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Electronic Supplementary Information

C-H Functionalization Directed by Transformable Nitrogen Heterocycles: A Strategy for the Synthesis of *ortho*-Oxygenated Arylnapthalenes

Shiva K. Rastogi, Derek C. Medellin and Alexander Kornienko*

Department of Chemistry and Biochemistry, Texas State University, San Marcos, TX 78666, USA

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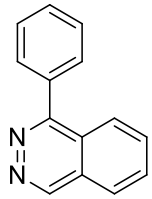
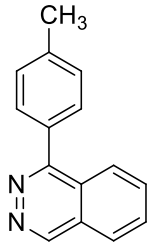
General Synthetic Methods. All reagents, solvents and catalysts were purchased from commercial sources (Acros Organics and Sigma-Aldrich) and used without purification. Dry solvents were obtained using a solvent purification system (Innovative Technology, Inc.). All reactions were performed in oven-dried flasks open to the atmosphere or under nitrogen and monitored by thin layer chromatography (TLC) on TLC precoated (250 μm) silica gel 60 F254 glass-backed plates (EMD Chemicals Inc.). Visualization was accomplished with UV light. Flash column chromatography was performed on silica gel (32-63 μm, 60 Å pore size). ^{1}H and ^{13}C NMR spectra were recorded on Bruker 400 (400.13 MHz for ^{1}H; 100.61 MHz for ^{13}C) spectrometer in $CDCl_3$ solvent. Chemical shifts (δ) are reported in ppm relative to the TMS internal standard. Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and coupling constant (*J*) in Hz. HRMS analyses were performed using Waters Synapt G2 LCMS.

General Procedure for the Synthesis of 3-Arylphthalazines 3a-d. A modified literature procedure was used.[1] Phthalazine (1 g, 7.5 mmol) was dissolved in dry benzene (30 mL) in a three-necked round bottom flask equipped with a condenser. In the synthesis of **3a** and **3b**, the solution was treated with commercially available aryl magnesium bromide (30 mmol). In the synthesis of **3c** and **3d** the Grignard reagents were prepared from magnesium and 4-bromoanisole or 3-bromotoluene, respectively, in THF using general Grignard preparation

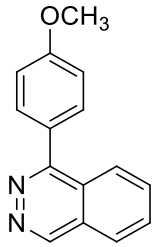
methods. The reaction mixtures were refluxed for 2 h, stirred overnight at rt, and then decomposed with a cold, saturated solution of ammonium chloride (50 mL). The mixtures were extracted with ether (3 x 100 mL), organic layers were combined, washed with water (30 mL), brine (30 mL) and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and resulting oil was purified by chromatography on silica gel.



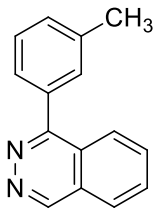
3-Phenylphthalazine (3a): 51%, R_f = 0.26 (20% hexanes / 80% EtOAc). ^{1}H and ^{13}C NMR spectra were identical to those reported in the literature.[1]



3-(*p*-Tolyl)phthalazine (3b): 70%, R_f = 0.25 (50% hexanes / 50% EtOAc). ^{1}H NMR ($CDCl_3$): δ (ppm) 9.49 (s, 1H), 8.09 (d, 1H, *J* = 8.6 Hz), 8.01 (d, 1H, *J* = 8.6 Hz), 7.92-7.83 (m, 2H), 7.64 (d, 2H, *J* = 8.0 Hz), 7.73 (d, 2H, *J* = 8.0 Hz), 2.45 (s, 3H); ^{13}C NMR δ 160.1, 150.4, 139.7, 133.0, 132.8, 132.4, 130.0, 129.4, 127.3, 126.8, 126.4, 125.7, 21.4; HRMS *m/z* (ESI) calcd for $C_{15}H_{13}N_2$ $(M+H)^+$ 221.1079, found 221.1079.

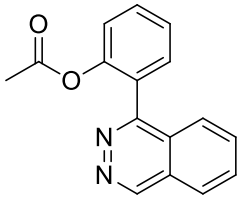


3-(4-Methoxyphenyl)phthalazine (3c): 30%, R_f = 0.32 (30% hexanes / 70% EtOAc). ^{1}H NMR ($CDCl_3$): δ (ppm) 9.49 (s, 1H), 8.14 (d, 1H, *J* = 8.6 Hz), 8.00 (d, 1H, *J* = 8.4 Hz), 7.90-7.80 (m, 2H), 7.75 (d, 2H, *J* = 8.8 Hz), 7.11 (d, 2H, *J* = 8.8 Hz), 3.9 (s, 3H); ^{13}C NMR δ (ppm) 160.8, 159.6, 150.3, 132.5, 132.1, 131.6, 128.7, 127.3, 126.7, 126.4, 125.6, 114.2, 55.5; HRMS m/z (ESI) calc for $C_{15}H_{12}N_2O$ $(M+H)^+$ 237.1028, found 237.1028.

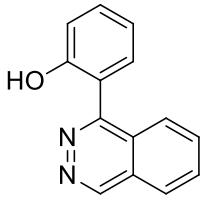


3-(*m*-Tolyl)phthalazine (3d): 60%, R_f = 0.30 (40% hexanes / 60% EtOAc). ^{1}H NMR ($CDCl_3$): δ (ppm) 9.51 (s, 1H), 8.09 (dd, 1H, *J* = 1.6, 8.6 Hz), 8.01 (dd, 1H, *J* = 1.8, 8.6 Hz), 7.9-7.8 (m, 2H), 7.58 (s, 1H), 7.53 (d, 1H, *J* = 7.5 Hz), 7.44 (t, 1H, *J* = 7.5 Hz), 7.36 (d, 1H, *J* = 8.2 Hz), 2.46 (s, 3H); ^{13}C NMR δ (ppm) 160.3, 150.7, 138.7, 136.3, 132.8, 132.4, 130.9, 130.4, 128.6, 127.4, 127.3, 126.9, 126.6, 125.8, 21.7; HRMS m/z (ESI) calcd. for $C_{15}H_{14}N_2$ $(M+H)^+$ 221.1079, found 221.1094.

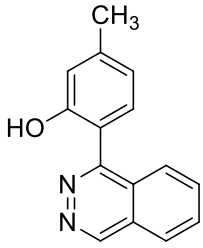
General procedure for the *ortho*-oxygenation Method A to obtain acetoxy compounds 4 or hydroxyl compounds 5. 3-Aryl phthalazine (1 mmol) was dissolved in acetic acid (5 mL) in a 25 mL vial. To this solution were added $PhI(OAc)_2$ (483 mg, 1.5 mmol) and $Pd(OAc)_2$ (11.2 mg, 0.05 mmol). The vial was sealed with a Teflon lined cap, and the reaction mixture was heated at 140 °C for 8 h. After this period of time, another portion of each $PhI(OAc)_2$ (483 mg, 1.5 mmol) and $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) were added and the reaction mixture was heated at 140 °C for additional 24 h. The solvent was removed under vacuum, and the resulting oil was purified by chromatography on silica gel to obtain acetoxy compounds **4** or sub*J*ected to hydrolysis without purification to obtain hydroxyl compounds **5**. In the latter case the crude material was dissolved into THF/MeOH (1:1, 25 mL) and filtered through a pad of Celite. Solid NaOH was added to the solution portion-wise until the pH turned 9-10. The solution was stirred at rt for 3 h and monitored by TLC. After the disappearance of the acetate, the solvent was removed under vacuum and the residue was dissolved in EtOAc (50 mL). The organic layer was washed with water (2 x 10 mL), brine (10 mL), dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel.



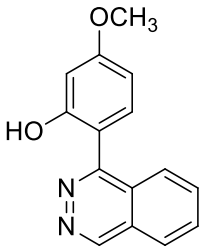
2-(Phthalazin-3-yl)phenyl acetate (4a): 70%, R_f = 0.29 (20% hexanes / 80% EtOAc). ^{1}H NMR ($CDCl_3$): δ (ppm) 9.55 (s, 1H), 8.01 (d, 1H, *J* = 8.0 Hz), 7.92 (dt, 1H, *J* = 6.8 Hz), 7.85 (dt, 1H, *J* = 8.2 Hz), 7.81-7.78 (m, 1H), 7.59 (dt, 2H, *J* = 7.4 Hz), 7.44 (dt, 2H, *J* = 7.5 Hz), 7.36 (dd, 1H, *J* = 8.5 Hz), 1.8 (s, 3H); ^{13}C NMR δ (ppm) 168.9, 150.98, 148.9, 132.7, 132.5, 131.7, 130.7, 129.1, 126.8, 126.6, 126.2, 126.1, 126.0, 123.3, 20.7; HRMS m/z (ESI) calcd for $C_{16}H_{13}N_2O_2$ $(M+H)^+$ 265.0977, found 265.0976.



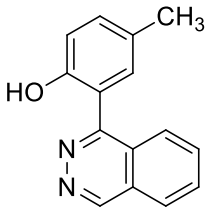
2-(Phthalazin-3-yl)phenol (5a): 60%, R_f = 0.33 (20% hexanes / 80% EtOAc). ^{1}H NMR ($CDCl_3$); δ (ppm) 9.45 (s, 1H), 8.45 (d, 1H, *J* = 8.0 Hz), 8.07 (dd, 1H, *J* = 2.4, 8.2 Hz), 8.0-7.95 (m, 2H), 7.74 (dd, 1H, *J* = 1.6, 7.8 Hz), 7.45 (dt, 2H, *J* = 1.6, 8.2 Hz), 7.24 (dd, 1H, *J* = 1.2, 8.2 Hz), 7.36 (dd, 1H, *J* = 1.2, 7.8 Hz); ^{13}C NMR δ (ppm) 159.0, 157.7, 150.4, 133.0, 132.8, 132, 131.5, 128.3, 127.2, 126.7, 125.3, 119.3, 118.8, 118.7; HRMS m/z (ESI) calcd. for $C_{14}H_{11}N_2O$ $(M+H)^+$ 223.0871, found 223.0872.



5-Methyl-2-(phthalazin-3-yl)phenol (5b): 51%, R_f = 0.35 (20% hexanes / 80% EtOAc). ^{1}H NMR ($CDCl_3$): δ (ppm) 9.40 (s, 1H), 8.44 (d, 1H, *J* = 8.6 Hz), 8.04 (d, 1H, *J* = 1.2, 8.6 Hz), 7.98-7.91 (m, 2H), 7.63-7.61 (d, *1H, J* = 7.9 Hz), 7.05 (s, 1H), 6.88 (dd, 1H, *J* = 1.7, 8.6 Hz), 2.42 (s, 3H); ^{13}C NMR δ (ppm) 157.9, 142.8, 132.9, 132.7, 131.3, 129.3, 127.1, 126.8, 125.2, 120.3, 119.0, 21.7; HRMS m/z (ESI) calc for $C_{16}H_{13}N_2O_2$ $(M+H)^+$ 265.0977, found 265.0976.



5-Methoxy-2-(phthalazin-3-yl)phenol (5c): 55%, R_f = 0.40 (50% hexanes / 50% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 9.36 (s, 1H), 8.44 (d, 1H, *J* = 8.6 Hz), 8.04-8.0 (m, 1H), 7.96-7.93 (m, 2H), 7.69 (d, 1H, *J* = 8.7 Hz), 6.7 (d, 1H, *J* = 2.6 Hz), 6.64 (dd, 1H, *J* = 2.6, 8.7 Hz), 3.89 (s, 3H) ^{13}C NMR δ (ppm) 162.6, 158.8, 149.5, 132.6, 132.5, 132.3, 128.0, 127.0, 126.6, 124.9, 111.5, 106.7, 102.5, 55.4; HRMS m/z (ESI) calc for $C_{15}H_{13}N_2O_2$ $(M+H)^+$ 253.0899, found 253.0975.

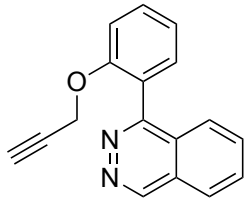


4-Methyl-2-(phthalazin-3-yl)phenol (5d): 63%, R_f = 0.30 (40% hexanes / 60% EtOAc). ^{1}H NMR ($CDCl_3$): δ (ppm) 9.43 (s, 1H), 8.43-8.4 (m, 1H), 8.05-8.02 (m, 1H), 7.99-7.95 (m, 2H), 7.51 (d, 1H, *J* = 1.8 Hz), 7.23 (d, 1H, *J* = 1.8 Hz), 7.14 (d, 1H, *J* = 8.4 Hz), 2.39 (s, 3H); ^{13}C NMR δ 158.9, 155.1, 150.1, 132.8, 132.6, 132.5, 131.4, 128.2, 128.0, 126.9, 126.6, 125.1, 118.5, 118.2, 20.6; HRMS m/z (ESI) calc for $C_{15}H_{13}N_2O$ $(M+H)^+$ 237.1028, found 237.1045.

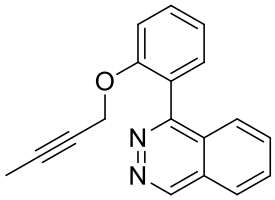
Procedure for the *ortho*-oxygenation Method B to obtain hydroxyl compounds 5 directly. 3-Arylphthalazine (0.48 mmol) was dissolved in the mixture of trifluoroacetic acid and trifluoroacetic anhydride (9:1, 2 mL) in a 15 mL vial. $K_2S_2O_8$ (144.2 mg, 0.53 mmol), $Pd(OAc)_2$ (5.5 mg, 0.024 mmol) were added to above solution. The vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 100 °C for 36 hr. After this time, the reaction mixture was allowed to cool to room temperature and diluted with CH_2Cl_2. The organic layer was washed with sat. $NaHCO_3$ (10 mL) and filtered through a pad of Celite. The filtrate was washed with brine (10 mL) and dried with Na_2SO_4. The solvent was removed under vacuum and the resulting oil was purified by chromatography on silica gel (20% hexanes / 80% EtOAc) to afford pure **5a** (60%), **5c** (65%) or **5d** (66%).

General procedure for the synthesis of propargylated compounds 6. A selected phthalazine phenol **5a-5d** (0.15 mmol) and NaH (5.4 mg, 0.225 mmol) were dissolved in dry

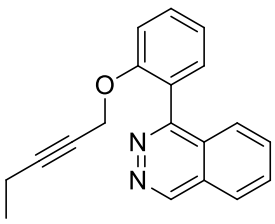
DMF (5 mL). The required propargyl bromide (0.18 mmol) was added to the solution and the reaction mixture was stirred at rt overnight. The solvent was removed under vacuum and heating (50 ^{o}C), residue was dissolved in EtOAc and washed with water (2 x 3 mL). The organic layer was washed with brine (3 mL), dried over Na_2SO_4 and concentrated under vacuum. The resulting oil was purified by chromatography on silica gel.



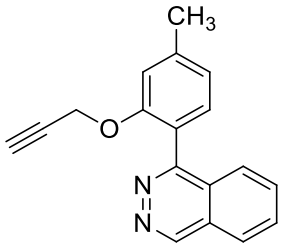
3-(2-(Prop-2-yn-1-yloxy)phenyl)phthalazine (6aa): 70%, R_f = 0.31 (20% hexanes / 80% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 9.54 (s, 1H), 8.2 (s, 1H), 8.0 (dt, 1H, *J* = 7.2 Hz), 7.88 (dt, 1H, *J* = 8.2 Hz), 7.81 (dt, 1H, *J* = 8.2 Hz), 7.76 (dt, 1H, *J* = 7.2 Hz), 7.54 (dt, 1H, *J* = 8.4 Hz), 7.23 (dt, 1H, *J* = 6.4 Hz), 7.45 (dd, 2H, *J* = 2.3, 7.4 Hz), 2.43 (t, 2H, *J* = 2.4 Hz); ^{13}C NMR δ (ppm) 158.6, 155.3, 151.0, 132.2, 131.9, 130.8, 127.1, 126.6, 126.5, 126.3, 126.3, 122.2, 113.1, 78.3, 75.7, 56.1; HRMS m/z (ESI) calc for $C_{17}H_{13}N_2O$ $(M+H)^+$ 261.1028, found 261.1026.



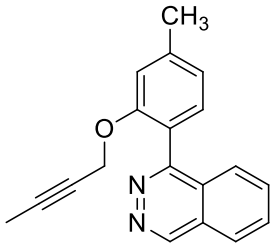
3-(2-(But-2-yn-1-yloxy)phenyl)phthalazine (6ab): 70%, R_f = 0.31 (20% hexanes / 80% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 9.53 (s, 1H), 7.99 (dt, 1H, *J* = 1.2, 7.9 Hz), 7.87 (td, 1H, *J* = 1.5, 9.6 Hz), 7.80 (dt, 1H, *J* = 1.3, 8.2, Hz), 7.77-7.74 (m, 1H), 7.52 (d, 2H, *J* = 8.2 Hz), 7.24-7.17 (m, 2H), 4.53 (t, 2H, *J* = 2.4 Hz), 1.78 (t, 3H, *J* = 2.3 Hz); ^{13}C NMR δ (ppm) 158.7, 155.6, 150.9, 132.1, 132.1, 131.8, 130.8, 127.2, 126.6, 126.4, 126.3, 126.2, 121.8, 113.2, 83.8, 73.9, 56.8; HRMS m/z (ESI) calcd. for $C_{18}H_{15}N_2O$ $(M+H)^+$ 275.1184, found 275.1185.



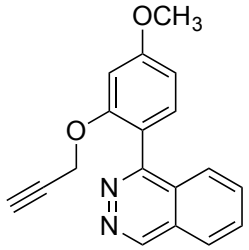
3-(2-(Pent-2-yn-1-yloxy)phenyl)phthalazine (6ac): 73%, R_f = 0.33 (20% hexanes / 80% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.55-8.50 (m, 1H), 8.02-8.00 (dd, 1H, *J* = 2.0, 7.8 Hz), 7.84-7.82 (m, 1H), 7.62 (s, 1H), 7.48-7.46 (q, 1H, *J* = 6.3 Hz), 7.30 (dt, 1H, *J* = 1.6, 8.8 Hz), 7.18-7.16 (m, 2H), 5.18 (s, 2H), 2.82-2.80 (q, 2H, *J* = 7.5 Hz), 1.32 (t, 1H, *J* = 7.5 Hz); ^{13}C NMR δ (ppm) 156.6, 136.9, 134.43, 132.6, 128.7, 128.4, 127.9, 127.3, 126.7, 126.0, 125.8, 125.3, 124.6, 121.8, 117.4, 66.8, 25.9, 14.9; HRMS m/z (ESI) calcd. for $C_{19}H_{17}O$ $(M+H)^+$ 261.1279, found 261.1279.



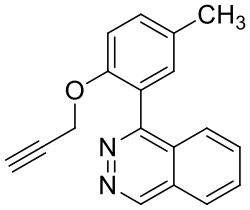
3-(4-Methyl-2-(prop-2-yn-1-yloxy)phenyl)phthalazine (6ba): 65%, R_f = 0.3 (20% hexanes / 80% EtOAc). ^{1}H NMR ($CDCl_3$): δ (ppm) 9.52 (s, 1H), 7.99 (dt, 1H, *J* = 8.6 Hz), 7.87 (td, 1H, *J* = 1.2, 8.2 Hz), 7.82-7.76 (m, 2H), 7.42 (d, 1H, *J* = 7.7 Hz), 7.42 (s, 1H), 7.04 (s, 1H), 7.02 (s, 1H), 4.57 (dd, 2H, *J* = 2.1, 8.2 Hz), 2.49 (s, 3H), 2.42 (s, 1H, *J* = 2.4 Hz); ^{13}C NMR δ (ppm) 155.2, 150.9, 141.3, 132.2, 132.1, 131.7, 127.2, 126.6, 126.3, 123.4, 122.9, 113.8, 78.5, 75.6, 56.1; HRMS m/z (ESI) calcd. for $C_{18}H_{15}N_2O$ $(M+H)^+$ 275.1184, found 275.1183.



3-(2-(But-2-yn-1-yloxy)-4-methylphenyl)phthalazine (6bb): 72%, R_f = 0.31 (20% hexanes / 80% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 9.51 (s, 1H), 7.98 (dt, 1H, *J* = 8.4 Hz), 7.88-7.84 (m, 1H), 7.79 (dd, *2H, J* = 4.6 Hz), 7.41 (d, 1H, *J* = 7.5 Hz), 7.02 (s, 1H), 7.01 (dd, 1H, *J* = 7.5 Hz), 4.51 (q, 2H), 2.48 (s, 3H), 1.79 (t, 3H, *J* = 2.3 Hz); ^{13}C NMR δ (ppm) 155.5, 150.6, 141.2, 132.0, 132.0, 131.6, 127.4, 126.6, 126.3, 123.4, 122.6, 114.0, 83.7, 74.1, 56.1, 22.0, 3.7; HRMS m/z (ESI) calcd. for $C_{19}H_{17}N_2O$ $(M+H)^+$ 289.1341, found 289.1341.

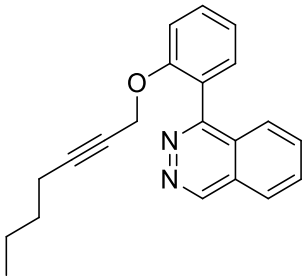


3-(4-Methoxy-2-(prop-2-yn-1-yloxy)phenyl)phthalazine (6ca): 64%, R_f = 0.32 (20% hexanes / 80% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 9.51 (s, 1H), 7.98 (dt, 1H, *J* = 1.1, 8.4 Hz), 7.88-7.84 (m, 1H), 7.79-7.78 (m, 2H), 7.48 (d, 1H, *J* = 8.4 Hz), 6.8 (d, 1H, *J* = 2.28 Hz), 6.75 (dd, 1H, *J* = 2.3, 8.4 Hz), 4.55 (q, 2H), 3.91 (s, 3H), 2.44 (t, 3H, *J* = 2.4 Hz); ^{13}C NMR δ (ppm) 162.0, 156.3, 150.8, 132.7, 132.1, 132.1, 127.2, 126.7, 126.6, 126.3, 78.2, 75.9, 56.1, 55.7; HRMS m/z (ESI) calcd. for $C_{18}H_{17}N_2O_2$ $(M+H)^+$ 291.1134, found 291.1137.

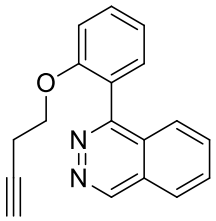


3-(5-methyl-2-(prop-2-yn-1-yloxy)phenyl)phthalazine (6da): 68%, R_f = 0.29 (40% hexanes / 60% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 9.52 (s, 1H), 7.99 (dt, 1H; *J* = 1.24, 7.8 Hz), 7.87 (dt, 1H, *J* = 1.7, 7.8 Hz), 7.80-7.75 (m, 2H), 7.35-7.31 (m, 2H), 7.13 (d, 1H, *J* = 8.2 Hz), 4.54-4.52 (q, 2H, *J* = 2.3, 7.5 Hz), 2.4 (s, 1H, *J* = 2.4 Hz), 2.3 (s, 3H); ^{13}C NMR δ 158.7, 153.1, 150.9, 132.4, 132.2, 132.1, 131.7, 131.2, 127.2, 126.5, 126.4, 126.3, 126.0, 113.2, 78.5, 75.6, 56.3, 20.6, HRMS m/z (ESI) calcd. for $C_{18}H_{16}N_2O$ $(M+H)^+$ 275.1184, found 275.1201.

General procedure for the synthesis of compounds 6ad and 6ae using the Mitsunobu reaction: To the solution of phthalazine phenol **5a** (0.14 mmol) and triphenylphosphine (110 mg, 0.42 mmol) dry THF was added a required alkynol (0.42 mmol) and the reaction mixture was cooled in an ice bath. Diisopropylazodicarboxylate (0.42 mmol) was added dropwise and the reaction mixture was stirred at rt for 24 h. The mixture was diluted into with ether (25 mL) and washed with water (2 x 5 mL). Organic layer was washed with brine (5 mL), dried over Na_2SO_4 and concentrated under vacuum. The resulting oil was purified by chromatography on silica gel.

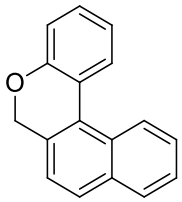


3-(2-(Hept-2-yn-1-yloxy)phenyl)phthalazine (6ad): 50%, R_f = 0.35 (50% hexanes / 50% EtOAc); ^{1}H NMR ($CDCl_3$) δ (ppm) 9.53 (s, 1H), 7.97 (dt, 1H, *J* = 1.2, 7.8 Hz); 7.89-7.87 (dt, 1H, *J* = 1.7, 8.4 Hz), 7.81-7.74 (m, 2H), 7.54-7.5 (m, 2H), 7.24-7.18 (m, 2H), 4.54-4.5 (dt, 2H, *J* = 1.6, 8.4 Hz), 2.17-2.13 (m, 2H), 1.46-1.39 (m, 2H), 1.36-1.23 (m, 2H), 0.88 (t,1H, *J* = 2.5 Hz); ^{13}C NMR δ (ppm) 158.8, 155.5, 150.9, 132.1, 132.1, 131.8, 130.7, 127.2, 126.6, 126.3, 126.5, 126.3, 126.1, 121.7, 121.6, 88.5, 74.7, 56.7, 30.5, 21.9, 18.5, 13.6. HRMS m/z (ESI) calcd. for $C_{21}H_{11}N_2O$ $(M+H)^+$ 317.1654, found 317.1657.

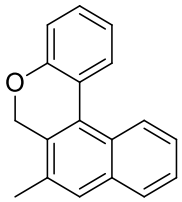


3-(2-(But-3-yn-1-yloxy)phenyl)phthalazine (6ae): 55%, R_f = 0.3 (50% hexanes / 50% EtOAc). ^{1}H NMR ($CDCl_3$) δ 9.53 (s, 1H), 8.0 (d, 1H, *J* = 8.0 Hz), 7.87 (t, 1H, *J* = 8.0 Hz), 7.79 (t, 1H, *J* = 8.2 Hz), 7.73 (t, 1H, *J* = 8.0 Hz), 7.53-7.48 (m, 2H), 7.18 (t, 1H, *J* = 7.2 Hz), 7.0 (d, 1H, *J* = 8.2 Hz) 4.0 (q, 2H, *J* = 14.5 Hz), 2.3-2.22 (m, 2H), 1.74 (t, 1H, *J* = 2.2 Hz); ^{13}C NMR δ (ppm) 158.7, 156.2, 132.7, 132.2, 132.1, 131.8, 131.0, 127.1, 126.6, 126.5, 126.3, 126.2, 121.8, 112.7, 79.9, 69.8, 66.7, 19.3. HRMS m/z (ESI) calcd. for $C_{18}H_{15}N_2O$ $(M+H)^+$ 275.1184, found 275.1183.

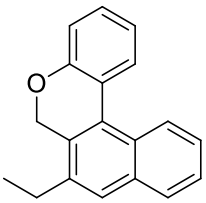
General procedure for the Intramolecular Inverse Electron Diels-Alder Reaction. A selected phthalazine-alkyne **6** (0.05 mmol) was dissolved in 1,2-dichlorobenzene (2 mL) in a 15 mL pressure vial. The vial was sealed with a Teflon-lined cap and the reaction mixture was heated at 140 – 200°C for 24 – 48 h. The solvent was removed under vacuum, and the resulting oil was purified by chromatography on silica gel.



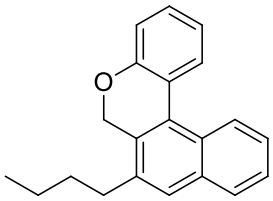
6*H*-Naphtho[2,1-*c*]chromene (7aa): 80%, R_f = 0.83 (80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.60 (dd, 1H, *J* = 8.4 Hz), 8.07 (dt, 1H, *J* = 8.4 Hz), 7.9 (dd, 1H, *J* = 8.4 Hz), 7.8 (d,1H, *J* = 8.2 Hz), 7.57-7.48 (m, 2H), 7.33-7.3 (m, 2H), 7.2-7.15 (m, 2H), 5.14 (s, 2H); ^{13}C NMR δ (ppm) 156.7, 134.7, 132.9, 129.3, 129.1, 128.9, 128.2, 128.1, 127.0, 126.9, 125.7, 125.3, 124.3, 122.6, 121.9, 117.7, 70.1; HRMS m/z (ESI) calcd. for $C_{17}H_{14}O$ $(M+H)^+$ 233.0966, found 233.0970.



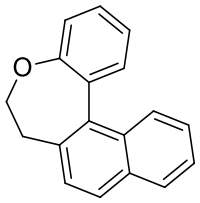
7-Methyl-6*H*-naphtho[2,1-*c*]chromene (7ab): 85%, R_f = 0.85 (80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.51-8.50 (m, 1H), 8.2 (s, 1H), 8.0 (dd, 1H, *J* = 2.0, 8.2 Hz), 7.81-7.79 (m, 1H), 7.59 (s, 1H), 7.49-7.44 (m, 2H), 7.30 (dt, 1H, *J* = 1.5, 8.4 Hz), 7.18-7.17 (m, 2H), 5.16 (s, 2H), 2.46 (s, 2H); ^{13}C NMR δ (ppm) 156.5, 134.3, 133.0, 130.7, 128.7, 128.3, 128.3, 128.2, 127.9, 127.1, 125.9, 125.8, 125.3, 124.5, 67.1, 19.1; HRMS m/z (ESI) calcd. for $C_{18}H_{16}O$ $(M+H)^+$ 247.1123, found 247.1124.



