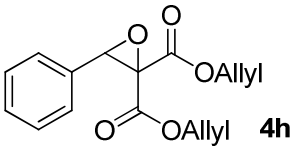
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	50.324	VV	0.7735	1.30278e4	258.87851	49.9211
2	54.767	VV	0.8571	1.30689e4	235.49992	50.0789

Area Percent Report

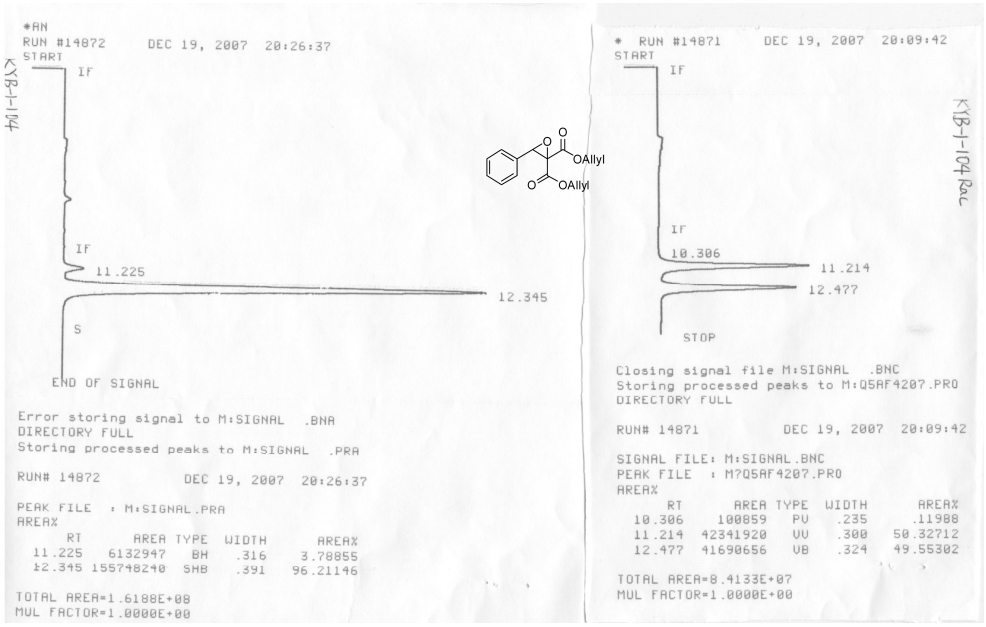
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

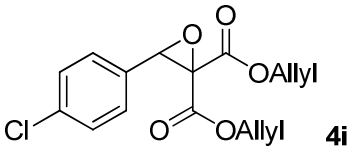
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	50.165	VV	0.7617	3.35428e4	680.19843	92.8466
2	54.652	VV	0.8244	2584.33081	48.13493	7.1534

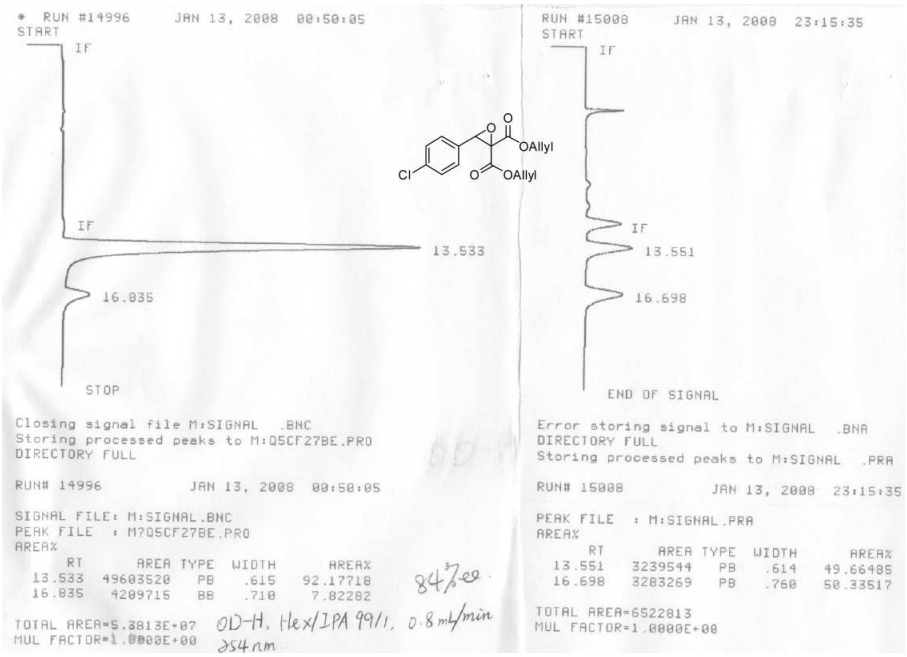

O
O
OAllyl
O
OAllyl

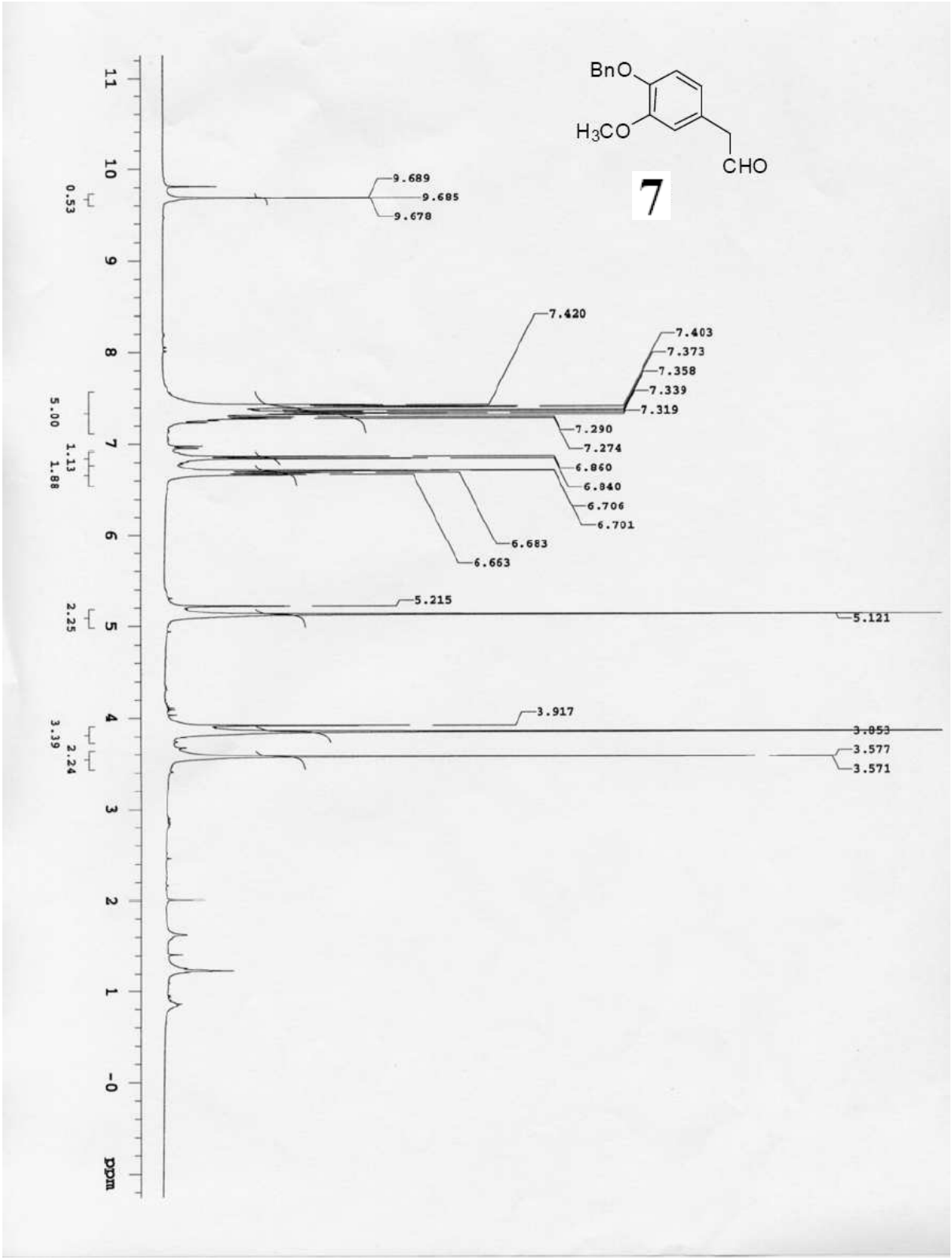
4h

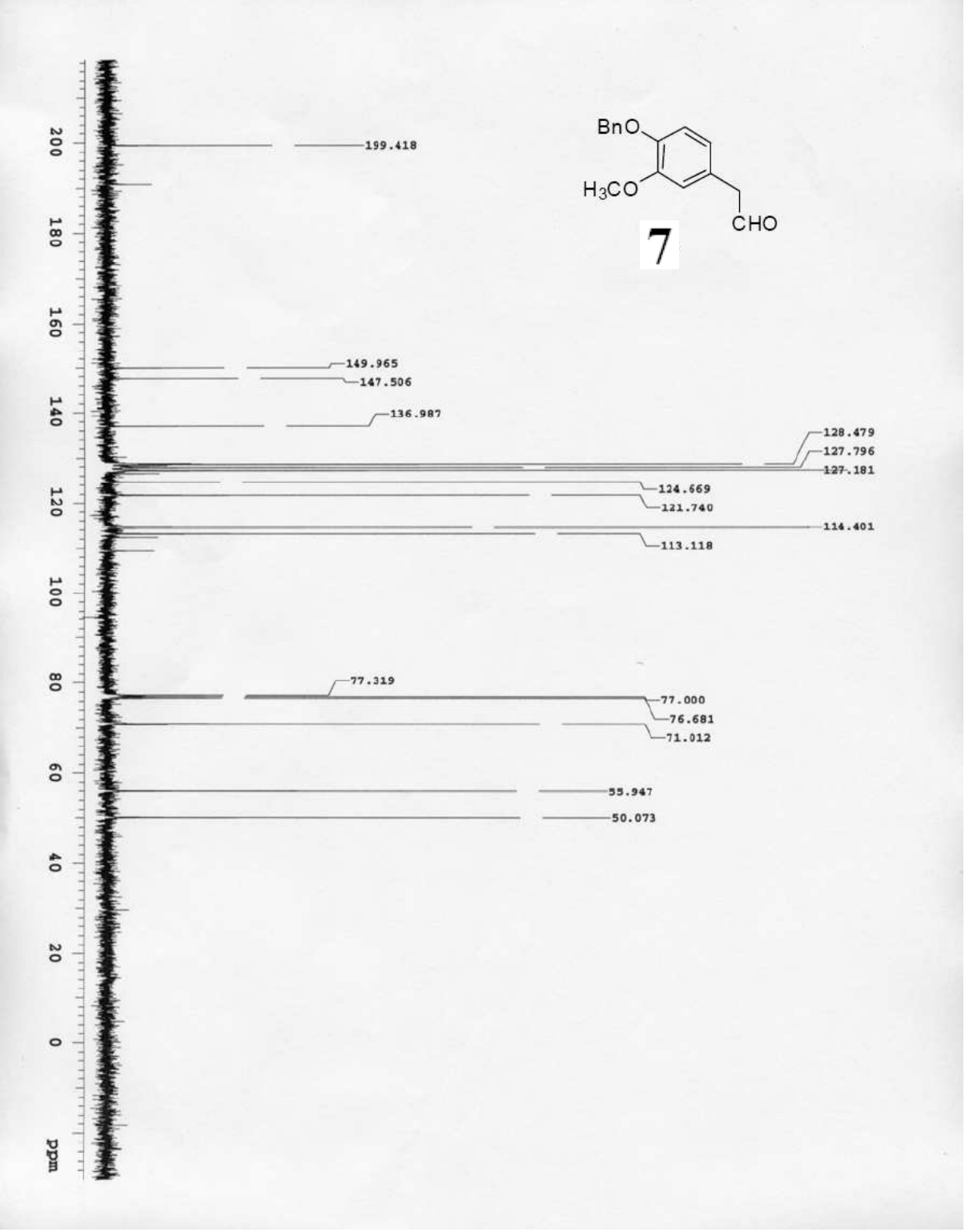

*AN
RUN #14872 DEC 19, 2007 20:26:37
START
IF
KYB-1-104
IF
11.225
12.345
S
END OF SIGNAL
Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 14872 DEC 19, 2007 20:26:37
PEAK FILE : M:SIGNAL.PRA
AREA%
RT AREA TYPE WIDTH AREA%
11.225 6132947 BH .316 3.78855
12.345 155748240 SHB .391 96.21146
TOTAL AREA=1.6188E+08
MUL FACTOR=1.0000E+00
* RUN #14871 DEC 19, 2007 20:09:42
START
IF
KYB-1-104 Rac
IF
10.306
11.214
12.477
STOP
Closing signal file M:SIGNAL .BNC
Storing processed peaks to M:Q5AF4207.PRO
DIRECTORY FULL
RUN# 14871 DEC 19, 2007 20:09:42
SIGNAL FILE: M:SIGNAL.BNC
PEAK FILE : M?Q5AF4207.PRO
AREA%
RT AREA TYPE WIDTH AREA%
10.306 100859 PV .235 .11988
11.214 42341920 VV .300 50.32712
12.477 41690656 VB .324 49.55302
TOTAL AREA=8.4133E+07
MUL FACTOR=1.0000E+00

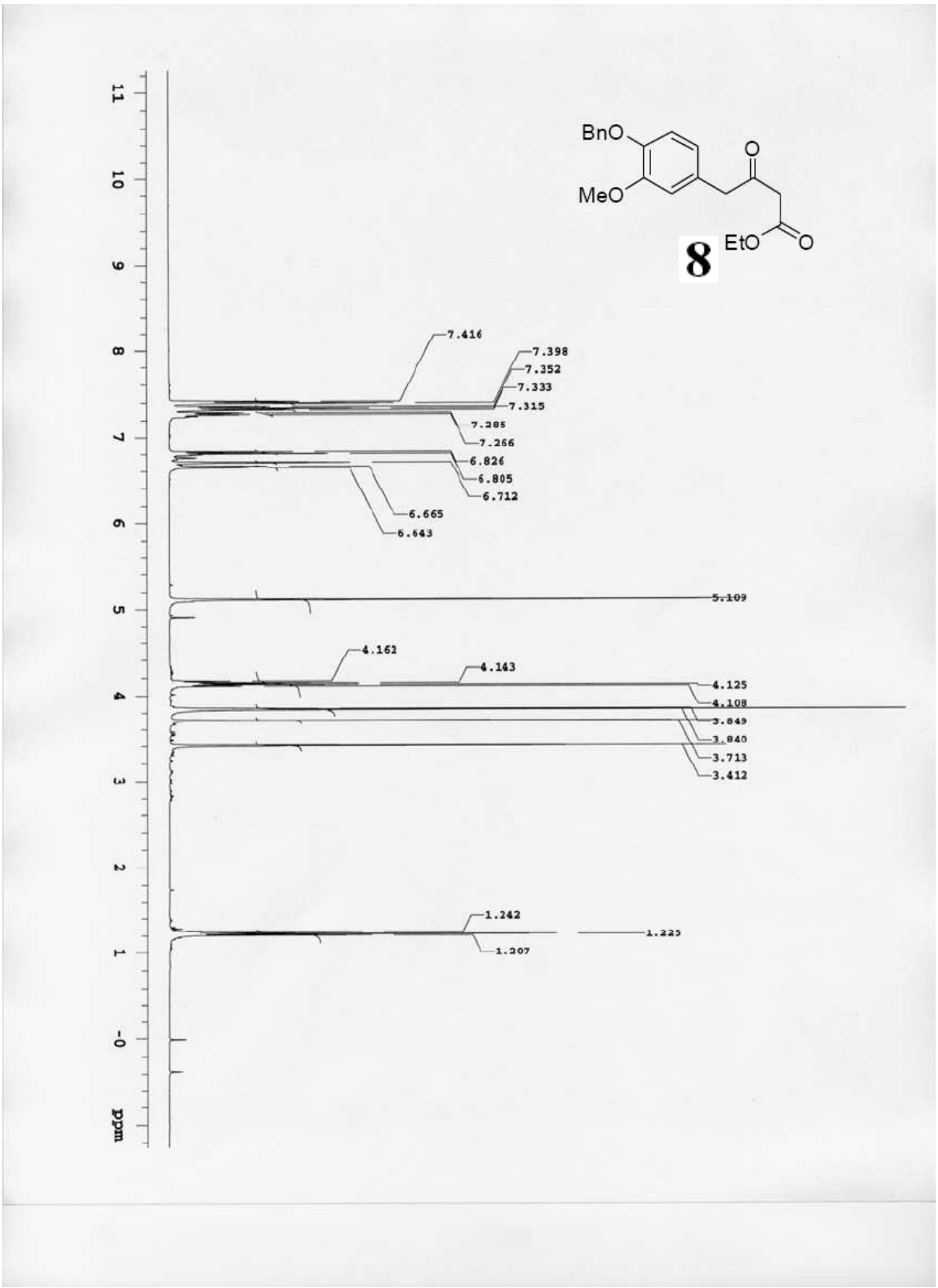

O
O
OAllyl
Cl
O
OAllyl

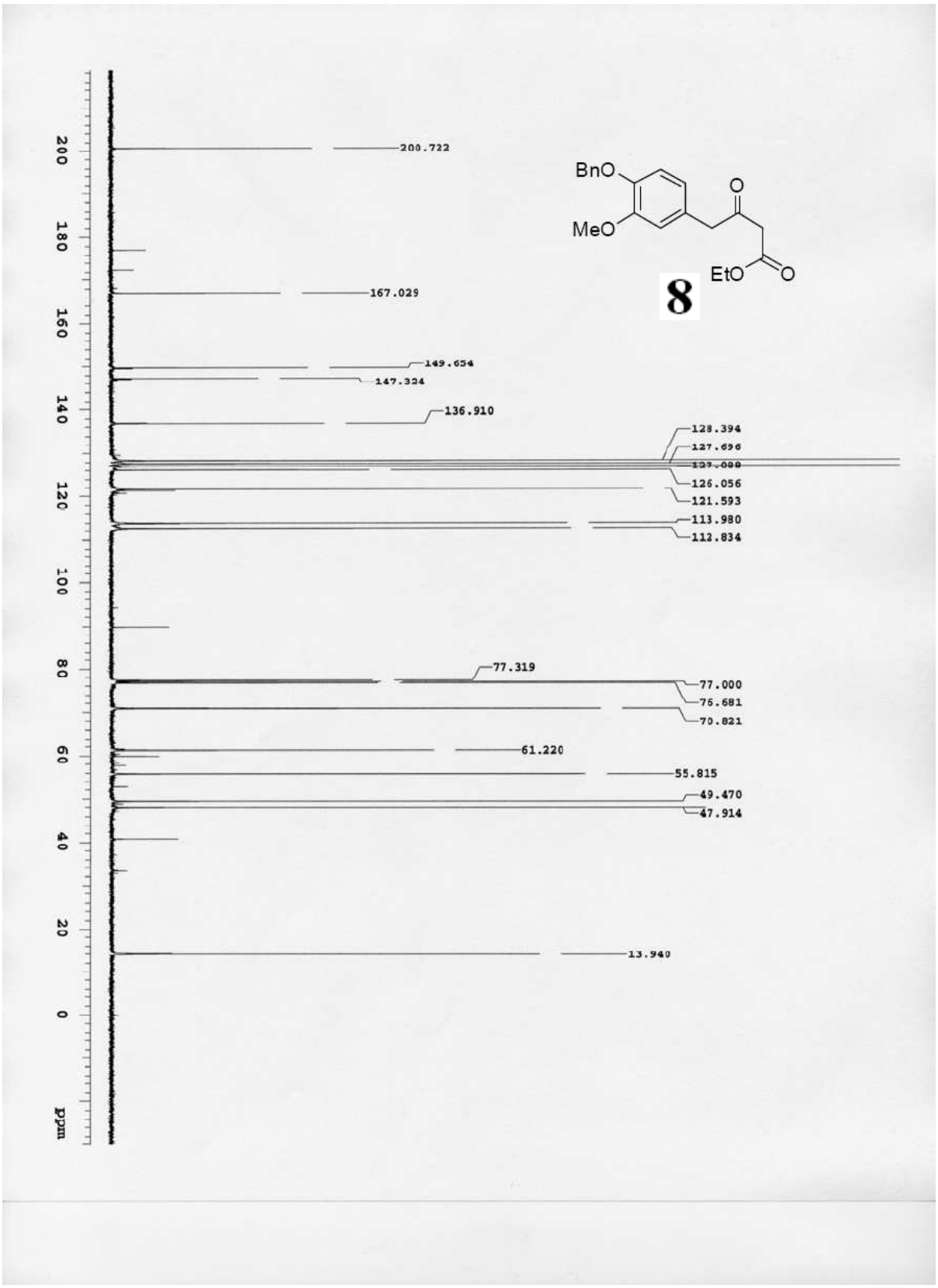
4i

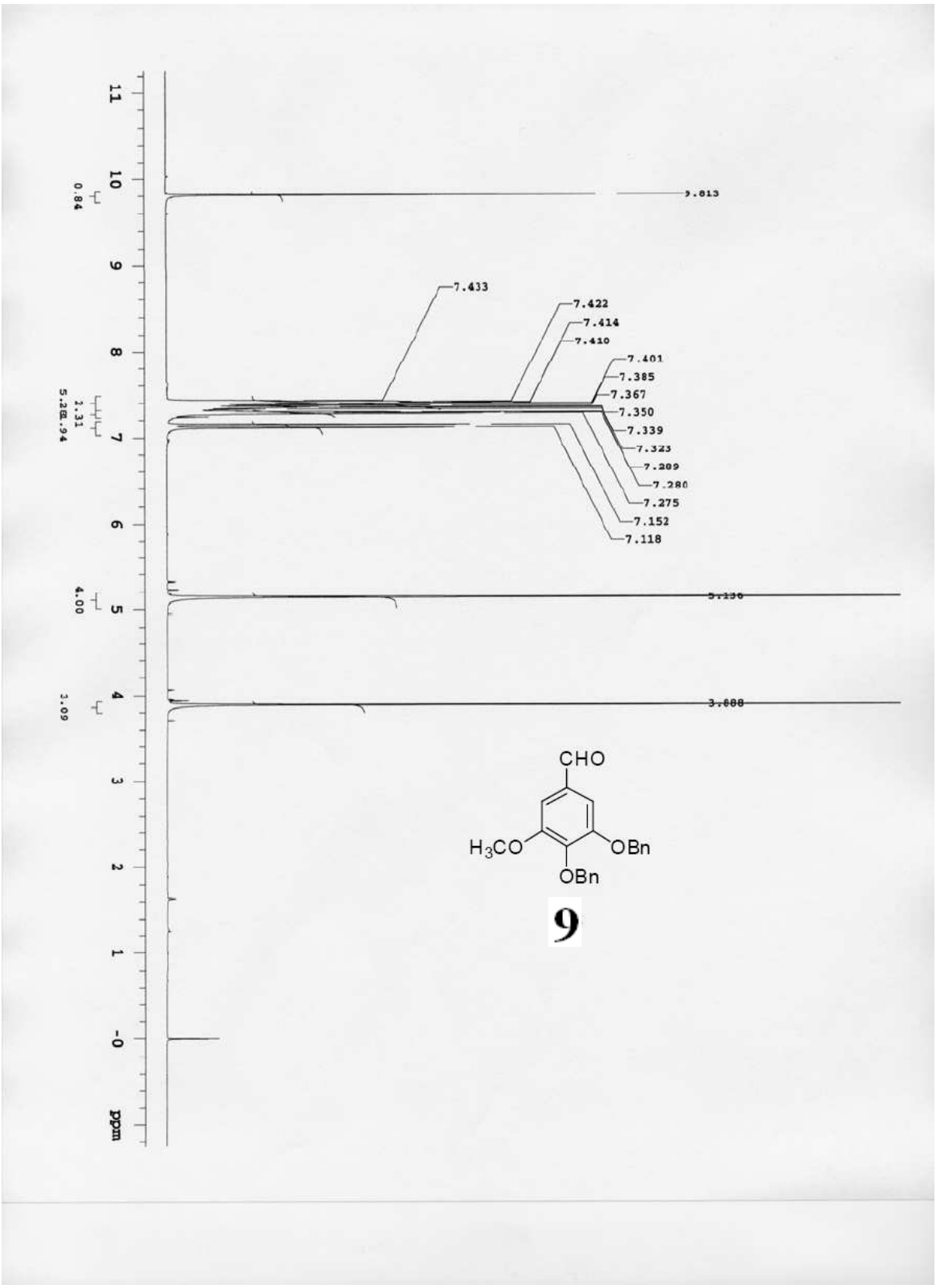

* RUN #14996 JAN 13, 2008 00:50:05
START
IF
IF
13.533
16.835
STOP
Closing signal file M:SIGNAL .BNC
Storing processed peaks to M:Q5CF27BE.PRO
DIRECTORY FULL
RUN# 14996 JAN 13, 2008 00:50:05
SIGNAL FILE: M:SIGNAL.BNC
PEAK FILE : M?Q5CF27BE.PRO
AREA%
RT AREA TYPE WIDTH AREA%
13.533 49603520 PB .615 92.17718
16.835 4209715 BB .710 7.82282
84%ee
TOTAL AREA=5.3813E+07 OD-H, Hex/IPA 99/1, 0.8 mL/min
MUL FACTOR=1.0000E+00 254 nm
RUN #15008 JAN 13, 2008 23:15:35
START
IF
IF
13.551
16.698
END OF SIGNAL
Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 15008 JAN 13, 2008 23:15:35
PEAK FILE : M:SIGNAL.PRA
AREA%
RT AREA TYPE WIDTH AREA%
13.551 3239544 PB .614 49.66485
16.698 3283269 PB .760 50.33517
TOTAL AREA=6522813
MUL FACTOR=1.0000E+00

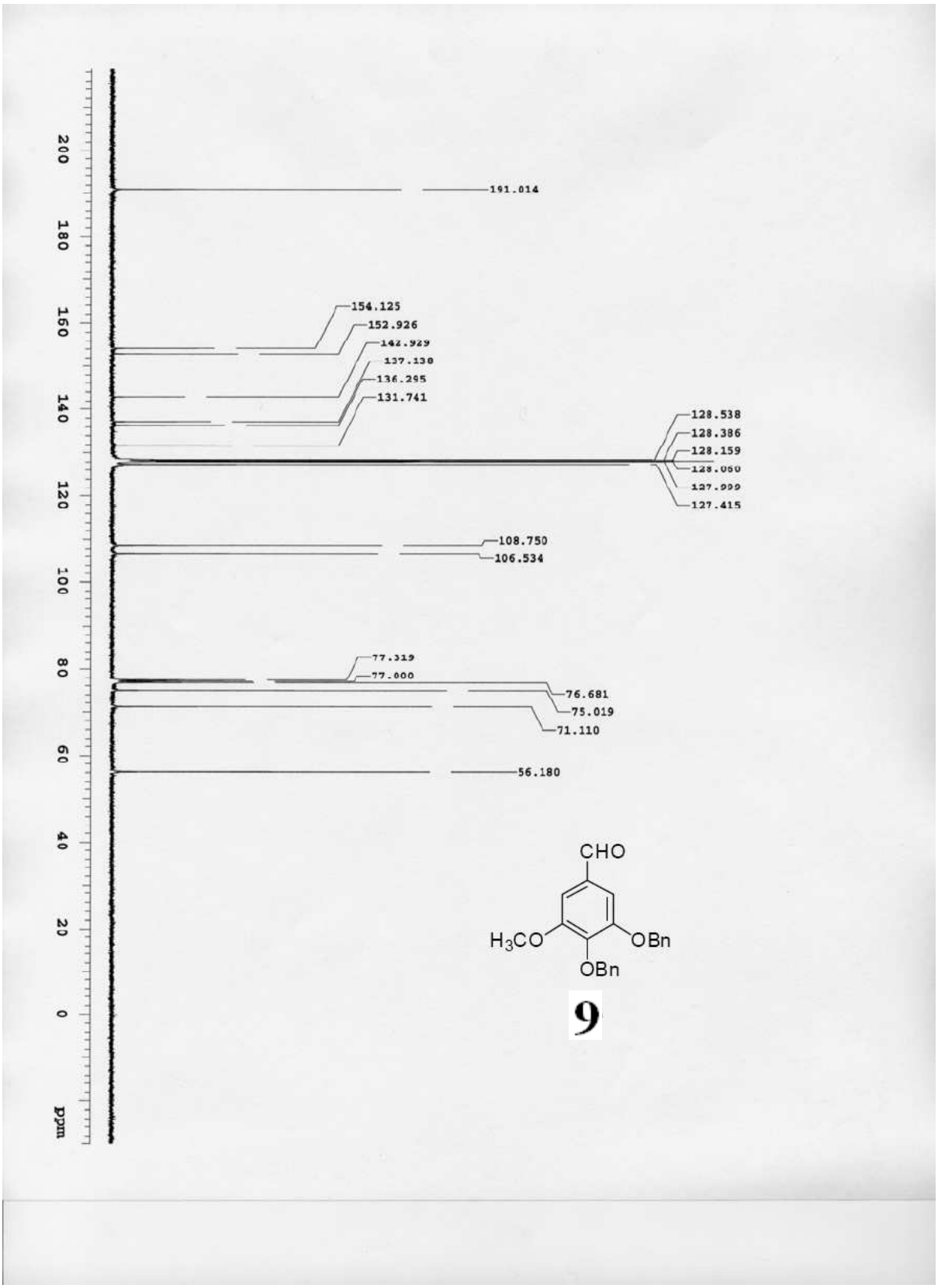

BnO
H3CO
CHO
7
9.689
9.685
9.678
7.420
7.403
7.373
7.358
7.339
7.319
7.290
7.274
6.860
6.840
6.706
6.701
6.683
6.663
5.215
5.121
3.917
3.853
3.577
3.571
0.53
5.00
1.13
1.88
2.25
3.39
2.24
ppm


BnO
H3CO
CHO
7
199.418
149.965
147.506
136.987
128.479
127.796
127.181
124.669
121.740
114.401
113.118
77.319
77.000
76.681
71.012
55.947
50.073
200
180
160
140
120
100
80
60
40
20
0
ppm

