A Copper-Catalyzed Regiospecific Synthesis of *N*-Alkyl Benzimidazoles

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Experimental Section

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General Considerations

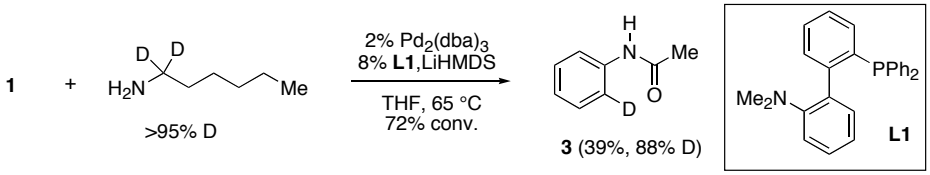
All reactions were carried out under an argon atmosphere in a Schlenk tube, with a stir bar and capped with a Teflon screw-cap. EtOAc was purchased from Mallinckrodt (ACS grade) and used as received. Anhydrous *t*-BuOH, DMF, and 1,4-dioxane were purchased from Aldrich in a Sure/Seal™ bottle, used as received and stored under Argon. Anhydrous granular K_3PO_4 was purchased from Fluka. K_2CO_3 powder (~325 mesh), NaO*t*-Bu and LHMDS (1M solution in THF) were purchased from Sigma-Aldrich. Cs_2CO_3 was a gift from Chemetall. Bulk quantities of K_2CO_3, K_3PO_4 and Cs_2CO_3 were stored in a nitrogen-filled glovebox. Small portions (1-2 g) were removed from the glovebox in glass vials and stored in a desiccator filled with anhydrous calcium sulfate. 4Å molecular sieves (purchased from Aldrich, activated powder, 5 μm) were activated by heating under vacuum prior to use.

$Pd(OAc)_2$ was a gift from Englehard. $Pd_2(dba)_3$ and CuI were purchased from Strem. Diamine ligands, *N*,*N*'-dimethylethylenediamine (**L3**) and *rac-trans-N,N'*-dimethylcyclohexane-1,2-diamine (**L2**), were purchased from Aldrich and used as received. 2-(Diphenylphosphino)-2'-(*N*,*N*-di-methylamino)biphenyl (**L1**) was synthesized following a published procedure.[1]

2-Bromo-*N*-methylaniline **13**, 2-bromoacetanilide **1**, and 2-bromo-4-methylacetanilide were purchased from Aldrich. 2-Bromo-4-trifluoromethylacetanilide was purchased from Acros. 2-Iodo-(4-trifluoromethyl)aniline was purchased from Alfa Aesar. The rest of starting materials were purchased from either Aldrich or Acros and used as received unless specified otherwise. *n*-Hexylamine was purified by distillation over CaH_2 and stored in a nitrogen-filled Schlenk tube. 2-Iodotrifluroacetanilide **8**[2] and labeled *n*-hexylamine[3] were prepared based on reported procedures. 2-Iodoacetanilide **6**[4] was synthesized using a published procedure.[5]

All new compounds were characterized by ^1H NMR, ^{13}C NMR, and IR spectroscopy, in addition to elemental analysis performed by Atlantic Microlabs Inc., Norcross, GA and/or low resolution mass spectroscopy. For starting materials, copies of the ^1H and ^{13}C NMR spectra are attached for those compounds of which a satisfactory elemental analysis was not obtained. Copies of the ^1H and ^{13}C NMR spectra are attached for all products. Nuclear Magnetic Resonance spectra were recorded on a Varian Mercury 300 or Varian Inova 500 instrument. All ^1H NMR experiments are reported in δ units, parts per million (ppm) and were measured relative to the signals for residual chloroform (7.27 ppm) and methanol (3.31 ppm) in the deuterated solvents. All ^{13}C NMR spectra (obtained with ^1H decoupling) are reported in ppm relative to deuterochloroform (77.23 ppm) and deuterodimethyl sulfoxide (39.51 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 a 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).

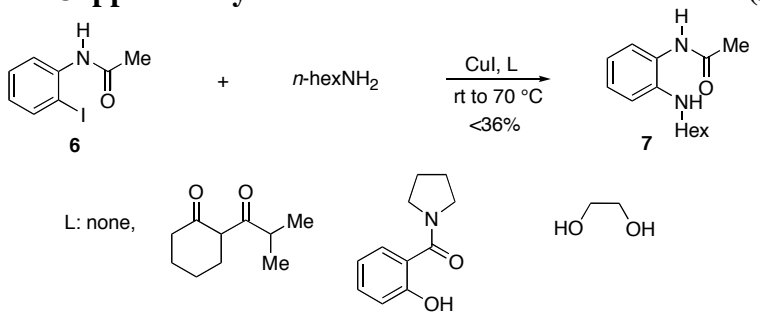
The yields for products (**9**, **12a-d**, **15**, and **18a-h**) are isolated yields (average of two runs). Yields for the preparation of starting materials refer to a single experiment. All compounds isolated were estimated to be ≥95% pure as determined by ^1H NMR and GC analysis and/or combustion analysis.



***N*-phenylacetamide d_1[6] (Scheme 1, 3)** 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), **L1** (0.04 mmol, 8 mol %), and 2-bromoacetanilide **1** (107.1 mg, 0.5 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (3 cycles). LiHMDS (1.0 M in THF, 1.5 mL) was added to the Schlenk tube through the septum via syringe at room temperature. The reaction mixture was stirred at room temperature for 5 min. Then 2,2-dideuterohexylamine (86 μL, 0.65 mmol) was 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 and put into a pre-heated oil bath at 65 °C. After stirring for 18 h, the reaction mixture was allowed to cool to 0 °C. 1N HCl (1.5 mL)

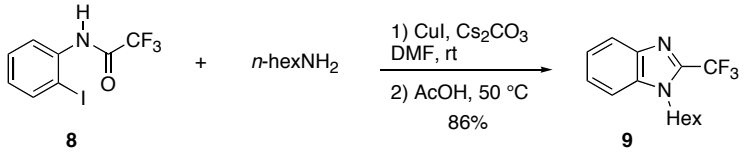
was added dropwise. 10 min later, saturated aqueous $NaHCO_3$ solution (2 mL) was added. The mixture was extracted with EtOAc (4 mL x 3). The combined EtOAc layers were dried over Na_2SO_4. The EtOAc extracts were analyzed by GC first (113 μL of dodecane was added as an internal standard) and then concentrated under vacuum. The residual was purified by flash column chromatography on silica gel (gradient elution: 2/1, and then 1.5/1 hexanes/EtOAc) to provide **3** (26.2 mg, 39 %, 88% D).

Ligand Screening for Copper-catalyzed Amination of *ortho*-Iodoanilides (Scheme 3)



A representative procedure for screening no added ligand, 2-isobutyrylcyclohexanone, and *N*-(2-hydroxybenzoyl)pyrrolidine is as follows: an oven-dried Schlenk tube containing a stir bar was charged with CuI (9.5 mg, 0.05 mmol, 5.0 mol % Cu), *ortho*-iodoacetanilide **6** (261 mg, 1 mmol), and Cs_2CO_3 (652 mg, 2.0 mmol) (*N*-(2-hydroxybenzoyl)pyrrolidine was added here). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (3 cycles). Ligand (0.20 mmol, 20 mol%), *n*-hexylamine (0.20 mL, 1.5 mmol), and DMF (0.5 mL) were added through the septum via syringe. The septum was replaced with a Teflon screw cap, and the Schlenk tube was sealed and stirred at rt or 70 °C for 12 h.

A representative procedure for screening ethylene glycol is as follows: an oven-dried Schlenk tube containing a stir bar was charged with CuI (19.0 mg, 0.10 mmol, 10 mol % Cu), *ortho*-iodoacetanilide **6** (261 mg, 1 mmol), and K_3PO_4 (425 mg, 2.0 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (3 cycles). Ethylene glycol (0.11 mL, 2 mmol), *n*-hexylamine (0.20 mL, 1.5 mmol), and *i*-PrOH (1 mL) were added through the septum via syringe. The septum was replaced with a Teflon screw cap, and the Schlenk tube was sealed and stirred at 70 °C for 12 h.



1-hexyl-2-(trifluoromethyl)-1*H*-benzimidazole[7] **(Scheme 3, 9)** To an oven-dried Schlenk tube containing a stir bar were added CuI (9.5 mg, 0.05 mmol, 5.0 mol % Cu), *ortho*-iodotrifluroacetanilide **8** (315 mg, 1 mmol), and preactivated 4Å molecular sieves (150 mg). The tube was evacuated and transferred to a nitrogen-filled glovebox. Cs_2CO_3 (652 mg, 2 mmol), *n*-hexylamine (0.20 mL, 1.5 mmol) and DMF (0.50 mL) were added. The Schlenk tube was removed from the glove box and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was diluted with EtOAc (4 mL) and then filtered through Celite with the aid of EtOAc. The filtrate was concentrated under reduced pressure to give a crude mixture that was dissolved in AcOH (1 mL). The formed solution was heated to 50 °C and stirred at 50 °C for 2 h. After cooling to room temperature, AcOH was removed by vacuum. The residual material was partitioned between dichloromethane (3 mL) and saturated aqueous $NaHCO_3$

solution (3 mL). The aqueous layer was separated and extracted by dichloromethane (3 mL x 2). The combined dichloromethane layers were dried over Na_2SO_4 and concentrated under vacuum. The residual was purified by flash chromatography on silica gel (Biotage, 3-28% ethyl acetate in hexanes gradient) to provide the title compound as a brown oil (235 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.89 (d, *J* = 7.6Hz, 1H), 7.48-7.34 (m, 3H), 4.29 (t, *J* = 7.9Hz, 2H), 1.93-1.82 (m, 2H), 1.46-1.27 (m, 6H), 0.90 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 141.3, 140.5 (q, *J* = 38.4 Hz), 135.5, 125.3, 123.6, 121.7, 119.3 (q, *J* = 271.2 Hz), 110.6, 45.3, 31.3, 30.0, 26.5, 22.5, 13.9.

General Procedures for Cu-Catalyzed Synthesis of *N*-Alkyl Benzimidazoles (Scheme 4 and Scheme 5)

Procedure A: an oven-dried Schlenk tube containing a stir bar was charged with CuI (9.5 mg, 0.05 mmol, 5.0 mol % Cu), *ortho*-iodo-*N*-alkylaniline (1 mmol), amide (1.2 mmol), and Cs_2CO_3 (652 mg, 2.0 mmol). The Schlenk tube was capped with a Teflon screw cap and then evacuated and backfilled with argon (3 cycles). *N,N'*-Dimethylethylenediamine **L3** (11 μL, 0.1 mmol, 10 mol%) was added via syringe to the Schlenk tube followed by the addition of 1,4-dioxane (1 mL) under a positive flow of Ar. The Schlenk tube was sealed and put into a pre-heated oil bath at 110 °C. After stirring for 17 h, the reaction mixture was allowed to cool to room temperature.

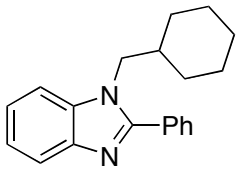
Procedure B: an oven-dried Schlenk tube containing a stir bar was charged with CuI (9.5 mg, 0.05 mmol, 5.0 mol % Cu), *ortho*-iodo-*N*-alkylaniline (1 mmol), amide (1.2 mmol), and Cs_2CO_3 (652 mg, 2.0 mmol). The Schlenk tube was capped with a Teflon screw cap and then evacuated and backfilled with argon (3 cycles). *rac-trans-N,N'*-Dimethylcyclohexane-1,2-diamine **L2** (32 μL, 0.2 mmol, 20 mol%) was added via syringe to the Schlenk tube followed by the addition of 1,4-dioxane (1 mL) under a positive flow of Ar. The Schlenk tube was sealed and put into a pre-heated oil bath at 90 °C. After stirring for 2 h, the reaction mixture was allowed to cool to room temperature.

Depending on the amides used, two procedures were developed for the cyclodehydration step.

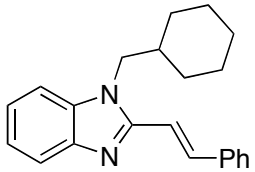
Procedure C: when benzamide and (*E*)-cinnamamide were used, the Schlenk tube was opened under a positive Ar flow. K_3PO_4 (318 mg, 1.5 mmol) was added followed by the addition of *t*-BuOH (1 mL). The Schlenk tube was resealed and put into a pre-heated oil bath at 110 °C. After stirring for 4 h or 8 h, the reaction mixture was allowed to cool to room temperature. The reaction mixture was first diluted with dichloromethane (4 mL) and then filtered through Celite with the aid of dichloromethane. The filtrate was concentrated under reduced presure. The residual material was purified by flash chromatography on silica gel.

Procedure D, in the case of cyclohexanecarboxamide and hexanamide, the reaction mixture was diluted with dichloromethane (4 mL) first. Then, the resulting mixture was filtered through Celite with the aid of dichloromethane. The filtrate was concentrated under reduced pressure. The residual material was dissolved in AcOH (1 mL) and then heated to 75 °C. After stirring for 2 h, the reaction mixture was allowed to cool to room temperature. AcOH was removed under vacuum. The residual material was partitioned between dichloromethane (3 mL) and saturated aqueous $NaHCO_3$ solution (3 mL) (if an emulsion formed, 2 mL of brine was added to aid in the separation). The aqueous layer was separated and extracted by dichloromethane (3 mL x 2). The combined dichloromethane layers were dried over Na_2SO_4 and

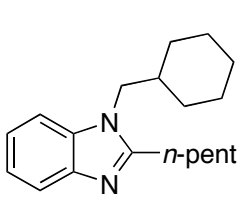
concentrated under reduced pressure. The residual material was purified by flash column chromatography on silica gel.



1-(cyclohexylmethyl)-2-phenyl-1*H*-benzimidazole (**Scheme 4**, **12a**) Following procedure A, *ortho*-iodo-*N*-alkylaniline **10** (240 mg, 0.76 mmol) was coupled with benzamide (111 mg, 0.91 mmol). The cyclodehydration step was accomplishing using procedure C (243 mg of K_3PO_4, 0.8 mL of *t*-BuOH, 4 h). The crude product was purified by flash chromatography on silica gel (gradient elution: 4/1, and then 3/1 hexanes/EtOAc) to provide the title compound as a red solid (150 mg, 68%). mp 97-98 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.85-7.82 (m, 1H), 7.71-7.67 (m, 2H), 7.55-7.49 (m, 3H), 7.45-7.41 (m, 1H), 7.33-7.29 (m, 2H), 4.12 (d, *J* = 7.5Hz, 2H), 1.85-1.76 (m, 1H), 1.62-1.55 (m, 3H), 1.45 (d, *J* = 12.8Hz, 2H), 1.11-0.99 (m, 3H), 0.81-0.74 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 154.3, 143.1, 135.9, 131.1, 129.60, 129.57, 128.7, 122.6, 122.3, 120.0, 110.7, 50.9, 38.1, 30.8, 26.1, 25.6. IR (neat, cm^{-1}): 3061, 2925, 2851, 1448, 1390, 1356, 1327, 1273, 774, 742, 699. Anal. Calcd for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64. Found: C, 82.45; H, 7.63.

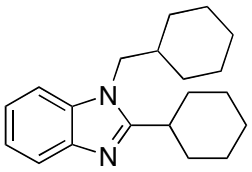


1-(cyclohexylmethyl)-2-[(*E*)-2-phenylethenyl]-1*H*-benzimidazole (**Scheme 4**, **12b**) Following procedure A, *ortho*-iodo-*N*-alkylaniline **10** (218 mg, 0.69 mmol) was coupled with (*E*)-cinnamamide (122 mg, 0.83 mmol). The cyclodehydration step was accomplishing using procedure C (220 mg of K_3PO_4, 0.7 mL of *t*-BuOH, 4 h). The crude product was purified by flash chromatography on silica gel (gradient elution: 5/1, and then 4/1 hexanes/EtOAc) to provide the title compound as a yellow solid (131 mg, 60%). mp 165-167 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.02 (d, *J* = 15.8Hz, 1H), 7.80-7.78 (m, 1H), 7.63 (d, *J* = 7.3Hz, 2H), 7.43 (t, *J* = 7.4Hz, 2H), 7.38-7.33 (m, 2H), 7.30-7.24 (m, 2H), 7.07 (d, *J* = 15.8Hz, 1H), 4.08 (d, *J* = 7.4Hz, 2H), 1.94-1.85 (m, 1H), 1.75-1.69 (m, 5H), 1.24-1.05 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 151.1, 143.2, 137.0, 136.2, 136.0, 129.1, 129.0, 127.4, 122.6, 122.5, 119.4, 113.4, 109.9, 49.9, 39.1, 31.3, 26.2, 25.8. IR (neat, cm^{-1}): 3059, 2926, 2852, 1635, 1500, 1449, 1405, 1329, 967, 755, 741, 700.

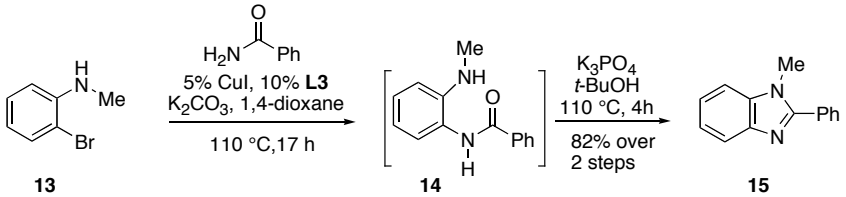


1-(cyclohexylmethyl)-2-pentyl-1*H*-benzimidazole (**Scheme 4**, **12c**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **10** (204 mg, 0.65 mmol) was coupled with hexanamide (89.6 mg, 0.78 mmol). The cyclodehydration step was accomplishing using procedure D (1 mL of AcOH). The crude product was purified by flash chromatography on silica gel (Biotage, 8-66% ethyl acetate

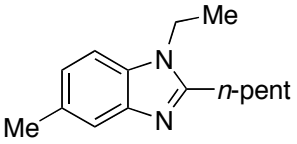
in hexanes gradient) to provide the title compound as a brown oil (160 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.76-7.70 (m, 1H), 7.32-7.28 (m, 1H), 7.25-7.19 (m, 2H), 3.92 (d, *J* = 7.4Hz, 2H), 2.84 (dd, *J* = 7.9, 8.0Hz, 2H), 1.98-1.80 (m, 3H), 1.75-1.62 (m, 5H), 1.50-1.34 (m, 4H), 1.24-0.98 (m, 5H), 0.93 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.6, 142.8, 135.6, 121.8, 121.6, 119.2, 109.7, 50.1, 38.7, 31.9, 31.2, 27.7, 27.6, 26.3, 25.8, 22.6, 14.2. IR (neat, cm^{-1}): 2926, 2853, 1615, 1508, 1458, 1409, 1328, 1285, 740. Anal. Calcd for $C_{17}H_{18}N_2$: C, 80.23; H, 9.92. Found: C, 79.97; H, 9.92.



