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Supporting Information

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A Palladium-Catalyzed Regiospecific Synthesis of *N*-Aryl Benzimidazoles

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Experimental Section

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General Considerations

All reactions were carried out under an argon atmosphere in a Schlenk tube with a stir bar capped with a Teflon screw-cap. Anhydrous *t*-BuOH was purchased from Aldrich in a Sure/Seal™ bottle, used as received and stored under Argon. EtOH (200 proof) was purchased from Pharmco and used as received. EtOAc was purchased from Mallinckrodt (ACS grade) and used as received. Anhydrous granular K_3PO_4 was purchased from Fluka. Bulk quantities of K_3PO_4 were stored in a nitrogen-filled glovebox. Small portions (2 g) were removed from the glovebox in glass vials, stored in a desiccator filled with anhydrous calcium sulfate and weighed in the air. 3Å molecular sieves were activated by heating under vacuum and then stored in a nitrogen-filled glovebox. 2-Bromo-4-methylacetanilide **16a** was purchased from Aldrich. 2-bromo-4-trifluoromethylacetanilide **18a** was purchased from Acros. *ortho*-Anisidine was

purchased from Alfa Aesar. The rest of starting materials were purchased from either Aldrich or Acros and used as received unless specified otherwise. Aniline, 2-bromo-4-methylaniline, *ortho*-toluidine, 2-chloroaniline, and 2-*i*-propylaniline were purified by distillation over CaH_2 and stored in a desiccator filled with anhydrous calcium sulfate. 2-Bromo-4-methylacetanilide was purified by recrystallization from a mixture of hexanes and ethyl acetate. *para*-Anisidine and *para*-toluidine were purified by vacuum sublimation and stored in a nitrogen-filled glovebox.

$Pd_2(dba)_3$ and iron powder were purchased from Strem. The following phosphorus ligands were purchased from the following companies, or received as gifts, and used as received: 2-(dicyclohexylphosphino)-2',4',6'-tri-*i*-propyl-1,1'-biphenyl **L1** (XPhos, a gift of Rhodia), 2-(di-*t*-butylphosphino)-2',4',6'-tri-*i*-propyl-1,1'-biphenyl **L2** (*t*-BuXPhos, Aldrich), 2-(di-*t*-butylphosphino)biphenyl **L3** (JohnPhos, Aldrich), 2-(dicyclohexylphosphino)-2'-(*N*,*N*-di-methylamino)biphenyl **L4** (DavePhos, a gift of Bayer), *rac*-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl **L6** (*rac*-BINAP, a gift of Rhodia), 1,1'-bis(di-*t*-butylphosphino)ferrocene **L7** (Strem), (R)-(-)-1-[(S)-2-(dicyclohexylphosphino)ferrocenyl)]ethyldicyclohexylphosphine **L8** (Strem), (R)-(-)-1-[(S)-2-(diphenylphosphino)ferrocenyl)]ethyldi-*t*-butylphosphine **L9** (Strem). 2-(Dicyclohexylphosphino)-2',6'-di-*i*-propoxy-1,1'-biphenyl **L5** (RuPhos)[1] and 2-(di-*t*-butylphosphino)-3,4,5,6-tetramethyl-2',4',6'-tri-*i*-propylbiphenyl **L10**[2] were synthesized following the published procedure.

All products were characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, in addition to elemental analysis performed by Atlantic Microlabs Inc., Norcross, GA. For those products for which a satisfactory elemental analysis was not obtained, copies of the ^{1}H and ^{13}C NMR spectra are attached. Regarding starting materials, all the new compounds were characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, in addition to elemental analysis performed by Atlantic Microlabs Inc., Norcross, GA. For those compounds for which a satisfactory elemental analysis was not obtained, copies of the ^{1}H and ^{13}C NMR spectra are attached. Nuclear Magnetic Resonance spectra were recorded on a Varian Mercury 300 or Varian Inova 500 instrument. All ^{1}H NMR experiments are reported in δ units, parts per million (ppm) and were measured relative to the signal for residual chloroform (7.27 ppm). All ^{13}C NMR spectra (obtained with ^{1}H decoupling) are reported in ppm relative to deuterochloroform (77.23 ppm). Infrared spectra were recorded using a Perkin-Elmer 2000 FT-IR. Melting points (uncorrected) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatography analyses were performed on an Agilent 6890 instrument with an FID detector and an Agilent DB-1 column (10 m x 0.1 mm i.d.). Flash column chromatography was performed manually or using a Biotage SP4 Flash Purification System with KP-Sil silica cartridges (methylene chloride was used to transfer the crude product onto the silica gel samplet).

The conversions and yields (average of two runs) in Tables 1 were determined by G.C. using dodecane as an internal standard, added during the reaction workup. The yields in Tables 2 and 3 as well as Scheme 2 are isolated yields (average of two runs). Yields for the preparation of starting materials refer to a single experiment and are not optimized. All compounds isolated were estimated to be ≥95% pure as determined by ^{1}H NMR and GC analysis.

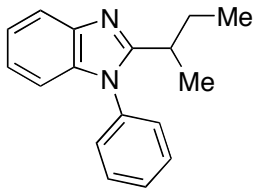
Screening of Phosphine Ligands for the Palladium-catalyzed Amination of *ortho*-Haloanilides (Table 1).

An oven-dried Schlenk tube containing a stir bar was charged with Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), ligand **L1**-**L9** (0.04 mmol, 8 mol %), and 2-bromoacetanilide (107 mg, 0.5 mmol). The Schlenk tube was capped with a Teflon screw cap, evacuated and sealed

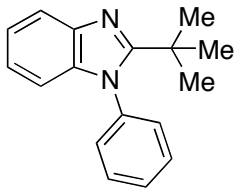
under vacuum. It was then transferred to a glove box in which *p*-toluidine (80.4 mg, 0.75 mmol) and K_3PO_4 (265 mg, 1.25 mmol) were added. The tube was sealed and removed from the box. It was connected to a double manifold and opened under a positive flow of Ar (the tube was evacuated and backfilled with Ar via 3 cycles). *t*-BuOH (1.0 mL) was added via syringe and the tube was sealed. It was put into a pre-heated oil bath at 110 °C and stirred for 18 h. After cooling to room temperature, dodecane (113 μL) was added as an internal standard. The reaction mixture was diluted with methylene chloride (3 mL). An aliquot was filtered through a plug of Celite (eluting with methylene chloride) and analyzed by GC.

General Procedure for Pd-Catalyzed Synthesis of *N*-Aryl Benzimidazoles (Tables 2 and 3)

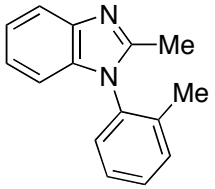
An oven-dried Schlenk tube containing a stir bar was charged with Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), ligand **L1** or **L5** (0.04 mmol, 8 mol %), *ortho*-haloanilides (0.5 mmol), aromatic amines (0.75 mmol) and K_3PO_4 (265 mg, 1.25 mmol). The Schlenk tube was capped with a Teflon screw cap and then evacuated and backfilled with argon (3 cycles). *t*-BuOH (1.0 mL) was added to the Schlenk tube under a positive flow of argon (if the aromatic amine was liquid, it was added to the Schlenk tube at this time). The Schlenk tube was sealed and put into a pre-heated oil bath at 110 °C or 120 °C. After stirring for 18 h, the reaction mixture was allowed to cool to room temperature and diluted with methylene chloride (4 mL). The diluted mixture was filtered through Celite with the aid of methylene chloride. The filtrate was concentrated under vacuum and the residual was purified by flash chromatography on silica gel. Most of the examples in Tables 2 and 3 followed the general procedure except **13b**, **13d**, **13q**, **17b** and **19a**.



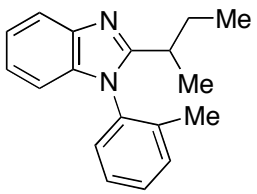
2-*sec*-butyl-1-phenyl-1*H*-benzimidazole (Table 2, **13a**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (128 mg, 0.5 mmol), aniline (68 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 5-40% ethyl acetate in hexanes gradient) to provide the title compound as a brown solid (107.4 mg, 86%). mp 62-65 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83 (d, J = 7.9Hz, 1H), 7.61-7.52 (m, 3H), 7.35 (d, J = 7.2Hz, 2H), 7.28 (ddd, J = 8.2, 7.3, 1.2Hz, 1H), 7.19 (ddd, J = 8.2, 7.3, 1.1Hz, 1H), 7.07 (d, J = 8.1Hz, 1H), 2.88-2.81 (m, 1H), 2.00-1.91 (m, 1H), 1.72-1.63 (m, 1H), 1.36 (d, J = 6.9Hz, 3H), 0.83 (t, J = 7.4Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 159.7, 142.8, 136.6, 136.2, 130.1, 129.1, 128.0, 122.5, 122.4, 119.4, 110.2, 33.5, 29.4, 20.2, 12.3. IR (neat, cm^{-1}): 2965, 1596, 1499, 1455, 1407, 1275, 1221, 1013, 745, 698. Anal. Calcd for $C_{17}H_{18}N_2$: C, 81.56; H, 7.25. Found: C, 81.30; H, 7.25.



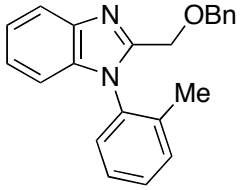
2-*tert*-butyl-1-phenyl-1*H*-benzimidazole (Table 2, **13b**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (128 mg, 0.5 mmol), aniline (68 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. After cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2 (4 mL) and then filtered through Celite with the aid of CH_2Cl_2. The filtrate was concentrated under vacuum. The residual was treated with 4N HCl (2 mL) in 1,4-dioxane at room temperature. The resulting mixture was heated to 100 °C and stirred at 100 °C for 2 h. The reaction mixture was cooled to 0 °C and 3N NaOH (3.4 mL) was added dropwise. Then saturated aq $NaHCO_3$ solution (4 mL) was added. The mixture was extracted with CH_2Cl_2 (4 mLx3). The combined extracts were dried over Na_2SO_4 and concentrated under vacuum. The residual was purified by flash chromatography on silica gel (Biotage, 8-66% ethyl acetate in hexanes gradient) to provide the title compound as an off-white solid (109.6 mg, 88%). mp 125-126 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 7.9Hz, 1H), 7.58-7.54 (m, 3H), 7.4-7.36 (m, 2H), 7.25 (ddd, *J* = 8.1, 7.2, 1.2Hz, 1H), 7.14 (ddd, *J* =8.2, 7.1, 1.2Hz, 1H), 6.76 (d, *J* = 7.8Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 161.6, 141.3, 139.4, 138.3, 129.68, 129.66, 129.5, 122.7, 122.3, 119.2, 110.2, 35.2, 30.4. IR (neat, cm^{-1}): 2986, 1594, 1497, 1456, 1365, 1308, 1266, 1198, 745, 705. Anal. Calcd for $C_{17}H_{18}N_2$: C, 81.56; H, 7.25. Found: C, 81.65; H, 7.27.



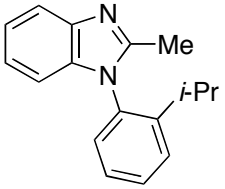
2-methyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 2, **13c**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (107 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a brown solid (62.5 mg, 56%). mp 72.5-74.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 8.0Hz, 1H), 7.49-7.36 (m, 3H), 7.29-7.15 (m, 3H), 6.91 (dt, *J* = 7.8, 0.9Hz, 1H), 2.40 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 151.9, 142.9, 136.5, 136.4, 134.9, 131.6, 129.8, 128.6, 127.6, 122.6, 122.3, 119.2, 110.1, 17.5, 14.2. IR (neat, cm^{-1}): 3052, 1615, 1499, 1458, 1391, 1320, 1245, 1016, 743, 583. See attached ^{1}H and ^{13}C.



2-*sec*-butyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 2, **13d**, 1:1 mixture of two rotamers) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (128 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 8-66% ethyl acetate in hexanes gradient) to provide the title compound as a viscous oil (85.6 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 7.9Hz, 1H), 7.47-7.42 (m, 2H), 7.40-7.36 (m, 1H), 7.28-7.25 (m, 1H), 7.22, (dd, *J* = 7.5, 3.2Hz, 1H), 7.17 (ddd, *J* = 8.1, 7.2, 1.1Hz, 1H), 6.89 (dd, *J* = 8.0, 4.2Hz, 1H), 2.67-2.59 (m, 1H), 2.02-1.90 (m, 1H), 1.99 (s, 1.5H), 1.97 (s, 1.5H), 1.71-1.62 (m, 1H), 1.34 (d, *J* = 5.6Hz, 1.5H), 1.32 (d, *J* = 5.7Hz, 1,5H), 0.86 (dd, *J* = 7.4, 3.1Hz, 1.5H), 0.84 (dd, *J* = 7.4, 3.1Hz, 1.5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 159.67, 159.56, 142.96, 142.88, 136.74, 136.57, 135.94, 134.84, 134.81, 131.61, 131.58, 129.64, 129.22, 128.87, 127.40, 127.36, 122.50, 122.25, 122.23, 119.41, 119.37, 110.18, 110.16, 33.92, 33.55, 29.73, 28.63, 20.52, 19.69, 17.58, 17.43, 12.43, 12.28. IR (neat, cm^{-1}): 2966, 2931, 1614, 1496, 1457, 1406, 1275, 1223, 1013, 764, 746, 724. See attached ^{1}H and ^{13}C.

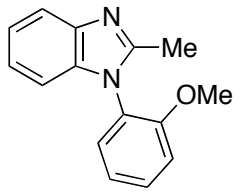


2-[(benzyloxy)methyl]-1-(2-methylphenyl)-1*H*-benzimidazole (Table 2, **13e**) Following the general procedure, a mixture of Pd_2dba_3 (5.4 mg, 0.0059 mmol, 2.0 mol % Pd), RuPhos **L5** (22.1 mg, 0.047 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (190 mg, 0.59 mmol), *ortho*-toluidine (95 μL, 0.89 mmol), K_3PO_4 (314 mg, 1.48 mmol), and *t*-BuOH (1.2 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in hexanes gradient) to provide the title compound as a viscous oil (165.6 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.88 (ddd, *J* = 7.9, 1.1, 0.8Hz, 1H), 7.47 (dt, *J* = 1.4, 7.5Hz, 1H), 7.42 (d, *J* = 6.6Hz, 1H), 7.36 (t, *J* = 7.5Hz, 1H), 7.32 (ddd, *J* = 8.2, 7.2, 1.2Hz, 1H), 7.30-7.24 (m, 5H), 7.17-7.15 (m, 2H), 6.97 (ddd, *J* = 7.9, 1.2, 0.8Hz, 1H), 4.63 (d, *J* = 12.2Hz, 1H), 4.55 (d, *J* = 12.2Hz), 4.54 (d, *J* = 11.9Hz, 1H), 4.50 (d, *J* = 11.9Hz, 1H), 1.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 150.5, 142.3, 137.4, 136.7, 136.5, 134.4, 131.3, 129.7, 128.6, 128.3, 127.72, 127.69, 127.1, 123.6, 122.6, 120.2, 110.5, 72.7, 64.2, 17.4. IR (neat, cm^{-1}): 3061, 3031, 2923, 2856, 1499, 1455, 1402, 1329, 1251, 1091, 1075, 1027, 742, 698. Anal. Calcd for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14. Found: C, 80.36; H, 6.24.

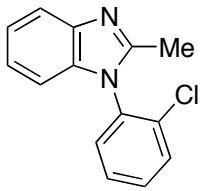


1-(2-isopropylphenyl)-2-methyl-1*H*-benzimidazole (Table 2, **13f**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (107 mg, 0.5 mmol), 2-*i*-propylaniline (106 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-

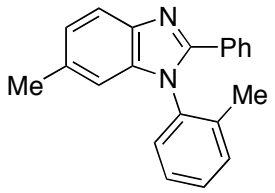
100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a gray solid (106.7 mg, 86%). mp 109-110.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 8.1Hz, 1H), 7.55-7.53 (m, 2H), 7.38-7.35 (m, 1H), 7.26 (t, *J* = 8.1Hz, 1H), 7.19-7.16 (m, 2H), 6.91 (d, *J* = 7.9Hz, 1H), 2.52-2.43 (m, 1H), 2.39 (s, 3H), 1.13 (d, *J* = 6.9Hz, 3H), 1.06 (d, *J* = 6.9Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 152.3, 147.4, 142.8, 137.3, 133.4, 130.3, 128.7, 127.4, 127.3, 122.7, 122.3, 119.1, 110.1, 28.0, 24.3, 23.7, 14.3. IR (neat, cm^{-1}): 2964, 1616, 1493, 1457, 1391, 1318, 1244, 1014, 765, 743, 667. Anal. Calcd for $C_{17}H_{18}N_2$: C, 81.56; H, 7.25. Found: C, 81.16; H, 7.30.



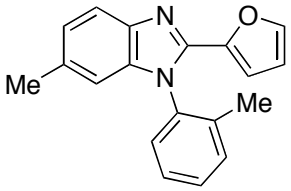
1-(2-methoxyphenyl)-2-methyl-1*H*-benzimidazole (Table 2, **13g**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (107 mg, 0.5 mmol), *ortho*-anisidine (85 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a gray solid (95.9 mg, 81%). mp 123-125 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.74 (d, *J* = 8.1Hz, 1H), 7.49 (dt, *J* = 1.6, 8.0Hz, 1H), 7.30 (dd, *J* = 7.6, 1.1Hz, 1H), 7.24 (t, *J* = 8.1Hz, 1H), 7.18-7.10 (m, 3H), 7.00 (d, *J* = 8.1Hz, 1H), 3.73 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.3, 152.8, 142.9, 136.8, 130.7, 129.3, 124.5, 122.3, 122.1, 121.2, 118.9, 112.5, 110.0, 55.7, 14.1. IR (neat, cm^{-1}): 3053, 2934, 2839, 1599, 1507, 1466, 1393, 1322, 1280, 1253, 1015, 744. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92. Found: C, 75.83; H, 5.95.



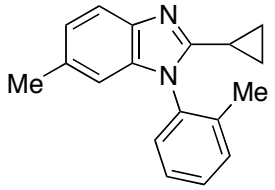
1-(2-chlorophenyl)-2-methyl-1*H*-benzimidazole (Table 2, **13h**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (107 mg, 0.5 mmol), 2-chloroaniline (79 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a pink solid (67.0 mg, 55%). mp 73-74 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 8.1Hz, 1H), 7.66 (dd, *J* = 7.7, 1.8Hz, 1H), 7.52 (dt, *J* = 2.0, 7.6Hz, 1H), 7.48 (dt, *J* = 1.5, 7.5Hz, 1H), 7.40 (dd, *J* = 7.6, 1.9Hz, 1H), 7.28 (dt, *J* = 1.1, 7.5Hz, 1H), 7.20 (dt, *J* = 1.1, 7.6Hz, 1H), 6.95 (d, *J* = 7.9Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 152.0, 142.9, 136.4, 133.8, 133.3, 131.1, 131.0, 130.2, 128.4, 122.9, 122.6, 119.3, 109.9, 14.3. IR (neat, cm^{-1}): 3055, 1615, 1528, 1490, 1455, 1392, 1321, 1243, 1074, 1015, 762, 743. Anal. Calcd for $C_{14}H_{11}ClN_2$: C, 69.28; H, 4.57. Found: C, 69.18; H, 4.64.



6-methyl-1-(2-methylphenyl)-2-phenyl-1*H*-benzimidazole (Table 2, **13i**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (145 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 120 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 5-40% ethyl acetate in hexanes gradient) to provide the title compound as an off-white solid (129.8 mg, 87%). mp 164-166 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.79 (d, *J* = 8.1Hz, 1H), 7.60 (d, *J* = 7.2Hz, 2H), 7.46-7.27 (m, 7H), 7.17 (d, *J* = 8.1Hz, 1H), 6.79 (s, 1H), 2.44 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 152.0, 141.2, 137.5, 136.3, 133.5, 131.8, 130.5, 129.50, 129.48, 128.8, 128.7, 128.5, 127.6, 124.6, 119.4, 110.5, 22.0, 17.7. IR (neat, cm^{-1}): 3029, 2919, 1496, 1472, 1378, 1332, 1276, 809, 761, 724, 697. Anal. Calcd for $C_{21}H_{18}N_2$: C, 84.53; H, 6.08. Found: C, 84.27; H, 6.08.

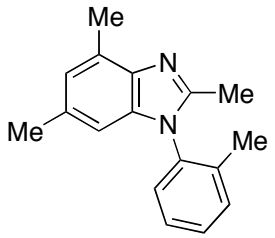


2-(2-furyl)-6-methyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 2, **13j**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (140 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 120 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 8-66% ethyl acetate in hexanes gradient) to provide the title compound as a viscous oil (125.6 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.76 (d, *J* = 8.2Hz, 1H), 7.54-7.46 (m, 3H), 7.42 (dt, *J* = 1.7, 7.8Hz, 1H), 7.30 (dd, *J* = 7.7, 1.3Hz, 1H), 7.15 (ddd, *J* = 8.3, 1.5, 0.5Hz, 1H), 6.741-6.735 (m, 1H), 6.32 (dd, *J* = 3.5, 1.8Hz, 1H), 5.90 (dd, *J* = 3.5, 0.7Hz, 1H), 2.42 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 144.8, 144.1, 143.8, 141.2, 136.9, 136.8, 135.5, 133.8, 131.7, 130.1, 128.8, 127.7, 124.8, 119.6, 111.6, 111.03, 109.99, 21.9, 17.4. IR (neat, cm^{-1}): 3028, 2920, 1623, 1499, 1423, 1373, 1332, 1227, 1022, 910, 809, 758, 724. See attached ^{1}H and ^{13}C.