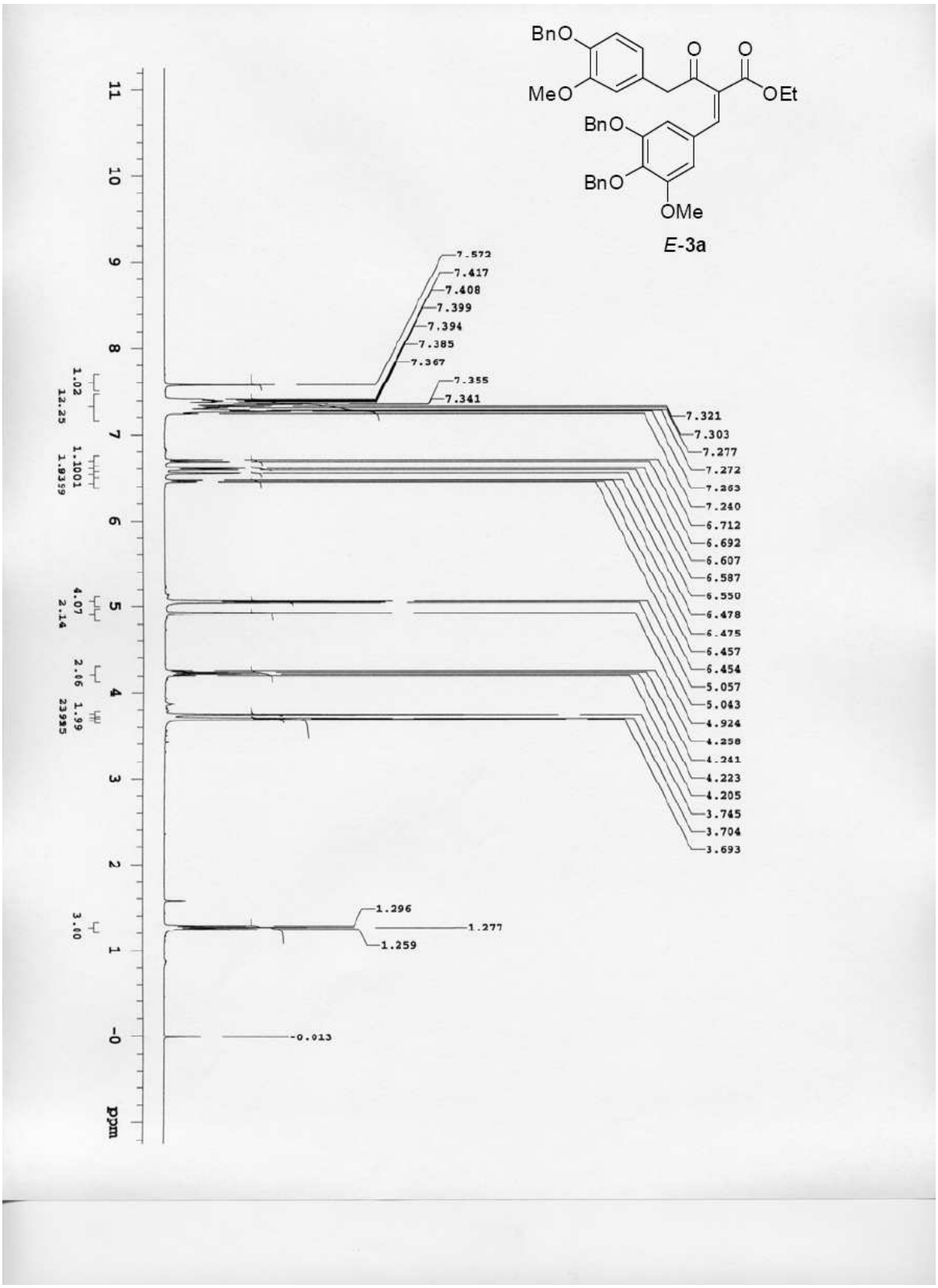

BnO
MeO
O
EtO
O
8
7.416
7.398
7.352
7.333
7.315
7.285
7.266
6.826
6.805
6.712
6.665
6.643
5.109
4.162
4.143
4.125
4.108
3.849
3.840
3.713
3.412
1.242
1.225
1.207
ppm

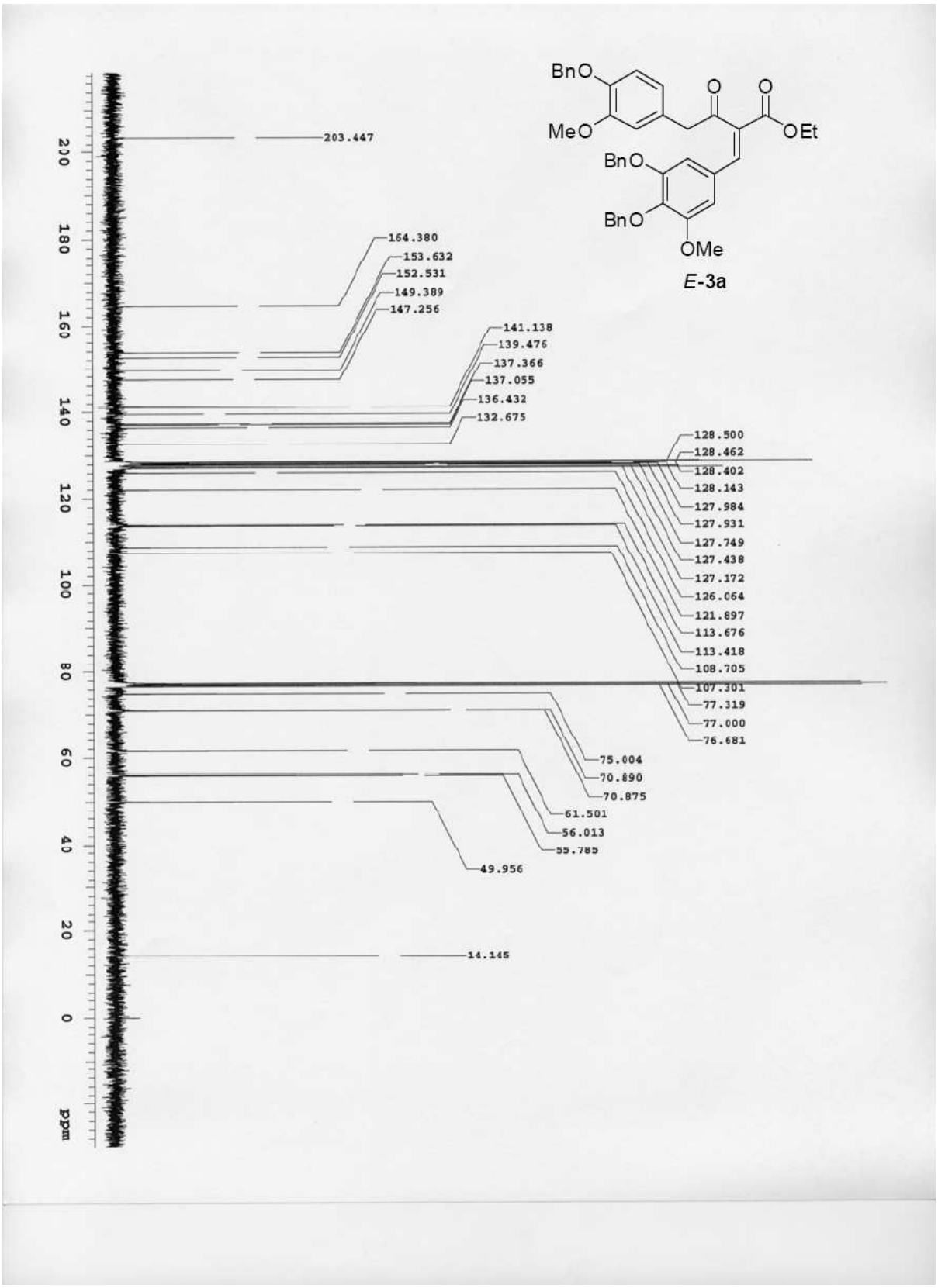

200.722
167.029
149.654
147.324
136.910
128.394
127.696
126.056
121.593
113.980
112.834
77.319
77.000
76.681
70.821
61.220
55.815
49.470
47.914
13.940
BnO
MeO
O
EtO
O
8
200
180
160
140
120
100
80
60
40
20
0
ppm

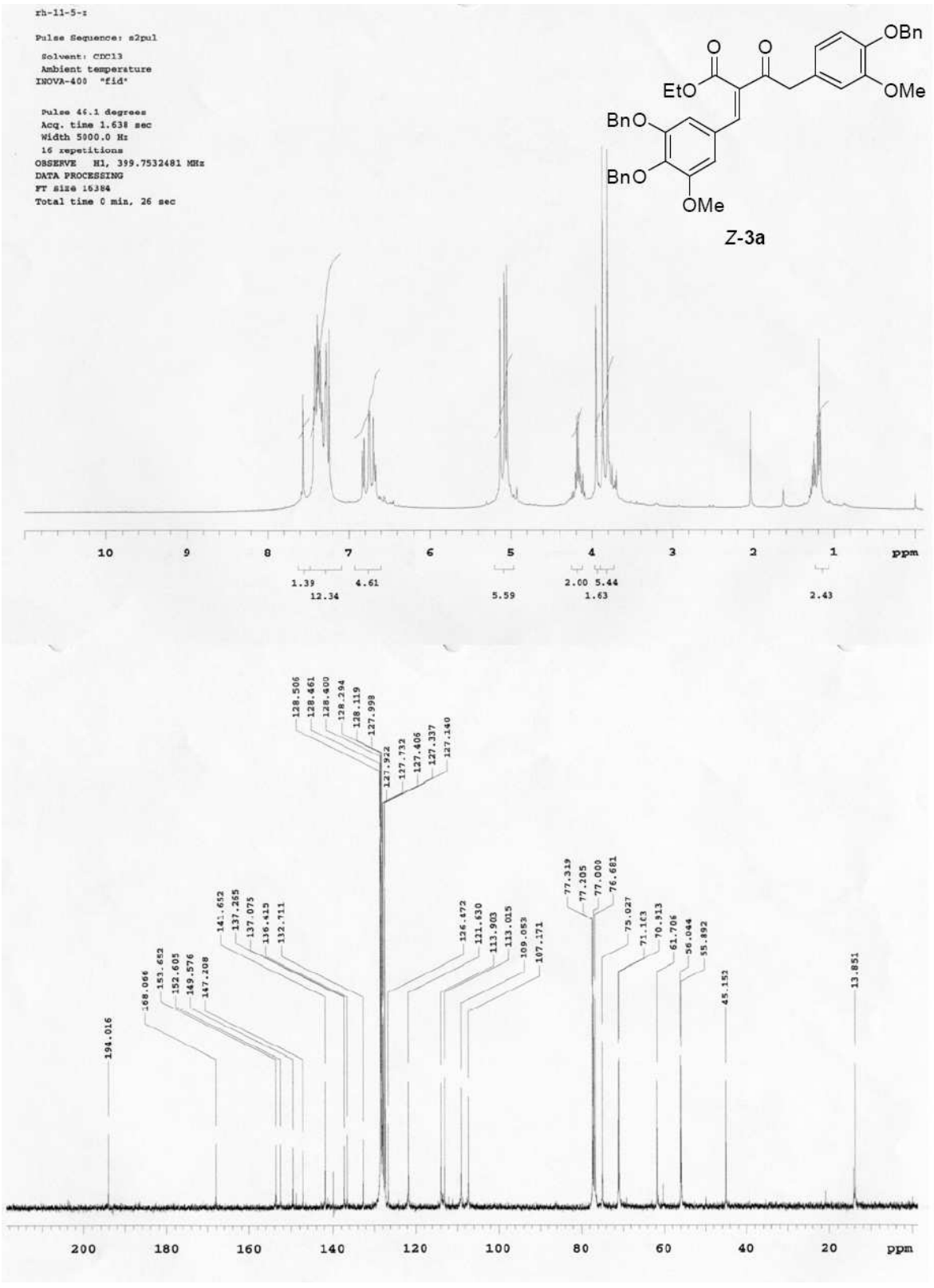

9.813
7.433
7.422
7.414
7.410
7.401
7.385
7.367
7.350
7.339
7.323
7.209
7.280
7.275
7.152
7.118
5.136
3.888
0.84
1.31
5.28
4.00
3.09
CHO
H3CO
OBn
OBn
9
ppm

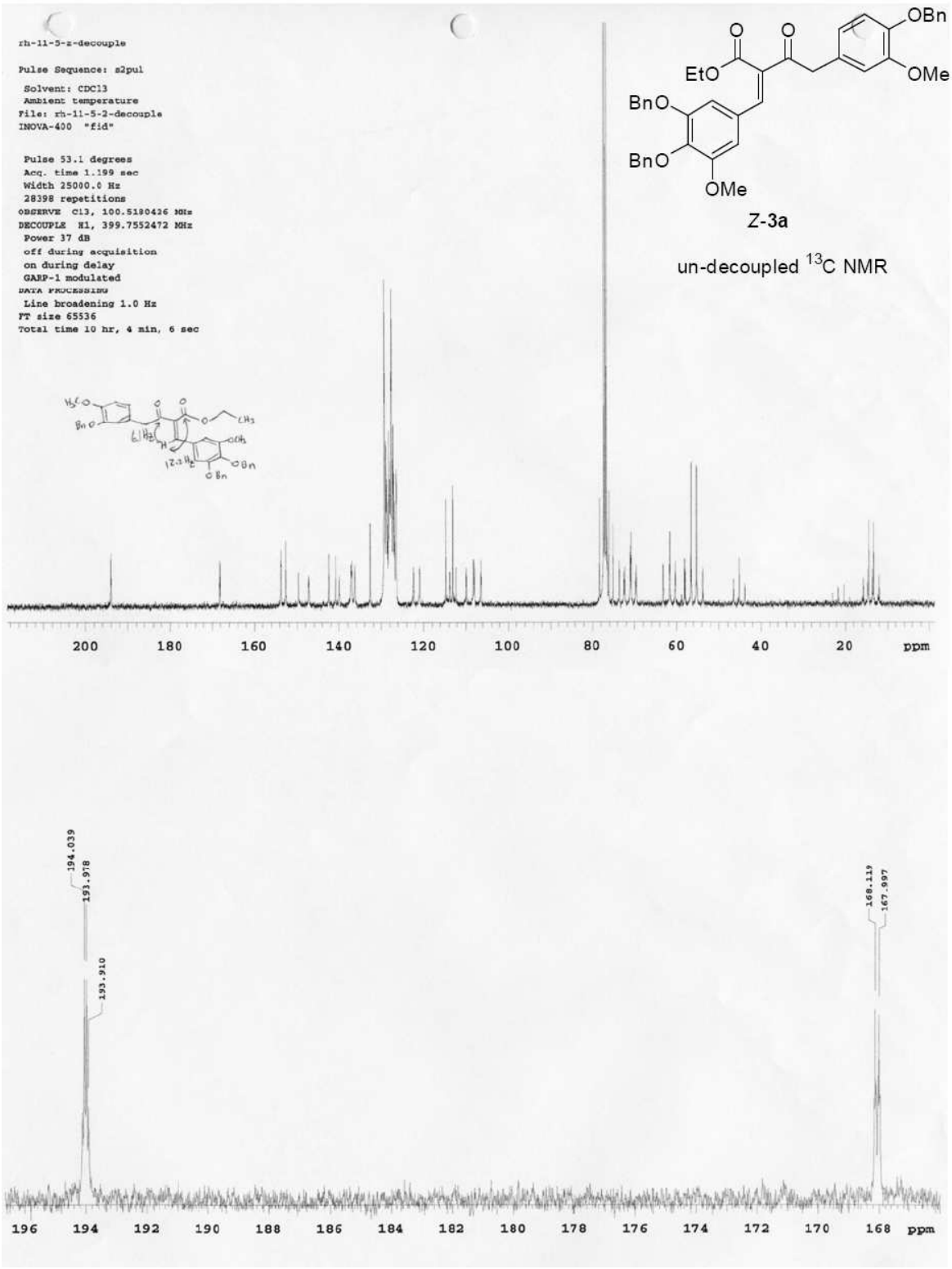

191.014
154.125
152.926
142.929
137.130
136.295
131.741
128.538
128.386
128.159
128.060
127.999
127.415
108.750
106.534
77.319
77.000
76.681
75.019
71.110
56.180
ppm
CHO
H3CO
OBn
OBn

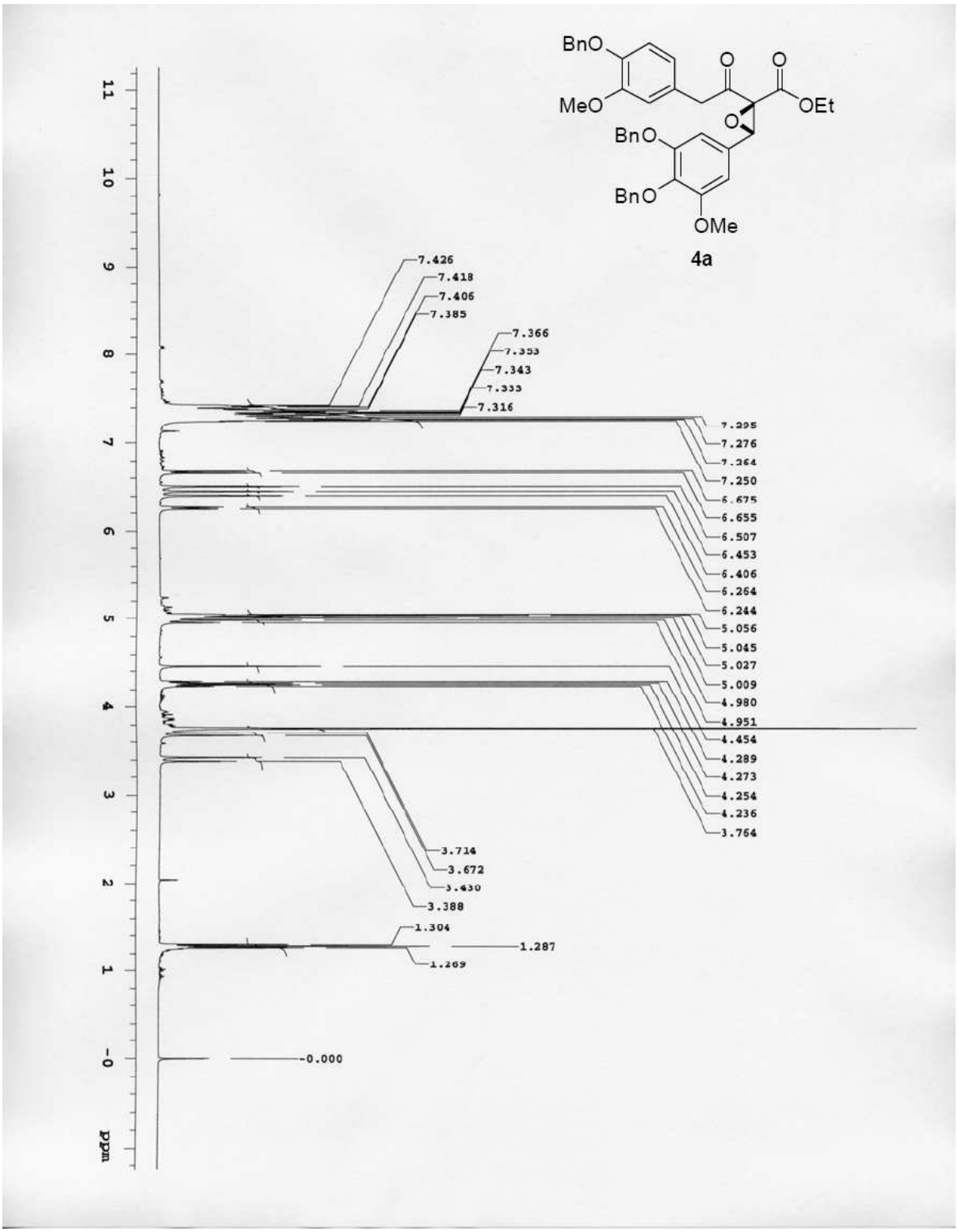
9

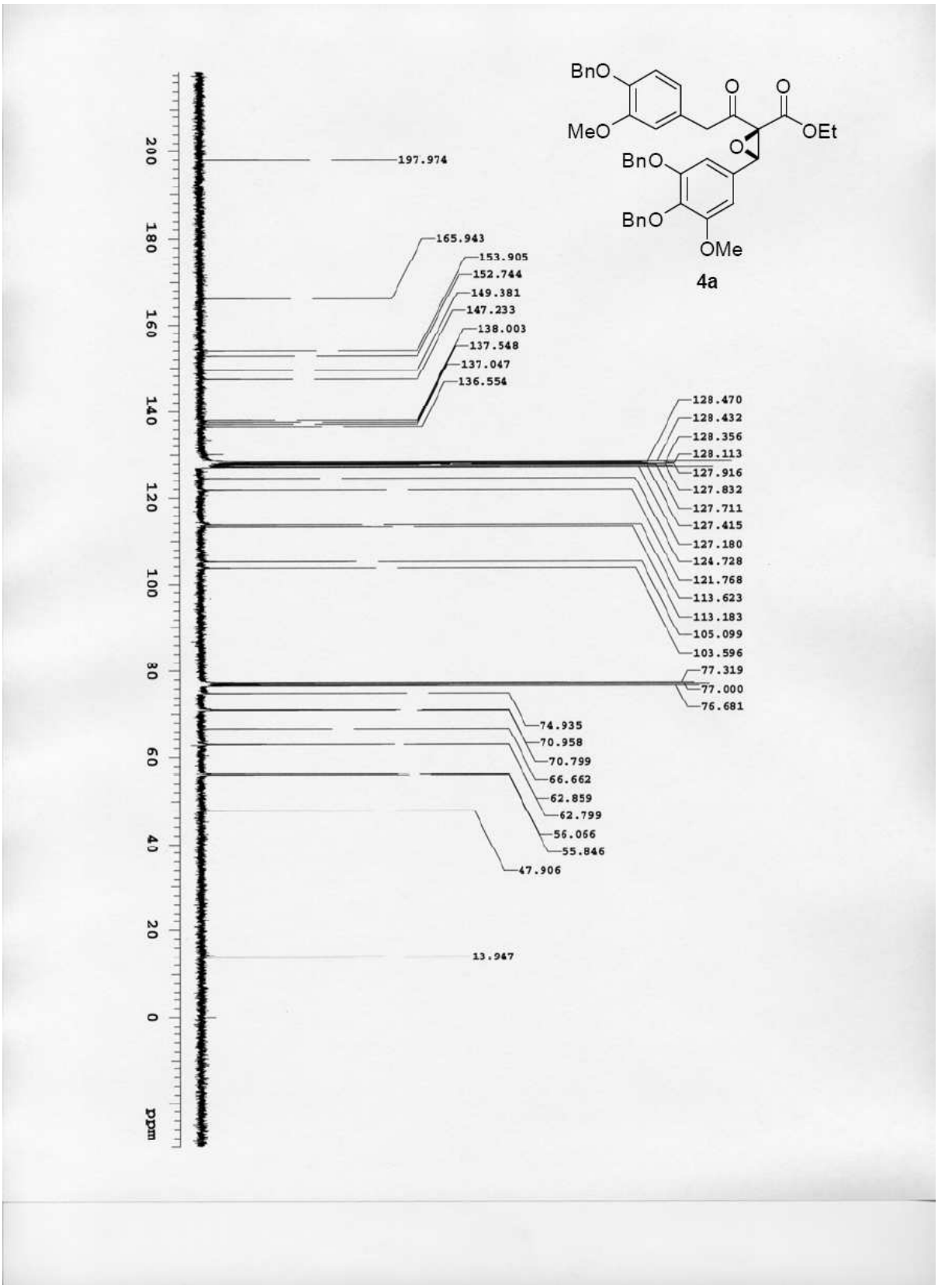

BnO
MeO
O
O
OEt
BnO
BnO
OMe
E-3a
7.572
7.417
7.408
7.399
7.394
7.385
7.367
7.355
7.341
7.321
7.303
7.277
7.272
7.263
7.240
6.712
6.692
6.607
6.587
6.550
6.478
6.475
6.457
6.454
5.057
5.043
4.924
4.258
4.241
4.223
4.205
3.745
3.704
3.693
1.296
1.277
1.259
-0.013
1.02
12.25
1.1001
1.9359
4.07
2.14
2.06
1.99
23935
3.00
ppm

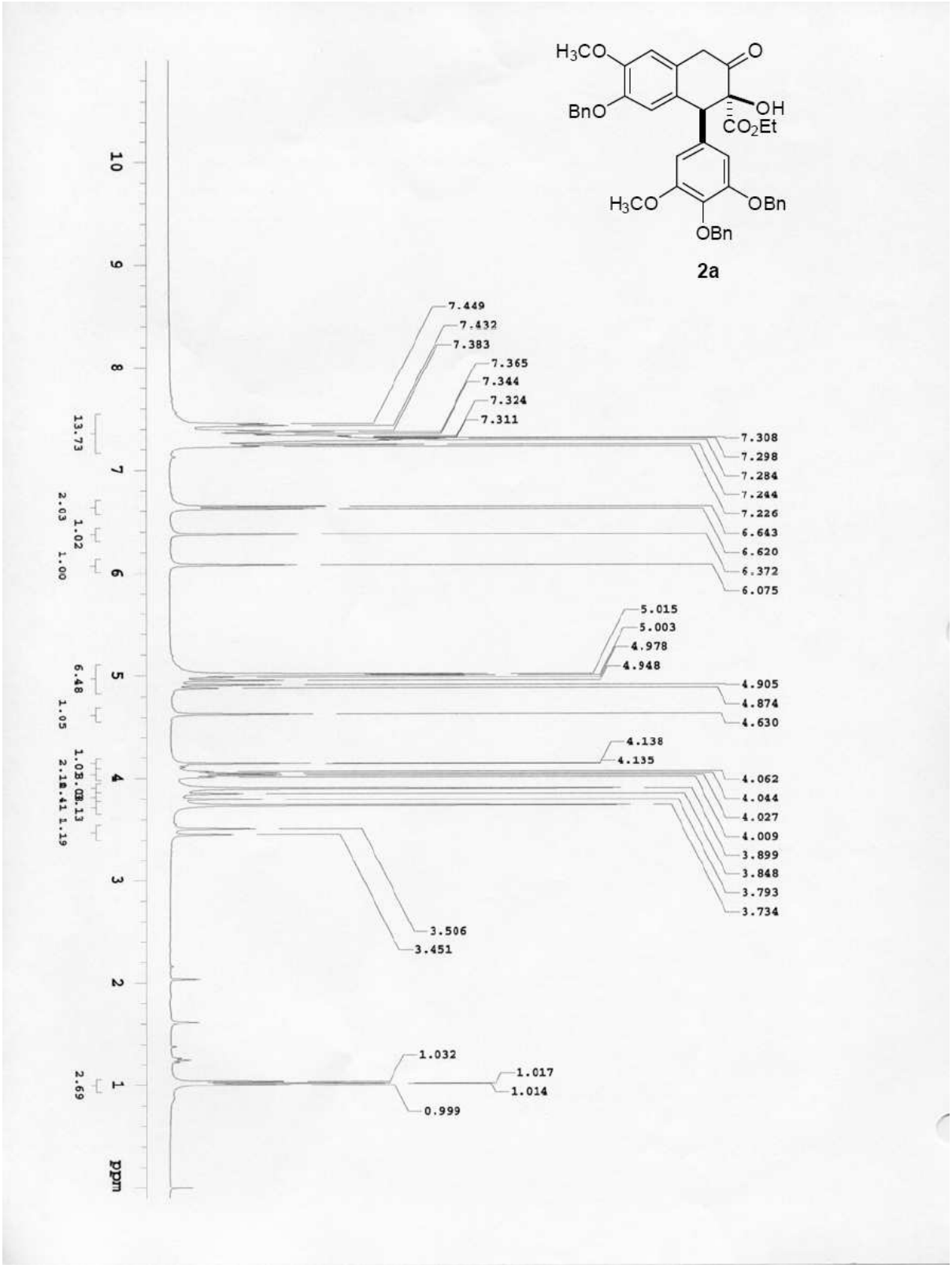

BnO
MeO
O
O
OEt
BnO
BnO
OMe
E-3a
203.447
164.380
153.632
152.531
149.389
147.256
141.138
139.476
137.366
137.055
136.432
132.675
128.500
128.462
128.402
128.143
127.984
127.931
127.749
127.438
127.172
126.064
121.897
113.676
113.418
108.705
107.301
77.319
77.000
76.681
75.004
70.890
70.875
61.501
56.013
55.785
49.956
14.145
200
180
160
140
120
100
80
60
40
20
0
ppm


rh-11-5-z
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
16 repetitions
OBSERVE H1, 399.7532481 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 26 sec
OBn
O
O
EtO
OMe
BnO
BnO
OMe
Z-3a
10
9
8
7
6
5
4
3
2
1
ppm
1.39
12.34
4.61
5.59
2.00
1.63
5.44
2.43
128.506
128.461
128.400
128.294
128.119
127.998
127.922
127.732
127.406
127.337
127.140
141.652
137.265
137.075
136.415
132.711
126.472
121.430
113.903
113.015
109.053
107.171
77.319
77.205
77.000
76.681
75.027
71.163
70.913
61.706
56.044
55.892
45.152
13.851
194.016
168.066
153.652
152.605
149.576
147.208
200
180
160
140
120
100
80
60
40
20
ppm

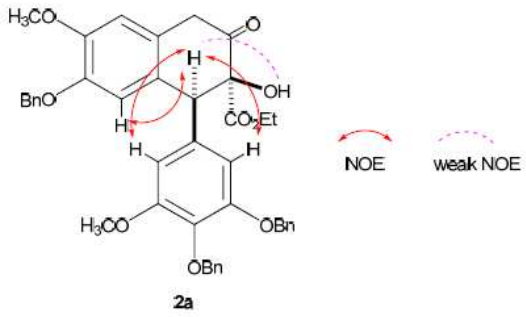

rh-11-5-z-decouple
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: rh-11-5-2-decouple
INOVA-400 "fid"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
28398 repetitions
OBSERVE C13, 100.5180426 MHz
DECOUPLE H1, 399.7552472 MHz
Power 37 dB
off during acquisition
on during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 10 hr, 4 min, 6 sec
OBn
EtO
OMe
BnO
BnO
OMe
Z-3a
un-decoupled 13C NMR
200 180 160 140 120 100 80 60 40 20 ppm
194.039
193.978
193.910
168.119
167.997
196 194 192 190 188 186 184 182 180 178 176 174 172 170 168 ppm


BnO
MeO
O
O
OEt
O
BnO
BnO
OMe
4a
7.426
7.418
7.406
7.385
7.366
7.353
7.343
7.333
7.316
7.276
7.250
6.655
6.507
6.453
6.406
6.264
6.244
5.056
5.045
5.027
5.009
4.980
4.951
4.454
4.289
4.273
4.254
4.236
3.764
3.714
3.672
3.430
3.388
1.304
1.287
1.269
0.000
ppm

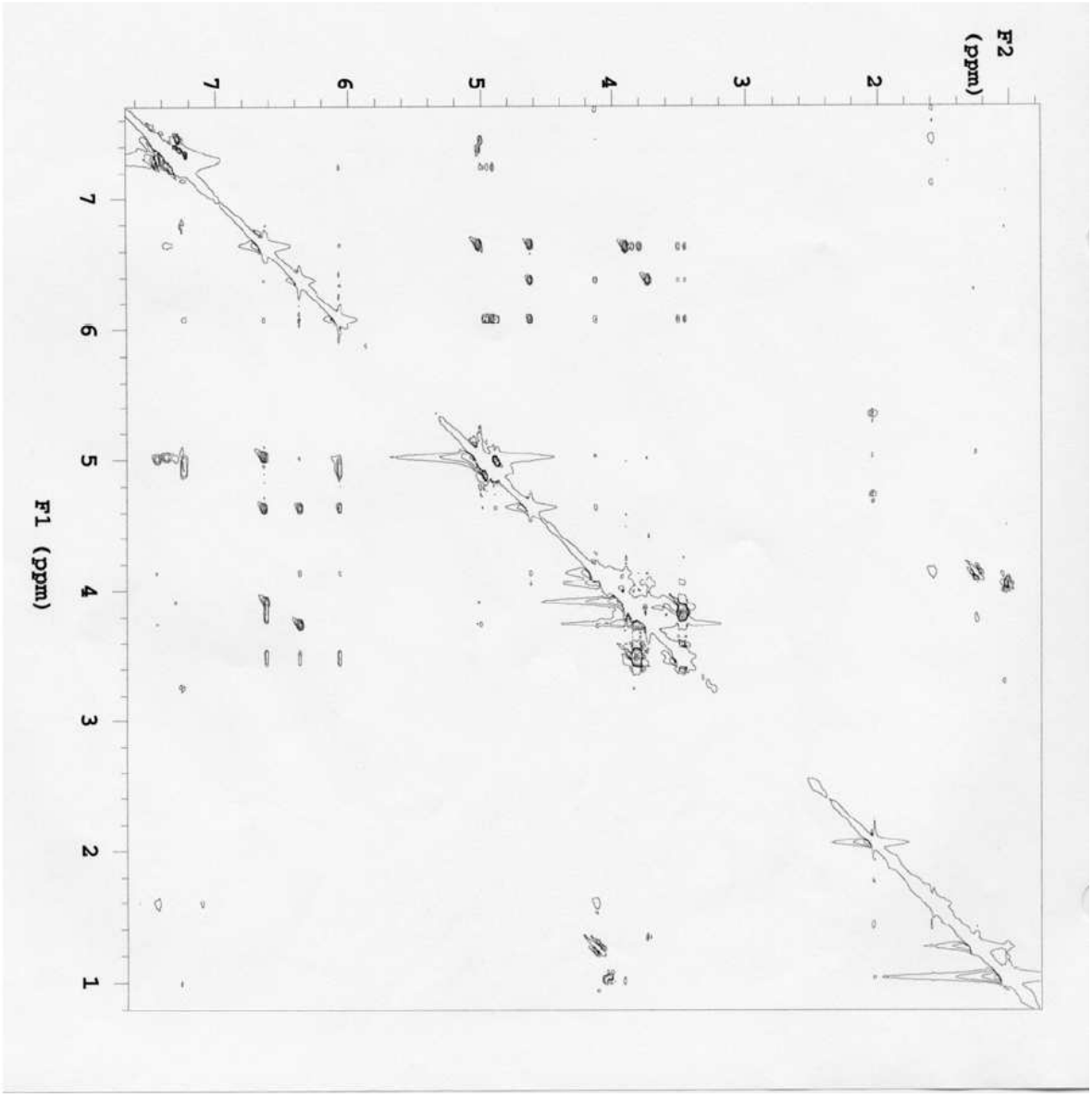

BnO
MeO
O
O
OEt
O
BnO
BnO
OMe
4a
197.974
165.943
153.905
152.744
149.381
147.233
138.003
137.548
137.047
136.554
128.470
128.432
128.356
128.113
127.916
127.832
127.711
127.415
127.180
124.728
121.768
113.623
113.183
105.099
103.596
77.319
77.000
76.681
74.935
70.958
70.799
66.662
62.859
62.799
56.056
55.846
47.906
13.947
200
180
160
140
120
100
80
60
40
20
0
ppm

