An Improved Cu-Based Catalyst System for the Reactions of Alcohols with Aryl Halides

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Supporting Information

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General Considerations

All reactions were carried out in resealable test tubes with teflon septa under a dry argon or nitrogen atmosphere. Copper(I) iodide (98%) was purchased from Strem. Me_4Phen was purchased from Acros. The *Anhydrous finely powdered* Cs_2CO_3 was a generous gift from Chemetall. This base was stored under nitrogen in a Vacuum Atmospheres glovebox. (The base is hygroscopic and excessive amounts of water lead to the formation of phenol and diaryl ether byproducts.) Small portions of the base (~5 g) were removed from the glovebox in glass vials, stored in the air in a desiccator filled with anhydrous calcium sulfate, and weighed in the air. Alcohols were purchased from commercial sources and used without further purification. Aryl halides were purchased from commercial sources and, when necessary, filtered through neutral alumina or distilled. Anhydrous toluene was purchased from J. T. Baker in CYCLE-TRAINER® solvent delivery kegs and vigorously purged with argon for 2 h. The solvent was further purified by passing it through two packed columns of neutral alumina under argon. The solvents were transferred by syringe from the solvent purification system to the reaction flask. Flash column chromatography was performed using a Biotage SP4 Flash Purification System using KP-Sil silica cartridges. In all cases, dichloromethane was used to transfer the crude reaction material onto the silica gel samplet. The samplet was dried in an oven prior to usage. A gradient elution using hexane and ethyl acetate was performed, based on the recommendation from the Biotage TLC Wizard.

Unless specified, yields reported in the publication are of the isolated material and represent an average of at least two independent runs. Yields reported in the supporting information refer to a single experiment. Compounds described in the literature were characterized by comparing their ^{1}H NMR and ^{13}C NMR spectra, and melting points (m.p.) to

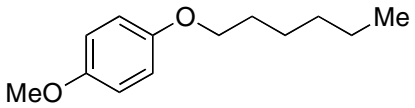
the previously reported data; their purity was confirmed by gas chromatography (GC) or elemental analysis. GC analyses were performed on a Hewlett Packard 6890 instrument with an FID detector and a Hewlett Packard 10 m x 0.2 mm i.d. HP-1 capillary column using dodecane as an internal standard. Elemental analyses were performed by Atlantic Microlabs, Inc., Norcross, GA. Previously unknown compounds were synthesized, purified and analyzed from a single run and were then repeated to determine an average yield. They were characterized by ^{1}H NMR, ^{13}C NMR, m.p., IR and elemental analysis. For those compounds that did not give a satisfactory elemental analysis, a copy of their ^{1}H NMR spectra is included. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 500 MHz instruments with chemical shifts reported relative to the deuterated solvent or TMS. IR spectra were recorded on a Perkin-Elmer System 2000 FT-IR instrument for all previously unknown compounds (KBr disc). Melting points (uncorrected) were obtained on a Mel-Temp II capillary melting point apparatus.

General procedure for the Cu-catalyzed cross-coupling of alcohols with aryl halides

An oven-dried screw-cap test tube was charged with CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), aryl halide (1.0 mmol, if solid), Cs_2CO_3 (490 mg, 1.5 mmol), and a magnetic stir bar. The reaction vessel was fitted with a rubber septum. The test tube was evacuated and back-filled with dry argon. Aryl halide (1. 0 mmol, if liquid), and toluene (0.50 mL) were then added by syringe. The rubber septum was removed and the reaction tube was quickly sealed with a Teflon-lined septum. The vessel was immersed in a pre-heated oil bath and stirred vigorously until TLC and/or GC analysis of the crude reaction mixture indicated that the aryl halide had been completely consumed. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (15 mL), and filtered through a plug of silica, eluting with additional ethyl acetate

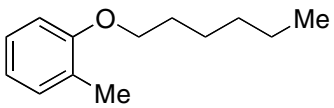
(30 mL). The filtrate was concentrated and the resulting residue was purified by flash chromatography (hexane/ethyl acetate) to provide the desired product.

Experimental procedures for compounds in Table 2



4-(hexyloxy)-anisole (Entries 1-3)

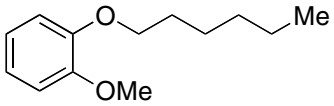
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (391 mg, 1.2 mmol), 4-iodoanisole (234 mg, 1.00 mmol), and *n*-hexanol (186 μL, 1.50 mmol) with toluene (0.50 mL) as solvent for 15 h at 80 °C. After cooling to room temperature, dodecane (225 mL, 1.0 mmol) and ethyl acetate (20 mL) were stirred into the reaction mixture. The mixture was filtered through a small plug of silica gel, and sampled for GC analysis. In order to standardize this compound for GC analysis, the product was purified by flash chromatography (hexane / ethyl acetate 1:0 → 9:1) to afford the title compound as a colorless oil (162 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (4H, s), 3.94-3.89 (3H, t, J = 6.6 Hz), 3.78 (3H, s), 1.79-1.72 (2H, m), 1.49-1.37 (2H, m), 1.36-1.32 (4H, m), 0.94-0.90 (3H, t, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 153.5, 115.6, 115.0, 68.9, 56.0, 31.9, 29.6, 26.0, 22.9, 14.3. IR (KBr disc, cm^{-1}) 2937, 1510, 1466, 1290, 1235, 1113, 1036, 827, 726, 532. Anal. Calc. for $C_{13}H_{20}O_2$: C 74.96, H 9.68. Found: C 74.78, H 9.74.



2-(hexyloxy)-toluene (Entry 4)[1]

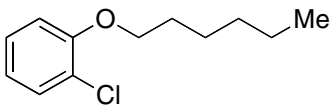
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10

mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 2-iodotoluene (127 μL, 1.00 mmol), and *n*-hexanol (187 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (159 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16-7.12 (2H, m), 6.85-6.80 (2H, m), 3.96 (2H, t, *J* = 6.4 Hz), 2.23 (3H, s), 1.85-1.76 (2H, m), 1.56-1.32 (6H, m), 0.94-0.88 (3H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 130.9, 127.1, 127.0, 120.3, 111.1, 68.1, 32.0, 29.7, 26.2, 23.0, 16.6, 14.4. IR (KBr disc, cm^{-1}) 2955, 2931, 2860, 1603, 1496, 1463, 1379, 1245, 119, 1122, 1050, 749, 713. Anal. Calc. for $C_{13}H_{20}O$: C 81.20, H 10.48. Found: C 81.41, H 10.33.



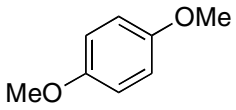
2-(hexyloxy)-anisole (Entry 5)[i]

The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 2-iodoanisole (130 μL, 1.00 mmol), and *n*-hexanol (187 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 30 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (195 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92-6.90 (4H, m), 4.03 (2H, t, *J* = 7.0 Hz), 3.88 (3H, s), 1.86 (2H, m), 7.49-1.34 (8H, m), 0.93-0.90 (3H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.6, 148.8, 121.0, 121.0, 113.2, 112.0, 69.2, 56.2, 31.9, 29.4, 25.9, 22.8, 14.3. IR (KBr disc, cm^{-1}) 2932, 2860, 1593, 1507, 1456, 1253, 1228, 1180, 1125, 1030, 740. Anal. Calc. for $C_{13}H_{20}O_2$: C 74.96, H 9.68. Found: C 74.69, H 9.68.



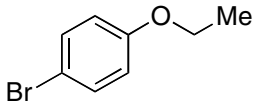
1-chloro-2-(hexyloxy)benzene (Entry 6)[ii]

The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 1-chloro-2-iodobenzene (122 μL, 1.00 mmol), and *n*-hexanol (187 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 1:3) afforded the title compound as a clear oil (185 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (1H, dd, *J* = 1.7, 7.9 Hz), 7.20 (1H, m), 6.94-6.85 (2H, m), 4.03 (2H, t, *J* = 6.5 Hz), 1.85 (2H, m), 1.54-1.31 (m, 6H), 0.94-0.89 (m, 3H).



1,4-dimethoxybenzene (Entry 7)[iii]

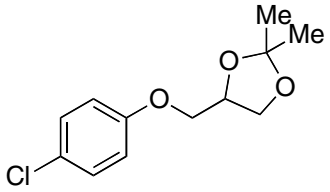
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (391 mg, 1.2 mmol), 4-iodoanisole (234 mg, 1.00 mmol), and methanol (81 μL, 2.00 mmol) with toluene (0.50 mL) as solvent for 15 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a colorless oil (108 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.84 (4H, s), 3.77 (6H, s). IR (KBr disc, cm^{-1}) 2933, 2860, 1509, 1467, 1233, 1181, 1107, 1042, 824, 742, 724, 523.



1-bromo-4-ethoxybenzene (Entry 8)[iv]

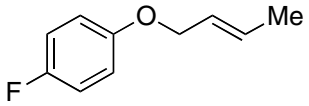
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 1,bromo-4-iodobenzene (283 mg, 1.00 mmol), and ethanol (116 μL, 2.0 mol) with toluene (0.50 mL) as solvent for 24 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (130

mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.36 (2H, m), 6.80-6.77 (2H, m), 4.00 (2H, q, *J* = 7.0 Hz), 1.42 (t, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.2, 132.4, 116.4, 112.8, 63.9, 14.9. IR (KBr disc, cm^{-1}) 2981, 2927, 1592, 1579, 1489, 1475, 1393, 1286, 1245, 1172, 1115, 1072, 1048, 1002, 923, 820, 639, 507. Anal. Calc. for C_8H_9BrO: C 47.79, H 4.51. Found: C 47.62, H 4.55.



4-((4-chlorophenoxy)methyl)-2,2-dimethyl-1,3-dioxolane (Entry 9)

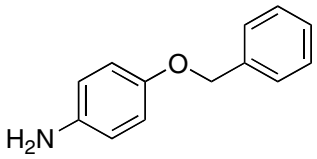
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (650 mg, 2.0 mmol), 4-chloro-1-iodobenzene (238 mg, 1.00 mmol), and solketal (249 μL, 2.00 mmol) with toluene (0.50 mL) as solvent for 15 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a colorless oil (202 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.268-7.209 (2H, m), 6.872-6.819 (2H, m), 4.512-4.434 (1H, m), 4.192-4.143 (1H, dd, *J* = 6.4, 8.5 Hz), 4.046-3.996 (1H, dd, *J* = 5.5, 9.5 Hz), 3.938-3.868 (2H, m), 1.465 (3H, s), 1.407 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 129.5, 126.2, 116.0, 110.0, 74.1, 69.2, 66.9, 27.0, 25.5. IR (KBr disc, cm^{-1}) 2980, 2932, 1489, 1451, 1371, 1240, 1203, 1169, 1152, 1075, 1051, 1000, 973, 893, 831, 658. Anal. Calc. for $C_{12}H_{15}ClO_3$: C 59.39, H 6.23. Found: C 59.57, H 6.30.



(*E*)-1-(but-2-enyloxy)-4-fluorobenzene (Entry 10)[v]

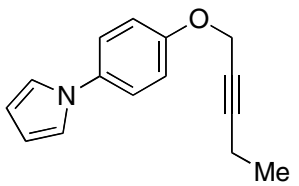
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10

mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 1-fluoro-4-iodobenzene (115 μL, 1.00 mmol), and (E)-crotyl alcohol (127 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (117 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00-6.95 (2H, m), 6.89-6.83 (2H, m), 5.90-5.83 (1H, m), 5.75-5.70 (1H, m), 4343 (2H, dd, *J* = 0.9, 6.2 Hz), 1.77 (3H, d, *J* = 6.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 155.0, 130.9, 126.1, 116.0, 115.8, 69.5, 18.1. IR (KBr disc, cm^{-1}) 3025, 2941, 2919, 2859, 1506, 1463, 1379, 1293, 1246, 1208, 1097, 1009, 967, 828, 780, 741, 514. Anal. Calc. for $C_{10}H_{11}FO$: C 72.27, H 6.67. Found: C 72.00, H 6.81.



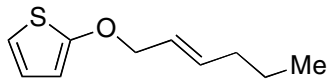
4-(benzyloxy)aniline (Entry 11)[vi]

The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (391 mg, 1.2 mmol), 4-iodoaniline (219 mg, 1.00 mmol), and benzyl alcohol (210 μL, 2.00 mmol) with toluene (0.50 mL) as solvent for 15 h at 80°C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a red solid (158 mg, 79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.32 (5H, m), 6.86-6.80 (2H, m), 6.68-6.63 (2H,m), 3.428 (2H, b s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 140.4, 137.7, 128.7, 128.0, 127.7, 116.5, 116.2, 70.9. IR (KBr disc, cm^{-1}) 2932, 2960, 1585, 1568, 1462, 1382, 1274, 1228, 1127, 1109, 1014, 829, 727, 673, 627, 423. m.p. 45-46.5 °C.



1-(4-(pent-2-ynyloxy)phenyl)-1*H*-pyrrole (Entry 12)

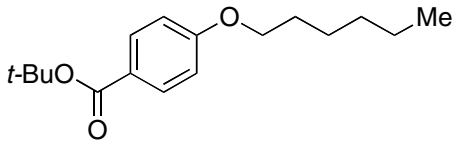
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (391 mg, 1.2 mmol), 1-(4-iodophenyl)pyrrole (269 mg, 1.00 mmol), and 2-pentyn-1-ol (139 μL, 1.50 mmol) with toluene (0.50 mL) as solvent for 24 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a white solid (209 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.30 (2H, m), 7.06-7.01 (4H, m), 6.34-6.33 (2H, t, *J* = 2.2 Hz), 4.71-4.70 (2H, , *J* = 2.2 Hz), 2.31-2.22 (2H, m), 1.19-1.14 (3H, t, *J* = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 122.2, 119.9, 115.9, 110.1, 90.0, 74.1, 57.0, 44.8, 13.8, 12.7. IR (KBr disc, cm^{-1}) 3132, 2977, 1522, 1325, 1258, 1243, 1190, 1070, 1018, 1006, 920, 824, 734. m.p. 57.5-59.0 °C.