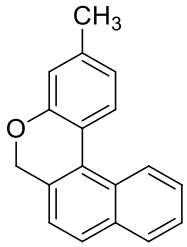
7-Ethyl-6*H*-naphtho[2,1-*c*]chromene (7ac): 86%, R_f = 0.85 in 80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.55-8.52 (m, 1H), 8.02 (dd, 1H, *J* = 1.5, 8.2 Hz), 7.84-7.82 (m, 1H), 7.62 (s, 1H), 7.48-7.46 (m, 2H), 7.30 (dt, 1H, *J* = 1.5, 8.4 Hz), 7.18-7.16 (m, 2H), 5.18 (s, 2H), 2.82 (q, 2H, *J* = 7.5 Hz), 1.32 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR δ (ppm) 156.6, 136.9, 134.4, 132.6, 128.7, 128.4, 127.9, 127.3, 126.7, 126.0, 125.8, 125.3, 124.6, 121.8, 117.4, 66.8, 25.9, 14.9; HRMS m/z (ESI) calcd. for $C_{19}H_{17}O$ $(M+H)^+$ 261.1279, found 261.1279.



7-Butyl-6*H*-naphtho[2,1-*c*]chromene (7ad): 79%, R_f = 0.71 (80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.51-8.50 (m, 1H), 8.02 (dd, 1H, *J* = 8.2 Hz), 7.83-7.81 (q, 1H), 7.60 (s, 1H), 7.49-7.44 (q, 2H), 7.30 (dt, 1H, *J* = 8.4 Hz), 7.18-7.17 (m, 2H), 5.17 (s, 2H), 2.79-2.72 (m, 2H), 1.67-1.61 (m, 2H), 1.49-1.42 (m, 2H), 0.97 (t, 1H, *J* = 7.3 Hz); ^{13}C NMR δ (ppm) 56.6, 135.6, 134.3, 132.6, 128.8, 128.7, 128.6, 128.4, 127.9, 127.6, 125.9, 125.7, 125.3, 124.6, 121.3, 117.4, 66.9, 33.0, 32.8, 22.7, 14.1; HRMS m/z (ESI) calcd. for $C_{19}H_{17}O$ $(M+H)^+$ 289.1592, found 289.1592.

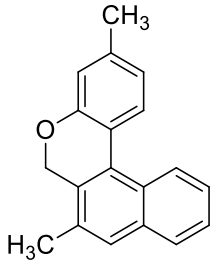


6,7-Dihydrobenzo[*b*]naphtho[1,2-*d*]oxepine (7ae): 48%, R_f = 0.65 (90% hexanes / 10% EtOAc); ^{1}H NMR ($CDCl_3$) δ (ppm) 8.14-8.11 (m, 1H), 7.89-7.87 (m, 1H), 7.84 (d, 1H, *J* = 8.6 Hz), 7.29-7.57 (dd, 1H, *J* = 7.6 Hz), 7.46-7.38 (m, 4H), 7.30 (dt, 1H, *J* = 1.4, 7.5 Hz), 7.27 (dd, 1H, *J* = 1.4, 8.2 Hz), 4.58 (dt, 2H, *J* = 1.6, 11.5 Hz), 3.08-2.99 (m, 1H), 2.73-2.68 (m, 1H, *J* = 2.0, 11.5 Hz); ^{13}C NMR δ (ppm) 155.4, 134.7, 134.4, 133.5, 133.1, 131.8, 131.3, 129.1, 128.5, 128.2, 126.7, 126.3, 125.6, 125.2, 123.9, 122.8, 78.9, 33.8; HRMS m/z (ESI) calcd. for $C_{18}H_{15}O$ $(M+H)^+$ 247.1123, found 247.1121.

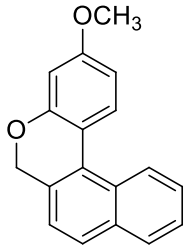


3-Methyl-6*H*-naphtho[2,1-*c*]chromene (**7ba**): 91%, R_f = 0.85 (80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.59 (d, 1H, *J* = 8.4 Hz), 7.96 (d, 1H, *J* = 8.4 Hz), 7.89, (dd, 1H, *J* = 1.6, 8.2 Hz), 7.77 (d, 1H, *J* = 8.2 Hz), 7.56-7.47 (m, 2H), 7.31 (d, 1H, *J* = 8.2 H), 7.01-7.0 (m, 2H), 5.12 (s, 2H), 2.42 (3H); ^{13}C NMR δ (ppm) 156.7, 139.3, 134.6, 132.3, 129.0, 129.0, 127.9,

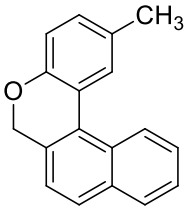
127.8, 127.2, 126.7, 125.6, 125.3, 122.8, 122.6, 121.5, 118.2 70.1, 21.5; HRMS m/z (ESI) calcd. for $C_{18}H_{16}O$ $(M+H)^+$ 247.1123 found 247.1129.



3,7-Dimethyl-6*H*-naphtho[2,1-*c*]chromene (7bb): 88%, R_f = 0.85 (80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.5-8.48 (m, 1H), 7.9 (d, 1H, *J* = 8.4 Hz), 7.8-7.77 (m, 1H), 7.56 (s, 1H), 7.47-7.43 (m, 2H), 6.99-6.98 (m, 2H), 5.12 (s, 2H), 2.45 (3H), 2.41 (3H); ^{13}C NMR δ 156.4, 139.1, 134.3, 132.4, 128.2, 128.1, 127.9, 127.9, 127.3, 125.8, 125.7, 125.4, 122.7, 121.7, 67.1, 21.5, 19.2; HRMS m/z (ESI) calcd. for $C_{19}H_{18}O$ $(M+H)^+$ 261.1279, found 261.1282.



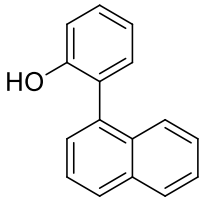
3-Methoxy-6*H*-naphtho[2,1-*c*]chromene (7ca): 74%, R_f = 0.80 (80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.56 (d, 1H, *J* = 8.4 Hz), 7.9 (d, 1H, *J* = 8.4 Hz), 7.89 (dd, 1H, *J* = 1.6, 7.8 Hz), 7.75 (dd, 1H, *J* = 8.2 Hz), 7.53-7.46 (m, 2H), 7.29 (d, 1H, *J* = 8.2 Hz), 6.77 (d, 1H, *J* = 2.68 Hz), 6.77-6.73 (m, 2H), 5.12 (s, 2H), 3.03 (s, 3H); ^{13}C NMR δ (ppm) 158.5, 134.7, 131.3, 129.0, 128.9, 127.3, 127.2, 126.7, 125.6, 125.3, 122.6, 117.3, 70.3, 55.6; HRMS m/z (ESI) calcd. for $C_{18}H_{16}O_2$ $(M+H)^+$ 263.1072, found 263.1081.



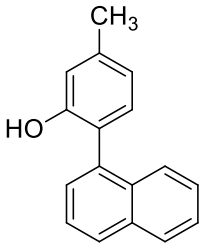
2-methyl-6H-naphtho[2,1-c]chromene (7da): 0.88%, R_f = 70% (80% hexanes / 20% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 8.61 (d, 1H, *J* = 8.4 Hz), 7.90-7.86 (m, 2H), 7.91 (d, 1H, *J* = 8.2 Hz), 7.58-7.4 (m, 2H), 7.31 (d, 1H, *J* = 8.2 Hz), 7.13 (dd, 1H, *J* = 2.6, 8.2 Hz), 7.07 (d, 1H, *J* = 8.2

Hz), 5.10 (s, 2H), 2.44 (s, 3H); ^{13}C NMR δ (ppm) 154.5, 134.6, 131.1, 129.4, 129.1, 128.5, 128.1, 127.2, 126.8, 125.6, 125.4, 122.6, 117.4, 70.2, 21.3; HRMS m/z (ESI) calcd. for $C_{18}H_{16}O$ $(M+H)^+$ 247.1123, found 247.1129.

General procedure for the Intermolecular Inverse Electron Diels-Alder Reaction. Phthalazine phenol **5a** or **5b** (0.023 mmol) was dissolved in 1,2 dichlorobenzene (1 mL) and added 2,5-norbornadiene (0.23 mmol) in a 15 mL pressure vial. The vial was sealed with a Teflon-lined cap and the reaction mixture was heated at 140 °C for 24 h. The solvent was removed under vacuum and the resulting oil was purified by chromatography on silica gel.



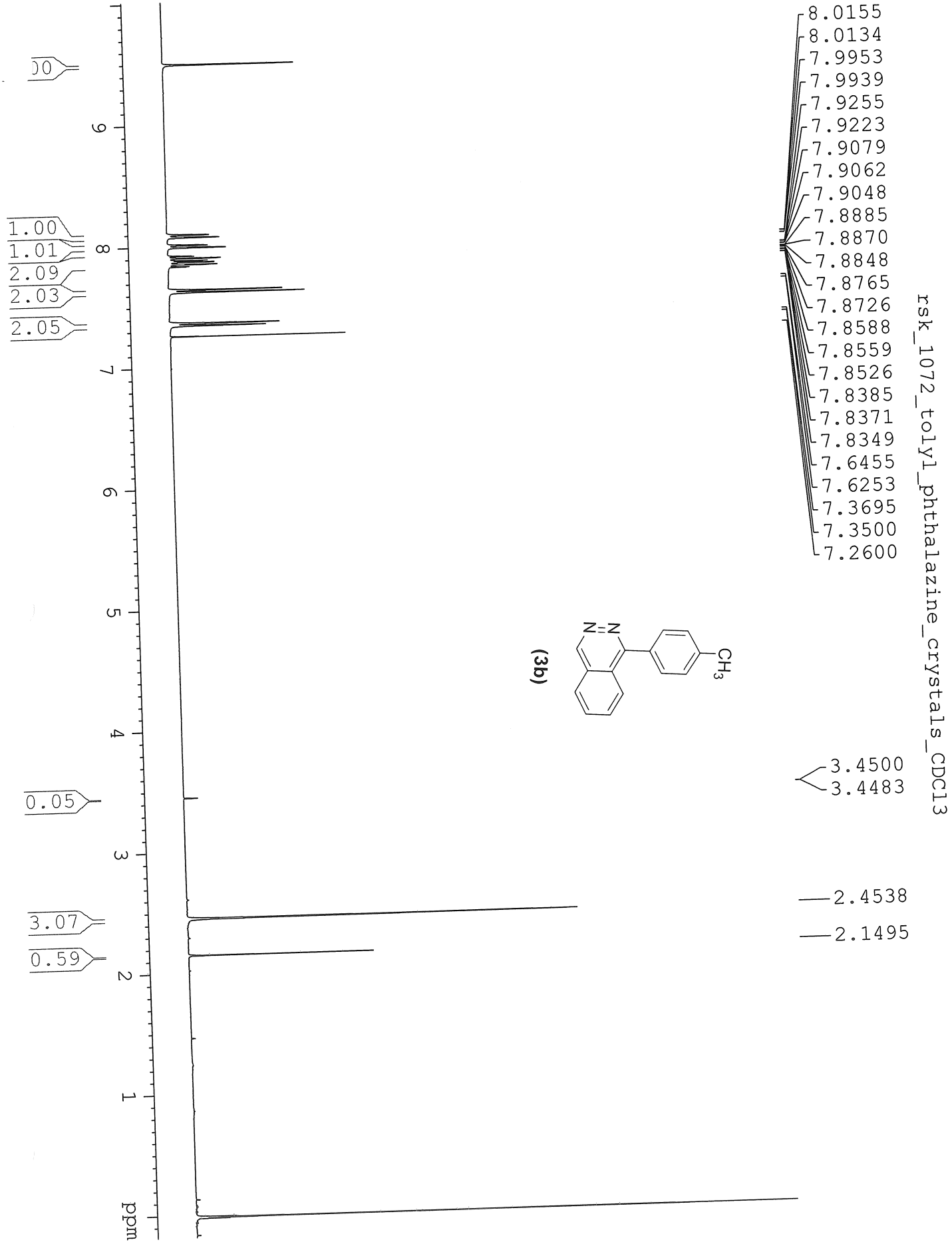
2-(Naphthalen-1-yl)phenol (8a): 80%, R_f = 0.6 (90% hexanes / 10% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 7.95 (d, 1H, *J* = 8.2 Hz), 7.68 (d, 1H, *J* = 8.2 Hz), 7.6-7.45 (m, 4H), 7.38 (dt, 1H, *J* = 8.4 Hz), 7.29 (dd, 1H, *J* = 4.2, 7.4 Hz), 7.09-7.06 (m, 2H); ^{13}C NMR δ (ppm) 153.3, 134.1, 132.0, 131.3, 129.7, 129.0, 128.6, 128.3, 126.9, 126.5, 125.9, 125.8, 120.7, 115.7; HRMS m/z (ESI) calcd. for $C_{16}H_{11}O$ $(M+H)^+$ 221.0966, found 221.0997.

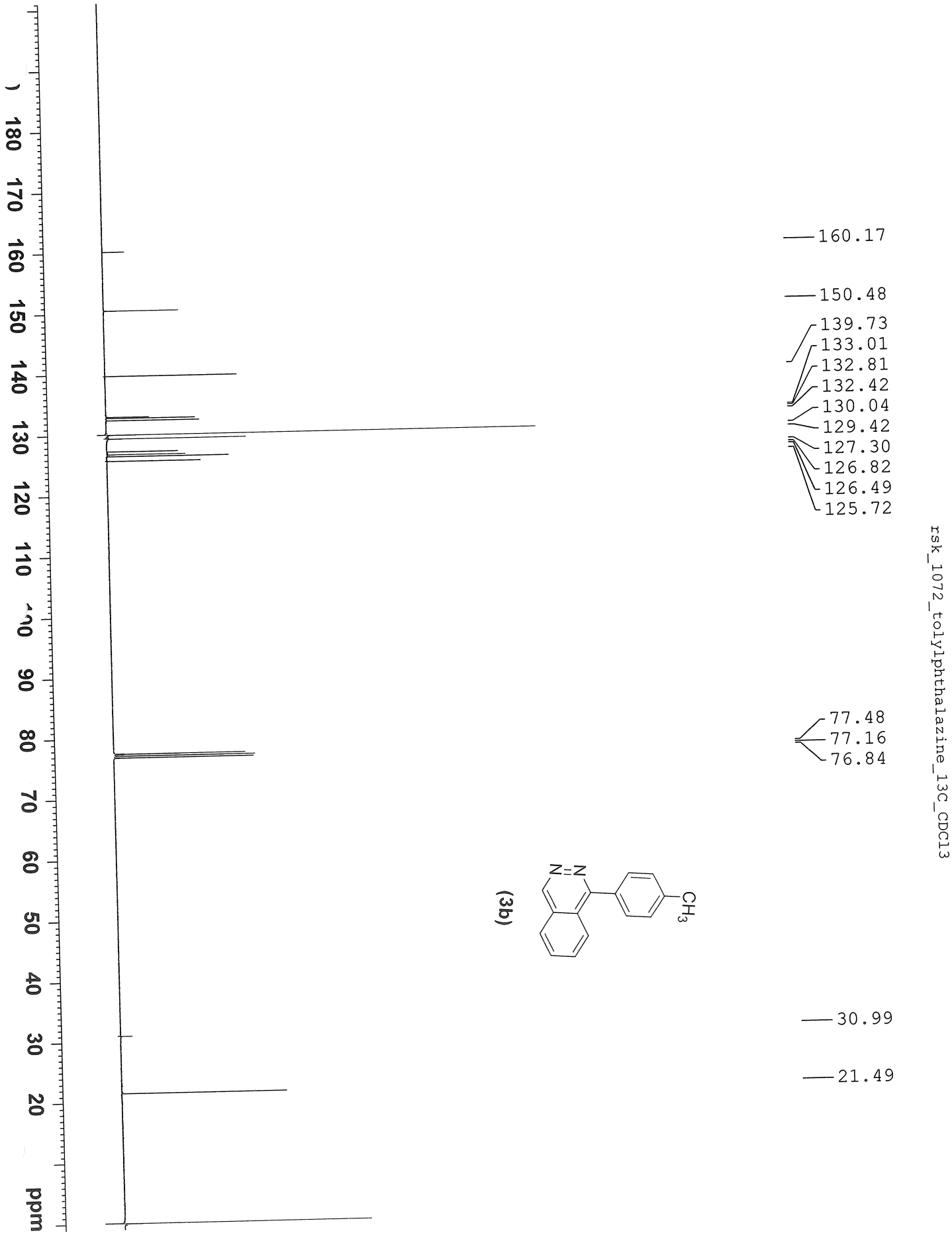


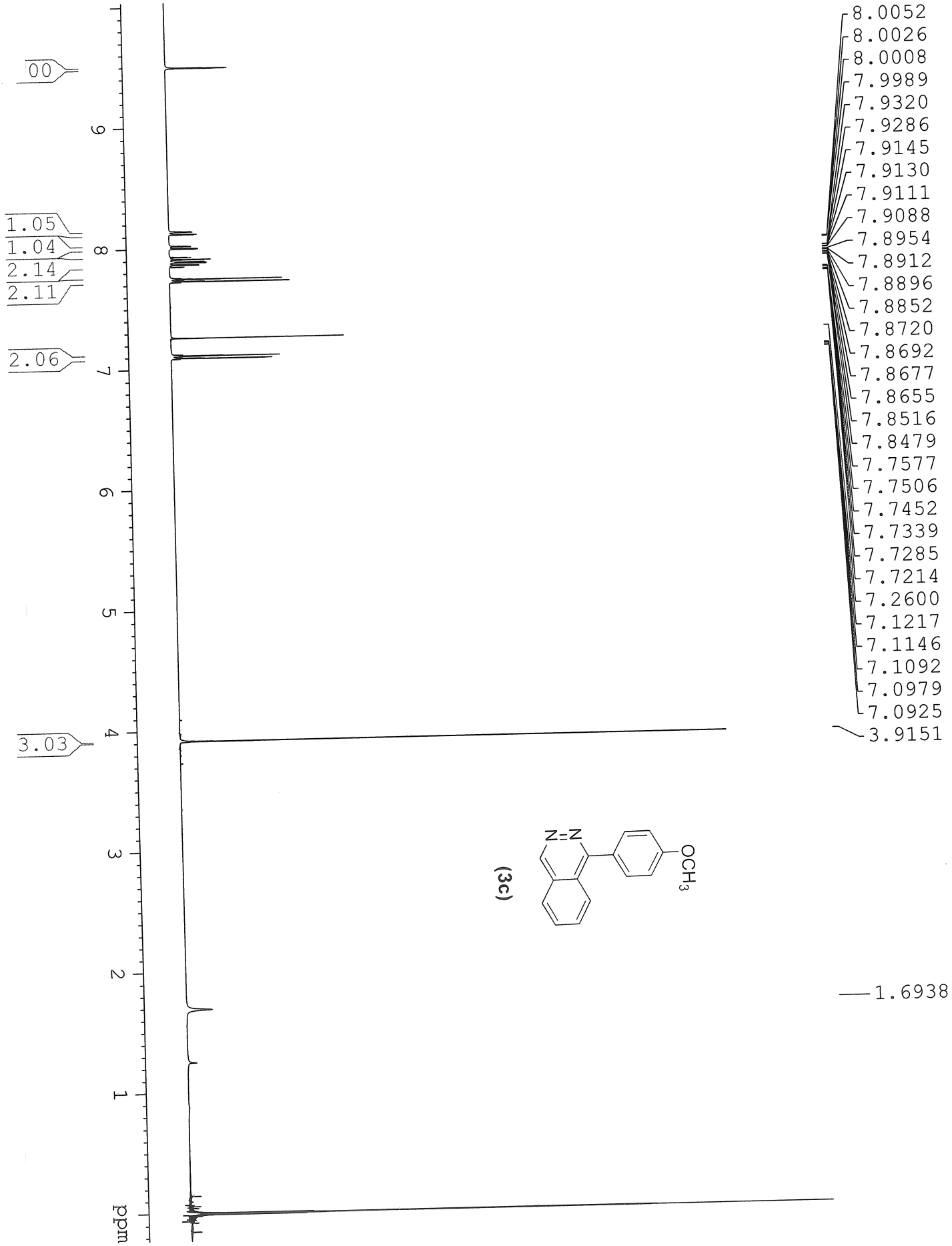
5-Methyl-2-(naphthalen-1-yl)phenol (8b): 65%, R_f = 0.61 (90% hexanes / 10% EtOAc); ^{1}H NMR ($CDCl_3$): δ (ppm) 7.93-7.91 (dd, 2H, *J* = 8.6 Hz), 7.76-7.67 (d, 1H, *J* = 1.2, 8.6 Hz), 7.58-7.43 (m, 4H), 7.16 (d, 1H, *J* = 7.6 Hz), 6.9- 6.88 (m, 2H), 2.42 (s, 3H); ^{13}C NMR δ (ppm) 153.1, 139.9, 134.1, 132.1, 131.3, 131.1, 128.8, 128.6, 128.4, 126.8, 126.5, 125.9, 125.8, 121.5, 116.3, 21.4; HRMS m/z (ESI) calcd. for $C_{17}H_{16}O$ $(M+H)^+$ 235.1123, found 235.1158.

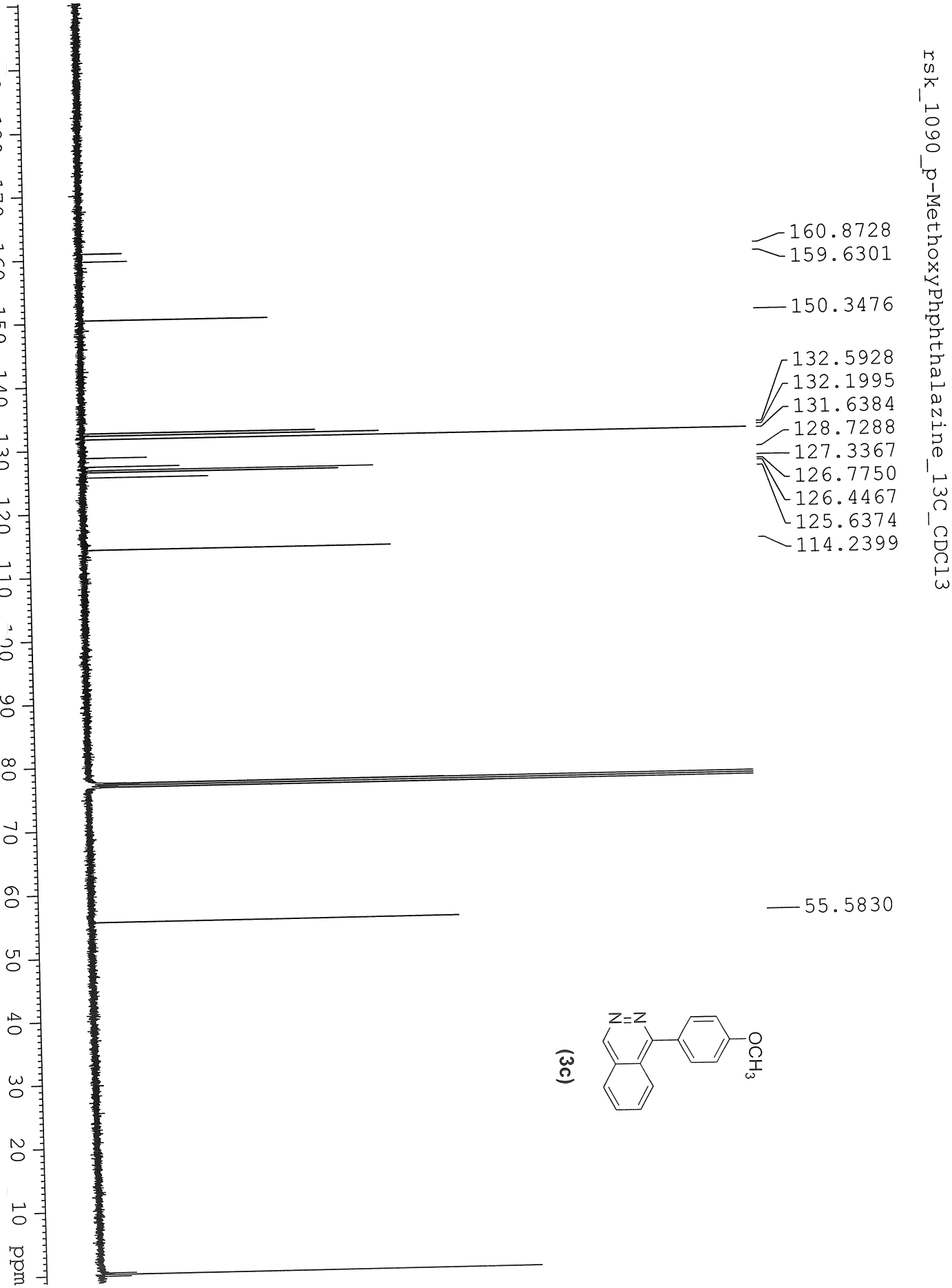
Reference:

1. Mustafa, A.; Harshah, A. H.; Saleh, A. A. S. *J. Am. Chem. Soc.*, **1960**, *82*, 2735-2739.









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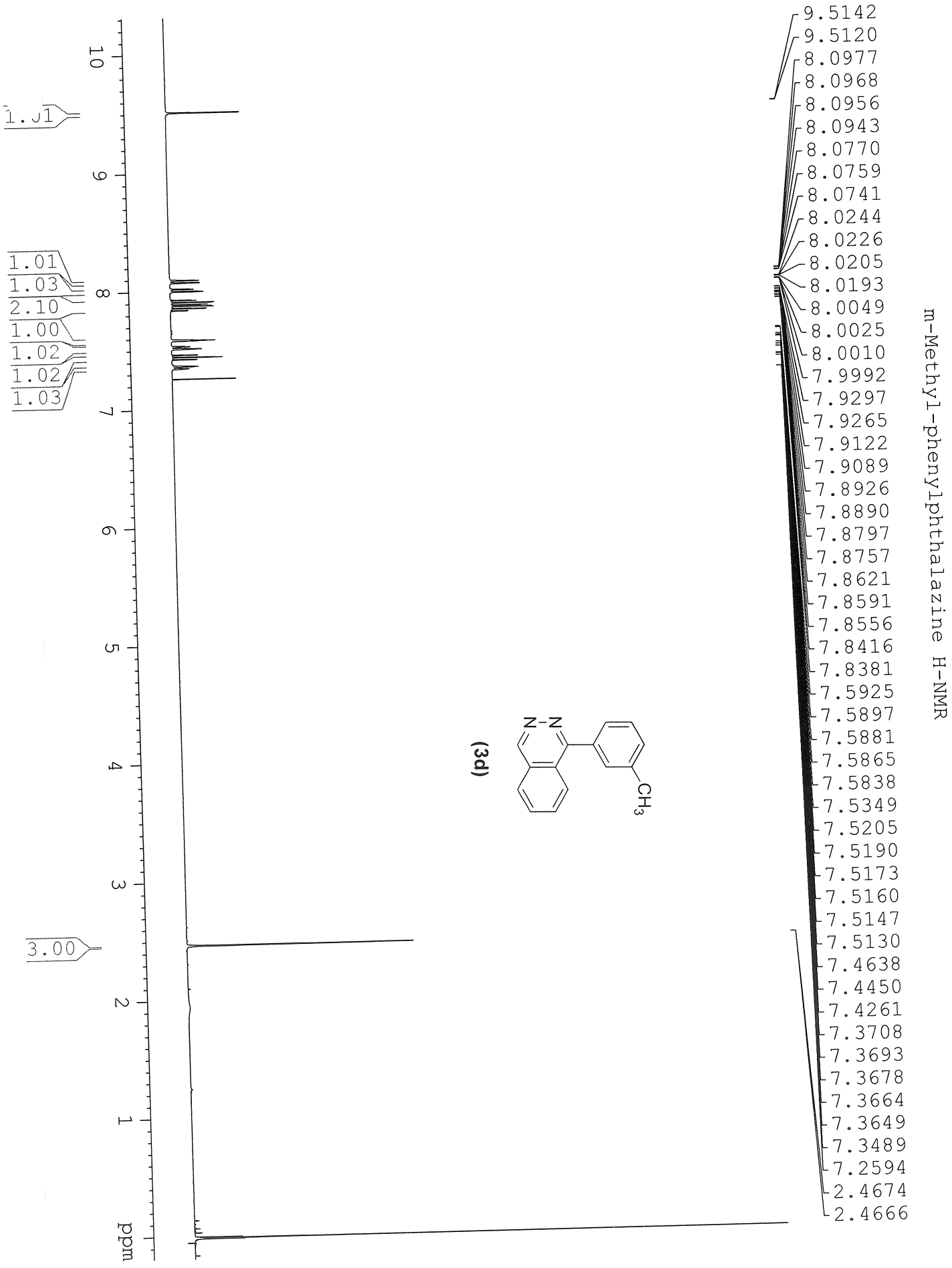