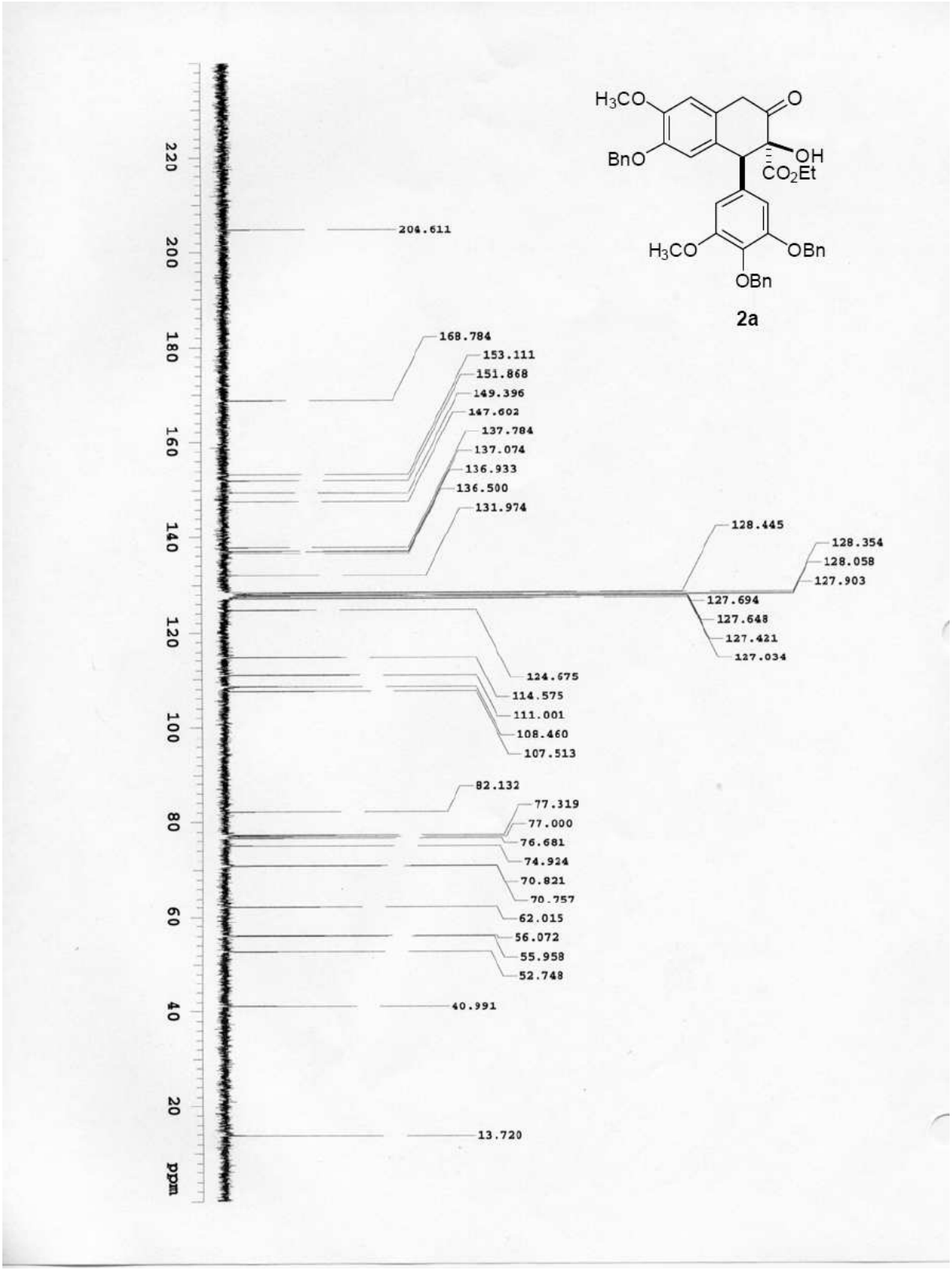

H3CO
O
BnO
OH
CO2Et
H3CO
OBn
OBn
2a
7.449
7.432
7.383
7.365
7.344
7.324
7.311
7.308
7.298
7.284
7.244
7.226
6.643
6.620
6.372
6.075
5.015
5.003
4.978
4.948
4.905
4.874
4.630
4.138
4.135
4.062
4.044
4.027
4.009
3.899
3.848
3.793
3.734
3.506
3.451
1.032
1.017
1.014
0.999
13.73
2.03
1.02
1.00
6.48
1.05
2.69
ppm

NOESY of **2a**

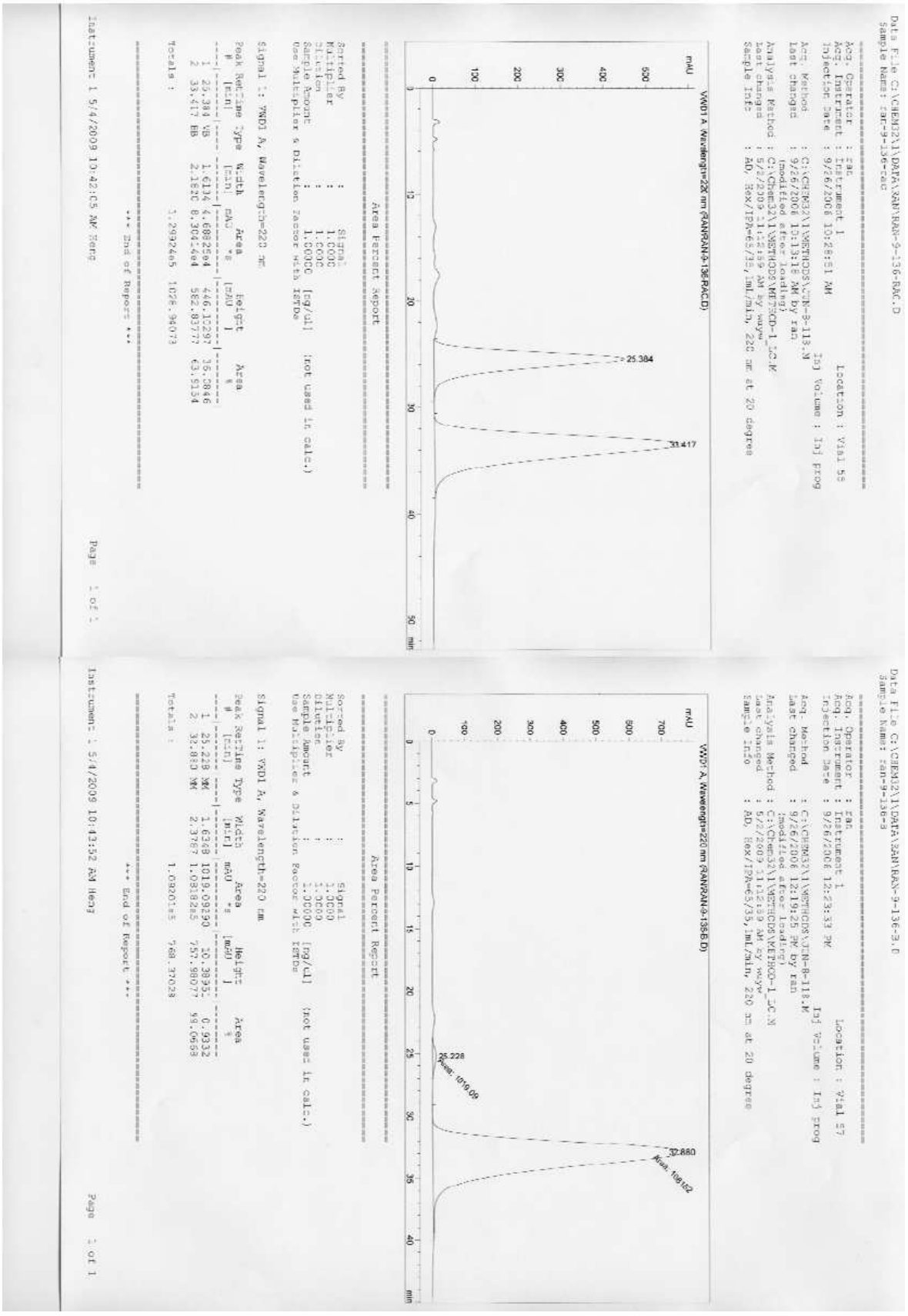


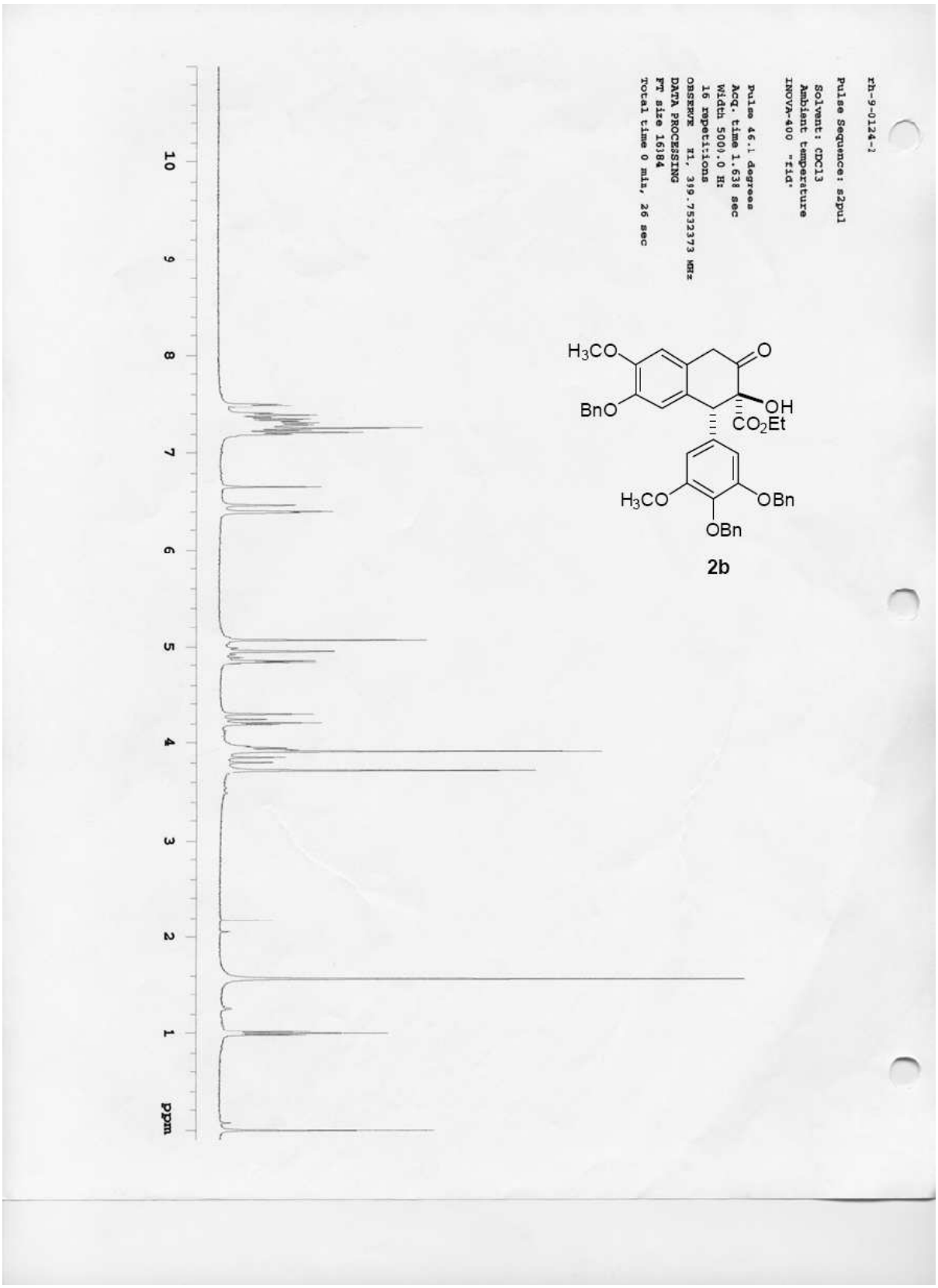
2a

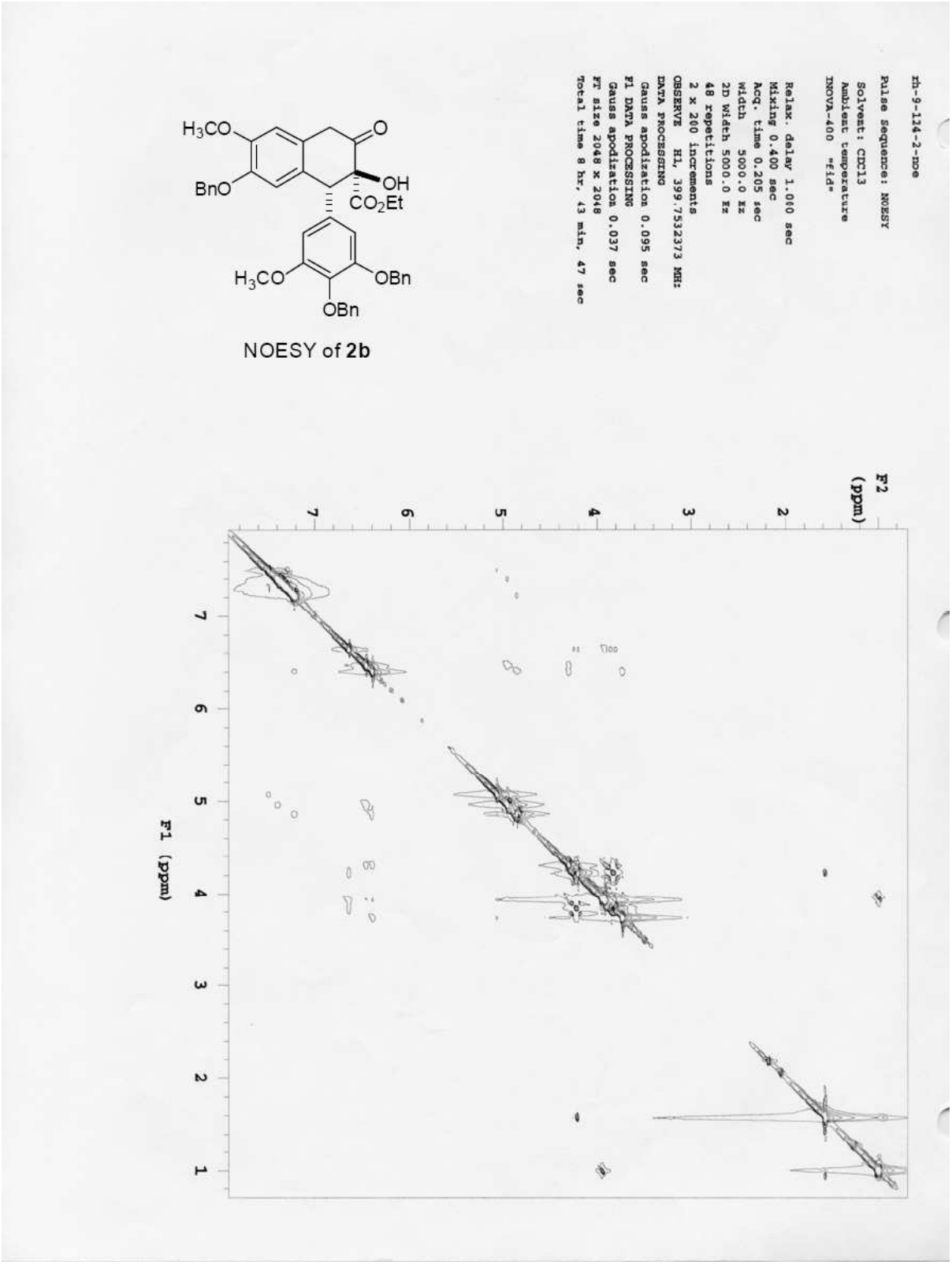



H3CO
O
BnO
OH
CO2Et
H3CO
OBn
OBn
2a
204.611
168.784
153.111
151.868
149.396
147.602
137.784
137.074
136.933
136.500
131.974
128.445
128.354
128.058
127.903
127.694
127.648
127.421
127.034
124.675
114.575
111.001
108.460
107.513
82.132
77.319
77.000
76.681
74.924
70.821
70.757
62.015
56.072
55.958
52.748
40.991
13.720
220
200
180
160
140
120
100
80
60
40
20
ppm

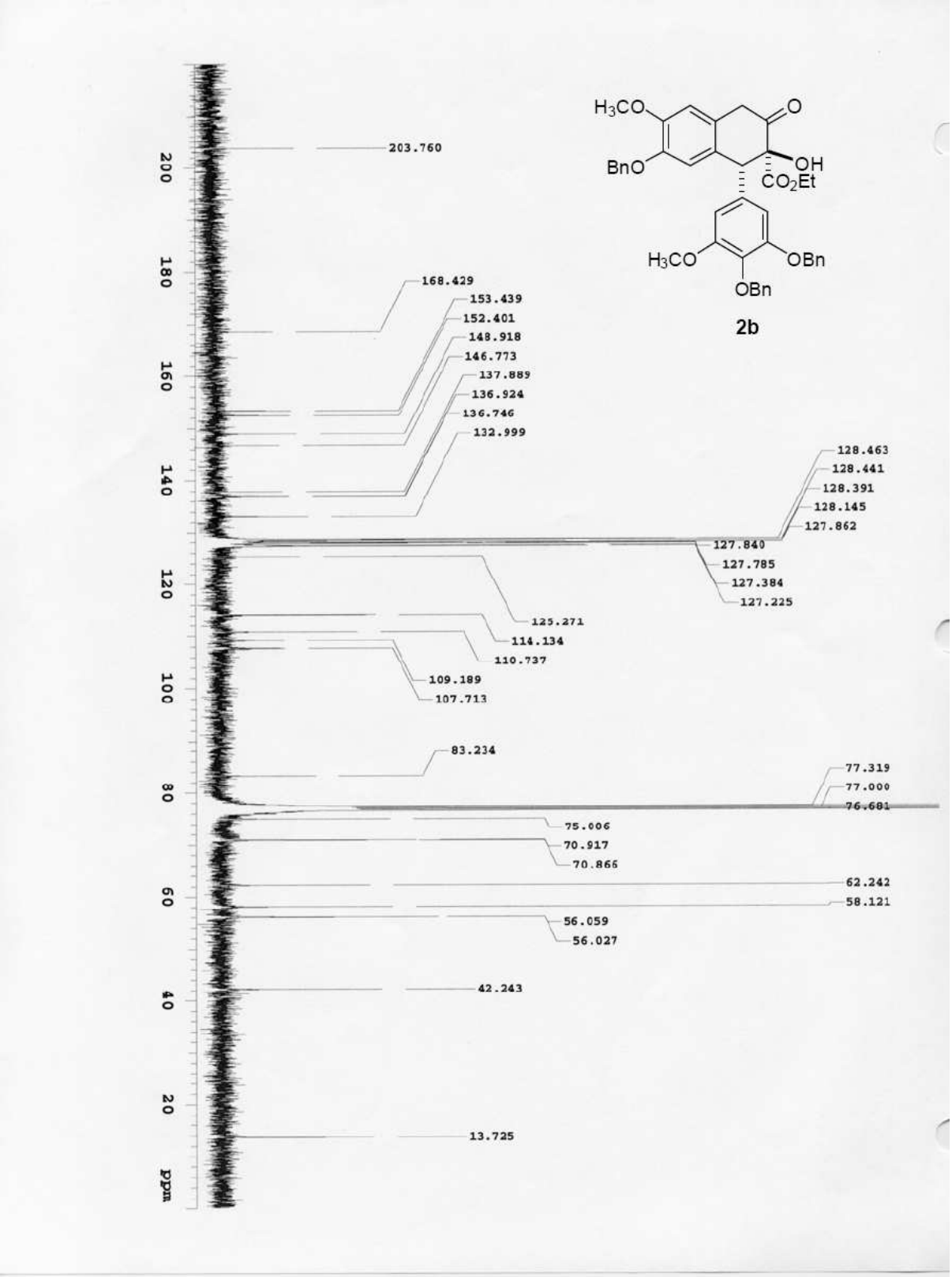
HPLC of **2a:** (The racemic sample was prepared by mixing both enantiomers.)

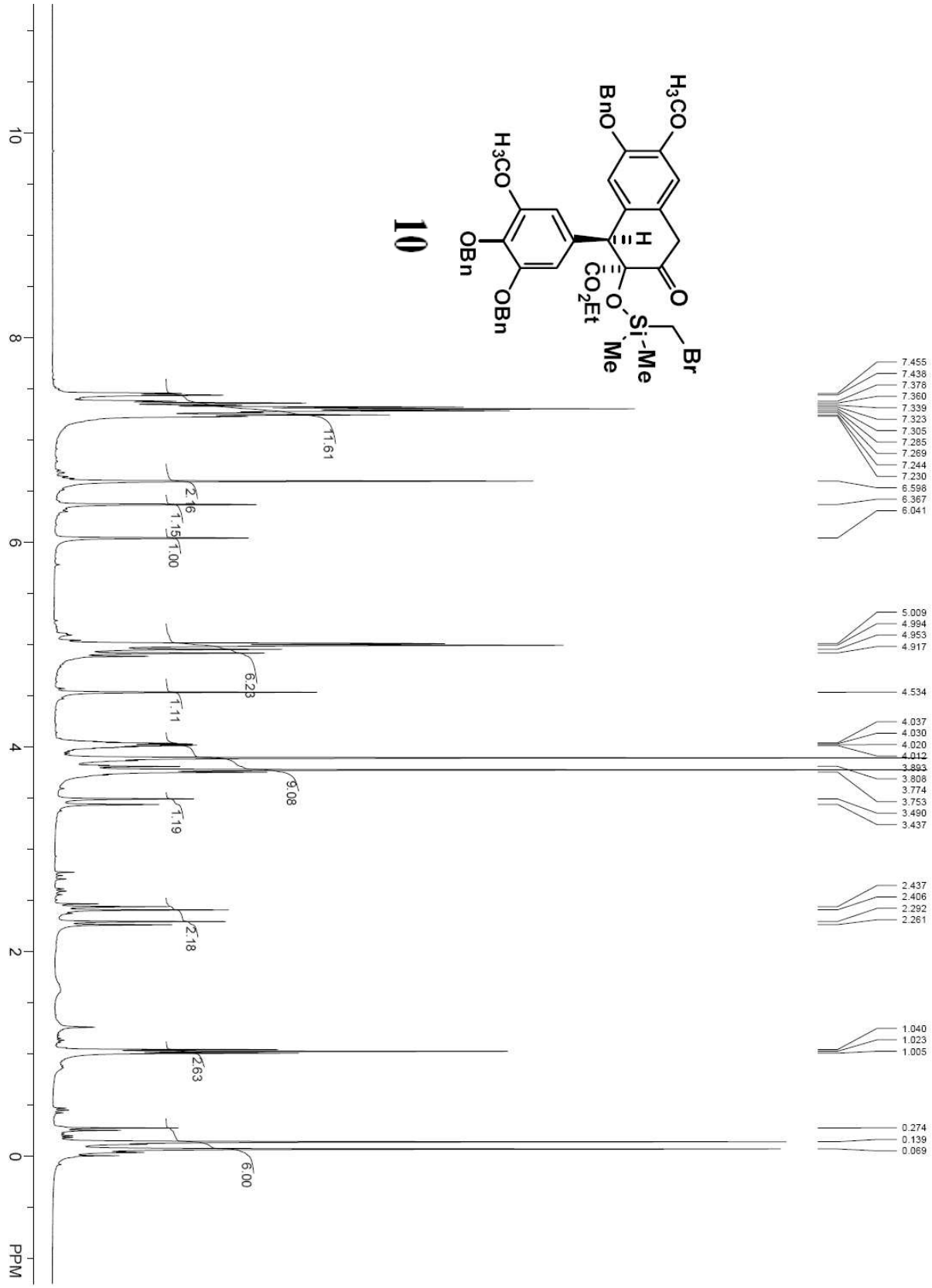


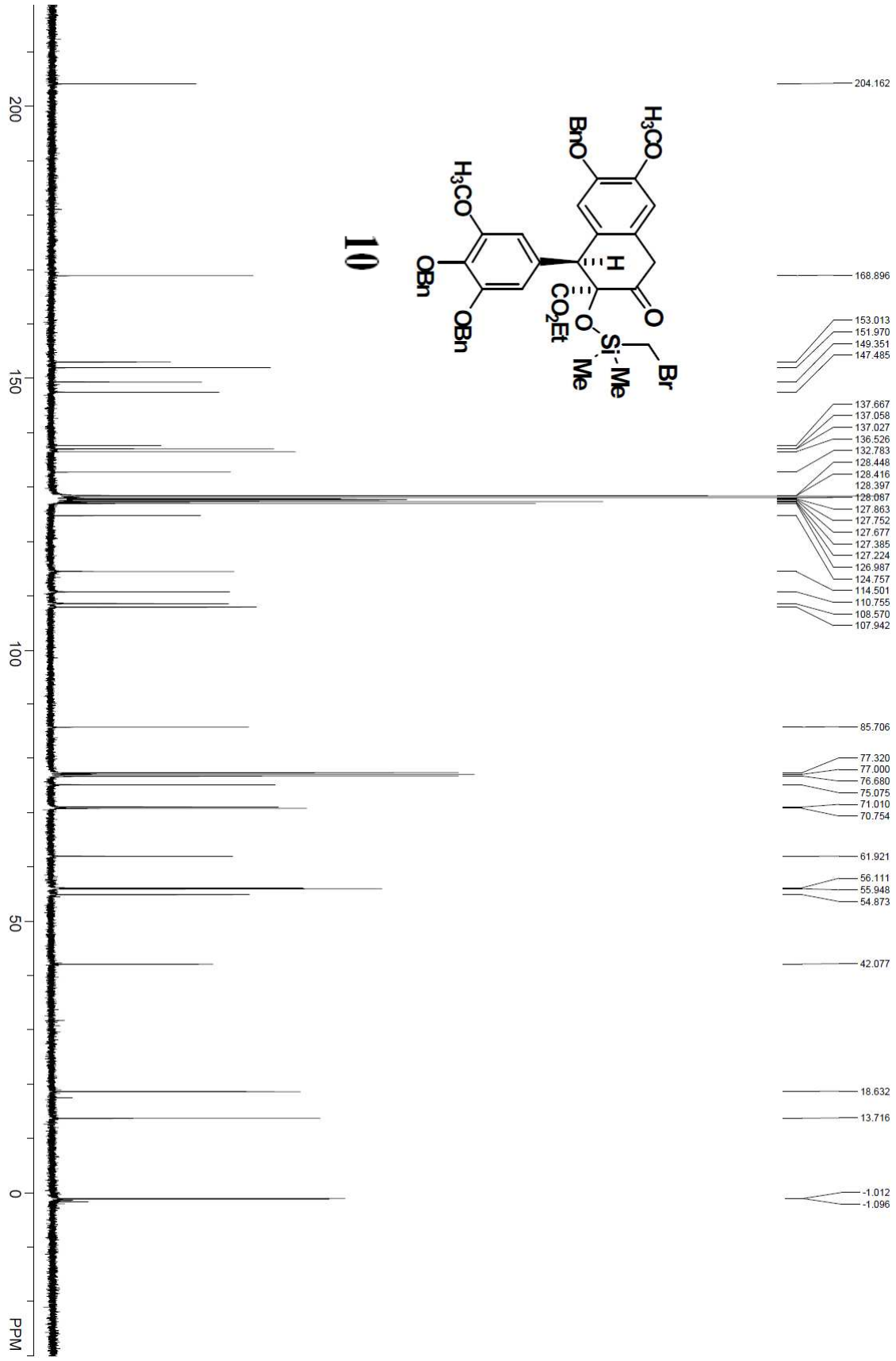

rh-9-0124-2
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-400 "rid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
16 repetitions
OBSERVE H1, 399.7532373 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 26 sec
H3CO
O
BnO
OH
CO2Et
H3CO
OBn
OBn
2b
10
9
8
7
6
5
4
3
2
1
ppm