2-cyclohexyl-1-(cyclohexylmethyl)-1*H*-benzimidazole (**Scheme 4**, **12d**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **10** (156 mg, 0.49 mmol) was coupled with cyclohexanecarboxamide (75.4 mg, 0.59 mmol). The cyclodehydration step was accomplishing using procedure D (1 mL of AcOH, 12 h at 75 °C instead of the standard 2 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 (122 mg, 83%). mp 90-91 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.76-7.73 (m, 1H), 7.32-7.28 (m, 1H), 7.23-7.20 (m, 2H), 3.94 (d, *J* = 7.5Hz, 2H), 2.81 (tt, *J* = 11.6, 3.4Hz, 1H), 1.95-1.63 (m, 13H), 1.47-1.37 (m, 3H), 1.24-1.14 (m, 3H), 1.09-1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 159.7, 142.9, 135.3, 121.8, 121.7, 119.4, 109.9, 49.9, 38.9, 36.6, 32.3, 31.3, 26.7, 26.4, 25.96, 25.95. IR (neat, cm^{-1}): 2927, 2852, 1503, 1459, 1420, 1347, 1272, 742.

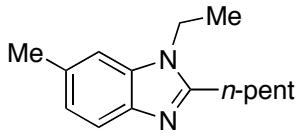


1-methyl-2-phenyl-1*H*-benzimidazole[8] (**Scheme 4**, **15**) Following procedure A, 2-Bromo-*N*-methylaniline **13** (123 μL, 1.0 mmol) was coupled with benzamide (145 mg, 1.2 mmol). The cyclodehydration step was accomplishing using procedure C (318 mg of K_3PO_4, 1 mL of *t*-BuOH, 4 h). The crude product was purified by flash chromatography on silica gel (gradient elution: 1.5/1, 1/1, and then 1/1.5 hexanes/ ethyl acetate) to provide **15** as a brown solid (171 mg, 82 %). mp 97-99 °C (lit. 92-94 °C).[8] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.88-7.81 (m, 1H), 7.80-7.74 (m, 2H), 7.57-7.50 (m, 3H), 7.43-7.30 (m, 3H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.8, 143.0, 136.6, 130.3, 129.8, 129.5, 128.7, 122.8, 122.5, 119.9, 109.7, 31.7. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81. Found: C, 80.48; H, 5.84.

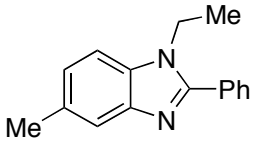


1-ethyl-5-methyl-2-pentyl-1*H*-benzimidazole (**Scheme 5**, **18a**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16a** (242 mg, 0.93 mmol) was coupled with hexanamide (128 mg, 1.1 mmol). The cyclodehydration step was accomplishing using procedure D (1 mL of AcOH). The

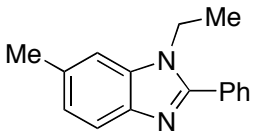
crude product was purified by flash chromatography on silica gel (gradient elution: 2/1, and then 1.5/1 hexanes/ ethyl acetate) to provide the title compound as a light yellow solid (166 mg, 78%). mp 48-50 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.51 (s, 1H), 7.19 (d, *J* = 8.2Hz, 1H), 7.06 (dd, *J* = 8.2, 1.6Hz, 1H), 4.14 (q, *J* = 7.3Hz, 2H), 2.84 (t, *J* = 7.9Hz, 2H), 2.47 (s, 3H), 1.94-1.83 (m, 2H), 1.48-1.36 (m, 4H), 1.40 (t, *J* = 7.2Hz, 3H), 0.92 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 154.8, 143.2, 132.8, 131.2, 123.2, 119.1, 108.6, 38.3, 31.8, 27.7, 27.5, 22.5, 21.6, 15.2, 14.1. IR (neat, cm^{-1}): 2956, 2931, 2871, 1508, 1456, 1410, 1324, 1277, 1107, 967, 791, 605. Anal. Calcd for $C_{15}H_{22}N_2$: C, 78.21; H, 9.63. Found: C, 78.30; H, 9.63.



1-ethyl-6-methyl-2-pentyl-1*H*-benzimidazole (**Scheme 5**, **18b**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16b** (231 mg, 0.88 mmol) was coupled with hexanamide (122 mg, 1.1 mmol). The cyclodehydration step was accomplishing using procedure D (1 mL of AcOH). The crude product was purified by flash chromatography on silica gel (gradient elution: 2/1, and then 1.5/1 hexanes/ ethyl acetate) to provide the title compound as a brown solid (133 mg, 65%). mp 48-49 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 8.2Hz, 1H), 7.10 (s, 1H), 7.05 (dd, *J* = 8.2, 1.6Hz, 1H), 4.14 (q, *J* = 7.3Hz, 2H), 2.84 (t, *J* = 7.9Hz, 2H), 2.50 (s, 3H), 1.94-1.84 (m, 2H), 1.49-1.33 (m, 4H), 1.41 (t, *J* = 7.2Hz, 3H), 0.92 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 154.4, 141.0, 135.0, 131.8, 123.2, 118.8, 109.2, 38.3, 31.9, 27.7, 27.6, 22.6, 21.9, 15.2, 14.1. IR (neat, cm^{-1}): 2956, 2930, 2860, 1515, 1471, 1413, 1332, 1282, 1097, 967, 808, 606. Anal. Calcd for $C_{15}H_{22}N_2$: C, 78.21; H, 9.63. Found: C, 78.46; H, 9.82.

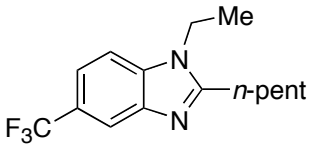


1-ethyl-5-methyl-2-phenyl-1*H*-benzimidazole (**Scheme 5**, **18c**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16a** (168 mg, 0.61 mmol) was coupled with benzamide (88.6 mg, 0.73 mmol). The cyclodehydration step was accomplishing using procedure C (194 mg of K_3PO_4, 0.6 mL of *t*-BuOH, 8 h). The crude product was purified by flash chromatography on silica gel (gradient elution: 3/1, and then 2/1 hexanes/ ethyl acetate) to provide the title compound as a yellow solid (120 mg, 79%). mp 90-92 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.75-7.70 (m, 2H), 7.63-7.62 (m, 1H), 7.56-7.49 (m, 3H), 7.32 (d, *J* = 8.2Hz, 1H), 7.15 (dd, *J* = 8.2, 1.6Hz, 1H), 4.26 (q, *J* = 7.2Hz, 2H), 2.52 (s, 3H), 1.46 (t, *J* = 7.2Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.4, 143.5, 133.5, 131.9, 130.7, 129.6, 129.2, 128.7, 124.1, 119.7, 109.5, 39.6, 21.6, 15.3. IR (neat, cm^{-1}): 2976, 1471, 1446, 1386, 1348, 1325, 1153, 793, 771, 700. Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82. Found: C, 81.18; H, 6.88.

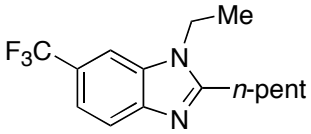


1-ethyl-6-methyl-2-phenyl-1*H*-benzimidazole (**Scheme 5**, **18d**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16b** (165 mg, 0.63 mmol) was coupled with benzamide (91.6 mg, 0.76 mmol). The cyclodehydration step was accomplishing using procedure C (201 mg of K_3PO_4, 0.6

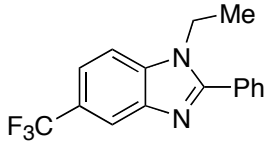
mL of *t*-BuOH, 8 h). The crude product was purified by flash chromatography on silica gel (gradient elution: 4/1, and then 3/1 hexanes/ ethyl acetate) to provide the title compound as a white solid (126 mg, 85%). mp 161-162 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.74-7.72 (m, 3H), 7.55-7.51 (m, 3H), 7.23 (s, 1H), 7.15 (d, *J* = 8.2Hz, 1H), 4.27 (q, *J* = 7.2Hz, 2H), 2.55 (s, 3H), 1.48 (t, *J* = 7.2Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.1, 141.5, 135.7, 132.7, 130.8, 129.7, 129.3, 128.8, 124.0, 119.6, 110.0, 39.6, 22.1, 15.4. IR (neat, cm^{-1}): 2981, 1467, 1399, 1356, 1330, 1269, 1098, 802, 782, 706, 699, 606. Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82. Found: C, 81.21; H, 6.84.



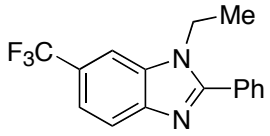
1-ethyl-2-pentyl-5-(trifluoromethyl)-1*H*-benzimidazole (**Scheme 5**, **18e**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16c** (230 mg, 0.73 mmol) was coupled with hexanamide (101 mg, 0.88 mmol). The cyclodehydration step was accomplishing using procedure D (1 mL of AcOH). The crude product was purified by flash chromatography on silica gel (gradient elution: 4/1, and then 3/1 hexanes/ ethyl acetate) to provide the title compound as a gray solid (163 mg, 78%). mp 41-43 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.00 (s, 1H), 7.49 (dd, *J* = 8.5, 1.6Hz, 1H), 7.39 (d, *J* = 8.4Hz, 1H), 4.21 (q, *J* = 7.3Hz, 2H), 2.88 (t, *J* = 7.9Hz, 2H), 1.95-1.89 (m, 2H), 1.49-1.37 (m, 4H), 1.44 (t, *J* = 7.3Hz, 3H), 0.94 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 157.1, 142.4, 136.8, 125.1 (q, *J* = 271.6Hz), 124.2 (q, *J* = 32.1Hz), 118.9 (q, *J* = 3.5Hz), 116.9 (q, *J* = 4.0Hz), 109.5, 38.7, 31.8, 27.6, 27.5, 22.5, 15.2, 14.1. IR (neat, cm^{-1}): 2959, 2874, 1515, 1444, 1405, 1329, 1158, 1142, 1117, 1050, 929, 807. Anal. Calcd for $C_{15}H_{19}F_3N_2$: C, 63.37; H, 6.74. Found: C, 63.29; H, 6.75.



1-ethyl-2-pentyl-6-(trifluoromethyl)-1*H*-benzimidazole (**Scheme 5**, **18f**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16d** (240 mg, 0.76 mmol) was coupled with hexanamide (105 mg, 0.91 mmol). The cyclodehydration step was accomplishing using procedure D (1 mL of AcOH). The crude product was purified by flash chromatography on silica gel (gradient elution: 4/1, and then 3/1 hexanes/ ethyl acetate) to provide the title compound as an off-white solid (189 mg, 87%). mp 57-59 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.79 (d, *J* = 8.4Hz, 1H), 7.59 (t, *J* = 0.8Hz, 1H), 7.49 (dd, *J* = 8.4, 1.2Hz, 1H), 4.23 (q, *J* = 7.3Hz, 2H), 2.89 (t, *J* = 7.9Hz, 2H), 1.96-1.90 (m, 2H), 1.49-1.37 (m, 4H), 1.46 (t, *J* = 7.3Hz, 3H), 0.94 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 157.6, 145.2, 134.2, 125.1 (q, *J* = 271.6Hz), 124.1 (q, *J* = 32.1Hz), 119.5, 118.8 (q, *J* = 3.6Hz), 106.7 (q, *J* = 4.2Hz), 109.5, 38.6, 31.8, 27.5, 27.4, 22.5, 15.2, 14.0. IR (neat, cm^{-1}): 2959, 2934, 2874, 1512, 1460, 1345, 1308, 1284, 1160, 1117, 1050, 823, 666. Anal. Calcd for $C_{15}H_{19}F_3N_2$: C, 63.37; H, 6.74. Found: C, 63.32; H, 6.77.

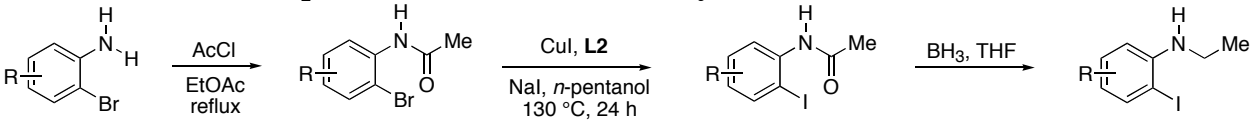


1-ethyl-2-phenyl-5-(trifluoromethyl)-1*H*-benzimidazole (**Scheme 5**, **18g**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16d** (116 mg, 0.37 mmol) was coupled with benzamide (53.4 mg, 0.44 mmol). The cyclodehydration step was accomplishing using procedure C (117 mg of K_3PO_4, 0.4 mL of *t*-BuOH, 8 h). The crude product was purified by flash chromatography on silica gel (gradient elution: 4/1, and then 3/1 hexanes/ ethyl acetate) to provide the title compound as a white solid (99.9 mg, 94%). mp 108-110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.11 (s, 1H), 7.75-7.70 (m, 2H), 7.59-7.50 (m, 5H), 4.33 (q, *J* = 7.2Hz, 2H), 1.49 (t, *J* = 7.3Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.6, 142.8, 137.5, 130.3, 130.0, 129.3, 129.0, 125.0 (q, *J* = 271.8Hz), 124.9 (q, *J* = 32.1Hz), 119.7 (q, *J* = 3.5Hz), 117.7 (q, *J* = 4.2Hz), 110.5, 40.0, 15.3. IR (neat, cm^{-1}): 1620, 1436, 1385, 1331, 1234, 1147, 1115, 1050, 885, 813, 775, 707. Anal. Calcd for $C_{16}H_{13}F_3N_2$: C, 66.20; H, 4.51. Found: C, 66.34; H, 4.55.

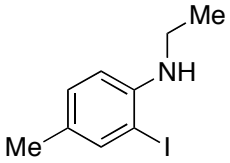


1-ethyl-2-phenyl-6-(trifluoromethyl)-1*H*-benzimidazole (**Scheme 5**, **18h**) Following procedure B, *ortho*-iodo-*N*-alkylaniline **16d** (149 mg, 0.47 mmol) was coupled with benzamide (68.8 mg, 0.57 mmol). The cyclodehydration step was accomplishing using procedure C (151 mg of K_3PO_4, 0.5 mL of *t*-BuOH, 8 h). The crude product was purified by flash chromatography on silica gel (gradient elution: 4/1, and then 3/1 hexanes/ ethyl acetate) to provide the title compound as a white solid (114 mg, 83%). mp 141-143 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.91 (dd, *J* = 8.6, 0.7Hz, 1H), 7.77-7.73 (m, 2H), 7.72 (t, *J* = 0.8Hz, 1H), 7.58-7.55 (m, 4H), 4.36 (q, *J* = 7.3Hz, 2H), 1.52 (t, *J* = 7.3Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.1, 145.5, 135.0, 130.4, 130.0, 129.4, 129.0, 125.0 (q, *J* = 272.0Hz), 124.9 (q, *J* = 32.1Hz), 120.5, 119.5 (q, *J* = 3.5Hz), 107.8 (q, *J* = 4.4Hz), 40.0, 15.5. IR (neat, cm^{-1}): 1467, 1400, 1345, 1309, 1158, 1113, 869, 821, 780, 711, 700, 664. Anal. Calcd for $C_{16}H_{13}F_3N_2$: C, 66.20; H, 4.51. Found: C, 66.08; H, 4.51.

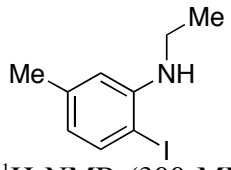
Procedure for the Preparation of *ortho*-Iodo-*N*-Alkylanilines 16a-d Used in Scheme 5



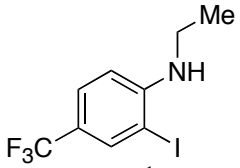
ortho-Iodo-*N*-alkylanilines **16a-d** were prepared via a three-step sequence (acetamide formation, copper-catalyzed halogen exchange, and borane reduction of acetamide) starting from the corresponding commercial available *ortho*-bromoanilines. The procedures for acetamide formation[5] and copper-catalyzed halogen exchange[9] have been previously disclosed. Full characterizations of **16a-d** are listed below.



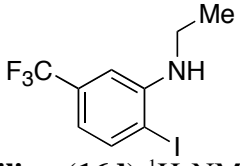
***N*-ethyl-2-iodo-4-methylaniline** (**16a**) ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 2.0Hz, 1H), 7.03 (dd, *J* = 8.3, 2.0Hz, 1H), 6.49 (d, *J* = 8.3Hz, 1H), 3.89 (bs, 1H), 3.18 (q, *J* = 7.1Hz, 2H), 2.22 (s, 3H), 1.31 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 145.4, 139.3, 130.1, 127.9, 110.6, 85.5, 39.1, 20.0, 14.9. IR (neat, cm^{-1}): 3389, 2968, 2867, 1608, 1514, 1312, 1273, 1163, 1029, 799, 664. Anal. Calcd for $C_9H_{12}IN$: C, 41.40; H, 4.63. Found: C, 41.68; H, 4.71.



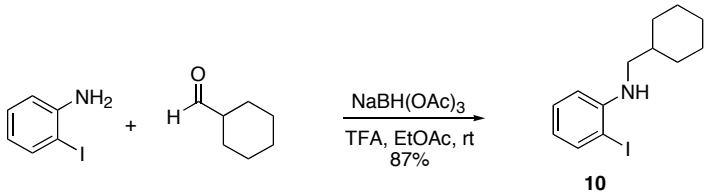
***N*-ethyl-2-iodo-5-methylaniline** (**16b**) ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 8.0Hz, 1H), 6.40 (d, *J* = 1.7Hz, 1H), 6.29 (ddd, *J* = 7.9, 2.0, 0.6Hz, 1H), 3.99 (bs, 1H), 3.19 (qd, *J* = 7.1, 5.2Hz, 2H), 2.28 (s, 3H), 1.32 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 147.2, 139.5, 138.6, 119.6, 111.5, 81.6, 38.8, 21.6, 14.8. IR (neat, cm^{-1}): 3391, 2968, 2869, 1591, 1505, 1419, 1304, 1187, 1004, 786, 584. Anal. Calcd for $C_9H_{12}IN$: C, 41.40; H, 4.63. Found: C, 41.16; H, 4.58.



***N*-ethyl-2-iodo-4-(trifluoromethyl)aniline** (**16c**) ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.88 (d, *J* = 1.5Hz, 1H), 7.45 (ddd, *J* = 8.6, 1.4, 0.7Hz, 1H), 6.54 (d, *J* = 8.6Hz, 1H), 4.44 (bs, 1H), 3.25 (qd, *J* = 7.1, 5.2Hz, 2H), 1.35 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 149.8, 136.1 (q, *J* = 3.8Hz), 126.9 (q, *J* = 3.8Hz), 124.1 (q, *J* = 270.8Hz), 119.8 (q, *J* = 33.0 Hz), 109.2, 83.7, 38.7, 14.5. IR (neat, cm^{-1}): 3398, 2975, 2875, 1607, 1532, 1322, 1280, 1154, 1112, 1079, 805, 675. Anal. Calcd for $C_9H_9F_3IN$: C, 34.31; H, 2.88. Found: C, 34.66; H, 2.87.



***N*-ethyl-2-iodo-5-(trifluoromethyl)aniline** (**16d**) ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.75 (dd, *J* = 8.1, 0.8Hz, 1H), 6.70 (s, 1H), 6.67 (ddd, *J* = 8.1, 2.1, 0.6Hz, 1H), 4.28 (bs, 1H), 3.24 (qd, *J* = 7.1, 5.2Hz, 2H), 1.36 (t, *J* = 7.1Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 147.8, 139.5, 132.1 (q, *J* = 32.1Hz), 124.4 (q, *J* = 272.4Hz), 114.6 (q, *J* = 4.0Hz), 106.4 (q, *J* = 4.0Hz), 88.8 (q, *J* = 1.2Hz), 38.8, 14.6. IR (neat, cm^{-1}): 3398, 2974, 1597, 1580, 1513, 1434, 1331, 1280, 1167, 1124, 1082, 1006, 854.



