

4,7-Dimethoxy-1,10-Phenanthroline: An Excellent Ligand for the Cu-Catalyzed *N*-Arylation of Imidazoles

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Supporting Information

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General Considerations.

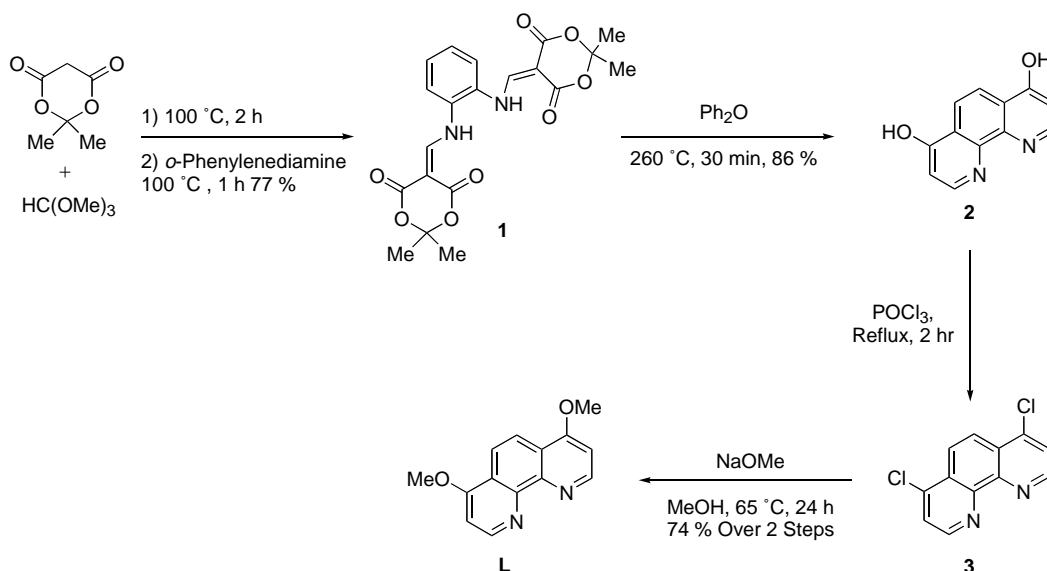
All reactions were carried out in resealable test tubes with teflon septa and run under a dry argon or nitrogen atmosphere. Copper (I) oxide (97%) was purchased from Aldrich company as a red powder. Anhydrous Cs_2CO_3 (99.9%) was purchased from Alfa Aesar; the bulk of the material was stored under nitrogen in a Vacuum Atmospheres glovebox. Small portions (~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. Poly(ethylene glycol) (M_n 3,400) was purchased from Aldrich. Generally, aryl halides and imidazoles were purchased from commercial sources and used without further purification. When necessary, aryl halides were filtered through neutral alumina, or distilled. Butyronitrile ($\geq 99\%$) was purchased from Aldrich and used without further purification. Anhydrous solvents were purchased from Aldrich in Sure-Seal® bottles. Flash column chromatography was performed with EM Science silica gel 60 (230-400 mesh). In all cases, dichloromethane was used to transfer the crude reaction material onto a silica gel column. A gradient elution technique was used for column chromatography, beginning with hexane and continuing to the specified concentration of ethyl acetate in hexane.

Yields reported in the publication are isolated (except where noted) 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 ^1H NMR, and melting point (m.p.) to the previously reported data; their purity was confirmed by gas chromatographic analyses (GC). For known compounds prepared using the new method (conditions) described, a copy of the ^1H NMR spectrum, of each, is included. 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. 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 ^1H NMR, ^{13}C NMR, m.p., and elemental analysis. Elemental analyses were performed by Atlantic Microlabs, Inc., Norcross, GA. For those compounds that did not give a satisfactory elemental analysis, a copy of their ^1H NMR spectrum is included. ^1H NMR and ^{13}C NMR were recorded on Varian 300 MHz and 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.

Synthesis of 4,7-dimethoxy-1,10-phenanthroline (L).

The synthesis of **L** was adapted from literature precedent.¹ A larger scale preparation of **L** can be performed as follows. Alternatively, **2** can be purchased in gram quantities from commercial sources.

Scheme 1. Synthesis of 4,7-Dimethoxy-1,10-Phenanthroline

1,2-Bis-[(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)methyl]amino]benzene (1).

An oven-dried 2 L 2-neck flask equipped with a mechanical stirrer was charged with trimethyl orthoformate (850 mL, 7.8 mol) and Meldrum's acid (101 g, 0.700 mmol). The flask was fitted with a reflux condenser; the contents were flushed with N₂ and brought to a gentle reflux for 2 h. The resulting red solution was cooled (~ 80 °C) and phenylene diamine (32.4 g, 300 mmol) was added portionwise (*exothermic reaction*) resulting in the formation of a yellow solid. The mixture was heated to reflux, stirred vigorously for an additional hour and then cooled to room temperature. The resulting solid was filtered, washed with cold acetone (slightly soluble) and dried to afford 95 g (77%) of product as a flaky light-yellow solid. ¹H NMR (CDCl₃, 400 MHz) δ 11.34 (br d, 2H), 8.50 (d, 2H), 7.41 (m, 4H, all ArH), 1.74 (s, 12H, Me). m.p. 208-210, decomp. (Lit. 209, decomp.).^{3a}

4,7-Dihydroxy-1,10-phenanthroline (2). A 5 L 3-neck flask equipped with a mechanical stirrer and a *large air-cooled* reflux condenser was charged with 3 L of diphenyl ether and was heated to 240 °C using a heating mantle. During the addition of **1**, the flask was open to atmospheric

pressure under a stream of N₂. Precursor **1** was added in small portions resulting in vigorous gas evolution (*Caution*). When the addition was complete, the mixture was brought to reflux (260 °C) for 30 min. The mixture was allowed to cool to 80 °C, and the precipitate was isolated by vacuum filtration and washed with acetone until the filtrate was colorless. The product was further washed with excess hexane and diethyl ether. Drying by vacuum filtration, then under hi-vac at 60 °C, afforded 41.5 g (86%) of a fine dark-brown powder. Although the title compound was essentially insoluble in common NMR solvents, a spectrum could be obtained using NaOH in D₂O. ¹H NMR (D₂O, NaOH, 400 MHz) δ 8.17 (d, 2H, *J* = 5.6 Hz), 7.75 (s, 2H), 6.43 (d, 2H *J* = 5.6 Hz). Anal Calc. for C₁₂H₈N₂: C 67.92, H 3.80. Found: C 67.60, H 3.59. m.p. stable up to 250 °C (Lit. 471-474, decomp.).²

4,7-Dichloro-1,10-phenanthroline (3). A 1 L 2-neck round bottom flask equipped with a stir bar, reflux condenser, and distillation apparatus was flame-dried and allowed to cool under an atmosphere of N₂. Phosphorous oxychloride (400 mL) and **2** (20.0 g, 94.3 mmol) were added to the flask under a N₂ purge. The apparatus was immersed in an oil bath and heated at reflux for 2 h (the condenser for the distillation apparatus was not filled with water at this time). After this period, the circulation of water for the distillation apparatus was turned on and roughly half of the excess phosphorous oxychloride was removed by gentle vacuum distillation. The solution was cooled to room temperature and crushed ice was slowly added to the reaction mixture (*Caution: very exothermic!*) while keeping the temperature between 10 and 30 °C with an ice bath. When HCl gas evolution ceased, the acidic solution was stirred for one hour at room temperature to dissolve the black solids that formed. The resulting dark cloudy solution was filtered through activated charcoal (Darco®) to give a translucent-beige solution, which was

brought to pH 13 by the slow addition of 20% KOH solution while maintaining the temperature below 25 °C. The white precipitate that formed was collected by suction filtration, washed with excess H₂O, and dried under vacuum overnight at 60 °C affording **3** as a white solid. The product was used in the subsequent step without further purification. ¹H NMR (DMSO, 400 MHz) δ 9.09 (d, 2H, *J* = 4.8 Hz), 8.41 (s, 2H), 8.08 (d, 2H, *J* = 4.8 Hz). m.p. 245-247 (Lit. 249-250).^{3c}

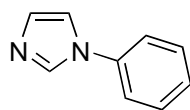
4,7-Dimethoxy-1,10-phenanthroline (L). An oven-dried 3-neck round bottom flask was cooled under a stream of nitrogen. Anhydrous methanol (1.2 L) was added, and purged with N₂ for 10 min. Sodium metal (9.20 g, 400 mmol) was slowly added in small pieces while the solution was stirred. A reflux condenser was attached, and **3** (all that was produced in the previous step) was added. The flask was heated to reflux for 24 hours under an atmosphere of N₂. Concentration of the resulting solution to ~30 mL and addition of cold water (250 mL) resulted in the precipitation of a tan solid. The flask was stored overnight in a refrigerator to allow complete precipitation of the solid. The product was collected by filtration, washed with excess water, and dried under vacuum overnight at 60 °C affording 16.7 g (74 % over 2 steps) of a tan solid, which can be recrystallized from benzene. ¹H NMR (CDCl₃, 300 MHz) δ 8.93 (d, 2H, *J* = 5.3 Hz), 8.18 (s, 2H), 7.03 (d, 2H, *J* = 5.3 Hz), 4.09 (s, 6H). m.p. 210-212 (Lit. 209-210).^{3e}

General procedure for the *N*-arylation of imidazoles with aryl iodides.

An oven-dried screw-cap test tube was charged with Cu₂O (0.025 mmol), **L** (0.075 mmol), imidazole (1.2 mmol), aryl iodide (1.00 mmol, if solid), poly(ethylene glycol) (200 mg), Cs₂CO₃ (1.4 mmol), and a magnetic stir bar. The reaction vessel was fitted with a rubber septum. The vessel was evacuated and back-filled with argon or nitrogen, and this sequence was repeated an

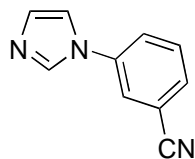
additional time. Aryl iodide (1.00 mmol, if liquid) and solvent (0.5 mL) were then added successively. The reaction tube was sealed, and stirred in a pre-heated oil bath for the designated time period. The reaction mixture was cooled to room temperature, diluted with dichloromethane (10 mL), and filtered through a plug of celite, eluting with additional dichloromethane (50 mL). The filtrate was concentrated and the resulting residue was purified by flash chromatography to provide the desired product.

Experimental procedures for the *N*-arylation of imidazole with aryl iodides.