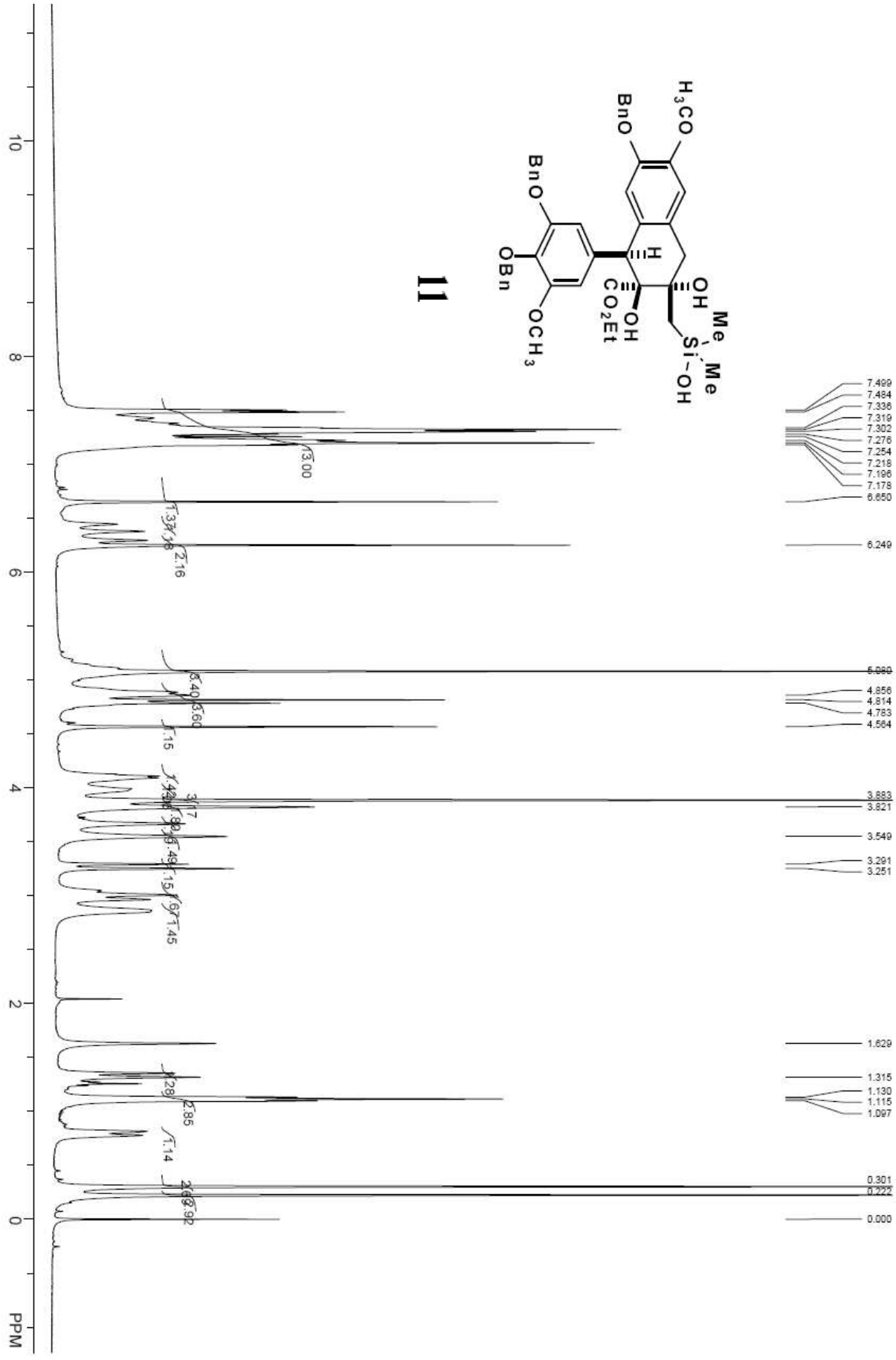

rh-9-124-2-noe
Pulse sequence: NOESY
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Relax. delay 1.000 sec
Mixing 0.400 sec
Acq. time 0.205 sec
Width 5000.0 Hz
2D Width 5000.0 Hz
48 repetitions
2 x 200 increments
OBSERVE H1, 399.7532373 MHz
DATA PROCESSING
Gauss apodization 0.095 sec
F1 DATA PROCESSING
Gauss apodization 0.037 sec
FT size 2048 x 2048
Total time 8 hr, 43 min, 47 sec
F2 (ppm)
F1 (ppm)
H3CO
BnO
O
OH
CO2Et
H3CO
OBn
OBn

NOESY of **2b**

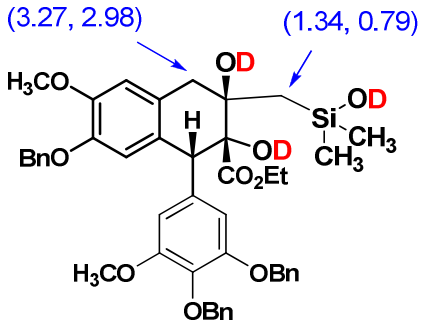

H3CO
O
BnO
OH
CO2Et
H3CO
OBn
OBn
2b
203.760
168.429
153.439
152.401
148.918
146.773
137.889
136.924
136.746
132.999
128.463
128.441
128.391
128.145
127.862
127.840
127.785
127.384
127.225
125.271
114.134
110.737
109.189
107.713
83.234
77.319
77.000
76.681
75.006
70.917
70.866
62.242
58.121
56.059
56.027
42.243
13.725
200
180
160
140
120
100
80
60
40
20
ppm


10
H3CO
BnO
H3CO
OBn
OBn
H
CO2Et
O
Si
Me
Me
Br
O
PPM
11.61
2.16
1.15
1.00
6.23
1.11
9.08
1.19
2.18
2.63
6.00
7.455
7.438
7.378
7.360
7.339
7.323
7.305
7.285
7.269
7.244
7.230
6.598
6.367
6.041
5.009
4.994
4.953
4.917
4.534
4.037
4.030
4.020
4.012
3.893
3.808
3.774
3.753
3.490
3.437
2.437
2.406
2.292
2.261
1.040
1.023
1.005
0.274
0.139
0.069

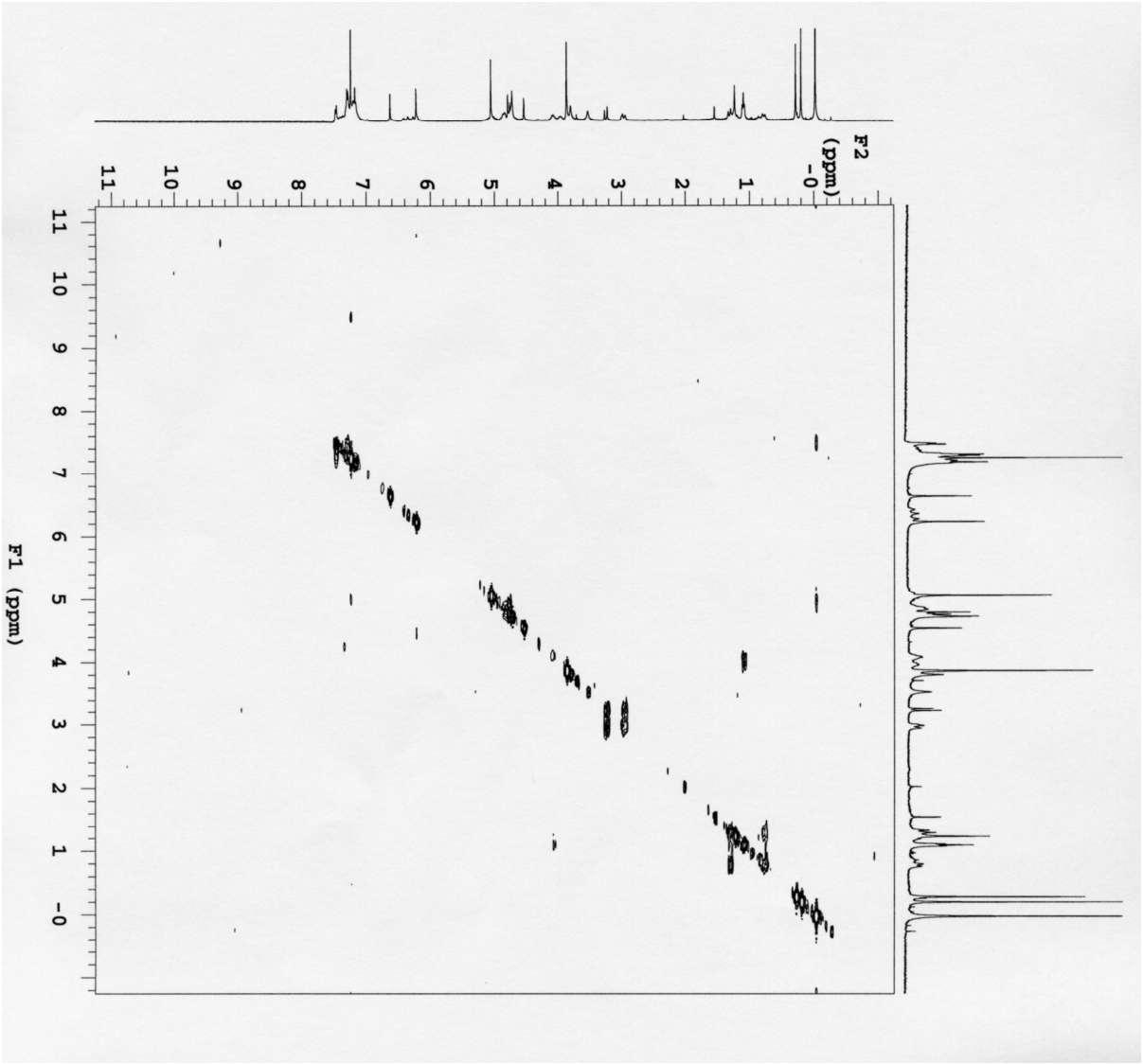

10
204.162
168.896
153.013
151.970
149.351
147.485
137.667
137.058
137.027
136.526
132.783
128.448
128.416
128.397
128.087
127.863
127.752
127.677
127.385
127.224
126.987
124.757
114.501
110.755
108.570
107.942
85.706
77.320
77.000
76.680
75.075
71.010
70.754
61.921
56.111
55.948
54.873
42.077
18.632
13.716
-1.012
-1.096
200
150
100
50
0
PPM


11
H3CO
BnO
BnO
OBn
OCH3
H
OH
CO2Et
OH
Me
Me
Si
OH
7.499
7.484
7.336
7.319
7.302
7.276
7.254
7.218
7.196
7.178
6.650
6.249
5.080
4.856
4.814
4.783
4.564
3.883
3.821
3.549
3.291
3.251
1.629
1.315
1.130
1.115
1.097
0.301
0.222
0.000
3.00
2.16
1.15
1.45
2.85
1.14
2.92
PPM

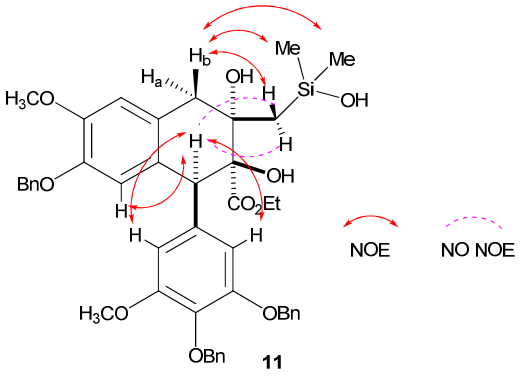
COSY of **11** (obtained with 1 drop of D_2O addition to the NMR sample)

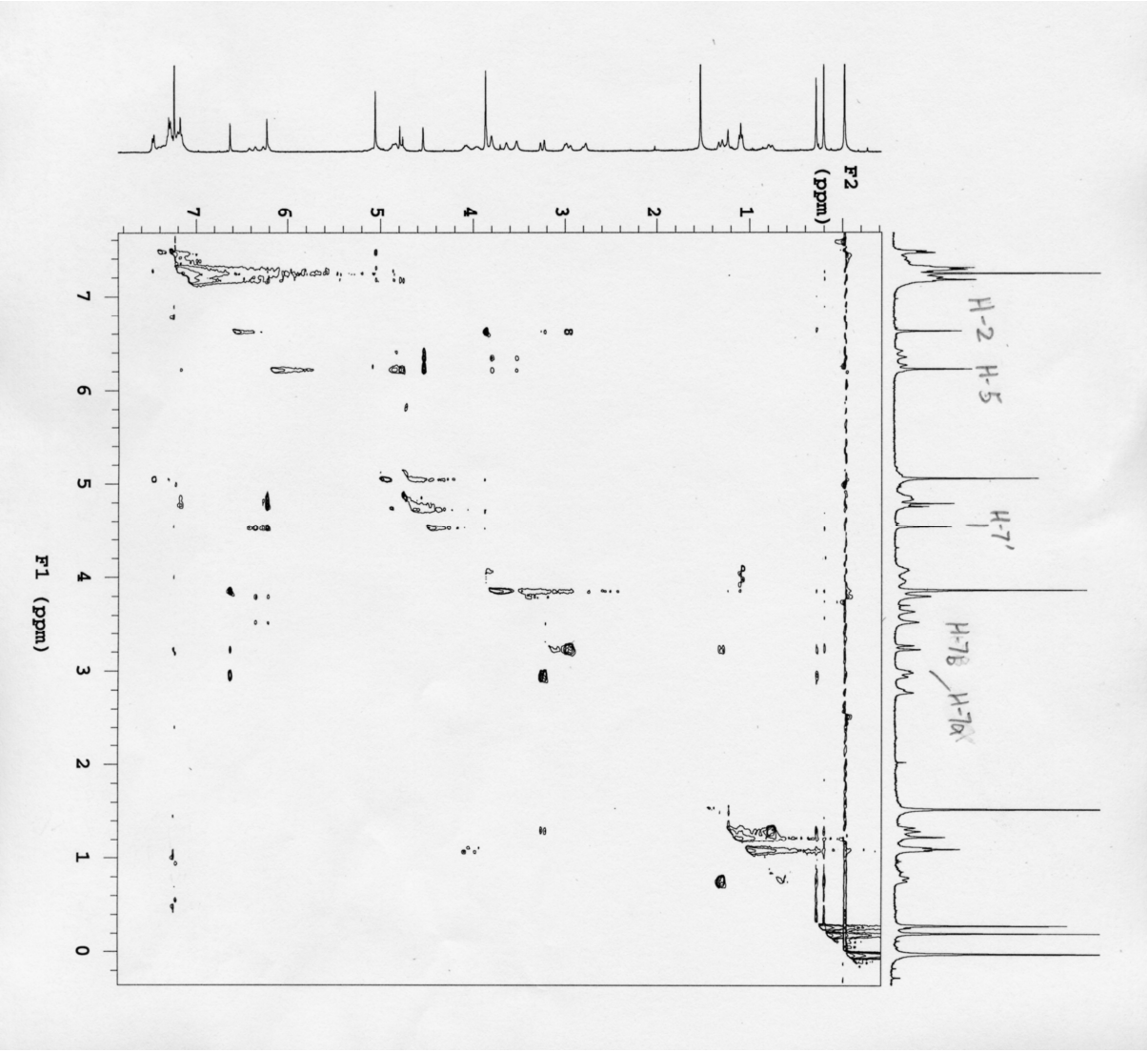


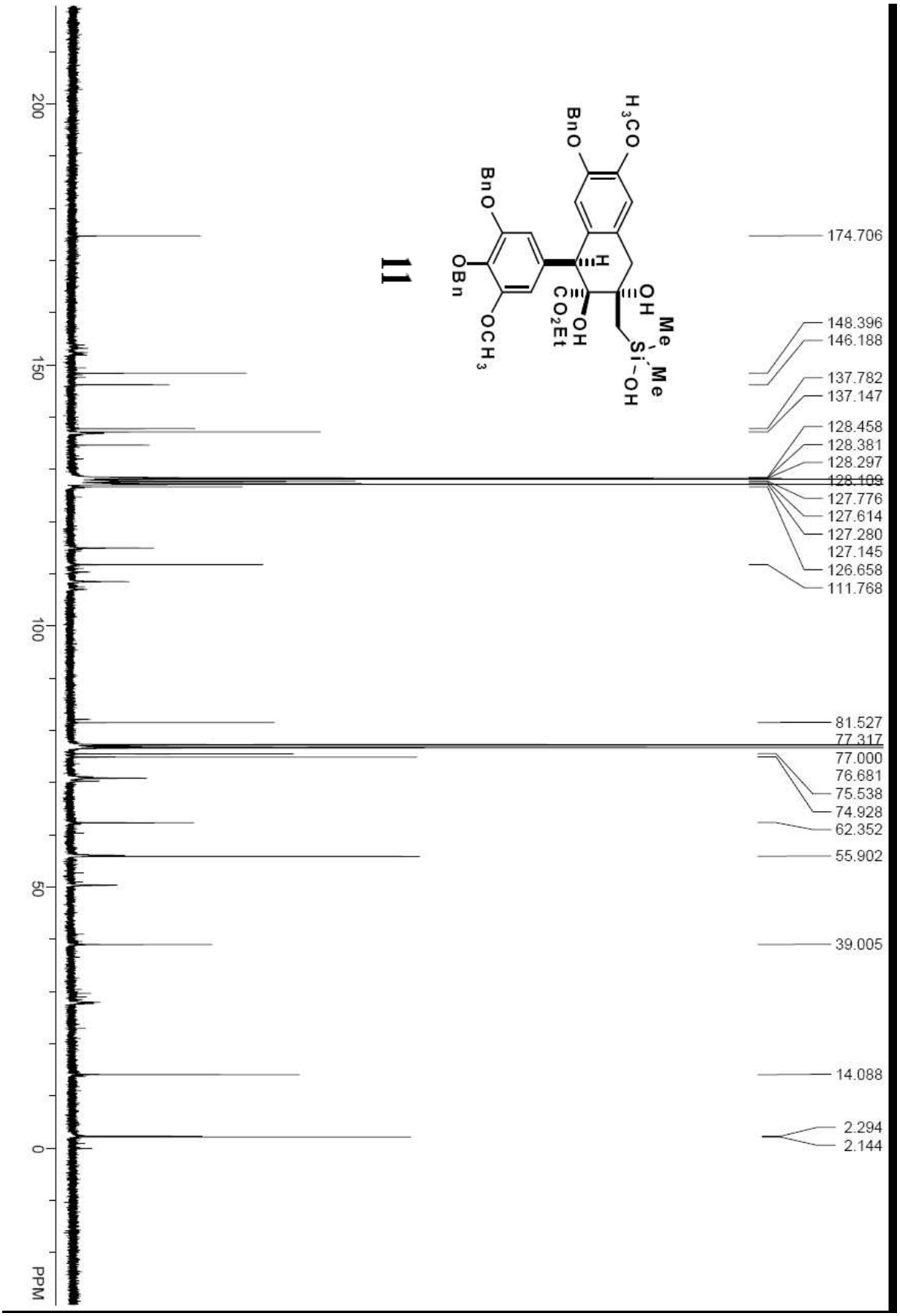
11

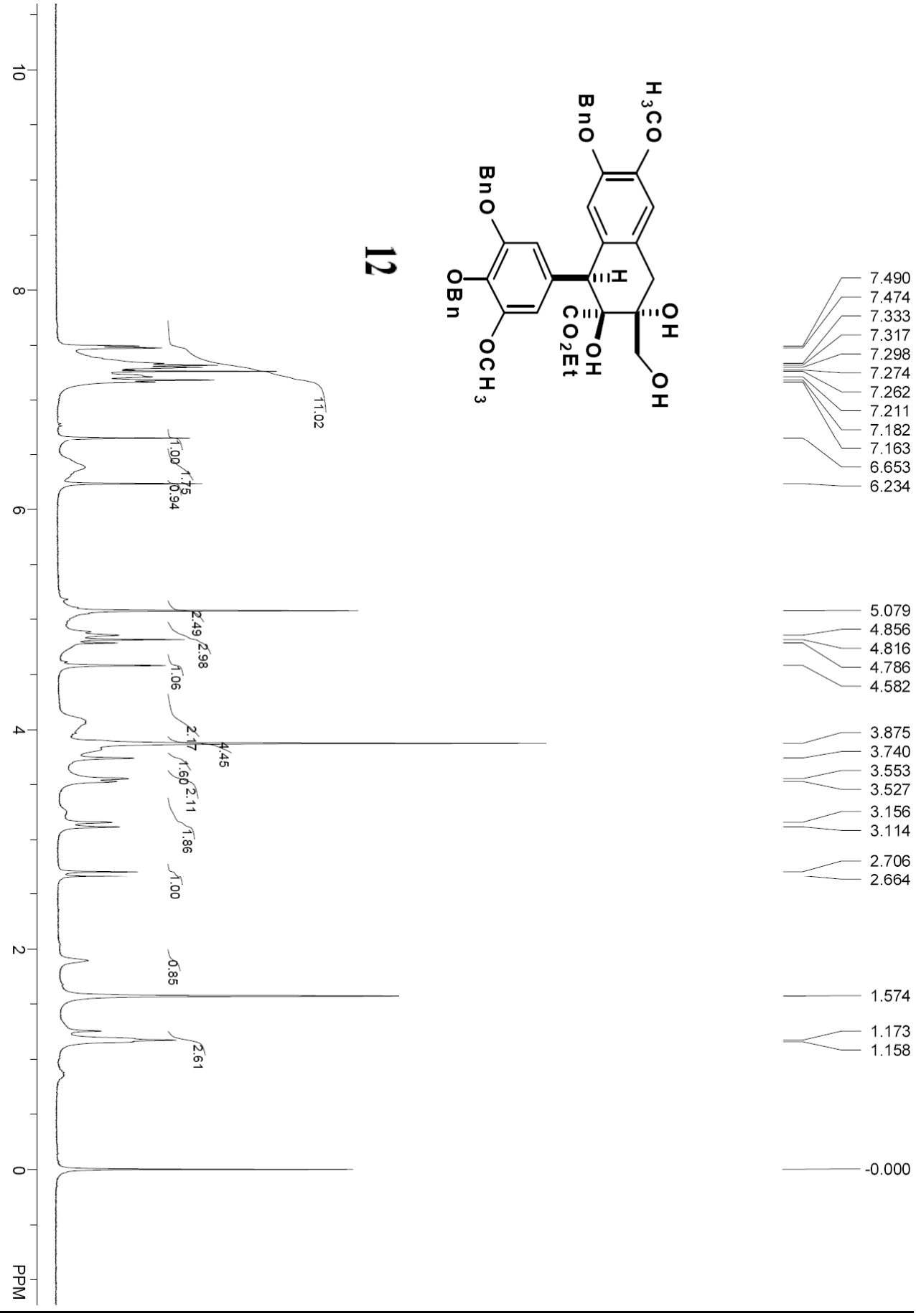


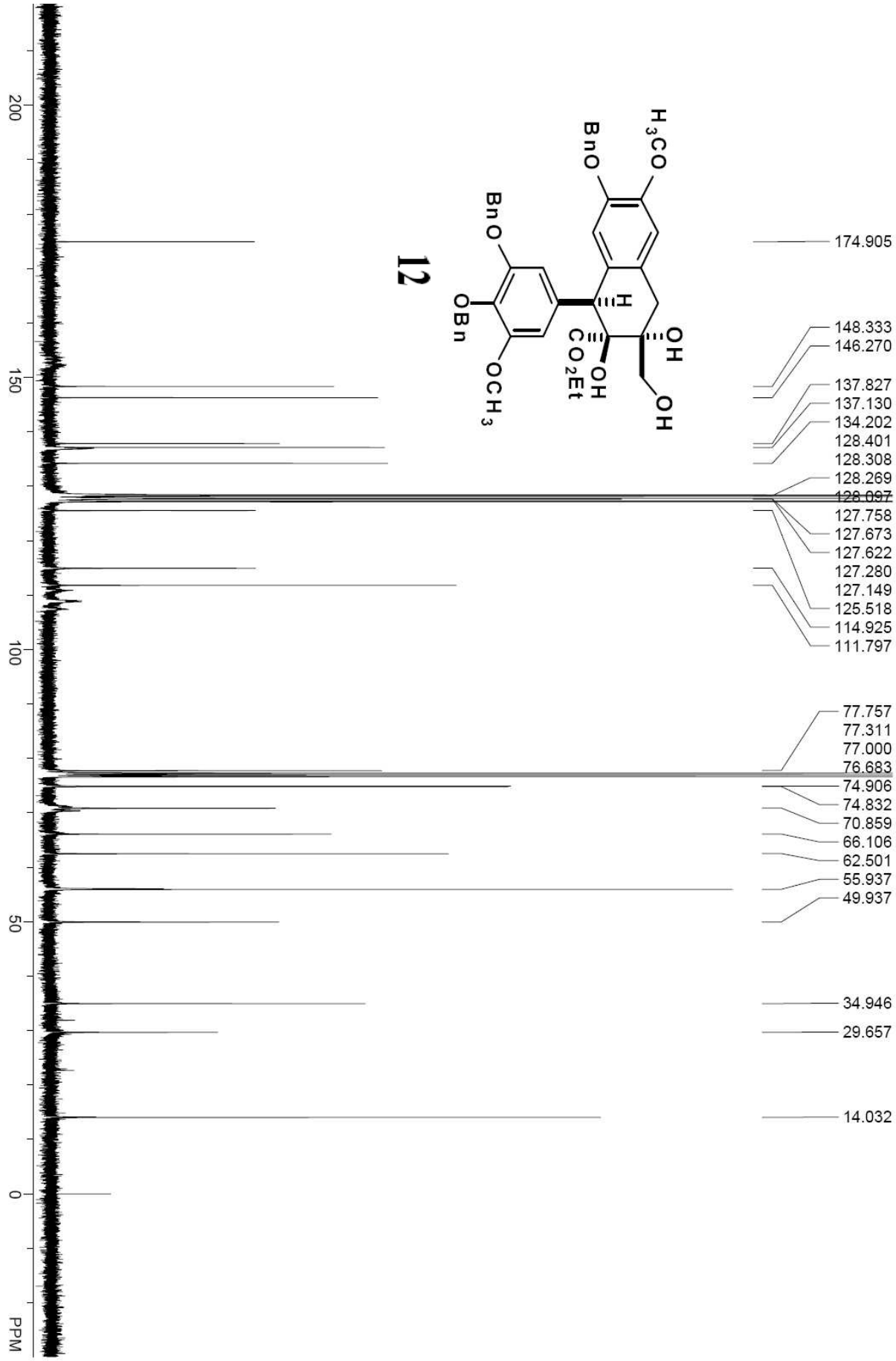
NOESY of **11**

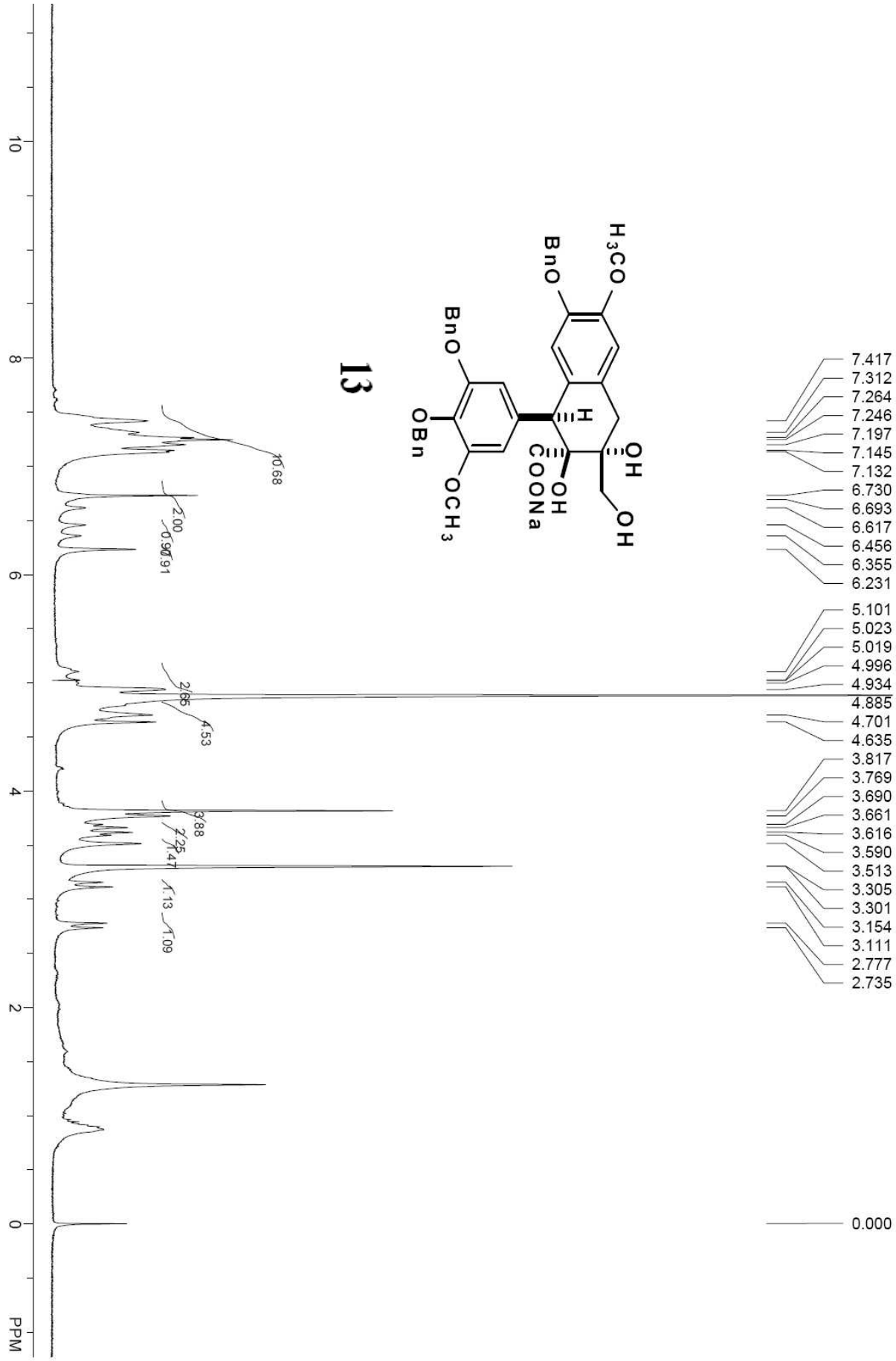

Me
Me
Si
OH
H_b
H_a
OH
H
H_3CO
BnO
H
H
OH
CO_2Et
H
H
H_3CO
OBn
OBn
NOE
NO NOE
11

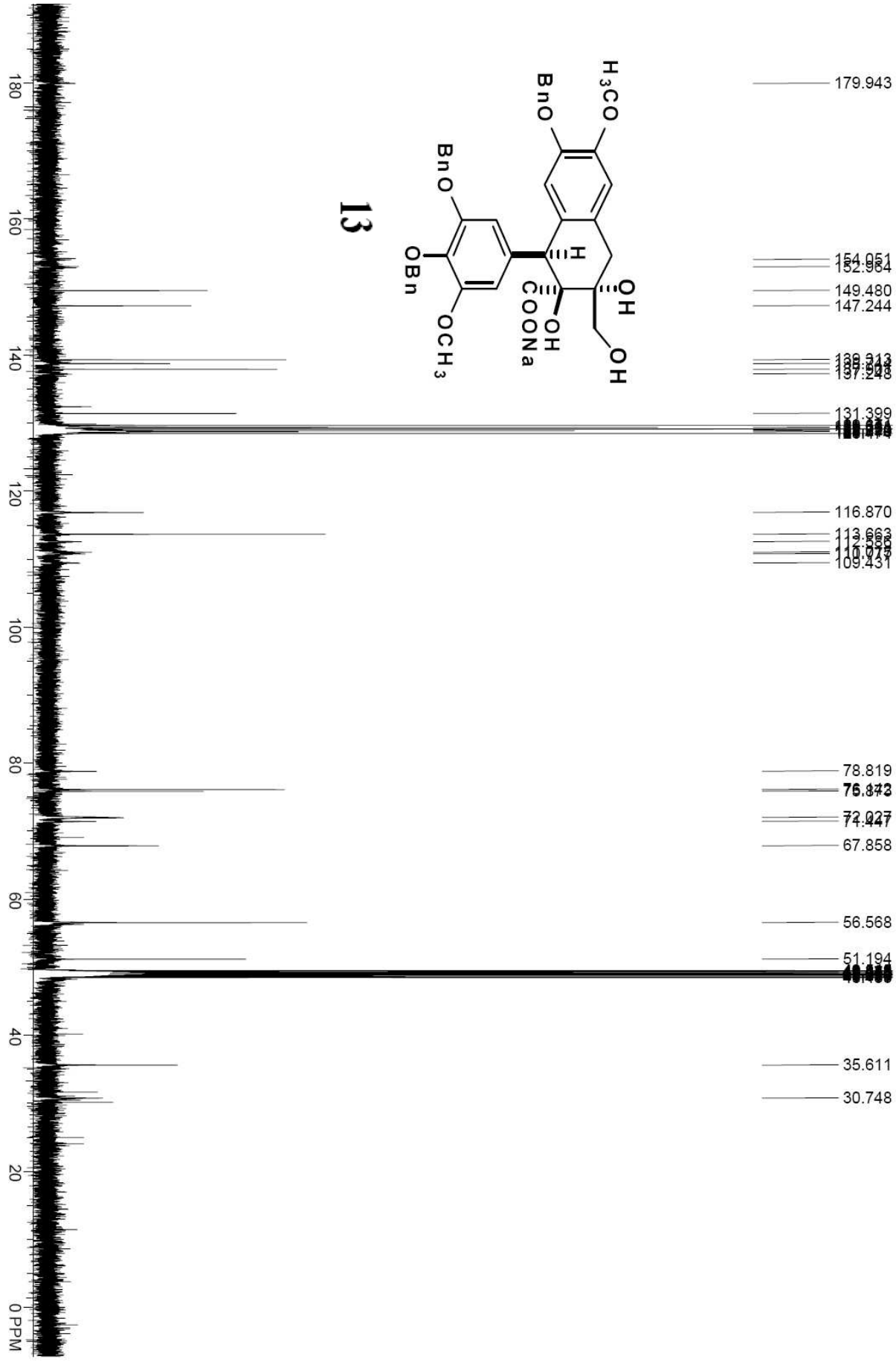

F2 (ppm)
F1 (ppm)
H-2
H-5
H-7'
H-7a
H-7a'

