Supporting Information

A Nucleophilic Strategy for Enantioselective Intermolecular α-Amination: Access to Enantioenriched α-Arylamino Ketones

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General Information

Unless otherwise noted, all reagents were obtained commercially and used without further purification. H-**3a** ((*R*)-TRIP) was prepared according to a published procedure[S1]. H-**3b** was prepared according to a published procedure[S2]. H-**3c** ((*R*)-TCYP) was prepared according to a published procedure[S3]. **3d** ((*R*)-DM-BDPA) was prepared according to a published procedure[S4]. **3e** was prepared according to a published procedure[S5]. Before use in the catalytic reaction, phosphoric acids **3** were dissolved in DCM, shaken with a 6M $HCl_{(aq)}$ solution, the layers separated, and the solvent removed under reduced pressure (without use of Na_2SO_4 or $MgSO_4$) to ensure protonation of the phosphate. Molecular sieves were activated under high vacuum at 150 °C for 15 h. Room temperature (r.t.) is defined as 22 °C. Dry and degassed solvents were used for reactions performed under nitrogen.

Chromatography. Analytical thin layer chromatography was performed on EMD glass-backed TLC plates (silica gel 60 F254) and visualized by UV lamp (254 nm), anisaldehyde, or potassium permanganate. Column chromatography was performed using Fisher 230-400 mesh, grade 60 silica gel. Purified compounds were further dried under high vacuum.

Nuclear magnetic resonance spectra. ^1H and ^{13}C spectra were recorded on Bruker AVQ-400, or AVB-400 spectrometers. Chemical shifts (δ) are reported in ppm. ^1H NMR spectra are referenced to residual $CHCl_3$ (7.26 ppm), ^{13}C NMR spectra are referenced to $CDCl_3$ (77.16 ppm), and ^{19}F spectra are referenced to $CFCl_3$ (0.00 ppm, external). ^{13}C spectra were recorded with proton decoupling. Peak multiplicities are designated by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; hept, heptet; m, multiplet; br, broad.

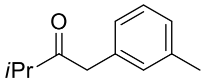
Mass spectrometry. Mass spectral data were obtained in the QB3/Chemistry Mass Spectrometry Facility, University of California, Berkeley.

HPLC analyses. Chiral phase high performance liquid chromatography (HPLC) was performed on Shimadzu VP and Shimadzu prominence series instruments using the specified column (5μm, 4.6 mm x 250 mm). Racemic traces were obtained by substituting 3,3',5,5'-tetra-tert-butyl-[1,1'-biphenyl]-2,2'-diyl hydrogenphosphate[S6] or anhydrous $Cu(OTf)_2$ in place of the chiral phosphoric acid.

X-ray crystallography. Data collection and analysis performed in the X-ray Crystallography Facility, College of Chemistry, University of California, Berkeley.

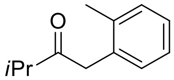
Synthesis of Arylazoalkene Substrates (1a-1p) and Their Corresponding Precursors

(3-Methylbenzyl) isopropyl ketone (**S1b**)



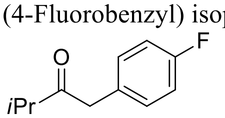
To a flame-dried 250 mL round-bottom flask equipped with a magnetic stir bar was added magnesium (1.52 g, 62.6 mmol) and the flask placed under a nitrogen atmosphere. Ether (anhydrous, degassed) (60 mL) and 3-methylbenzyl chloride (8.44 g, 60.0 mmol) were added and the reaction mixture stirred at r.t. for 1 h. Isobutyronitrile (4.48 mL, 50.0 mmol) was added, the reaction mixture heated to 35 °C, and stirred at this temperature for 16 h. The reaction mixture was quenched by dropwise addition of 6M $HCl_{(aq)}$ solution (25 mL), the layers separated, and the aqueous phase extracted with ether (2 x 30 mL). The combined organic phases were washed with $NaHCO_{3(sat., aq)}$ and $NaCl_{(sat., aq)}$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (19:1 hexanes:ether) to afford **S1b** (7.80 g, 88%) as a clear oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.03 (s, 1H), 7.01 (d, *J* = 8.1 Hz, 1H), 3.72 (s, 2H), 2.74 (hept, *J* = 6.9 Hz, 1H), 2.35 (s, 3H), 1.11 (d, *J* = 6.9 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.2, 138.3, 134.4, 130.3, 128.6, 127.7, 126.5, 47.8, 40.1, 21.5, 18.4; **HRMS** (EI): found $[M]^+$ 176.1196 $C_{12}H_{16}O$ requires 176.1201

(2-Methylbenzyl) isopropyl ketone (**S1c**)



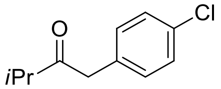
To a 250 mL round-bottom flask equipped with a magnetic stir bar was added ethyl isobutyrate (5.81 g, 50.0 mmol), anhydrous THF (167 mL), and potassium *tert*-butoxide (11.2 g, 100 mmol). o-Tolylacetonitrile (6.56 g, 50.0 mmol) was added, the flask capped, and the reaction mixture stirred at r.t. for 15 h. Ethyl acetate (240 mL), water (300 mL), and 12M $HCl_{(aq)}$ were added and the layers separated. The organic phase was washed with $NaHCO_{3(sat., aq)}$ and $NaCl_{(sat., aq)}$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude ketonitrile product was decarboxylated as follows: to a 250 mL round-bottom flask equipped with a magnetic stir bar containing was added the crude ketonitrile product. The flask was cooled to at 0°C and a solution of $H_2SO_{4(conc.)}$ (25 mL) and water (6 mL) was added dropwise. The reaction mixture was heated to 80°C and stirred at this temperature for 30 min. Water (94 mL) was added cautiously. The reaction mixture was heated to 130°C and stirred at this temperature for 4 h at which point it was allowed to cool to r.t. and ether (100 mL) was added. The layers were separated and the organic phase was washed with $NaHCO_{3(sat., aq)}$ and $NaCl_{(sat., aq)}$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (19:1 to 9:1 hexanes:ether) to afford **S1c** (2.93 g, 33%) as a yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 3H), 7.14 – 7.08 (m, 1H), 3.78 (s, 2H), 2.74 (hept, *J* = 6.9 Hz, 1H), 2.24 (s, 3H), 1.13 (d, *J* = 6.9 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.0, 137.0, 133.4, 130.5, 127.3, 126.2, 46.1, 40.0, 19.8, 18.6; **HRMS** (EI): found $[M]^+$ 176.1198 $C_{12}H_{16}O$ requires 176.1201

(4-Fluorobenzyl) isopropyl ketone (**S1d**)



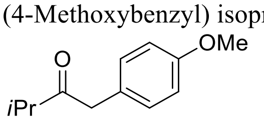
To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added magnesium (761 mg, 31.3 mmol) and one crystal of iodine (~5 mg) and the flask placed under a nitrogen atmosphere. Ether (anhydrous, degassed) (30 mL) and 4-fluorobenzyl chloride (4.34 g, 30.0 mmol) were added and the reaction mixture stirred at r.t. for 1 h. Isobutyronitrile (2.24 mL, 25.0 mmol) was added, the reaction mixture heated to 35 °C, and stirred at this temperature for 17 h. The reaction mixture was quenched by dropwise addition of 6M $HCl_{(aq)}$ solution (25 mL), the layers separated, and the aqueous phase extracted with ether (2 x 30 mL). The combined organic phases were washed with $NaHCO_{3(sat., aq)}$ and $NaCl_{(sat., aq)}$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (19:1 to 9:1 hexanes:ethyl acetate) to afford **S1d** (3.05g, 68%) as a yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.18 – 7.11 (m, 2H), 7.04 – 6.96 (m, 2H), 3.72 (s, 2H), 2.71 (hept, *J* = 7.0 Hz, 1H), 1.11 (d, *J* = 7.0 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 211.8, 162.0 (d, *J* = 245.0 Hz), 131.1 (d, *J* = 8.0 Hz), 130.2 (d, *J* = 3.3 Hz), 115.5 (d, *J* = 21.3 Hz), 46.7, 40.4, 18.4; **^{19}F NMR** (376 MHz, $CDCl_3$) -115.30 – -115.39 (m); **HRMS** (EI): found $[M]^+$ 180.0951 $C_{11}H_{13}FO$ requires 180.095

(4-Chlorobenzyl) isopropyl ketone (**S1e**)



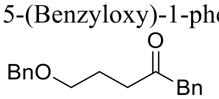
To a flame-dried 250 mL round-bottom flask equipped with a magnetic stir bar was added magnesium (2.13 g, 87.5 mmol) and the flask placed under a nitrogen atmosphere. Ether (anhydrous, degassed) (42 mL) and 4-chlorobenzyl chloride (13.5 g, 84.0 mmol) were added and the reaction mixture stirred at r.t. for 2 h. Isobutyronitrile (2.24 mL, 25.0 mmol) and ether (anhydrous, degassed) (42 mL) was added, the reaction mixture heated to 35 °C, and stirred at this temperature for 15 h. The reaction mixture was quenched by dropwise addition of 6M $HCl_{(aq)}$ solution (50 mL), the layers separated, and the aqueous phase extracted with ether (3 x 30 mL). The combined organic phases were washed with $NaHCO_{3(sat., aq)}$ and $NaCl_{(sat., aq)}$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (19:1 to 9:1 hexanes:ether) to afford **S1e** (9.71 g, 70%) as a white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.5 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 3.71 (s, 3H), 2.71 (hept, *J* = 6.9 Hz, 1H), 1.11 (d, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 211.4, 133.0, 132.9, 130.9, 128.8, 46.8, 40.5, 18.4; **HRMS** (EI): found $[M]^+$ 196.0654 $C_{11}H_{13}{}^{35}ClO$ requires 196.0655

(4-Methoxybenzyl) isopropyl ketone (**S1f**)



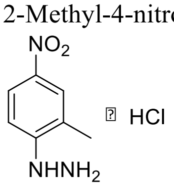
The same procedure for **S1c** was performed, except 4-methoxyphenylacetonitrile (7.36 g, 50 mmol) was used instead. The crude product was purified by column chromatography (9:1 hexanes:ether) to afford **S1f** (3.91 g, 41%) as a colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 3.78 (s, 3H), 3.68 (s, 2H), 2.72 (hept, *J* = 6.8 Hz, 1H), 1.09 (d, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.4, 158.6, 130.5, 126.5, 114.1, 55.3, 46.9, 39.9, 18.4; **HRMS** (EI): found $[M]^+$ 192.1149 $C_{12}H_{16}O_2$ requires 192.1150

5-(Benzyloxy)-1-phenylpentan-2-one (**S1p**)



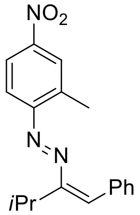
To a 500 mL round-bottom flask equipped with a magnetic stir bar was added 4-(benzyloxy)-*N*-methoxy-*N*-methylbutanamide[S7] (8.39 g, 35.4 mmol) and the flask placed under a nitrogen atmosphere. THF (anhydrous, degassed) (71 mL) was added and the reaction mixture cooled to 0 °C. Benzylmagnesium chloride (26.5 mL, 53 mmol, 2M solution in THF) was added dropwise at this temperature. The reaction mixture was allowed to warm to r.t. and stirred at this temperature for 15 h. The reaction mixture was cooled to 0 °C and $NH_4Cl_{(sat., aq)}$ (50 mL) and water (50 mL) were carefully added. The formed layers were separated and the aqueous layer extracted with ether (2 x 100 mL). The combined organic phases were washed with $NaCl_{(sat., aq)}$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (9:1 hexanes:ether) to afford **S1p** (6.85 g, 72%) as a clear oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.24 (m, 8H), 7.22 (d, J = 6.7 Hz, 2H), 4.47 (s, 2H), 3.71 (s, 2H), 3.47 (t, J = 6.1 Hz, 2H), 2.61 (t, J = 7.1 Hz, 2H), 1.91 (p, J = 7.1, 6.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.0, 138.4, 134.4, 129.5, 128.7, 128.4, 127.7, 127.6, 127.0, 72.8, 69.2, 50.2, 38.7, 23.9; **HRMS** (EI): found $[M]^+$ 268.1465 $C_{18}H_{20}O_2$ requires 268.1463

2-Methyl-4-nitrophenylhydrazine hydrochloride (**S2**)



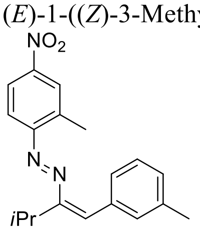
To a 1000 mL round-bottom flask equipped with a magnetic stir bar was added 1-fluoro-2-methyl-4-nitrobenzene (50.0 g, 322 mmol), isopropyl alcohol (488 mL), and hydrazine monohydrate (32.6 mL, 672 mmol). The reaction mixture was then heated to 90 °C and then stirred at this temperature for 2 h. Additional hydrazine monohydrate (32.6 mL, 672 mmol) was added at 90 °C and the reaction mixture stirred at this temperature for an additional 2 h. The reaction mixture was allowed to cool slowly to room temperature at which point ether (400 mL) was added. The precipitated solid was collected by filtration, washing with water (200 mL) and ether (200 mL). The orange solid was added to a 6M $HCl_{(aq)}$ solution (300 mL) and allowed to stir for 1 h, at which point the pale yellow slurry was filtered and dried by pulling vacuum through the solid for 16 h. The solid was dried further under high vacuum over P_2O_5 for 8 h of afford **S2** (43.3 g, 66%) as a off-white solid; **^{1}H NMR** (400 MHz, DMSO-*d*$_6$) δ 10.66 (br s, 1H), 8.92 (br s, 1H), 8.08 (dd, *J* = 9.0, 2.5 Hz, 1H), 8.01 (d, *J* = 2.5 Hz, 1H), 7.05 (d, *J* = 9.0 Hz, 1H), 2.27 (s, 3H); **^{13}C NMR** (101 MHz, DMSO-*d*$_6$) δ 149.4, 140.3, 125.4, 124.5, 123.0, 111.3, 39.5, 17.3; **HRMS** (EI): found $[M\text{-}HCl]^+$ 167.0693 $C_7H_9N_3O_2$ requires 167.0695

(*E*)-1-((*Z*)-3-Methyl-1-phenylbut-1-en-2-yl)-2-(2-methyl-4-nitrophenyl)diazene (**1a**)



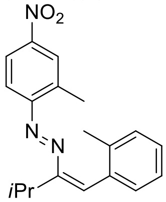
To a 250 mL round-bottom flask equipped with a magnetic stir bar was added benzyl isopropyl ketone (1.62 g, 10.0 mmol), **S2** (2.44 g, 12.0 mmol), anhydrous sodium acetate (8.20 g, 100 mmol), and ethanol (50 mL). The reaction mixture was heated to 60 °C and stirred at this temperature for 14 h. The reaction mixture was cooled, dichloromethane (50 mL) was added, and filtered. The filtrate was concentrated under reduced pressure and passed through a plug of silica (dry load, 9:1 to 4:1 hexanes:ethyl acetate), collecting the first yellow band to afford the crude hydrazone (1.99 g, 6.39 mmol; mixture of both (*E*) and (*Z*) isomers). To a 100 mL round-bottom flask equipped with a magnetic stir bar and containing the crude hydrazone was added pyridine (3.6 mL). The flask was protected from light and a solution of iodine (1.62 g, 6.39 mmol) in pyridine (7.1 mL) was added dropwise to the hydrazone solution. The reaction mixture was then stirred in the absence of light at r.t. for 14 h. The reaction mixture was then cooled to 0 °C and a 1M $NaOH_{(aq)}$ solution (19 mL) was added dropwise. After addition, ether (50 mL) and water (50 mL) were added, the mixture was filtered to remove any solids, the filtrate layers were separated, and the aqueous layer extracted with ether (2 x 50 mL). The combined organic phases were washed with 2M $HCl_{(aq)}$ (3 x 50 mL), $NaHCO_{3(sat., aq),}$ and $NaCl_{(sat., aq)}$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (dry load, 19:1 hexanes:ether) and then triturated with methanol (~4 mL) to afford **1a** (281 mg, 9%, two steps) as a dark purple solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 2.1 Hz, 1H), 8.09 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.73 (d, *J* = 7.2 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.45 – 7.33 (m, 3H), 7.12 (s, 1H), 3.41 (hept, *J* = 6.8 Hz, 1H), 2.76 (s, 3H), 1.27 (d, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.2, 154.5, 148.2, 139.2, 135.8, 135.2, 132.3, 128.7, 128.3, 126.4, 122.1, 116.5, 27.1, 21.7, 17.9; **HRMS** (ESI): found $[M+H]^+$ 310.1550 $C_{18}H_{20}N_3O_2$ requires 310.1550

(*E*)-1-((*Z*)-3-Methyl-1-(*m*-tolyl)but-1-en-2-yl)-2-(2-methyl-4-nitrophenyl)diazene (**1b**)



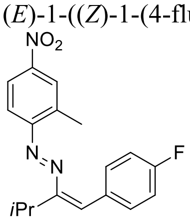
The same procedure for **1a** was performed, except (3-Methylbenzyl) isopropyl ketone (**S1b**) (3.08 g, 17.5 mmol) was used instead. The reaction afforded **1b** (727 mg, 13%, two steps) as a dark purple solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 2.3 Hz, 1H), 8.10 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.58 – 7.46 (m, 3H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.10 (s, 1H), 3.41 (hept, *J* = 6.9 Hz, 1H), 2.76 (s, 3H), 2.40 (s, 3H), 1.26 (d, *J* = 6.9 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.2, 154.5, 148.2, 139.2, 137.8, 135.8, 135.4, 133.1, 129.5, 129.5, 128.2, 126.4, 122.1, 116.5, 27.1, 21.7, 21.6, 17.9; **HRMS** (ESI): found $[M+H]^+$ 324.1707 $C_{19}H_{22}N_3O_2$ requires 324.1707

(E)-1-((Z)-3-methyl-1-(o-tolyl)but-1-en-2-yl)-2-(2-methyl-4-nitrophenyl)diazene (**1c**)



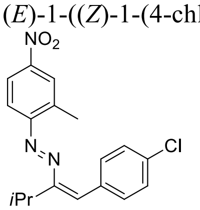
The same procedure for **1a** was performed, except (2-Methylbenzyl) isopropyl ketone (**S1c**) (2.64g, 15.0 mmol) was used instead. The reaction afforded **1c** (449 mg, 9%, two steps) as a dark purple solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (d, J = 2.5 Hz, 1H), 8.03 (dd, J = 8.8, 2.5 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.37 (s, 1H), 7.32 – 7.20 (m, H), 3.42 (hept, J = 7.0 Hz, 1H), 2.76 (s, 3H), 2.45 (s, 3H), 1.30 (d, J = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.3, 154.3, 148.2, 139.2, 137.2, 134.6, 134.1, 133.5, 130.0, 128.6, 126.4, 125.3, 122.0, 116.5, 27.2, 21.8, 20.5, 17.8; **HRMS** (ESI): found $[M+H]^+$ 324.1707 $C_{19}H_{22}N_3O_2$ requires 324.1707

(E)-1-((Z)-1-(4-fluorophenyl)-3-methylbut-1-en-2-yl)-2-(2-methyl-4-nitrophenyl)diazene (**1d**)



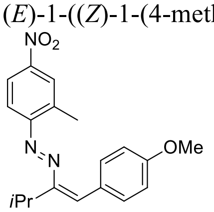
The same procedure for **1a** was performed, except (4-Fluorobenzyl) isopropyl ketone (**S1d**) (3.00g, 16.6 mmol) was used instead. The reaction afforded **1d** (480 mg, 9%, two steps) as a dark purple solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (d, J = 2.4 Hz, 1H), 8.09 (dd, J = 8.8, 2.1 Hz, 1H), 7.71 (dd, J = 8.6, 5.6 Hz, 2H), 7.45 (d, J = 8.8 Hz, 1H), 7.09 (t, J = 8.8 Hz, 2H), 7.06 (s, 1H), 3.38 (hept, J = 6.8 Hz, 1H), 2.74 (s, 3H), 1.24 (d, J = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.1 (d, J = 250.5 Hz), 160.0, 154.5, 148.3, 139.2, 134.1 (d, J = 8.1 Hz), 134.0, 132.1 (d, J = 3.5 Hz), 126.5, 122.2, 116.4, 115.4 (d, J = 21.6 Hz), 27.1, 21.7, 17.9; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.18 – -111.28 (m); **HRMS** (ESI): found $[M+H]^+$ 328.1456 $C_{18}H_{19}FN_3O_2$ requires 328.1456

(E)-1-((Z)-1-(4-chlorophenyl)-3-methylbut-1-en-2-yl)-2-(2-methyl-4-nitrophenyl)diazene (**1e**)



The same procedure for **1a** was performed, except (4-Chlorobenzyl) isopropyl ketone (**S1e**) (3.44g, 17.5 mmol) was used instead. The reaction afforded **1e** (1.20 g, 20%, two steps) as a dark purple solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (d, J = 2.4 Hz, 1H), 8.09 (dd, J = 8.8, 2.5 Hz, 1H), 7.64 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.8 Hz, 1H), 7.36 (d, J = 8.6 Hz, 2H), 7.04 (s, 1H), 3.38 (hept, J = 6.9 Hz, 1H), 2.75 (s, 3H), 1.24 (d, J = 6.9 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.6, 154.4, 148.4, 139.4, 134.8, 134.3, 133.8, 133.4, 128.5, 126.5, 122.2, 116.4, 27.1, 21.6, 17.9; **HRMS** (ESI): found $[M+H]^+$ 344.1159 $C_{18}H_{19}{}^{35}ClN_3O_2$ requires 344.1160

(E)-1-((Z)-1-(4-methoxyphenyl)-3-methylbut-1-en-2-yl)-2-(2-methyl-4-nitrophenyl)diazene (**1f**)

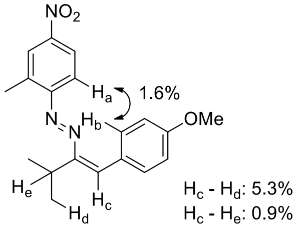


The same procedure for **1a** was performed, except (4-Methoxybenzyl) isopropyl ketone (**S1f**) (2.31g, 12.0 mmol) was used instead. The reaction afforded **1f** (1.20 g, 23%, two steps) as a black solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (d, J = 2.0 Hz, 1H), 8.10 (dd, J = 8.8, 2.3 Hz, 1H), 7.72 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.8 Hz, 1H), 7.04 (s, 1H), 6.94 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 3.39 (hept, J

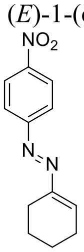
= 7.2 Hz, 1H), 2.74 (s, 3H), 1.24 (d, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.4, 159.1, 154.8, 148.0, 138.9, 135.2, 134.1, 128.7, 126.4, 122.2, 116.5, 114.0, 55.4, 27.1, 21.7, 17.9; **HRMS** (ESI): found $[M+H]^+$ 340.1654 $C_{19}H_{22}N_3O_3$ requires 340.1656

NOE experiments:

The diastereomeric assignment of **1f** (and by analogy **1a-1e**) was performed by irradiation of H_a and H_c, which gave the following relevant enhancements. Additionally, although a negative observation, no communication between H_b and H_d/H_e was observed.

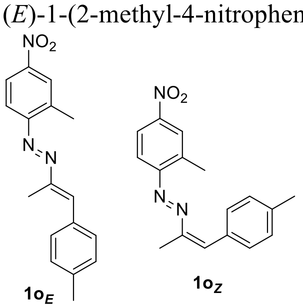


(*E*)-1-(cyclohex-1-en-1-yl)-2-(4-nitrophenyl)diazene (**1n**)



Adapted from a published procedure[S8]. To a 50 mL round bottom flask with a magnetic stir bar was added 2-chlorocyclohexanone (1.33 g, 10.0 mmol) and pyridine (1.01 mL, 12.5 mmol). The reaction mixture was heated to 100 °C (pre-heated oil bath) and stirred at this temperature for 5 min. The reaction mixture was cooled and THF (2 mL) was added to obtain solution **A**. In a separate 250 mL round bottom flask with a magnetic stir bar was added 4-nitrophenyl hydrazine and THF (10 mL). The reaction mixture was cooled to 0 °C and solution **A** was added dropwise. After addition, the reaction mixture was stirred at 0 °C for 2 h at which point ice water (140 mL) was added. A 1M $NaOH_{(aq)}$ solution (16 mL) was then added dropwise and The reaction mixture extracted with DCM (3 x 50 mL). The combined organic phases were washed with $NaCl_{(sat., aq)}$, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography (19:1 hexanes:ethyl acetate) to afford **1n** (1.63 g, 71%) as a orange solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 9.0 Hz, 2H), 7.82 (d, *J* = 9.0 Hz, 2H), 7.13 (t, *J* = 4.4 Hz, 1H), 2.57 – 2.47 (m, 2H), 2.45 – 2.36 (m, 2H), 1.83 – 1.69 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.29, 156.25, 148.1, 146.5, 124.7, 123.0, 26.9, 22.8, 22.2, 21.9; **HRMS** (EI): found $[M]^+$ 231.1008 $C_{12}H_{13}N_3O_2$ requires 231.1008

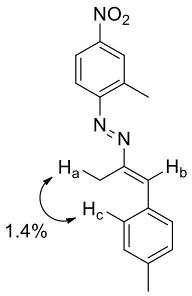
(*E*)-1-(2-methyl-4-nitrophenyl)-2-((*E*)-1-(*p*-tolyl)prop-1-en-2-yl)diazene (**1o*$_E$***)
(*E*)-1-(2-methyl-4-nitrophenyl)-2-((*Z*)-1-(*p*-tolyl)prop-1-en-2-yl)diazene (**1o*$_Z$***)

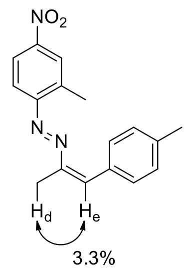


The same procedure for **1a** was performed, except 4-Methylphenylacetone (1.48 g, 10.0 mmol) was used instead. The reaction afforded **1o** (400 mg, 14%, two steps) as a red solid (2:1 **1o*$_E$***:**1o*$_Z$***); **^{1}H NMR** (400 MHz, $CDCl_3$) δ (**1o*$_E$***) 8.20 (d, *J* = 2.7 Hz, 1H), 8.10 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.79 (s, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 2.72 (s, 3H), 2.43 (s, 3H), 2.31 (s, 3H); δ (**1o*$_Z$***) 8.20 (d, *J* = 3.4 Hz, 1H), 8.10 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.13 (s, 1H), 2.73 (s, 3H), 2.40 (s, 3H), 2.17 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ (**1o*$_E$***+**1o*$_Z$***) 154.6, 154.2, 154.1, 151.0, 148.1, 147.9, 146.1, 139.6, 139.2, 139.1, 138.6, 138.3, 132.9, 132.9, 132.3, 130.2, 129.5, 129.2, 126.3, 126.3, 122.0, 122.0, 116.6, 116.3, 21.5, 21.5, 17.9, 17.7, 17.7, 12.1; **HRMS** (ESI): found $[M+H]^+$ 296.1395 $C_{17}H_{18}N_3O_2$ requires 296.1394

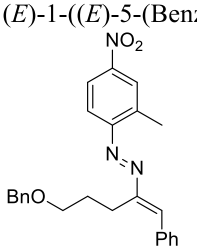
NOE experiments:

The diastereomeric assignment of **1o$_E$** and **1o$_Z$** was performed by irradiation of H_a, H_b, H_d, and H_e which gave the following relevant enhancements. Additionally, although a negative observation, no communication between H_a and H_b was observed.





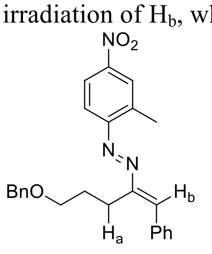
(*E*)-1-((*E*)-5-(Benzyloxy)-1-phenylpent-1-en-2-yl)-2-(2-methyl-4-nitrophenyl)diazene (**1p**)



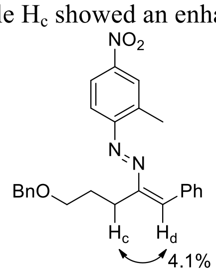
The same procedure for **1a** was performed, except (5-(benzyloxy)-1-phenylpentan-2-one (**S1p**) (2.68 g, 10.0 mmol) was used instead. The crude product was purified by column chromatography (dry load, 19:1 hexanes:ether, first orange band) to afford **1p** (274 mg, 7%, two steps) as a red solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (d, J = 2.1 Hz, 1H), 8.11 (dd, J = 8.8, 2.5 Hz, 1H), 7.81 (s, 1H), 7.69 (d, J = 6.3 Hz, 2H), 7.64 (d, J = 8.8 Hz, 1H), 7.47 – 7.30 (m, 8H), 4.55 (s, 2H), 3.62 (t, J = 6.1 Hz, 2H), 3.03 – 2.95 (m, 2H), 2.70 (s, 3H), 2.00 – 1.90 (m, 2H)f; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.9, 154.1, 148.1, 146.3, 138.6, 138.4, 135.4, 130.1, 129.3, 128.9, 128.4, 127.6, 127.5, 126.3, 122.0, 116.2, 73.0, 70.2, 27.7, 22.4, 17.8.; **HRMS** (EI): found $[M+H]^+$ 415.1894 $C_{25}H_{25}N_3O_3$ requires 415.1896

NOE experiments:

The diastereomeric assignment of **1p** was performed by irradiation of a mixture of **1p** and iso-**1p**. H_a showed no enhancement upon irradiation of H_b, while H_c showed an enhancement of 4.1% upon irradiation of H_d.



1p

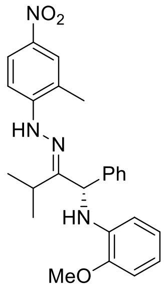


iso-**1p**

Chiral Phosphoric Acid-Catalyzed Enantioselective Nucleophilic Addition Products

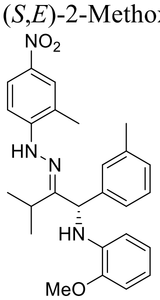
General procedure **A** for the addition reaction (substrates **2a**-**2m**): To a 1 dram (3.7 mL) glass vial equipped with a magnetic stir bar was added the appropriate arylazoalkene **1** (0.30 mmol), (*R*)-TCYP (H-**3c**) (9.9 mg, 0.010 mmol), and 5A molecular sieves (100 mg). A solution of the appropriate aniline (0.10 mmol) in benzene (1 mL) was added, the vial capped with a PTFE screw cap, protected from ambient light, and stirred at r.t. for the designated time. The reaction mixture was loaded directly onto the column and purified by column chromatography to obtain the desired product.

(*S*,*E*)-2-Methoxy-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)aniline (**2a**)



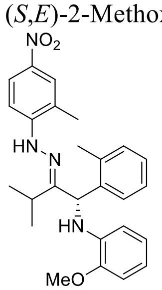
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and 2-methoxyaniline (12.3 mg, 0.10 mmol) with a reaction time of 24 h after column chromatography (4:1 to 3:1 hexanes:ether) afforded **2a** (39.7 mg, 92%) as a yellow film; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 9.0, 2.6 Hz, 1H), 8.03 (d, *J* = 1.9 Hz, 1H), 7.74 (br s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.49 (d, *J* = 7.1 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.23 (m, 1H), 6.83 – 6.73 (m, 2H), 6.70 – 6.59 (m, 2H), 5.93 (br s, 1H), 5.21 (s, 1H), 3.94 (s, 3H), 2.88 (hept, *J* = 7.1 Hz, 1H), 2.25 (s, 3H), 1.21 (d, *J* = 7.1 Hz, 3H), 1.07 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.2, 148.3, 147.2, 140.4, 139.9, 136.8, 128.8, 128.2, 127.9, 126.4, 124.3, 121.2, 119.8, 117.1, 111.4, 111.0, 109.7, 60.7, 55.8, 28.7, 18.6, 18.6, 17.0; **HRMS** (ESI): found $[M+H]^+$ 443.2236 $C_{25}H_{29}N_4O_3$ requires 433.2234; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 15.17 min, minor enantiomer t_r = 13.46 min, 92% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-2-Methoxy-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-(*m*-tolyl)butyl)aniline (**2b**)



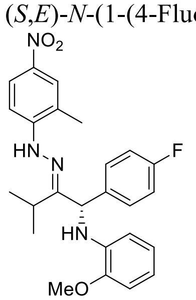
General procedure **A** using arylazoalkene **1b** (97.0 mg, 0.30 mmol) and 2-methoxyaniline (12.3 mg, 0.10 mmol) with a reaction time of 24 h after column chromatography (4:1 to 3:1 hexanes:ether) afforded **2b** (38.9 mg, 87%) as a yellow foam; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 9.0, 2.6 Hz, 1H), 8.03 (d, *J* = 1.9 Hz, 1H), 7.74 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.49 (d, *J* = 7.1 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.23 (m, 1H), 6.83 – 6.73 (m, 2H), 6.70 – 6.59 (m, 2H), 5.93 (br s, 1H), 5.21 (s, 1H), 3.94 (s, 3H), 2.88 (hept, *J* = 7.1 Hz, 1H), 2.25 (s, 3H), 1.21 (d, *J* = 7.1 Hz, 3H), 1.07 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.2, 148.4, 147.2, 140.2, 139.8, 138.4, 136.9, 128.8, 128.7, 128.6, 126.4, 125.3, 124.3, 121.2, 119.8, 117.0, 111.3, 111.0, 109.6, 60.8, 55.7, 28.7, 21.6, 18.6, 18.6, 17.0; **HRMS** (ESI): found $[M+H]^+$ 447.2394 $C_{26}H_{31}N_4O_3$ requires 447.2391; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 11.83 min, minor enantiomer t_r = 9.58 min, 93% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-2-Methoxy-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-(*o*-tolyl)butyl)aniline (**2c**)



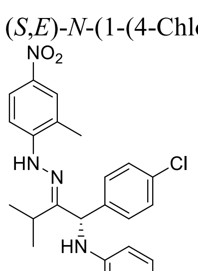
General procedure **A** using arylazoalkene **1c** (97.0 mg, 0.30 mmol) and 2-methoxyaniline (12.3 mg, 0.10 mmol) with a reaction time of 24 h after column chromatography (4:1 to 3:1 hexanes:ether) afforded **2c** (39.8 mg, 89%) as a yellow foam; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 – 7.98 (m, 2H), 7.75 (s, 1H), 7.41 – 7.35 (m, 1H), 7.30 (d, *J* = 9.0 Hz, 1H), 7.25 – 7.18 (m, 3H), 6.84 – 6.77 (m, 2H), 6.72 – 6.60 (m, 2H), 5.51 (s, 1H), 5.34 (br s, 1H), 3.93 (s, 3H), 2.87 (hept, *J* = 7.3 Hz, 1H), 2.52 (s, 3H), 2.24 (s, 3H), 1.25 (d, *J* = 7.1 Hz, 3H), 1.11 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.7, 148.4, 147.4, 139.7, 137.9, 137.4, 136.5, 131.1, 127.9, 127.7, 126.3, 126.3, 124.2, 121.2, 119.6, 117.4, 111.3, 111.0, 109.7, 57.5, 55.6, 28.5, 19.5, 18.7, 18.5, 17.0; **HRMS** (ESI): found $[M+H]^+$ 447.2393 $C_{26}H_{31}N_4O_3$ requires 447.2391; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 7.07 min, minor enantiomer t_r = 5.54 min, 94% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-*N*-(1-(4-Fluorophenyl)-3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)butyl)-2-methoxyaniline (**2d**)



General procedure **A** using arylazoalkene **1d** (98.2 mg, 0.30 mmol) and 2-methoxyaniline (12.3 mg, 0.10 mmol) with a reaction time of 24 h after column chromatography (4:1 to 2:1 hexanes:ether) afforded **2d** (41.8 mg, 93%) as a yellow foam; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 9.0, 2.6 Hz, 1H), 8.04 (d, *J* = 2.0 Hz, 1H), 7.73 (s, 1H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.45 (dd, *J* = 8.6, 5.3 Hz, 2H), 7.04 (t, *J* = 8.6 Hz, 2H), 6.83 – 6.73 (m, 2H), 6.69 – 6.63 (m, 1H), 6.56 (d, *J* = 7.8 Hz, 1H), 5.93 (br s, 1H), 5.19 (s, 1H), 3.93 (s, 3H), 2.86 (hept, *J* = 7.6 Hz, 1H), 2.26 (s, 3H), 1.21 (d, *J* = 7.1 Hz, 3H), 1.08 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3 (d, *J* = 246.4 Hz), 154.9, 148.2, 147.2, 139.9, 136.6, 136.3 (d, *J* = 3.1 Hz), 129.7 (d, *J* = 8.1 Hz), 126.4, 124.3, 121.2, 119.9, 117.2, 115.7 (d, *J* = 21.6 Hz), 111.3, 110.8, 109.7, 59.7, 55.7, 28.7, 18.6, 18.6, 17.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.66 – -113.75 (m); **HRMS** (ESI): found $[M+H]^+$ 451.2142 $C_{25}H_{28}FN_4O_3$ requires 451.2140; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 11.72 min, minor enantiomer t_r = 15.62 min, 91% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

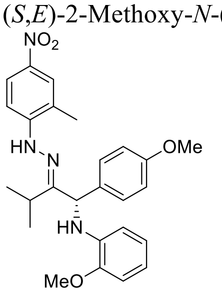
(*S*,*E*)-*N*-(1-(4-Chlorophenyl)-3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)butyl)-2-methoxyaniline (**2e**)



General procedure **A** using arylazoalkene **1e** (103 mg, 0.30 mmol) and 2-methoxyaniline (12.3 mg, 0.10 mmol) with a reaction time of 24 h after column chromatography (4:1 to 2:1 hexanes:ether) afforded **2e** (38.9 mg, 87%) as a yellow film; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 9.1, 2.5 Hz, 1H), 8.03 (d, *J* = 2.0 Hz, 1H), 7.74 (s, 1H), 7.52 (d, *J* = 9.1 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.32

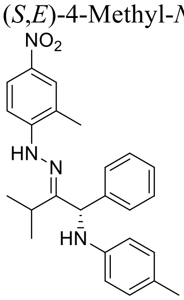
(d, J = 8.5 Hz, 2H), 6.83 – 6.73 (m, 2H), 6.67 (td, J = 7.7, 1.5 Hz, 1H), 6.58 – 6.51 (m, 1H), 5.92 (br s, 1H), 5.19 (s, 1H), 3.94 (s, 3H), 2.88 (hept, J = 6.8 Hz, 1H), 2.26 (s, 3H), 1.22 (d, J = 7.1 Hz, 3H), 1.10 (d, J = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.6, 148.1, 147.2, 140.0, 139.1, 136.4, 133.6, 129.5, 128.9, 126.5, 124.3, 121.2, 119.9, 117.4, 111.3, 110.9, 109.7, 59.8, 55.8, 28.7, 18.7, 18.6, 17.0; **HRMS** (ESI): found $[M+H]^+$ 467.1850 $C_{25}H_{28}{}^{35}ClN_4O_3$ requires 467.1844; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 10.39 min, minor enantiomer t_r = 15.78 min, 93% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-2-Methoxy-*N*-(1-(4-methoxyphenyl)-3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)butyl)aniline (**2f**)



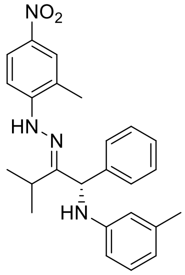
General procedure **A** using arylazoalkene **1f** (102 mg, 0.30 mmol) and 2-methoxyaniline (12.3 mg, 0.10 mmol) with a reaction time of 1.5 h after column chromatography (3:1 to 2:1 hexanes:ether) afforded **2e** (42.4 mg, 92%) as a yellow foam; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (dd, J = 9.2, 2.6 Hz, 1H), 8.03 (d, J = 2.4 Hz, 1H), 7.74 (s, 1H), 7.56 (d, J = 9.1 Hz, 1H), 7.40 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.78 (t, J = 7.5 Hz, 2H), 6.69 – 5.97 (m, 2H), 6.00 (s, 1H), 5.17 (s, 1H), 3.93 (s, 3H), 3.79 (s, 3H), 2.87 (hept, J = 7.2 Hz, 1H), 2.25 (s, 3H), 1.21 (d, J = 7.1 Hz, 3H), 1.06 (d, J = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.2, 155.3, 148.3, 147.2, 139.8, 136.6, 132.1, 129.3, 126.4, 124.3, 121.2, 119.8, 117.1, 114.1, 111.3, 111.1, 109.7, 60.0, 55.7, 55.4, 28.7, 18.6, 18.6, 17.0; **HRMS** (EI): found $[M]^+$ 462.2264 $C_{26}H_{30}N_4O_4$ requires 462.2267; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 14.04 min, minor enantiomer t_r = 22.16 min, 91% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-4-Methyl-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)aniline (**2g**)



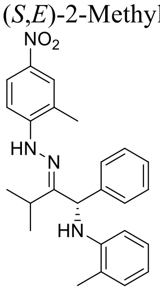
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and 4-methylaniline (10.7 mg, 0.10 mmol) with a reaction time of 16 h after column chromatography (9:1 to 4:1 hexanes:ether) afforded **2g** (29.9 mg, 72%) as a yellow foam; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (dd, J = 9.1, 2.6 Hz, 1H), 8.02 (d, J = 1.8 Hz, 1H), 7.73 (s, 1H), 7.50 – 7.43 (m, 3H), 7.36 (t, J = 7.5 Hz, 2H), 7.31 – 7.25 (m, 1H), 6.96 (d, J = 8.1 Hz, 2H), 6.63 (d, J = 8.4 Hz, 2H), 5.22 (s, 1H), 5.02 (br s, 1H), 2.90 (hept, J = 7.5 Hz, 1H), 2.25 (s, 3H), 2.21 (s, 3H), 1.22 (d, J = 7.1 Hz, 3H), 1.08 (d, J = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.7, 148.2, 144.5, 140.4, 139.8, 129.8, 128.8, 128.0, 127.9, 127.1, 126.4, 124.3, 119.8, 114.0, 111.2, 60.7, 28.6, 20.5, 18.6, 18.6, 17.0; **HRMS** (EI): found $[M]^+$ 416.2210 $C_{25}H_{28}N_4O_2$ requires 416.2212; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 15.04 min, minor enantiomer t_r = 8.75 min, 95% ee; absolute configuration assigned as (*S*) by X-ray crystal structure analysis; crystals obtained by slow evaporation of toluene solution.

(*S*,*E*)-3-Methyl-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)aniline (**2h**)



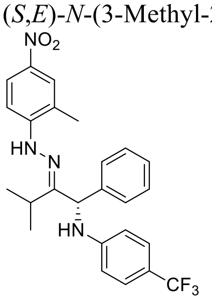
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and 3-methylaniline (10.7 mg, 0.10 mmol) with a reaction time of 16 h after column chromatography (9:1 to 4:1 hexanes:ether) afforded **2h** (21.3 mg, 51%) as a yellow foam; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 9.0, 2.6 Hz, 1H), 8.03 (d, *J* = 2.6 Hz, 1H), 7.72 (s, 1H), 7.50 – 7.43 (m, 3H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.31 – 7.25 (m, 1H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.56 – 6.48 (m, 3H), 5.23 (s, 1H), 5.13 (br s, 1H), 2.90 (hept, *J* = 7.1 Hz, 1H), 2.26 (s, 3H), 2.25 (s, 3H), 1.22 (d, *J* = 7.1 Hz, 3H), 1.08 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.6, 148.1, 146.8, 140.4, 139.9, 139.0, 129.2, 128.8, 128.1, 127.9, 126.4, 124.3, 119.8, 118.8, 114.7, 111.2, 110.7, 60.4, 28.7, 21.7, 18.6, 18.6, 17.0; **HRMS** (EI): found $[M]^+$ 416.2206 $C_{25}H_{28}N_4O_2$ requires 416.2212; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 10.66 min, minor enantiomer t_r = 7.40 min, 94% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-2-Methyl-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)aniline (**2i**)



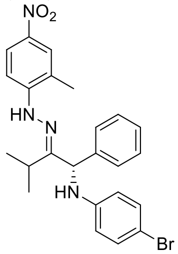
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and 2-methylaniline (10.7 mg, 0.10 mmol) with a reaction time of 24 h after column chromatography (9:1 to 4:1 hexanes:ether) afforded **2h** (26.2 mg, 63%) as a yellow film; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 9.1, 2.6 Hz, 1H), 8.04 (d, *J* = 2.6 Hz, 1H), 7.76 (s, 1H), 7.53 – 7.45 (m, 3H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.31 – 7.24 (m, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.9 Hz, 1H), 6.67 – 6.58 (m, 2H), 5.40 (br s, 1H), 5.25 (s, 1H), 2.91 (hept, *J* = 7.2 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H), 1.21 (d, *J* = 7.1 Hz, 3H), 1.09 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.5, 148.1, 144.6, 140.3, 139.9, 130.3, 128.8, 128.2, 127.9, 127.1, 126.5, 124.4, 122.1, 119.9, 117.2, 110.9, 110.6, 60.3, 29.0, 18.6, 18.5, 17.8, 17.0; **HRMS** (EI): found $[M]^+$ 416.2209 $C_{25}H_{28}N_4O_2$ requires 416.2212; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 10.26 min, minor enantiomer t_r = 5.27 min, 89% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-*N*-(3-Methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)-4-(trifluoromethyl)aniline (**2j**)



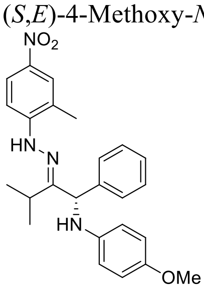
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and 4-(trifluoromethyl)aniline (16.1 mg, 0.10 mmol) with a reaction time of 16 h after column chromatography (7:3 to 2:1 hexanes:ether) afforded **2j** (33.5 mg, 71%) as a yellow foam; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 9.0, 2.5 Hz, 1H), 8.04 (d, *J* = 1.8 Hz, 1H), 7.73 (s, 1H), 7.50 – 7.41 (m, 3H), 7.41 – 7.33 (m, 4H), 7.33 – 7.27 (m, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 5.65 (br d, *J* = 6.6 Hz, 1H), 5.20 (d, *J* = 6.5 Hz, 1H), 2.88 (hept, *J* = 7.4 Hz, 1H), 2.26 (s, 3H), 1.21 (d, J = 7.1 Hz, 3H), 1.08 (d, J = 7.2 Hz, 3H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 154.6, 149.0, 147.9, 140.0, 139.5, 129.0, 128.3, 128.1, 126.65 (q, J = 3.8 Hz), 126.5, 125.01 (q, J = 270.4 Hz), 124.3, 120.0, 119.15 (q, J = 32.5 Hz), 112.7, 111.1, 59.8, 28.9, 18.6, 18.5, 17.0; ^{19}**F NMR** (376 MHz, $CDCl_3$) δ -60.26 (s); **HRMS** (EI): found $[M]^+$ 470.1924 $C_{25}H_{25}F_3N_4O_2$ requires 470.1930; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 259 nm); major enantiomer t_r = 8.52 min, minor enantiomer t_r = 6.16 min, 91% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-4-Bromo-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)aniline (**2k**)



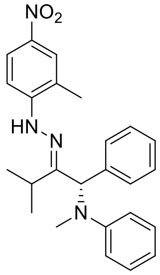
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and 4-bromoaniline (17.2 mg, 0.10 mmol) with a reaction time of 16 h after column chromatography (9:1 to 3:1 hexanes:ether) afforded **2k** (41.4 mg, 86%) as a yellow foam; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 9.0, 2.6 Hz, 1H), 8.01 (d, J = 2.0 Hz, 1H), 7.73 (s, 1H), 7.47 – 7.40 (m, 3H), 7.38 – 7.33 (m, 2H), 7.32 – 7.27 (m, 1H), 7.21 (d, J = 8.9 Hz, 2H), 6.57 (d, J = 8.9 Hz, 2H), 5.29 (br d, J = 6.6 Hz, 1H), 5.16 (d, J = 5.6 Hz, 1H), 2.89 (hept, J = 7.3 Hz, 1H), 2.24 (s, 3H), 1.21 (d, J = 7.1 Hz, 3H), 1.07 (d, J = 7.2 Hz, 3H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 154.9, 148.0, 145.6, 139.9, 139.7, 131.9, 128.9, 128.1, 128.0, 126.4, 124.3, 119.9, 115.3, 111.1, 109.4, 60.3, 28.7, 18.6, 18.5, 17.0; **HRMS** (EI): found $[M]^+$ 482.1132 $C_{24}H_{25}{}^{81}BrN_4O_2$ requires 482.1140; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 15.35 min, minor enantiomer t_r = 9.32 min, 94% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-4-Methoxy-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)aniline (**2l**)



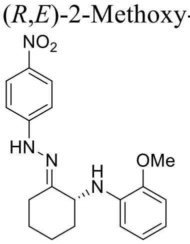
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and 4-methoxyaniline (12.3 mg, 0.10 mmol) with a reaction time of 16 h after column chromatography (4:1 to 2:1 hexanes:ether) afforded **2l** (36.6 mg, 85%) as a yellow foam; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.13 (dd, J = 9.0, 2.6 Hz, 1H), 8.03 (d, J = 2.4 Hz, 1H), 7.71 (s, 1H), 7.48 – 7.42 (m, 3H), 7.34 (t, J = 7.4 Hz, 2H), 7.27 (t, J = 7.3 Hz, 1H), 6.74 (d, J = 9.0 Hz, 2H), 6.66 (d, J = 9.0 Hz, 2H), 5.16 (s, 1H), 4.84 (br s, 1H), 3.71 (s, 3H), 2.88 (hept, J = 7.2 Hz, 1H), 2.25 (s, 3H), 1.20 (d, J = 7.1 Hz, 3H), 1.05 (d, J = 7.2 Hz, 3H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 155.8, 152.4, 148.2, 141.0, 140.4, 139.8, 128.8, 128.0, 127.9, 126.4, 124.3, 119.8, 115.4, 114.8, 111.2, 61.5, 55.8, 28.6, 18.6, 18.6, 17.0; **HRMS** (EI): found $[M]^+$ 432.2155 $C_{25}H_{28}N_4O_3$ requires 432.2161; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 21.71 min, minor enantiomer t_r = 12.56 min, 94% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*S*,*E*)-*N*-Methyl-*N*-(3-methyl-2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-phenylbutyl)aniline (**2m**)



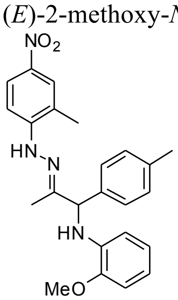
General procedure **A** using arylazoalkene **1a** (92.8 mg, 0.30 mmol) and *N*-methylaniline (10.7 mg, 0.10 mmol) with a reaction time of 24 h after column chromatography (9:1 to 4:1 hexanes:ether) afforded **2m** (28.2 mg, 68%) as a orange film; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 – 7.92 (m, 2H), 7.79 (br s, 1H), 7.41 – 7.22 (m, 7H), 7.06 (d, *J* = 9.0 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 5.81 (s, 1H), 3.02 – 2.92 (m, 4H), 2.25 (s, 3H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 149.7, 148.2, 139.8, 139.0, 129.4, 128.7, 128.3, 127.3, 126.3, 124.2, 119.7, 117.3, 113.1, 111.5, 63.9, 34.7, 28.4, 18.9, 18.5, 16.9; **HRMS** (EI): found $[M]^+$ 416.2204 $C_{25}H_{28}N_4O_2$ requires 416.2212; **HPLC** Chiralpak AD-H column (98:02 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 10.01 min, minor enantiomer t_r = 9.46 min, 90% ee; absolute configuration assigned as (*S*) by analogy to **2g**.

(*R*,*E*)-2-Methoxy-*N*-(2-(2-(4-nitrophenyl)hydrazono)cyclohexyl)aniline (**2n**)



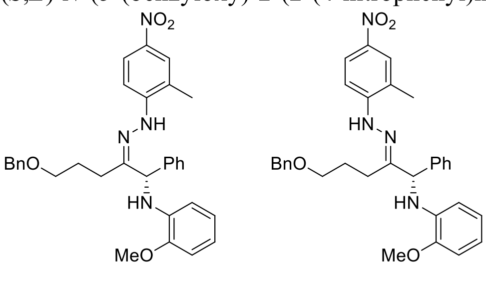
To a 2 dram (7.4 mL) glass vial equipped with a magnetic stir bar was added **1n** (46.3 mg, 0.20 mmol), (*R*)-TRIP (H-**3a**) (7.5 mg, 0.010 mmol), and 5A molecular sieves (400 mg). A solution of 2-methoxyaniline (29.6 mg, 0.24 mmol) in benzene (4 mL) was added, the vial capped with a PTFE screw cap, protected from ambient light, and stirred at r.t. for 2 h. The reaction mixture was loaded directly onto the column and purified by column chromatography (petroleum ether:acetone 4:1) and additional column chromatography (1:1 petroleum ether:ether) to afford **2n** (44.1 mg, 62%) as a yellow foam; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.21 (s, 1H), 8.11 (d, *J* = 9.0 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 6.58 (t, *J* = 7.5 Hz, 1H), 5.61 (br s, 1H), 4.06 – 3.95 (m, 1H), 3.89 (s, 3H), 3.04 (d, *J* = 14.0 Hz, 1H), 2.40 – 2.27 (m, 1H), 2.15 – 2.03 (m, 1H), 1.93 – 1.62 (m, 3H), 1.54 – 1.33 (m, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 152.7, 151.8, 146.5, 138.0, 137.2, 125.9, 121.0, 116.0, 111.0, 110.2, 109.8, 56.1, 55.5, 35.2, 26.0, 25.8, 23.3; **HRMS** (EI): found $[M]^+$ 354.1693 $C_{19}H_{22}N_4O_3$ requires 354.1692; **HPLC** Chiralpak AD-H column (90:10 hexanes:isopropanol, 1.0 mL/min, 259 nm); major enantiomer t_r = 21.37 min, minor enantiomer t_r = 18.73 min, 90% ee; absolute configuration tentatively assigned as (*R*) by analogy to **4n**.

(*E*)-2-methoxy-*N*-(2-(2-(2-methyl-4-nitrophenyl)hydrazono)-1-(*p*-tolyl)propyl)aniline (**2o**)



To a 2 dram (7.4 mL) glass vial equipped with a magnetic stir bar was added **1o** (58.9 mg, 0.20 mmol), (*R*)-TRIP (H-**3a**) (30.1 mg, 0.040 mmol), and 5A molecular sieves (400 mg). A solution of 2-methoxyaniline (73.9 mg, 0.60 mmol) in benzene (4 mL) was added, the vial capped with a PTFE screw cap, protected from ambient light, and stirred at r.t. for 14 h. The reaction mixture was loaded directly onto the column and purified by column chromatography (hexanes:ether 3:1 to 2:1) to afford **2o** (41.0 mg, 49%) as a yellow film; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 9.1, 2.5 Hz, 1H), 8.02 (d, *J* = 2.1 Hz, 1H), 7.64 (d, *J* = 9.2 Hz, 1H), 7.41 – 7.32 (m, 3H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.83 – 6.74 (m, 2H), 6.68 (td, *J* = 7.7, 1.6 Hz, 1H), 6.60 (dd, *J* = 7.8, 1.5 Hz, 1H), 5.83 (br s, 1H), 5.09 (s, 1H), 3.94 (s, 3H), 2.35 (s, 3H), 2.23 (s, 3H), 1.88 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.8, 148.2, 147.1, 139.8, 137.8, 137.1, 136.8, 129.7, 127.4, 126.4, 124.2, 121.3, 119.9, 117.2, 111.6, 111.1, 109.6, 63.8, 55.7, 21.2, 16.9, 12.3; **HRMS** (EI): found $[M]^+$ 418.2004 $C_{24}H_{26}N_4O_3$ requires 418.2005; **HPLC** Chiralpak AD-H column (80:20 hexanes:isopropanol, 1.0 mL/min, 356 nm); major enantiomer t_r = 8.22 min, minor enantiomer t_r = 14.30 min, 90% ee.

(*S*,*Z*)-*N*-(5-(benzyloxy)-2-(2-(4-nitrophenyl)hydrazono)-1-phenylpentyl)-2-methoxyaniline (**$2p_Z$**)
(*S*,*E*)-*N*-(5-(benzyloxy)-2-(2-(4-nitrophenyl)hydrazono)-1-phenylpentyl)-2-methoxyaniline (**$2p_E$**)

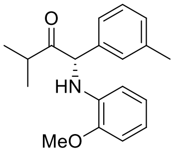


$2p_Z$ **$2p_E$**

To a 1 dram (3.7 mL) glass vial equipped with a magnetic stir bar was added **1p** (124 mg, 0.30 mmol), (*R*)-TRIP (H-**3a**) (7.6 mg, 0.010 mmol), 5A molecular sieves (200 mg). 2-methoxyaniline (12.4 mg, 0.10 mmol) in benzene (2 mL) was added, the vial capped with a PTFE screw cap, protected from ambient light, and stirred at r.t. for 14 h. The reaction mixture was loaded directly onto the column and purified by column chromatography (hexanes:ether 4:1 to 3:1) to afford a mixture **$2p_Z$** (37.5 mg, 70%) and **$2p_E$** (9.7 mg, 18%) as a yellow film; **^{1}H NMR** (400 MHz, $CDCl_3$) δ (**$2p_Z$**) 11.21 (br s, 1H), 8.06 (dd, J = 9.2, 2.5 Hz, 1H), 7.91 (d, J = 2.5 Hz, 1H), 7.48 – 7.26 (m, 11H), 6.91 – 6.85 (m, 3H), 6.69 – 6.65 (m, 1H), 4.98 (d, J = 1.6 Hz, 1H), 4.75 (br d, J = 1.5 Hz, 1H), 4.50 (s, 2H), 3.84 (s, 3H), 3.64 – 3.50 (m, 2H), 2.67 – 2.55 (m, 1H), 2.47 – 2.37 (m, 1H), 2.15 – 1.97 (m, 2H), 1.92 (s, 3H); δ (**$2p_E$**) δ 8.18 – 8.12 (m, 1H), 7.97 (d, J = 2.2 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.49 – 7.25 (m, 8H), 6.82 (dd, J = 7.6, 1.0 Hz, 1H), 6.76 (td, J = 7.7, 1.3 Hz, 1H), 6.71 – 6.64 (m, 1H), 6.55 (dd, J = 7.8, 1.3 Hz, 1H), 6.13 (br s, 1H), 5.08 (br s, 1H), 4.49 (s, 2H), 3.97 (s, 3H), 3.43 – 3.30 (m, 2H), 2.50 – 2.43 (m, 2H), 2.15 – 1.96 (m, 5H).; **^{13}C NMR** (101 MHz, $CDCl_3$) δ (**$2p_Z$+$2p_E$**) 151.7, 149.3, 149.0, 148.7, 147.5, 147.1, 140.4, 139.6, 138.9, 138.5, 137.8, 137.6, 136.9, 135.9, 129.7, 129.1, 128.9, 128.6, 128.5, 128.14, 128.12, 128.09, 128.0, 127.71, 127.69, 127.65, 126.4, 126.3, 124.2, 124.0, 121.6, 121.2, 120.7, 120.3, 120.0, 116.9, 112.0, 111.5, 110.9, 109.9, 109.7, 109.5, 73.1, 73.0, 69.7, 68.4, 64.6, 63.3, 55.7, 55.4, 32.4, 26.5, 25.6, 23.6, 16.8, 16.6.; **HRMS** (ESI): found $[M+H]^+$ 539.2647 $C_{32}H_{35}N_4O_4$ requires 539.2653; **HPLC** Chiralpak AD-H column (90:10 hexanes:isopropanol, 1.0 mL/min, 356 nm); **$2p_Z$:** major enantiomer t_r = 6.86 min, minor enantiomer t_r = 9.98 min, 91% ee; **$2p_Z$:** major enantiomer t_r = 12.20 min, minor enantiomer t_r = 20.27 min, 42% ee; absolute configuration tentatively assigned as (*S*) by analogy to **2g**; major product assigned as (*Z*) by based on the presence of the downfield hydrazone proton according to ref. S9.

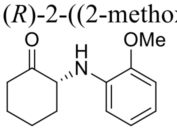
Hydrolysis of products 2b, 2n, 2o to respective ketones 4b, 4n, 4o

(*S*)-1-(4-chlorophenyl)-1-((2-methoxyphenyl)amino)-3-methylbutan-2-one (**4b**)



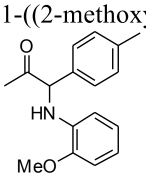
To a 1 dram (3.7 mL) glass vial equipped with a magnetic stir bar was added **2b** (26 mg, 0.058 mmol), paraformaldehyde (14 mg, 0.47 mmol), acetone (0.7 mL) and water (0.07 mL). To the resulting suspension was added Amberlyst-15 ion-exchange resin (10 mg) and the mixture was stirred at room temperature for 15 h until TLC showed complete consumption of starting hydrazone **2b**. The mixture was then passed through a celite plug and the filtrate was extracted with DCM (2 x 3mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography (hexanes:ether 19:1) to afford **4b** (12.5 mg, 72%) as a pale yellow film; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 3H), 7.10 (d, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.71 (td, *J* = 7.6, 1.1 Hz, 1H), 6.62 (td, *J* = 7.7, 1.5 Hz, 1H), 6.39 (dd, *J* = 7.8, 1.2 Hz, 1H), 5.99 (br d, *J* = 4.4 Hz, 1H), 5.08 (d, *J* = 4.7 Hz, 1H), 3.90 (s, 3H), 2.85 (hept, *J* = 7.0 Hz, 1H), 2.34 (s, 3H), 1.16 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 210.4, 147.1, 138.9, 138.1, 136.3, 129.2, 129.0, 128.6, 125.4, 121.0, 116.9, 110.6, 109.5, 66.3, 55.6, 37.0, 21.6, 19.7, 18.5; **HRMS** (ESI): found $[M+H]^+$ 298.1804 $C_{19}H_{24}NO_2$ requires 298.1802; **HPLC** Chiralpak AD-H column (98:02 hexanes:isopropanol, 1.0 mL/min, 285 nm); major enantiomer t_r = 9.24 min, minor enantiomer t_r = 6.10 min, 93% ee; absolute configuration assigned as (*S*) by analogy to **2b**.