(*E*)-2-(hex-2-enyloxy)thiophene (Entry 13)

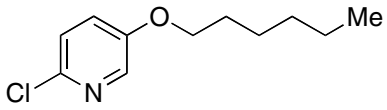
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (650 mg, 2.0 mmol), 3-iodothiophene (102 μL, 1.00 mmol), and *n*-hexanol (236 μL, 2.00 mmol) with toluene (0.50 mL) as solvent for 15 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 12.5:1) afforded the title compound as a yellow oil (125 mg, 69%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.191-7.163 (1H, dd, *J* = 3.1, 5.3 Hz), 6.789-6.767 (1H, dd, *J* = 1.6, 5.3 Hz), 6.274-6.258 (1H, q, *J* = 1.6 Hz), 5.906-5.811 (1H, m), 5.765-5.666 (1H, m), 4.461-4.438 (2H, dd, *J* = 1.0, 6.0 Hz), 2.119-2.045 (2H, m), 1.507-1.384 (2H, m), 0.951-0.902 (3H, t, *J* = 7.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 136.1, 124.9, 124.7, 119.8, 97.6, 71.1, 34.6, 22.3, 13.9. IR (KBr disc, cm^{-1}) 3118, 2959, 2929, 2871, 1544, 1421, 1366, 1234, 1177, 1010, 970, 873, 831, 752, 627. Anal. Calc. for $C_{10}H_{14}OS$: C 65.89, H 7.74.

Found: C 66.05, H 7.92.



tert-butyl 4-(hexyloxy)benzoate (Entry 14)

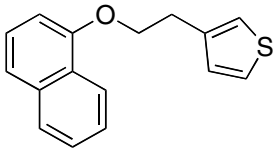
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), *tert*-butyl-4-iodo benzoate[vii] (304 mg, 1.00 mmol), and *n*-hexanol (187 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 19:1) afforded a mixture of the title compound and *n*-hexyl 4-(hexyloxy)benzoate (7:1 by ^1H NMR and GC) as a clear oil (264 mg, 95%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.98-7.92 (2H, m), 6.92-6.87 (2H, m), 4.00 (2H, t, *J* = 6.6 Hz), 1.83-1.76 (2H, m), 1.49-1.44 (2H, m), 1.35-1.30 (2H, m), 0.92 (3H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9 ,162.8, 131.5, 124.4, 114.0, 80.6, 68.3, 31.8, 29.3, 28.5, 25.9, 22.8, 14.2. IR (KBr disc, cm^{-1}) 2933, 2872, 1710, 1607, 1510, 1368, 1293, 1253, 1160, 1116, 1010, 848, 771, 696.



2-chloro-5-(hexyloxy)pyridine (Entry 15)

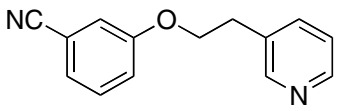
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (391 mg, 1.2 mmol), 2-chloro-5-iodopyridine (239 mg, 1.00 mmol), and *n*-hexanol (249 μL, 2.00 mol) with toluene (0.50 mL) as solvent for 15 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a colorless oil (179 mg, 84%). ^1H NMR (300 MHz, $CDCl_3$) δ 8.03-8.02 (1H, dd, *J* = 0.8, 2.9 Hz), 7.22-7.19 (1H, dd, *J* = 0.8, 8.7 Hz), 7.17-7.14 (1H, dd, *J* = 2.9, 8.7 Hz), 3.99-3.94 (2H, t, *J* =

6.4), 1.80-1.73 (2H, m), 1.47-1.30 (6H, m), 0.92-0.87 (3H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 142.6, 137.0, 125.2, 124.7, 69.3, 31.9, 29.4, 26.0, 23.0, 14.4. IR (KBr disc, cm^{-1}) 2902, 2863, 1516, 1454, 1245, 1016, 917, 814, 736, 697, 517. Anal. Calc. for $C_{11}H_{16}ClNO$: C 61.82, H 7.55. Found: C 62.02, H 7.65.



3-(2-(naphthalen-1-yloxy)ethyl)thiophene (Entry 16)

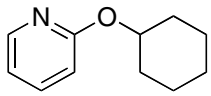
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 1-iodonaphthalene (175μL, 1.00 mmol), and 2-(3-thieno)-ethanol (168 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a tan oil (252 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31-8.29 (1H, m), 7.82 (1H, dd, *J* = 2.1, 6.4 Hz), 7.53-7.48 (1H, m), 7.45 (1H, d, *J* = 8.2 Hz), 7.39 (1H, d, *J* = 8.0 Hz), 7.31 (1H, dd, *J* = 2.9, 4.9 Hz), 7.19-7.18 (1H, m), 7.14 (1H, dd, *J* = 1.2, 4.9 Hz), 6.83 (1H, d, *J* = 7.5 Hz), 4.38 (2H, d, *J* = 6.7 Hz), 3.31 (2H, d, *J* = 6.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7. 138.9. 134.7. 128.7. 127.7. 126.6. 126.0. 125.9. 125.7. 125.4. 122.2. 121.8. 120.5. 104.8. 68.4. 30.5. IR (KBr disc, cm^{-1}) 3052, 2928, 2873, 1594, 1580, 1508, 1460, 1405, 1269, 1240, 1100, 1071, 1020, 790. Anal. for $C_{16}H_{14}OS$: C 75.55, H 5.55. Found: C 75.28, H 5.50.



3-(2-(pyridin-3-yl)ethoxy)benzonitrile (Entry 17)

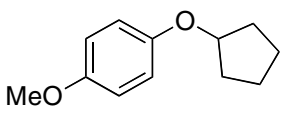
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 3-iodobenzonitrile (229 mg, 1.00 mmol), and 2-(3-

pyridyl)ethanol (172 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 3:1) afforded the title compound as a clear oil (174 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (1H, d, *J* = 2.2 Hz), 8.22 (1H, dd, *J* = 1.6, 4.7 Hz), 7.65-7.60 (1H, m), 7.40-7.33 (1H, m), 7.29-7.23 (2H, m), 7.13-7.09 (2H, m), 4.20 (2H, t, *J* = 6.5 Hz), 3.12 (2H, t, *J* = 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 150.5, 148.5, 136.6, 133.6, 130.6, 125.0, 123.6, 119.9, 118.8, 117.6, 113.4, 68.5, 33.0. IR (KBr disc, cm^{-1}) 3033, 2934, 2878, 2230, 1597, 1578, 1480, 1431, 1328, 1292, 1148, 1033, 971, 715, 682. Anal. Calc. for $C_{14}H_{12}N_2O$: C 74.98, H 5.39.



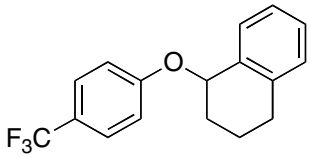
2-(cyclohexyloxy)pyridine (Entry 18)

The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 4 Å molecular sieves (200 mg, flame activated under vacuum) 2-iodopyridine (106 μL, 1.00 mmol), and cyclohexanol (158 μL, 1.50 mmol) with toluene (0.50 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (164 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (1H, ddd, *J* = 0.8, 2.1, 5.0 Hz), 7.54 (1H, ddd, *J* = 2.0, 7.2, 8.4 Hz), 6.81 (1H, ddd, *J* = 0.9, 5.0, 7.1 Hz), 6.69 (1H, dt, *J* = 8.4, 0.8 Hz), 5.06-5.00 (1H, m), 2.05-2.01 (2H, m), 1.82-1.76 (2H, m), 1.66-1.39 (4H, m), 1.34-1.25 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.7, 147.1, 138.7, 116.4, 111.9, 73.2, 32.1, 25.9, 24.2. IR (KBr disc, cm^{-1}) 3025, 2942, 1614, 1516, 1328, 1249, 1161, 1110, 1061, 961, 837, 749. Anal. Calc. for $C_{11}H_{15}NO$: C 74.54, H 8.53. Found: C 74.50, H 8.63.



1-(cyclopentyloxy)-4-methoxybenzene (Entry 19)[viii]

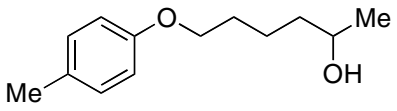
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 4-iodoanisole (234 mg, 1.00 mmol), and cyclopentanol (136 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (168 mg mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (4H, s), 4.71-4.66 (1H, m), 3.78 (3H, s), 1.90-1.76 (6H, m), 1.65-1.56 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 116.8, 114.8, 80.0, 55.9, 33.0, 24.2. IR (KBr disc, cm^{-1}) 2960, 2872, 1833, 1507, 1465, 1441, 1231, 1173, 1106, 1040, 990, 824. Anal. Calc. for $C_{12}H_{16}O_2$: C 74.97, H 8.39. Found: C 74.56, H 8.25.



1-(4-(trifluoromethyl)phenoxy)-1,2,3,4-tetrahydronaphthalene (Entry 20)

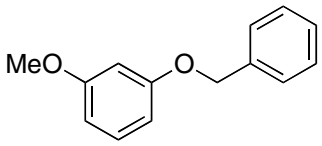
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 4-iodobenzotrifluoride (147 μL, 1.00 mmol), and (±)-1-tetralol (222 mg, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (217 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (2H, d, J = 8.8 Hz), 7.36-7.19 (4H, m), 7.10 (d, J = 8.8 Hz), 5.47 (1H, t, J = 4.3 Hz), 2.96-2.91 (1H, m), 2.84-2.78 (1H, m), 2.21-2.15 (1H, m), 2.09-1.99 (2H, m), 1.87-1.80 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 135.1, 129.6, 129.4, 128.4, 127.3, 127.2, 127.1, 126.4, 116.1, 74.2, 29.2, 28.0, 18.9. IR (KBr

disc, cm^{-1}) 3024, 2942, 1614, 1516, 1328, 1250, 1161, 1110, 1061, 961, 837, 749. Anal. Calc. for $C_{17}H_{15}F_3OX$: C 69.85, H 5.17. Found: C 69.74, H 5.24.



1-(*p*-tolyloxy)hexan-5-ol (Entry 21)

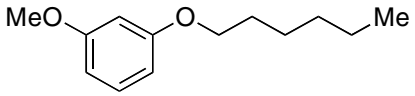
The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 4-iodotoluene (218 mg, 1.00 mmol), and 1,5-hexanediol (181 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 4:1) afforded the title compound as a clear oil (156 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09-7.07 (2H, m), 6.82-6.79 (2H, m), 3.95 (2H, t, *J* = 6.5 Hz), 6.87-3.81 (1H, m), 2.30 (3H, t), 1.83-1.78 (2H, m), 1.61-1.47 (6H, m), 1.22 (3H, dd, *J* = 0.6, 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 130.0, 129.9, 114.5, 68.2, 68.0, 39.2, 29.5, 23.7, 22.6, 20.7. IR (KBr disc, cm^{-1}) 3363 (br), 3031, 2940, 2867, 1614, 1584, 1512, 1474, 1376, 1291, 1244, 1176, 1111, 1037, 952, 818, 511.



1-(benzyloxy)-3-methoxybenzene (Entry 22)[ix]

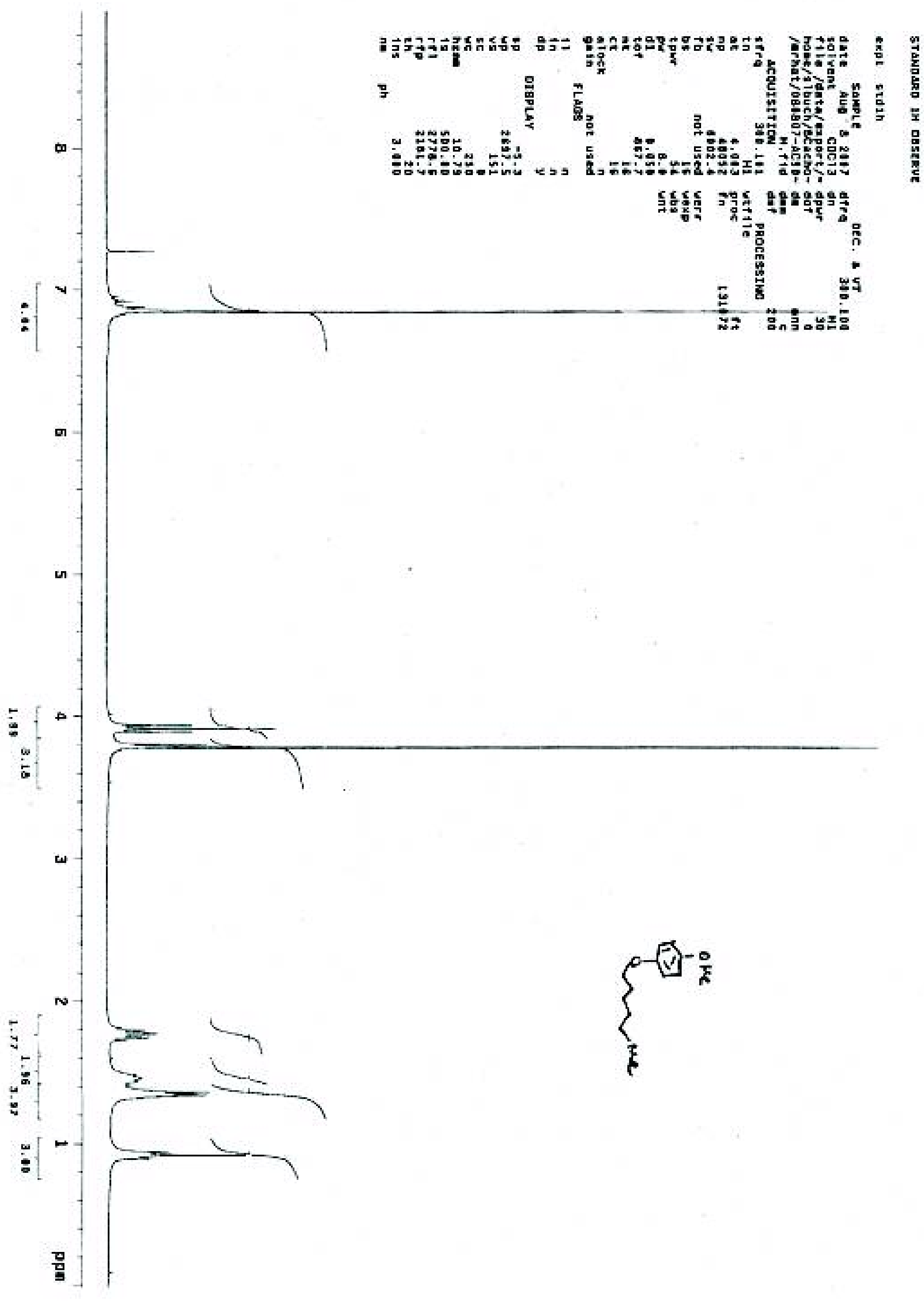
The general procedure was followed using CuI (19 mg, 0.050 mmol), Me_4Phen (48 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 3-bromoanisole (127 μL, 1.00 mmol), and benzyl alcohol (155 μL, 1.50 mol) with toluene (0.50 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (199 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.36 (5H, m), 7.23 (1H, m), 6.64-6.57 (3H, m), 5.08 (2H, s), 3.82 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 160.2, 137.1, 130.1, 128.8,