***N*-(cyclohexylmethyl)-2-iodoaniline** Following a published procedure,[10] 2-iodoaniline (2.0 g, 9.1 mmol) and cyclohexylcarboxyaldehyde (1.2 mL, 10.0 mmol) were converted to the title compound. The crude compound was purified by flash column chromatography on silica gel (gradient elution: hexanes and then 50/1 hexanes/ethyl acetate) to provide **10** as a light yellow oil (2.81 g, 87 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.65 (dd, *J* = 7.8, 1.6Hz, 1H), 7.20 (td, *J* = 8.2, 1.5Hz, 1H), 6.55 (dd, *J* = 8.2, 1.3Hz, 1H), 6.42 (td, *J* = 7.6, 1.5Hz, 1H), 4.24 (bs, 1H), 3.00 (t, *J* = 6.1Hz, 2H), 1.88-1.55 (m, 6H), 1.36-1.12 (m, 3H), 1.08-0.95 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 147.6, 139.1, 129.6, 118.3, 110.6, 85.6, 51.0, 37.4, 31.5, 26.7, 26.1. IR (neat, cm^{-1}): 3400, 2922, 2850, 1591, 1507, 1449, 1426, 1320, 1004, 739. Anal. Calcd for $C_{13}H_{18}IN$: C, 49.54; H, 5.76. Found: C, 49.78; H, 5.73.

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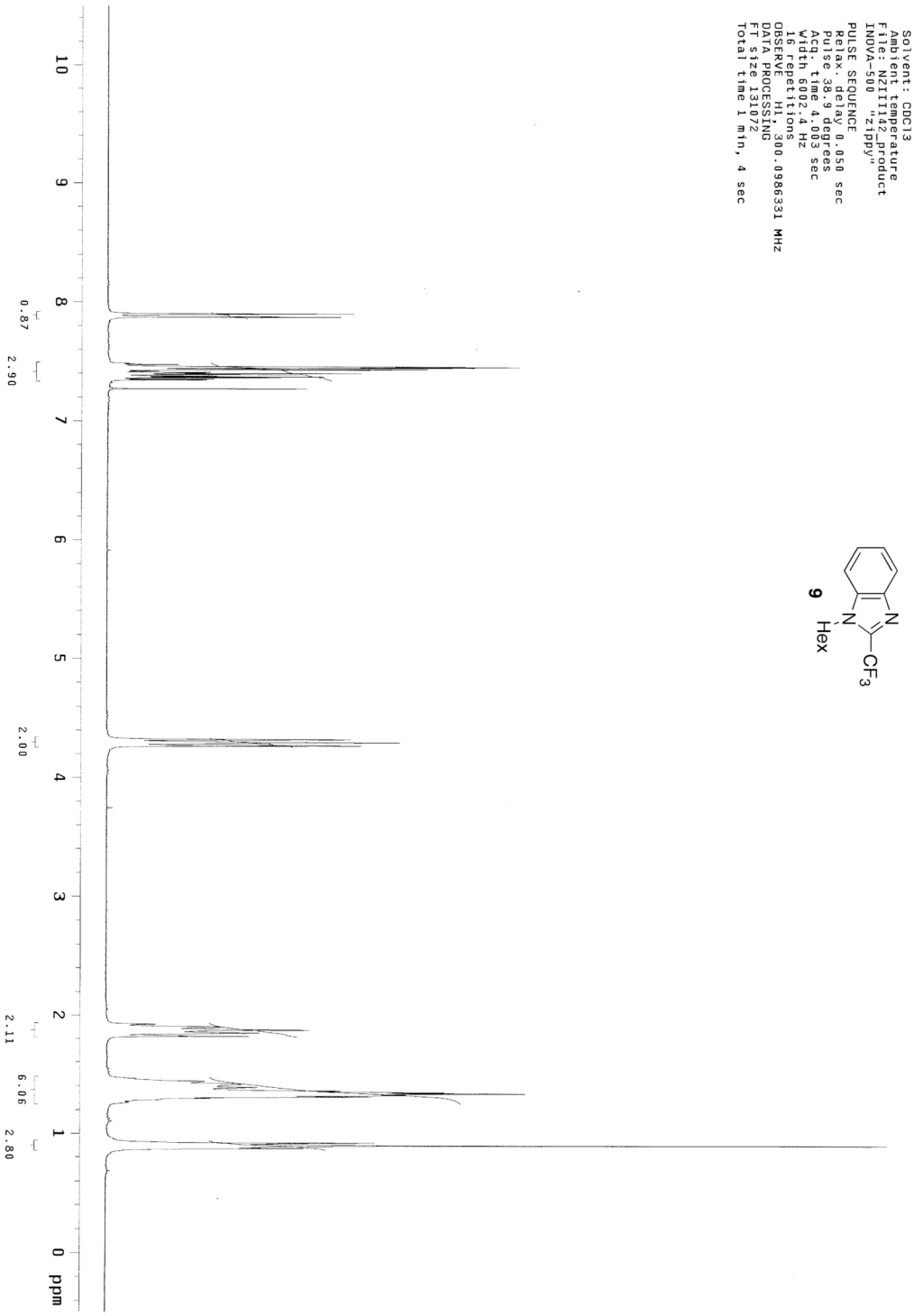
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Ambient temperature
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Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986331 MHz
DATA PROCESSING
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Total time 1 min, 4 sec
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N
CF3
Hex
9
10
9
8
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6
5
4
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2
1
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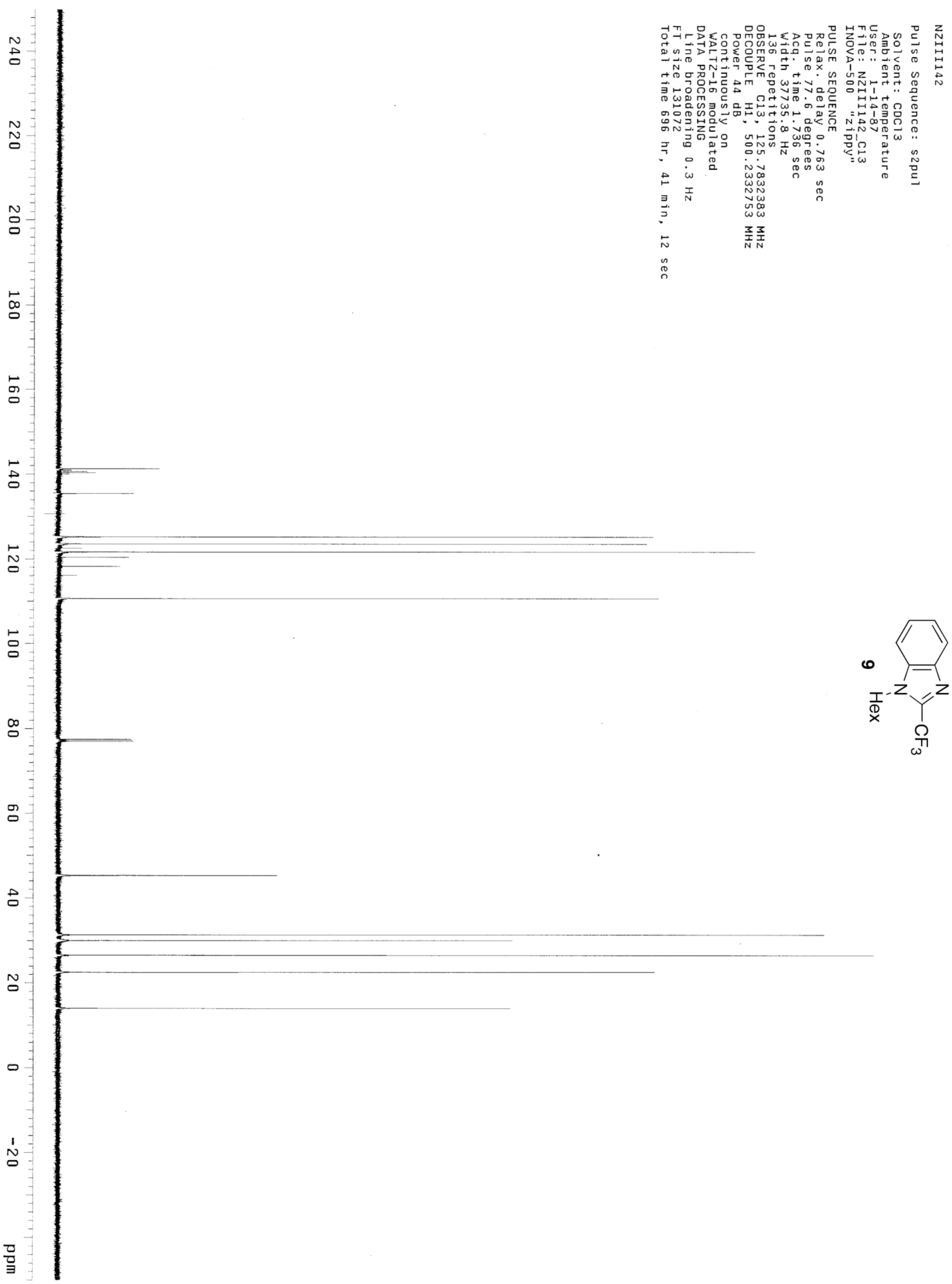
2.90
2.00
2.11
6.06
2.80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Ambient temperature
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INOVA-500 "zippy"
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Pulse 77.6 degrees
Acq. time 1.736 sec
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DECOUPLE H1, 500.2332753 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
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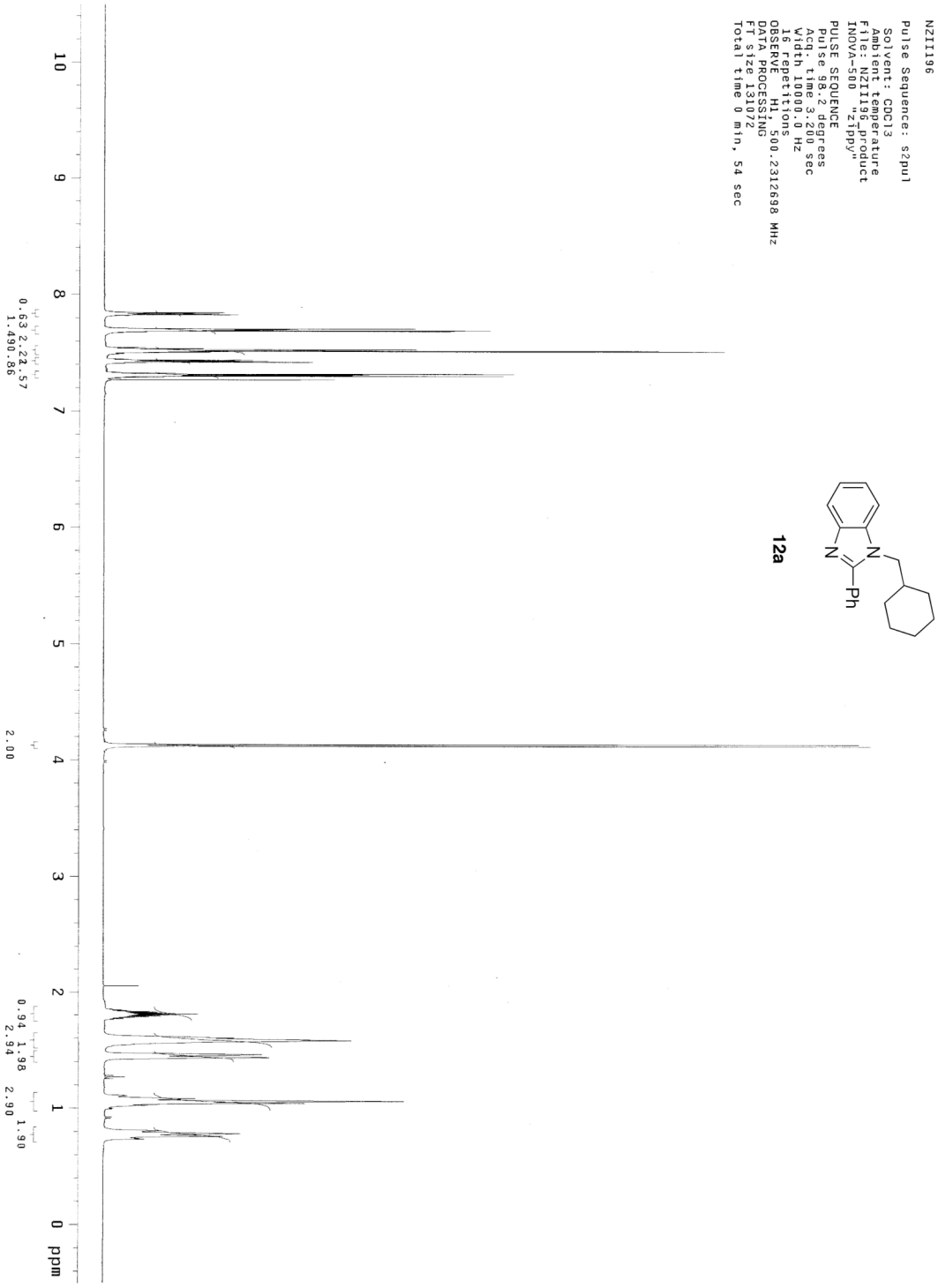
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Ambient temperature
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INOVA-500 "Tippy"
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Width 10000.0 Hz
16 repetitions
OBSERVE H1, 500.2312698 MHz
DATA PROCESSING
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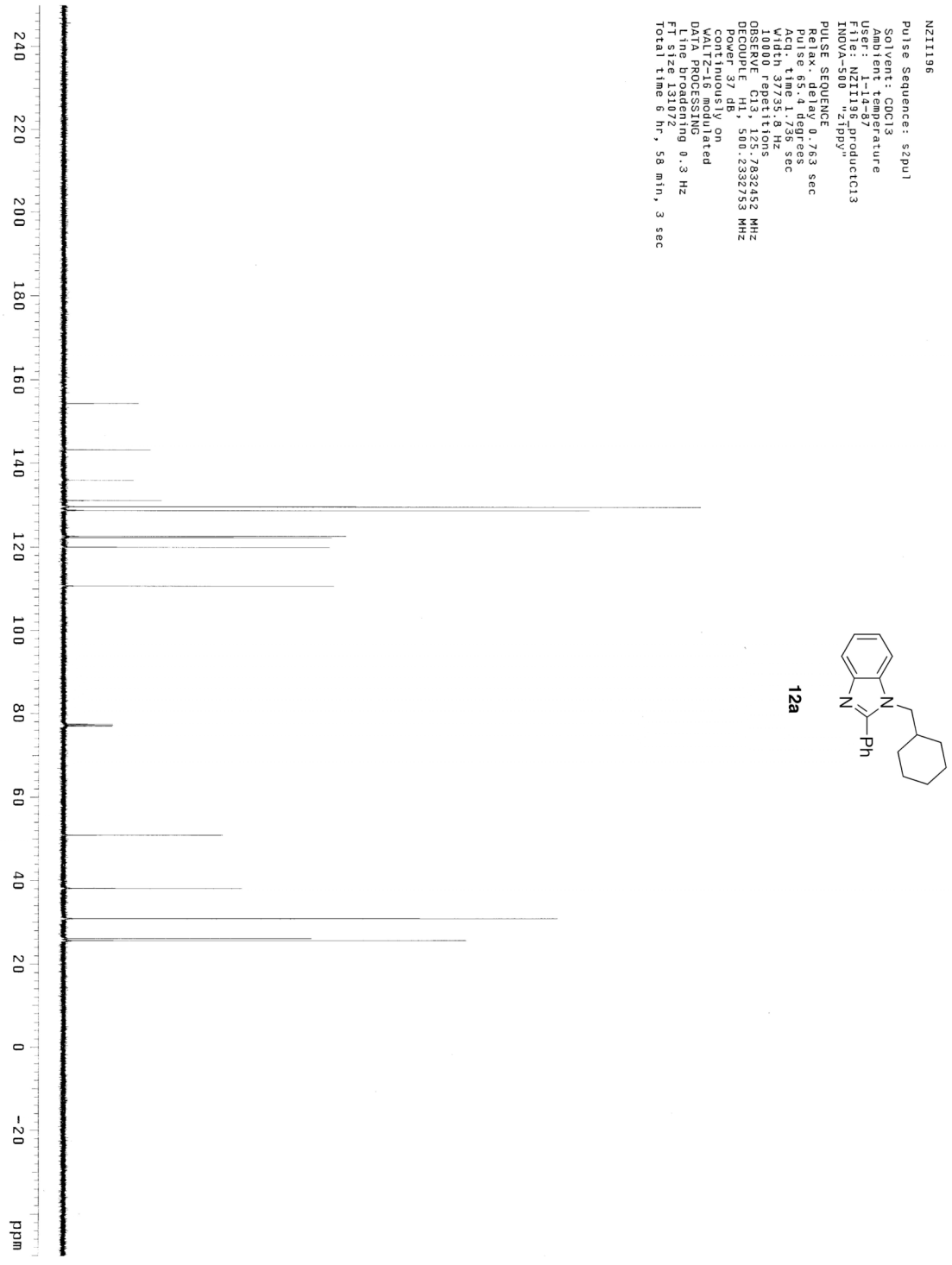
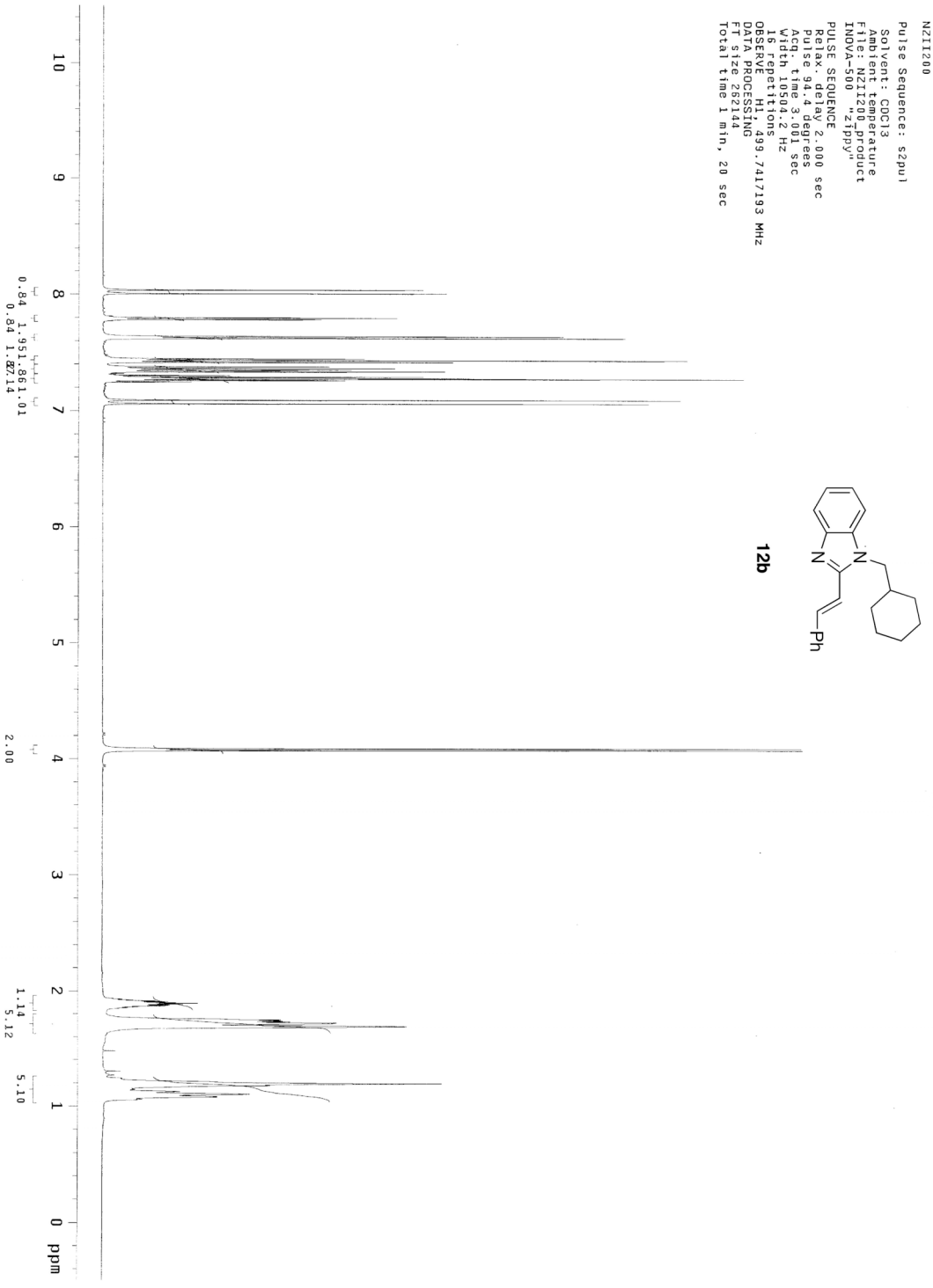
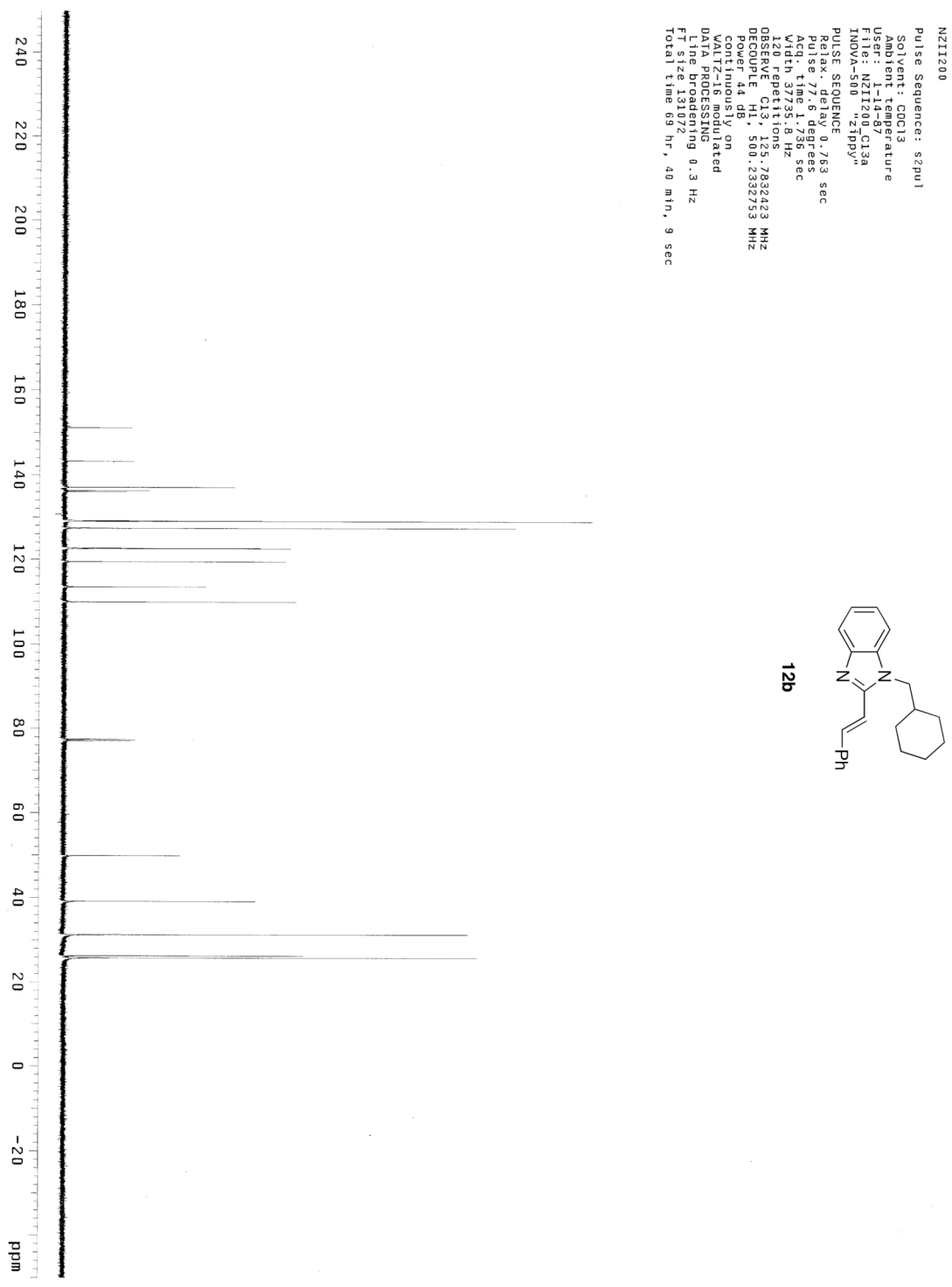
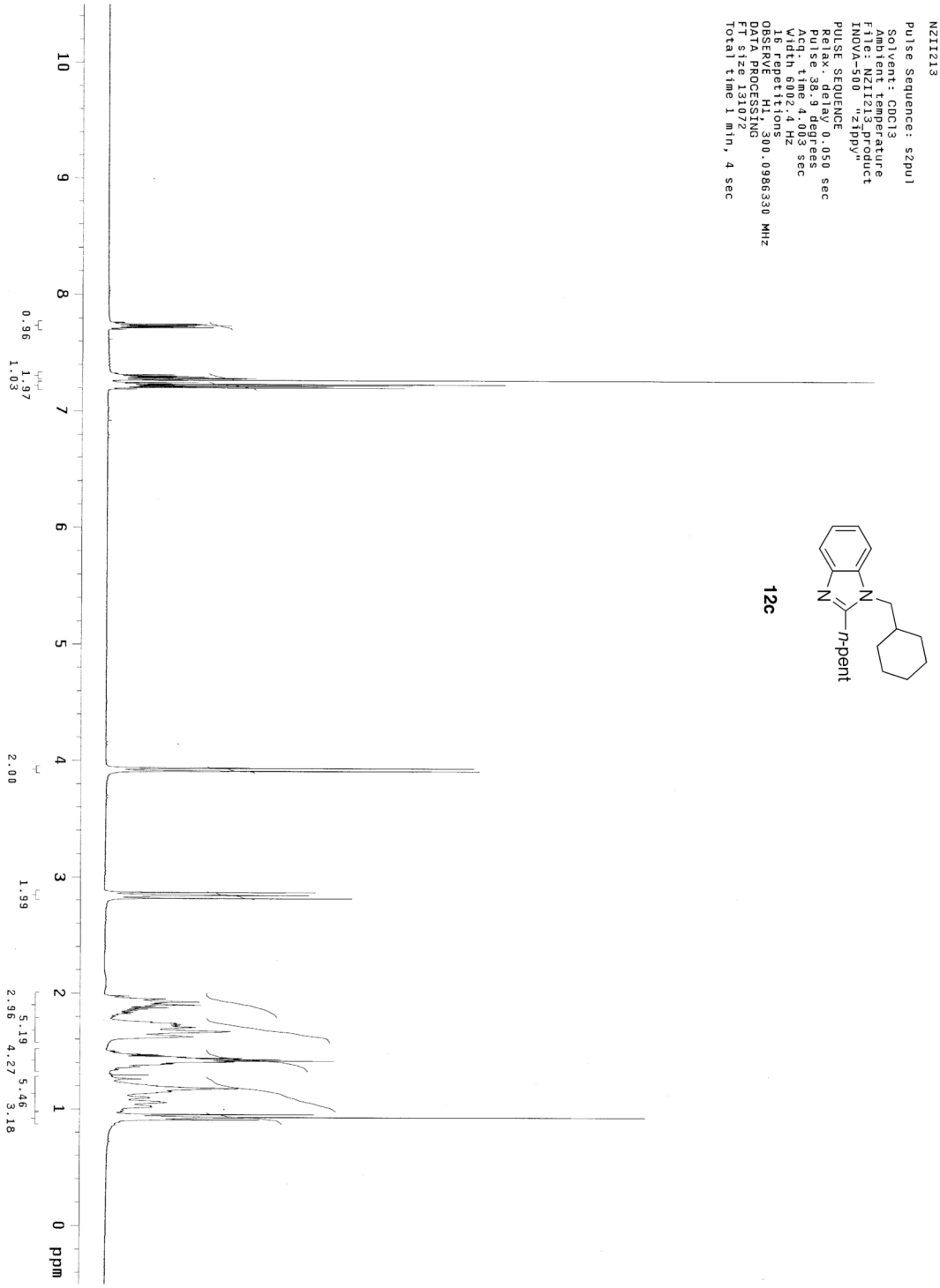
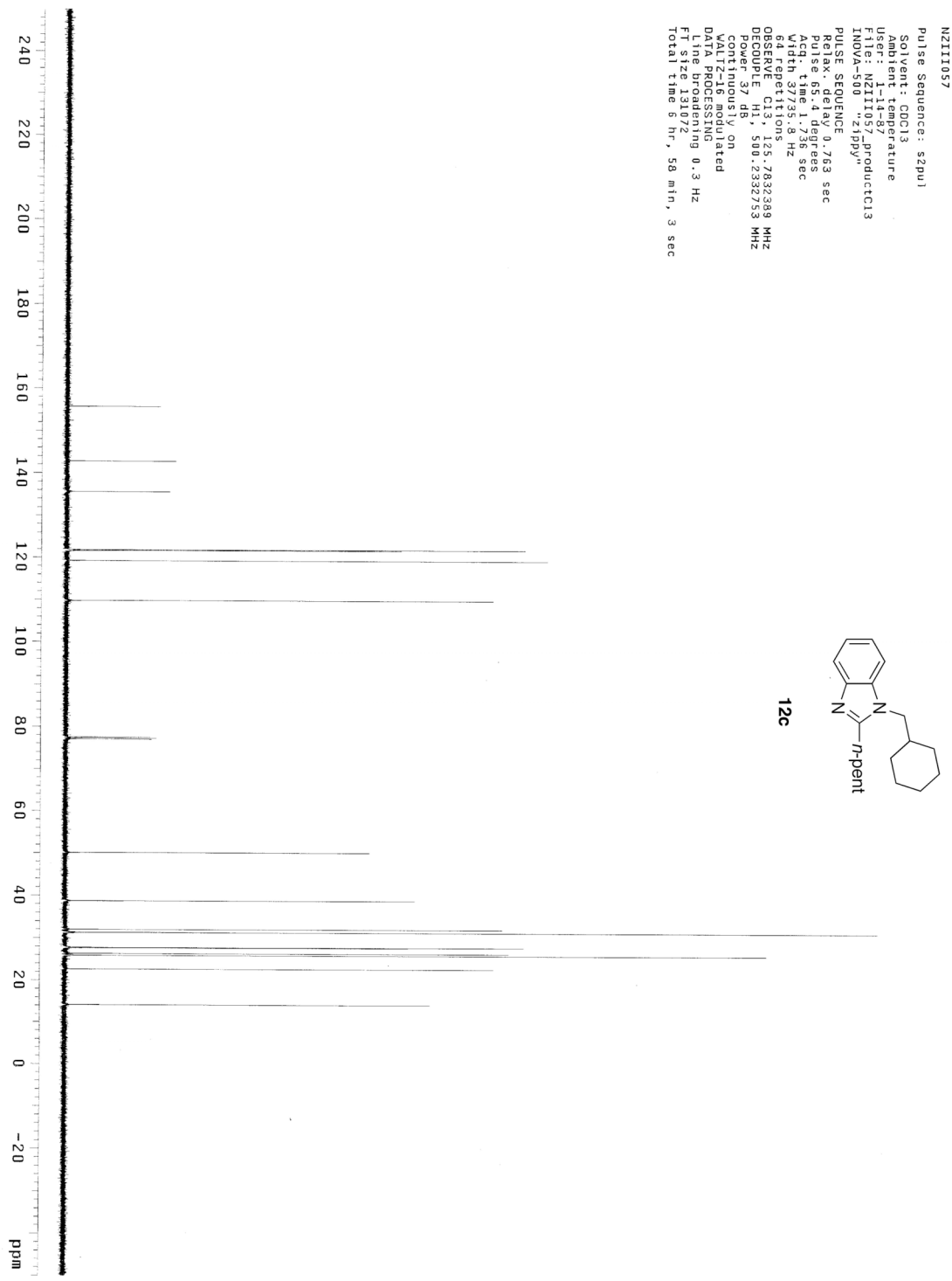
Total time 0 min, 54 sec
12a
N
N
Ph
10
9
8
7
6
5
4
3
2
1
0 ppm
0.63 2.22 2.57
1.49 0.86
2.00
0.94 1.98
2.94
1.90
2.90