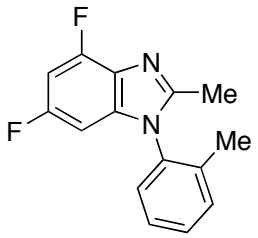


2-cyclopropyl-6-methyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 2, **13k**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (127 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 120 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage,

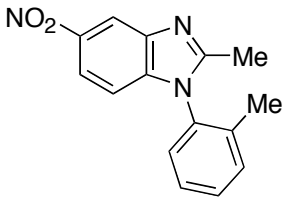
5-40% ethyl acetate in hexanes gradient) to provide the title compound as a viscous oil (105.7 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 8.1Hz, 1H), 7.48-7.44 (m, 2H), 7.41-7.38 (m, 1H), 7.32 (d, *J* = 7.5Hz, 1H), 7.06 (dd, *J* = 8.2, 1.1Hz, 1H), 6.70 (s, 1H), 2.39 (s, 3H), 2.06 (s, 3H), 1.64-1.59 (m, 1H), 1.31-1.25 (m, 2H), 1.00-0.93 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.7, 140.7, 137.0, 136.7, 134.9, 132.1, 131.5, 129.5, 128.9, 127.4, 123.7, 118.4, 109.7, 21.8, 17.6, 9.3, 9.2, 8.0. IR (neat, cm^{-1}): 3011, 2921, 1617, 1524, 1499, 1458, 1414, 1273, 1089, 809, 760, 724. See attached ^{1}H and ^{13}C.



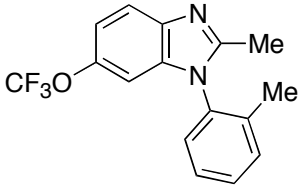
2,4,6-trimethyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 2, **13l**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (121 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a viscous oil (118.0 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.47-7.33 (m, 3H), 7.2 (d, *J* = 7.6Hz, 1H), 6.90 (s, 1H), 6.53 (d, *J* = 0.6Hz, 1H), 2.68 (s, 3H), 2.38 (s, 3H), 2.35 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 150.5, 139.9, 136.5, 136.2, 135.1, 132.4, 131.5, 129.6, 128.5, 128.4, 127.4, 124.4, 107.5, 21.7, 17.4, 16.8, 14.1. IR (neat, cm^{-1}): 3015, 2920, 1602, 1529, 1499, 1461, 1390, 1321, 1224, 1008, 833, 750. See attached ^{1}H and ^{13}C.



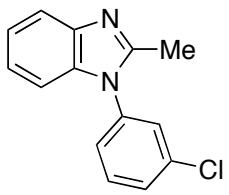
4,6-difluoro-2-methyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 2, **13m**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (125 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 8-66% ethyl acetate in hexanes gradient) to provide the title compound as a brown solid (83.2 mg, 65%). mp 112.5-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.49-7.35 (m, 3H), 7.20 (d, *J* = 7.8 Hz, 1H), 6.73 (td, *J* = 10.1, 2.2Hz, 1H), 6.39 (ddd, *J* = 8.2, 2.2, 0.7Hz, 1H), 2.35 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 160.1 (d, *J* = 10.9 Hz), 158.2 (d, *J* = 10.4 Hz), 153.8 (d, *J* = 15.0 Hz), 152.7 (d, *J* = 2.9 Hz), 151.8 (d, *J* = 14.4 Hz), 136.2, 134.1, 131.8, 130.3, 128.3, 127.8, 97.9 (dd, *J* = 28.8, 21.9 Hz), 93.1 (dd, *J* = 27.6, 4.6 Hz), 17.3, 14.1. IR (neat, cm^{-1}): 3067, 2923, 1639, 1596, 1492, 1396, 1332, 1240, 1127, 1010, 842, 754. Anal. Calcd for $C_{15}H_{12}F_2N_2$: C, 69.76; H, 4.68. Found: C, 69.82; H, 4.89.



2-methyl-1-(2-methylphenyl)-5-nitro-1*H*-benzimidazole (Table 2, **13n**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-chloroanilide (107 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 120 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in hexanes gradient) to provide the title compound as a brown solid (109.5 mg, 87%). mp 153-155 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.59 (d, *J* = 2Hz, 1H), 8.08 (dd, *J* = 8.9, 2.1Hz, 1H), 7.51-7.45 (m, 2H), 7.41 (dt, *J* = 1.5, 7.3Hz, 1H), 7.24 (dd, *J* = 7.6, 0.8Hz, 1H), 6.94 (d, *J* = 8.9Hz, 1H), 2.41 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.9, 143.8, 142.2, 140.4, 136.1, 133.7, 132.0, 130.5, 128.2, 127.9, 118.7, 115.8, 109.9, 17.3, 14.3. IR (neat, cm^{-1}): 3058, 2926, 1617, 1520, 1498, 1344, 1309, 1064, 831, 765, 740. Anal. Calcd for $C_{15}H_{13}N_3O_2$: C, 67.40; H, 4.90. Found: C, 67.37; H, 4.85.

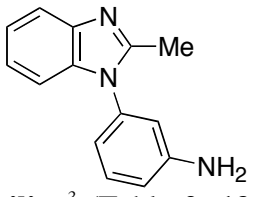


2-methyl-1-(2-methylphenyl)-6-(trifluoromethoxy)-1*H*-benzimidazole (Table 2, **13o**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (149 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in hexanes gradient) to provide the title compound as a viscous oil (113.3 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.71 (d, *J* = 8.9Hz, 1H), 7.48-7.43 (m, 2H), 7.39 (dt, *J* = 2.0, 7.0Hz, 1H), 7.22 (dd, *J* = 7.7, 0.8Hz, 1H), 7.13 (ddd, *J* = 8.7, 2.3, 0.9Hz, 1H), 6.77 (d, *J* = 1.1Hz, 1H), 2.38 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.6, 145.2 (d, *J* = 2.3Hz), 141.4, 136.3 (d, *J* = 1.7Hz), 134.2, 131.9, 130.2, 128.4, 127.8, 121.0, 120.7 (q, *J* = 256.2Hz), 119.7, 116.3, 103.5, 17.4, 14.2. IR (neat, cm^{-1}): 3056, 1623, 1500, 1479, 1463, 1391, 1255, 1218, 1161, 1010, 763, 722. See attached ^{1}H and ^{13}C.

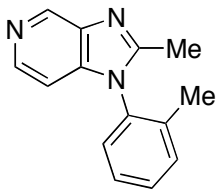


1-(3-chlorophenyl)-2-methyl-1*H*-benzimidazole (Table 2, **13p**) Following the general procedure (note: only 1.1 equiv 3-chloroaniline was used), a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (107 mg, 0.5 mmol), 3-chloroaniline (58 μL, 0.55 mmol), K_3PO_4 (265 mg, 1.25

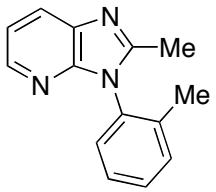
mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as an off-white solid (101.0 mg, 83%). mp 164-167 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 7.9Hz, 1H), 7.54-7.50 (m, 2H), 7.40 (s, 1H), 7.30-7.26 (m, 2H), 7.21 (t, *J* = 7.6Hz, 1H), 7.13 (d, *J* = 8.1Hz, 1H), 2.52 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 151.3, 142.7, 137.4, 136.3, 135.6, 131.1, 129.2, 127.4, 125.4, 123.0, 122.8, 119.3, 109.9, 14.6. IR (neat, cm^{-1}): 3067, 1595, 1482, 1457, 1394, 1317, 1242, 786, 748, 692. Anal. Calcd for $C_{14}H_{11}ClN_2$: C, 69.28; H, 4.57. Found: C, 68.99; H, 4.75.



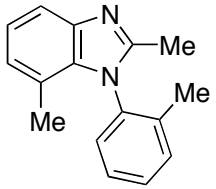
3-(2-methyl-1*H*-benzimidazol-1-yl)aniline[3] (Table 2, **13q**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), XPhos **L1** (19.1 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (107 mg, 0.5 mmol), 1,3-phenylenediamine (81.1 mg, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (gradient: 1/2 Hexanes/EtOAc, then EtOAc) to provide the title compound as a viscous oil (57.6 mg, 52%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.73 (d, *J* = 8.1Hz, 1H), 7.31 (t, *J* = 7.9Hz, 1H), 7.26-7.23 (m, 1H), 7.20-7.15 (m, 2H), 6.79 (ddd, *J* = 8.2, 2.4, 0.9Hz, 1H), 6.70 (ddd, *J* = 7.7, 1.8, 0.9Hz, 1H), 6.60 (t, *J* = 2.1Hz, 1H), 3.96 (bs, 2H), 2.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 151.8, 148.1, 142.7, 137.1, 136.6, 130.7, 122.6, 122.3, 119.0, 116.9, 115.3, 113.2, 110.3, 14.6. IR (neat, cm^{-1}): 3330, 3206, 1605, 1497, 1455, 1396, 1330, 1273, 996, 744, 696. See attached ^{1}H and ^{13}C.



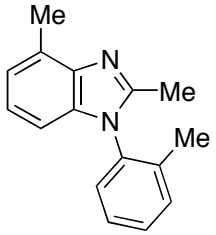
2-methyl-1-(2-methylphenyl)-1*H*-imidazo[4,5-*c*]pyridine (Table 2, **13r**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-chloroanilide (85.3 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (gradient: 1/2 hexanes/EtOAc, EtOAc, EtOAc/MeOH 20/1, and EtOAc/MeOH 10/1) to provide the title compound as a gray solid (96.9 mg, 87%). mp 170.5-173 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.07 (d, *J* = 0.9Hz, 1H), 8.35 (d, *J* = 5.6Hz, 1H), 7.52-7.38 (m, 3H), 7.23 (d, *J* = 7.6Hz, 1H), 6.89 (dd, *J* = 5.5, 4.5Hz, 1H), 2.42 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.6, 142.4, 141.9, 141.1, 140.0, 136.2, 133.8, 131.9, 130.3, 128.2, 127.8, 105.5, 17.4, 14.2. IR (neat, cm^{-1}): 3057, 2924, 1610, 1500, 1470, 1387, 1303, 1184, 1030, 932, 828, 766, 726, 623. Anal. Calcd for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87. Found: C, 75.19; H, 5.87.



2-methyl-3-(2-methylphenyl)-3*H*-imidazo[4,5-*b*]pyridine (Table 2, **13s**) Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-chloroanilide (85.3 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a brown solid (92.4 mg, 83%). mp 87-89 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.29 (dd, *J* = 4.8, 1.5Hz, 1H), 8.02 (dd, *J* = 7.9, 1.4Hz, 1H), 7.47-7.42 (m, 2H), 7.41-7.37 (m, 1H), 7.24 (d, *J* = 8.7Hz, 1H), 7.22 (dd, *J* = 8.0, 4.8Hz, 1H), 2.43 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.5, 149.2, 144.0, 136.6, 135.0, 133.8, 131.7, 130.0, 128.6, 127.6, 126.7, 118.6, 17.8, 14.8. IR (neat, cm^{-1}): 3053, 1602, 1515, 1501, 1419, 1386, 1299, 1282, 1234, 1001, 774, 720. See attached ^{1}H and ^{13}C.

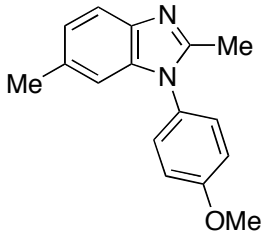


2,7-dimethyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 3, **15a**). Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (114 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a viscous oil (104.1 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 7.9Hz, 1H), 7.43 (dt, *J* = 1.4, 7.6Hz, 1H), 7.38-7.33 (m, 2H), 7.27 (dd, *J* = 7.8, 1.1Hz, 1H), 7.14 (t, *J* = 7.6Hz, 1H), 6.90 (d, *J* = 7.3Hz, 1H), 2.30 (s, 3H), 1.96 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 151.9, 143.1, 137.1, 136.9, 134.3, 131.0, 129.8, 129.1, 127.1, 124.7, 122.1, 121.3, 117.2, 17.5, 16.9, 14.2. IR (neat, cm^{-1}): 3052, 2924, 1526, 1499, 1456, 1388, 1312, 1083, 785, 746, 723, 595. See attached ^{1}H and ^{13}C.

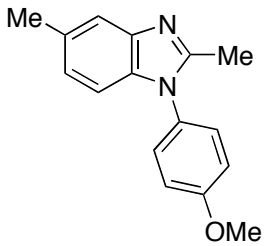


2,4-dimethyl-1-(2-methylphenyl)-1*H*-benzimidazole (Table 3, **15b**). Following the general procedure, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (114 mg, 0.5 mmol), *ortho*-toluidine (80 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a gray solid (113.5 mg, 97%).

mp 61-63 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.45-7.40 (m, 2H), 7.35 (dt, *J* = 2.4, 7.2Hz, 1H), 7.20 (d, *J* = 7.6Hz, 1H), 7.08-7.04 (m, 2H), 6.75-6.72 (m, 1H), 2.72 (s, 3H), 2.40 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 150.9, 142.0, 136.4, 136.0, 135.0, 131.5, 129.6, 129.0, 128.5, 127.4, 122.7, 122.5, 107.6, 17.4, 16.9, 14.2. IR (neat, cm^{-1}): 3053, 2923, 1603, 1525, 1496, 1460, 1387, 1320, 1231, 1154, 1006, 753, 719. See attached ^{1}H and ^{13}C.

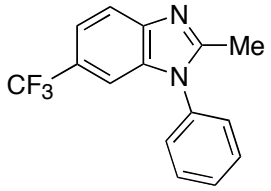


1-(4-methoxyphenyl)-2,6-dimethyl-1*H*-benzimidazole (Table 3, **17a**). An oven-dried Schlenk tube containing a stir bar was charged with Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), and 2-bromo-4-methylacetanilide (114 mg, 0.5 mmol). The Schlenk tube was capped with a Teflon screw cap, evacuated and sealed under vacuum. It was then transferred to a glove box in which *para*-anisidine (92.4 mg, 0.75 mmol) and K_3PO_4 (265 mg, 1.25 mmol) were added. The tube was sealed and removed from the box. It was connected to a double manifold and opened under a positive flow of Ar (the tube was evacuated and backfilled with Ar via 3 cycles). *t*-BuOH (1.0 mL) was added and the tube was sealed. It was put into a pre-heated oil bath at 110 °C and stirred for 18 h. After cooling to room temperature, the reaction mixture was diluted with methylene chloride (4 mL) and then filtered through Celite with the aid of methylene chloride. The filtrate was concentrated under vacuum and the residual was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a gray solid (121.7 mg, 96%). mp 110-111 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 8.2Hz, 1H), 7.26 (d, *J* = 9.0Hz, 2H), 7.08-7.05 (m, 3H), 6.88-6.87 (m, 1H), 3.90 (s, 3H), 2.46 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 159.8, 151.5, 140.7, 137.2, 132.5, 128.9, 128.5, 123.8, 118.6, 115.1, 110.0, 55.7, 21.8, 14.5. IR (neat, cm^{-1}): 2929, 1611, 1515, 1456, 1395, 1293, 1250, 1034, 834, 809. See attached ^{1}H and ^{13}C.

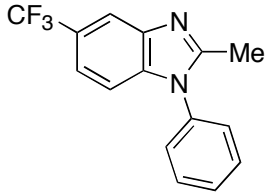


1-(4-methoxyphenyl)-2,5-dimethyl-1*H*-benzimidazole (Table 3, **17b**). An analogous procedure to the preparation of **17a** was employed except that double the amount of Pd_2dba_3 and RuPhos **L5** was used. A mixture of Pd_2dba_3 (9.2 mg, 0.01 mmol, 4.0 mol % Pd), RuPhos **L5** (37.3 mg, 0.08 mmol, 16 mol %), 2-bromo-5-methylacetanilide (114 mg, 0.5 mmol), *para*-anisidine (92.4 mg, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a brown solid (110.7 mg, 88%). mp 97-98.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.52 (s, 1H), 7.26 (d, *J* = 8.9Hz, 2H),

7.05 (d, *J* = 8.9Hz, 2H), 7.03-6.95 (m, 2H), 3.89 (s, 3H), 2.48 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 159.7, 152.0, 143.0, 135.1, 132.0, 129.0, 128.4, 123.9, 118.9, 115.1, 109.5, 55.7, 21.7, 14.5. IR (neat, cm^{-1}): 2930, 1515, 1457, 1394, 1321, 1295, 1249, 1036, 834, 796. See attached ^{1}H and ^{13}C.



2-methyl-1-phenyl-6-(trifluoromethyl)-1*H*-benzimidazole (Table 3, **19a**). An oven-dried Schlenk tube containing a stir bar was charged with Pd_2dba_3 (9.2 mg, 0.01 mmol, 4.0 mol % Pd), RuPhos **L5** (37.3 mg, 0.08 mmol, 16 mol %), and 2-bromo-4-trifluoromethylacetanilide (141 mg, 0.5 mmol). The Schlenk tube was capped with a Teflon screw cap, evacuated and sealed under vacuum. It was then transferred to a glove box in which K_3PO_4 (265 mg, 1.25 mmol) and activated 3Å molecular sieves (250 mg) were added. The tube was sealed and removed from the box. It was connected to a double manifold and opened under a positive flow of Ar (the tube was evacuated and backfilled with Ar via 3 cycles). Aniline (68 μL, 0.75 mmol) and *t*-BuOH (1.0 mL) were added and the tube was sealed. It was put into a pre-heated oil bath at 110 °C and stirred for 18 h. After cooling to room temperature, the reaction mixture was diluted with methylene chloride (4 mL) and then filtered through Celite with the aid of methylene chloride. The filtrate was concentrated under vacuum and the residual was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a viscous oil (117.3 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.80 (d, *J* = 8.4Hz, 1H), 7.63-7.54 (m, 3H), 7.51 (d, *J* = 8.4Hz, 1H), 7.37-7.35 (m, 3H), 2.52 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 154.4, 145.0 (d, *J* = 1.2Hz), 136.1, 135.4, 130.3, 129.5, 127.1, 124.94 (q, *J* = 32.2Hz), 124.89 (q, *J* = 271.8Hz), 119.54 (q, *J* = 3.5Hz), 119.47, 107.8 (q, *J* = 4.0Hz), 14.6. IR (neat, cm^{-1}): 3064, 1599, 1501, 1453, 1331, 1274, 1159, 1115, 1053, 824, 699. Anal. Calcd for $C_{15}H_{11}F_3N_2$: C, 65.21; H, 4.01. Found: C, 65.13; H, 4.01.

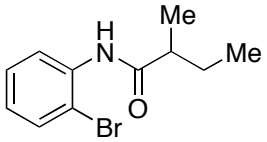


2-methyl-1-phenyl-6-(trifluoromethyl)-1*H*-benzimidazole (Table 3, **19b**). Following the general procedure except that the reaction was conducted at 100 °C, a mixture of Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), the corresponding *ortho*-bromoanilide (141 mg, 0.5 mmol), aniline (68 μL, 0.75 mmol), K_3PO_4 (265 mg, 1.25 mmol), and *t*-BuOH (1.0 mL) was heated at 110 °C for 18 h. The crude product was purified by flash chromatography on silica gel (Biotage, 12-100% ethyl acetate in hexanes gradient) to provide the title compound as an off-white solid (90.8 mg, 66%). mp 114-115.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.00 (s, 1H), 7.62-7.53 (m, 3H), 7.42 (dd, *J* =8.5, 1.3Hz, 1H), 7.36-7.33 (m, 2H), 7.17 (d, *J* = 8.4Hz, 1H), 2.52 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.9, 142.3, 138.5, 135.5, 130.3, 129.5, 127.1, 124.99 (q, *J* = 271.8Hz), 124.97 (q, *J* = 32.2Hz), 119.7 (q, *J* = 3.5Hz), 116.7 (q, *J* = 4.2Hz), 110.4, 14.6. IR (neat, cm^{-1}): 3034, 1596, 1501, 1394, 1331, 1164,

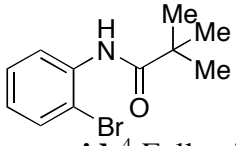
1113, 1054, 921, 809, 698. Anal. Calcd for $C_{15}H_{11}F_3N_2$: C, 65.21; H, 4.01. Found: C, 65.34; H, 3.98.

General Procedure for the Preparation of *ortho*-Haloanilides Used in Tables 2 and 3

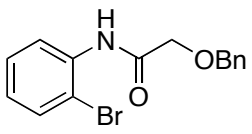
ortho-Haloaniline (10 mmol) was dissolved in EtOAc (20 mL). Neat acid chloride (22 mmol) was added to the solution dropwise at room temperature. A slurry was formed during or after the addition of the acid chloride. The resulting slurry was heated to 85 °C and stirred at 85 °C until it became homogeneous (ca. 0.5 h). The reaction mixture was cooled to 0 °C. 3N NaOH was added dropwise until the pH of the reaction mixture reached 8. Saturated $NaHCO_3$ solution (25 mL) was added. The aqueous layer was separated and extracted with EtOAc (15 mL x 2). The combined EtOAc layers were dried over Na_2SO_4 and concentrated under vacuum. The residual was purified by flash chromatography on silica gel or crystallization.