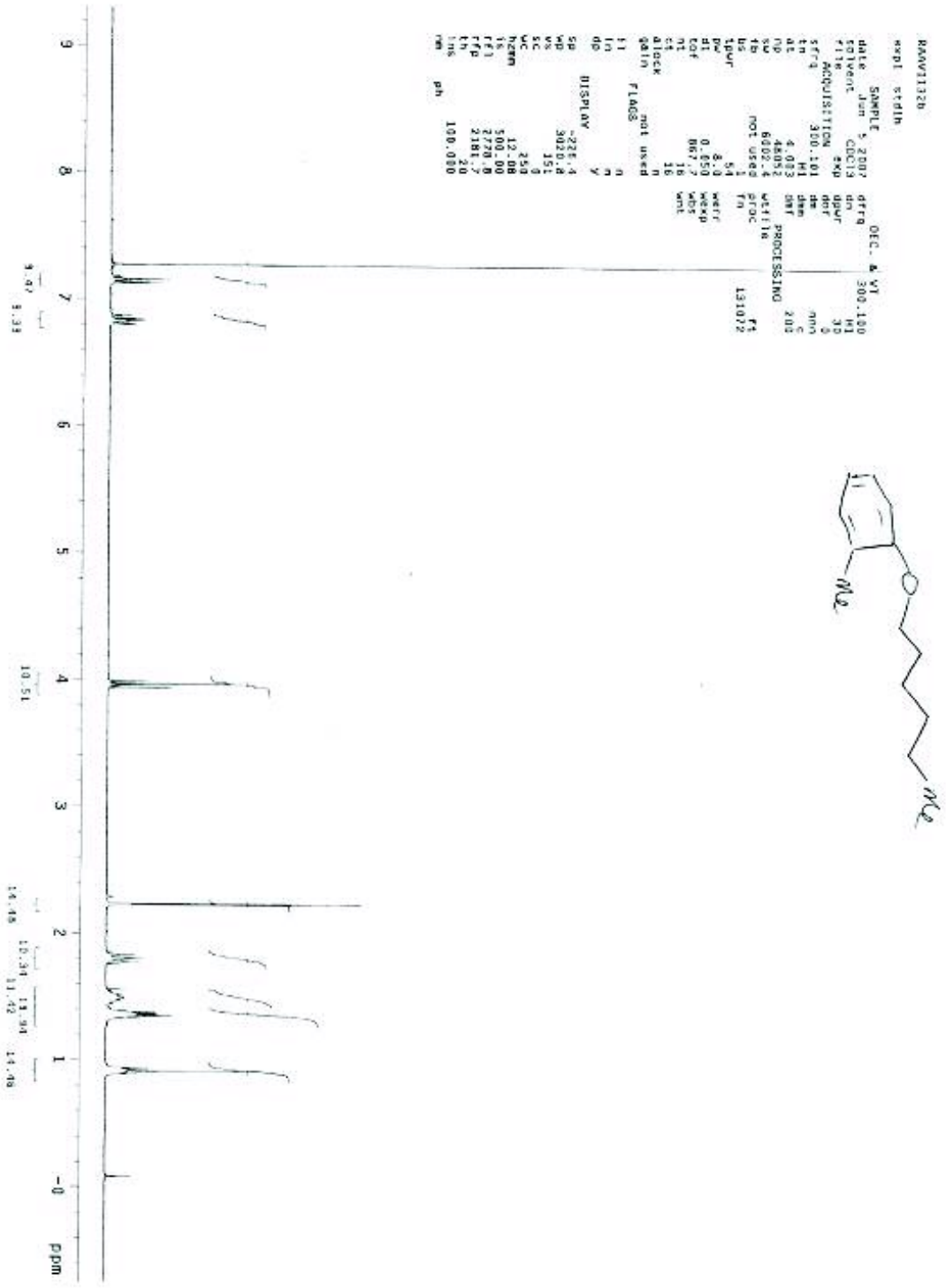
128.1, 127.7, 107.1, 106.7, 101.5, 70.2, 55.4. IR (KBr disc, cm^{-1}) 3032, 2939, 2835, 1592, 1492, 1453, 1381, 1288, 1264, 1199, 1151, 1082, 1045, 835, 761, 734, 697. Anal. Calc. for $C_{14}H_{14}O_2$: C 78.48, H 6.59. Found: C 78.39, H 6.59.



3-(hexyloxy)-anisole (Entry 23)[x]

The general procedure was followed using CuI (9.5 mg, 0.050 mmol), Me_4Phen (24 mg, 0.10 mmol), Cs_2CO_3 (490 mg, 1.5 mmol), 3-bromoanisole (127 μL, 1.00 mmol), and *n*-hexanol (0.5 mL) as solvent for 24 h at 130 °C. Chromatographic purification (hexane / ethyl acetate 1:0 → 9:1) afforded the title compound as a clear oil (160 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (1H, t, *J* = 4.5 Hz), 6.53-6.48 (3H, m), 3.95 (2H, t, *J* = 6.7 Hz), 3.79 (3H, s), 1.81-1.76 (2H, m), 1.49-1.45 (2H, m), 1.38-1.33 (4H, m), 0.94-0.91 (3H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 160.6, 130.0, 106.8, 106.3, 101.1, 77.0, 55.5, 31.8, 29.5, 26.0, 22.8, 14.3. IR (KBr disc, cm^{-1}) 3000, 2933, 28871, 1599, 1493, 1468, 1455, 1334, 1287, 1265, 1201, 1153, 1046, 835, 762, 687.

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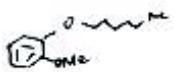

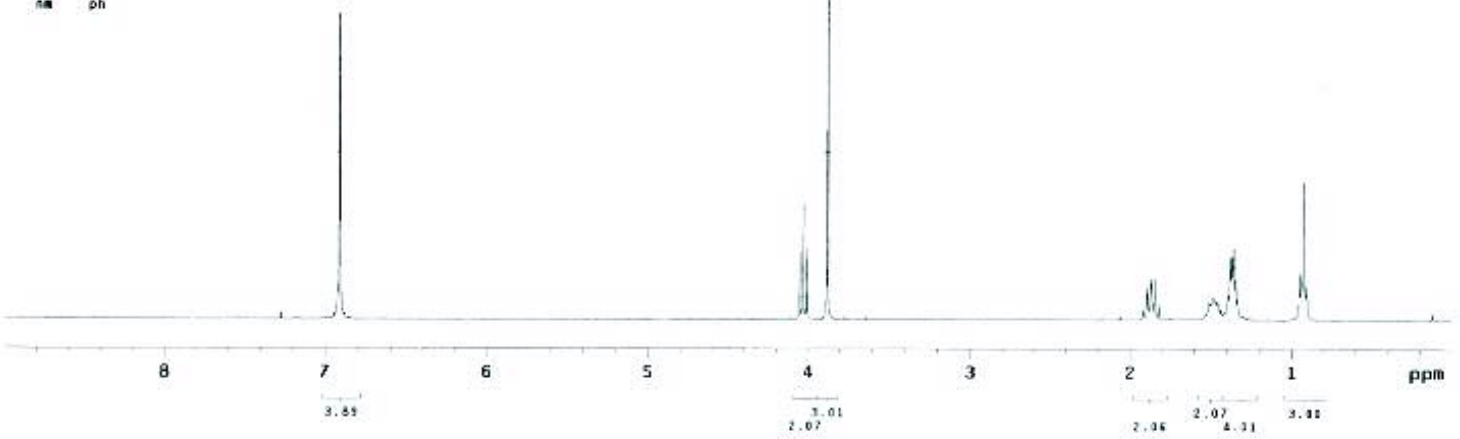

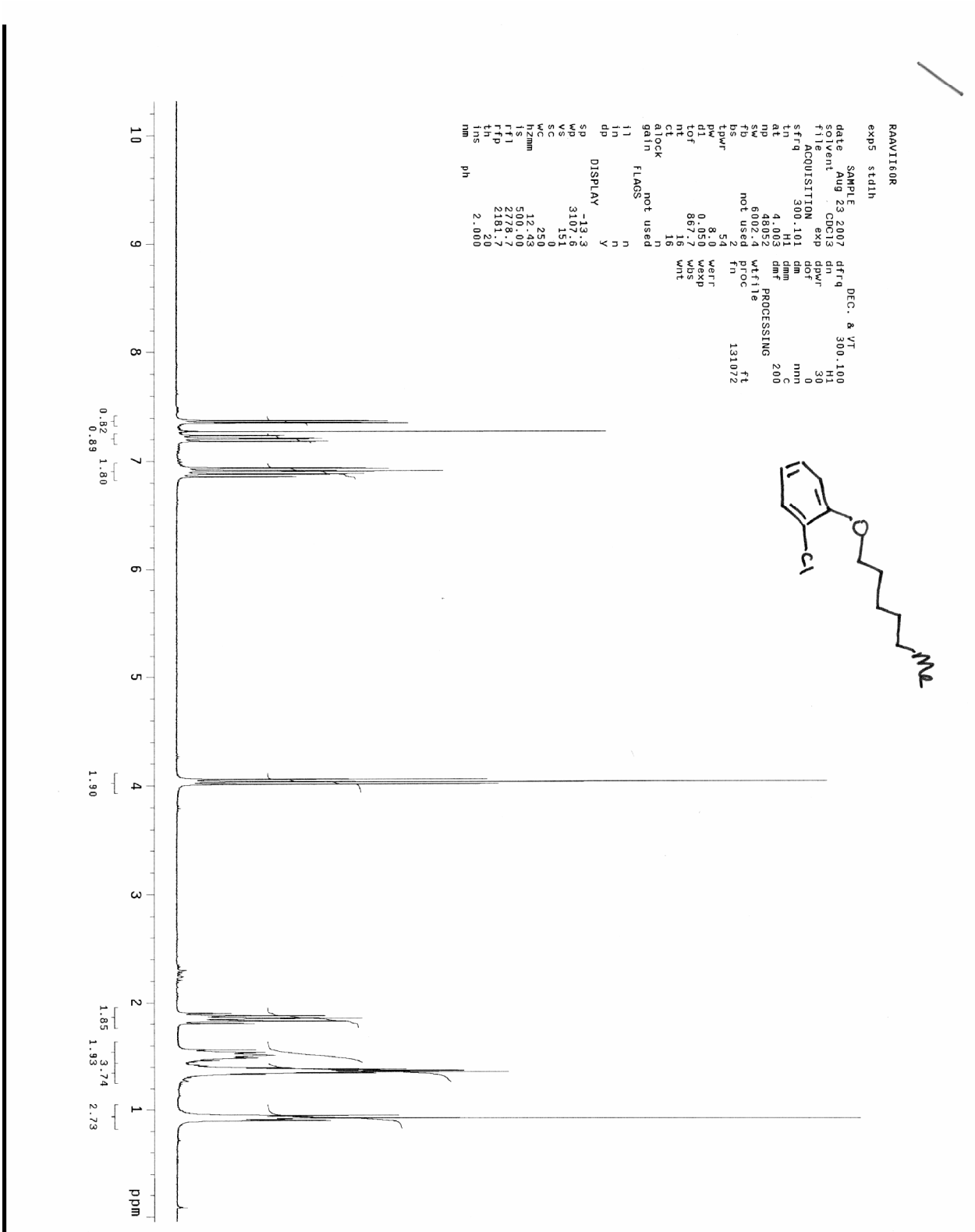
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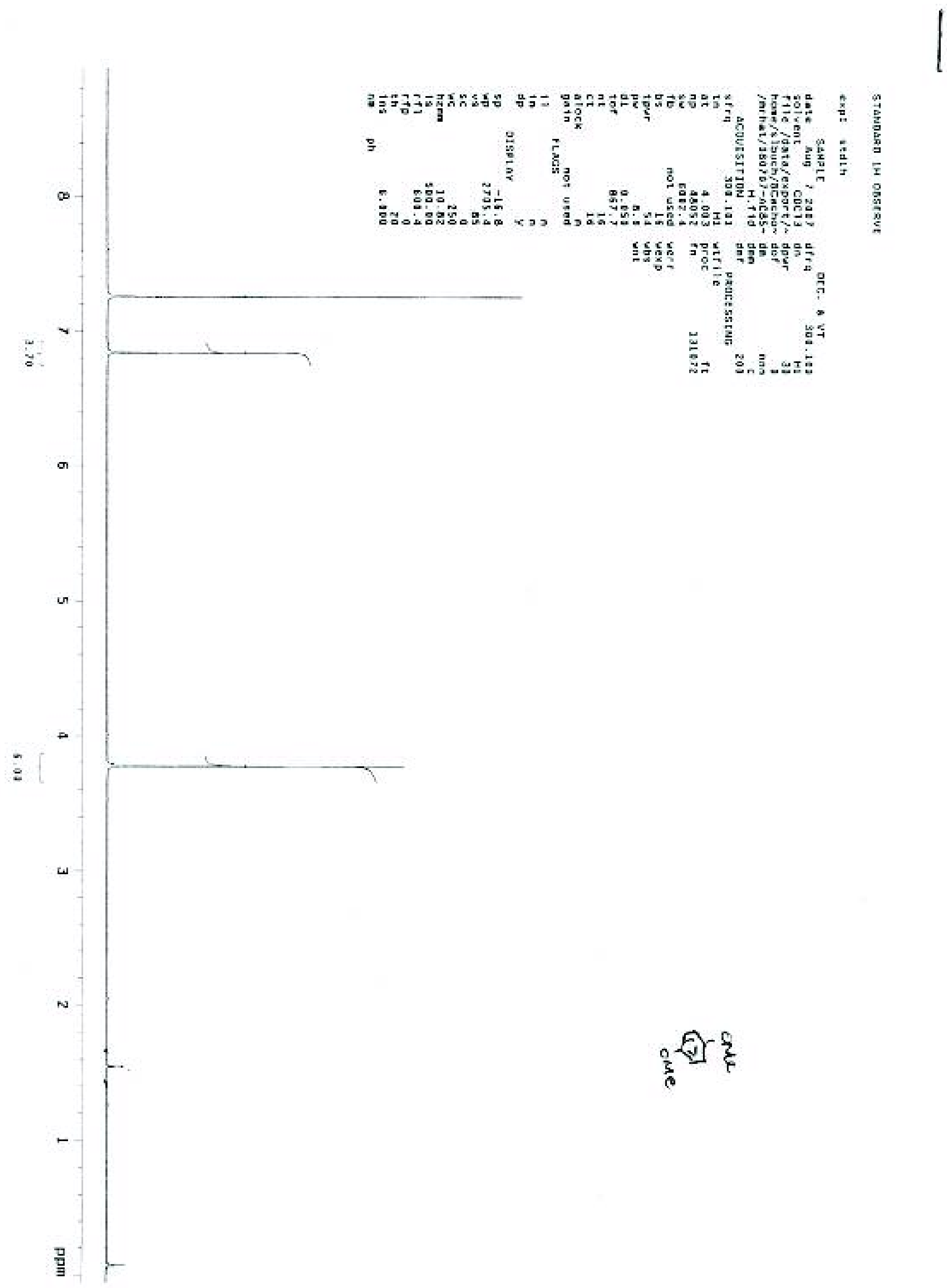