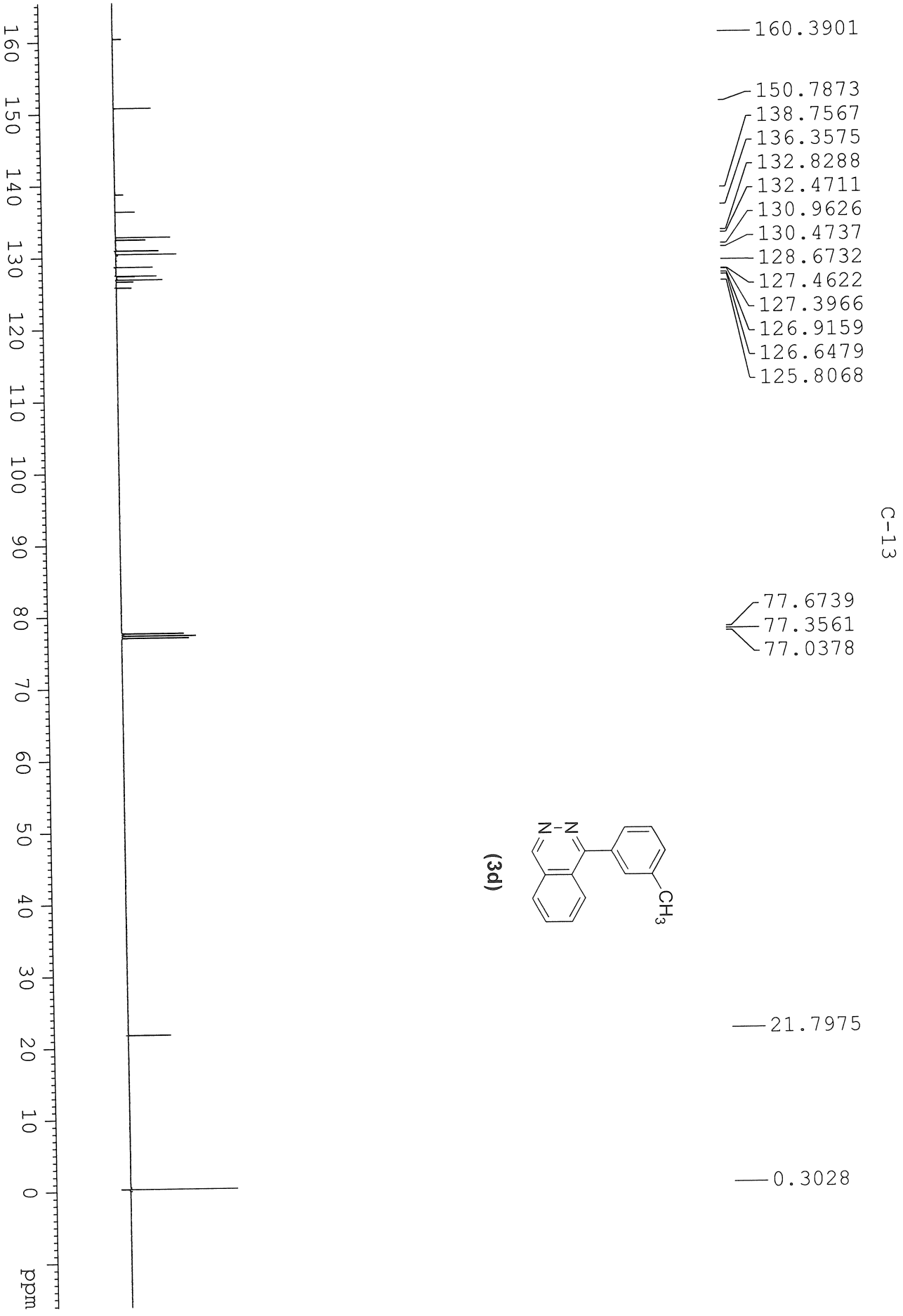

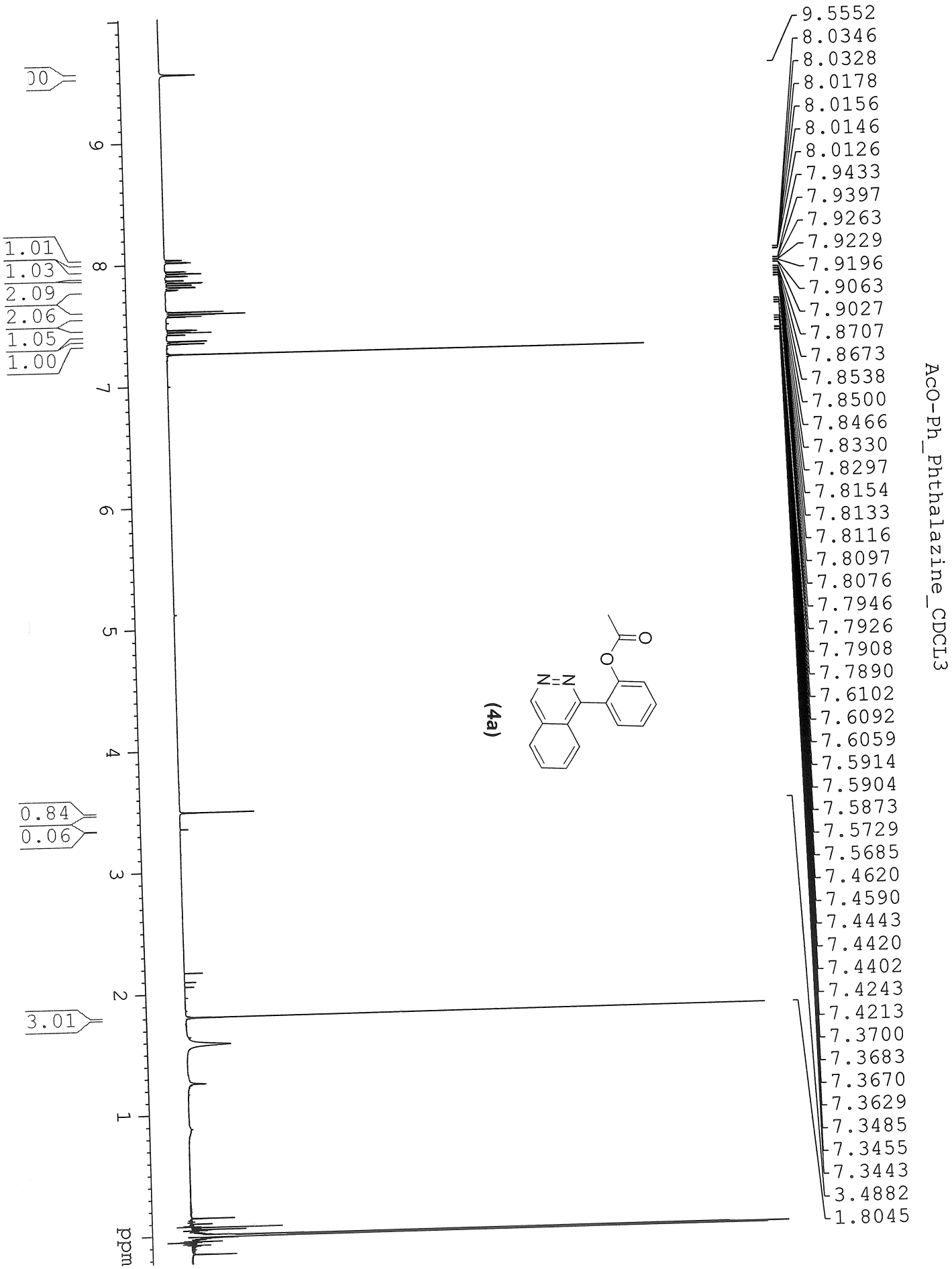

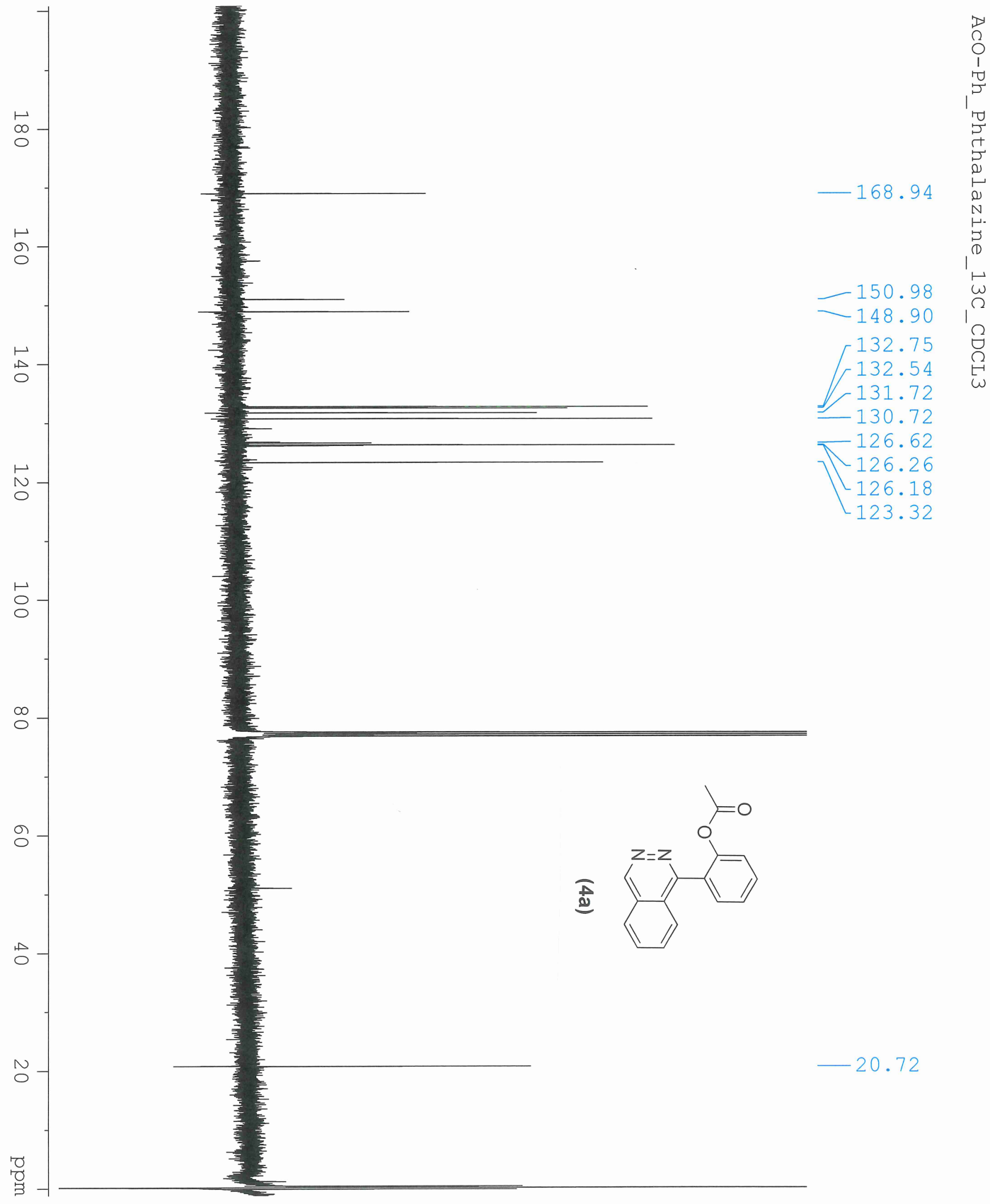

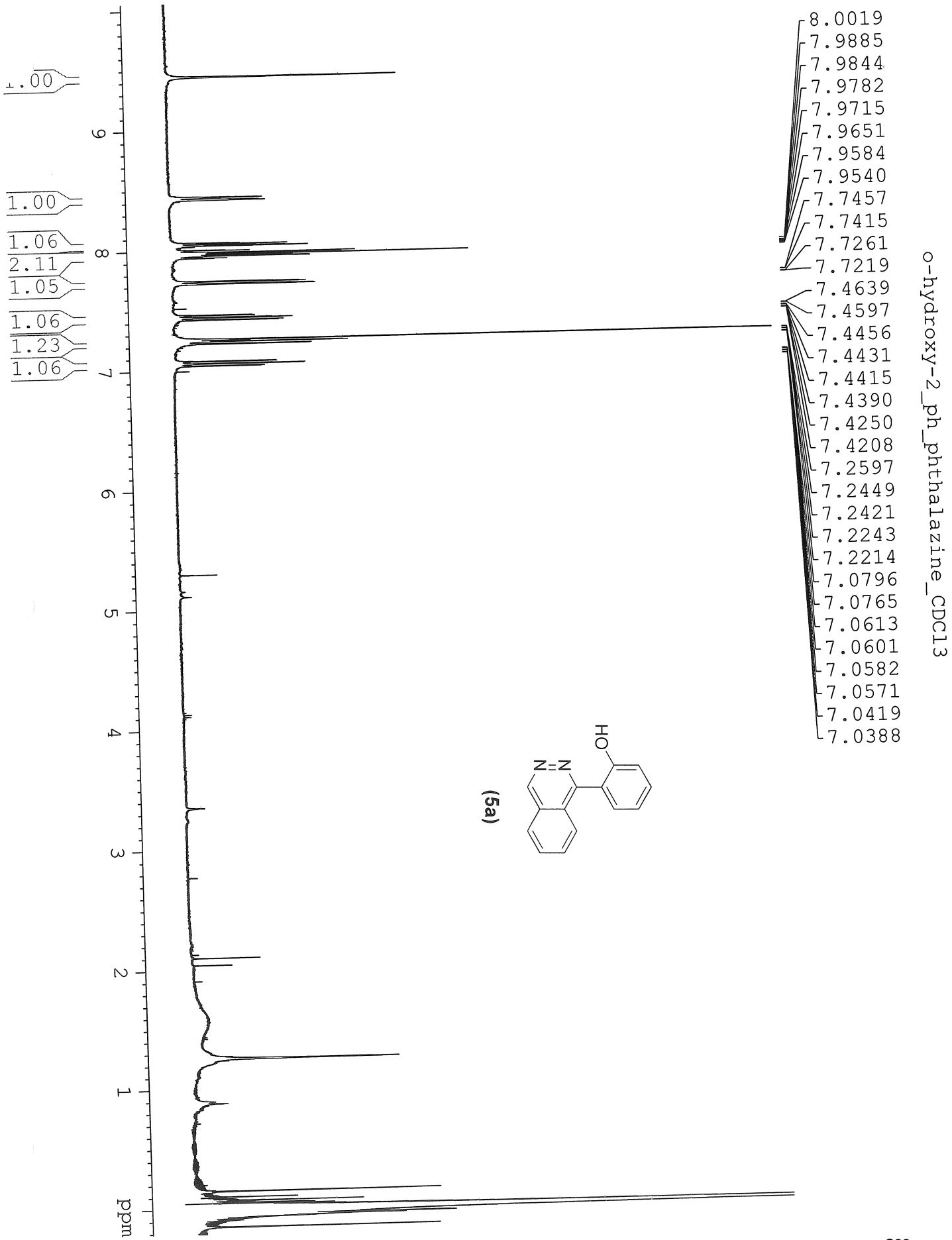

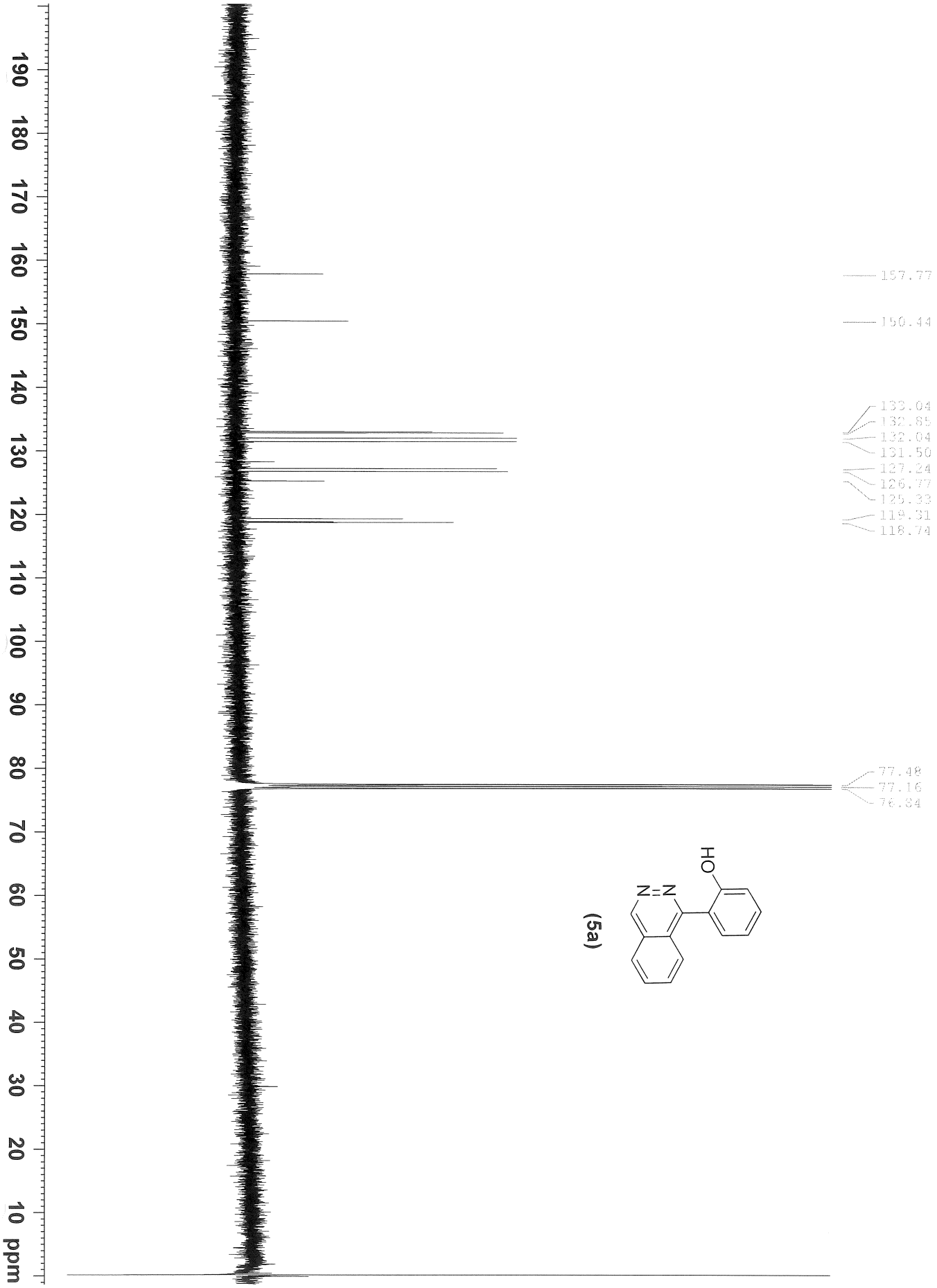

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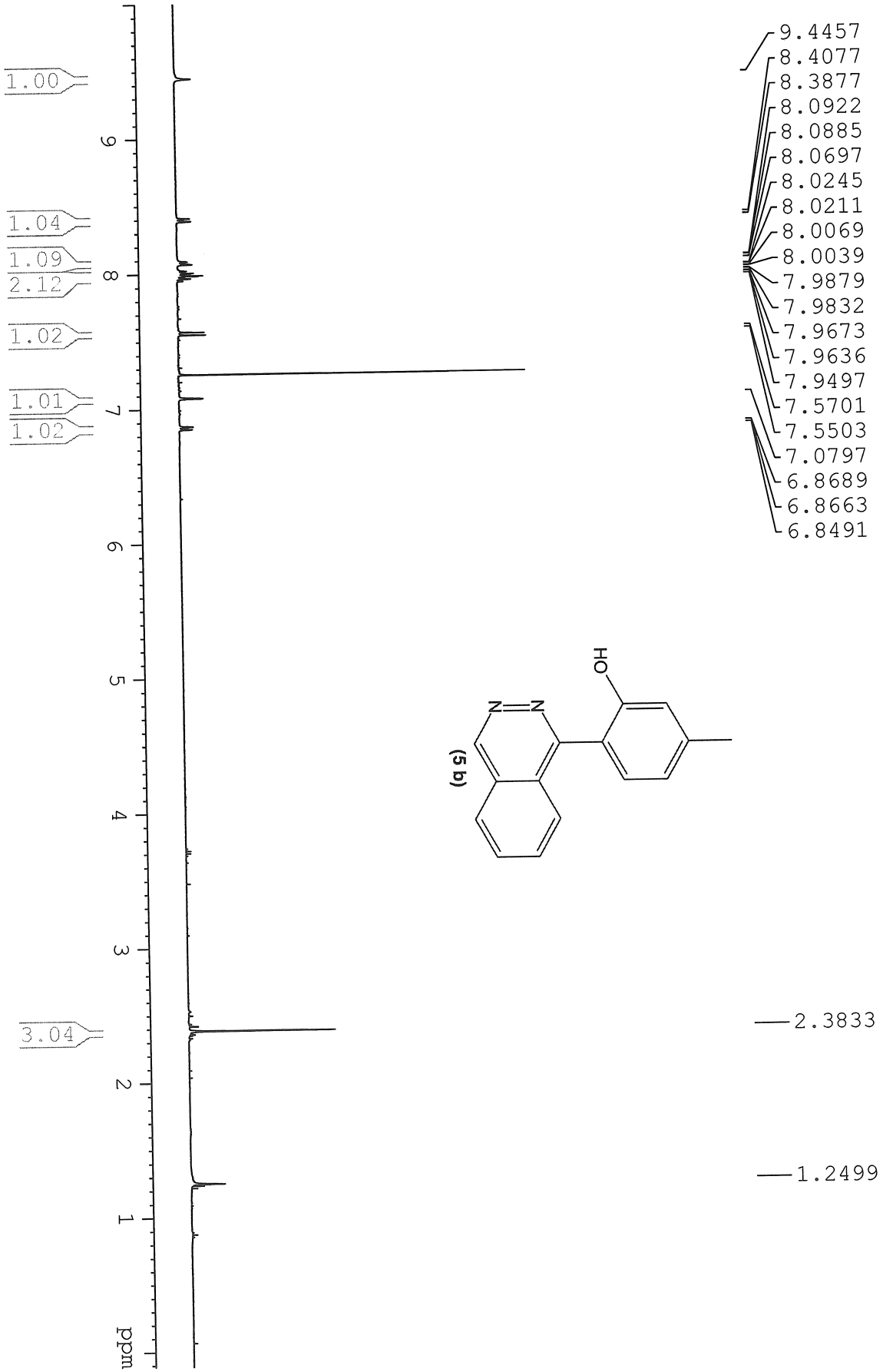