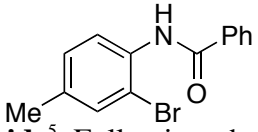
***N*-(2-bromophenyl)-2-methylbutanamide** Following the general procedure, a mixture of 2-bromoaniline (2.05 g, 11.9 mmol), 2-methylbutyryl chloride (3.3 mL, 26.3 mmol) in EtOAc (20 ml) was refluxed until the reaction mixture became homogeneous. The crude product was purified by flash chromatography on silica gel (8/1 hexanes/ethyl acetate) to provide the title compound as a white solid (2.95 g, 97%). mp 86-87.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.38 (d, *J* = 8.2Hz, 1H), 7.68 (bs, 1H), 7.53 (dd, *J* = 8.0, 1.4Hz, 1H), 7.31 (ddd, *J* = 8.4, 8.2, 1.5Hz, 1H), 6.97 (dt, *J* = 1.5, 7.7Hz, 1H), 2.40-2.33 (m, 1H), 1.84-1.75 (m, 1H), 1.61-1.53 (m, 1H), 1.27 (d, *J* = 7.0Hz, 3H), 1.00 (t, *J* = 7.5Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 174.9, 135.9, 132.3, 128.5, 125.2, 122.1, 113.6, 44.6, 27.6, 17.6, 12.0. IR (neat, cm^{-1}): 3268, 2965, 1661, 1528, 1438, 1283, 1047, 1028, 749, 677. Anal. Calcd for $C_{11}H_{14}BrNO$: C, 51.58; H, 5.51. Found: C, 51.46; H, 5.56.



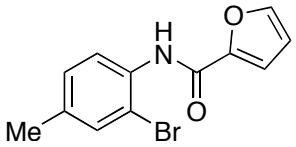
***N*-(2-bromophenyl)-2,2-dimethylpropanamide**[4] Following the general procedure, a mixture of 2-bromoaniline (1.80 g, 10.5 mmol), pivaloyl chloride (2.8 mL, 23.1 mmol) in EtOAc (20 ml) was refluxed until the reaction mixture became homogeneous. The crude product was purified by flash chromatography on silica gel (8/1 hexanes/ethyl acetate) to provide the title compound as a white solid (2.69 g, 100%). mp 65-65.5 °C (lit.[4] 61-61.5 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.40 (dd, *J* = 8.3, 1.5Hz, 1H), 8.02 (bs, 1H), 7.53 (dd, *J* = 8.1, 1.4Hz, 1H), 7.31 (ddd, *J* = 8.2, 6.9, 1.4Hz, 1H), 6.96 (ddd, *J* = 8.1, 7.3, 1.5Hz, 1H), 1.36 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 176.8, 136.0, 132.2, 128.6, 125.0, 121.8, 113.8, 40.4, 27.8. IR (neat, cm^{-1}): 3421, 2963, 1693, 1587, 1520, 1432, 1301, 1156, 1024, 748, 567. Anal. Calcd for $C_{11}H_{14}BrNO$: C, 51.58; H, 5.51. Found: C, 51.74; H, 5.61.



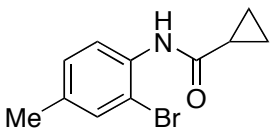
2-(benzyloxy)-*N*-(2-bromophenyl)acetamide Following the general procedure, a mixture of 2-bromoaniline (2.09 g, 12.2 mmol), benzoyl chloride (2.4 mL, 20.9 mmol) in EtOAc (20 ml) was refluxed for 60 min. The crude product was purified by flash chromatography on silica gel (6/1 hexanes/ethyl acetate) to provide the title compound as a viscous oil (3.81 g, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.09 (bs, 1H), 8.45 (dd, *J* = 8.3, 1.6Hz, 1H), 7.56 (dd, *J* = 8.1, 1.5Hz, 1H), 7.44-7.32 (m, 6H), 7.00 (ddd, *J* = 8.1, 7.5, 1.7Hz, 1H), 4.72 (s, 2H), 4.16 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 167.9, 136.7, 135.3, 132.5, 128.8, 128.6, 128.5, 128.0, 125.5, 121.6, 113.6, 73.8, 69.8. IR (neat, cm^{-1}): 3357, 3064, 3032, 2908, 2864, 1700, 1593, 1521, 1437, 1301, 1099, 1025, 751, 698. Anal. Calcd for $C_{15}H_{14}BrNO_2$: C, 56.27; H, 4.41. Found: C, 56.37; H, 4.36.



***N*-(2-bromo-4-methylphenyl)benzamide**[5] Following the general procedure, a mixture of 2-bromo-4-methylaniline (1.77 g, 9.5 mmol), benzyloxyacetyl chloride (4.2 mL, 26.8 mmol) in EtOAc (24 ml) was refluxed for 20 min. The crude product was purified by crystallization from EtOAc to provide the title compound as a white solid (2.48 g, 98%). mp 148-149 °C (lit.[5] 149-150 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.41 (d, *J* = 8.4Hz, 2H), 7.95-7.93 (m, 2H), 7.60-7.57 (m, 1H), 7.54-7.51 (m, 2H), 7.41 (dd, *J* = 1.4, 0.5Hz, 1H), 7.18 (dd, *J* = 8.4, 1.4Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 165.3, 135.6, 134.8, 133.4, 132.7, 132.3, 129.3, 129.1, 127.2, 121.8, 113.8, 20.8. IR (neat, cm^{-1}): 3265, 1646, 1579, 1522, 1494, 1386, 1309, 820, 713, 688. Anal. Calcd for $C_{14}H_{12}BrNO$: C, 57.95; H, 4.17. Found: C, 58.22; H, 4.19.

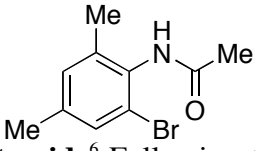


***N*-(2-bromo-4-methylphenyl)-2-furamide** Following the general procedure, a mixture of 2-bromo-4-methylaniline (1.60 g, 8.6 mmol), 2-furoyl chloride (1.9 mL, 18.9 mmol) in EtOAc (18 ml) was refluxed for 60 min. The crude product was purified by crystallization from a mixture of EtOAc and hexanes to provide the title compound as an off-white solid (1.29 g, 54%). mp 98-100 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.62 (bs, 1H), 8.36 (d, *J* = 8.2Hz, 1H), 7.55 (dd, *J* = 1.8, 0.9Hz, 1H), 7.39 (dd, *J* = 1.1, 0.8Hz, 1H), 7.25 (dd, *J* = 3.5, 0.8Hz, 1H), 7.15 (d, *J* = 8.4Hz, 1H), 6.57 (ddd, *J* = 3.5, 1.8, 0.7Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.0, 147.9, 144.7, 135.5, 133.0, 132.7, 129.2, 121.6, 115.6, 113.5, 112.8, 20.8. IR (neat, cm^{-1}): 3389, 3106, 1682, 1595, 1530, 1464, 1311, 1165, 1009, 818, 769, 741. Anal. Calcd for $C_{12}H_{10}BrNO_2$: C, 51.45; H, 3.60. Found: C, 51.44; H, 3.56.

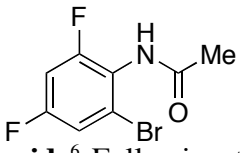


***N*-(2-bromo-4-methylphenyl)cyclopropanecarboxamide** Following the general procedure, a mixture of 2-bromo-4-methylaniline (1.71 g, 9.2 mmol), cyclopropanecarbonyl chloride (1.8 mL, 20.2 mmol) in EtOAc (18 ml) was refluxed for 60 min. The crude product was purified by crystallization from a mixture of EtOAc and hexanes to provide the title compound as a white solid (2.01 g, 86%). mp 139-140.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.19 (d, *J* = 7.2Hz, 1H),

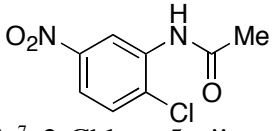
7.77 (bs, 1H), 7.35 (s, 1H), 7.09 (dd, *J* = 8.4, 1.4Hz, 1H), 2.29 (s, 3H), 1.61-1.56 (m, 1H), 1.12-1.09 (m, 2H), 0.90-0.86 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.9, 135.0, 133.5, 132.5, 129.1, 121.8, 113.0, 20.7, 16.2, 8.4. IR (neat, cm^{-1}): 3270, 2917, 1652, 1531, 1398, 1289, 1198, 1042, 818, 651. Anal. Calcd for $C_{11}H_{12}BrNO$: C, 51.99; H, 4.76. Found: C, 51.78; H, 4.61.



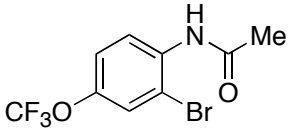
***N*-(2-bromo-4,6-dimethylphenyl)acetamide**[6] Following the general procedure, the synthesis of the title compound and its full characterization have been previously reported by us.



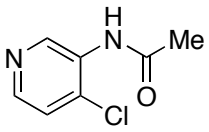
***N*-(2-bromo-4,6-difluorophenyl)acetamide**[6] Following the general procedure, the synthesis of the title compound and its full characterization have been previously reported by us.



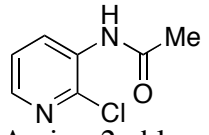
***N*-(2-chloro-5-nitrophenyl)acetamide**[7] 2-Chloro-5-niitroaniline (5 g, 29.0 mmol) was mixed with acetic anhydride (25 mL). The mixture was refluxed for 2 h and then poured to water. Saturated aqueous Na_2CO_3 solution was added to neutralize the mixture. The formed solid was collected by filtration to provide the title compound as an orange solid (2.95g, 47%). mp 157-159 °C (lit.[7] 160 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.33 (d, *J* = 2.7Hz, 1H), 7.92 (dd, *J* = 8.8, 2.7Hz, 1H), 7.74 (bs, 1H), 7.55 (d, *J* = 8.8Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.6, 147.3, 135.7, 129.7, 128.6, 119.2, 116.5, 25.1. Anal. Calcd for $C_8H_7ClN_2O_3$: C, 44.77; H, 3.29. Found: C, 45.08; H, 3.02.



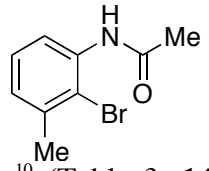
***N*-[2-chloro-4-(trifluoromethoxy)phenyl]acetamide** Following the general procedure, a mixture of 2-bromo-4-trifluoromethoxyaniline (1.15 g, 4.5 mmol), acetyl chloride (0.7 mL, 9.9 mmol) in EtOAc (9 ml) was refluxed for 20 min. The crude product was purified by crystallization from a mixture of EtOAc and hexanes to provide the title compound as a white solid (0.92 g, 69%). mp 125-127 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.38 (d, *J* = 9.2Hz, 1H), 7.61 (bs, 1H), 7.43 (d, *J* = 2.4Hz, 1H), 7.20 (dd, *J* = 9.1, 2.1Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.5, 144.9, 134.8, 125.2, 122.6, 121.3, 120.5 (q, *J* = 258.0Hz), 113.2, 25.0. IR (neat, cm^{-1}): 3288, 1663, 1533, 1478, 1389, 1293, 1208, 1152, 1041, 940, 879, 655. Anal. Calcd for $C_9H_7BrF_3NO_2$: C, 36.27; H, 2.37. Found: C, 36.42; H, 2.30.



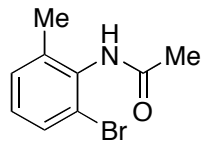
***N*-(4-chloro-3-pyridinyl)acetamide**[8] Following the general procedure, a mixture of 3-amino-4-chloropyridine (1.01 g, 7.84 mmol), acetyl chloride (1.2 mL, 17.24 mmol) in EtOAc (16 ml) was refluxed for 60 min (Note: because the title product was quite water soluble, the basified mixture was extracted with $CHCl_3$ instead of EtOAc. The extraction process was followed by TLC.). The crude product was purified by flash chromatography on silica gel (gradient: 20/1 CH_2Cl_2/MeOH, then 15/1 CH_2Cl_2/MeOH) to provide the title compound as a brown solid (1.15 g, 86%). mp 102-104 °C (dec). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.48 (s, 1H), 8.26 (d, *J* = 5.2Hz, 1H), 7.67 (bs, 1H), 7.33 (d, *J* = 5.2Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.5, 145.5, 144.1, 132.5, 132.2, 124.1, 24.6. IR (neat, cm^{-1}): 3232, 3198, 1696, 1578, 1522, 1411, 1303, 1257, 1240, 1082, 848, 718, 605. Anal. Calcd for $C_7H_7ClN_2O$: C, 49.28; H, 4.14. Found: C, 49.55; H, 4.09.



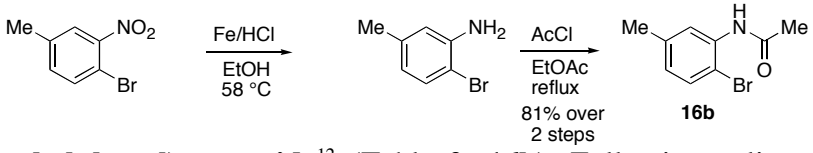
***N*-(2-chloro-3-pyridinyl)acetamide**[9] 3-Amino-2-chloropyridine (2.57 g, 20 mmol) and acetic anhydride (2.83 mL, 30 mmol) were mixed with acetic acid (20 mL) under a nitrogen atmosphere. The resulting mixture was refluxing for 1 h under a nitrogen atmosphere. Acetic acid was removed under vacuum. The residual was dissolved in benzene (10 mL) and then hexanes (20 mL) was added. The resulting solution was kept at 4 °C overnight to give an off-white solid (3.02 g, 89%). mp 93-94 °C (lit.[9] 81-83 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.67 (dd, *J* = 8.1, 1.4Hz, 1H), 8.08 (dd, *J* =4.7, 1.7Hz, 1H), 7.72 (bs, 1H), 7.23 (ddd, *J* = 8.2, 4.7, 0.5Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.9, 144.0, 139.8, 132.0, 129.3, 123.5, 123.4, 25.0. Anal. Calcd for $C_7H_7ClN_2O$: C, 49.28; H, 4.14. Found: C, 49.41; H, 4.13.



***N*-(2-bromo-3-methylphenyl)acetamide**[10] (Table 3, **14a**). Following the general procedure, a mixture of 2-bromo-3-methylaniline (1.5 mL, 12.0 mmol), acetyl chloride (1.9 mL, 26.4 mmol) in EtOAc (24 ml) was refluxed for 40 min. The crude product was purified by crystallization from a mixture of EtOAc and hexanes to provide the title compound as a white solid (2.71 g, 99%). mp 145-147 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.14 (d, *J* = 8.1Hz, 1H), 7.74 (bs, 1H), 7.20 (t, *J* = 7.9Hz, 1H), 7.00 (d, *J* = 7.3Hz, 1H), 2.41 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.4, 138.5, 135.9, 127.7, 126.3, 119.6, 116.3, 25.1, 24.0. IR (neat, cm^{-1}): 3277, 3041, 1664, 1538, 1467, 1403, 1371, 1300, 1028, 791, 678. See attached ^{1}H and ^{13}C.

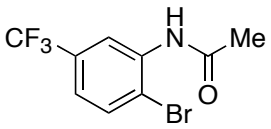


***N*-(2-bromo-6-methylphenyl)acetamide**[11] (Table 3, **14b**, 1:6 mixture of two rotamers). Following the general procedure, a mixture of 2-bromo-6-methylaniline (1.03 g, 5.5 mmol), acetyl chloride (0.9 mL, 12.1 mmol) in EtOAc (11 ml) was refluxed until the reaction mixture became homogeneous. The crude product was purified by crystallization from a mixture of EtOAc and hexanes to provide the title compound as a white solid (0.97 g, 77%). mp 175-177 °C (lit.[11] 164-166 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.51 (d, *J* =7.6Hz, 0.14H), 7.40 (dd, *J* = 8.0, 0.7Hz, 0.86H), 7.29 (bs, 0.86H), 7.24 (d, *J* = 7.6Hz, 0.14H), 7.14 (d, *J* = 7.3Hz, 0.86H), 7.06 (bs, 0.14H), 7.01 (t, *J* = 7.8Hz, 1H), 2.34 (s, 0.43H), 2.25 (s, 2.57H), 2.19 (s, 2.57H), 1.78 (s, 0.43H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 173.18, 168.92, 139.20, 138.57, 135.20, 134.24, 131.19, 130.31, 130.29, 130.02, 129.71, 128.51, 125.21, 122.43, 23.36, 20.45, 19.35, 19.30. IR (neat, cm^{-1}): 3228, 3032, 1658, 1532, 1452, 1369, 1296, 1172, 770, 672. Anal. Calcd for $C_9H_{10}BrNO$: C, 47.39; H, 4.42. Found: C, 47.42; H, 4.36.



***N*-(2-bromo-5-methylphenyl)acetamide**[12] (Table 3, **16b**). Following a literature procedure,[13] EtOH (200 proof, 7 mL) was added to a 50 mL round bottom flask equipped with a stir bar. Fe powder (from Strem, 1.40 g) was added via two portions followed by the slow addition of concentrated HCl (0.21 mL). The mixture was heated to 65 °C and stirred at 65 °C for 2 h. After cooling to 58 °C, 25% aqueous NH_4Cl (4 mL) was added. 4-Bromo-3-nitrotoluene, dissolved in EtOH (200 proof, 1 mL), was added dropwise to the activated Fe powder. Upon the completion of the addition, the mixture was stirred at 58 °C for 2 h and then cooled to 40 °C. EtOH (200 proof, 8 mL) and Celite (2 g) were added sequentially. The mixture was filtered through Celite with the aid of EtOH (200 proof, 30 mL). The filtrate was concentrated under vacuum. The residual was directly used in the next step.

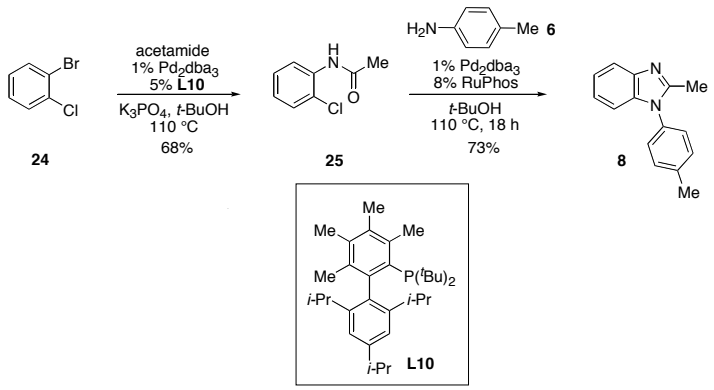
Following the general procedure for the preparation of *ortho*-haloanilides, a mixture of crude 2-bromo-5-methylaniline and acetyl chloride (0.8 mL, 11 mmol) in EtOAc (10 mL) was refluxed until it became homogeneous. The crude product, obtained after aqueous workup, was purified by flash column chromatography on silica gel (gradient elution: 6/1 Hexanes/EtOAc to 4/1 Hexanes/EtOAc) to provide **16b** as a white solid (0.928 g, 81 % over two steps). mp 124-125 °C (lit.[12] 120-121°C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.17 (s, 1H), 7.56 (bs, 1H), 7.39 (d, *J* = 8.1Hz, 1H), 6.80 (d, *J* = 7.9Hz, 1H), 2.33 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.4, 138.8, 135.5, 131.9, 126.3, 122.7, 110.1, 25.1, 21.5. IR (neat, cm^{-1}): 3288, 1664, 1580, 1532, 1466, 1410, 1292, 1037, 800, 610. Anal. Calcd for $C_9H_{10}BrNO$: C, 47.39; H, 4.42. Found: C, 47.60; H, 4.39.



***N*-[2-bromo-5-(trifluoromethyl)phenyl]acetamide** (Table 3, **18b**). Following the general procedure, a mixture of 2-bromo-5-trifluoromethylaniline (2.51 g, 10.5 mmol), acetyl chloride (2.0 mL, 23.0 mmol) in EtOAc (20 ml) was refluxed until the reaction mixture became homogeneous. The crude product was purified by crystallization from a mixture of EtOAc and hexanes to provide the title compound as a white solid (2.10 g, 71%). mp 142.5-145 °C. ^{1}H

NMR (500 MHz, $CDCl_3$) δ: 8.70 (s, 1H), 7.73 (bs, 1H), 7.65 (d, *J* = 8.4Hz, 1H), 7.22 (dd, *J* = 8.4, 1.8Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 136.5, 132.9, 131.0 (q, *J* = 32.8Hz), 123.7 (q, *J* = 272.4Hz), 121.6 (d, *J* = 4.0Hz), 118.7, 116.6, 25.1. IR (neat, cm^{-1}): 3283, 1669, 1538, 1332, 1278, 1183, 1122, 1079, 1034, 890, 825. Anal. Calcd for $C_9H_7BrF_3NO$: C, 38.32; H, 2.50. Found: C, 38.55; H, 2.44.