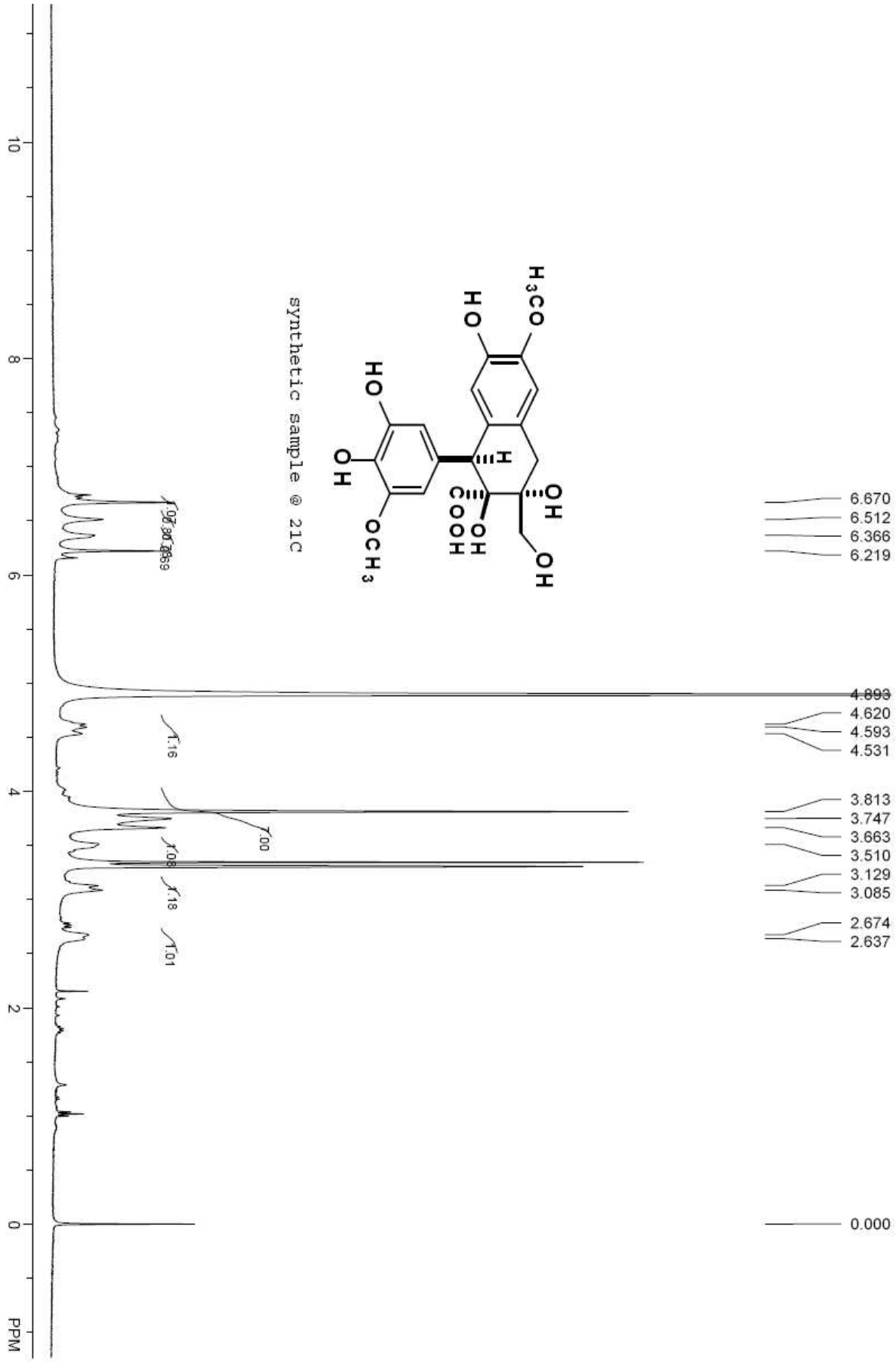

11
174.706
148.396
146.188
137.782
137.147
128.458
128.381
128.297
128.109
127.776
127.614
127.280
127.145
126.658
111.768
81.527
77.317
77.000
76.681
75.538
74.928
62.352
55.902
39.005
14.088
2.294
2.144
200
150
100
50
0
PPM

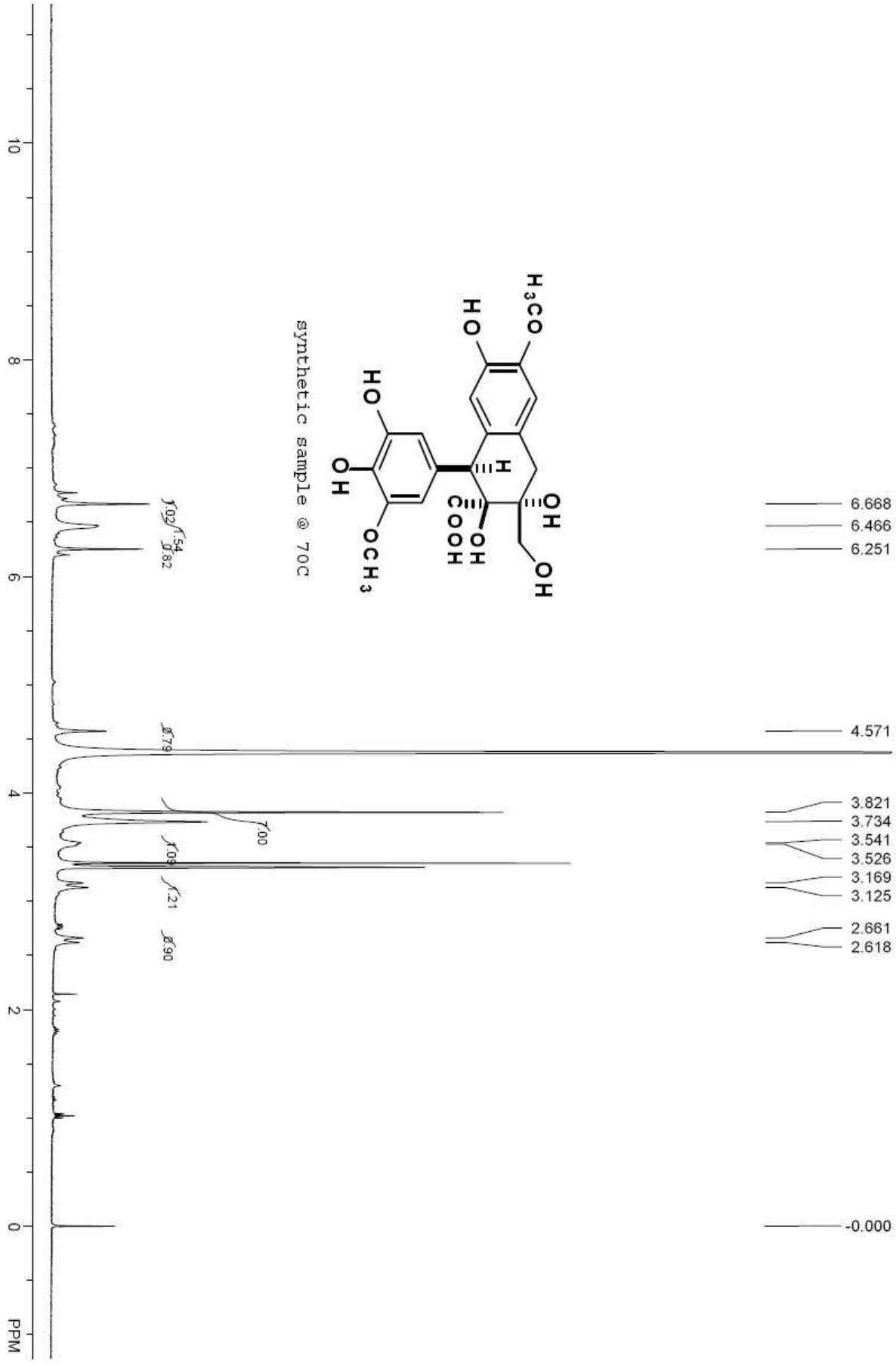

12
H3CO
BnO
BnO
OBn
OCH3
H
CO2Et
OH
OH
OH
7.490
7.474
7.333
7.317
7.298
7.274
7.262
7.211
7.182
7.163
6.653
6.234
5.079
4.856
4.816
4.786
4.582
3.875
3.740
3.553
3.527
3.156
3.114
2.706
2.664
1.574
1.173
1.158
-0.000
11.02
1.00
1.75
0.94
2.49
2.98
1.06
2.17
4.45
1.60
2.11
1.86
1.00
0.85
2.61
10
8
6
4
2
0
PPM

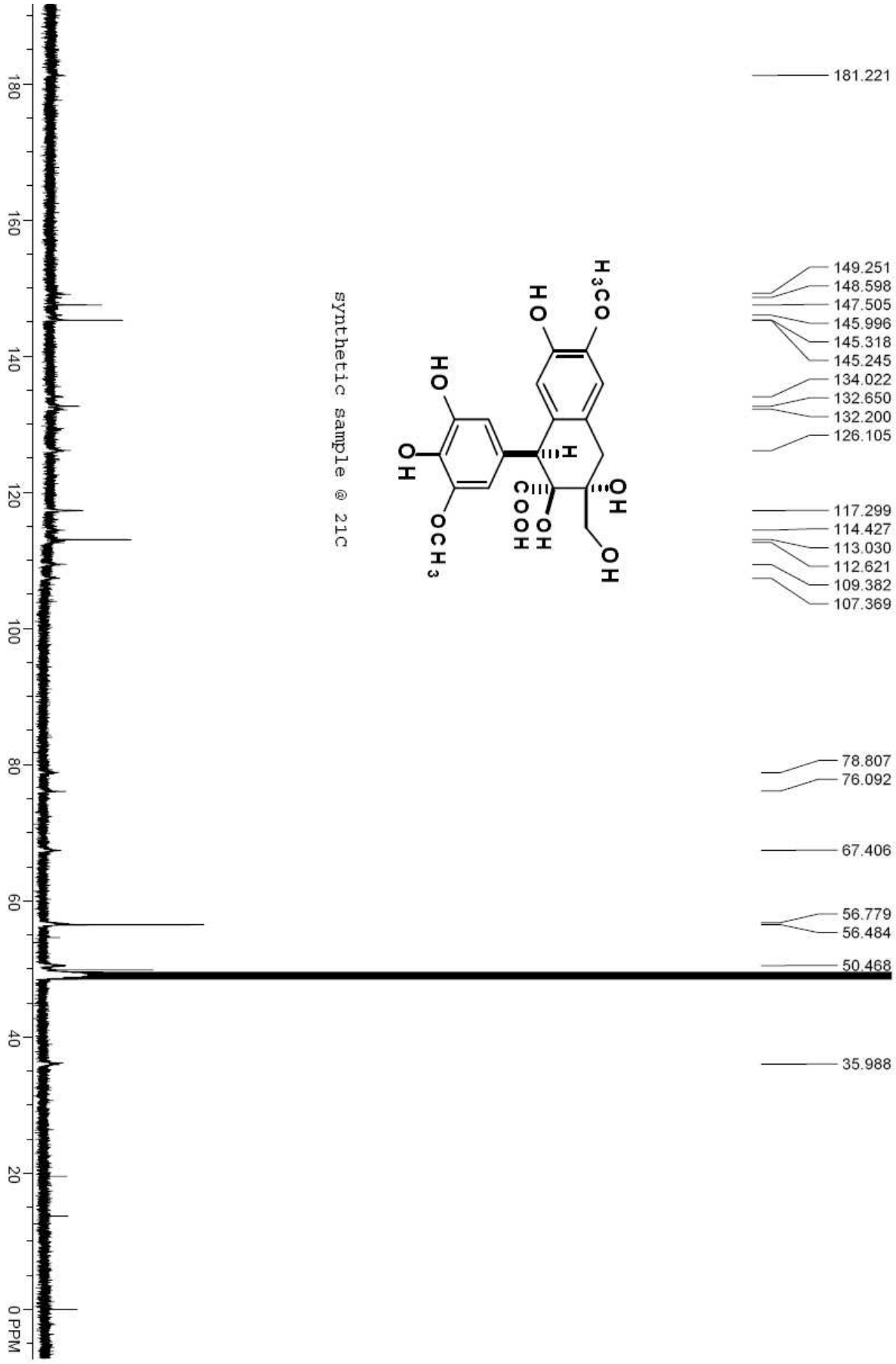

12
174.905
148.333
146.270
137.827
137.130
134.202
128.401
128.308
128.269
128.097
127.758
127.673
127.622
127.280
127.149
125.518
114.925
111.797
77.757
77.311
77.000
76.683
74.906
74.832
70.859
66.106
62.501
55.937
49.937
34.946
29.657
14.032
200
150
100
50
0
PPM


13
7.417
7.312
7.264
7.246
7.197
7.145
7.132
6.730
6.693
6.617
6.456
6.355
6.231
5.101
5.023
5.019
4.996
4.934
4.885
4.701
4.635
3.817
3.769
3.690
3.661
3.616
3.590
3.513
3.305
3.301
3.154
3.111
2.777
2.735
0.000
10.68
2.00
0.90
0.91
2.65
4.53
3.88
2.25
4.47
1.13
1.09
PPM

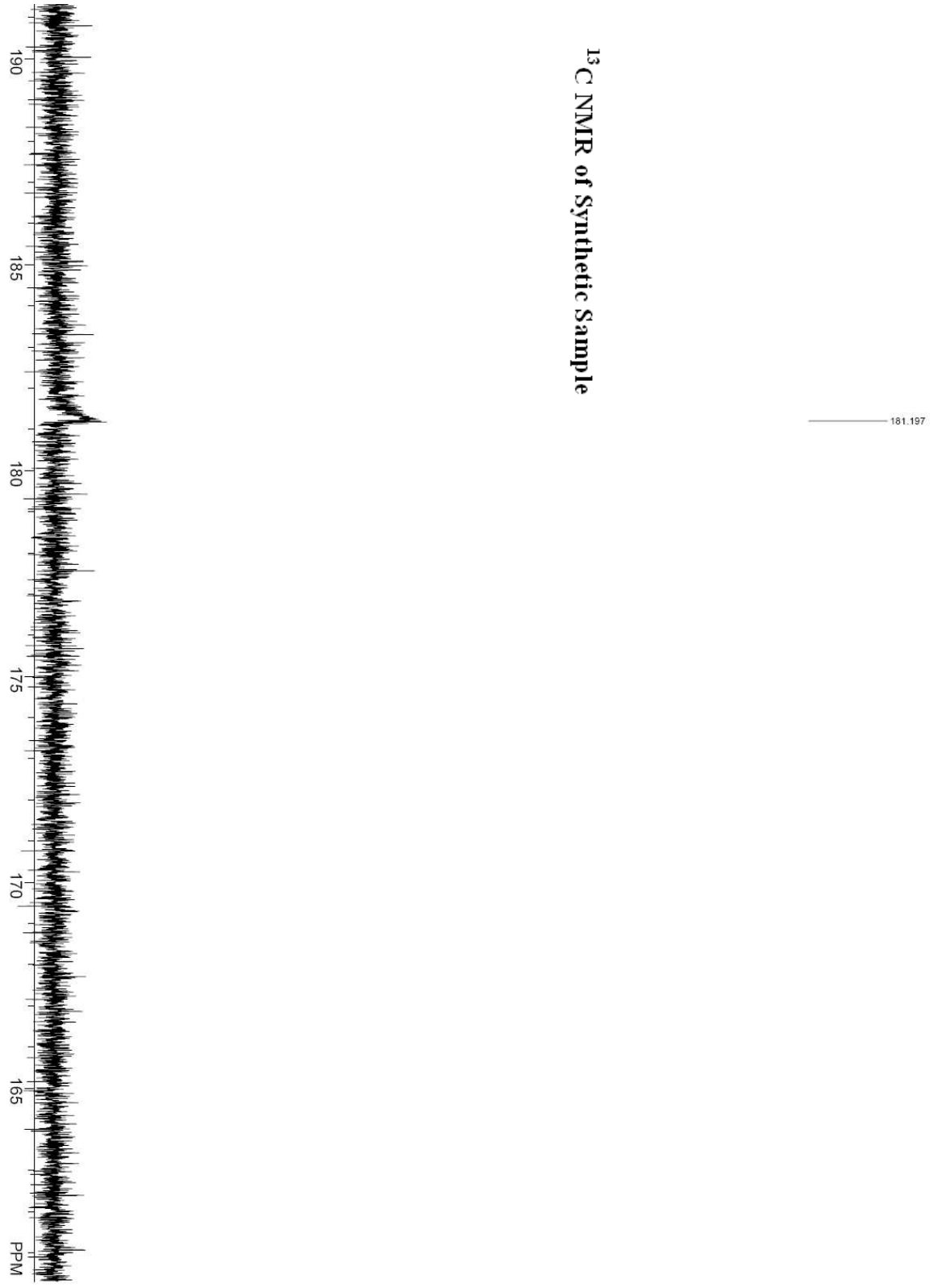

13
BnO
H3CO
BnO
OBn
OCH3
COONa
OH
OH
OH
179.943
154.051
152.964
149.480
147.244
139.313
137.248
131.399
116.870
113.663
109.431
78.819
72.027
67.858
56.568
51.194
35.611
30.748
180
160
140
120
100
80
60
40
20
0 PPM


synthetic sample @ 21C
6.670
6.512
6.366
6.219
4.893
4.620
4.593
4.531
3.813
3.747
3.663
3.510
3.129
3.085
2.674
2.637
0.000
1.16
7.00
1.08
1.18
1.01
PPM

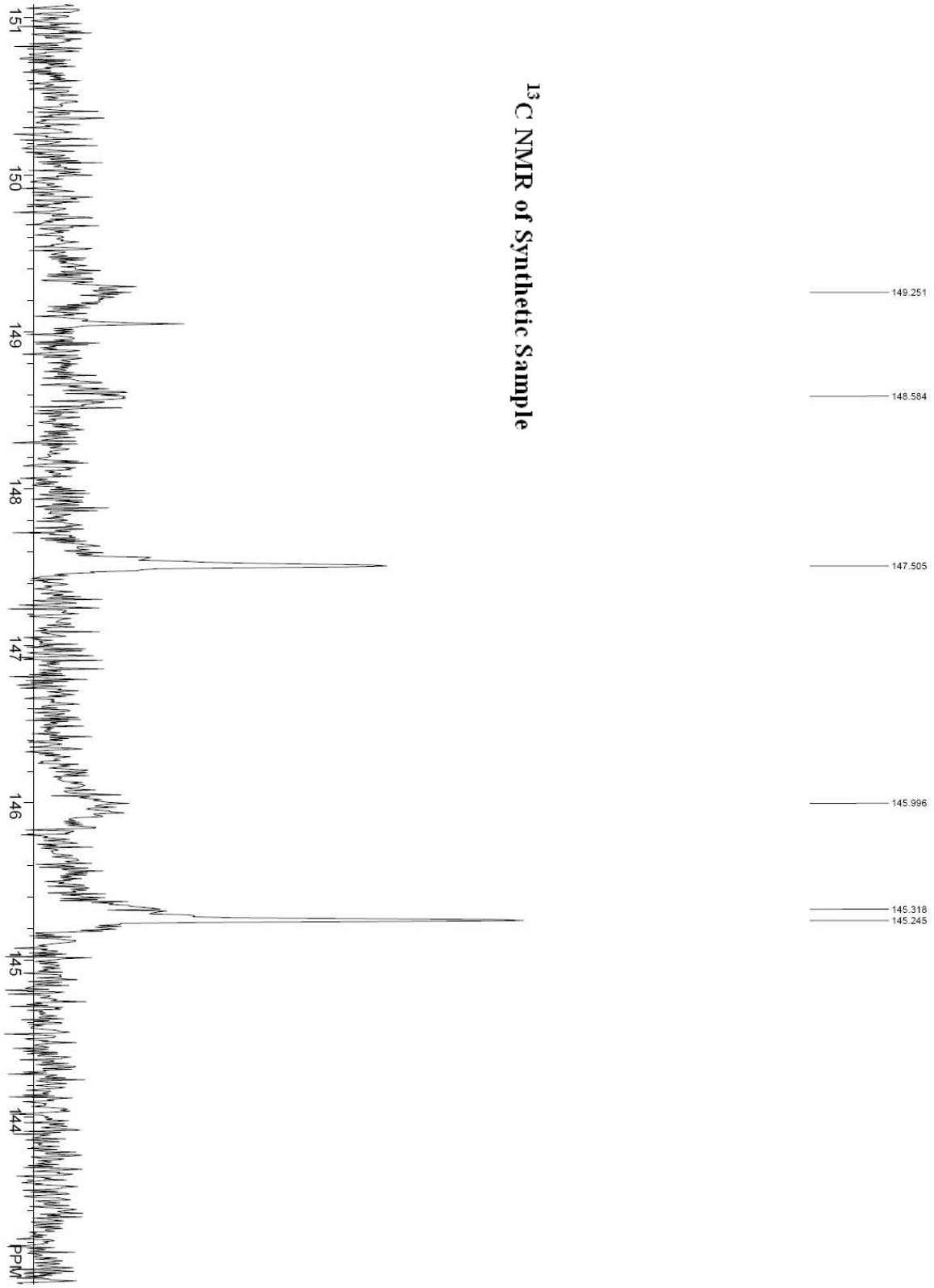

synthetic sample @ 70C
6.668
6.466
6.251
4.571
3.821
3.734
3.541
3.526
3.169
3.125
2.661
2.618
-0.000
PPM


synthetic sample @ 21C
181.221
149.251
148.598
147.505
145.996
145.318
145.245
134.022
132.650
132.200
126.105
117.299
114.427
113.030
112.621
109.382
107.369
78.807
76.092
67.406
56.779
56.484
50.468
35.988
180
160
140
120
100
80
60
40
20
0 PPM