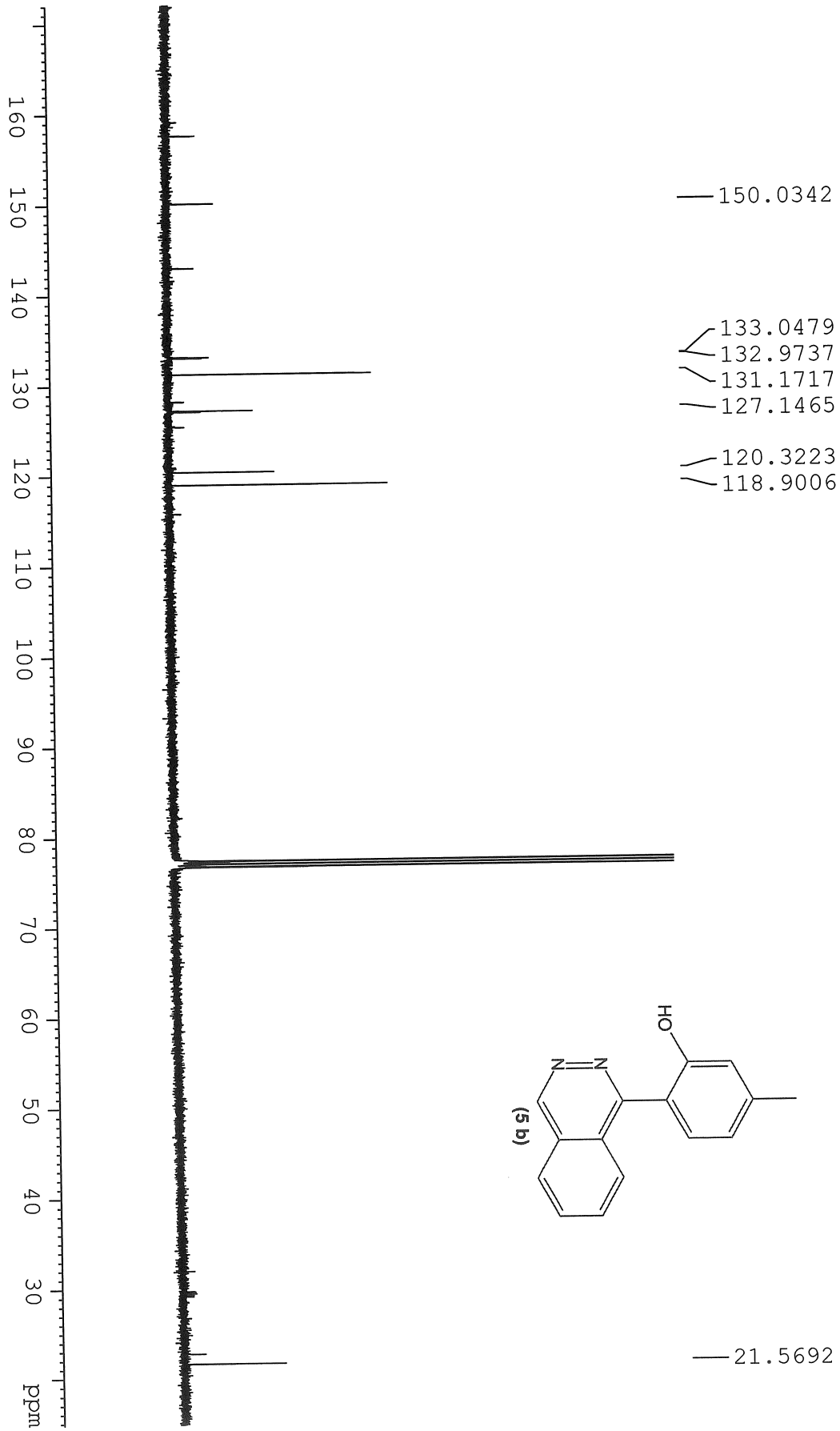

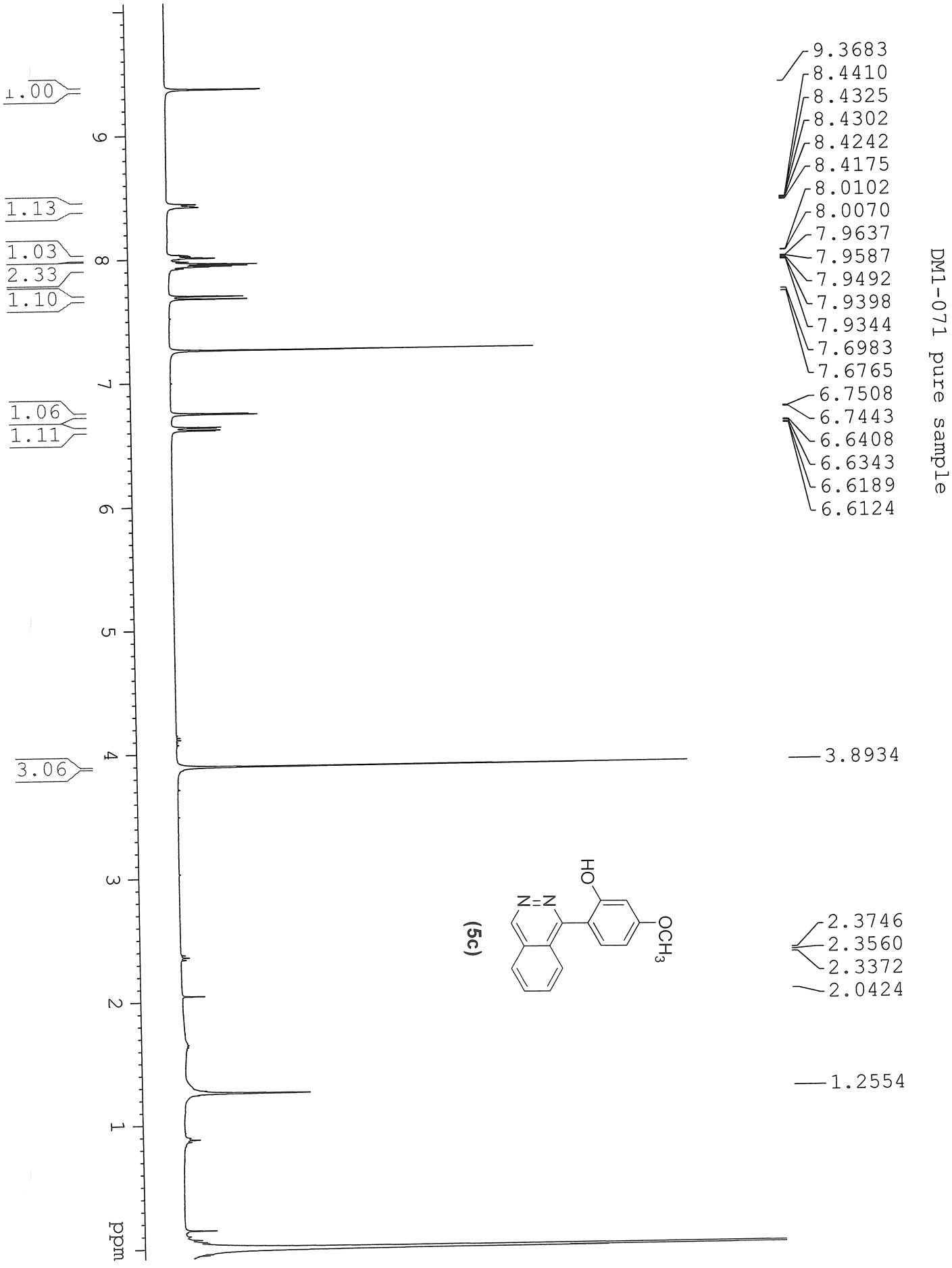

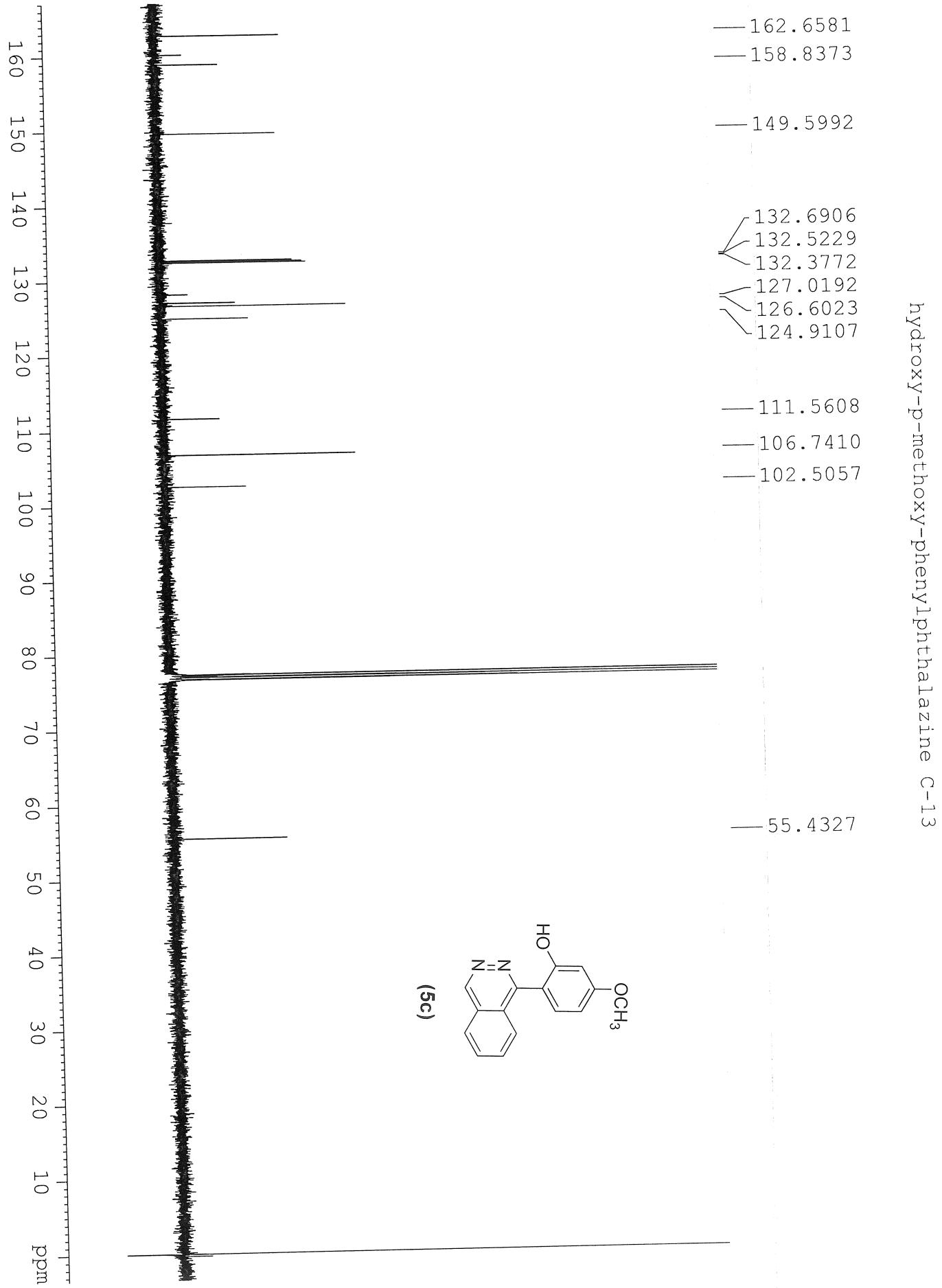

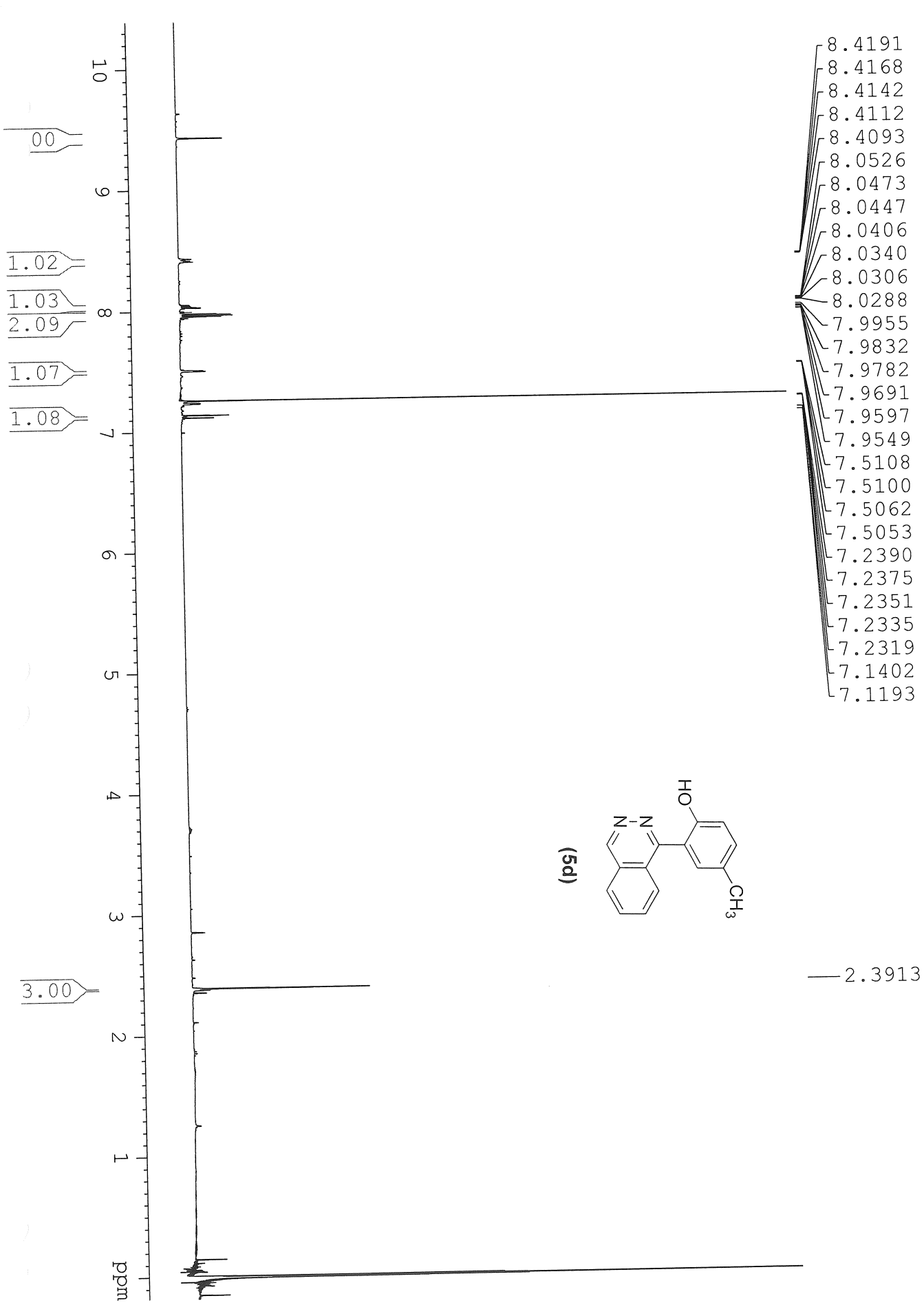

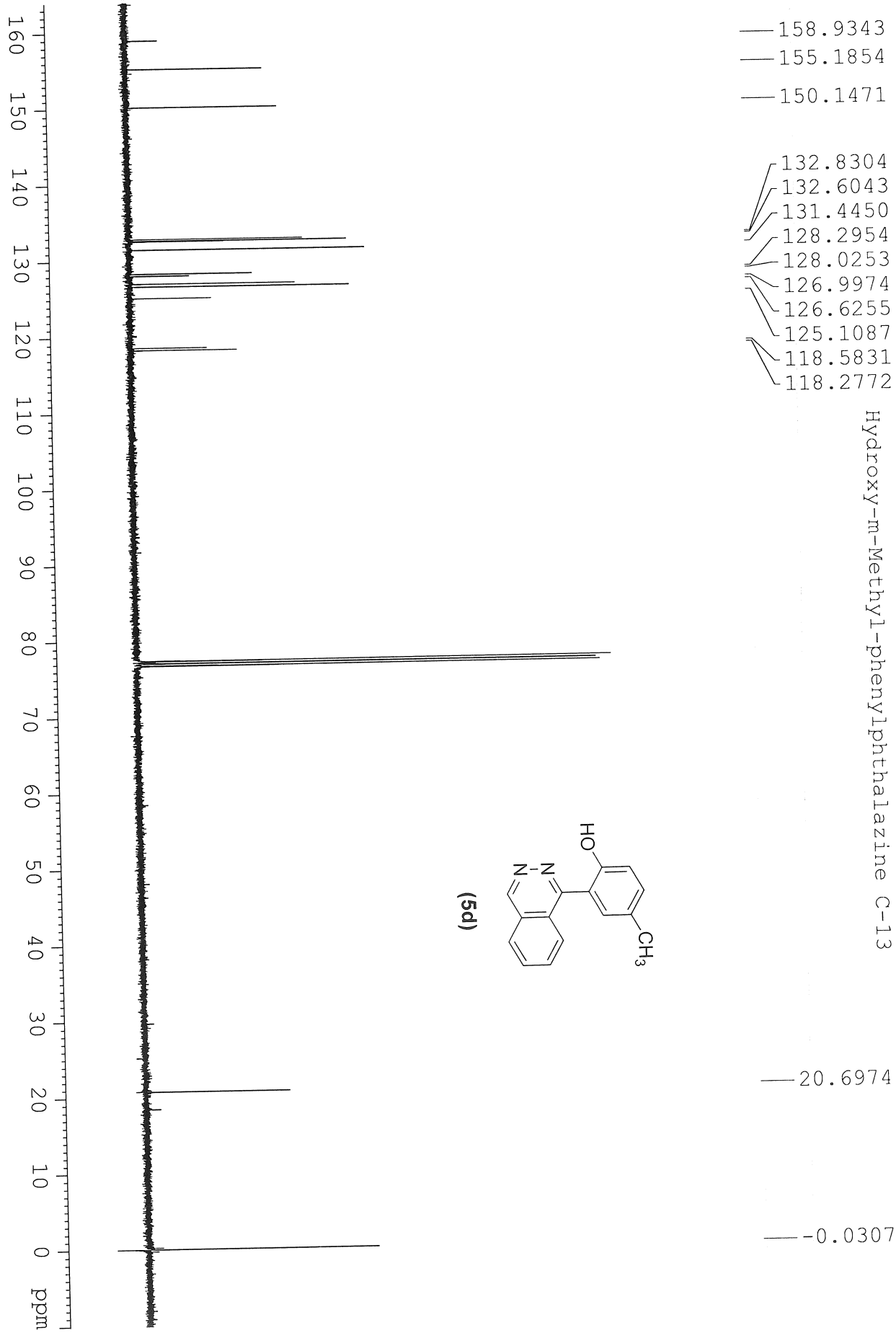

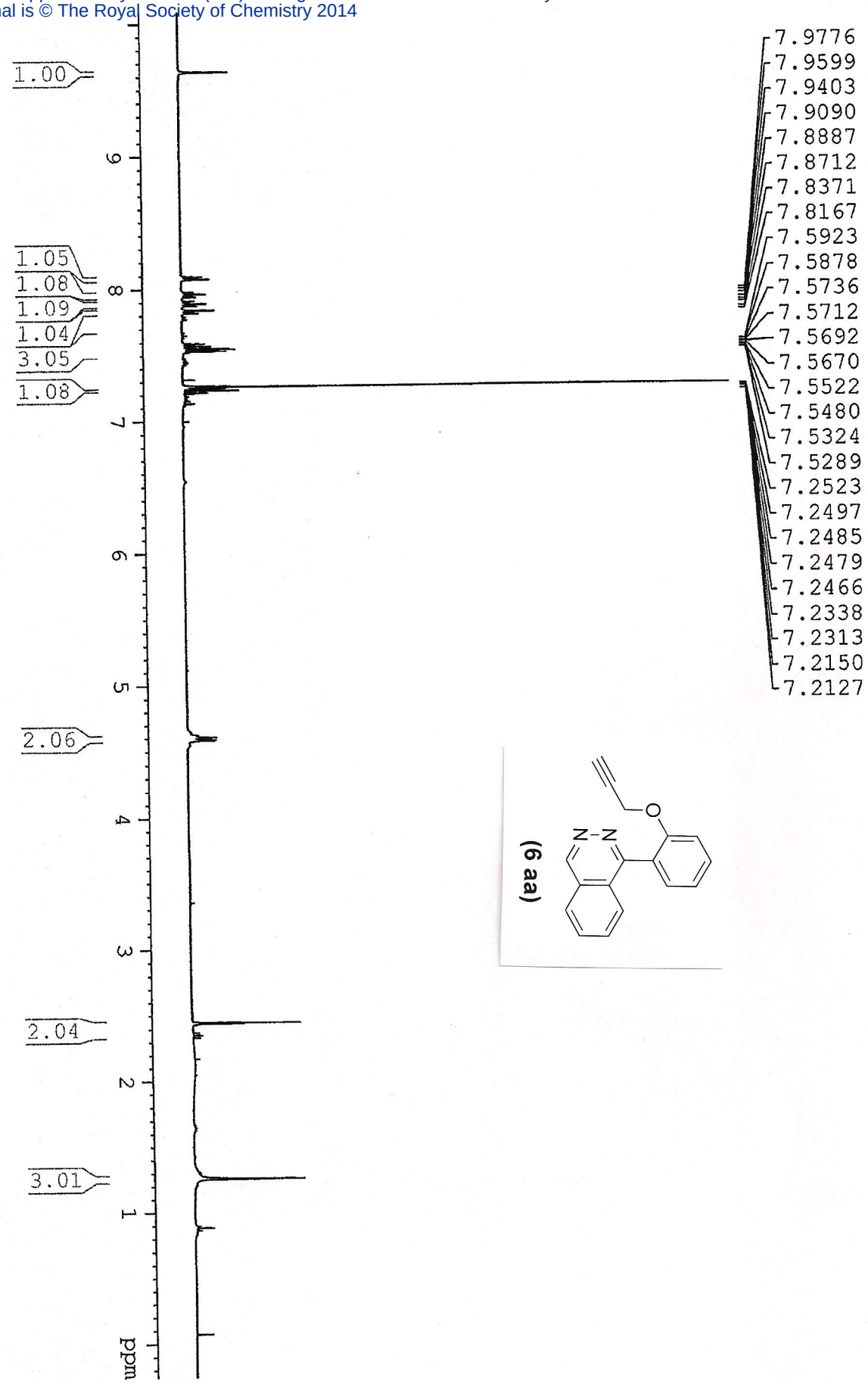

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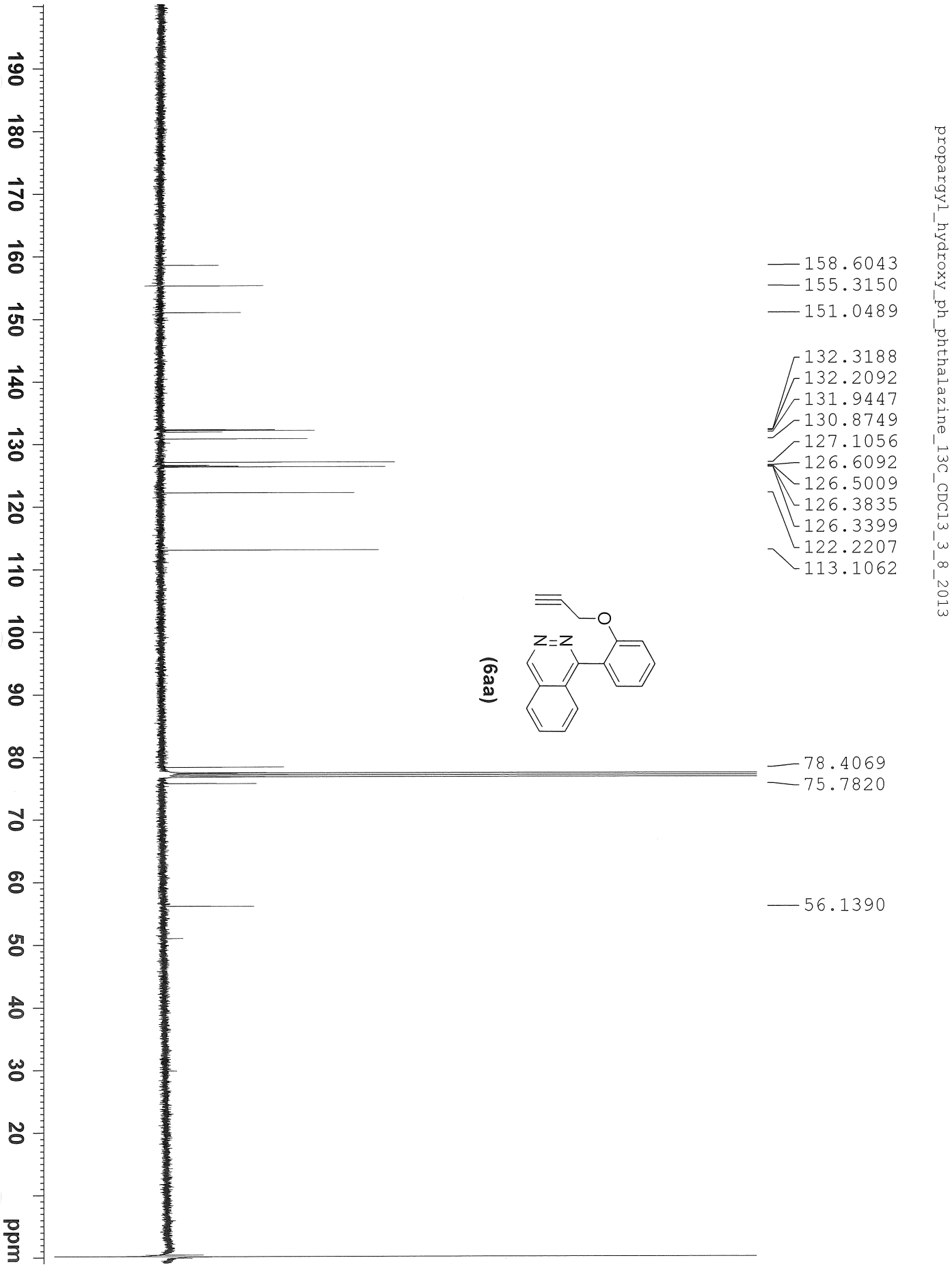
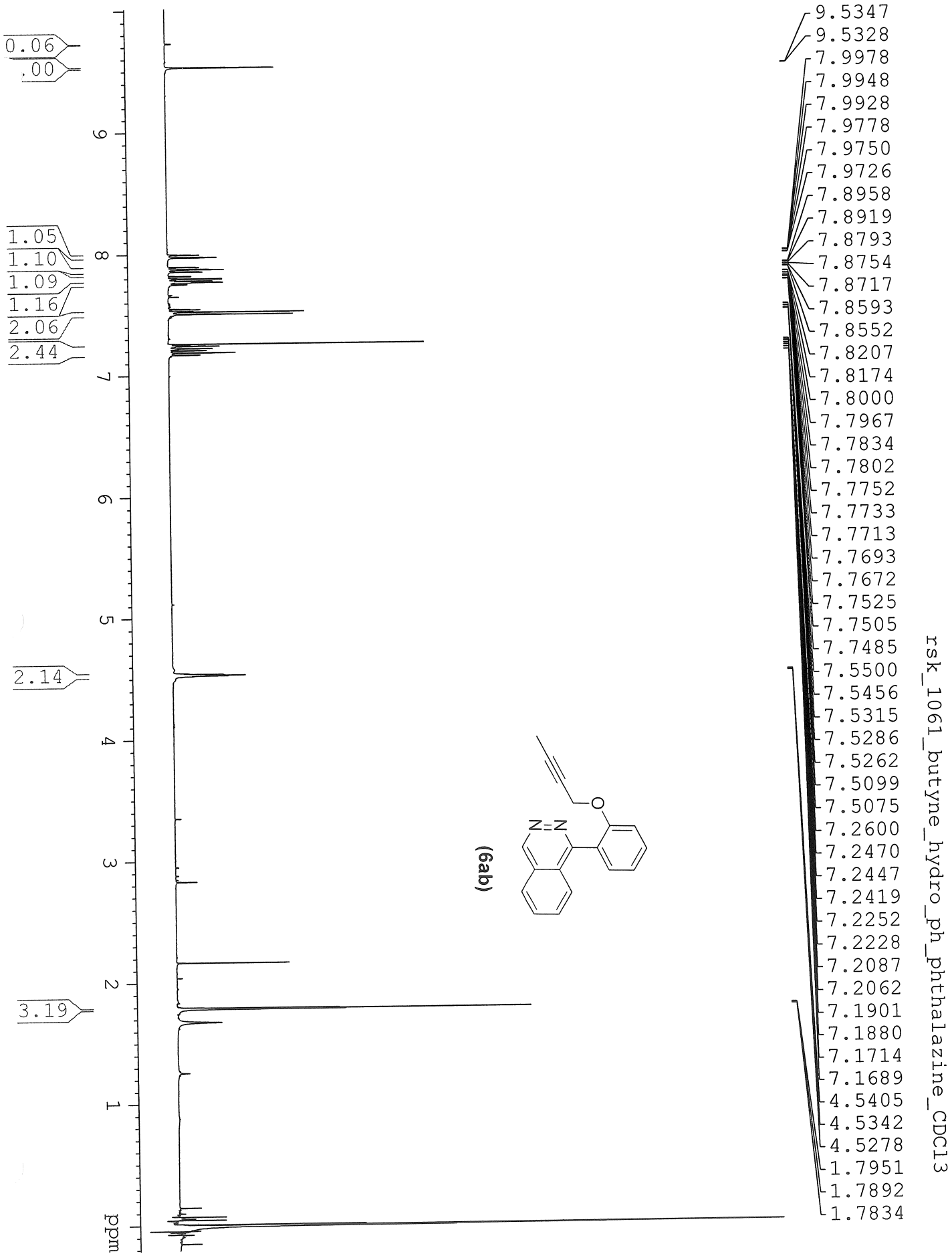
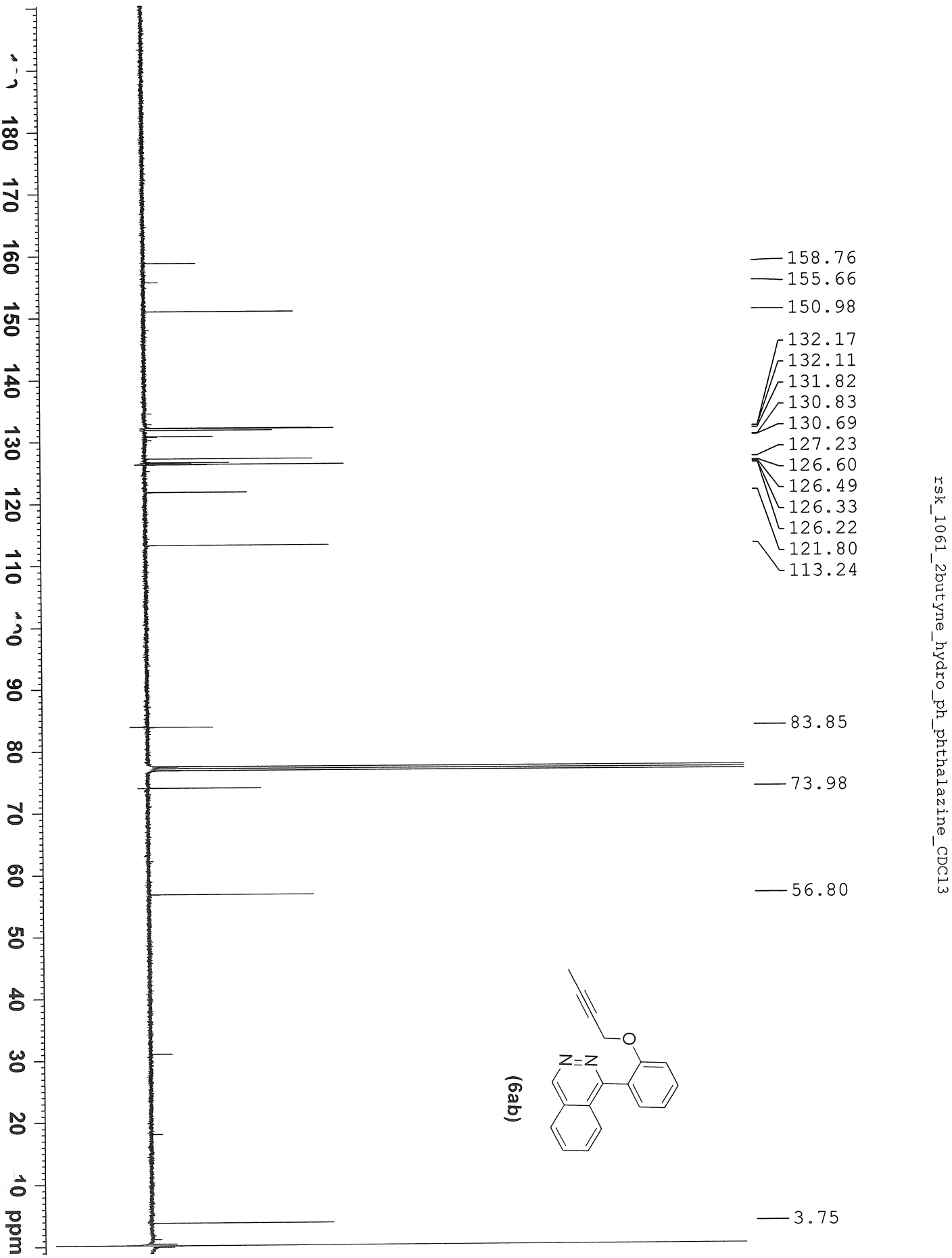
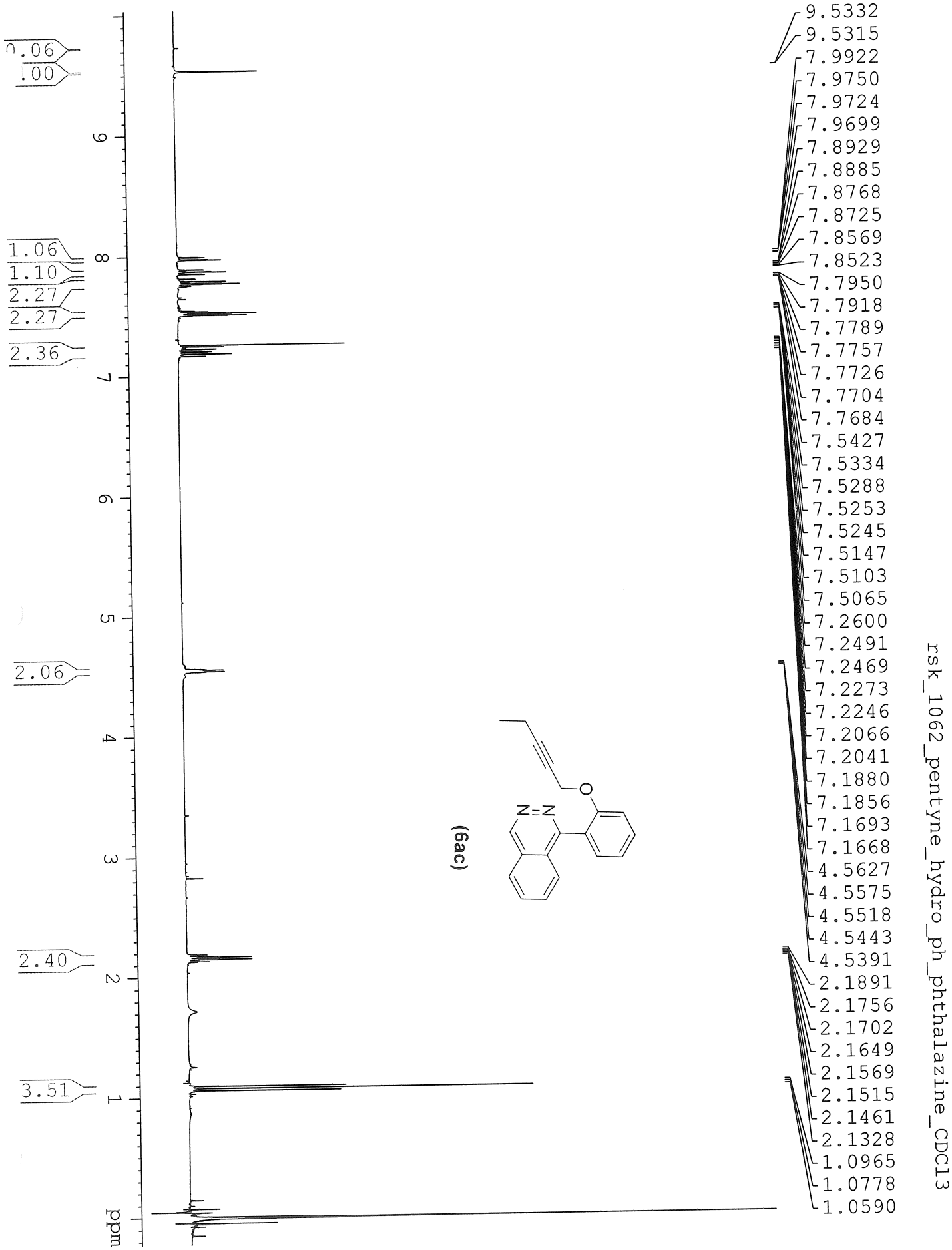
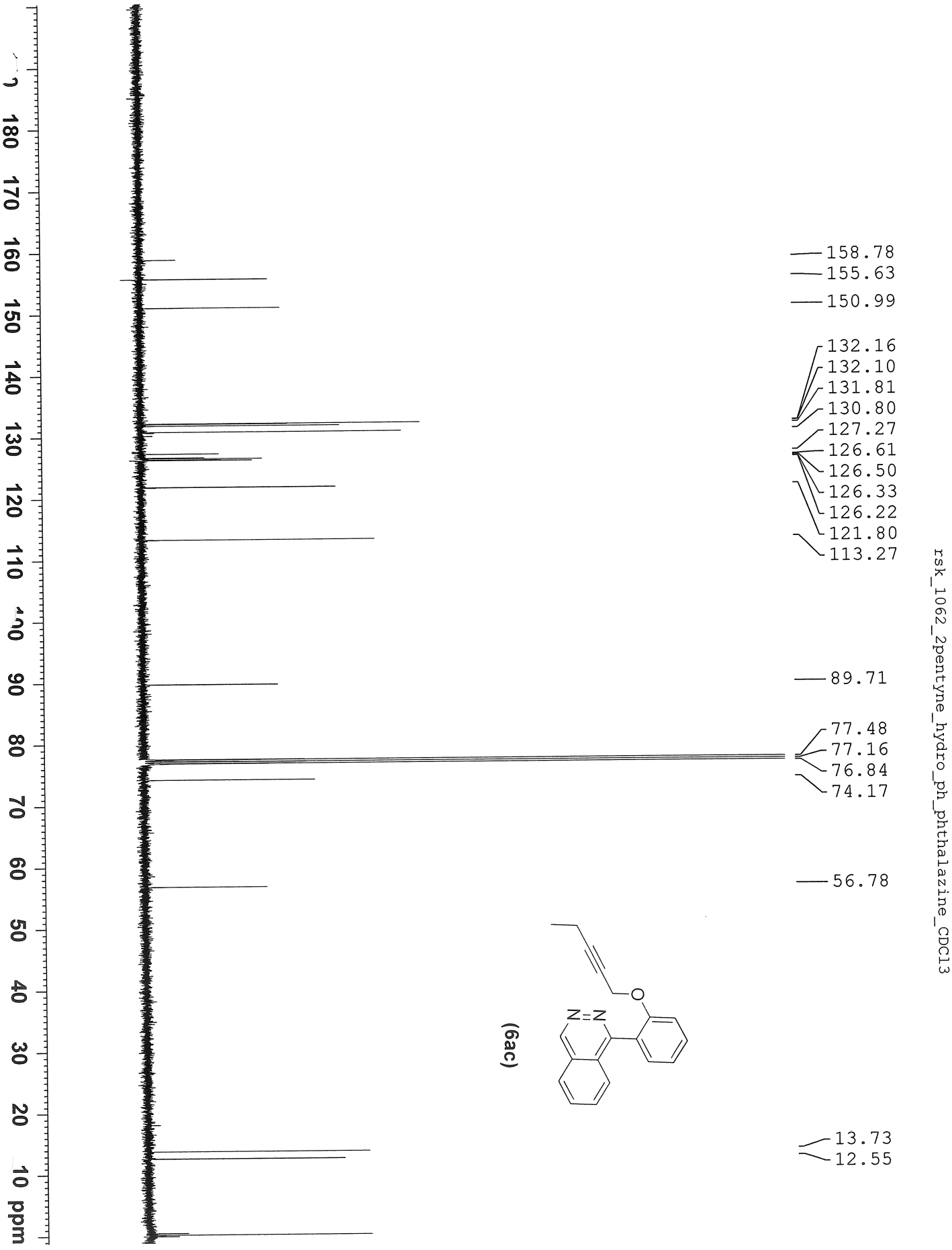
RSK-1041 (3), 1-H