Procedure for the Synthesis of *N*-Aryl Benzimidazoles via Sequential Amidation/Amination (Scheme 2)



Following a previously disclosed procedure from this group,[14] an oven-dried Schlenk tube was evacuated and backfilled with argon. 3Å molecular sieves (100 mg) were activated by heating under vacuum and backfilled with argon (this sequence was repeated three times) prior to use. The Schlenk tube was charged with Pd_2dba_3 (9.2 mg, 0.01 mmol, 2.0 mol % Pd), ligand **L12** (24.0 mg, 0.05 mmol, 5 mol %), acetamide (89 mg, 1.5 mmol), and K_3PO_4 (318 mg, 1.5 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (3 cycles). Bromochlorobenzene **24** (116 μL, 1.0 mmol) and *t*-BuOH (2.0 mL) were added to the Schlenk tube through the septum via syringe. The septum was replaced with a Teflon screw cap and the Schlenk tube was sealed. After the mixture was stirred in a pre-heated oil bath at 110 °C for 10 h, it was allowed to cool to room temperature. EtOAc (4 mL) was added and the diluted reaction mixture was filtered through Celite with the aid of EtOAc. The filtrate was concentrated under reduced pressure. The residual was purified by flash column chromatography on silica gel (elution: 8/1 hexanes/EtOAc) to give **25** as a white solid (115 mg, 68%).

2-methyl-1-(4-methylphenyl)-1*H*-benzimidazole (Scheme 2, **8**) An oven-dried Schlenk tube containing a stir bar was charged with Pd_2dba_3 (4.6 mg, 0.005 mmol, 2.0 mol % Pd), RuPhos **L5** (18.7 mg, 0.04 mmol, 8 mol %), and **25** (84.8 mg, 0.5 mmol). The Schlenk tube was capped with a Teflon screw cap, evacuated and then sealed under vacuum. It was then transferred to a glove box in which *p*-toluidine (80.4 mg, 0.75 mmol) and K_3PO_4 (265 mg, 1.25 mmol) were added. The tube was sealed and removed from the box. It was connected to a double manifold and then opened under a positive flow of Ar (the tube was evacuated and backfilled with Ar via 3 cycles). *t*-BuOH (1.0 mL) was added to the Schlenk tube under a positive flow of argon. The Schlenk tube was sealed and put into a pre-heated oil bath at 110 °C. After stirring for 18 h, the reaction mixture was allowed to cool to room temperature and diluted with methylene chloride (4 mL). The diluted mixture was filtered through Celite with the aid of methylene chloride. The filtrate was concentrated under vacuum and the residual was purified by flash chromatography

on silica gel (Biotage, 12-100% ethyl acetate in CH_2Cl_2 gradient) to provide the title compound as a white solid (80.5 mg, 73%). mp 89-91 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 7.9Hz, 1H), 7.38 (d, *J* = 7.9Hz, 2H), 7.28-7.24 (m, 3H), 7,21 (dt, *J* = 1.1, 8.2Hz, 1H), 7.12 (d, *J* = 7.8Hz, 1H), 2.51 (s, 3H), 2.48 (3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 151.8, 142.7, 139.0, 136.7, 133.5, 130.6, 127.0, 122.6, 122.3, 119.1, 110.1, 21.4, 14.6. IR (neat, cm^{-1}): 3037, 2925, 1615, 1515, 1457, 1393, 1321, 1246, 1015, 818, 742, 573.

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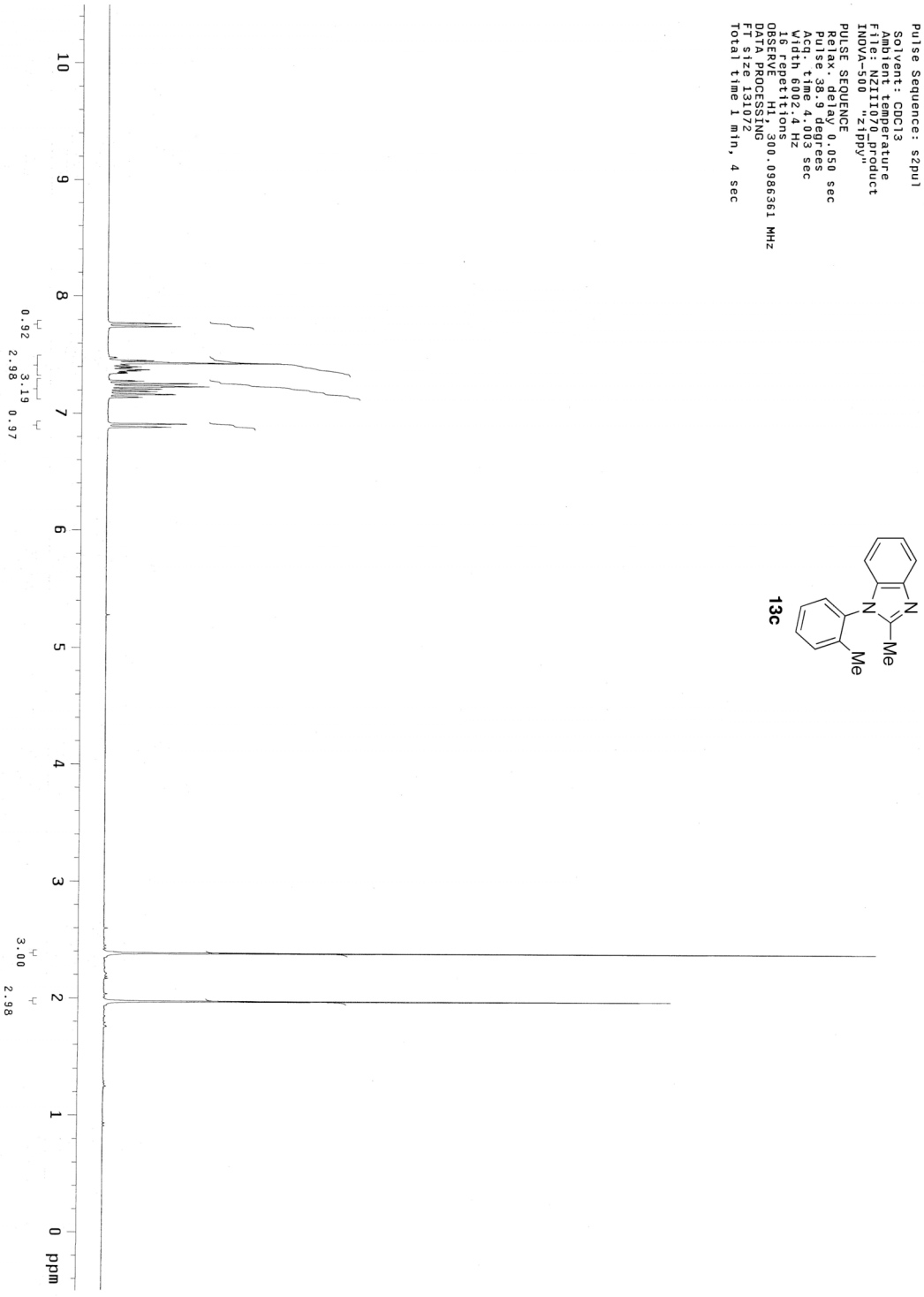
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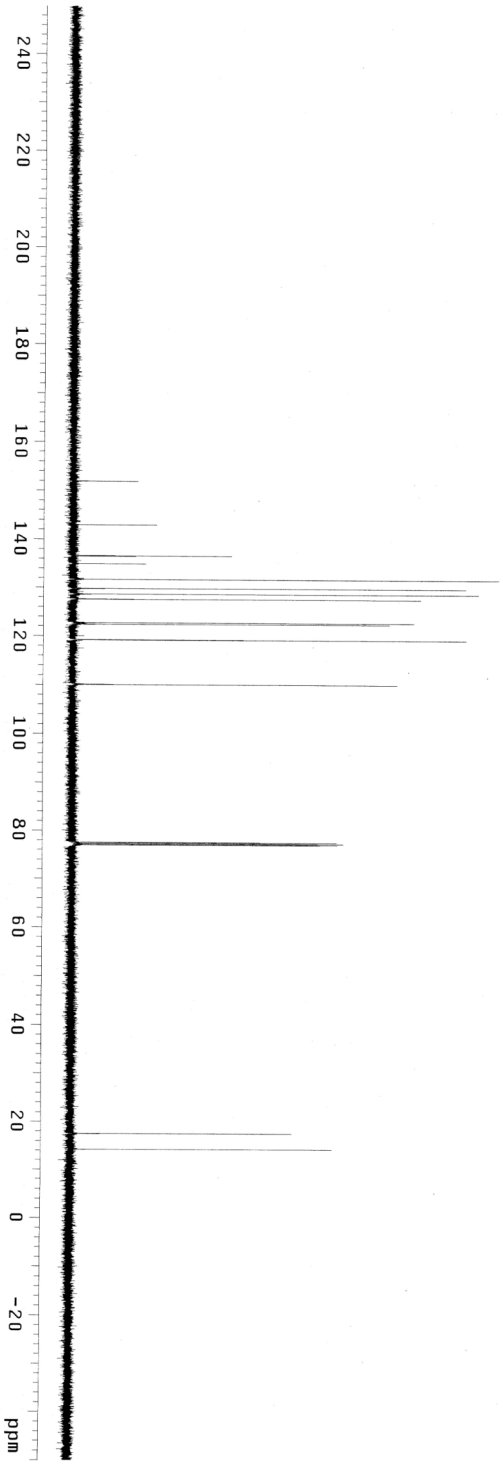
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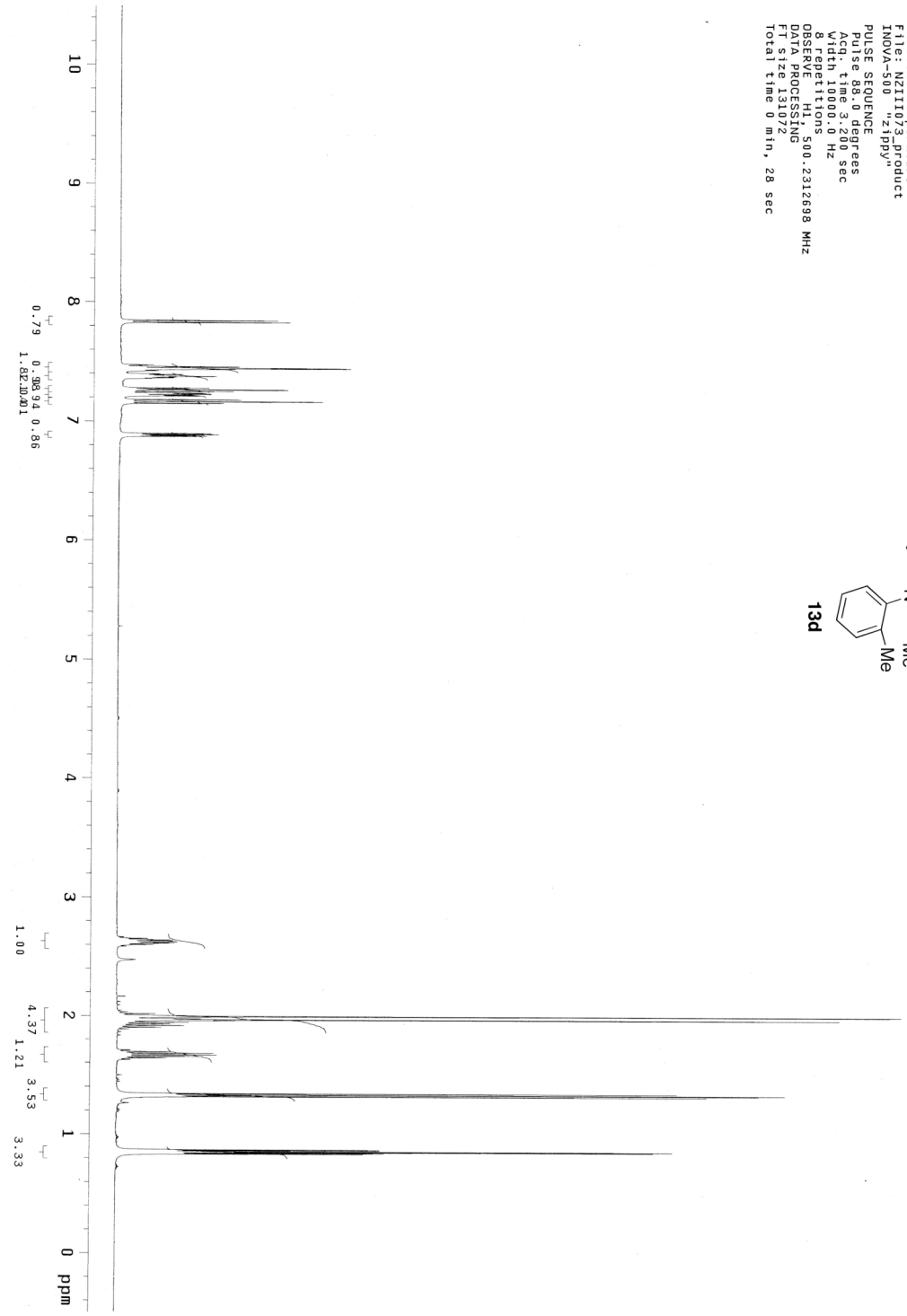
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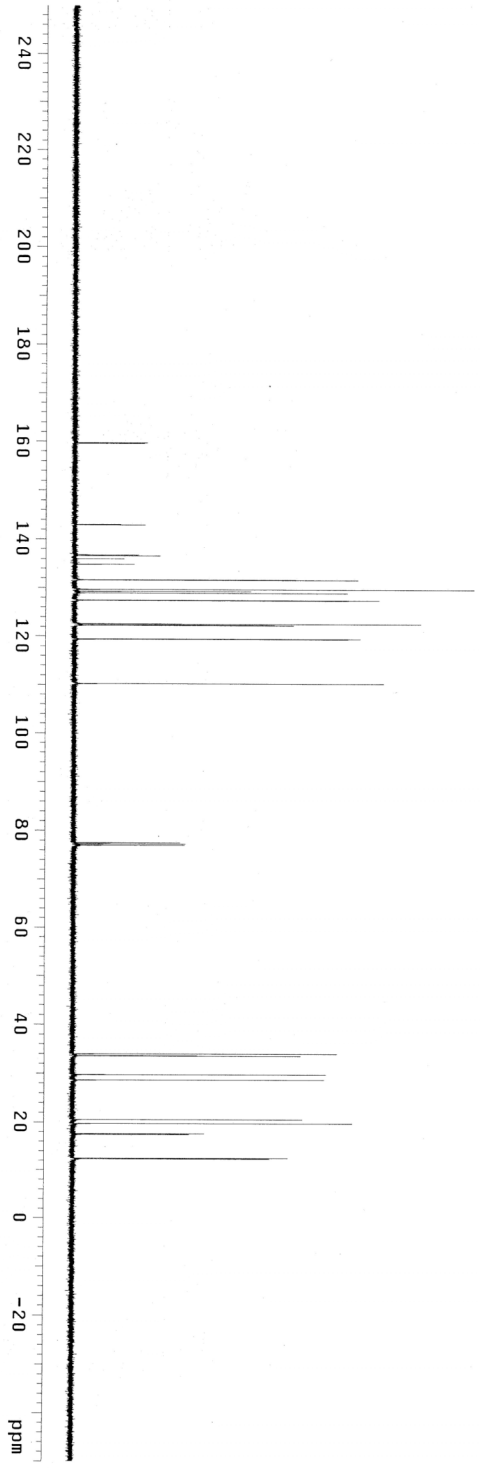