(*R*)-2-((2-methoxyphenyl)amino)cyclohexanone (**4n**)



To a 1 dram (3.7 mL) glass vial equipped with a magnetic stir bar was added **2n** (25 mg, 0.07 mmol), paraformaldehyde (10 mg, 0.35 mmol), acetone (1.4 mL) and water (1.4 mL). To the resulting suspension was added Amberlyst-15 ion-exchange resin (7.3 mg) and the mixture was stirred at room temperature for 40 h until TLC showed complete consumption of starting hydrazone **2n**. The mixture was then passed through a celite plug and the filtrate was extracted with DCM (2 x 3mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography (hexanes:ether 9:1) to afford **4n** (12.9 mg, 84%) as a colorless film; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.83 (td, *J* = 7.6, 1.4 Hz, 1H), 6.78 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.67 (td, *J* = 7.7, 1.5 Hz, 1H), 6.50 (dd, *J* = 7.9, 1.5 Hz, 1H), 5.34 (br s, 1H), 4.05-3.95 (m, 1H), 3.87 (s, 3H), 2.70-2.63 (m, 1H), 2.63-2.56 (m, 1H), 2.43 (tdd, *J* = 13.4, 6.2, 1.4 Hz, 1H), 2.20-2.11 (m, 1H), 1.99-1.95 (m, 1H), 1.88-1.78 (m, 1H), 1.73 (qt, *J* = 13.0, 4.0 Hz, 1H), 1.51 (dq, *J* = 12.5, 3.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 208.5, 147.2, 136.6, 121.2, 116.9, 109.8, 109.8, 61.8, 55.6, 41.3, 35.8, 28.3, 24.2; **HRMS** (ESI): found $[M+H]^+$ 220.1332 $C_{13}H_{18}NO_2$ requires 220.1331; **HPLC** Chiralpak IA column (97:03 hexanes:isopropanol, 1.0 mL/min, 285 nm); major enantiomer t_r = 7.76 min, minor enantiomer t_r = 12.00 min, 90% ee; absolute configuration tenatively assigned as (*R*) by an ethanolic sodium borohydride reduction and subsequent comparison previously reported HPLC retention times.[S10]

1-((2-methoxyphenyl)amino)-1-(*p*-tolyl)propan-2-one (**4o**)



To a 1 dram (3.7 mL) glass vial equipped with a magnetic stir bar was added **2o** (34 mg, 0.08 mmol), paraformaldehyde (11.4 mg, 0.4 mmol), acetone (1.7 mL) and water (1.7 mL). To the resulting suspension was added Amberlyst-15 ion-exchange resin (8.3 mg) and the mixture was stirred at room temperature for 48 h until TLC showed complete consumption of starting hydrazone **2o**. The mixture was then passed through a celite plug and the filtrate was extracted with DCM (2 x 3mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography (hexanes:ether 9:1) to afford **4o** (18.9 mg, 82%) as a colorless film; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 7.8 Hz, 2H), 6.75 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.69

(td, *J* = 7.6, 1.4 Hz, 1H), 6.62 (td, *J* = 7.7, 1.6 Hz, 1H), 6.33 (dd, *J* = 7.7, 1.6 Hz, 1H), 5.86 (br d, *J* = 4.3 Hz, 1H), 4.95 (d, *J* = 4.2 Hz, 1H), 3.89 (s, 3H), 2.33 (s, 3H), 2.14 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.5, 147.1, 138.3, 136.2, 135.2, 130.0, 127.8, 121.1, 117.0, 110.7, 109.5, 68.0, 55.6, 26.8, 21.3; **HRMS** (ESI): found $[M+H]^+$ 220.1332 $C_{17}H_{20}NO_2$ requires 220.1331; **HPLC** Chiralpak IA column (97:03 hexanes:isopropanol, 1.0 mL/min, 285 nm); major enantiomer t_r = 7.33 min, minor enantiomer t_r = 8.81 min, 90% ee.

References

(S1) Romanov-Michailidis, F.; Guénée, L; Alexakis, A. *Angew. Chem. Int. Ed.* **2013**, *52*, 9266.

(S2) Romanov-Michailidis, F.; Guénée, L; Alexakis, A. *Org. Lett.* **2013**, *15*, 5890.

(S3) Rauniyar, V.; Wang, Z. J.; Burks, H. E.; Toste F. D. *J. Am. Chem. Soc.* **2011**, *133*, 8486.

(S4) Nelson, H. M.; Patel, J. S.; Shunatona, H. P.; Toste, F. D. *Chem. Sci.* **2015**, *6*, 170.

(S5) Neel, A. J.; Hehn, J. P.; Tripet, P. F.; Toste, F. D. *J. Am. Chem. Soc.* **2013**, *135*, 14044.

(S6) Yao, L.-H.; Shao, S.-X.; Jiang, L.; Tang, N.; Wu, J.-C. *Chem. Pap.* **2014**, *68*, 1381.

(S7) Maryanoff, B. E.; Kinney, W. A.; Lawson, E. C.; Luci, D. K.; Marchenko, N.; Sviridov, S; Ghosh, S. U.S. Patent US2011136824, June 9, 2011.

(S8) Brodka, S; Simon, H. *Chem. Ber.* **1969**, *102*, 3647.

(S9) Bozzini, S.; Felluga, F.; Nardin, G.; Pizzioli, A.; Pitacco, G.; Valentin, E. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1961.

(S10) (a) Gao, B.; Wen, Y.; Yang, Z.; Huang, X.; Liu, X.; Feng, X. *Adv. Synth. Catal.* **2008**, *350*, 385. (b) Bao, H.; Wu, J.; Li, H.; Wang, Z.; You, T.; Ding, K. *Eur. J. Org. Chem.* **2010**, 6722. (c) Bao, H.; Wang, Z.; You, T.; Ding, K. *Chin. J. Chem.* **2013**, *31*, 67.

S1b (1H NMR)
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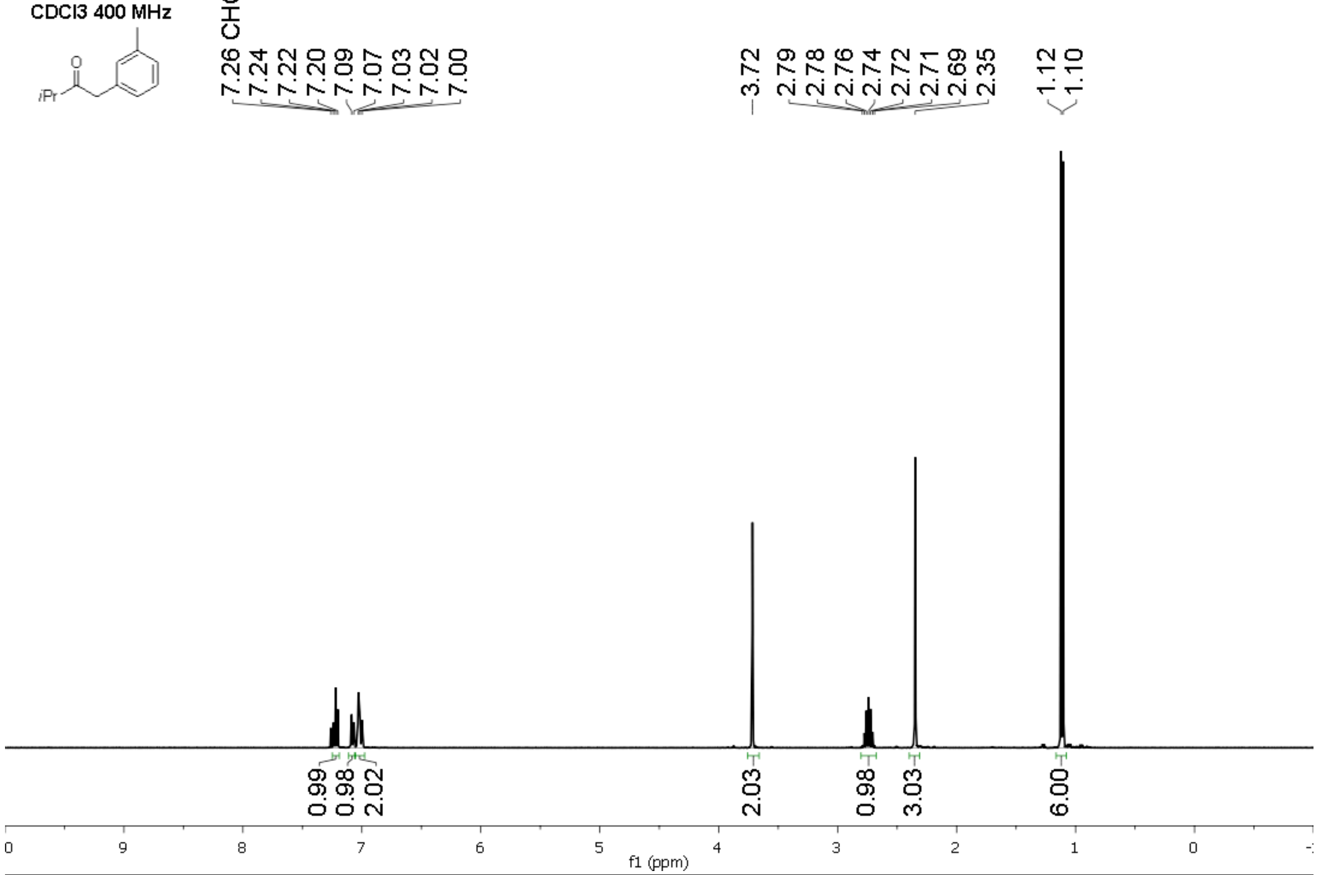
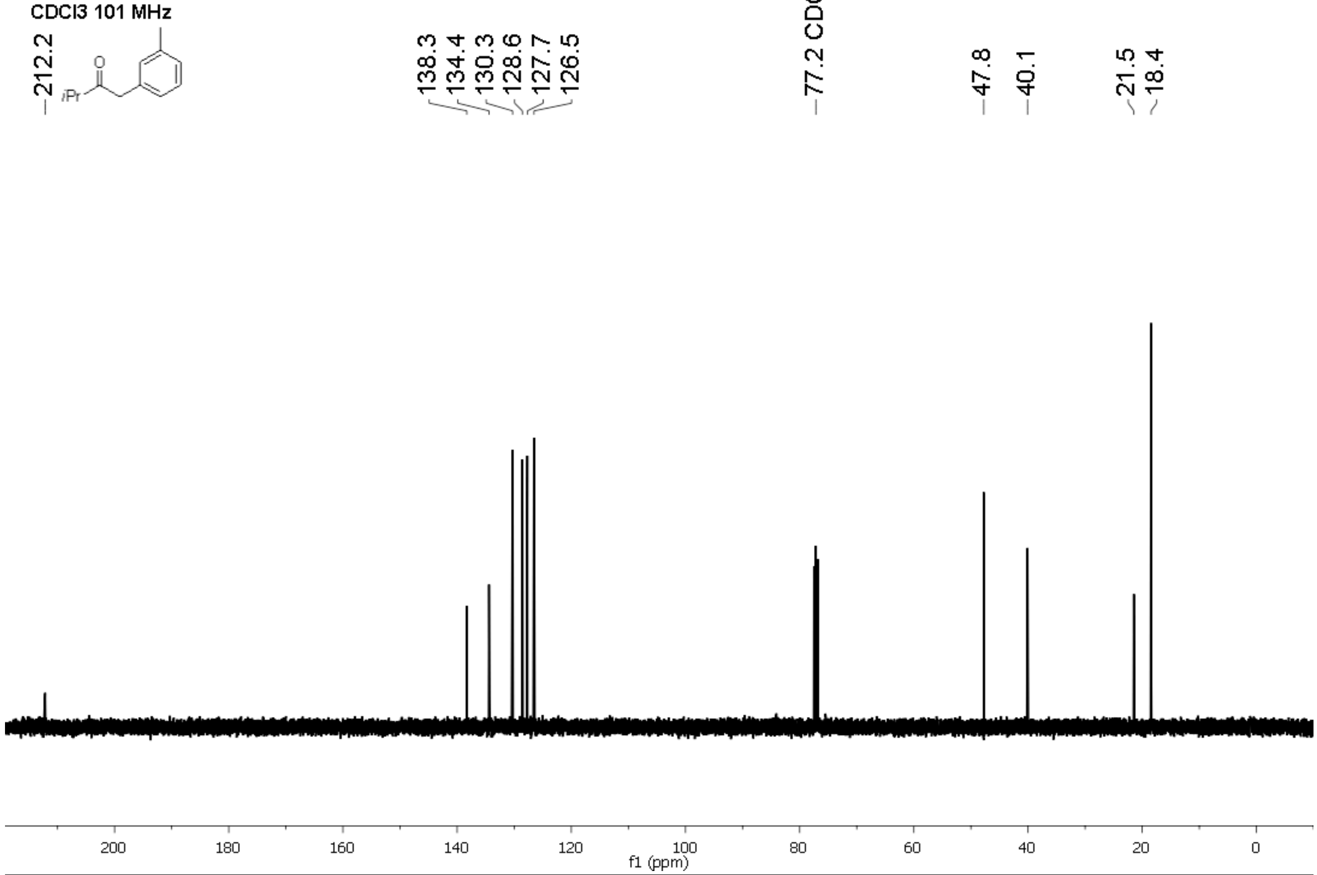
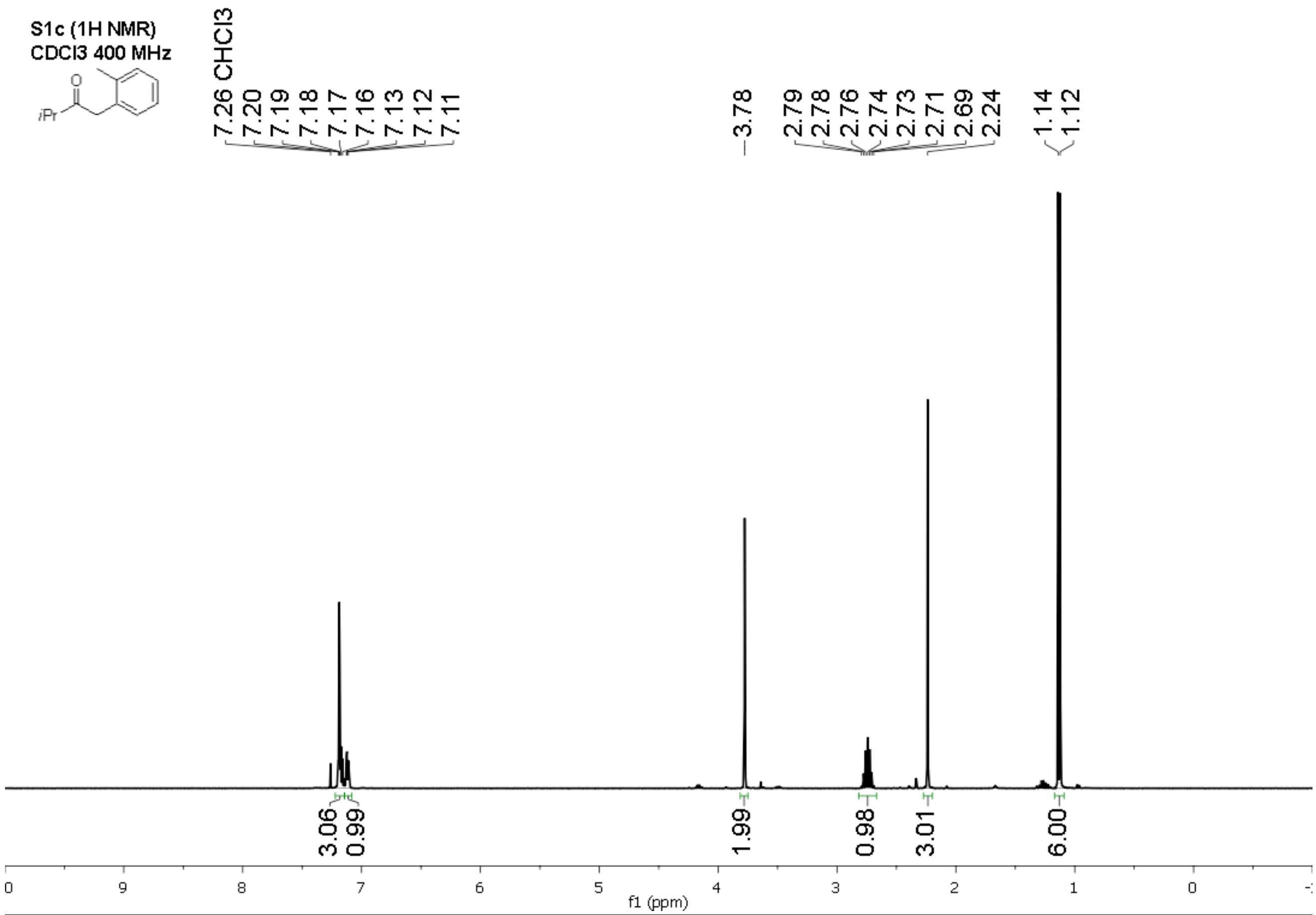


S1b (13C NMR)
CDCl3 101 MHz

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CDCl3 400 MHz
O
iPr
7.26 CHCl3
7.20
7.19
7.18
7.17
7.16
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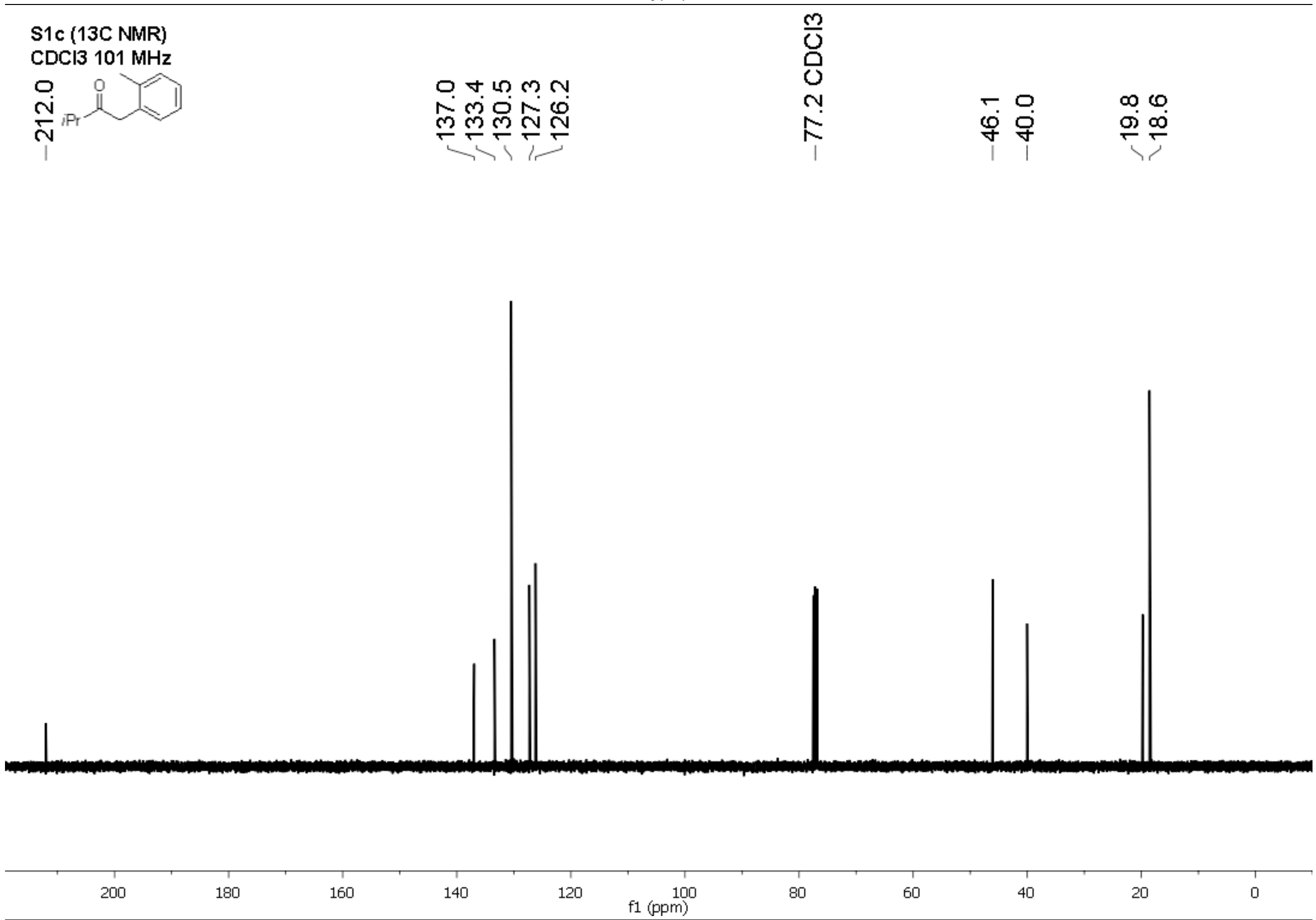
7.12
7.11
3.78
2.79
2.78
2.76
2.74
2.73
2.71
2.69
2.24
1.14
1.12
3.06
0.99
1.99
0.98
3.01
6.00
f1 (ppm)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O
iPr
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126.2
77.2 CDCl3
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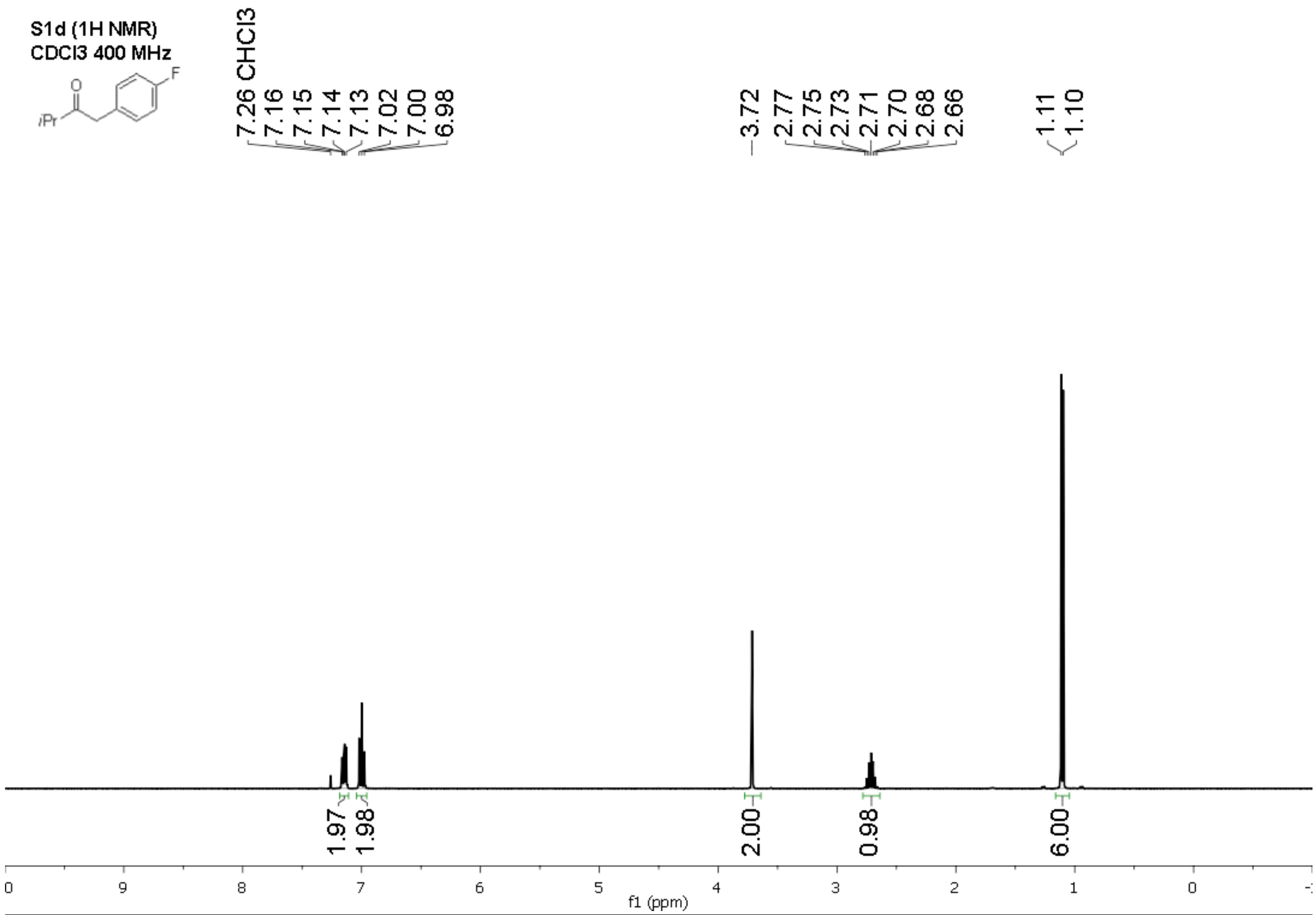
40.0
19.8
18.6
f1 (ppm)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F
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7.13
7.02
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6.98
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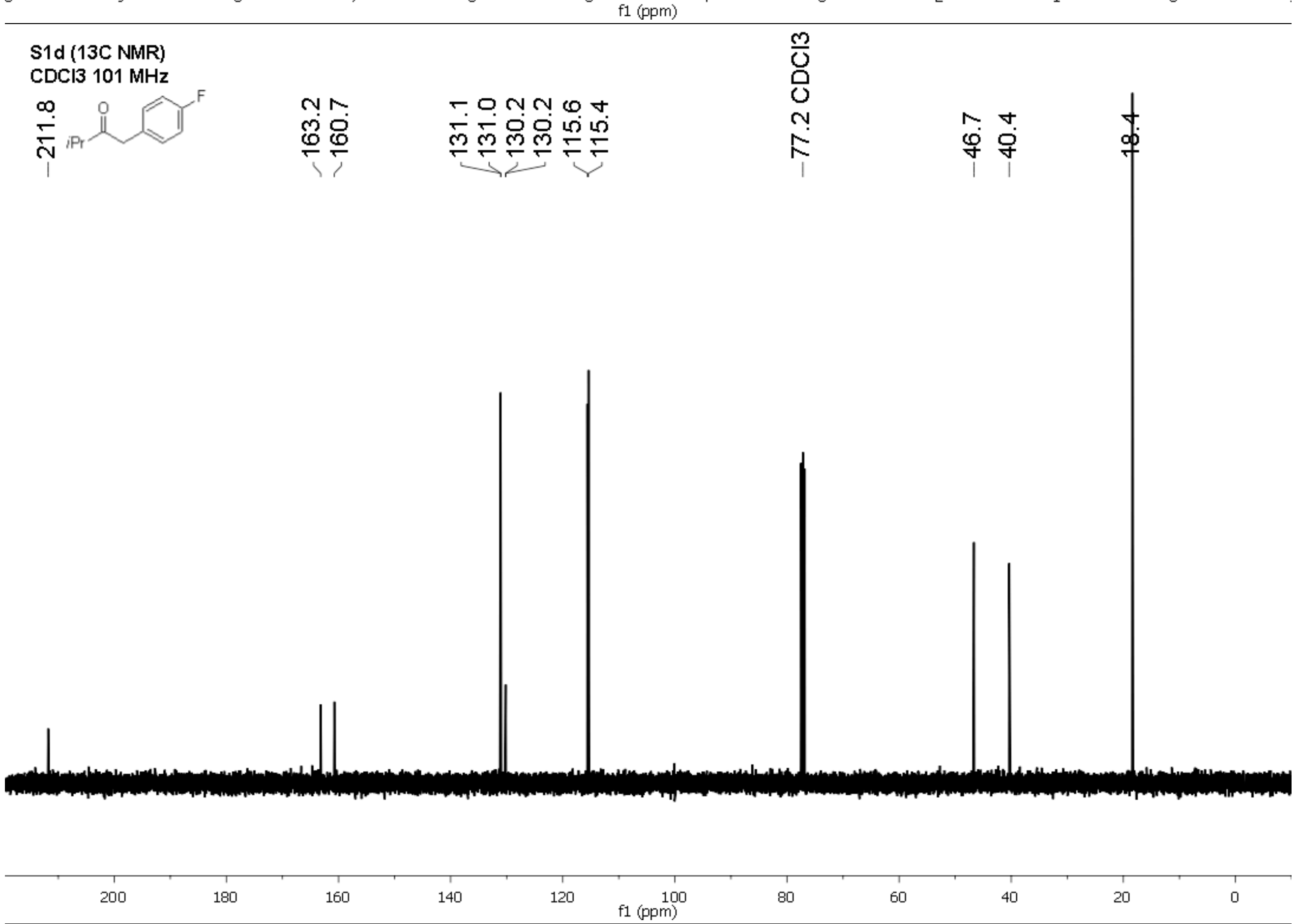
2.77
2.75
2.73
2.71
2.70
2.68
2.66
1.11
1.10
1.97
1.98
2.00
0.98
6.00
f1 (ppm)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O
F
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160.7
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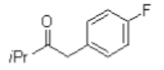
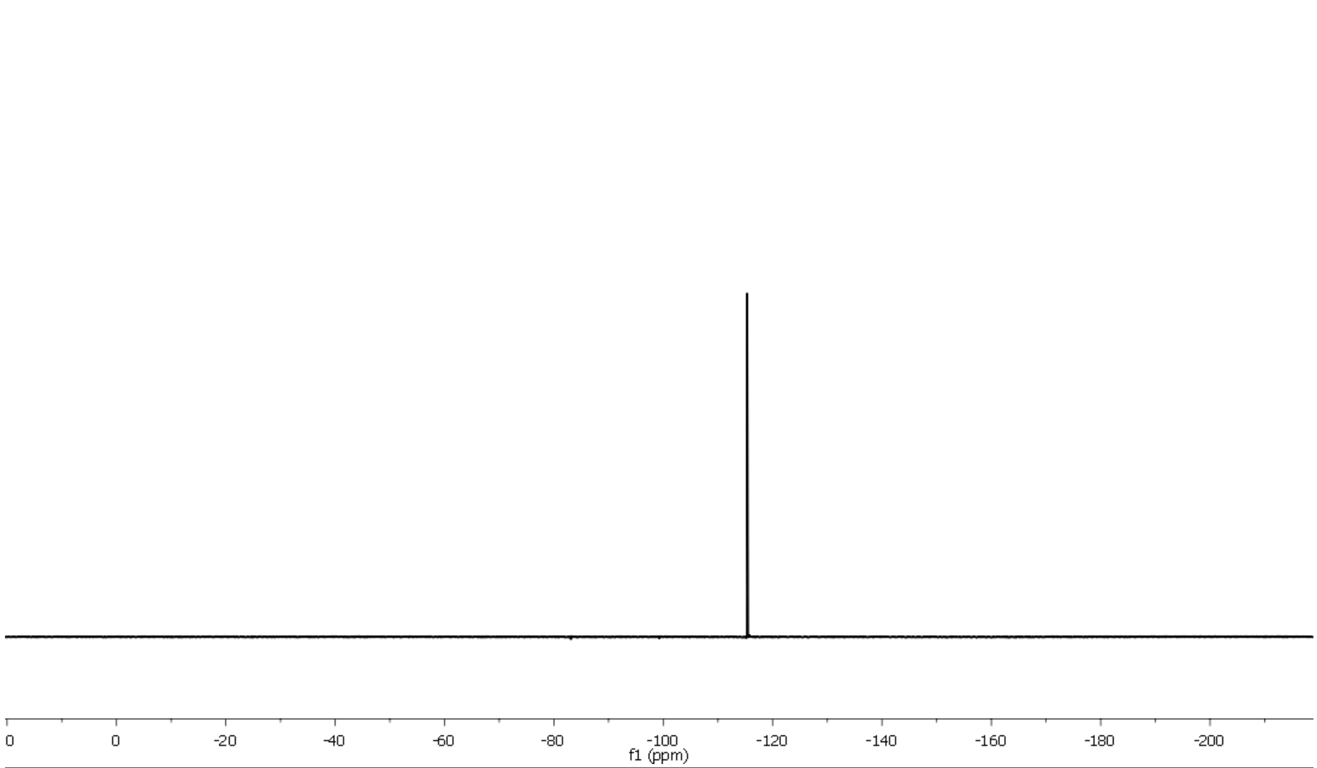
131.0
130.2
130.2
115.6
115.4
77.2 CDCl3
46.7
40.4
18.4
f1 (ppm)

S1d (19F NMR)
CDCl3 376 MHz





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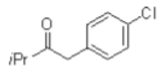

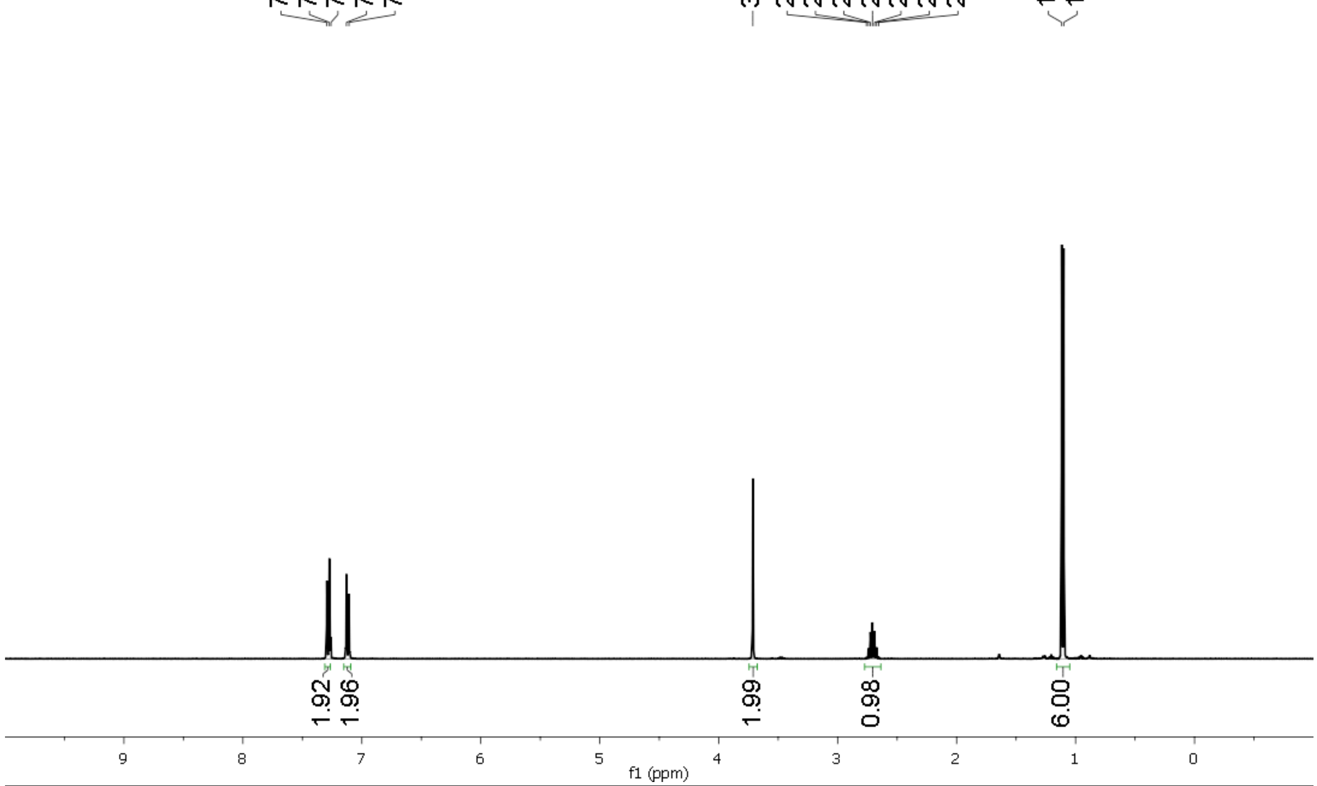

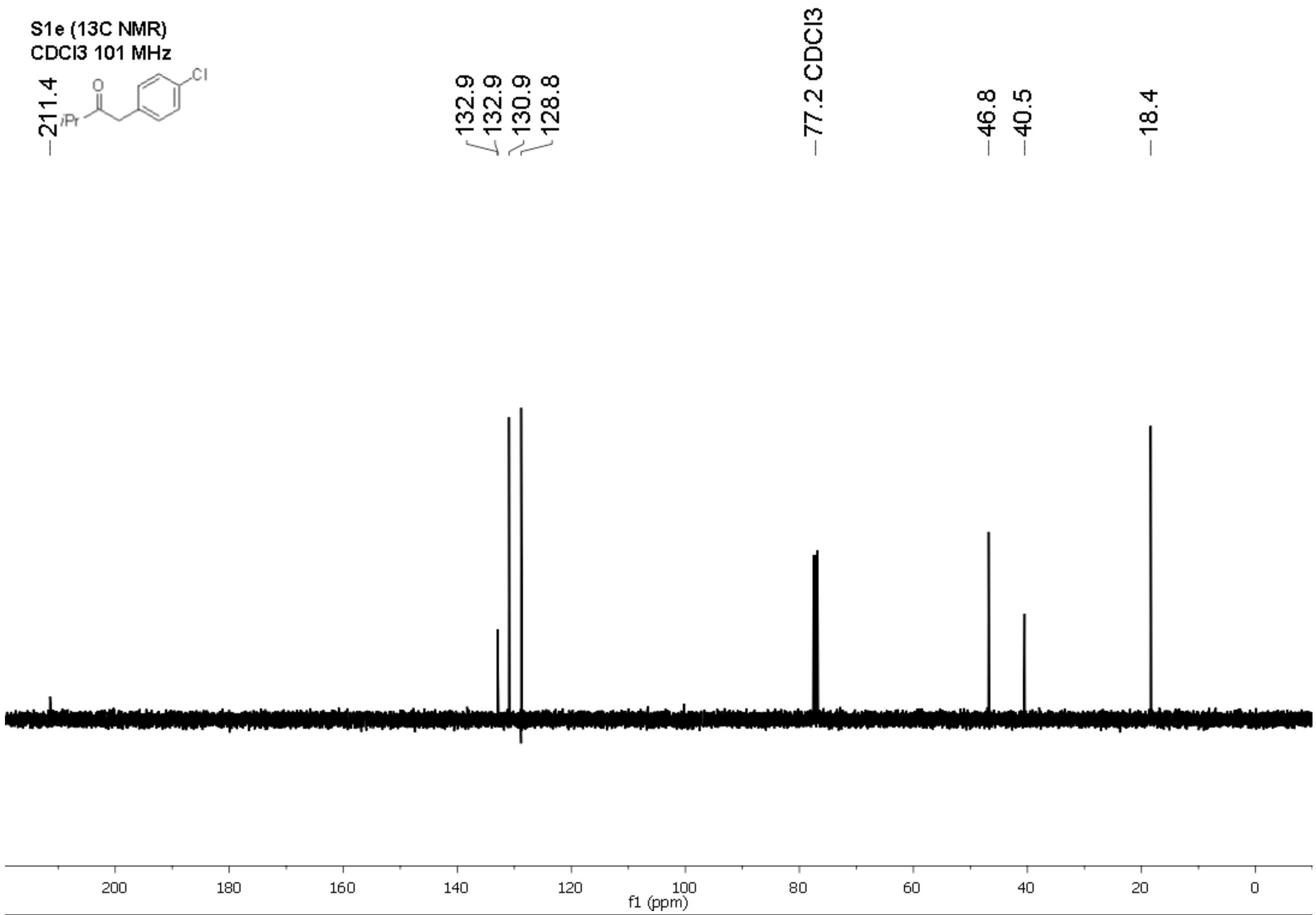
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iPr
O
Cl
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132.9
132.9
130.9
128.8
77.2 CDCl3
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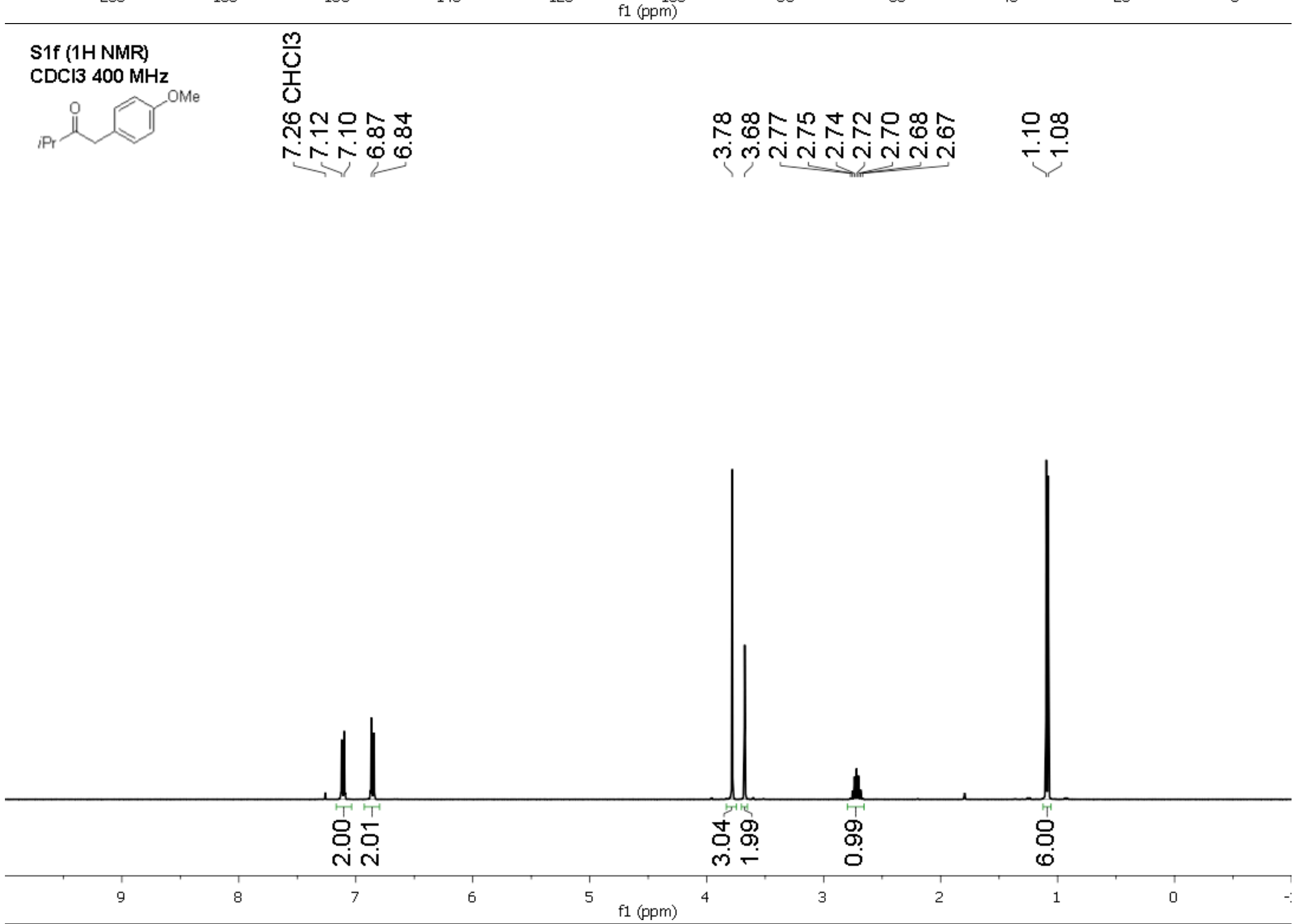
40.5
18.4
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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O
OMe
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3.68
2.77
2.75
2.74
2.72
2.70
2.68
2.67
1.10
1.08
2.00
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9
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5
4
3
2
1
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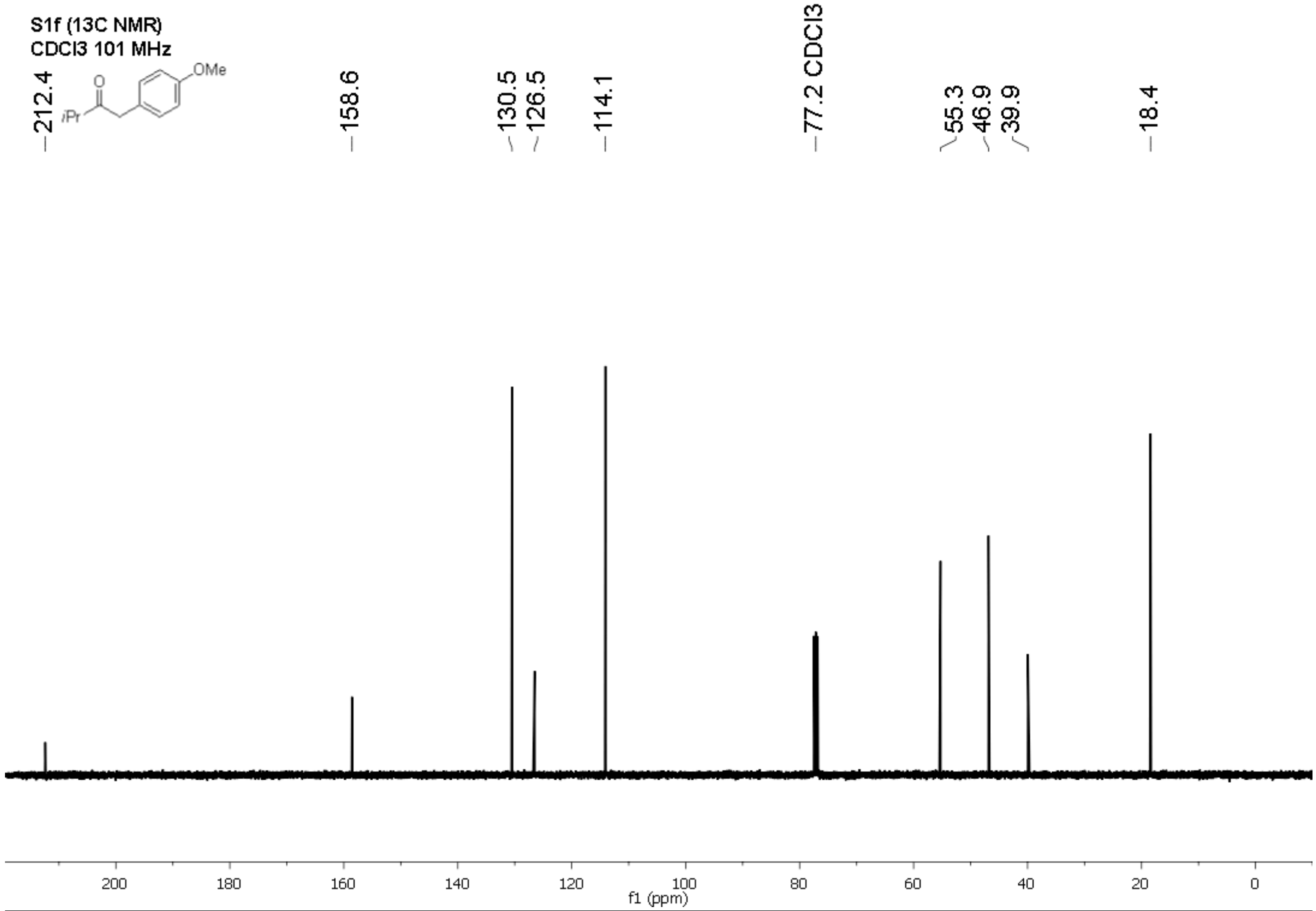
f1 (ppm)



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OMe
O
iPr
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126.5
114.1
77.2 CDCl3
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39.9
18.4
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180
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140
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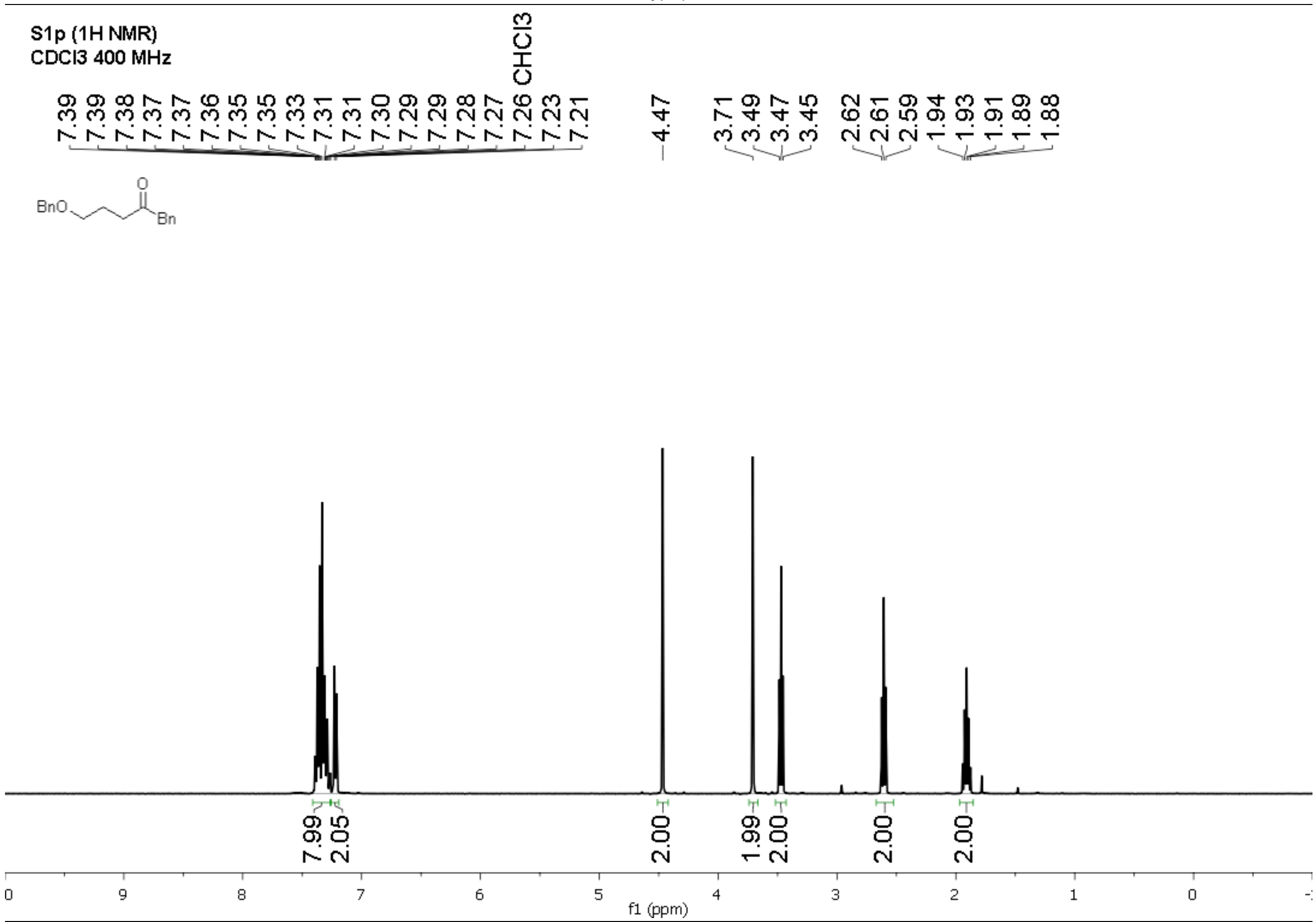
100
80
60
40
20
0
f1 (ppm)



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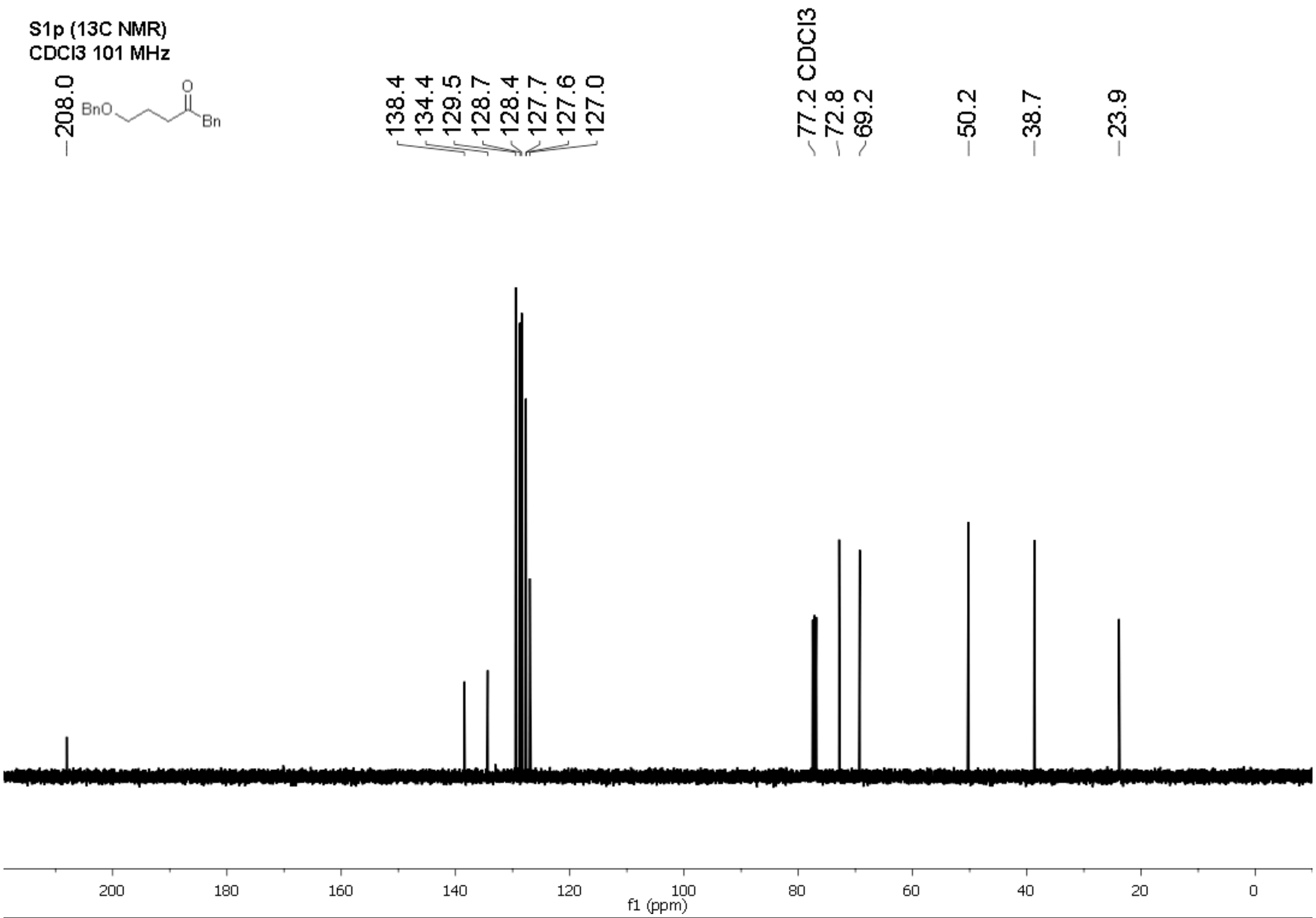
7.39
7.38
7.37
7.37
7.36
7.35
7.35
7.33
7.31
7.31
7.30
7.29
7.29
7.28
7.27
7.26 CHCl3
7.23
7.21
4.47
3.71
3.49
3.47
3.45
2.62
2.61
2.59
1.94
1.93
1.91
1.89
1.88
BnO
O
Bn
7.99
2.05
2.00
1.99
2.00
2.00
2.00
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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O
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129.5
128.7
128.4
127.7
127.6
127.0
77.2 CDCl3
72.8
69.2
50.2
38.7
23.9
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140
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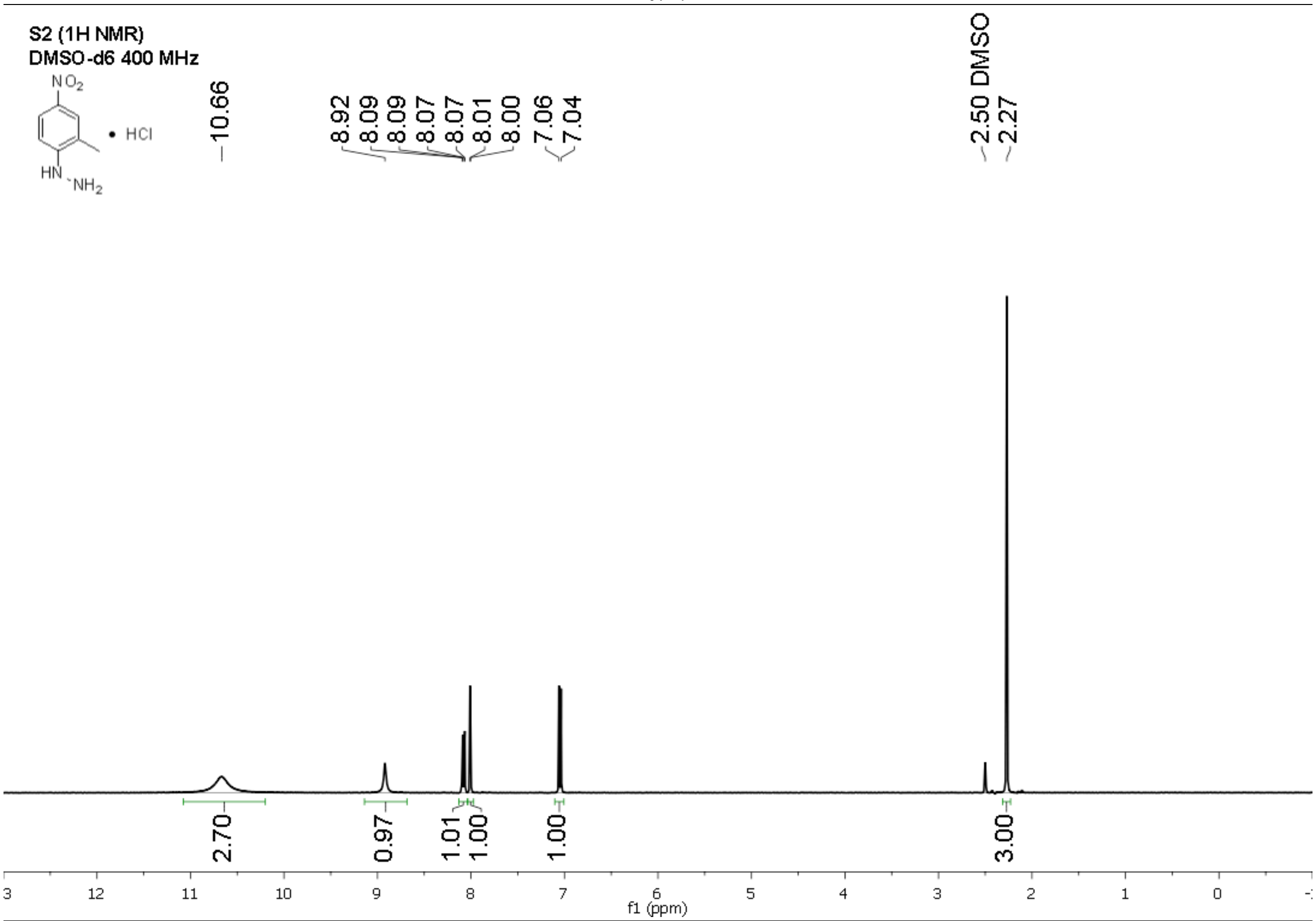
100
80
60
40
20
0
f1 (ppm)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• HCl
HN
NH2
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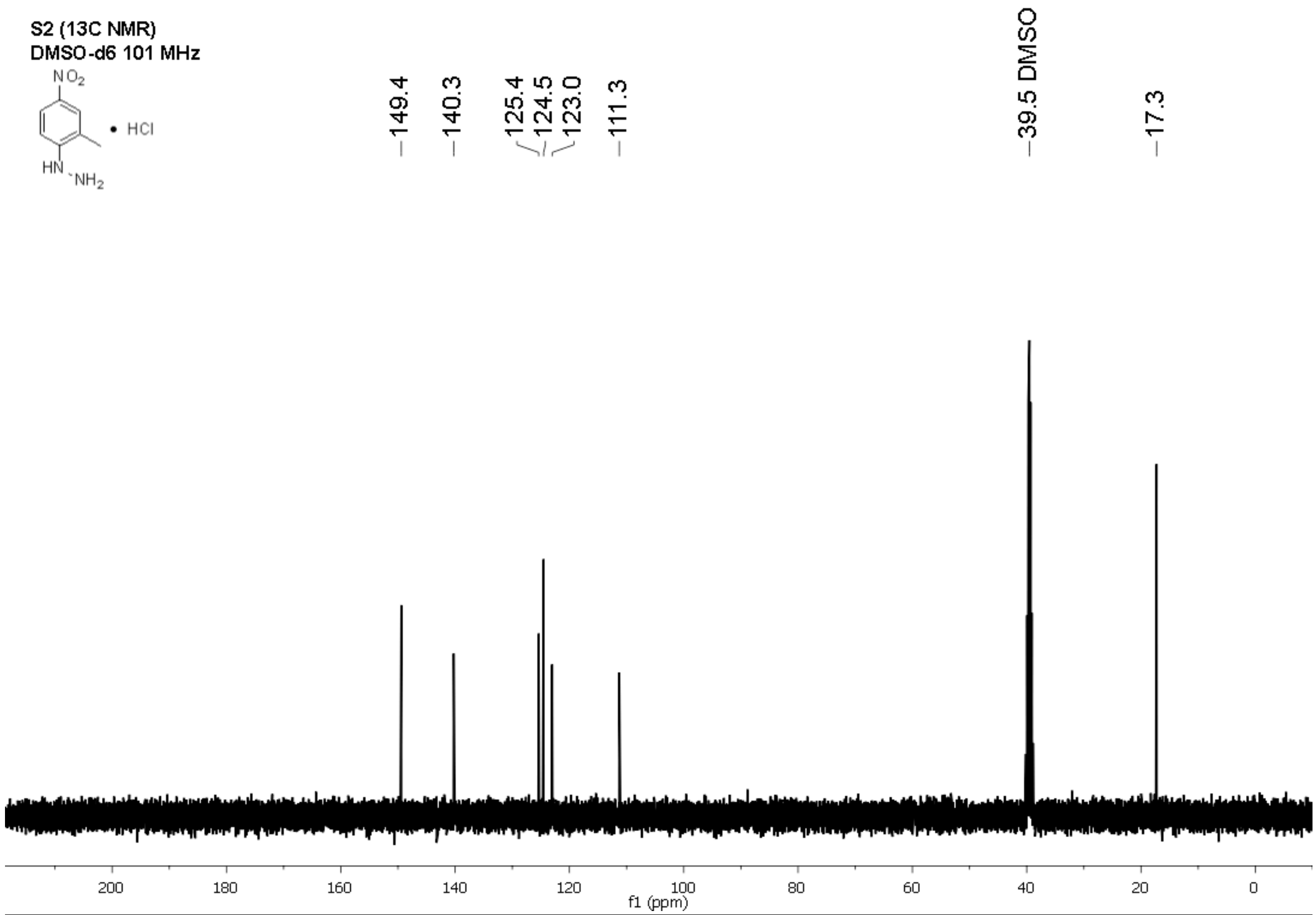
8.92
8.09
8.09
8.07
8.07
8.01
8.00
7.06
7.04
2.50 DMSO
2.27
2.70
0.97
1.01
1.00
1.00
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)