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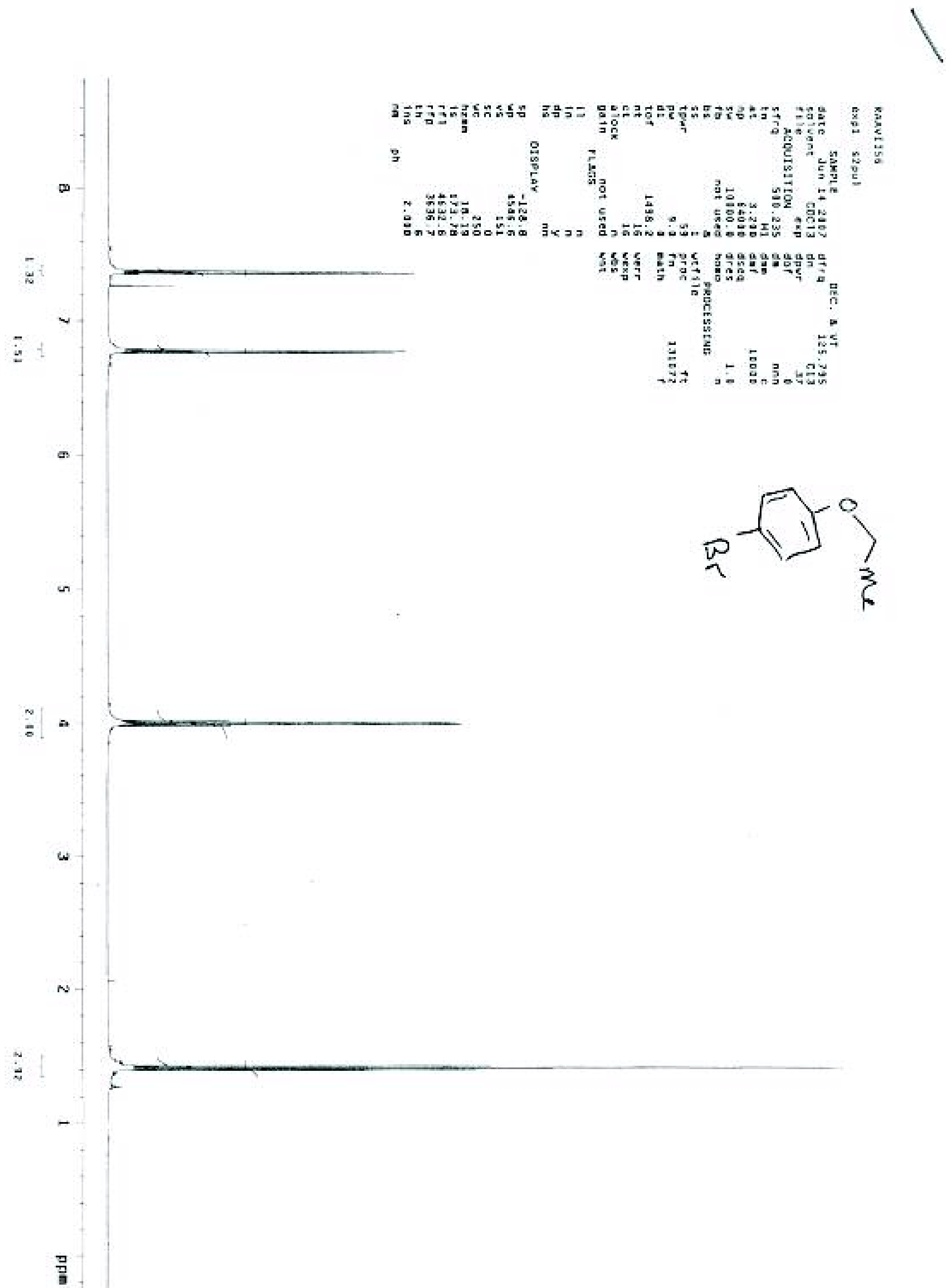
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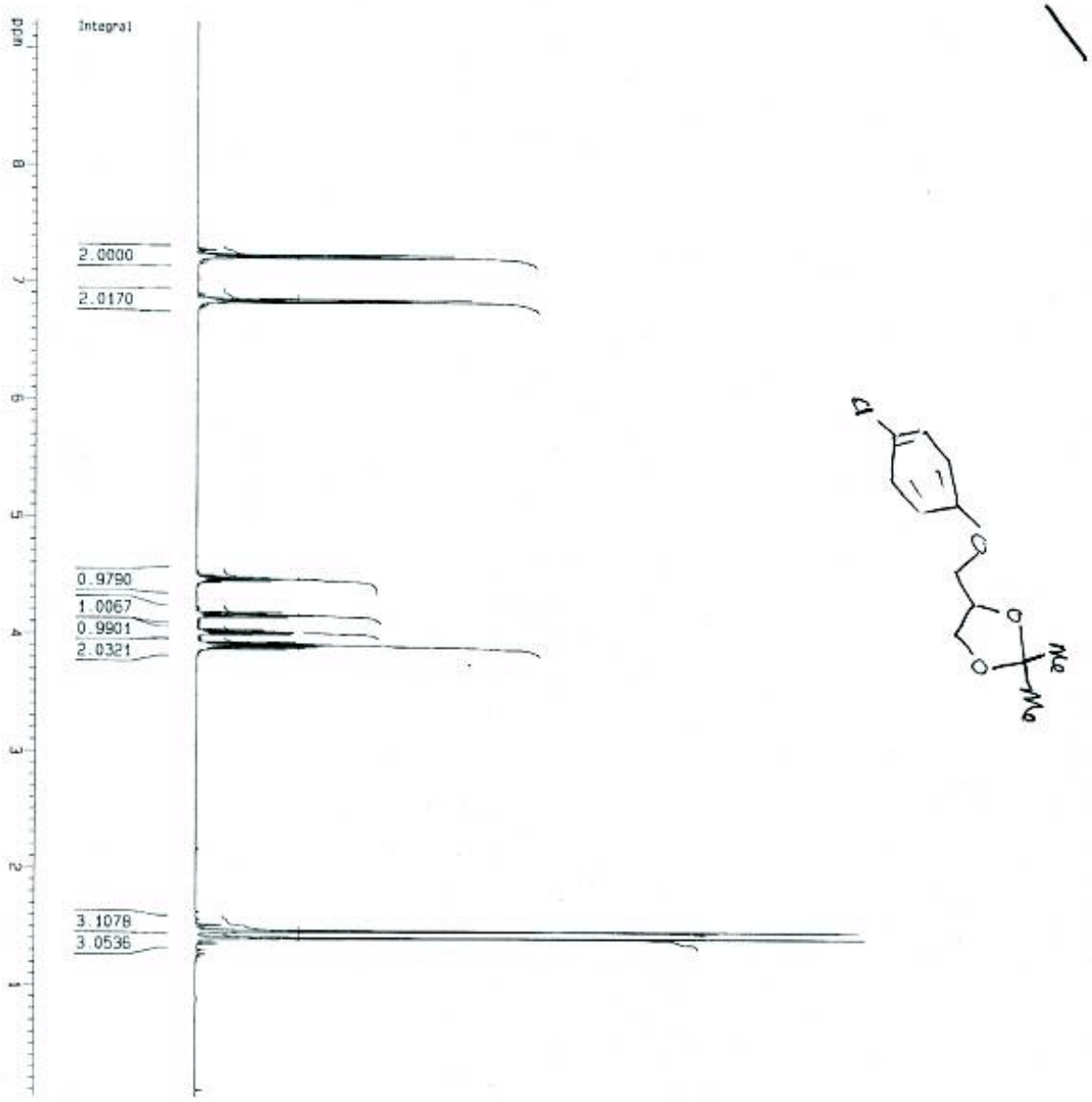