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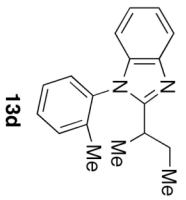
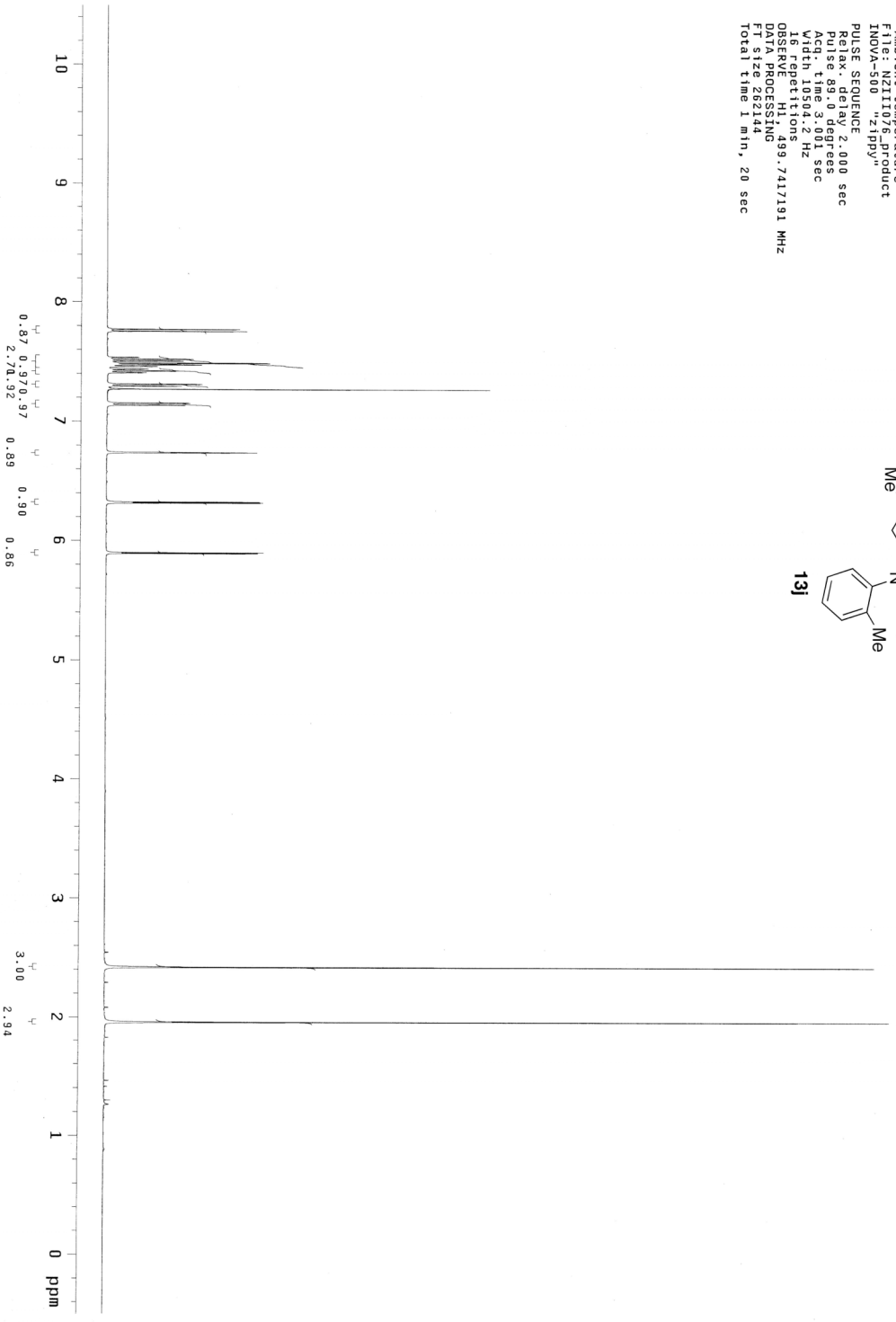
DECOUPLE  H1, 500.2332753 MHz
  Power 37 dB
  continuously on
  WALTZ-16 modulated
DATA PROCESSING
  Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
```

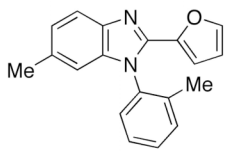


13d

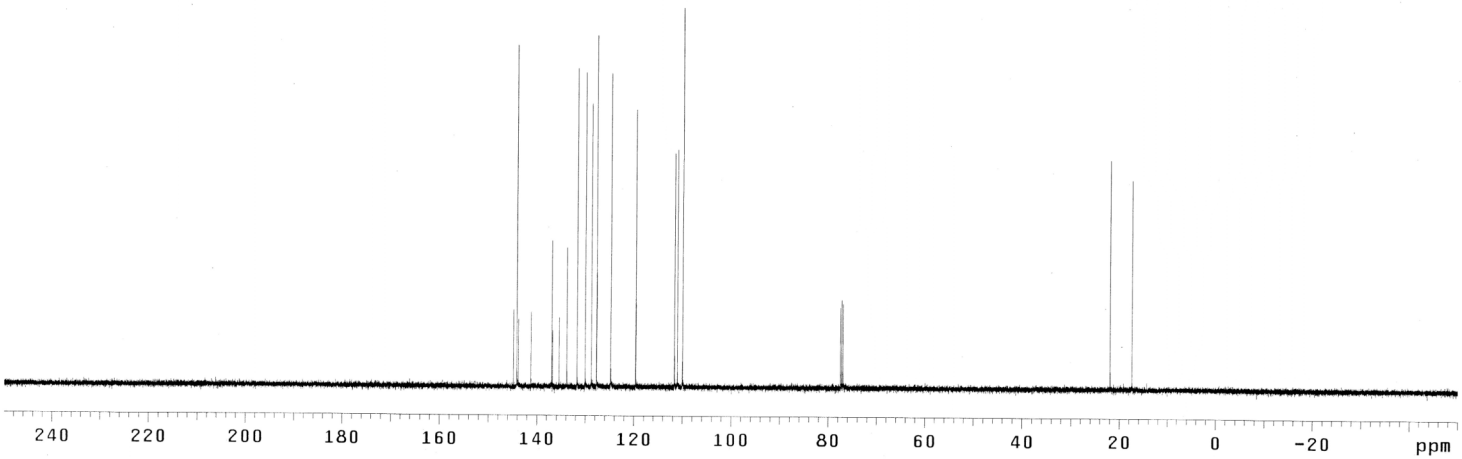

NZIII076
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII076_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
16 repetitions
OBSERVE H1, 499.7417191 MHz
DATA PROCESSING
FT size 262144
Total time 1 min, 20 sec
Me
N
N
O
Me
13j
10
9
8
7
6
5
4
3
2
1
0 ppm
0.87
0.97
0.97
2.70
1.92
0.89
0.90
0.86
3.00
2.94

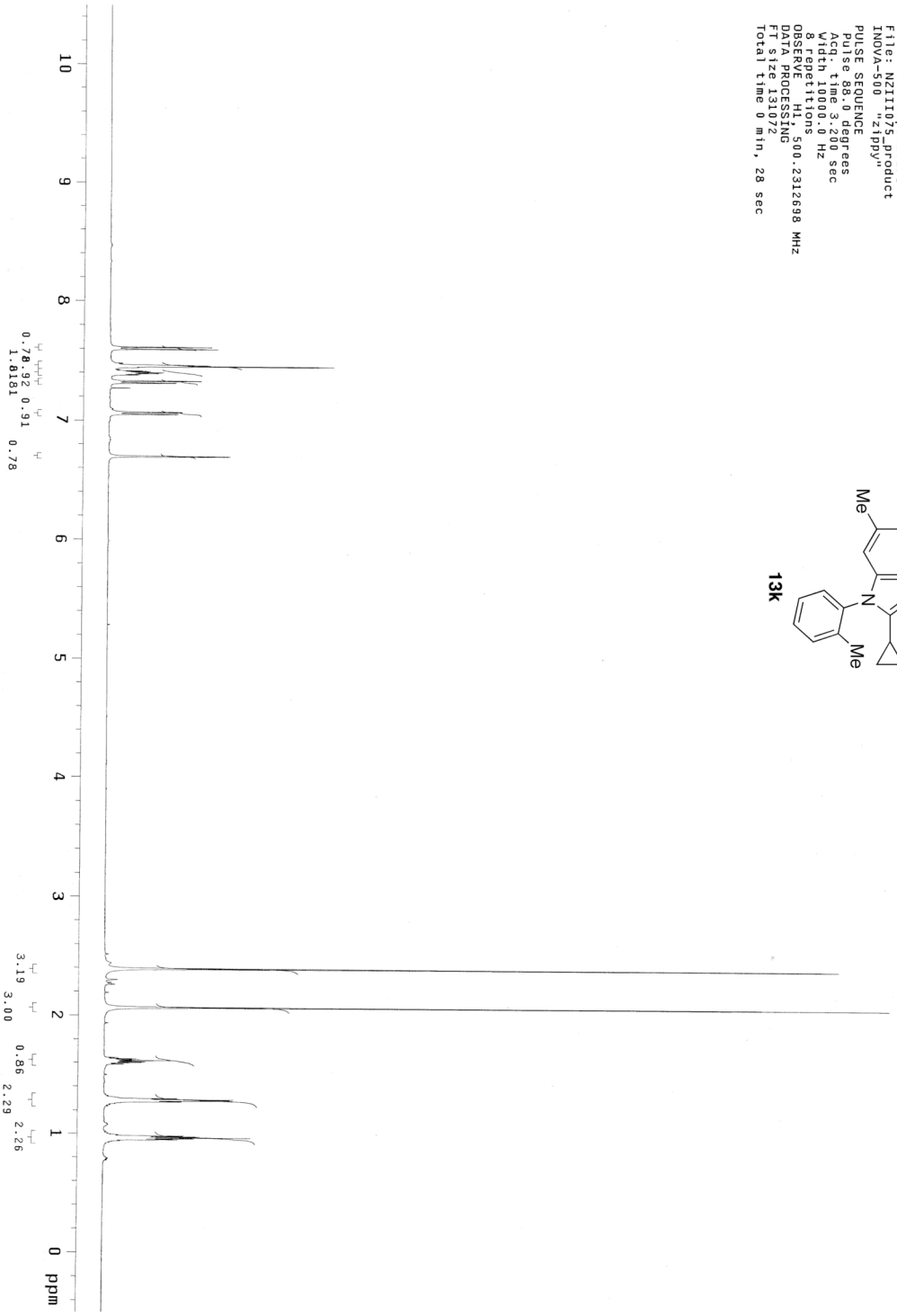
NZIII076

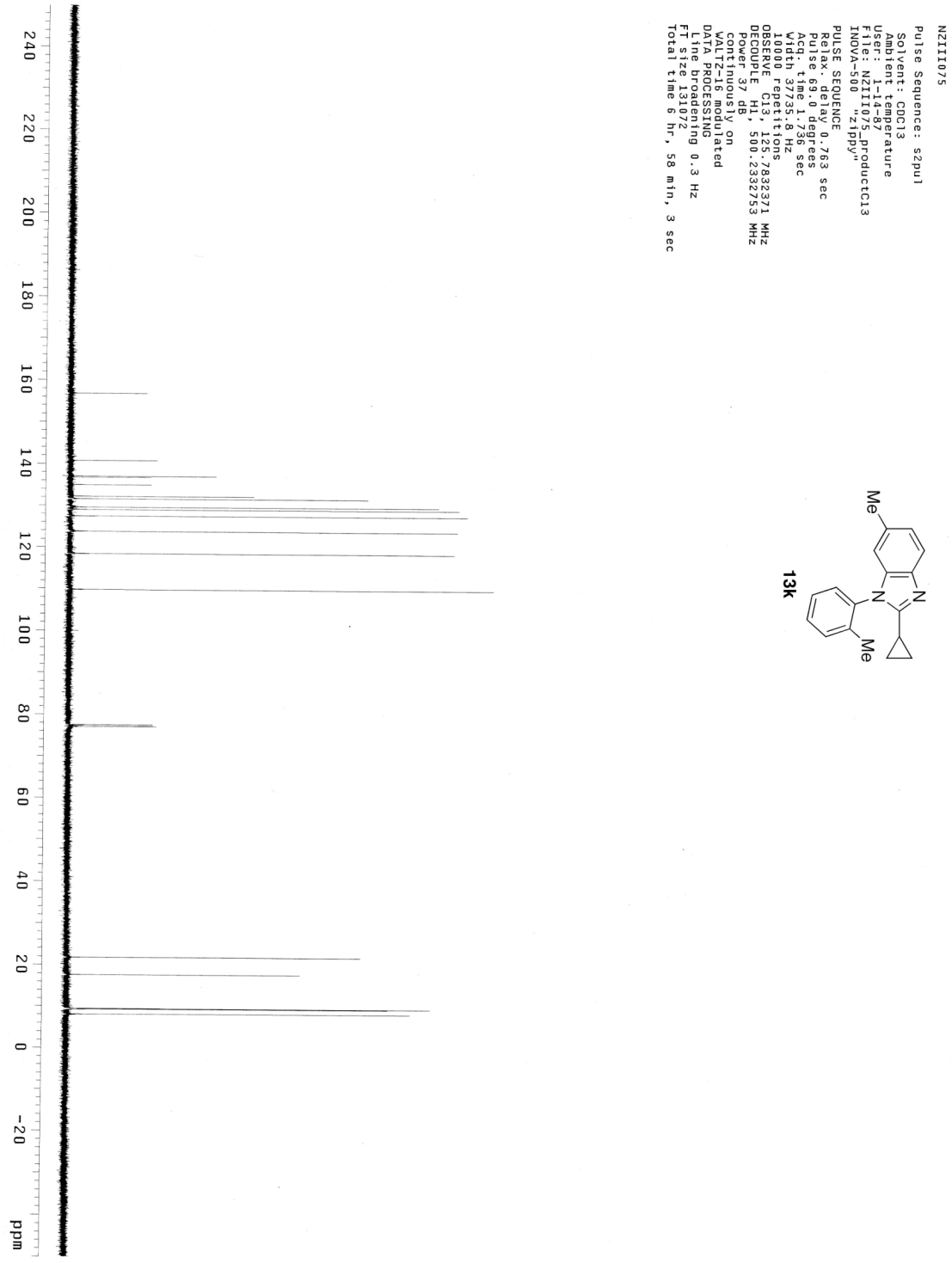
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZIII076_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
72 repetitions
OBSERVE C13, 125.7832366 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 41 min, 50 sec

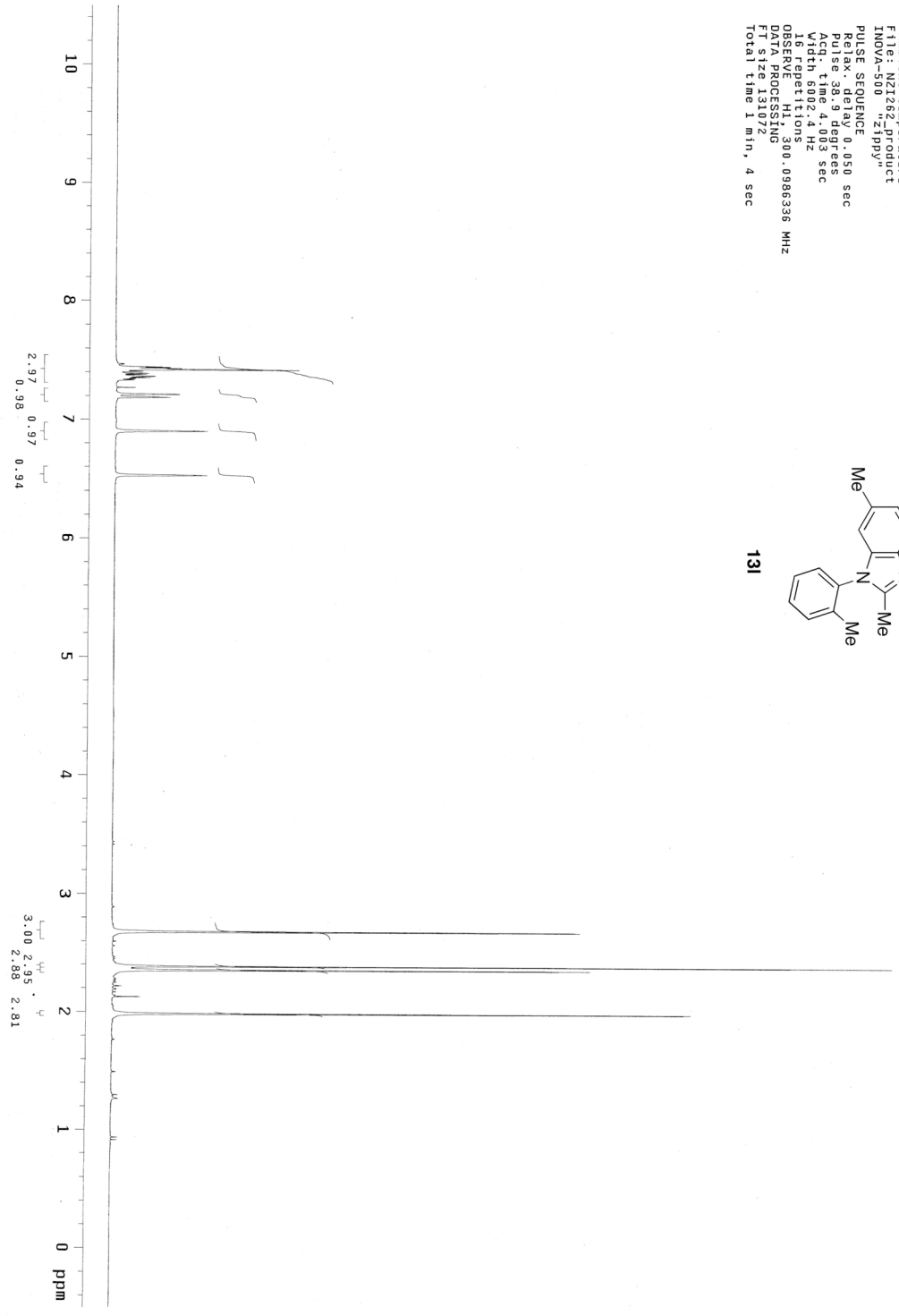


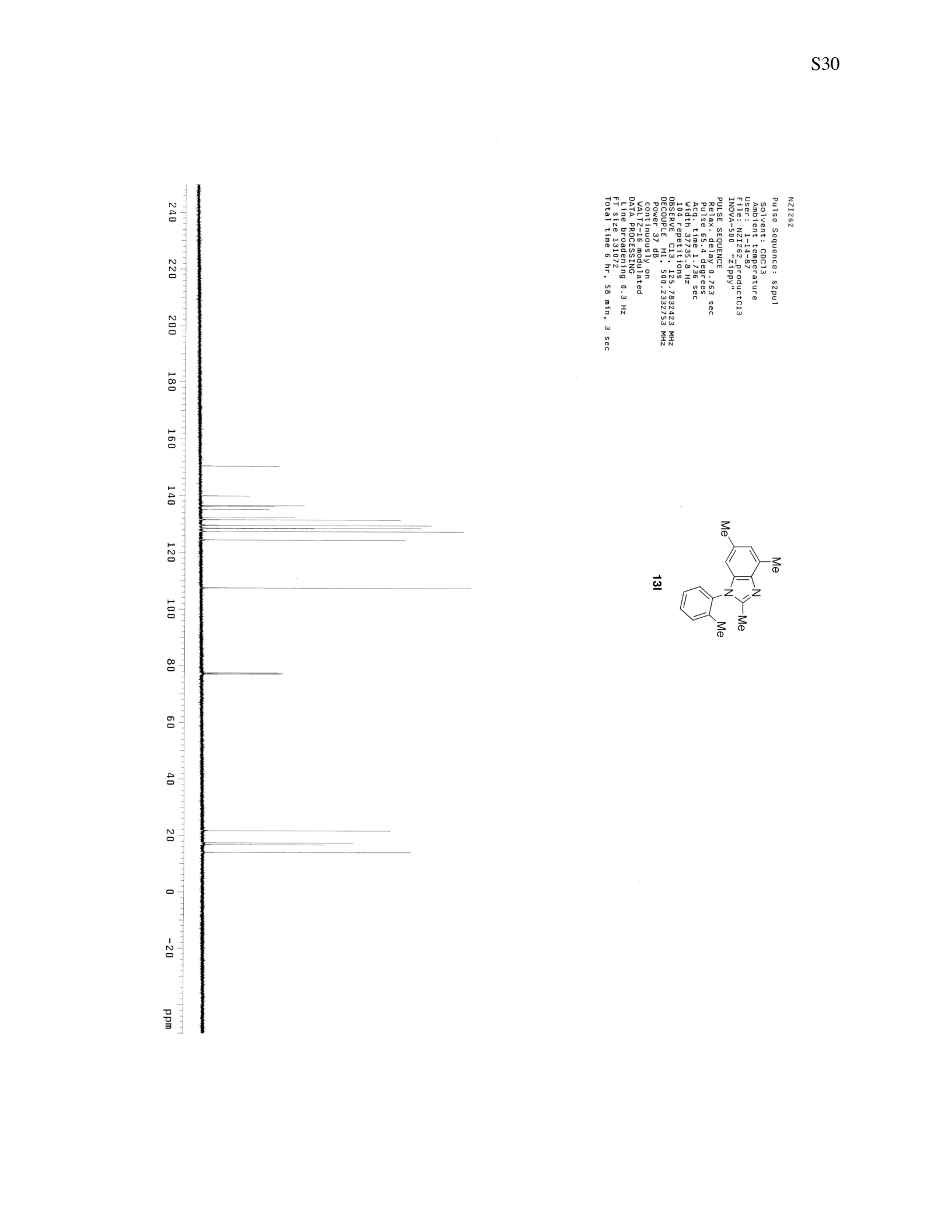
13j

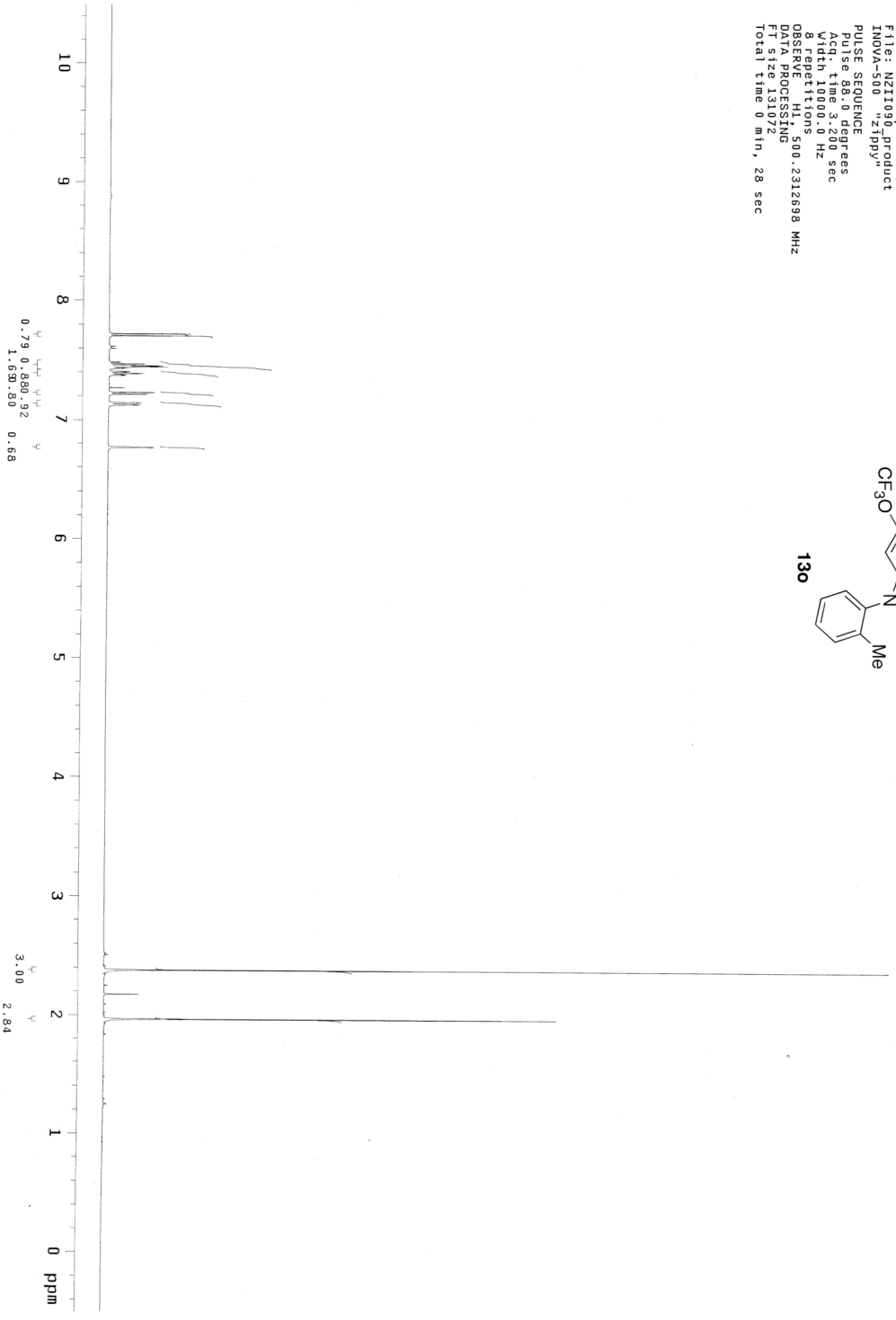


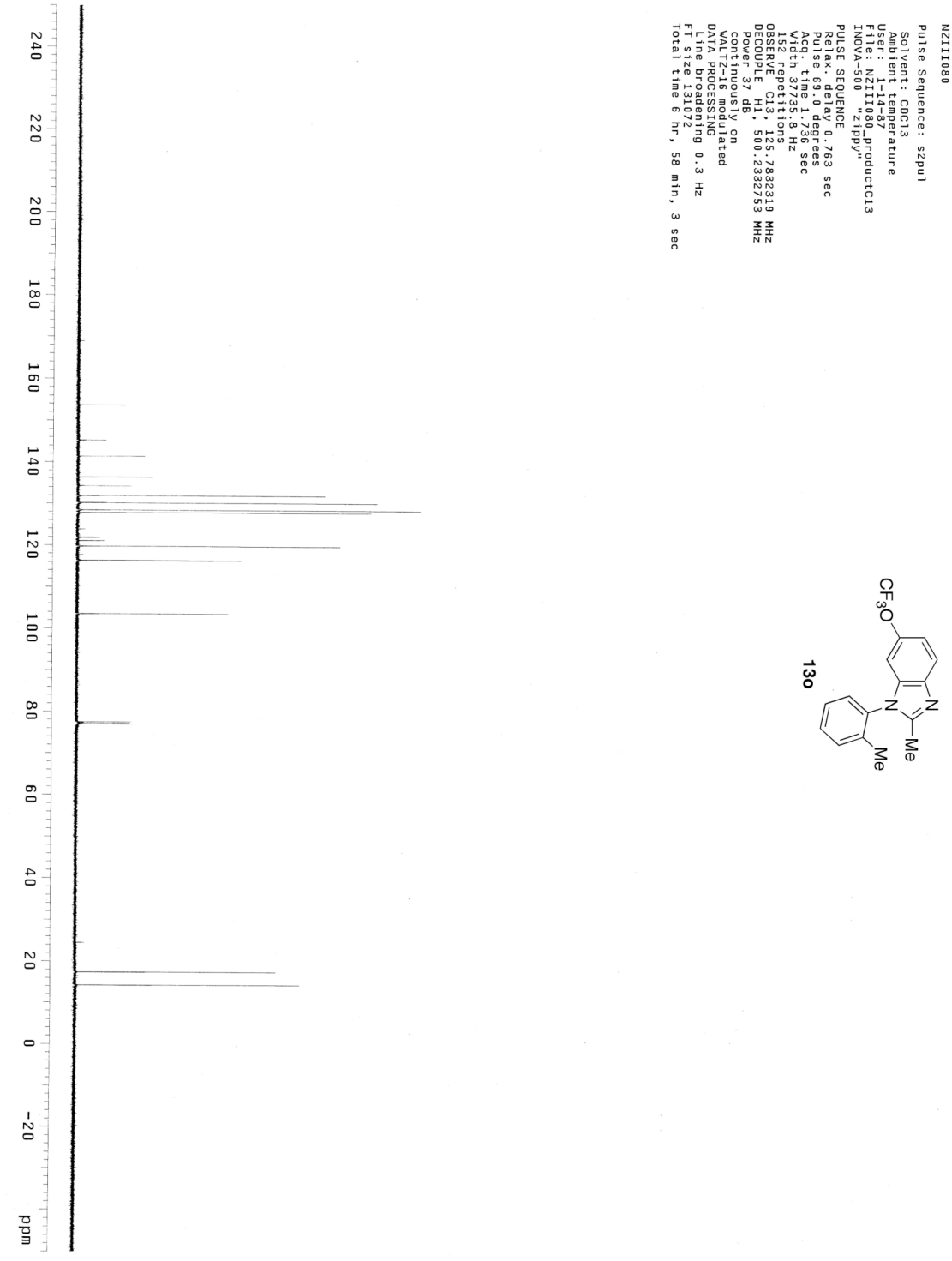

NZII1075
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII1075_product
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 500.2312698 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 28 sec
Me
N
N
Me
13k
10
9
8
7
6
5
4
3
2
1
0 ppm
0.78
0.92
0.91
1.8181
0.78
3.19
3.00
0.86
2.29
2.26

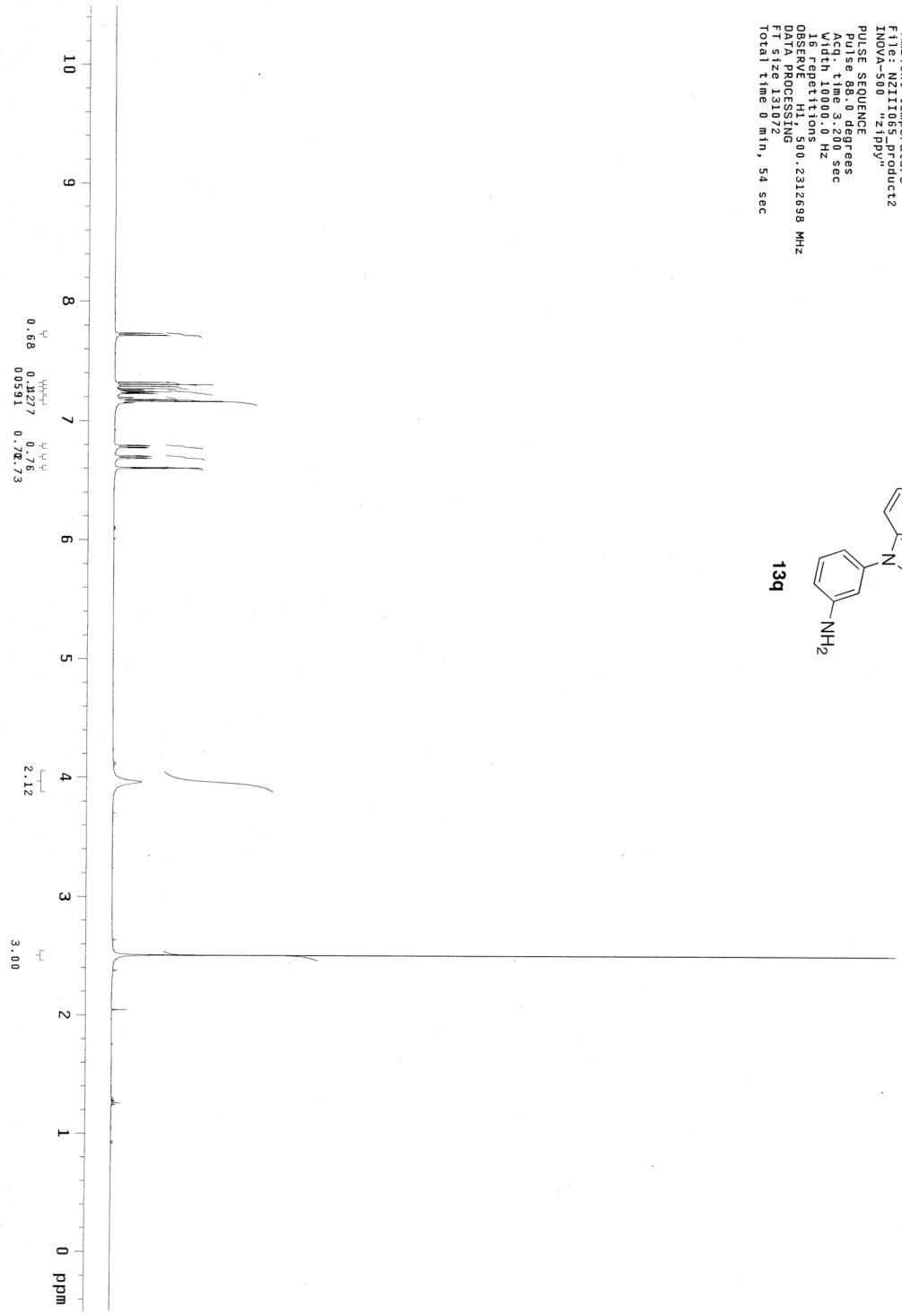

NZIII075
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZIII075_productc13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
10000 repetitions
OBSERVE C13, 125.7832371 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
Me
N
N
Me
13k
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

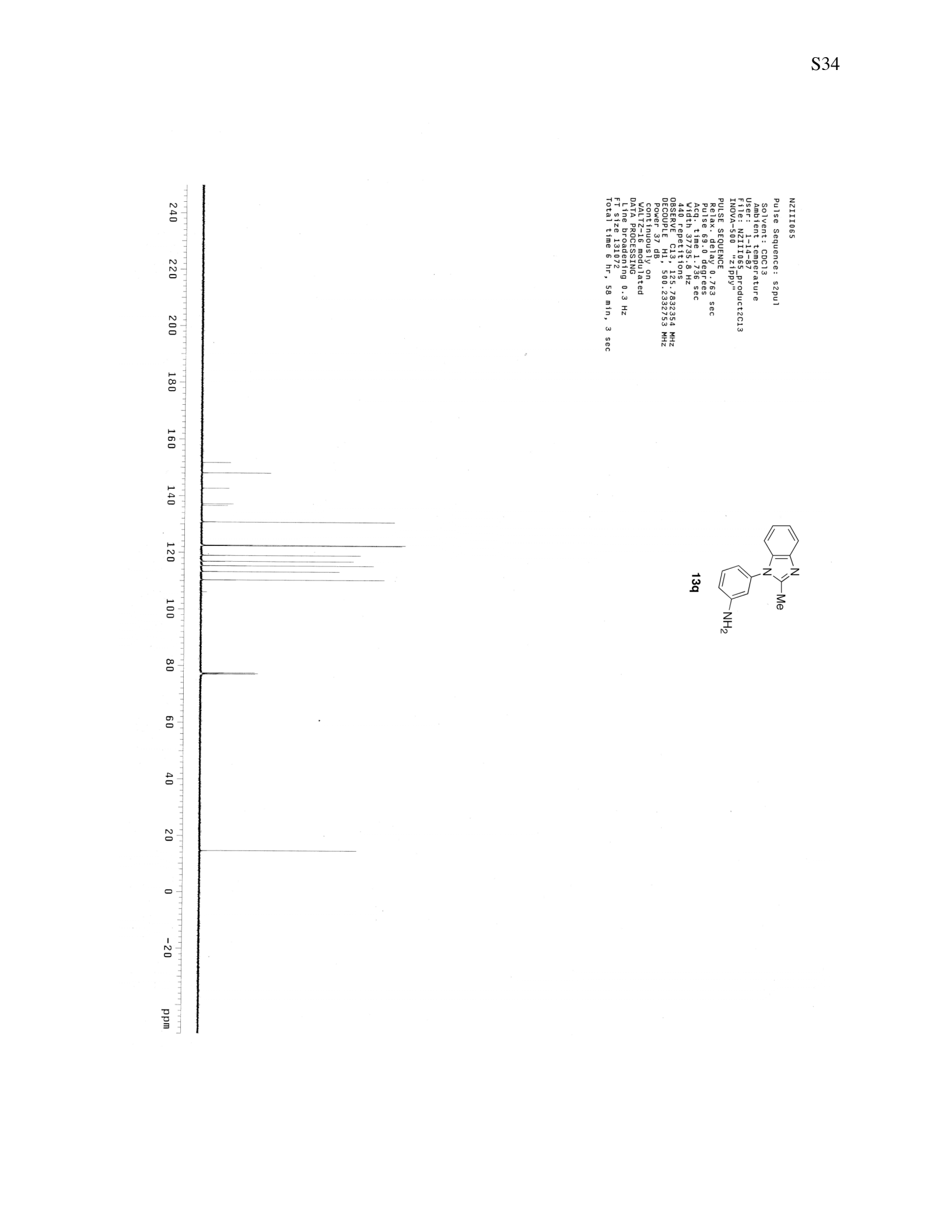

NZI262
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZI262_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986336 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
Me
Me
Me
Me
N
N
13l
10
9
8
7
6
5
4
3
2
1
0 ppm
2.97
0.98
0.97
0.94
3.00
2.95
2.88