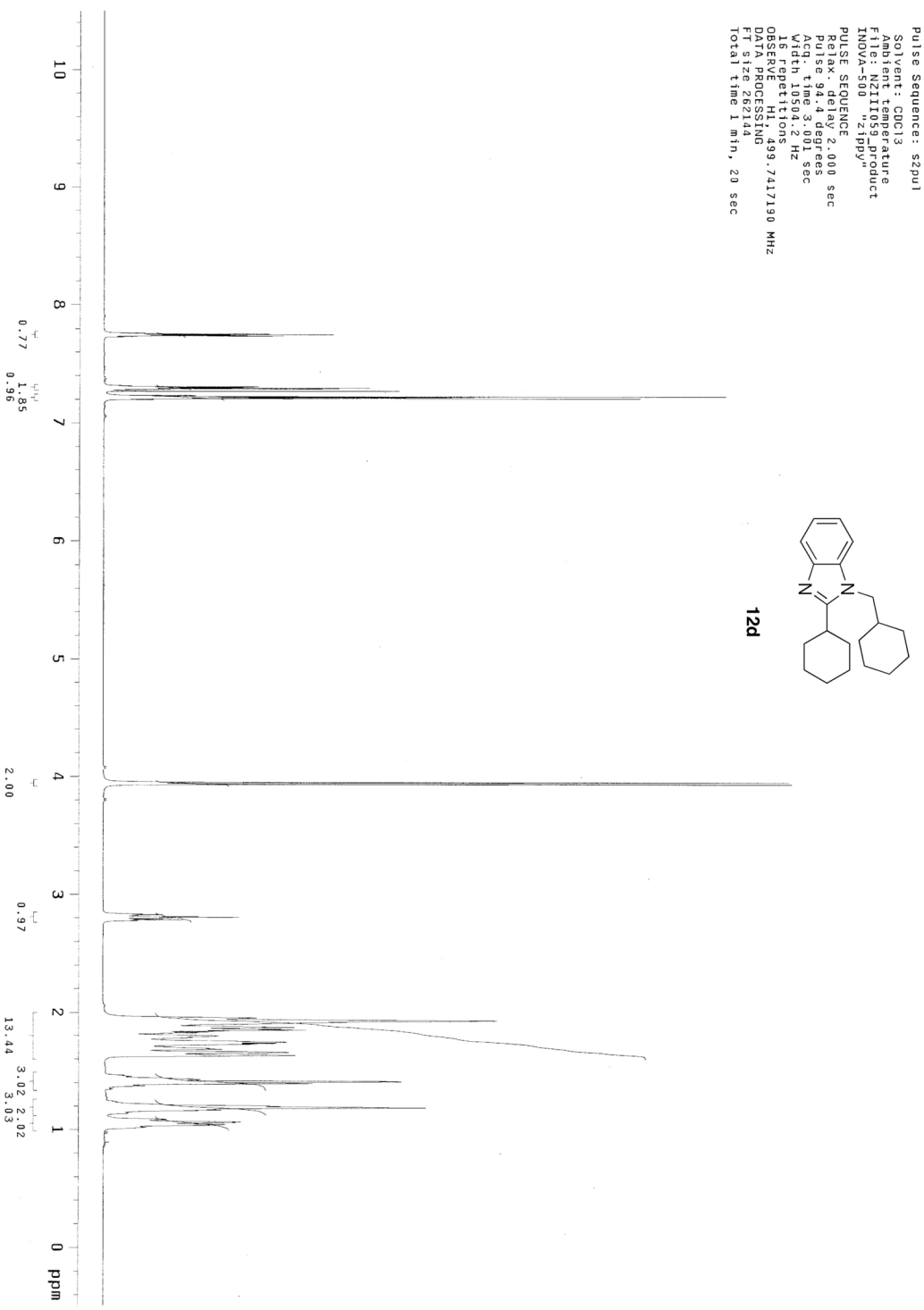

NZII196
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: ti14-8
File: NZII196_product13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
10000 repetitions
OBSERVE C13, 125.7832452 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
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
Ph
12a
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