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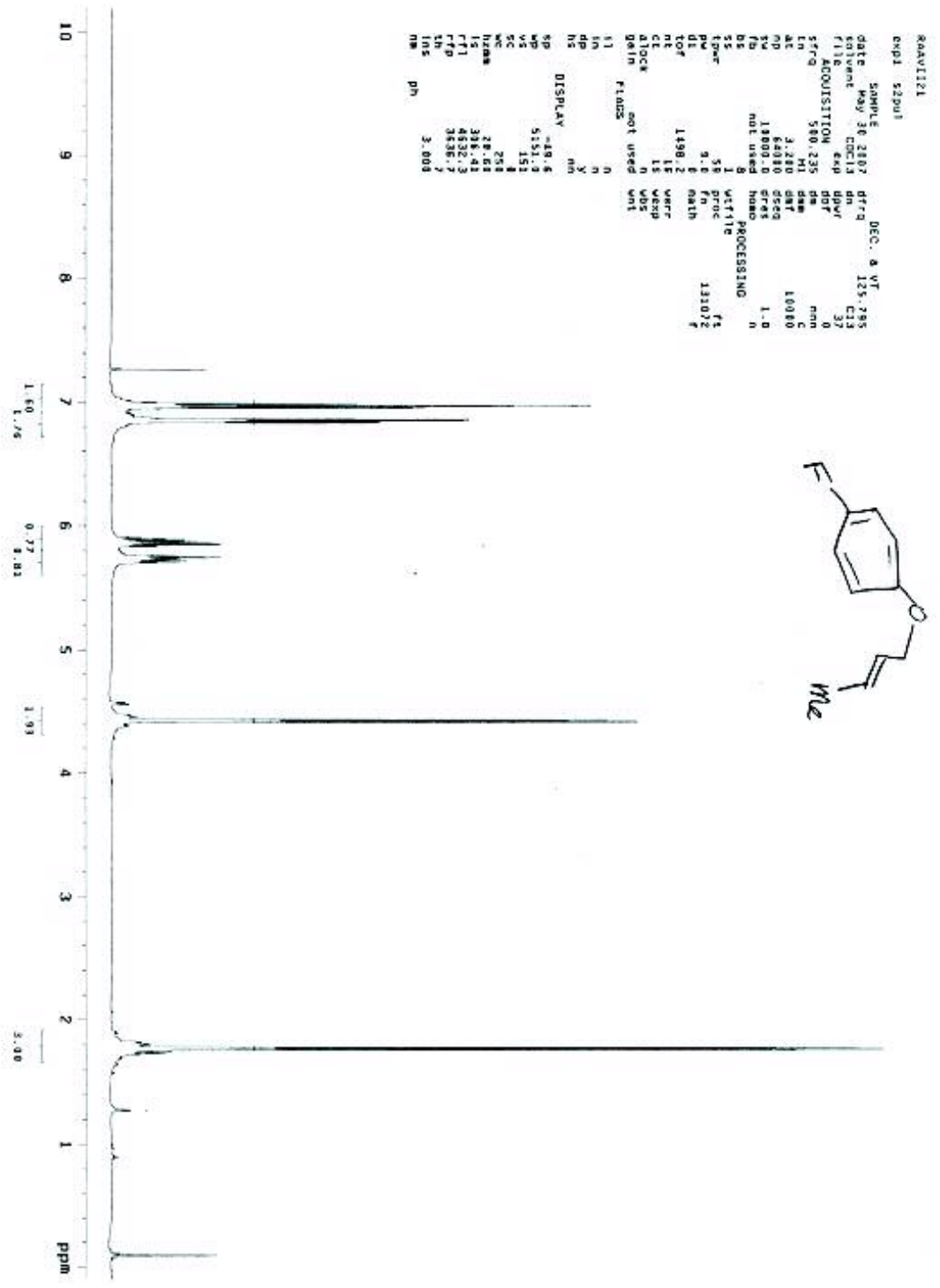
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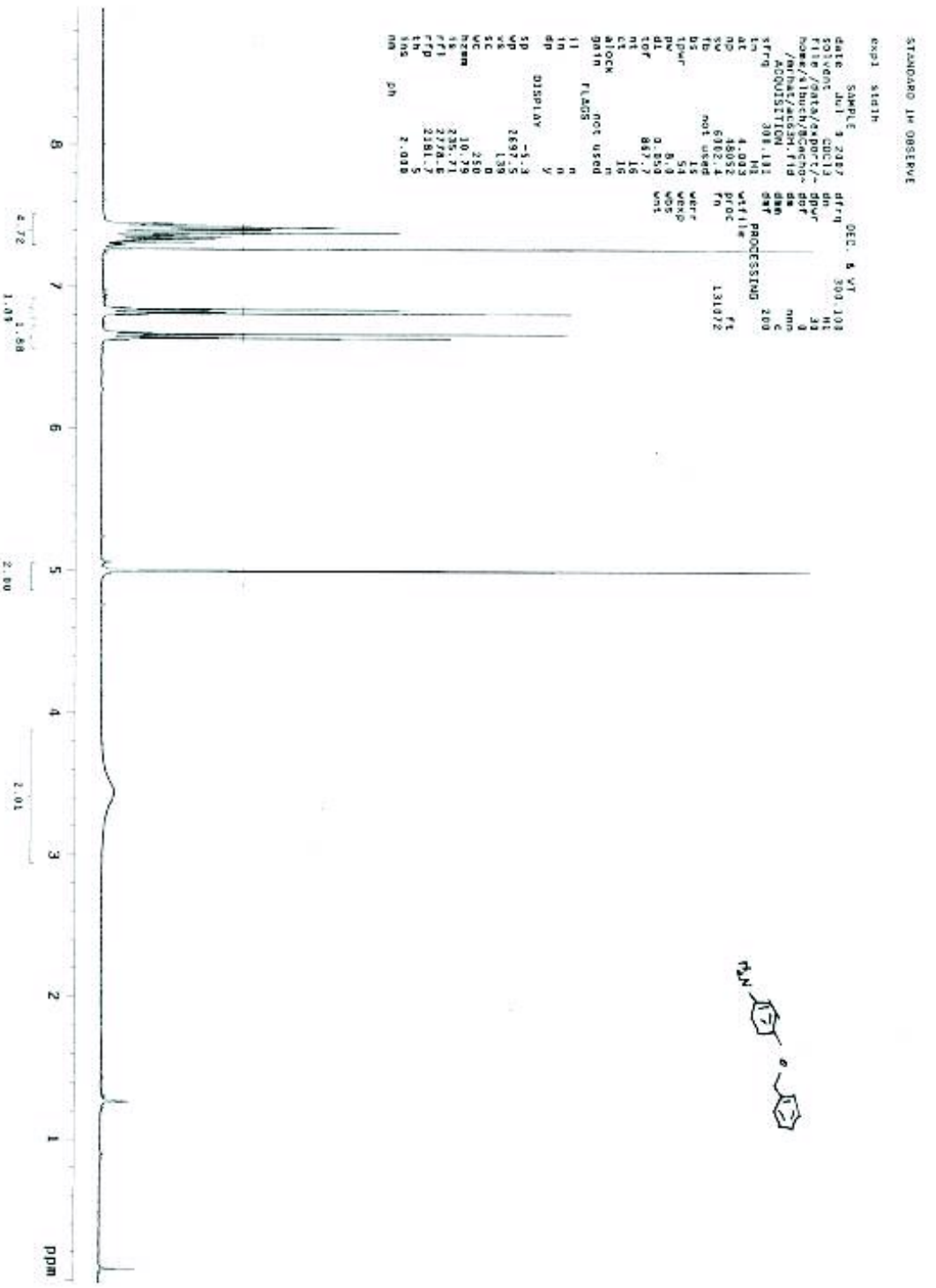
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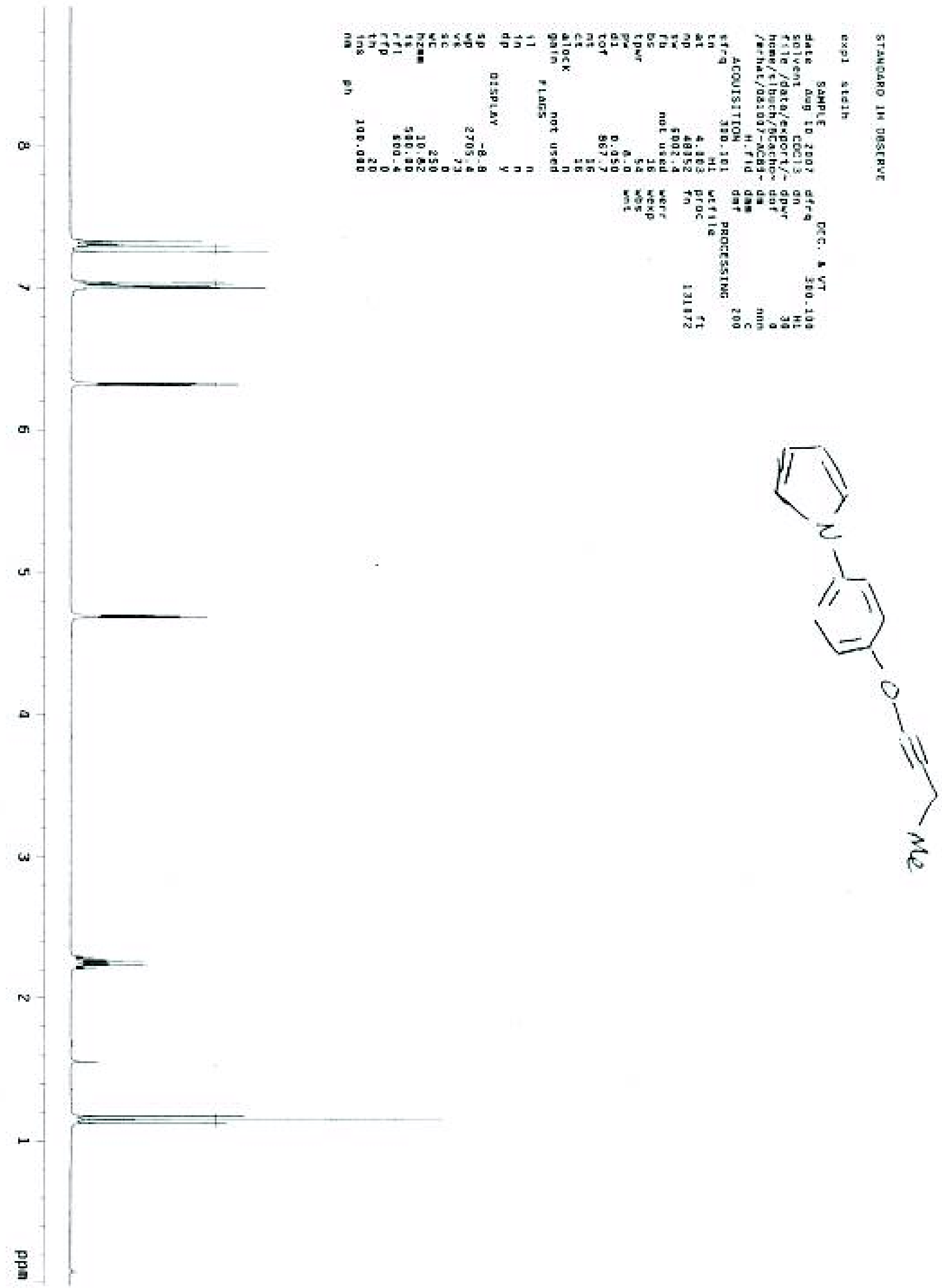
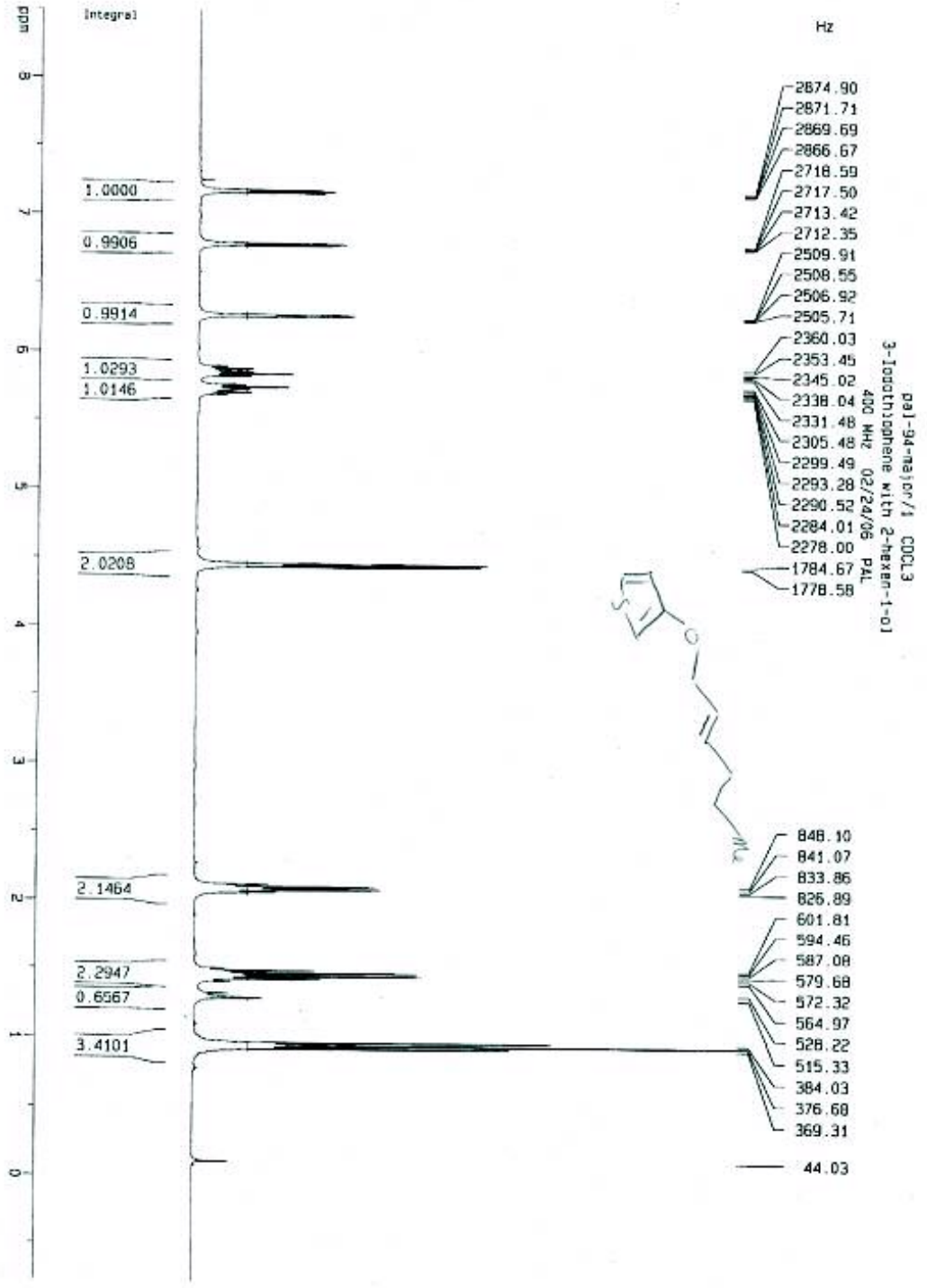