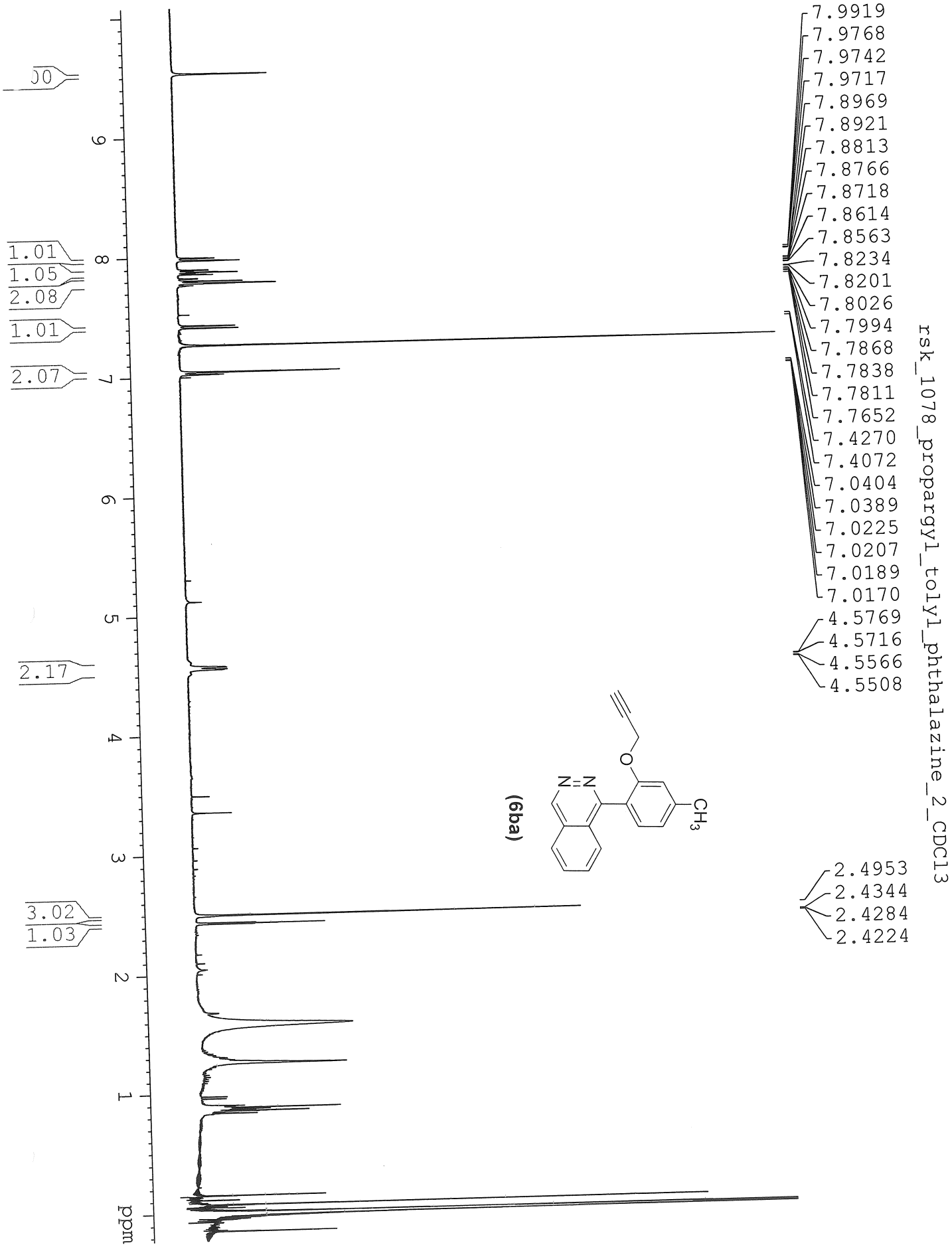


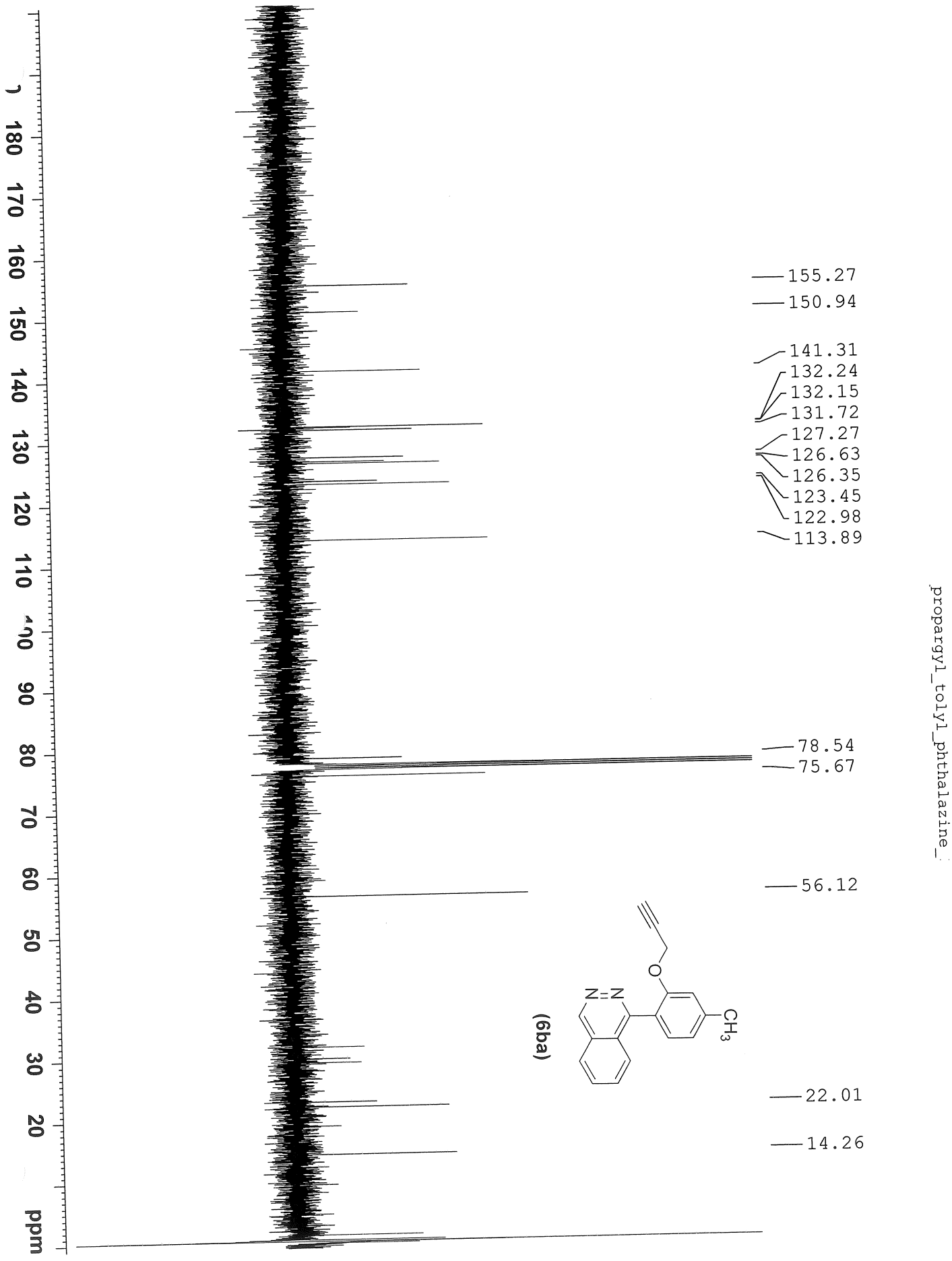


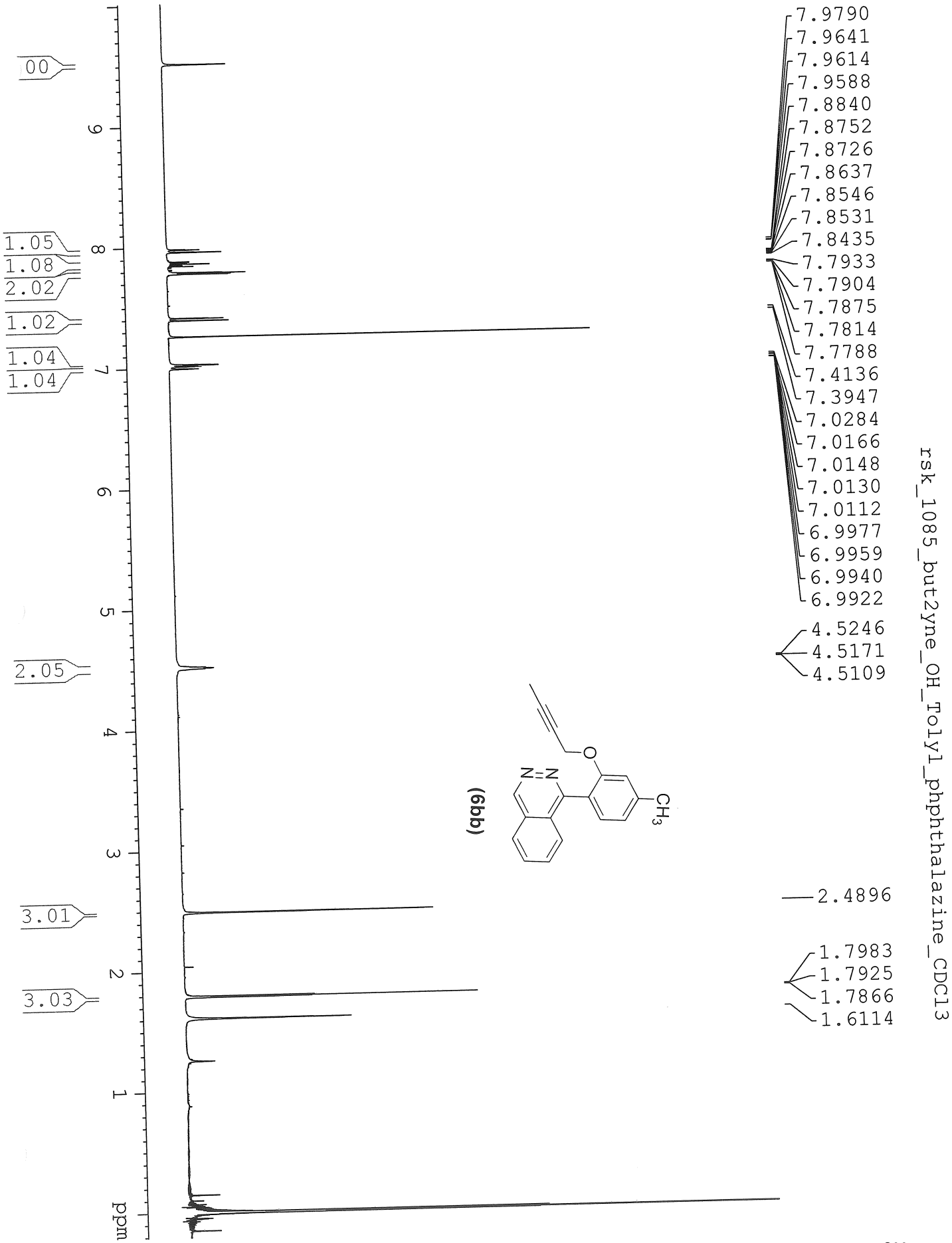


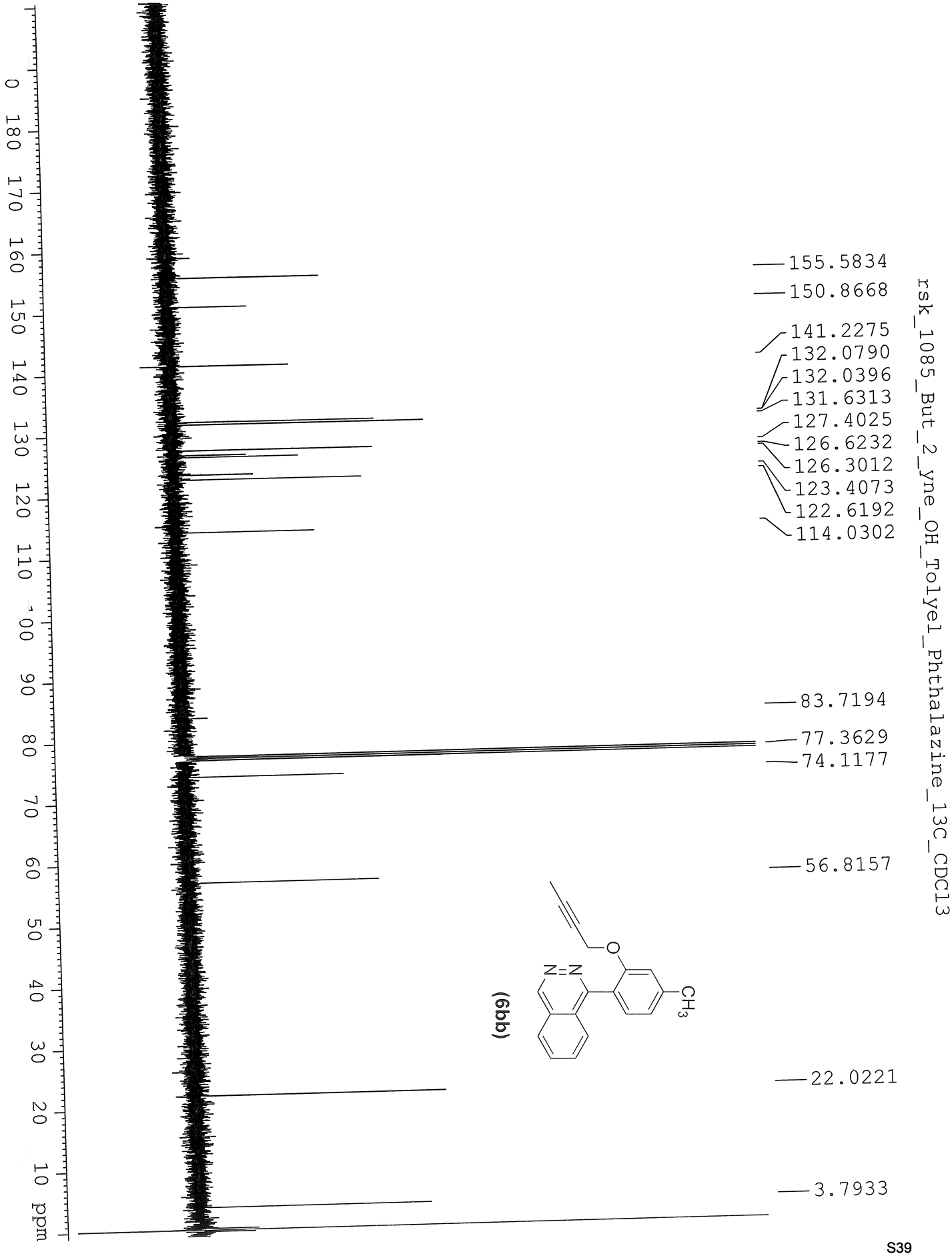


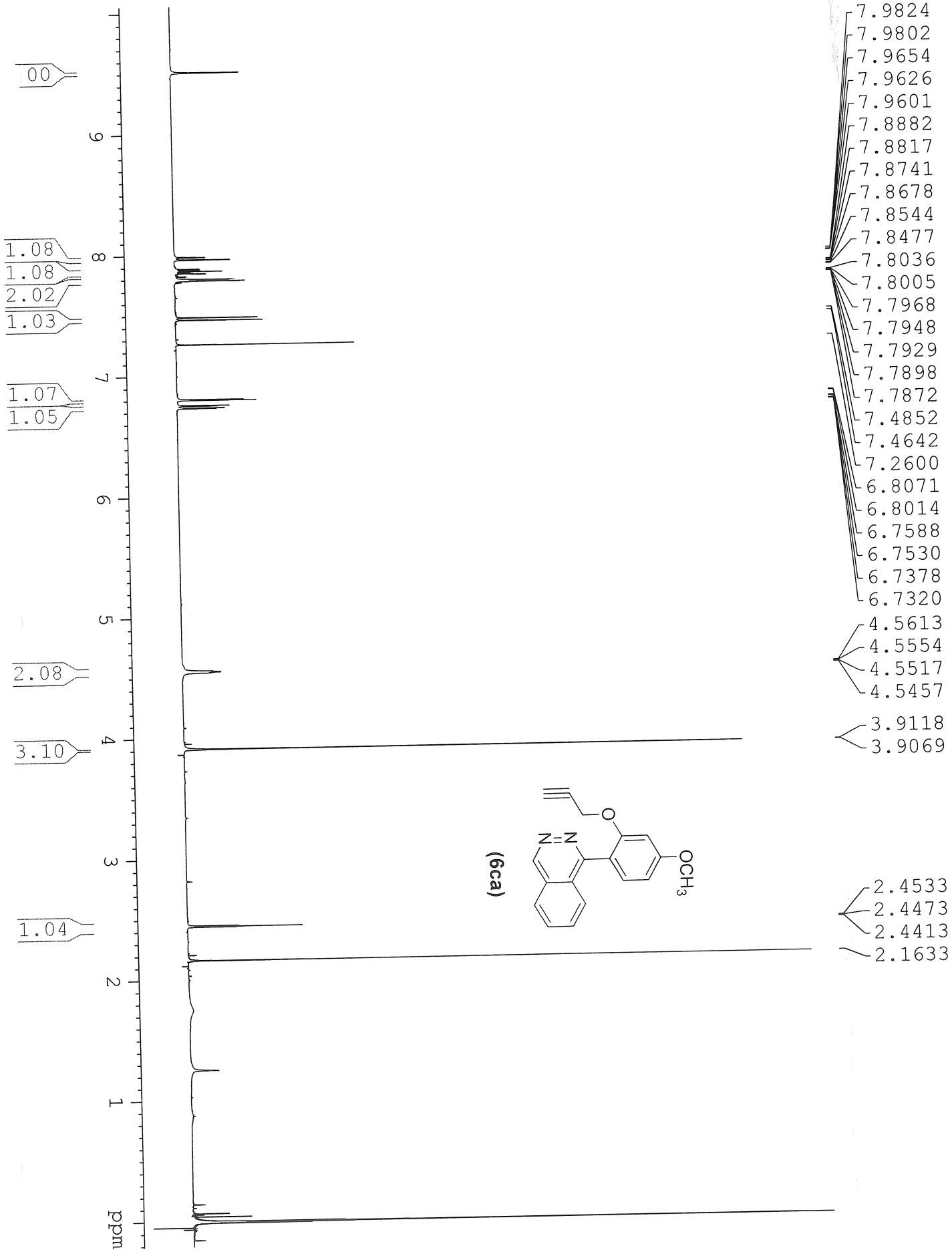


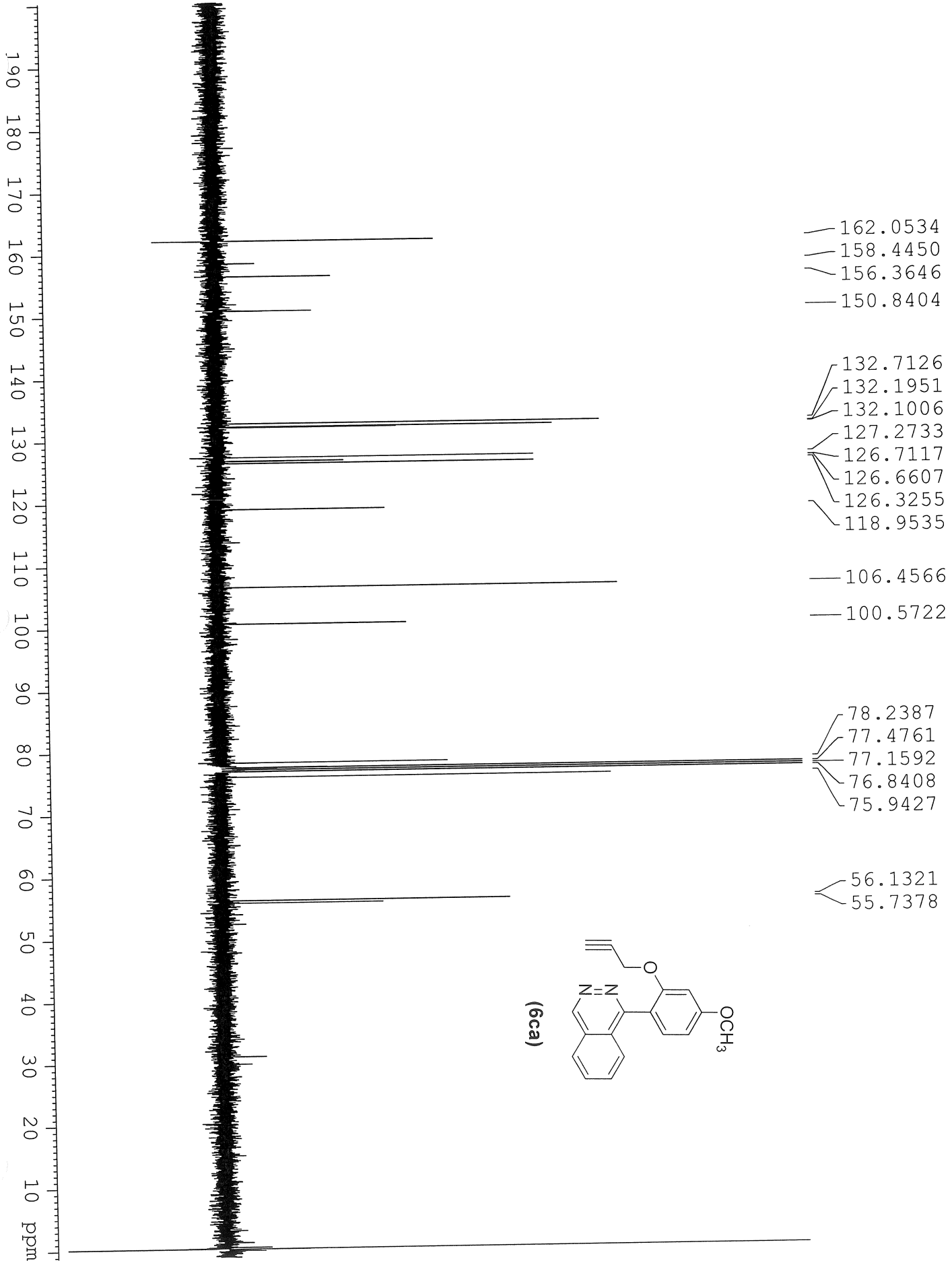


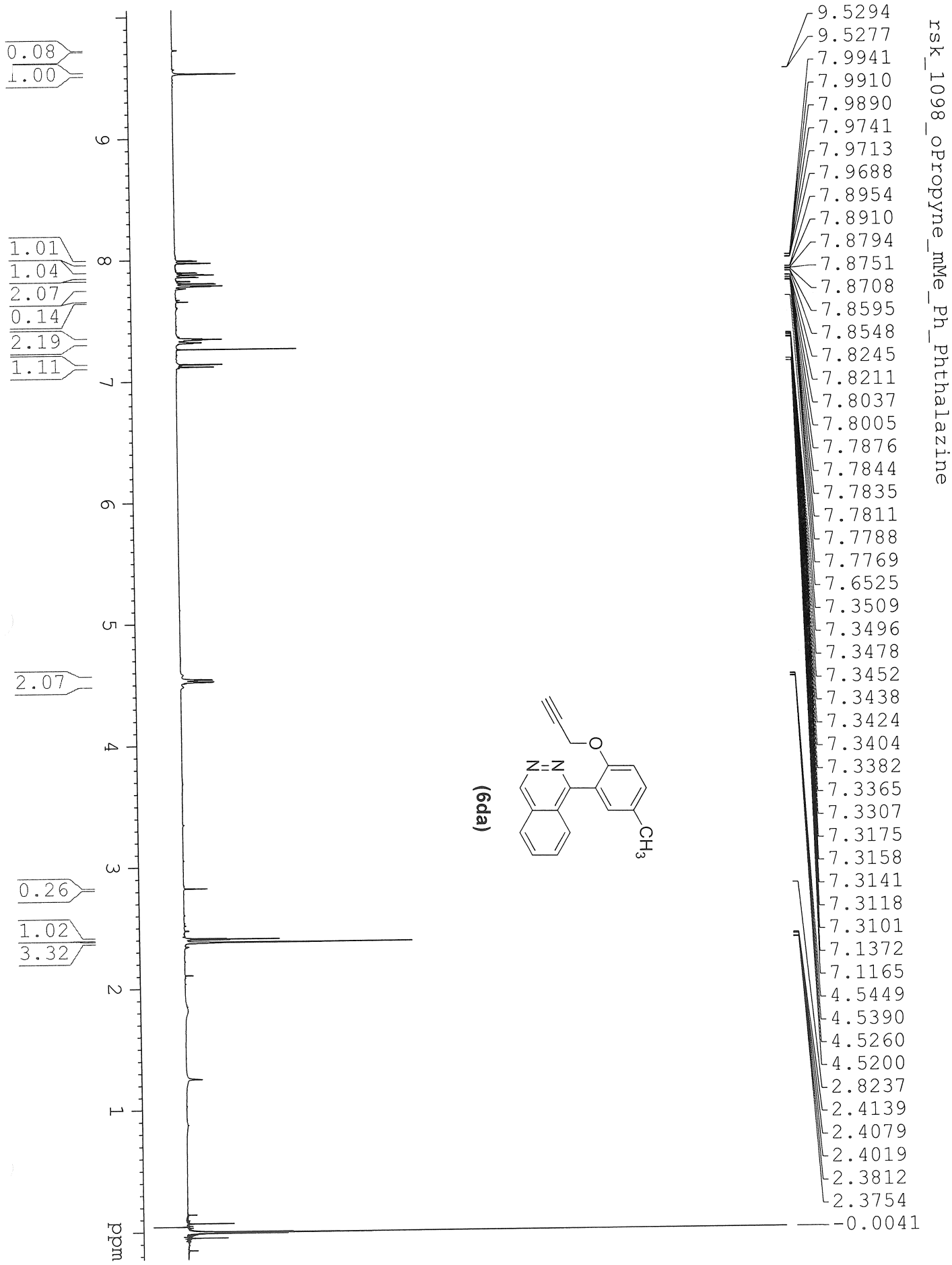


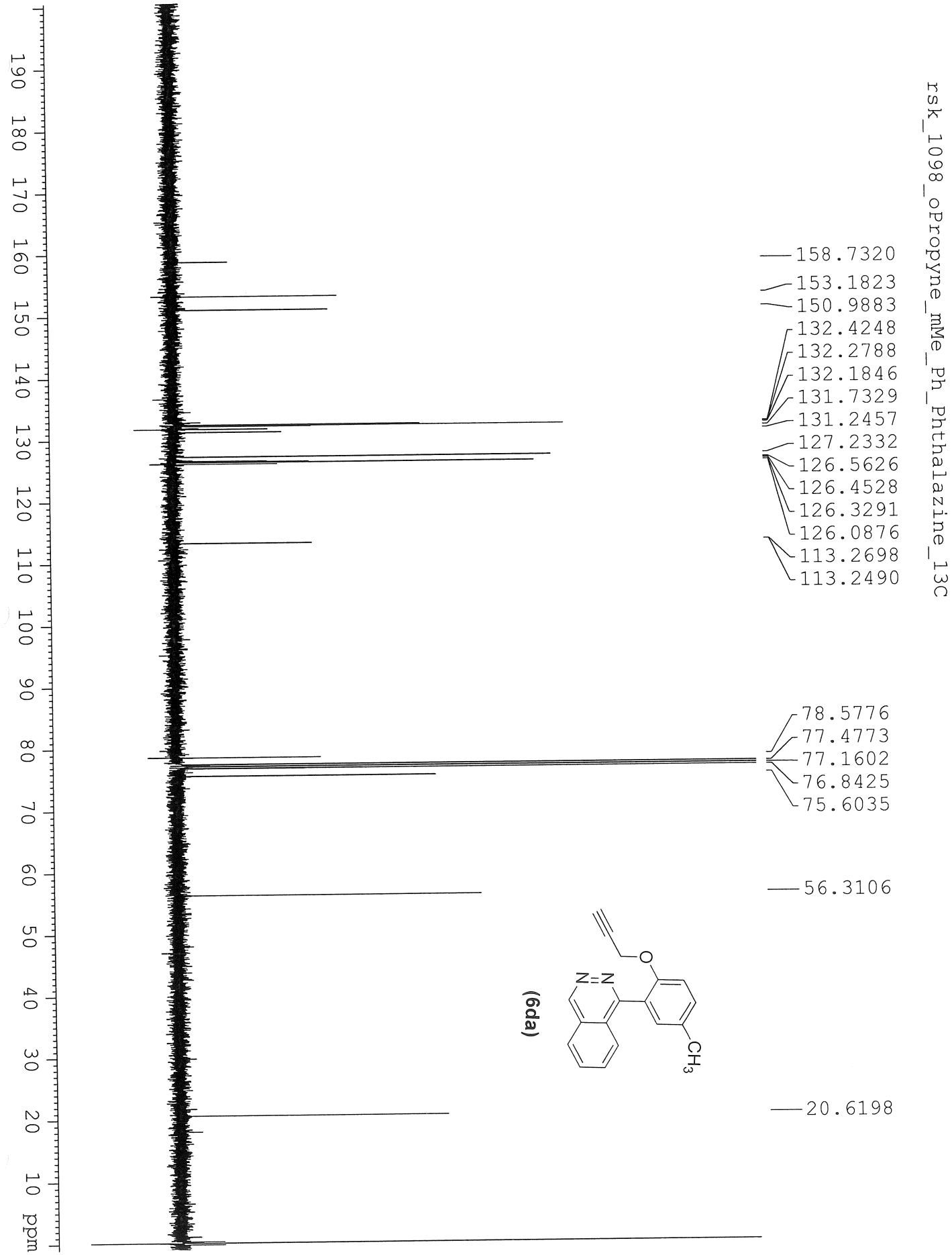