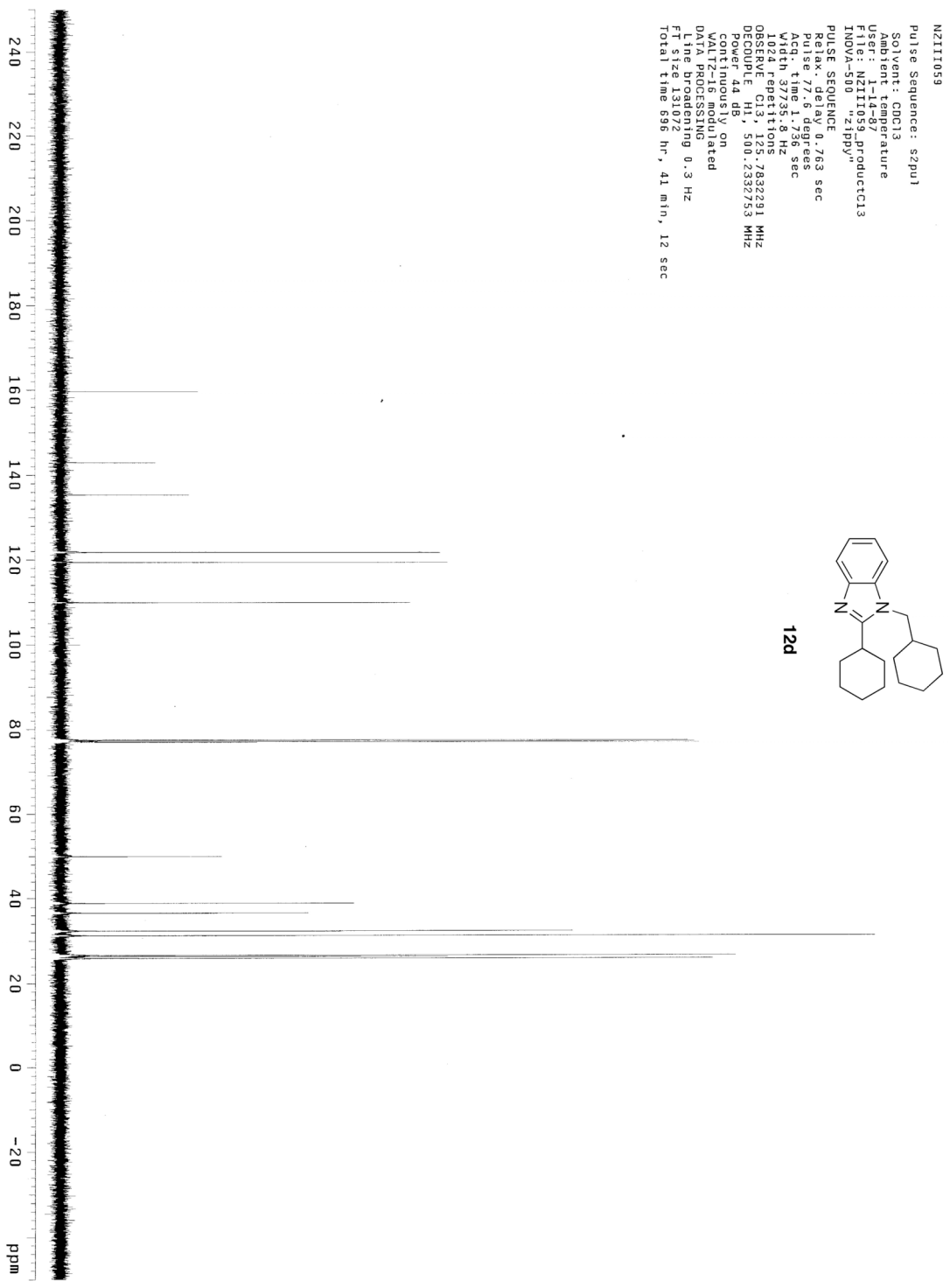

NZII200
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: nzii200_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 94.4 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
16 repetitions
OBSERVE H1, 499.7417193 MHz
DATA PROCESSING
FT size 262144
Total time 1 min, 20 sec
12b
N
N
Ph
10
9
8
7
6
5
4
3
2
1
0
ppm
0.84
1.95
1.86
1.01
0.84
1.82
7.14
2.00
1.14
5.12
5.10

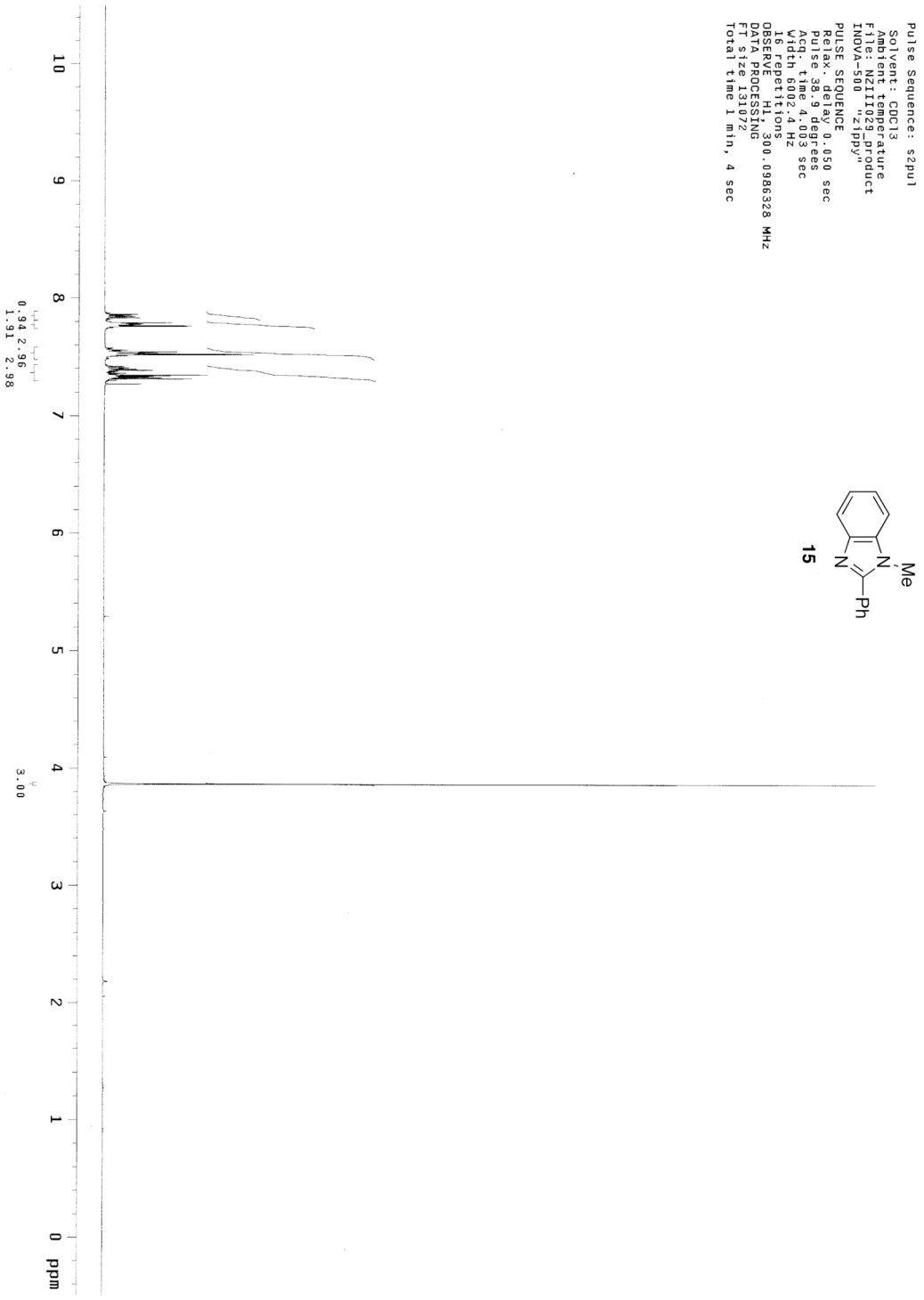

NZII200
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient_temperature
Using: NZII200/_C13a
File: NZII200/_C13a
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 77.6 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
128 repetitions
OBSERVE C13, 125.7832423 MHz
DECOUPLE H1, 500.2332753 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 69 hr, 40 min, 9 sec
N
N
Ph
12b
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

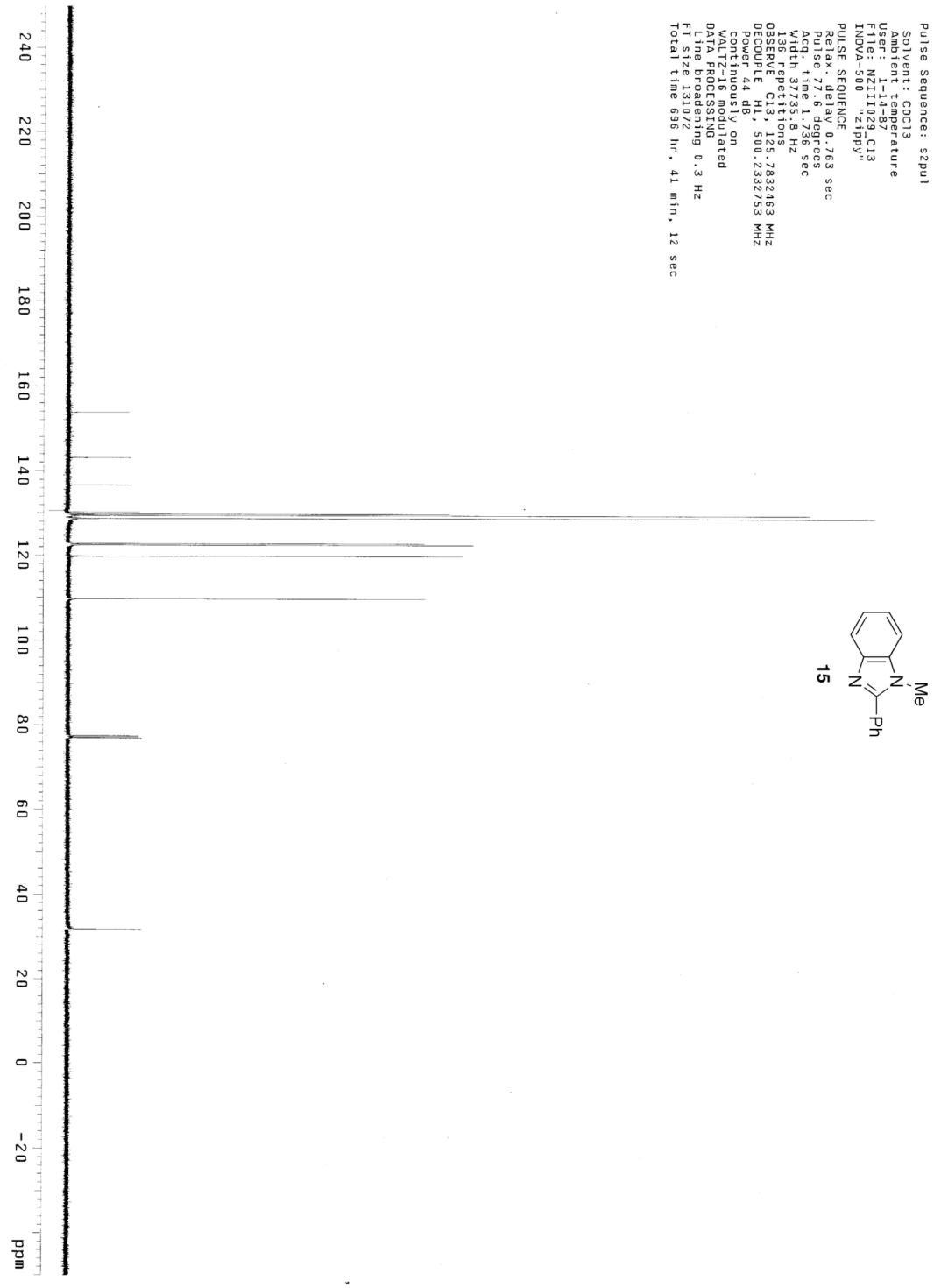

NZII213
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Field: NZII213_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986330 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
N
N
n-pent
12c
10
9
8
7
6
5
4
3
2
1
0 ppm
0.96
1.97
1.03
2.00
1.99
2.96
5.19
4.27
5.46
3.18

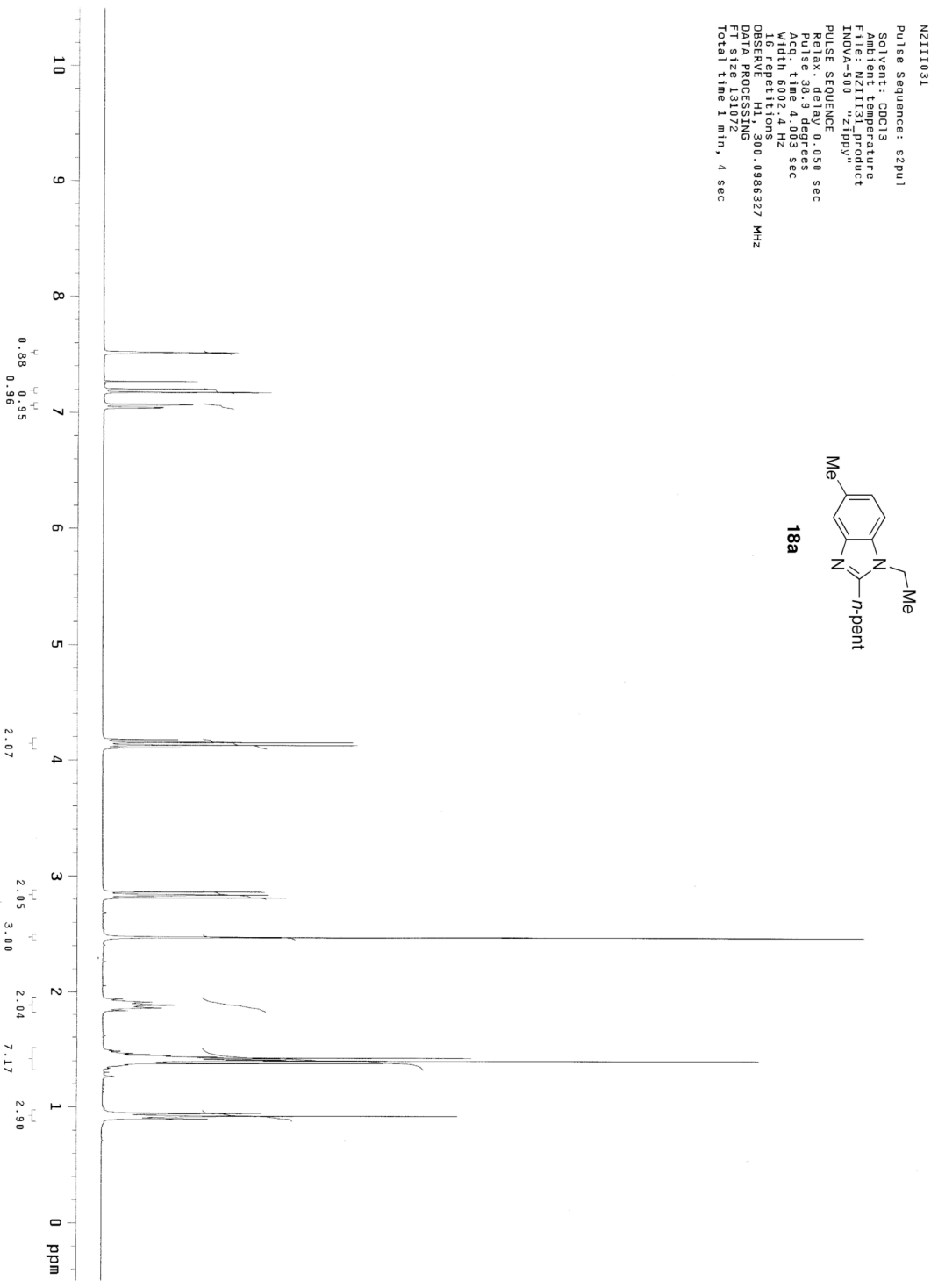

NZIII057
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZIII057_productC13
INOVA-500 "z1py"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
68 repetitions
OBSERVE C13, 125.7832389 MHz
DECOUPLE H1, 500.2332753 MHz
Continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
N
N
n-pent
12c
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

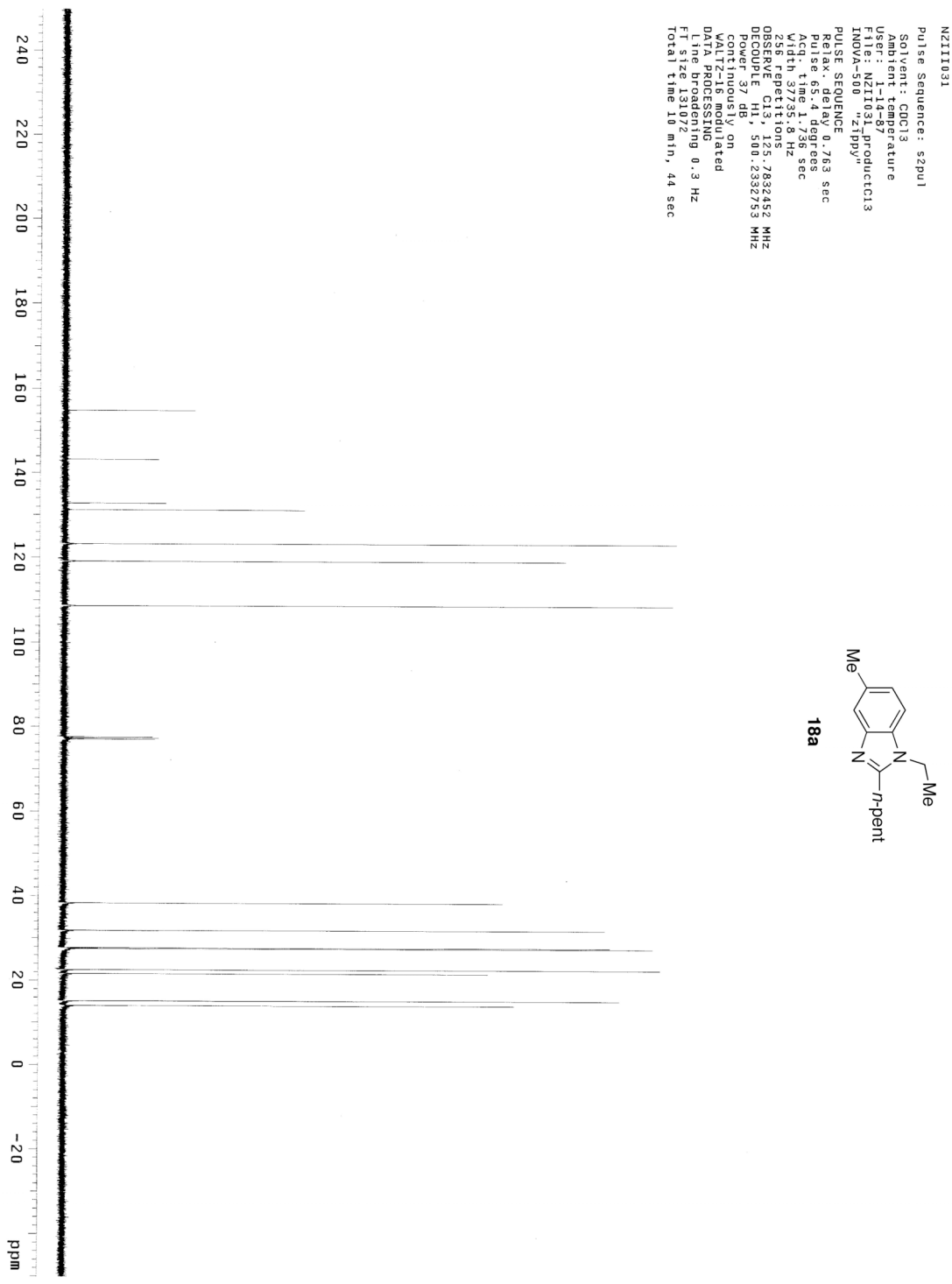

NZII059
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII059_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 94.4 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
16 repetitions
OBSERVE H1, 499.7417190 MHz
DATA PROCESSING
FT size 262144
Total time 1 min, 20 sec
12d
0.77
1.85
0.96
2.00
0.97
13.44
3.02
2.02
3.03
10
9
8
7
6
5
4
3
2
1
0
ppm