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• HCl
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NH2
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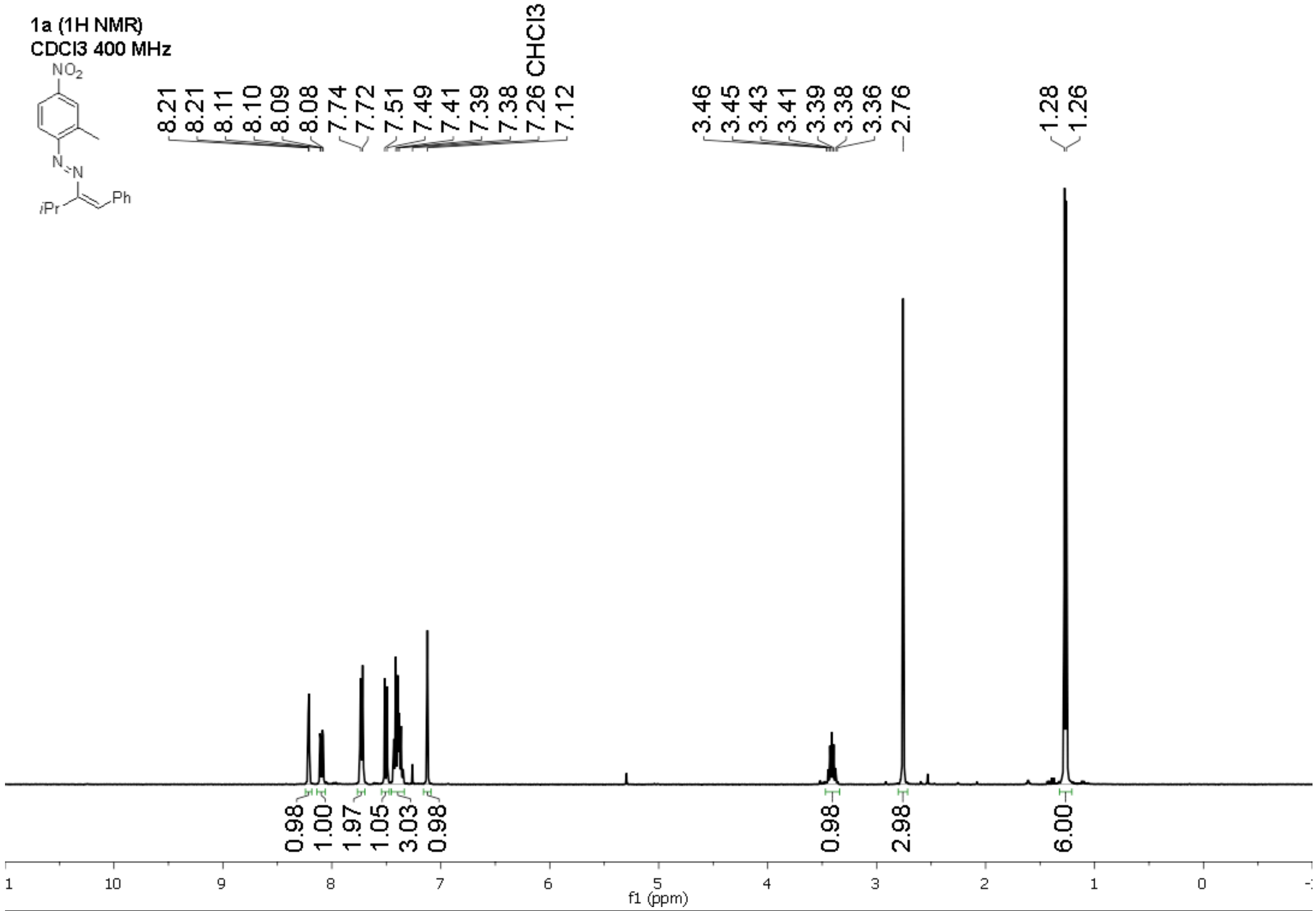
111.3
39.5 DMSO
17.3
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



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N=N
iPr
Ph
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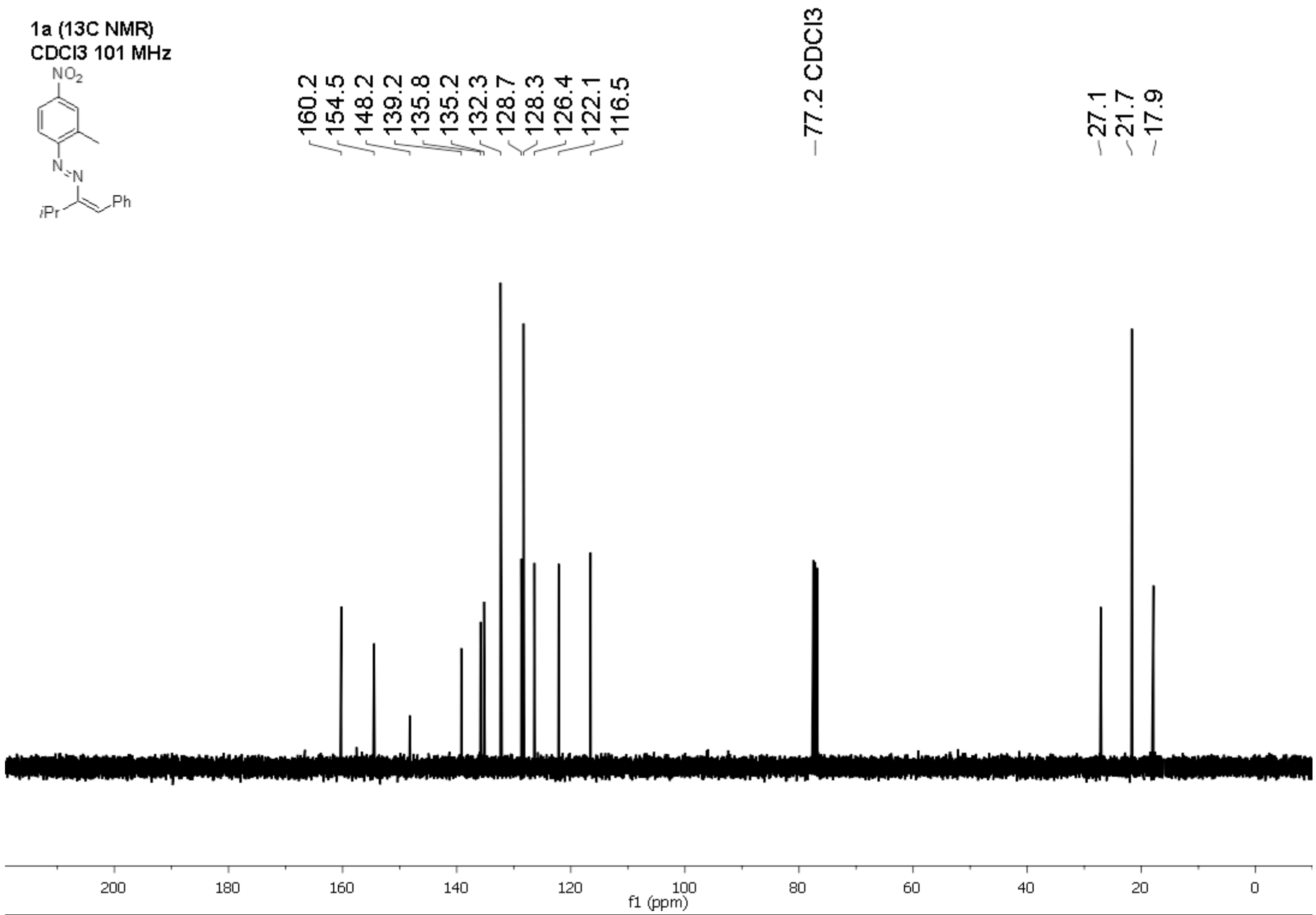
3.46 3.45 3.43 3.41 3.39 3.38 3.36 2.76
1.28 1.26
0.98 1.00 1.97 1.05 3.03 0.98
0.98
2.98
6.00
11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


1a (13C NMR)
CDCl3 101 MHz
NO2
N=N
iPr
Ph
160.2
154.5
148.2
139.2
135.8
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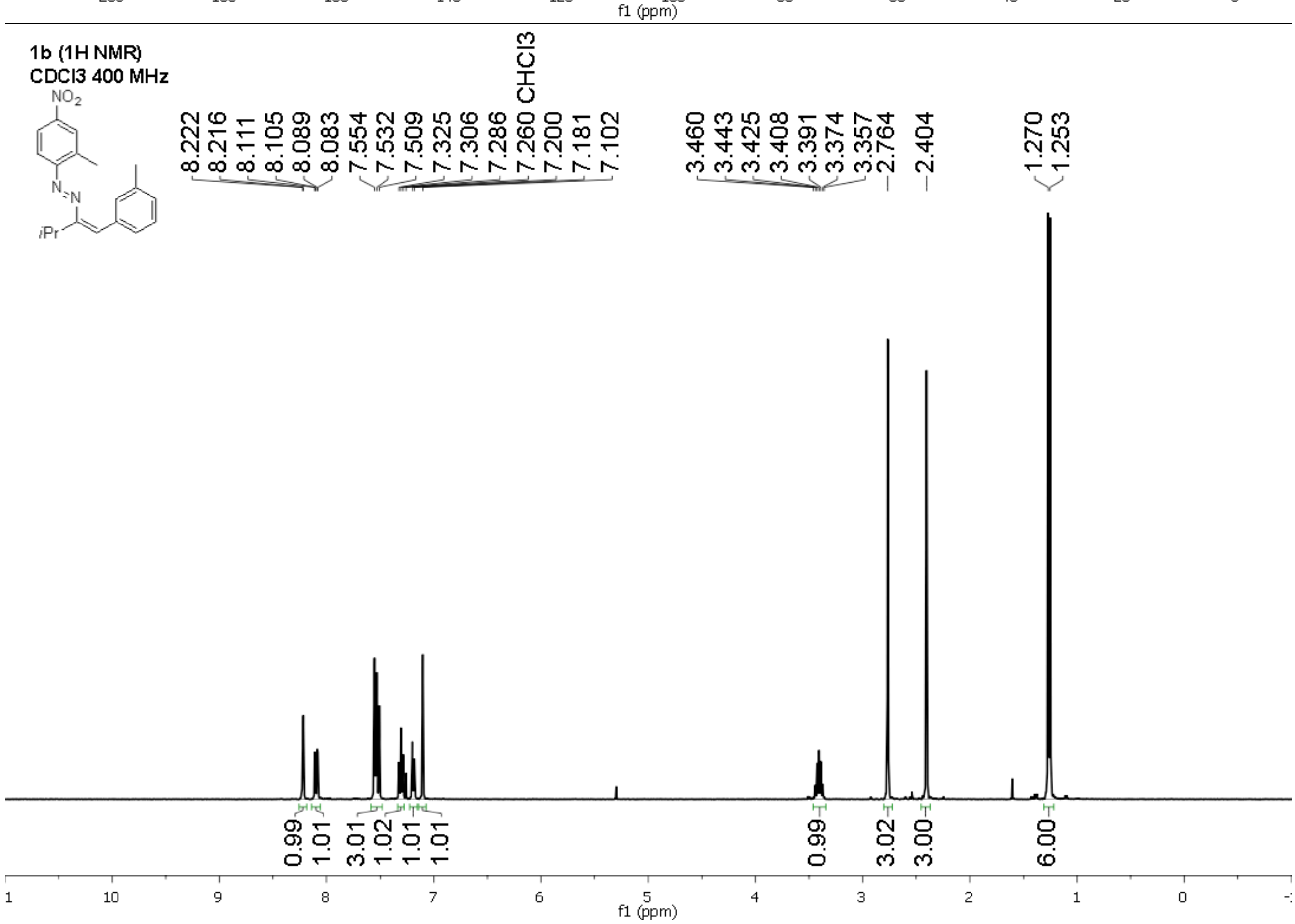
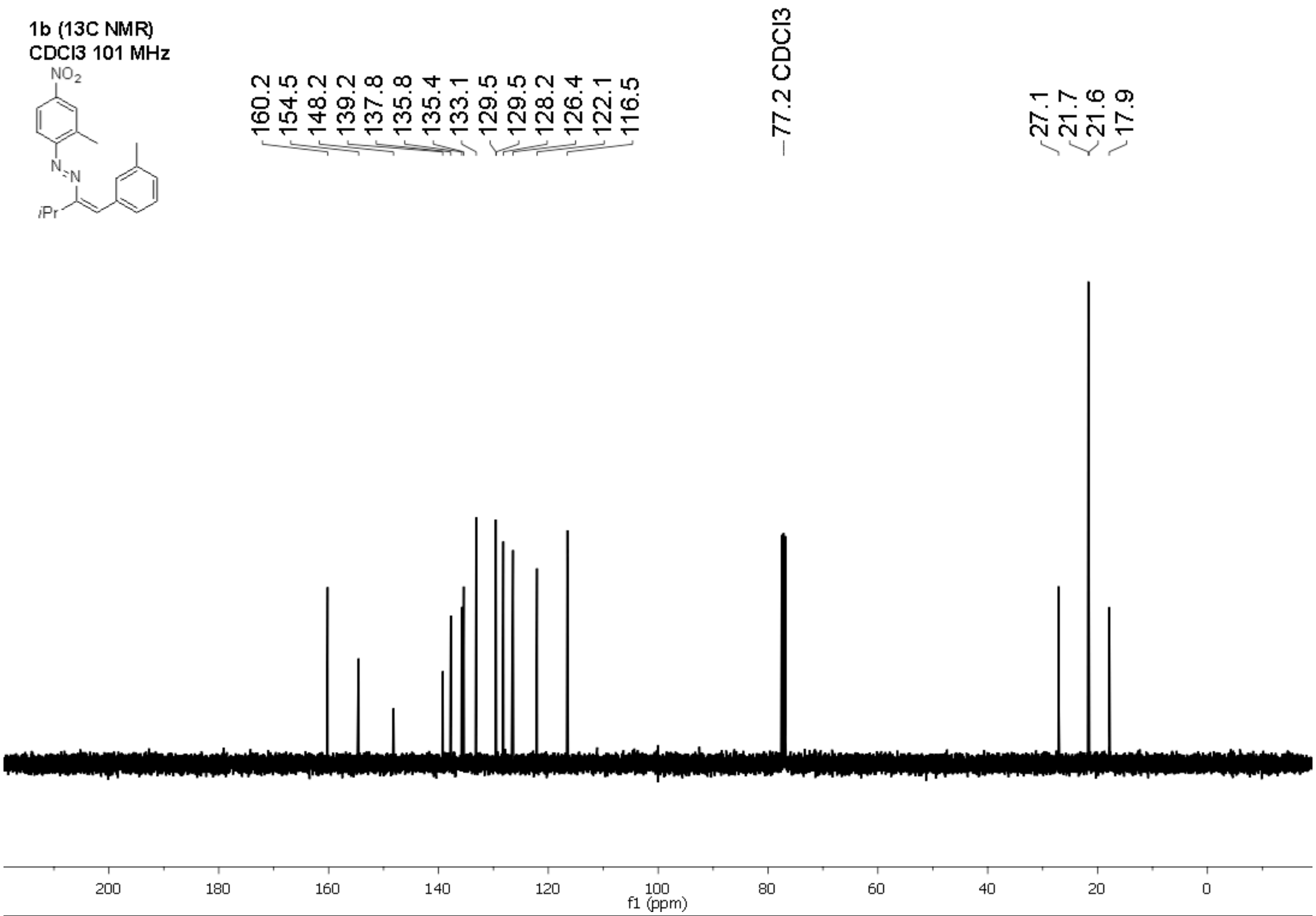
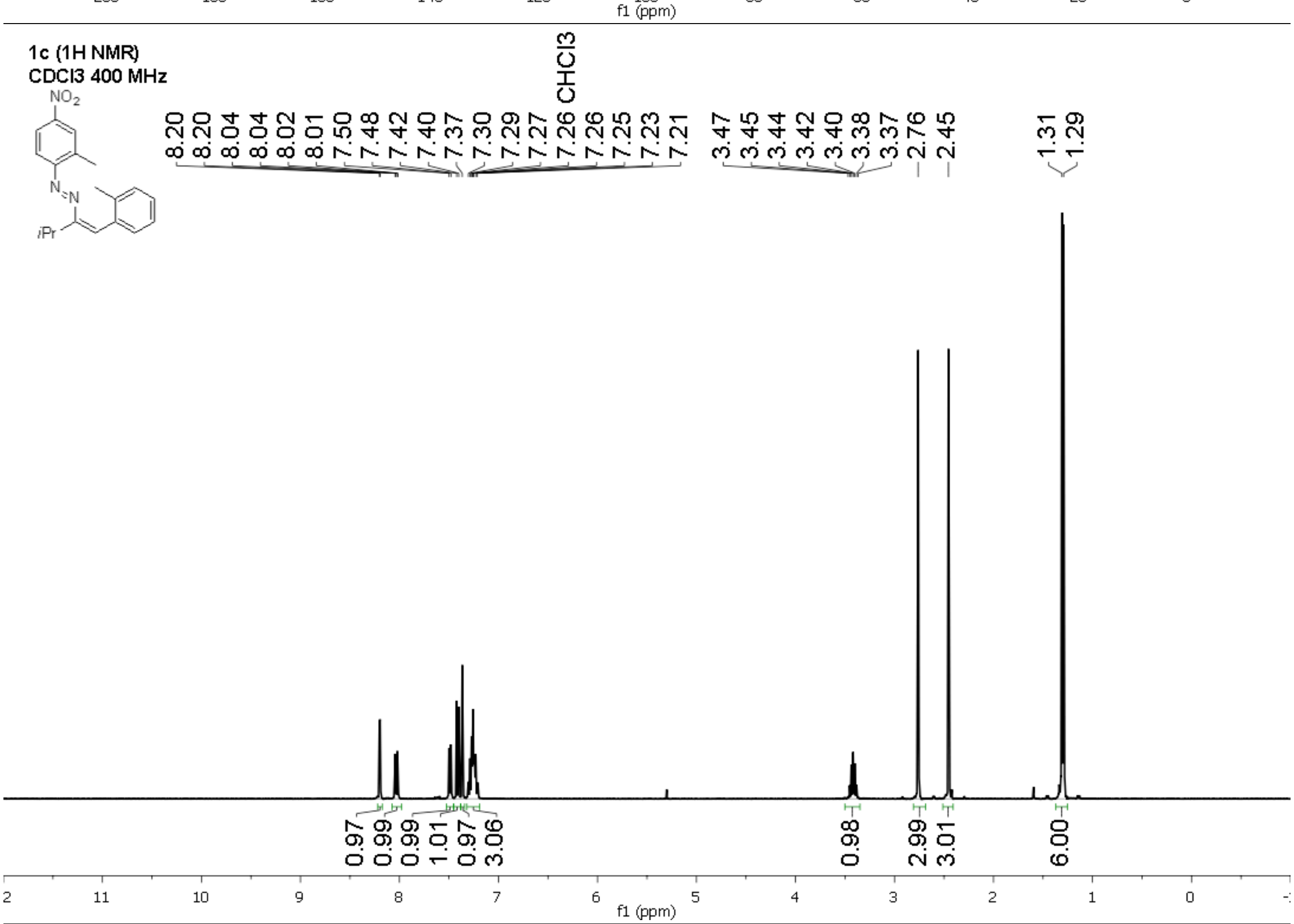
132.3
128.7
128.3
126.4
122.1
116.5
77.2 CDCl3
27.1
21.7
17.9
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

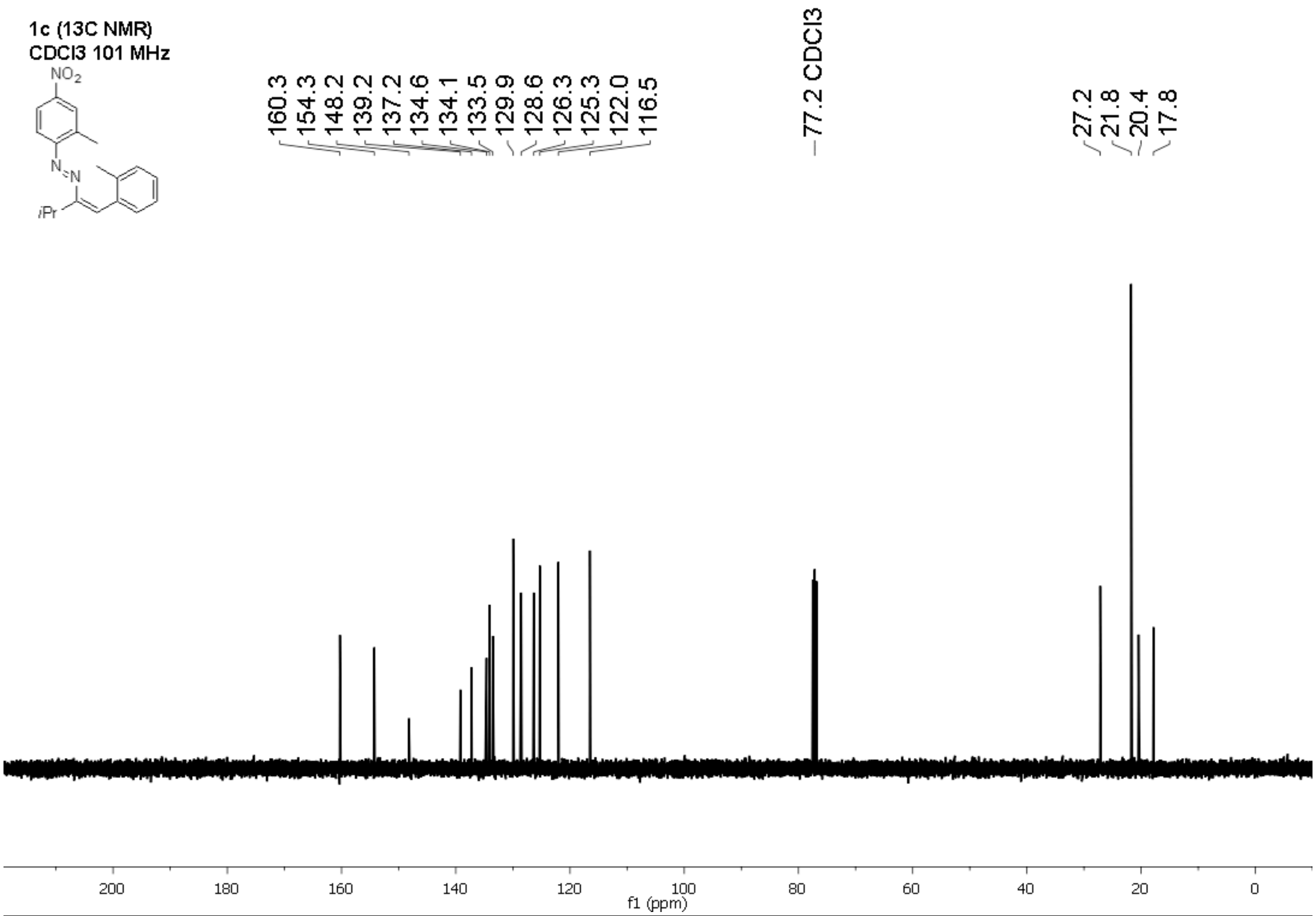

1b (1H NMR)
CDCl3 400 MHz
NO2
N=N
iPr
8.222
8.216
8.111
8.105
8.089
8.083
7.554
7.532
7.509
7.325
7.306
7.286
7.260 CHCl3
7.200
7.181
7.102
3.460
3.443
3.425
3.408
3.391
3.374
3.357
2.764
2.404
1.270
1.253
0.99
1.01
3.01
1.02
1.01
1.01
0.99
3.02
3.00
6.00
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

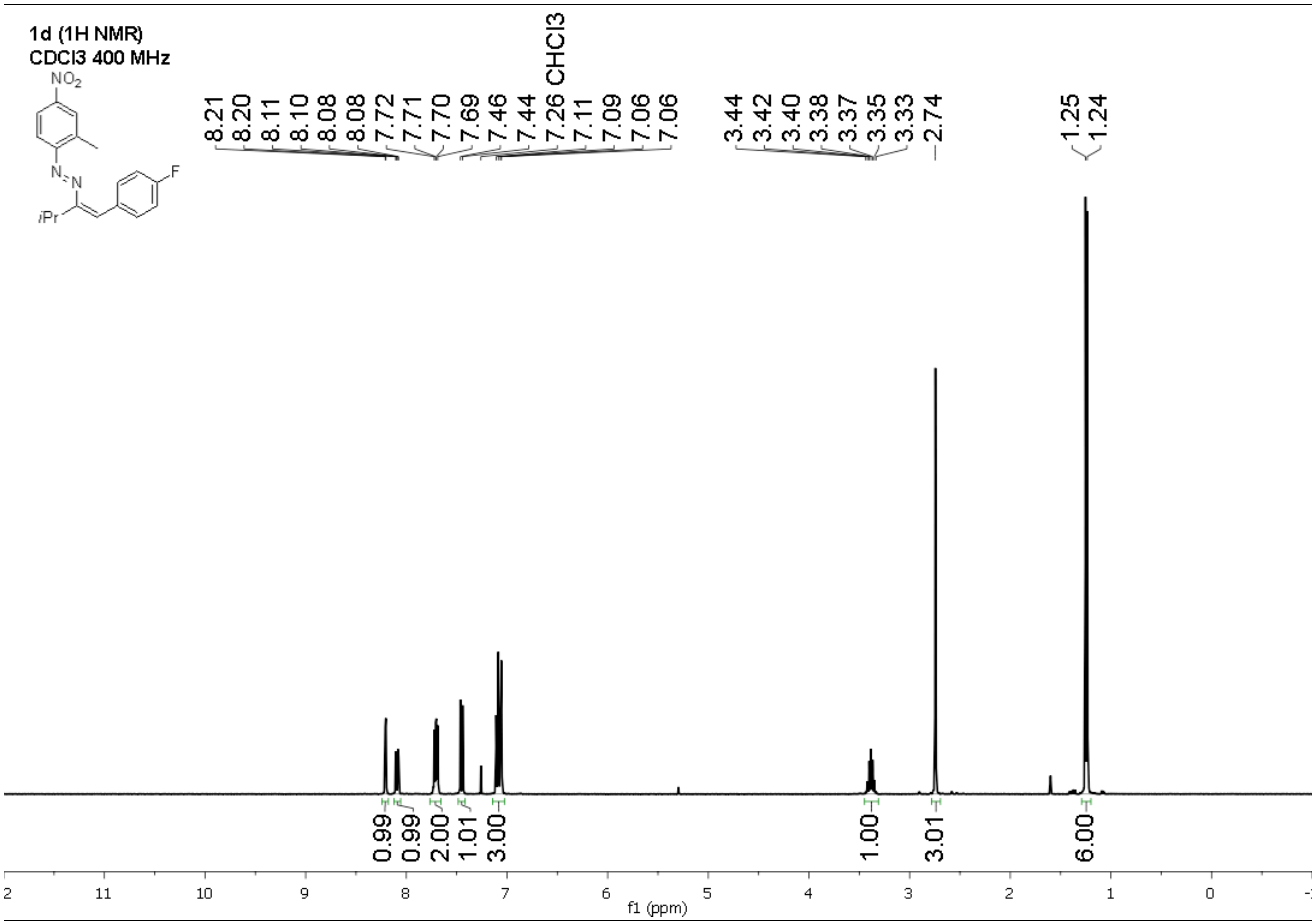
1b (13C NMR)
CDCl3 101 MHz

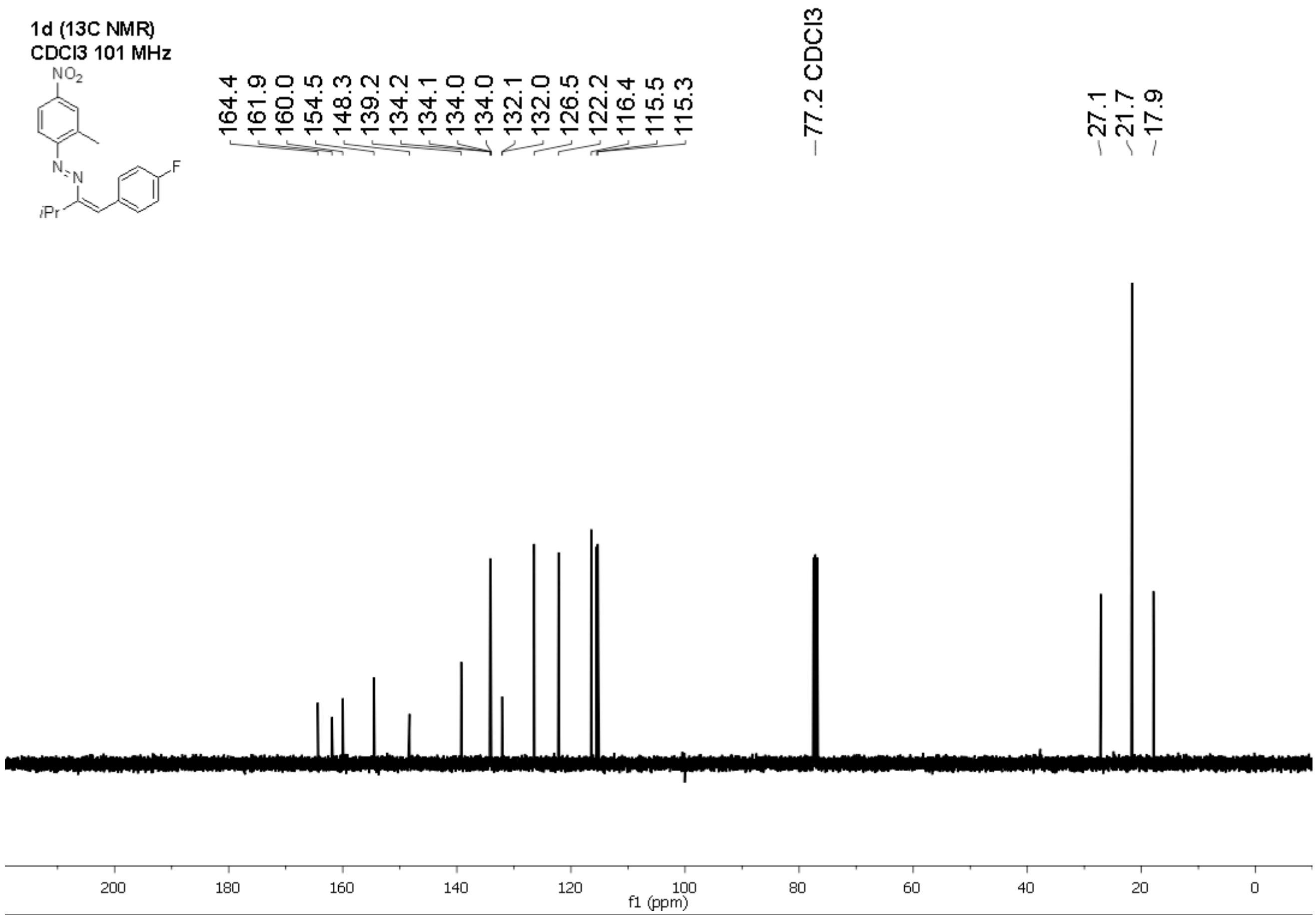


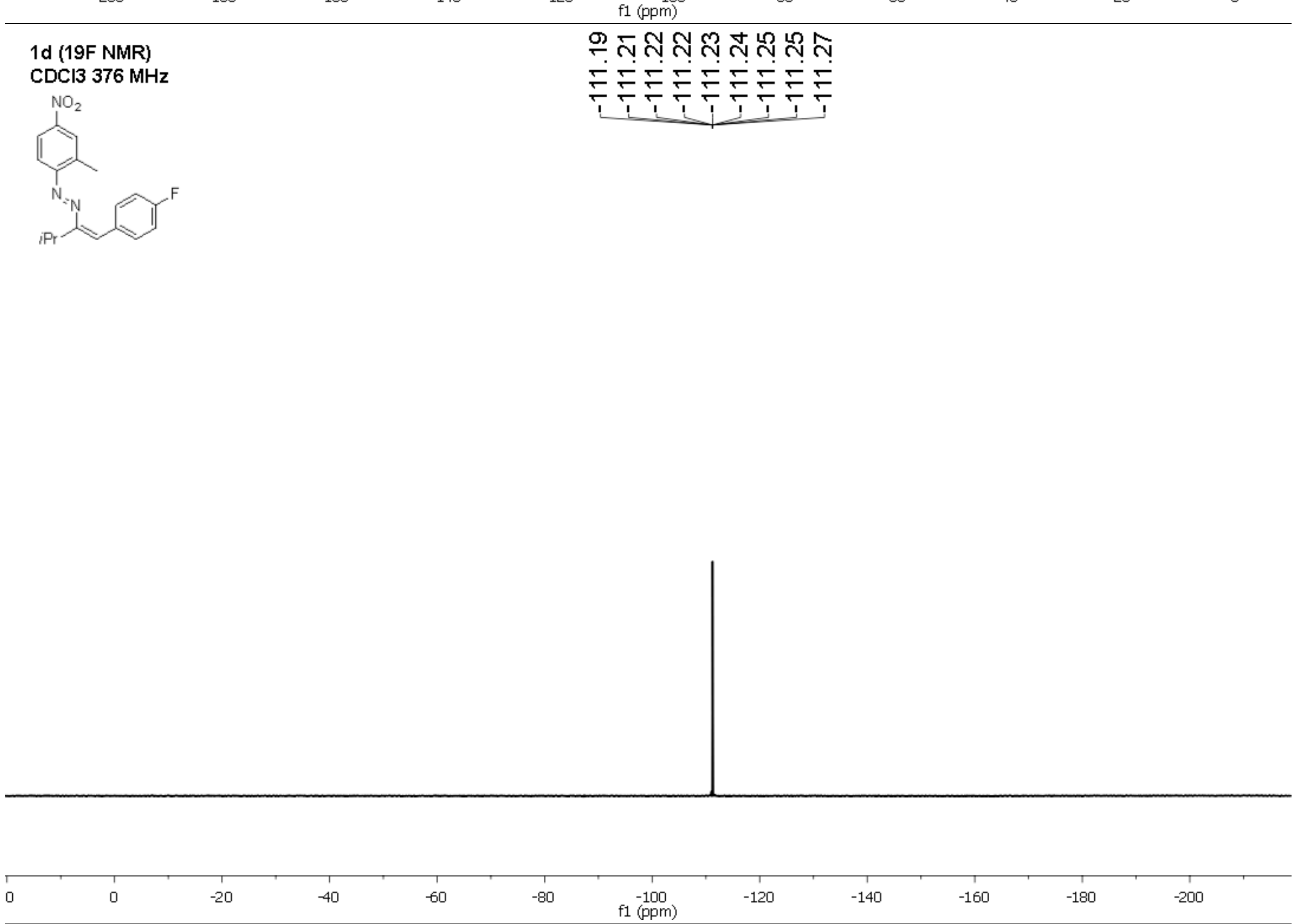
1c (1H NMR)
CDCl3 400 MHz

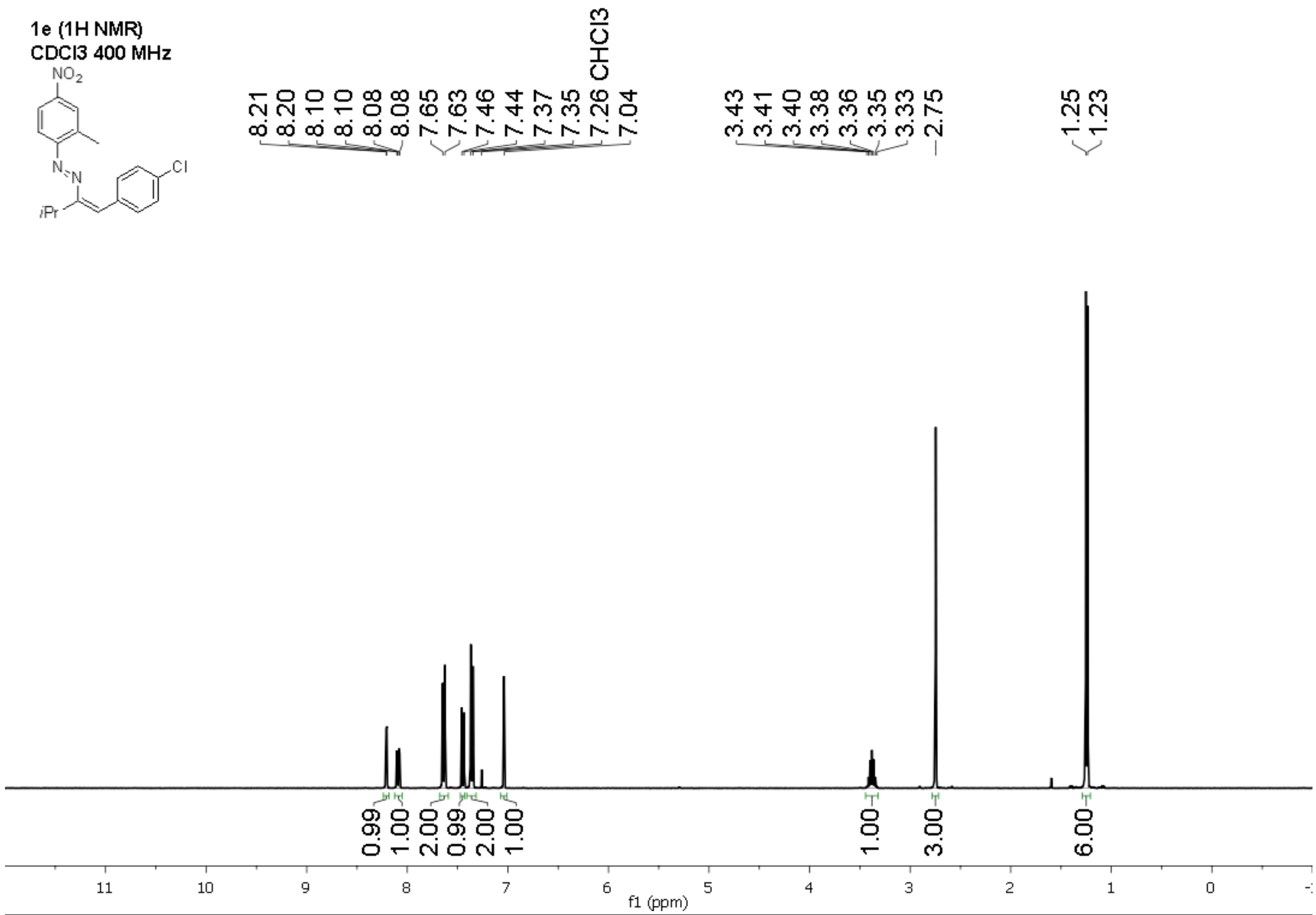


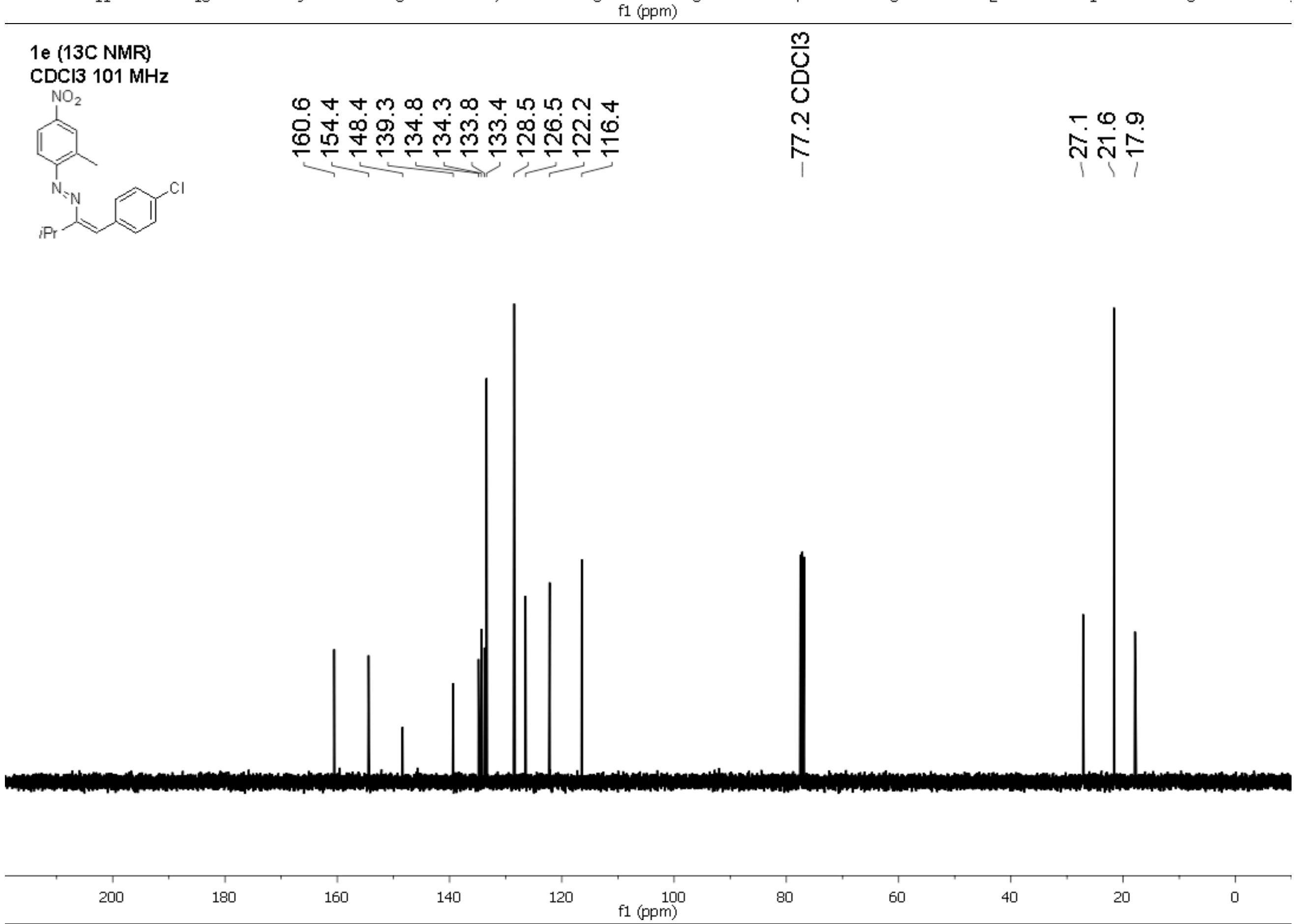

1c (13C NMR)
CDCl3 101 MHz
NO2
N
N
iPr
160.3
154.3
148.2
139.2
137.2
134.6
134.1
133.5
129.9
128.6
126.3
125.3
122.0
116.5
77.2 CDCl3
27.2
21.8
20.4
17.8
f1 (ppm)

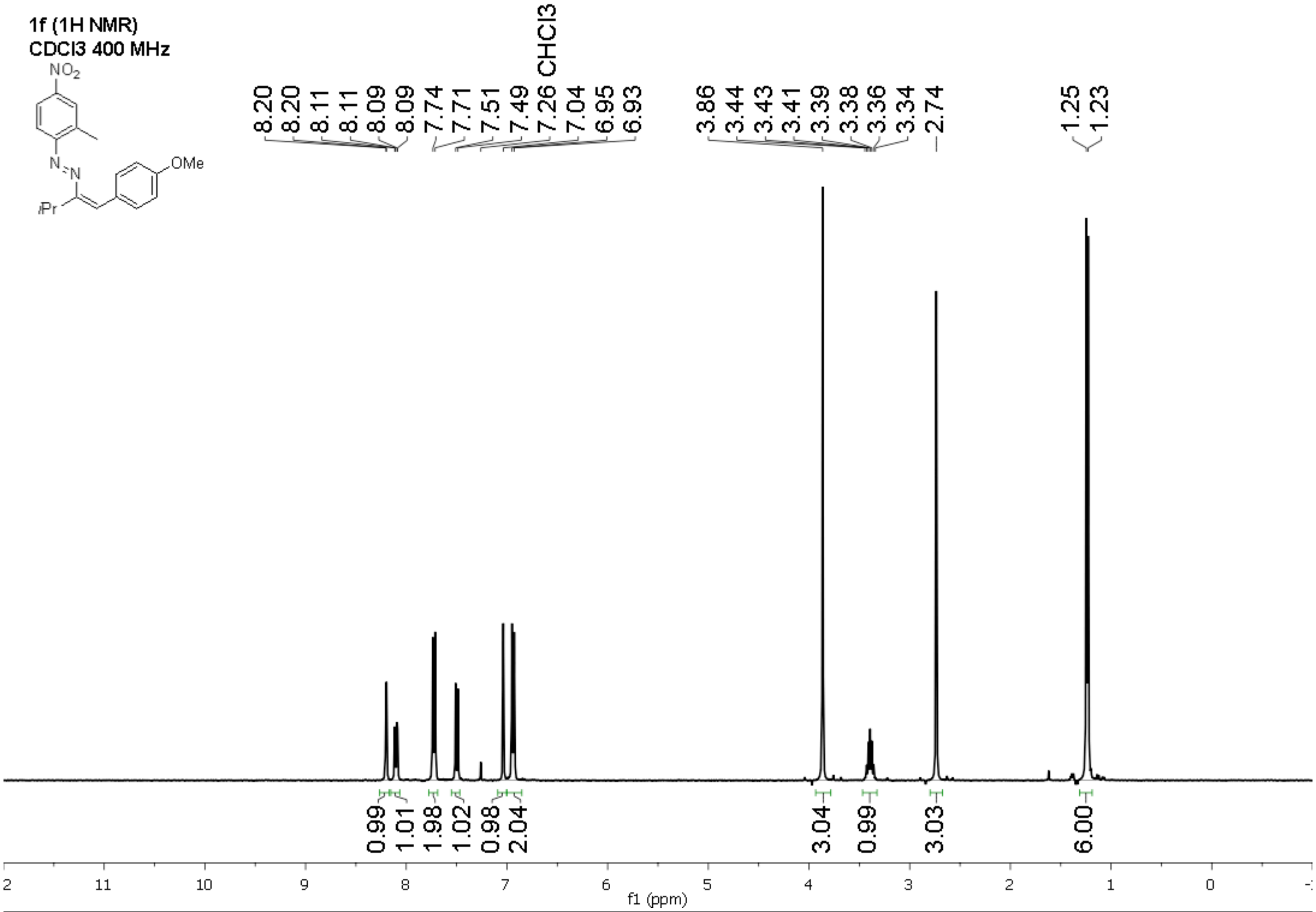

1d (1H NMR)
CDCl3 400 MHz
NO2
N
N
F
iPr
8.21
8.20
8.11
8.10
8.08
8.08
7.72
7.71
7.70
7.69
7.46
7.44
7.26 CHCl3
7.11
7.09
7.06
7.06
3.44
3.42
3.40
3.38
3.37
3.35
3.33
2.74
1.25
1.24
0.99
0.99
2.00
1.01
3.00
1.00
3.01
6.00
f1 (ppm)

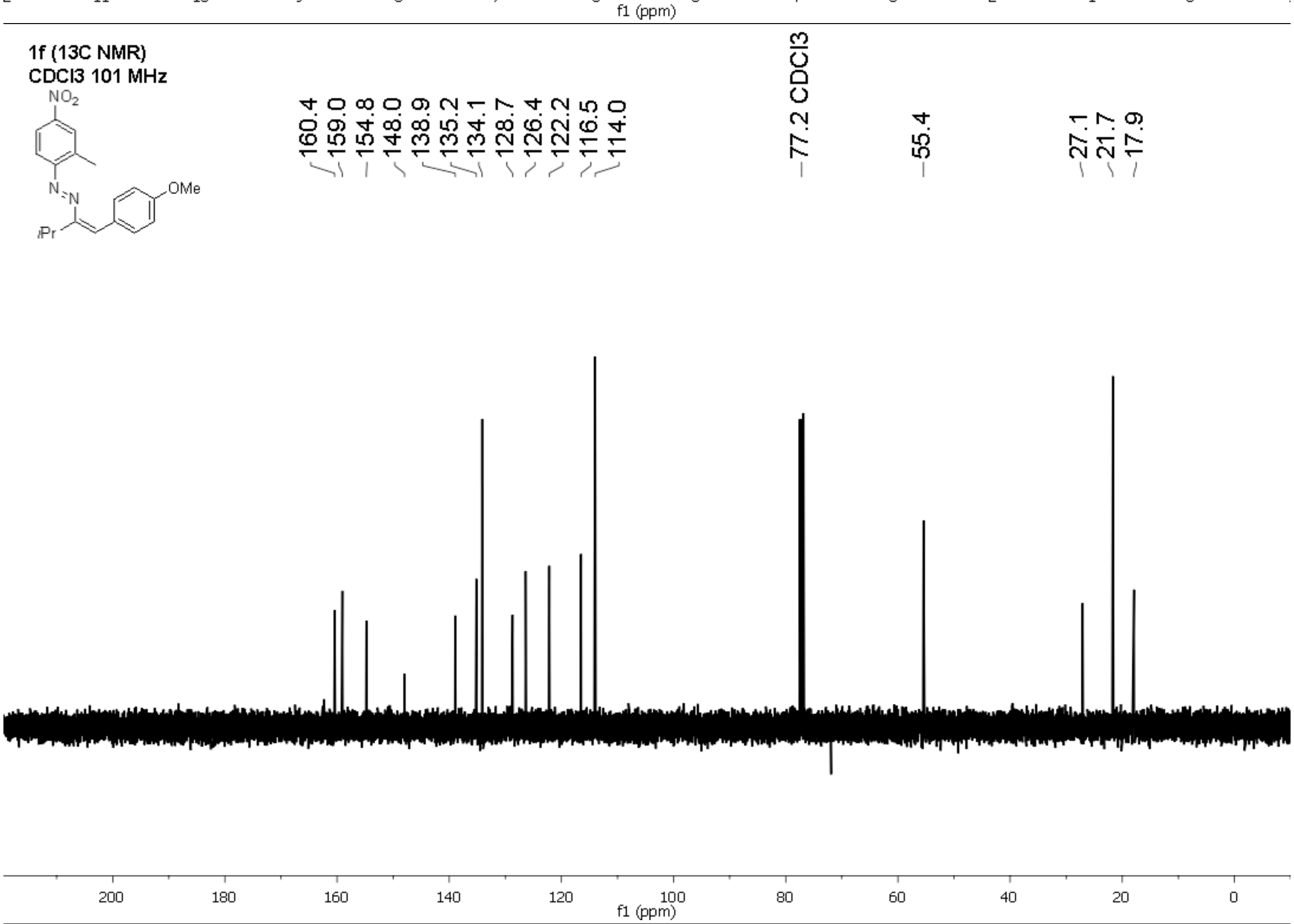

1d (13C NMR)
CDCl3 101 MHz
NO2
F
N
N
iPr
164.4
161.9
160.0
154.5
148.3
139.2
134.2
134.1
134.0
134.0
132.1
132.0
126.5
122.2
116.4
115.5
115.3
77.2 CDCl3
27.1
21.7
17.9
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

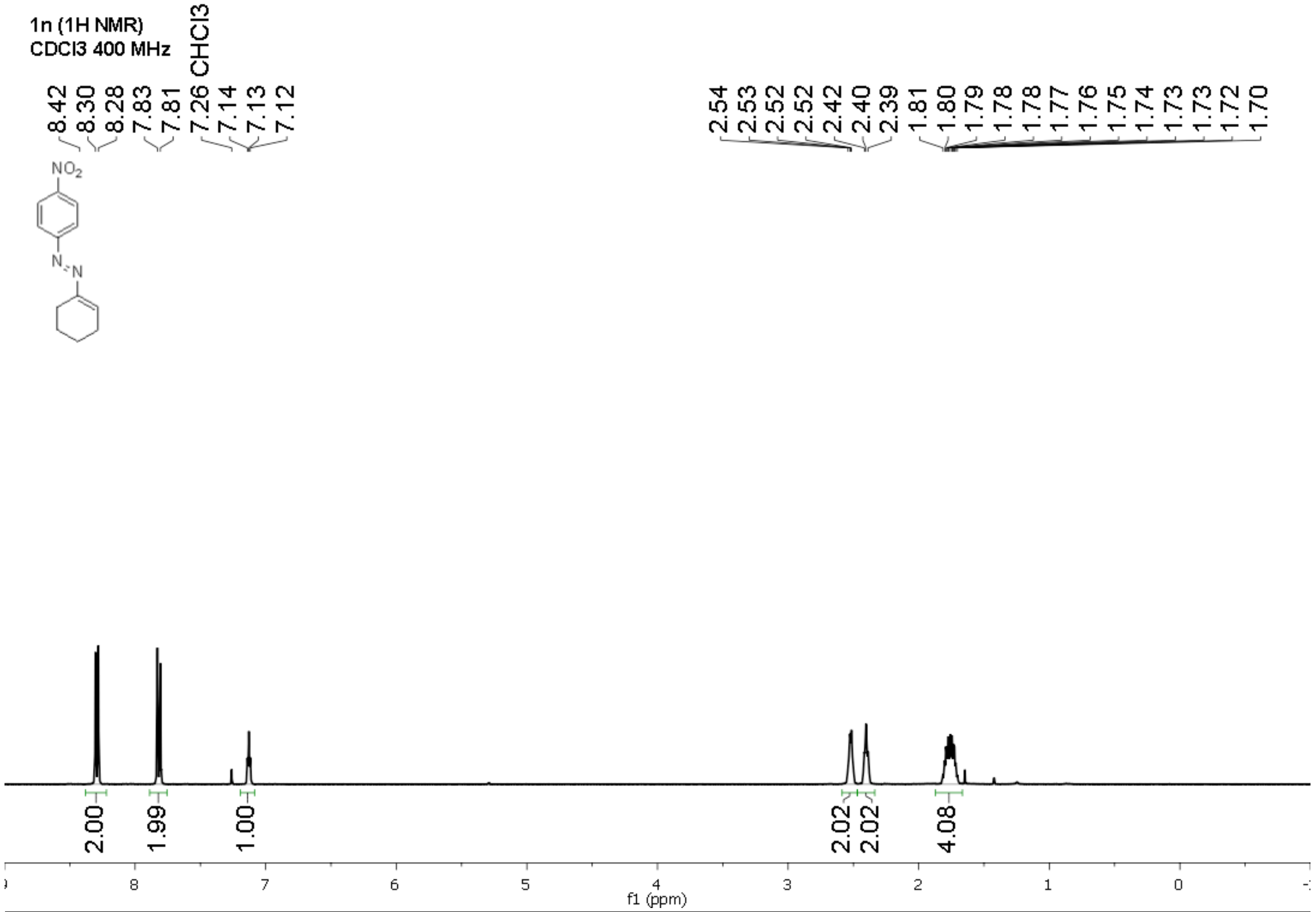

1d (19F NMR)
CDCl3 376 MHz
NO2
F
N
N
iPr
-111.19
-111.21
-111.22
-111.22
-111.23
-111.24
-111.25
-111.25
-111.27
0
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

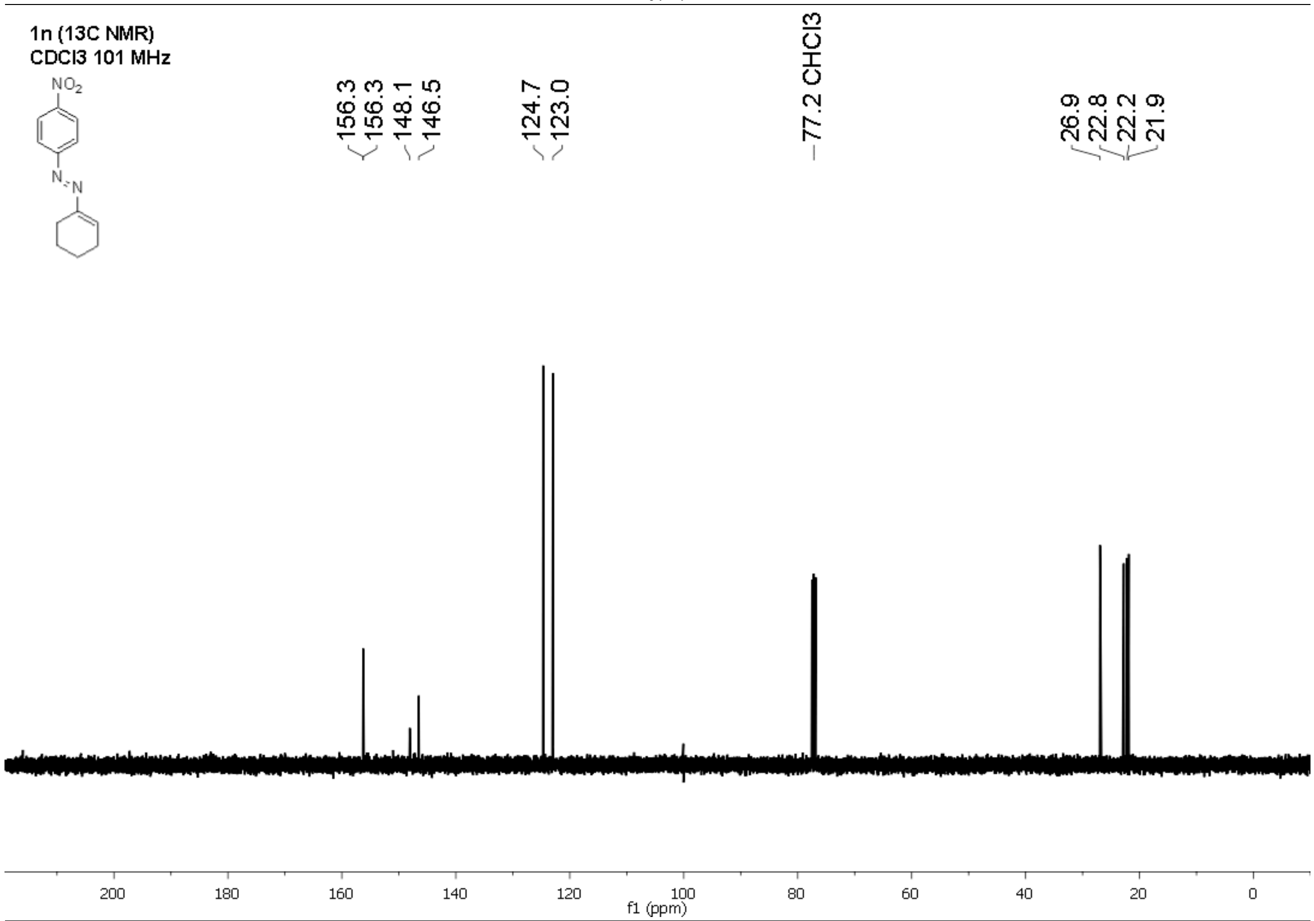

1e (1H NMR)
CDCl3 400 MHz
NO2
Cl
iPr
8.21 8.20 8.10 8.10 8.08 8.08 7.65 7.63 7.46 7.44 7.37 7.35 7.26 CHCl3 7.04
3.43 3.41 3.40 3.38 3.36 3.35 3.33 2.75
1.25 1.23
0.99 1.00 2.00 0.99 2.00 1.00
1.00 3.00 6.00
f1 (ppm)

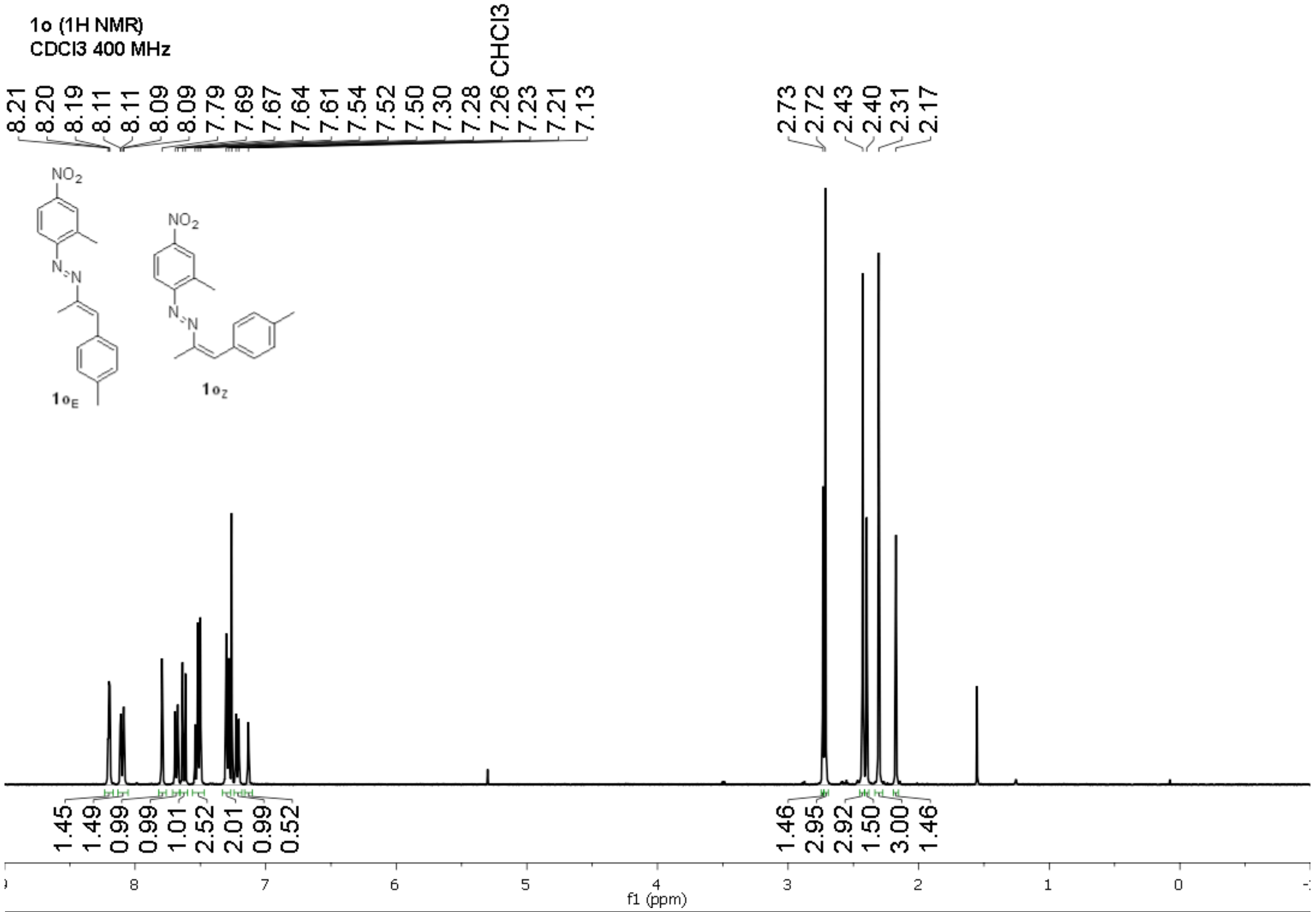

1e (13C NMR)
CDCl3 101 MHz
NO2
Cl
iPr
160.6 154.4 148.4 139.3 134.8 134.3 133.8 133.4 128.5 126.5 122.2 116.4
77.2 CDCl3
27.1 21.6 17.9
f1 (ppm)