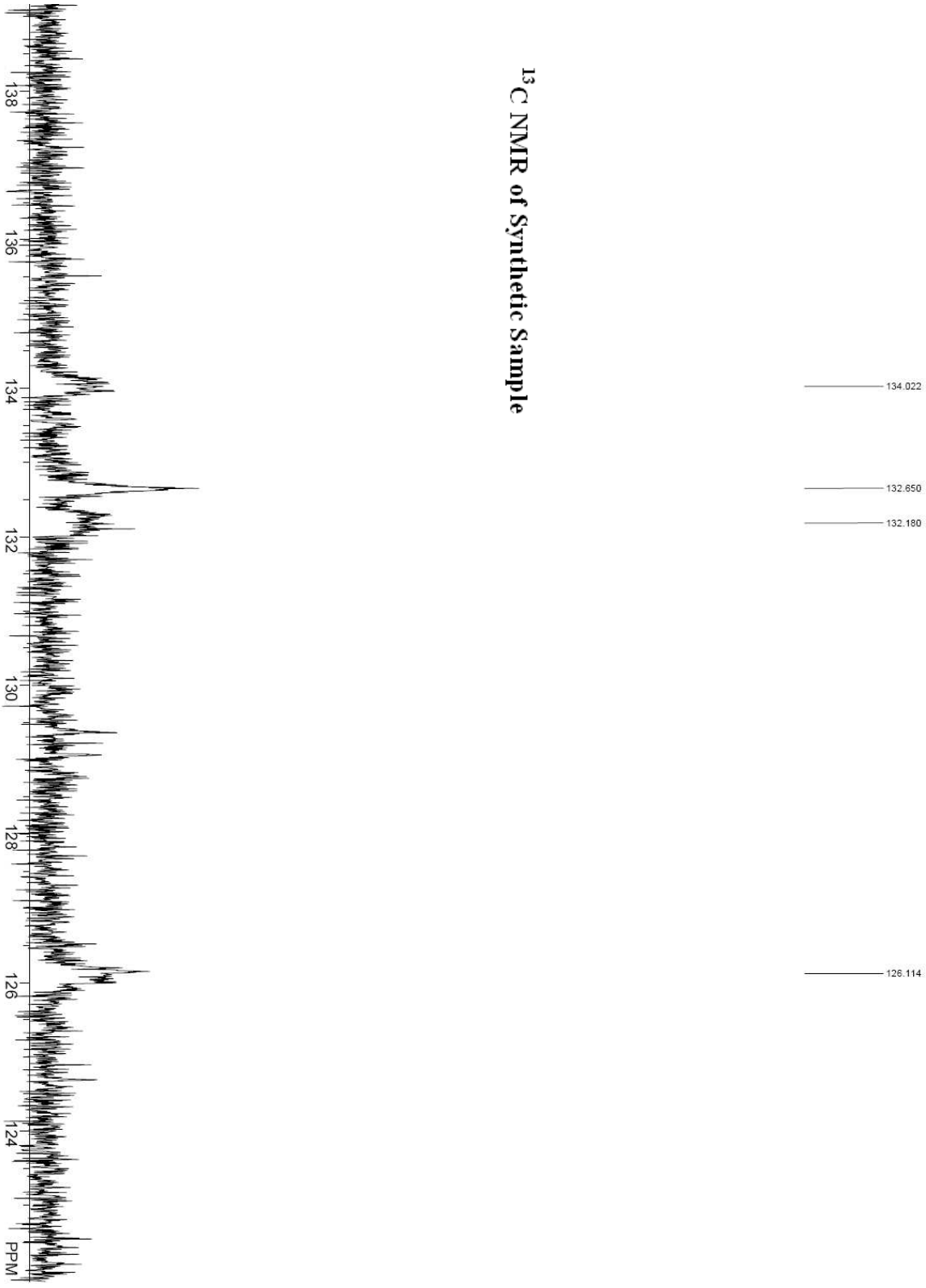
^{13}C NMR of Synthetic Sample



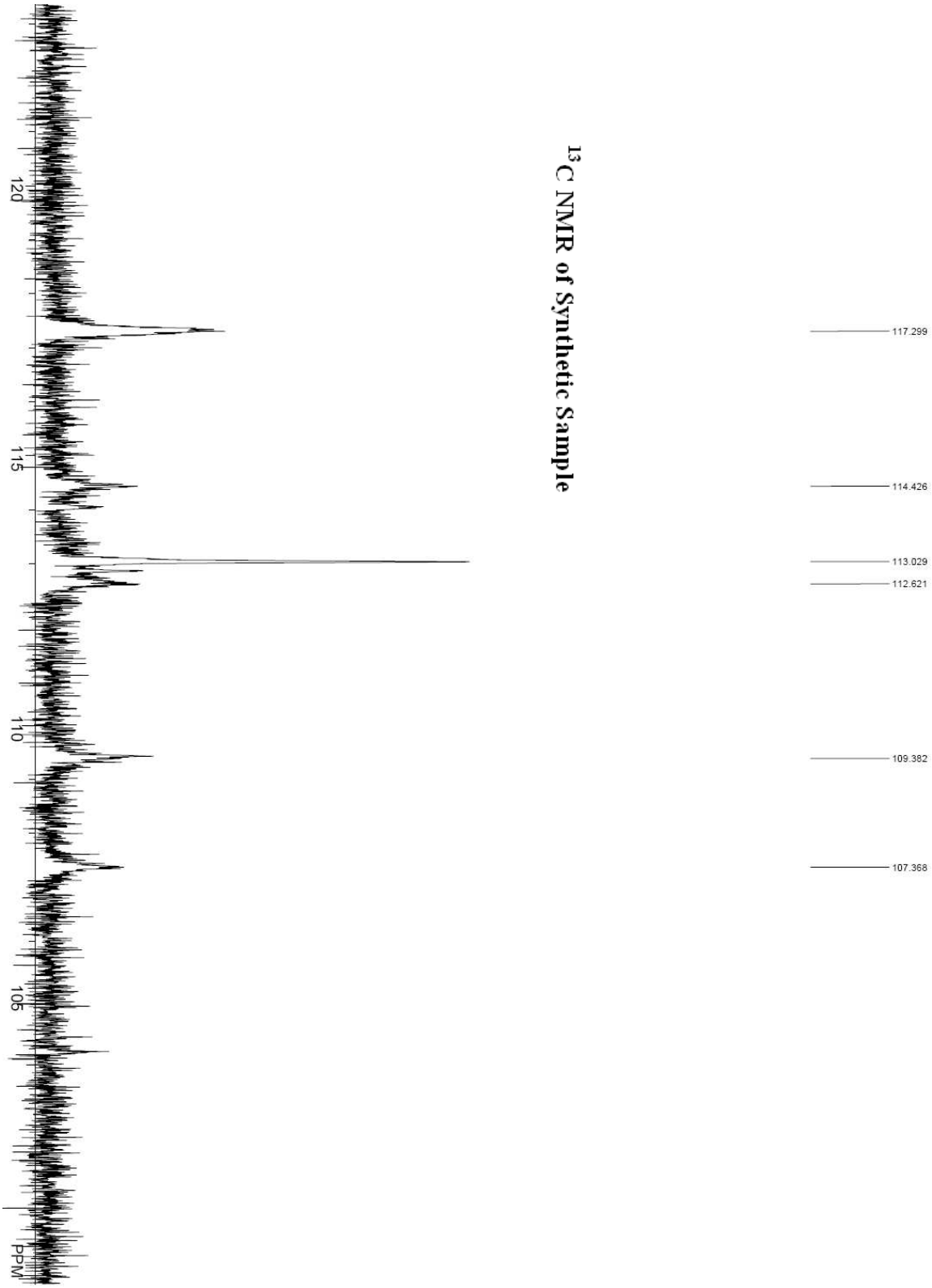
^{13}C NMR of Synthetic Sample



^{13}C NMR of Synthetic Sample

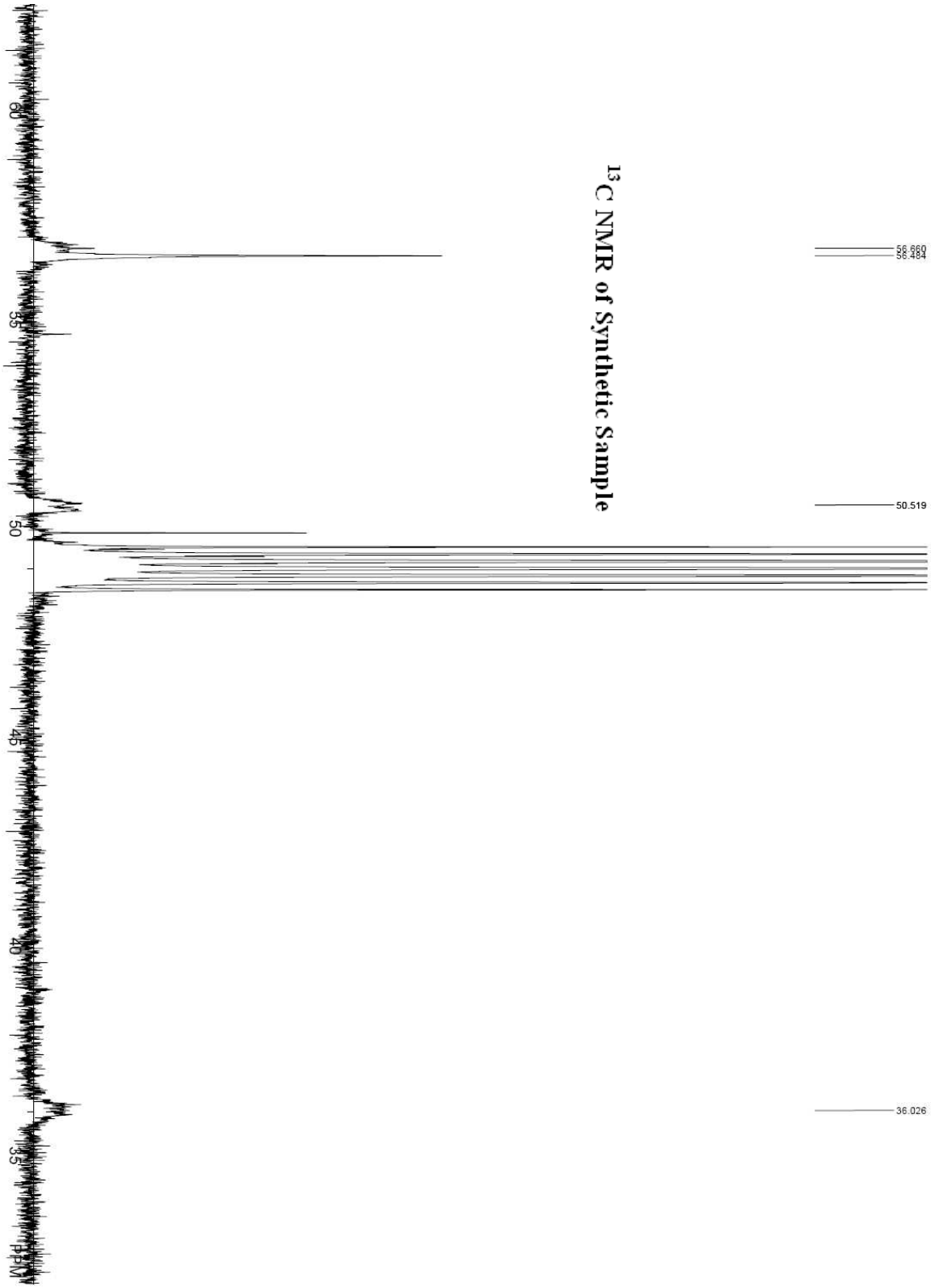


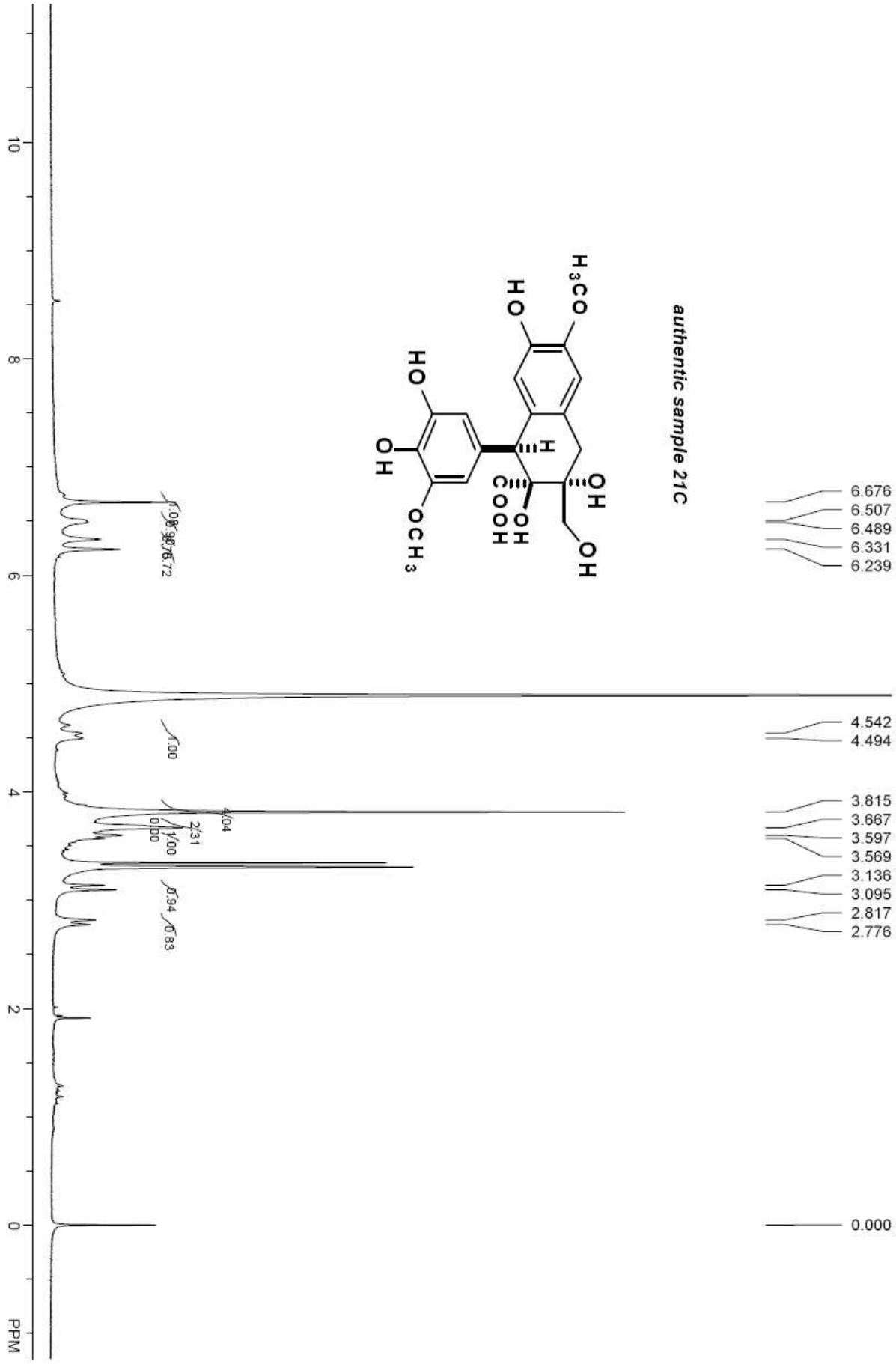
^{13}C NMR of Synthetic Sample

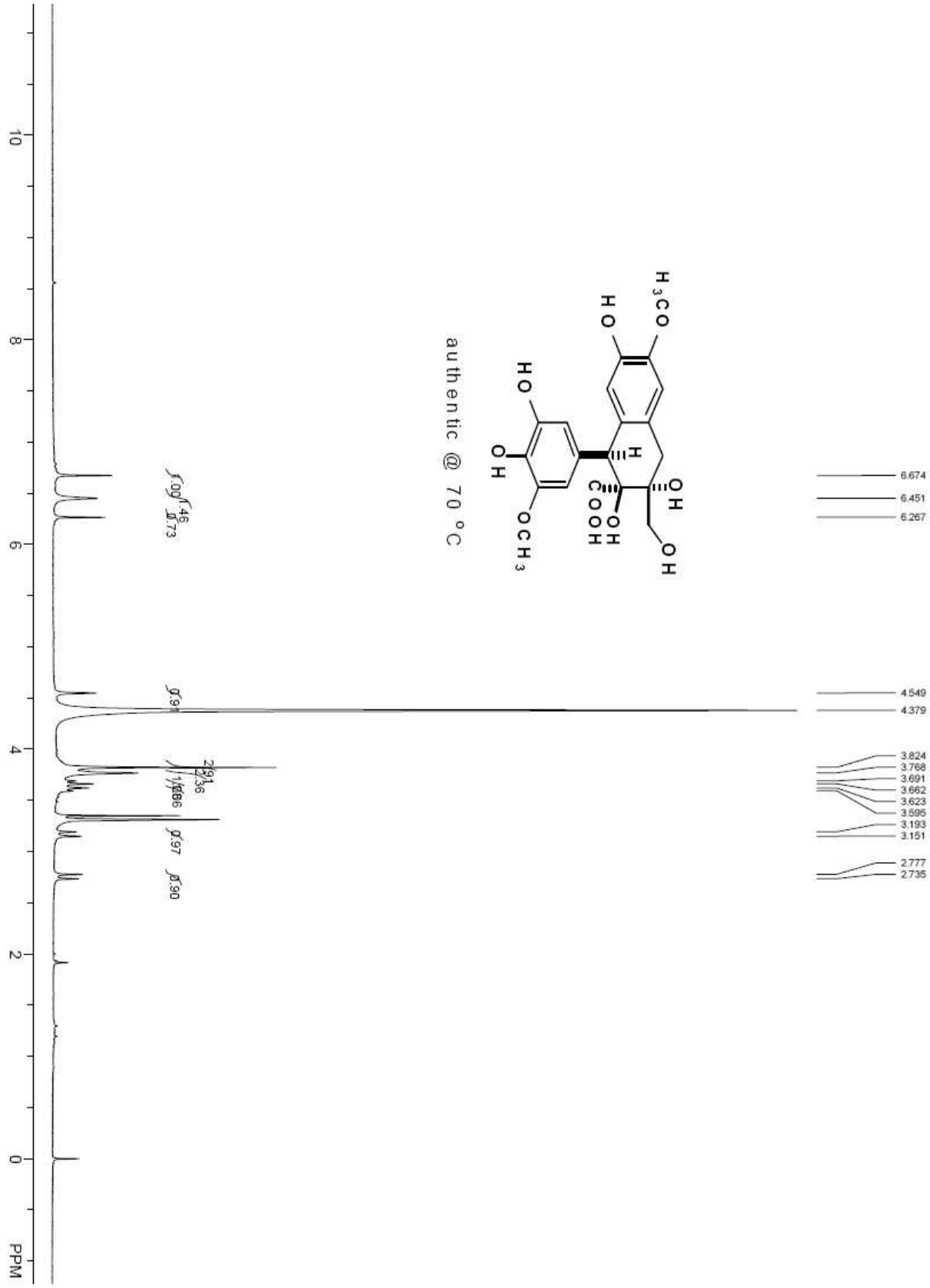


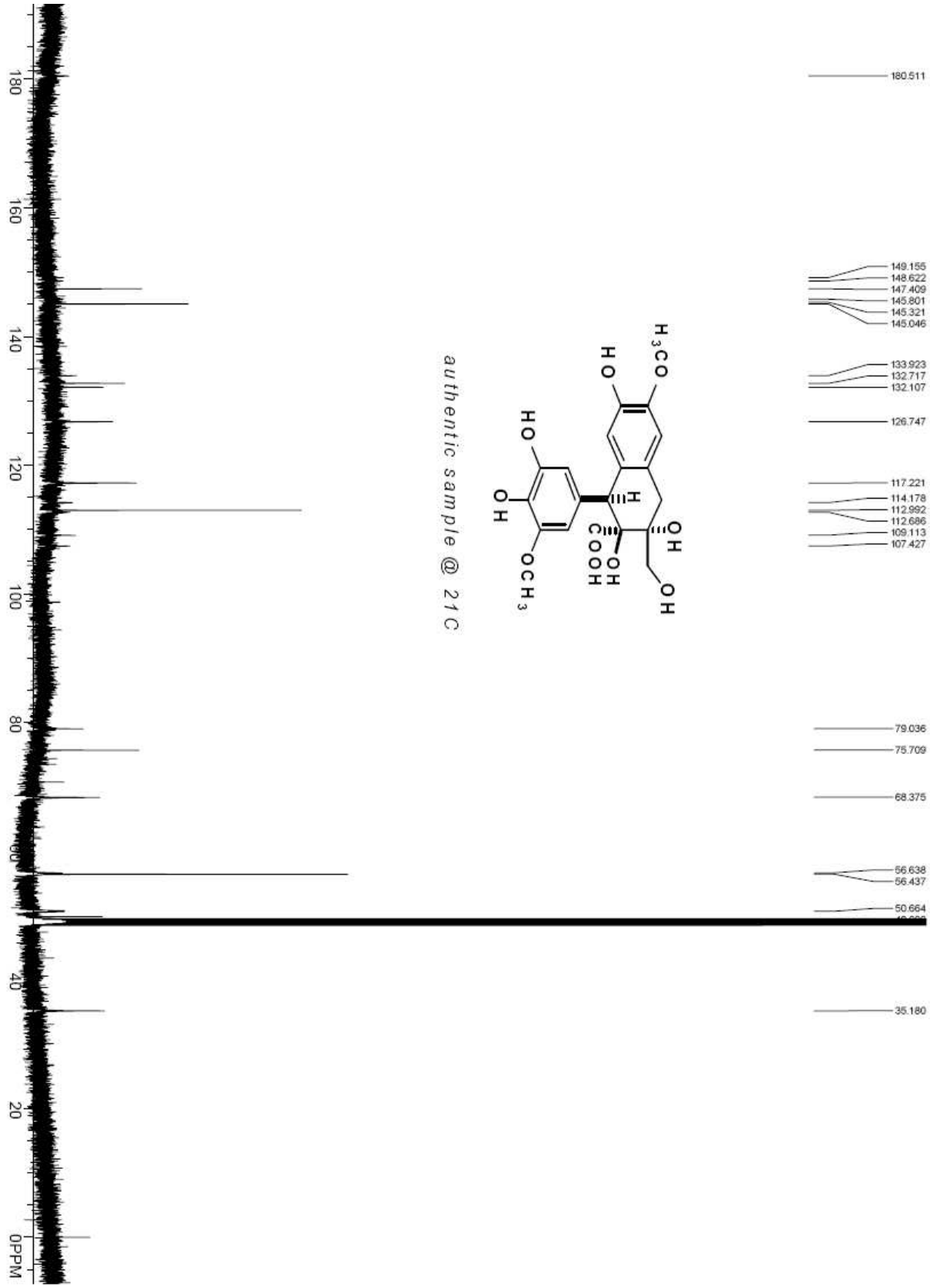
^{13}C NMR of Synthetic Sample

^{13}C NMR of Synthetic Sample



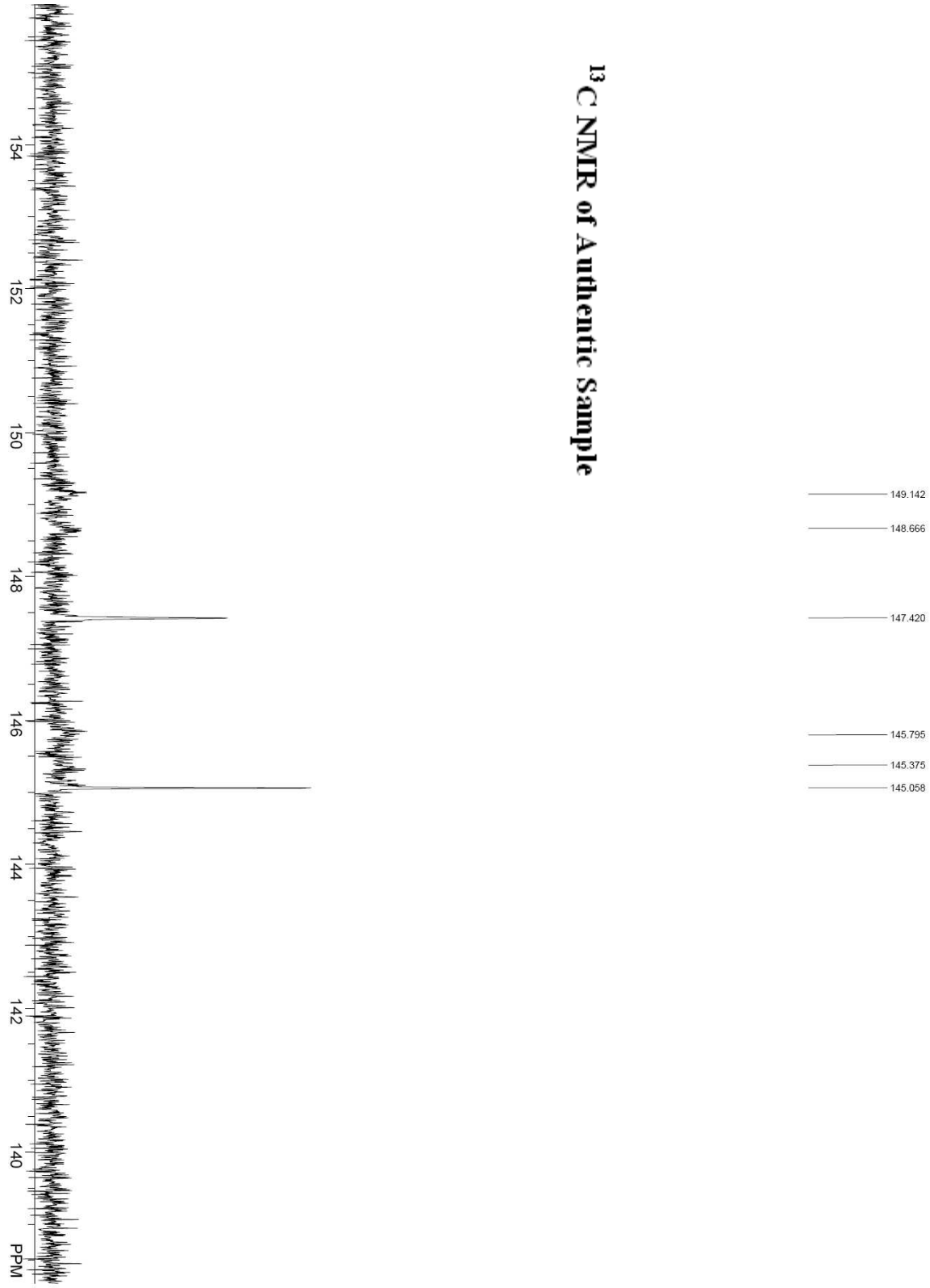

authentic sample 21C
6.676
6.507
6.489
6.331
6.239
4.542
4.494
3.815
3.667
3.597
3.569
3.136
3.095
2.817
2.776
0.000
PPM


authentic @ 70 °C
6.674
6.451
6.267
4.549
4.379
3.824
3.768
3.691
3.662
3.623
3.595
3.193
3.151
2.777
2.735
PPM

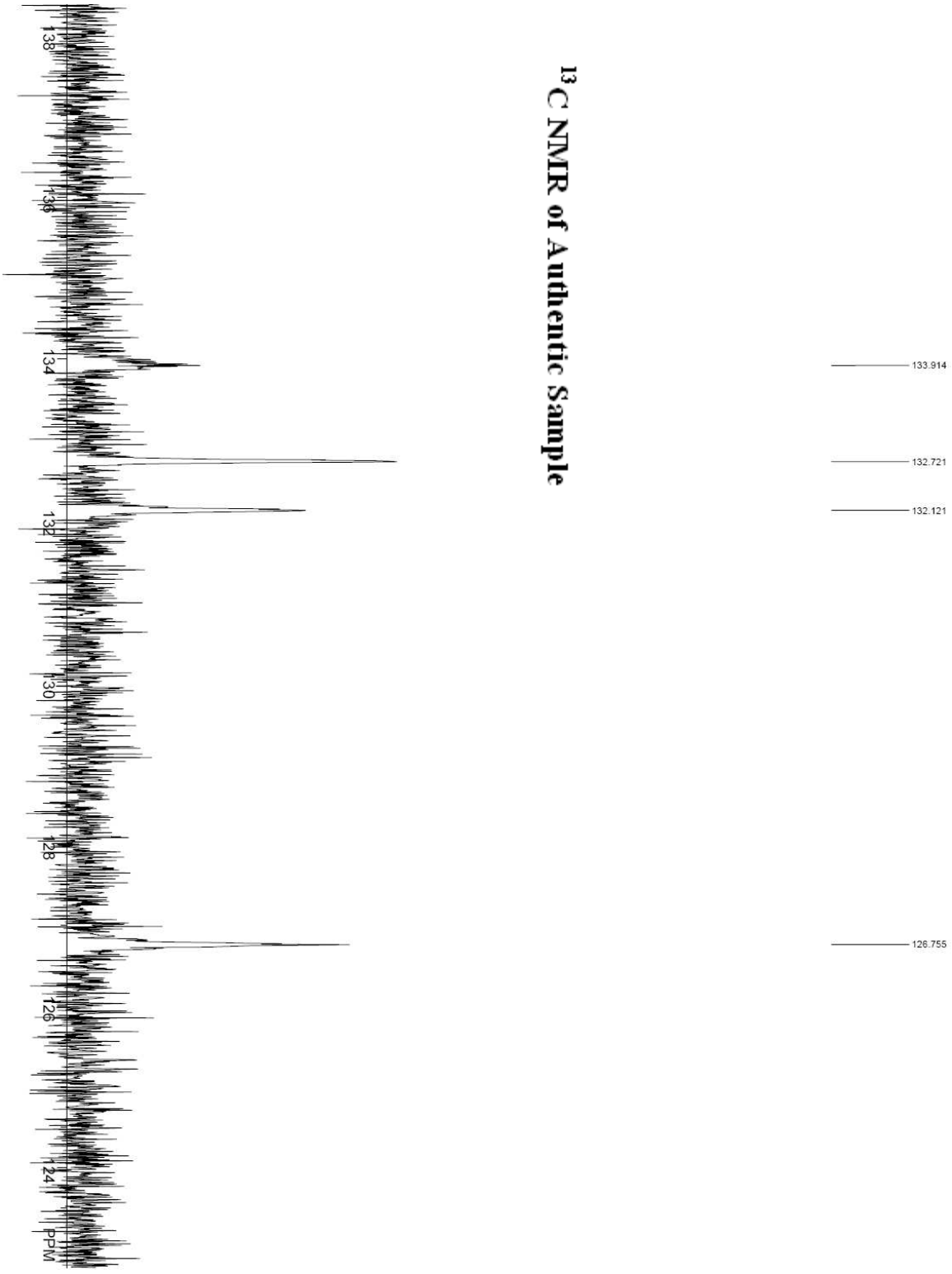

180.511
149.155
148.622
147.409
145.801
145.321
145.046
133.923
132.717
132.107
126.747
117.221
114.178
112.992
112.686
109.113
107.427
79.036
75.709
68.375
56.638
56.437
50.664
35.180
180
160
140
120
100
80
60
40
20
0PPM
authentic sample @ 21C
H3CO
HO
HO
O
H
OCH3
H
COOH
OH
OH