STANDARD 1H OBSERVE
ppm
Me


ppm
Integral
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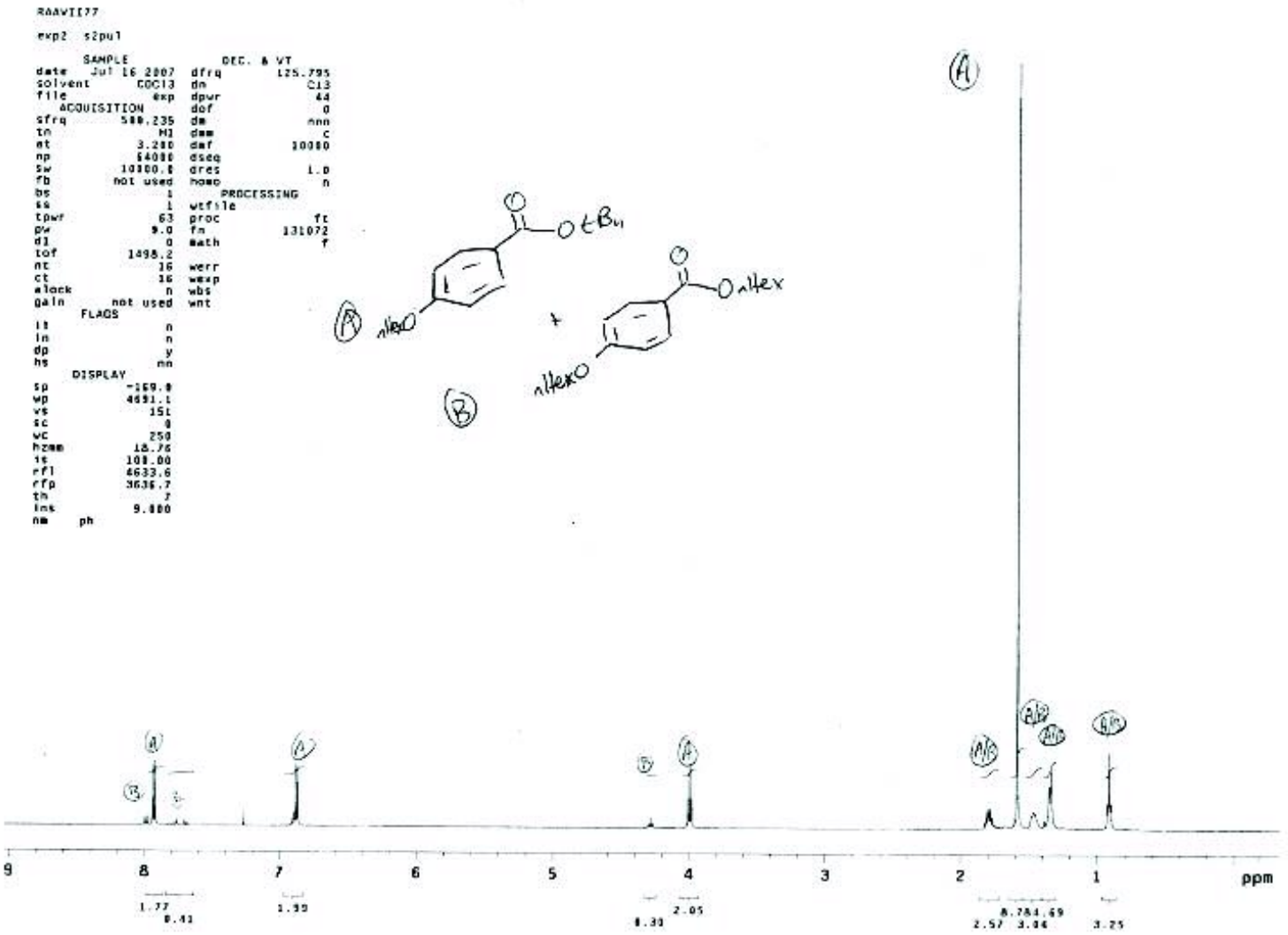
0.9906
0.9914
1.0293
1.0146
2.0208
2.1464
2.2947
0.6567
3.4101
Hz
2874.90
2871.71
2869.69
2866.67
2718.59
2717.50
2713.42
2712.35
2509.91
2508.55
2506.92
2505.71
2360.03
2353.45
2345.02
2338.04
2331.48
2305.48
2299.49
2293.28
2290.52
2284.01
2278.00
1784.67
1778.58
848.10
841.07
833.86
826.89
601.81
594.46
587.08
579.68
572.32
564.97
528.22
515.33
384.03
376.68
369.31
44.03
pal-94-major/1 CDCL3
3-Isopthiophene with 2-hexen-1-ol
400 MHz 02/24/06 PAL


RAAVII77
exp2 s2pul
SAMPLE
date Jul 16 2007
solvent CDCl3
file exp
ACQUISITION
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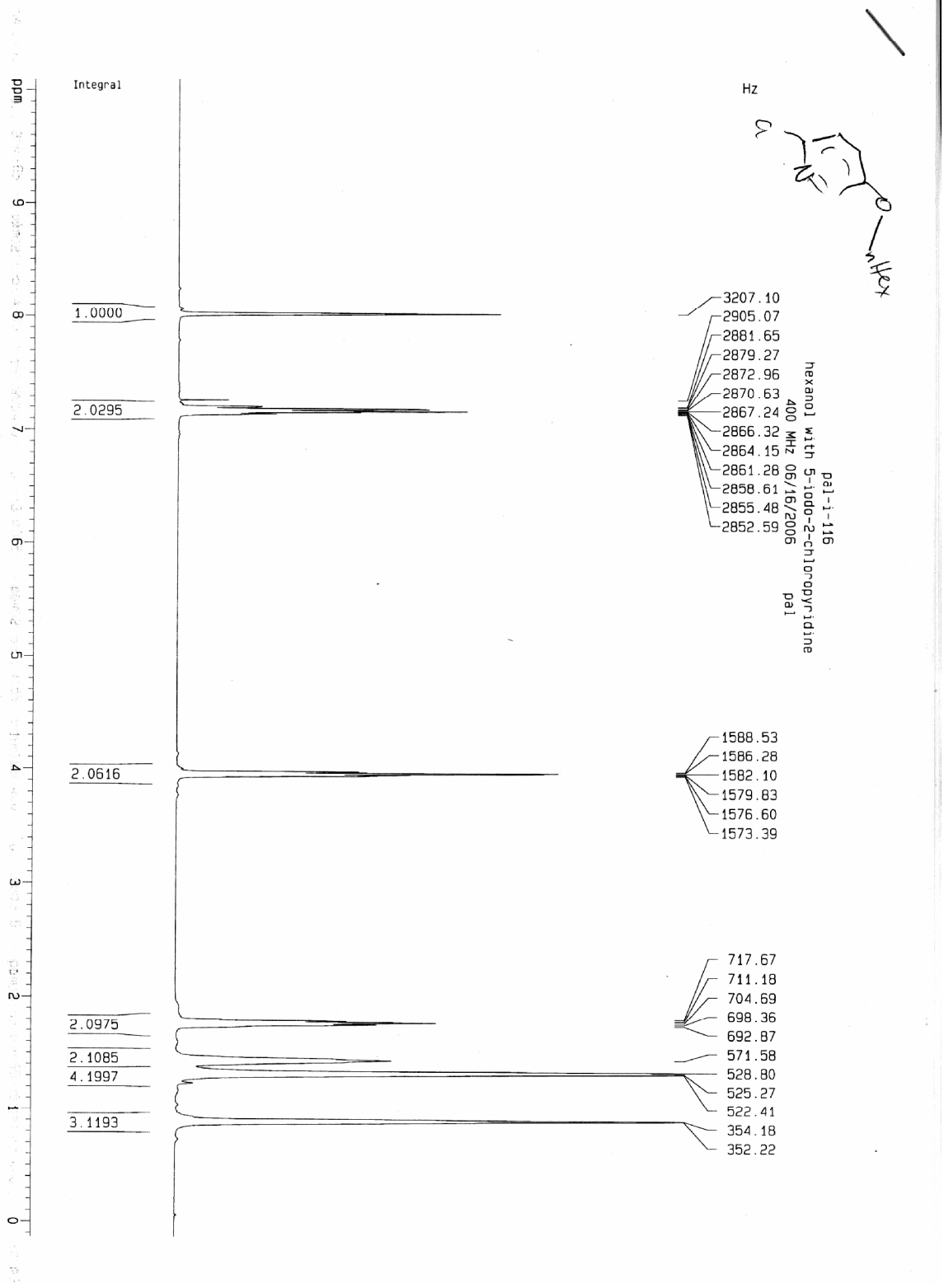
tn H1
at 3.280
np 64000
sw 10000.8
fb not used
bs 1
ss 1
tpwr 63
pw 9.0
d1 0
tof 1498.2
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -169.8
wp 4691.1
vs 151
sc 0
wc 250
hzmm 18.76
is 108.00
rfl 4633.6
rfp 3636.7
th 7
ins 9.000
nm ph
DEC. & VT
dfrq 125.795
dn C13
dpwr 44
dof 0
dm nnn
dmm c
dmf 10080
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
OtBu
nHexO
nHexO
nHex
A
B
ppm
9
8
7
6
5
4
3
2
1
1.77
0.41
1.00
0.30
2.05
8.78
4.69
2.57
3.04
3.25


Integral
Hz
ppm
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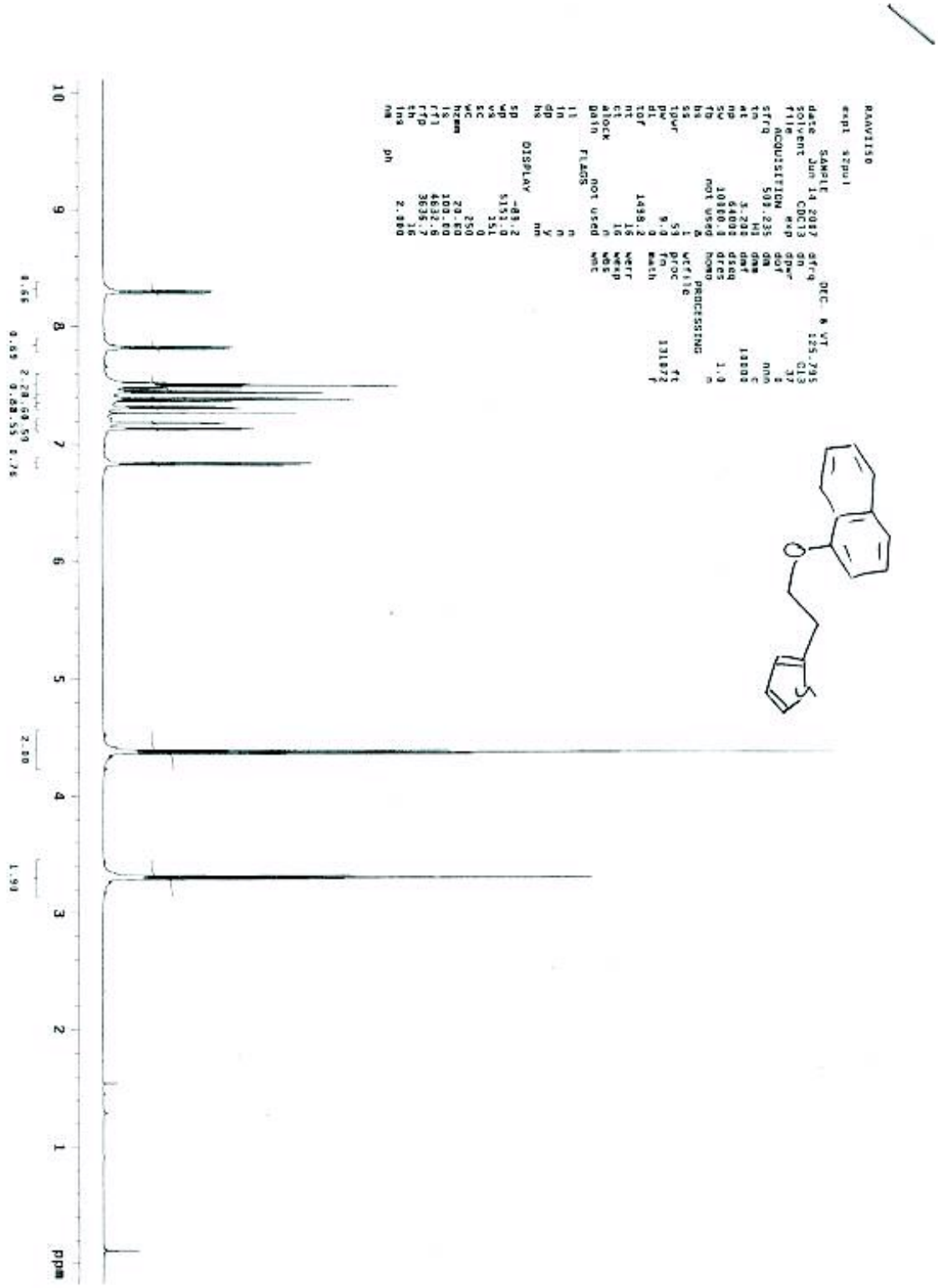
2.0616
2.0975
2.1085
4.1997
3.1193
3207.10
2905.07
2881.65
2879.27
2872.96
2870.63
2867.24
2866.32
2864.15
2861.28
2858.61
2855.48
2852.59
1588.53
1586.28
1582.10
1579.83
1576.60
1573.39
717.67
711.18
704.69
698.36
692.87
571.58
528.80
525.27
522.41
354.18
352.22
pal-i-116
hexanol with 5-iodo-2-chloropyridine
400 MHz 06/16/2006
pal