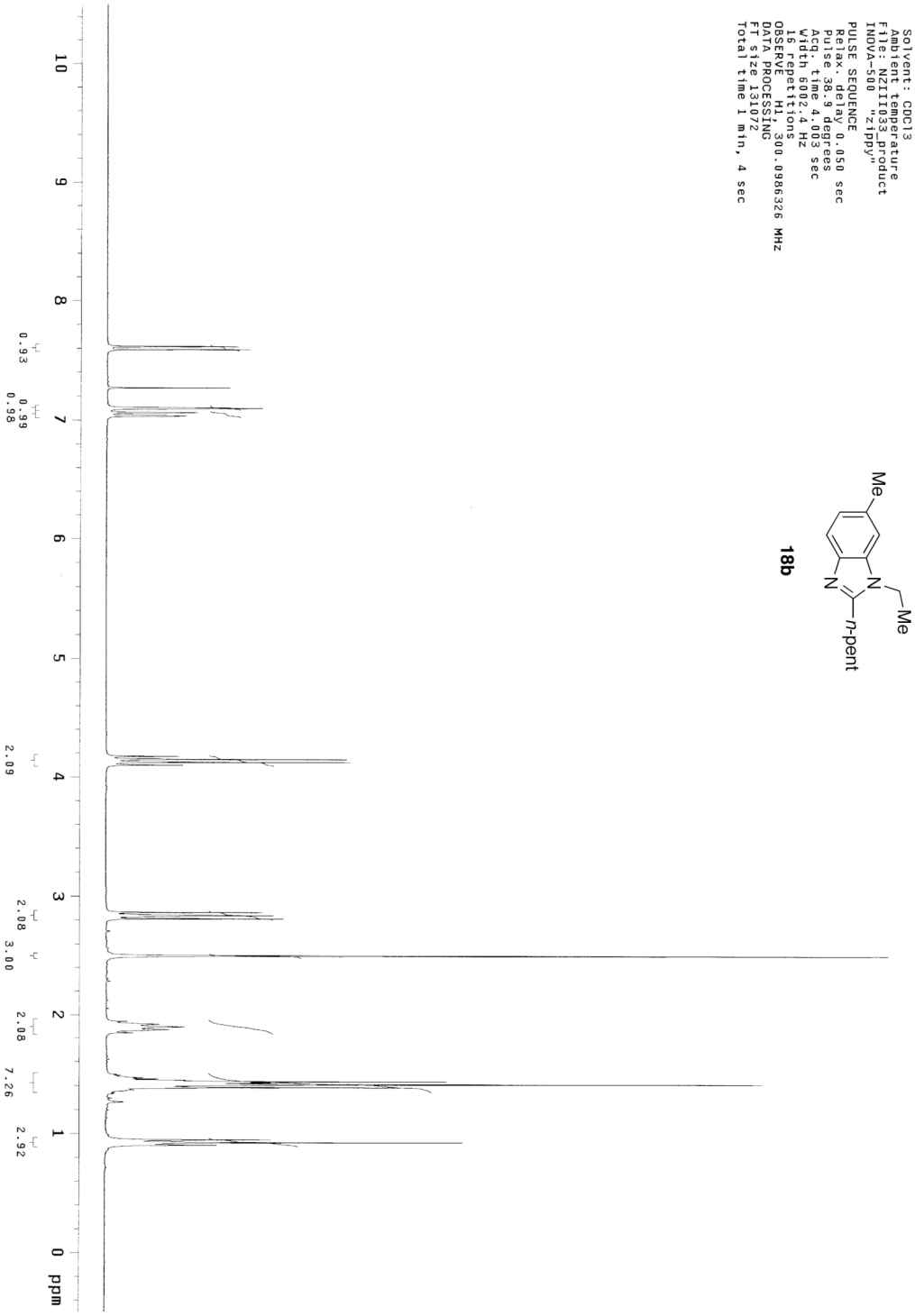

NZII059
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII059_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 75.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
1024 repetitions
OBSERVE C13, 125.7832291 MHz
DECOUPLE H1, 500.2332753 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 696 hr, 41 min, 12 sec
12d
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

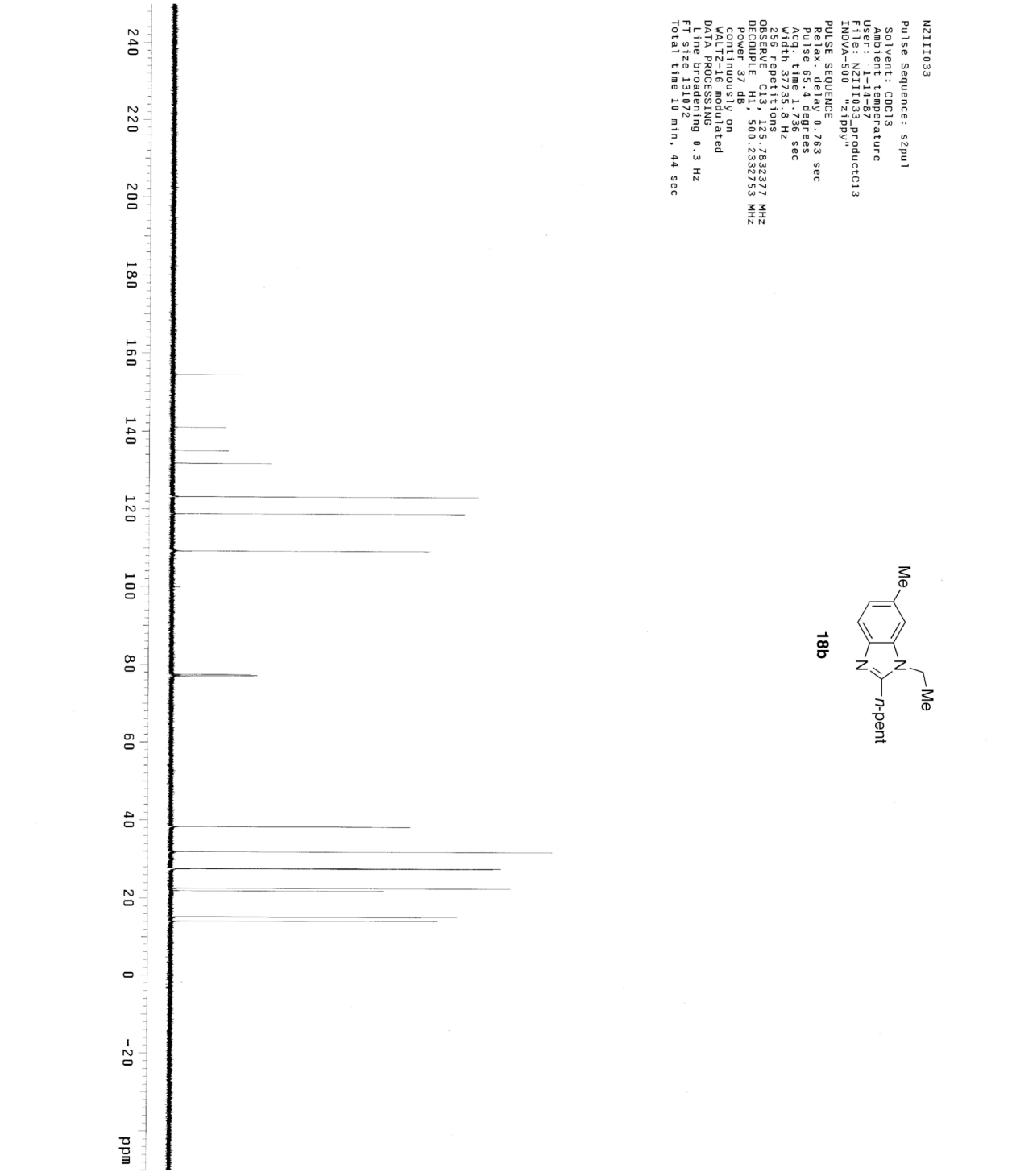

NZIII029
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII029_product
INOVA-500 "21ppy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986328 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
Me
N
N
Ph
15
0.94 2.96
1.91 2.98
3.00
10
9
8
7
6
5
4
3
2
1
0
ppm

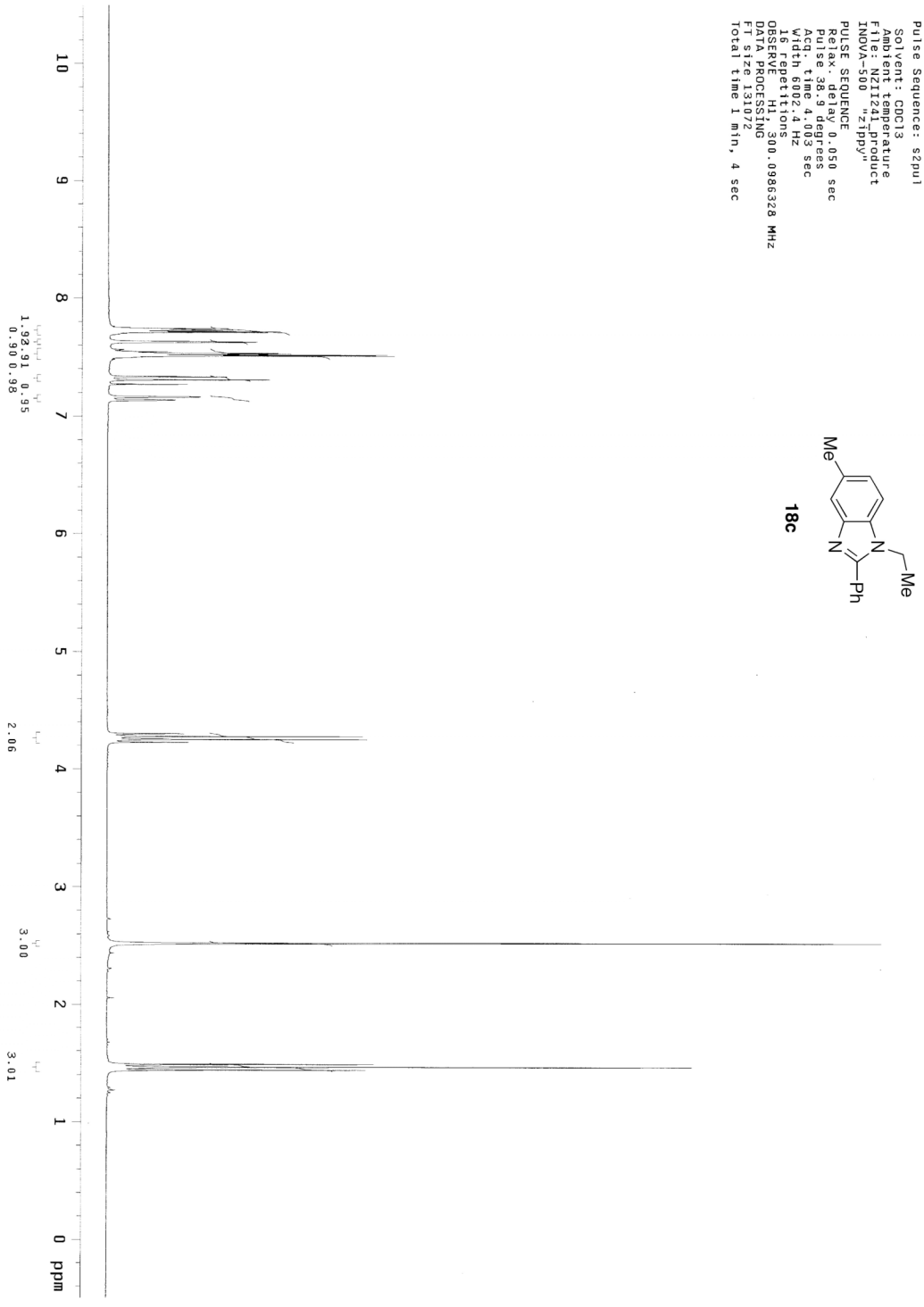

NZIII029
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: l-14-87
File: NZIII029_C13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 77.6 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
1536 repetitions
OBSERVE C13, 125.7832463 MHz
DECOUPLE H1, 500.2332753 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 696 hr, 41 min, 12 sec
Me
N
N
Ph
15
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

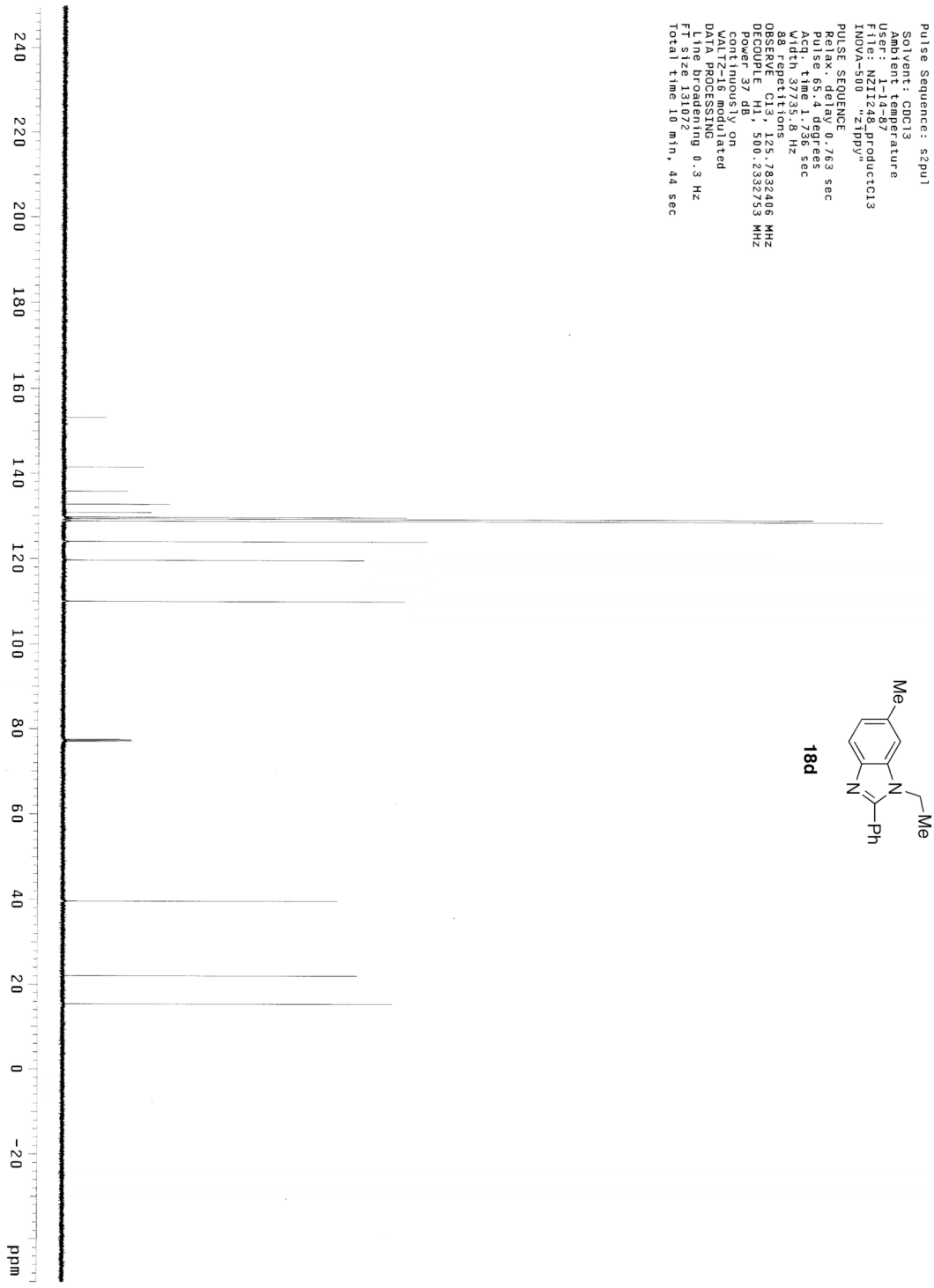

NZIII031
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII31_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986327 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
Me
N
N
Me
n-pent
18a
10
9
8
7
6
5
4
3
2
1
0
ppm
0.88
0.95
0.96
2.07
2.05
3.00
2.04
7.17
2.90

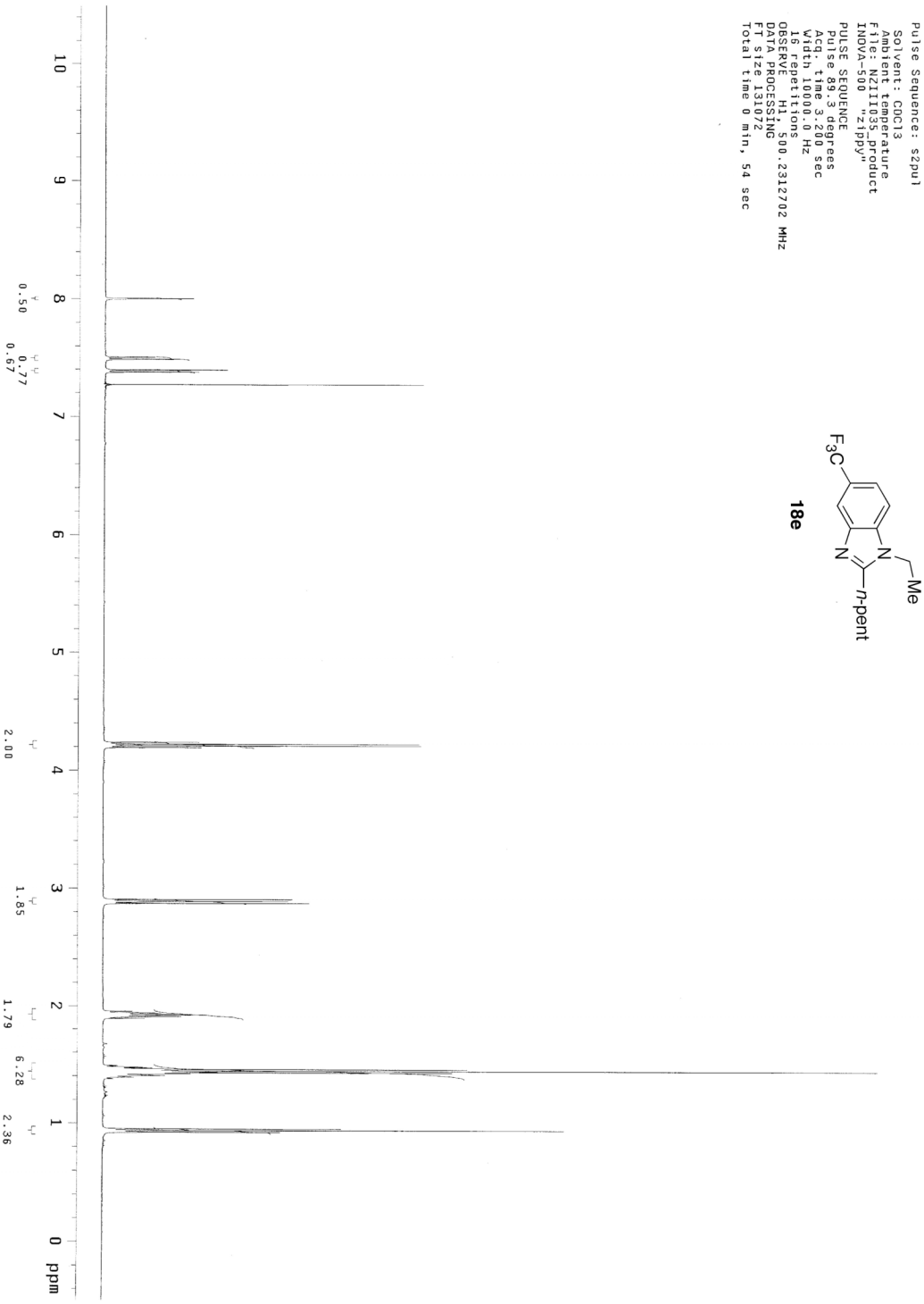

NZIII031
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: lia-87
File: NZI031_productc13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
256 repetitions
OBSERVE C13, 125.7832452 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 10 min, 44 sec
Me
N
N
Me
n-pent
18a
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