^{13}C NMR of Authentic Sample

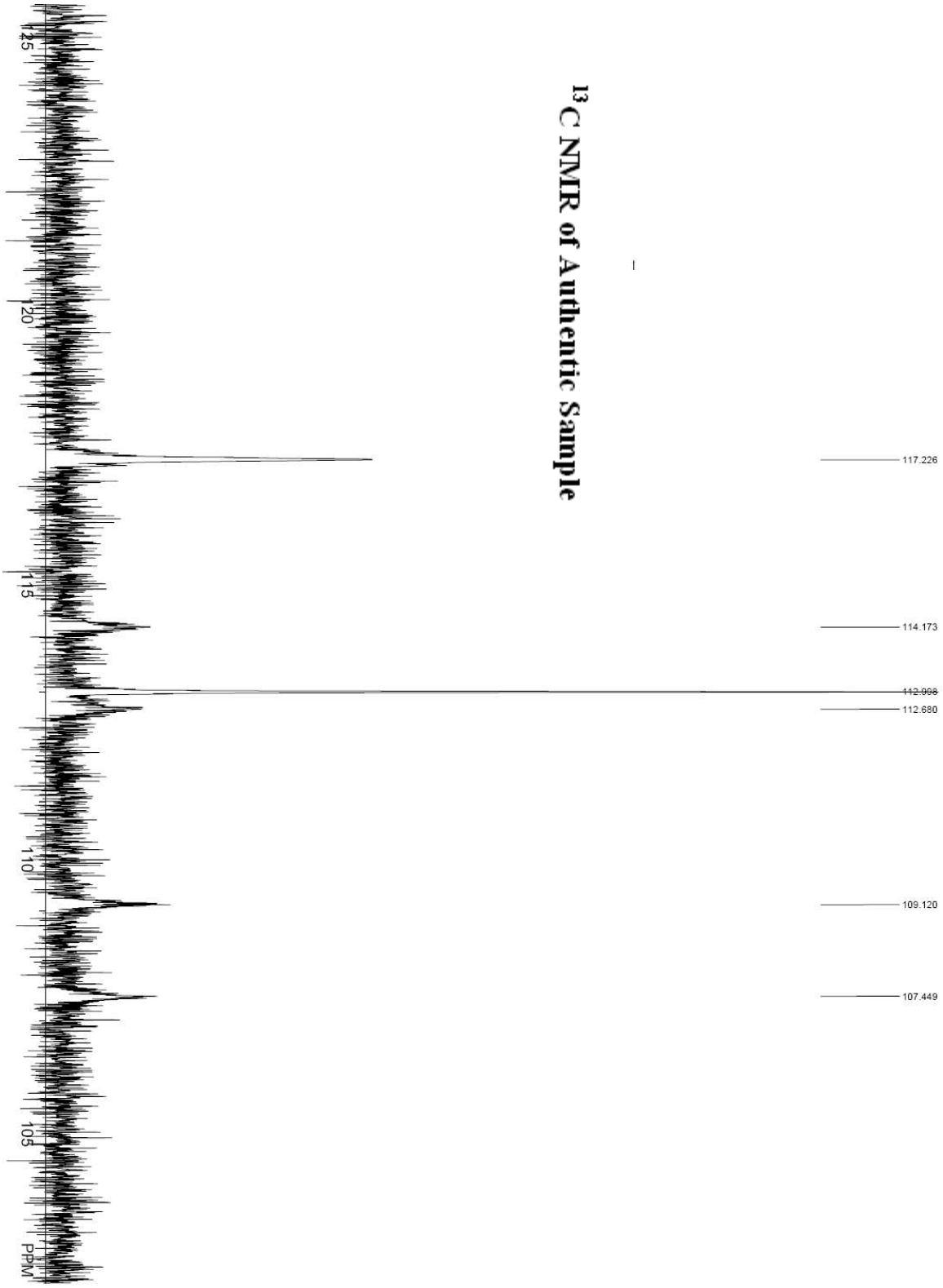
^{13}C NMR of Authentic Sample



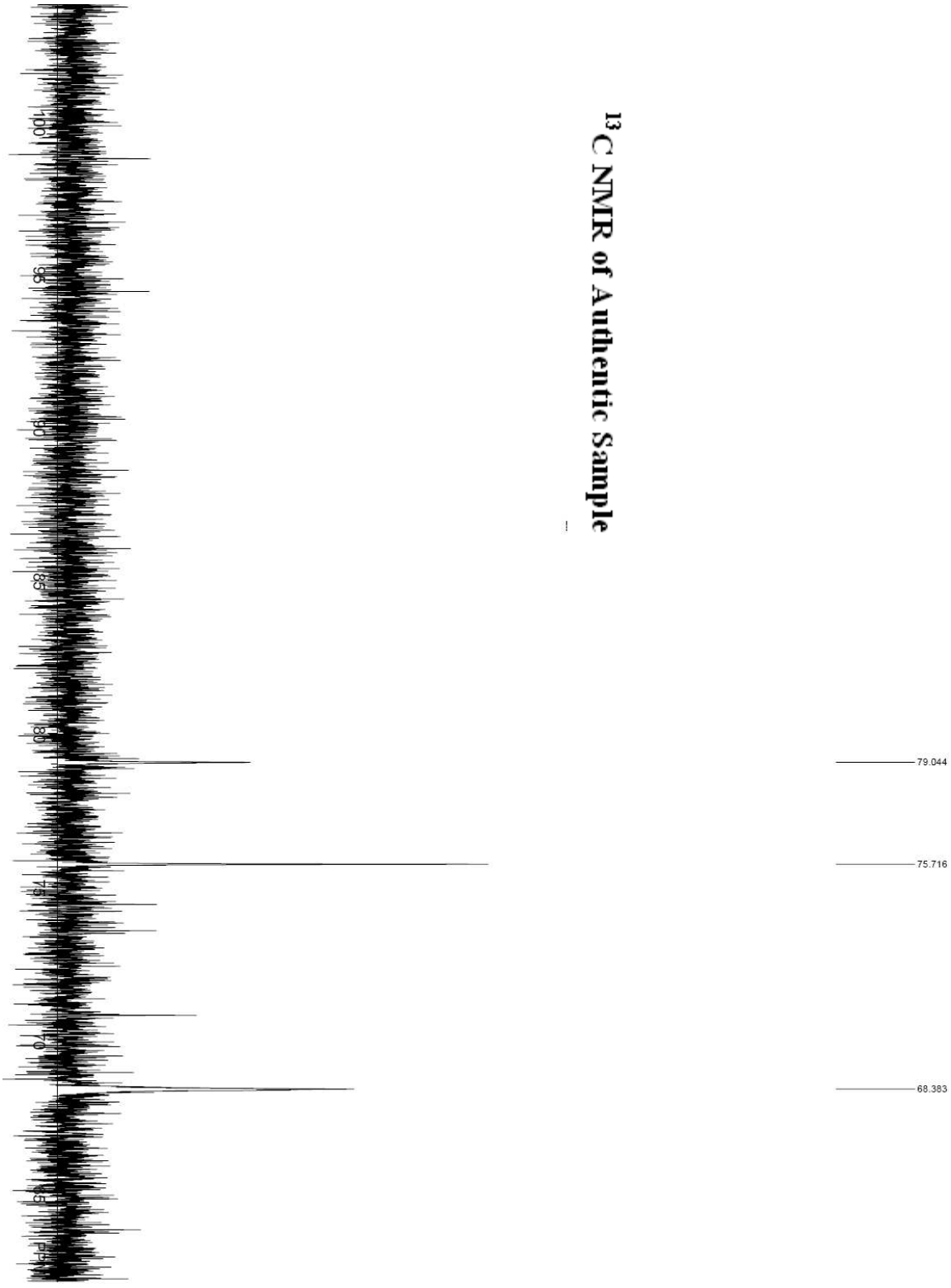
^{13}C NMR of Authentic Sample



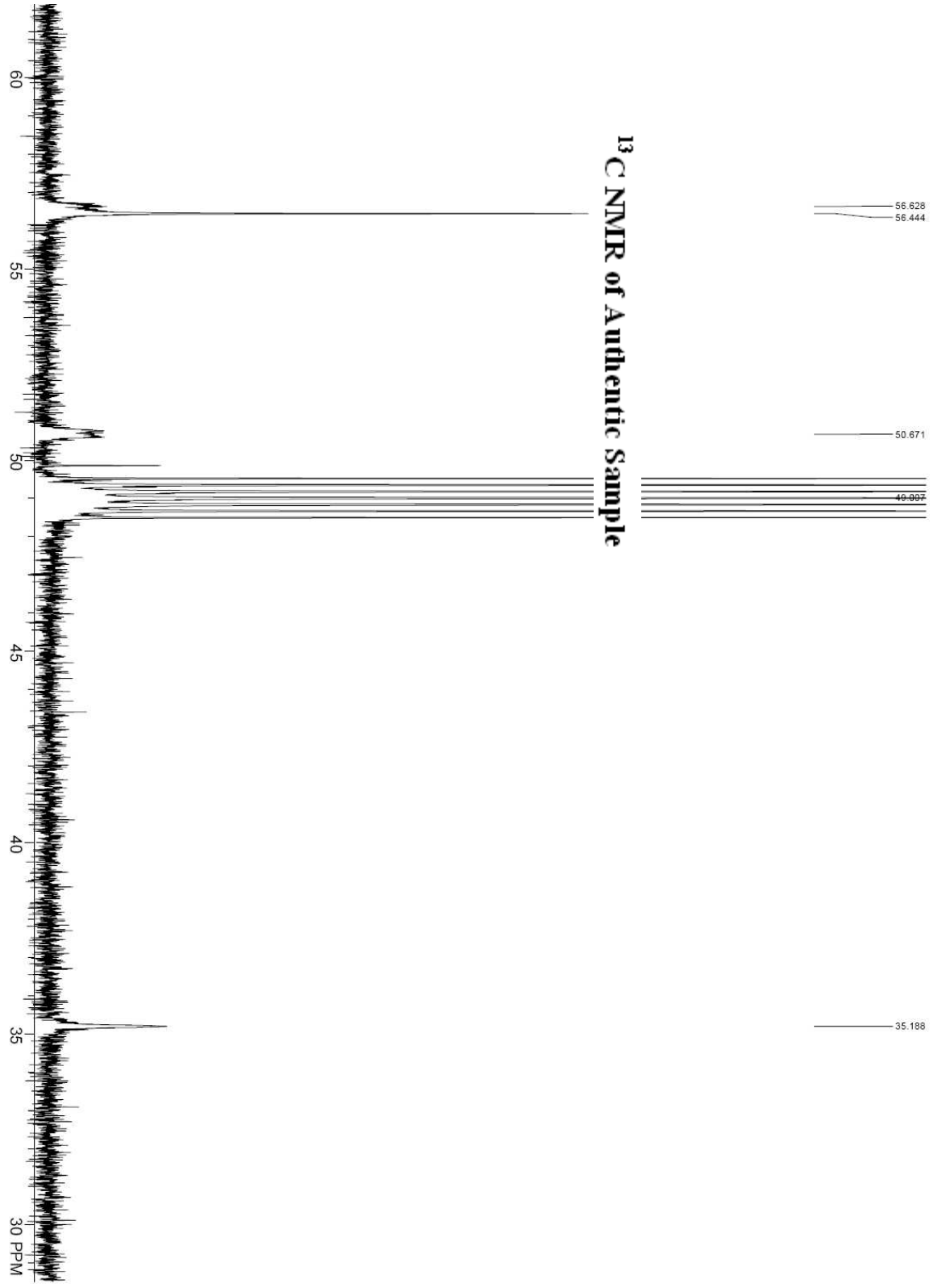
^{13}C NMR of Authentic Sample

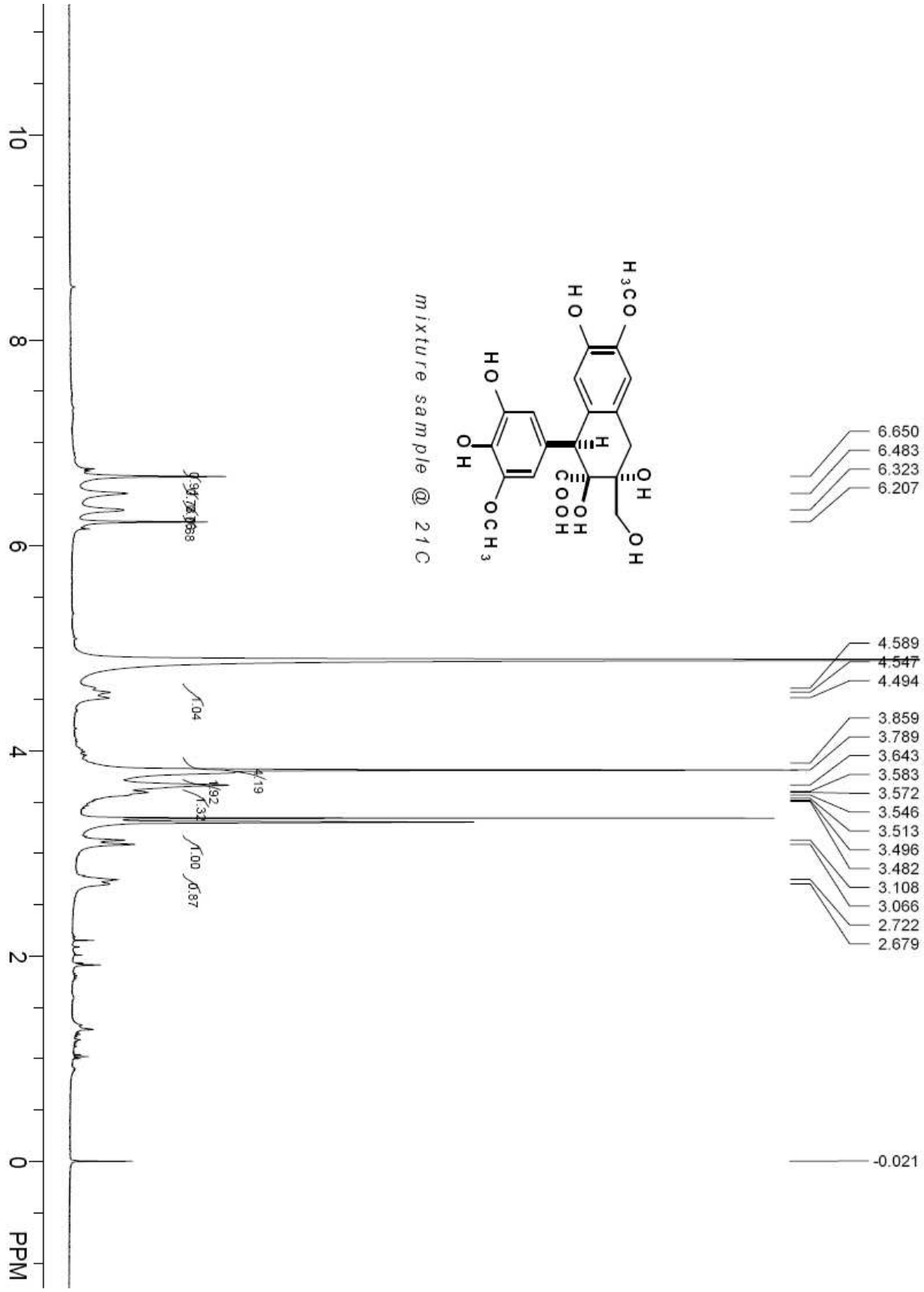


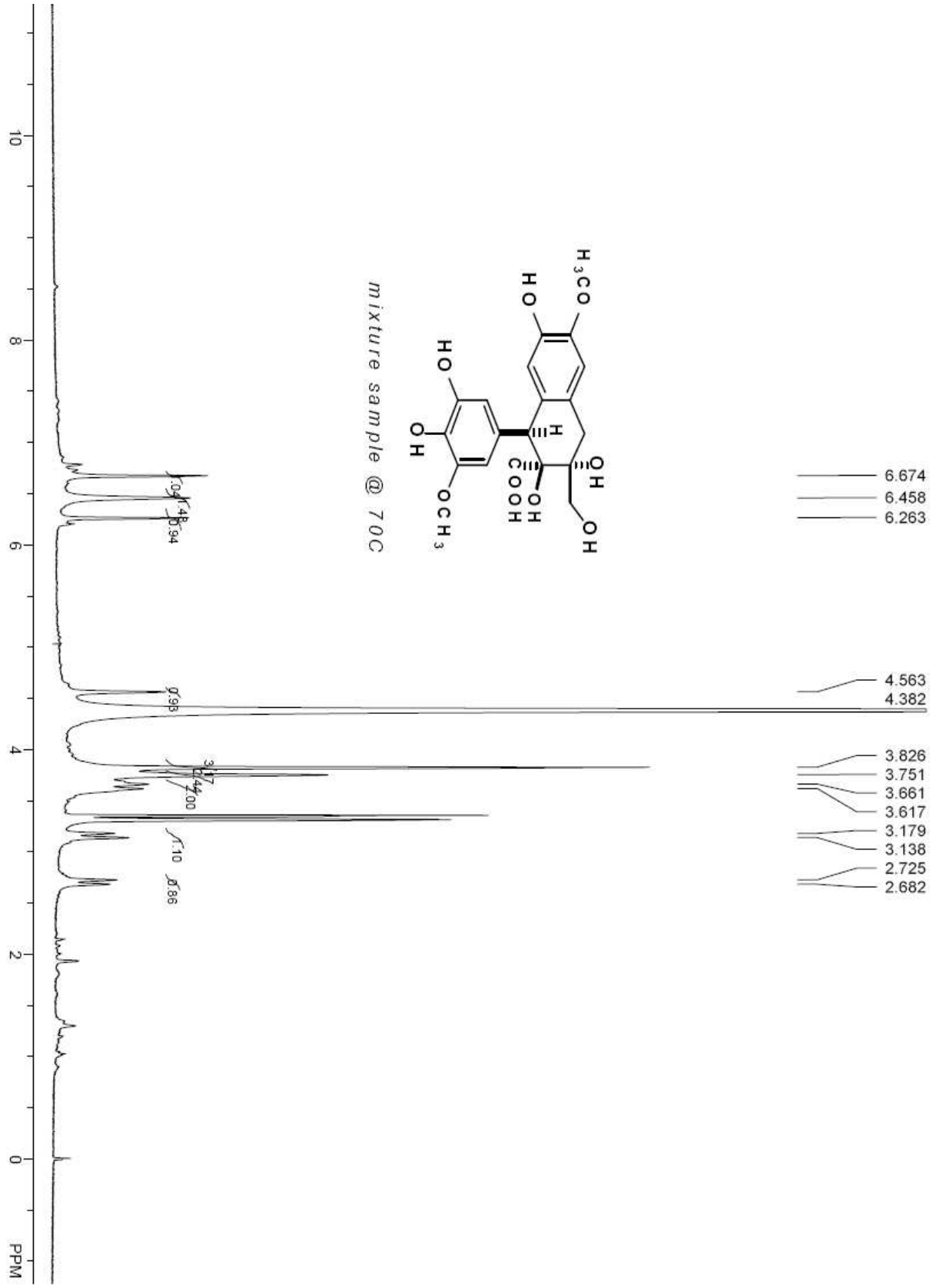
^{13}C NMR of Authentic Sample

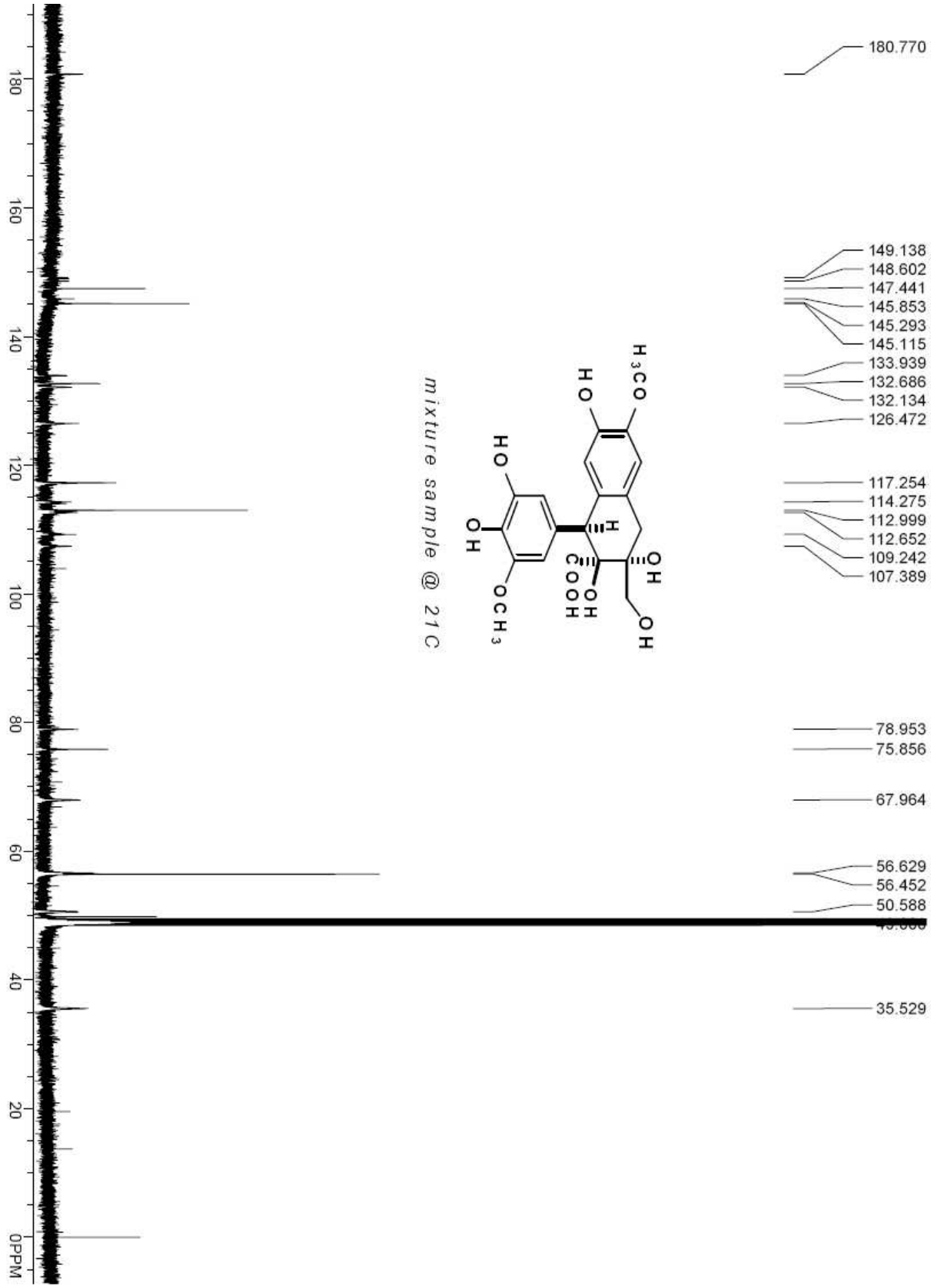


^{13}C NMR of Authentic Sample

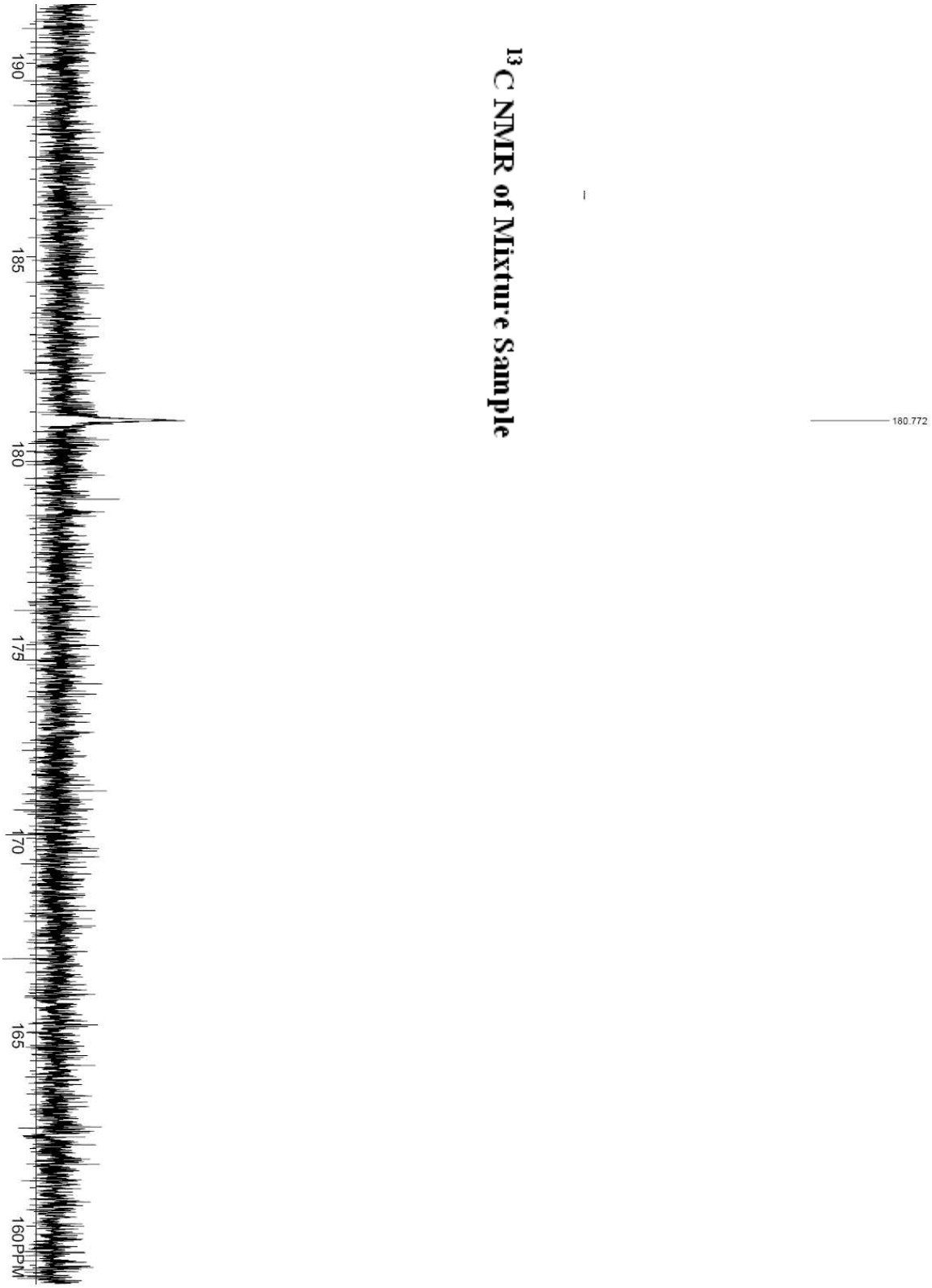



mixture sample @ 21 C
6.650
6.483
6.323
6.207
4.589
4.547
4.494
3.859
3.789
3.643
3.583
3.572
3.546
3.513
3.496
3.482
3.108
3.066
2.722
2.679
-0.021
1.04
4.19
1.92
1.32
1.00
0.87
PPM

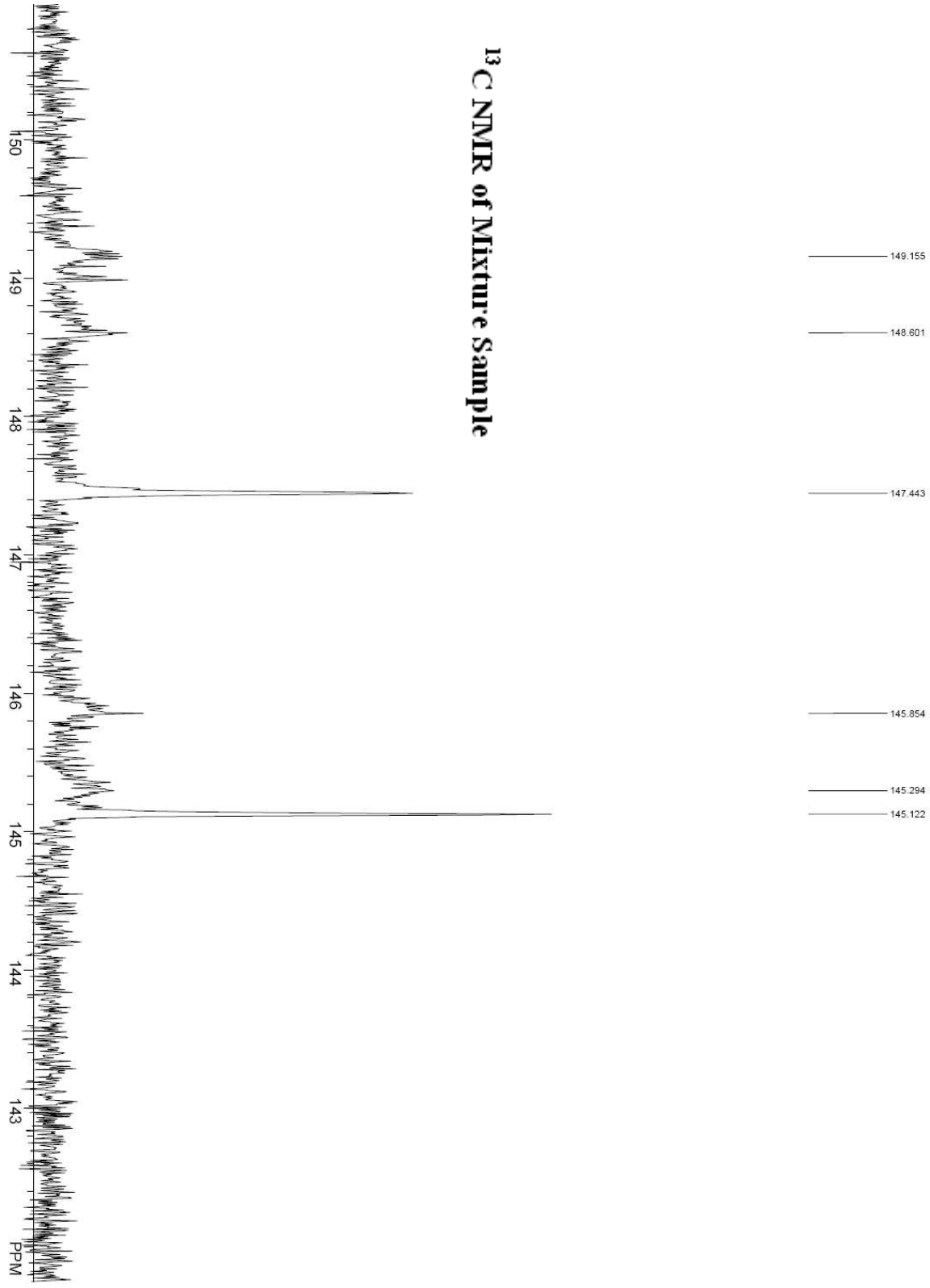

mixture sample @ 70C
6.674
6.458
6.263
4.563
4.382
3.826
3.751
3.661
3.617
3.179
3.138
2.725
2.682
0.93
1.48
0.94
3.17
2.44
4.00
1.10
0.86
PPM


180.770
149.138
148.602
147.441
145.853
145.293
145.115
133.939
132.686
132.134
126.472
117.254
114.275
112.999
112.652
109.242
107.389
78.953
75.856
67.964
56.629
56.452
50.588
35.529
mixture sample @ 21C
180
160
140
120
100
80
60
40
20
0PPM