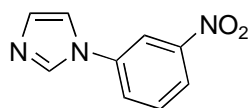
1-Phenyl-1*H*-imidazole

The general procedure was followed using Cu₂O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs₂CO₃ (0.45 g, 1.4 mmol), iodobenzene (112 μ L, 1.00 mmol), and imidazole (82 mg, 1.2 mmol), with NMP (0.5 mL) as solvent for 3 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1 : 3) afforded 1-phenyl-1*H*-imidazole (slightly yellow oil, 131 mg, 92 %). The low catalyst loading experiment was performed using the general procedure with Cu₂O (0.4 mg, 0.0025 mmol), **L** (1.8 mg, 0.0075 mmol), PEG (2.0 g), Cs₂CO₃ (4.50 g, 14 mmol), iodobenzene (1.12 mL, 10 mmol), and imidazole (820 mg, 12 mmol), in butyronitrile (2.0 mL) as solvent for 48 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1 : 3) provided 1-phenyl-1*H*-imidazole (slightly yellow oil, 1.34 g, 93 %). ¹H NMR (300 MHz, CDCl₃) δ 7.82 (s, 1H), 7.47-7.41 (m, 2H), 7.36-7.29 (m, 3H), 7.25 (bs, 1H), 7.18 (bs, 1H).³ A copy of the ¹H NMR spectrum is provided.



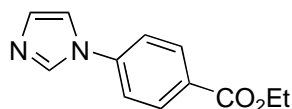
3-Imidazol-1-yl-benzonitrile

The general procedure was followed using Cu₂O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs₂CO₃ (0.45 g, 1.4 mmol), 3-iodobenzonitrile (229 mg, 1.00 mmol), and imidazole (82 mg, 1.2 mmol), with butyronitrile (0.5 mL) as solvent for 24 h at 90 °C. Chromatographic purification (hexane / ethyl acetate 1 : 3) 3-imidazol-1-yl-benzonitrile (white needles, 158 mg, 94 %). ¹H NMR (500 MHz, CDCl₃) δ 7.89 (s, 1H), 7.71-7.60 (m, 4H), 7.30 (bs, 1H), 7.25 (bs, 1H). m.p. 151-154 °C (Lit. 156-157 °C).⁴ A copy of the ¹H NMR spectrum is provided.



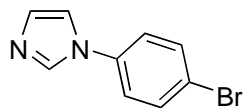
1-(3-Nitro-phenyl)-1H-imidazole

The general procedure was followed using Cu₂O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs₂CO₃ (0.45 g, 1.4 mmol), 3-nitroiodobenzene (249 mg, 1.00 mmol), and imidazole (83 mg, 1.2 mmol) with acetonitrile (0.5 mL) as solvent for 29 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1 : 3) 1-(3-nitro-phenyl)-1H-imidazole (white solid, 177 mg, 93 %). ¹H NMR (500 MHz, CDCl₃) δ 8.25 (t, 1H, *J* = 1.9), 8.19 (ddd, 1H, *J* = 1.1, 1.9, 7.9 Hz), 7.94 (s, 1H), 7.75 (ddd, 1H, *J* = 1.4, 2.2, 8.1 Hz), 7.69 (t, 1H, *J* = 8.0 Hz), 7.36 (s, 1H), 7.23 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 149.1, 138.3, 125.5, 131.5, 131.2, 126.9, 122.1, 118.0, 116.2. m.p. 109-110 °C (Lit. 109-110 °C).⁵ A copy of the ¹H NMR spectrum is provided.

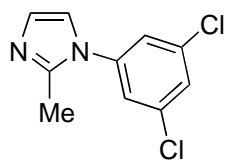


4-Imidazol-1-yl-benzoic acid ethyl ester

The general procedure was followed using Cu_2O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), ethyl-4-iodobenzoate (168 μL , 1.00 mmol), and imidazole (82 mg, 1.2 mmol), 3 Å molecular sieves (200 mg, powdered, flame activated) with acetonitrile (0.5 mL) as solvent for 23 h at 80 °C. Chromatographic purification (hexane / ethyl acetate 1 : 3) 4-imidazol-1-yl-benzoic acid ethyl ester (white crystals, 184 mg, 84 %). ^1H NMR (500 MHz, CDCl_3) δ 8.18 (td, 2H, $J = 1.8, 8.5$ Hz), 7.96 (s, 1H), 7.48 (td, 2H, $J = 1.8, 8.8$), 7.37 (s, 1H), 7.26 (s, 1H), 4.43 (q, 2H, $J = 7.1$ Hz), 1.44 (t, 3H, $J = 7.0$ Hz). m.p. 101-103 °C (Lit. 100-102 °C).⁶ A copy of the ^1H NMR spectrum is provided.

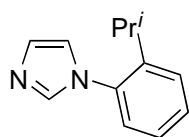
**1-(4-Bromo-phenyl)-1H-imidazole⁷**

The general procedure was followed using Cu_2O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 1-bromo-4-iodobenzene (340 mg, 1.20 mmol), and imidazole (68 mg, 1.0 mmol) with butyronitrile (0.5 mL) as solvent for 24 h at 90 °C. Chromatographic purification (hexane / ethyl acetate 1 : 1) provided 1-(4-bromo-phenyl)-1H-imidazole (white crystals, 171 mg, 78 %). ^1H NMR (300 MHz, CDCl_3) δ 7.83 (bs, 1H), 7.63 (m, 2H), 7.32-7.20 (m, 4H). m.p. 120-122 °C. GC/MS of the crude material showed a 6.1 : 1 mixture of 1-(4-bromo-phenyl)-1H-imidazole to 1-(4-iodo-phenyl)-1H-imidazole. A copy of the ^1H NMR spectrum is provided.

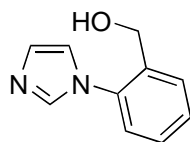


1-(3,5-Dichloro-phenyl)-2-methyl-1*H*-imidazole

The general procedure was followed using Cu₂O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (200 mg), Cs₂CO₃ (0.45 g, 1.4 mmol), 1,3-dichloro-5-iodobenzene (273 mg, 1.00 mmol), 2-methylimidazole (100 mg, 1.2 mmol) with butyronitrile (0.5 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1 : 3) provided 1-(3,5-dichloro-phenyl)-2-methyl-1*H*-imidazole (white needles, 194 mg, 86 %). ¹H NMR (300 MHz, CDCl₃) δ 7.44 (t, 1H, *J* = 1.8), 7.23 (d, 2H, *J* = 1.9), 7.05 (d, 1H, *J* = 1.2), 6.99 (d, 1H, *J* = 1.2), 2.40 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 139.8, 135.8, 128.5, 128.4, 124.1, 14.0. IR (KBr disc, cm⁻¹) 1534, 1501, 1463, 1451, 1405, 1305, 1176, 1143, 1115, 1099, 985, 850, 781. Anal. Calc. for C₁₀H₈N₂Cl₂: C 52.89, H 3.55. Found: C 52.95, H 3.44. m.p. 122-125 °C.

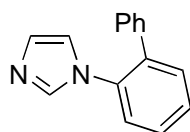
**1-(2-Isopropyl-phenyl)-1*H*-imidazole**

The general procedure was followed using Cu₂O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs₂CO₃ (0.45 g, 1.4 mmol), 2-isopropyl iodobenzene (246 mg, 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with butyronitrile (0.5 mL) as solvent for 48 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1 : 1) provided 1-(2-isopropyl-phenyl)-1*H*-imidazole (white crystals, 171 mg, 92 %). ¹H NMR (300 MHz, CDCl₃) δ 7.57 (bs, 1H), 7.46-7.42 (m, 2H), 7.31-7.11 (m, 3H), 7.05 (m, bs), 2.74 (heptet, 1H, *J* = 6.9 Hz), 1.16 (d, 6H, *J* = 6.9 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 145.0, 135.1, 129.4, 129.2, 127.0, 126.7, 126.4, 121.1, 27.4, 24.0. m.p. 76-77 °C (Lit. 67-68 °C).⁸ Anal. Calc. for C₁₂H₁₄N₂: C 77.38, H 7.58. Found: C 77.42, H 7.78. A copy of the ¹H NMR spectrum is provided.



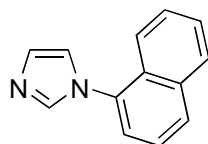
(2-Imidazol-1-yl-phenyl)-methanol

The general procedure was followed using Cu_2O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 2-iodobenzylalcohol (234 mg, 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with butyronitrile (0.3 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1 : 1) provided (2-imidazol-1-yl-phenyl)-methanol (clear crystals, 165 mg, 95 %). ^1H NMR (300 MHz, CDCl_3) δ 7.62 (dd, 2H, $J = 1.7, 7.6$ Hz), 7.45 (td, 1H, $J = 1.4, 7.5$ Hz), 7.38 (td, 1H, $J = 1.4, 7.4$ Hz), 7.23 (dd, 1H, $J = 1.1, 7.7$ Hz), 7.13 (s, 1H), 7.08 (s, 1H), 4.90 (bs, 1H), 4.46 (s, 1H). m.p. 102-104 °C (Lit. 100.5-102.5 °C).⁹ A copy of the ^1H NMR spectrum is provided.



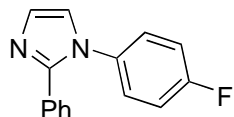
1-Biphenyl-2-yl-1H-imidazole

The general procedure was followed using Cu_2O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 2-iodobiphenyl (176 μL , 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with butyronitrile (0.6 mL) as solvent for 72 h at 120 °C. Chromatographic purification (hexane / ethyl acetate 1 : 1) provided 1-biphenyl-2-yl-1H-imidazole (slightly yellow crystals, 179 mg, 81 %). ^1H NMR (300 MHz, CDCl_3) δ 7.50-7.33 (m, 5H), 7.30-7.24 (m, 3H), 7.02 (bs, 1H), 6.82 (bs, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 137.8, 137.5, 135.2, 131.5, 128.7, 128.7, 128.6, 128.3, 127.8, 126.3. Anal. Calc. for $\text{C}_{15}\text{H}_{12}\text{N}_2$: C 81.79, H 5.49. Found: C 81.50, H 5.46. m.p. 93-95 °C.



1-Naphthalen-1-yl-1H-imidazole

The general procedure was followed using Cu_2O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 1-iodonaphthalene (146 μL , 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with NMP (0.3 mL) as solvent for 24 h at 110 °C. The crude reaction mixture was dissolved in 20 mL of water, and extracted with dichloromethane (5 x 30 mL). The combined organic layers were dried with MgSO_4 , and the solvent was removed *in vacuo*. Chromatographic purification (hexane / ethyl acetate 1 : 1) provided 1-naphthalen-1-yl-1H-imidazole (yellow-white solid, 179 mg, 92 %). ^1H NMR (300 MHz, CDCl_3) δ 7.94-7.92 (m, 2H), 7.76, (bs, 1H), 7.61-7.48 (m, 4 H), 7.43 (d, 1H, $J = 7.0$ Hz), 7.30 (bs, 1H), 7.25 (bs, 1H). m.p. 63-64 °C (Lit. 62 °C).¹⁰ A copy of the ^1H NMR spectrum is provided.



1-(4-Fluoro-phenyl)-2-phenyl-1H-imidazole

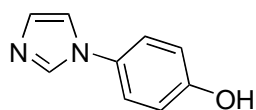
The general procedure was followed using Cu_2O (3.6 mg, 0.025 mmol), **L** (18 mg, 0.075 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 4-fluoroiodobenzene (222 mg, 1.00 mmol), 2-phenylimidazole (173 mg, 1.2 mmol) with butyronitrile (0.3 mL) as solvent for 24 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 3 : 1) provided 1-(4-fluoro-phenyl)-2-phenyl-1H-imidazole (white solid, 211 mg, 89 %). ^1H NMR (300 MHz, CDCl_3) δ 7.36-7.30 (m, 2H), 7.24-7.16 (m, 4H), 7.15-7.09 (m, 2H), 7.06 (s, 1H), 7.03-6.96 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.5, 160.2, 134.5, 129.0, 128.5, 128.4, 128.2, 127.6, 127.5, 116.5, 116.2. IR (KBr disc, cm^{-1}) 1509, 1501, 1466, 1414, 1303, 1285, 1233, 1212, 1151, 1128, 1091, 1068, 970, 915, 840, 775,

747, 715, 697. Anal. Calc. for $C_{15}H_{11}N_2F$: C 75.62, H 4.65. Found: C 75.39, H 4.62. m.p. 111-114 °C.

General procedure for the *N*-arylation of imidazoles with aryl bromides.

An oven-dried screw-cap test tube was charged with Cu_2O (0.05 mmol), **L** (0.15 mmol), imidazole (1.2 mmol), aryl bromide (1.00 mmol, if solid), poly(ethylene glycol) (200 mg), Cs_2CO_3 (1.4 mmol), and a magnetic stir bar. The reaction vessel was fitted with a rubber septum. The vessel was evacuated and back-filled with argon or nitrogen, and this sequence was repeated an additional time. Aryl bromide (1.00 mmol, if liquid), and solvent (0.5 mL) were then added successively. The reaction tube was sealed, immersed, and stirred in a preheated oil bath for the designated time period. The reaction mixture was cooled to room temperature, diluted with dichloromethane (10 mL), filtered through a plug of celite, and eluted with additional dichloromethane (50 mL). The filtrate was concentrated and the resulting residue was purified by flash chromatography to provide the desired product.

Experimental procedures for the *N*-arylation of imidazole with aryl bromides.

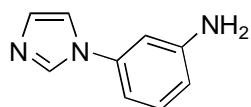


4-Imidazol-1-yl-phenol

The general procedure was followed using Cu_2O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (400 mg), Cs_2CO_3 (1.0 g, 3.0 mmol), 4-bromophenol (172 mg, 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with butyronitrile (0.5 mL) as solvent for 15 h at 110 °C. After cooling to ambient temperature, the crude reaction mixture was dissolved in 20 mL 2M $HCl_{(aq)}$, and washed once with diethyl ether. The aqueous layer was brought to pH 8 with Na_2CO_3 , and extracted repeatedly with CH_2Cl_2 . The combined organic layers were dried with anhydrous $MgSO_4$, and concentrated.

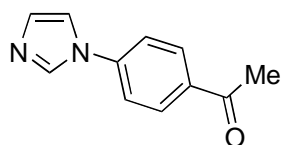
Chromatographic purification (1 % ethanol in ethyl acetate, dry pack) afforded 4-imidazol-1-yl-phenol (white crystals, 198 mg, 90 %). ^1H NMR (300 MHz, CD_3OD) δ 7.95 (bs, 1H), 7.41 (bs, 1H), 7.35-7.30 (m, 2H), 7.01 (bs, 1H), 6.92-6.87 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.7, 130.8, 129.8, 124.3, 117.4, 24.0. m.p. 196-198 °C (Lit. 188-190 °C [203-205 °C MeOH, H_2O]).¹¹

A copy of the ^1H NMR spectrum is provided.



3-Imidazol-1-yl-phenylamine

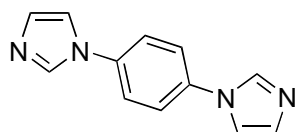
The general procedure was followed using Cu_2O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 3-bromoaniline (109 μL , 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with butyronitrile (0.25 mL) as solvent for 20 h at 110 °C. Chromatographic purification (ethyl acetate) afforded 3-imidazol-1-yl-phenylamine (white powder, 141 mg, 88 %). ^1H NMR (300 MHz, CDCl_3) δ 7.79 (bs, 1H), 7.21-7.15 (m, 3H), 6.72-6.68 (m, 1H), 6.64-6.60 (m, 2H). 4.01 (bs, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 148.2, 138.4, 135.6, 130.7, 130.1, 118.4, 114.0, 111.1, 107.7. m.p. 112-114 °C (Lit. 111-113 °C).¹² A copy of the ^1H NMR spectrum is provided.



1-(4-Imidazol-1-yl-phenyl)-ethanone

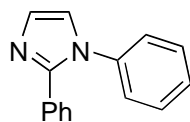
The general procedure was followed using Cu_2O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 4-bromoacetophenone (199 mg, 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with butyronitrile (0.4 mL) as solvent for 48 h at 110 °C. Chromatographic

purification (hexane / ethyl acetate 1 : 3) afforded 1-(4-imidazol-1-yl-phenyl)-ethanone (white solid, 159 mg, 86 %). ^1H NMR (300 MHz, CDCl_3) δ 8.04, (m, 2H), 7.92 (bs, 1H), 7.46 (m, 2H), 7.33 (bs, 1H), 7.19 (bs, 1H), 2.59 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.6, 140.7, 135.7, 135.4, 131.2, 130.4, 120.7, 117.8, 26.7. m.p. 112-114 °C (Lit. 110-112 °C).¹³ A copy of the ^1H NMR spectrum is provided.



1,4-*bis*(Imidazol-1-yl)-benzene¹⁴

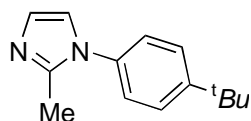
The general procedure was followed using Cu_2O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), Cs_2CO_3 (0.90 g, 2.8 mmol), 1,4-dibromobenzene (236 mg, 1.00 mmol), and imidazole (164 mg, 2.4 mmol) with NMP (0.5 mL) as solvent for 30 h at 110 °C. The crude reaction mixture was diluted in excess CH_2Cl_2 , and filtered through a celite plug. After removal of the solvent *in vacuo*, the product was crystallized from EtOAc and stored in a freezer overnight, to afford 1,4-*bis*(imidazol-1-yl)-benzene (white solid, 200 mg, 95 %). ^1H NMR (500 MHz, CDCl_3) δ 7.90 (bs, 2H), 7.54 (s, 4H), 7.32 (bs, 1H), 7.26 (bs, 1H). m.p. 190 °C (decomp.). IR (KBr disc, cm^{-1}) 1534, 1485, 1304, 1248, 1105, 1059. Anal Calc. for $\text{C}_{12}\text{H}_{10}\text{N}_4$: C 68.56, H 4.79. Found C 68.49, H 4.90.



1,2-Diphenyl-1*H*-imidazole

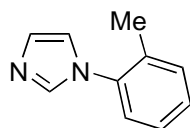
The general procedure was followed using Cu_2O (14.4 mg, 0.10 mmol), **L** (72 mg, 0.30 mmol), PEG (200 mg), Cs_2CO_3 (0.45 g, 1.4 mmol), 4-*t*-butylbromobenzene (173 μL , 1.00 mmol), and imidazole (82 mg, 1.2 mmol) with butyronitrile (0.6 mL) as solvent for 72 h at 120 °C.

Chromatographic purification (hexane / ethyl acetate 1 : 1) afforded 1,2-diphenyl-1*H*-imidazole (white crystals, 198 mg, 90 %). ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.32 (m, 5H), 7.28-7.16 (m, 6H), 7.14 (d, 1H, *J* = 1.1 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 138.6, 130.4, 129.5, 129.1, 128.6, 128.4, 128.2, 128.2, 125.9, 123.0. m.p. 88-89 °C (Lit. 90 °C).¹⁵ A copy of the ¹H NMR spectrum is provided.



1-(4-*tert*-Butyl-phenyl)-2-methyl-1*H*-imidazole

The general procedure was followed using Cu₂O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (200 mg), Cs₂CO₃ (0.45 g, 1.4 mmol), 4-*t*-butylbromobenzene (173 μL, 1.00 mmol), 2-methylimidazole (100 mg, 1.2 mmol) with butyronitrile (0.25 mL) as solvent for 48 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1 : 3) afforded 1-(4-*tert*-butyl-phenyl)-2-methyl-1*H*-imidazole (yellow oil, 207 mg, 97 %). ¹H NMR (300 MHz, CDCl₃) δ 7.41 (m, 2H), 7.12 (m, 1H), 6.94 (bs, 1H), 6.91 (bs, 1H), 2.28 (s, 3H), 1.29 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 151.1, 135.3, 127.5, 126.3, 124.9, 12.7, 34.6, 31.3, 13.8. IR (KBr Disc, cm⁻¹) 2962, 2870, 1608, 1579, 1513, 1463, 1419, 1365, 1302, 1269, 1178, 1139, 1114, 996, 986, 842, 730, 674, 571. A copy of the ¹H NMR spectrum is provided.



1-*ortho*-Tolyl-1*H*-imidazole

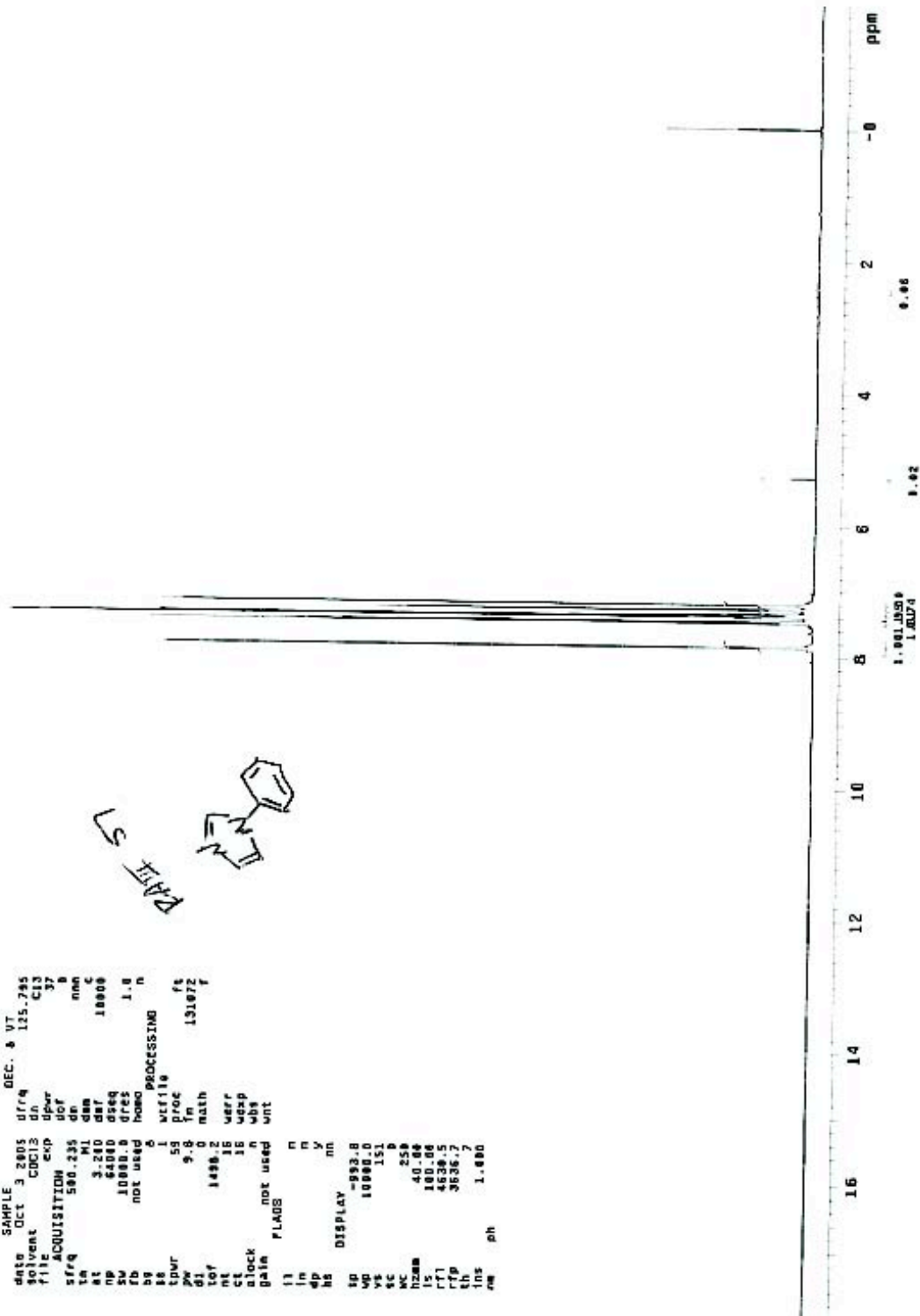
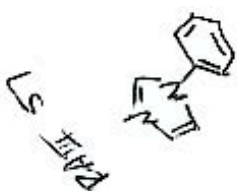
The general procedure was followed using Cu₂O (7.2 mg, 0.05 mmol), **L** (36 mg, 0.15 mmol), PEG (200 mg), Cs₂CO₃ (0.45 g, 1.4 mmol), 2-bromotoluene (120 μL, 1.00 mmol), and imidazole (82

mg, 1.2 mmol) with butyronitrile (0.3 mL) as solvent for 28 h at 110 °C. Chromatographic purification (hexane / ethyl acetate 1 : 1) afforded 1-*ortho*-tolyl-1*H*-imidazole (yellow oil, 140 mg, 89 %). ¹H NMR (300 MHz, CDCl₃) δ 7.59 (bs, 1H), 7.37-7.28 (m, 3H), 7.23-7.20 (m, 2H), 7.06 (bs, 1H), 2.19 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 148.2, 138.4, 135.6, 130.7, 130.1, 118.4, 114.0, 111.1, 107.7.¹⁶ A copy of the ¹H NMR spectrum is provided.

STANDARD PROTON PARAMETERS

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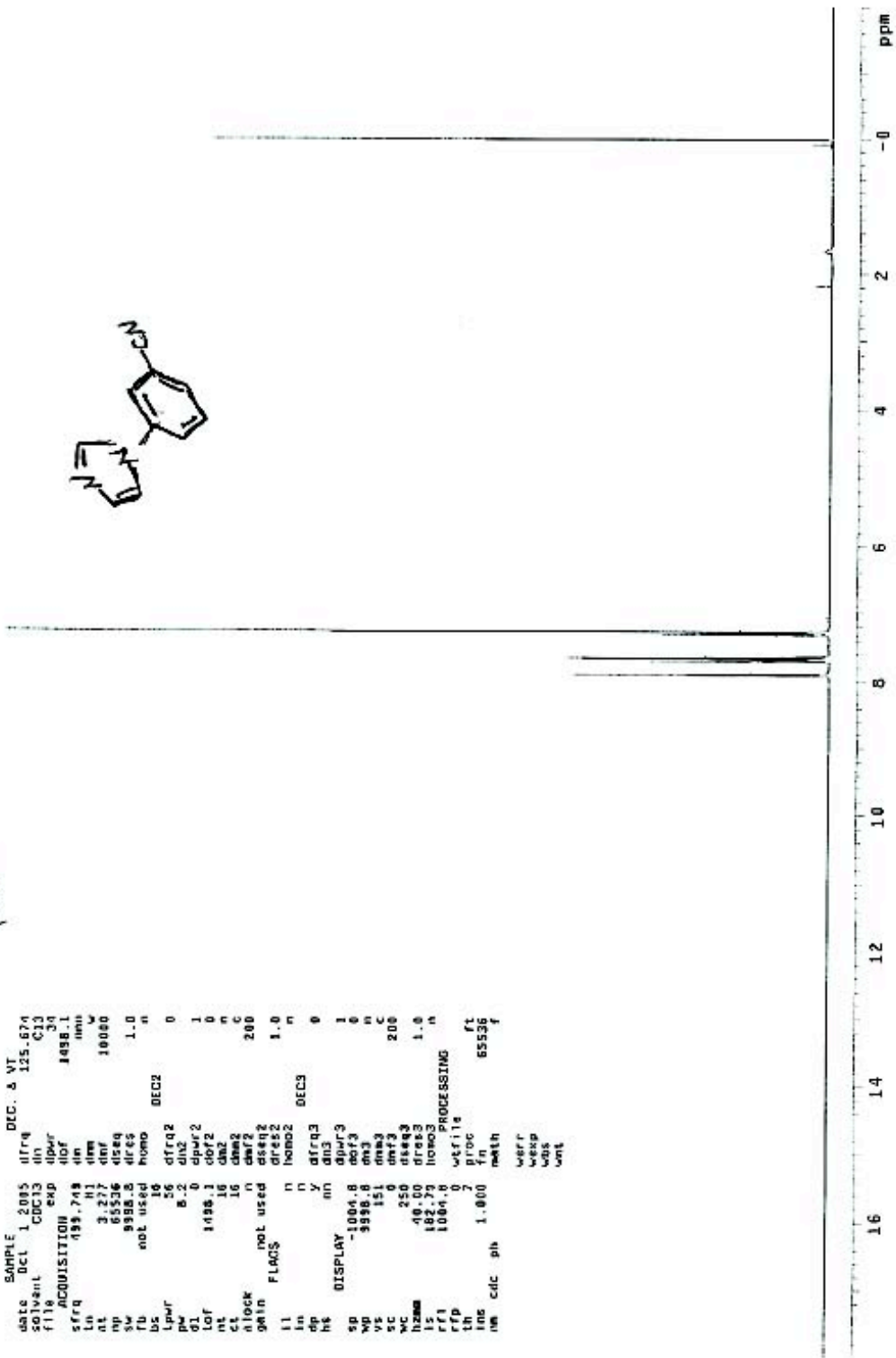
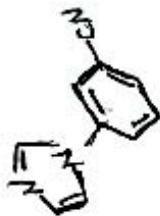


RAA III 157

STANDARD PROTON PARAMETERS

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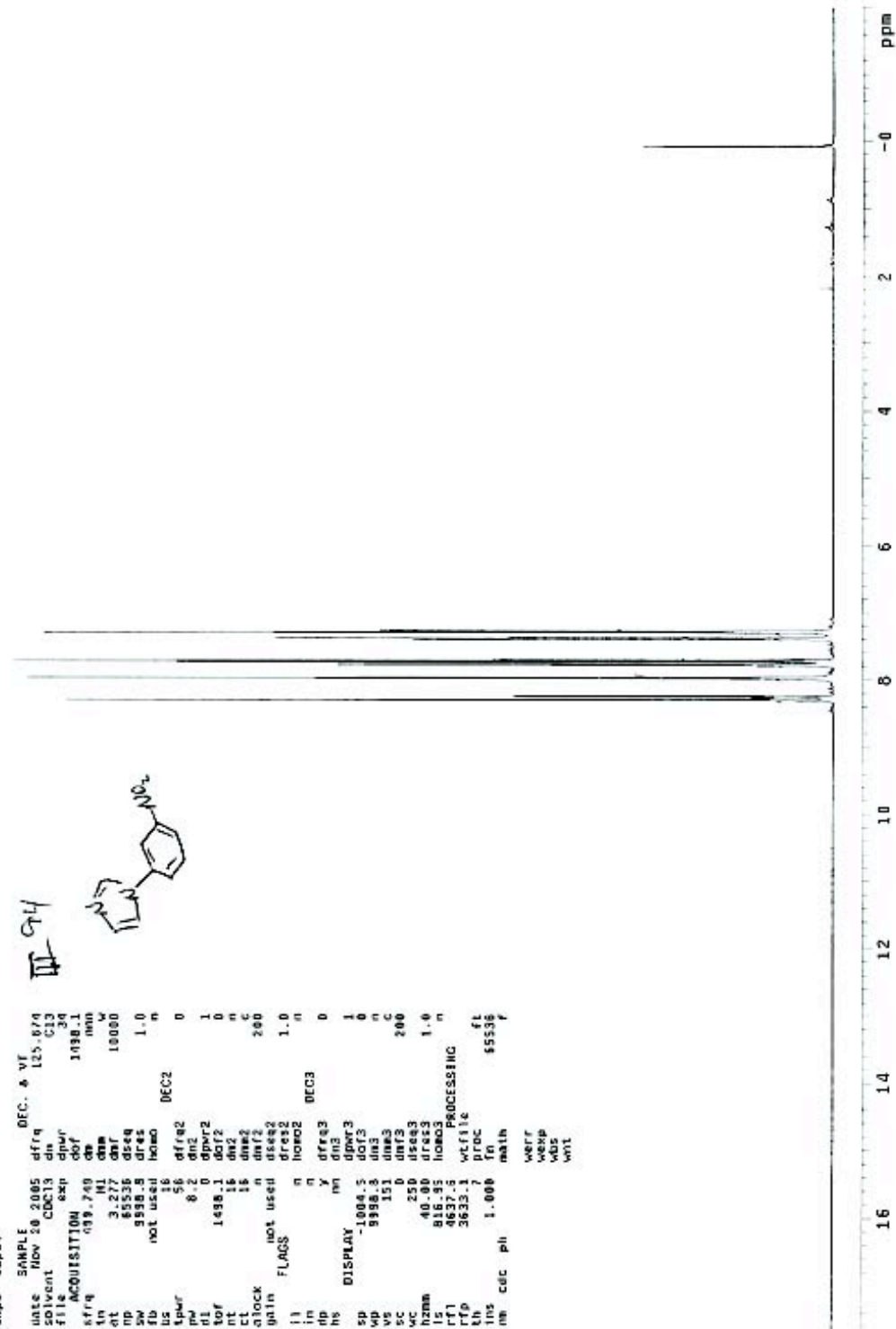
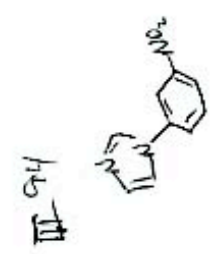
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STANDARD PROTON PARAMETERS

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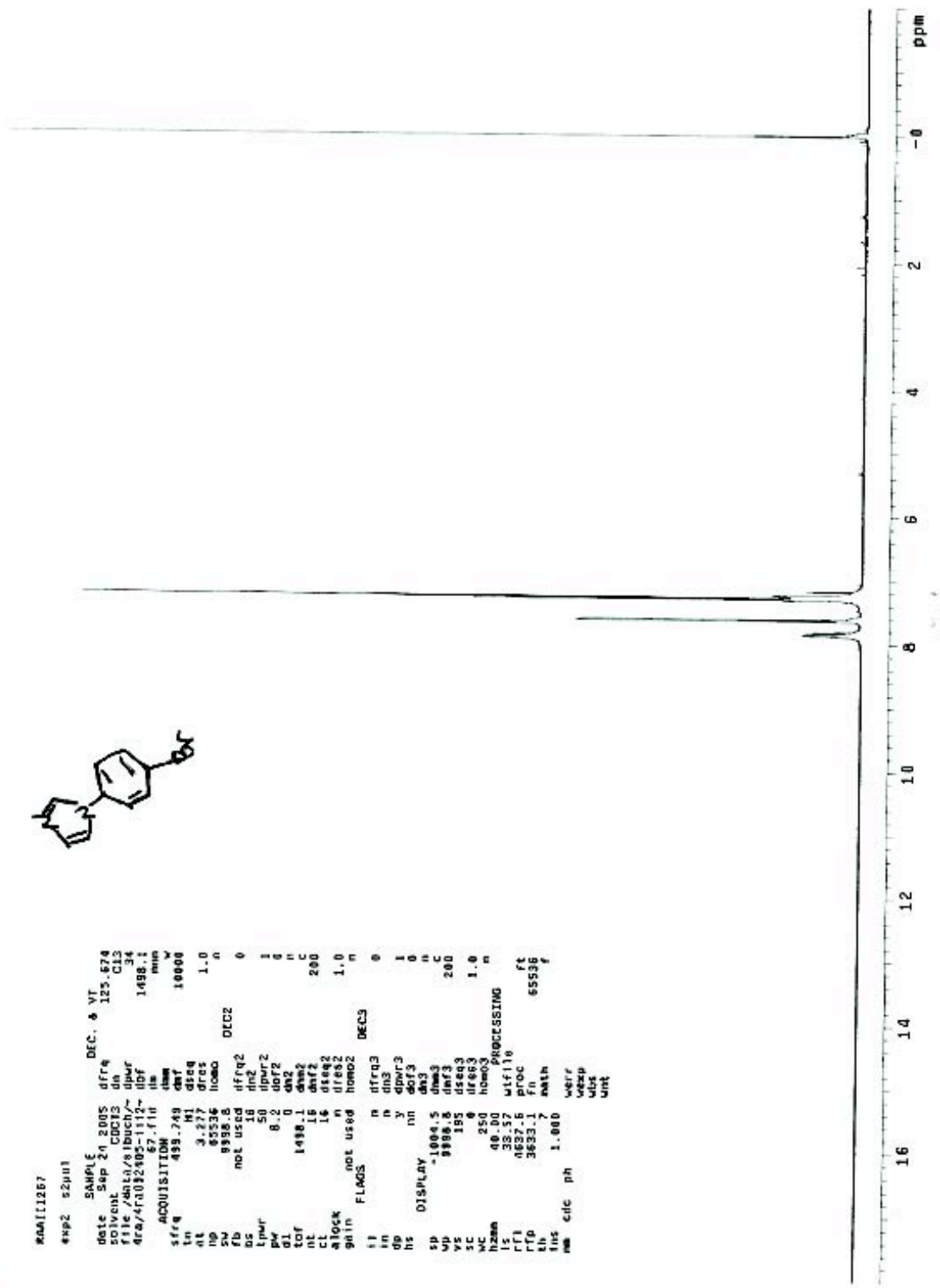


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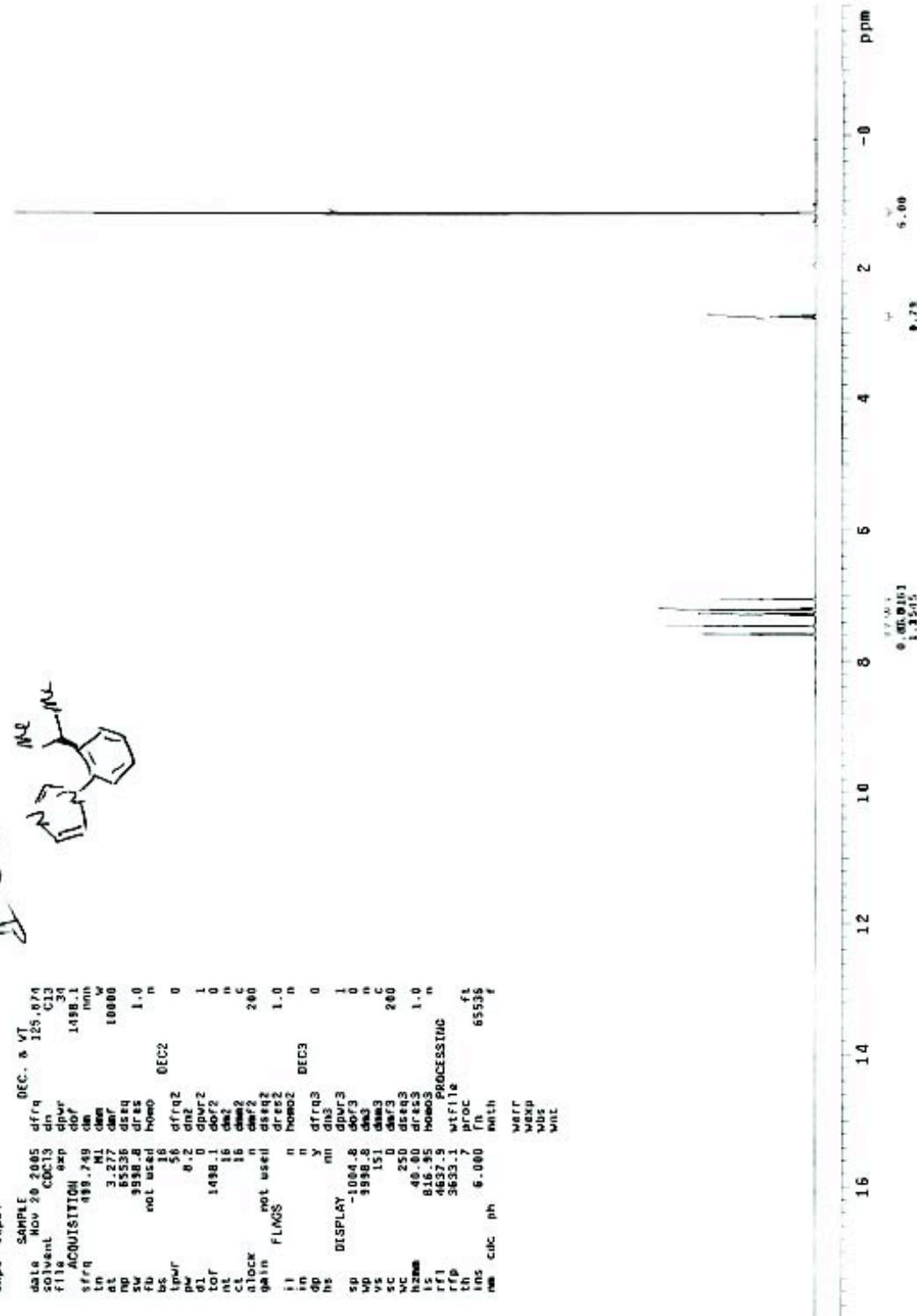
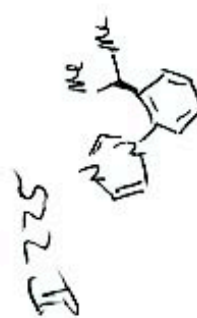
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STANDARD PROTON PARAMETERS

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0.000103
1.3515

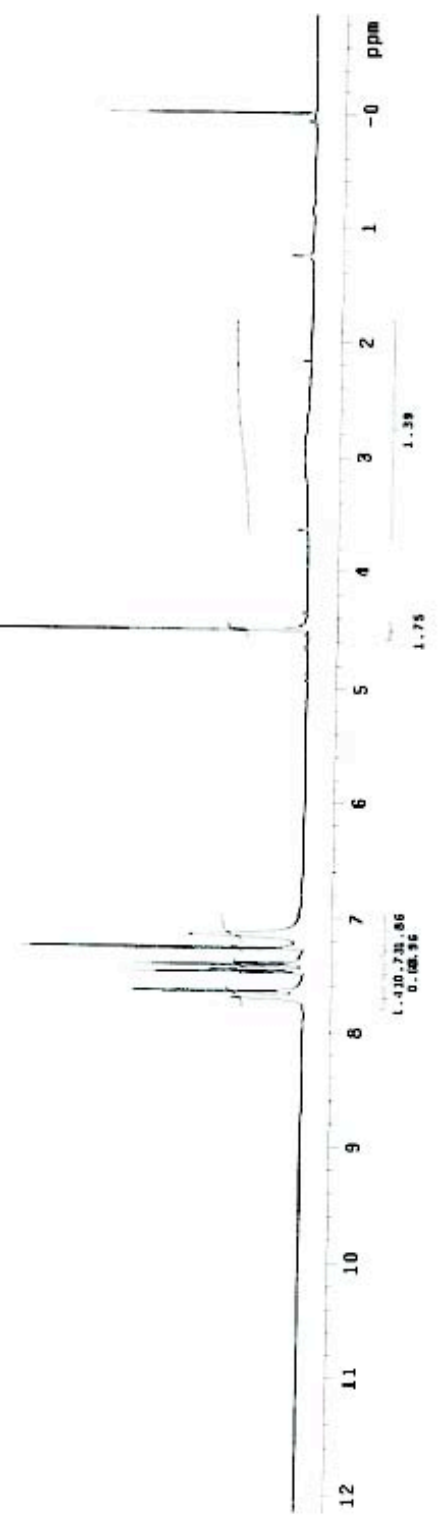
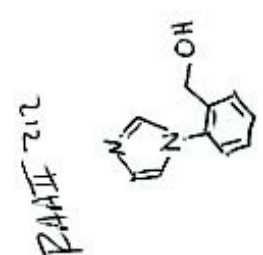
5.00

9.79

STANDARD PROTON PARAMETERS

```

EXP2  s2(hu)
SAMPLE 3 2065 DEC. 4 VI
DATE Oct 3 2065 dfrq 125.785
SOLVENT CDCl3 dn 0.013
FILE 001 exp dprv 37
ACQUISITION exp dof 8
SFRq 500.235 dm nnn
IN 3.288 dam nnc
AQ 6800 dsdq c
SFR 10000.0 dres 1.0
not used nmo PROCESSING n
cs 1 vtc17c
tpvr 39 ptec ft
pw 9.9 fn 131072
d1 0 math f
tof 1499.2 nerr f
nt 16 wexp
ct 16 wds
clock n
dain not used vnt
f1 FLAG3
f2 n
f3 n
f4 u
f5 n
f6 n
f7 n
f8 n
f9 n
f10 n
f11 n
f12 n
DISPLAY
SP -447.8
AP 8536.9
VS 151
SC 9
Nznm 259
IS 358.40
rfl 4536.3
rfp 5836.7
th 1.000
ns pH
  
```

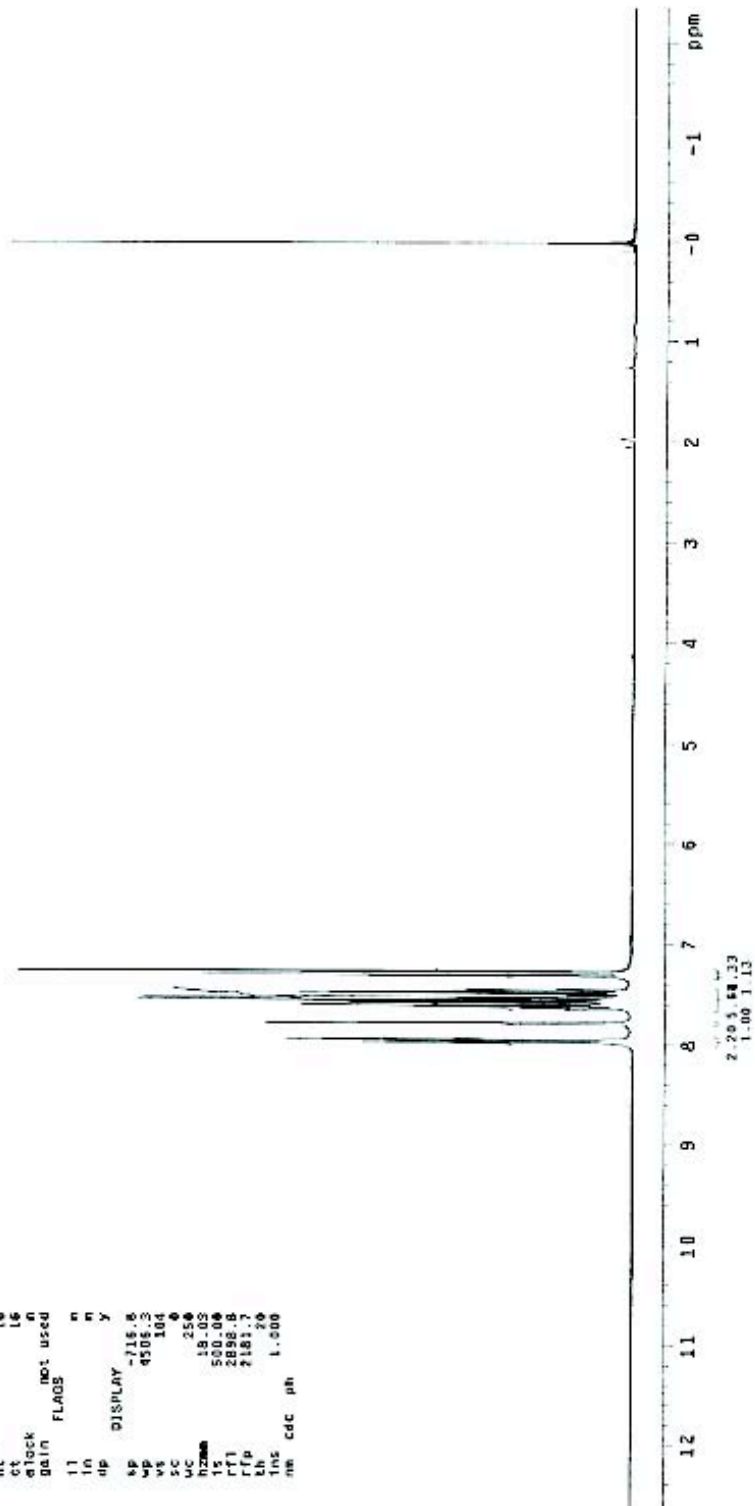
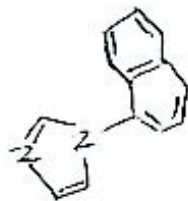


Ryan Atteem 1-is-naphthalene

exp2 stullh

SAMPLE DEC. & VT
 date Dec 8 2004 dfrq 300.100
 solvent CDCl3 dr H1
 file /data/export/~dpar 30
 host/s bluchy/ra/mc dcf 0
 nat/frn-1-is-naph- dr mm
 nolene.fid dem c
 ACQUISITION def PROCESSING 200
 sfrq 300.100 wflfa
 at 1.941 wflfa
 us 17880 proc not used
 sr 4508.5 fr
 fb not used werr
 bs L6 w8xp
 spwr 54 w0s
 pu 7.0 wnt
 d3 1.000
 tof 0
 nt L6
 ct L6
 d lock n
 gain not used
 FLAGB n
 ln n
 in n
 dp DISPLAY y

sp -718.8
 up 4508.3
 vs 104
 sc 250
 wctm 18.00
 rs 500.00
 rft 2898.8
 rfp 2183.7
 lb 20
 lns cdc ph 1.000



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STANDARD 1H OBSERVE

```

exp1 std1h
SAMPLE
date Jun 23 2005 DECI 6 VY
solvent CDCl3 dfrq 300.100
file /data/export/~dpwr 30
home/sibuch/ak/mr-00f
nat/edg-1-13.fid dm
ACQUISITION
sfrq 300.100 dmf PROCESSING 200
tr 1.495 utfile
ns 17484 proc not used
su d$66.5 fa
fb not used
bs 18 warr
tpwr 54 wexp
pu 7.0 uba
dl 1.000 wnt
tof 0
nt 16
ct 16
clock not used
gain FLAGS
ll n
ln n
lp y
ep DISPLAY
pp -147.9
vs 2732.7
vc 151
cc 250
hzmm 476.84
ls 2086.2
rft 883.2
rff 286.5
lh 200.5
ins cdc ph
nm 2.000
  
```

Me CDCl₃

Me CDCl₃

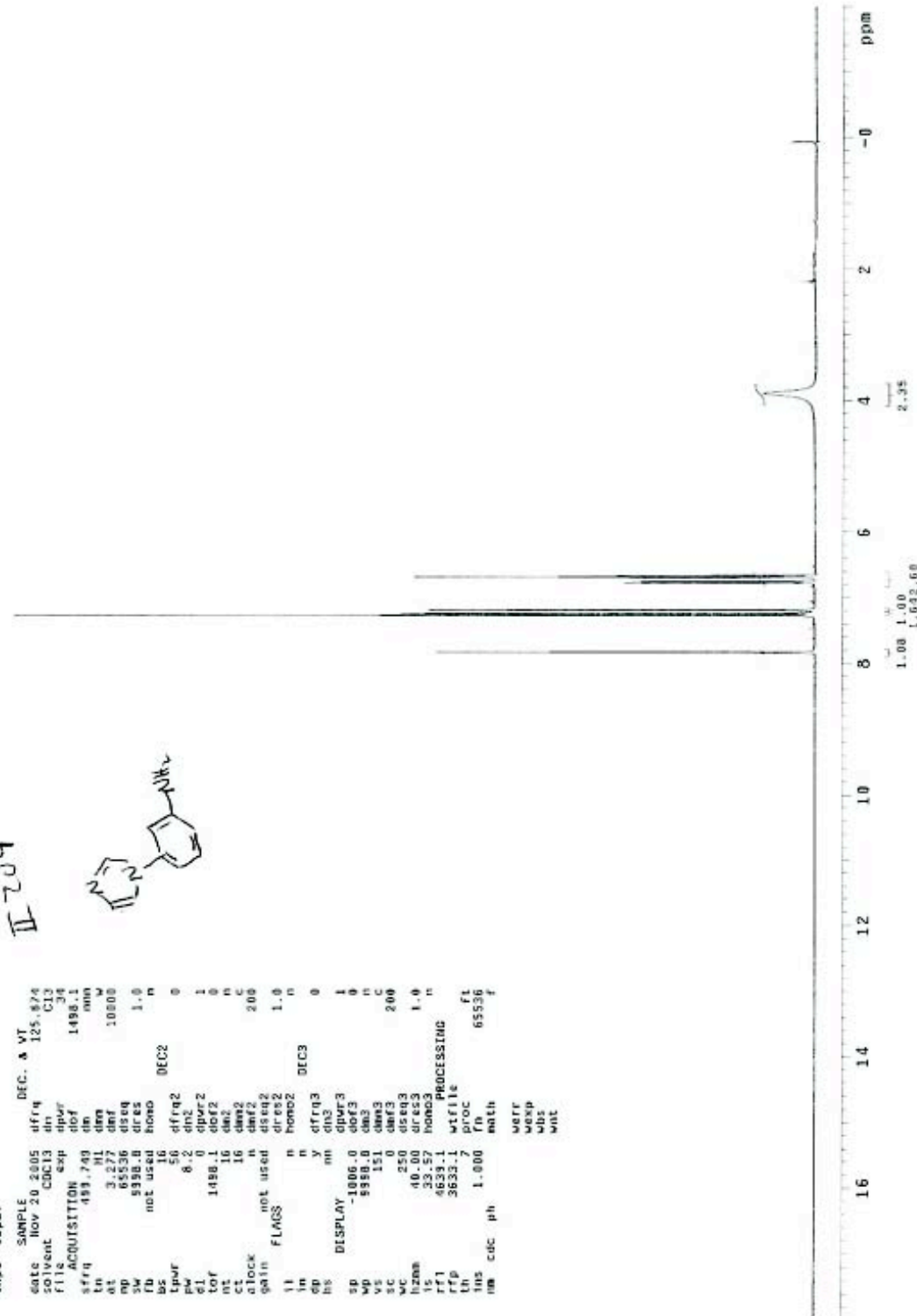
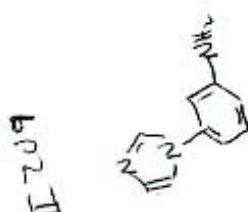


0.81 1.81 1.05
 0.81 1.81 1.05

STANDARD PROTON PARAMETERS

```

exp1 12pul
SAMPLE
date Nov 20 2005 DEC. & VT 125.874
solvent Nov CDC13 dn C13
file 34
ACQUISITION exp dprvr 1498.1
sfrq 499.749 dn 10000
ln ml dmw
dt 3.277 dmf
sp 6536 dseq
fn 59384 dres 1.0
ls not used hnmw DEC2
Lpwr 50 dfrq2 0
pw 8.2 dn2 1
d1 0 dprvr2 1
tof 1498.1 ddf2 0
nt 16 dm2 n
ct 16 dmw2 C
atlock not used dseq2 200
gain not used dres2 1.0
FLAGS n hnmw2 DEC3
ln n y dfrq3 0
op n dn3
hs n dprvr3 1
sp -1006.0 ddf3 0
wp 5938.0 dm3 n
vs 151 dmw3 C
vc 250 ddf2 200
hzmw 40.00 ddf3 1.0
rs 33.57 hnmw3 n
rf1 4639.1 wifile
rfp 3633.1 wifile
th 1.000 proc f1
tus 65536
nm cdc ph 1.000 ansh
          usff
          wexp
          wbs
          wnt
  
```

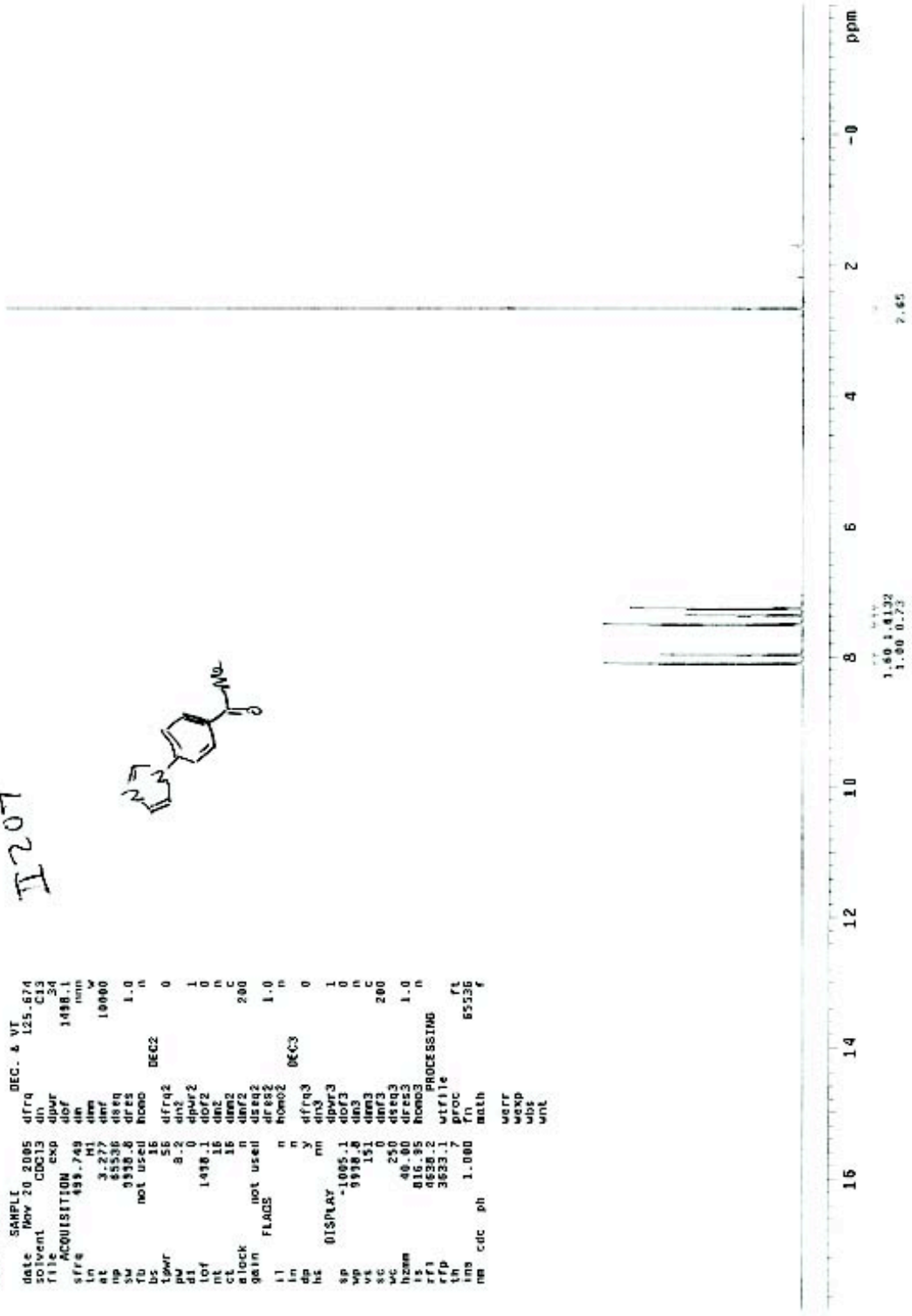
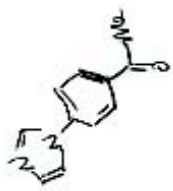


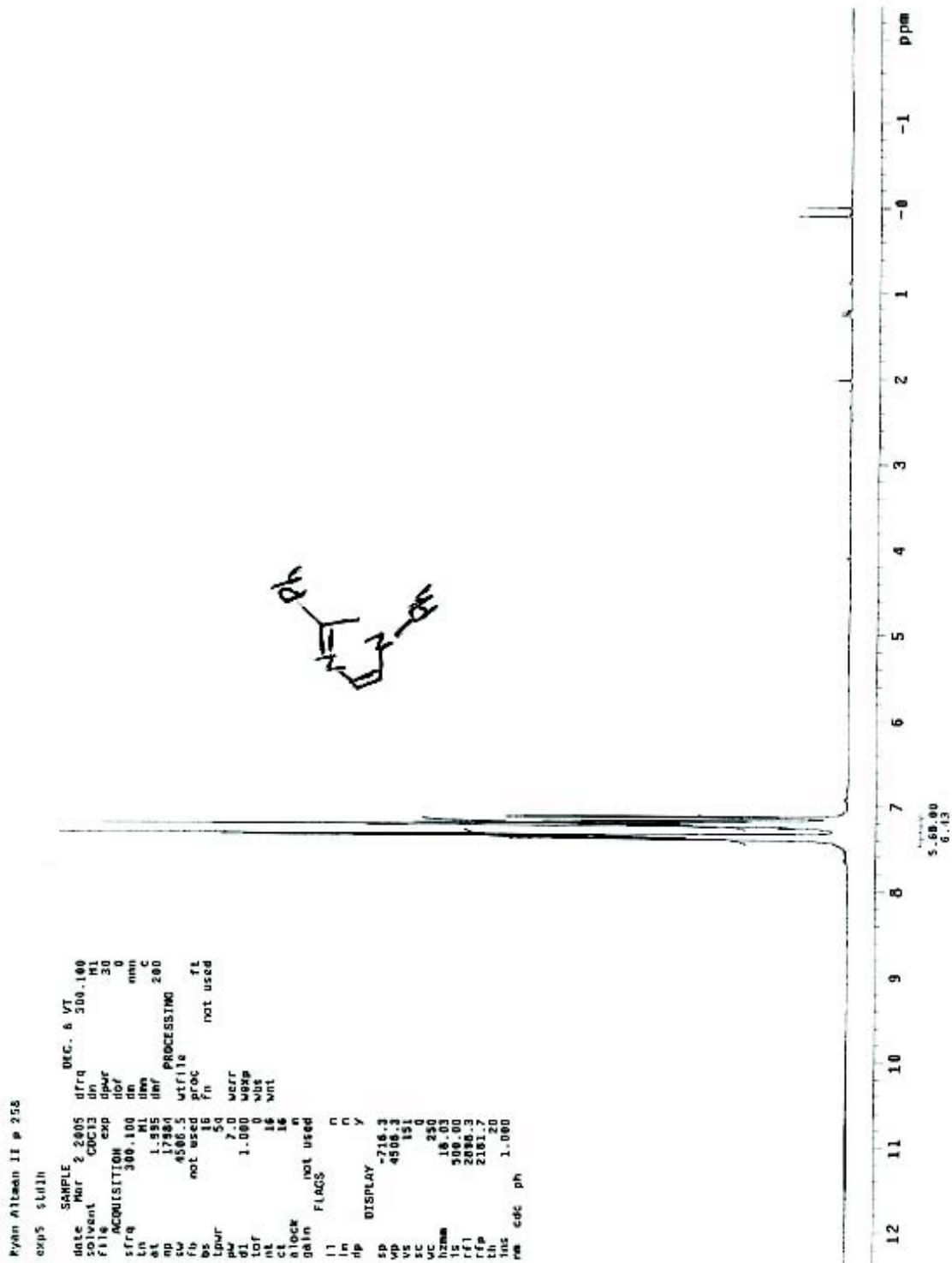
STANDARD PROTON PARAMETERS

```

exp1 02jul
SAMPLE
date Nov 20 2005 DEC. & VI
solvent CDC13 d1h 125.674
file ACQUISITION exp d1pvr 34
sfrq 499.749 d1h 1498.1
ln n1 d1m 10000
at 3.277 d1m
sp 933.8 d1m
T0 not used NMR5 1.0
bs 56 d1m DEC2
LAWT 56 d1m2 0
pw 8.2 d1m2 1
d1 0 d1pvr2 0
lof 1498.1 d1m2 0
nt 16 d1m2 n
ct 16 d1m2 C
d1ock not used d1m2 200
gain FLAGE not used d1m2 1.0
l1 n n1m02 DEC3
ln n y d1m3 0
hs DISPLAY nm d1m3 1
sp -1095.1 d1m3 0
vt 9998.0 d1m3 n
vc 191 d1m3 C
lc 250 d1m3 200
hzam 46.80 d1m3 1.0
is 816.95 n1m03
rfi 4628.2 PROCESSING
rfp 3623.1 wifile
th 7 proc
ms cdc ph 1.000 fn 85236 f
math
warr
wexp
wbs
wnt
  
```

I207





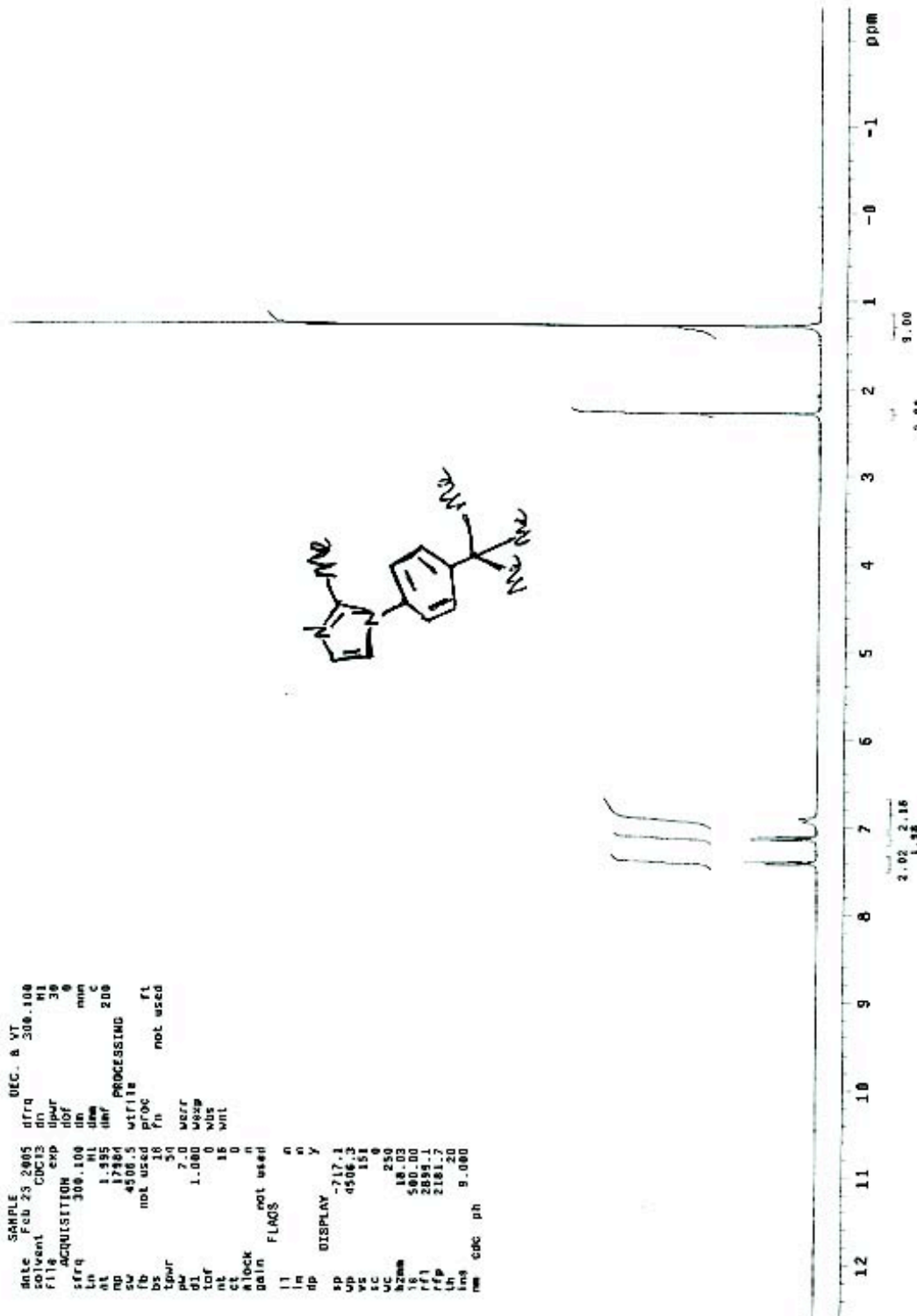
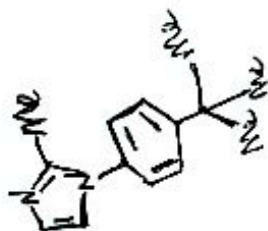
Pyan Altman 11 0245

exp5 stillh

SAMPLE DEC. 8 VT
 date Feb 25 2005 dfrq 300.100
 filvent CUC13 dn HI
 fl1 39
 ACQUISITION exp uper 30
 ln 300.100 dn mnc
 at 1.995 dnf
 no 17984 dnf PROCESSING 200
 sv 4500.5 wfl1a
 fb not used proc fl
 bs 18 fn not used

ipwr 50
 pw 7.0 werr
 ol 1.000 wexp
 cor 0 wos
 ct 16 wnt
 clock 0
 gain not used
 flags

ll 0
 ln 0
 dp 0
 display -717.1
 sp 4506.3
 re 151
 uc 280
 szam 18 03
 lb 500.00
 rfl 2899.1
 rfp 2181.7
 lh 20
 lng 9.080
 nm cdc ph

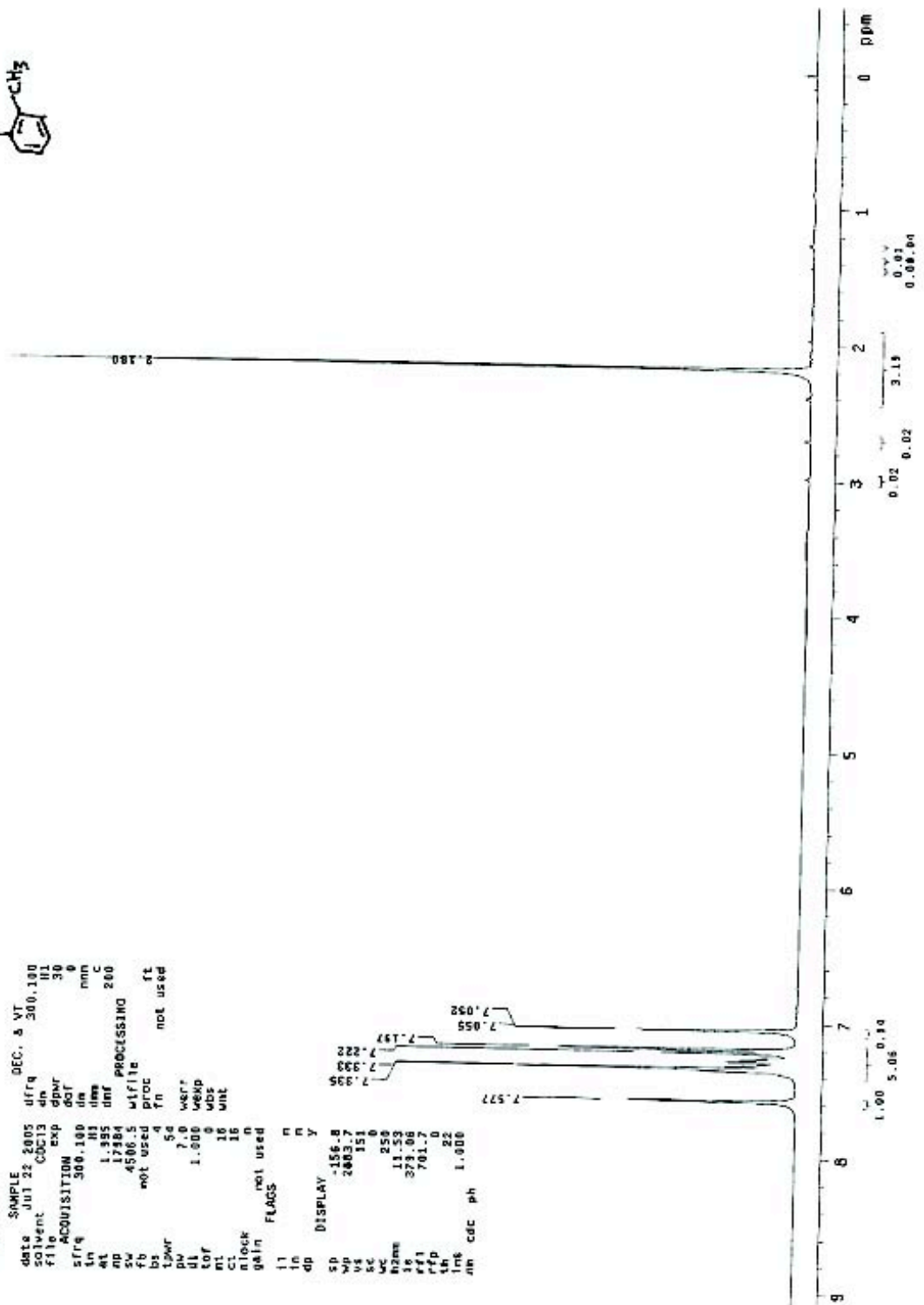




STANDARD IH OBSERVE

```

exp1 std1h
SAMPLE DEC. & VT
date JUL 22 2005 300.100
solvent CDCl3 dn
file CDC13 exp 30
ACQUISITION exp 30
sfrq 300.100 dn mm
in H3 dmms C
ap 1.295
aq 17284 dmf PROCESSING 200
aw 4506.5 wfile
bx not used proc fl
bx not used proc fn
tavr 4
pv 5.0 wsr
dl 7.0 wsr
dl 1.000 wsr
nt 16 wsr
ct 16 wsr
gain not used n
l1 not used n
l2 not used n
l3 not used n
l4 not used n
l5 not used n
l6 not used n
l7 not used n
l8 not used n
l9 not used n
l0 not used n
DP DISPLAY y
SD -156.8
Wp 2003.7
Vp 151
Vt 250
bc 11.53
bzms 573.06
Fp 701.7
rff 0
ln 2
lns cdc ph 1.000
  
```



-
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