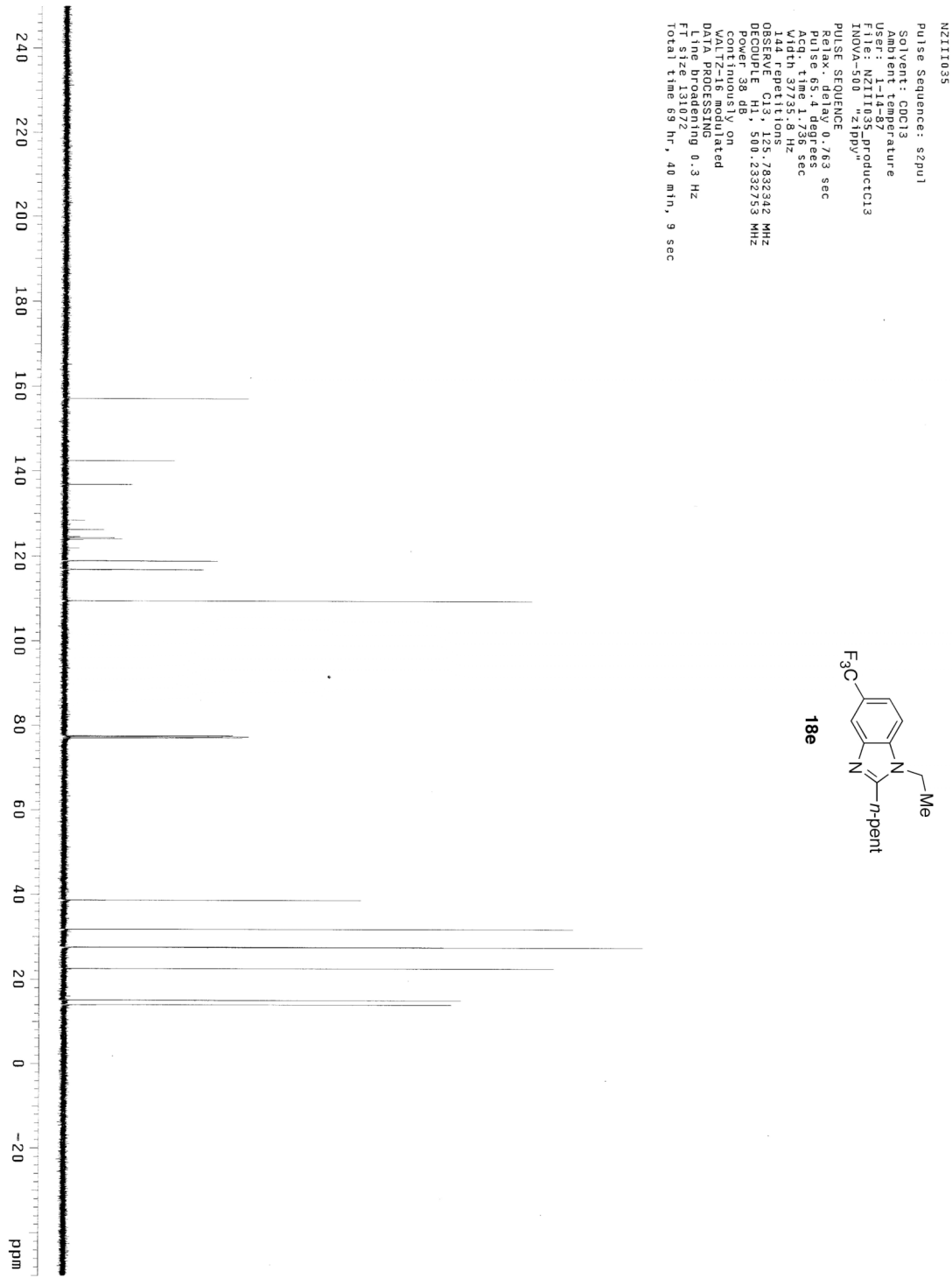

NZIII033
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII033_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986326 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
Me
N
N
Me
n-pent
18b
10
9
8
7
6
5
4
3
2
1
0 ppm
0.93
0.99
0.98
2.09
2.08
3.00
2.08
7.26
2.92

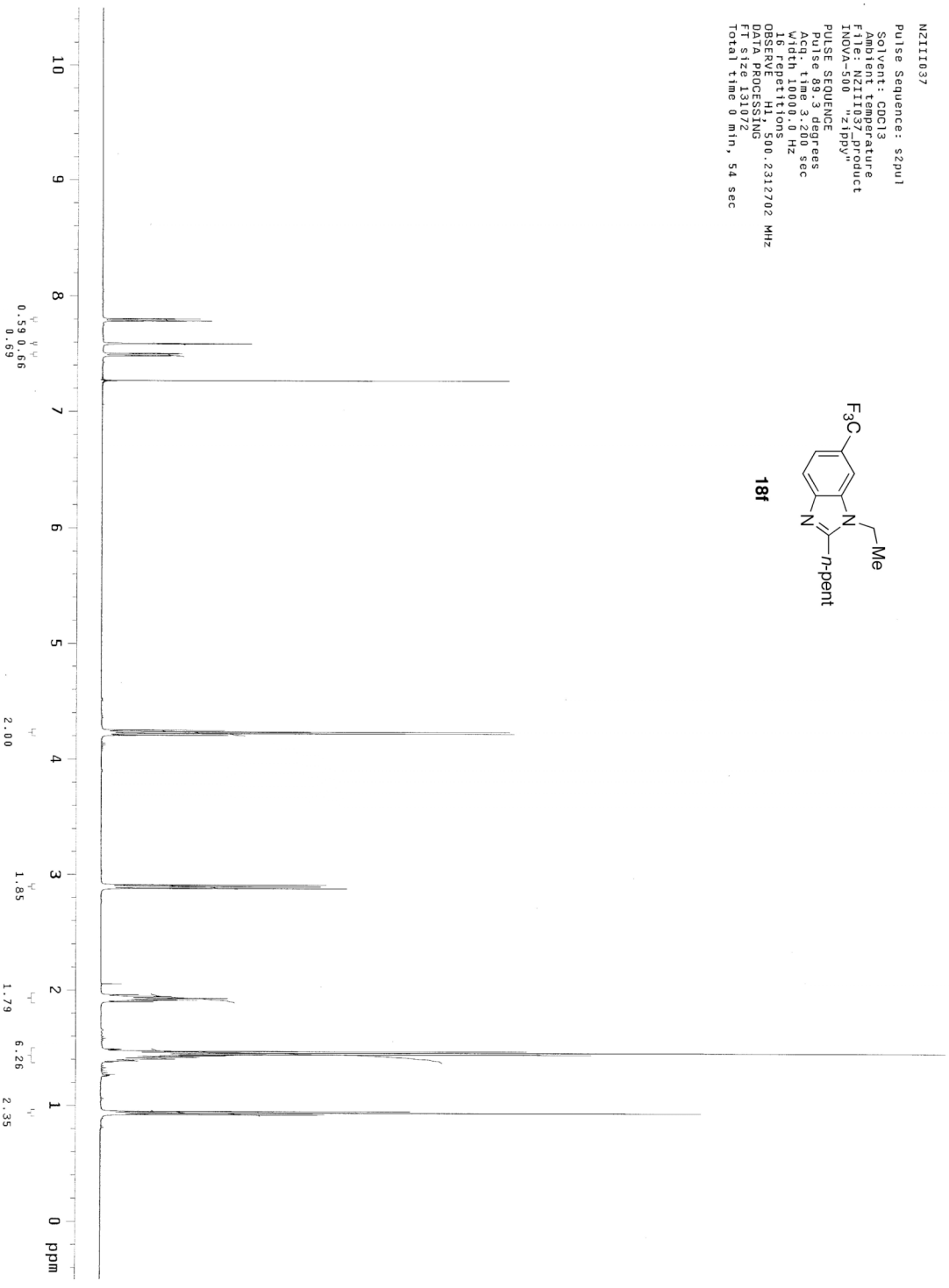

NZIII033
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZIII033_productC13
INOVA-500 "zipy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 63.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
256 repetitions
OBSERVE C13, 125.7833377 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 10 min, 44 sec
Me
N
N
Me
n-pent
18b
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

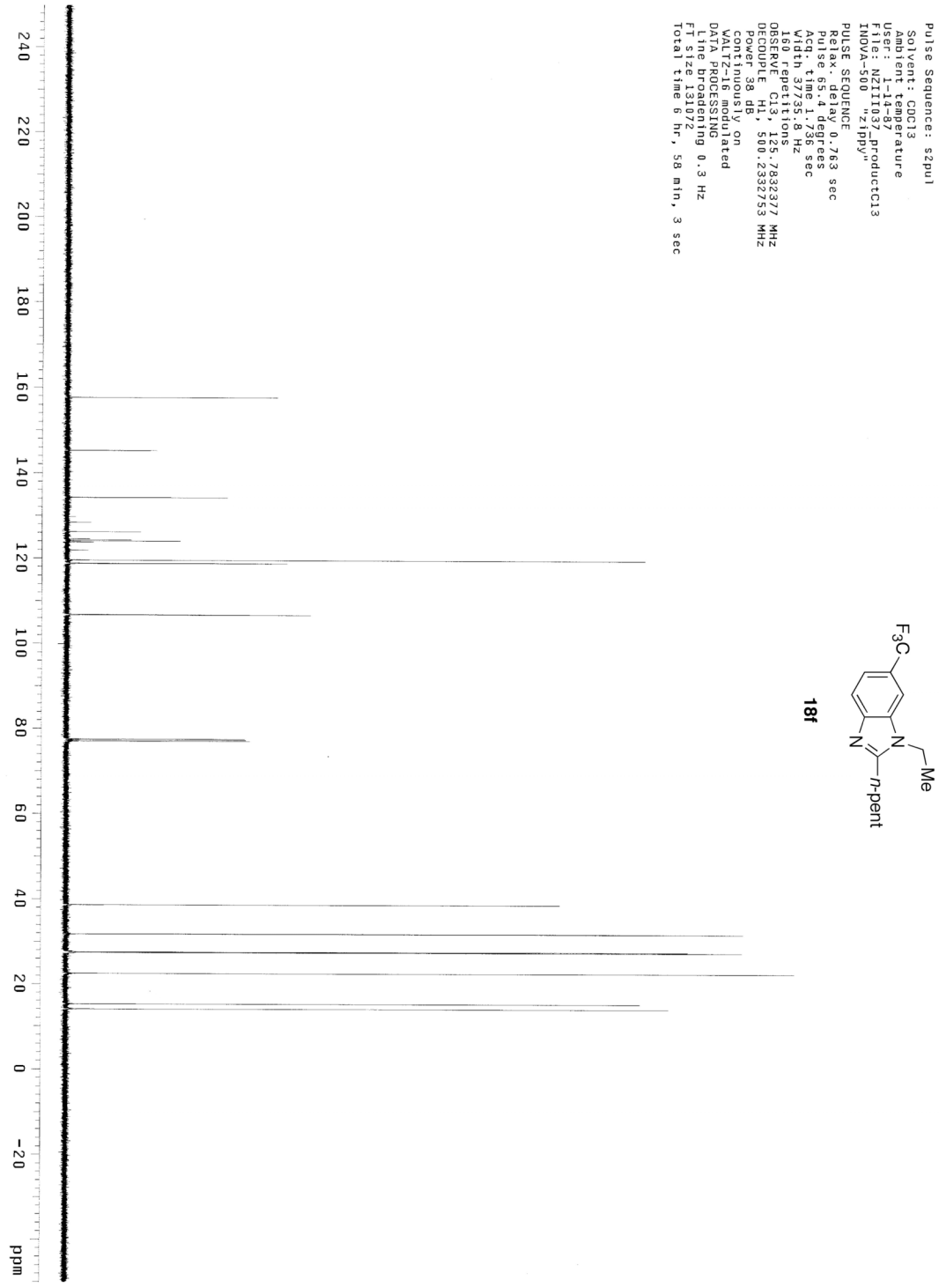

NZII241
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII41_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986328 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
Me
N
N
Me
Ph
18c
10
9
8
7
6
5
4
3
2
1
0
ppm
1.92
1.91
0.95
0.90
0.98
2.06
3.00
3.01

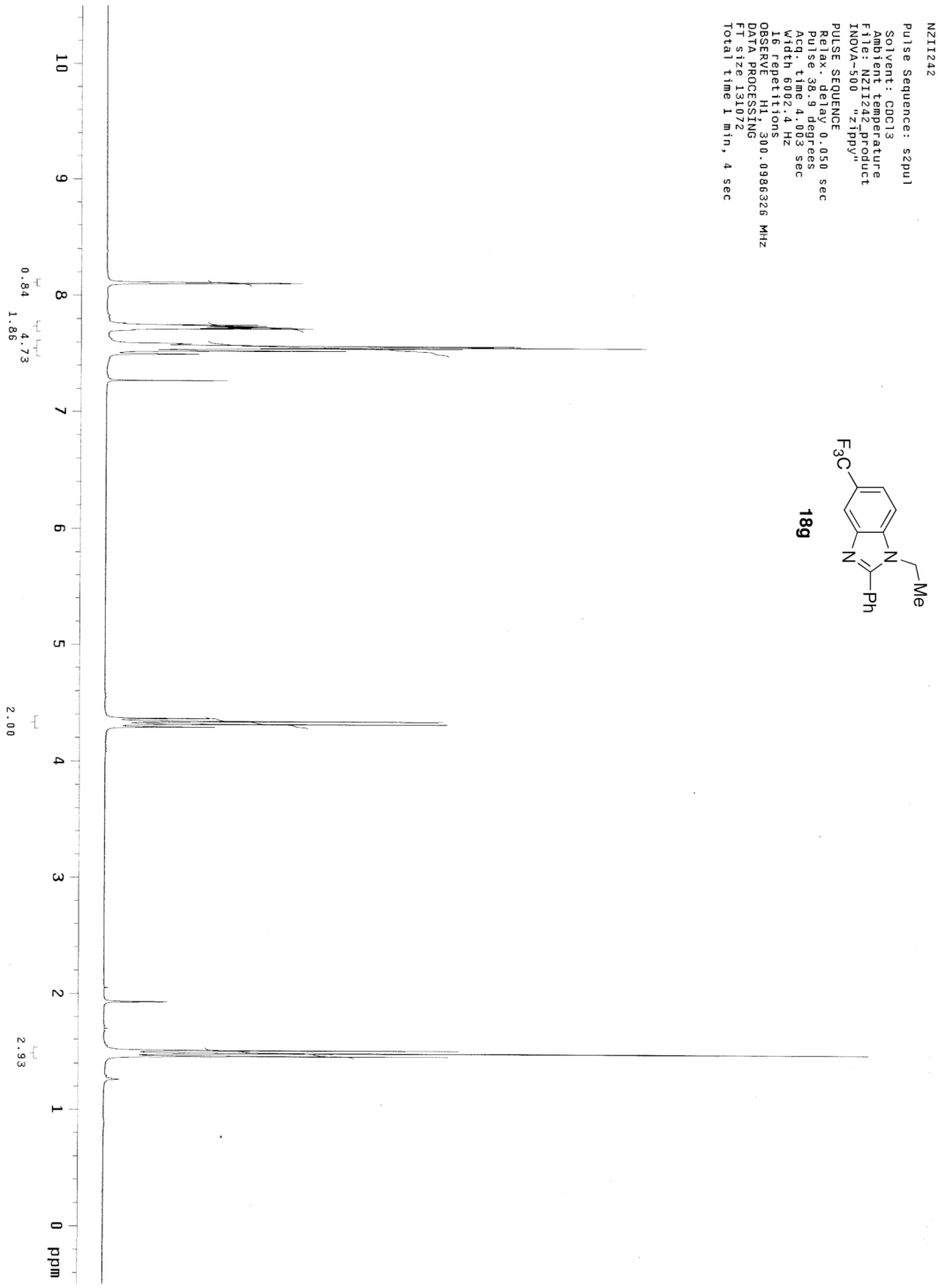

NZII248
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: l-14-87
File: NZII248_productC13
INOVA-500 "z1ppy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.4 degrees
Acq. time 1.536 sec
Width 37735.8 Hz
88 repetitions
OBSERVE C13, 125.7832406 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 10 min, 44 sec
Me
N
N
Me
Ph
18d
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

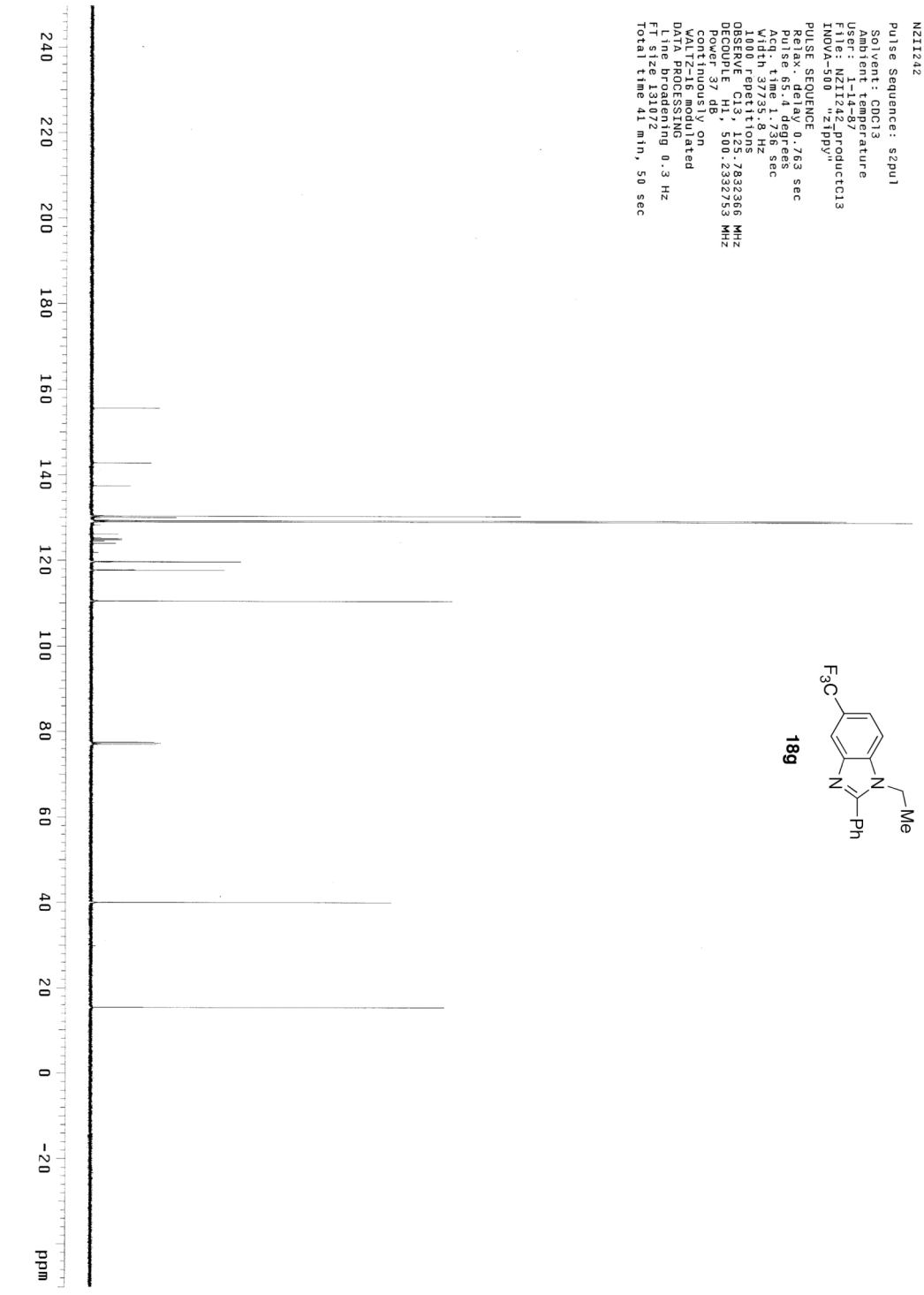

NZIII035
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZIII035_proton
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 89.3 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
16 repetitions
OBSERVE H1, 500.2312702 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 54 sec
F3C
N
N
Me
n-pent
18e
10
9
8
7
6
5
4
3
2
1
0 ppm
0.50
0.77
0.67
2.00
1.85
1.79
6.28
2.36