RAAV1150
expt s2pul
SAMPLE
date Jun 14 2017
solvent CDCl3
file
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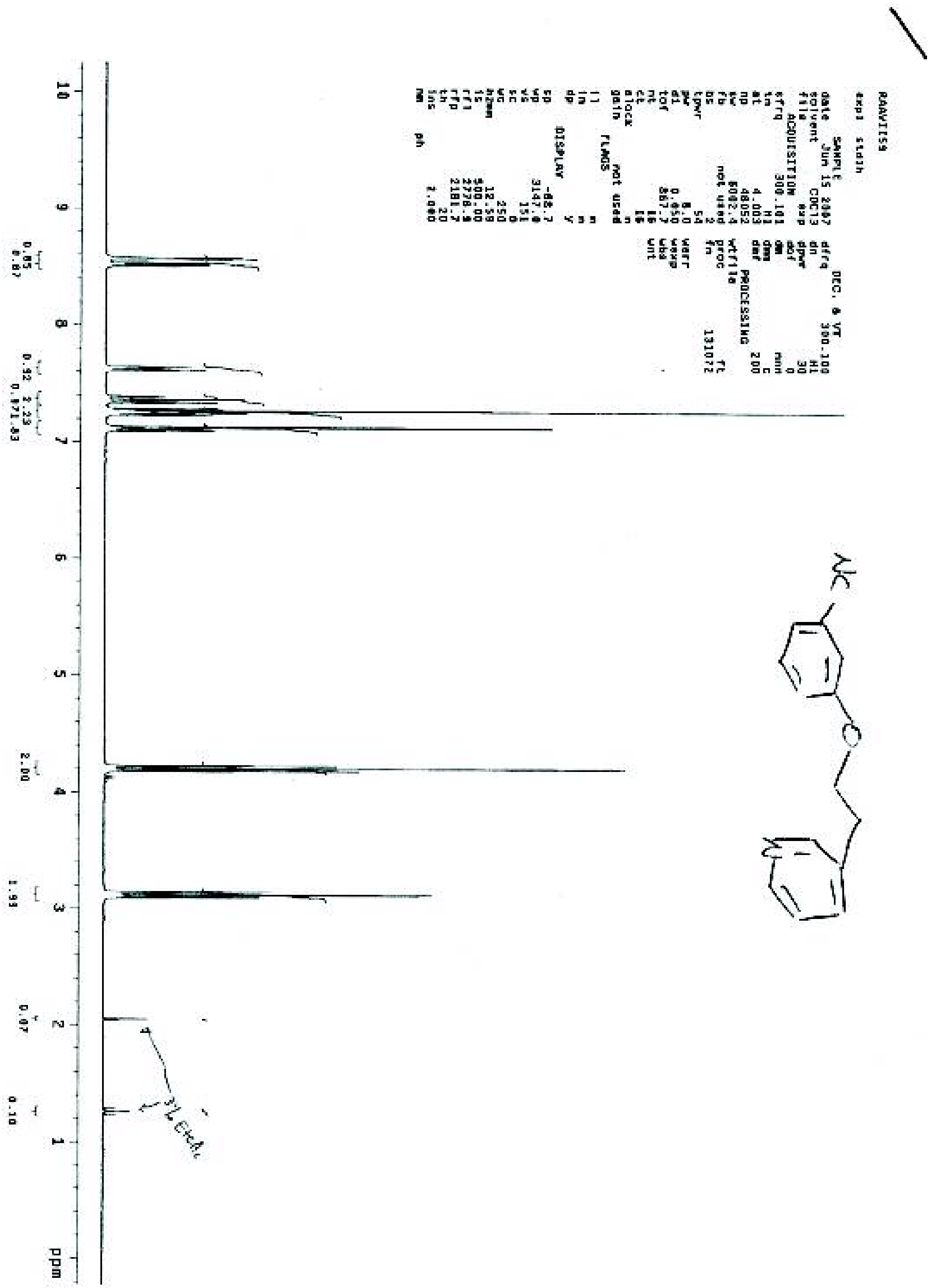
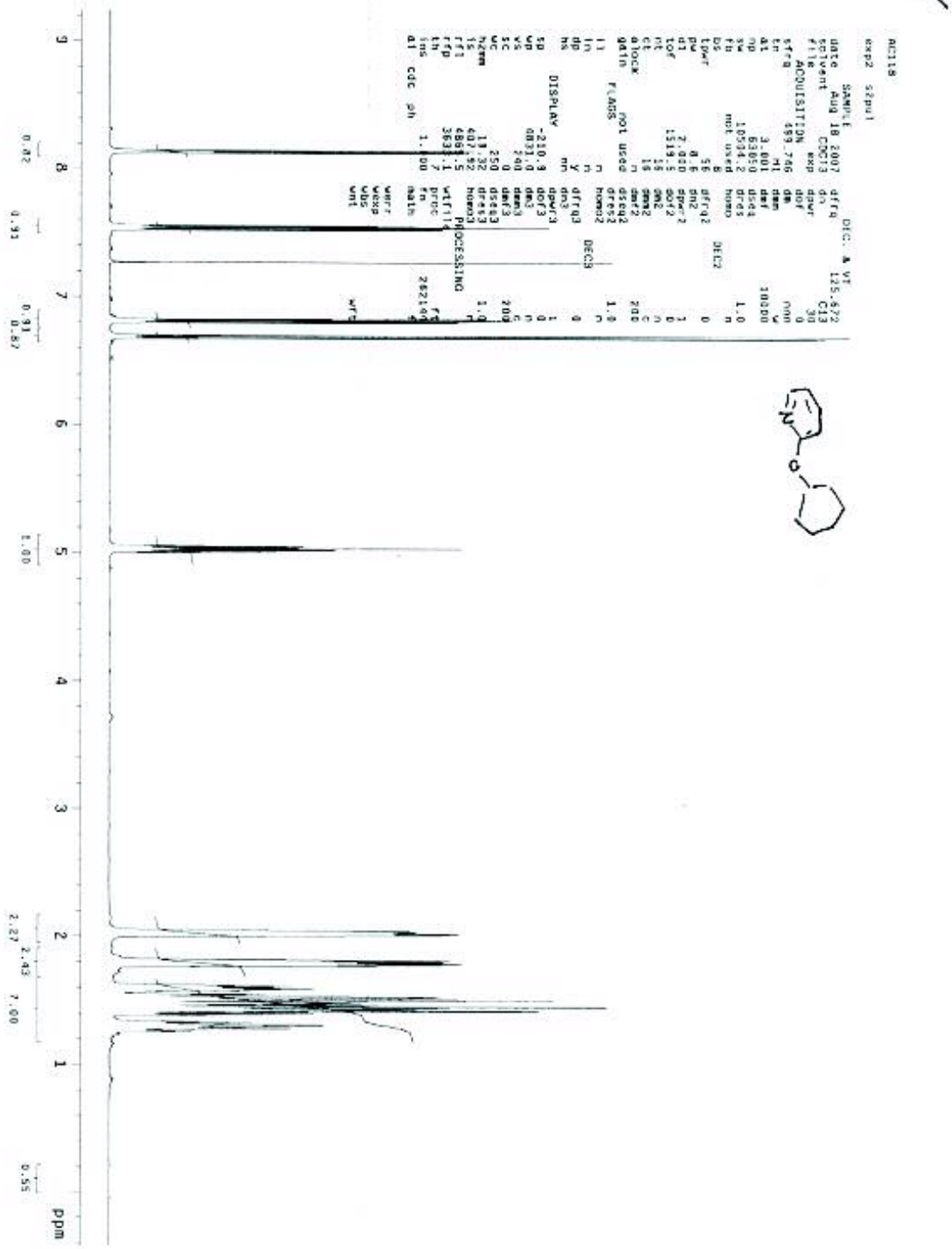
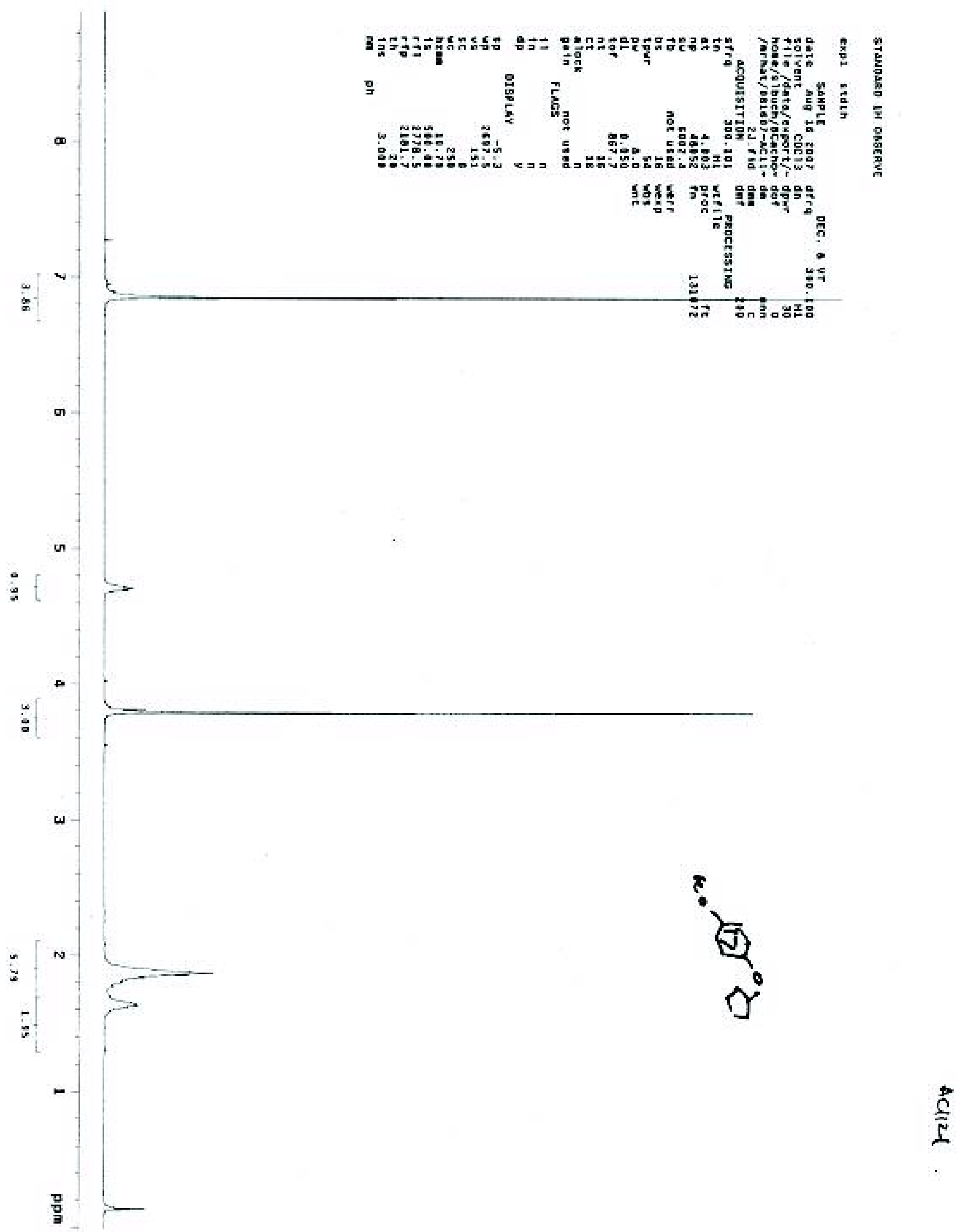
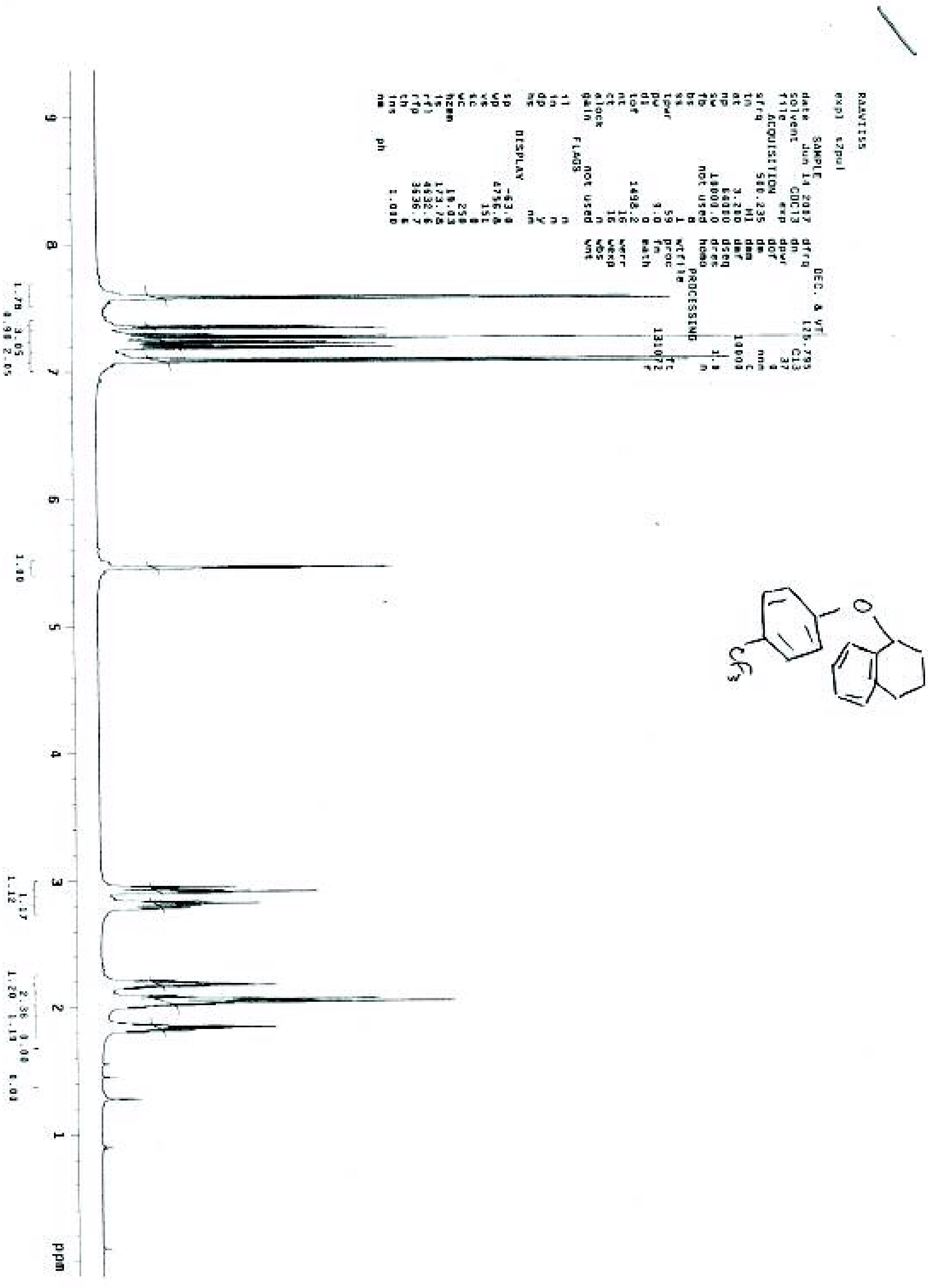
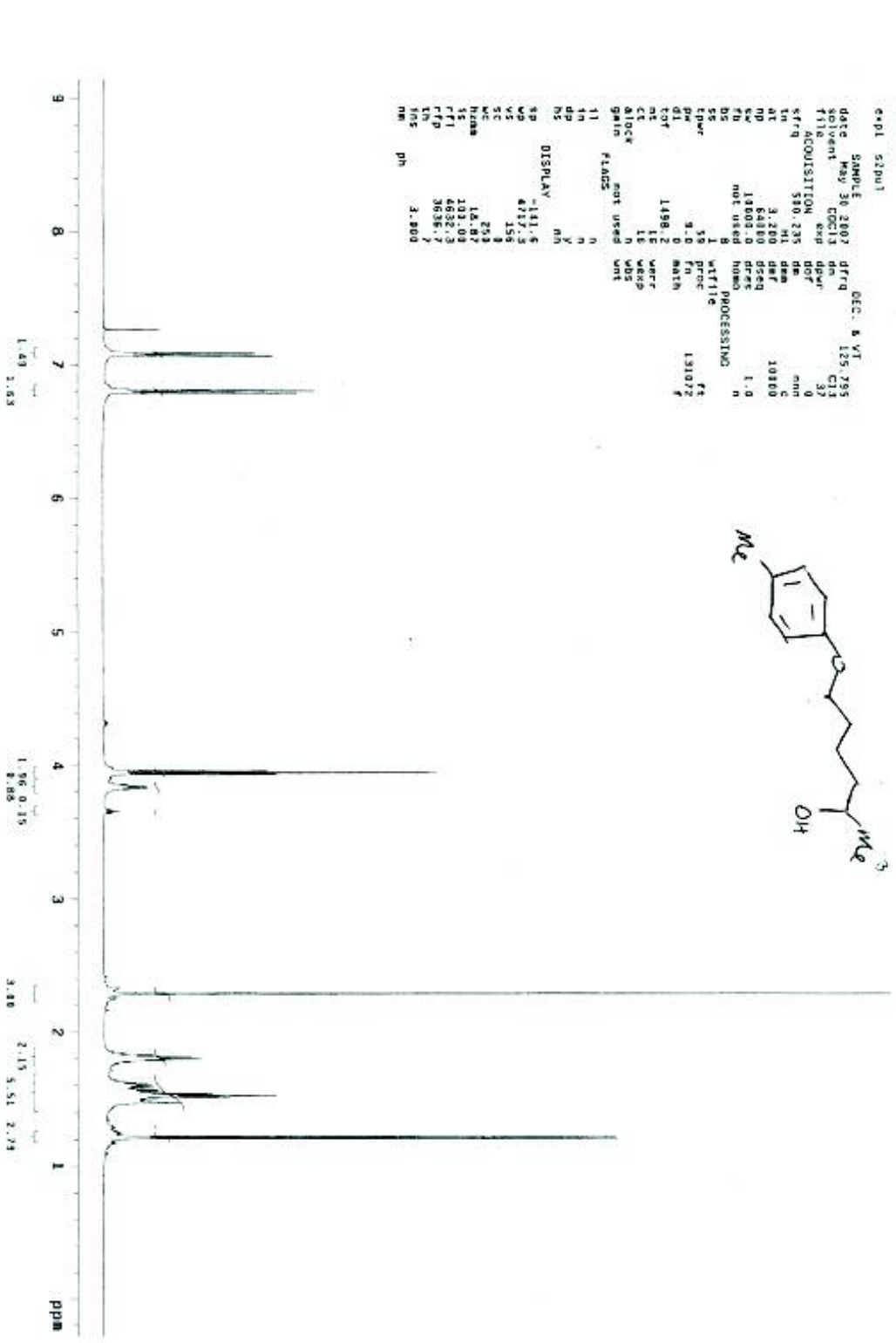
at 3.208
np 64008
sw 10160.8
fb not used
bs 8
ss 1
tpwr 53
pw 9.0
pl 0
tof 1499.2
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -81.2
wp 5151.0
vs 151
sc 0
wc 250
hzcm 20.60
is 100.80
rfl 4632.6
rfp 3635.7
th 16
ins 2.880
nm ph
DEC
sfrq 125.795
dn C13
dpwr 37
dof 0
dm nnn
dmm c
dmf 13808
dmg
dres 1.0
homo
PROCESSING
lb 0.
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
8.66
2.28.69.59
0.69 0.68.55 0.75
2.00
1.93
10
9
8
7
6
5
4
3
2
1
ppm