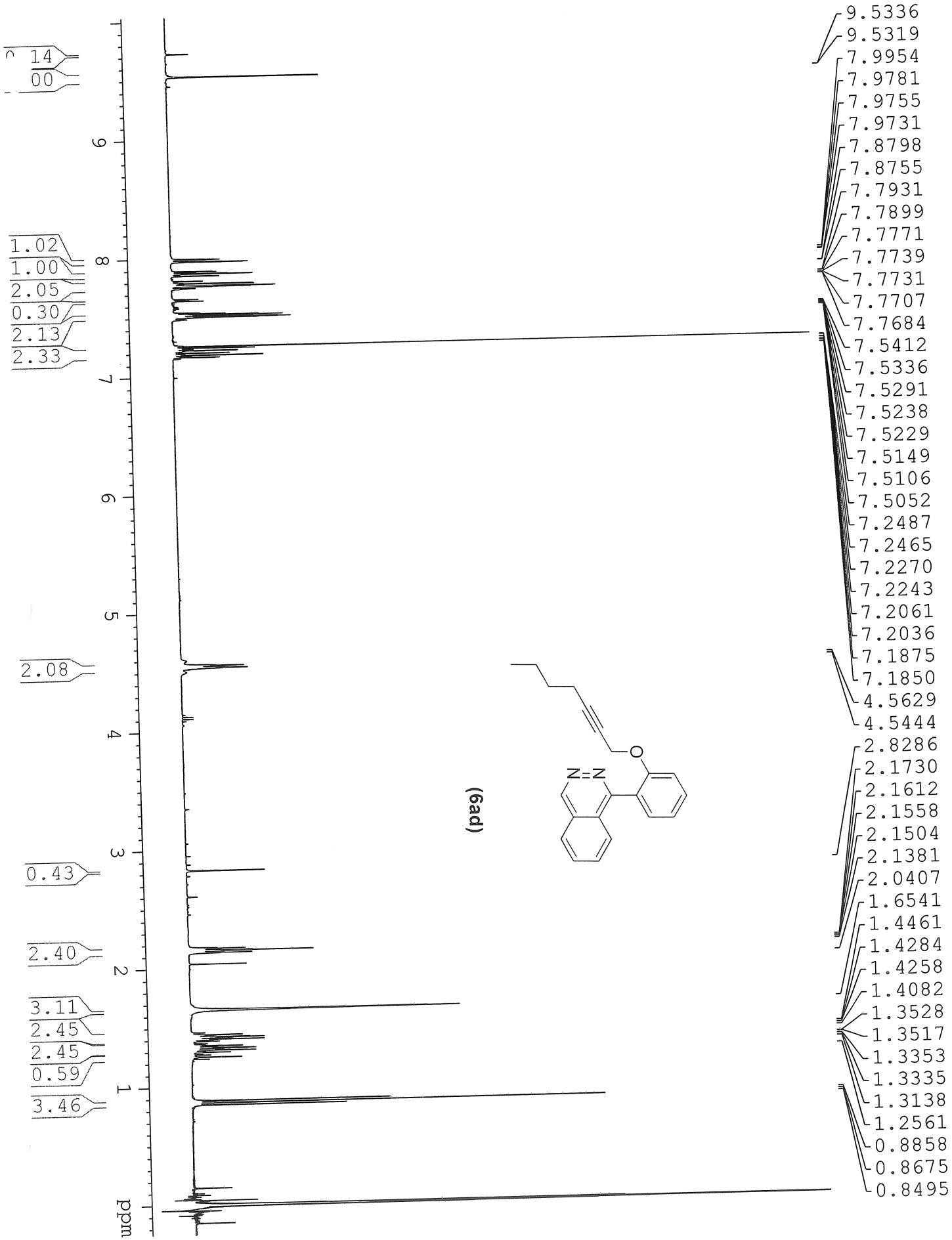


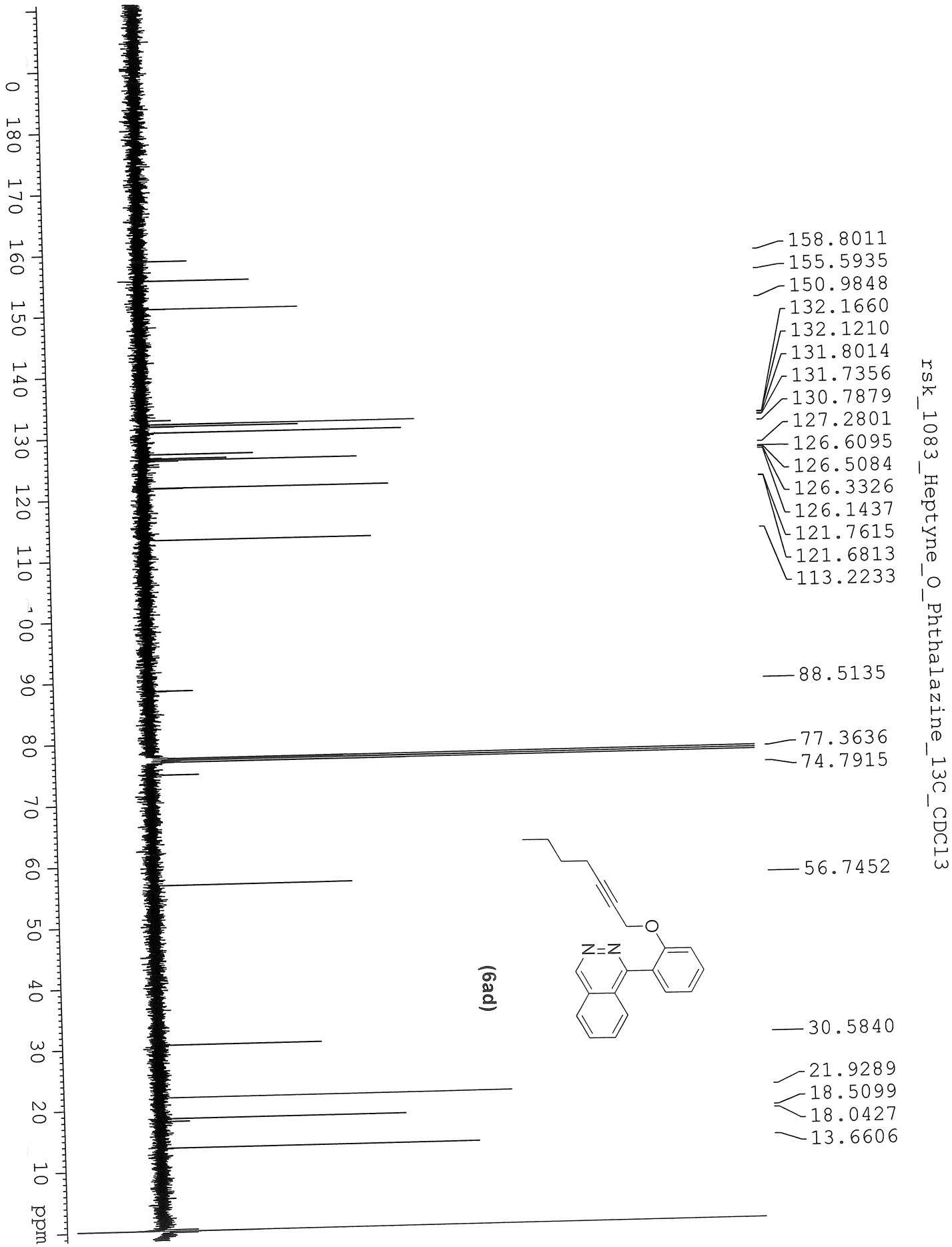


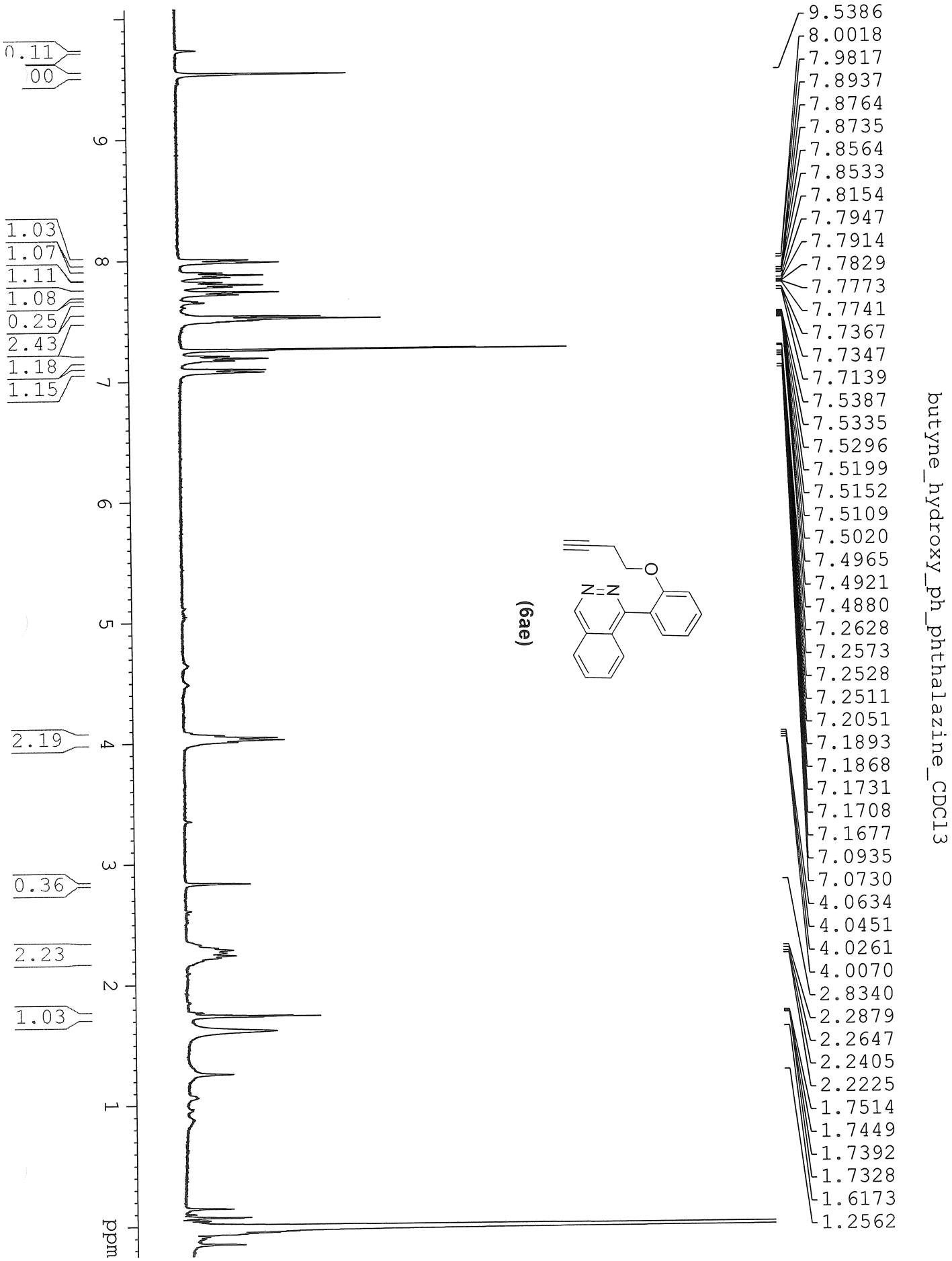


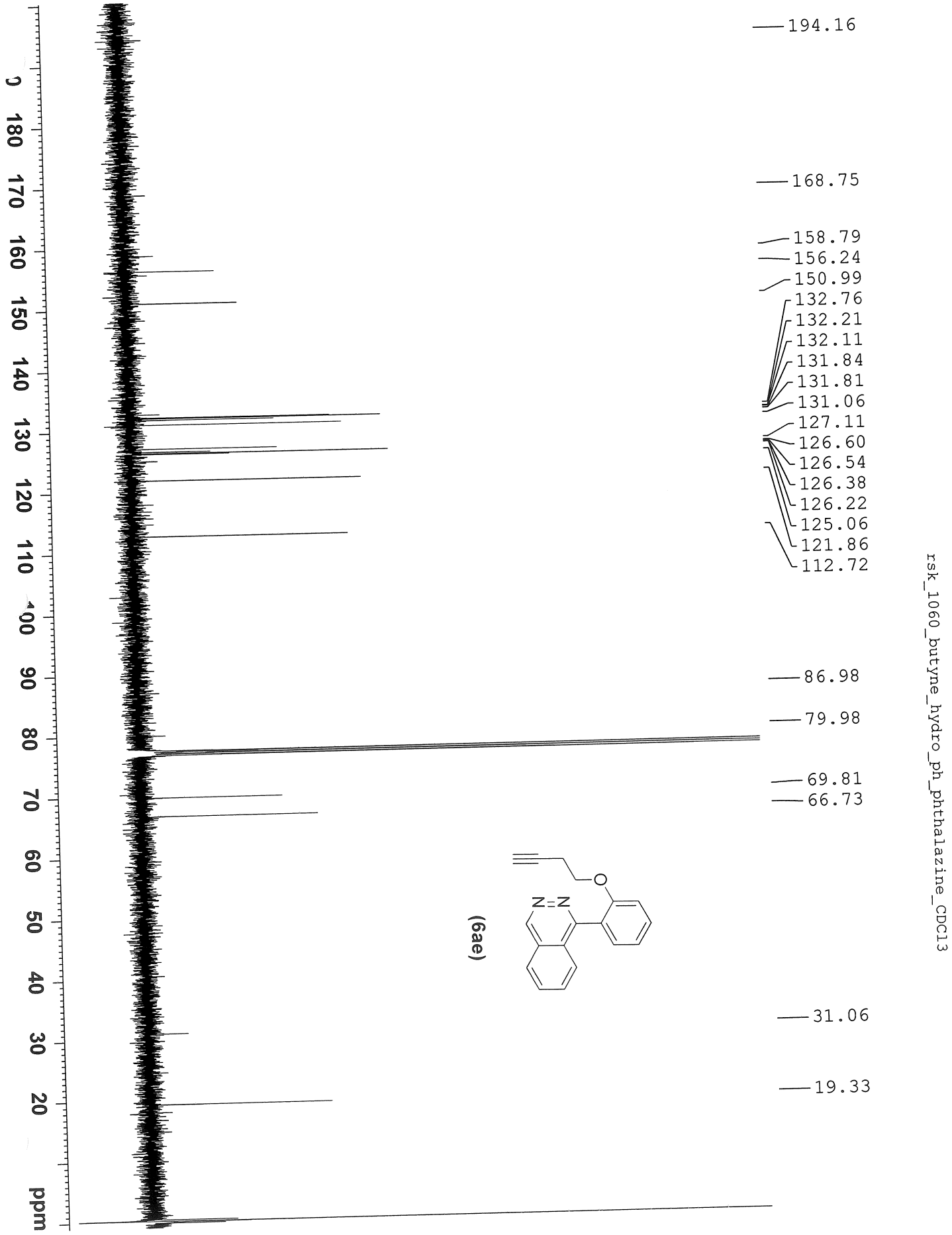


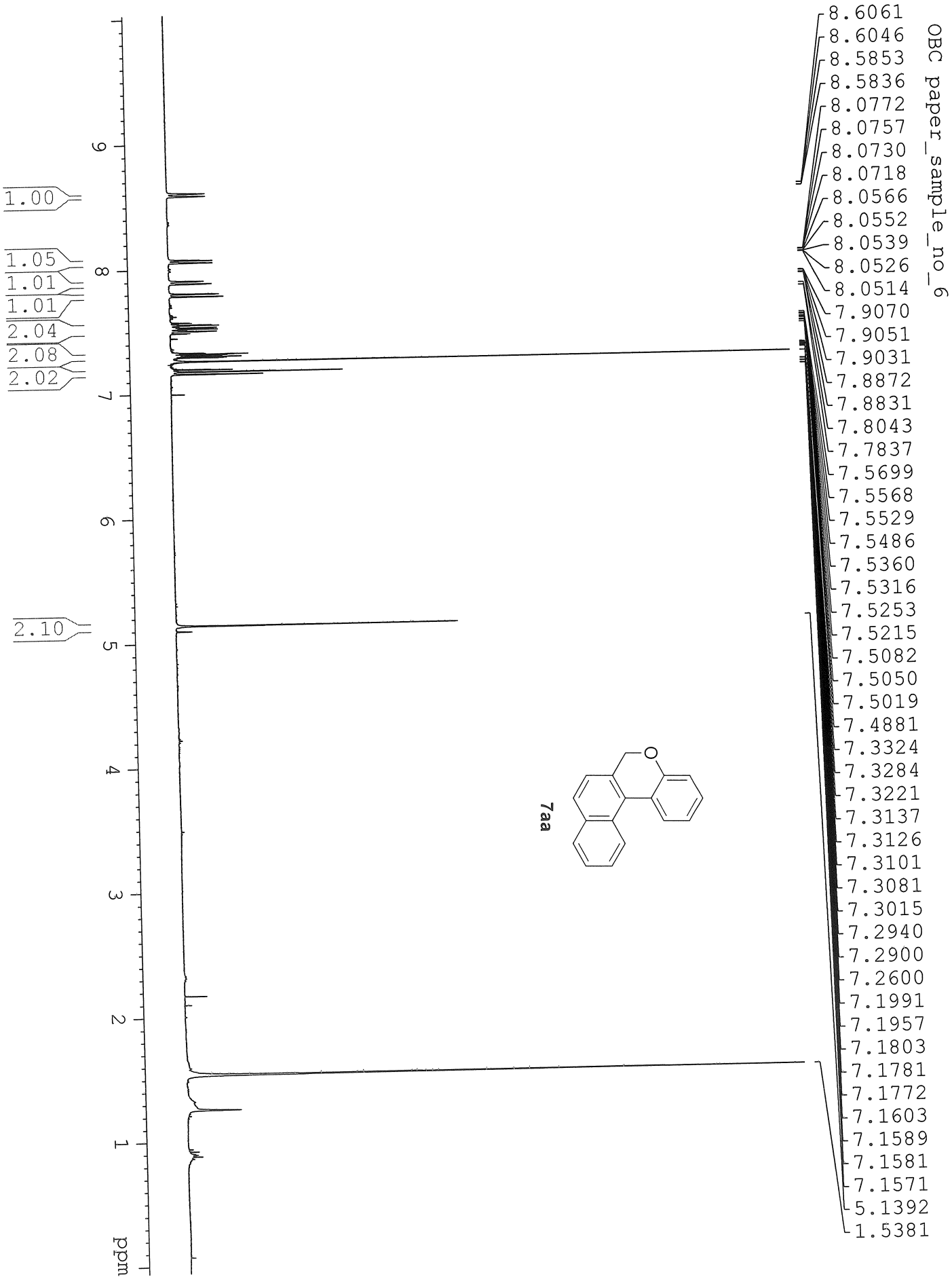


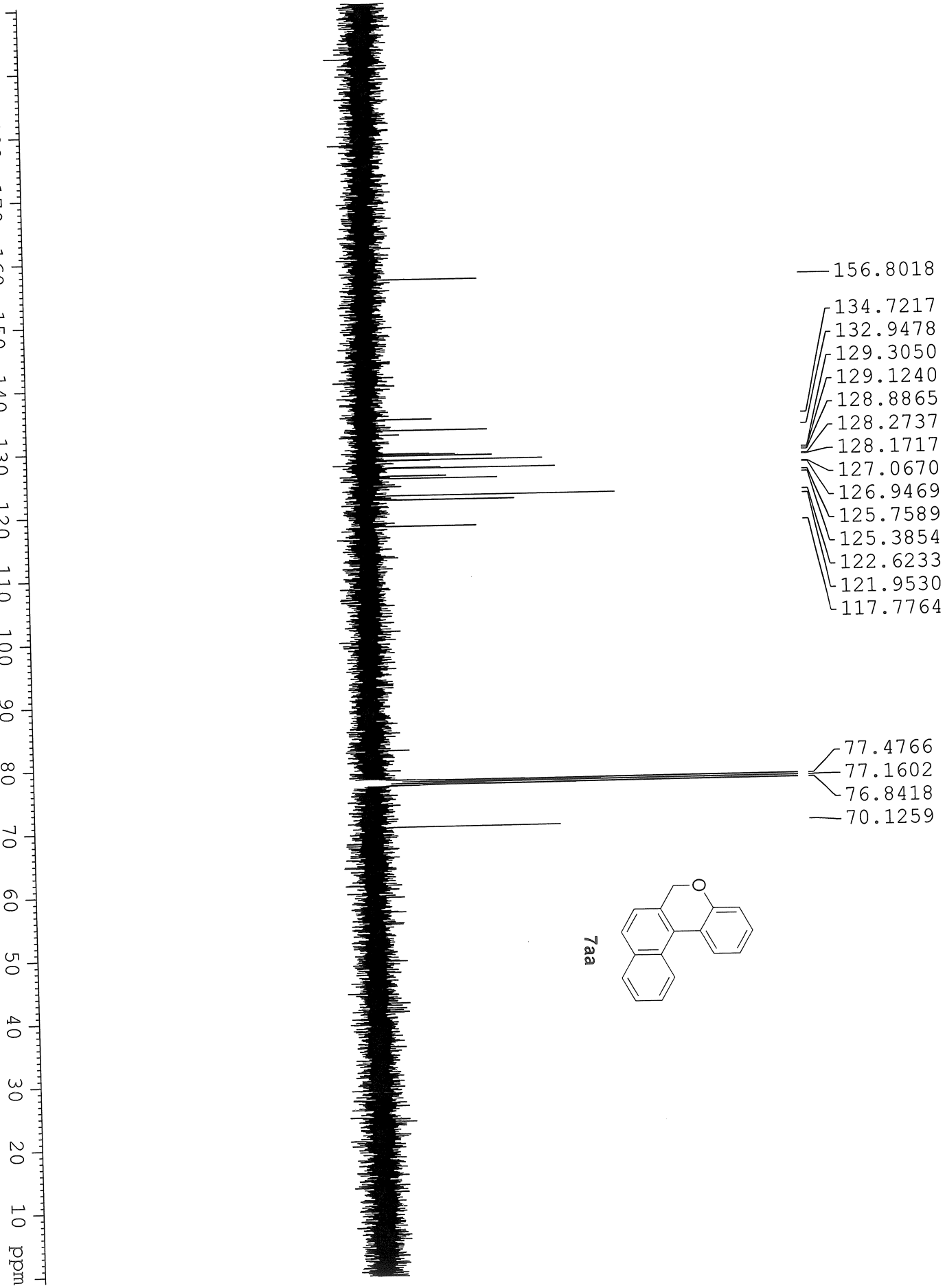


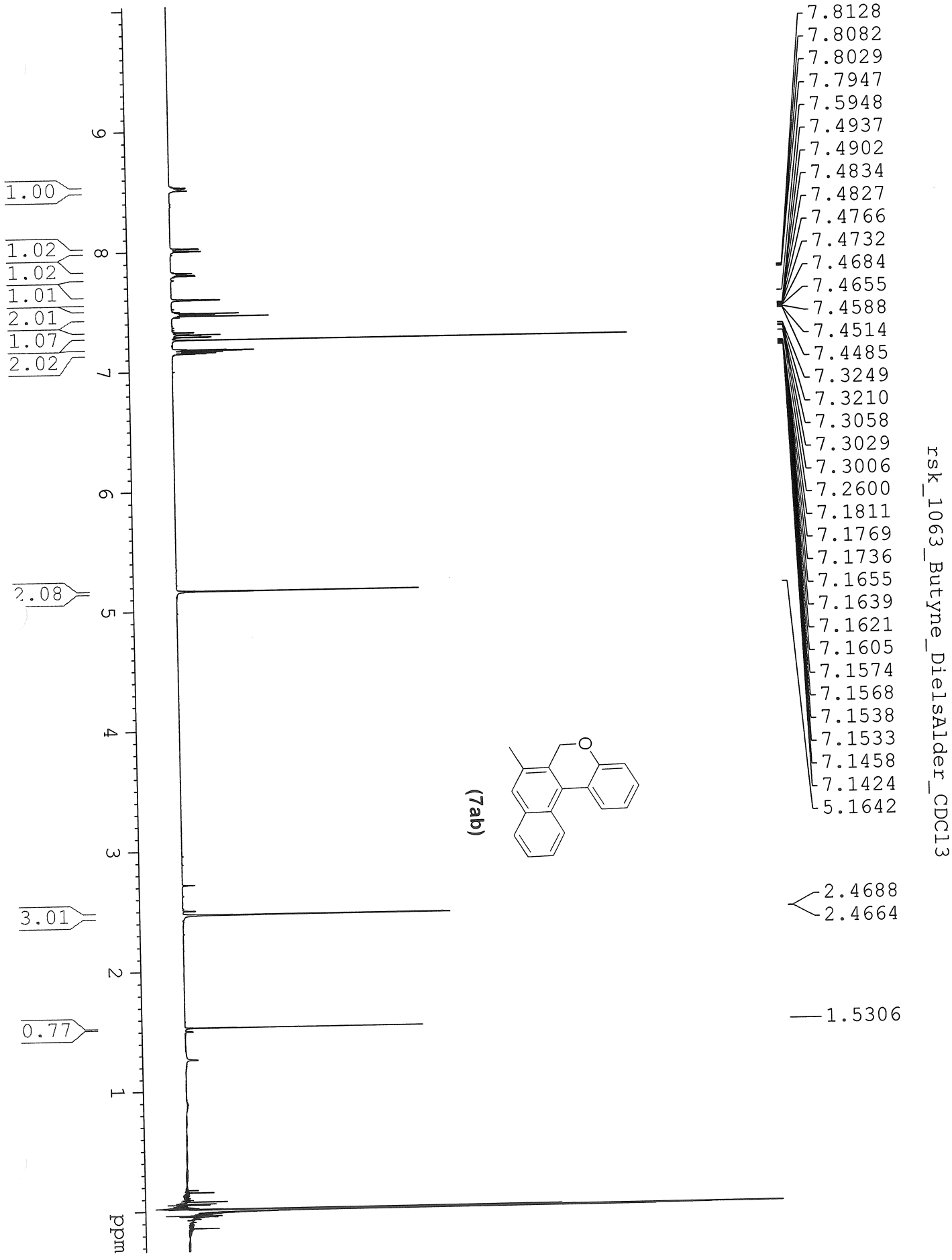


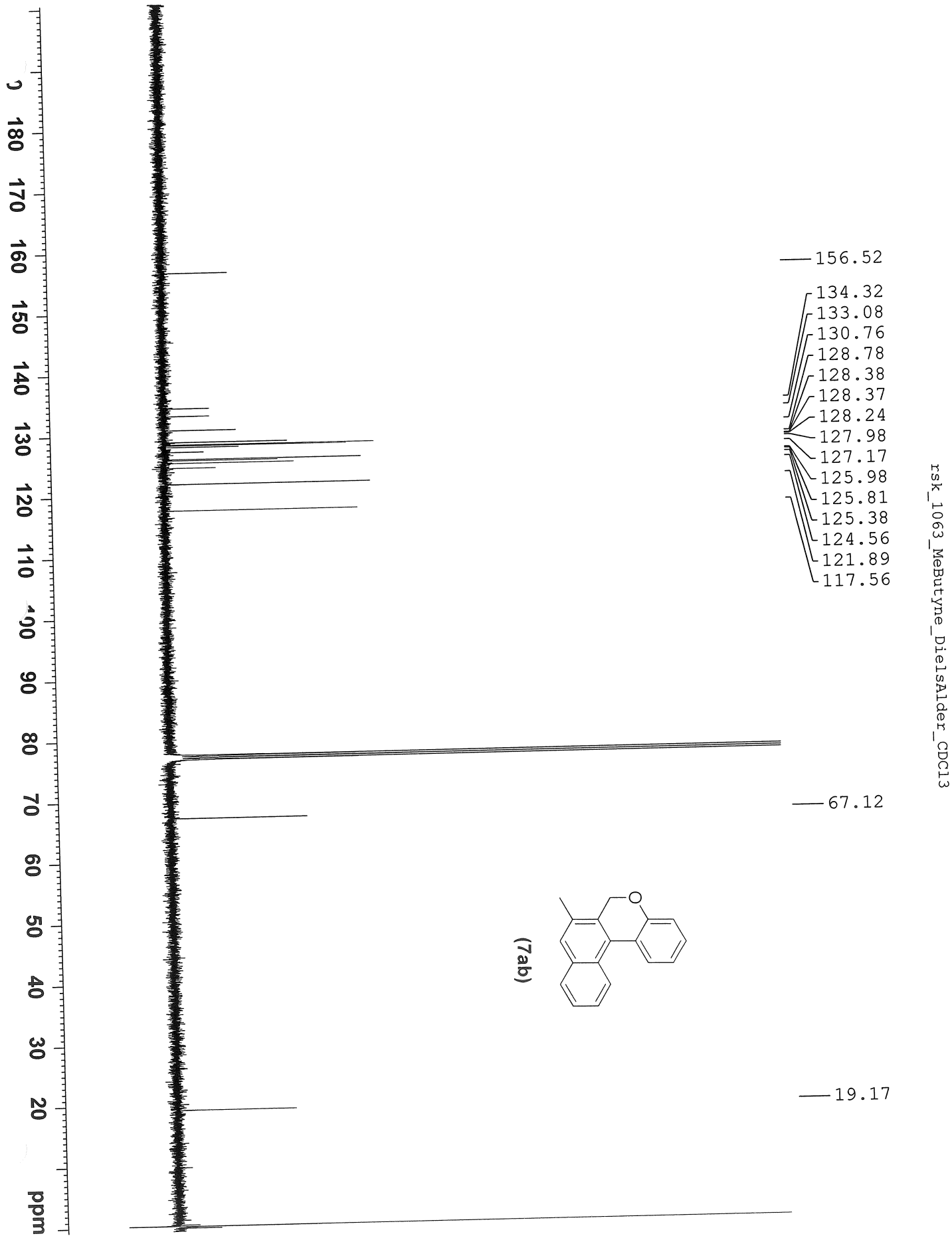


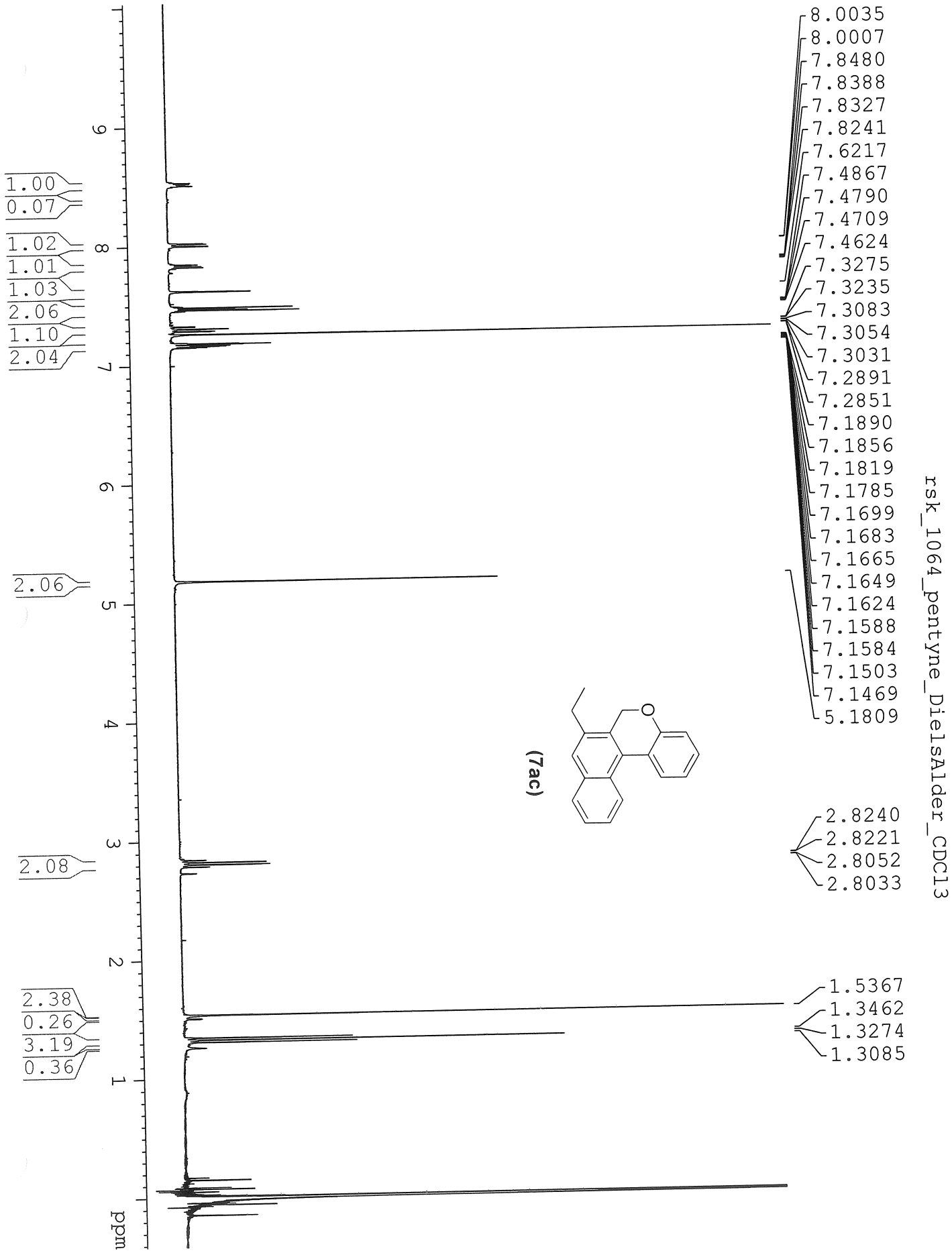