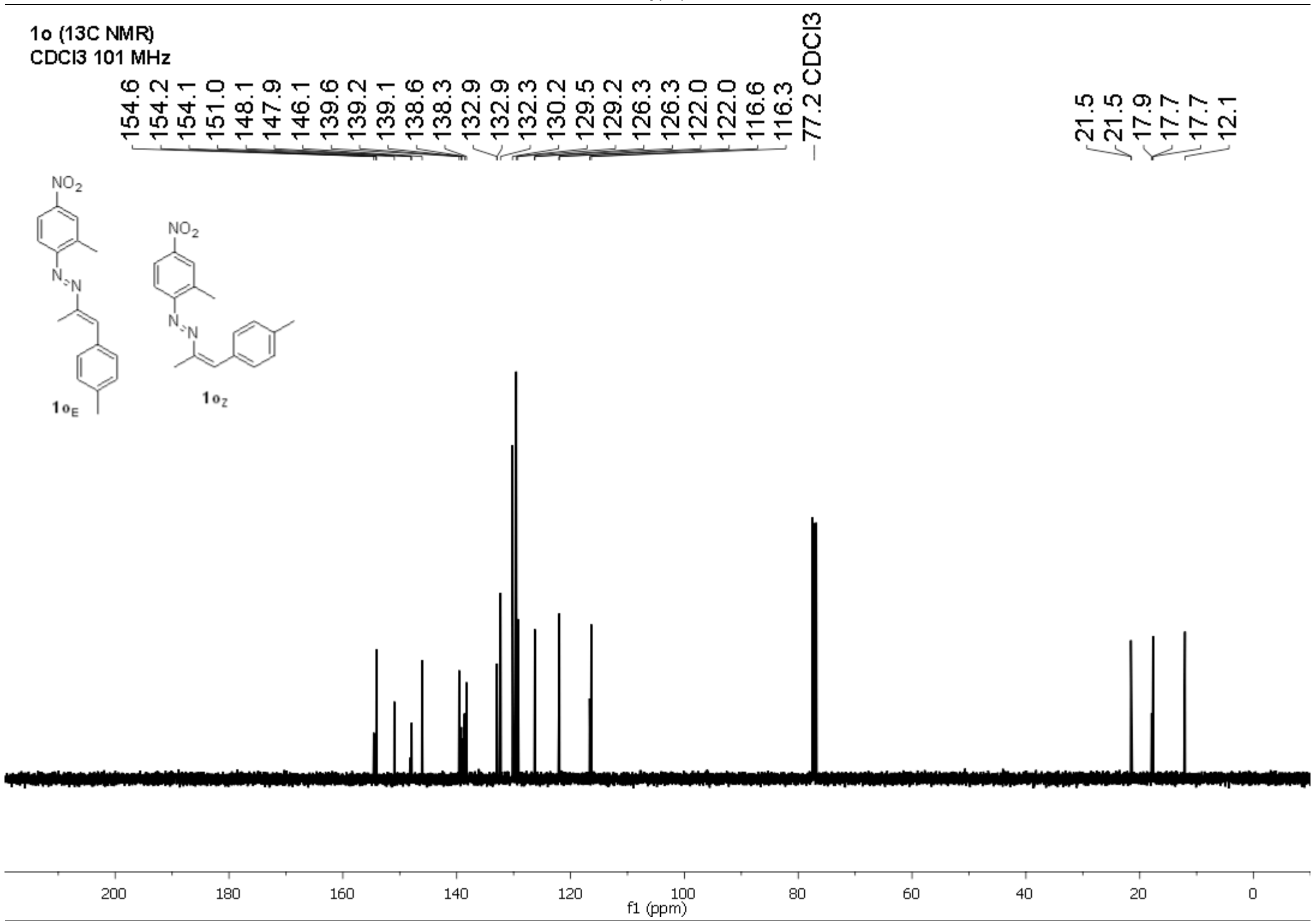

1f (1H NMR)
CDCl3 400 MHz
NO2
OMe
iPr
8.20 8.20 8.11 8.11 8.09 8.09 7.74 7.71 7.51 7.49 7.26 CHCl3 7.04 6.95 6.93
3.86 3.44 3.43 3.41 3.39 3.38 3.36 3.34 2.74
1.25 1.23
0.99 1.01 1.98 1.02 0.98 2.04
3.04 0.99 3.03
6.00
f1 (ppm)

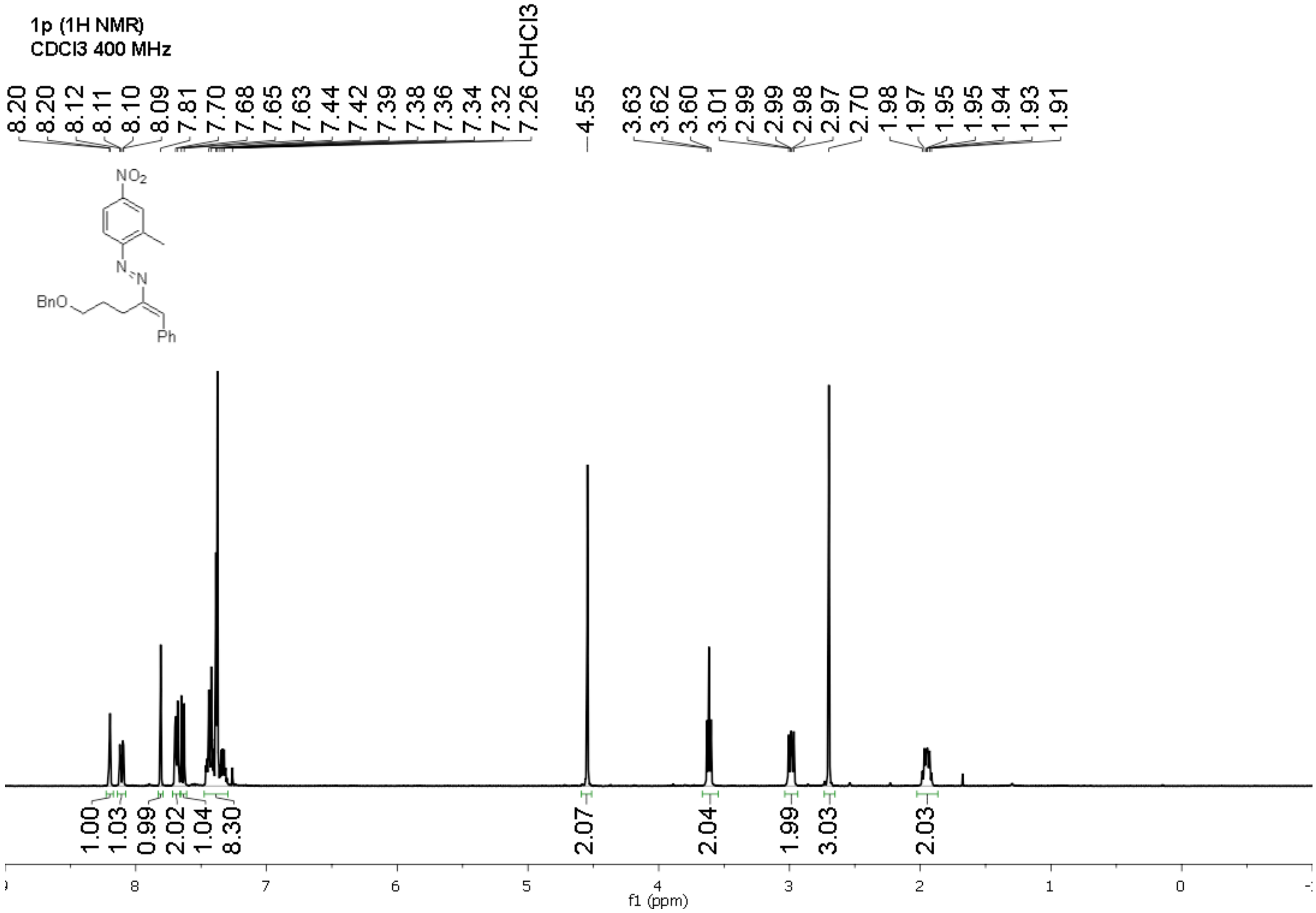

1f (13C NMR)
CDCl3 101 MHz
NO2
OMe
iPr
160.4 159.0 154.8 148.0 138.9 135.2 134.1 128.7 126.4 122.2 116.5 114.0
77.2 CDCl3
55.4
27.1 21.7 17.9
f1 (ppm)

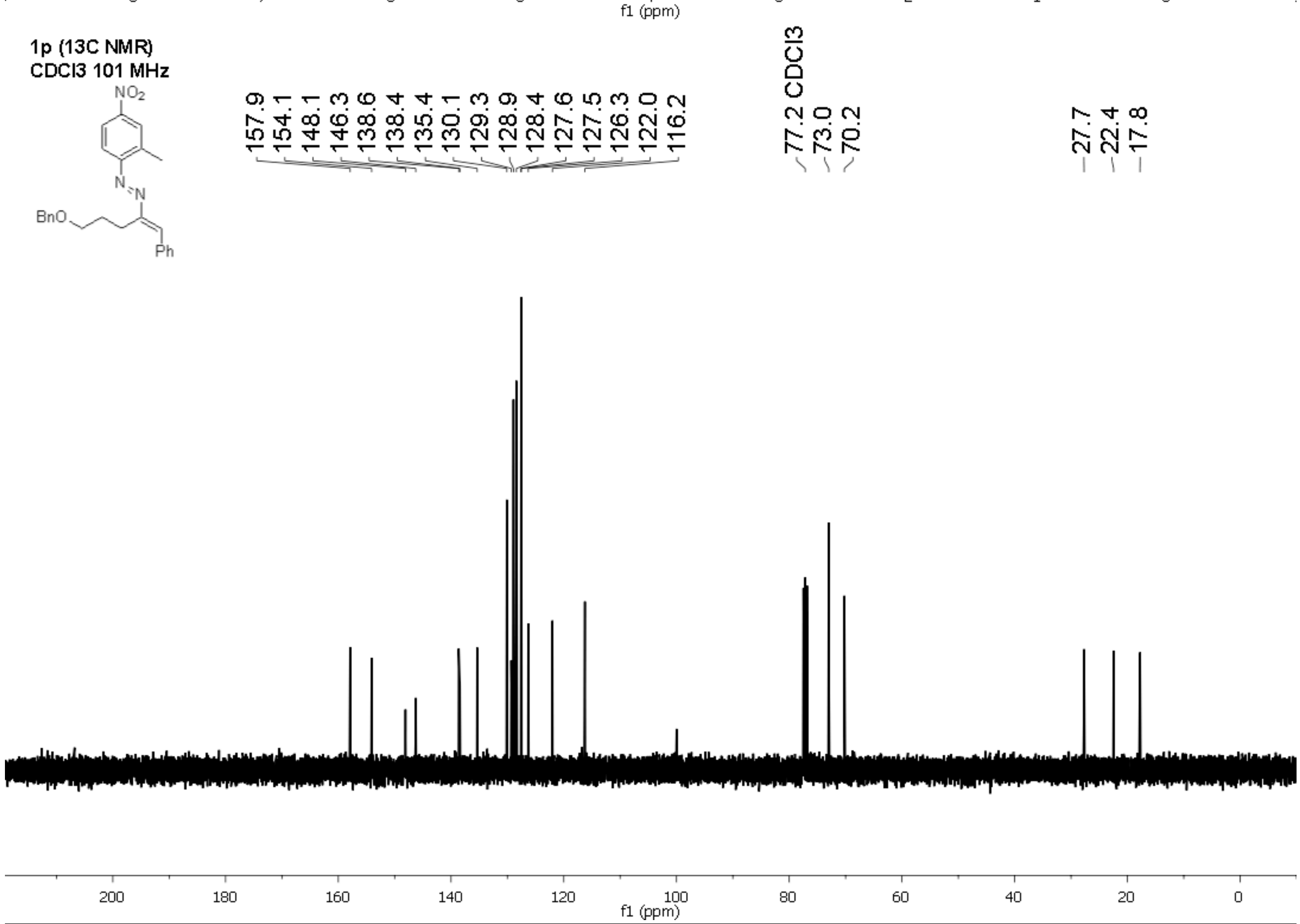

1n (1H NMR)
CDCl3 400 MHz
8.42
8.30
8.28
7.83
7.81
7.26 CHCl3
7.14
7.13
7.12
2.54
2.53
2.52
2.52
2.42
2.40
2.39
1.81
1.80
1.79
1.78
1.78
1.77
1.76
1.75
1.74
1.73
1.73
1.72
1.70
NO2
N
N
2.00
1.99
1.00
2.02
2.02
4.08
8
7
6
5
4
3
2
1
0
f1 (ppm)

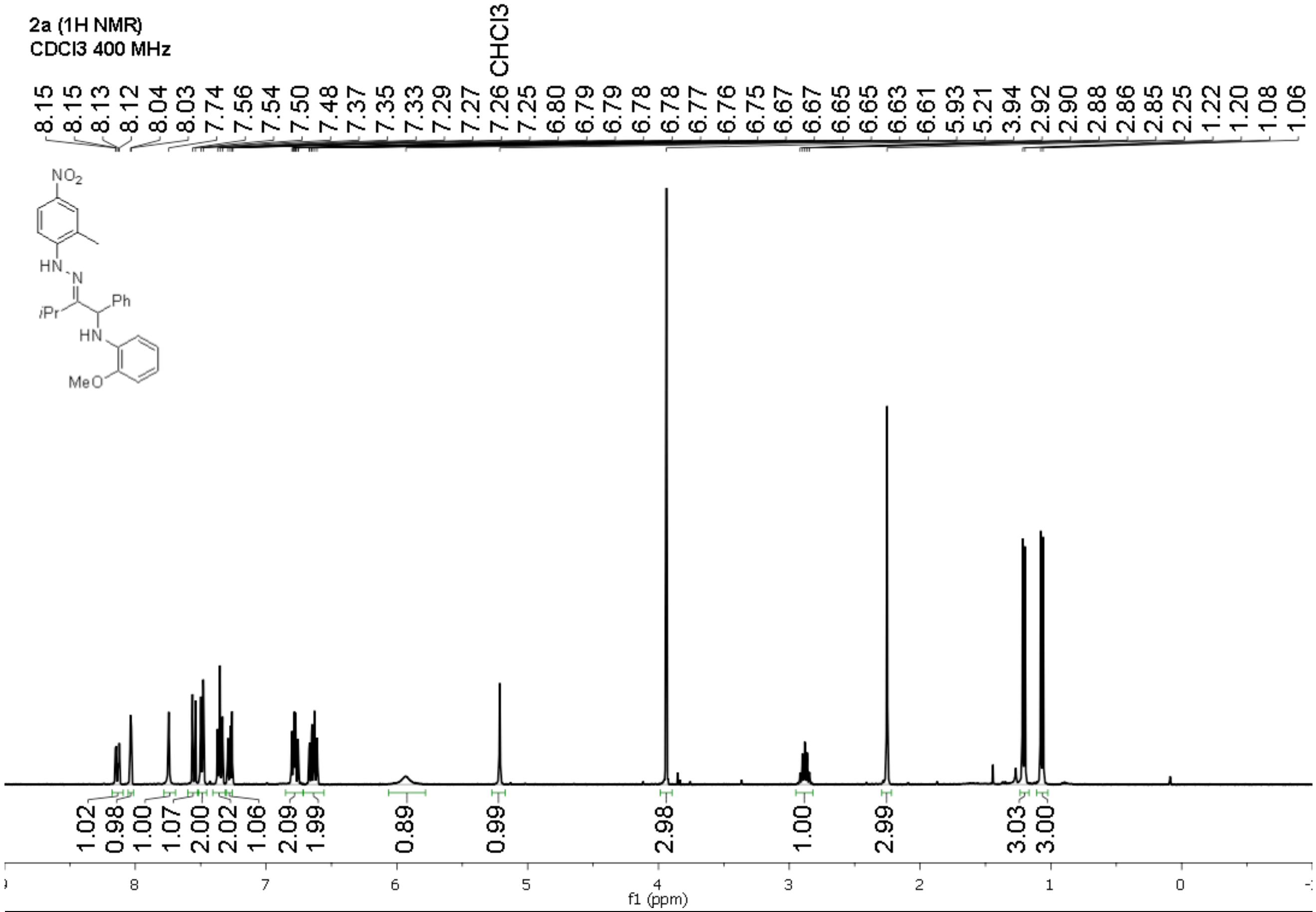

1n (13C NMR)
CDCl3 101 MHz
NO2
N
N
156.3
156.3
148.1
146.5
124.7
123.0
77.2 CHCl3
26.9
22.8
22.2
21.9
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

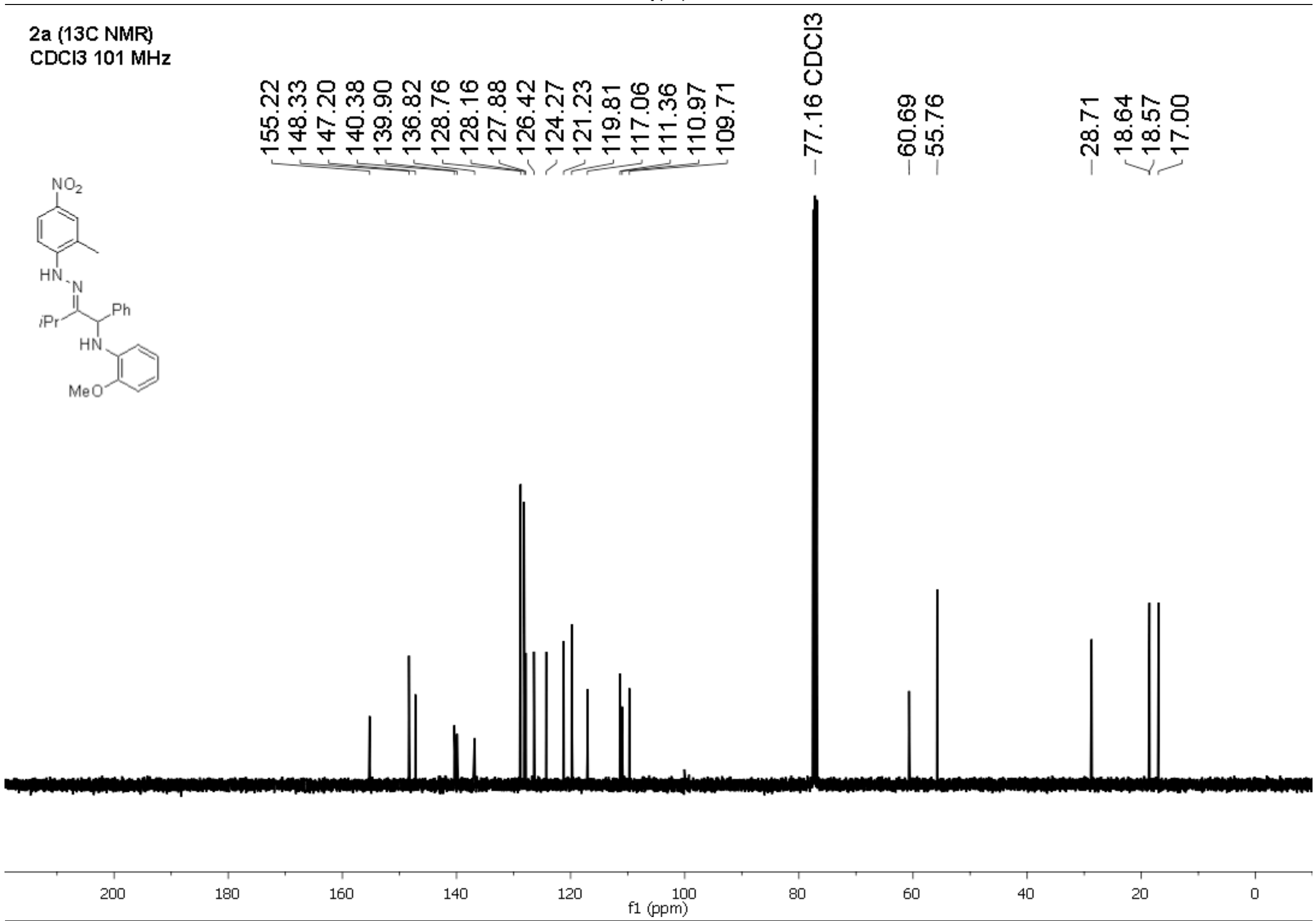

1o (1H NMR)
CDCl3 400 MHz
8.21 8.20 8.19 8.11 8.11 8.09 8.09 7.79 7.69 7.67 7.64 7.61 7.54 7.52 7.50 7.30 7.28 7.26 CHCl3 7.23 7.21 7.13
2.73 2.72 2.43 2.40 2.31 2.17
NO2
N
N
1oE
1oZ
1.45 1.49 0.99 0.99 0.91 1.01 2.52 2.01 0.99 0.52
1.46 2.95 2.92 1.50 3.00 1.46
8 7 6 5 4 3 2 1 0
f1 (ppm)

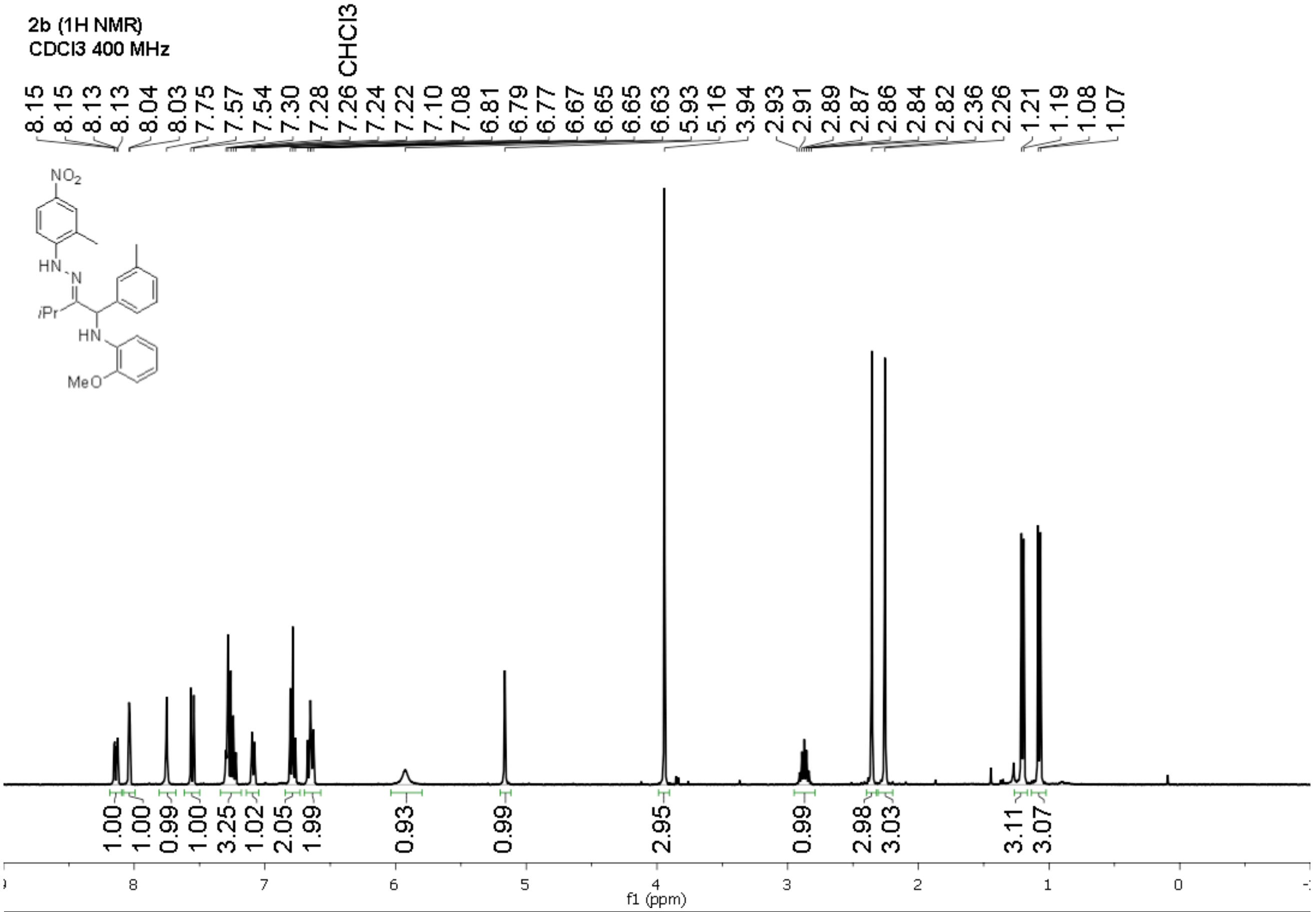

1o (13C NMR)
CDCl3 101 MHz
154.6 154.2 154.1 151.0 148.1 147.9 146.1 139.6 139.2 139.1 138.6 138.3 132.9 132.9 132.3 130.2 129.5 129.2 126.3 126.3 122.0 122.0 116.6 116.3
77.2 CDCl3
21.5 21.5 17.9 17.7 17.7 12.1
NO2
N
N
1oE
1oZ
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

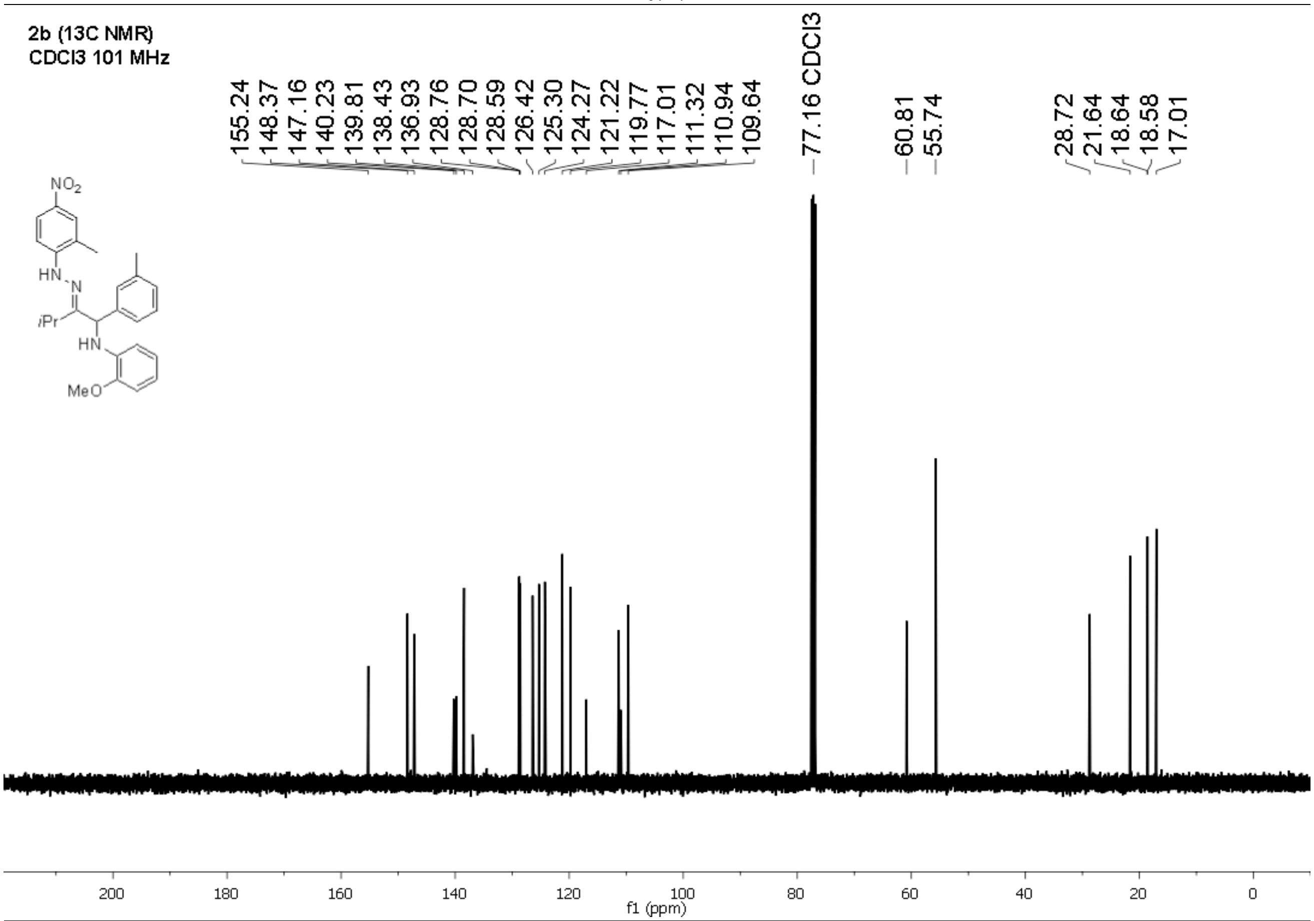

1p (1H NMR)
CDCl3 400 MHz
8.20 8.20 8.12 8.11 8.10 8.09 7.81 7.70 7.68 7.65 7.63 7.44 7.42 7.39 7.38 7.36 7.34 7.32 7.26 CHCl3
4.55
3.63 3.62 3.60 3.01 2.99 2.99 2.98 2.97 2.70 1.98 1.97 1.95 1.95 1.94 1.93 1.91
NO2
N
N
BnO
Ph
1.00 1.03 0.99 2.02 2.04 1.04 8.30 2.07 2.04 1.99 3.03 2.03
8 7 6 5 4 3 2 1 0
f1 (ppm)

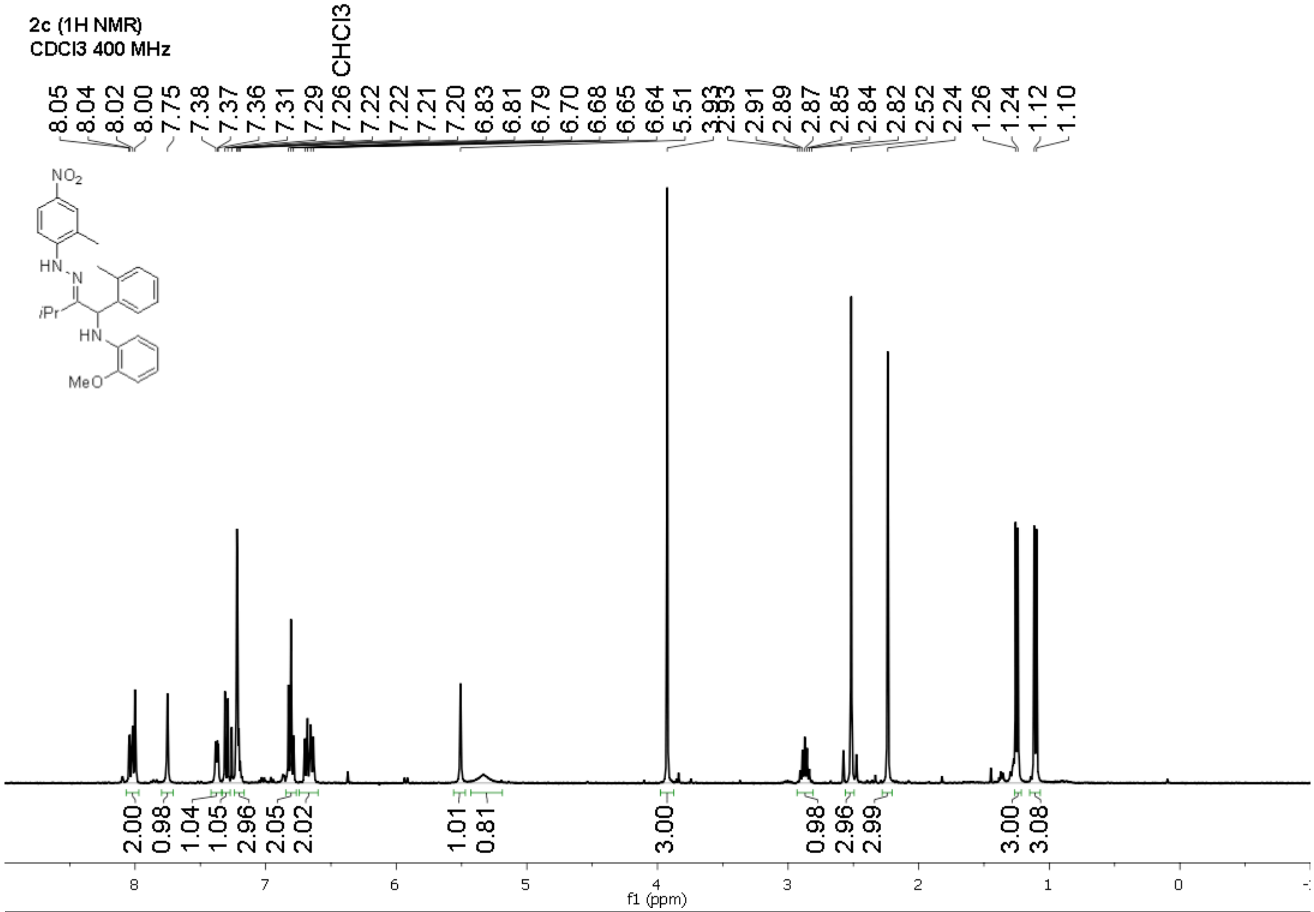

1p (13C NMR)
CDCl3 101 MHz
NO2
N
N
BnO
Ph
157.9 154.1 148.1 146.3 138.6 138.4 135.4 130.1 129.3 128.9 128.4 127.6 127.5 126.3 122.0 116.2
77.2 CDCl3 73.0 70.2
27.7 22.4 17.8
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

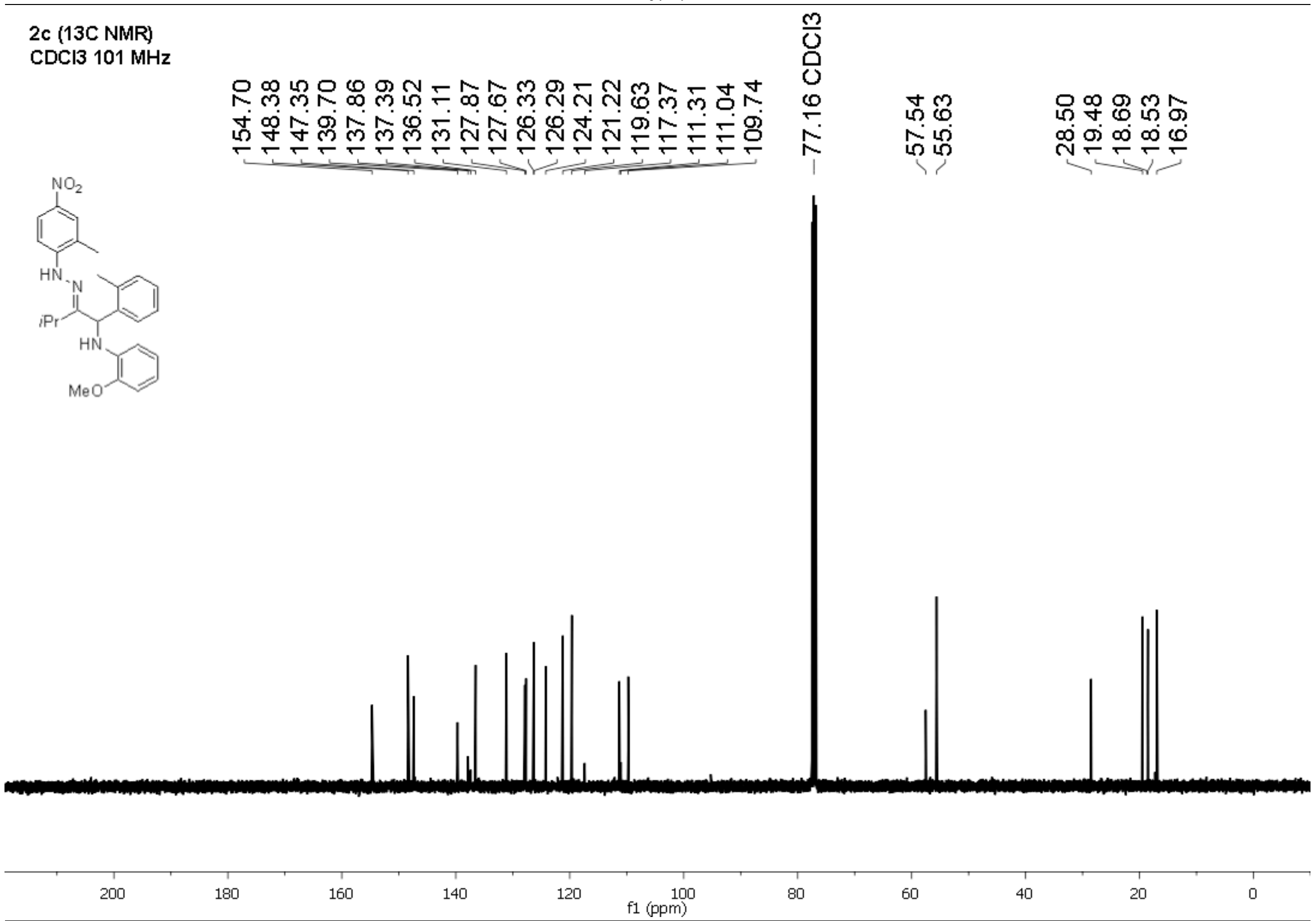

2a (1H NMR)
CDCl3 400 MHz
8.15 8.15 8.13 8.12 8.04 8.03 7.74 7.56 7.54 7.50 7.48 7.37 7.35 7.33 7.29 7.27 7.26 CHCl3 7.25 6.80 6.79 6.79 6.78 6.78 6.77 6.76 6.75 6.67 6.67 6.65 6.65 6.63 6.61 5.93 5.21 3.94 2.92 2.90 2.88 2.86 2.85 2.25 1.22 1.20 1.08 1.06
NO2
HN
N
Ph
iPr
HN
MeO
1.02 0.98 1.00 1.07 2.00 2.02 1.06 2.09 1.99 0.89 0.99 2.98 1.00 2.99 3.03 3.00
f1 (ppm)

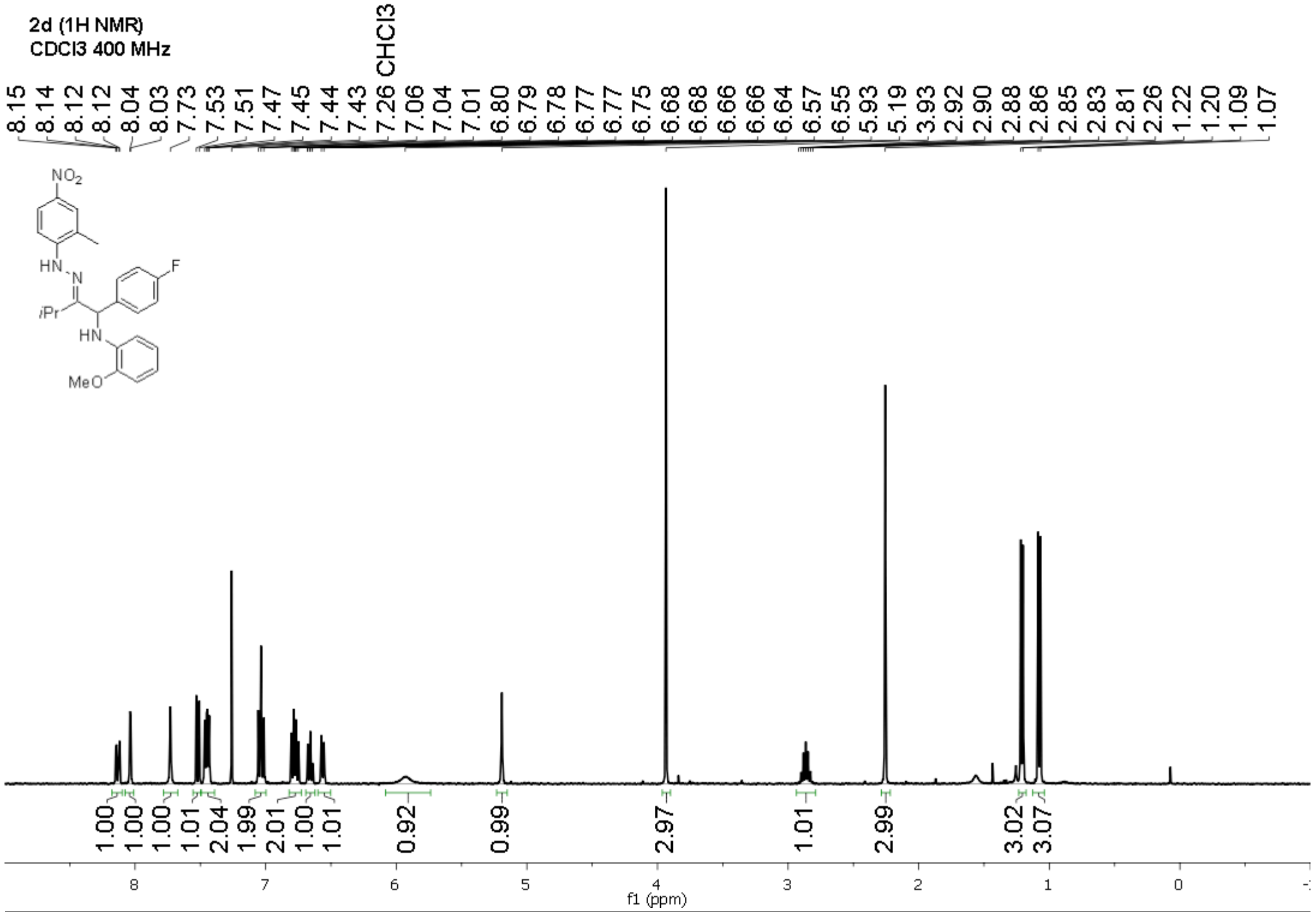

2a (13C NMR)
CDCl3 101 MHz
155.22 148.33 147.20 140.38 139.90 136.82 128.76 128.16 127.88 126.42 124.27 121.23 119.81 117.06 111.36 110.97 109.71
77.16 CDCl3
60.69 55.76
28.71 18.64 18.57 17.00
NO2
HN
N
Ph
iPr
HN
MeO
f1 (ppm)

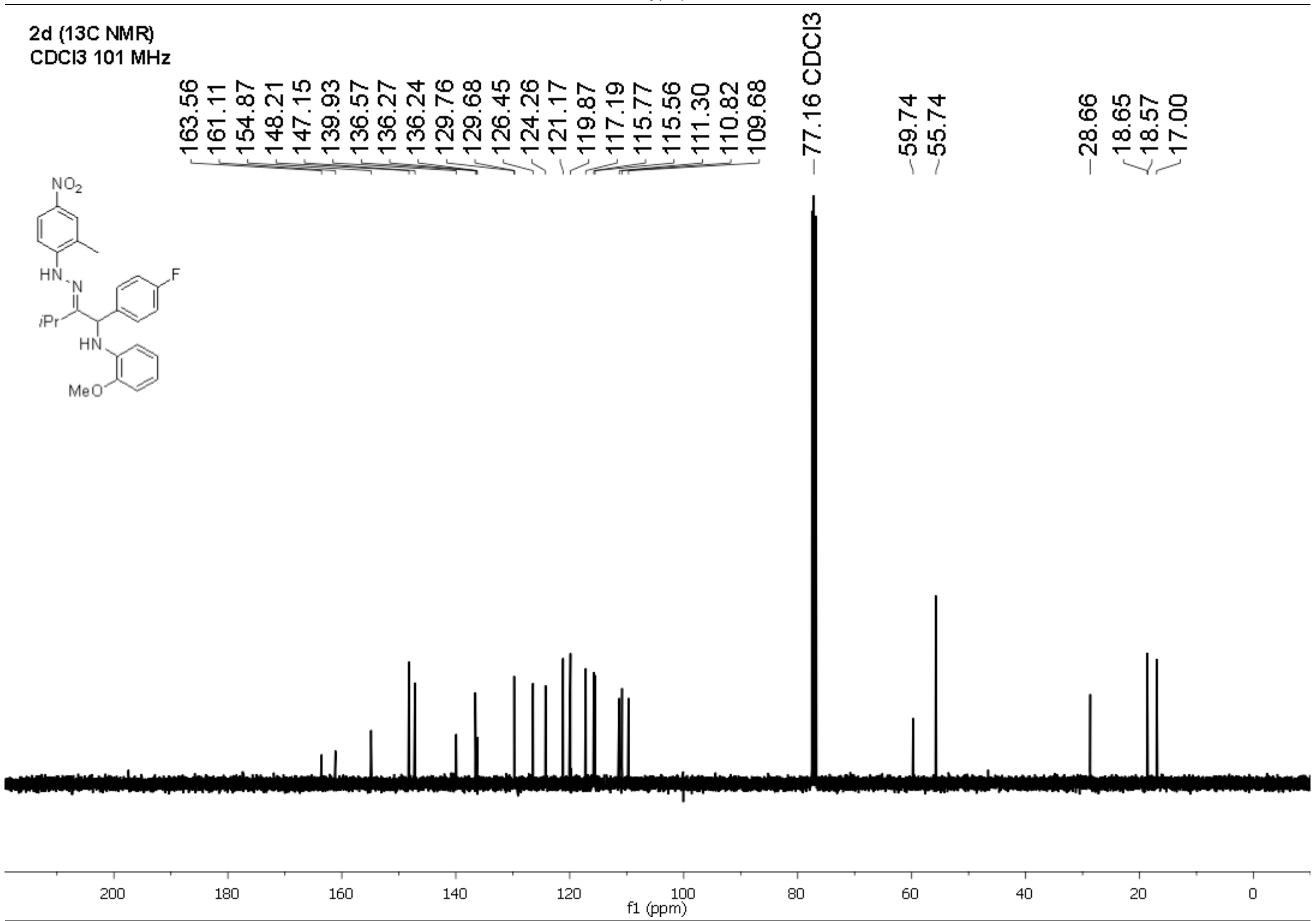

2b (1H NMR)
CDCl3 400 MHz
8.15 8.15 8.13 8.13 8.04 8.03 7.75 7.57 7.54 7.30 7.28 7.26 CHCl3 7.24 7.22 7.10 7.08 6.81 6.79 6.77 6.67 6.65 6.65 6.63 5.93 5.16 3.94 2.93 2.91 2.89 2.87 2.86 2.84 2.82 2.36 2.26 1.21 1.19 1.08 1.07
NO2
HN
N
iPr
HN
MeO
1.00 1.00 0.99 1.00 3.25 1.02 2.05 1.99 0.93 0.99 2.95 0.99 2.98 3.03 3.11 3.07
f1 (ppm)


2b (13C NMR)
CDCl3 101 MHz
155.24 148.37 147.16 140.23 139.81 138.43 136.93 128.76 128.70 128.59 126.42 125.30 124.27 121.22 119.77 117.01 111.32 110.94 109.64
77.16 CDCl3
60.81 55.74
28.72 21.64 18.64 18.58 17.01
NO2
HN
N
iPr
HN
MeO
f1 (ppm)

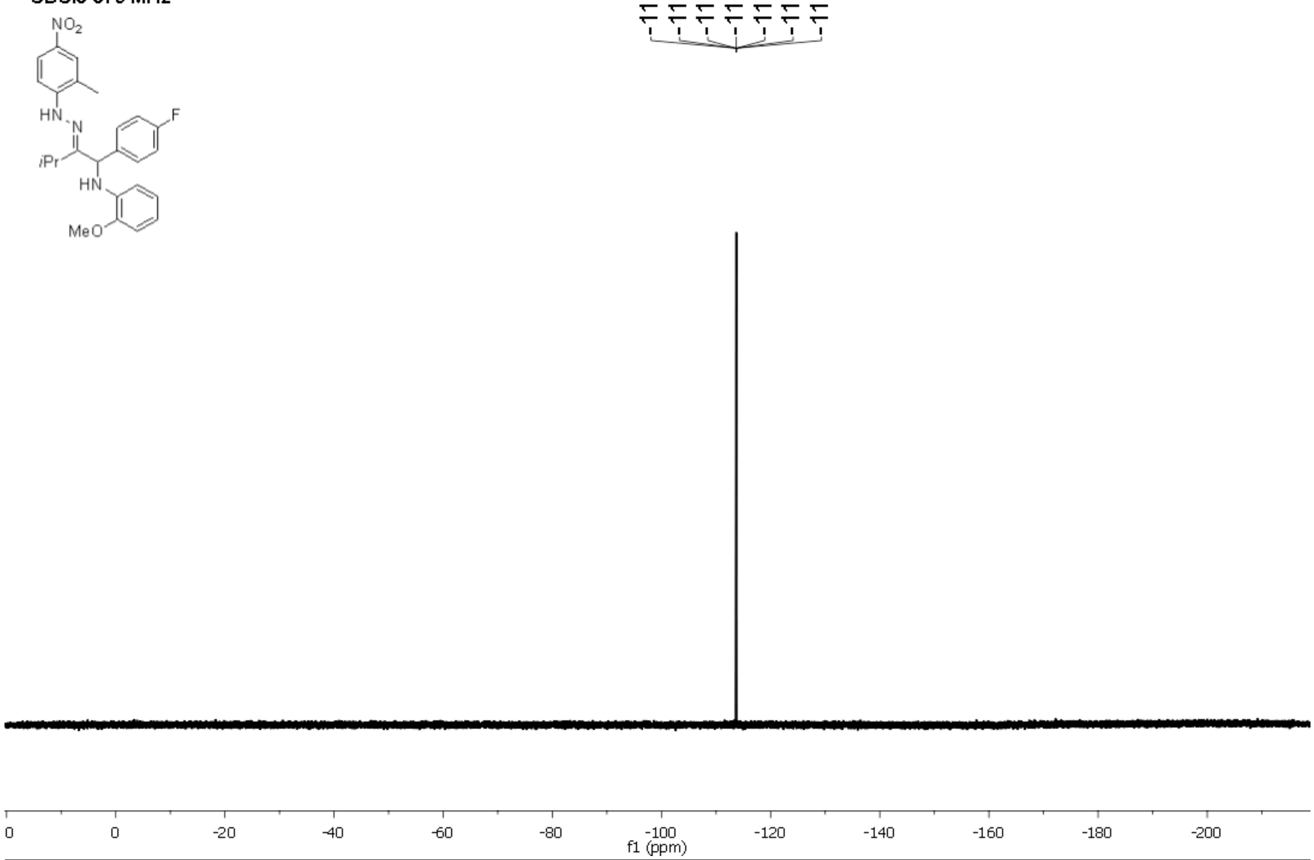

2c (1H NMR)
CDCl3 400 MHz
8.05 8.04 8.02 8.00 7.75 7.38 7.37 7.36 7.31 7.29 7.26 CHCl3 7.22 7.22 7.21 7.20 6.83 6.81 6.79 6.70 6.68 6.65 6.64 5.51 3.93 3.93 2.91 2.89 2.87 2.85 2.84 2.82 2.52 2.24 1.26 1.24 1.12 1.10
2.00 0.98 1.04 1.05 2.96 2.05 2.02 1.01 0.81 3.00 0.98 2.96 2.99 3.00 3.08
f1 (ppm)


2c (13C NMR)
CDCl3 101 MHz
154.70 148.38 147.35 139.70 137.86 137.39 136.52 131.11 127.87 127.67 126.33 126.29 124.21 121.22 119.63 117.37 111.31 111.04 109.74
77.16 CDCl3
57.54 55.63
28.50 19.48 18.69 18.53 16.97
f1 (ppm)

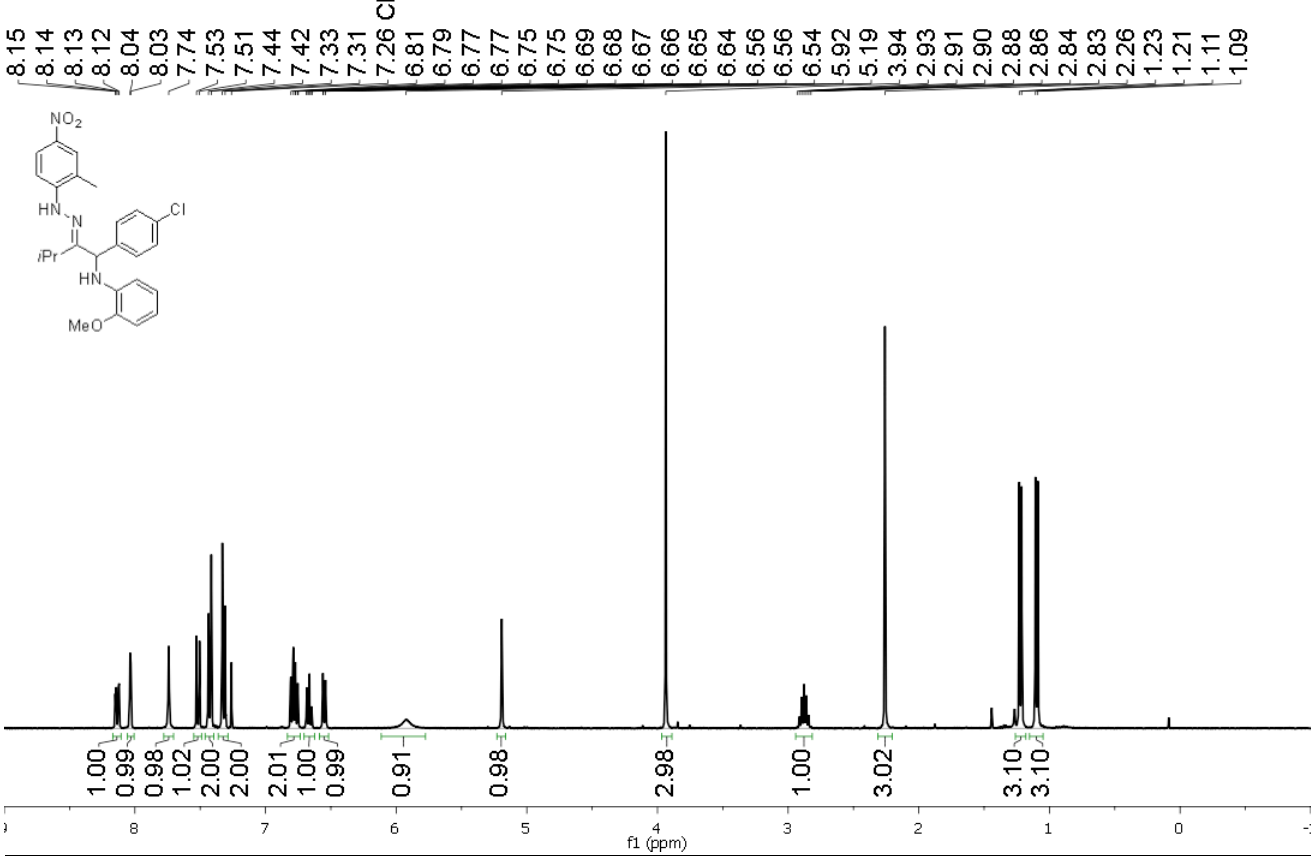

2d (1H NMR)
CDCl3 400 MHz
8.15 8.14 8.12 8.12 8.04 8.03 7.73 7.53 7.51 7.47 7.45 7.44 7.43 7.26 CHCl3 7.06 7.04 7.01 6.80 6.79 6.78 6.77 6.77 6.75 6.68 6.68 6.66 6.66 6.64 6.57 6.55 5.93 5.19 3.93 2.92 2.90 2.88 2.86 2.85 2.83 2.81 2.26 1.22 1.20 1.09 1.07
NO2
HN
N
F
iPr
HN
MeO
1.00 1.00 1.00 1.01 2.04 1.99 2.01 1.00 1.01 0.92 0.99 2.97 1.01 2.99 3.02 3.07
f1 (ppm)

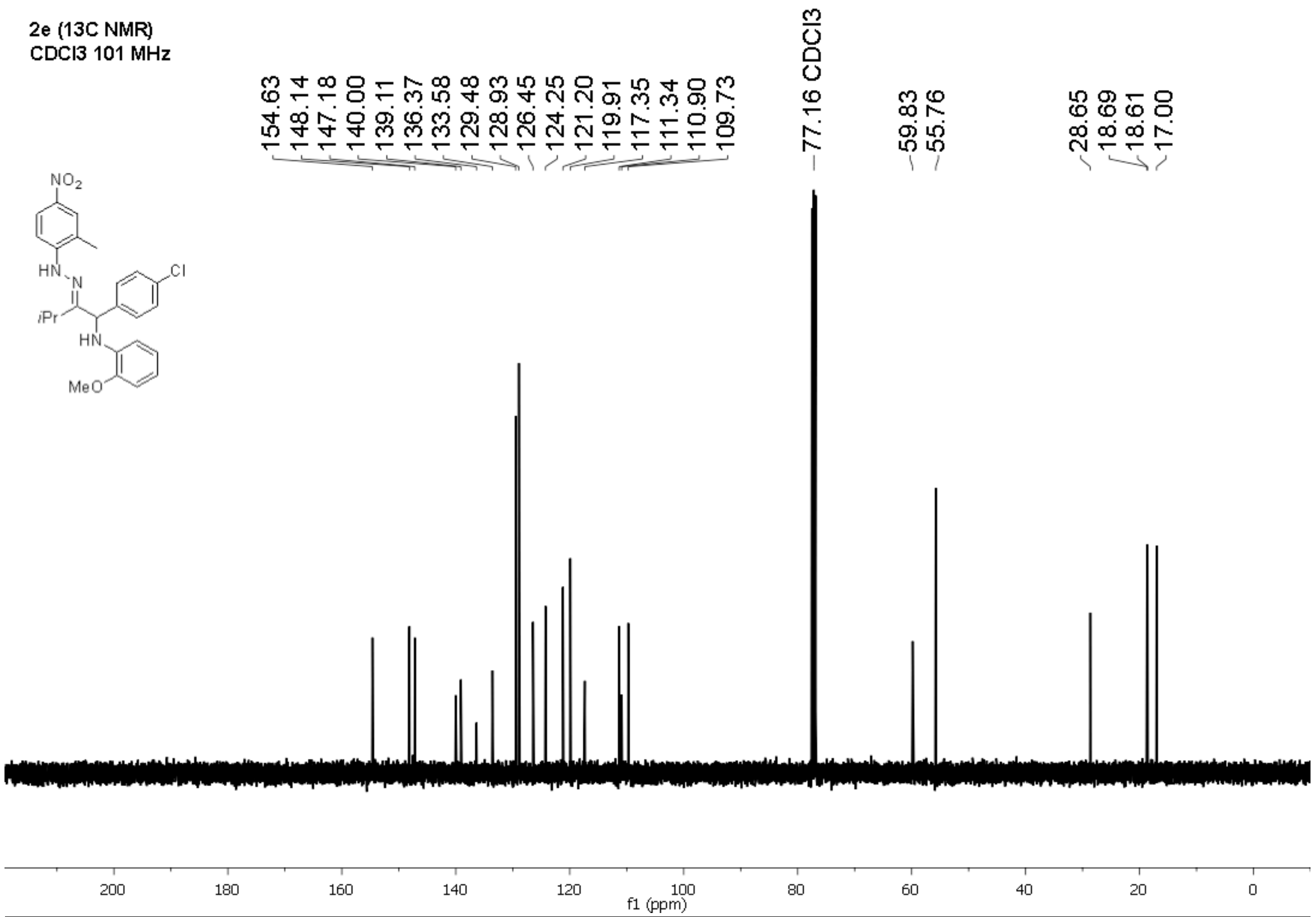

2d (13C NMR)
CDCl3 101 MHz
163.56 161.11 154.87 148.21 147.15 139.93 136.57 136.27 136.24 129.76 129.68 126.45 124.26 121.17 119.87 117.19 115.77 115.56 111.30 110.82 109.68
77.16 CDCl3
59.74 55.74
28.66 18.65 18.57 17.00
NO2
HN
N
F
iPr
HN
MeO
f1 (ppm)

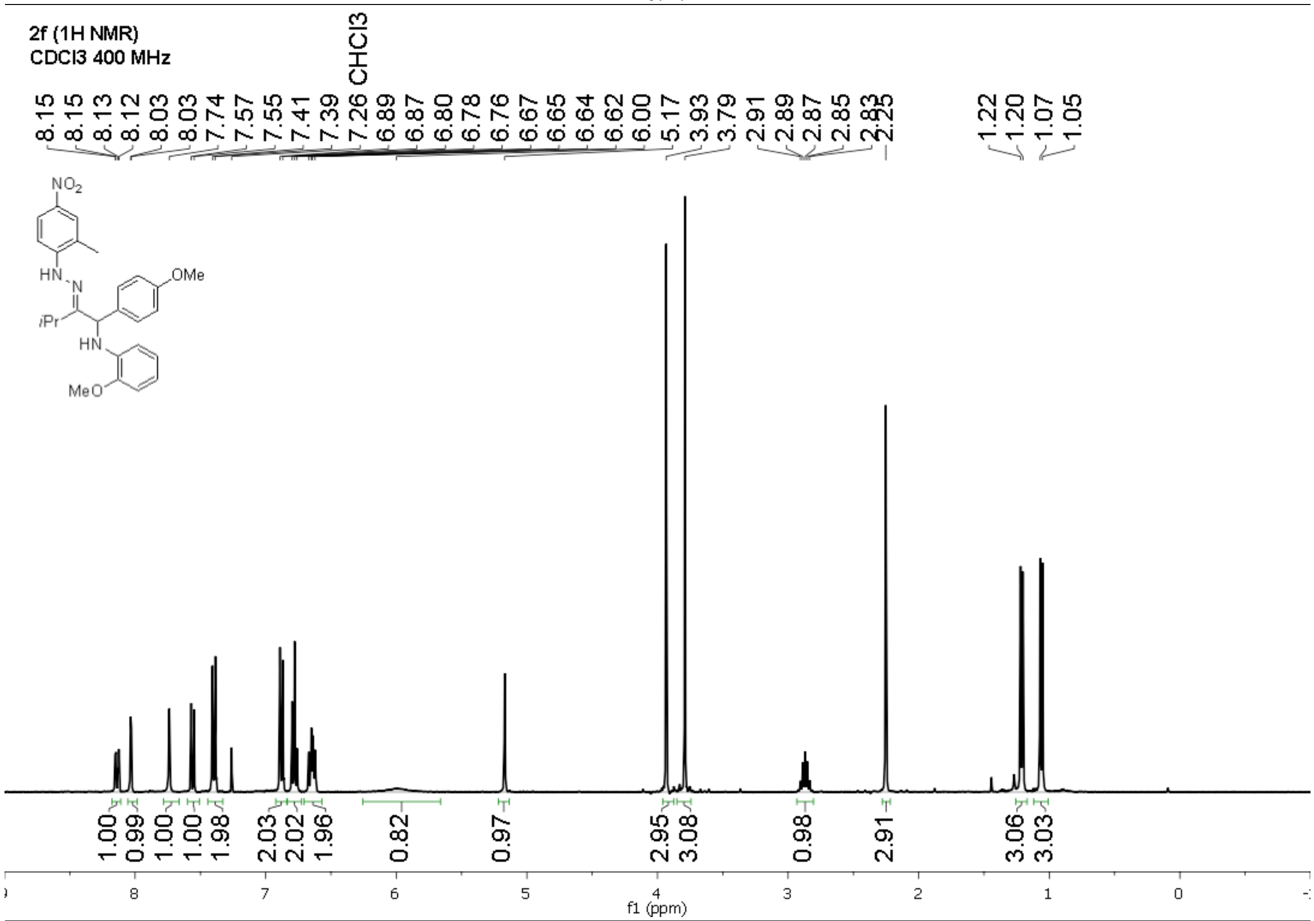
2d (19F NMR)
CDCl3 376 MHz



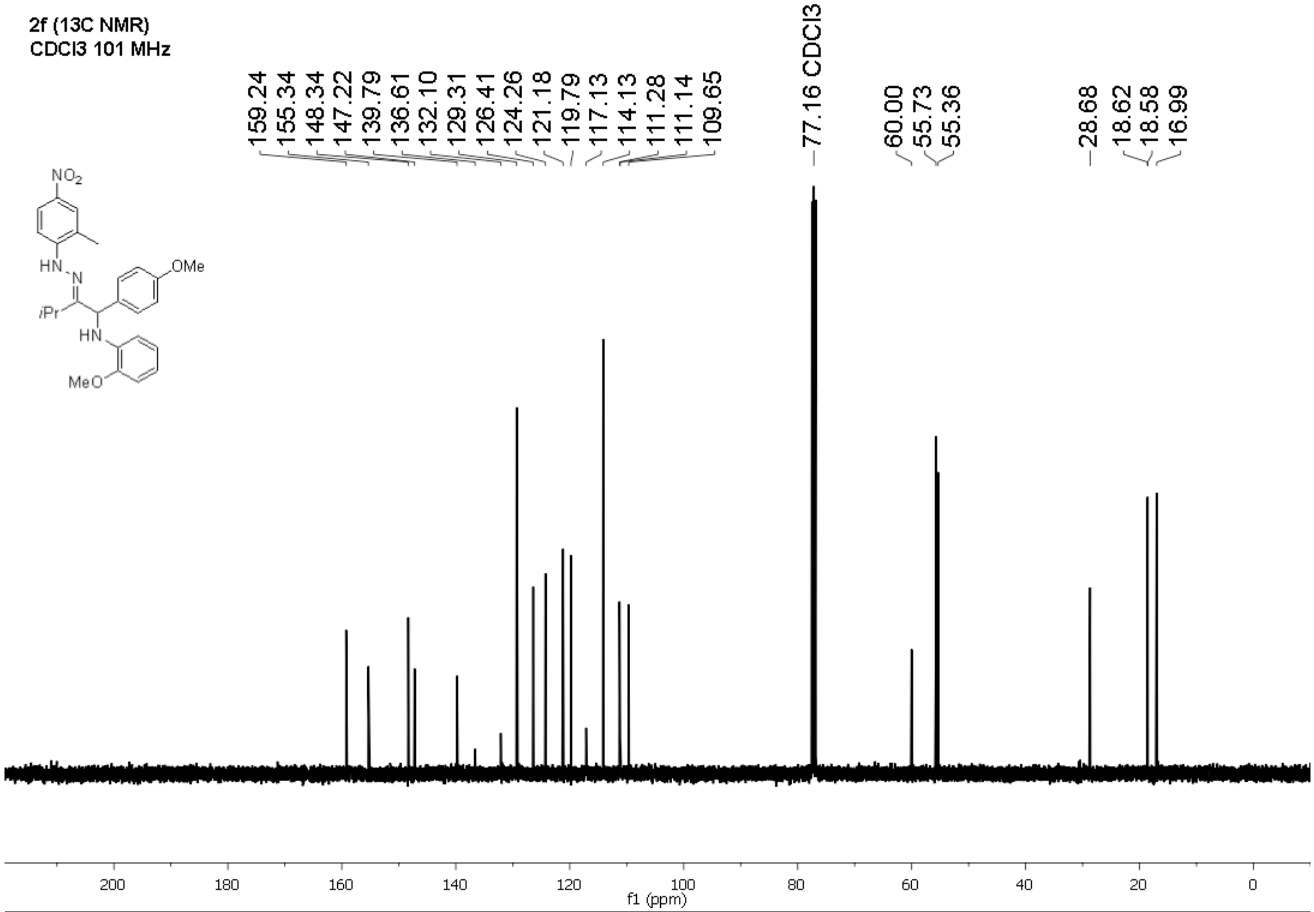
2e (1H NMR)
CDCl3 400 MHz



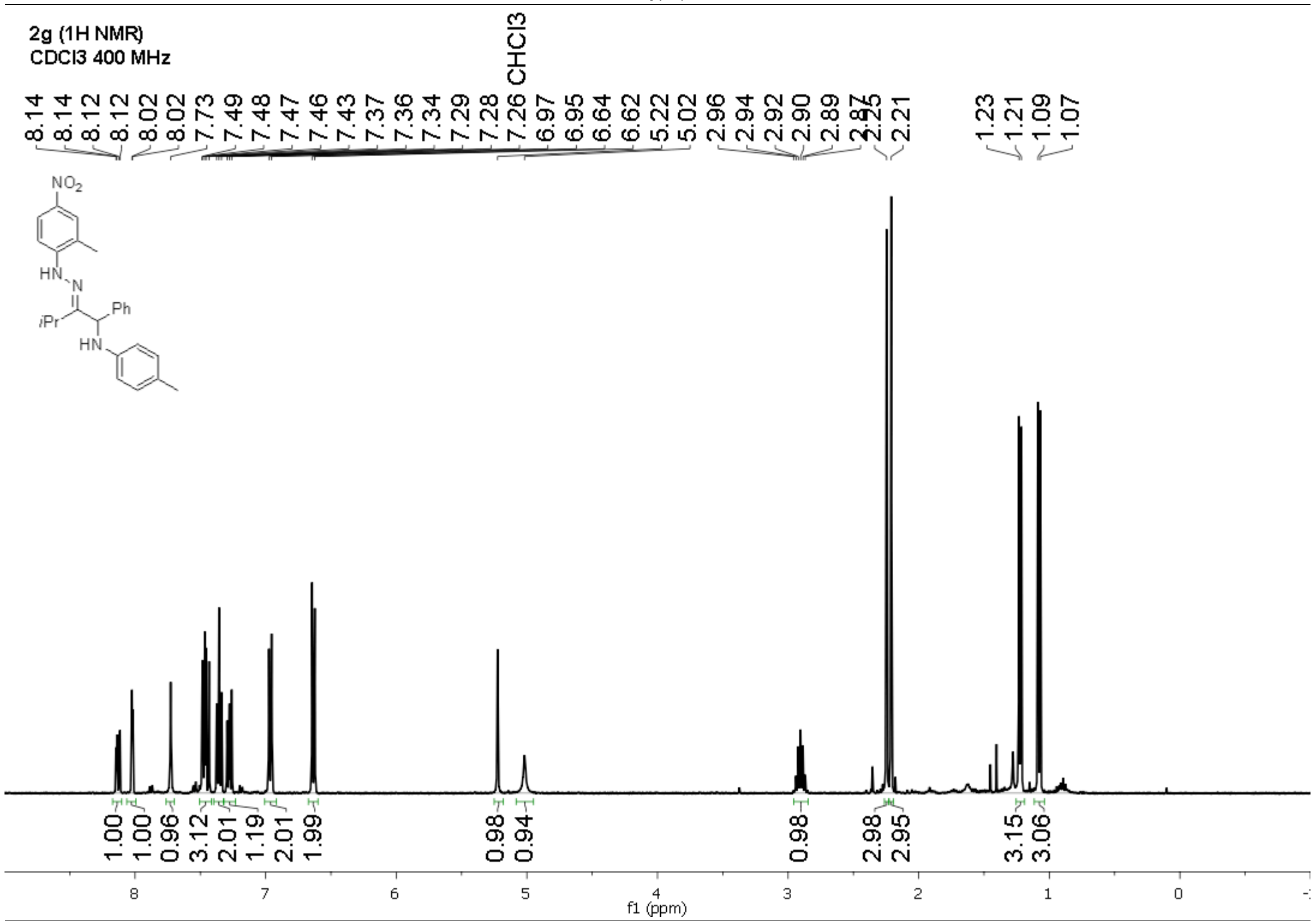

2e (13C NMR)
CDCl3 101 MHz
154.63 148.14 147.18 140.00 139.11 136.37 133.58 129.48 128.93 126.45 124.25 121.20 119.91 117.35 111.34 110.90 109.73
77.16 CDCl3
59.83 55.76
28.65 18.69 18.61 17.00
NO_2
HN
N
Cl
iPr
HN
MeO
f1 (ppm)

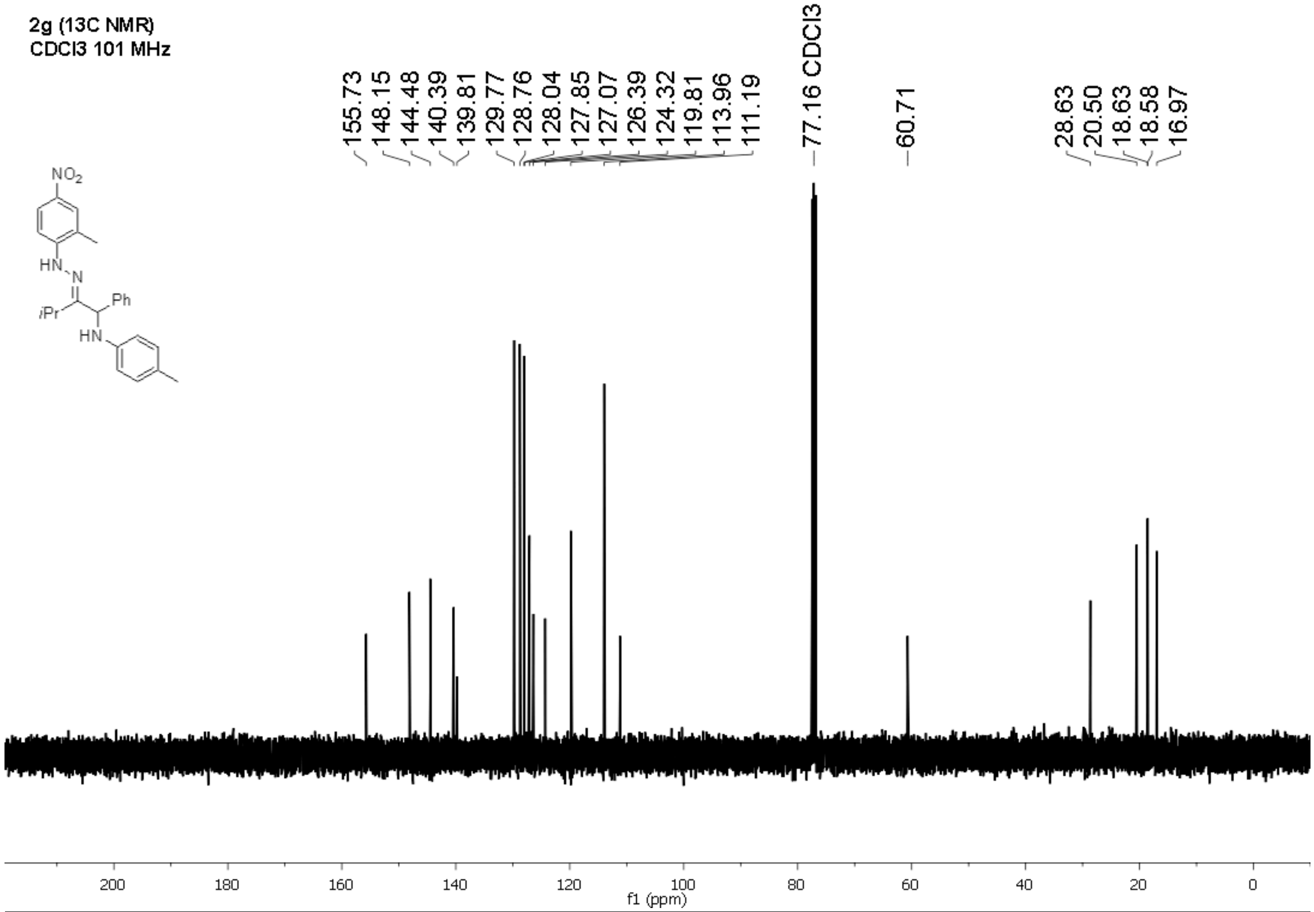

2f (1H NMR)
CDCl3 400 MHz
8.15 8.15 8.13 8.12 8.03 8.03 7.74 7.57 7.55 7.41 7.39 7.26 CHCl3 6.89 6.87 6.80 6.78 6.76 6.67 6.65 6.64 6.62 6.00 5.17 3.93 3.79 2.91 2.89 2.87 2.85 2.83 2.25
1.22 1.20 1.07 1.05
NO_2
HN
N
OMe
iPr
HN
MeO
1.00 0.99 1.00 1.00 1.98 2.03 2.02 1.96 0.82 0.97 2.95 3.08 0.98 2.91 3.06 3.03
f1 (ppm)

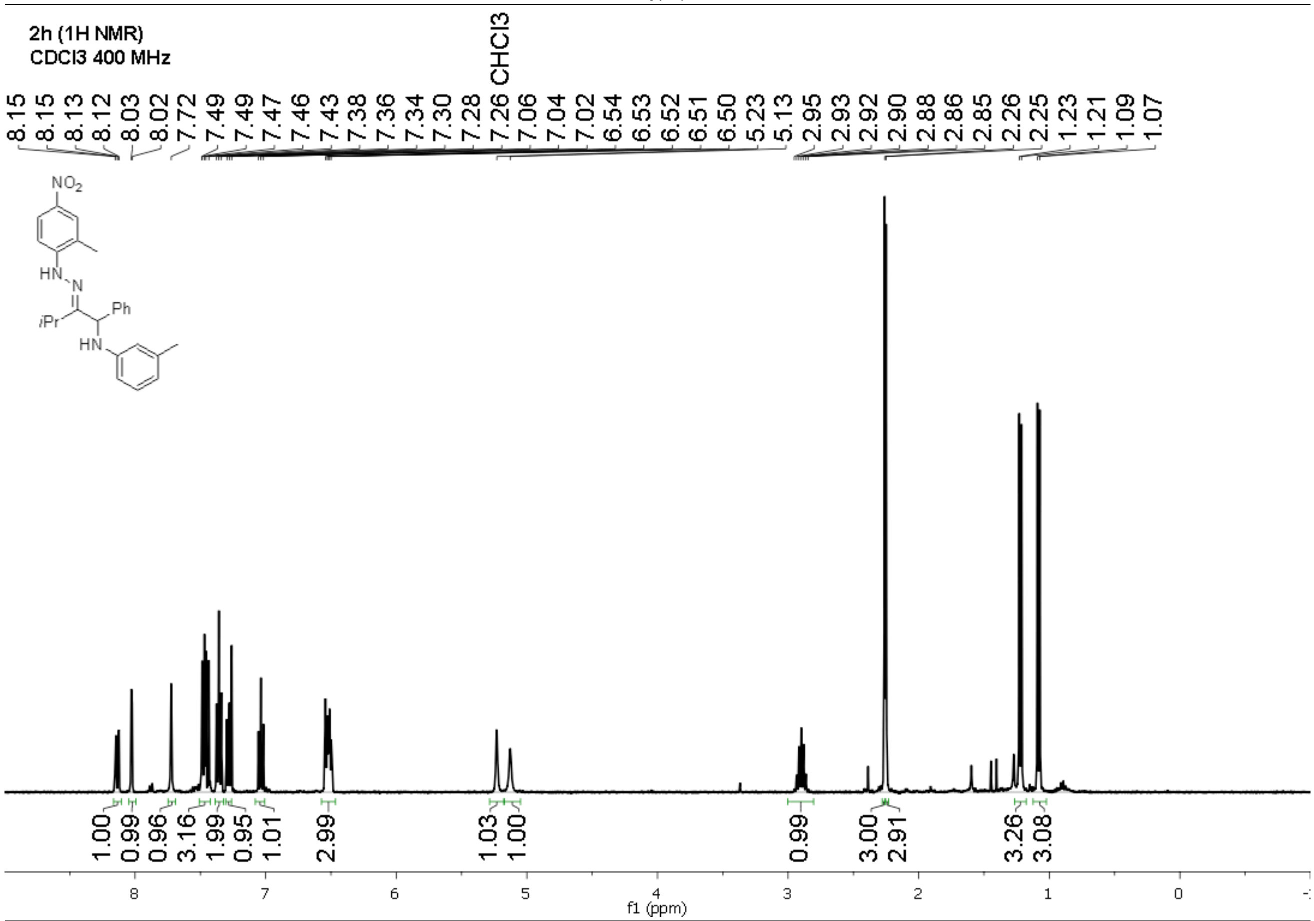
2f (13C NMR)
CDCl3 101 MHz



2g (1H NMR)
CDCl3 400 MHz




2g (13C NMR)
CDCl3 101 MHz
155.73
148.15
144.48
140.39
139.81
129.77
128.76
128.04
127.85
127.07
126.39
124.32
119.81
113.96
111.19
77.16 CDCl3
60.71
28.63
20.50
18.63
18.58
16.97
NO2
HN
N
Ph
iPr
HN
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


2h (1H NMR)
CDCl3 400 MHz
8.15
8.15
8.13
8.12
8.03
8.02
7.72
7.49
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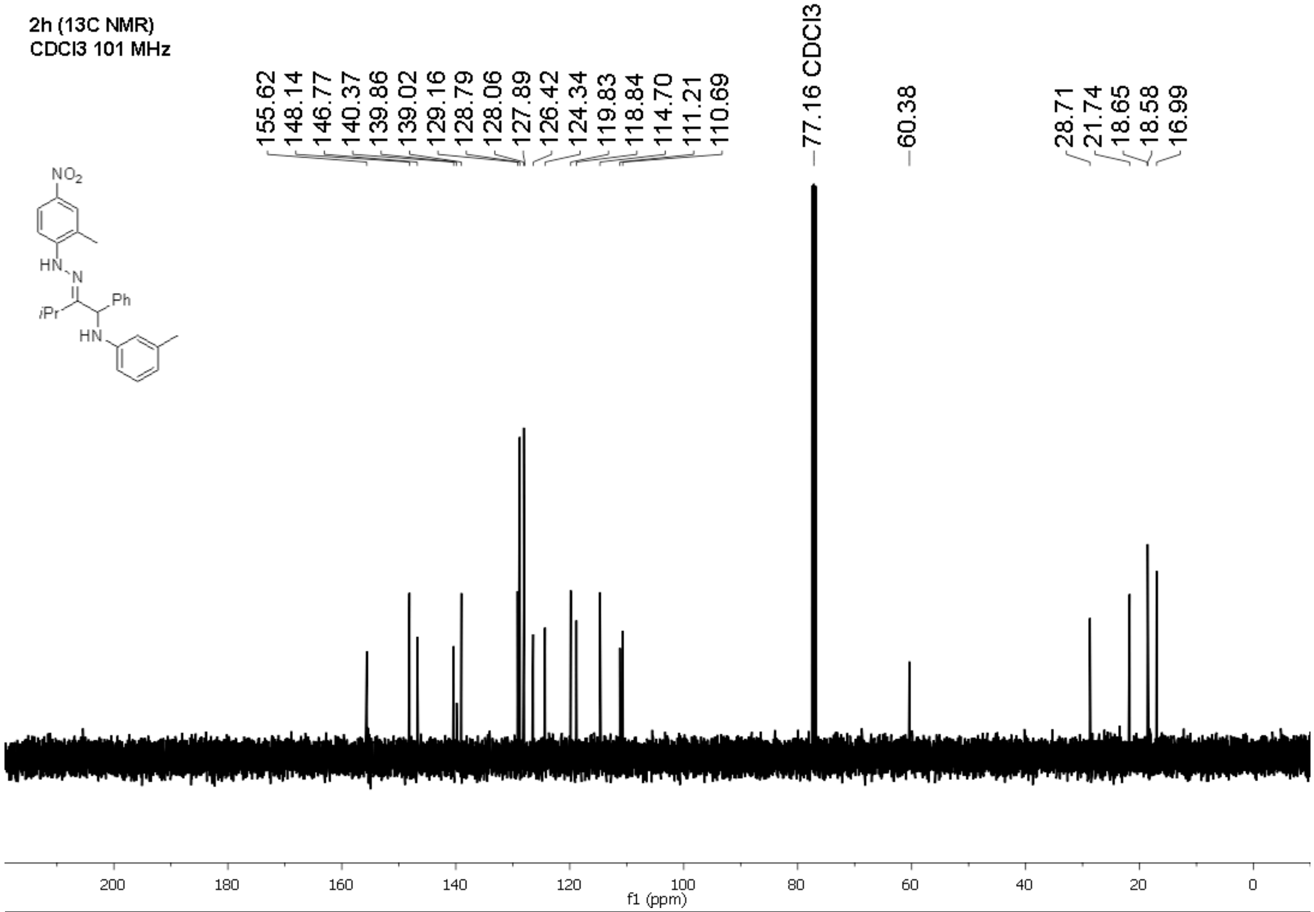
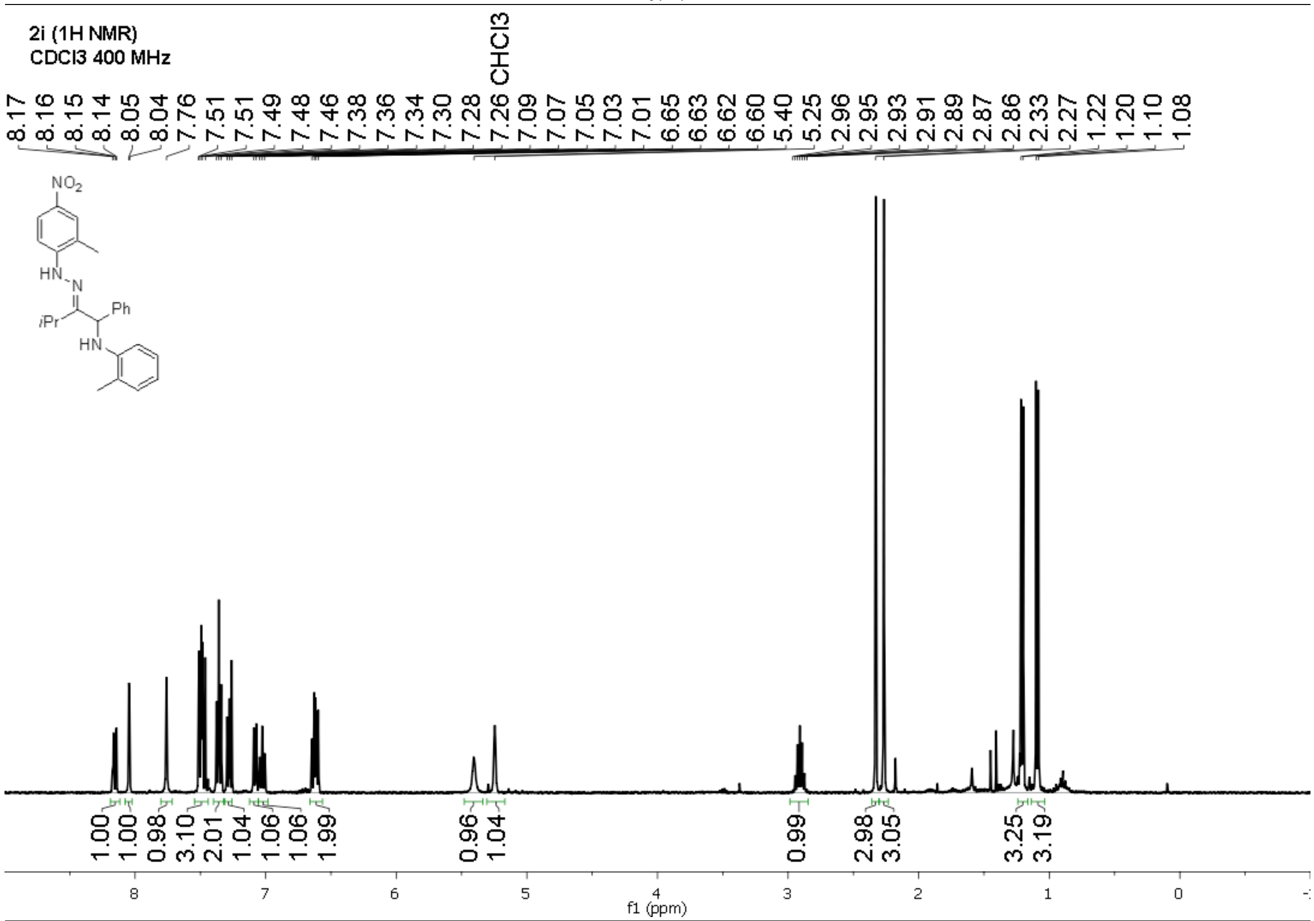
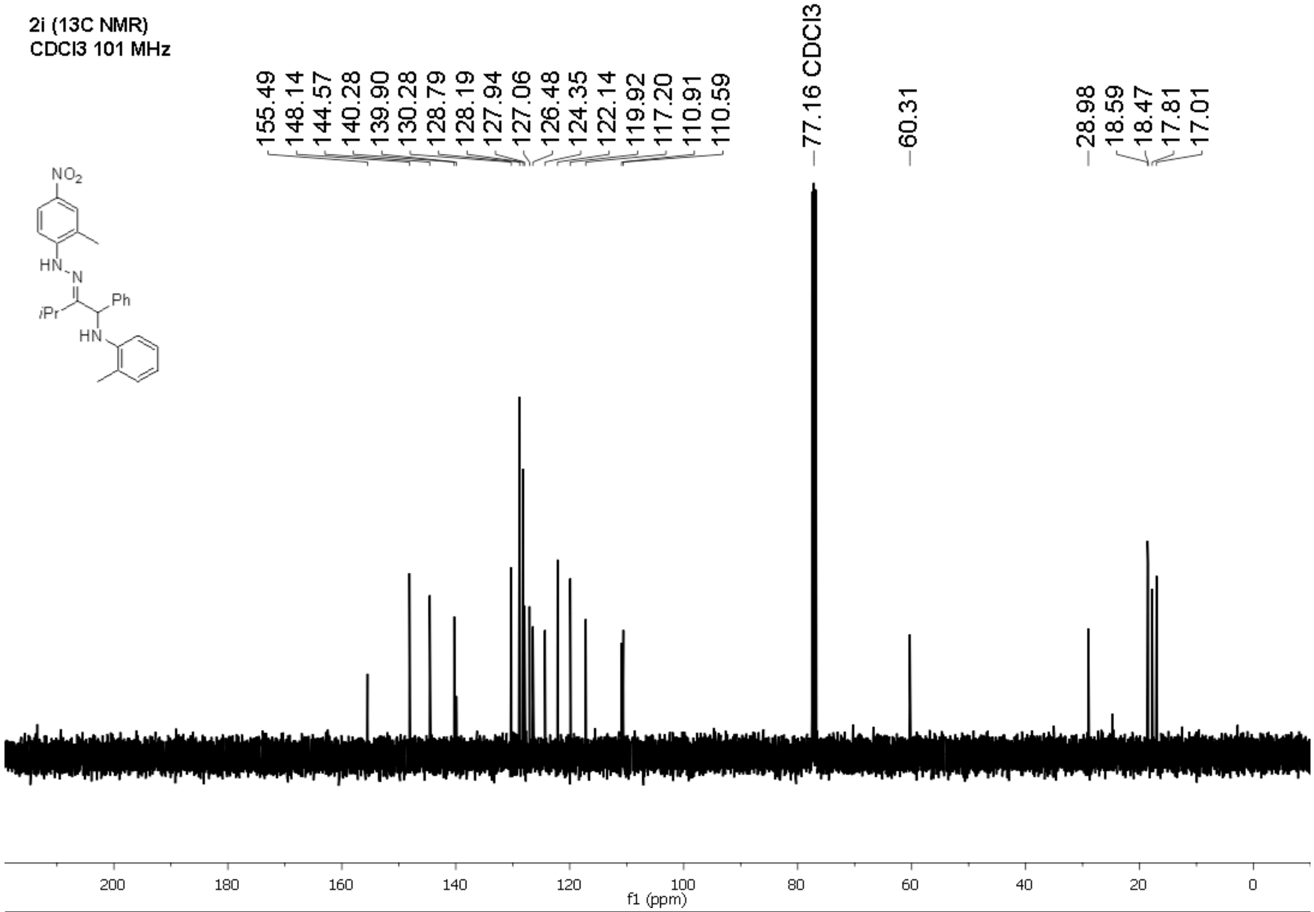
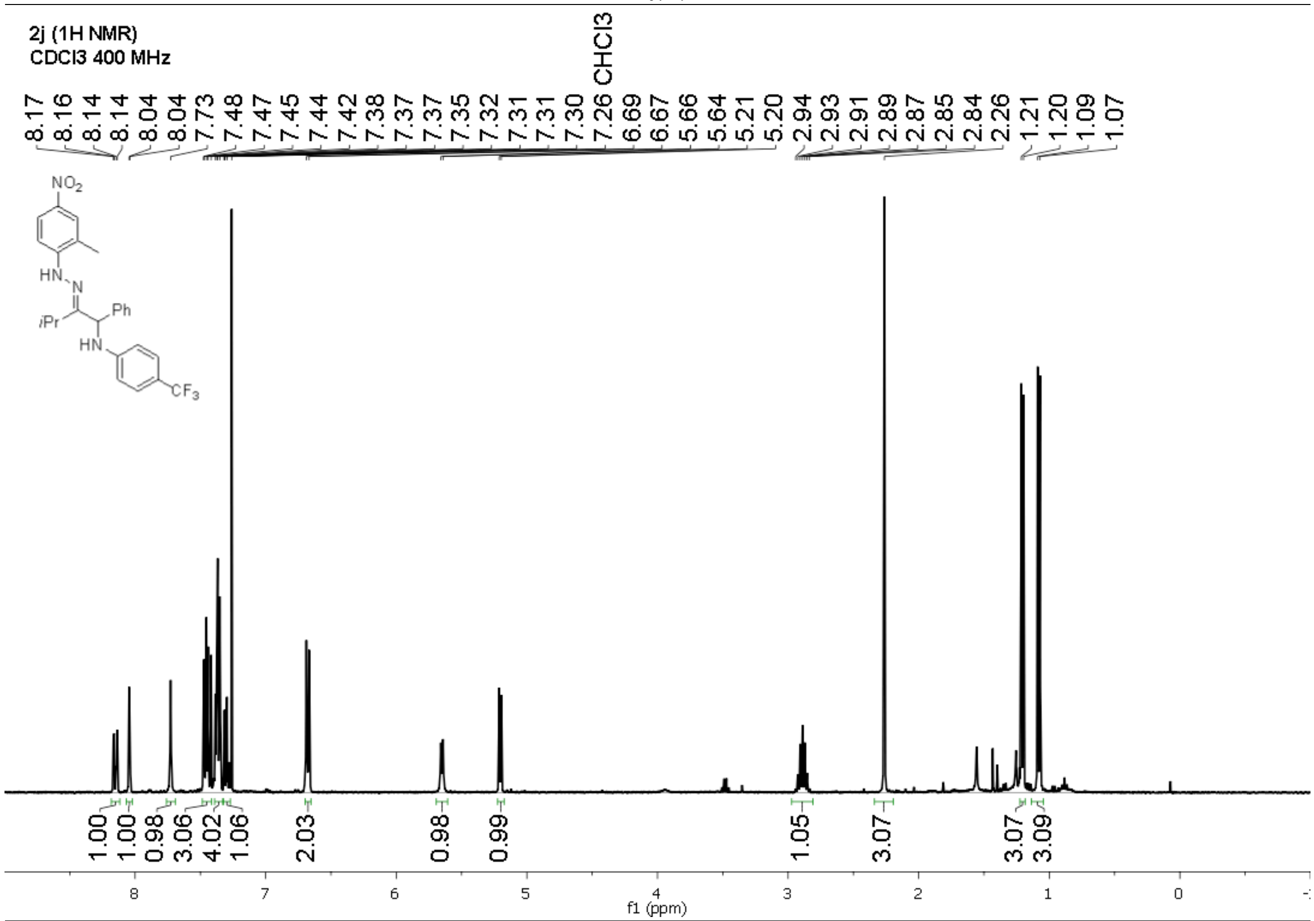
7.47
7.46
7.43
7.38
7.36
7.34
7.30
7.28
7.26 CHCl3
7.06
7.04
7.02
6.54
6.53
6.52
6.51
6.50
5.23
5.13
2.95
2.93
2.92
2.90
2.88
2.86
2.85
2.26
2.25
1.23
1.21
1.09
1.07
NO2
HN
N
Ph
iPr
HN
1.00
0.99
0.96
3.16
1.99
0.95
1.01
2.99
1.03
1.00
0.99
3.00
2.91
3.26
3.08
8
7
6
5
4
3
2
1
0
f1 (ppm)

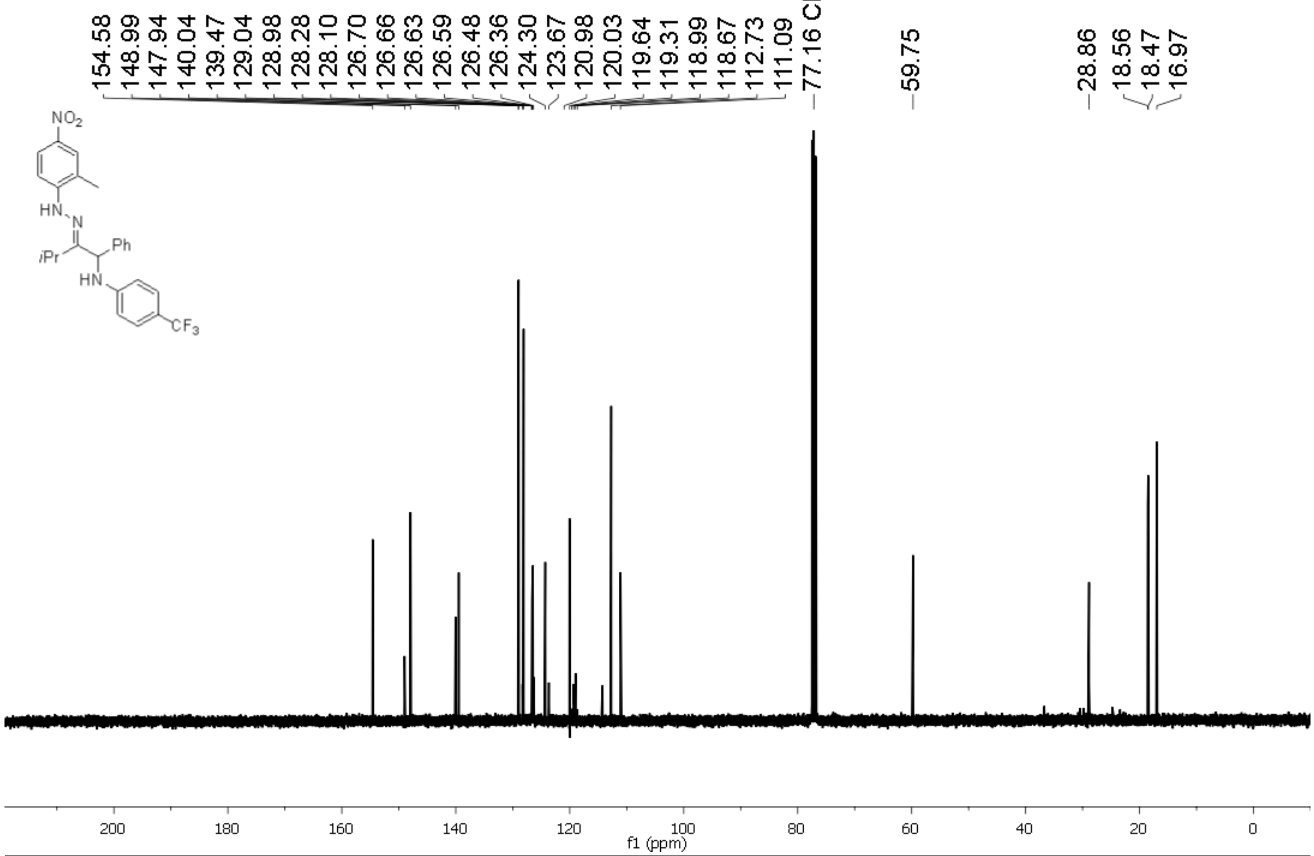

2h (13C NMR)
CDCl3 101 MHz
155.62
148.14
146.77
140.37
139.86
139.02
129.16
128.79
128.06
127.89
126.42
124.34
119.83
118.84
114.70
111.21
110.69
77.16 CDCl3
60.38
28.71
21.74
18.65
18.58
16.99
NO2
HN
N
Ph
iPr
HN
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


2i (1H NMR)
CDCl3 400 MHz
8.17
8.16
8.15
8.14
8.05
8.04
7.76
7.51
7.51
7.49
7.48
7.46
7.38
7.36
7.34
7.30
7.28
7.26 CHCl3
7.09
7.07
7.05
7.03
7.01
6.65
6.63
6.62
6.60
5.40
5.25
2.96
2.95
2.93
2.91
2.89
2.87
2.86
2.33
2.27
1.22
1.20
1.10
1.08
NO2
HN
N
Ph
iPr
HN
1.00
1.00
0.98
3.10
2.01
1.04
1.06
1.06
1.99
0.96
1.04
0.99
2.98
3.05
3.25
3.19
8
7
6
5
4
3
2
1
0
f1 (ppm)

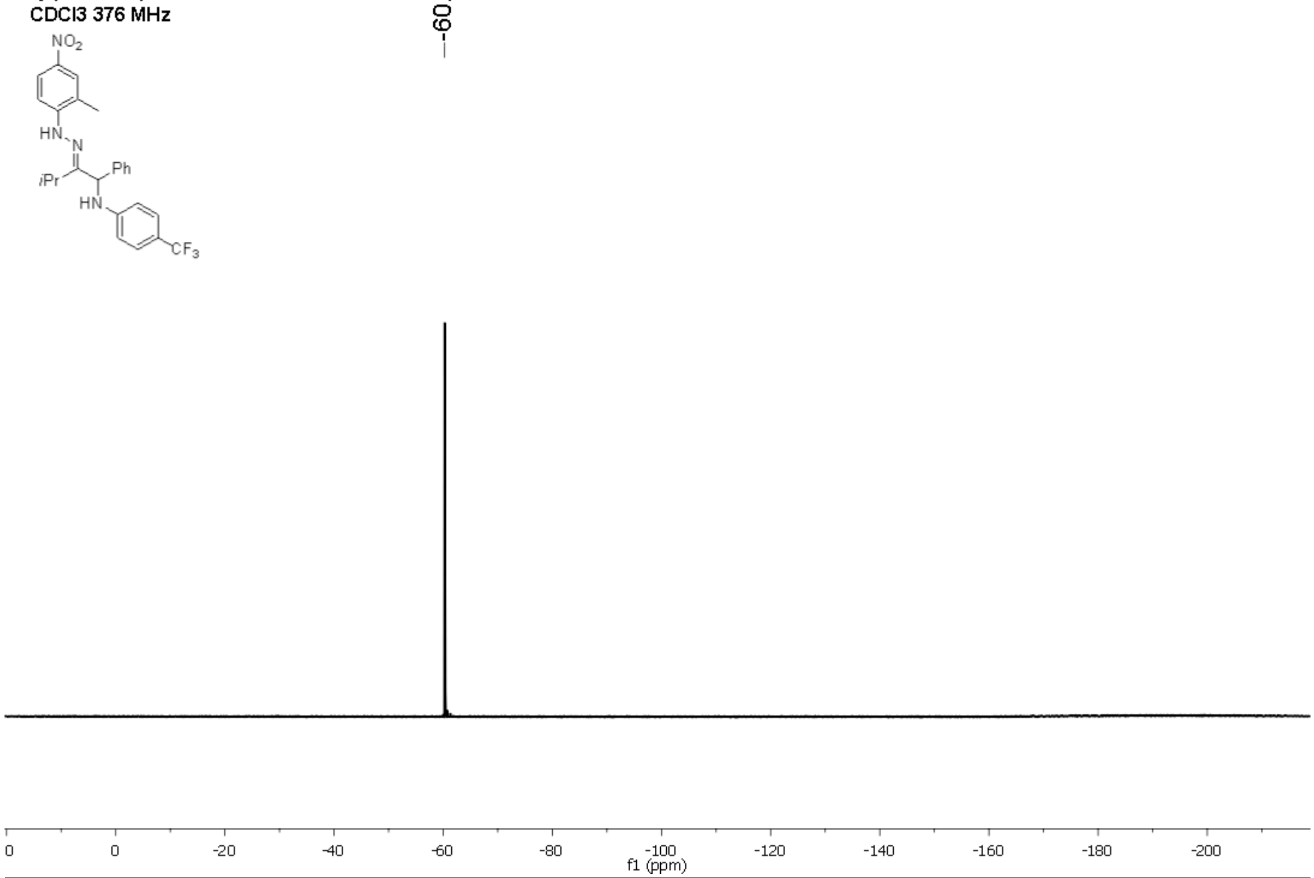

2i (13C NMR)
CDCl3 101 MHz
155.49 148.14 144.57 140.28 139.90 130.28 128.79 128.19 127.94 127.06 126.48 124.35 122.14 119.92 117.20 110.91 110.59
77.16 CDCl3
60.31
28.98 18.59 18.47 17.81 17.01
NO_2
HN
N
iPr
Ph
HN
f1 (ppm)


2j (1H NMR)
CDCl3 400 MHz
8.17 8.16 8.14 8.14 8.04 8.04 7.73 7.48 7.47 7.45 7.44 7.42 7.38 7.37 7.37 7.35 7.32 7.31 7.31 7.30 7.26 CHCl3 6.69 6.67 5.66 5.64 5.21 5.20 2.94 2.93 2.91 2.89 2.87 2.85 2.84 2.26 1.21 1.20 1.09 1.07
NO_2
HN
N
iPr
Ph
HN
CF_3
1.00 1.00 0.98 3.06 4.02 1.06 2.03 0.98 0.99 1.05 3.07 3.07 3.09
f1 (ppm)

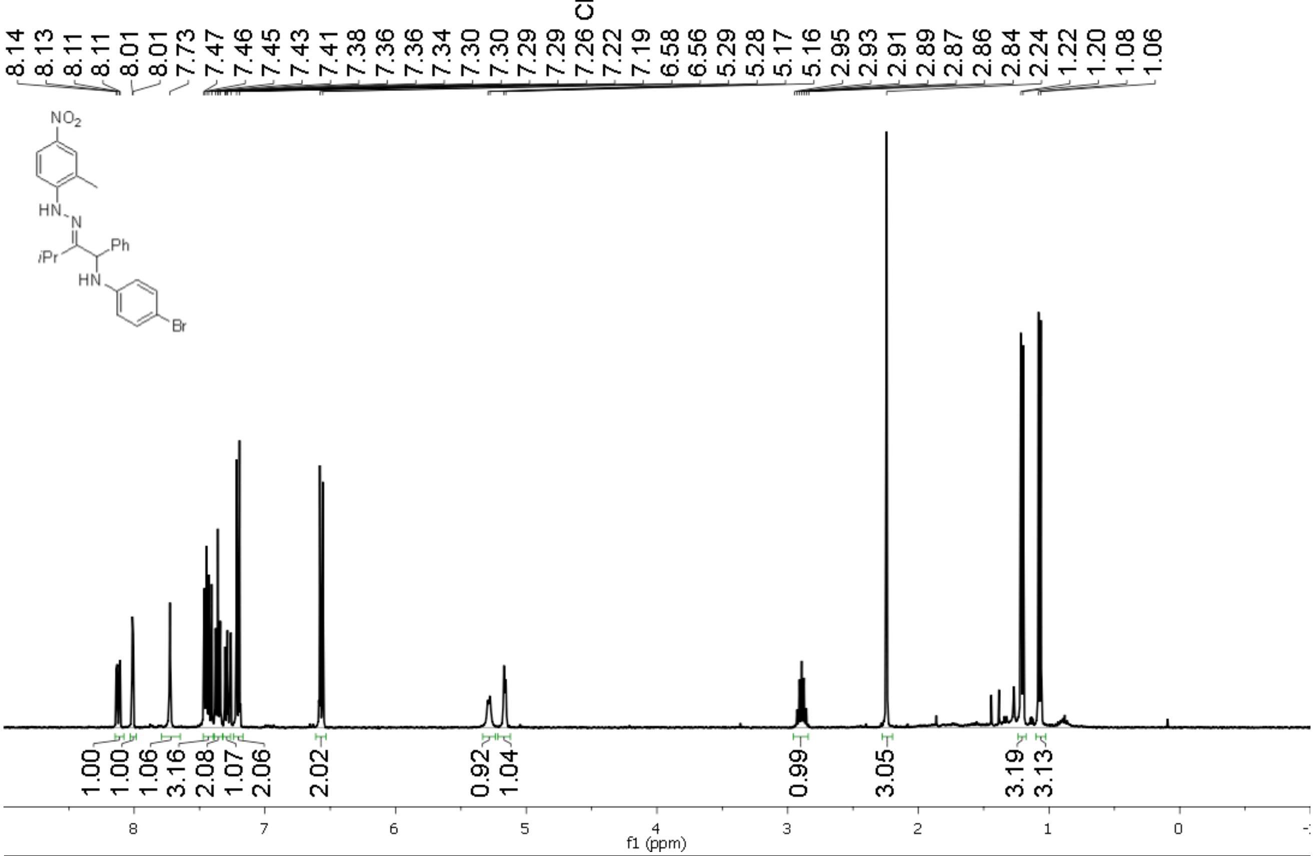
2j (13C NMR)
CDCl3 101 MHz



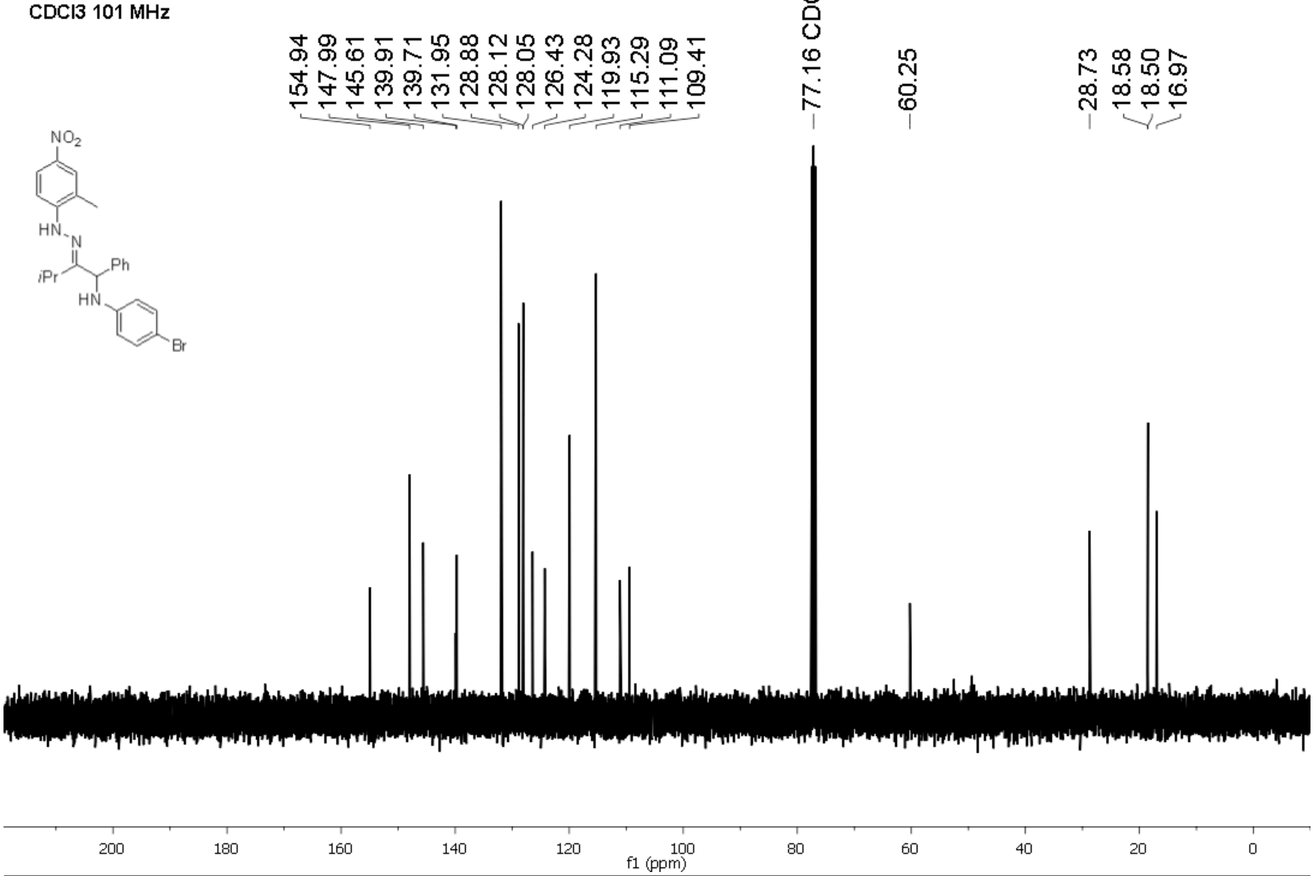
2j (19F NMR)
CDCl3 376 MHz

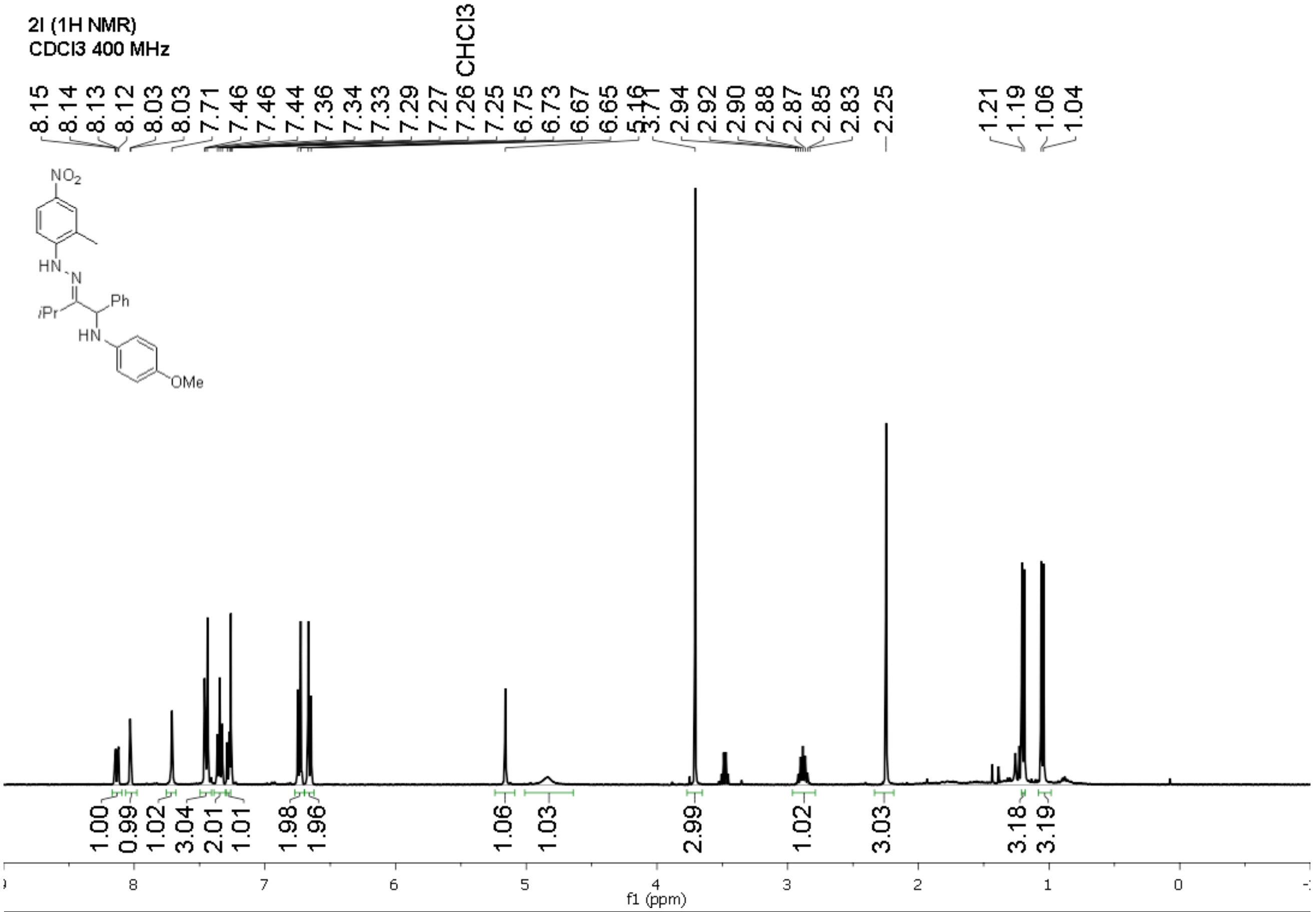


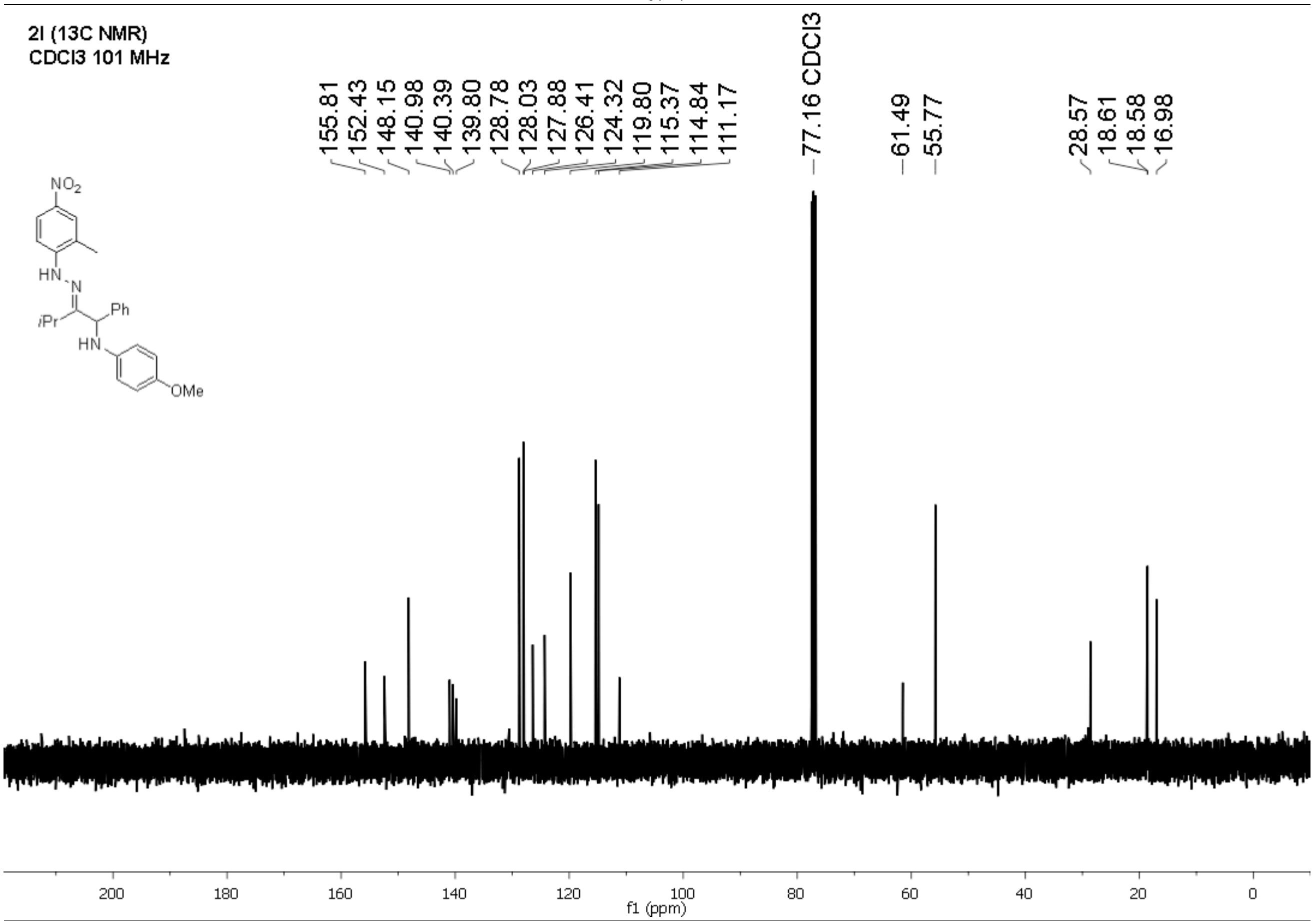
2k (1H NMR)
CDCl3 400 MHz

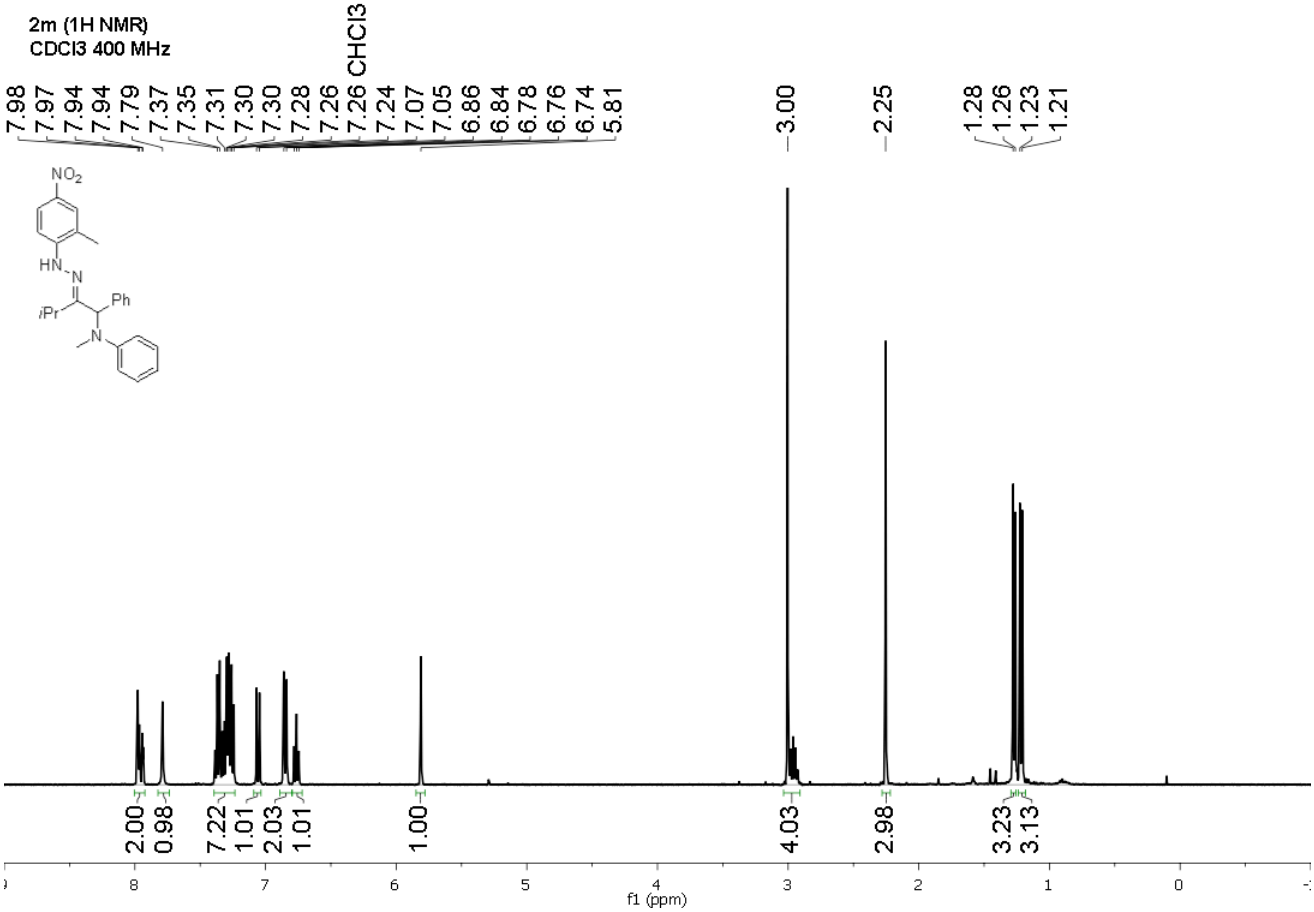


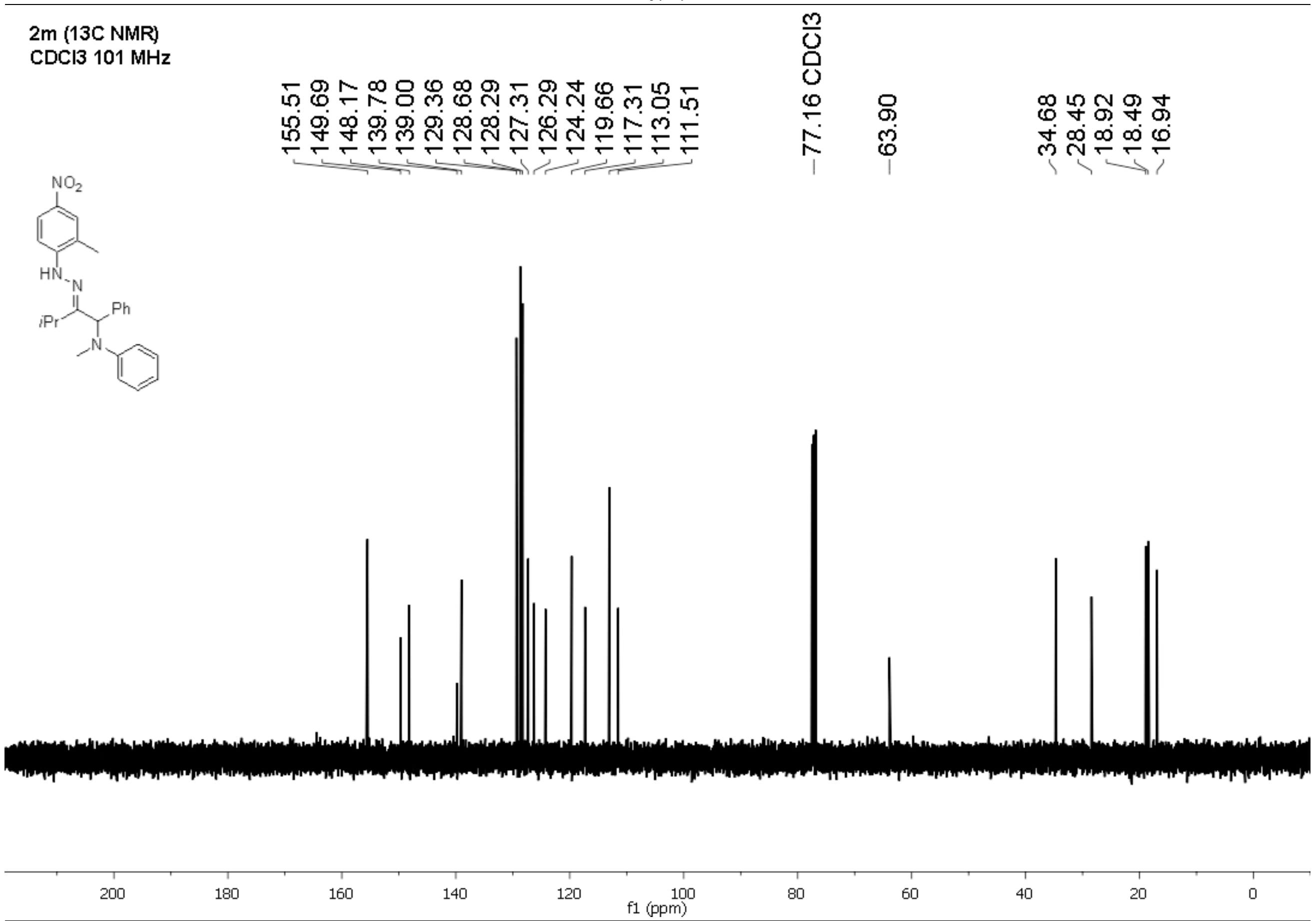
2k (13C NMR)
CDCl3 101 MHz

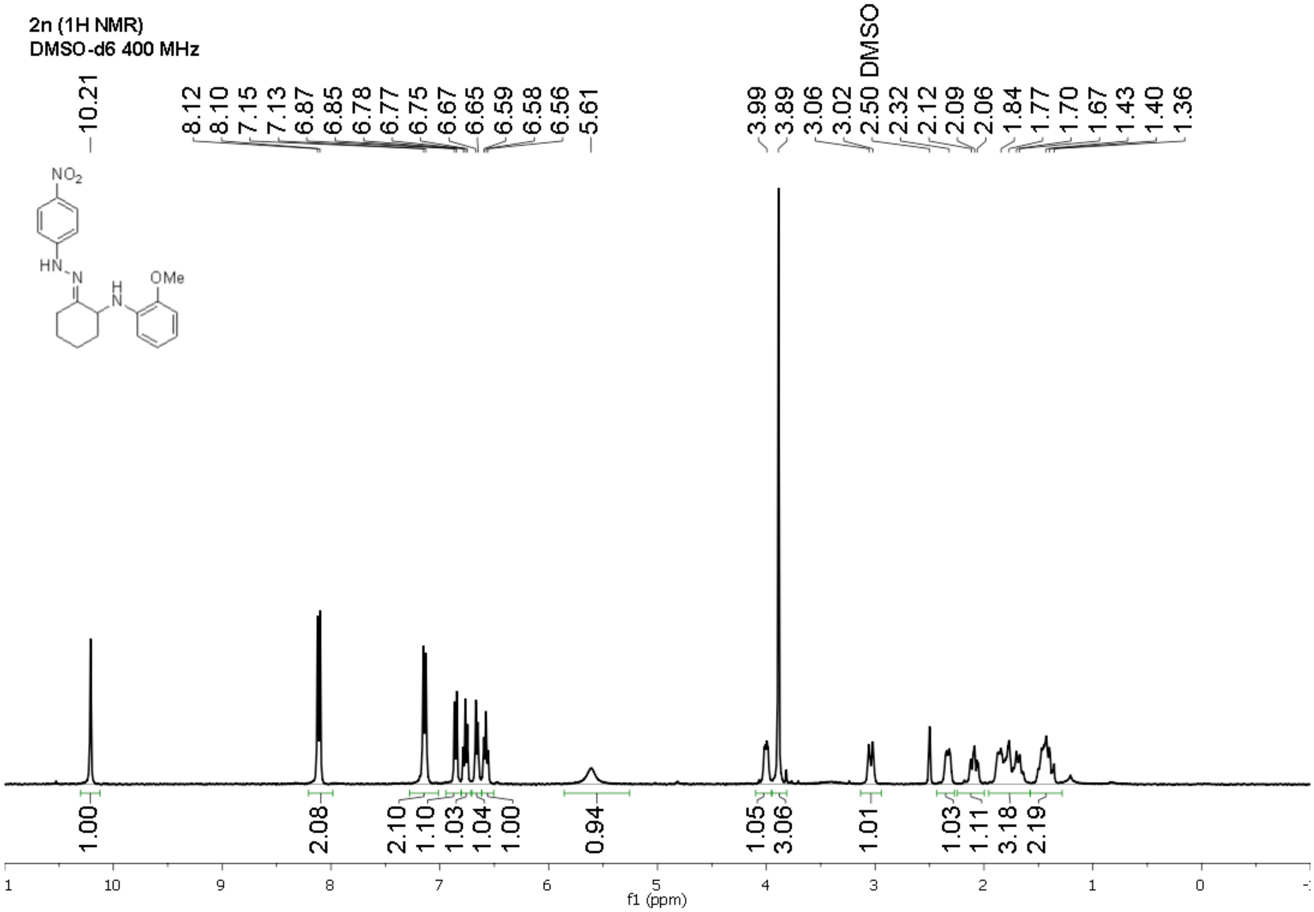



2l (1H NMR)
CDCl3 400 MHz
8.15 8.14 8.13 8.12 8.03 8.03 7.71 7.46 7.46 7.44 7.36 7.34 7.33 7.29 7.27 7.26 CHCl3 7.25 6.75 6.73 6.67 6.65 5.16 3.71 2.94 2.92 2.90 2.88 2.87 2.85 2.83 2.25 1.21 1.19 1.06 1.04
NO2
HN
N
iPr
Ph
HN
OMe
1.00 0.99 1.02 3.04 2.01 1.01 1.98 1.96 1.06 1.03 2.99 1.02 3.03 3.18 3.19
8 7 6 5 4 3 2 1 0
f1 (ppm)

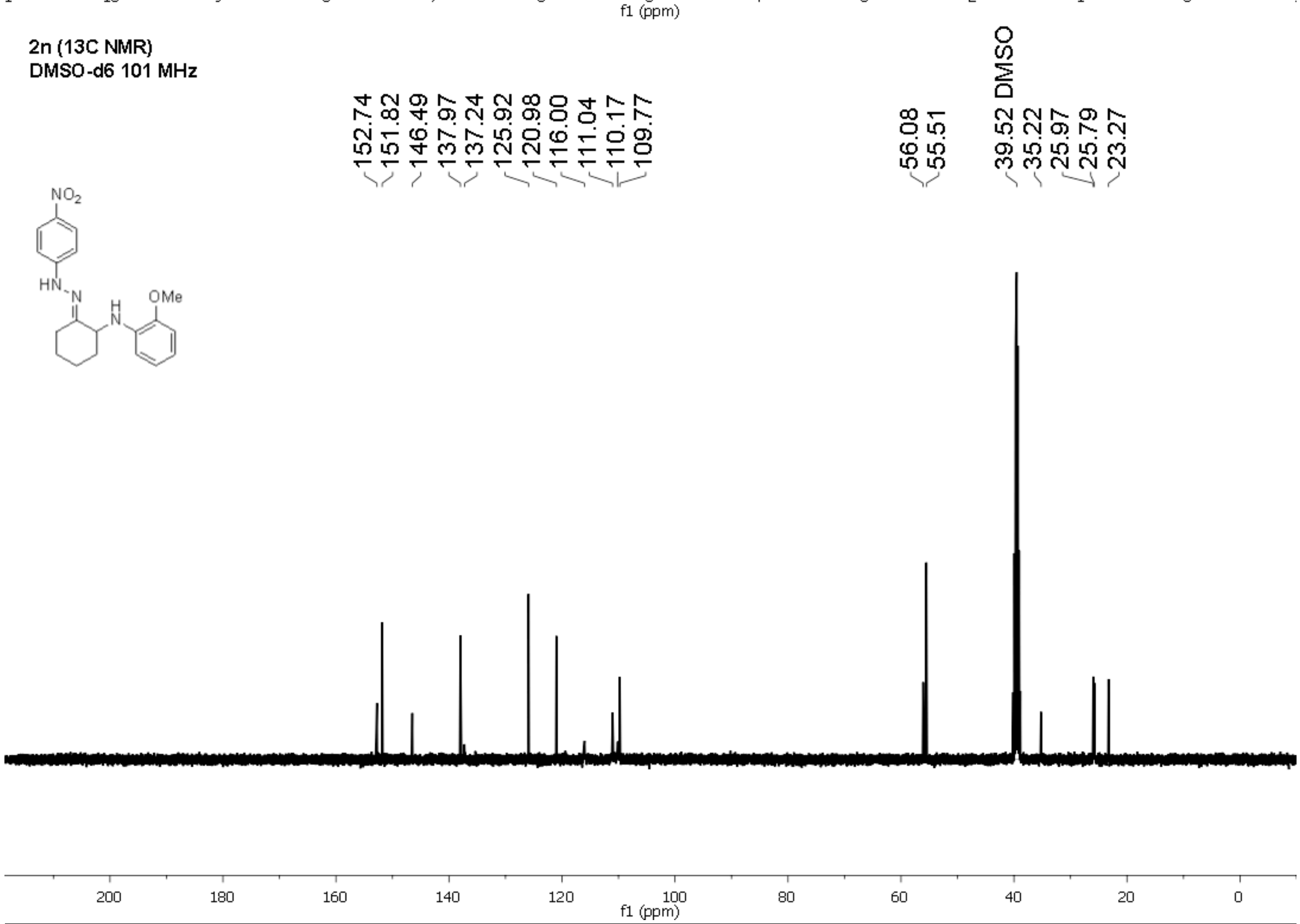

2l (13C NMR)
CDCl3 101 MHz
155.81 152.43 148.15 140.98 140.39 139.80 128.78 128.03 127.88 126.41 124.32 119.80 115.37 114.84 111.17
77.16 CDCl3
61.49 55.77
28.57 18.61 18.58 16.98
NO2
HN
N
iPr
Ph
HN
OMe
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


2m (1H NMR)
CDCl3 400 MHz
7.98 7.97 7.94 7.94 7.79 7.37 7.35 7.31 7.30 7.30 7.28 7.26 7.26 CHCl3 7.24 7.07 7.05 6.86 6.84 6.78 6.76 6.74 5.81
3.00
2.25
1.28 1.26 1.23 1.21
NO2
HN
N
iPr
Ph
N
2.00 0.98 7.22 1.01 2.03 1.01 1.00 4.03 2.98 3.23 3.13
8 7 6 5 4 3 2 1 0
f1 (ppm)

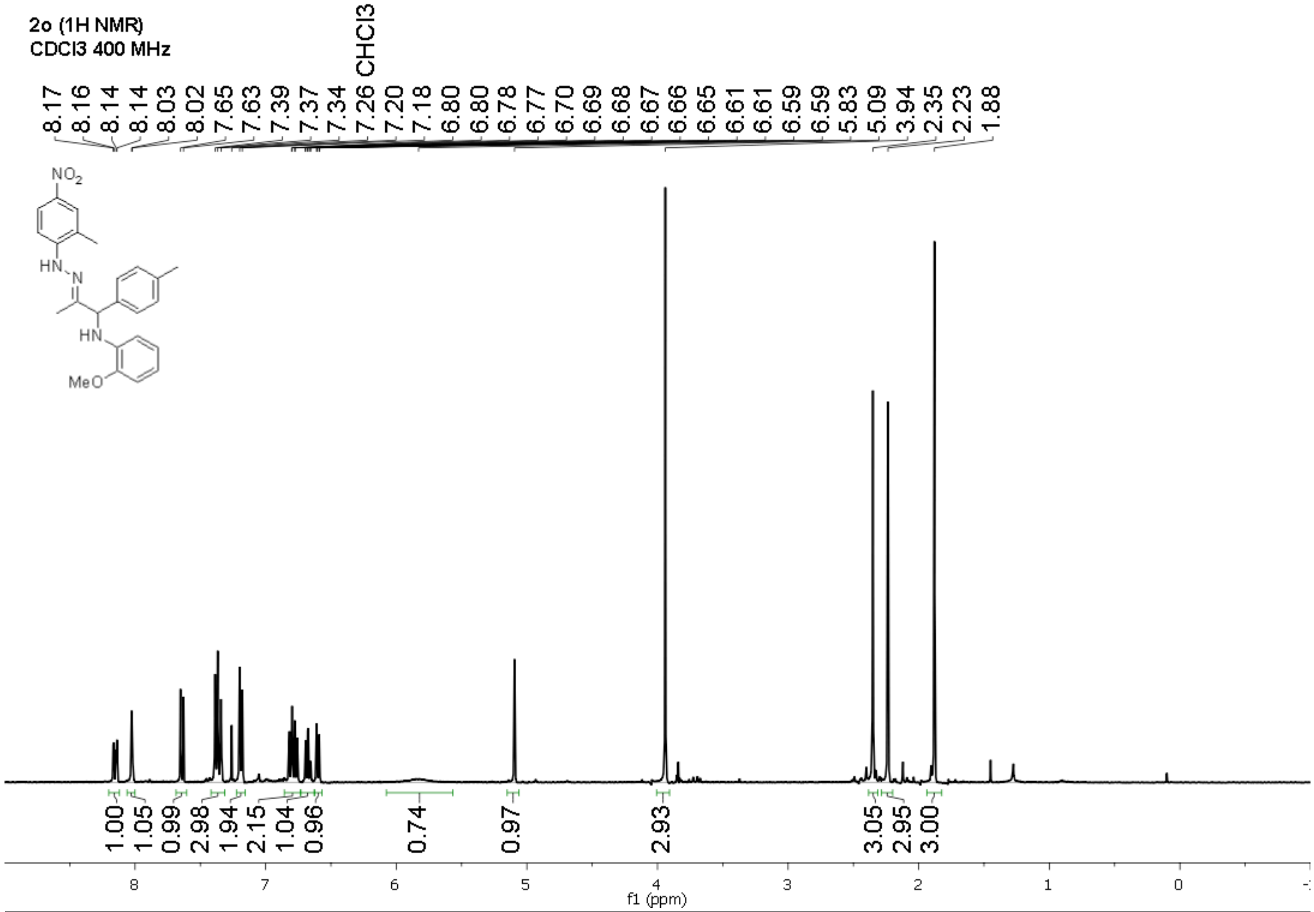

2m (13C NMR)
CDCl3 101 MHz
155.51 149.69 148.17 139.78 139.00 129.36 128.68 128.29 127.31 126.29 124.24 119.66 117.31 113.05 111.51
77.16 CDCl3
63.90
34.68 28.45 18.92 18.49 16.94
NO2
HN
N
iPr
Ph
N
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

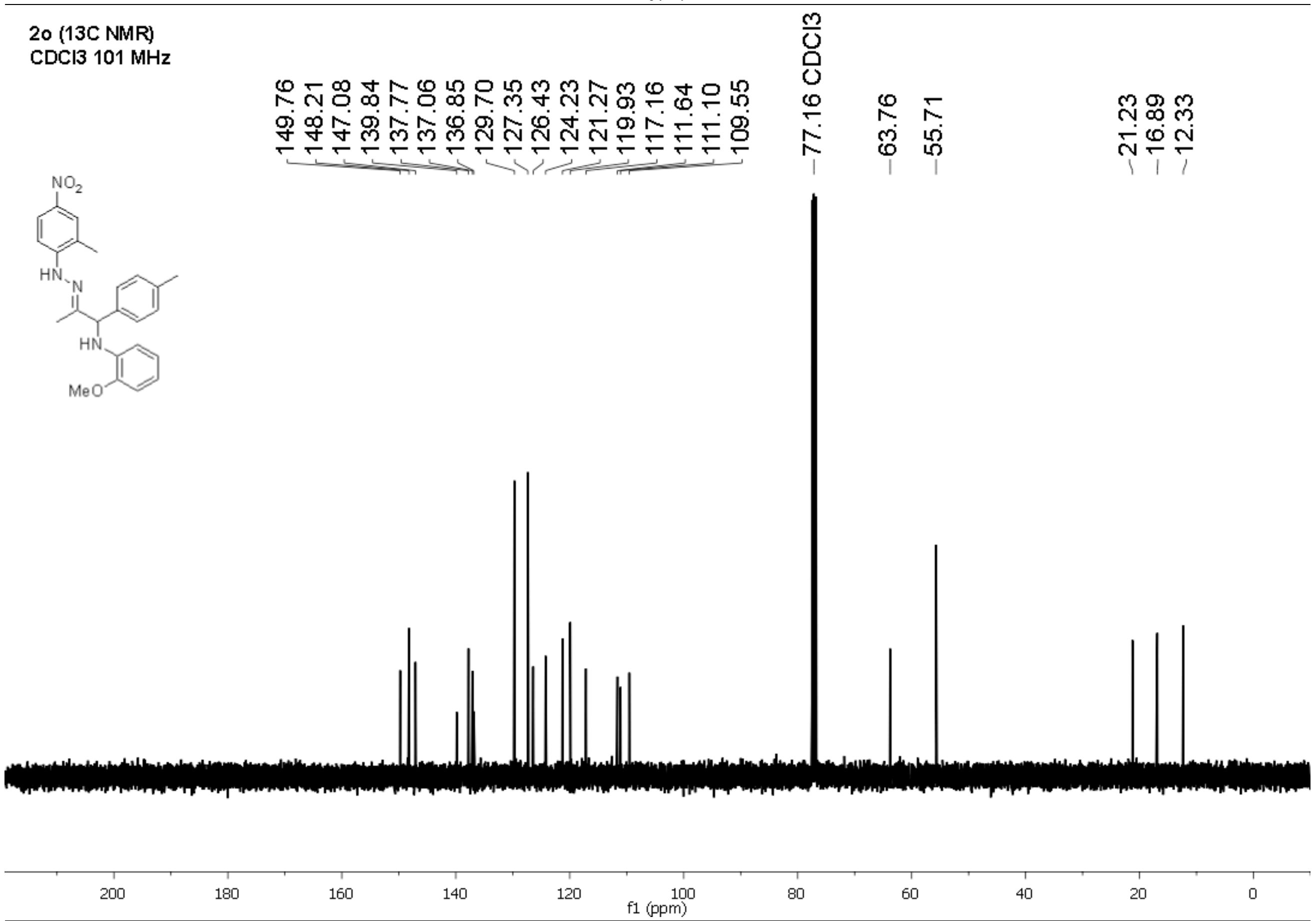


2n (1H NMR)
DMSO-d6 400 MHz
10.21
8.12 8.10 7.15 7.13 6.87 6.85 6.78 6.77 6.75 6.67 6.65 6.59 6.58 6.56 5.61
3.99 3.89 3.06 3.02 2.50 DMSO 2.32 2.12 2.09 2.06 1.84 1.77 1.70 1.67 1.43 1.40 1.36
NO2
HN
N
H
N
OMe
1.00 2.08 2.10 1.10 1.03 1.04 1.00 0.94 1.05 3.06 1.01 1.03 1.11 3.18 2.19
f1 (ppm)

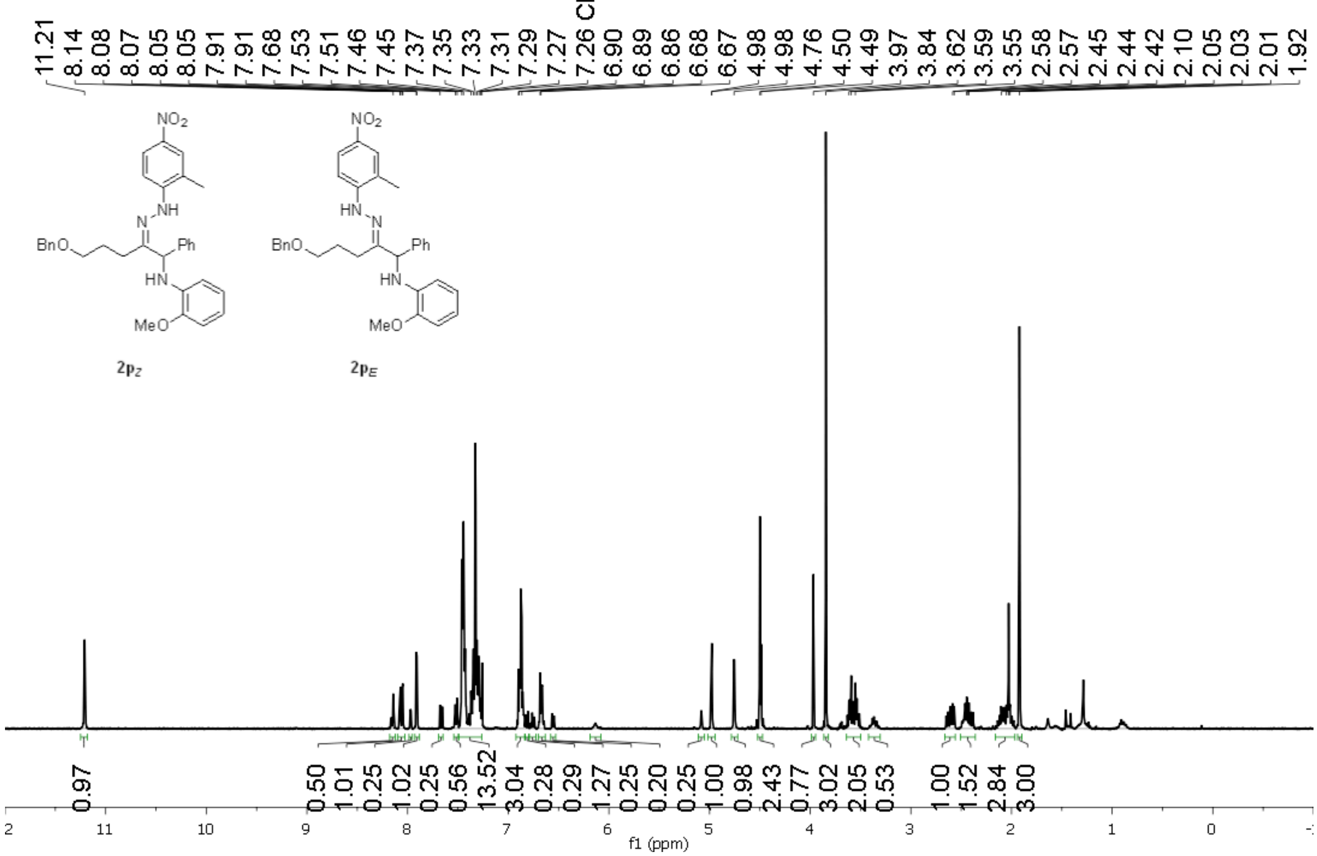


2n (13C NMR)
DMSO-d6 101 MHz
152.74 151.82 146.49 137.97 137.24 125.92 120.98 116.00 111.04 110.17 109.77
56.08 55.51
39.52 DMSO 35.22 25.97 25.79 23.27
NO2
HN
N
H
N
OMe
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

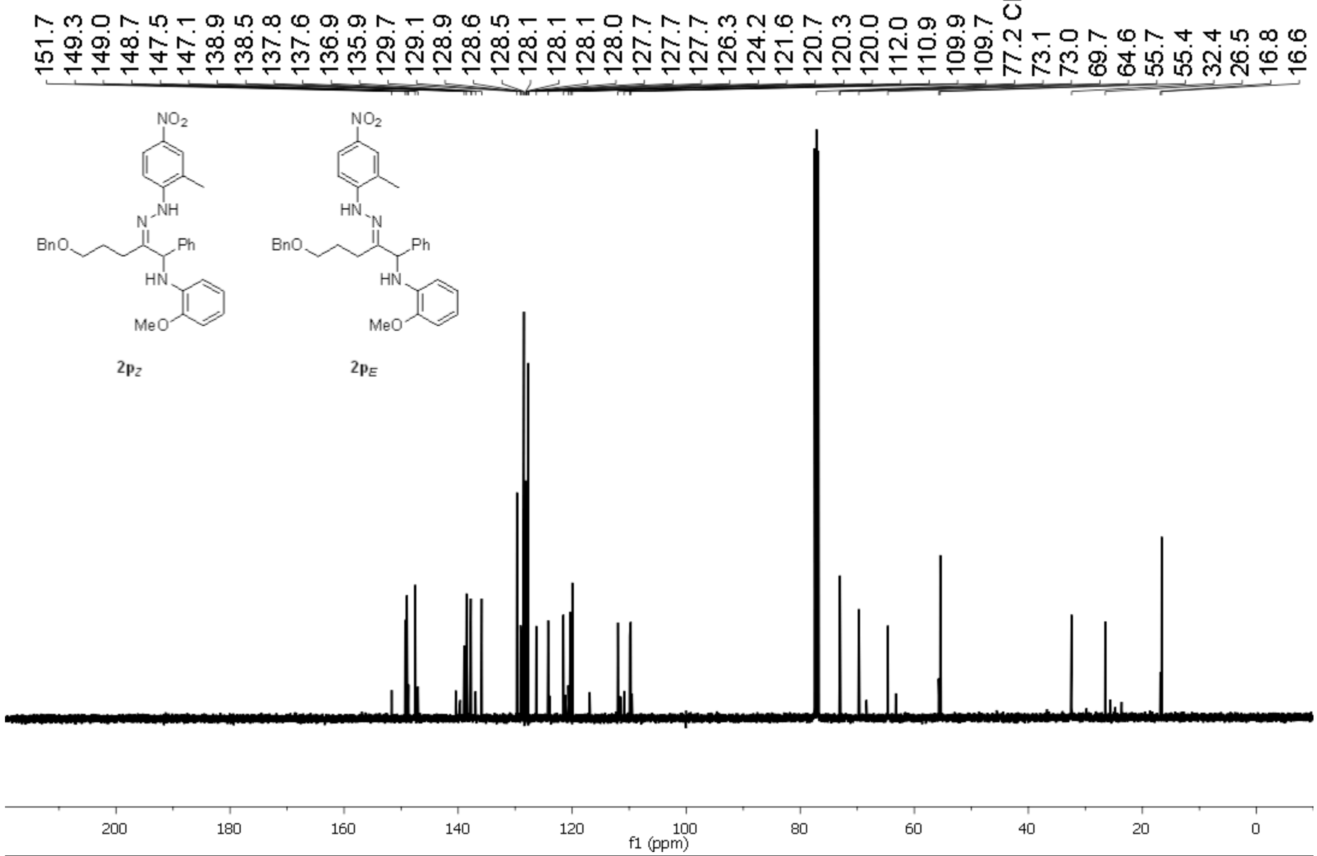

2o (1H NMR)
CDCl3 400 MHz
8.17 8.16 8.14 8.14 8.03 8.02 7.65 7.63 7.39 7.37 7.34 7.26 CHCl3 7.20 7.18 6.80 6.80 6.78 6.77 6.70 6.69 6.68 6.67 6.66 6.65 6.61 6.61 6.59 6.59 5.83 5.09 3.94 2.35 2.23 1.88
NO2
HN
N
HN
MeO
1.00 1.05 0.99 2.98 1.94 2.15 1.04 0.96 0.74 0.97 2.93 3.05 2.95 3.00
f1 (ppm)

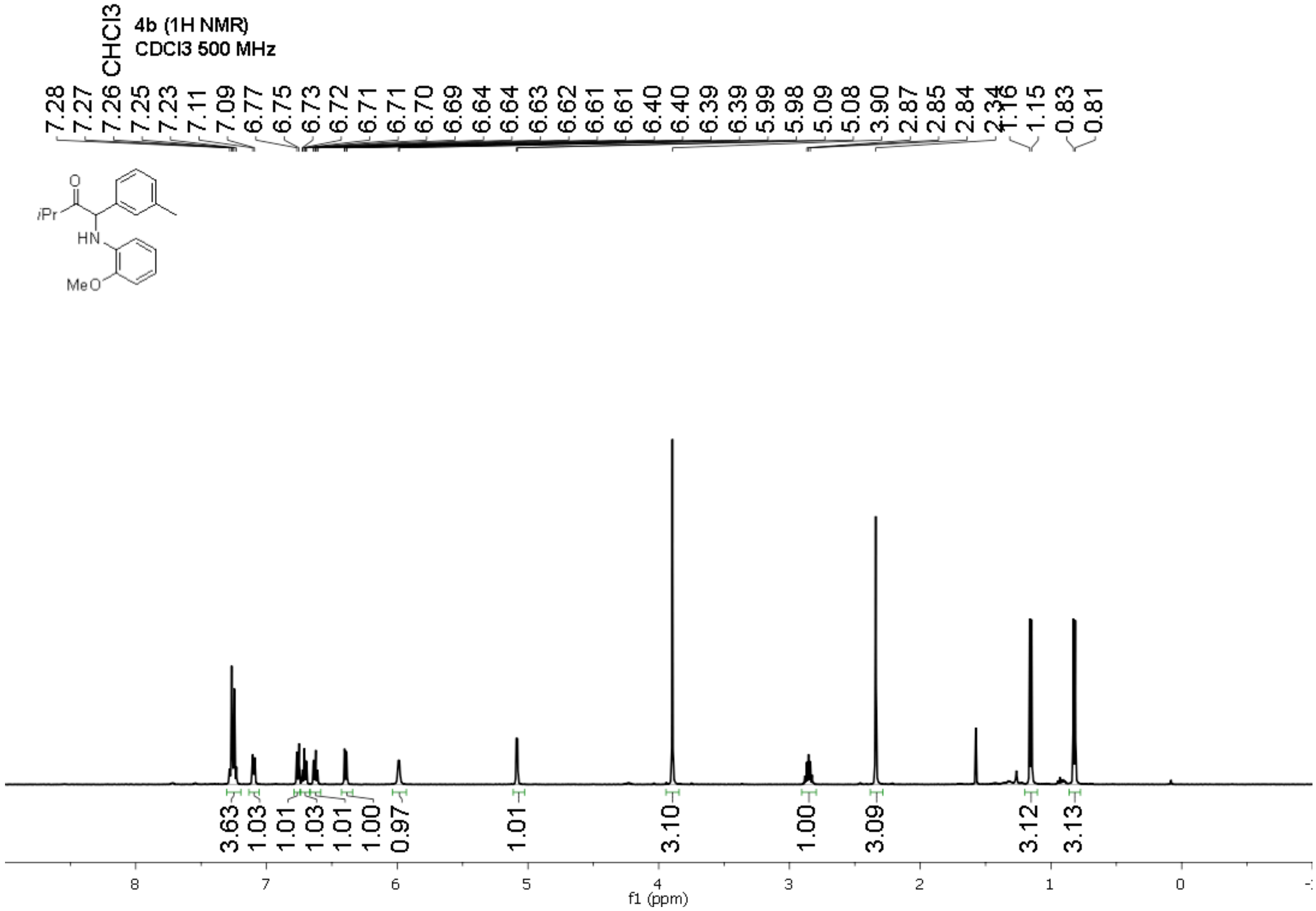

2o (13C NMR)
CDCl3 101 MHz
149.76 148.21 147.08 139.84 137.77 137.06 136.85 129.70 127.35 126.43 124.23 121.27 119.93 117.16 111.64 111.10 109.55
77.16 CDCl3
63.76
55.71
21.23 16.89 12.33
NO2
HN
N
HN
MeO
f1 (ppm)

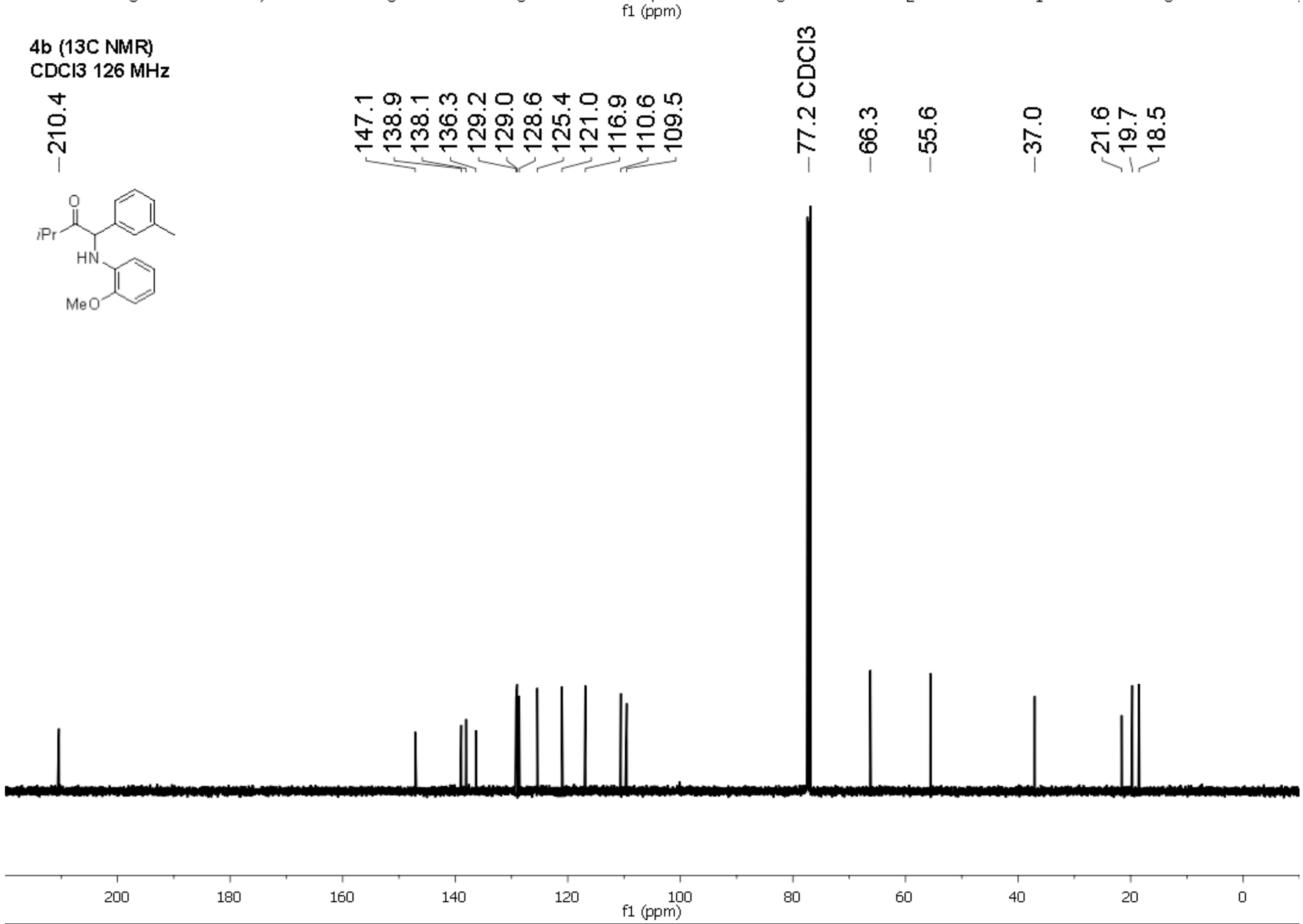
2p (1H NMR)
CDCl3 400 MHz

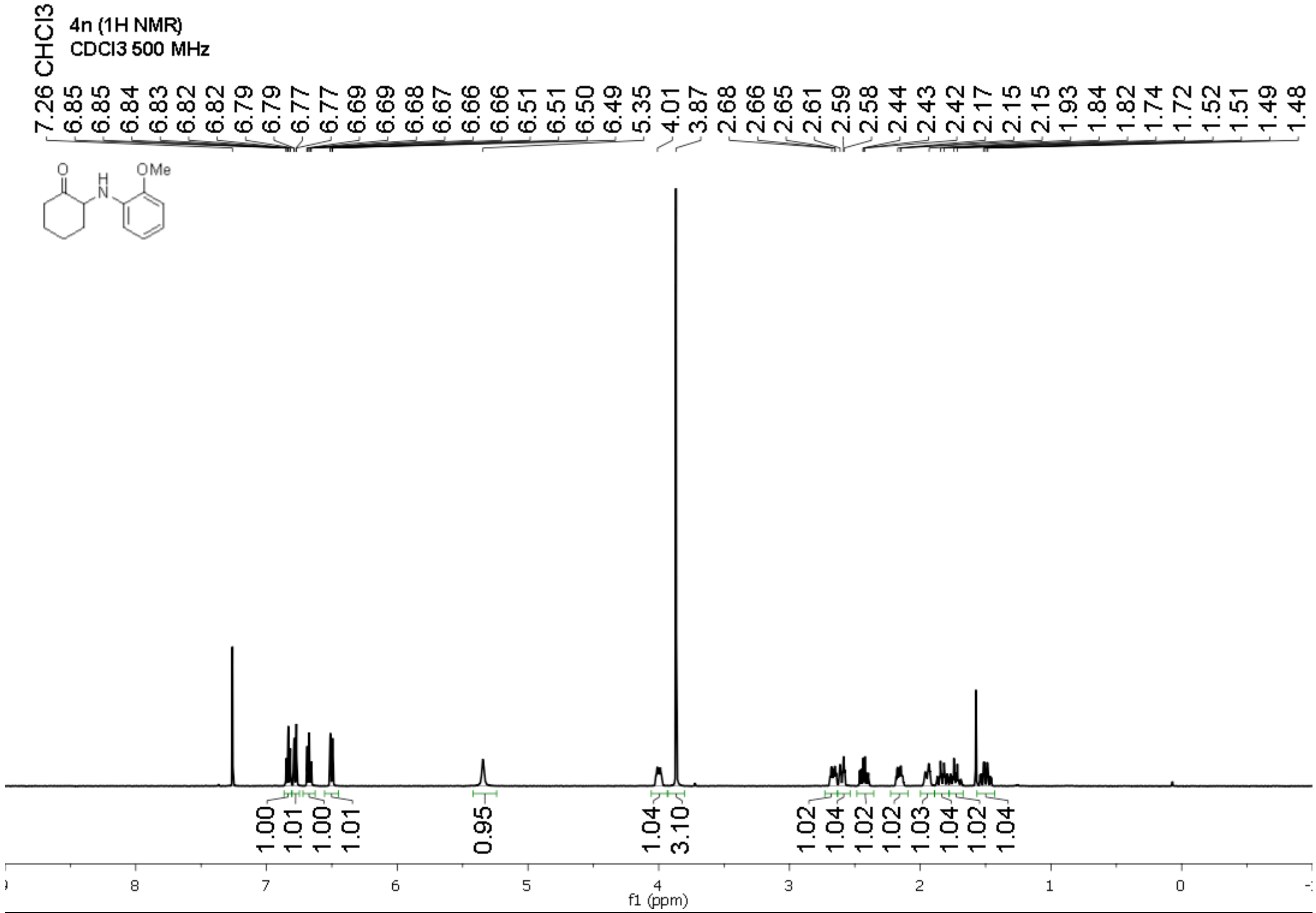


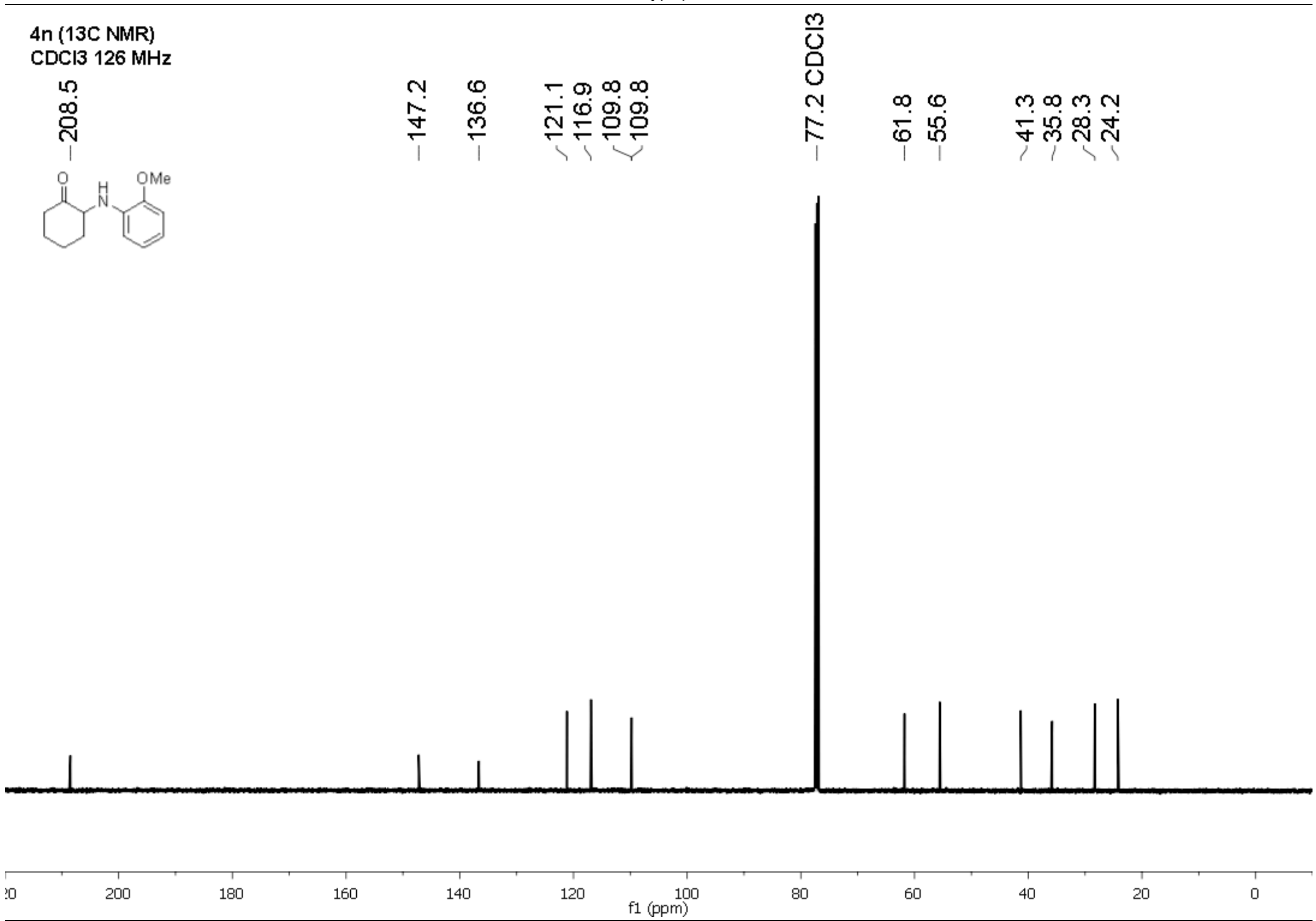
2p (13C NMR)
CDCl3 101 MHz

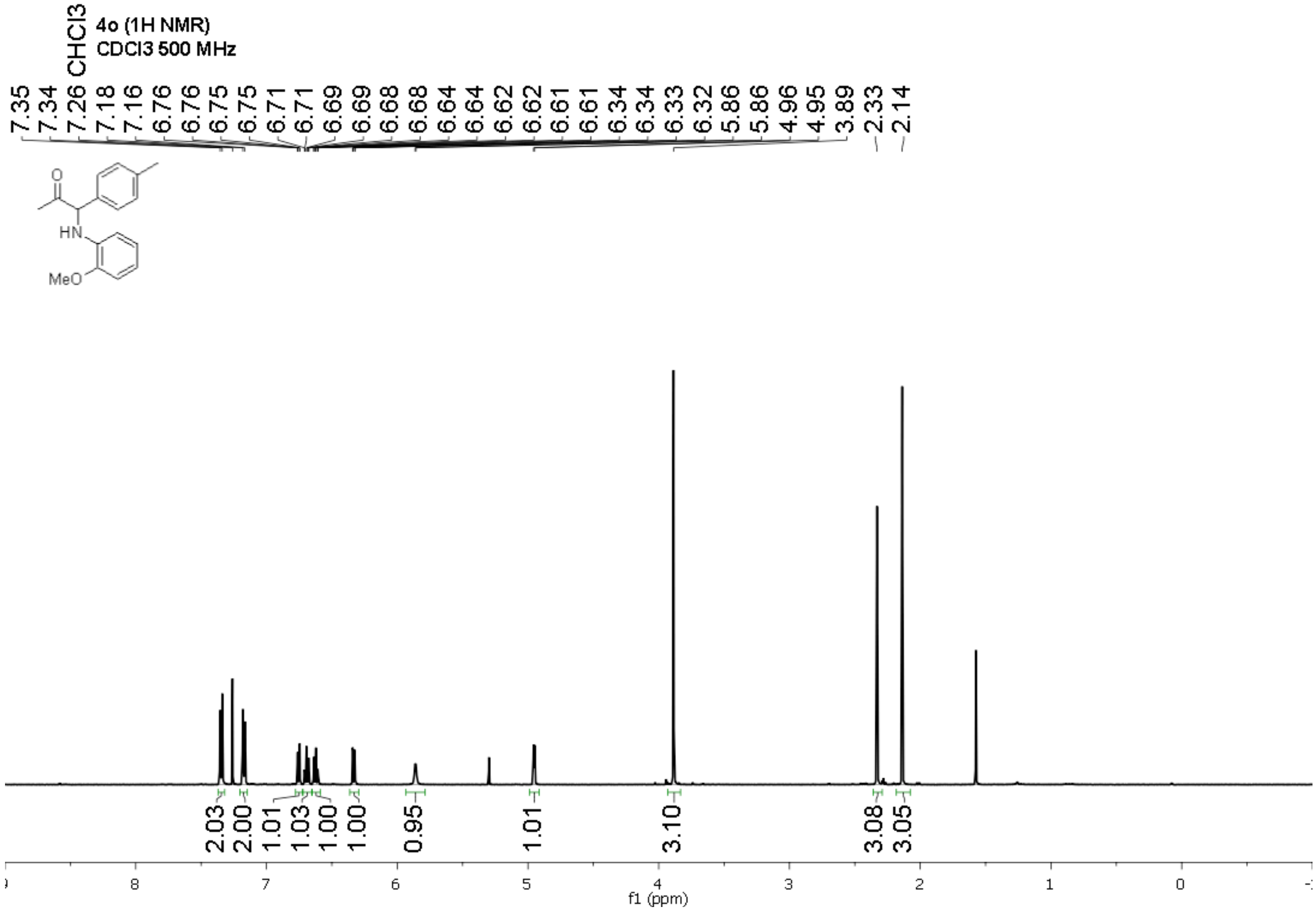



4b (1H NMR)
CDCl3 500 MHz
7.28 7.27 7.26 CHCl3 7.25 7.23 7.11 7.09 6.77 6.75 6.73 6.72 6.71 6.71 6.70 6.69 6.64 6.64 6.63 6.62 6.61 6.61 6.40 6.40 6.39 6.39 5.99 5.98 5.09 5.08 3.90 2.87 2.85 2.84 2.34 1.16 1.15 0.83 0.81
iPr
O
HN
MeO
3.63 1.03 1.01 1.03 1.01 1.00 0.97 1.01 3.10 1.00 3.09 3.12 3.13
8 7 6 5 4 3 2 1 0
f1 (ppm)

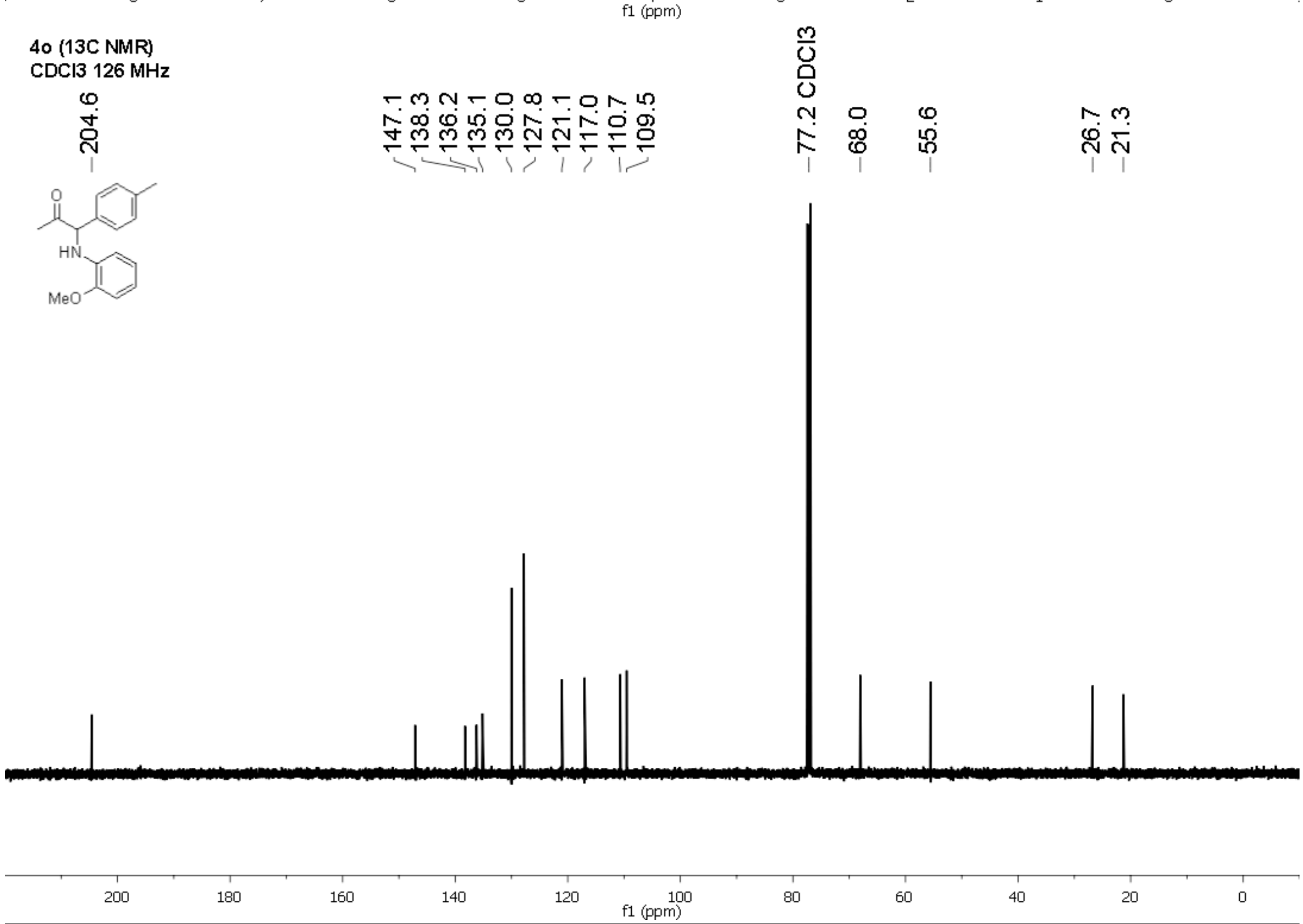

4b (13C NMR)
CDCl3 126 MHz
210.4
147.1 138.9 138.1 136.3 129.2 129.0 128.6 125.4 121.0 116.9 110.6 109.5
77.2 CDCl3
66.3
55.6
37.0
21.6 19.7 18.5
iPr
O
HN
MeO
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


4n (1H NMR)
CDCl3 500 MHz
7.26 CHCl3
6.85 6.85 6.84 6.83 6.82 6.82 6.79 6.79 6.77 6.77 6.69 6.69 6.68 6.67 6.66 6.66 6.51 6.51 6.50 6.49 5.35 4.01 3.87 2.68 2.66 2.65 2.61 2.59 2.58 2.44 2.43 2.42 2.17 2.15 2.15 1.93 1.84 1.82 1.74 1.72 1.52 1.51 1.49 1.48
O
H
N
OMe
1.00 1.01 1.00 1.01 0.95 1.04 3.10 1.02 1.04 1.02 1.02 1.03 1.04 1.02 1.04
8 7 6 5 4 3 2 1 0
f1 (ppm)

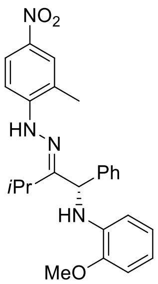

4n (13C NMR)
CDCl3 126 MHz
208.5
147.2
136.6
121.1 116.9 109.8 109.8
77.2 CDCl3
61.8 55.6
41.3 35.8 28.3 24.2
O
H
N
OMe
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



4o (1H NMR)
CDCl3 500 MHz
7.35 7.34 7.26 CHCl3 7.18 7.16 6.76 6.76 6.75 6.75 6.71 6.71 6.69 6.69 6.68 6.68 6.64 6.64 6.62 6.62 6.61 6.61 6.34 6.34 6.33 6.32 5.86 5.86 4.96 4.95 3.89 2.33 2.14
HN
MeO
2.03 2.00 1.01 1.03 1.00 1.00 0.95 1.01 3.10 3.08 3.05
8 7 6 5 4 3 2 1 0
f1 (ppm)

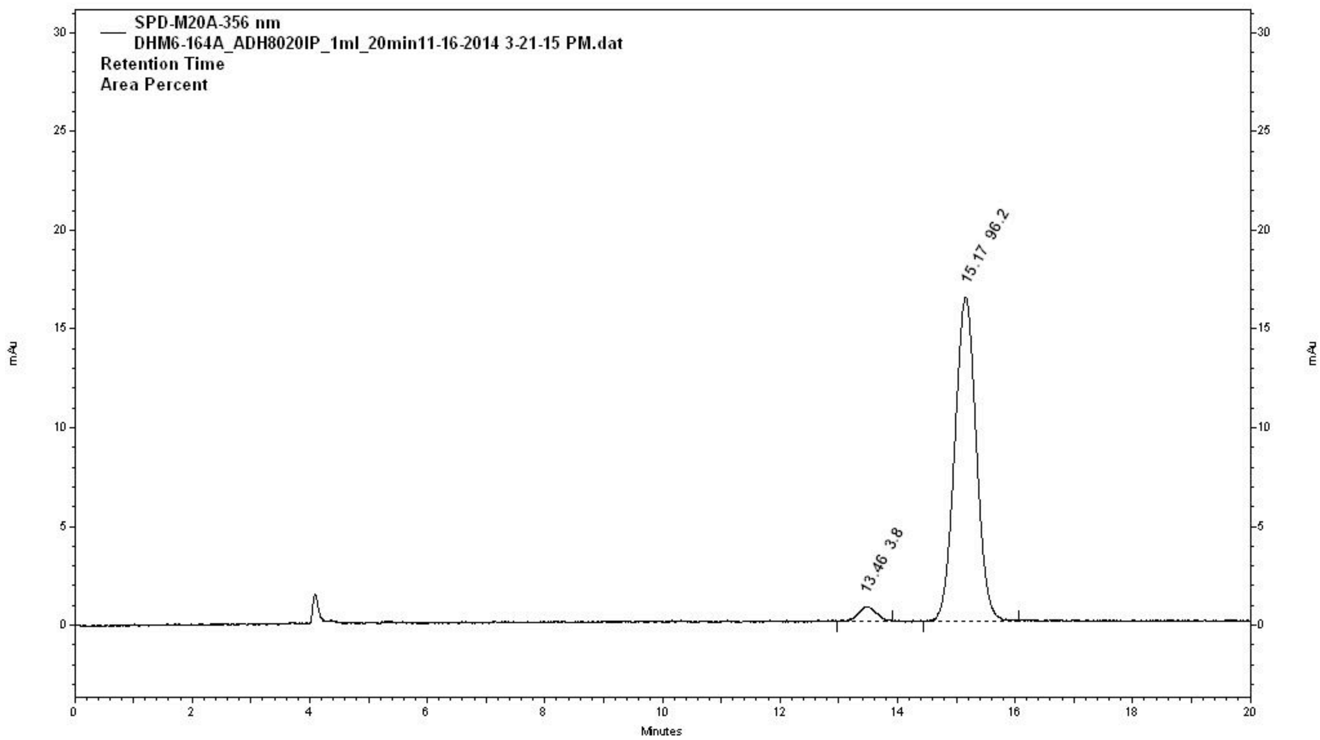


4o (13C NMR)
CDCl3 126 MHz
204.6
147.1 138.3 136.2 135.1 130.0 127.8 121.1 117.0 110.7 109.5
77.2 CDCl3
68.0
55.6
26.7 21.3
HN
MeO
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

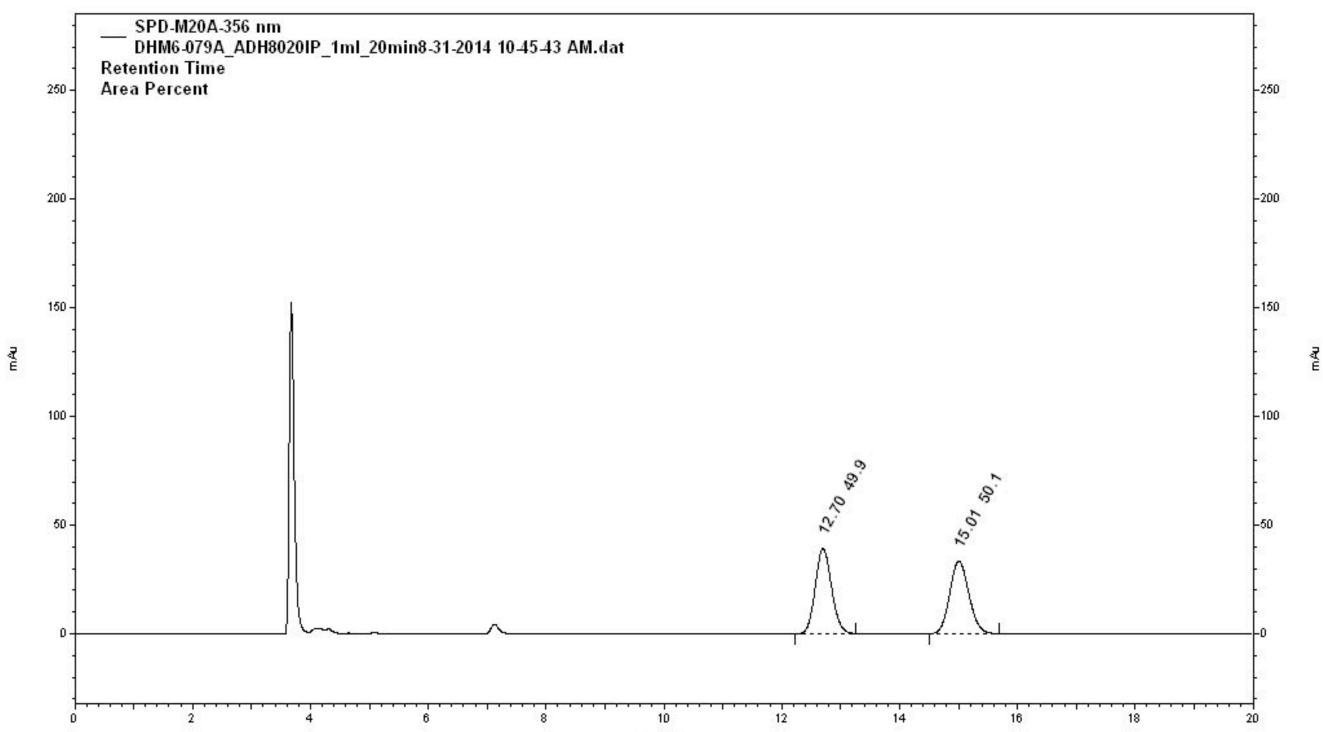


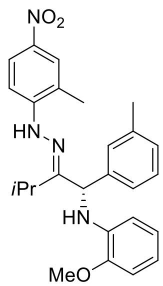
2a

Enantioenriched



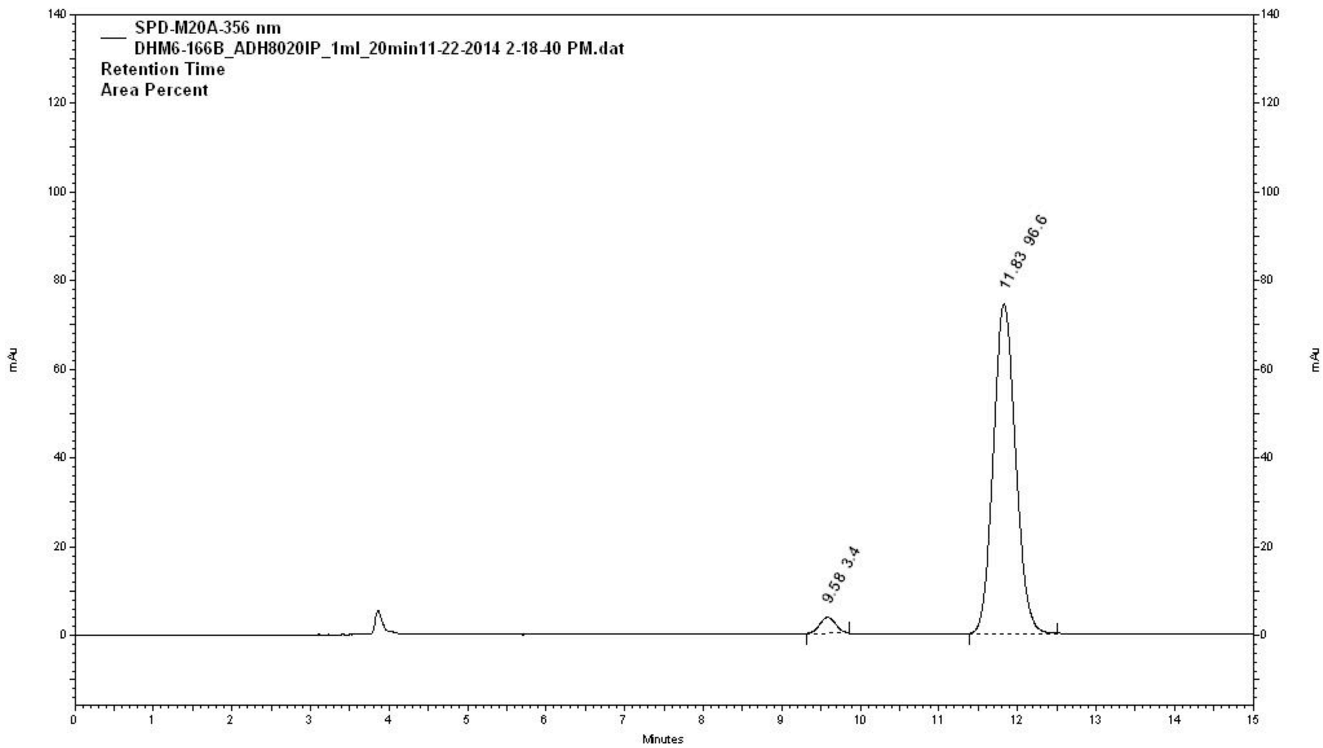
Racemic



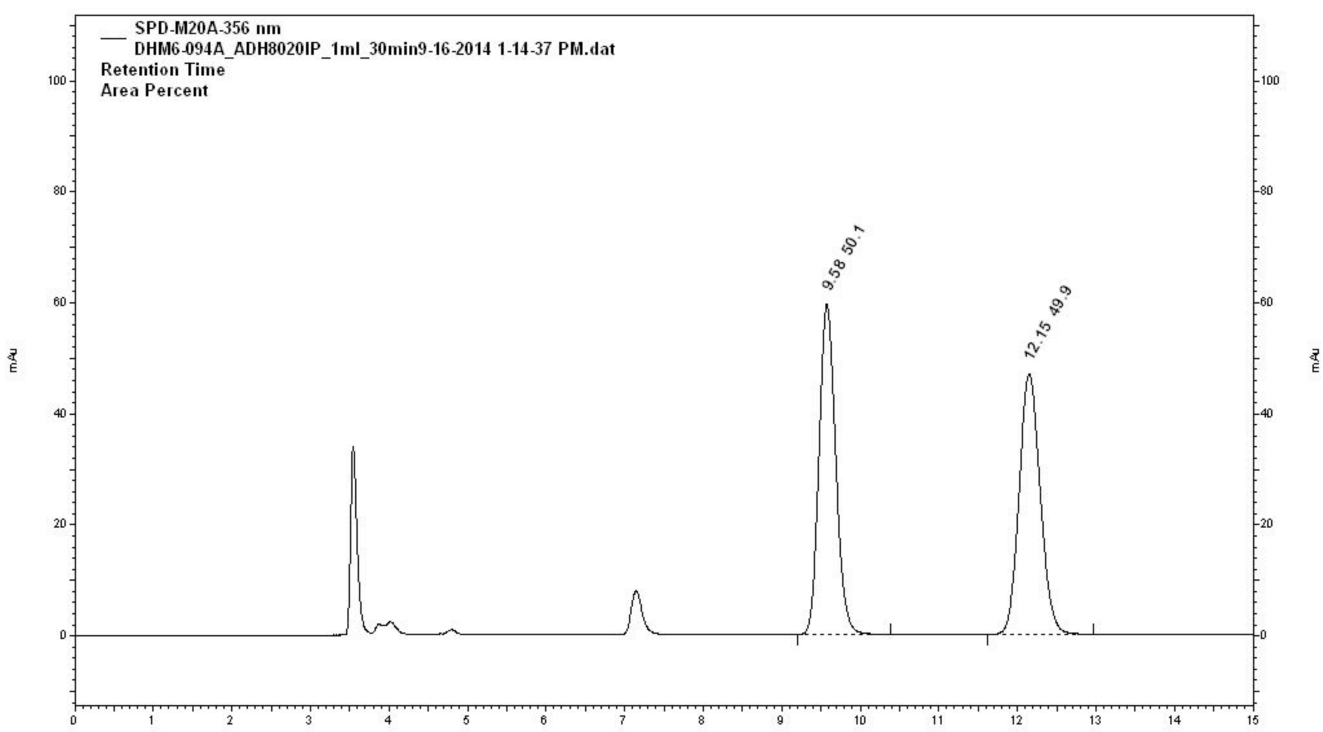


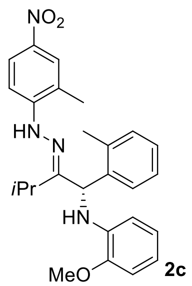
2b

Enantioenriched

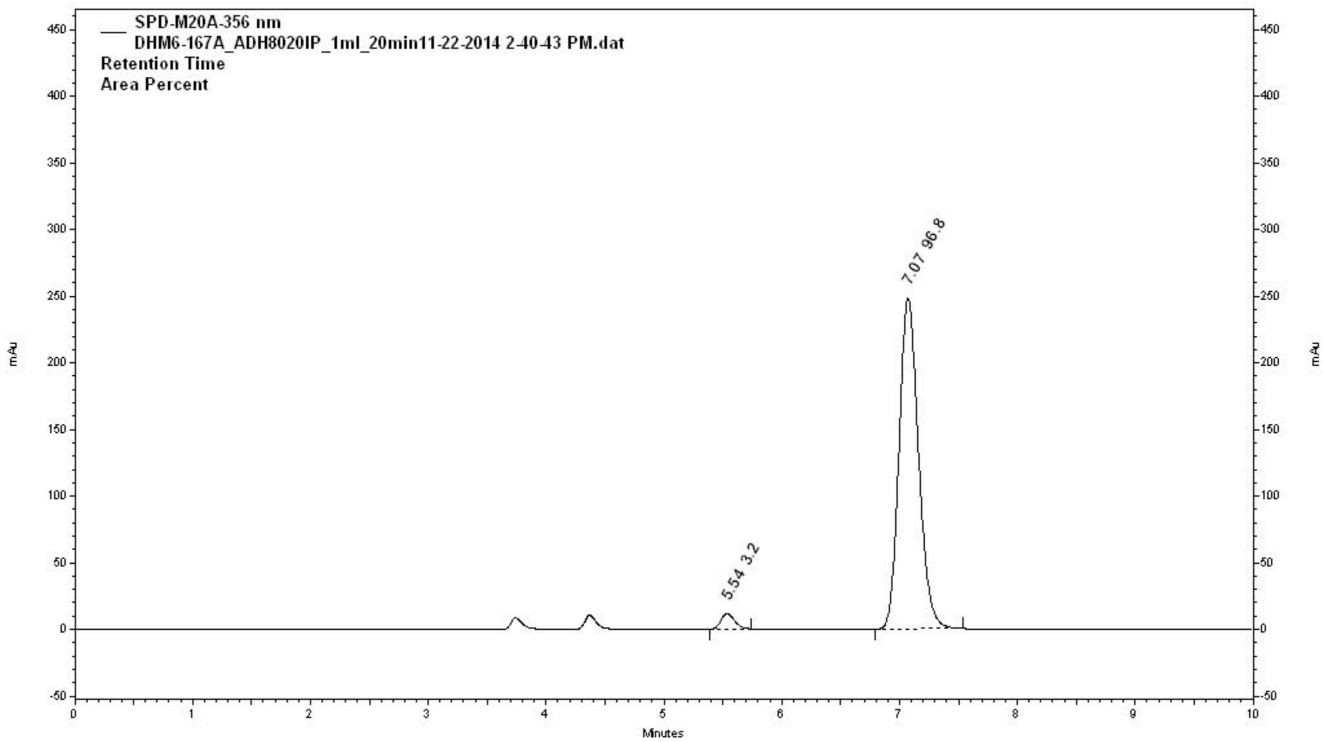


Racemic

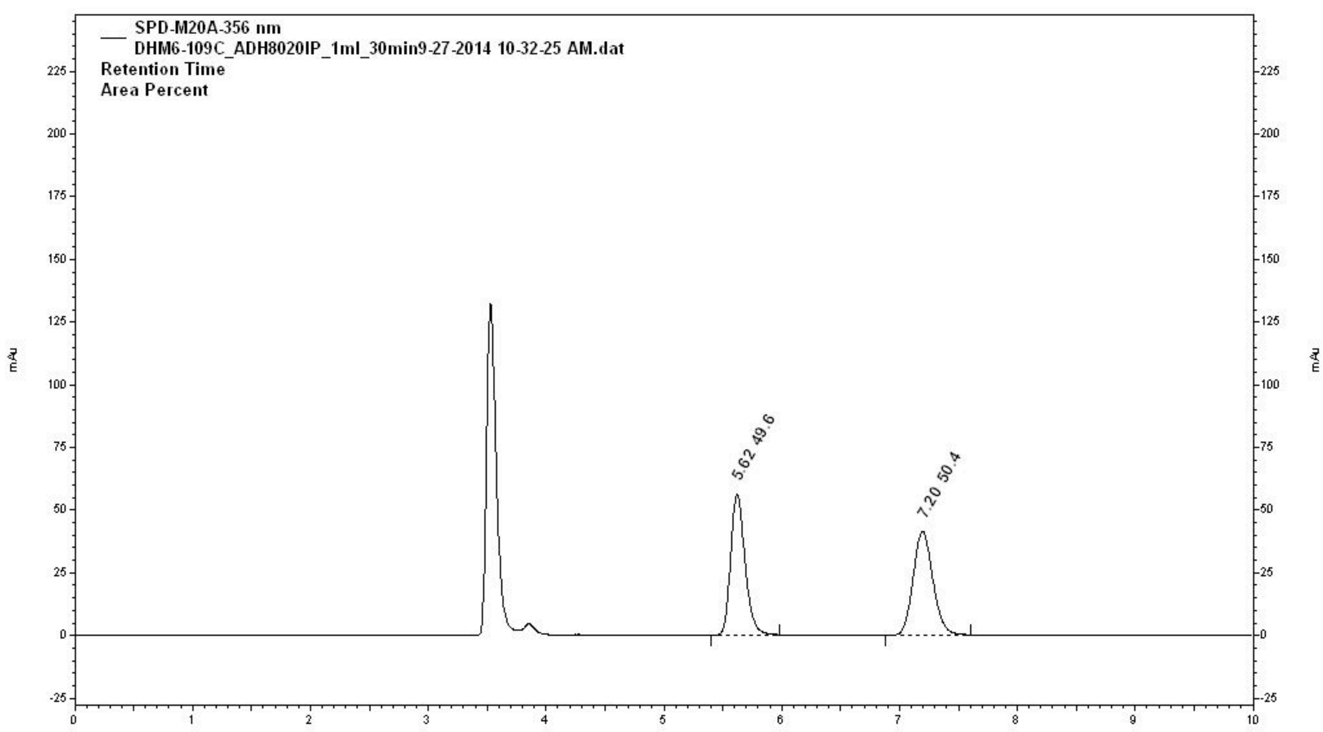


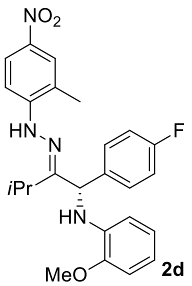


Enantioenriched



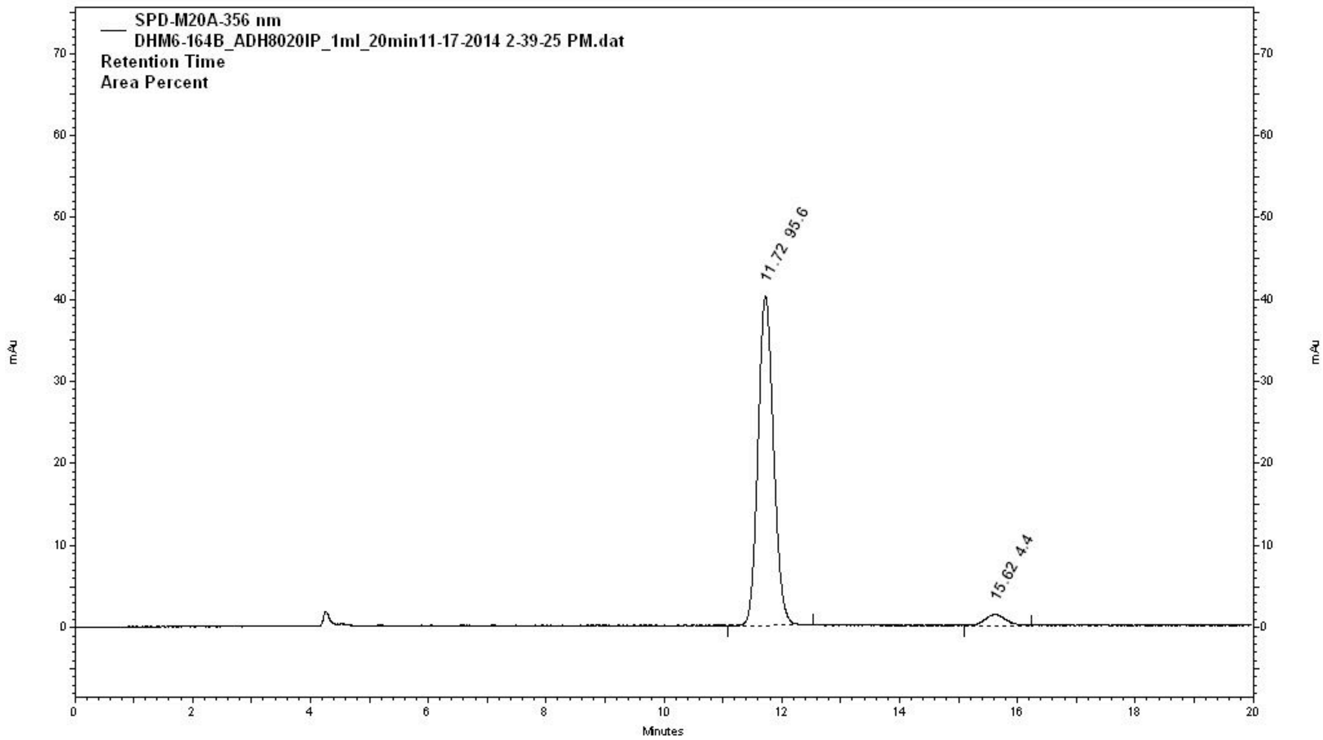
Racemic



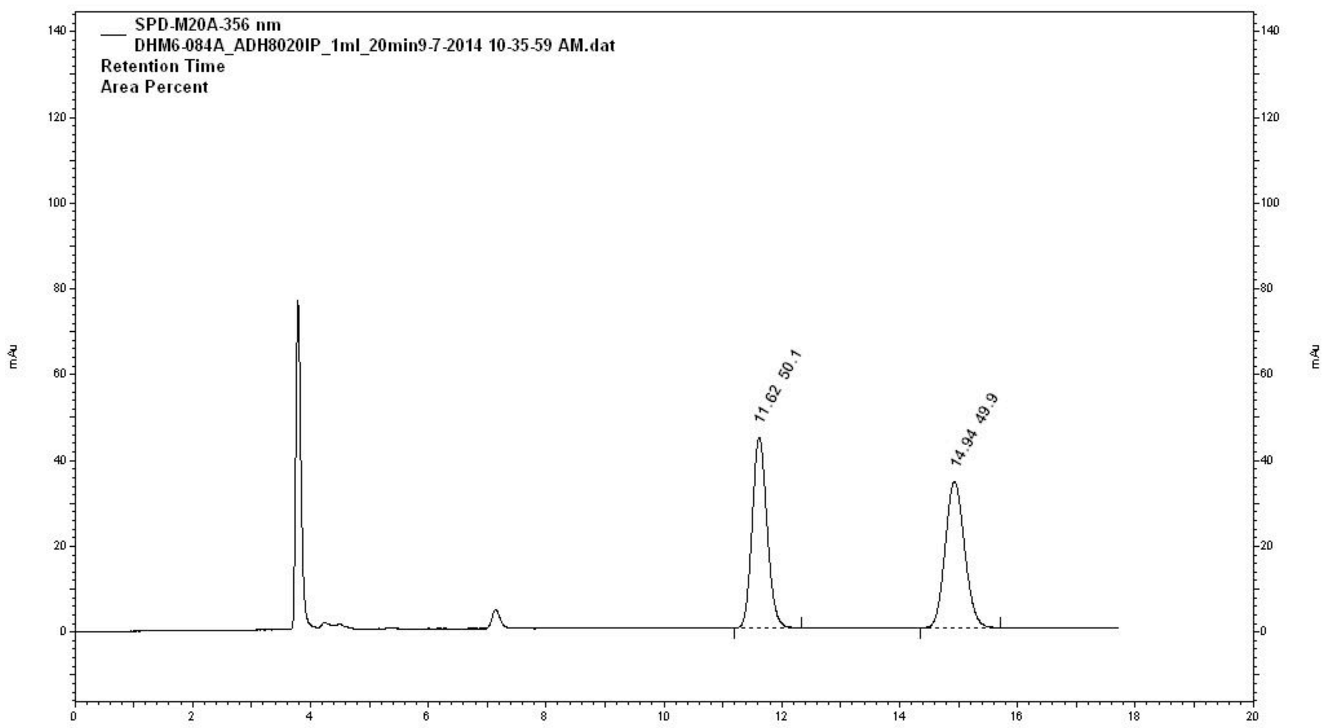


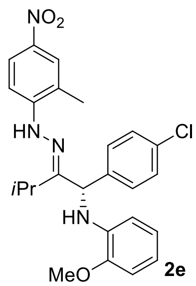
2d

Enantioenriched

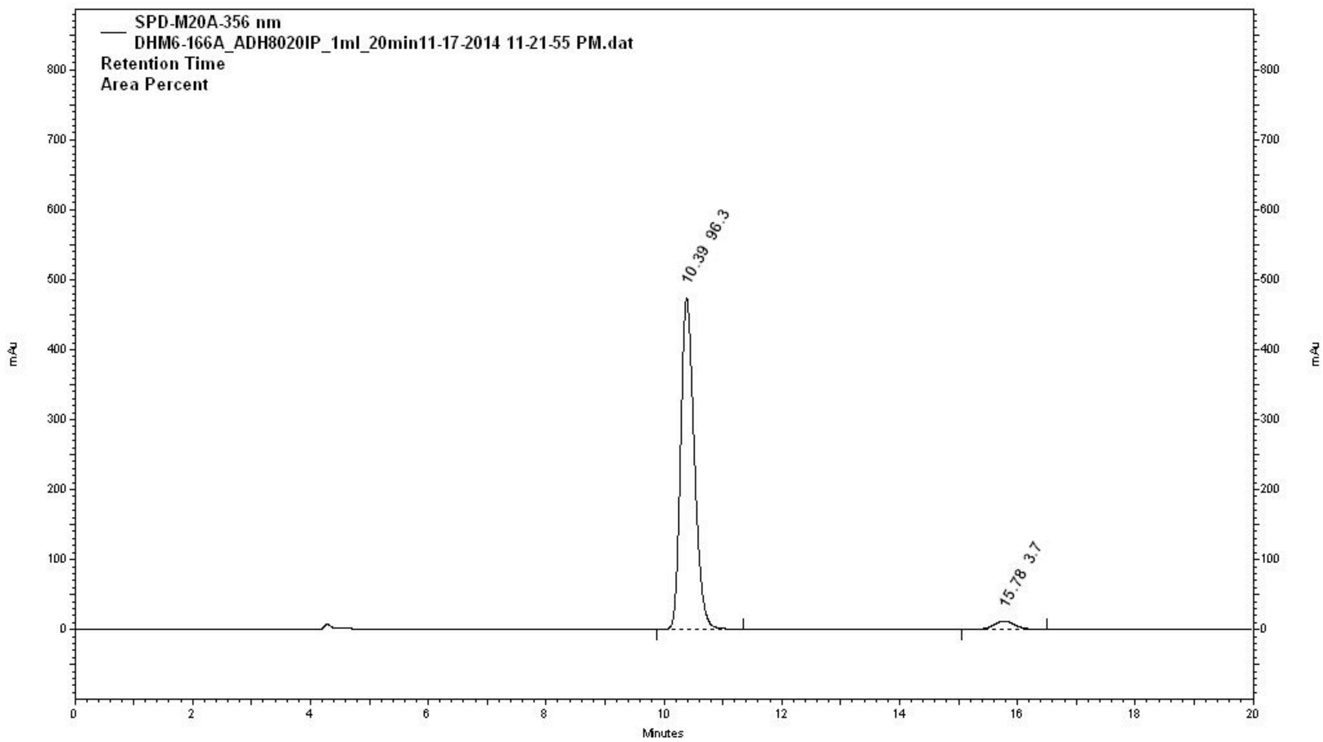


Racemic

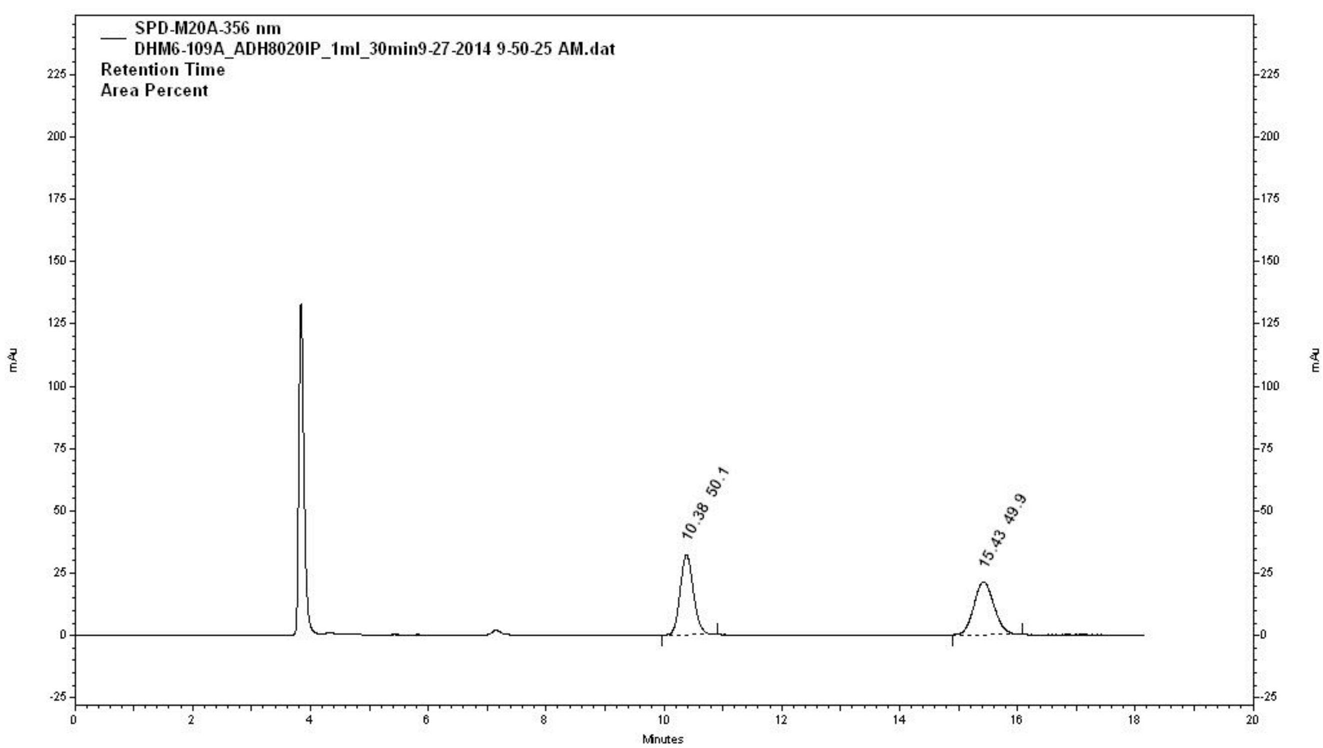


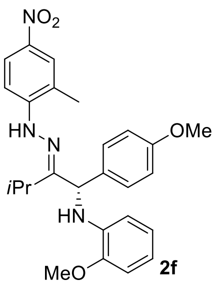


Enantioenriched



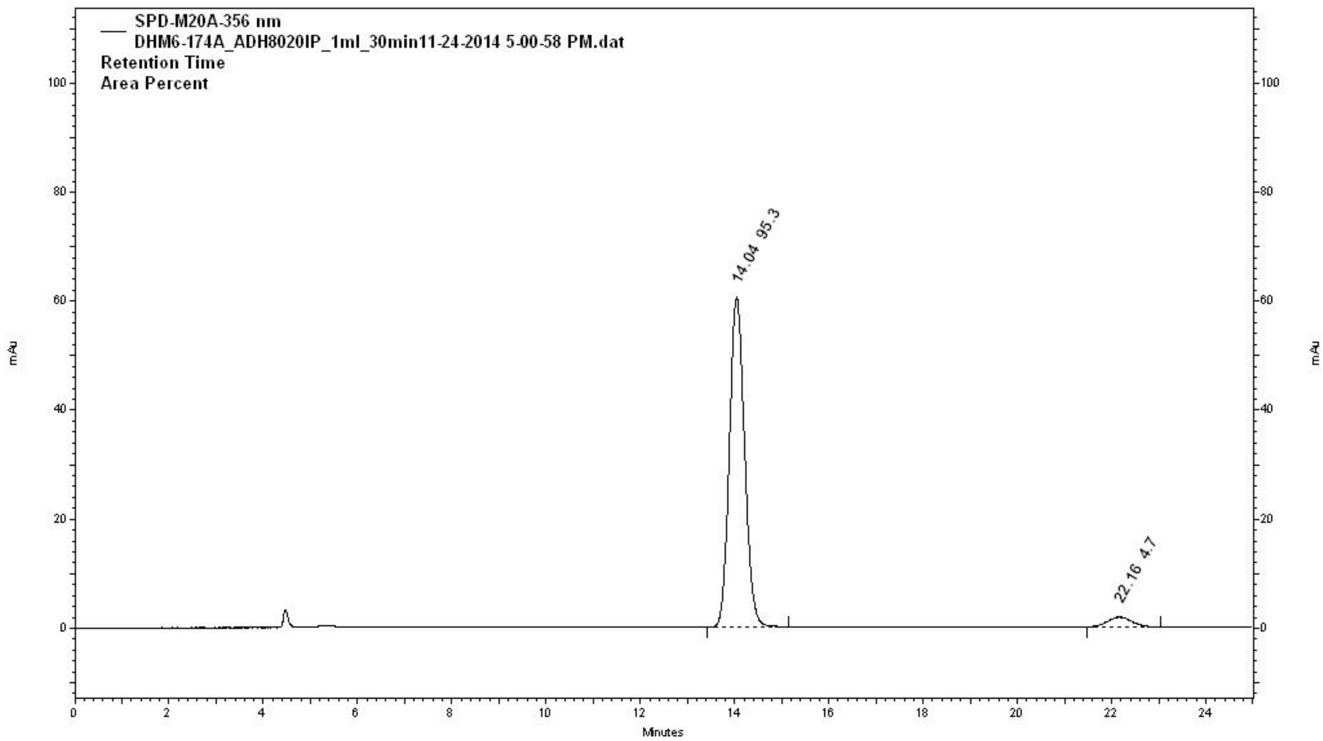
Racemic



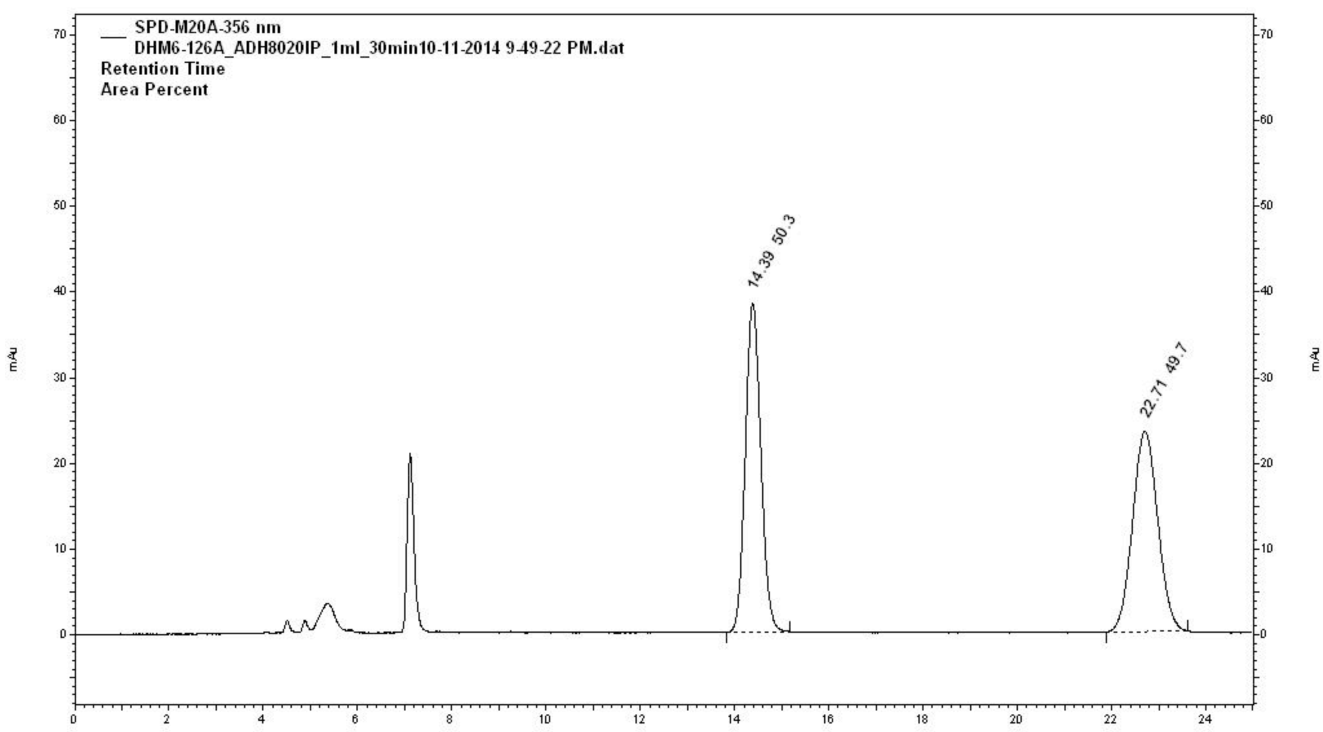


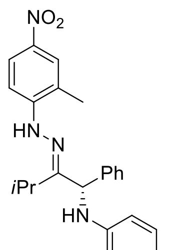
2f

Enantioenriched



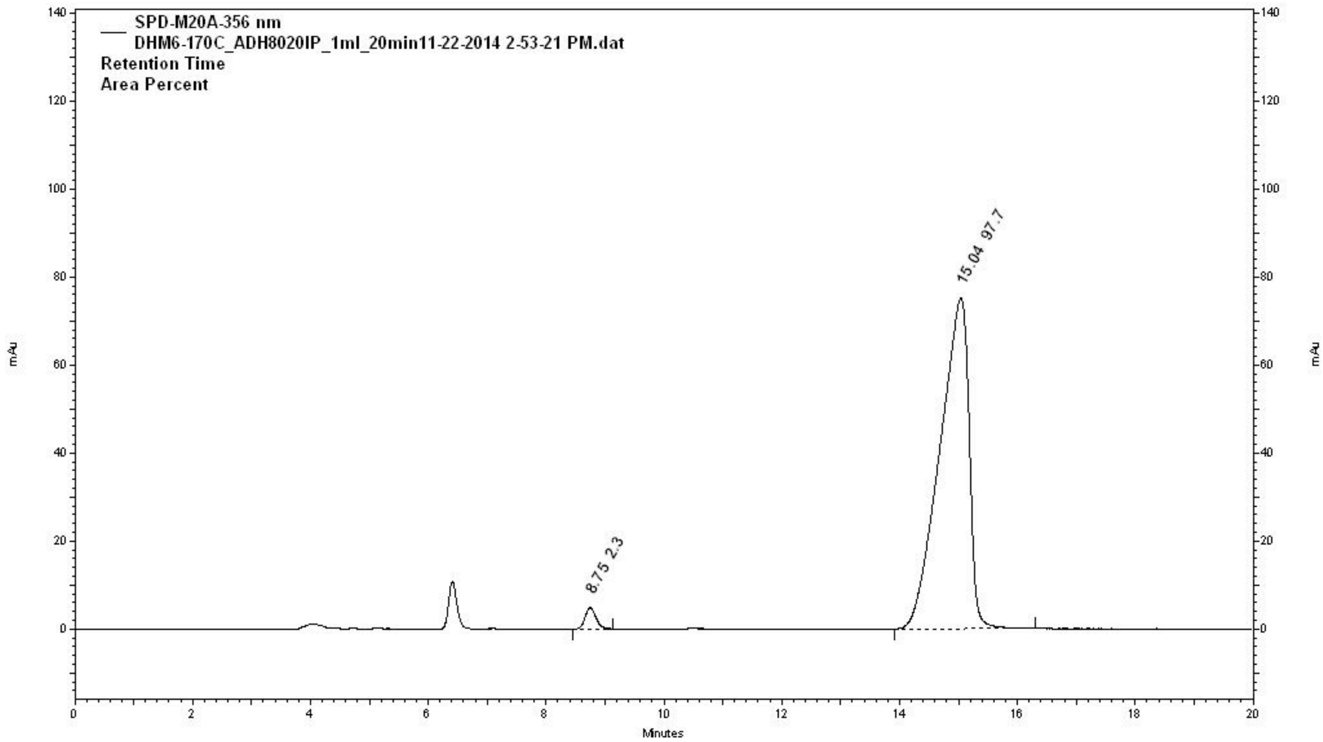
Racemic



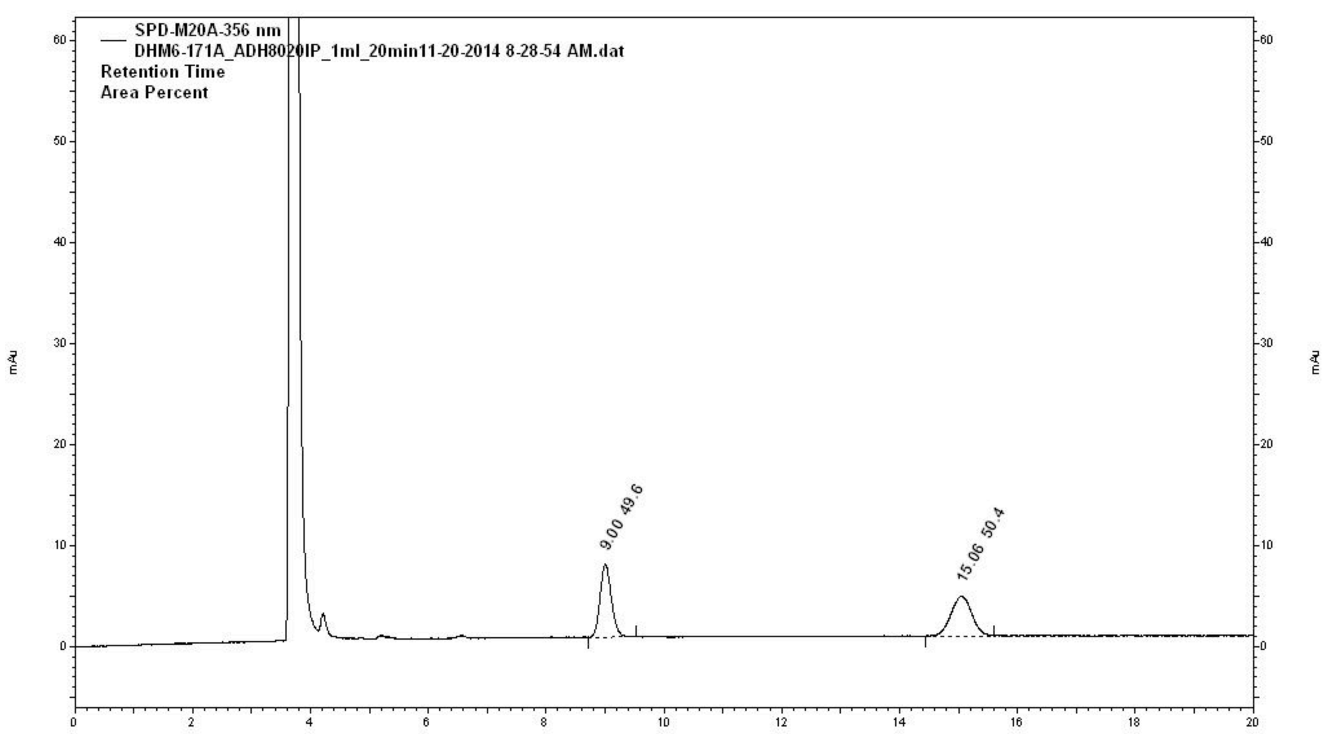


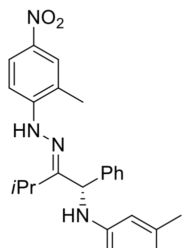
2g

Enantioenriched



Racemic





2h

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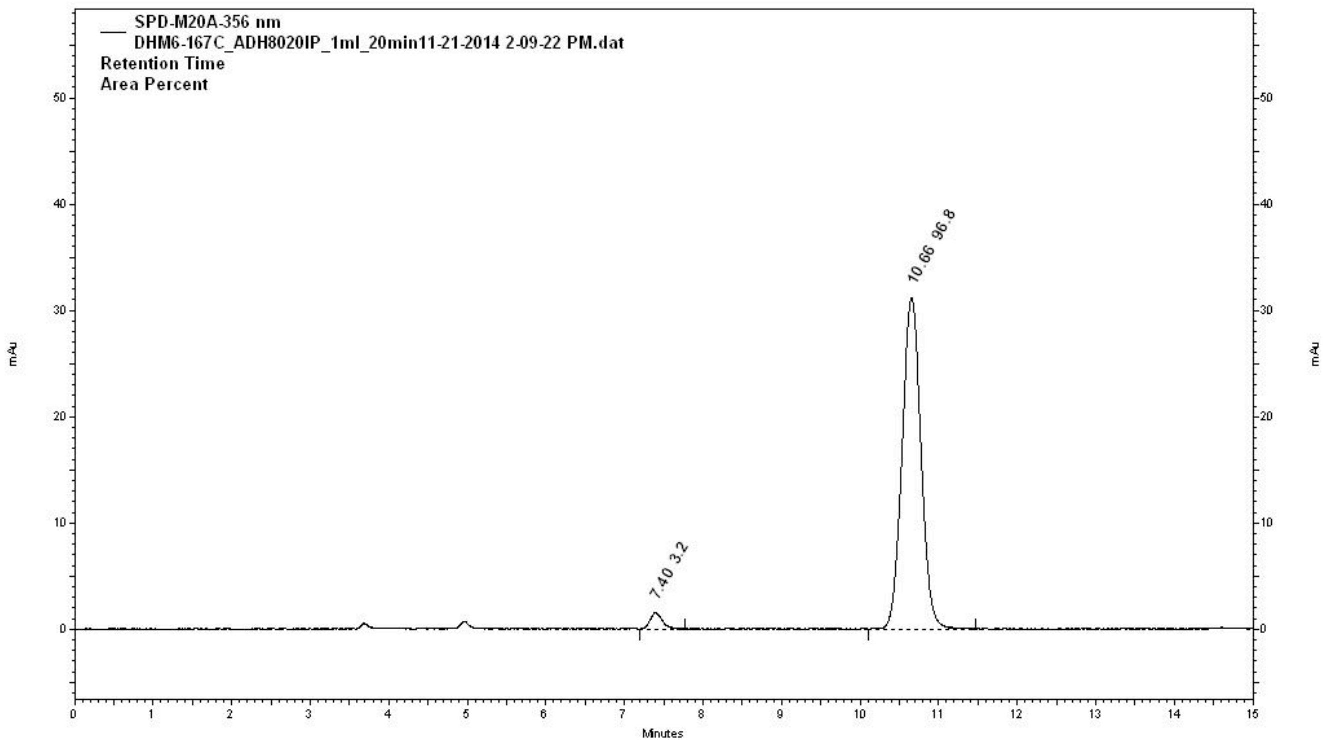

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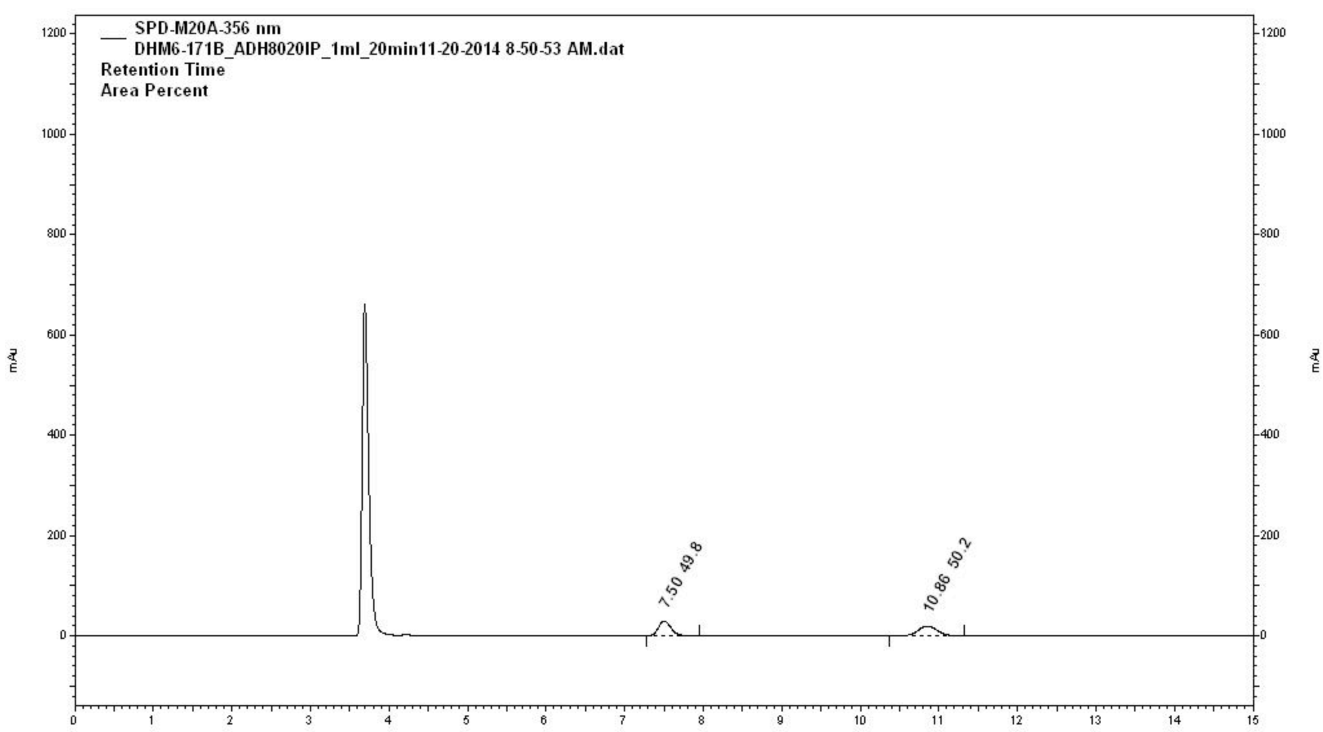

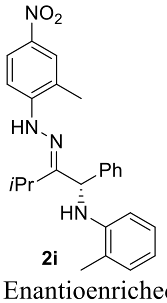

2i

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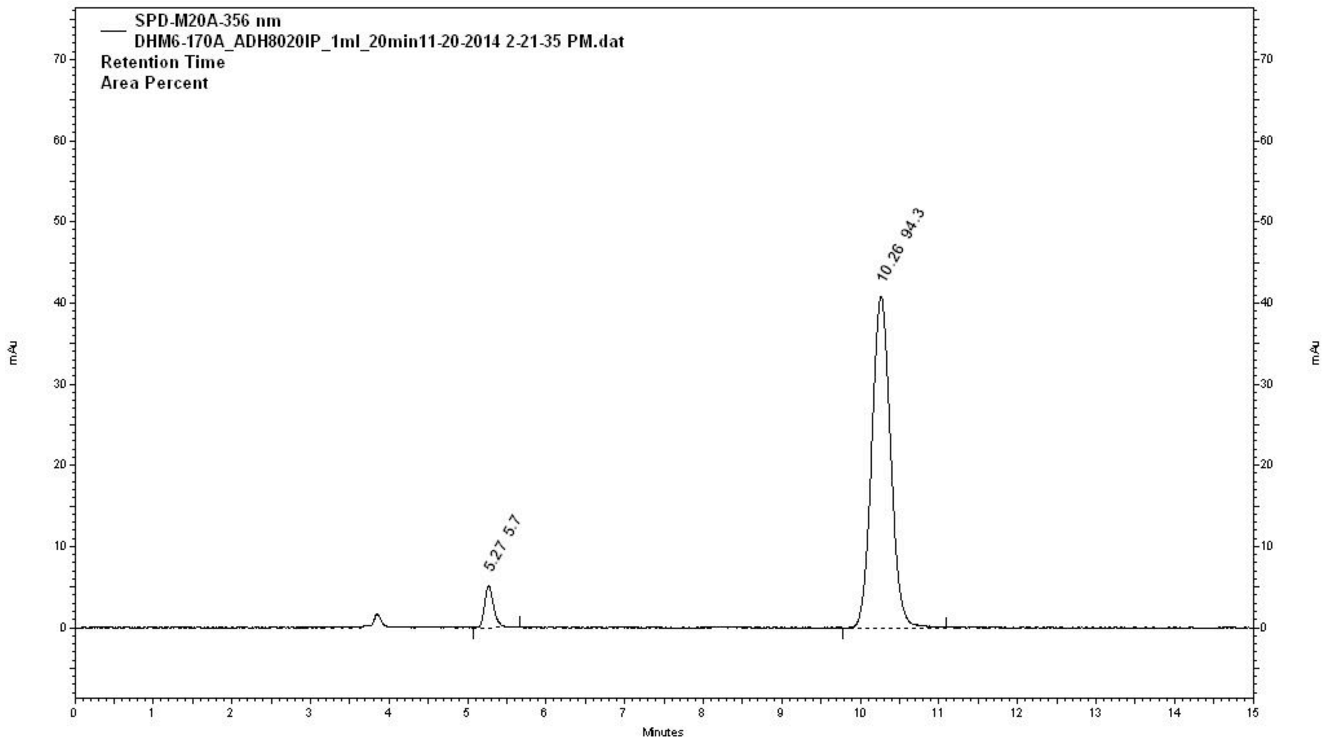

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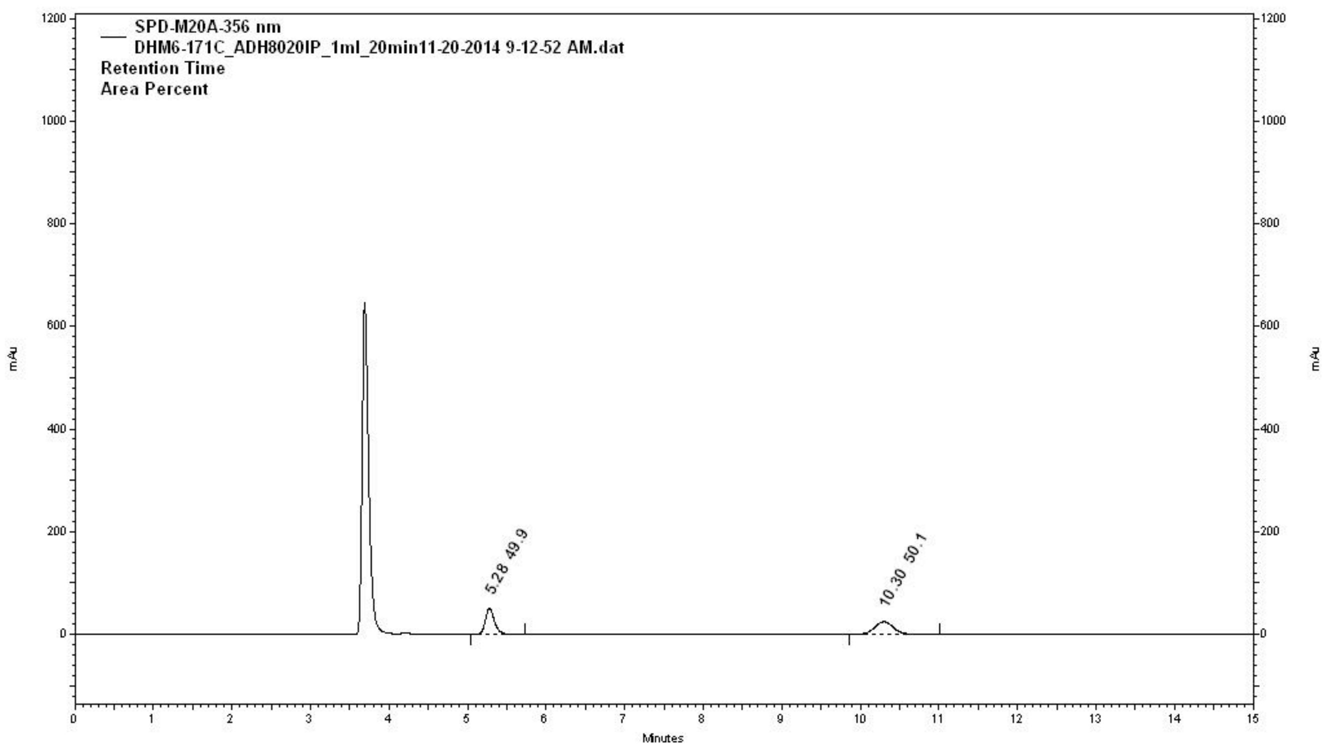

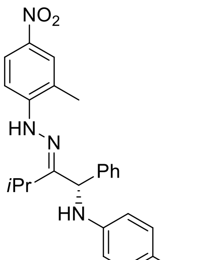

2j

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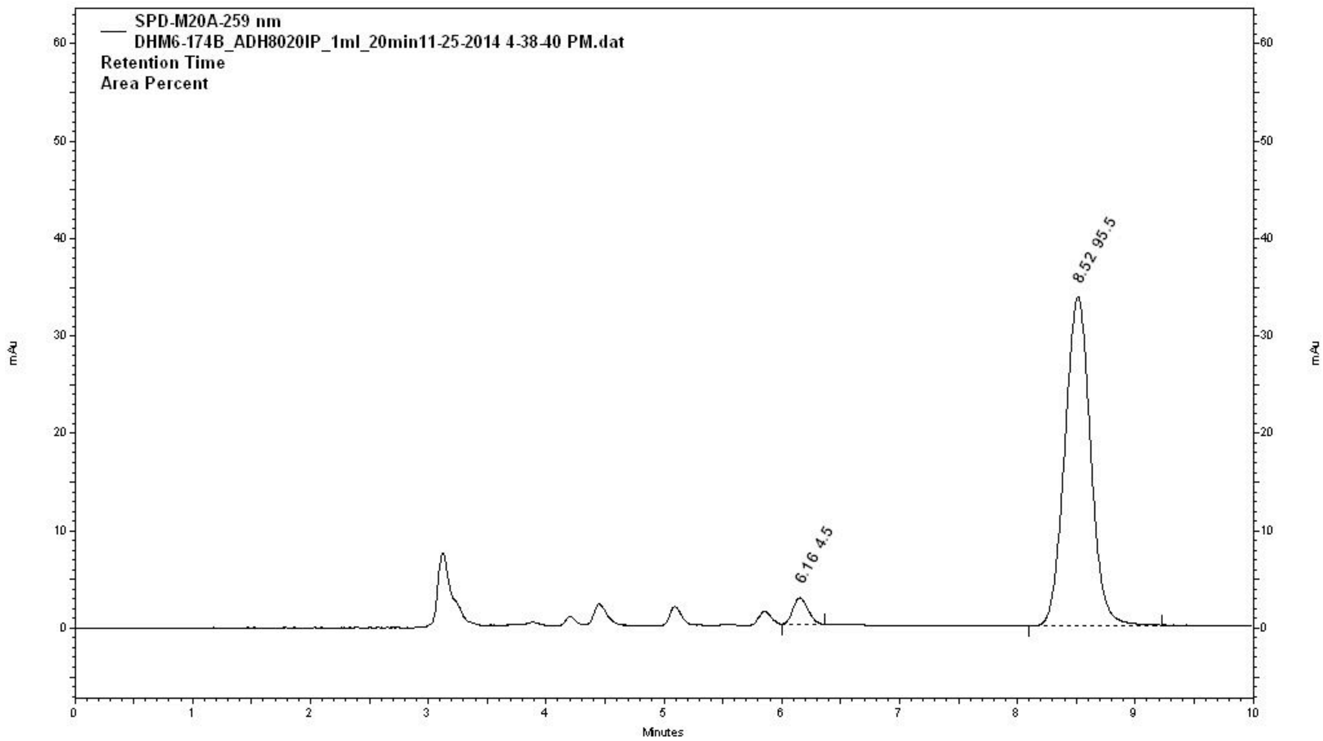

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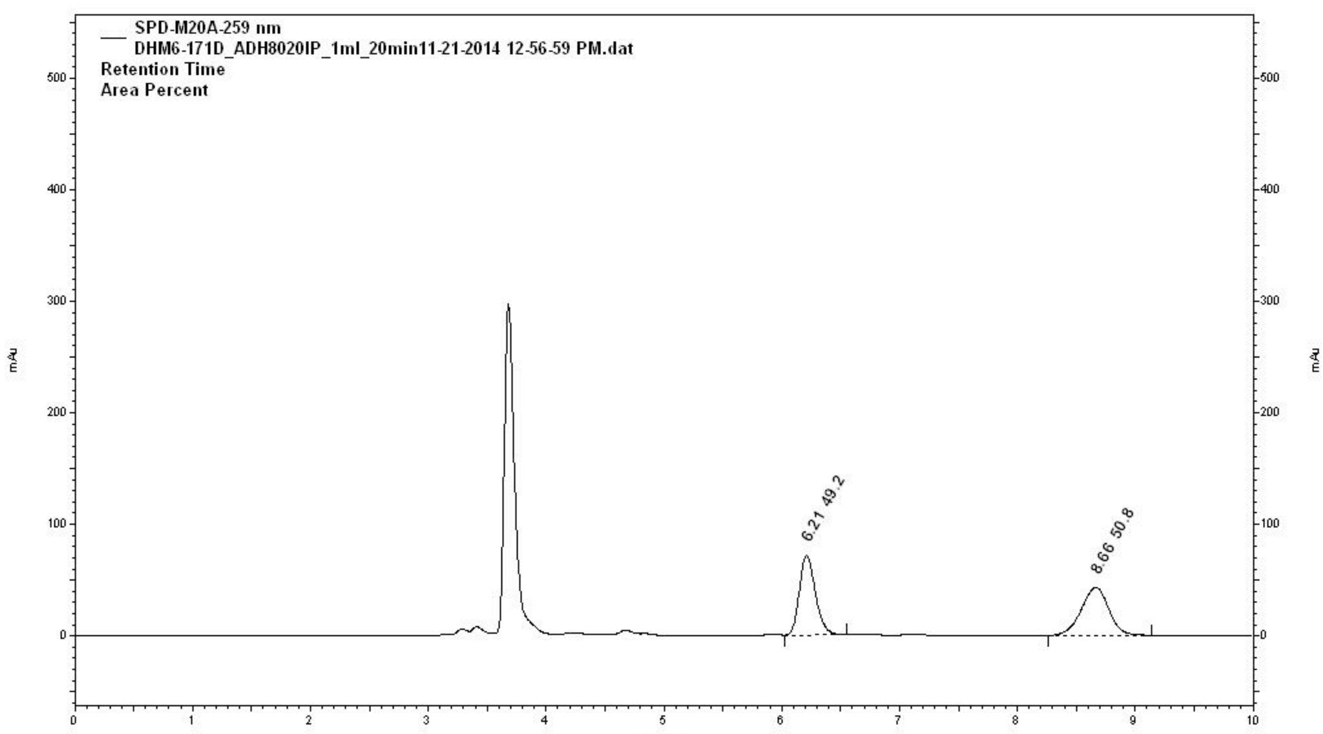

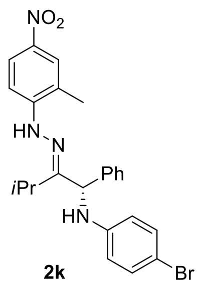

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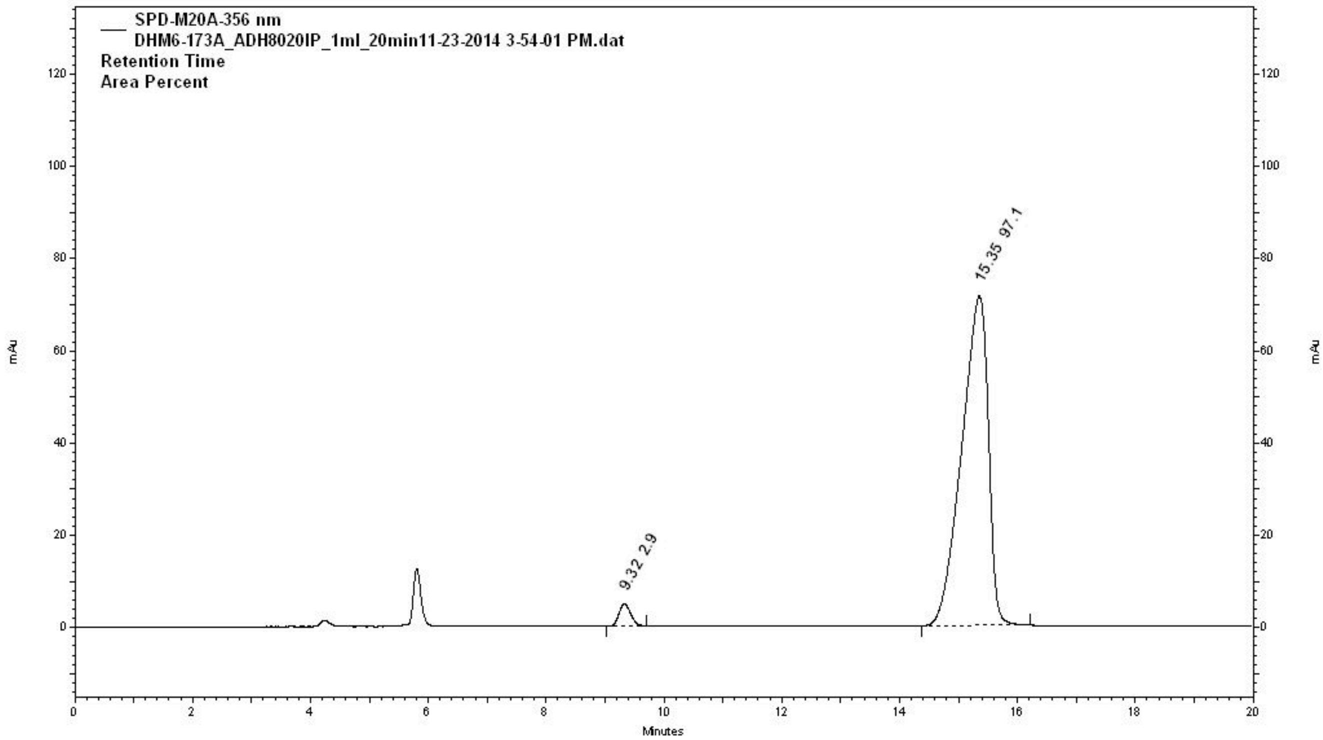

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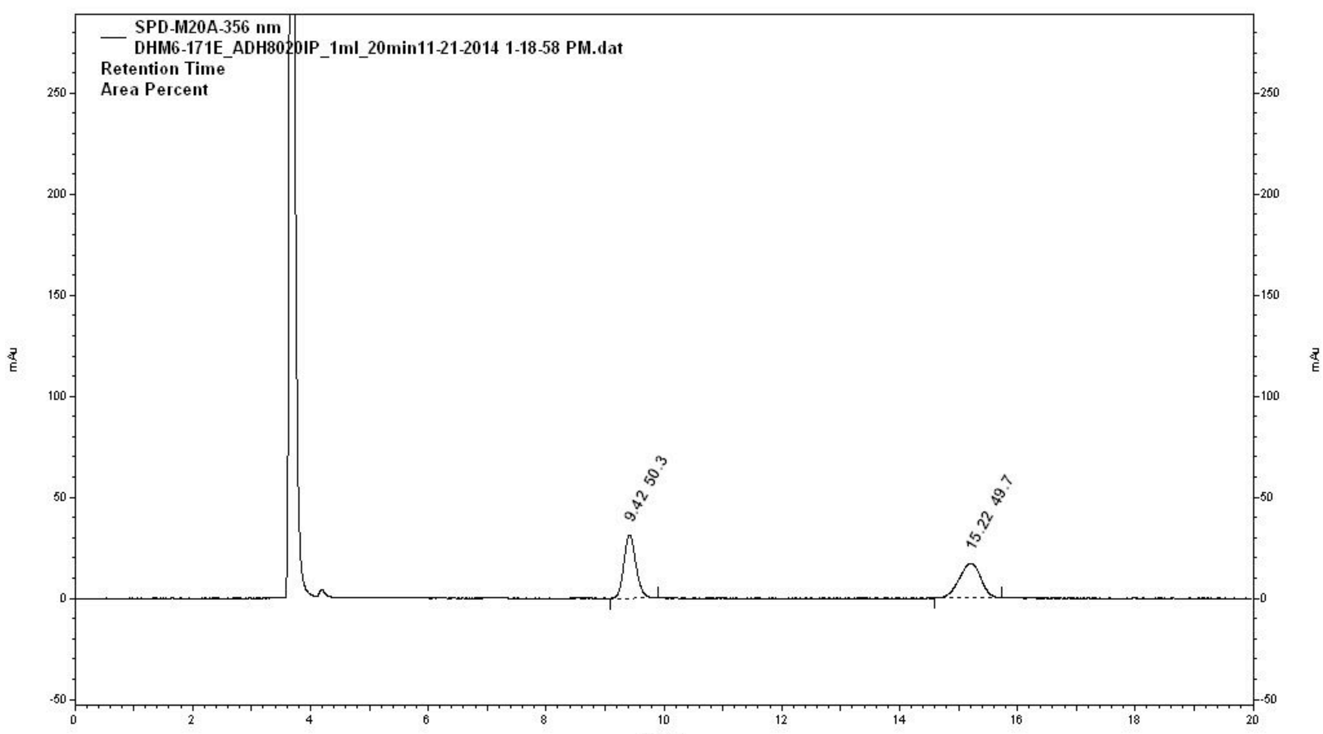

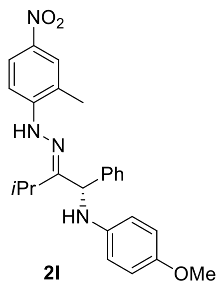

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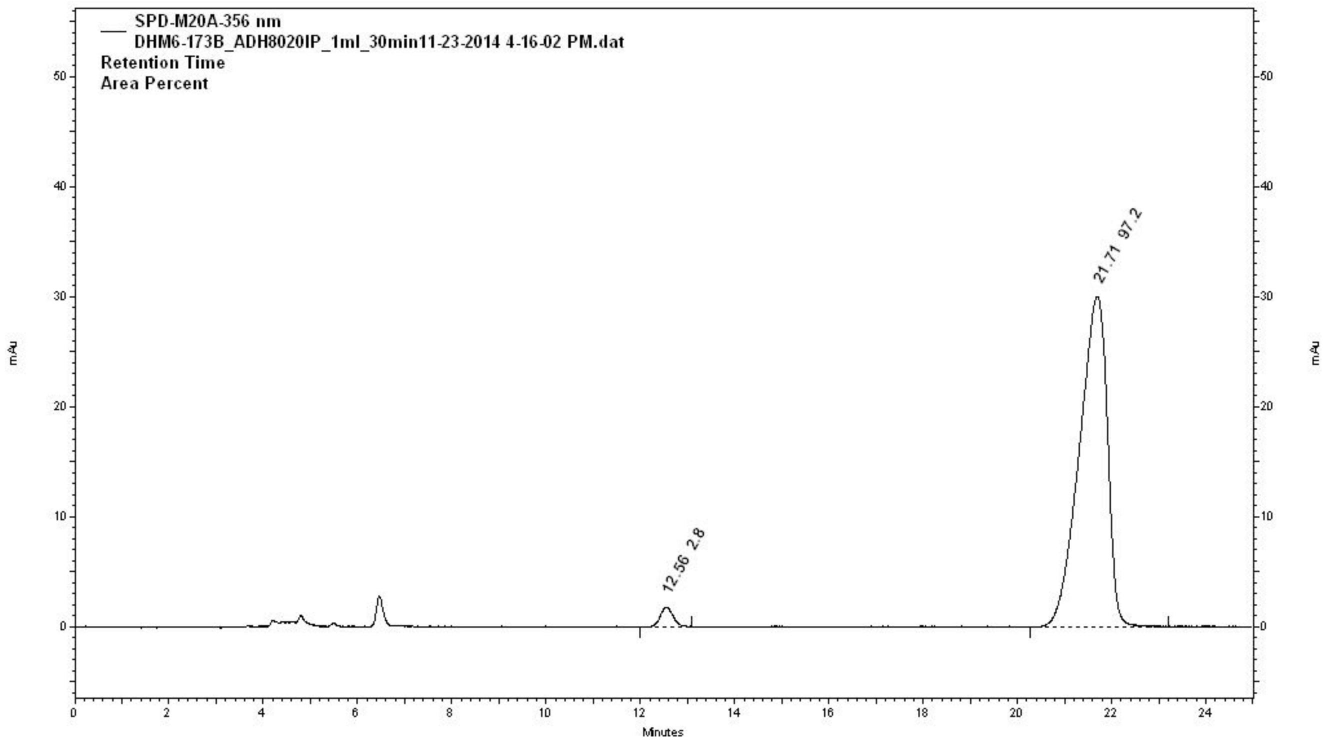

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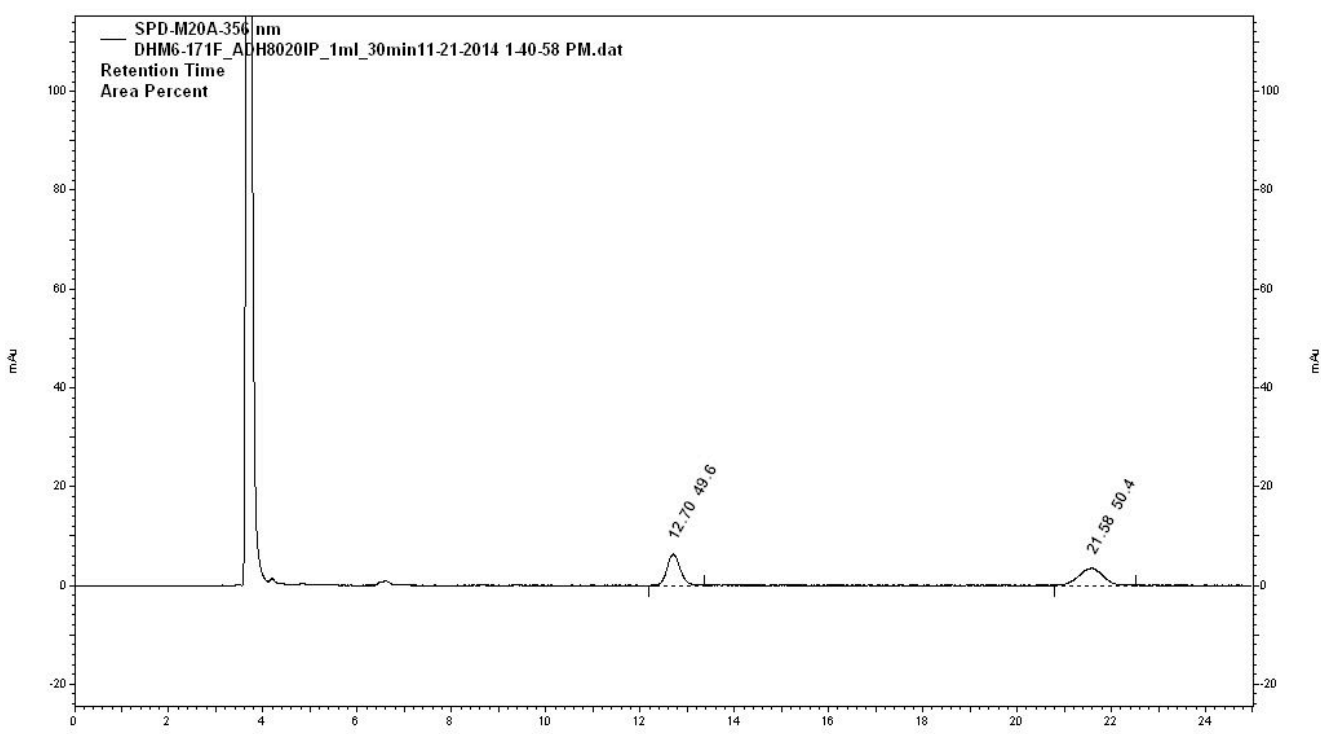

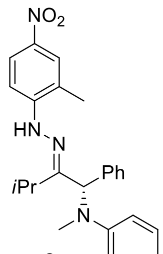

2m

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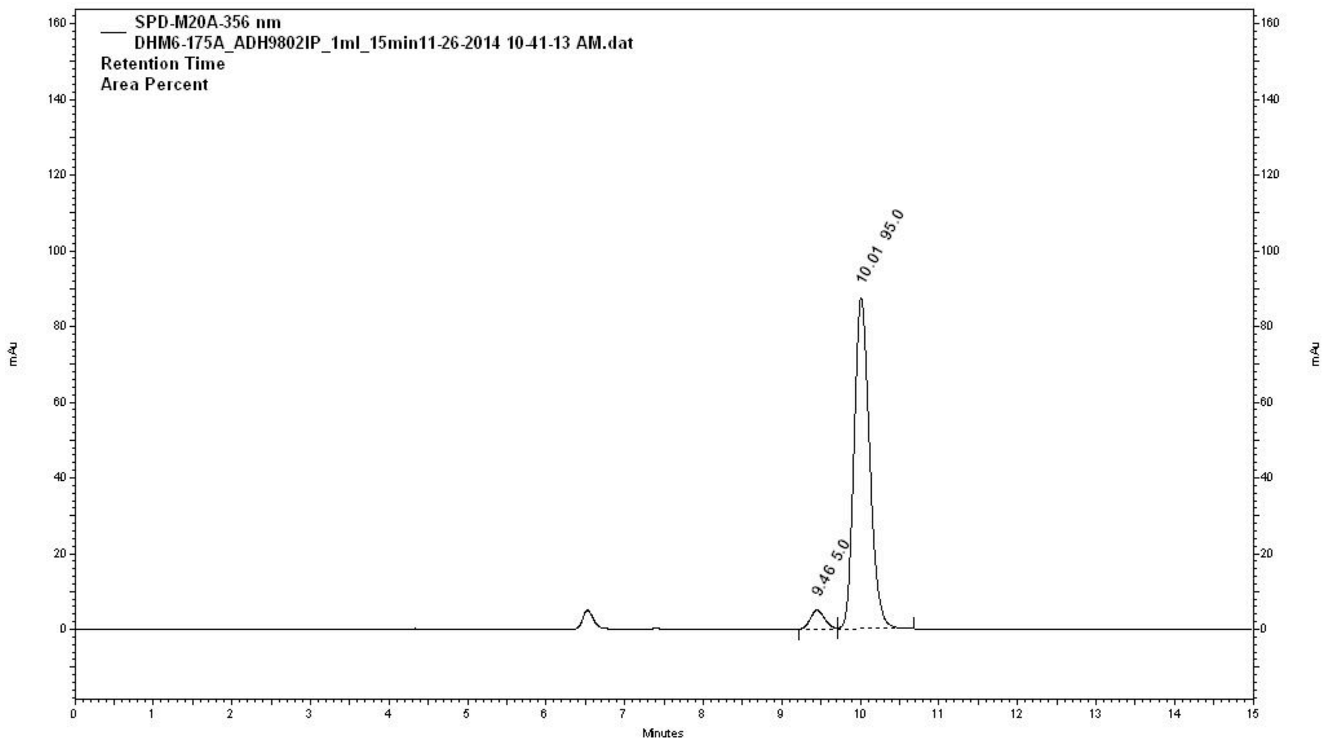

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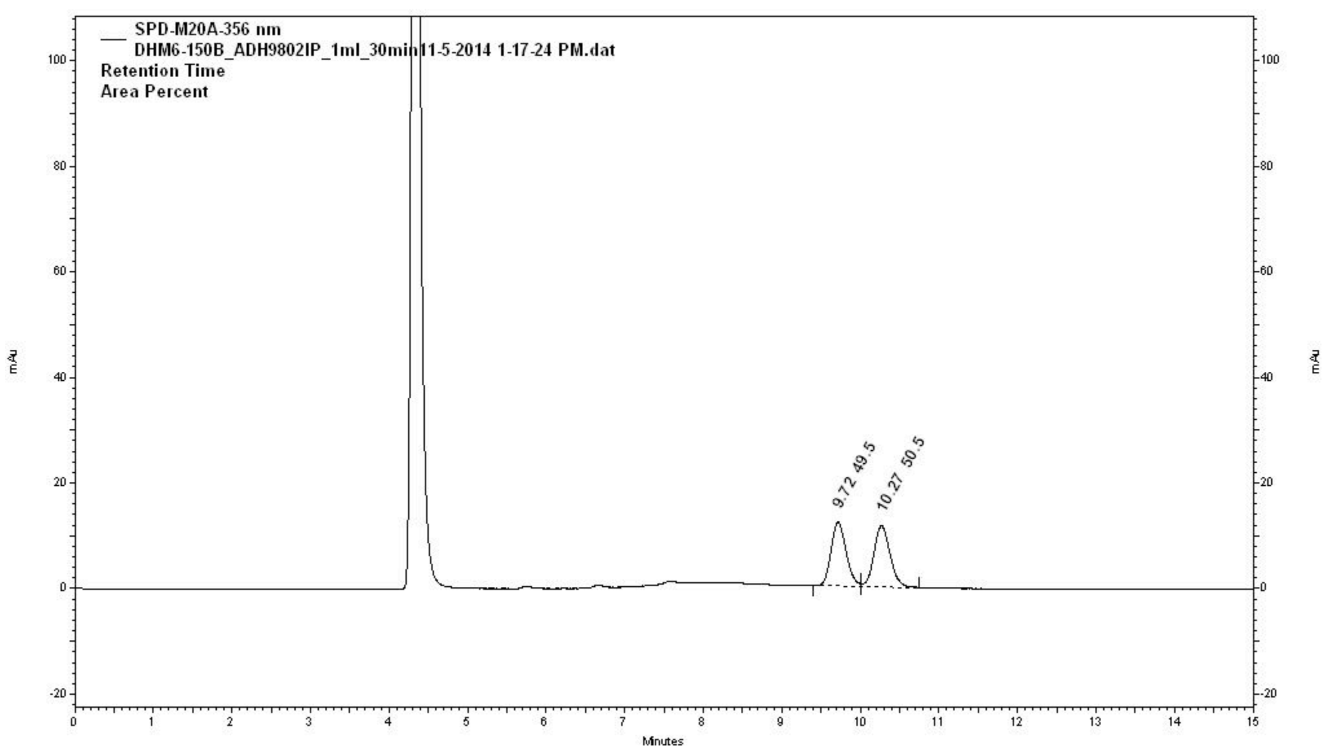

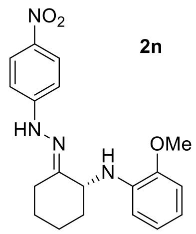

2n

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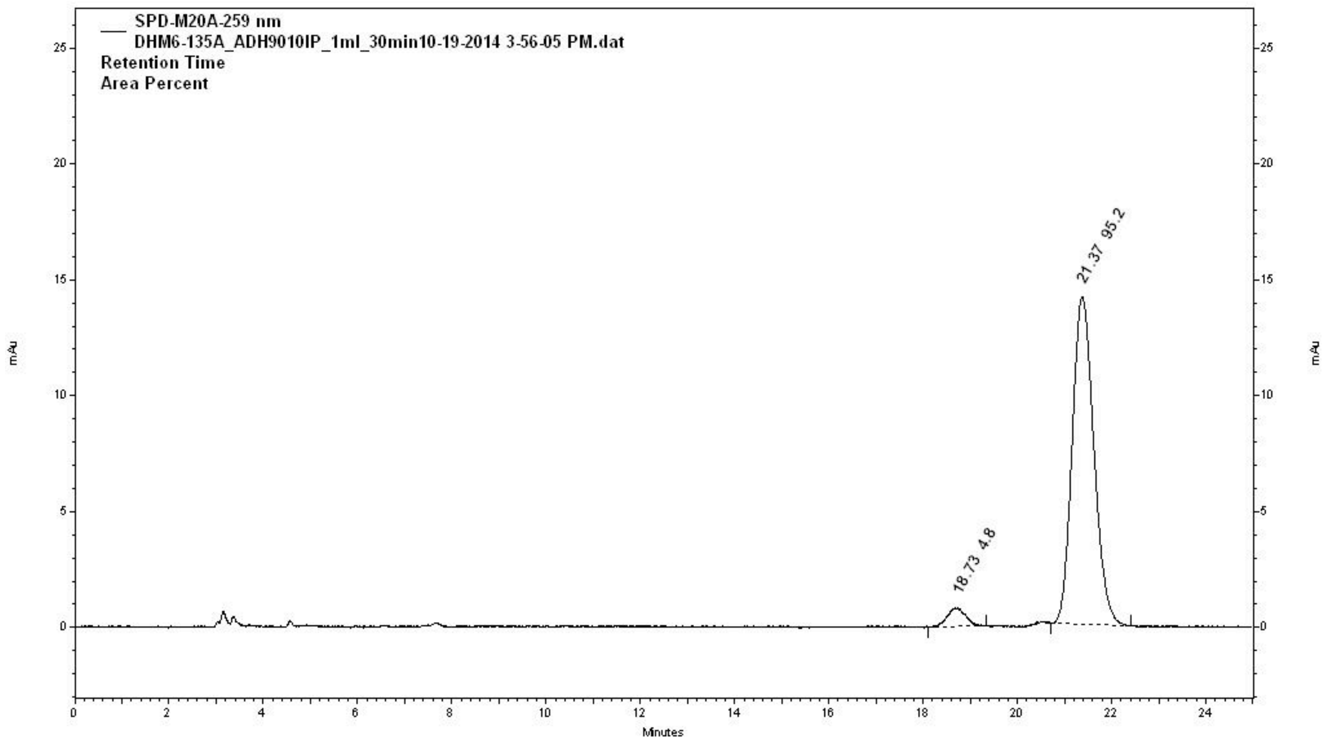

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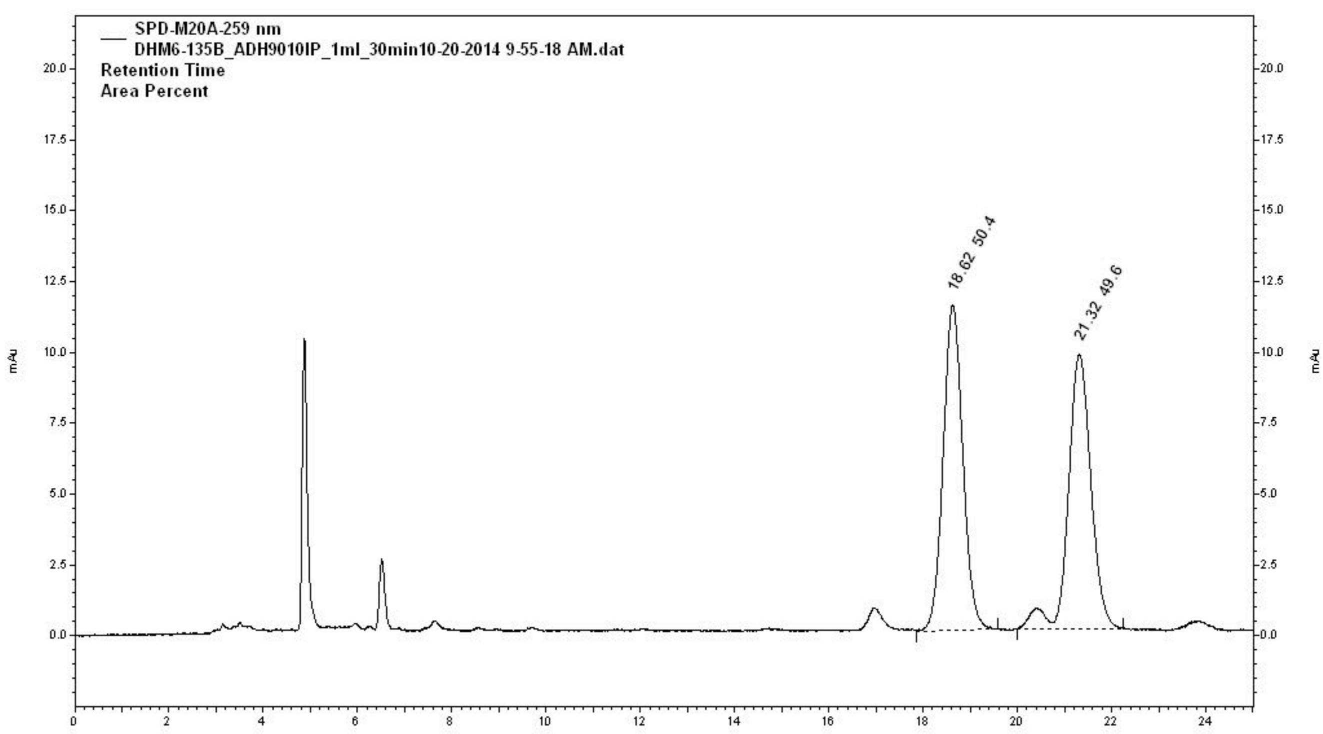

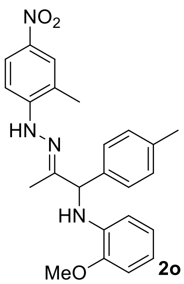

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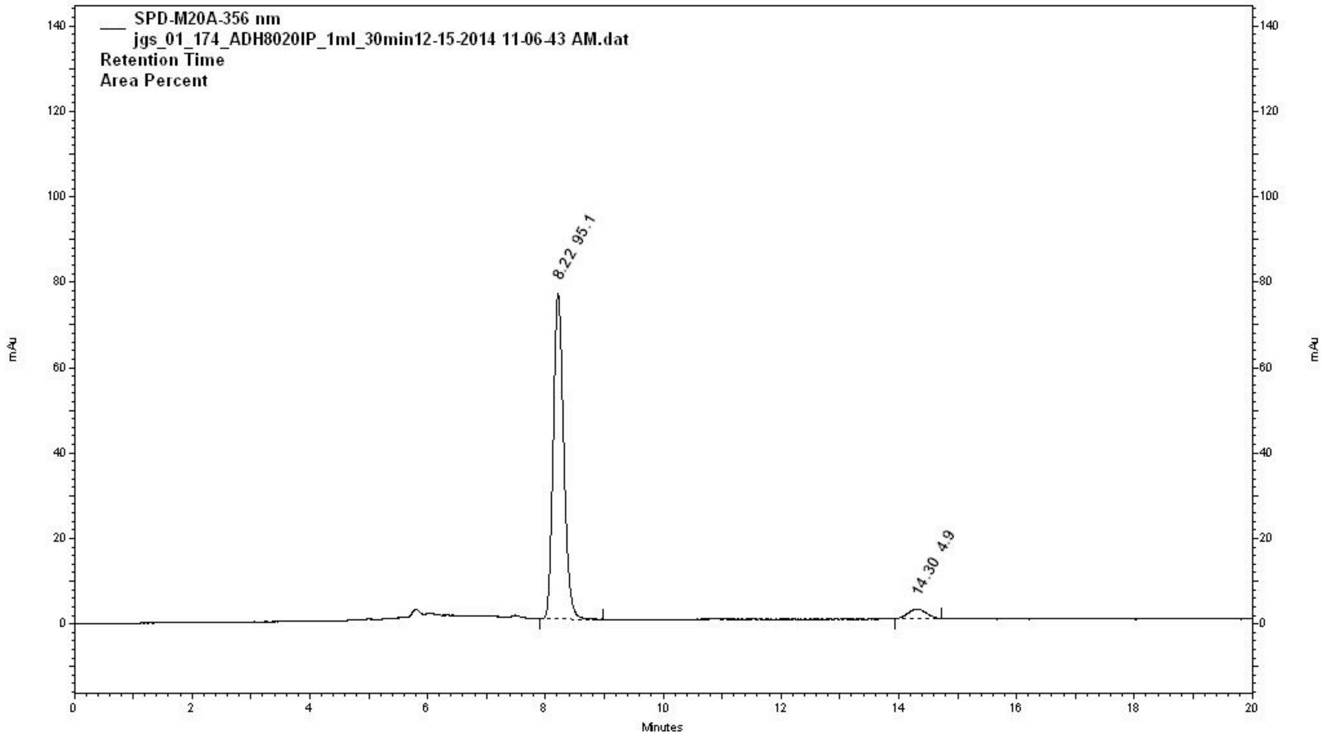

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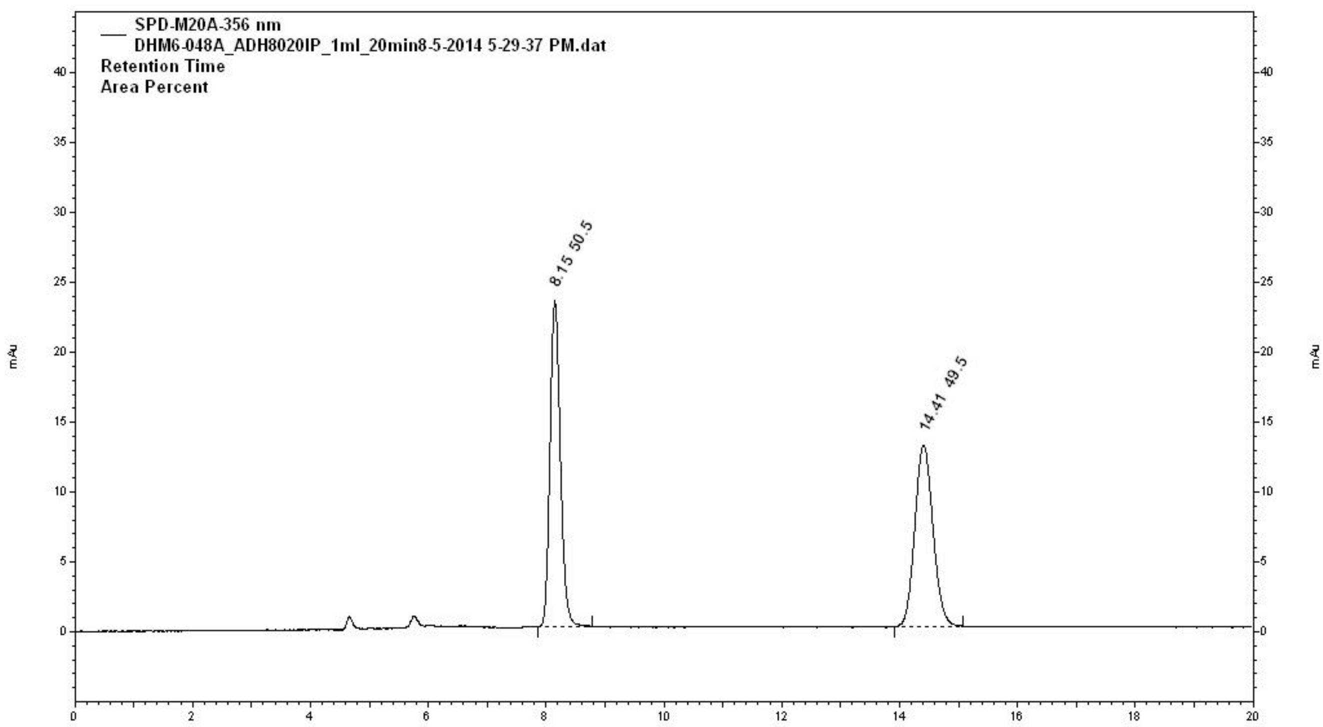

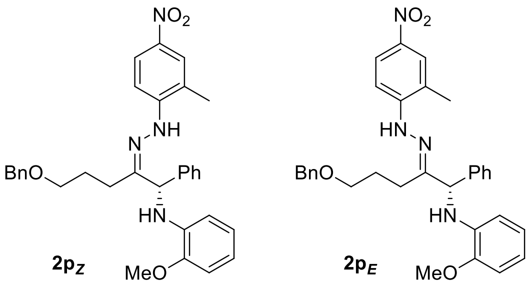

2p*Z* **2p*E***

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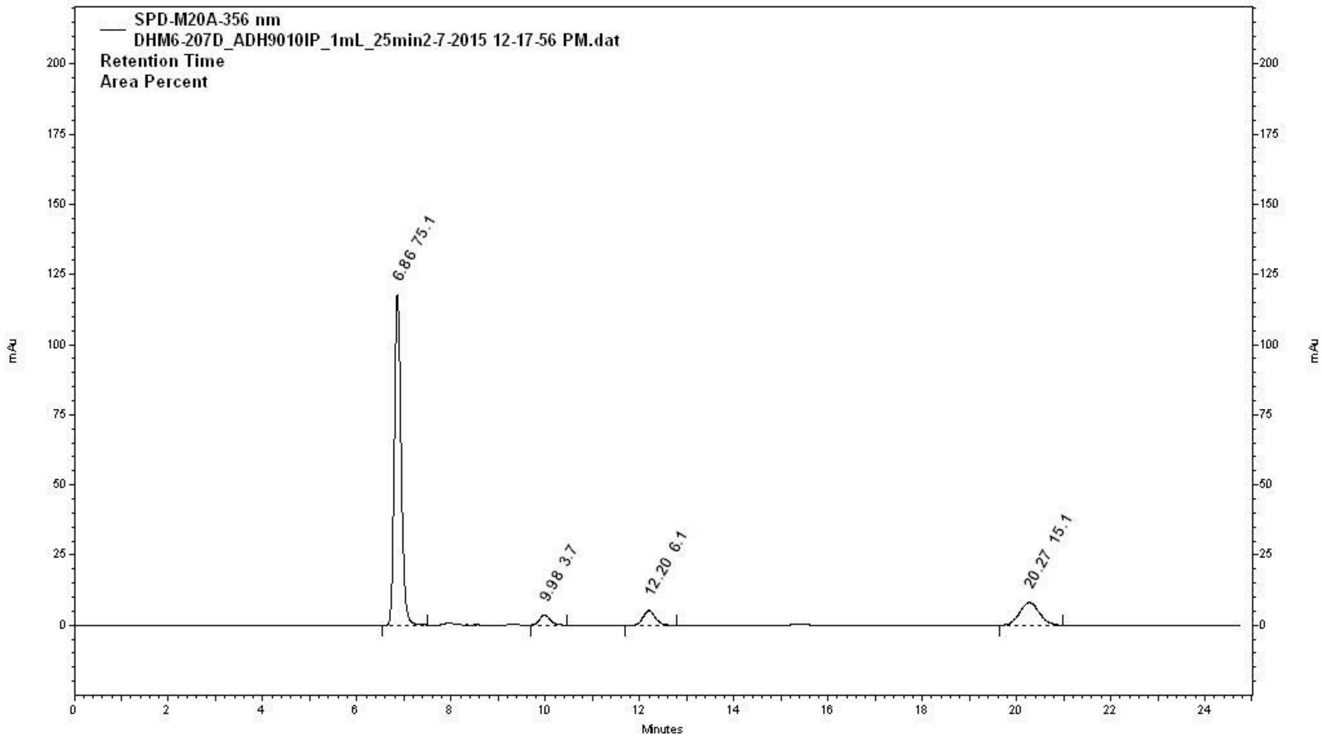

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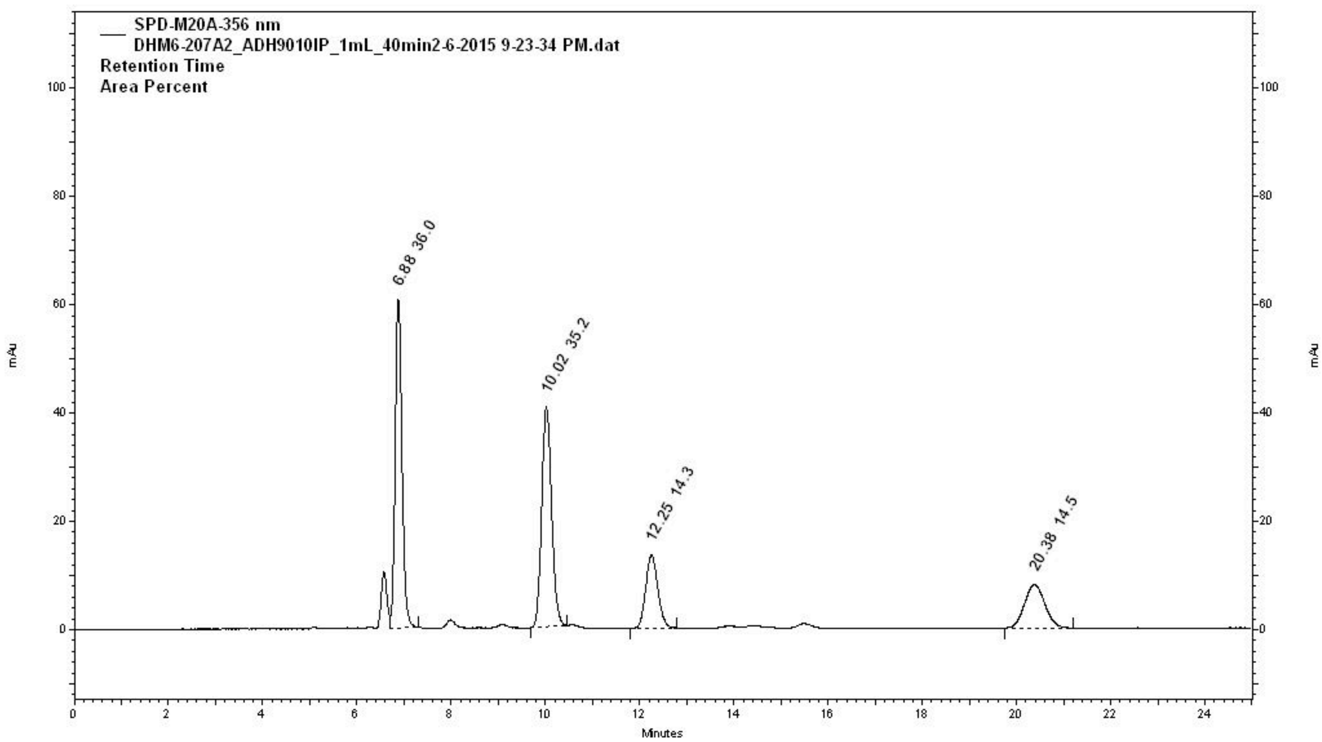

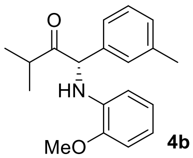

4b

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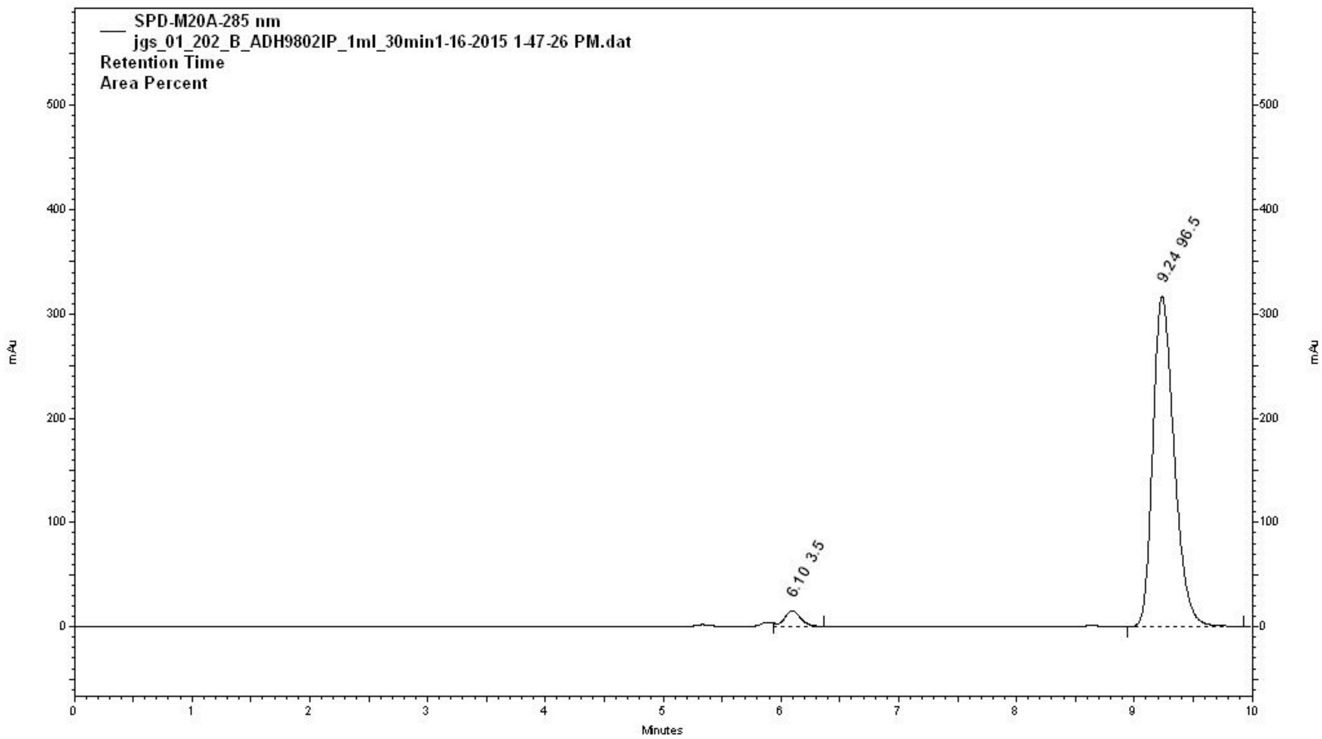

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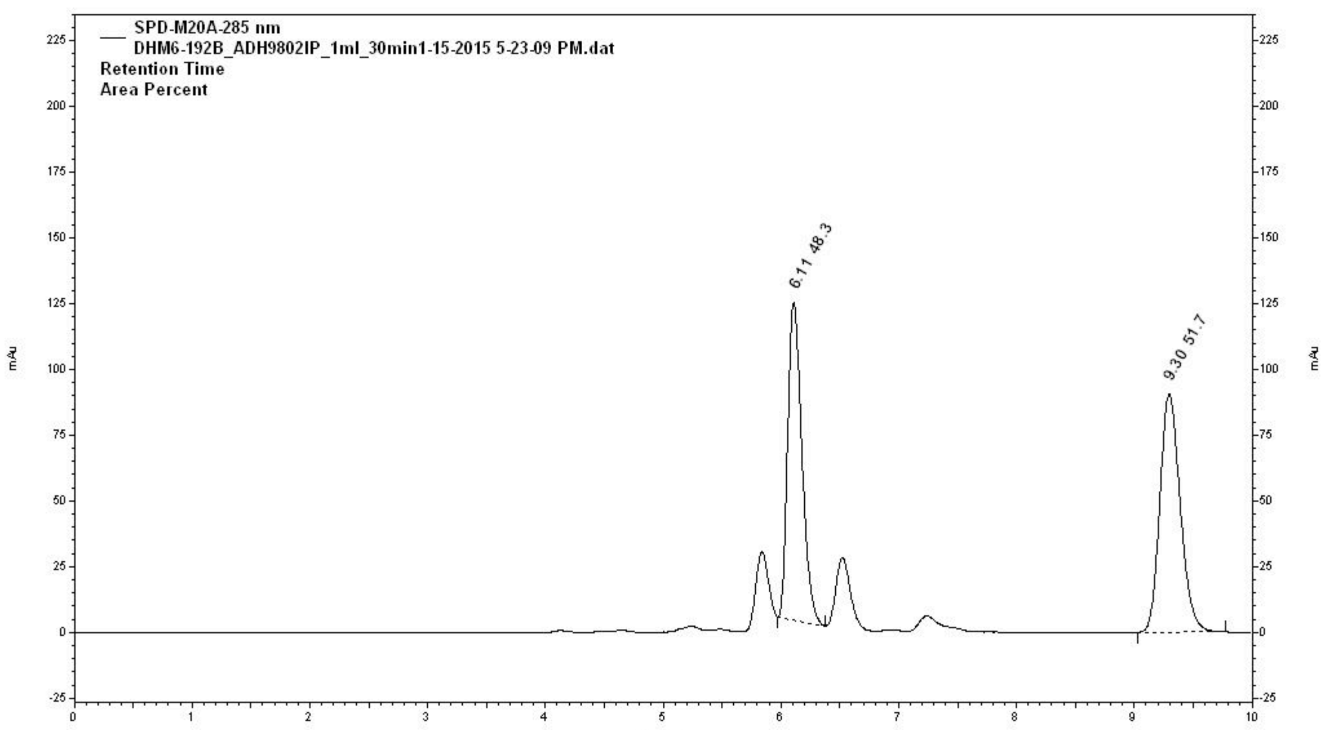

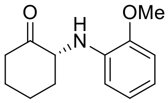

4n

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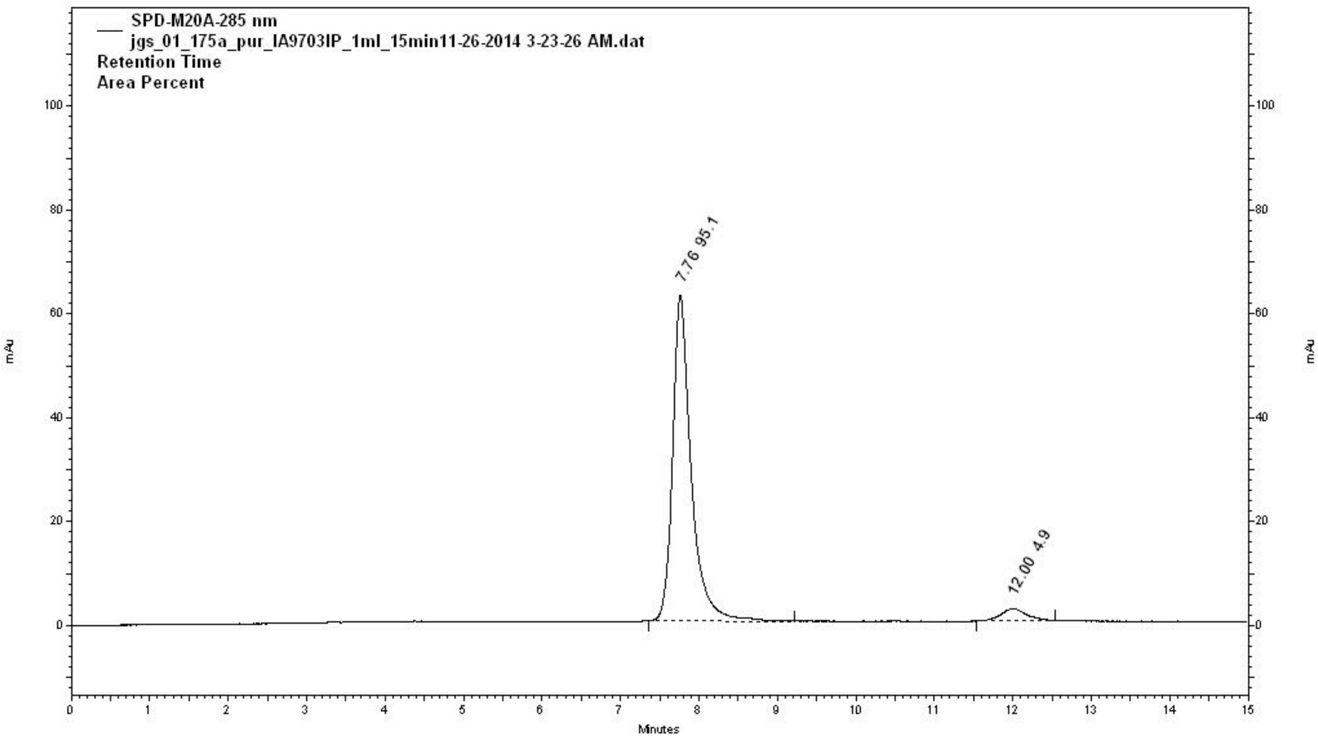

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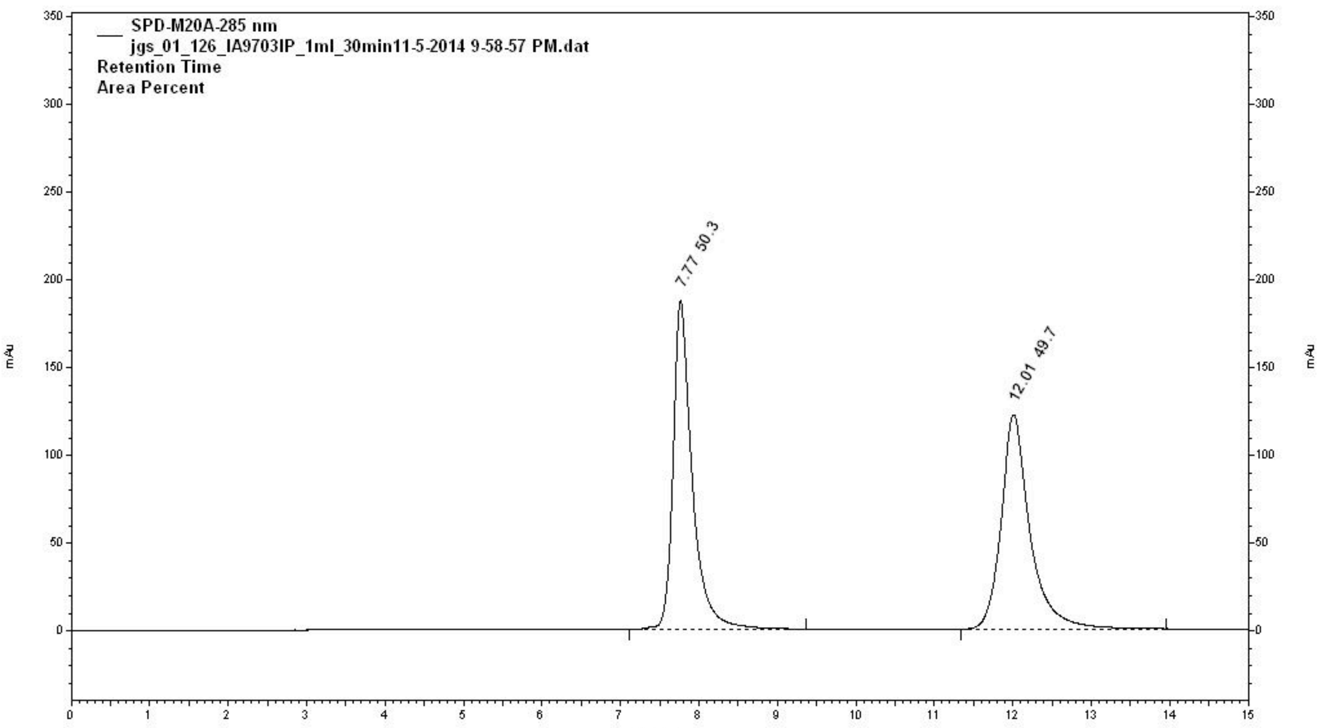

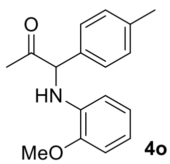

4o

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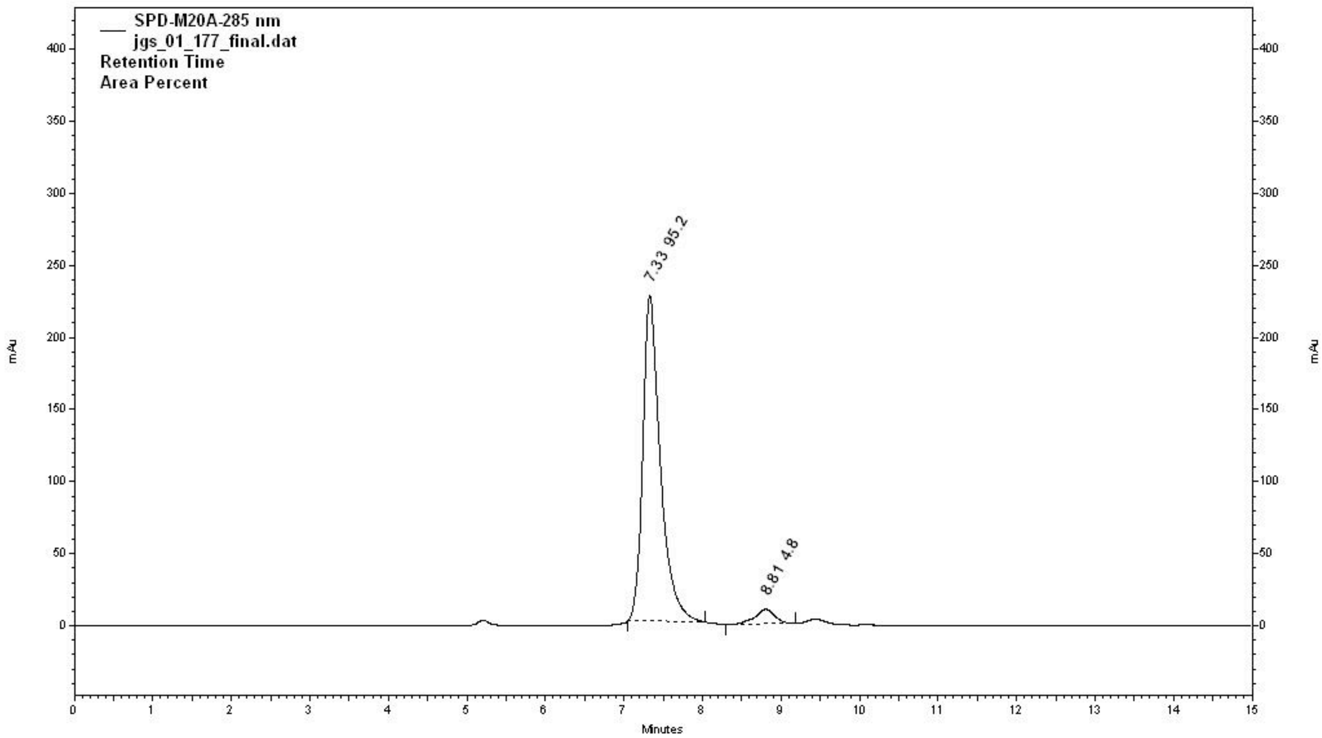

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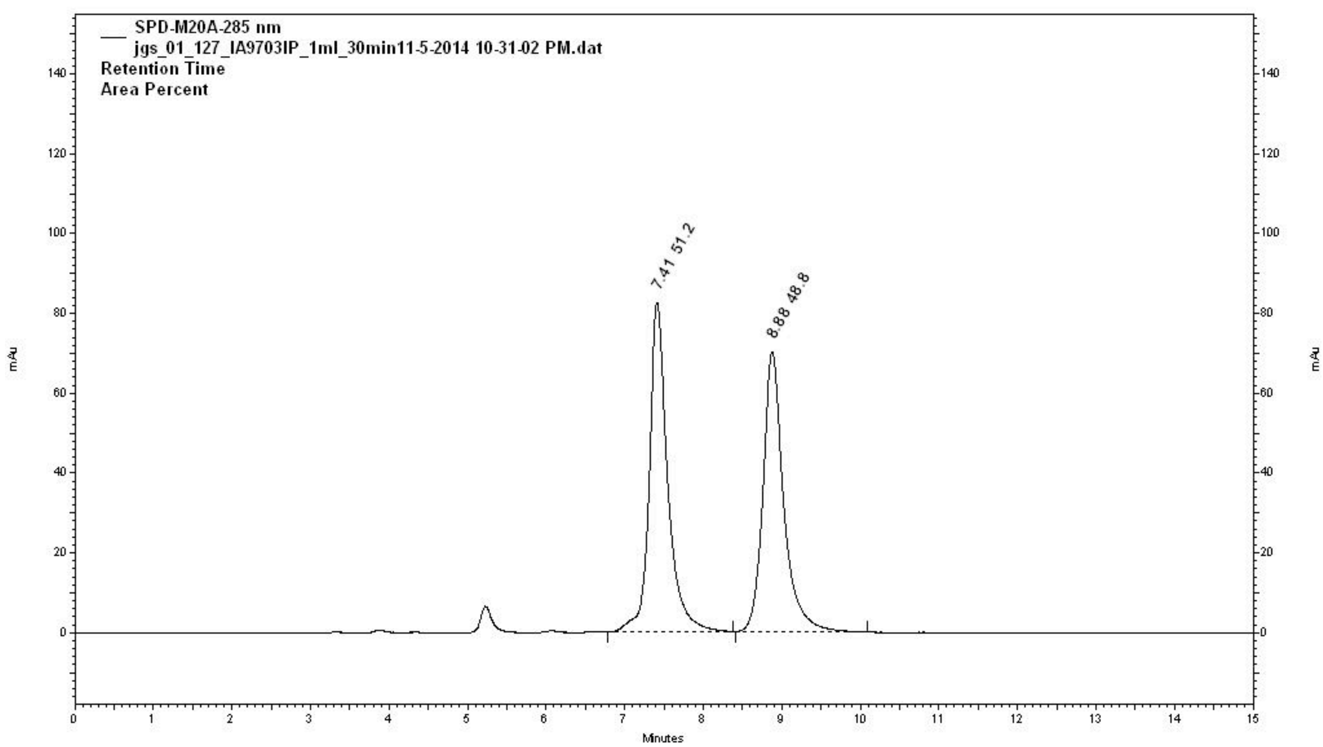
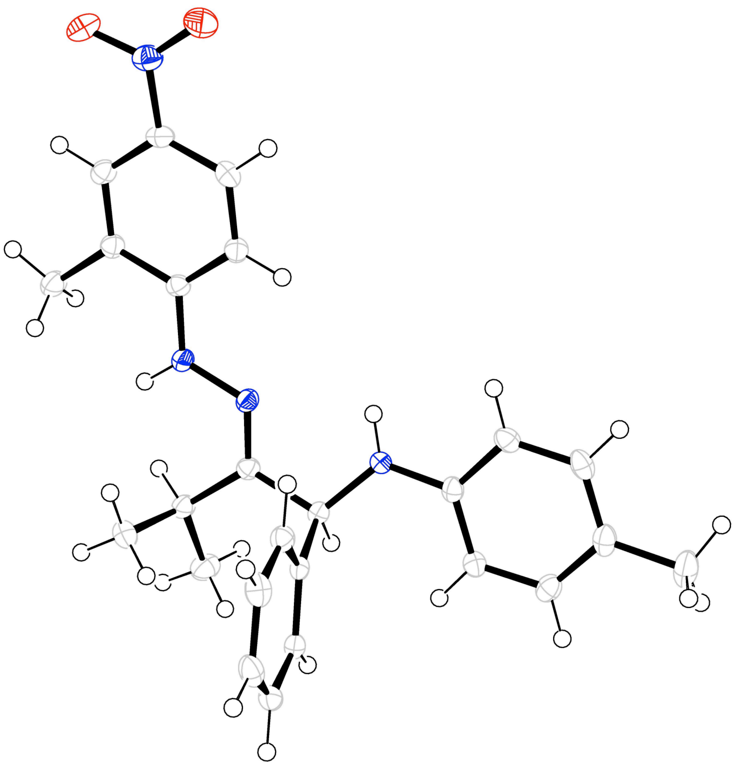


Crystal Structure of **2g**

ORTEP Representation:



Experimental Details:

A yellow prism 0.080 x 0.060 x 0.040 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 5 seconds per frame using a scan width of 2.0°. Data collection was 99.9% complete to 67.000° in q. A total of 68854 reflections were collected covering the indices, -9<=h<=9, -11<=k<=11, -33<=l<=33. 4089 reflections were found to be symmetry independent, with an Rint of 0.0264. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014/7). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014/7. Absolute stereochemistry was unambiguously determined to be S at C12.

Table S1. Crystal data and structure refinement

Empirical formula	C25 H28 N4 O2	
Formula weight	416.51	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.2090(11) Å	α= 90°.
	b = 9.9163(13) Å	β= 90°.
	c = 27.474(4) Å	γ= 90°.
Volume	2236.5(5) Å^3	
Z	4	
Density (calculated)	1.237 Mg/m^3	
Absorption coefficient	0.638 mm^{-1}	
F(000)	888	
Crystal size	0.080 x 0.060 x 0.040 mm^3	
Theta range for data collection	3.217 to 68.357°.	

Index ranges	-9<=h<=9, -11<=k<=11, -33<=l<=33
Reflections collected	68854
Independent reflections	4089 [R(int) = 0.0264]
Completeness to theta = 67.000°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.844
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4089 / 0 / 284
Goodness-of-fit on F2	1.068
Final R indices [I>2sigma(I)]	R1 = 0.0284, wR2 = 0.0747
R indices (all data)	R1 = 0.0286, wR2 = 0.0749
Absolute structure parameter	0.07(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.245 and -0.281 e.$Å^{-3}$

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	x	y	z	U(eq)
C(1)	5797(2)	2329(2)	1948(1)	18(1)
C(2)	7273(2)	2847(2)	2122(1)	20(1)
C(3)	8231(2)	2080(2)	2428(1)	22(1)
C(4)	7703(2)	800(2)	2557(1)	20(1)
C(5)	6226(2)	282(2)	2396(1)	21(1)
C(6)	5243(2)	1041(2)	2095(1)	20(1)
C(7)	3643(2)	497(2)	1912(1)	26(1)
C(8)	4370(2)	4921(2)	1173(1)	18(1)
C(9)	2867(2)	4305(2)	939(1)	21(1)
C(10)	3358(2)	3361(2)	518(1)	27(1)
C(11)	1586(2)	5319(2)	775(1)	28(1)
C(12)	4971(2)	6296(2)	1006(1)	18(1)
C(13)	5690(2)	6112(2)	493(1)	18(1)
C(14)	7094(2)	5340(2)	434(1)	21(1)
C(15)	7695(2)	5078(2)	-29(1)	26(1)
C(16)	6900(2)	5586(2)	-435(1)	26(1)
C(17)	5522(2)	6376(2)	-379(1)	24(1)
C(18)	4927(2)	6647(2)	85(1)	20(1)
C(19)	6893(2)	8073(2)	1280(1)	18(1)
C(20)	8269(2)	8404(2)	1554(1)	21(1)
C(21)	9027(2)	9640(2)	1498(1)	23(1)
C(22)	8460(2)	10601(2)	1169(1)	24(1)
C(23)	7093(2)	10263(2)	898(1)	23(1)
C(24)	6314(2)	9029(2)	947(1)	20(1)
C(25)	9321(3)	11921(2)	1094(1)	32(1)
N(1)	8773(2)	-50(2)	2842(1)	25(1)
N(2)	4865(2)	3025(2)	1616(1)	20(1)
N(3)	5291(2)	4314(1)	1481(1)	18(1)
N(4)	6118(2)	6844(2)	1355(1)	21(1)
O(1)	10050(2)	428(2)	3004(1)	40(1)
O(2)	8377(2)	-1240(1)	2910(1)	29(1)

Table S3. Bond lengths [Å] and angles [°]

C(1)-N(2)	1.377(2)
C(1)-C(2)	1.400(3)
C(1)-C(6)	1.414(2)
C(2)-C(3)	1.380(3)
C(2)-H(2)	0.9500
C(3)-C(4)	1.388(3)
C(3)-H(3)	0.9500
C(4)-C(5)	1.388(3)
C(4)-N(1)	1.448(2)
C(5)-C(6)	1.380(2)
C(5)-H(5)	0.9500
C(6)-C(7)	1.506(3)
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-N(3)	1.285(2)
C(8)-C(9)	1.520(2)
C(8)-C(12)	1.521(2)
C(9)-C(11)	1.522(3)
C(9)-C(10)	1.541(3)
C(9)-H(9)	1.0000
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-N(4)	1.450(2)
C(12)-C(13)	1.539(2)
C(12)-H(12)	1.0000
C(13)-C(18)	1.389(2)
C(13)-C(14)	1.394(3)
C(14)-C(15)	1.387(3)
C(14)-H(14)	0.9500
C(15)-C(16)	1.388(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.385(3)
C(16)-H(16)	0.9500
C(17)-C(18)	1.391(2)
C(17)-H(17)	0.9500
C(18)-H(18)	0.9500
C(19)-N(4)	1.391(2)
C(19)-C(20)	1.397(2)
C(19)-C(24)	1.401(2)
C(20)-C(21)	1.383(3)
C(20)-H(20)	0.9500
C(21)-C(22)	1.394(3)
C(21)-H(21)	0.9500
C(22)-C(23)	1.388(3)
C(22)-C(25)	1.502(3)
C(23)-C(24)	1.387(2)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
N(1)-O(1)	1.233(2)
N(1)-O(2)	1.238(2)
N(2)-N(3)	1.376(2)
N(2)-H(2A)	0.8800
N(4)-H(4)	0.88
N(2)-C(1)-C(2)	121.51(16)
N(2)-C(1)-C(6)	117.60(16)
C(2)-C(1)-C(6)	120.84(16)
C(3)-C(2)-C(1)	119.90(16)
C(3)-C(2)-H(2)	120.0
C(1)-C(2)-H(2)	120.0
C(2)-C(3)-C(4)	118.81(17)
C(2)-C(3)-H(3)	120.6
C(4)-C(3)-H(3)	120.6
C(3)-C(4)-C(5)	122.00(16)
C(3)-C(4)-N(1)	118.76(17)
C(5)-C(4)-N(1)	119.12(16)
C(6)-C(5)-C(4)	120.00(17)
C(6)-C(5)-H(5)	120.0
C(4)-C(5)-H(5)	120.0
C(5)-C(6)-C(1)	118.38(16)
C(5)-C(6)-C(7)	120.99(16)
C(1)-C(6)-C(7)	120.61(16)
C(6)-C(7)-H(7A)	109.5
C(6)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(6)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
N(3)-C(8)-C(9)	124.64(15)
N(3)-C(8)-C(12)	115.35(15)
C(9)-C(8)-C(12)	119.72(14)
C(8)-C(9)-C(11)	114.86(15)
C(8)-C(9)-C(10)	110.46(14)
C(11)-C(9)-C(10)	111.11(15)
C(8)-C(9)-H(9)	106.6
C(11)-C(9)-H(9)	106.6
C(10)-C(9)-H(9)	106.6
C(9)-C(10)-H(10A)	109.5
C(9)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(9)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(9)-C(11)-H(11A)	109.5
C(9)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(9)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
N(4)-C(12)-C(8)	110.30(13)
N(4)-C(12)-C(13)	113.64(14)
C(8)-C(12)-C(13)	107.13(13)
N(4)-C(12)-H(12)	108.6
C(8)-C(12)-H(12)	108.6
C(13)-C(12)-H(12)	108.6
C(18)-C(13)-C(14)	119.25(16)
C(18)-C(13)-C(12)	121.37(15)
C(14)-C(13)-C(12)	119.30(15)
C(15)-C(14)-C(13)	120.26(16)
C(15)-C(14)-H(14)	119.9
C(13)-C(14)-H(14)	119.9
C(14)-C(15)-C(16)	120.10(17)
C(14)-C(15)-H(15)	120.0

C(16)-C(15)-H(15)	120.0	C(24)-C(23)-C(22)	122.28(17)
C(17)-C(16)-C(15)	119.98(16)	C(24)-C(23)-H(23)	118.9
C(17)-C(16)-H(16)	120.0	C(22)-C(23)-H(23)	118.9
C(15)-C(16)-H(16)	120.0	C(23)-C(24)-C(19)	120.24(16)
C(16)-C(17)-C(18)	119.91(17)	C(23)-C(24)-H(24)	119.9
C(16)-C(17)-H(17)	120.0	C(19)-C(24)-H(24)	119.9
C(18)-C(17)-H(17)	120.0	C(22)-C(25)-H(25A)	109.5
C(13)-C(18)-C(17)	120.46(17)	C(22)-C(25)-H(25B)	109.5
C(13)-C(18)-H(18)	119.8	H(25A)-C(25)-H(25B)	109.5
C(17)-C(18)-H(18)	119.8	C(22)-C(25)-H(25C)	109.5
N(4)-C(19)-C(20)	119.67(16)	H(25A)-C(25)-H(25C)	109.5
N(4)-C(19)-C(24)	122.39(16)	H(25B)-C(25)-H(25C)	109.5
C(20)-C(19)-C(24)	117.91(16)	O(1)-N(1)-O(2)	122.34(16)
C(21)-C(20)-C(19)	120.81(17)	O(1)-N(1)-C(4)	119.18(16)
C(21)-C(20)-H(20)	119.6	O(2)-N(1)-C(4)	118.48(16)
C(19)-C(20)-H(20)	119.6	N(3)-N(2)-C(1)	120.16(15)
C(20)-C(21)-C(22)	121.81(16)	N(3)-N(2)-H(2A)	119.9
C(20)-C(21)-H(21)	119.1	C(1)-N(2)-H(2A)	119.9
C(22)-C(21)-H(21)	119.1	C(8)-N(3)-N(2)	117.54(15)
C(23)-C(22)-C(21)	116.96(17)	C(19)-N(4)-C(12)	121.80(14)
C(23)-C(22)-C(25)	121.17(18)	C(19)-N(4)-H(4)	119.1
C(21)-C(22)-C(25)	121.83(17)	C(12)-N(4)-H(4)	119.1

Symmetry transformations used to generate equivalent atoms:
-none-

Table S4. Anisotropic displacement parameters ($Å^2$x 10^3). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U11	U22	U33	U23	U13	U12
C(1)	22(1)	19(1)	13(1)	0(1)	2(1)	2(1)
C(2)	22(1)	19(1)	19(1)	0(1)	0(1)	-1(1)
C(3)	22(1)	24(1)	20(1)	-4(1)	-2(1)	-1(1)
C(4)	23(1)	23(1)	16(1)	1(1)	0(1)	7(1)
C(5)	26(1)	20(1)	17(1)	2(1)	4(1)	0(1)
C(6)	22(1)	19(1)	18(1)	1(1)	2(1)	-1(1)
C(7)	25(1)	22(1)	30(1)	6(1)	-4(1)	-4(1)
C(8)	19(1)	18(1)	15(1)	1(1)	2(1)	0(1)
C(9)	21(1)	20(1)	23(1)	4(1)	-1(1)	-4(1)
C(10)	30(1)	26(1)	26(1)	-2(1)	-5(1)	-6(1)
C(11)	20(1)	30(1)	35(1)	9(1)	-4(1)	0(1)
C(12)	19(1)	15(1)	19(1)	1(1)	-1(1)	-1(1)
C(13)	20(1)	14(1)	19(1)	0(1)	-1(1)	-5(1)
C(14)	19(1)	20(1)	24(1)	0(1)	-2(1)	-2(1)
C(15)	21(1)	25(1)	31(1)	-6(1)	4(1)	-2(1)
C(16)	29(1)	28(1)	21(1)	-7(1)	5(1)	-9(1)
C(17)	29(1)	23(1)	19(1)	2(1)	-3(1)	-8(1)
C(18)	23(1)	15(1)	22(1)	0(1)	-3(1)	-3(1)
C(19)	21(1)	17(1)	17(1)	-3(1)	4(1)	-1(1)
C(20)	23(1)	25(1)	16(1)	-2(1)	0(1)	0(1)
C(21)	22(1)	27(1)	20(1)	-9(1)	2(1)	-4(1)
C(22)	26(1)	21(1)	24(1)	-6(1)	8(1)	-5(1)
C(23)	26(1)	18(1)	24(1)	0(1)	4(1)	2(1)
C(24)	20(1)	19(1)	21(1)	-2(1)	-1(1)	0(1)
C(25)	37(1)	24(1)	36(1)	-4(1)	8(1)	-11(1)
N(1)	26(1)	26(1)	23(1)	1(1)	-1(1)	6(1)
N(2)	21(1)	17(1)	22(1)	3(1)	-4(1)	-4(1)
N(3)	20(1)	16(1)	18(1)	1(1)	1(1)	-1(1)
N(4)	26(1)	18(1)	18(1)	2(1)	-6(1)	-5(1)
O(1)	34(1)	35(1)	50(1)	2(1)	-21(1)	5(1)
O(2)	32(1)	25(1)	32(1)	10(1)	2(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3)

	x	y	z	U(eq)
H(2)	7614	3726	2029	24
H(3)	9234	2422	2548	26
H(5)	5893	-594	2494	25
H(7A)	3472	-413	2042	39
H(7B)	3659	462	1556	39
H(7C)	2756	1087	2020	39
H(9)	2341	3727	1192	25
H(10A)	3824	3895	252	40
H(10B)	2394	2878	400	40
H(10C)	4168	2710	634	40
H(11A)	1324	5926	1045	43
H(11B)	600	4838	673	43
H(11C)	2010	5845	501	43
H(12)	4016	6919	984	21
H(14)	7642	4991	711	25
H(15)	8652	4550	-67	31
H(16)	7301	5392	-752	31
H(17)	4984	6733	-656	29
H(18)	3991	7201	123	24
H(20)	8689	7772	1781	26
H(21)	9960	9839	1690	28
H(23)	6677	10899	671	27
H(24)	5384	8832	753	24
H(25A)	10021	11861	806	49
H(25B)	9989	12125	1381	49
H(25C)	8516	12639	1047	49
H(2A)	3994	2645	1489	24
H(4)	6330	6386	1622	25