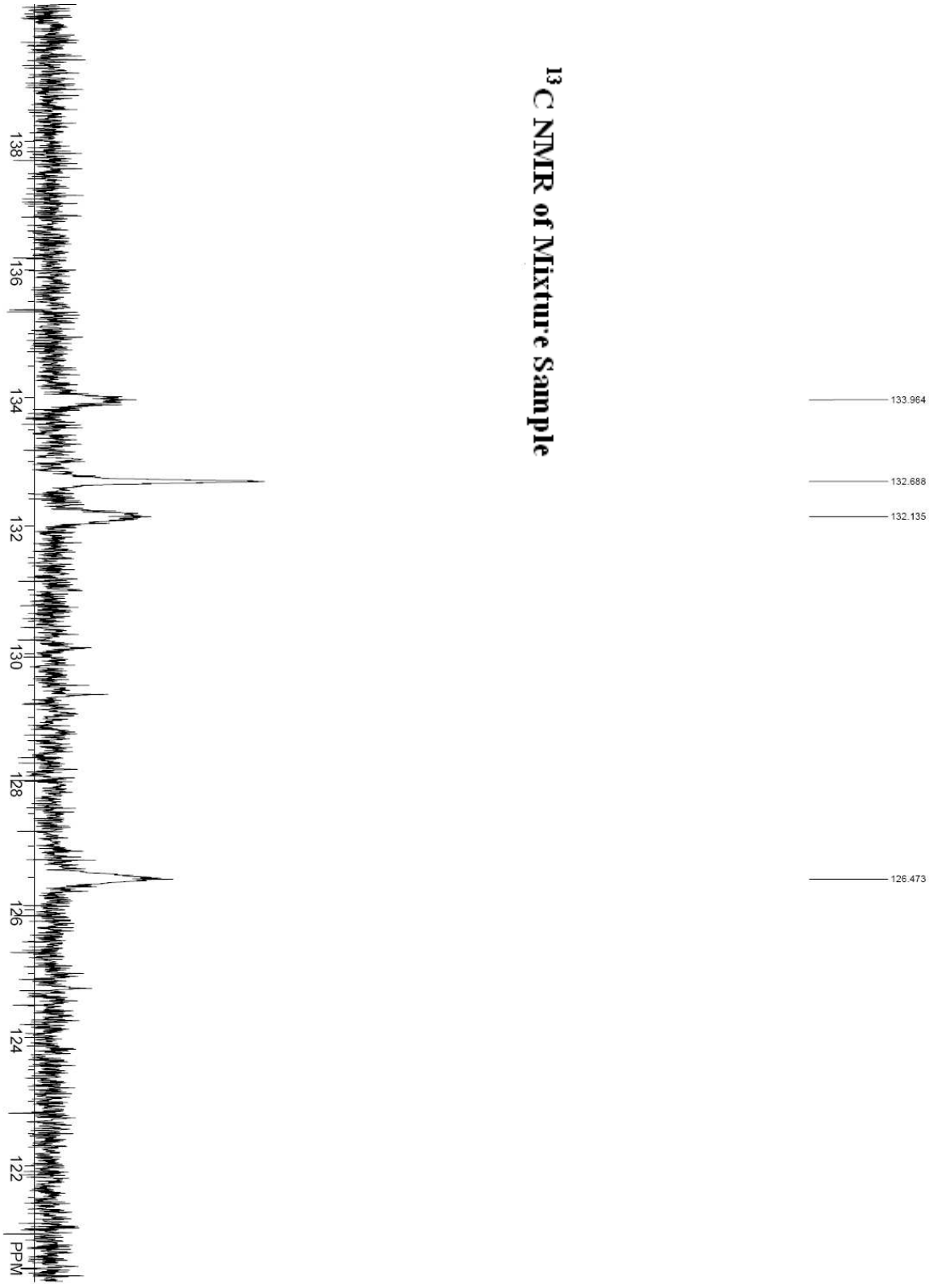
^{13}C NMR of Mixture Sample



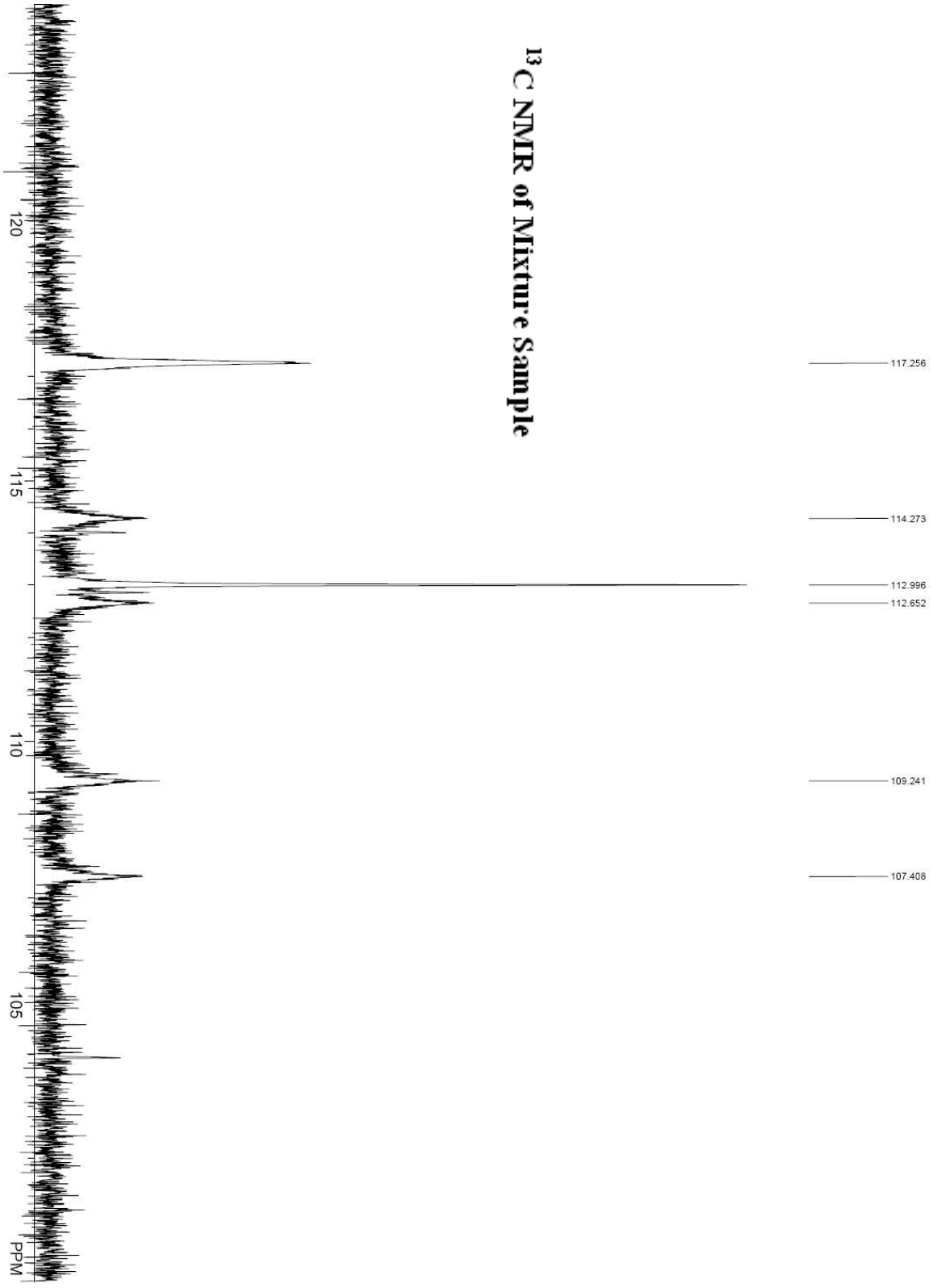
^{13}C NMR of Mixture Sample



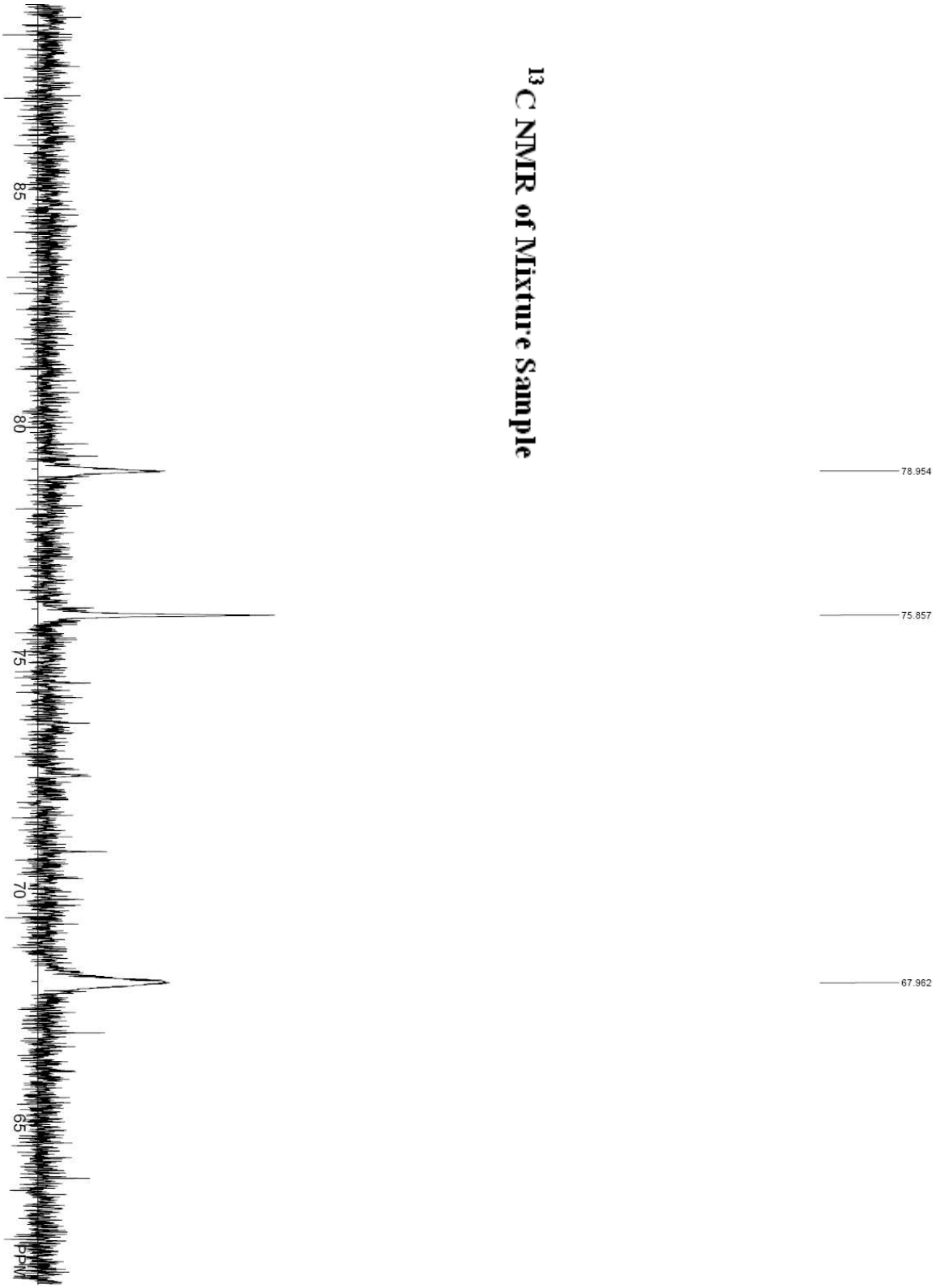
^{13}C NMR of Mixture Sample

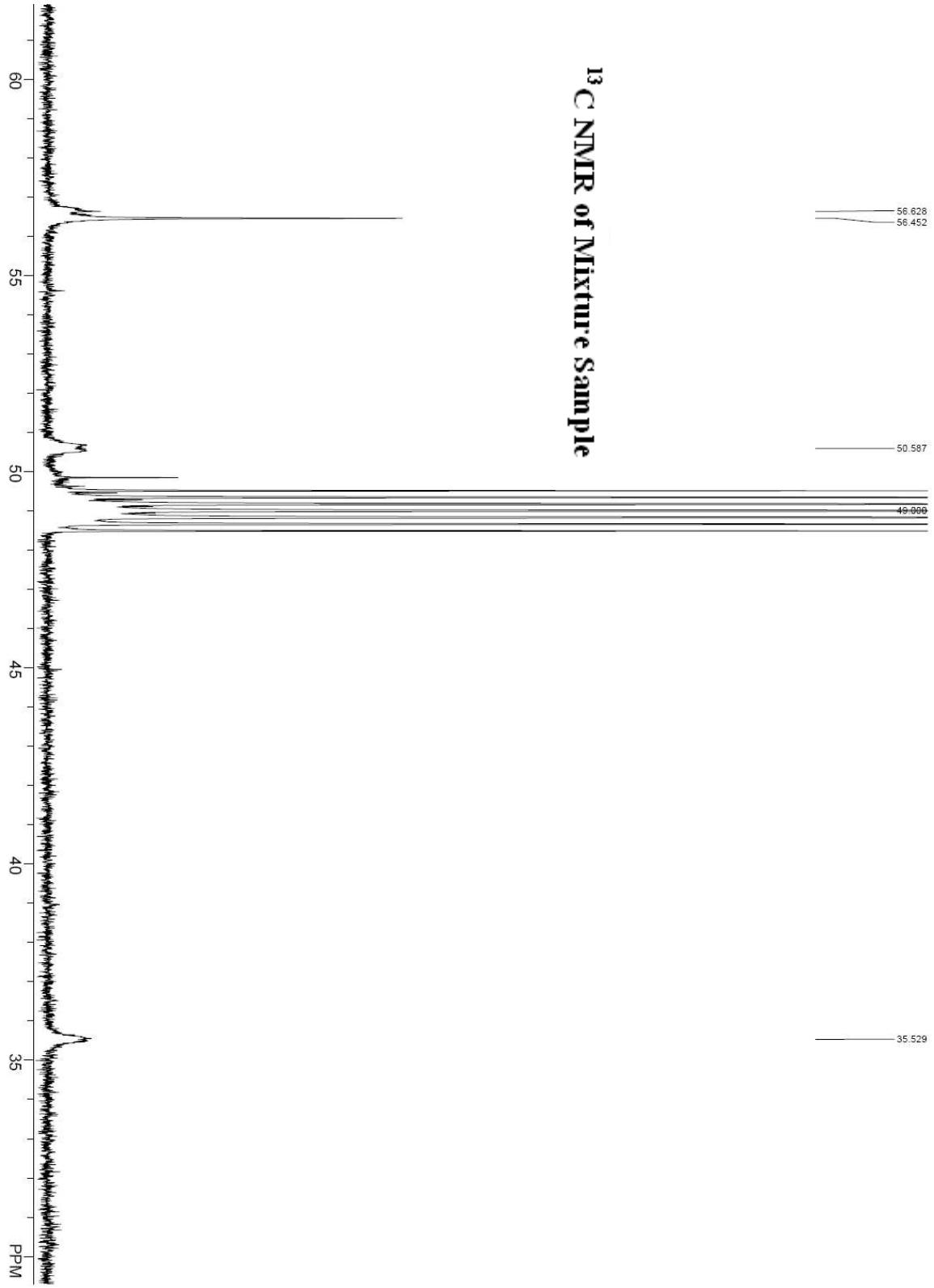


^{13}C NMR of Mixture Sample

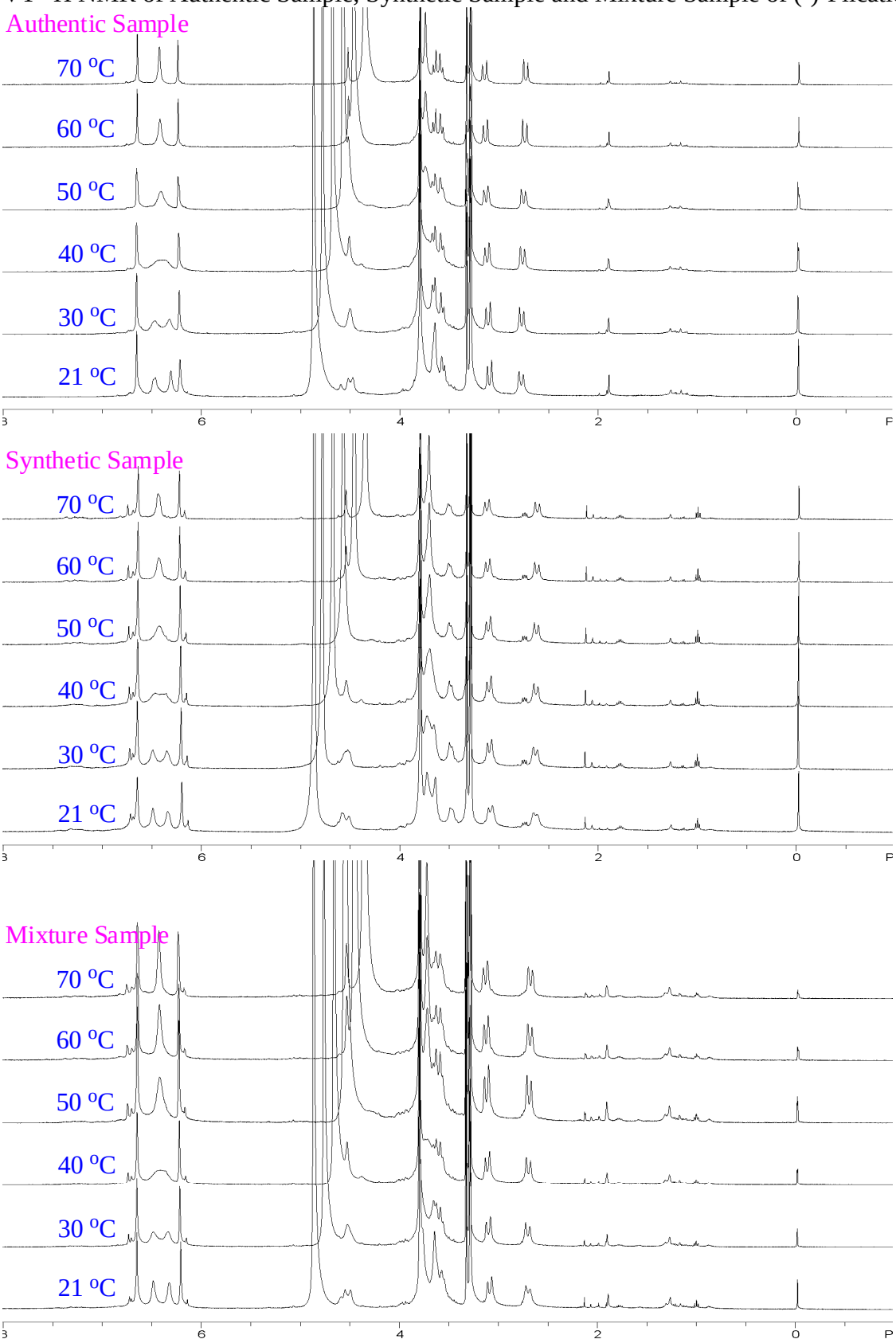


^{13}C NMR of Mixture Sample

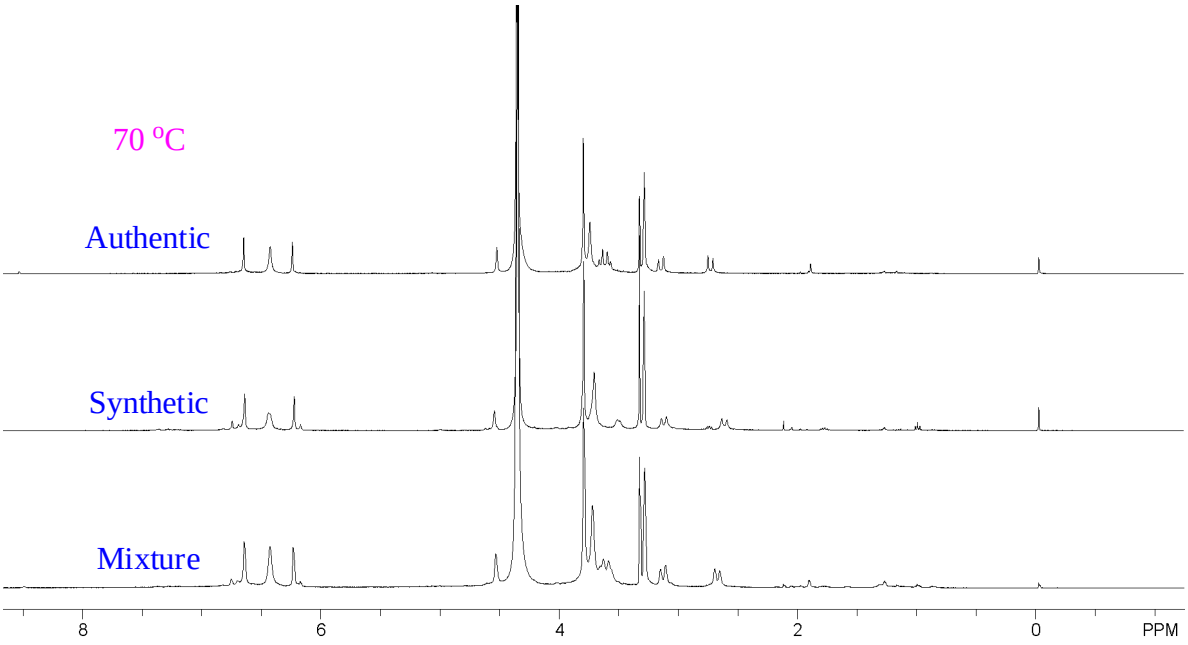



^{13}C NMR of Mixture Sample
56.628
56.452
50.587
49.000
35.529
60
55
50
45
40
35
PPM

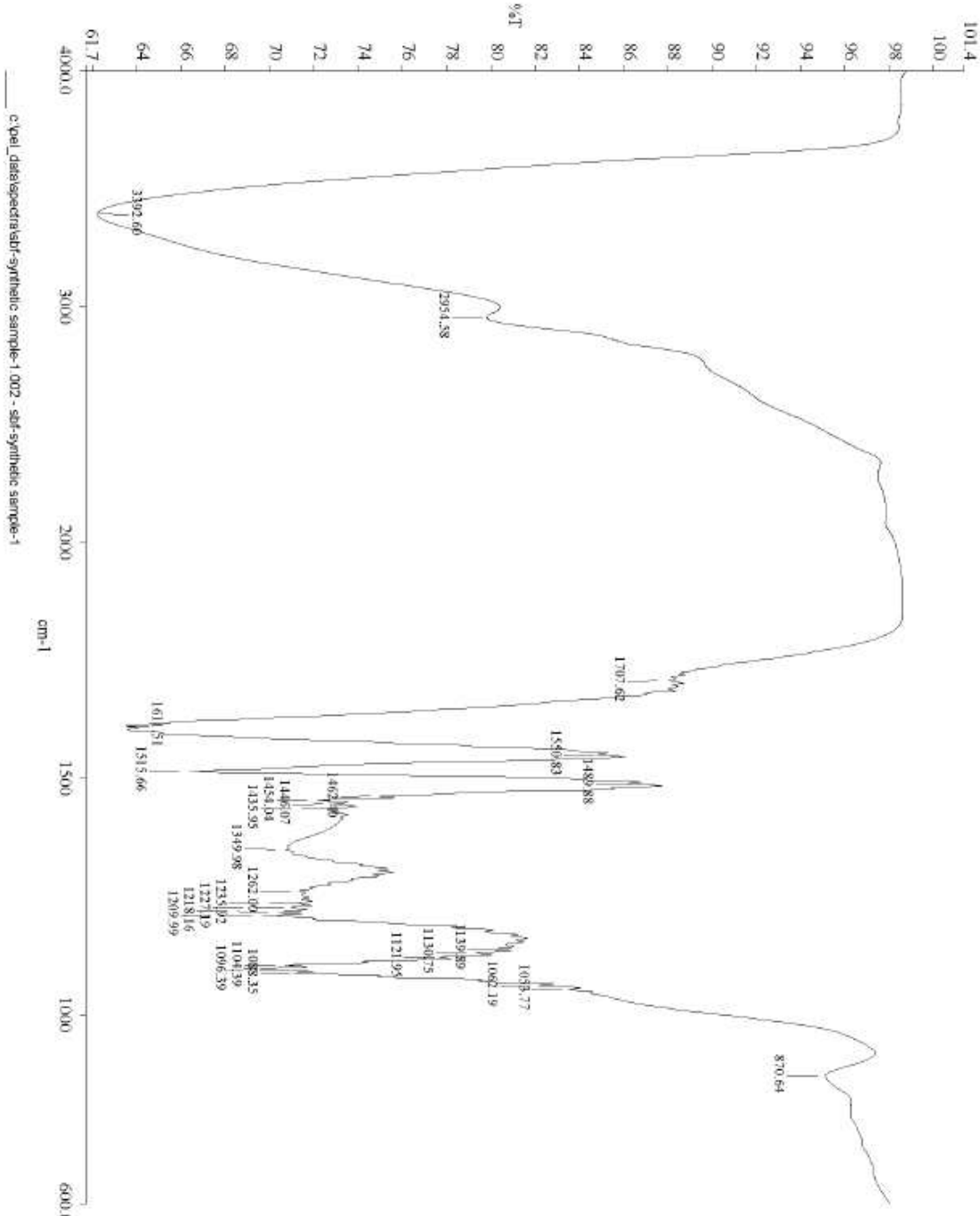
VT-^{1}H NMR of Authentic Sample, Synthetic Sample and Mixture Sample of (-)-Plicatic Acid



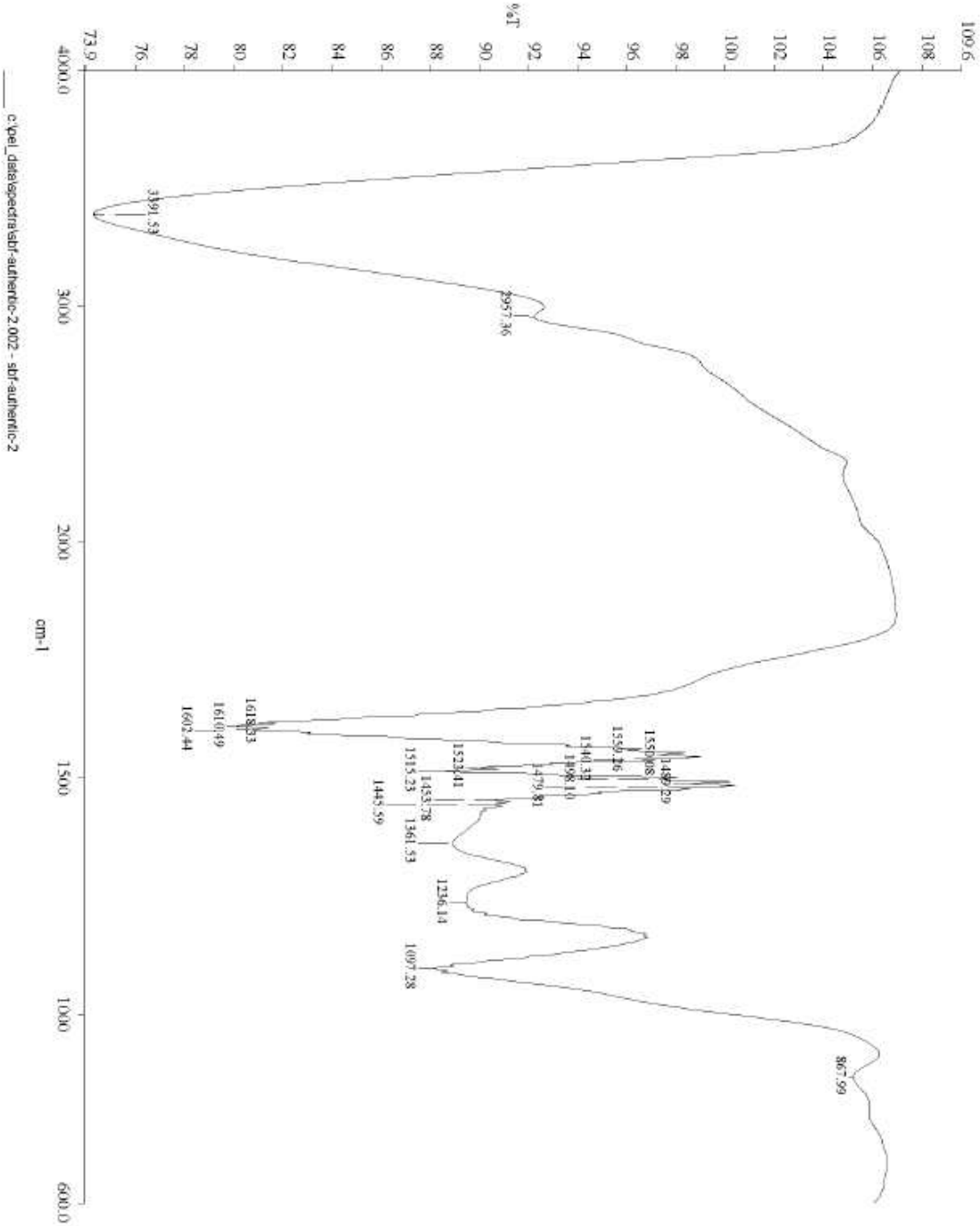
^{1}H NMR Spectra of Authentic Sample, Synthetic Sample and Mixture Sample of (-)-Plicatic Acid (**1**) at 70 ^{o}C



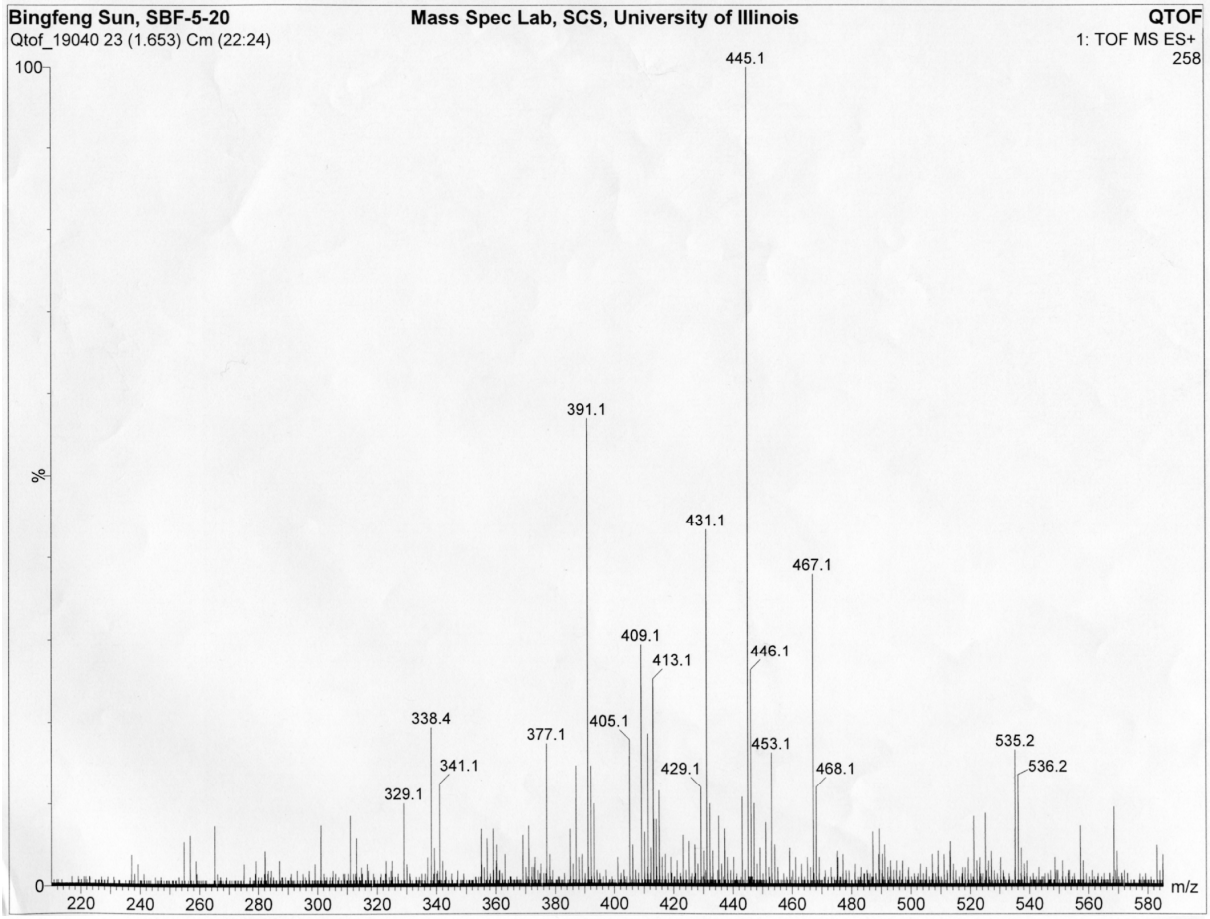
IR of Synthetic Sample of (-)-Plicatic Acid



IR of Authentic Sample of (-)-Plicatic Acid



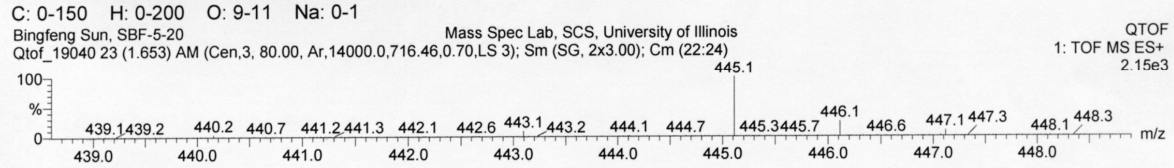
MS and HRMS of Synthetic Sample of (-)-Plicatic Acid



Elemental Composition Report **Page 1**

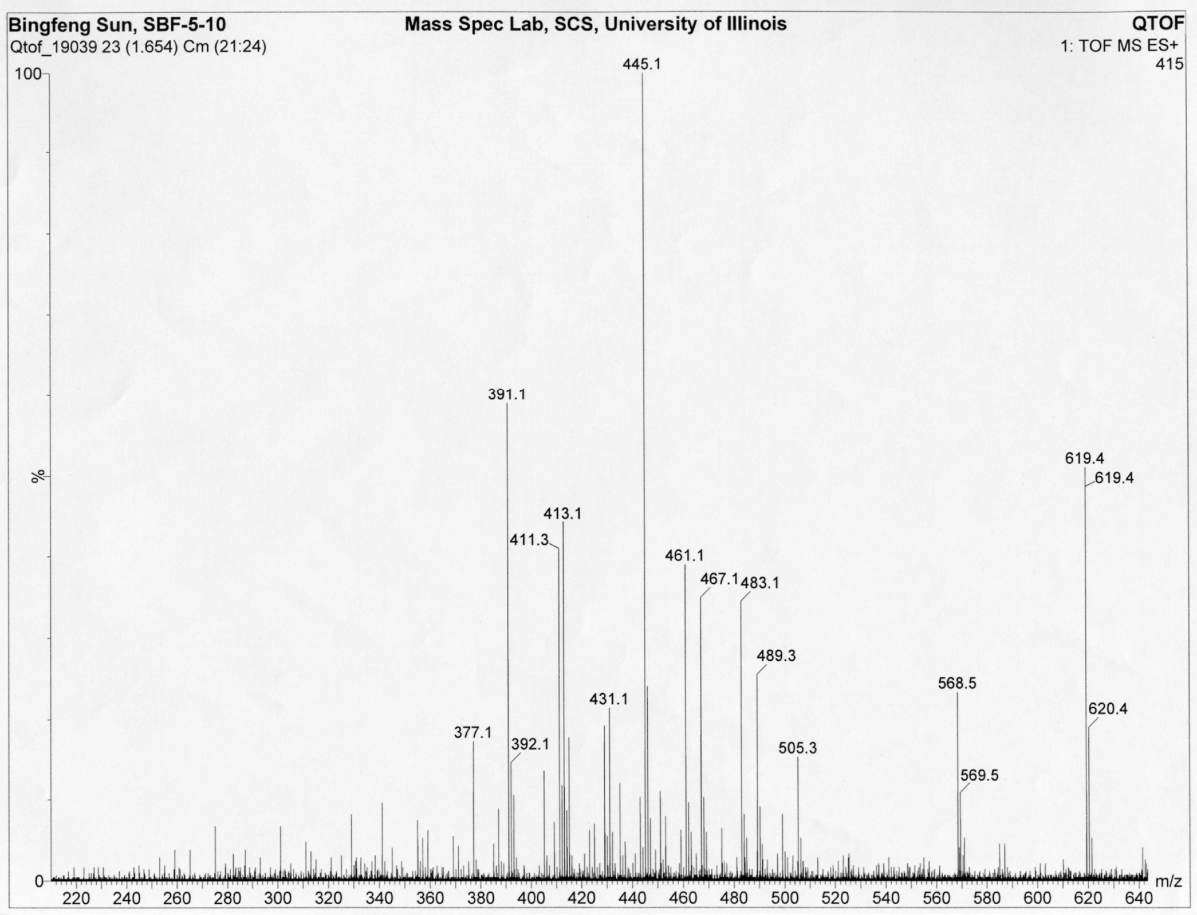
Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 100.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
25 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-150 H: 0-200 O: 9-11 Na: 0-1



Minimum:				-1.5		
Maximum:		5.0	10.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
445.1112	445.1111	0.1	0.2	9.5	28.1	C20 H22 O10 Na
	445.1135	-2.3	-5.2	12.5	22.6	C22 H21 O10

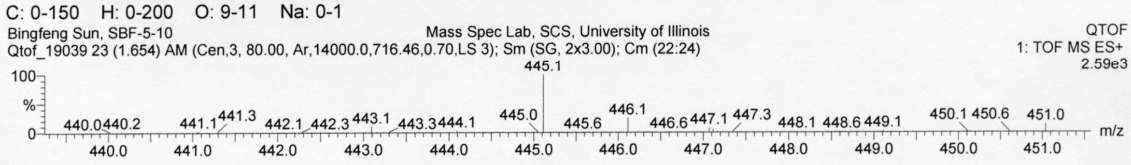
MS and HRMS of Authentic Sample of (-)-Plicatic Acid



Elemental Composition Report Page 1

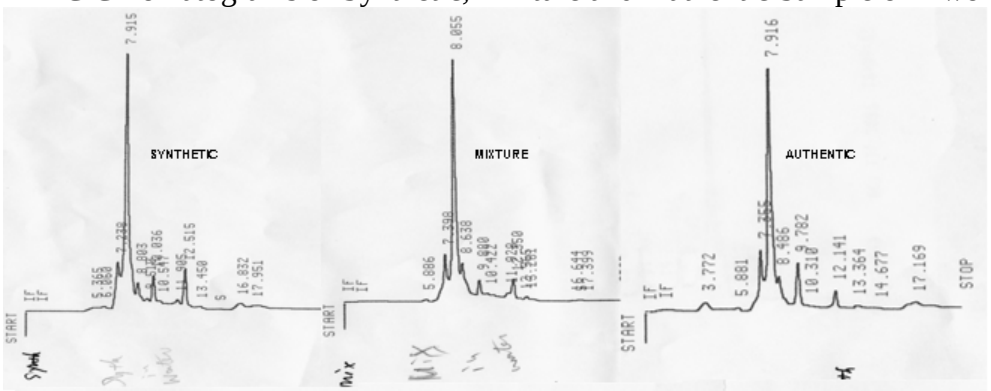
Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 100.0
Selected filters: None

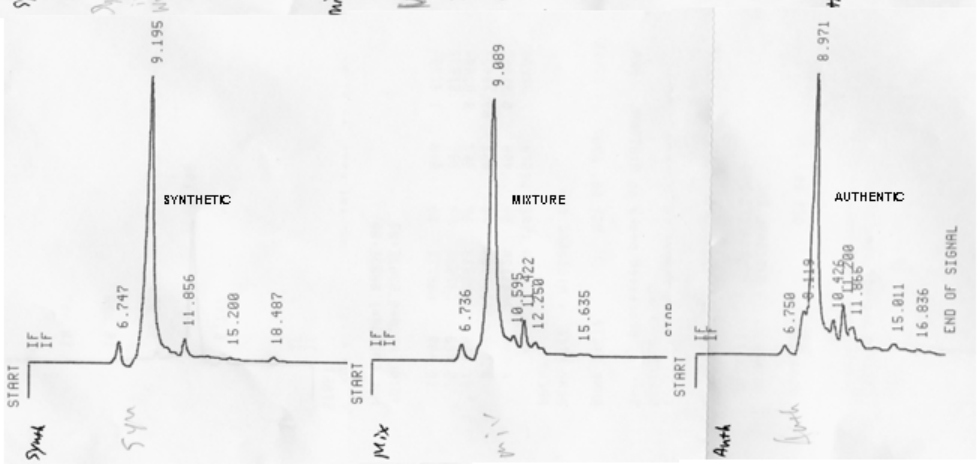
Monoisotopic Mass, Even Electron Ions
25 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-150 H: 0-200 O: 9-11 Na: 0-1



Minimum:				-1.5		
Maximum:		5.0	10.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
445.1111	445.1111	0.0	0.0	9.5	1.2	C20 H22 O10 Na
	445.1135	-2.4	-5.4	12.5	0.7	C22 H21 O10

HPLC Chromatograms of Synthetic, Mixture and Authentic Sample on Two Columns





CD Spectra of Synthetic and Authentic Sample of (-)-Plicatic Acid