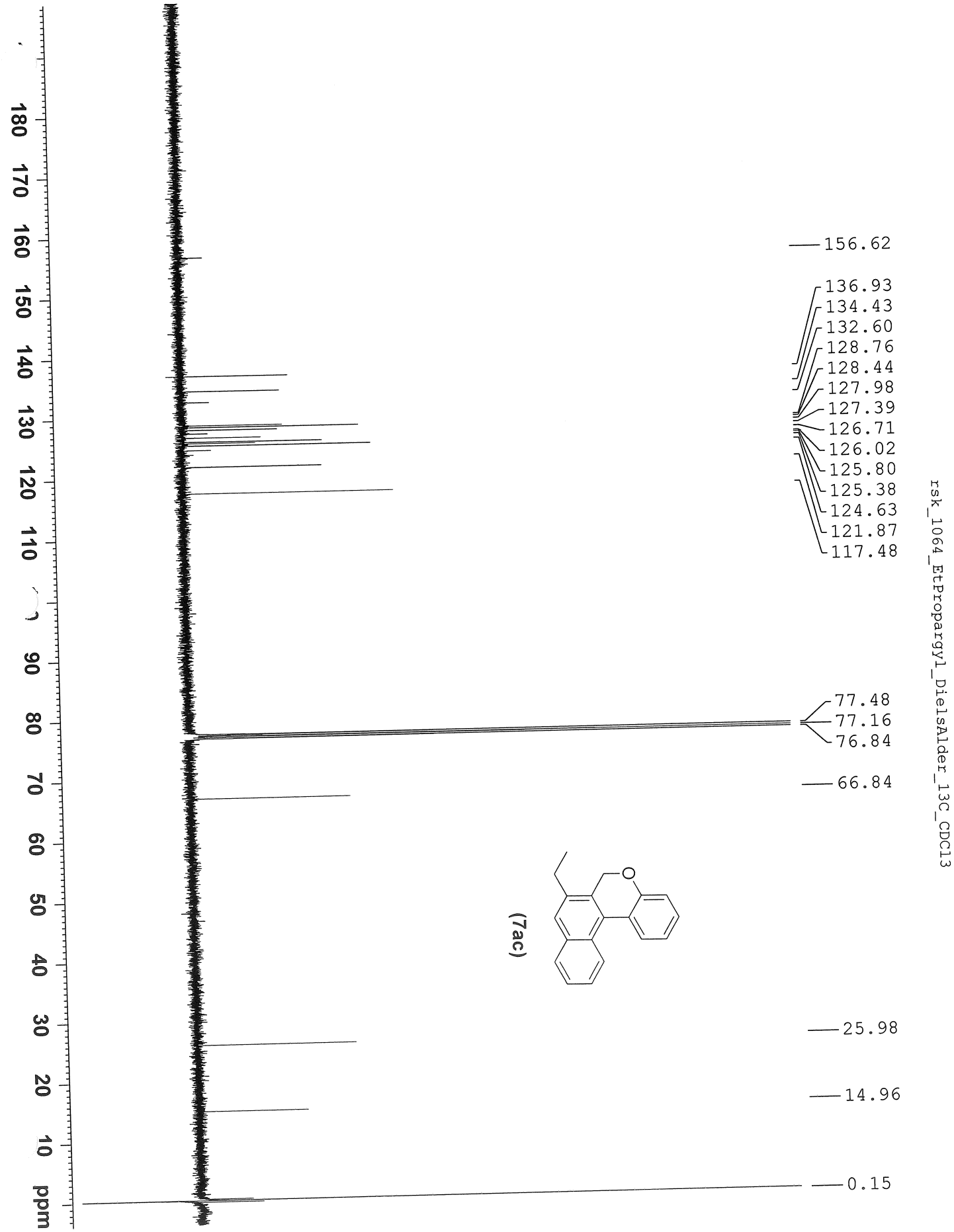


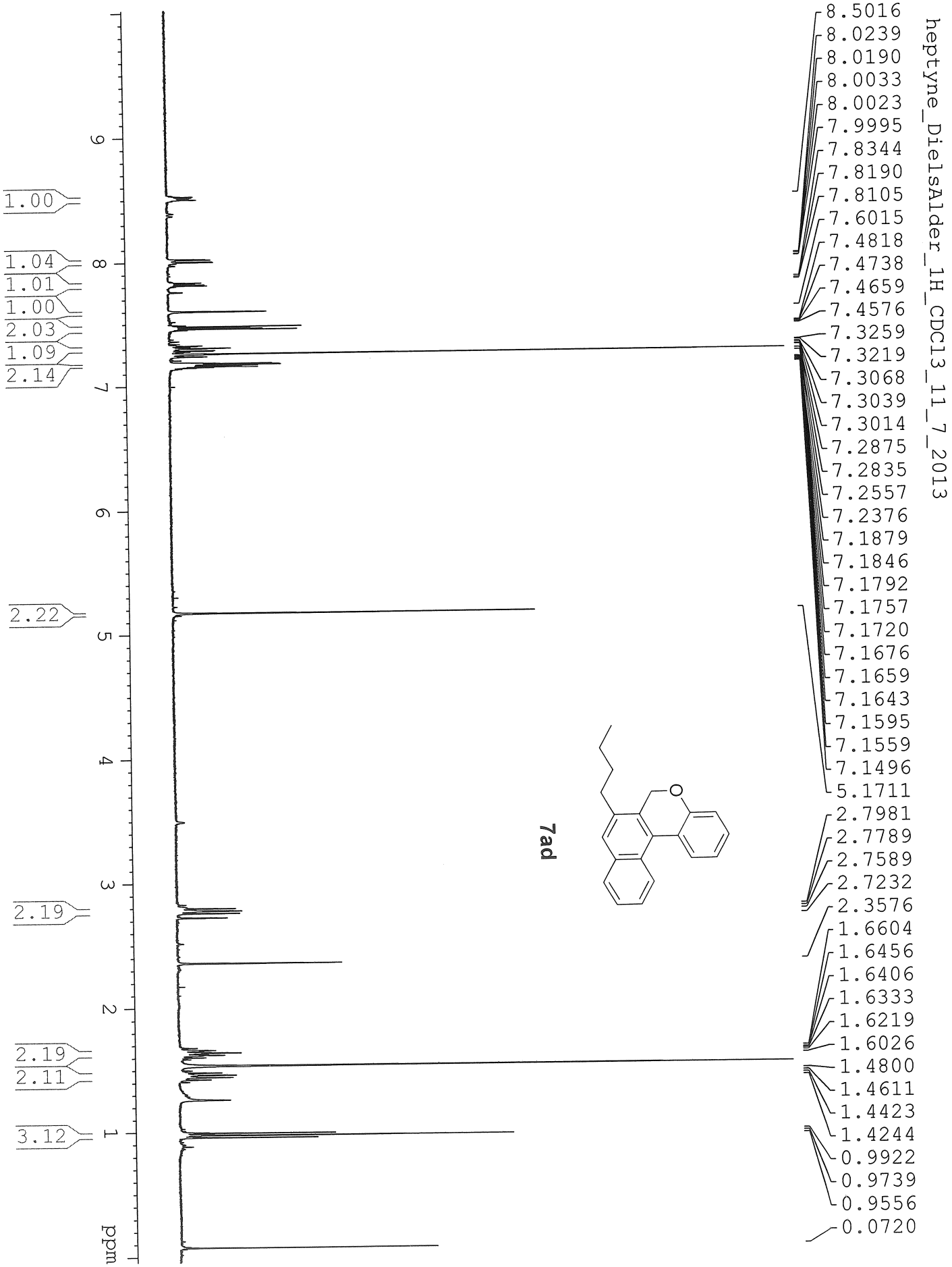


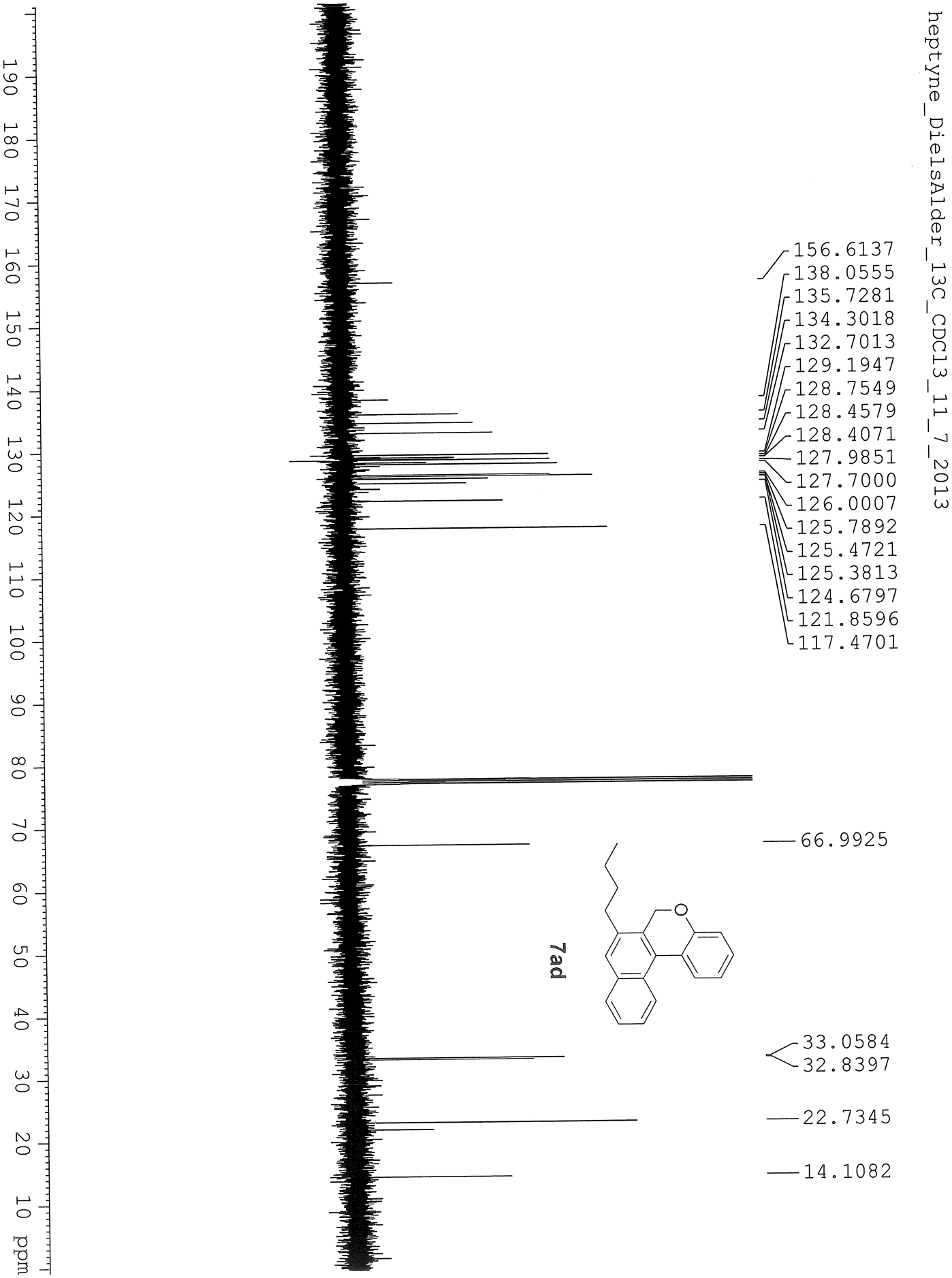


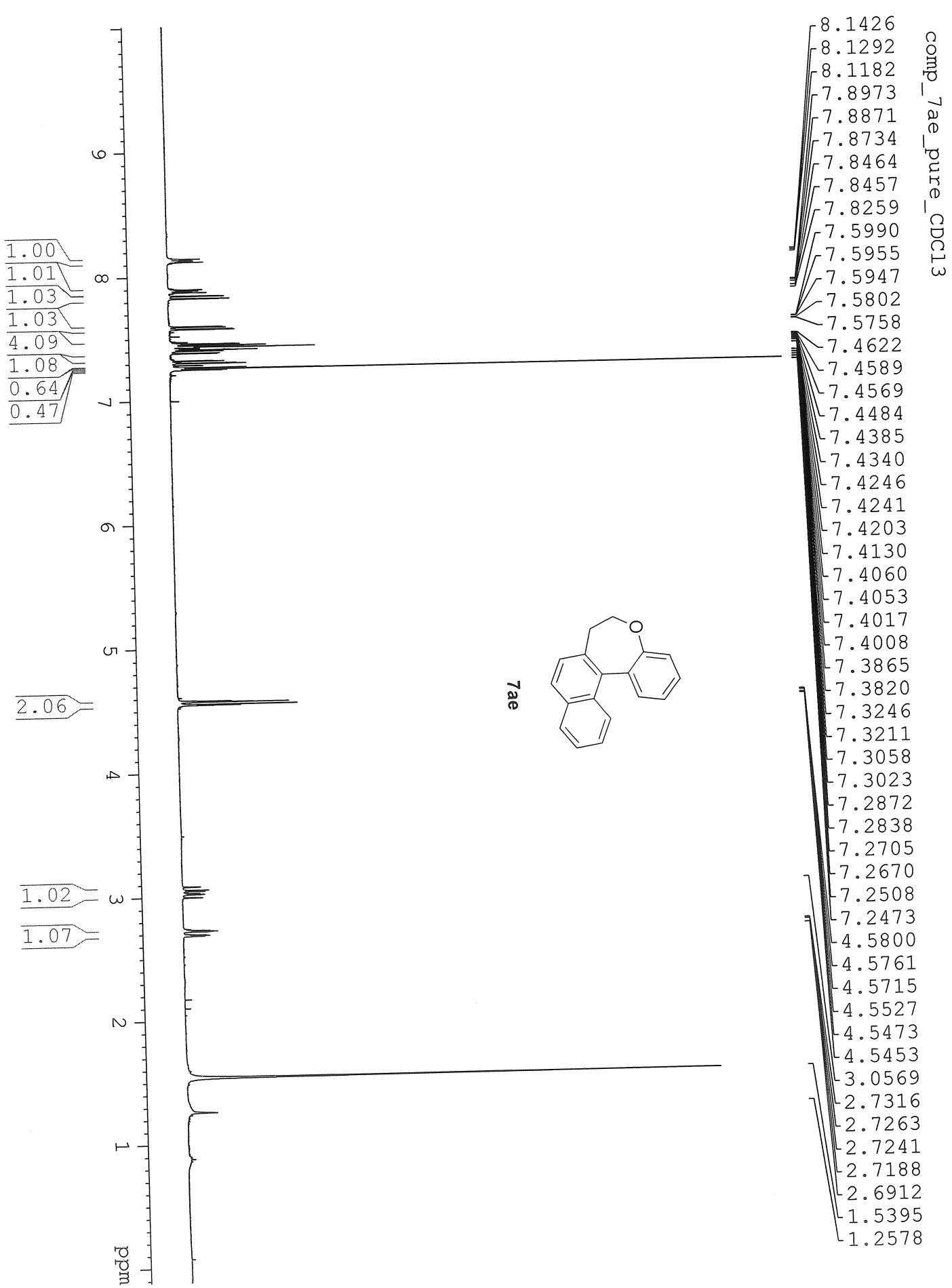


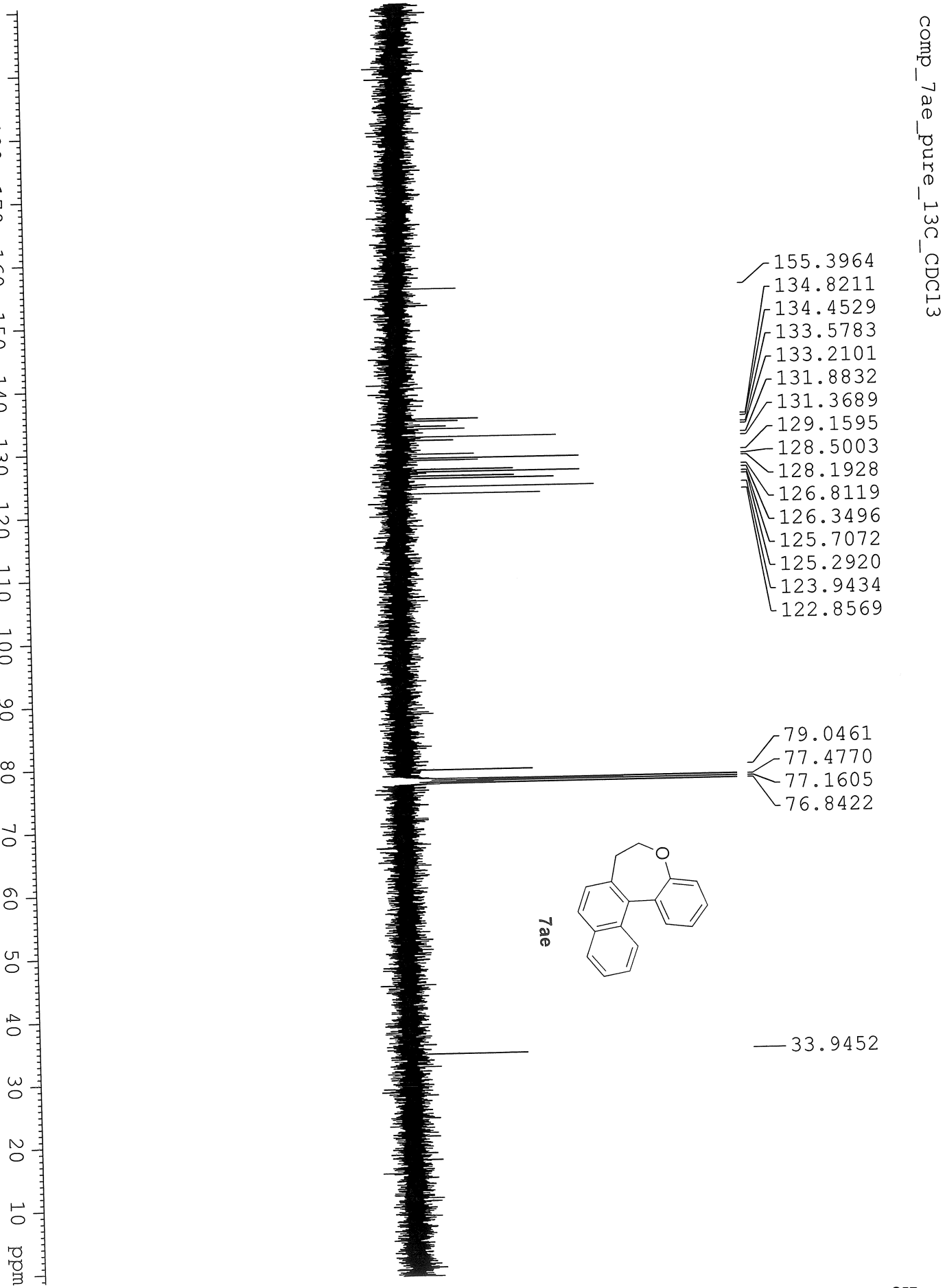


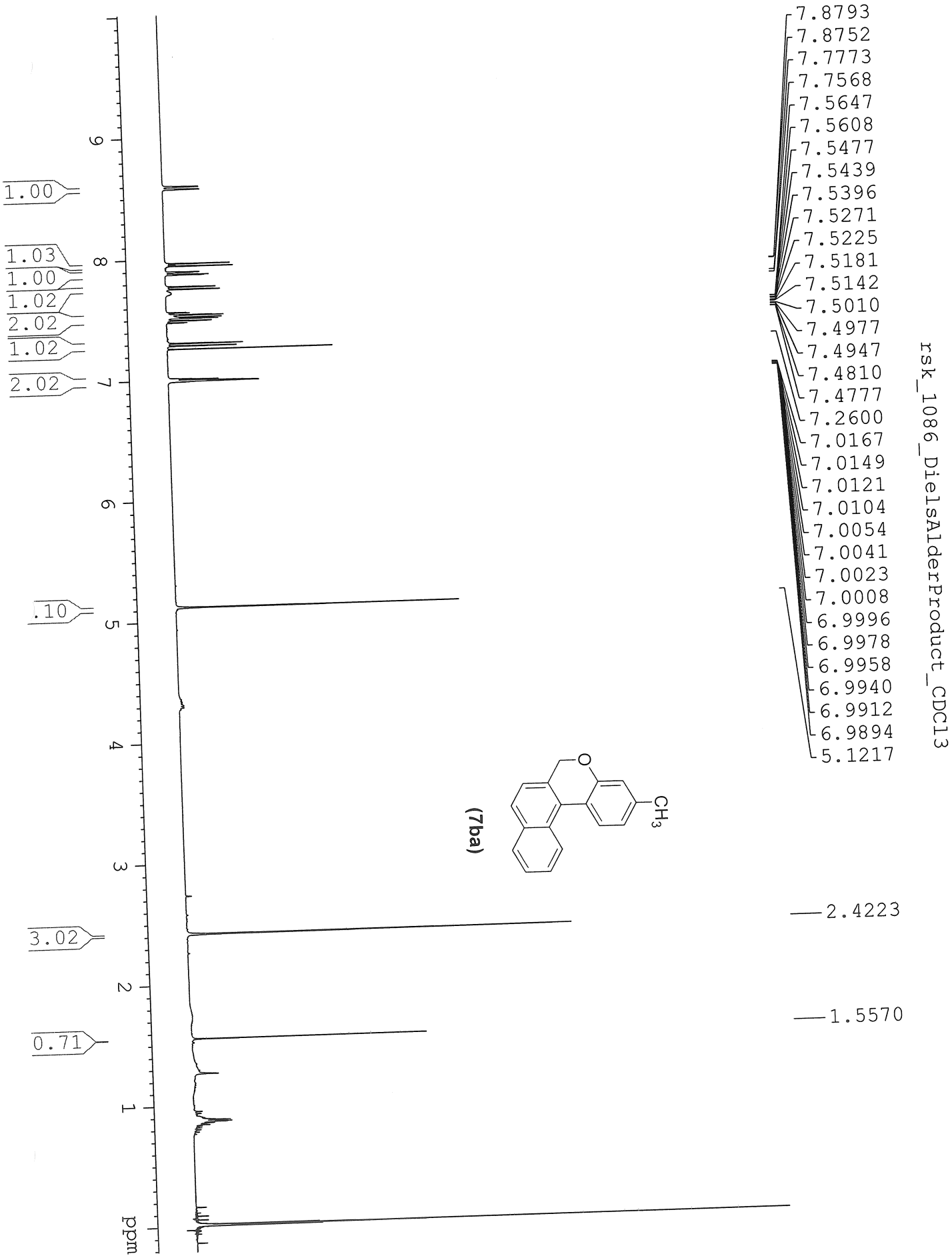


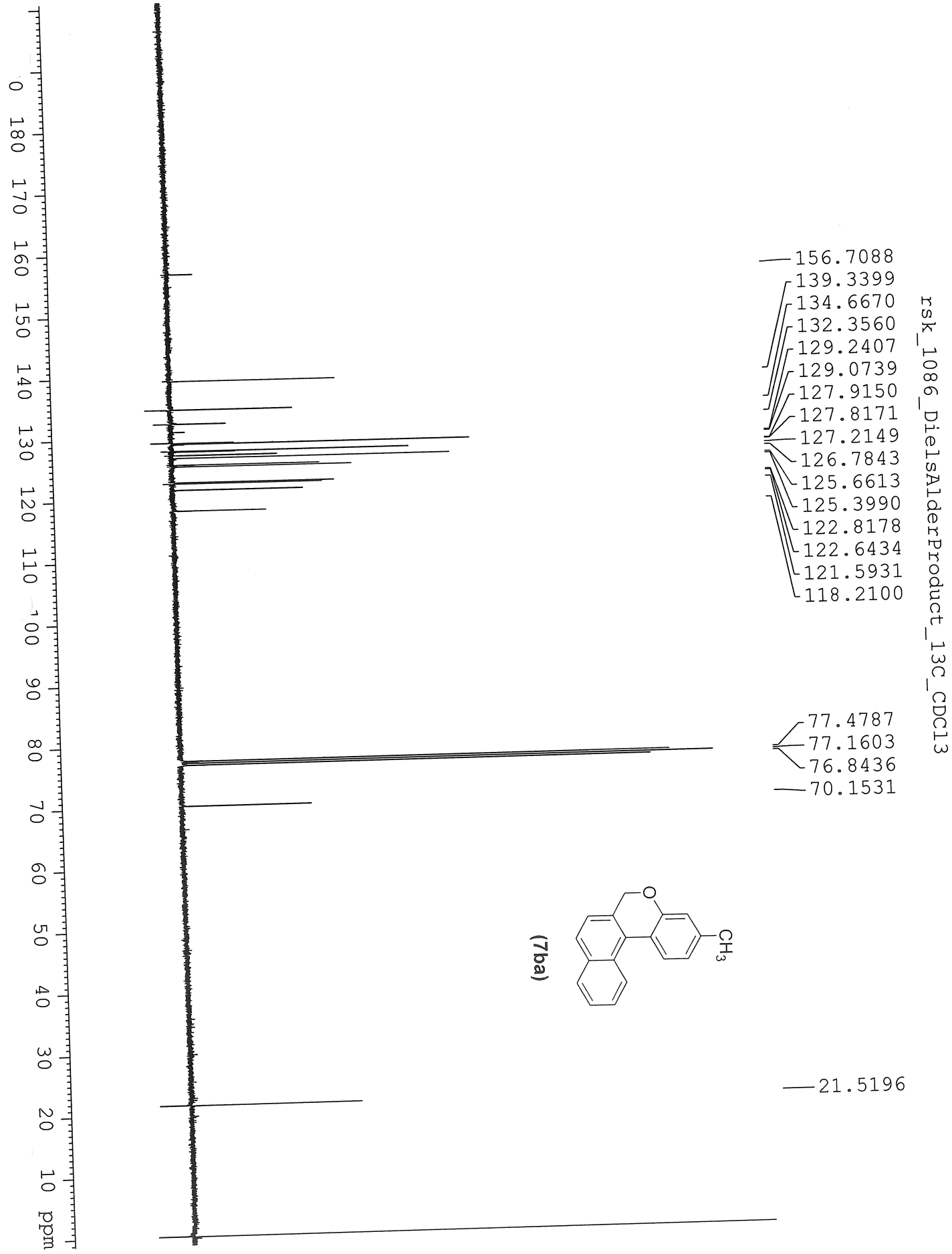


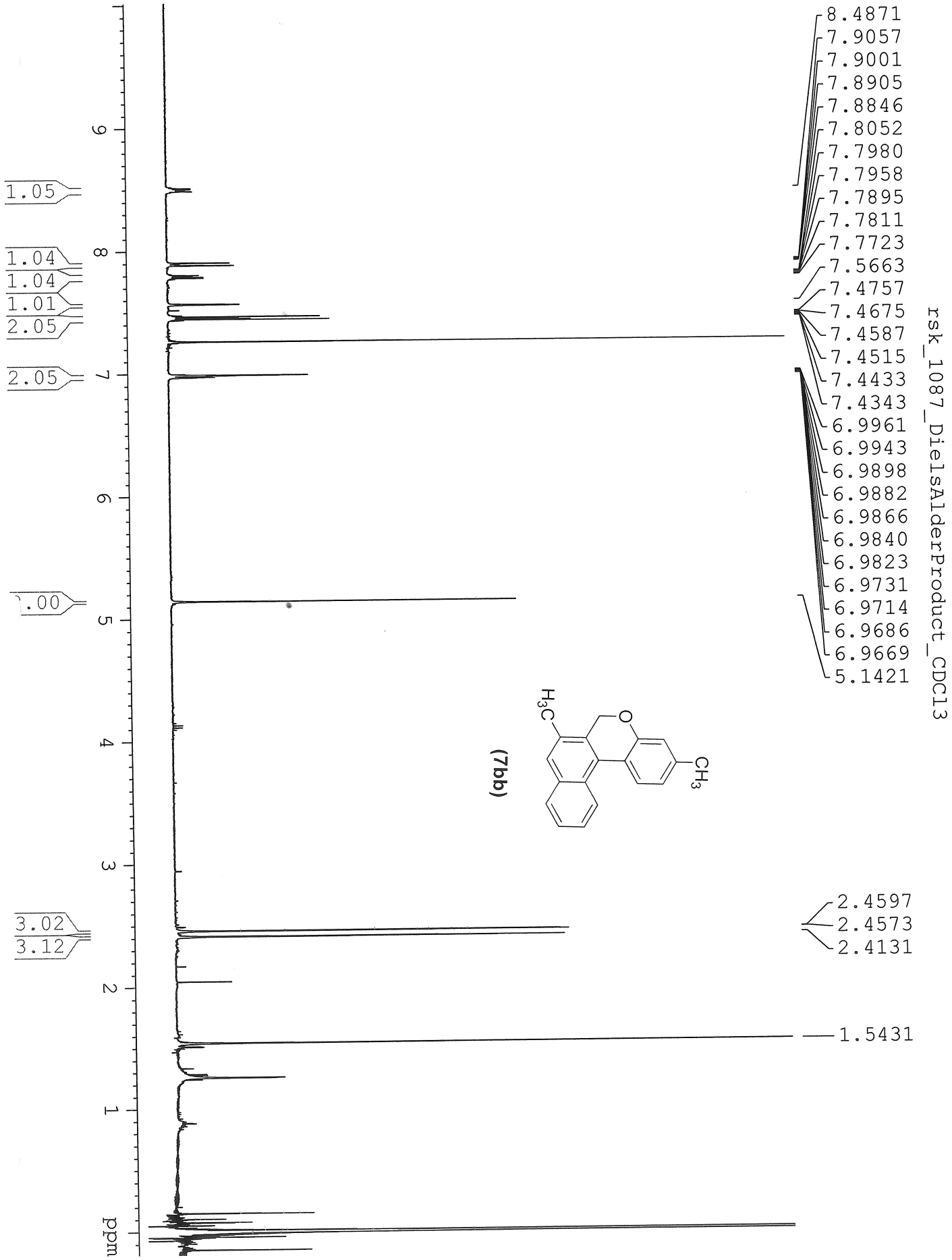


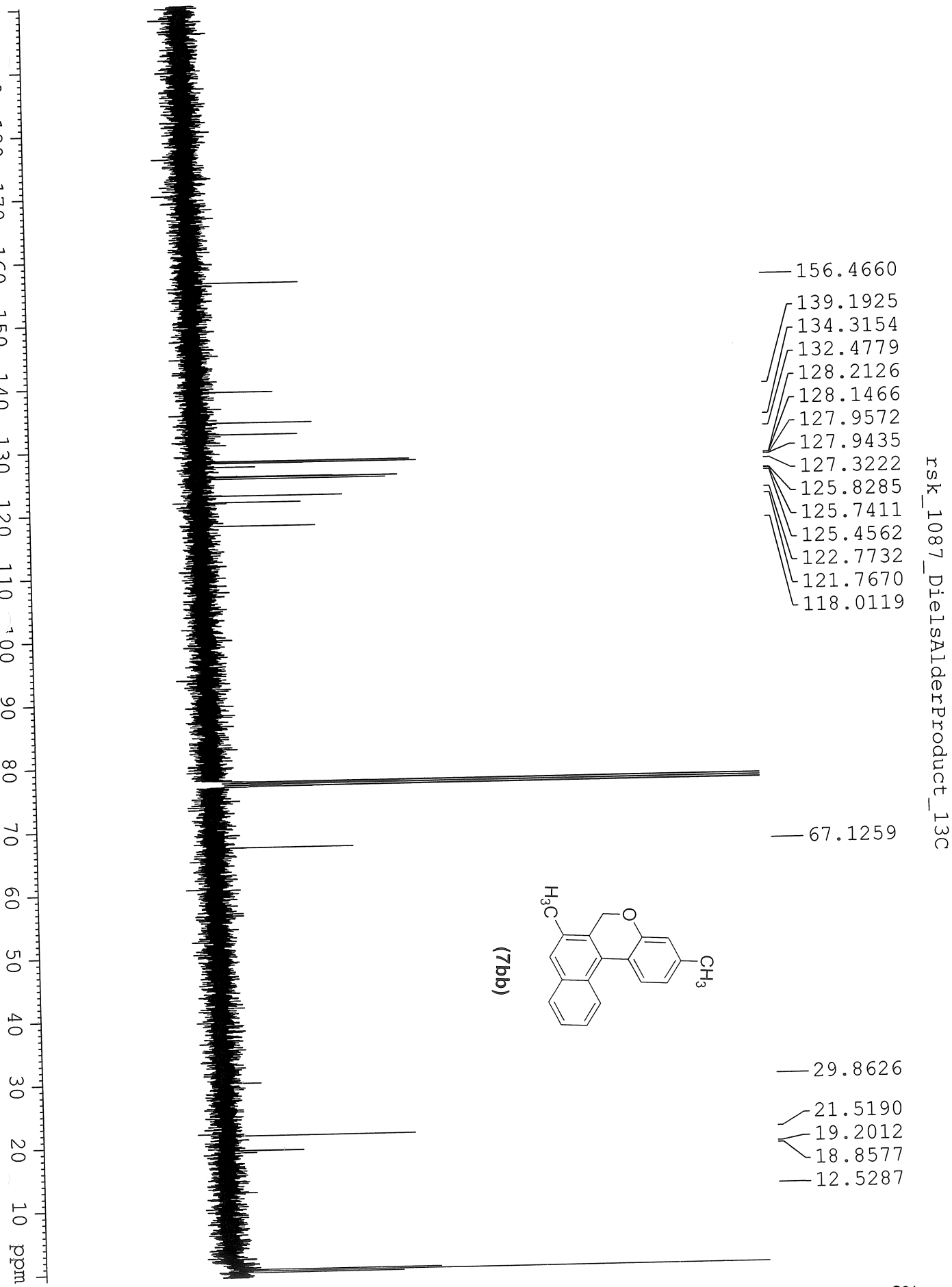


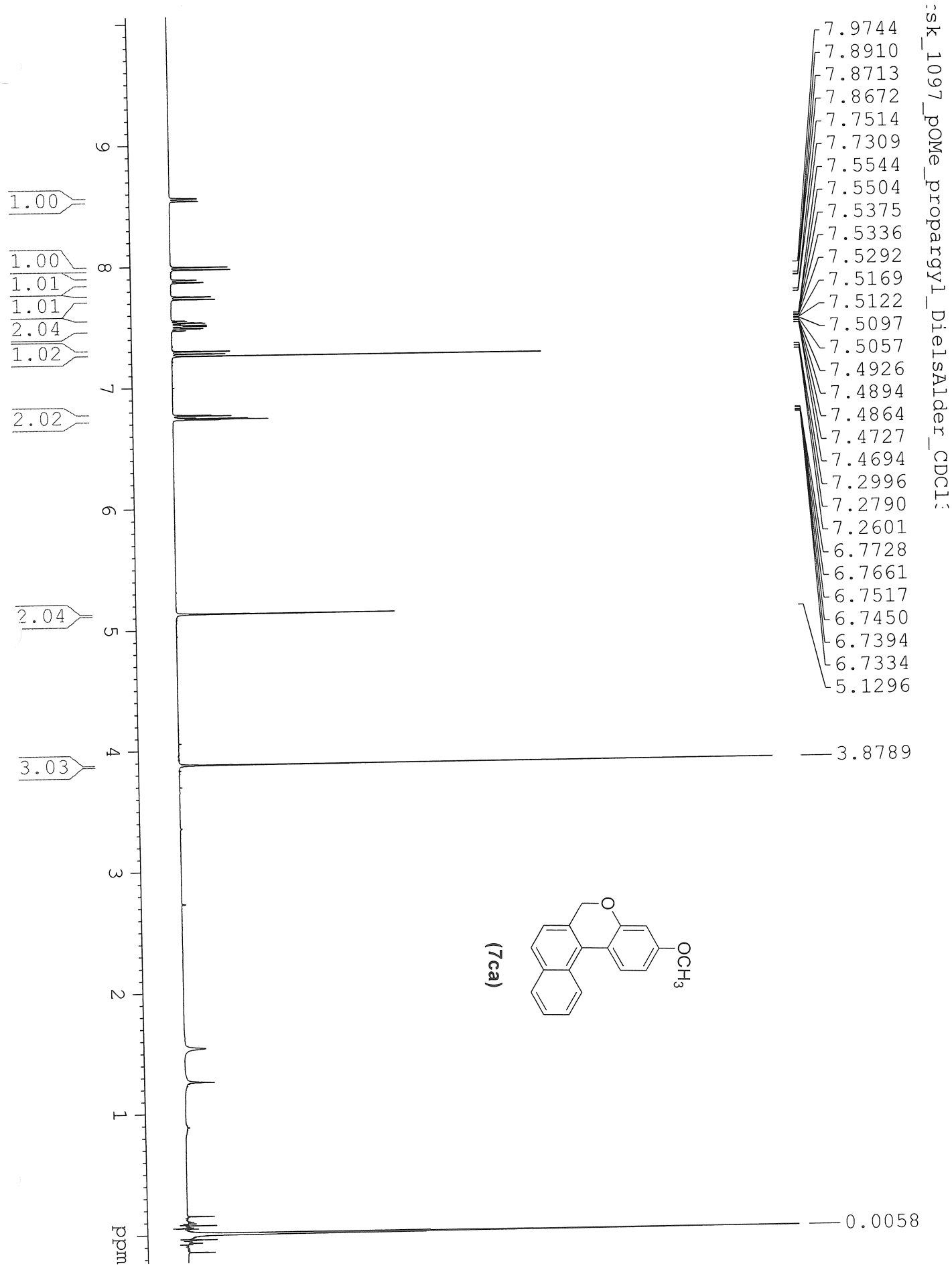


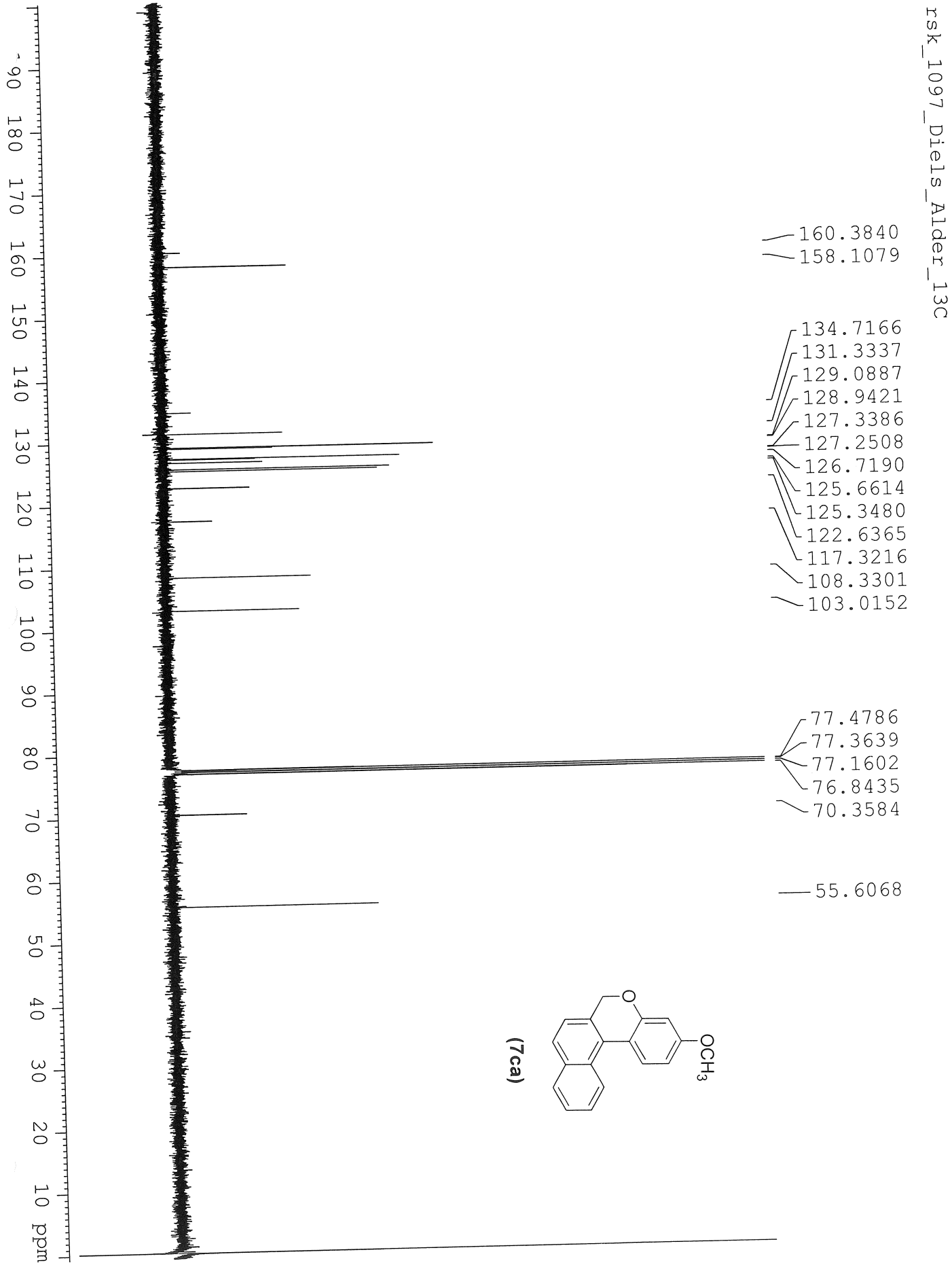


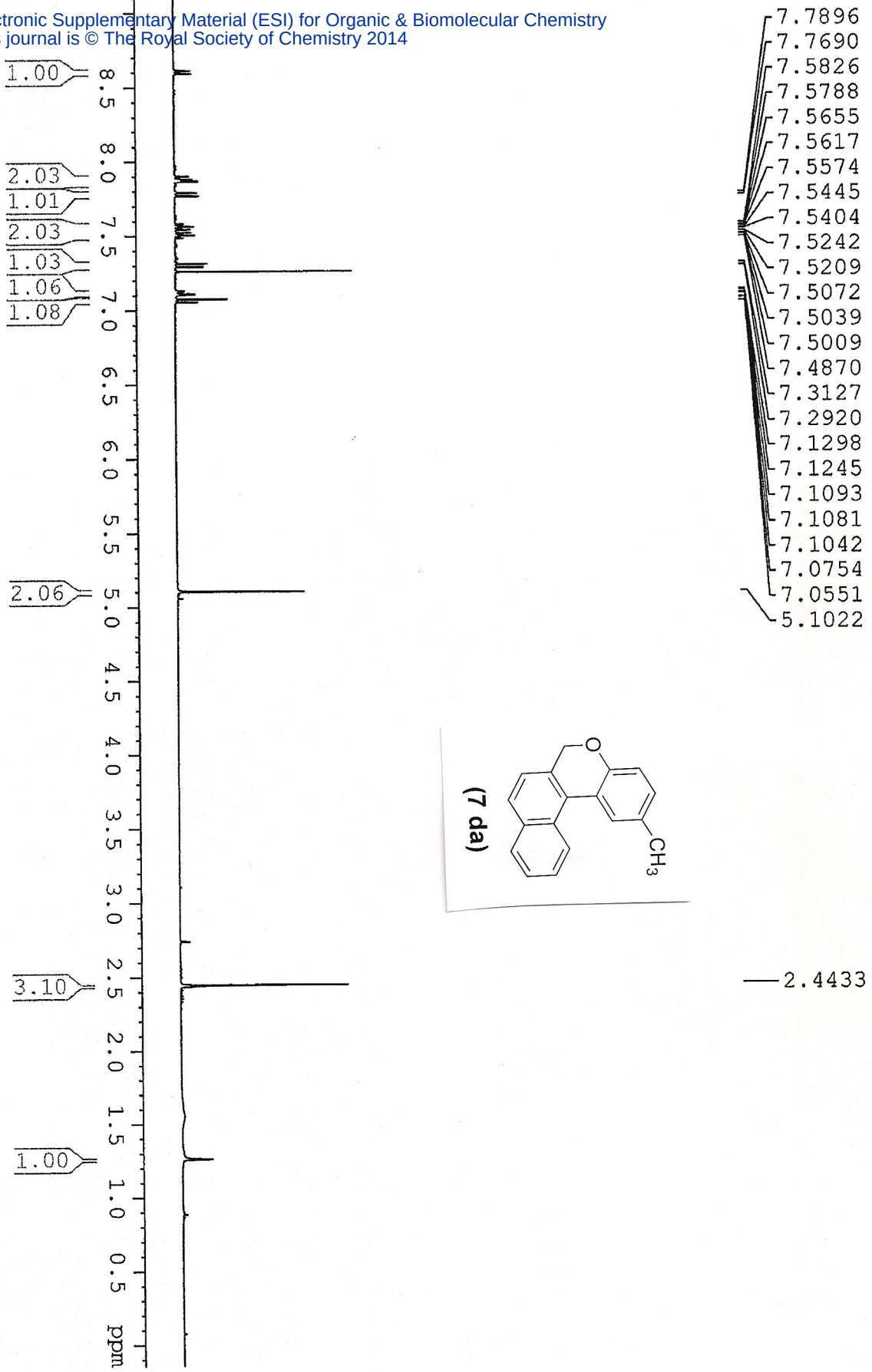












RSK-1099 (9); 1-H

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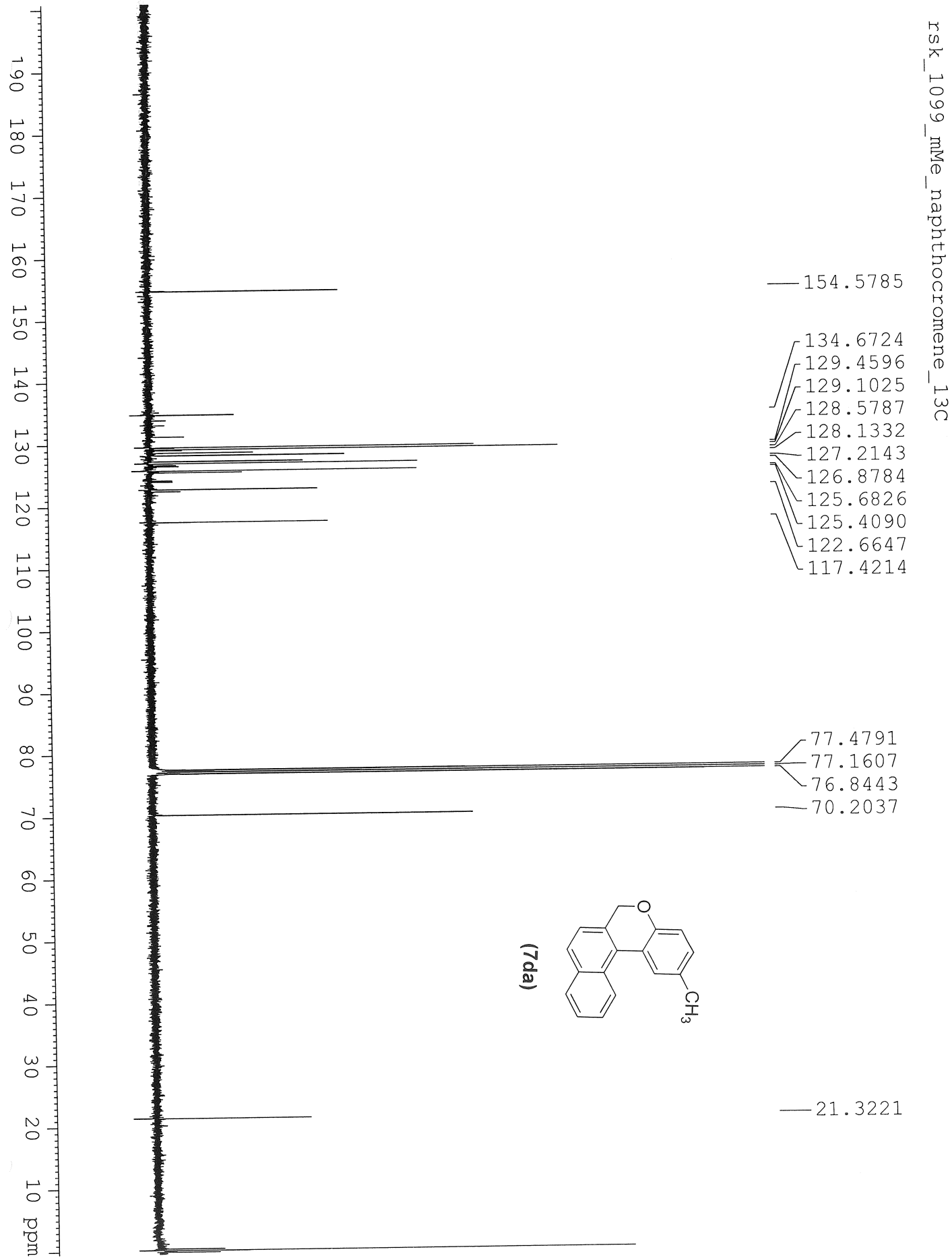

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