ppm






RAAVEII3
Me
OH
Me
ppm

4c100

STANDARD 1H OBSERVE

expl stdih

SAMPLE		DEC. & VT	
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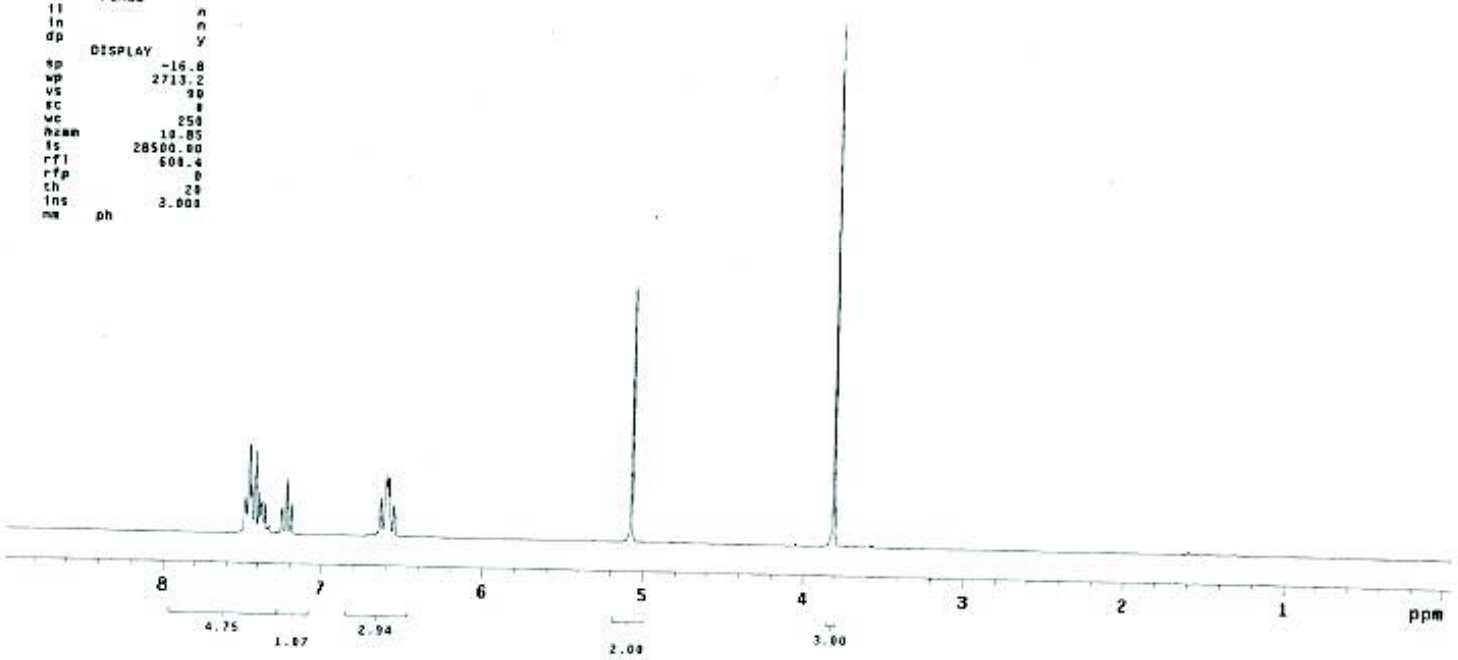
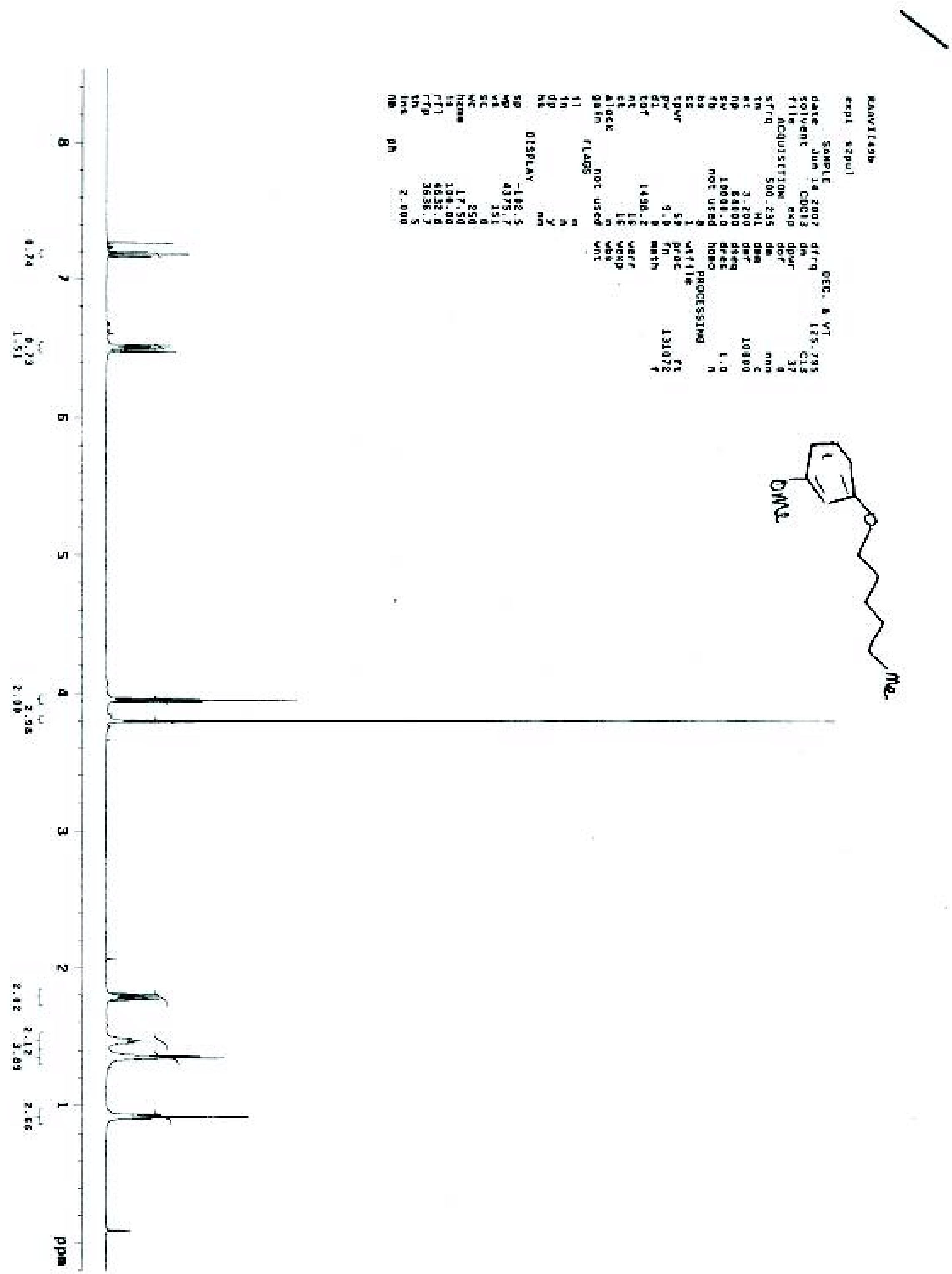
solvent	CDCl3	dn	H1
file	/data/export/~	dpwr	38
	home/slbuch/BCacho~	dof	0
	/mrhat/080807-AC10~	dm	nnn
	0H.fid	dmm	c
ACQUISITION		dmf	280
sfrq	300.101	PROCESSING	
tn	H1	wtfile	
at	4.083	proc	ft
np	48052	fn	131072
sw	6002.4		
fb	not used	werr	
bs	16	wexp	
tpwr	54	wbs	
pw	8.0	wnt	
dl	8.050		
tof	867.7		
nt	16		
ct	16		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-16.8		
wp	2713.2		
vs	90		
sc	0		
wc	250		
hzmm	18.85		
is	28500.00		
rfl	608.4		
rfp	0		
th	28		
ins	3.000		
ns	ph		





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