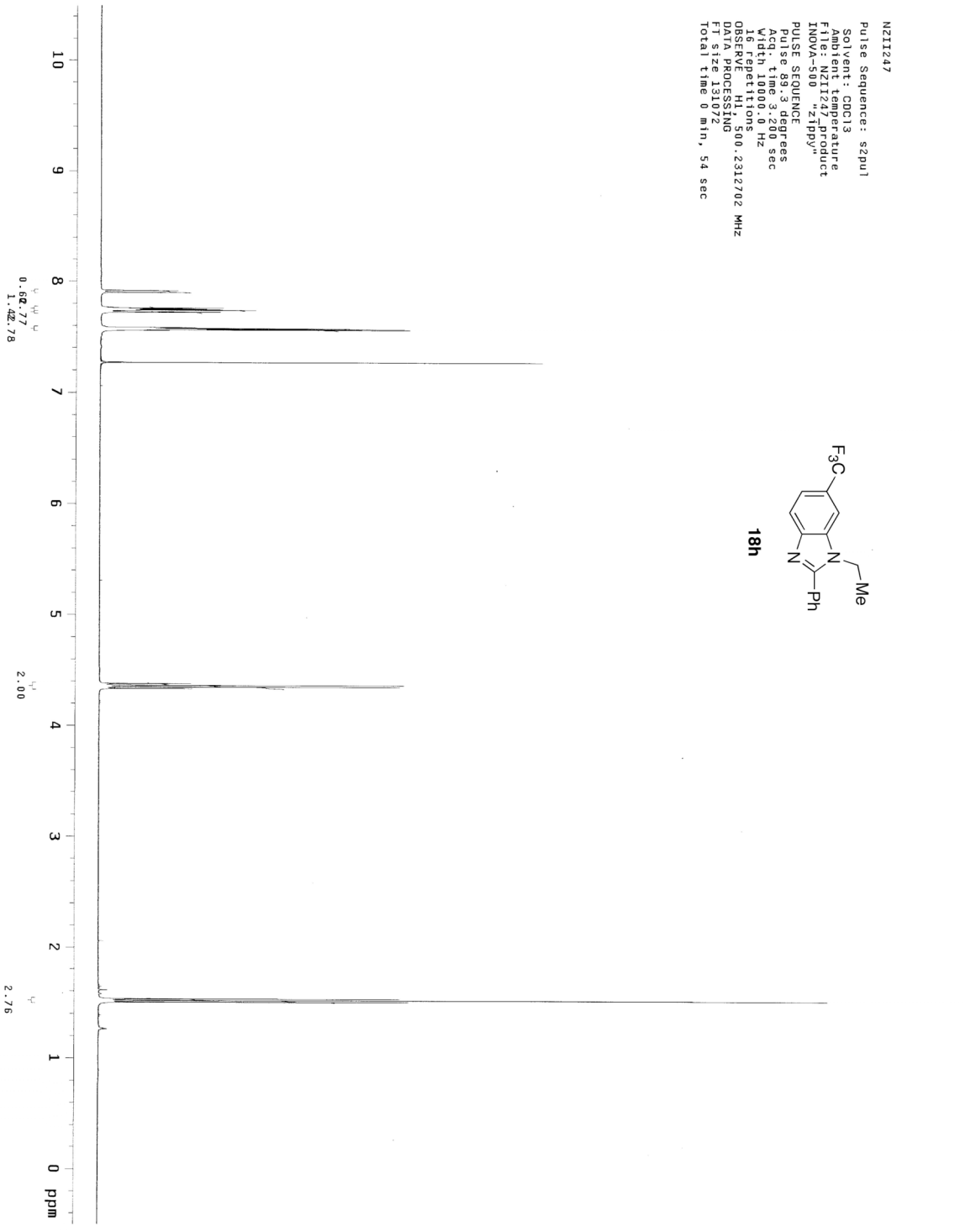

NZIII035
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: I-14-87
File: NZIII035_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
144 repetitions
OBSERVE C13, 125.7832342 MHz
DECOUPLE H1, 500.2332753 MHz
Power 38 dB
Continuously on
WALTZ16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 69 hr, 40 min, 9 sec
F3C
N
N
Me
n-pent
18e
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

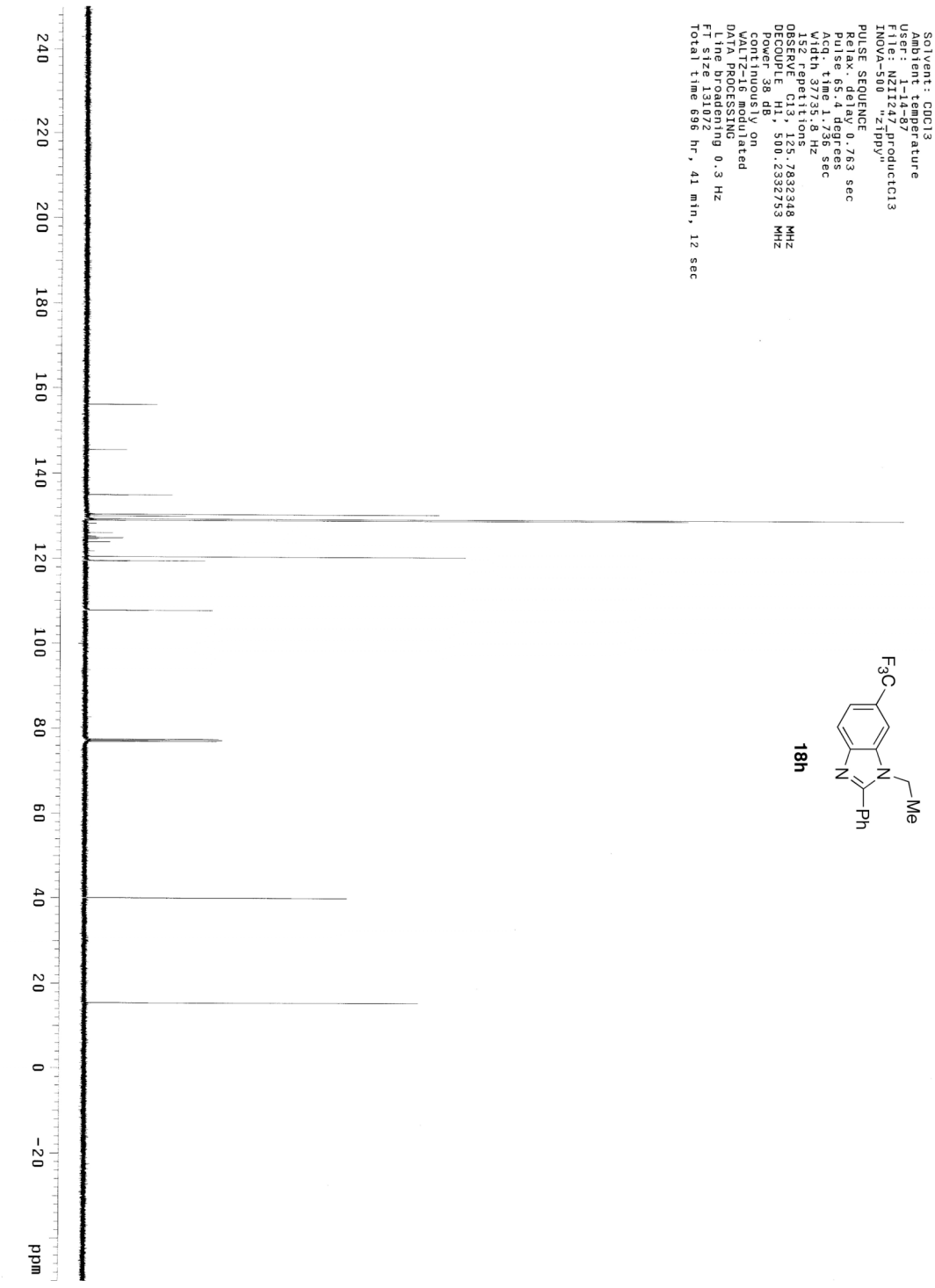

NZIII037
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Flags: NZIII037_pr.oduct
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 89.3 degrees
Acq. time 3.200 sec
width 10000.0 Hz
16 repetitions
OBSERVE H1, 500.2312702 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 54 sec
F3C
N
N
Me
n-pent
18f
0.59 0.66
0.69
2.00
1.85
1.79
6.26
2.35
10
9
8
7
6
5
4
3
2
1
0 ppm

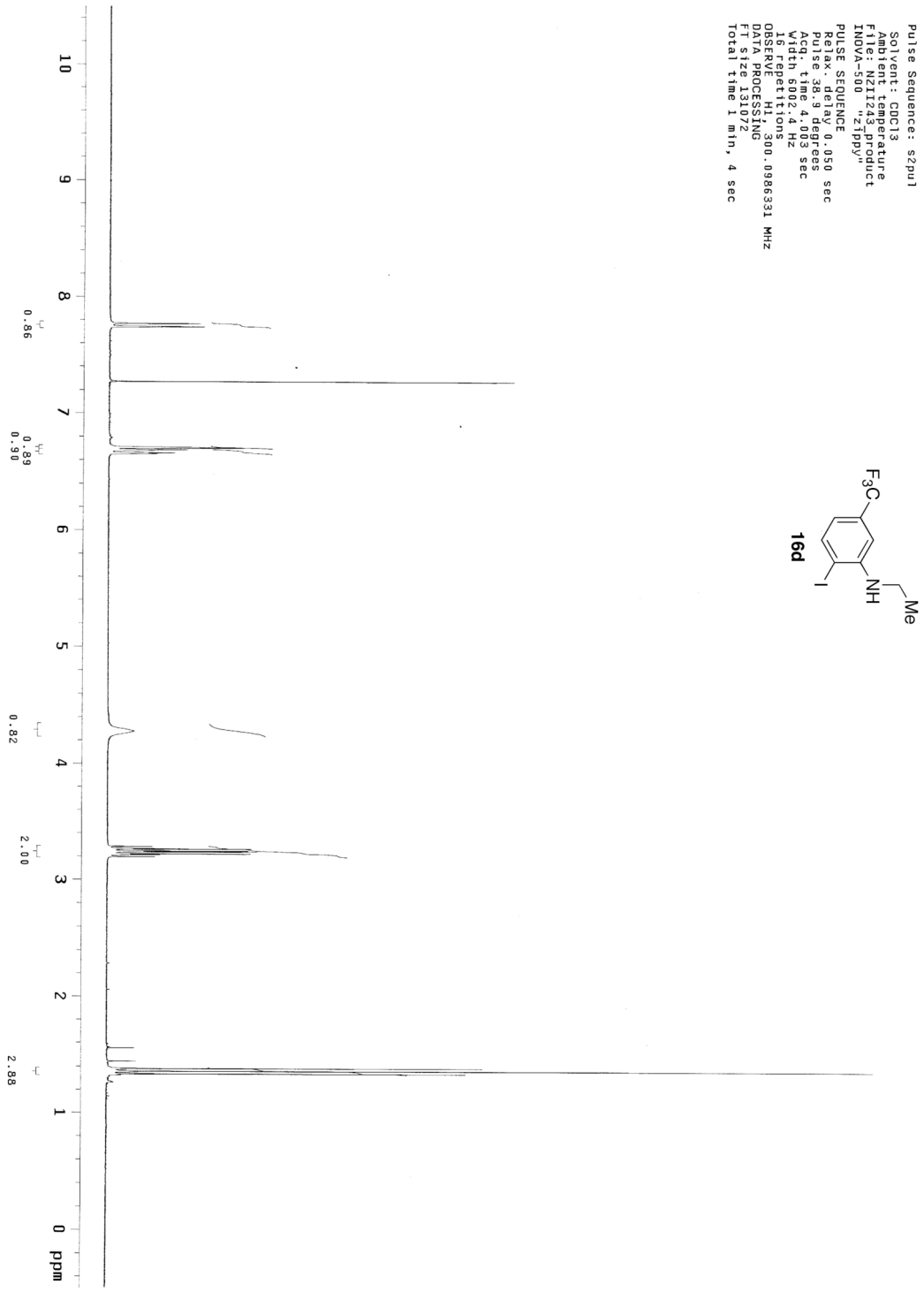

NZII1037
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: i-14-87
File: NZII1037.productCl3
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
160 repetitions
OBSERVE Cl3, 125.7832377 MHz
DECOUPLE H1, 500.2332753 MHz
Power 38 dB
continuously on
WALTZ16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 6 hr, 58 min, 3 sec
F3C
N
N
Me
n-pent
18f
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

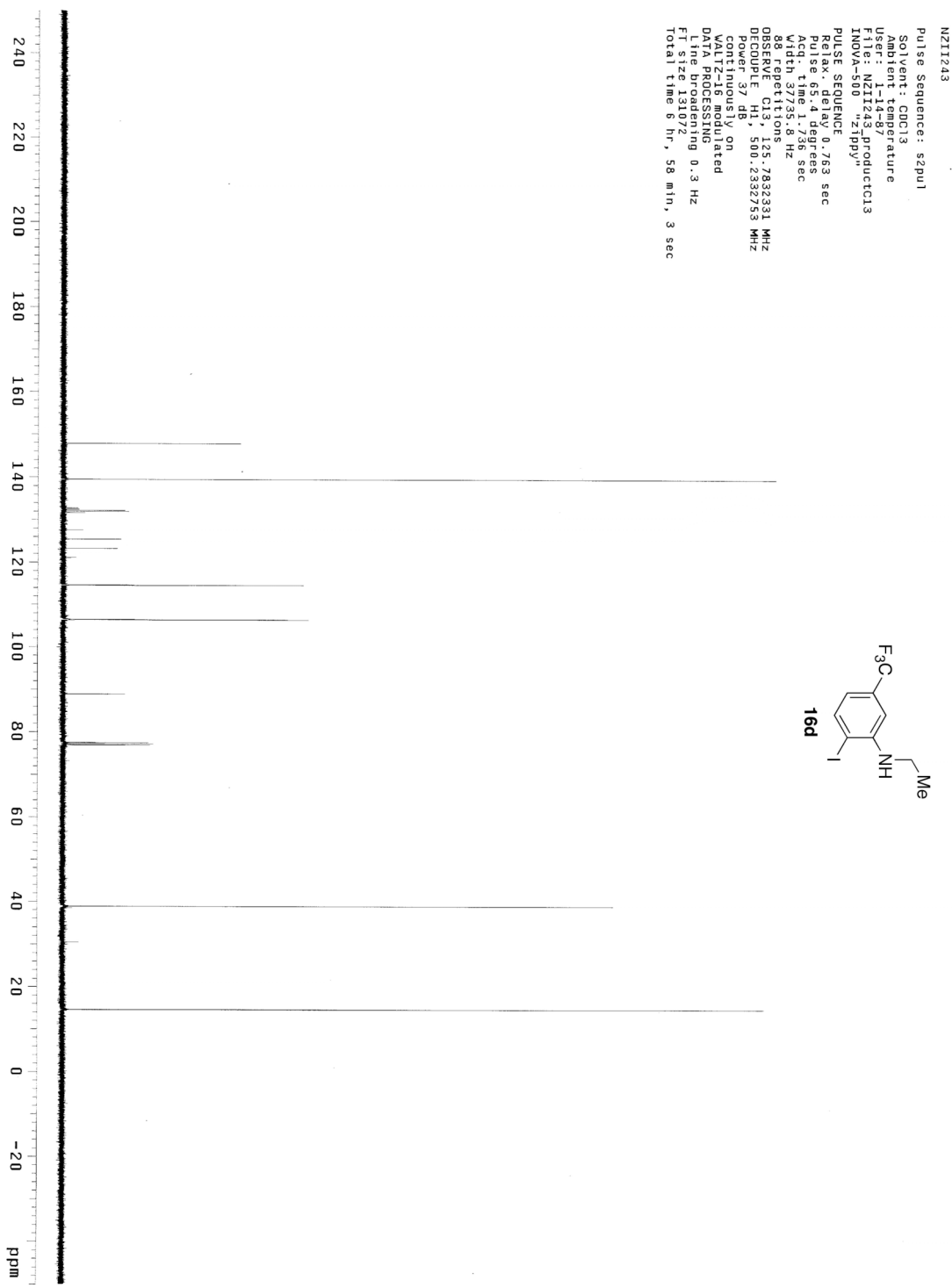

NZII242
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII242_product
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
1 repetitions
OBSERVE H1, 500.0986326 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
F3C
N
N
Me
Ph
18g
10
9
8
7
6
5
4
3
2
1
0 ppm
0.84
4.73
1.86
2.00
2.93


NZII242
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: l-14-07
File: NZII242/productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
1000 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
F3C
N
N
Me
Ph
18g
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


NZII247
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII247_product
INOVA-500 "zippy"
PULSE SEQUENCE
Pulse 89.3 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
16 repetitions
OBSERVE H1, 500.2312702 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 54 sec
F3C
N
N
Me
Ph
18h
10
9
8
7
6
5
4
3
2
1
0 ppm
0.62
7.77
1.42
7.78
2.00
2.76


NZII247
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII247_productC13
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 60.4 degrees
Acq. time 1.796 sec
Width 37735.8 Hz
152 repetitions
OBSERVE C13, 125.7832348 MHz
DECOUPLE H1, 500.2332753 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 696 hr, 41 min, 12 sec
F3C
N
N
Me
Ph
18h
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


NZII243
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: NZII243_product
INOVA-500 "z1ppy"
PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986331 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 4 sec
F3C
NH
Me
I
16d
0.86
0.89
0.90
0.82
2.00
2.88
10
9
8
7
6
5
4
3
2
1
0 ppm


NZII243
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: NZII243_productC13
INOVA-500 "z1ppy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 63.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
8848 repetitions
OBSERVE C13, 125.7832331 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
F3C
NH
Me
I
16d
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm