Supplemental information for:

Copper-Catalyzed Synthesis of Enantioenriched Tetraarylethanes

Wendy S. Jen*, Matthew Truppo, Deborah Amos, Paul Devine,
Michael McNevin, Mirlinda Biba, and Kevin R. Campos

Department of Process Research, Merck Research Laboratories, P.O. Box 2000, Rahway, New Jersey 07065

General Information. Commercial grade reagents were purchased and used without further purification. Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on Sigma grade 9385 silica mesh 230-400 according to the method described by Still.[1] Thin-layer chromatography (TLC) was performed on EMD 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by florescence quenching.

The ketoreductase (KRED) enzymes, glucose dehydrogenase (GDH-103) and NADP were purchased from Biocatalytics Inc. (Pasadena, CA). Enzymatic reaction conversion was monitored by analytical high performance liquid chromatography (HPLC) at 215 nm using an Agilent 1100 series HPLC and a Zorbax Eclipse XDB-C18 (50 x 4.6 mm) column with a flow rate of 1 mL/min (50% acetonitrile / 50% water) for 10 minutes. Enantiomeric excess for the enzymatic reactions were was determined using a Berger SFC and a Chiralpak AD-H (250 x 4.6 mm) column with a flow rate of 1.5 mL/min (25% MeOH modifier, 215 nm, 200 bar, 35 ºC) unless otherwise stated.

^{1}H and ^{13}C spectra were recorded on Bruker AM-400 (400 MHz and 100 MHz, respectively), Bruker DRX-500 (500 MHz and 125 MHz, respectively) instruments, as noted, and are internally referenced to residual protio solvent signals. Data for ^{1}H are reported with chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz), and assignment. Data for ^{13}C are reported with chemical shift. Optical Rotations were recorded on a Jasco P-1010 polarimeter (WI

[1] Still, W.C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

lamp, 589 nm, 25°C). Mass spectra (high resolution) were obtained from Agilent LC/MSD TOF. Chiral HPLC analysis was performed on a Berger SFC at 215nm using Chiralcel columns. Dimerization reactions were monitored and diastereomeric ratios were determined using an Agilent 1100 series HPLC and a ACE-C18 column under the following conditions: flow rate of 0.75ml/min, 35 deg Celsius, 60min total time, 95:5 to 0:100 AQ/ORG over 50 min. Stock solution: 2L water, 25.2g ammonium formate, 15.8ml formic acid. AQ: 990ml water, 10 ml stock solution. ORG: 900 ml acetonitile, 90ml water, 10 ml stock solution.

General Procedure A: Ketone Reduction. The ketone reductions were run in 100 mM potassium phosphate buffer using the following conditions and concentrations: 30 ºC, pH 7.0, 2 g/L ketoreductase (KRED) enzyme, 2 g/L glucose dehydrogenase (GDH-103), 10 g/L glucose, 1 g/L NADP cofactor, 5 g/L ketone, 10% v/v tetrahydrofuran (THF). The enzymes, cofactor and glucose were first dissolved in the buffer. Next, the substrate was dissolved in the THF and the substrate solution was then added to the reaction mixture. The reactions were run for 24 hours at 30 ºC with automatic pH control using 2 N NaOH. Upon completion, the reaction solution was extracted with 2X volumes of ethyl acetate. The organic phase was washed with 10mL DI water and then dried using vacuum distillation. The resulting oil or solid was then puried by column chromatography or recrystallized using the specified solvents.

General Procedure B: Dimerization Reaction. To a cooled solution (0^o C) of alcohol (1.0 equiv) in THF (0.5M) was added ClP(O)(OEt)2 (1.2 equiv) dropwise, followed by *i*PrMgCl (2.0M in THF, 1.3 equiv). The reaction was warmed to room temperature an aged until phosphonate ester formation was complete by HPLC. The reaction mixture was then cooled back to 0^o C. CuCN (0.05 equivalents, unless stated otherwise), MTBE (0.75M relative to alcohol), and *i*PrMgCl (2.0 equiv) were then added sequentially. The reaction was aged for 15 min at 0^o C, then warmed to room temperature. Upon completion of the reaction (after aging approximately 30-60 minutes, unless otherwise stated), the reaction was quenched with saturated aqueous ammonium chloride solution, and extracted 3X with EtOAc. The combined organics were washed with brine, dried over sodium sulfate, and concentrated. The crude oil/solids were then purified by flash chromatography with 5 to 15% EtOAc/Hexanes.

(*R*)-(6-bromopyridin-2-yl)(phenyl)methanol (12). Prepared according to general procedure A from the corresponding ketone (6.0g, 22.8 mmol) using KRED19 to provide alcohol **12** (80% ee). The crude product was then recrystallized to upgrade the ee from MTBE/hexanes to provide the title compound as a white solid in 53% yield (3.22g), >99% ee. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (t, *J* = 7.7 Hz, 1H, py**H**), 7.41-7.27 (m, 6H, C_6**H**$_5$, py**H**), 7.14 (d, *J* = 7.5 Hz, 1H, py**H**), 5.76 (s, 1H, PhC**H**OHpy); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 142.3, 140.9, 139.2, 128.7, 128.2, 127.1, 126.9, 120.1, 75.1; HRMS (MALDI-TOF) exact mass calculated for ($C_{12}H_{11}BrNO$) requires *m/z* 264.00185, found *m/z* 264.00223 $(M+H)^+$; $[\alpha]_D$ = -9.86° (c = 1.0, $CHCl_3$). Melting point 108.9 °C to 109.7 °C. Enantiomeric ratios were determined by SFC with a Chiralcel OF column (250x4.6mm 10 μm SFC, isocratic 15% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r = 7.09 min and 8.29 min.

*Single-Crystal X-Ray Crystallography of **12***

The structure of **12**, $C_{12}H_{10}BrNO$, was determined by single-crystal X-ray crystallography on a crystal isolated from methylene chloride/hexanes. The crystal selected was representative of the bulk sample. Crystal data at 100 K:

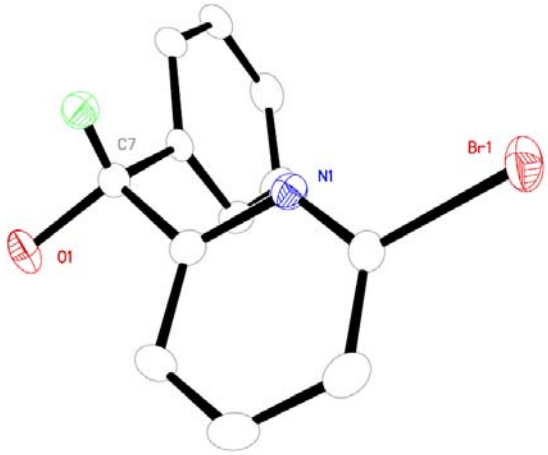
a = 8.7335(6) Å	α = 90.00 °	V = 1076.98(13) Å^3
b = 9.1351(6)	β = 90.00	Space group = $P2_12_12_1$, #19
c = 13.4992(9)	γ = 90.00	Z = 4

Data were collected on a Bruker CCD diffractometer using molybdenum Kα radiation and integrated to a resolution of 0.79 Å^{-1} which yielded 2235 unique reflections from 11423 measured reflections.

The structure was solved using direct methods. The refined model has all non-H atoms refined anisotropically, and H atoms at their calculated positions, with agreement statistics of: R_1 = 2.4%, for 138 variables and 2208 reflections and wR_2 = 5.5% using all 2235 reflections. Based on this structure, the absolute configuration of the compound was determined to be (*R*)-(6-bromopyridin-2-yl)(phenyl)methanol.

The structure model is shown below and a perspective view calculated from the

crystallographic coordinates is presented in Figure 1 and below.



(6-bromopyridin-2-yl)(4-fluorophenyl)methanol (13). Prepared according to general procedure A from the corresponding ketone (4.0g, 14.2 mmol) and KRED124 to provide alcohol **13** (>99%ee). The crude product was chromatographed with 15% EtOAc/Hexanes to provide the title compound as a white solid in 82% yield (3.75 g), >99% ee. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (t, *J* = 7.7 Hz, 1H, py**H**), 7.41-7.33 (m, 3H, $C_6\mathbf{H_4}F$, py**H**), 7.11 (d, *J* = 7.6 Hz, 1H, py**H**), 7.07-7.03 (m, 2H, 5.76, $C_6\mathbf{H_4}F$), 5.74 (s, 1H, PhC**H**OHpy); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 162.8, 161.4, 141.0, 139.3, 138.1, 120.0, 115.7, 115.5, 74.42; ^{19}F NMR (400 MHz, $CDCl_3$) δ -114.6; HRMS (MALDI-TOF) exact mass calculated for ($C_{12}H_{10}BrFNO$) requires *m/z* 281.99243, found *m/z* 281.99283 $(M+H)^+$; $[\alpha]_D$ = -10.7° (c = 1.0, $CHCl_3$); Melting point 53.0 °C to 54.3 °C. Enantiomeric ratios were determined by SFC with a Chiralcel OF column (250x4.6mm 10 μm SFC, MeOH/CO2, 1.5 mL/min, 35 °C, 200bar, 215nm, 4% modifier for 4 min then 4% to 40% modifier at 2% per min); t_r = 10.9 min and 11.9 min.

(6-bromopyridin-2-yl)(4-chlorophenyl)methanol (14). Prepared according to general procedure A from the corresponding ketone (1.0g, 3.4 mmol) and KRED24 to provide alcohol **14** (>99% ee). The crude product was chromatographed with 15% ethyl acetate/hexanes to provide the title compound as an oil in 79% yield (0.80g), >99% ee. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (t, *J* = 7.7 Hz, 1H, py**H**), 7.38 (d, *J* = 7.8 Hz, 1H, py**H**), 7.33-7.29 (m, 4H, $C_6\mathbf{H_4}Cl$), 7.12 (d, *J* = 7.6 Hz, 1H, py**H**), 5.72 (s, 1H, PhC**H**OHpy); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 162.6, 141.0, 140.8, 139.4, 134.0, 128.9, 128.4, 127.1, 120.0, 74.4; HRMS (MALDI-TOF) exact mass calculated for ($C_{12}H_{10}BrClNO$) requires *m/z* 297.96288, found *m/z* 297.96440 $(M+H)^+$; $[\alpha]_D$ = -7.0° (c = 1.0, $CHCl_3$). Enantiomeric ratios were determined by SFC with a Chiralcel AD-H column (250x4.6mm 10 μm SFC, isocratic 15% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r = 9.3 min and 10.8 min.

(6-bromopyridin-2-yl)(*m*-tolyl)methanol (15). Prepared according to general procedure A from the corresponding ketone (10.0g, 36 mmol) and KRED8 to provide alcohol **15** (70%ee). The crude product was recrystallized from MTBE/hexanes. The mother liquors were concentrated and then purified by flash chromatography to provide the title compound as a white solid in 49% yield (4.9g), 83% ee. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (t, *J* = 7.7 Hz, 1H, py**H**), 7.38 (d, *J* = 7.8 Hz, 1H, py**H**), 7.27-7.10 (m, 5H, $C_6\mathbf{H_4}$, py**H**), 5.72 (s, 1H, PhC**H**OHpy), 2.38 (s, 3H, PhC$\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3,142.4, 141.0, 139.3, 138.6, 129.1, 128.8, 127.8, 126.9, 124.3, 120.3, 75.3, 21.6; HRMS (MALDI-TOF) exact mass calculated for ($C_{13}H_{12}BrNONa$) requires *m/z* 299.99945, found *m/z* 299.99903 $(M+Na)^+$; $[\alpha]_D$ = -9.2° (c = 1.0, $CHCl_3$); Melting point 62.3 °C to 64.0 °C. Enantiomeric ratios were determined by SFC with a Chiralcel AD-H column (250x4.6mm 10 μm SFC, isocratic 15% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r = 7.1 min and 8.1 min.

(6-bromopyridin-2-yl)(3-methoxyphenyl)methanol (16). Prepared according to general procedure A from the corresponding ketone (1.0g, 3.42g) to provide the desired alcohol (87% ee). The crude product was purified by flash chromatography with 20% ethyl acetate/hexanes to provide the title compound as a white solid in 76% yield (0.76g), 87% ee. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, *J* = 7.7 Hz, 1H, py**H**), 7.39 (d, *J* = 7.8 Hz, 1H, py**H**), 7.27 (t, *J* = 8.3 Hz, 1H, Ph**H**), 7.15 (d, *J* = 7.6 Hz, 1H, py**H**), 6.98-6.95 (m, 2H, $C_6\mathbf{H_4}$), 6.83 (dd, *J* = 8.2, 2.4, 1H, $C_6\mathbf{H_4}$), 5.72 (s, 1H, PhC**H**OHpy), 3.80 (s, 3H, PhOC$\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 160.0, 143.8, 140.9, 139.3, 129.8, 126.9, 120.1, 119.4, 113.7, 113.5, 75.0, 55.3; HRMS (MALDI-TOF) exact mass calculated for ($C_{13}H_{13}BrNO_2$) requires *m/z* 294.01242, found *m/z* 294.01216 $(M+H)^+$; $[\alpha]_D$ = -17.3° (c = 1.0, $CHCl_3$); Melting point 68.1 °C to 69.0 °C. Enantiomeric ratios were determined by SFC with a Chiralcel AD-H column

(250x4.6mm 5 μm SFC, isocratic 25% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r = 5.8 min and 6.2 min.

(6-methylpyridin-2-yl)(phenyl)methanol (20). Prepared according to general procedure A from the corresponding ketone (10g, 50.7mmol) to provide the desired alcohol (92%ee). The crude product was recrystallized from MTBE to provide the title compound as a white solid in 67% yield (6.7g), >99% ee. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (t, *J* = 7.7 Hz, 1H, py**H**), 7.41-7.27 (m, 5H, Ph**H**), 7.05 (d, *J* = 7.7 Hz, 1H, py**H**), 6.91 (d, *J* =7.8 Hz, 1H, py**H**), 5.72 (s, 1H, PhC**H**OHpy), 2.60 (s, 3H, pyC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 156.7, 143.5, 137.2, 128.6, 127.8, 127.2, 121.9, 118.4, 74.6 24.3; HRMS (MALDI-TOF) exact mass calculated for ($C_{13}H_{14}NO$) requires *m/z* 200.10699, found *m/z* 200.10793 $(M+H)^+$; $[\alpha]_D$ = +5.4° (c = 1.0, $CHCl_3$); melting point 112.5 °C to 113.9 °C. Enantiomeric ratios were determined by SFC with a Chiralpak AD-H (250 x 4.6 mm) column with a flow rate of 1.5 mL/min (25% MeOH modifier, 215 nm, 200 bar, 35 ºC); t_r = 16.6 min and 17.7 min.

(6-chloropyridin-2-yl)(phenyl)methanol (21). Prepared according to general procedure A from the corresponding ketone (1.0g, 4.6 mmol) and KRED8 to provide the desired alcohol (83%ee). The crude product was purified by column chromatography with 15% ethyl acetate/hexanes to provide the title compound as a white solid in 88% yield (0.88g), 83% ee. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, *J* = 7.8 Hz, 1H, py**H**), 7.41-7.30 (m, 5H, Ph**H**), 7.23 (d, *J* = 7.8 Hz, 1H, py**H**), 7.12 (d, *J* =7.8 Hz, 1H, py**H**), 5.76 (s, 1H, PhC**H**OHpy); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 150.4, 142.3, 139.5, 128.7, 128.2, 127.1, 123.0, 119.7, 75.1; HRMS (MALDI-TOF) exact mass calculated for ($C_{12}H_{11}ClNO$) requires *m/z* 220.05237, found *m/z* 220.05261 $(M+H)^+$; $[\alpha]_D$ = -14.2° (c = 1.0, $CHCl_3$); melting point 82.5 °C to 84.1 °C. Enantiomeric ratios were determined by SFC with a Chiralpak AD-H (250 x 4.6 mm) column with a flow rate of 1.5 mL/min (25% MeOH modifier, 215 nm, 200 bar, 35 ºC); t_r = 15.2 min and 15.8 min.

(*S*)-(3-chlorophenyl)(phenyl)methanol (33). Prepared according to general procedure A from the corresponding ketone (1.0g, 4.8 mmol) and KRED108 to provide the desired alcohol (>99% ee). The crude product was purified by flash chromatography with

10% ethyl acetate/hexanes to provide the title compound as a colorless oil in 81% yield (0.81g), >99% ee. All data corresponds to know data.[2] $[\alpha]_D$ = -3.5° (c = 1.0, $CHCl_3$). Enantiomeric ratios were determined by SFC with a Chiralcel AD-H column (250x4.6mm 5 μm SFC, isocratic 10% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r = 8.3 min and 8.9 min.

(1*S*,2*S*)-(1,2-bis(6-bromopyridin-2-yl)-1,2-diphenylethane) (5). Prepared according to general procedure B from the alcohol **12** (528 mg, 2.0 mmol, >99%ee)**.** Crude product was analyzed by HPLC to be a 86:14 diastereomeric mixture of C_2:meso isomers and chromatographed from 10% EtOAc/hexanes to provide the title compound as a white solid in 89% yield (440 mg); >99% ee (C_2 symmetric isomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 8H, Ph**H** and py**H**), 7.21 (dd, *J* = 0.67, 7.6 Hz, 2H, py**H**), 7.11 (dt, *J* =0.67, 8.0 Hz, 4H, py**H**), 7.06-6.97 (m, 2H, Ph**H**), 5.29 (s, 2H, PhC**H**py); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 141.2, 141.1, 138.5, 129.0, 128.3, 126.6, 125.4, 123.5, 57.2; HRMS (MALDI-TOF) exact mass calculated for ($C_{24}H_{19}N_2Br_2$) requires *m/z* 492.99095, found *m/z* 492.99203 $(M+H)^+$; $[\alpha]_D$ = +25.35° (c = 1.0, $CHCl_3$). Melting point 151.9 °C to 153.0 °C. Enantiomeric ratios were determined by SFC with a Chiralcel AD-H column (250x4.6mm 5 μm SFC, isocratic 8% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r (*C*$_2$ symmetric) = 8.5 min and 9.0 min, t_r (*meso*) = 10.1 min.

*Single-Crystal X-Ray Crystallography of **5***

The structure of **5**, $C_{24}H_{18}Br_2N_2$, was determined by single-crystal X-ray crystallography on a crystal isolated from dichloromethane/hexanes vapor diffusion. The crystal selected was representative of the bulk sample. Crystal data at 100 K:

a = 9.0694(5) Å	α = 90.00 °	*V* = 2081.4(2) Å^3
b = 11.7804(6)	β = 90.00	Space group = $P2_12_12_1$, #19
c = 19.4812(11)	γ = 90.00	*Z* = 4

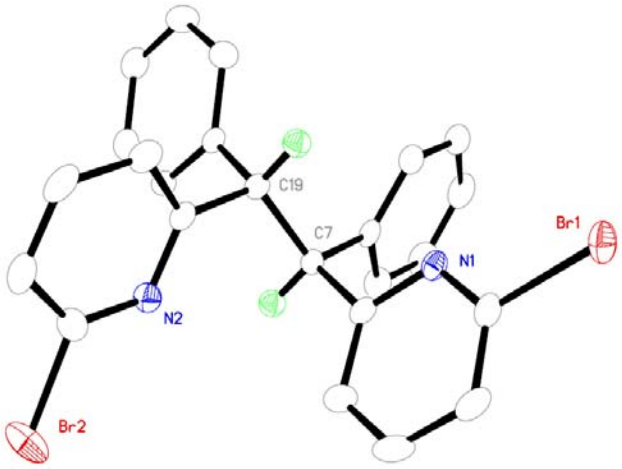
Data were collected on a Bruker CCD diffractometer using molybdenum Kα radiation and

[2] (a) Wu, P-Y; Wu, H-L; Uang, B-J. *J. Org. Chem*. **2006**, *71*, 833. (b) Truppo, M.D.; Pollard, D.; Devine, P. *Org. Lett.* **2007**, *9*, 335.

integrated to a resolution of 0.79 $Å^{-1}$ which yielded 4584 unique reflections from 23314 measured reflections.

The structure was solved using direct methods. The refined model has all non-H atoms refined anisotropically, and H atoms at their calculated positions, with agreement statistics of: R_1 = 2.0%, for 253 variables and 4408 reflections and wR_2 = 5.1% using all 4584 reflections. Based on this structure, the absolute configuration of the compound was determined to be (1*S*,2*S*)-(1,2-bis(6-bromopyridin-2-yl)-1,2-diphenylethane).

The structure model is shown below and a perspective view calculated from the crystallographic coordinates is presented in Figure 1 and below.



1,2-bis(6-bromopyridin-2-yl)-1,2-bis(4-fluorophenyl)ethane (22). Prepared according to general procedure B from alcohol **13** (564mg, 2.0 mmol, >99% ee). The crude product was analyzed by HPLC to be a 73:27 diastereomeric mixture of *C_2:meso* isomers and chromatographed from 5% EtOAc/Hexanes to provide the title compound (inseparable mixture of diastereomers) as a white solid in 86% yield (456 mg); >99% ee (*C_2* symmetric isomer). *C_2* symmetric isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, *J* =10.1 Hz, 2H, py**H**), 7.27 (dd, *J* = 8.9, 5.4 Hz, 4H, Ph**H**), 7.15 (d, *J* =10.0 Hz, 2H, py**H**), 7.15 (d, *J* =10.0 Hz, 2H, py**H**), 6.83 (t, *J* =8.9 Hz, 4H, Ph**H**), 5.06 (s, 2H, PhC**H**py); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 141.2, 138.5, 136.6, 130.2, 125.5, 123.4, 115.1, 114.9, 56.5; HRMS (MALDI-TOF) exact mass calculated for ($C_{24}H_{17}N_2Br_2F_2$) requires *m/z* 528.97211, found *m/z* 528.97418

$(M+H)^+$; $[\alpha]_D$ = + 10.3° (c = 1.0, $CHCl_3$). Melting point 97 °C to 98.5°C. Enantiomeric ratios were determined by SFC with a Chiralcel OD-H column (250x4.6mm 5 μm SFC, IPA/CO_2, 4% modifier for 4 min then ramp to 40% at 2% per minute and hold for 3 min at 40% IPA, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r (*C*$_2$ symmetric) = 11.9 min and 12.3 min, t_r (*meso*) = 13.2 min.

1,2-bis(6-bromopyridin-2-yl)-1,2-bis(4-chlorophenyl)ethane (23). Prepared according to general procedure B from alcohol **14** (448 mg, 1.5 mmol, >99%ee). The crude product was analyzed by HPLC to be a 75:25 diastereomeric mixture of *C*$_2$*:meso* isomers and chromatographed from 10% EtOAc/Hexanes to provide the title compound (inseparable mixture of diastereomers) as a white solid in 91% yield (384 mg); >99% ee (*C*$_2$ symmetric isomer). *C*$_2$ symmetric and meso isomers (75:25 mixture): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* =8.5 Hz, 1H, py**H**), 7.32-7.23 (m, 5H, Ph**H,** py**H**), 7.17-7.10 (m, 7.5H, Ph**H,** py**H**), 6.98 (d, *J* =6.7 Hz, .5H, py**H**), 5.07 (s, 1.5H, C_2 symmetric PhC**H**py), 5.05 (s, .5H, meso PhC**H**py); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 162.2, 141.6, 141.3, 139.6, 139.2, 138.6, 132.6, 132.5, 130.5, 128.5, 128.4, 125.8, 125.6, 123.4, 122.8, 56.9, 56.5; HRMS (MALDI-TOF) exact mass calculated for ($C_{24}H_{17}N_2Br_2Cl_2$) requires *m/z* 560.91301, found *m/z* 560.01797 $(M+H)^+$; $[\alpha]_D$ = + 13.5° (c = 1.0, $CHCl_3$). Melting point 151.0 °C to 152.1 °C. Enantiomeric ratios were determined by SFC with a Chiralpak OJ-H column (250x4.6mm 5 μm SFC, isocratic 20% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 15 min); t_r (*C*$_2$ symmetric) = 7.11 min and 9.93 min, t_r (*meso*) = 8.59 min.

1,2-bis(6-bromopyridin-2-yl)-1,2-di-*p*-tolylethane (24). Prepared according to general procedure B from alcohol **15** (556 mg, 2.0 mmol, 83%ee). The crude product was analyzed by NMR to be a >95:5 diastereomeric mixture of *C*$_2$*:meso* isomers and chromatographed from 5% EtOAc/Hexanes to provide the title compound (inseparable mixture of diastereomers) as a white solid in 89% yield (464 mg); 44% ee (*C*$_2$ symmetric isomer). *C*$_2$ symmetric isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* =7.6 Hz, 2H, py**H**), 7.20 (d, *J* = 7.6 Hz, 2H, py**H**), 7.12-7.10 (m, 6H, py**H**, Ph**H**), 7.11 (t, *J* =7.6 Hz, 2H, Ph**H**), 6.86 (d, *J* =7.5 Hz, 2H, Ph**H**), 5.10 (s, 2H, PhC**H**py), 2.21 (s, 6H, Ph**Me**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 141.0, 140.9, 138.4, 137.5, 129.7, 129.0, 127.2, 125.9, 125.2, 123.4,

57.0, 21.4; HRMS (MALDI-TOF) exact mass calculated for ($C_{26}H_{23}N_2Br_2$) requires *m/z* 521.02225, found *m/z* 521.02345 $(M+H)^+$; $[\alpha]_D$ = + 18.3° (c = 1.0, $CHCl_3$). Melting point 181.0 °C to 182.1 °C. Enantiomeric ratios were determined by SFC with a Chiralcel OJ-H (250x4.6mm 5 μm SFC, isocratic 15% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 10 min); t_r (*C*$_2$ symmetric) = 5.8 min and 7.9 min.

1,2-bis(6-bromopyridin-2-yl)-1,2-bis(4-methoxyphenyl)ethane (25). Prepared according to general procedure B from alcohol **16** (441 mg, 1.5 mmol, 87% ee). Crude reaction mixture was analyzed by HPLC to be a 86:14 diastereomeric mixture of *C*$_2$*:meso* isomers and chromatographed from EtOAc/Hexanes to provide the title compound (inseparable mixture of diastereomers) as a white solid in 80% yield (332 mg); 64% ee (*C*$_2$ symmetric isomer). *C*$_2$ symmetric isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* =7.6 Hz, 2H, py**H**), 7.27 (d, *J* = 7.5 Hz, 2H, py**H**), 7.21 (d, *J* = 7.6 Hz, 2H, py**H**), 7.12 (d, *J* =7.7 Hz, 2H, Ph**H**), 7.04 (t, *J* = 7.5 Hz, 2H, Ph**H**), 6.92-6.90 (m, 4H, Ph**H**), 6.60 (d, *J* =7.5 Hz, 2H, Ph**H**), 5.10 (s, 2H, PhC**H**py), 3.70 (s, 6H, PhO**Me**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 159.4, 142.5, 141.1, 138.4, 129.1, 125.3, 123.4, 121.4, 114.4, 112.4, 57.1, 55.2; HRMS (MALDI-TOF) exact mass calculated for ($C_{26}H_{23}N_2Br_2O_2$) requires *m/z* 553.01208, found *m/z* 553.01377 $(M+H)^+$; $[\alpha]_D$ = + 10.7° (c = 1.0, $CHCl_3$). Melting point 152.4 °C to 152.8 °C. Enantiomeric ratios were determined by SFC with a Chiralcel AD-H (250x4.6mm 5 μm SFC, isocratic 15% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 10 min); t_r (*C*$_2$ symmetric) = 4.7 min and 5.8 min.

1,2-bis(6-methylpyridin-2-yl)-1,2-diphenylethane (29). Prepared according to general procedure B from the corresponding alcohol **20** (398 mg, 2.0 mmol, >99% ee). The crude product was analyzed by HPLC to be a 72:28 diastereomeric mixture of *C*$_2$*:meso* isomers and chromatographed from EtOAc/Hexanes to provide the title compound (inseparable mixture of diastereomers) as a white solid in 51% yield (186 mg); 50% ee (*C*$_2$ symmetric isomer). *C*$_2$ symmetric and *meso* isomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* =7.44 Hz, 1H, pyH), 7.48 (d, *J* = 7.35 Hz, 3H, pyH), 7.35 (m, 2H, PhH), 7.12-6.95 (m, 8H, PhH and pyH), 6.75 (d, *J* = 7.5 Hz, 2H, pyH), 5.19 (s, 2H, PhC**H**py), 2.47 and 2.43 (s, 6H, py**Me**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 157.1, 129.0, 128.9, 127.9, 127.8, 126.0, 120.8,

120.4, 120.2, 109.6, 58.0, 24.5; HRMS (MALDI-TOF) exact mass calculated for ($C_{26}H_{25}N_2$) requires *m/z* 365.20123, found *m/z* 365.20244 $(M+H)^+$; $[\alpha]_D$ = -4.3° (c = 1.0, $CHCl_3$). Melting point 156.4 °C to 158.0 °C. Enantiomeric ratios were determined by SFC with a Sepapak-2 (250x4.6mm 5 μm SFC, 4% MeOH/CO_2 for 4 min then to 40% for 3 min, 1.5 mL/min, 35 °C, 200 bar, 215nm, 25 min); t_r (*C_2* symmetric) = 10.3 min and 10.7 min, t_r (*meso*) = 10.4 min.

1,2-bis(6-chloropyridin-2-yl)-1,2-diphenylethane (30). Prepared according to general procedure B from the corresponding alcohol **21** (438mg, 2.0 mmol, 83% ee), Crude reaction mixture was analyzed by HPLC to be a 85:15 diastereomeric mixture of *C_2:meso* isomers and chromatographed from EtOAc/Hexanes to provide the title compound (inseparable mixture of diastereomers) as a white solid in 90% yield (364 mg); 83% ee (*C_2* symmetric isomer). *C_2* symmetric isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (t, *J* =7.7 Hz, 2H, py**H**), 7.32 (d, *J* = 7.6 Hz, 4H, Ph**H**), 7.19 (d, *J* =7.6 Hz, 4H, Ph**H**), 7.09 (t, *J* =7.6 Hz, 2H, Ph**H**), 7.05 (d, J = 7.7 Hz, 2H, py**H**), 6.95 (d, *J* =7.8 Hz, 2H, py**H**), 5.18 (s, 2H, PhC**H**py); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 150.3, 141.0, 138.7, 128.9, 128.2, 126.5, 123.1, 121.5, 57.1; HRMS (MALDI-TOF) exact mass calculated for ($C_{24}H_{19}N_2Cl_2$) requires *m/z* 405.09198, found *m/z* 405.09308 $(M+H)^+$; $[\alpha]_D$ = + 18.6° (c = 1.0, $CHCl_3$). Melting point 157.8 °C to 159.51 °C. Enantiomeric ratios were determined by SFC with a tandem Chiralpak AS-H and Chiralpak OJ-H column (250x4.6mm 5 μm SFC, isocratic 8% MeOH/CO_2, 1.5 mL/min, 35 °C, 200bar, 215nm, 25 min); t_r (*C_2* symmetric) = 16.2 min and 18.0 min, t_r (*meso*) = 17.0 min.

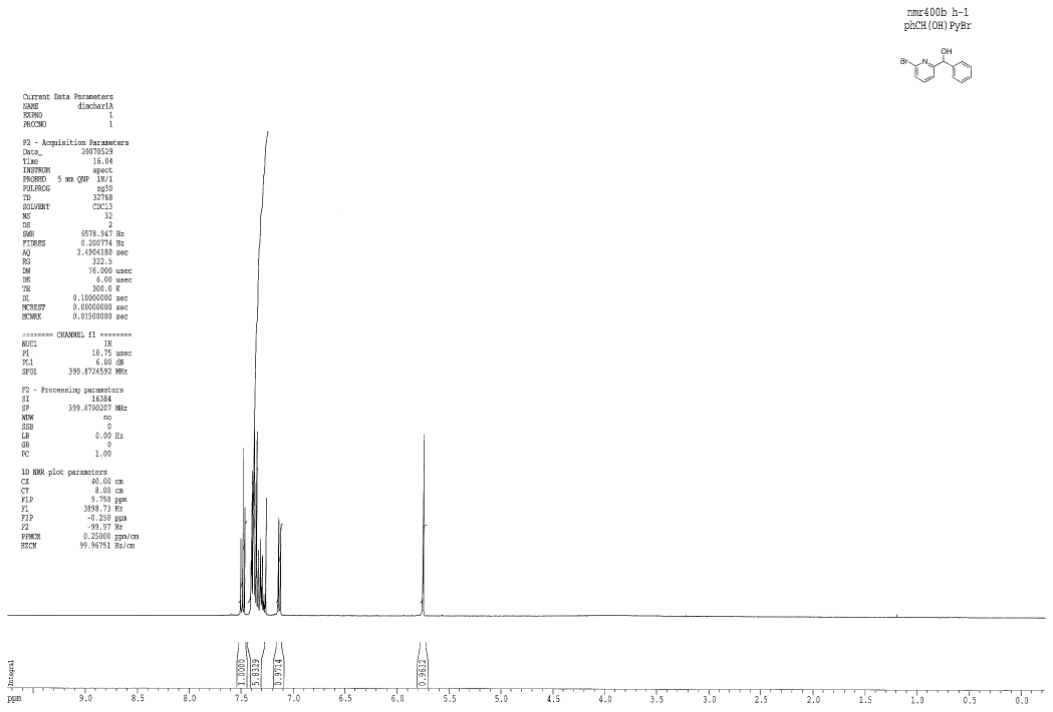
1,1,2,2-tetraphenylethane (32). Prepared according to general procedure B from benzhydrol (500 mg, 2.7 mmol) and 100 mol% CuCN (2.7 mmol) and aging reaction overnight. Crude reaction mixture chromatographed using EtOAc/Hexanes to provide the title compound as a white solid in 30% yield (135 mg). Spectral data is consistent with that previously reported in the literature for this compound.[3]

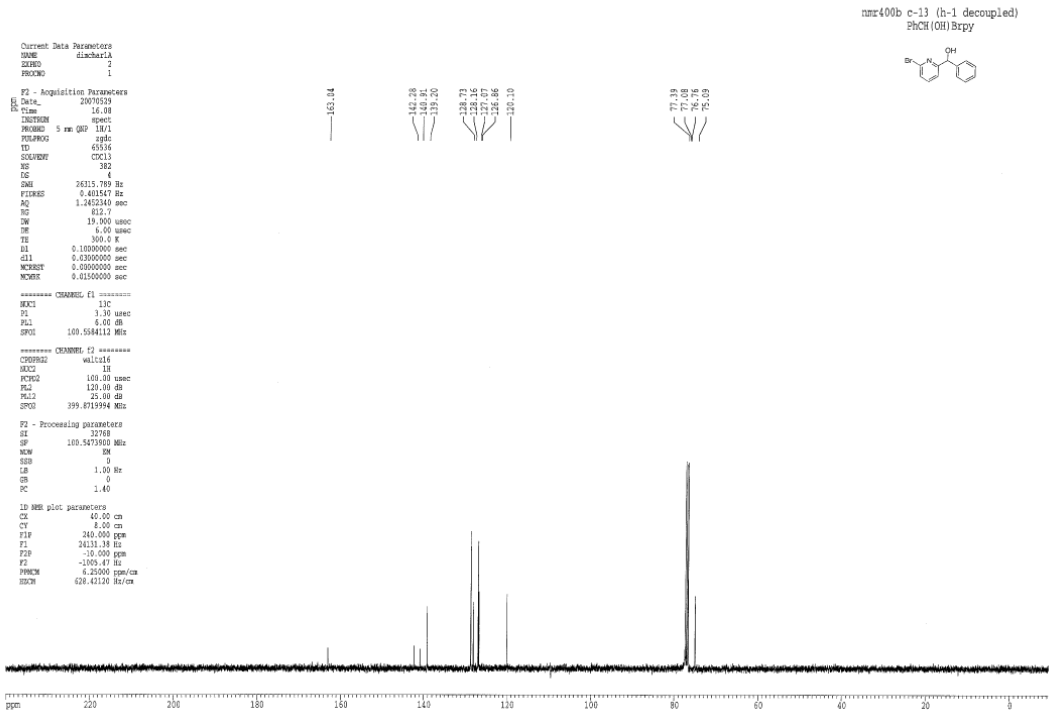
[3] Inaba, Shin-ichi; Matsumoto, Hideyuki; Rieke, Reuben D. *J. Org. Chem.* **1984**, *49*, 2093-2098.

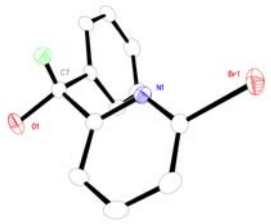
1,2-bis(3-chlorophenyl)-1,2-diphenylethane (34). Prepared according to general procedure B from the corresponding alcohol **33** (436mg, 2.0 mmol, >99% ee) and 10 mol% CuCN. Crude reaction mixture was analyzed by HPLC to be a 64:36 diastereomeric mixture of *C_2:meso* isomers and chromatographed from EtOAc/Hexanes to provide the title compound (inseparable mixture of diastereomers) as a white solid in 54% yield (218 mg); 93% ee (*C_2* symmetric isomer). *C_2* symmetric and *meso* isomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17-7.14 (m, 10H, Ph**H**), 7.08-7.02 (m, 8H, Ph**H**), 4.71 (s, 2H, PhC**H**Ph); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 142.2, 134.1, 134.0, 129.6, 129.5, 128.7, 128.7, 128.5, 128.4, 126.6, 126.5, 126.5, 126.4, 126.3, 56.0; HRMS (MALDI-TOF) exact mass calculated for ($C_{26}H_{21}Cl_2$) requires *m/z* 403.10148, found *m/z* 403.10203 $(M+H)^+$; $[\alpha]_D$ = –11.0° (c = 1.0, $CHCl_3$). Melting point 178.9 °C to 181.1 °C. Enantiomeric ratios were determined by SFC with a tandem Chiralpak OJ-H and Chiralpak OJ-H column (250x4.6mm 5 μm SFC, isocratic 8% MeOH/CO_2, 1.5 mL/min, 30 °C, 200bar, 215nm, 35 min); t_r (*C_2* symmetric) = 28.0 min and 30.5 min, t_r (*meso*) = 29.4 min.

Spectral and Crystallographic Data

*Spectra for Alcohol **12***

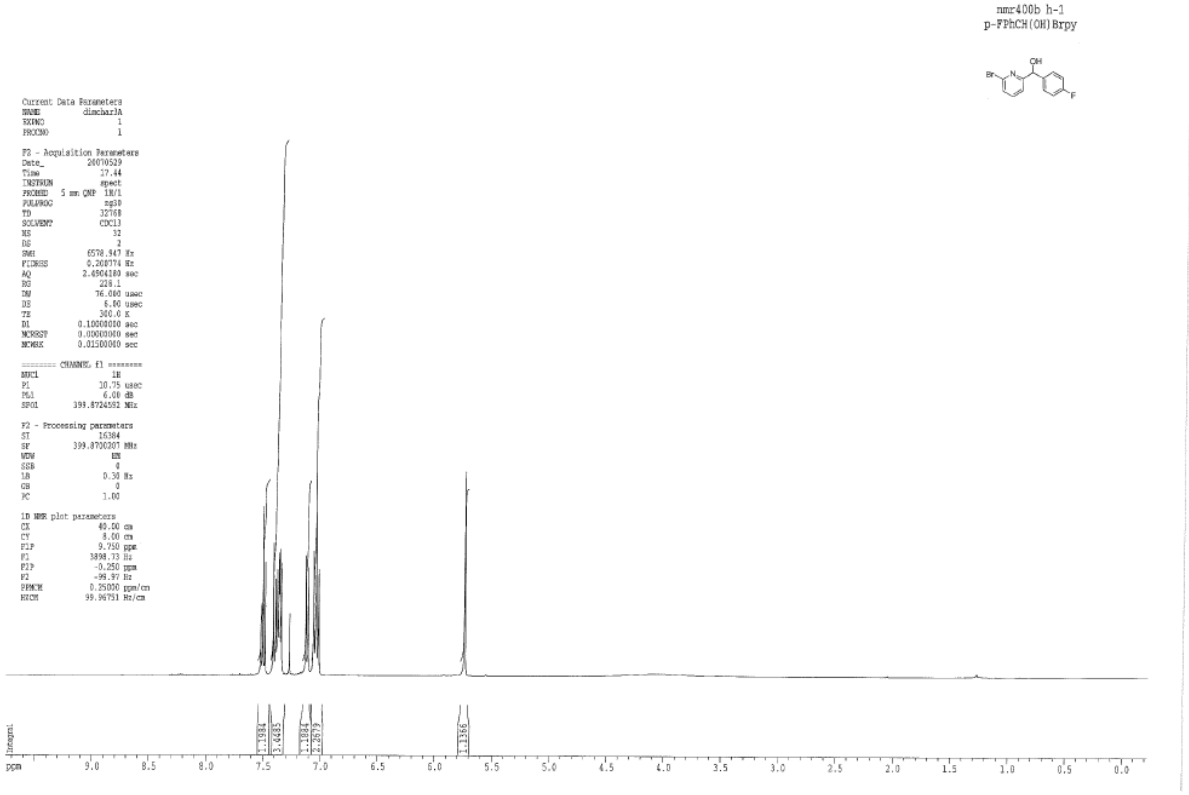


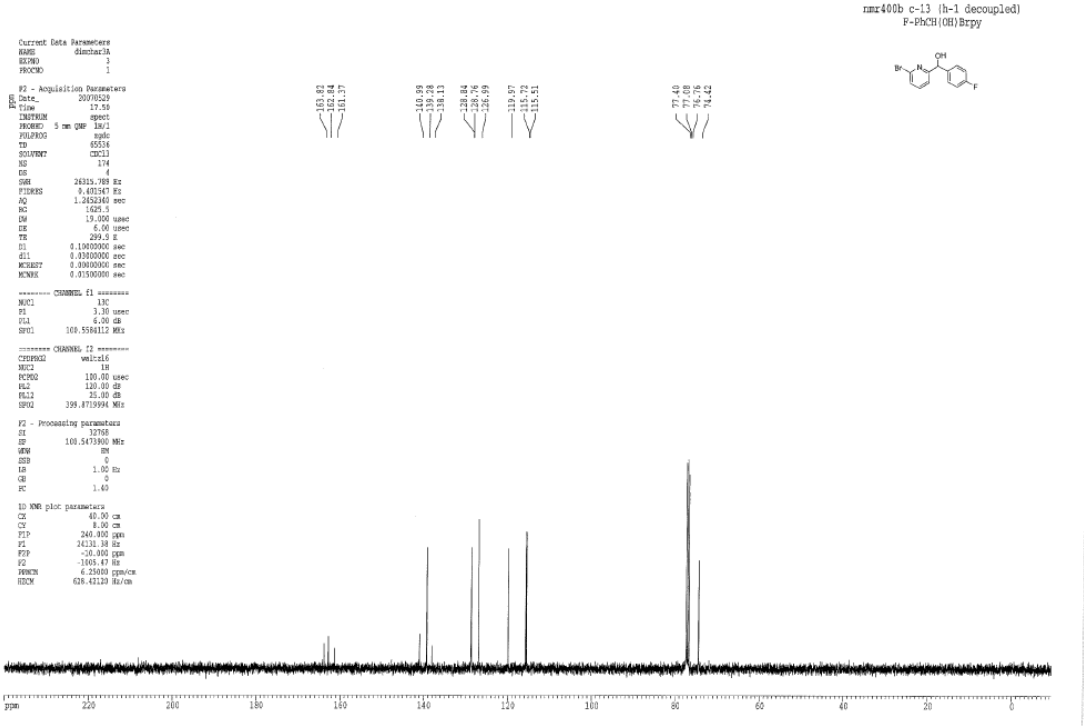




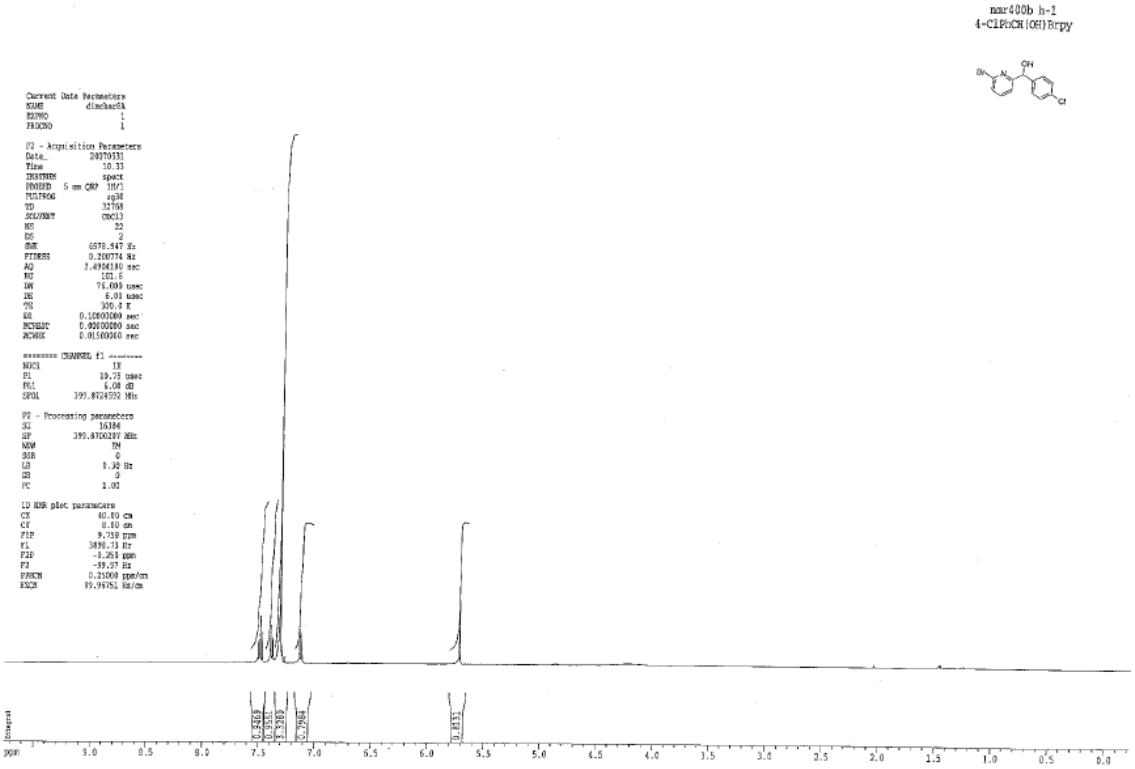
Crystal structure data: Compound $C_{12}H_{10}Br\ N\ O$, M_r = 264.120, orthorhombic, $P2_12_12_1$, a = 8.7335(6), b = 9.1351(6), c = 13.4992(9) Å, V = 1076.98(13) Å^3, Z = 4, D_x = 1.629 gcm^{-3}, monochromatized radiation λ(Mo) = 0.71073 Å, μ = 3.79 mm^{-1}, F(000) = 528, T = 100° K. Data were collected on a Bruker CCD diffractometer to a θ limit of 26.73° which yielded 11423 reflections. There are 2235 unique reflections with 2208 observed at the 2σ level. The structure was solved by direct methods (SHELXS-97, Sheldrick, G.M. *Acta Crystallogr.*, 1990, A46, 467-473) and refined using full-matrix least-squares on F^2 (SHELXL-97, Sheldrick, G.M. *SHELXL-97. Program for the Refinement of Crystal Structures.* Univ. of Göttingen, Germany). The final model was refined using 138 parameters and all 2235 data. All non-hydrogen atoms were refined with anisotropic thermal displacements. The final agreement statistics are: R = 0.024 (based on 2208 reflections with $I > 2\sigma(I)$), wR = 0.055, S = 1.07 with $(\Delta/\sigma)_{max} < 0.01$. The maximum peak height in a final difference Fourier map is 0.456 e Å^{-3} and this peak is without chemical significance. CCDC 667023 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

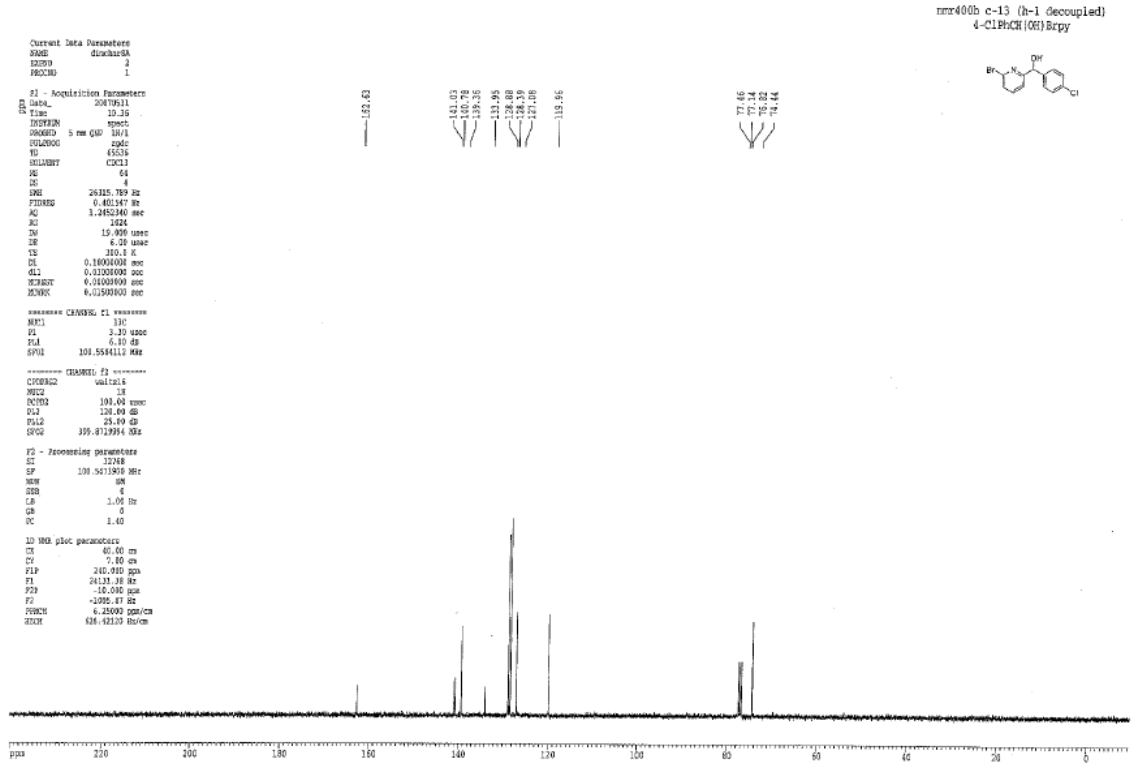
*Spectra for Alcohol **13***



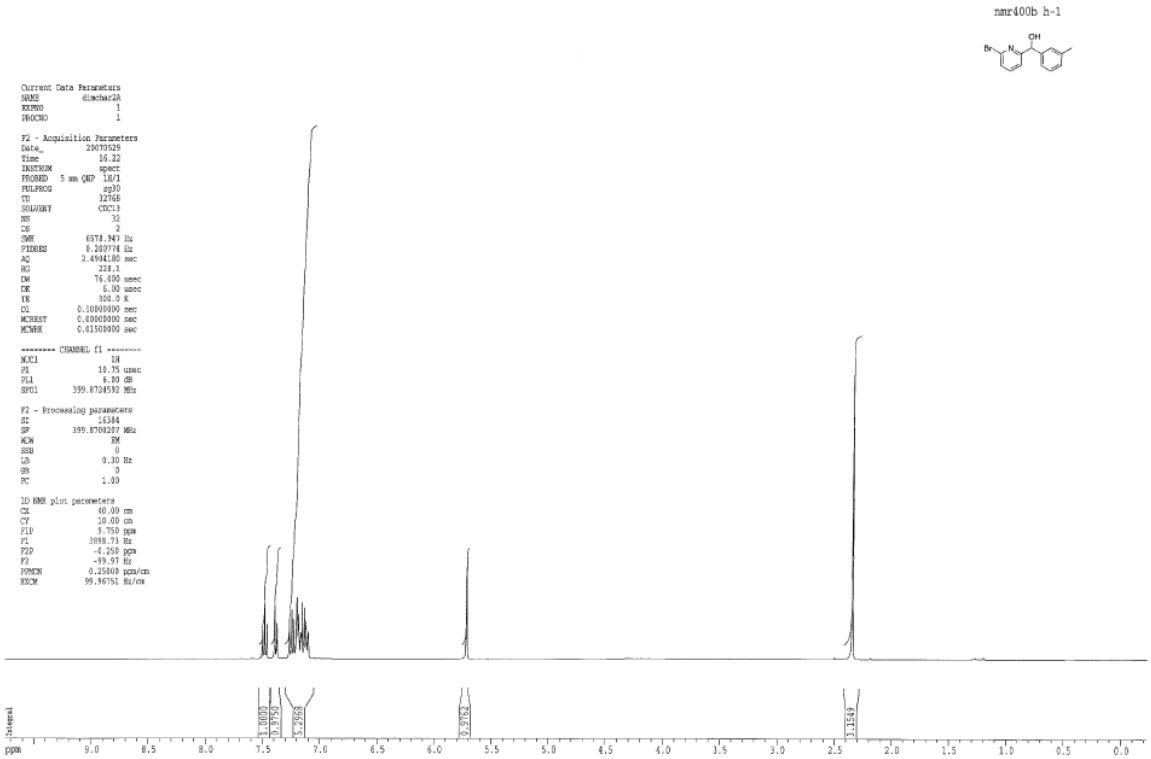


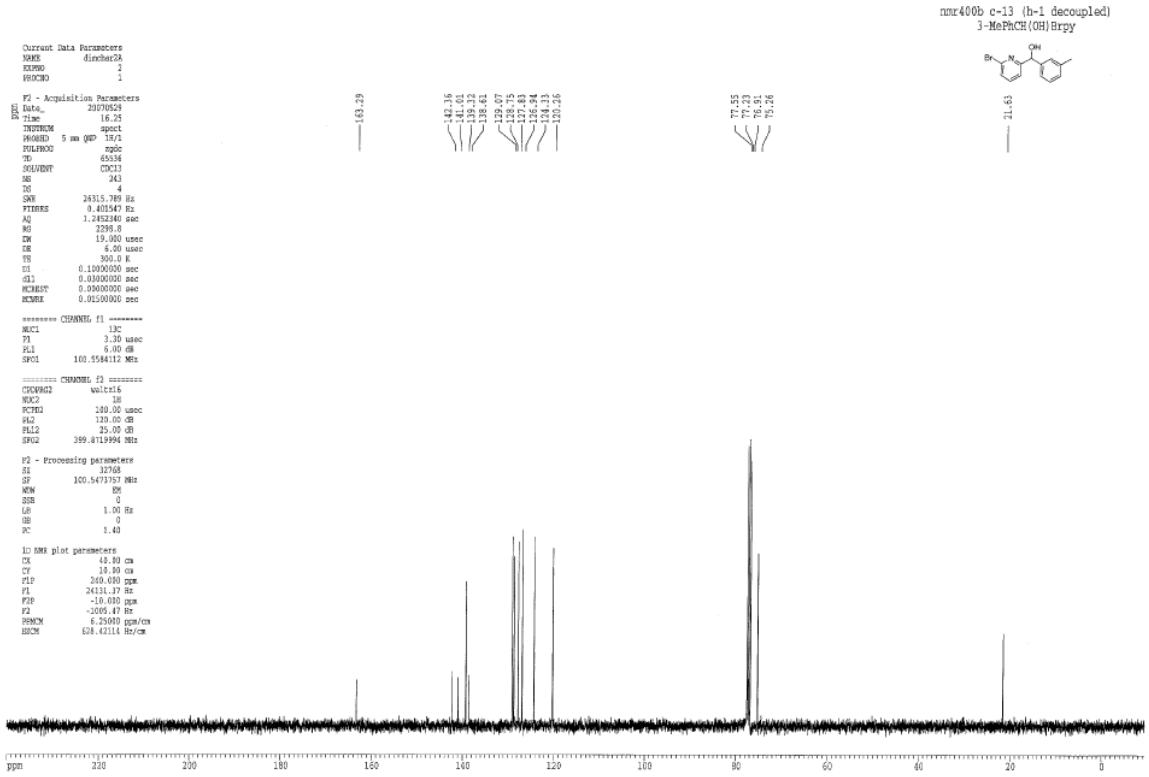
*Spectra for Alcohol **14***



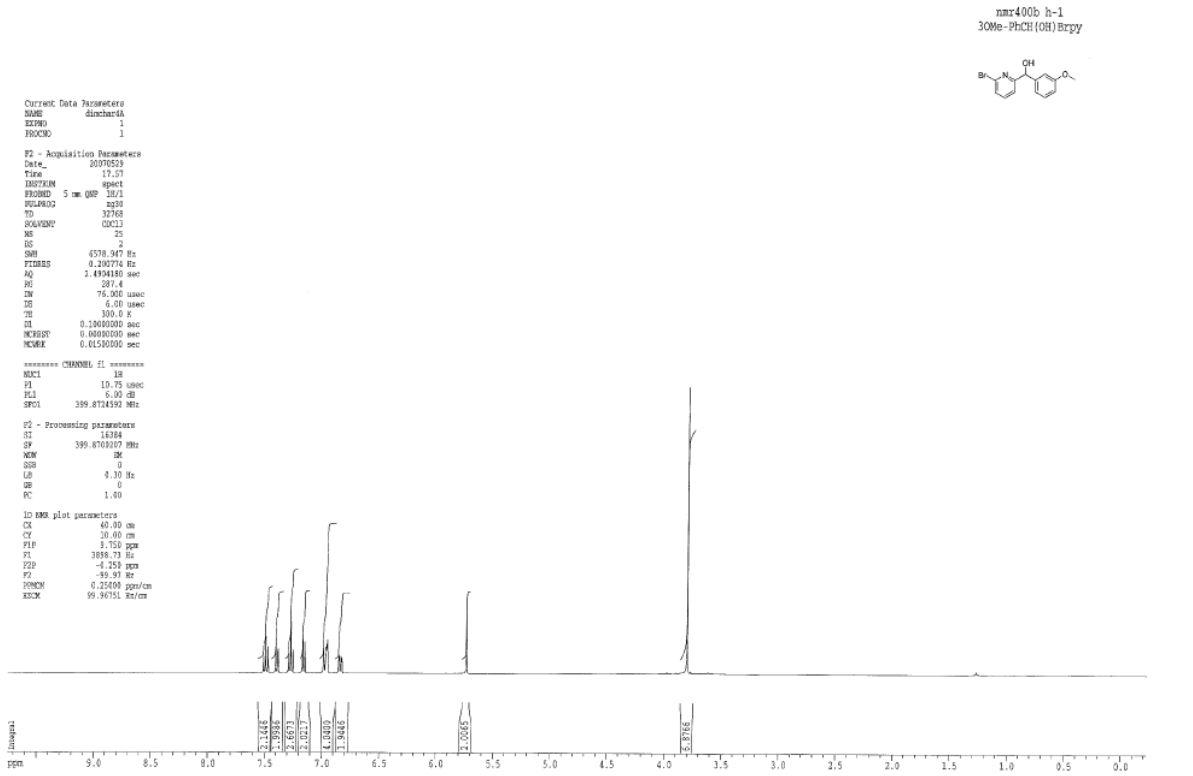


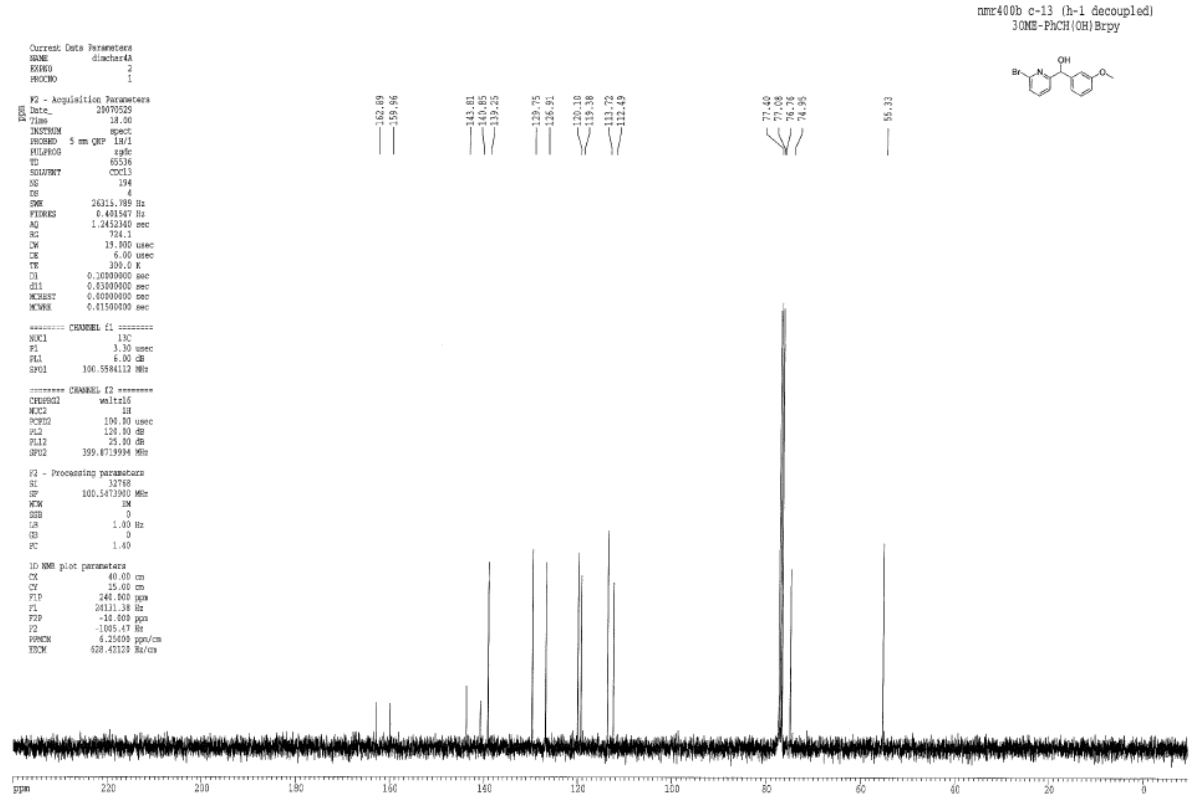
*Spectra for Alcohol **15***



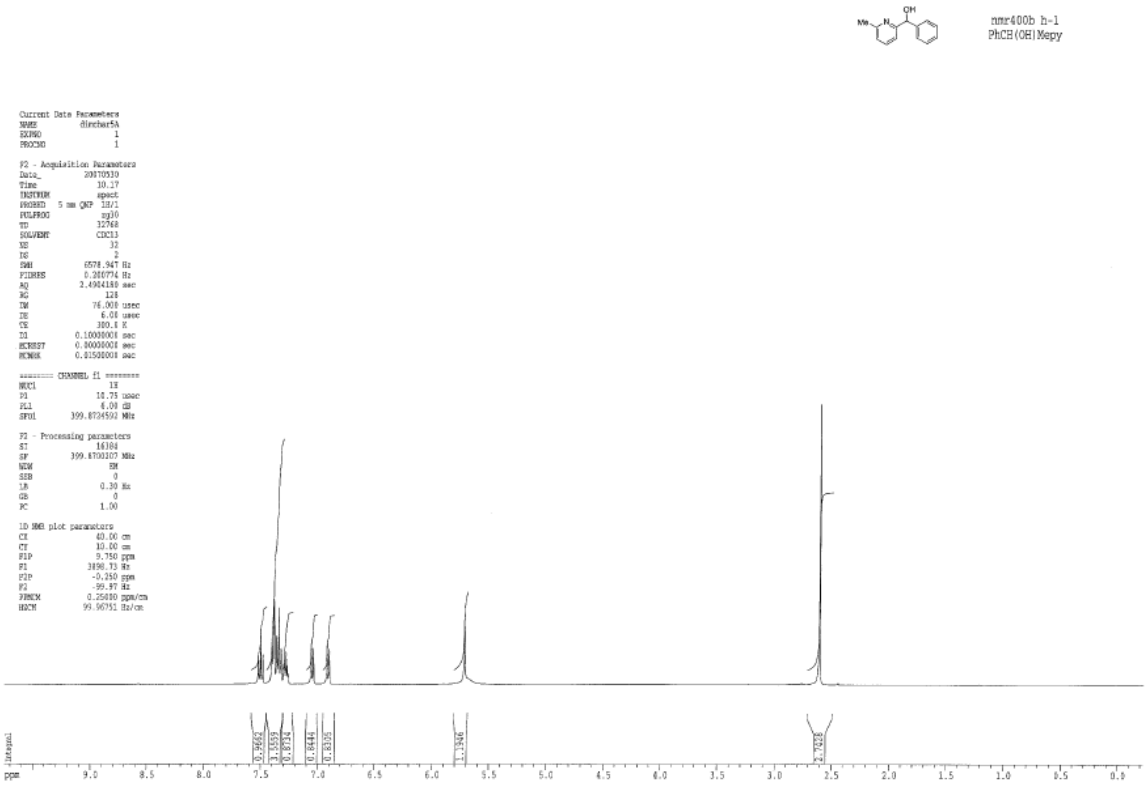


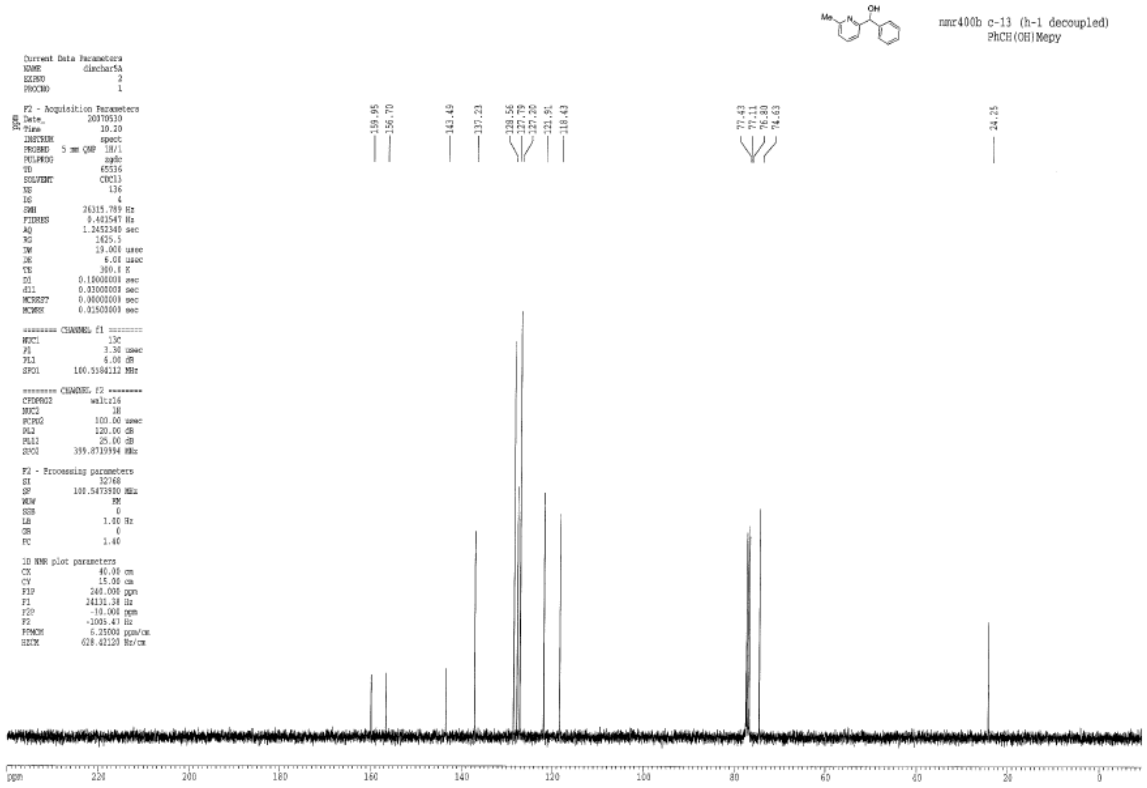
*Spectra for Alcohol **16***



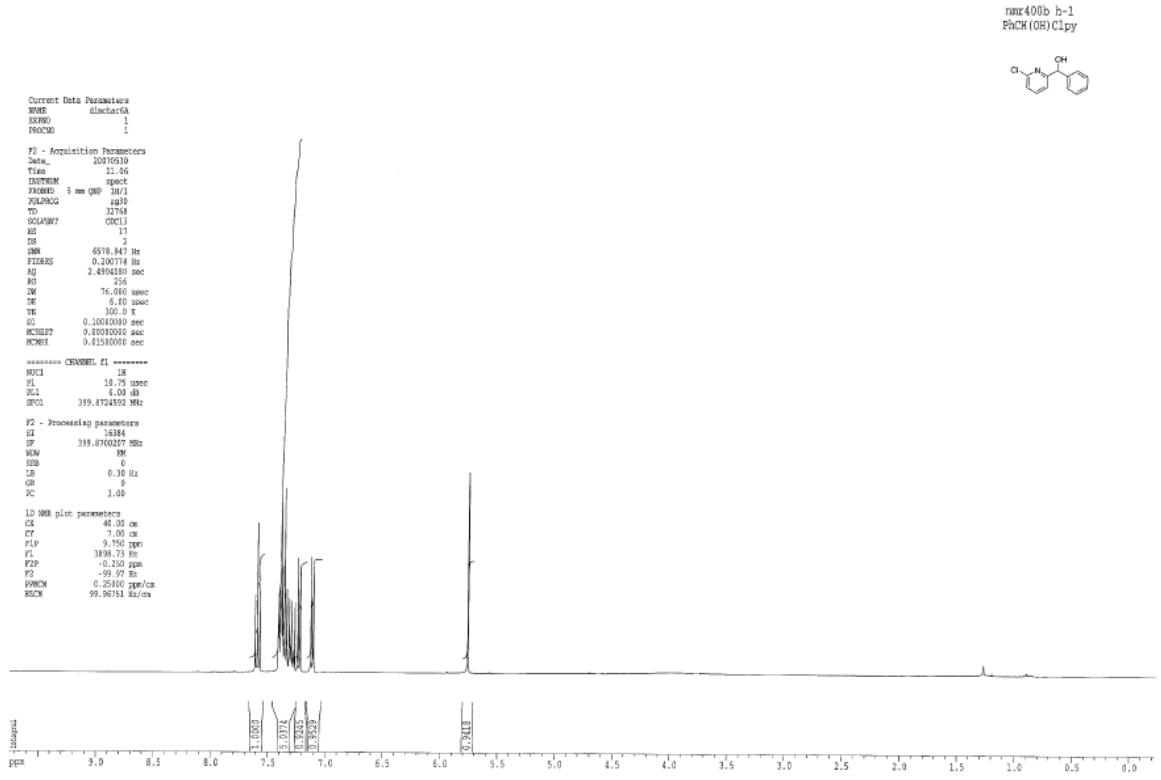


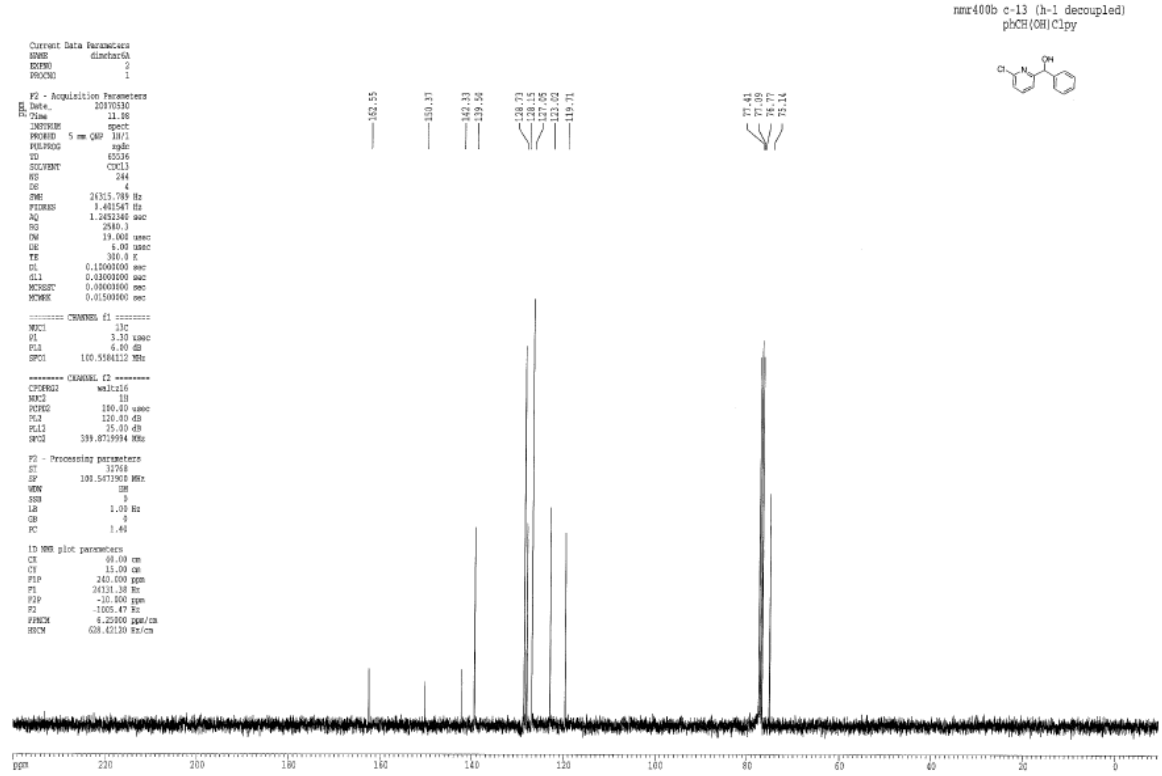
*Spectral Data for **20***



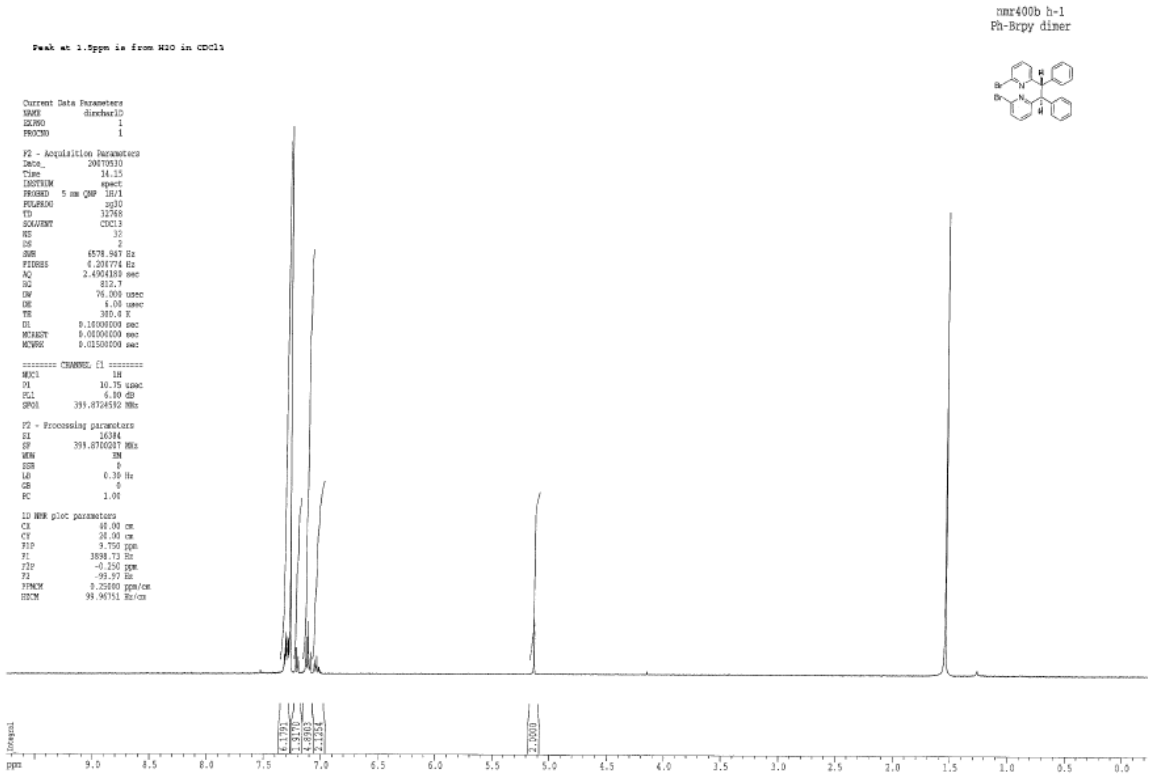


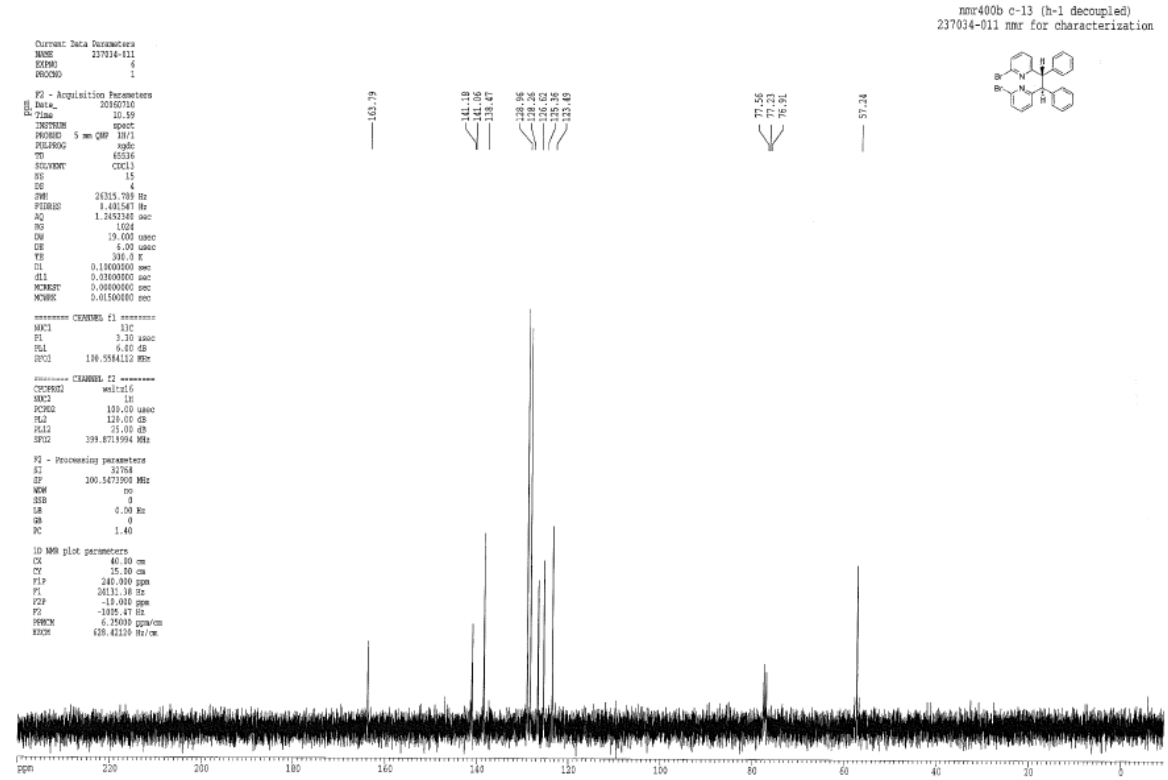
*Spectra Data for **21***



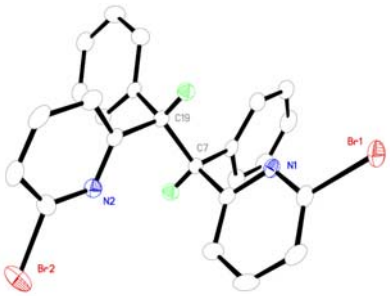


*Spectral Data for **5***



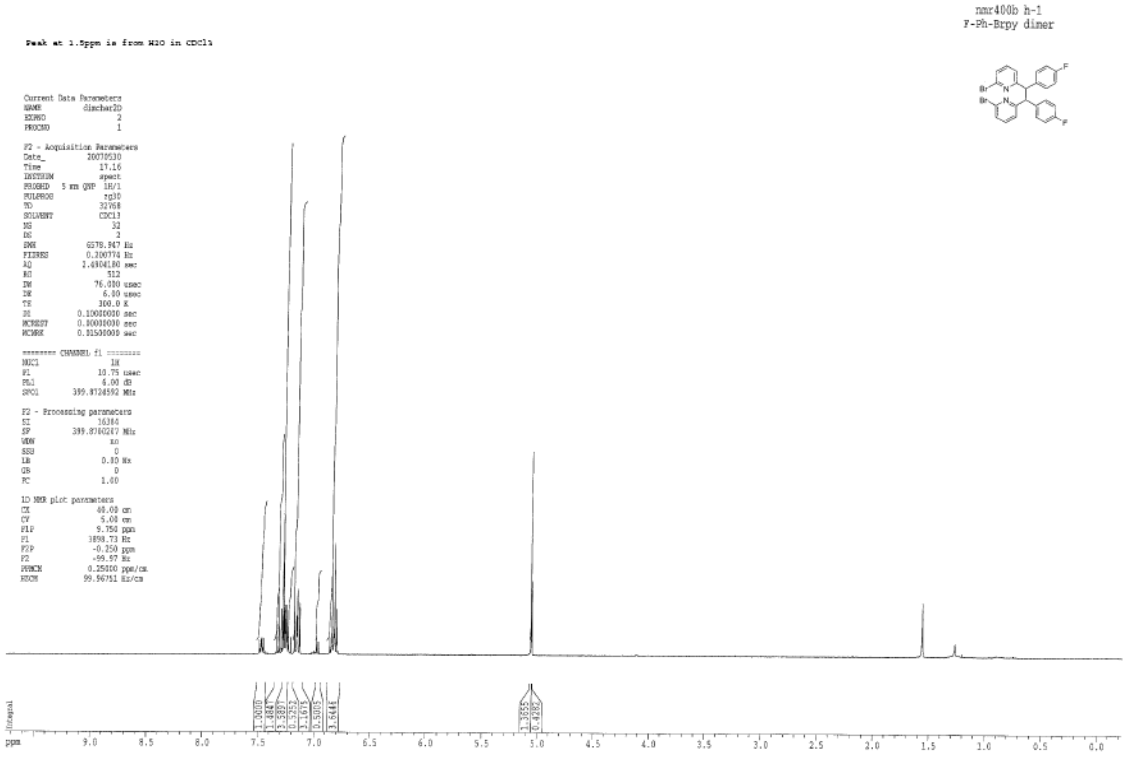


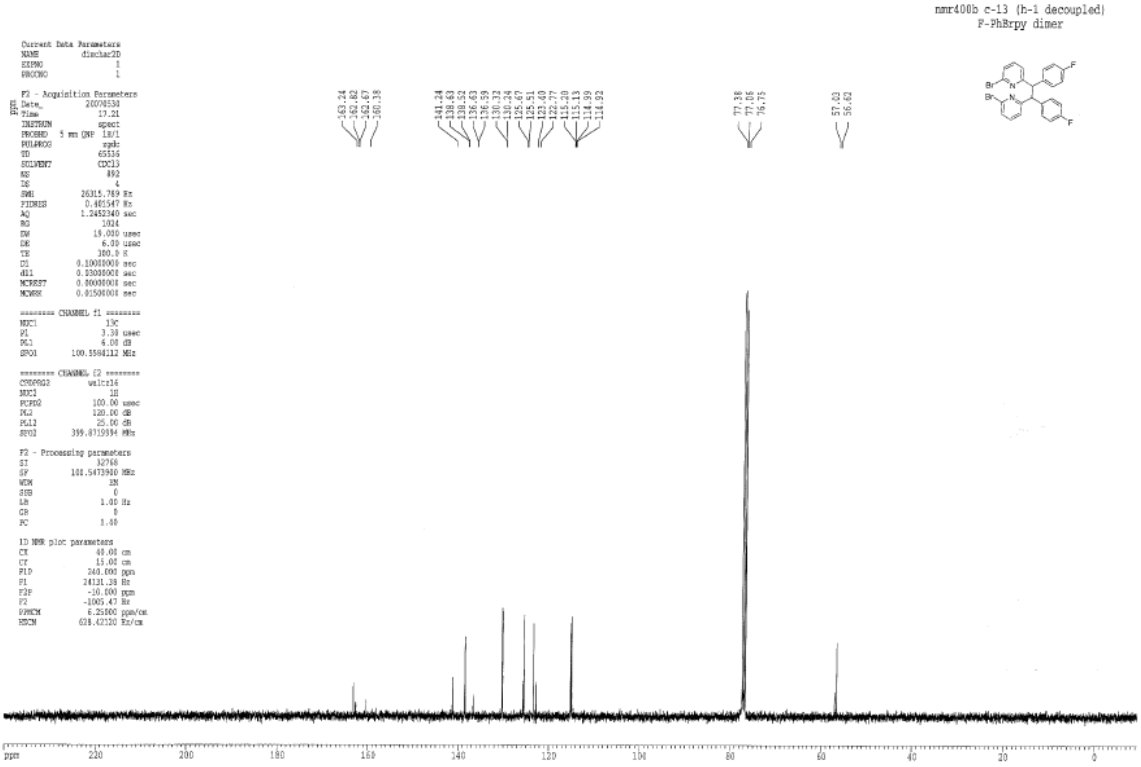
Crystal Structure of ***5***



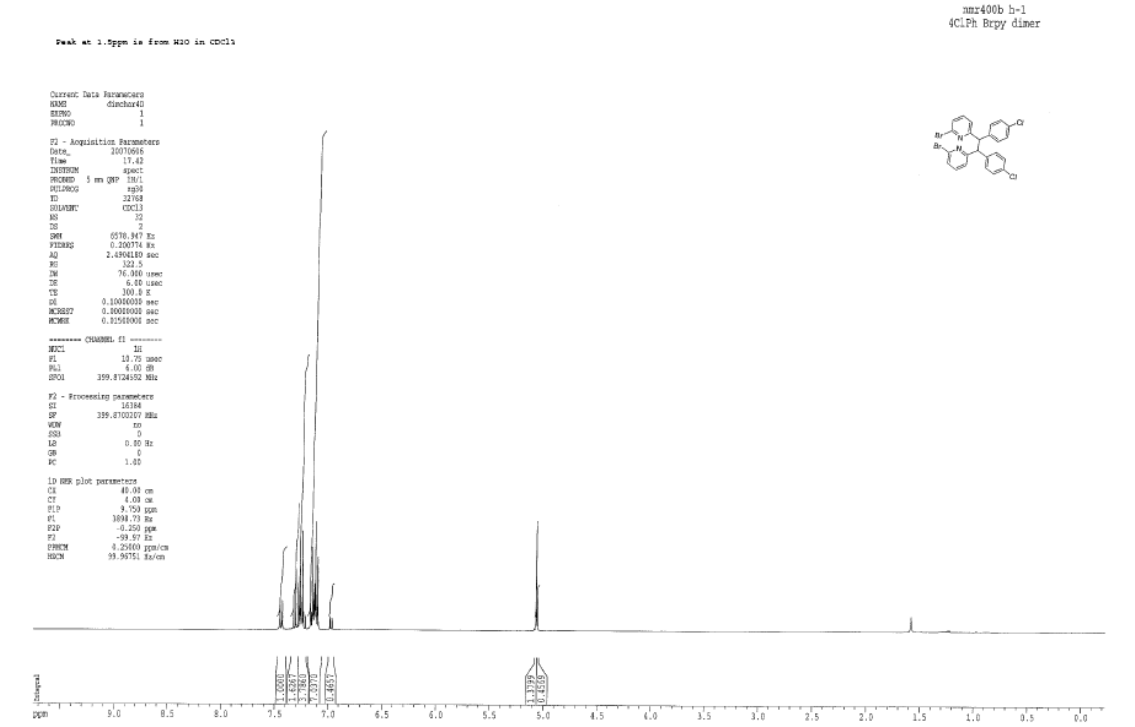
Compound $C_{24}H_{18}Br_2N_2$, M_r = 494.220, orthorhombic, $P2_12_12_1$, a = 9.0694(5), b = 11.7804(6), c = 19.4812(11) Å, V = 2081.4(2) Å^3, Z = 4, D_x = 1.577 gcm^{-3}, monochromatized radiation λ(Mo) = 0.71073 Å, μ = 3.91 mm^{-1}, F(000) = 984, T = 100° K. Data were collected on a Bruker CCD diffractometer to a θ limit of 27.17° which yielded 23314 reflections. There are 4584 unique reflections with 4408 observed at the 2σ level. The structure was solved by direct methods (SHELXS-97, Sheldrick, G.M. *Acta Crystallogr.*, 1990, A46, 467-473) and refined using full-matrix least-squares on F^2 (SHELXL-97, Sheldrick, G.M. *SHELXL-97. Program for the Refinement of Crystal Structures.* Univ. of Göttingen, Germany). The final model was refined using 253 parameters and all 4584 data. All non-hydrogen atoms were refined with anisotropic thermal displacements. The final agreement statistics are: R = 0.020 (based on 4408 reflections with $I > 2\sigma(I)$), wR = 0.051, S = 1.10 with $(\Delta/\sigma)_{max} < 0.01$. The maximum peak height in a final difference Fourier map is 0.544 e Å^{-3} and this peak is without chemical significance. CCDC 667024 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

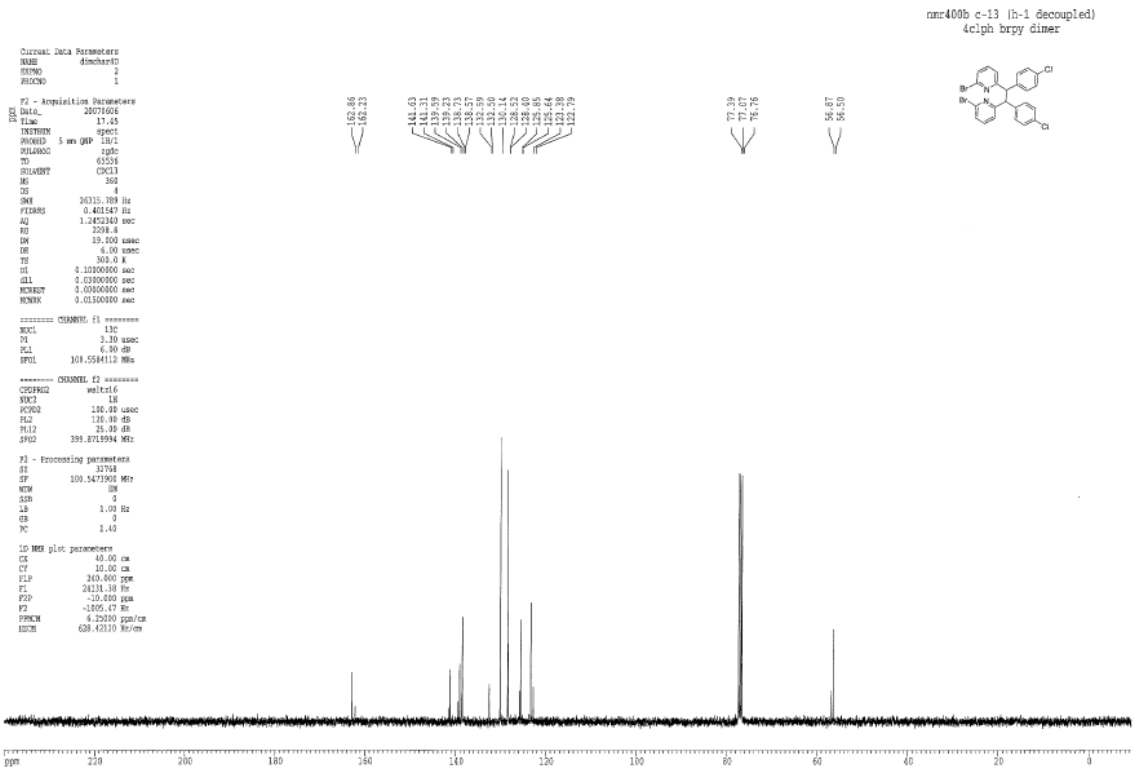
*Spectral Data for **22***



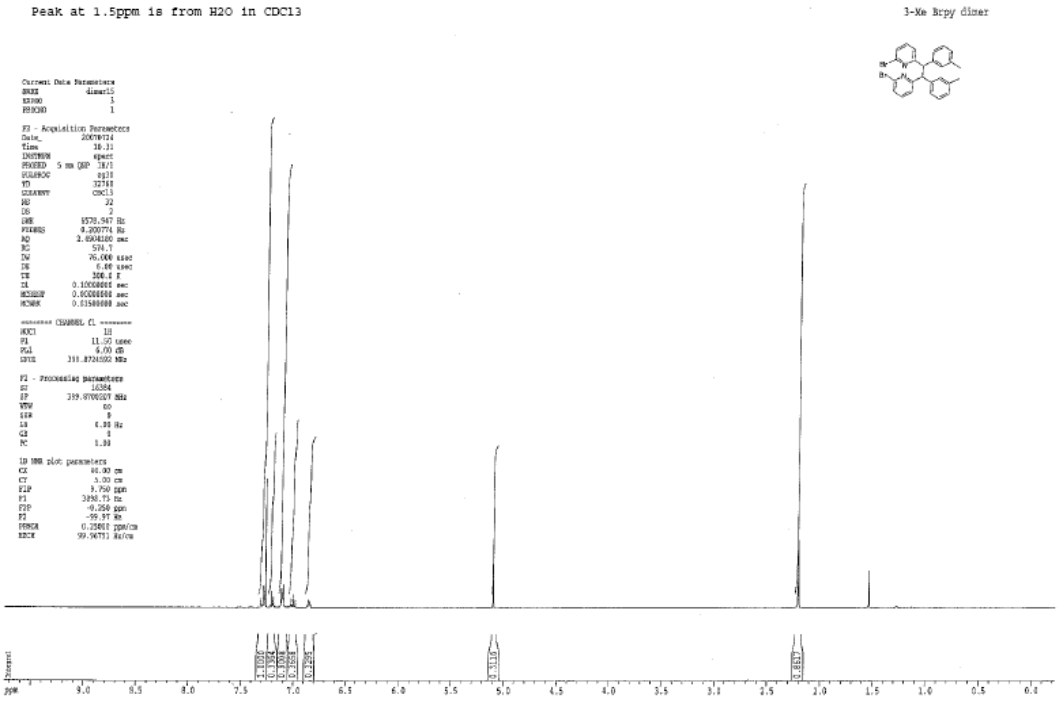


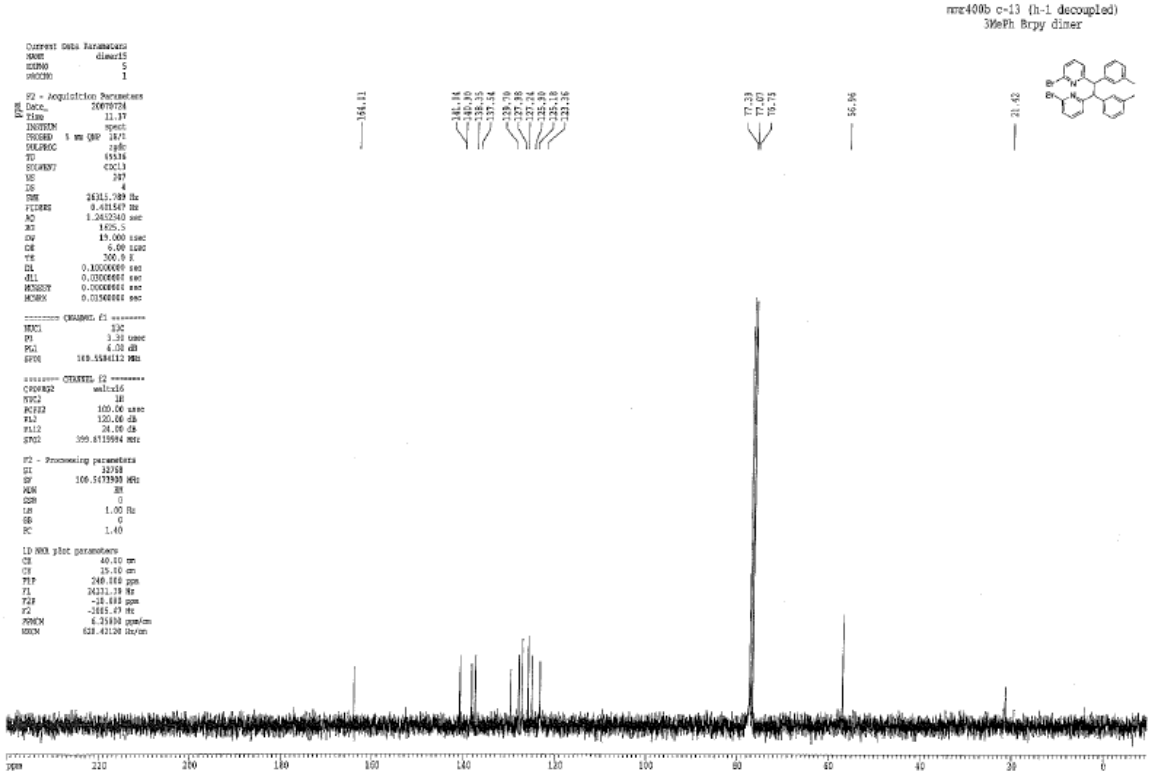
*Spectral Data for **23***



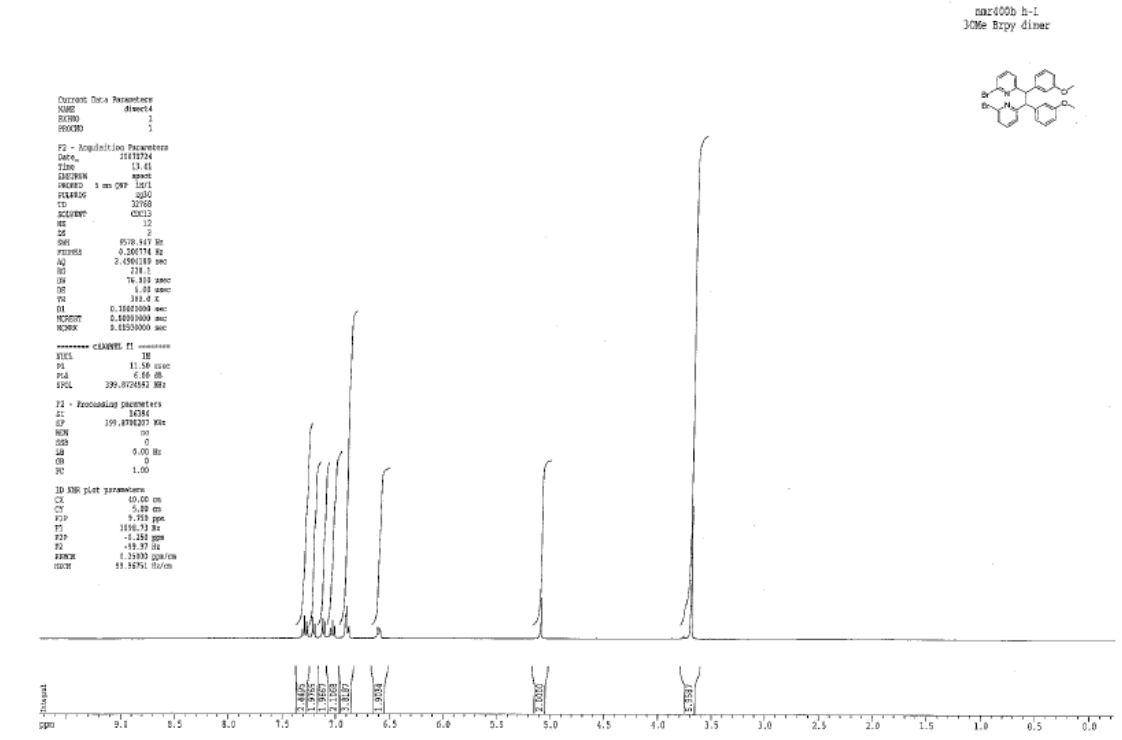


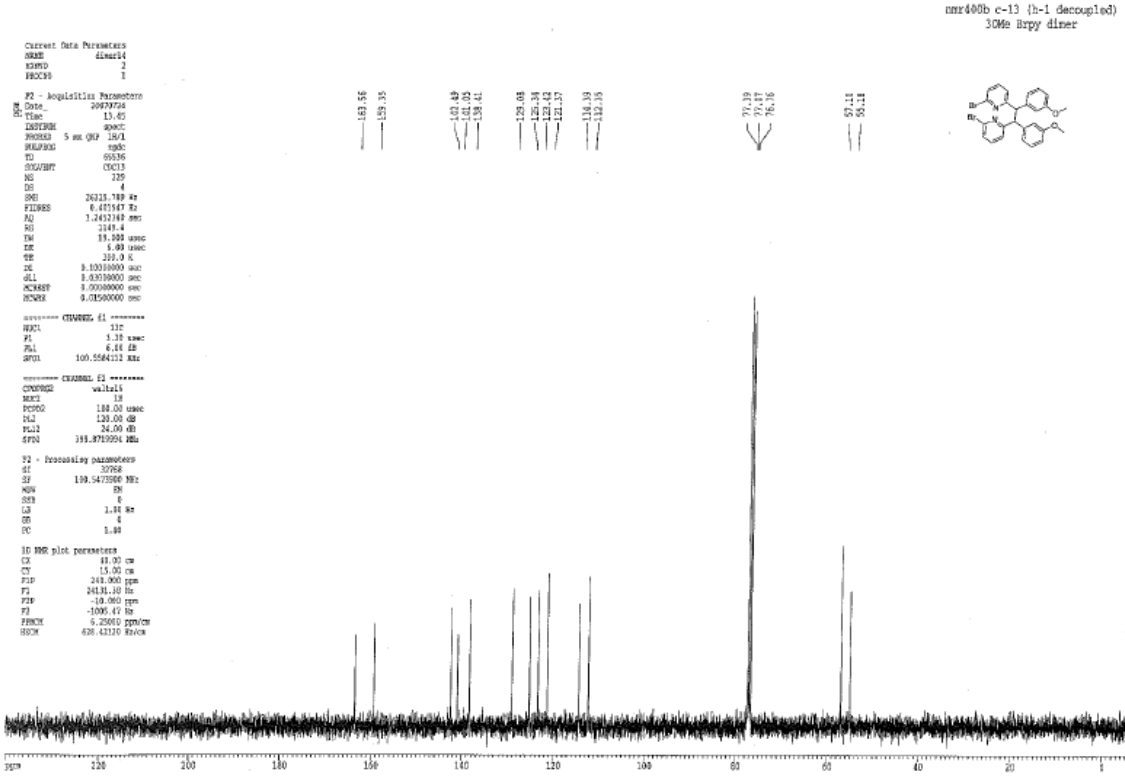
*Spectral Data for **24***



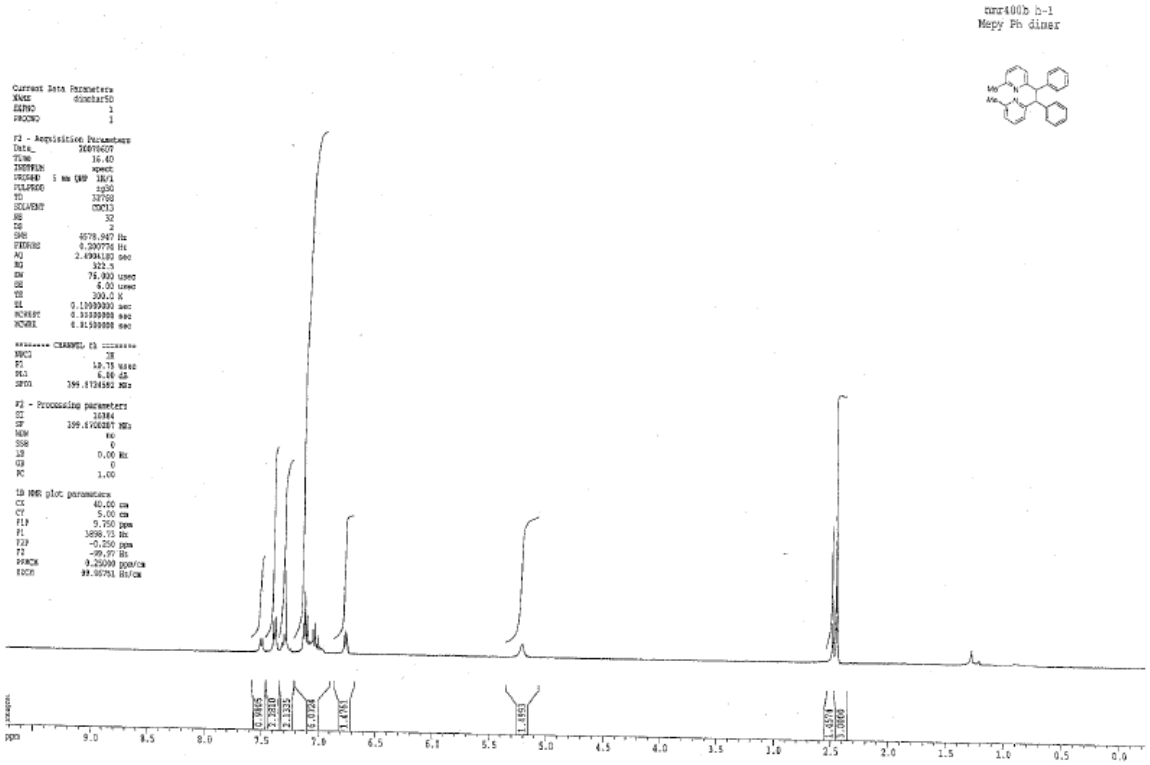


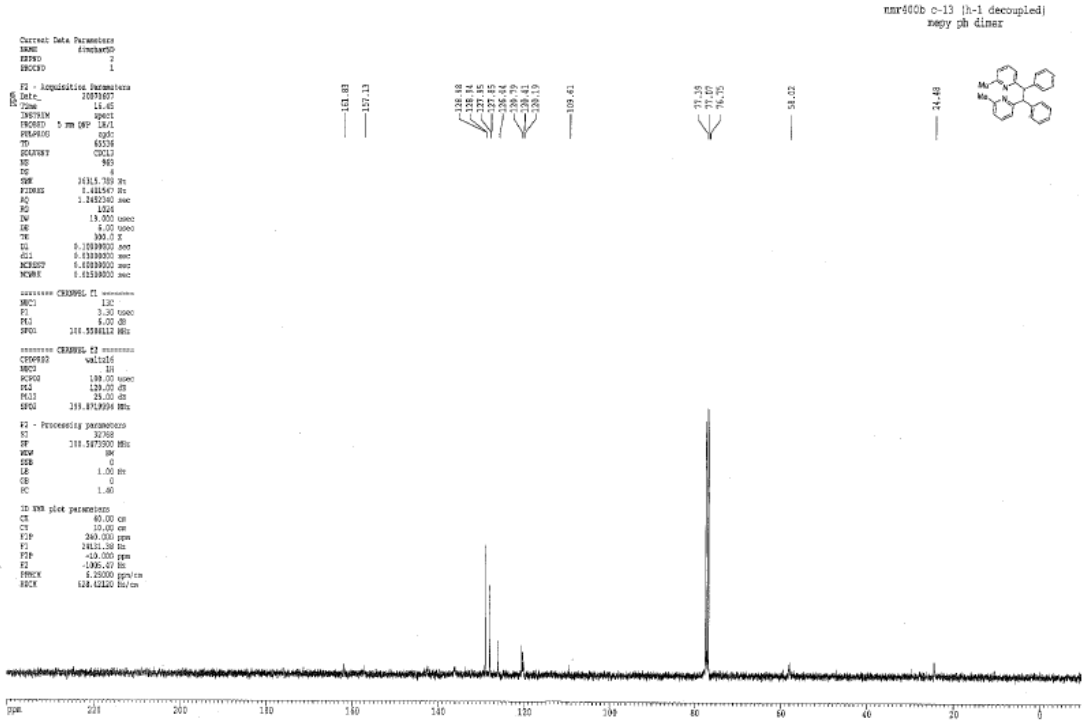
*Spectra Data for **25***



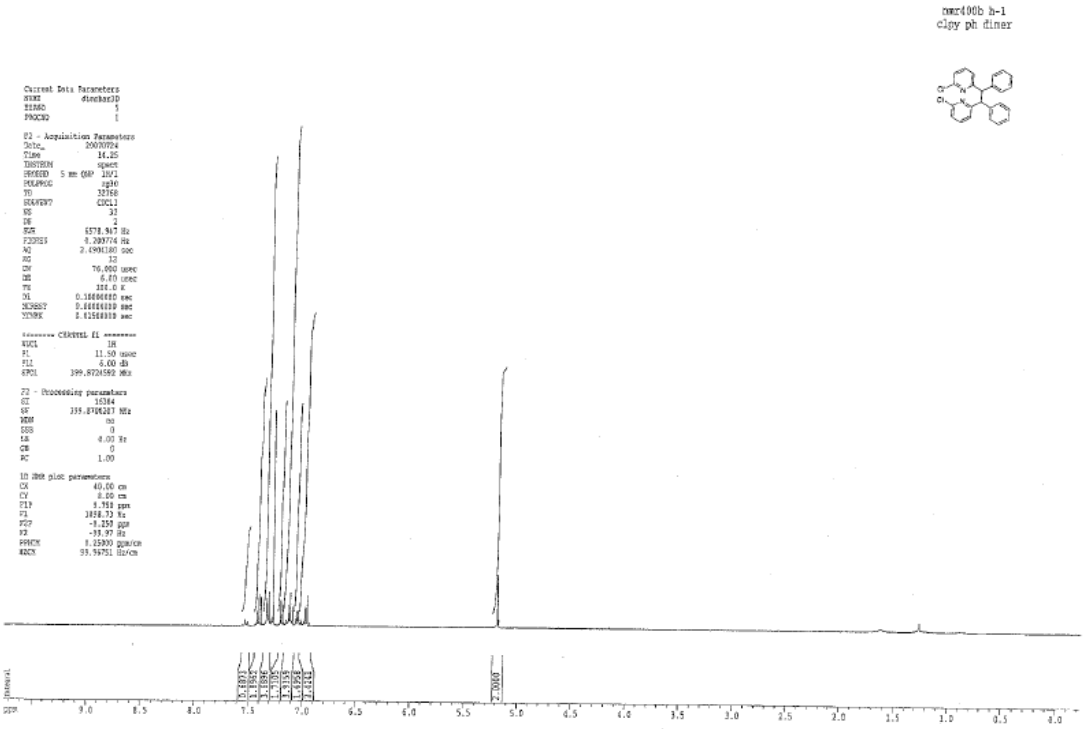


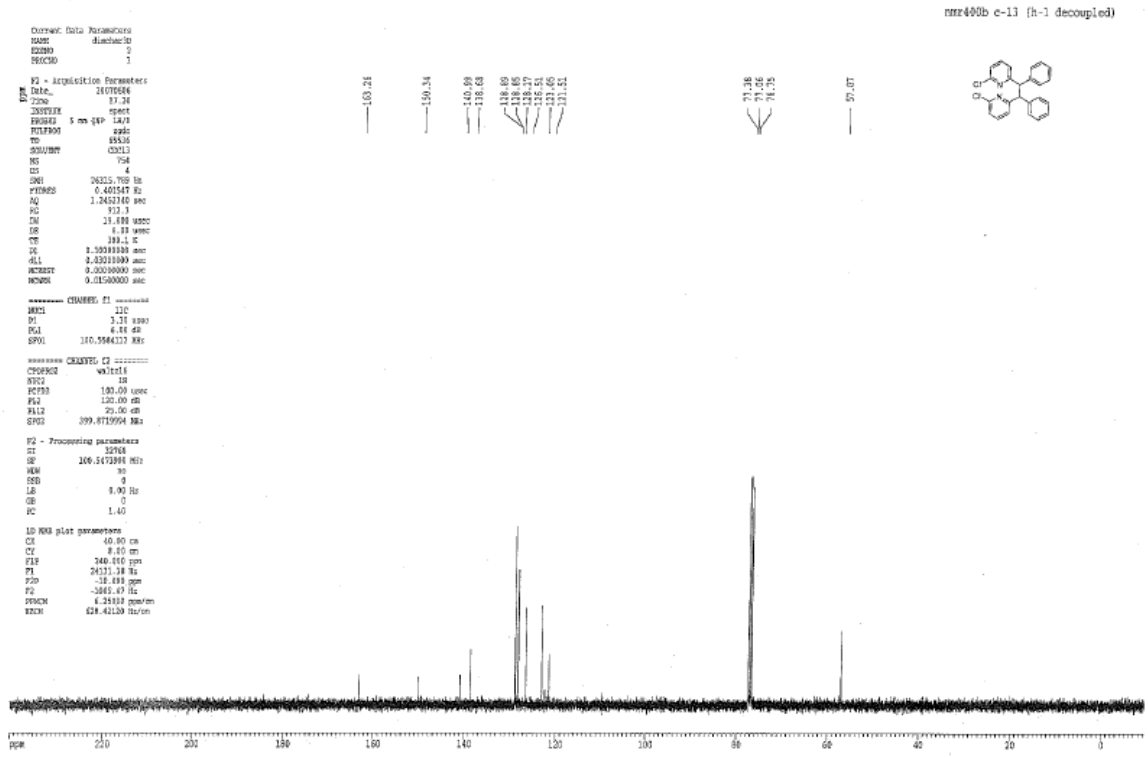
Spectral Data for **29**



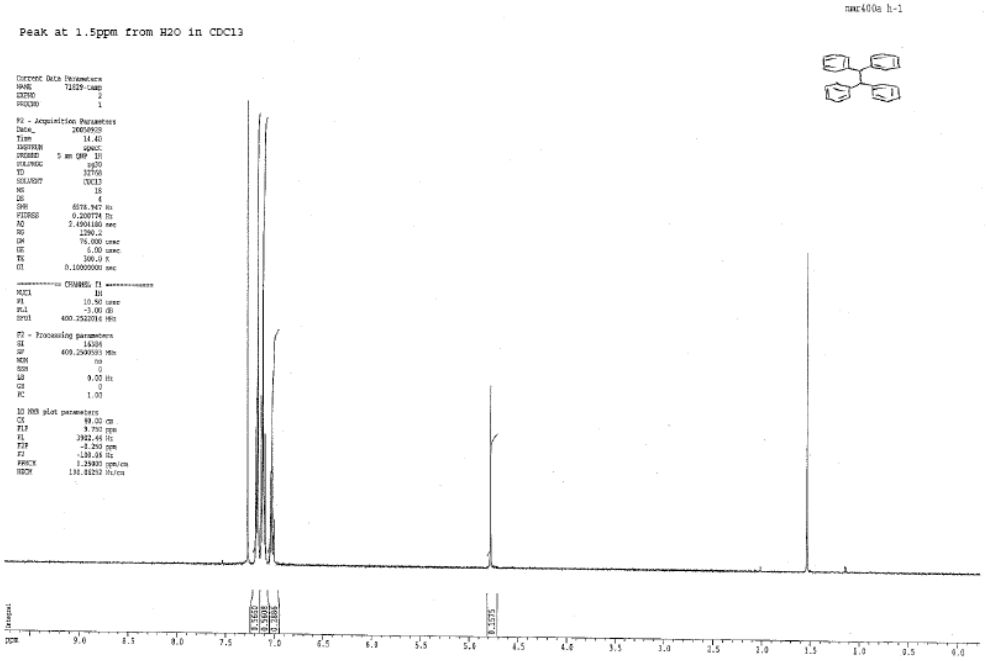


*Spectra Data for **30***

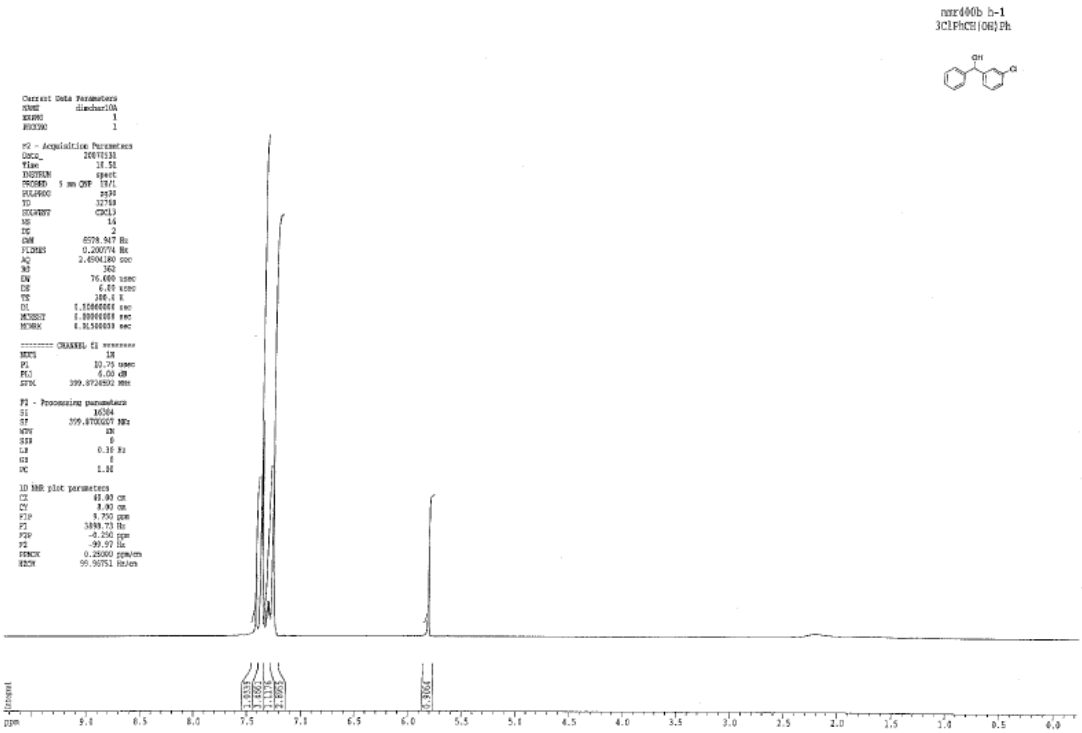




Spectra Data for 32



*Spectral Data for **33***



*Spectra Data for **34***