2.81

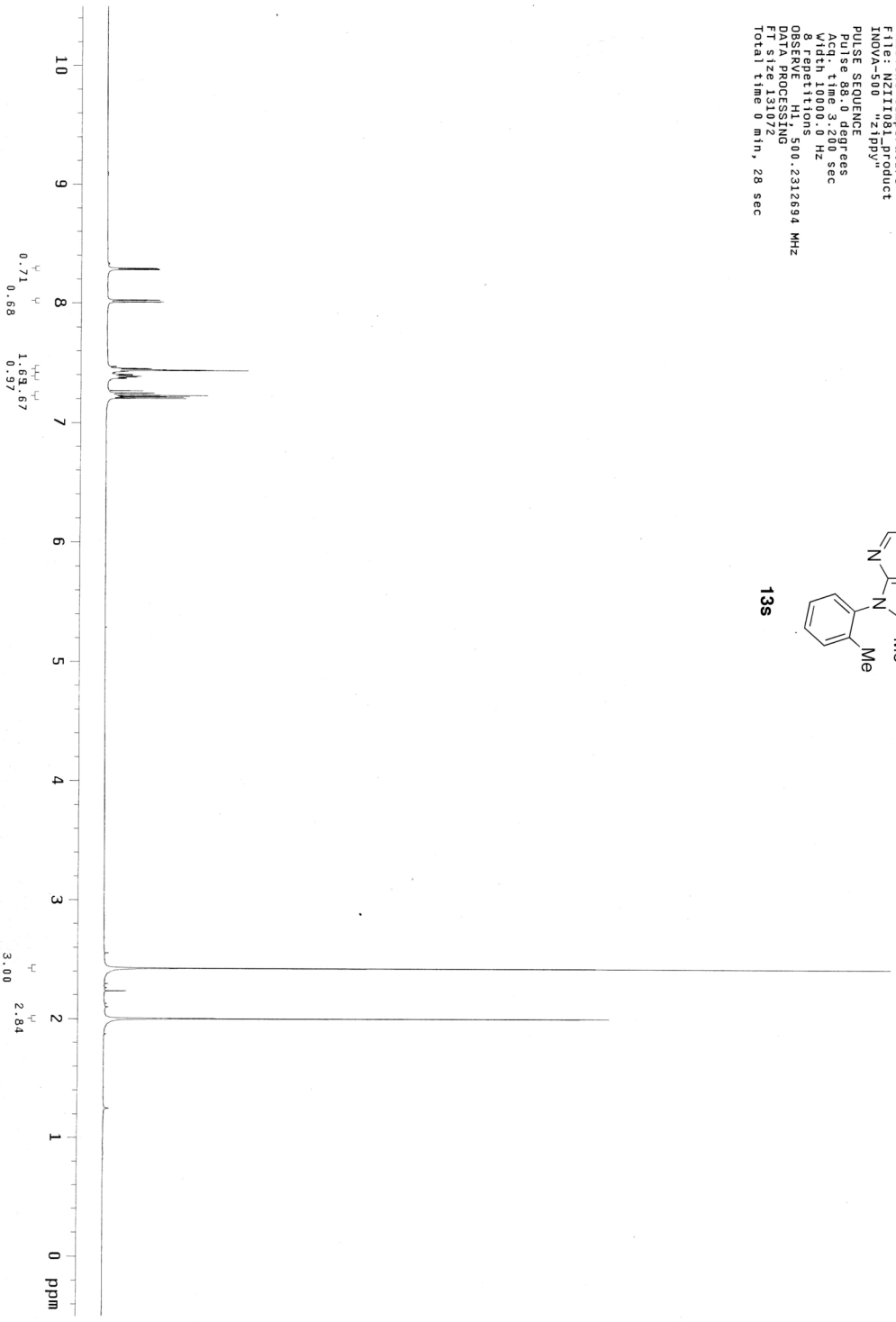

NZI262
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZI262_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
104 repetitions
OBSERVE C13, 125.7832423 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
Me
Me
N
N
Me
Me
131
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


NZII090
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII090_product
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
width 10000.0 Hz
8 repetitions
OBSERVE H1, 500.2312698 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 28 sec
CF3O
N
N
Me
Me
13o
10
9
8
7
6
5
4
3
2
1
0 ppm
0.79
0.88
0.92
1.63
1.68
0.68
3.00
2.84


NZII1080
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII1080_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
152 repetitions
OBSERVE C13, 125.7832319 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
CF3O
N
N
Me
Me
13o
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

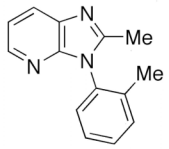

NZIII065
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII065_product2
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
16 repetitions
OBSERVE H1, 500.2312698 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 54 sec
N
N
Me
NH2
13q
10
9
8
7
6
5
4
3
2
1
0 ppm
0.68
1.27
0.91
0.76
0.73
2.12
3.00


NZII1065
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII1065_product2C13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
440 repetitions
OBSERVE C13, 125.7832354 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
N
N
Me
NH2
13q
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

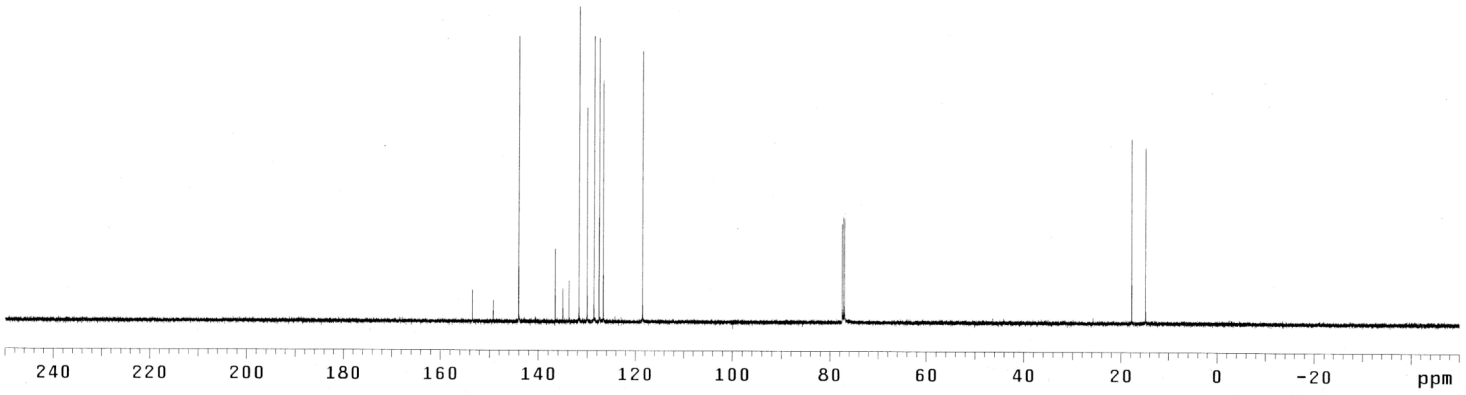

NZIII087
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII08I_product
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 500.2312694 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 28 sec
13s
N
N
N
Me
Me
0.71
0.68
1.68
1.67
0.97
3.00
2.84
10
9
8
7
6
5
4
3
2
1
0 ppm

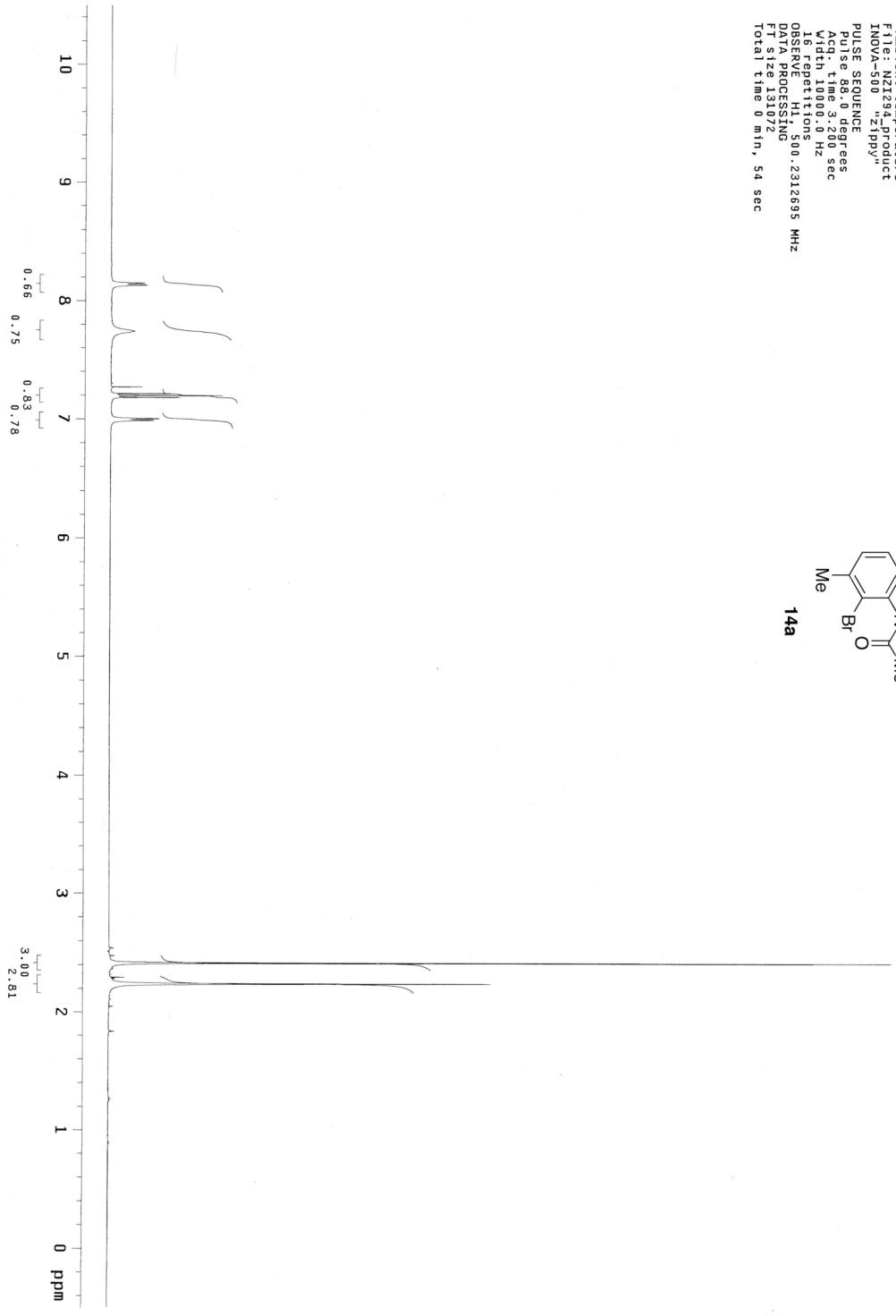
NZIII081

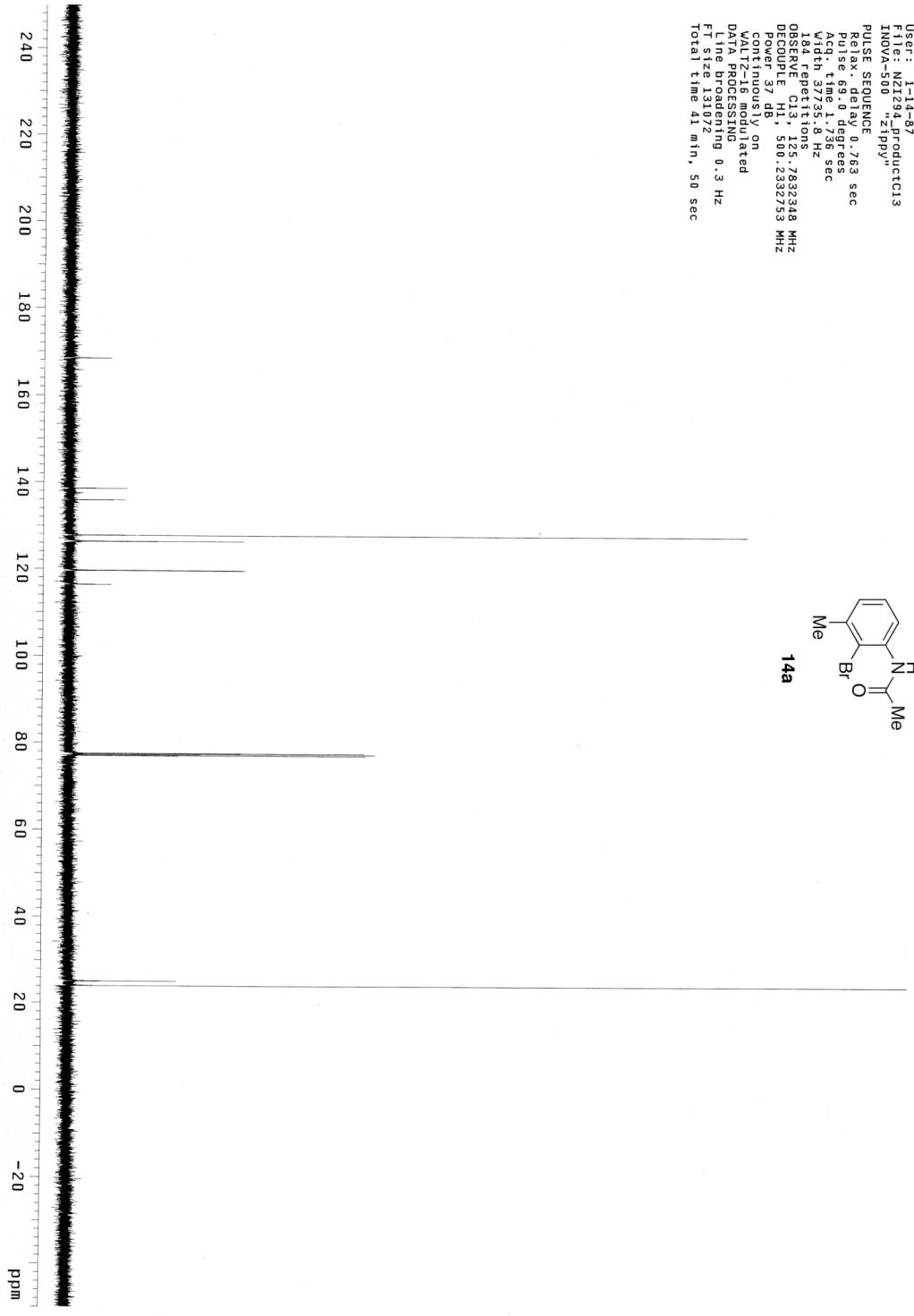
Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
User: 1-14-87
File: NZIII081_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
 Relax. delay 0.763 sec
 Pulse 69.0 degrees
 Acq. time 1.736 sec
 Width 37735.8 Hz
 408 repetitions
OBSERVE C13, 125.7832319 MHz
DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec

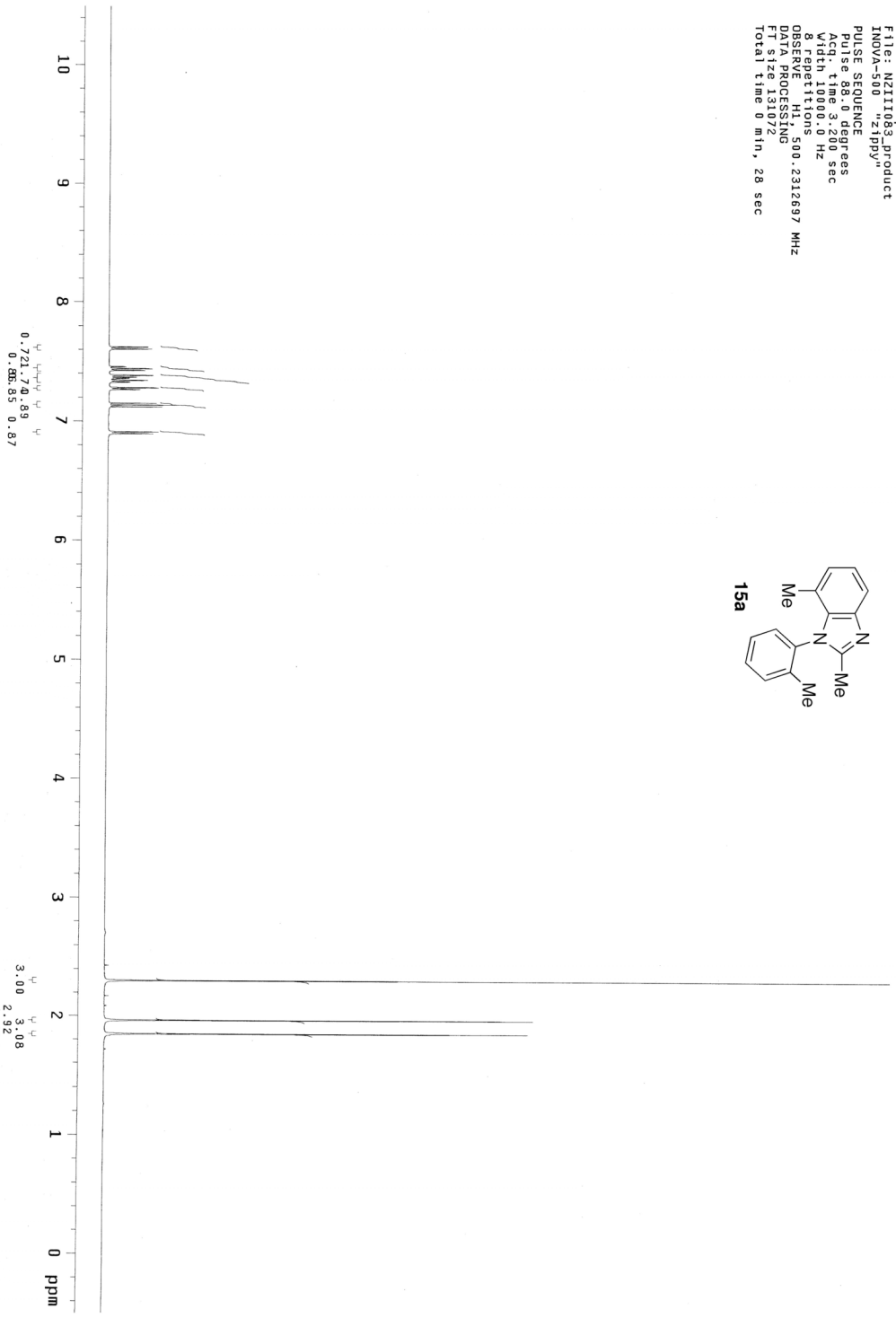


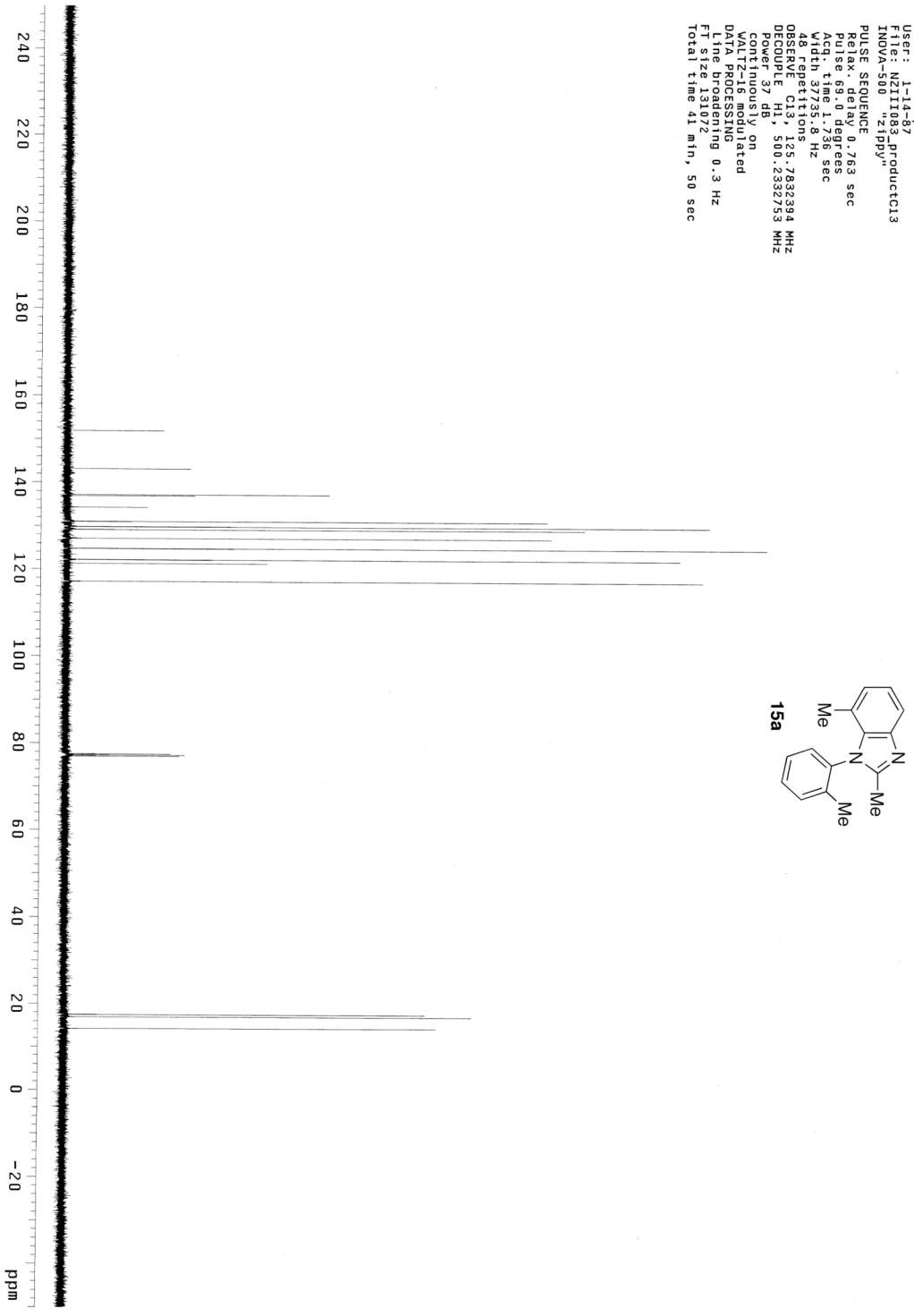
13s

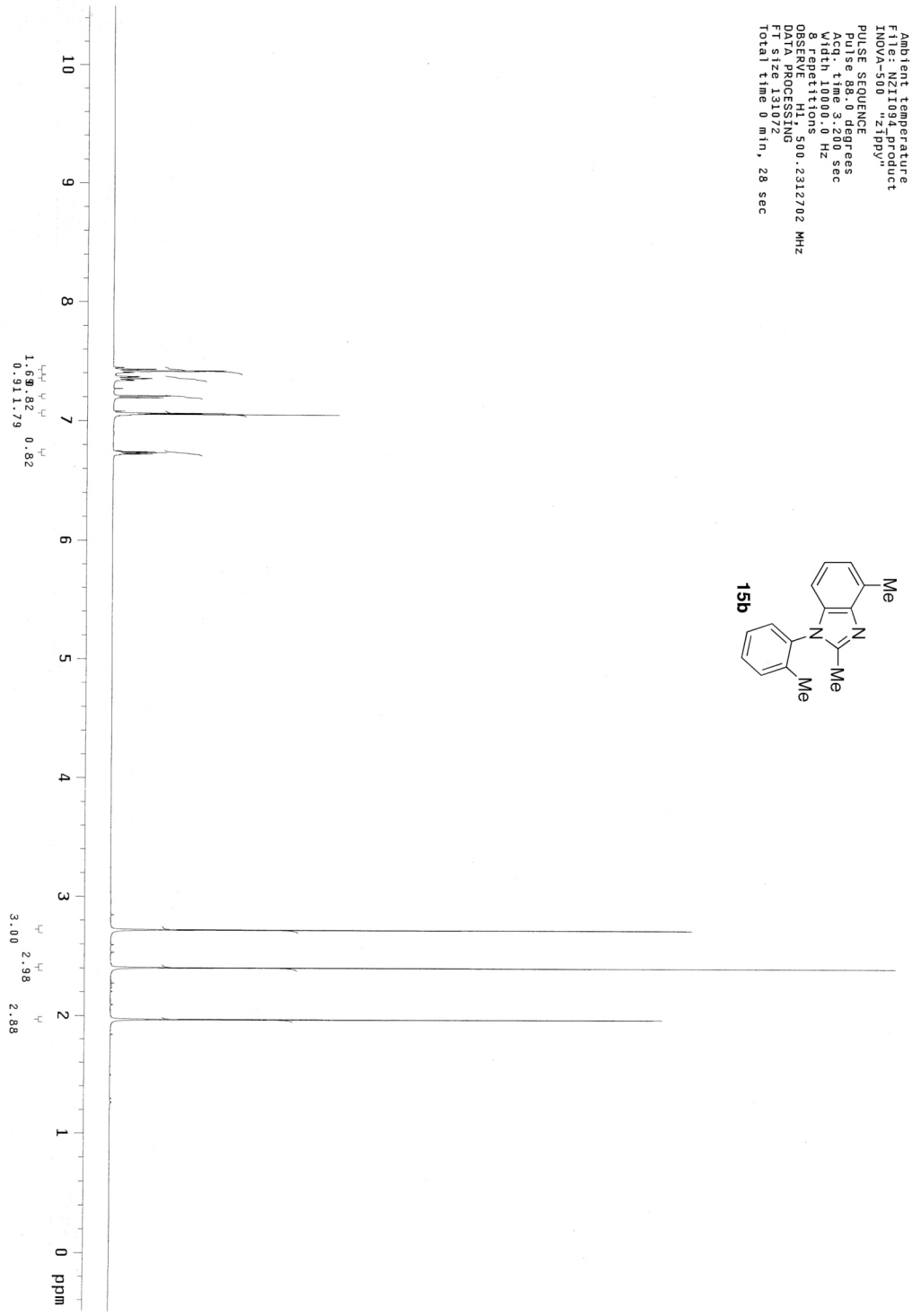


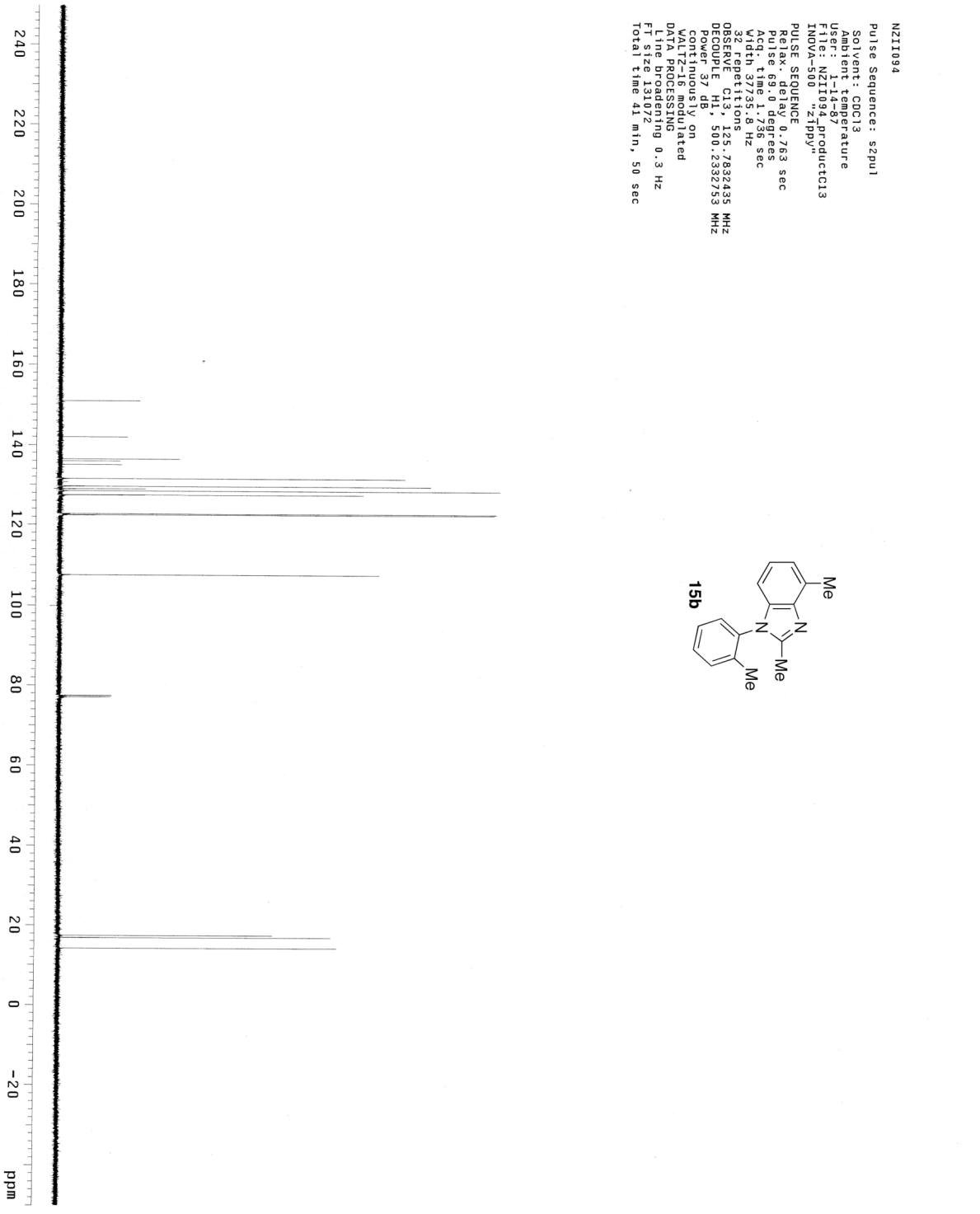

NZI294
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZI294_product
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
16 repetitions
OBSERVE H1, 500.2312695 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 54 sec
Me
Br
H
N
O
Me
14a
0.66
0.75
0.83
0.78
3.00
2.81
10
9
8
7
6
5
4
3
2
1
0
ppm

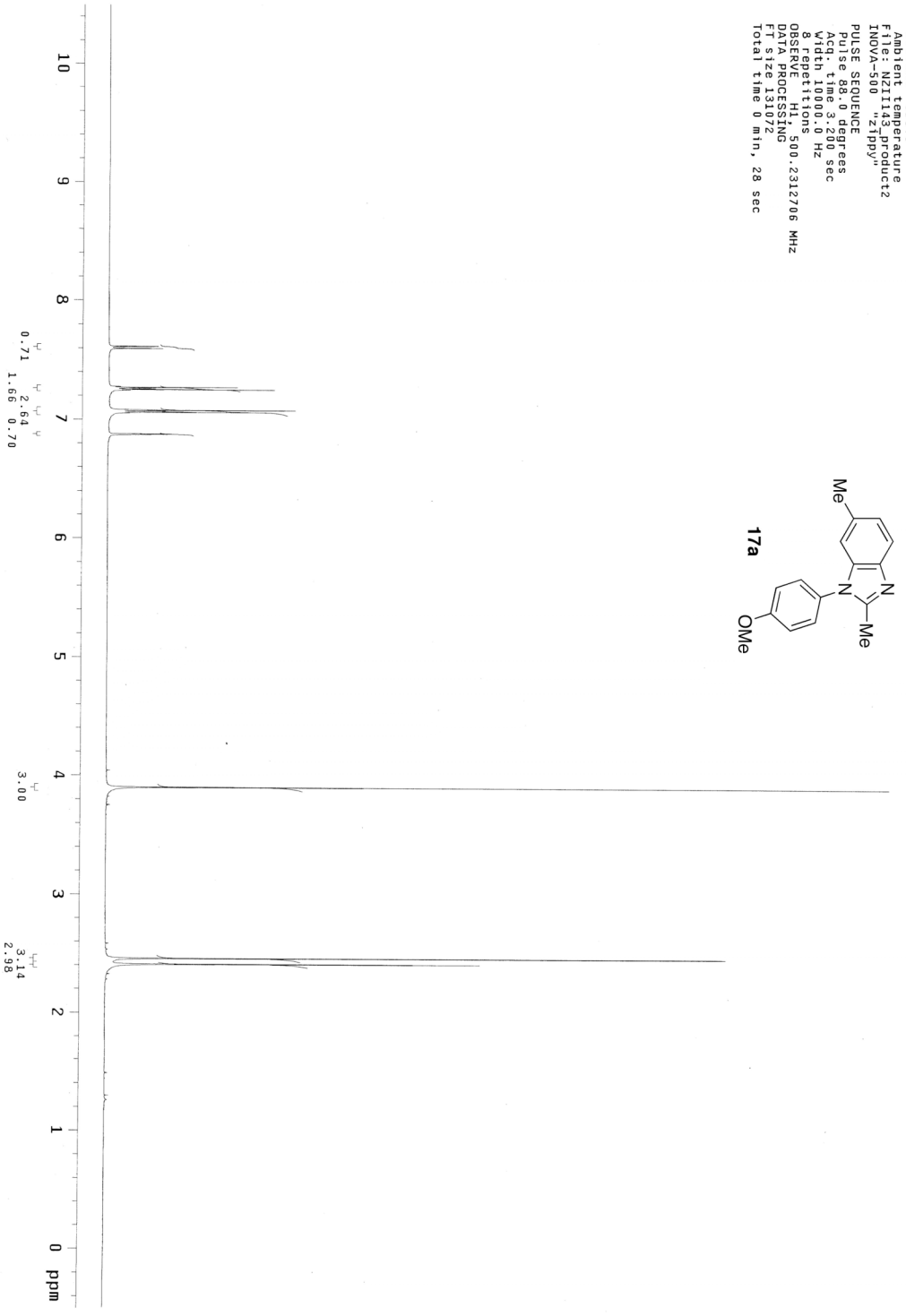

NZI294
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZI294_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
184 repetitions
OBSERVE C13, 125.7832348 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 41 min, 50 sec
Me
Br
H
N
O
Me
14a
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

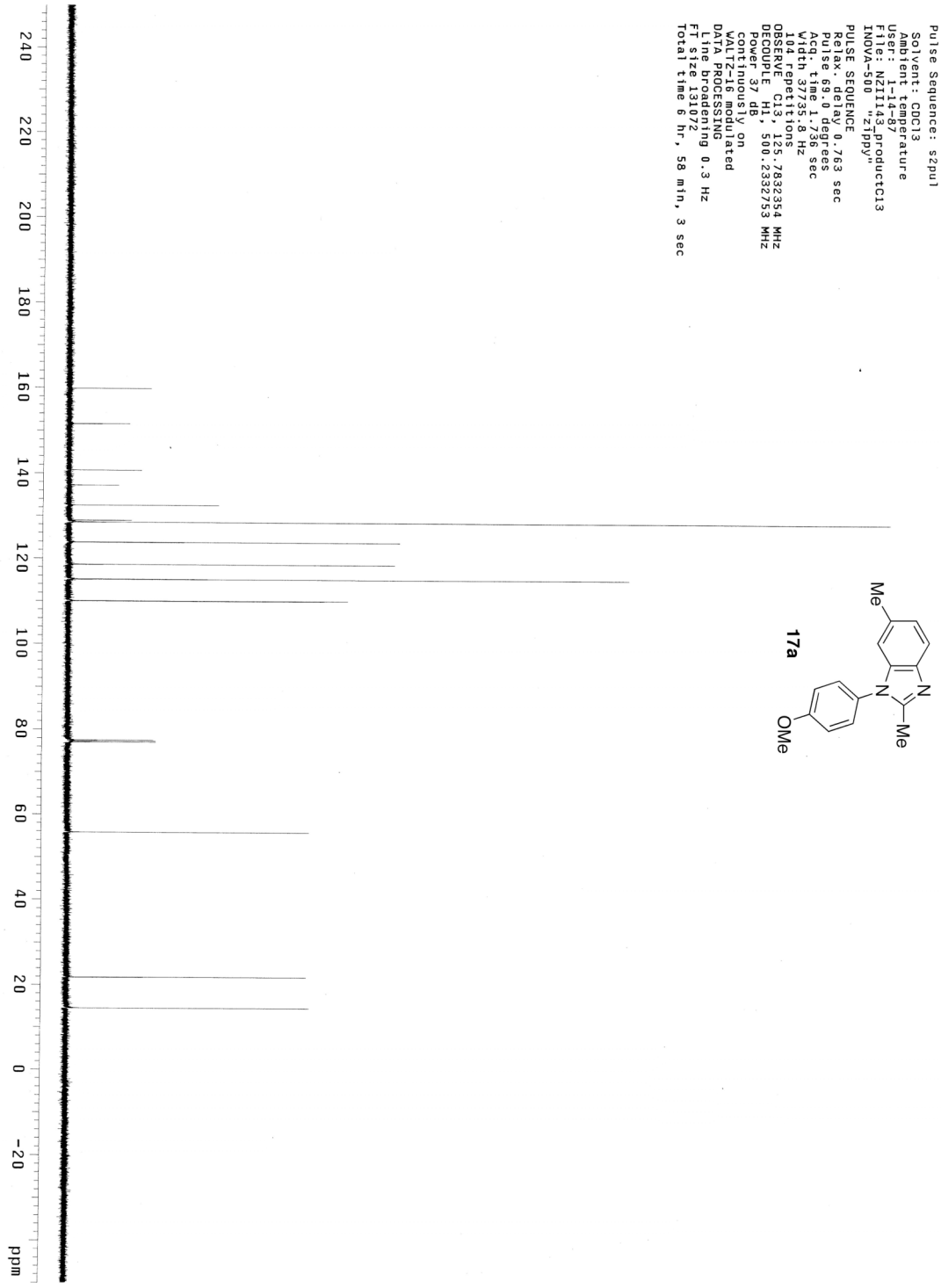

NZIII083
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII083_product
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 500.2312697 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 28 sec
Me
N
N
Me
Me
15a
0.72
1.70
0.89
1.85
0.87
3.00
3.08
2.92
10
9
8
7
6
5
4
3
2
1
0 ppm

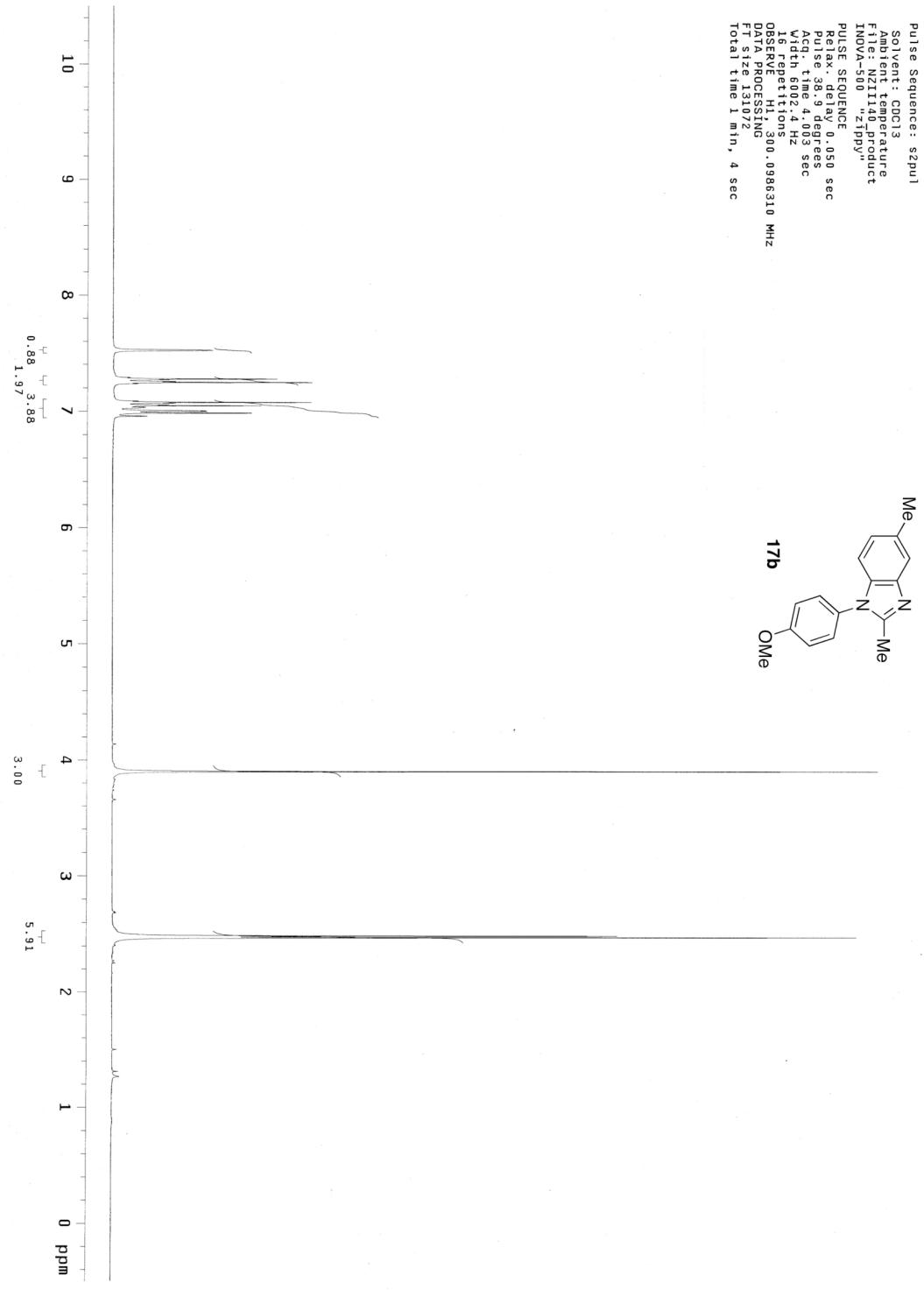

NZIII083
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZIII083_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
48 repetitions
OBSERVE C13, 125.7832394 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 41 min, 50 sec
Me
N
N
Me
Me
15a
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


NZII094
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII094_product
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 500.2312702 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 28 sec
Me
N
N
Me
Me
15b
10
9
8
7
6
5
4
3
2
1
0 ppm
1.69
0.91
0.82
1.79
0.82
3.00
2.98
2.88


NZI094
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZI094_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
32 repetitions
OBSERVE C13, 125.7832435 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 41 min, 50 sec
Me
N
N
Me
Me
15b
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


NZII143
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII143_product2
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
width 10000.0 Hz
8 repetitions
OBSERVE H1, 500.2312706 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 28 sec
Me
N
N
Me
OMe
17a
10
9
8
7
6
5
4
3
2
1
0 ppm
0.71
2.64
1.66
0.70
3.00
3.14
2.98


NZII143
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII143_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
104 repetitions
OBSERVE C13, 125.7832354 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
Me
N
N
Me
OMe
17a
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

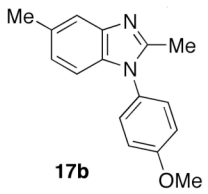

NZII140
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII140_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986310 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
Me
N
N
Me
17b
OMe
10
9
8
7
6
5
4
3
2
1
0 ppm
0.88
1.97
3.88
3.00
5.91

STANDARD CARBON PARAMETERS

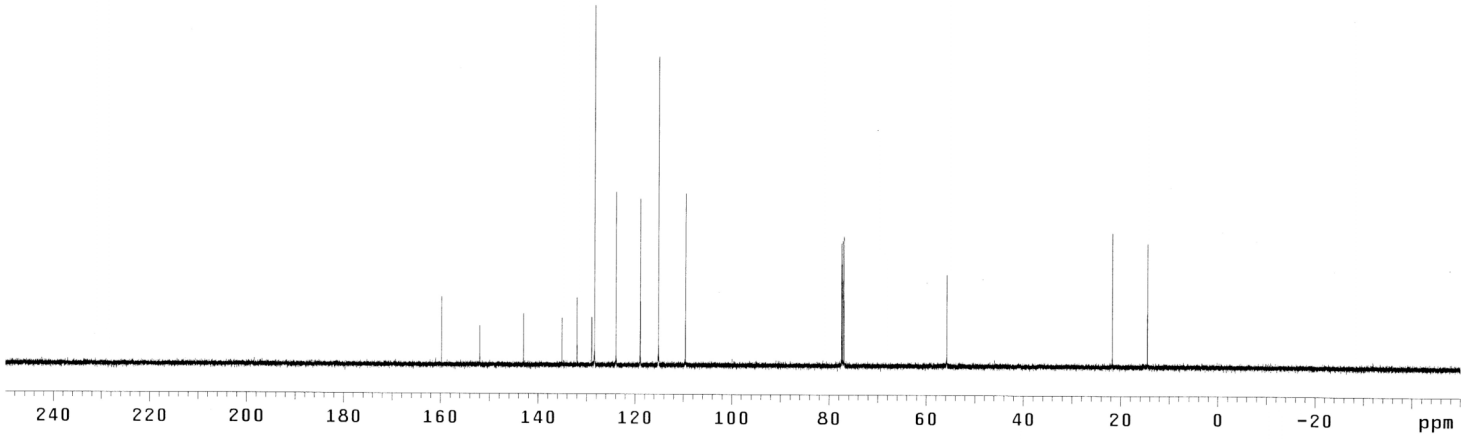
Pulse Sequence: s2pul

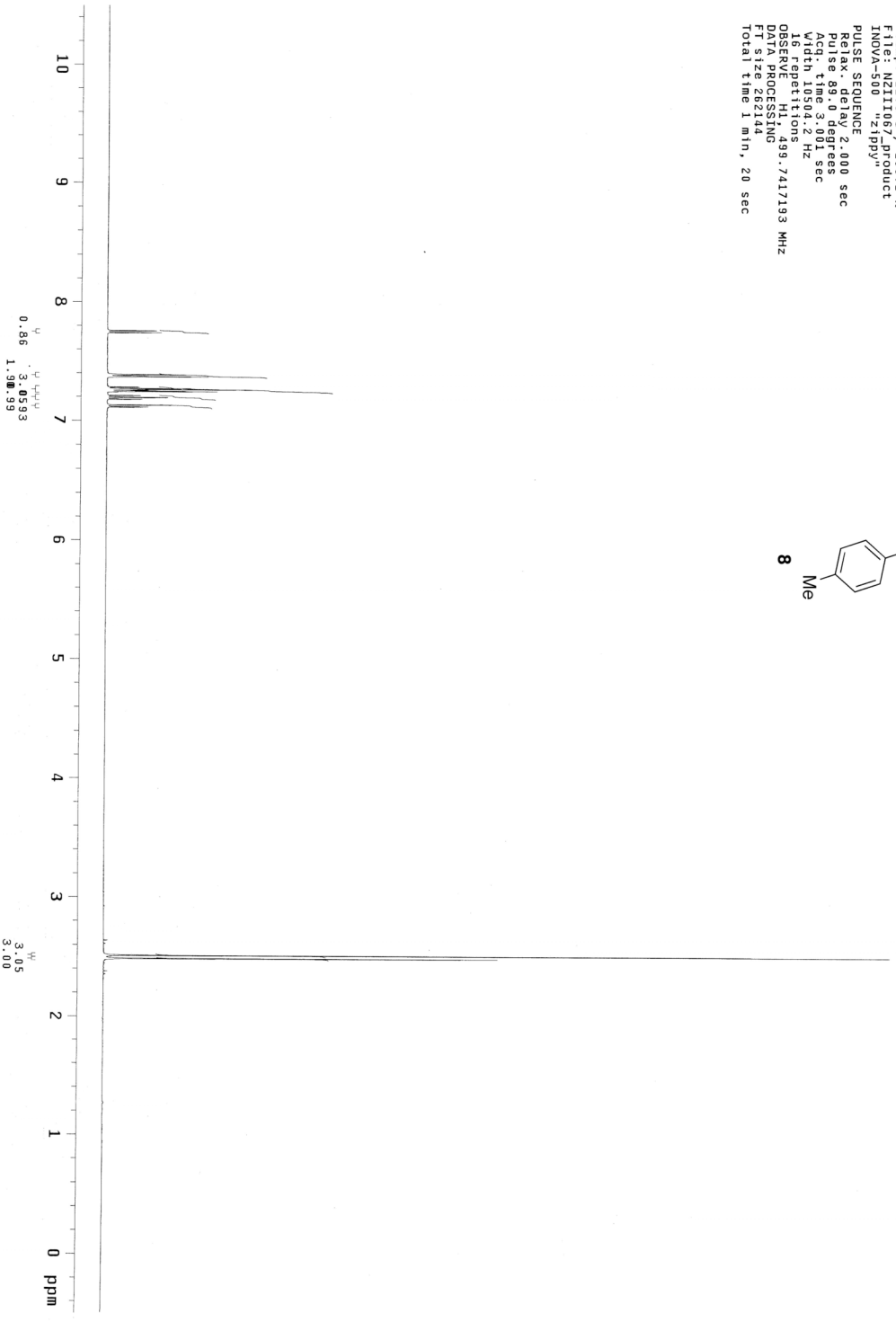
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII140_productC13
INOVA-500 "zippy"

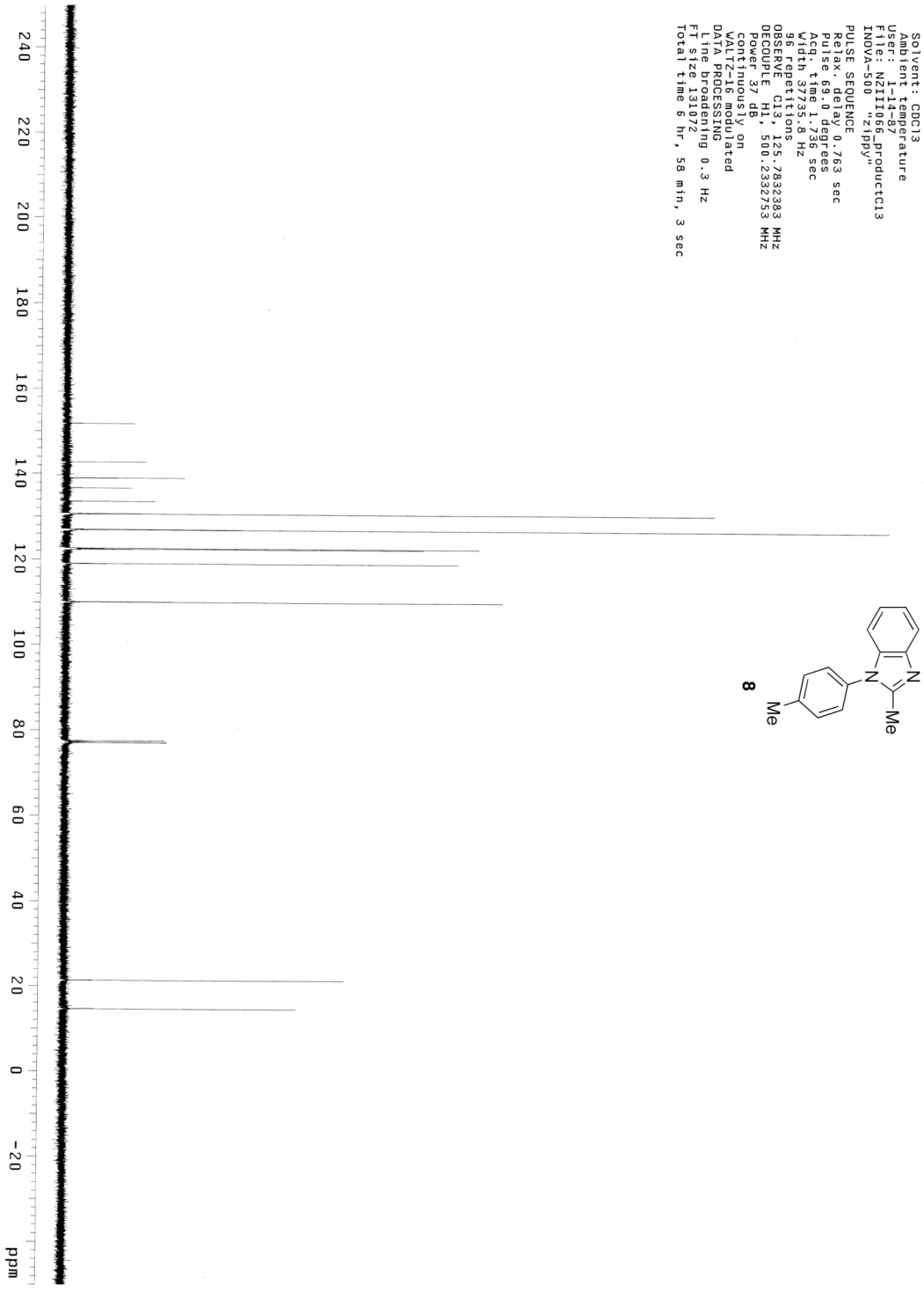
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
136 repetitions
OBSERVE C13, 125.7832348 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec



17b




NZII167
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 22.0 C / 295.1 K
File: NZII167_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
width 10504.2 Hz
16 repetitions
OBSERVE H1, 499.7417193 MHz
DATA PROCESSING
FT size 262144
Total time 1 min, 20 sec
N
N
Me
Me
8
0.86
1.99
2.99
3.05
3.00
10
9
8
7
6
5
4
3
2
1
0 ppm


NZII1066
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII1066_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
96 repetitions
OBSERVE C13, 125.7832383 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
N
N
Me
Me
8
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm