

Synthesis of Cyclic Guanidines Bearing *N*-Arylsulfonyl and *N*-Cyano Protecting Groups via Pd-Catalyzed Alkene Carboamination Reactions

Luke J. Peterson, Jingyi Luo, and John P. Wolfe*

Department of Chemistry, University of Michigan, 930 N. University Avenue, Ann Arbor, Michigan 48109-1055

Supporting Information

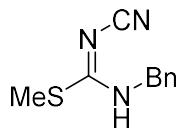
Experimental procedures and characterization data for new compounds in Tables 1-3, Scheme 2, and Equations 4-8.

Table of Contents

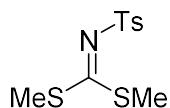
General Considerations	S1
Preparation and Characterization of Substrates	S2
Preparation and Characterization of Products	S16
Deuterium Labeling Studies	S36
Computational Details	S42
References	S51
Copies of ^1H and ^{13}C NMR Spectra	S52

General: All reactions were carried out under a nitrogen atmosphere in flame-dried glassware. Tris(dibenzylideneacetone)dipalladium(0) and palladium(II) acetate were purchased from Strem Chemical Co. and used without purification, and C-Phos and X-Phos were purchased from Sigma-Aldrich Co. and was used without further purification. Aryl triflates were prepared according to a procedure published by Frantz and coworkers,^[1] except the products were purified by column chromatography. Bulk quantities of lithium *tert*-butoxide and sodium *tert*-butoxide were stored in nitrogen-filled glove box and small amounts were removed shortly before use. Toluene, THF, dichloromethane and diethyl ether were purified using a GlassContour solvent purification system. Structural and stereochemical assignments were made on the basis of 2-D COSY, and NOESY experiments. Ratios of diastereomers were determined by ^1H NMR analysis. Yields refer to isolated yields of compounds estimated to be $\geq 95\%$ pure as determined by ^1H NMR analysis unless otherwise noted.

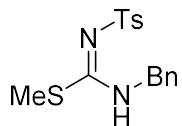
Preparation and Characterization of Substrates



Methyl N-benzyl-N'-cyanocarbamimidothioate (S1). A flame dried flask was cooled under a stream of nitrogen and charged with dimethyl cyanocarbonimidodithioate (2 g, 13.6 mmol) and ethanol (40 mL). Benzylamine (2.2 mL, 20.6 mmol) was then added via syringe, and the solution was heated to reflux with stirring for 2 h. The solution was then cooled to rt, a stream of nitrogen was blown over the solution for 20 min, and then the solution was placed in the freezer overnight. The white precipitate that had formed was then isolated via filtration using a fritted glass funnel to yield 2.61 g (94%) of the desired product as a white solid. ^1H NMR (400 MHz, CDCl_3) δ 7.41–7.23 (m, 5 H), 6.60 (s, br, 1 H), 4.50 (s, br, 2 H), 2.48 (s, br, 3 H).

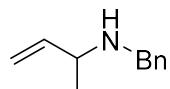


Dimethyl tosylcarbonimidodithioate (S2). A flame dried flask was cooled under a stream of nitrogen and charged with 4-methylbenzenesulfonamide (25.68 g, 150 mmol), carbon disulfide (14.2 mL, 240 mmol), and DMF (200 mL). The mixture was cooled to 0 °C in an ice bath, and then a solution of KOH (19.9 g, 354 mmol) in water (60 mL) was added dropwise at a rate sufficiently slow that the reaction temperature remained below 10 °C at all times. The reaction mixture was then stirred at 0 °C for 30 min, and then methyl iodide (21.7 mL, 348 mmol) was added dropwise at a rate sufficiently slow that the reaction temperature remained below 10 °C at all times. The reaction mixture was then warmed to rt and stirred for 30 min. Water was then added (150 mL), and the white precipitate that had formed was then isolated via filtration using a fritted glass funnel. The white solid was washed with water followed by ethanol, then was dried *in vacuo* to afford 31.27 g (75%) of the title compound as a white solid. ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, J = 8.0 Hz, 2 H), 7.30 (d, J = 8.1 Hz, 2 H), 2.53 (s, 6 H), 2.43 (s, 3 H).

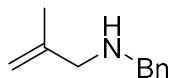


Methyl N-benzyl-N'-tosylcarbamimidothioate (S3). A flame dried flask was cooled under a stream of nitrogen and charged with dimethyl tosylcarbonimidodithioate (**S2**) (2.00 g, 7.26

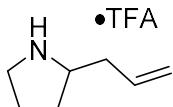
mmol) and ethanol (40 mL). Benzylamine (1.2 mL, 10.89 mmol) was then added slowly, and the reaction was then heated to reflux with stirring for 2 h. The solution was then cooled to rt, a stream of nitrogen was blown over the solution for 20 min, and then the solution was placed in the freezer overnight. The white precipitate that had formed was then isolated via filtration using a fritted glass funnel to yield 2.19 g (90%) of the title compound as a white solid. ^1H NMR (400 MHz, CDCl_3) δ 8.50 (s, br, 1 H), 7.79 (d, J = 8.0 Hz, 2 H), 7.41–7.31 (m, 3 H), 7.31–7.17 (m, 4 H), 4.48 (d, J = 5.9 Hz, 2 H), 2.42 (s, 3 H), 2.38 (s, 3 H).



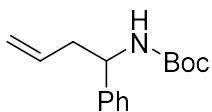
N-Benzylbut-3-en-2-ylamine (S4). A flame dried flask was cooled under a stream of nitrogen and charged with *N*-(but-3-en-2-yl)benzamide^[2] (1.32 g, 7.53 mmol) in diethyl ether (30 mL). The solution was cooled on an ice bath, and a solution of LiAlH_4 (30 mL, 30 mmol, 1 M in THF) was added slowly. The reaction mixture was then heated to reflux with stirring overnight. The mixture was then cooled in an ice bath, and water (7.53 mL) was slowly added followed by 1 M NaOH (7.5 mL). The mixture was then transferred to a separatory funnel and extracted with diethyl ether (3 x 10 mL). The organic layers were combined, dried, filtered, and concentrated *in vacuo* to afford 1.2 g (99%) of the title compound as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.38–7.29 (m, 4 H), 7.28–7.21 (m, 1 H), 5.80–5.64 (m, 1 H), 5.19–5.02 (m, 2 H), 3.80 (d, J = 13.1 Hz, 1 H), 3.68 (d, J = 13.1 Hz, 1 H), 3.28–3.16 (m, 1 H), 1.50 (s, br, 1 H), 1.18 (d, J = 6.5 Hz, 3 H).



N-Benzyl-2-methylprop-2-en-1-ylamine (S5). A flame dried flask was cooled under a stream of nitrogen and charged with benzylamine (10.9 mL, 100.0 mmol) and potassium carbonate (4.15 g, 30.0 mmol), then cooled on an ice bath. 3-bromo-2-methylprop-1-ene (3.38 g, 25.0 mmol) was then added slowly, and the resulting mixture was heated to 65 °C with stirring overnight. The reaction mixture was then cooled to rt and filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was then purified via flash column chromatography on silica gel (ethyl acetate:hexanes = 1:4) to afford 3.00 g (75%) of the title compound as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.40–7.30 (m, 4 H), 7.30–7.21 (m, 1 H), 4.94–4.82 (m, 2 H), 3.78 (s, 2 H), 3.20 (s, 2 H), 1.78 (s, 3 H).

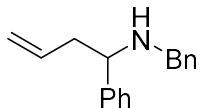


2-Allylpyrrolidinium trifluoroacetate (S6). This compound was synthesized by modifying procedure by published by Dieter, et al.^[3] A flame dried flask was cooled under a stream of nitrogen and charged with *N*-Boc pyrrolidine (3.40 g, 20.0 mmol), TMEDA (3.6 mL, 24.0 mmol), and diethyl ether (80 mL). The solution was cooled to $-78\text{ }^{\circ}\text{C}$ and *s*-BuLi (20 mL, 1.4 M in cyclohexane) was added slowly dropwise. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 2 h, then a solution of zinc chloride (3.81 g, 28 mmol) in THF (30 mL) was added slowly. The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 1.5 h, and then a solution of copper cyanide (2.15 g, 24.0 mmol) and lithium chloride (1.7 g, 40.0 mmol) in THF (60 mL) was added slowly. The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 1.5 h, and then allyl bromide (5.2 mL, 60 mmol) was added slowly. The cooling bath was removed and the mixture was allowed to stir at rt overnight. The reaction was then quenched with aqueous ammonium hydroxide (60 mL), and the mixture was stirred at rt for 5 h. The mixture was transferred to a separatory funnel, the layers were separated, and the aqueous layer was extracted with diethyl ether (2 x 60 mL). The combined organic layers were washed with brine, dried, filtered, and concentrated *in vacuo*. The crude product was purified via flash chromatography on silica gel to afford *N*-Boc 2-allylpyrrolidine. This material was then dissolved in dichloromethane (23 mL) and the resulting solution was cooled to 0 $^{\circ}\text{C}$ in an ice bath. Trifluoroacetic acid (22.5 mL, 293 mmol) was then added slowly, and the mixture was stirred at rt for 3 h. The mixture was then concentrated and residual trifluoroacetic acid was then removed by adding toluene (10 mL) and then concentrating the resulting solution (this was repeated four times) to afford 3.2 g (97%) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 8.88 (s, br, 2 H), 5.82–5.68 (m, 1 H), 5.29–5.17 (m, 2 H), 3.69–3.61 (m, 1 H), 3.41–3.31 (m, 2 H), 2.64–2.40 (m, 2 H), 2.29–1.96 (m, 3 H), 1.82–1.74 (m, 1 H).

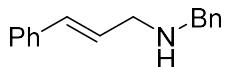


tert-Butyl (1-phenylbut-3-en-1-yl)carbamate (S7). The title compound was prepared by modifying a procedure published by Veenstra *et al.*^[4] A flame dried flask was cooled under a stream of nitrogen and charged with dichloromethane (50 mL), benzaldehyde (2.00 g, 18.78 mmol), allyl trimethylsilane (3.0 mL, 18.78 mmol), and *tert*-butyl carbamate (2.20 g, 18.78 mmol). The solution was then cooled to 0 $^{\circ}\text{C}$ in an ice bath, and $\text{BF}_3\cdot\text{EtO}_2$ (1.40 mL, 11.27

mmol) was added slowly. The resulting mixture was stirred at 0 °C for 30 min, and was then warmed to rt and stirred for 30 min. The reaction was then quenched with saturated aqueous NaHCO₃ (30 mL), and transferred to a separatory funnel. The layers were separated, the aqueous layer was extracted with dichloromethane (25 mL), and then the combined organic layers were dried, filtered, and concentrated *in vacuo* to afford a white solid. The crude product was purified via flash column chromatography on silica gel (ethyl acetate:hexanes = 1:4) to afford 1.66 g (36%) of the title compound as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.40–7.18 (m, 5 H), 5.73–5.62 (m, 1 H), 5.19–5.02 (m, 2 H), 4.86 (s, br, 1 H), 2.52 (s, br, 2 H), 1.41 (s, br, 9 H).

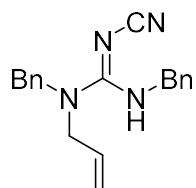


N-Benzyl-1-phenylbut-3-en-1-ylamine (S8). A flame dried flask was cooled under a stream of nitrogen and charged with *tert*-butyl (1-phenylbut-3-en-1-yl)carbamate (**S7**) (1.66 g, 6.7 mmol) and dichloromethane (10 mL). The resulting solution was cooled to 0 °C then trifluoroacetic acid (10.3 mL, 134 mmol) was added slowly. The mixture was warmed to rt and stirred for 3 h. The mixture was then concentrated and residual trifluoroacetic acid was then removed by adding toluene (10 mL) and then concentrating the resulting solution (this was repeated three times). The resulting crude material was dissolved in THF (10 mL), then potassium carbonate (1.85 g, 13.4 mmol) and benzyl bromide (0.8 mL, 6.7 mmol) were added. The resulting mixture was heated to 50 °C overnight, then was cooled to rt and filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate:hexanes = 1:4) to afford 0.853 g (54%) of the title compound as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.40–7.13 (m, 10 H), 5.79–5.63 (m, 1 H), 5.14–5.01 (m, 2 H), 3.73–3.59 (m, 2 H), 3.51 (d, *J* = 13.3 Hz, 1 H), 2.48–2.33 (m, 2 H), 1.73 (s, br, 1 H).

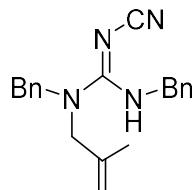


(E)-N-Benzyl-3-phenylprop-2-en-1-ylamine (S9). A flame dried flask was cooled under a stream of nitrogen and charged with benzylamine (8.7 mL, 80.0 mmol) and potassium carbonate (3.32 g, 24.0 mmol). The mixture was cooled to 0 °C and (*E*)-(3-bromoprop-1-en-1-yl)benzene (3.93 g, 20.0 mmol) was then added slowly. The mixture was then warmed to rt and

stirred overnight. The mixture was filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate:hexanes = 1:4) to afford 1.30 g (38%) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.48–7.16 (m, 10 H), 6.54 (d, J = 16.0 Hz, 1 H), 6.38–6.28 (m, 2 H), 3.85 (s, 3 H), 3.45 (dd, J = 6.3, 1.5 Hz, 2 H).

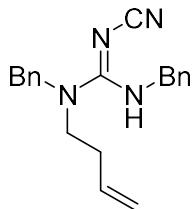


1-Allyl-1,3-dibenzyl-2-cyanoguanidine (6a). A round bottom flask was charged with methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.93 g, 4.53 mmol), ethanol (45 mL), and mercuric oxide (1.47 g, 6.80 mmol), then purged with nitrogen. Triethylamine (2.5 mL, 18.12 mmol) was added followed by *N*-benzylprop-2-en-1-ylamine (1.00 g, 6.80 mmol). The reaction mixture was then stirred at rt for 72 h. The mixture was filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate:hexanes 4:6) to yield 1.00 g (72%) of the title compound as a clear, viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.39–7.27 (m, 6 H), 7.23–7.18 (m, 4 H), 5.81–5.71 (m, 1 H), 5.28–5.08 (m, 3 H), 4.72 (d, J = 5.3 Hz, 2 H), 4.58 (s, 2 H), 3.94 (dt, J = 5.6, 1.6 Hz, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.0, 137.0, 135.8, 132.1, 129.0, 128.9, 28.1, 127.7, 127.3, 118.5, 117.2, 52.2, 51.5, 47.7; IR (film) 3255, 2162, 1536 cm^{-1} ; MS (ESI+) 305.1758 (305.1761 calcd for $\text{C}_{19}\text{H}_{20}\text{N}_4$, $\text{M} + \text{H}^+$).

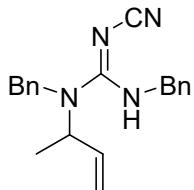


1,3-Dibenzyl-2-cyano-1-(2-methylallyl)guanidine (6b). The title compound was prepared from methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.825 g, 4.0 mmol), ethanol (40 mL), mercuric oxide (1.30 g, 6.0 mmol), triethylamine (2.2 mL, 16.0 mmol), and *N*-benzyl-2-methylprop-2-en-1-ylamine (**S5**) (0.972 g, 6.0 mmol) using a procedure analogous to that described above for the synthesis of **6a**. This procedure afforded 0.589 g (46%) of the title compound as a clear, viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.38–7.26 (m, 6 H), 7.24–7.20

(m, 4 H), 5.28 (t, J = 5.4 Hz, 1 H), 4.94 (s, 1 H), 4.79 (s, 1 H), 4.74 (d, J = 5.4 Hz, 2 H), 4.60 (s, 2 H), 3.80 (s, 2 H), 1.65 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.2, 139.6, 137.1, 135.9, 128.9, 128.1, 128.0, 127.7, 127.5, 117.2, 112.9, 54.2, 52.5, 47.7, 19.8; IR (film) 3268, 2164, 1539 cm^{-1} ; MS (ESI+) 319.1915 (319.1917 calcd for $\text{C}_{20}\text{H}_{22}\text{N}_4$, $\text{M} + \text{H}^+$).

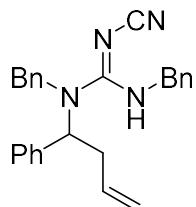


1,3-Dibenzyl-1-(but-3-en-1-yl)-2-cyanoguanidine (6c). The title compound was prepared from methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.75 g, 3.65 mol), ethanol (35 mL), mercuric oxide (1.187 g, 5.5 mmol), triethylamine (2.0 mL, 14.6 mmol) and *N*-benzylbut-3-en-1-ylamine (1.147 g, 7.1 mmol) using a procedure analogous to that described above for the synthesis of **6a**. This procedure afforded 0.82 g (71%) of the title compound as a pale yellow solid, m.p. 92–93 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.39–7.22 (m, 6 H), 7.18–7.07 (m, 4 H), 5.73 (ddt, J = 17.1, 10.2, 6.9 Hz, 1 H), 5.13–4.96 (m, 3 H), 4.67 (d, J = 5.3 Hz, 2 H), 4.51 (s, 2 H), 3.48 (t, J = 7.2 Hz, 2 H), 2.39–2.32 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.8, 137.1, 135.6, 134.3, 129.2, 128.9, 128.1, 128.0, 127.7, 126.7, 117.9, 52.7, 49.5, 47.7, 32.4; IR (film) 3256, 2161, 1536 cm^{-1} ; MS (ESI+) 319.1919 (319.1917 calcd for $\text{C}_{20}\text{H}_{22}\text{N}_4$, $\text{M} + \text{H}^+$).

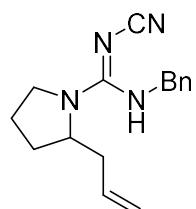


1,3-Dibenzyl-1-(but-3-en-2-yl)-2-cyanoguanidine (6d). The title compound was prepared from methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.888 g, 4.53 mmol), ethanol (40 mL), mercuric oxide (1.40 g, 6.5 mmol), triethylamine (2.4 mL, 17.3 mmol) and *N*-benzylbut-3-en-2-ylamine (**S4**) (0.837 g, 5.2 mmol) using a procedure analogous to that described above for the synthesis of **6a**. This procedure afforded 0.316 g (23%) of an off white solid, m.p. 104–105 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.27 (m, 3 H), 7.26–7.19 (m, 3 H), 7.18–7.16 (m, 2 H), 6.97–6.95 (m, 2 H), 5.92–5.86 (m, 1 H), 5.25–5.15 (m, 2 H), 5.11–5.09 (m, 1 H), 4.97 (d, J = 5.3 Hz, 1 H), 4.70–4.58 (m, 2 H), 4.46–4.28 (m, 2 H), 1.31 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.7, 137.5, 136.6, 136.3, 129.2, 128.8, 128.0, 127.9, 127.7, 126.4, 117.3, 117.2,

55.1, 48.4, 47.8, 16.6; IR (film) 3265, 2160, 1533 cm^{-1} ; MS (ESI+) 319.1920 (319.1917 calcd for $\text{C}_{20}\text{H}_{22}\text{N}_4$, $\text{M} + \text{H}^+$).

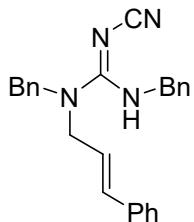


1,3-Dibenzyl-2-cyano-1-(1-phenylbut-3-en-1-yl)guanidine (6e). The title compound was prepared from methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.616 g, 3.0 mmol), ethanol (30 mL), mercuric oxide (0.975 g, 4.5 mmol), triethylamine (1.7 mL, 12 mmol), and *N*-benzyl-1-phenylbut-3-en-1-ylamine (**S8**) (0.853 g, 3.6 mmol) using a procedure analogous to that described above for the synthesis of **6a**. This procedure afforded 0.40 g (34%) of the title compound as a clear, viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.45–7.27 (m, 5 H), 7.25–7.13 (m, 6 H), 6.85 (d, J = 6.8 Hz, 2 H), 6.78 (d, J = 6.4 Hz, 2 H), 6.03 (t, J = 7.8 Hz, 1 H), 5.92–5.82 (m, 1 H), 5.24–5.08 (m, 2 H), 4.75 (t, J = 4.9 Hz, 1 H), 4.71–4.52 (m, 2 H), 4.32 (d, J = 16.9 Hz, 1 H), 4.16 (d, J = 17.0 Hz, 1 H), 2.76 (t, J = 6.8 Hz, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.8, 138.3, 136.4, 135.6, 134.2, 129.2, 128.9, 128.8, 128.3, 128.2, 128.1, 127.9, 127.8, 126.5, 118.3, 117.3, 59.9, 47.9, 47.8, 35.3; IR (film) 3263, 2163, 1541 cm^{-1} ; MS (ESI+) 395.2229 (395.2230 calcd for $\text{C}_{26}\text{H}_{26}\text{N}_4$, $\text{M} + \text{H}^+$).

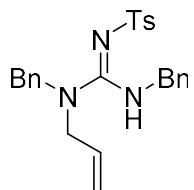


2-Allyl-*N*-benzyl-*N'*-cyanopyrrolidine-1-carboximidamide (6f). The title compound was prepared from methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (1.112 g, 5.4 mmol), ethanol (55 mL), mercuric oxide (1.75 g, 8.1 mmol), triethylamine (3.8 mL, 27 mmol), and 2-allylpyrrolidinium trifluoroacetate (**S6**) (1.46 g, 6.5 mmol) using a procedure analogous to that described above for the synthesis of **6a**. This procedure afforded 0.628 g (43%) of the title compound as a clear, viscous oil. ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.24 (m, 5 H), 5.78–5.64 (m, 1 H), 5.16 (t, J = 5.6 Hz, 1 H), 5.10–5.00 (m, 2 H), 4.68–4.51 (m, 2 H), 4.28–4.24 (m, 1 H),

3.51–3.43 (m, 2 H), 2.50–2.46 (m, 1 H), 2.16 (dt, J = 14.1, 8.3 Hz, 1 H), 2.02–1.82 (m, 3 H), 1.79–1.74 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.0, 137.8, 133.7, 128.8, 127.9, 127.8, 118.3, 117.9, 58.1, 48.4, 46.9, 37.8, 29.6, 23.4; IR (film) 3252, 2156, 1527 cm^{-1} ; MS (ESI+) 269.1760 (269.1761 calcd for $\text{C}_{16}\text{H}_{20}\text{N}_4$, $\text{M} + \text{H}^+$).

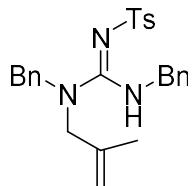


1,3-dibenzyl-1-cinnamyl-2-cyanoguanidine (6g). The title compound was prepared from methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.60 g, 2.90 mmol), ethanol (30 mL), mercuric oxide (0.94 g, 4.35 mmol), triethylamine (1.6 mL, 11.60 mmol), and (*E*)-*N*-benzyl-3-phenylprop-2-en-1-ylamine (**S9**) (0.61 g, 3.5 mmol) using a procedure analogous to that described above for the synthesis of **6a**. This procedure afforded 0.438 g (40%) of the title compound as a pale yellow solid, m.p. 74–77 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.40–7.05 (m, 15 H), 6.38 (d, J = 16.4 Hz, 1 H), 6.08 (dt, J = 16.0, 6.1 Hz, 1 H), 5.38 (t, J = 5.4 Hz, 1 H), 4.70 (d, J = 5.3 Hz, 2 H), 4.60 (s, 2 H), 4.09 (d, J = 6.4 Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.0, 137.1, 135.8, 135.7, 129.0, 128.9, 128.7, 128.2, 128.1, 128.0, 127.8, 127.3, 126.5, 123.1, 117.3, 52.2, 51.2, 47.6; IR (film) 3257, 2164, 1542 cm^{-1} ; MS (ESI+) 381.2072 (381.2074 calcd for $\text{C}_{25}\text{H}_{24}\text{N}_4$, $\text{M} + \text{H}^+$).

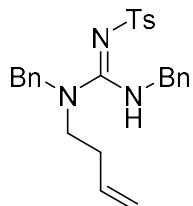


***N*-{[Allyl(benzyl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (7a).** The title compound was prepared from methyl *N*-benzyl-*N'*-tosylcarbamimidothioate (**S3**) (1.06 g, 3.17 mmol), ethanol (30 mL), mercuric oxide (1.03 g, 4.75 mmol), triethylamine (1.8 mL, 12.68 mmol), and *N*-benzylprop-2-en-1-ylamine (0.70 g, 4.75 mmol) using a procedure analogous to that described above for the synthesis of **6a** except with a reaction time of 48 h. This procedure afforded 1.06 g (77%) of the title compound as a white solid, m.p. 91–92 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.62 (d, J = 8.0 Hz, 2 H), 7.34–7.22 (m, 6 H), 7.20–7.08 (m, 6 H), 6.99 (t, J = 5.7 Hz, 1 H), 5.74 (ddt, J = 16.4, 9.8, 5.8 Hz, 1 H), 5.24–5.05 (m, 2 H), 4.48 (s, 2 H), 4.39

(d, $J = 5.7$ Hz, 2 H), 3.82 (d, $J = 5.7$ Hz, 2 H), 2.39 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.9, 141.7, 141.0, 136.9, 136.4, 132.4, 129.1, 128.9, 128.7, 128.0, 127.6, 127.4, 126.1, 118.9, 51.9, 51.8, 49.7, 21.4; IR (film) 3320, 1563 cm^{-1} ; MS (ESI+) 434.1894 (434.1897 calcd for $\text{C}_{25}\text{H}_{27}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

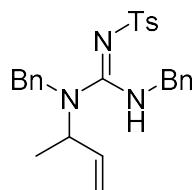


***N*-{[Benzyl(2-methylallyl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (7b).** The title compound was prepared from methyl *N*-benzyl-*N*'-tosylcarbamimidothioate (**S3**) (1.30 g, 3.88 mmol), ethanol (30 mL), mercuric oxide (1.26 g, 5.82 mmol), triethylamine (2.2 mL, 15.70 mmol), and *N*-benzyl-2-methylprop-2-en-1-ylamine (**S5**) (0.75 g, 4.65 mmol) using a procedure analogous to that described above for the synthesis of **6a** except with a reaction time of 48 h. This procedure afforded 0.78 g (45%) of the title compound as a white solid, m.p. 115–117 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.62 (d, $J = 8.0$ Hz, 2 H), 7.35–7.21 (m, 6 H), 7.19–7.05 (m, 6 H), 6.98 (t, $J = 5.8$ Hz, 1 H), 4.92 (s, 1 H), 4.79 (s, 1 H), 4.48 (s, 2 H), 4.42 (d, $J = 5.8$ Hz, 2 H), 3.71 (s, 2 H), 2.39 (s, 3 H), 1.57 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) 160.1, 141.6, 141.1, 140.0, 137.0, 136.5, 129.1, 128.9, 128.7, 128.0, 127.8, 127.6, 127.3, 126.1, 113.4, 54.5, 51.8, 49.7, 21.4, 20.0; IR (film) 3316, 1559 cm^{-1} ; MS (ESI+) 448.2048 (448.2053 calcd for $\text{C}_{26}\text{H}_{29}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

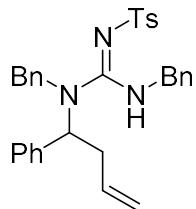


***N*-{[Benzyl(but-3-en-1-yl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (7c).** The title compound was prepared from methyl *N*-benzyl-*N*'-tosylcarbamimidothioate (**S3**) (1.13 g, 3.37 mmol), ethanol (30 mL), mercuric oxide (1.10 g, 5.09 mmol), triethylamine (1.9 mL, 13.84 mmol) and *N*-benzylbut-3-en-1-ylamine (0.77 g, 5.09 mmol) using a procedure analogous to that described above for the synthesis of **6a** except with a reaction time of 48 h. This procedure afforded 1.39 g (91%) of the title compound as a white solid, m.p. 123–124 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.60 (d, $J = 8.0$ Hz, 2 H), 7.36–7.22 (m, 7 H), 7.21–7.09 (m, 7 H), 7.06

(t, $J = 5.7$ Hz, 1 H), 5.55 (ddt, $J = 17.1, 10.2, 6.8$ Hz, 1 H), 5.01–4.86 (m, 2 H), 4.47 (s, 2 H), 4.36 (d, $J = 5.7$ Hz, 2 H), 3.32–3.20 (m, 2 H), 2.39 (s, 3 H), 2.23–2.19 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3) 160.1, 141.7, 140.9, 136.8, 136.3, 134.5, 129.1, 128.9, 128.8, 128.0, 127.7, 127.4, 127.3, 126.1, 117.3, 53.0, 49.9, 48.5, 32.0, 21.4; IR (film) 3313, 1560 cm^{-1} ; MS (ESI+) 448.2049 (448.2053 calcd for $\text{C}_{26}\text{H}_{29}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

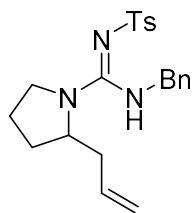


***N*-{[Benzyl(but-3-en-2-yl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (7d).** The title compound was prepared from methyl *N*-benzyl-*N'*-tosylcarbamimidothioate (**S3**) (1.018 g, 3.05 mmol), ethanol (30 mL), mercuric oxide (0.991 g, 4.58 mmol), triethyl amine (1.7 mL, 12.2 mmol), and *N*-benzylbut-3-en-2-ylamine (**S4**) (0.590 g, 3.66 mmol) using a procedure analogous to that described above for the synthesis of **6a** except with a reaction time of 48 h. This procedure afforded 1.21 g (89%) of the title compound as an off white solid, m.p. 69–71 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.33–7.27 (m, 2 H), 7.27–7.11 (m, 6 H), 7.10–7.02 (m, 2 H), 6.97 (dd, $J = 7.9, 1.9$ Hz, 4 H), 6.87 (t, $J = 5.7$ Hz, 1 H), 5.95–5.86 (m, 1 H), 5.24–5.11 (m, 2 H), 4.55–4.50 (m, 1 H), 4.38 (t, $J = 5.5$ Hz, 2 H), 4.31 (s, 2 H), 2.33 (s, 3 H), 1.30 (d, $J = 6.8$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.8, 141.4, 140.6, 138.0, 137.5, 136.7, 129.0, 128.8, 128.5, 127.9, 127.5, 127.0, 126.8, 126.0, 117.3, 57.4, 49.6, 47.4, 21.4, 16.8; IR (film) 3320, 1557 cm^{-1} ; MS (ESI+) 448.2056 (448.2053 calcd for $\text{C}_{26}\text{H}_{29}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

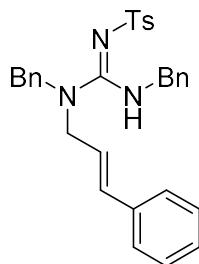


***N*-{[Benzyl(1-phenylbut-3-en-1-yl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (7e).** The title compound was prepared from methyl *N*-benzyl-*N'*-tosylcarbamimidothioate (**S3**) (1.390 g, 3.9 mmol), ethanol (39 mL), mercuric oxide (1.26 g, 5.8 mmol), triethylamine (2.1 mL, 15 mmol), and *N*-benzyl-1-phenylbut-3-en-1-ylamine (**S8**) (1.100 g, 4.6 mmol) using a procedure analogous to that described above for the synthesis of **6a**.

except with a reaction time of 96 h. This procedure afforded 1.46 g (71%) of the title compound as a white solid, m.p. 117–118 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.56–7.49 (m, 2 H), 7.33–7.17 (m, 8 H), 7.17–7.05 (m, 5 H), 7.00–6.93 (m, 2 H), 6.92–6.85 (m, 2 H), 6.48 (t, J = 5.4 Hz, 1 H), 5.58 (ddt, J = 16.9, 10.3, 6.7 Hz, 1 H), 5.35 (t, J = 7.7 Hz, 1 H), 5.08–4.94 (m, 2 H), 4.53–4.40 (m, 2 H), 4.30 (d, J = 16.3 Hz, 1 H), 4.12 (d, J = 16.3 Hz, 1 H), 2.81–2.62 (m, 2 H), 2.35 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.1, 141.4, 141.3, 138.0, 136.8, 136.6, 129.0, 128.8, 128.7, 128.6, 128.2, 128.1, 127.9, 127.7, 127.3, 126.7, 126.0, 118.1, 61.9, 49.9, 48.1, 35.6, 21.4; IR (film) 3335, 1495 cm^{-1} ; MS (ESI+) 524.2367 (524.2366 calcd for $\text{C}_{32}\text{H}_{33}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

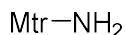


2-Allyl-N-benzyl-N'-tosylpyrrolidine-1-carboximidamide (7f). The title compound was prepared from methyl *N*-benzyl-*N'*-tosylcarbamimidothioate (**S3**) (1.60 g, 4.78 mmol), ethanol (40 mL), mercuric oxide (1.50 g, 6.92 mmol), triethylamine (3.3 mL, 23.42 mmol) and 2-allylpyrrolidinium trifluoroacetate (**S6**) (7.0 mmol) using a procedure analogous to that described above for the synthesis of **6a** except with a reaction time of 48 h. This procedure afforded 0.89 g (48%) of the title compound as a white solid, m.p. 76–78 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.66 (d, 8.0 Hz, 2 H), 7.38–7.28 (m, 3 H), 7.24–7.13 (m, 4 H), 5.44 (ddt, J = 17.3, 10.2, 7.2 Hz, 1 H), 4.87 (dd, J = 10.3, 2.1 Hz, 1 H), 4.74 (dd, J = 17.1, 1.6 Hz, 1 H), 4.36–4.18 (m, 3 H), 3.44–3.38 (m, 1 H), 3.36–3.30 (m, 1 H), 2.38 (s, 3 H), 2.20–2.08 (m, 1 H), 2.03–1.91 (m, 2 H), 1.88 (dtt, J = 12.2, 6.0, 2.7 Hz, 1 H), 1.73 (dtt, J = 12.0, 10.2, 7.3 Hz, 1 H), 1.57–1.49 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) 157.7, 141.7, 141.1, 137.1, 133.8, 129.1, 128.9, 128.0, 127.5, 126.2, 117.6, 58.4, 51.1, 49.0, 38.1, 29.6, 25.2, 21.4; IR (film) 3314, 1560 cm^{-1} ; MS (ESI+) 398.1892 (398.1897 calcd for $\text{C}_{22}\text{H}_{27}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

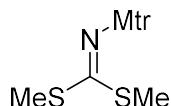


***N*-{[Benzyl(cinnamyl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (7g).**

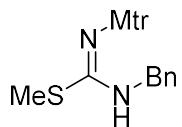
The title compound was prepared from methyl *N*-benzyl-*N'*-tosylcarbamimidothioate (**S3**) (0.65 g, 1.94 mmol), ethanol (30 mL), mercuric oxide (0.65 g, 3.00 mmol), triethylamine (1.1 mL, 7.95 mmol), and (E)-*N*-benzyl-3-phenylprop-2-en-1-ylamine (**S9**) (0.70 g, 3.14 mmol) using a procedure analogous to that described above for the synthesis of **6a** except with a reaction time of 48 h. This procedure afforded 0.35 g (33%) of the title compound as a white solid, m.p. 120–121 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.65 (d, *J* = 8.1 Hz, 2 H), 7.35–7.20 (m, 12 H), 7.17–7.11 (m, 5 H), 7.09 (t, *J* = 5.8 Hz, 1 H), 6.33 (d, *J* = 15.9 Hz, 1 H), 6.05 (dt, *J* = 15.9, 6.3 Hz, 1 H), 4.52 (s, 2 H), 4.41 (d, *J* = 5.8 Hz, 2 H), 3.98 (d, *J* = 6.3, 1.4 Hz, 2 H), 2.38 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) 160.0, 141.7, 141.0, 136.8, 136.3, 136.0, 134.0, 129.1, 128.9, 128.8, 128.6, 128.1, 128.1, 128.0, 127.7, 127.5, 127.4, 126.5, 126.1, 123.6, 52.2, 51.5, 49.8, 21.5; IR (film) 3314, 1564 cm⁻¹; MS (ESI+) 510.2205 (510.2210 calcd for C₃₁H₃₁N₃O₂S, M + H⁺).



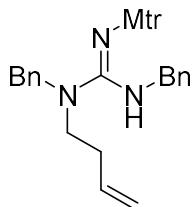
4-methoxy-2,3,6-trimethylbenzenesulfonamide (S10). A round bottom flask equipped was charged with ammonia in ethanol (10 mL, 20 mmol) and cooled on an ice bath. A solution of 4-methoxy-2,3,6-trimethylbenzenesulfonyl chloride (2.48 g, 10 mmol) in ethanol (10 mL) was added, followed by triethylamine (1.4 mL, 10 mmol). The reaction was allowed to warm to rt and stir for 6 hours. Concentration of the reaction mixture *in vacuo* afforded the crude product that was purified via flash column chromatography to yield 1.26 g (55%) of the desired product as a tan solid.



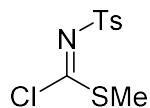
Dimethyl [(4-methoxy-2,3,6-trimethylphenyl)sulfonyl]carbonimidodithioate (S11). A flame dried flask was cooled under a stream of nitrogen and charged with 4-methoxy-2,3,6-trimethylbenzenesulfonamide (**S10**) (1.26 g, 5.5 mmol), carbon disulfide (0.5 mL, 8.8 mmol), and DMF (10 mL). The solution was then cooled on an ice bath. A solution of potassium hydroxide (0.73 g, 13 mmol) in water (5 mL) was added dropwise, and the reaction was stirred at 0 °C for 30 minutes. Iododomethane (0.8 mL, 13 mmol) was added dropwise, and then the reaction was allowed to warm to rt and stirred for 30 minutes. Water (10 mL) was then added, and a light yellow solid precipitated from solution. The solid was isolated to afford 1.1 g (60%) of the desired product.



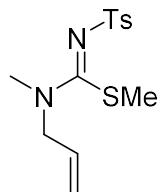
Methyl (E)-N-benzyl-N'-(4-methoxy-2,3,6-trimethylphenyl)sulfonyl]carbamimidothioate (S12). A flame dried flask was cooled under a stream of nitrogen and charged with Dimethyl {(4-methoxy-2,3,6-trimethylphenyl)sulfonyl}carbonimidodithioate (**S11**) (1.1 g, 3.3 mmol) in ethanol (20 mL). Benzylamine (0.55 mL, 4.95 mmol) was added slowly, and the reaction was then heated to reflux with stirring for 2 h. The solution was then cooled to rt, a stream of nitrogen was blown over the solution for 20 min, and then the solution was placed in the freezer overnight. The white precipitate that had formed was then isolated via filtration using a fritted glass funnel to yield 1.04 g (80%) of the title compound as a light tan solid.



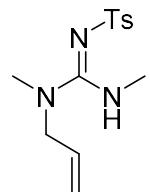
(E)-N-{[benzyl(but-3-en-1-yl)amino][benzylamino]methylene}-4-methoxy-2,3,6-trimethylbenzenesulfonamide (20). A round bottom flask was charged with Methyl (E)-N-benzyl-N'-(4-methoxy-2,3,6-trimethylphenyl)sulfonyl]carbamimidothioate (**S12**) (1.04 g, 2.65 mmol), ethanol (26 mL), and mercuric oxide (0.86 g, 3.97 mmol), then purged with nitrogen. Triethylamine (1.5 mL, 10.6 mmol) was added followed by *N*-benzylbut-3-en-1-ylamine (0.64 g, 3.97 mmol). The reaction mixture was then stirred at rt for 72 h. The mixture was filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate:hexanes = 3:7) to yield 0.62 g (46%) of the title compound as a light tan solid, m.p. 96–99 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.24 (m, 6 H), 7.18–7.13 (m, 2 H), 7.11–7.03 (m, 2 H), 7.00 (t, *J* = 6.0 Hz, 1 H), 6.50 (s, 1 H), 5.60–5.51 (m, 1 H), 4.98–4.90 (m, 2 H), 4.47 (s, 3 H), 4.34 (d, *J* = 6.0 Hz, 2 H), 3.84 (s, 3 H), 3.25–3.15 (m, 2 H), 2.59 (s, 3 H), 2.57 (s, 3 H), 2.24 (q, *J* = 7.3 Hz, 2 H), 2.11 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 160.1, 158.4, 138.6, 136.9, 136.7, 136.5, 134.5, 133.7, 128.8, 128.7, 127.9, 127.6, 127.3, 127.2, 124.7, 117.2, 111.7, 55.4, 52.6, 49.8, 48.2, 31.8, 24.0, 18.5, 11.9; IR (film) 3316, 1560, 1118 cm⁻¹; MS (ESI+) 506.2474 (506.2472 calcd for C₂₉H₃₅N₃O₃S, M + H⁺).



Methyl tosylcarbonochloridoimidothioate (S13). A flame dried flask was cooled under a stream of nitrogen and charged with dimethyl tosylcarbonimidodithioate (**S2**) (4.00 g, 14.4 mmol) and dichloromethane (50 mL). Sulfonyl chloride (2.4 mL, 28.8 mmol) was added dropwise, and the reaction was refluxed for 3 hours. After cooling to rt, the reaction mixture was concentrated, and the crude product was purified via flash column chromatography (EtOAc/Hexanes) to afford 2.63 g (69%) of the title compound. ^1H NMR (CDCl_3 , 400 MHz) δ 7.86 (d, J = 8.1 Hz, 2 H), 7.33 (d, J = 8.2 Hz, 2 H), 2.45 (s, 3 H), 2.43 (s, 3 H).



Methyl-*N*-allyl-*N*-methyl-*N'*-tosylcarbamimidothioate (S14). A flame dried flask was cooled under a stream of nitrogen, charged with methyl tosylcarbonochloridoimidothioate (**S13**) (1.5 g, 5.69 mmol) and acetonitrile (38 mL), and cooled on an ice bath. Triethyl amine (0.95 mL, 6.83 mmol) was added dropwise, followed by dropwise addition of *N*-allylmethylamine in 9.5 mL acetonitrile. The reaction was allowed to stir at rt for 48 h, then concentrated. The crude product was purified via flash column chromatography on silica gel (EtOAc:Hexanes = 30:70) to afford 1.568 g (92%) of the title compound as a yellow oil. ^1H (400 MHz, CDCl_3) δ 7.73 (d, J = 7.8 Hz, 2 H), 7.17 (d, J = 7.8 Hz, 2 H), 5.61–5.70 (m, 1 H), 5.16 (dd, J = 10.3, 1.2 Hz, 1 H), 5.09 (dd, J = 17.1, 1.2 Hz, 1 H), 4.08 (d, J = 5.6 Hz, 2 H), 3.07 (s, 3 H), 2.45 (s, 3 H), 2.31 (s, 3 H).



***N*-{[Allyl(methyl)amino](methylamino)methylene}-4-methylbenzenesulfonamide (23).** A round bottom flask was charged with Methyl-*N*-allyl-*N*-methyl-*N'*-tosylcarbamimidothioate (**S14**) (1.57 g, 5.25 mmol), ethanol (50 mL), and mercuric oxide (1.71 g, 7.88 mmol), then purged with nitrogen. Triethylamine (2.9 mL, 21 mmol) was added followed by methylamine (3.15 mL,

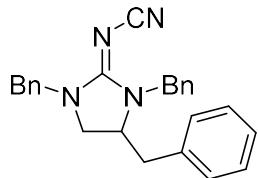
6.3 mmol) as a 2M solution in methanol. The reaction mixture was then stirred at rt for 72 h. The mixture was filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate:hexanes = 40:60) to yield 1.15 g (78%) of the title compound as a white solid, m.p. 63–65 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, J = 8.0 Hz, 2 H), 7.21 (d, J = 8.0 Hz, 2 H), 5.79–5.71 (m, 1 H), 5.20–5.13 (m, 2 H), 3.81 (d, J = 5.6 Hz, 2 H), 2.82 (s, 3 H), 2.80 (d, J = 5.2 Hz, 3 H), 2.37 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.4, 141.8, 141.2, 132.5, 129.2, 125.9, 118.4, 53.9, 36.7, 32.4, 21.4; IR (film) 3356.1, 1590.3 cm^{-1} ; MS (ESI+) 282.1271 (282.1271 calcd for $\text{C}_{13}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

Preparation and Characterization of Products

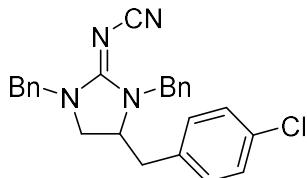
General Procedure A for Pd-Catalyzed Carboamination Reactions of Aryl Bromides. A flame dried Schlenk tube equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with $\text{Pd}_2(\text{dba})_3$ (1 mol%), XPhos or CPhos (4 mol%), and NaO^tBu (2 equiv). The tube was purged with nitrogen and then a solution of the aryl bromide (1.5 equiv) in toluene was added, and the resulting solution was stirred at rt for 1 min. A solution of the *N*-protected guanidine substrate (1 equiv) in toluene (0.1 M) was added, and the solution was heated to 90 °C with stirring until the starting material had been consumed as judged by TLC or ^1H NMR analysis of the reaction mixture (ca 1 h). The mixture was then cooled to rt and saturated aqueous NH_4Cl (1 mL) was added. The resulting mixture was then extracted with ethyl acetate (3 x 2 mL), and the combined organic layers were filtered through a plug of silica gel. The organic layer was then concentrated *in vacuo*, and the crude product was purified via flash column chromatography on silica gel (methanol:dichloromethane = 1:99).

General Procedure B for Pd-Catalyzed Carboamination Reactions of Aryl Triflates. A flame dried Schlenk tube equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with $\text{Pd}(\text{OAc})_2$ (2 mol%), CPhos (4 mol%), and LiO^tBu (2 equiv). The tube was purged with nitrogen and then a solution of the aryl triflate (1.5 equiv) in PhCF_3 was added, and the resulting solution was stirred at rt for 1 min. A solution of the *N*-protected guanidine substrate (1 equiv) in CF_3Ph (0.2 M) was added, and the solution was heated to 100 °C with stirring until the starting material had been consumed as judged by TLC or ^1H NMR analysis of the reaction mixture (ca 2 h). The mixture was then cooled to rt and saturated aqueous NH_4Cl (1 mL) was added. The resulting mixture was then extracted with ethyl acetate (3 x 2 mL), and the

combined organic layers were filtered through a plug of silica gel. The organic layer was then concentrated *in vacuo*, and the crude product was purified via flash column chromatography on silica gel (methanol:dichloromethane = 1:99).

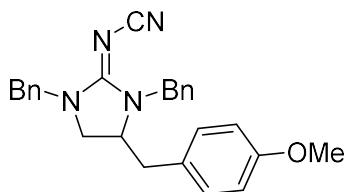


N-(1,3,4-Tribenzylimidazolidin-2-ylidene)cyanamide (8a). The general procedure A was employed for the coupling of bromobenzene (47 mg, 0.30 mmol) with 1-allyl-1,3-dibenzyl-2-cyanoguanidine (**6a**) (61 mg, 0.20 mmol). This procedure afforded 65 mg (86%) of the title compound as a white, viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.42–7.25 (m, 8 H), 7.25–7.15 (m, 5 H), 6.90 (dd, J = 7.3, 2.1 Hz, 2 H), 5.36 (d, J = 15.6 Hz, 1 H), 4.74–4.56 (m, 2 H), 4.19 (d, J = 15.6 Hz, 1 H), 3.70 (tdd, J = 9.1 Hz, 6.2 Hz, 4.4 Hz, 1 H), 3.20 (t, J = 9.6 Hz, 1 H), 3.04–2.93 (m, 2 H), 2.54 (dd, J = 13.6 Hz, 8.8 Hz, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.2, 135.7, 135.4, 135.3, 129.0, 128.9, 128.2, 128.1, 128.1, 128.0, 127.2, 116.5, 55.8, 49.5, 49.4, 47.3, 38.2 (one carbon signal is absent due to incidental equivalence); IR (film) 2171, 1595 cm^{-1} ; MS (ESI+) 381.2074 (381.2074 calcd for $\text{C}_{25}\text{H}_{24}\text{N}_4$, $\text{M} + \text{H}^+$).

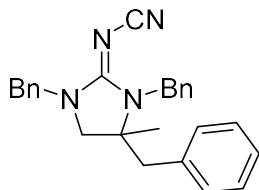


N-[1,3-Dibenzyl-4-(4-chlorobenzyl)imidazolidin-2-ylidene]cyanamide (8b). The general procedure A was employed for the coupling of 4-bromochlorobenzene (57.4 mg, 0.30 mmol) with 1-allyl-1,3-dibenzyl-2-cyanoguanidine (**6a**) (61 mg, 0.20 mmol). This procedure afforded 68 mg (82%) of the title compound as a pale yellow, foamy solid, m.p. 158–160 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.43–7.25 (m, 8 H), 7.18–7.15 (m, 4 H), 6.80 (d, J = 8.1 Hz, 2 H), 5.35 (d, J = 15.5 Hz, 1 H), 4.76 (d, J = 15.2 Hz, 1 H), 4.52 (d, J = 15.2 Hz, 1 H), 4.19 (d, J = 15.6 Hz, 1 H), 3.70–3.65 (m, 1 H), 3.20 (t, J = 9.6 Hz, 1 H), 2.96–2.88 (m, 2 H), 2.53 (dd, J = 13.7, 8.5, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.1, 135.5, 135.2, 133.7, 133.2, 130.4, 129.0, 128.9, 128.2, 128.1, 128.0, 116.3, 55.4, 49.4, 49.2, 47.3, 37.3 (two carbon signals are absent due to

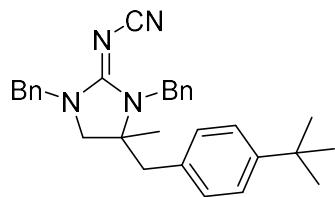
incidental equivalence); IR (film) 2162, 1599 cm^{-1} ; MS (ESI+) 415.1681 (415.1684 calcd for $\text{C}_{25}\text{H}_{23}\text{ClN}_4$, $\text{M} + \text{H}^+$).



***N*-[1,3-Dibenzyl-4-(4-methoxybenzyl)imidazolidin-2-ylidene]cyanamide (8c).** The general procedure A was employed for the coupling of 4-bromoansole (56.1 mg, 0.30 mmol) with 1-allyl-1,3-dibenzyl-2-cyano guanidine (**6a**) (61 mg, 0.20 mmol). This procedure afforded 70 mg (85%) of the title compound as a pale yellow solid, m.p. 98–100 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.41–7.27 (m, 8 H), 7.22–7.16 (m, 2 H), 6.86–6.80 (m, 2 H), 6.80–6.74 (m, 2 H), 5.37 (d, J = 15.6 Hz, 1 H), 4.72 (d, J = 15.2 Hz, 1 H), 4.60 (d, J = 15.3 Hz, 1 H), 4.21 (d, J = 15.6 Hz, 1 H), 3.77 (s, 3 H), 3.72–3.65 (m, 1 H), 3.21 (t, J = 9.6 Hz, 1 H), 3.00 (dd, J = 9.8, 6.3 Hz, 1 H), 2.92 (dd, J = 13.8, 4.4 Hz, 1 H), 2.52 (dd, J = 13.8, 8.6 Hz, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.6, 156.7, 136.4, 136.2, 130.0, 128.8, 128.7, 128.3, 128.2, 128.1, 128.0, 117.8, 114.3, 56.2, 55.3, 54.4, 53.7, 42.8, 37.4, 24.9 (one carbon signal is absent due to incidental equivalence); IR (film) 2170, 1595 cm^{-1} ; MS (ESI+) 411.2179 (411.2179 calcd for $\text{C}_{26}\text{H}_{26}\text{N}_4\text{O}$, $\text{M} + \text{H}^+$).

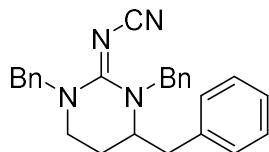


***N*-(1,3,4-Tribenzyl-4-methylimidazolidin-2-ylidene)cyanamide (8d).** The general procedure A was employed for the coupling of bromobenzene (35.3 mg, 0.225 mmol) with 1,3-dibenzyl-2-cyano-1-(2-methylallyl)guanidine (**6b**) (47.8 mg, 0.15 mmol). This procedure afforded 52 mg (88%) of the title compound as an off-white solid, m.p. 92–94 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.39–7.30 (m, 7 H), 7.30–7.23 (m, 4 H), 7.20 (dd, J = 7.7, 1.8 Hz, 2 H), 6.94–6.87 (m, 2 H), 5.01 (d, J = 16.2 Hz, 1 H), 4.69–4.55 (m, 2 H), 4.40 (d, J = 16.2 Hz, 1 H), 3.30 (d, J = 9.8 Hz, 1 H), 2.92 (d, J = 9.8 Hz, 1 H), 2.77 (d, J = 13.6 Hz, 1 H), 2.59 (d, J = 13.6 Hz, 1 H), 1.16 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.5, 138.2, 135.4, 135.0, 129.9, 129.0, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.7, 127.5, 127.4, 127.3, 116.4, 62.4, 55.7, 49.4, 44.7, 43.5, 24.5; IR (film) 2167, 1593 cm^{-1} ; MS (ESI+) 395.2227 (395.2230 calcd for $\text{C}_{26}\text{H}_{26}\text{N}_4$, $\text{M} + \text{H}^+$).

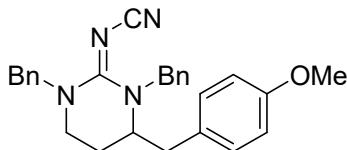


***N*-{1,3-Dibenzyl-4-[4-(*tert*-butyl)benzyl]-4-methylimidazolidin-2-ylidene}cyanamide (8e).**

The general procedure A was employed for the coupling of 1-bromo-4-*tert*-butylbenzene (48 mg, 0.225 mmol) with 1,3-dibenzyl-2-cyano-1-(2-methylallyl)guanidine (**6b**) (47.8 mg, 0.15 mmol). This procedure afforded 58 mg (86%) of the title compound as a yellow solid, m.p. 142–144 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.38–7.27 (m, 7 H), 7.25–7.20 (m, 5 H), 6.82 (d, *J* = 8 Hz, 2 H), 4.97 (d, *J* = 16.2 Hz, 1 H), 4.70–4.54 (m, 2 H), 4.42 (d, *J* = 16.2 Hz, 1 H), 3.30 (d, *J* = 9.8 Hz, 1 H), 2.90 (d, *J* = 9.8 Hz, 1 H), 2.71 (d, *J* = 13.5 Hz, 1 H), 2.58 (d, *J* = 13.6 Hz, 1 H), 1.30 (s, 9 H), 1.15 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 157.5, 150.2, 138.2, 135.5, 131.9, 130.0, 128.8, 128.6, 128.4, 128.0, 127.5, 127.4, 125.4, 116.4, 62.5, 55.7, 49.4, 44.7, 43.0, 34.5, 31.3, 24.2; IR (film) 2170, 1593 cm⁻¹; MS (ESI+) 451.2854 (451.2856 calcd for C₃₀H₃₄N₄, M + H⁺).

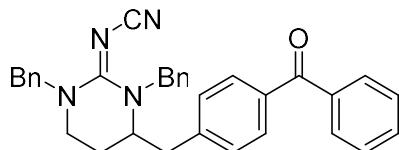


***N*-(1,3,4-Tribenzyltetrahydropyrimidin-2-[1*H*]-ylidene)cyanamide (8f).** The general procedure A was employed for the coupling of bromobenzene (35.3 mg, 0.225 mmol) with 1,3-dibenzyl-1-(but-3-en-1-yl)-2-cyanoguanidine (**6c**) (47.8 mg, 0.15 mmol). This procedure afforded 58 mg (98%) of the title compound as a pale yellow solid, m.p. 87–89 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.41–7.20 (m, 13 H), 7.00–6.93 (m, 2 H), 5.43 (d, *J* = 15.2 Hz, 1 H), 5.15 (d, *J* = 15.0 Hz, 1 H), 4.65 (d, *J* = 15.0 Hz, 1 H), 4.03 (d, *J* = 15.2 Hz, 1 H), 3.48–3.43 (m, 1 H), 3.60–3.12 (m, 2 H), 2.76 (dd, *J* = 13.6, 6.5 Hz, 1 H), 2.50 (dd, *J* = 13.5, 8.2 Hz, 1 H), 1.71–1.60 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 156.7, 136.8, 136.3, 136.1, 129.0, 128.9, 128.8, 128.8, 128.3, 128.2, 128.1, 128.0, 127.0, 117.8, 56.1, 54.4, 53.7, 42.7, 38.2, 24.8; IR (film) 2165, 1526 cm⁻¹; MS (ESI+) 395.2231 (395.2230 calcd for C₂₆H₂₆N₄, M + H⁺).



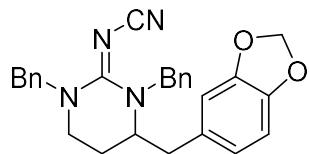
***N*-[1,3-Dibenzyl-4-(4-methoxybenzyl)tetrahydropyrimidin-2-[1*H*]-ylidene]cyanamide (8g).**

The general procedure A was employed for the coupling of 4-bromoanisole (42.1 mg, 0.225 mmol) with 1,3-dibenzyl-1-(but-3-en-1-yl)-2-cyanoguanidine (**6c**) (47.8 mg, 0.15 mmol). This procedure afforded 60 mg (94%) of the title compound as a pale yellow solid, m.p. 43–46 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.42–7.21 (m, 11 H), 6.93–6.77 (m, 4 H), 5.43 (d, *J* = 15.3 Hz, 1 H), 5.14 (d, *J* = 15.0 Hz, 1 H), 4.63 (d, *J* = 15.1 Hz, 1 H), 4.02 (d, *J* = 15.3 Hz, 1 H), 3.78 (s, 3 H), 3.45–3.35 (m, 1 H), 3.29–3.11 (m, 2 H), 2.69 (dd, *J* = 13.7, 6.6 Hz, 1 H), 2.46 (dd, *J* = 13.7, 7.9 Hz, 1 H), 1.67–1.62 (m, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 158.6, 156.7, 136.4, 136.2, 130.0, 128.8, 128.7, 128.3, 128.2, 128.1, 128.0, 117.8, 114.3, 56.2, 55.3, 54.4, 53.7, 42.8, 37.4, 24.9 (one carbon signal is absent due to incidental equivalence); IR (film) 2164, 1511 cm⁻¹; MS (ESI+) 425.2337 (425.2336 calcd for C₂₇H₂₈N₄O, M + H⁺).

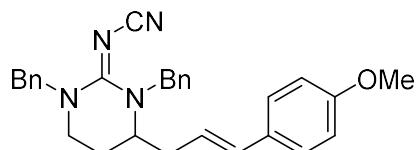


***N*-[4-(4-Benzoylbenzyl)-1,3-dibenzyltetrahydropyrimidin-2-[1*H*]-ylidene]cyanamide (8h).**

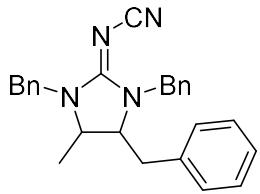
The general procedure A was employed for the coupling of 4-bromobenzophenone (78.3 mg, 0.30 mmol) with 1,3-dibenzyl-1-(but-3-en-1-yl)-2-cyanoguanidine (**6c**) (63.7 mg, 0.20 mmol). This procedure afforded 80.5 mg (81%) of the title compound as a pale yellow solid, m.p. 53–56 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.80–7.70 (m, 4 H), 7.63–7.56 (m, 1 H), 7.48 (t, *J* = 7.6 Hz, 2 H), 7.44–7.23 (m, 9 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 5.41 (d, *J* = 15.2 Hz, 1 H), 5.17 (d, *J* = 15.0 Hz, 1 H), 4.64 (d, *J* = 15.0 Hz, 1 H), 4.13 (d, *J* = 15.3 Hz, 1 H), 3.55–3.45 (m, 1 H), 3.31–3.15 (m, 2 H), 2.83 (dd, *J* = 13.5, 6.4 Hz, 1 H), 2.59 (dd, *J* = 13.5, 8.2 Hz, 1 H), 1.79–1.46 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 196.1, 156.8, 141.6, 137.4, 136.4, 136.1, 136.0, 132.5, 130.7, 129.9, 129.0, 128.9, 128.8, 128.3, 128.2, 128.1, 117.6, 55.8, 54.4, 53.9, 42.7, 38.2, 25.0 (one carbon signal is absent due to incidental equivalence); IR (film) 2164, 1523 cm⁻¹; MS (ESI+) 499.2490 (499.2490 calcd for C₃₃H₃₀N₄O, M + H⁺).



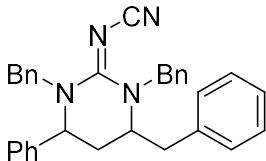
***N*-[4-(Benzo[d][1,3]dioxol-5-ylmethyl)-1,3-dibenzyltetrahydropyrimidin-2-[1H]-ylidene]cyanamide (8i).** The general procedure A was employed for the coupling of 1-bromo-3,4-(methylenedioxy)benzene (45.2 mg, 0.225 mmol) with 1,3-dibenzyl-1-(but-3-en-1-yl)-2-cyanoguanidine (**6c**) (47.8 mg, 0.15 mmol). This procedure afforded 64 mg (97%) of the title compound as a pale yellow, viscous oil. ^1H NMR (500 MHz, CDCl_3) δ 7.42–7.26 (m, 10 H), 6.75–6.68 (m, 1 H), 6.39 (d, J = 6.9 Hz, 2 H), 5.93 (s, 2 H), 5.40 (d, J = 15.2 Hz, 1 H), 5.16 (d, J = 15.0 Hz, 1 H), 4.64 (d, J = 15.0 Hz, 1 H), 4.12 (d, J = 15.2 Hz, 1 H), 3.39 (ddt, J = 8.4, 6.1, 4.2 Hz, 1 H), 3.27–3.11 (m, 2 H), 2.66 (dd, J = 13.7, 6.4 Hz, 1 H), 2.39 (dd, J = 13.7, 8.4 Hz, 1 H), 1.68–1.62 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.7, 147.9, 146.6, 136.3, 136.2, 130.4, 128.9, 128.3, 128.2, 128.1, 128.0, 122.0, 117.7, 109.1, 108.6, 101.1, 56.2, 54.5, 53.7, 42.8, 37.9, 24.6; IR (film) 2162, 1525 cm^{-1} ; MS (ESI+) 439.2124 (439.2129 calcd for $\text{C}_{27}\text{H}_{26}\text{N}_4\text{O}_2$, $\text{M} + \text{H}^+$).



(E)-*N*-{1,3-Dibenzyl-4-[3-(4-methoxyphenyl)allyl]tetrahydropyrimidin-2-[1H]-ylidene}cyanamide (8j). The general procedure A was employed for the coupling of (*E*)-1-(2-bromovinyl)-4-methoxybenzene (47.9 mg, 0.225 mmol) with 1,3-dibenzyl-1-(but-3-en-1-yl)-2-cyanoguanidine (**6c**) (47.8 mg, 0.15 mmol). This procedure afforded 64 mg (95%) of the title compound as a pale yellow, viscous oil. ^1H NMR (500 MHz, CDCl_3) δ 7.40–7.28 (m, 10 H), 7.25–7.20 (m, 2 H), 6.86–6.81 (m, 2 H), 6.22 (d, J = 15.7 Hz, 1 H), 5.86–5.76 (m, 1 H), 5.51 (d, J = 15.3 Hz, 1 H), 5.09 (d, J = 15.0 Hz, 1 H), 4.67 (d, J = 15.1 Hz, 1 H), 4.36 (d, J = 15.3 Hz, 1 H), 3.80 (s, 3 H), 3.39–3.35 (m, 1 H), 3.21–3.13 (m, 2 H), 2.42–2.37 (m, 1 H), 2.25–2.14 (m, 1 H), 1.83–1.68 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.3, 157.0, 136.5, 136.2, 133.4, 129.4, 128.9, 128.8, 128.3, 128.1, 128.0, 127.9, 127.3, 117.8, 55.3, 54.8, 54.4, 53.5, 24.7, 35.5, 25.2; IR (film) 2933, 2164, 1510 cm^{-1} ; MS (ESI+) 451.2490 (451.2492 calcd for $\text{C}_{29}\text{H}_{30}\text{N}_4\text{O}$, $\text{M} + \text{H}^+$).

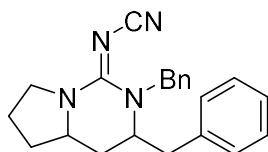


***N*-(1,3,4-Tribenzyl-5-methylimidazolidin-2-ylidene)cyanamide (8k).** The general procedure A was employed for the coupling of bromobenzene (47.1 mg, 0.30 mmol) with 1,3-dibenzyl-1-(but-3-en-2-yl)-2-cyanoguanidine (**6d**) (63.7 mg, 0.20 mmol). This procedure afforded 56 mg (71%) of the title compound as a pale yellow, viscous oil. This compound was obtained as a 1.5:1 mixture of diastereomers as judged by ¹H NMR analysis. Data are for the mixture. ¹H NMR (400 MHz, CDCl₃) δ 7.42–7.17 (m, 24 H), 7.11 (dd, *J* = 7.4, 2.0 Hz, 2 H), 7.07–7.01 (m, 2 H), 6.86–6.79 (m, 2 H), 5.41 (d, *J* = 15.5 Hz, 1 H), 5.39–5.32 (m, 2 H), 5.24 (d, *J* = 15.4 Hz, 1 H), 4.19–4.03 (M, 3 H), 3.88–3.74 (m, 2 H), 3.60–3.46 (m, 1 H), 3.26–3.13 (m, 1 H), 3.00 (dd, *J* = 14.2, 6.7 Hz, 1 H), 2.87 (dd, *J* = 13.6, 4.3 Hz, 1 H), 2.76 (dd, *J* = 14.2, 7.9 Hz, 1 H), 2.42 (dd, *J* = 13.6, 7.9 Hz, 1 H), 1.14 (d, *J* = 6.6 Hz, 3 H), 0.76 (d, *J* = 5.9 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 158.6, 157.6, 136.7, 136.0, 135.8, 135.7, 135.3, 129.2, 129.0, 128.9, 128.8, 128.2, 128.1, 128.0, 127.9, 127.9, 127.82, 127.8, 127.0, 116.8, 116.5, 63.2, 59.6, 55.3, 54.4, 47.7, 47.4, 46.8, 46.2, 38.2, 33.7, 18.6, 12.3; IR (film) 2171, 1592 cm⁻¹; MS (ESI+) 395.2228 (395.2230 calcd for C₂₆H₂₆N₄, M + H⁺).

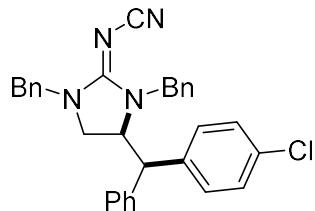


***N*-(1,3,4-Tribenzyl-6-phenyltetrahydropyrimidin-2-[1H]-ylidene)cyanamide (8l).** The general procedure A was employed for the coupling of bromobenzene (35.3 mg, 0.225 mmol) with 1,3-dibenzyl-2-cyano-1-(1-phenylbut-3-en-1-yl)guanidine (**6e**) (59.2 mg, 0.15 mmol). This procedure afforded 60 mg (85%) of the title compound as a pale yellow solid, m.p. 68–75 °C. This compound was obtained as a 1.7:1 mixture of diastereomers as judged by ¹H NMR analysis; data are for the mixture. ¹H NMR (400 MHz, CDCl₃) δ 7.48–7.25 (m, 10 H), 7.25–7.11 (m, 6 H), 6.90–6.84 (d, *J* = 6.8 Hz, 2 H), 6.68–6.60 (m, 2 H), 5.85–5.67 (m, 3 H), 5.36 (d, *J* = 14.9 Hz, 1 H), 4.55–4.40 (m, 2 H), 4.34 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.97 (d, *J* = 15.7 Hz, 1 H), 3.85 (t, *J* = 15.4 Hz, 1 H), 3.57 (dq, *J* = 10.2, 5.1 Hz, 1 H), 3.36 (dp, *J* = 11.0, 3.8 Hz, 1 H), 2.58 (dd, *J* = 13.5, 7.6 Hz, 1 H), 2.39–2.33 (m, 2 H), 2.06–1.92 (m, 3 H), 1.88 (ddd, *J* = 14.0, 6.7, 3.1 Hz, 1 H), 1.67 (ddd, *J* = 14.0, 11.4, 4.6 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 158.3, 157.3, 139.6,

139.5, 137.0, 136.9, 136.6, 136.0, 135.8, 129.4, 129.3, 129.2, 129.0, 128.91, 128.86, 128.84, 128.77, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.84, 127.78, 127.7, 127.4, 127.0, 126.83, 126.80, 126.3, 117.8, 117.1, 58.2, 56.6, 56.5, 55.2, 54.2, 52.1, 51.8, 51.5, 38.3, 36.1, 33.2; IR (film) 2165, 1515 cm^{-1} ; MS (ESI+) 471.2542 (471.2543 calcd for $\text{C}_{32}\text{H}_{30}\text{N}_4$, $\text{M} + \text{H}^+$).

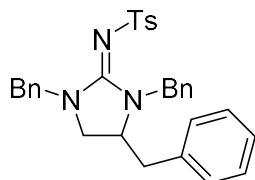


***N*-(2,3-Dibenzylhexahydropyrrolo[1,2-c]pyrimidin-1-[2H]-ylidene)cyanamide (8m).** The general procedure A was employed for the coupling of bromobenzene (47.1 mg, 0.30 mmol) with 2-allyl- N -benzyl- N' -cyanopyrrolidine-1-carboximidamide (**6f**) (58.0 mg, 0.22 mmol). This procedure afforded 72 mg (97%) of the title compound as a pale yellow solid, m.p. 52–55 °C. This compound was obtained as a 2:1 mixture of diastereomers as judged by ^1H NMR analysis; data are for the mixture. ^1H NMR (500 MHz, CDCl_3) δ 7.42–7.17 (m, 7 H), 7.09–7.05 (m, 1 H), 6.97–6.91 (m, 2 H), 5.53–5.44 (m, 2 H), 4.44–4.32 (m, 2 H), 4.15–4.13 (m, 2 H), 3.95 (td, J = 10.4, 7.4 Hz, 1 H), 3.75–3.66 (m, 2 H), 3.53 (dtd, J = 10.1, 5.0, 1.6 Hz, 1 H), 3.44–3.35 (m, 3 H), 3.24 (dd, J = 13.2, 3.9 Hz, 1 H), 3.12 (dd, J = 13.8, 4.8 Hz, 1 H), 2.62 (dd, J = 13.7, 9.9 Hz, 1 H), 2.43 (dd, J = 13.2, 9.6 Hz, 1 H), 2.14 (dtd, J = 12.1, 6.2, 2.2 Hz, 1 H), 2.11–2.06 (m, 2 H), 1.98–1.82 (m, 2 H), 1.53 (dq, J = 13.1, 6.8 Hz, 1 H), 1.50–1.42 (m, 1 H), 1.37 (dt, J = 13.3, 11.2 Hz, 1 H), 1.30–1.17 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.9, 154.1, 137.3, 137.0, 136.9, 136.8, 129.0, 128.9, 128.8, 128.7, 128.6, 127.9, 127.8, 127.7, 127.6, 127.0, 126.9, 118.4, 55.4, 55.2, 54.8, 54.0, 51.2, 50.9, 49.1, 49.0, 39.8, 38.9, 35.3, 32.4, 31.5, 29.1, 23.8, 23.3; IR (film) 2163, 1512 cm^{-1} ; MS (ESI+) 345.2072 (345.2074 calcd for $\text{C}_{22}\text{H}_{24}\text{N}_4$, $\text{M} + \text{H}^+$).

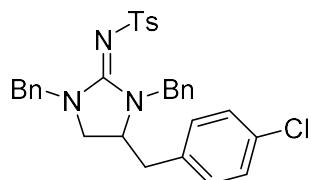


***(4S,4'R)-N*-(1,3-dibenzyl-4-[(4-chlorophenyl)(phenyl)methyl]imidazolidin-2-ylidene)cyanamide (8n).** The general procedure A was employed for the coupling of 4-bromochlorobenzene (43 mg, 0.225 mmol) with 1,3-dibenzyl-1-cinnamyl-2-cyanoguanidine (**6g**) (57.1 mg, 0.15 mmol). This procedure afforded 18 mg (24%) of the title compound as a pale yellow solid, m.p. 59–63 °C. This compound was obtained as a >20:1 mixture of diastereomers

as judged by ^1H NMR analysis; data are for the major diastereomer. ^1H NMR (400 MHz, CDCl_3) δ 7.34–7.26 (m, 9 H), 7.22–7.17 (m, 2 H), 7.17–7.07 (m, 4 H), 7.05–6.98 (m, 2 H), 6.93–6.86 (m, 2 H), 5.27 (d, J = 16.0 Hz, 1 H), 4.65–4.49 (m, 2 H), 4.22–4.17 (m, 1 H), 4.03 (d, J = 7.9 Hz, 1 H), 3.45 (t, J = 9.9 Hz 1 H), 3.32 (d, J = 16.0 Hz, 1 H), 3.01 (dd, J = 10.2, 4.3 Hz, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.9, 139.7, 138.1, 135.9, 135.1, 133.3, 129.6, 129.2, 129.0, 128.9, 128.4, 128.1, 128.1, 128.0, 127.8, 127.7, 116.4, 57.6, 54.2, 49.2, 49.1, 48.4 (one carbon signal is absent due to incidental equivalence); IR (film) 2172, 1598 cm^{-1} ; MS (ESI+) 491.1992 (491.1997 calcd for $\text{C}_{31}\text{H}_{27}\text{ClN}_4$, $\text{M} + \text{H}^+$).

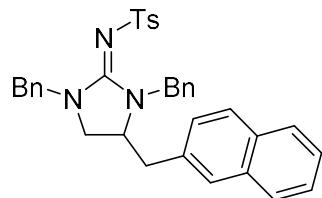


4-Methyl-N-(1,3,4-tribenzylimidazolidin-2-ylidene)benzenesulfonamide (9a). The general procedure B was employed for the coupling of phenyl trifluoromethanesulfonate (101.8 mg, 0.45 mmol) with *N*-{[allyl(benzyl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7a**) (134.3 mg, 0.30 mmol). This procedure afforded 140 mg (92%) of the title compound as a pale yellow solid, m.p. 102–104 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.91–7.83 (m, 2 H), 7.39–7.28 (m, 6 H), 7.28–7.14 (m, 9 H), 6.89–6.81 (m, 2 H), 5.29 (d, J = 15.3 Hz, 1 H), 4.77 (d, J = 15.1 Hz, 1 H), 4.53 (d, J = 15.1 Hz, 1 H), 4.17 (d, J = 15.3 Hz, 1 H), 3.71–3.65 (m, 1 H), 3.23 (t, J = 9.9 Hz, 1 H), 3.03–2.89 (m, 2 H), 2.51 (dd, J = 13.6, 8.8 Hz, 1 H), 2.36 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.2, 142.9, 141.1, 136.0, 135.5, 129.2, 129.0, 128.9, 128.8, 128.7, 128.6, 128.3, 128.2, 127.9, 127.8, 127.0, 125.8, 55.5, 50.8, 48.8, 48.7, 38.3, 21.4; IR (film) 2922, 1562 cm^{-1} ; MS (ESI+) 510.2204 (510.2210 calcd for $\text{C}_{31}\text{H}_{31}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

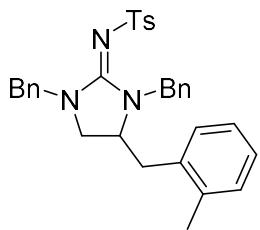


***N*-[1,3-Dibenzyl-4-(4-chlorobenzyl)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (9b).** The general procedure B was employed for the coupling of 4-chlorophenyl trifluoromethanesulfonate (78.2 mg, 0.30 mmol) with *N*-{[allyl(benzyl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7a**) (86.7 mg, 0.20

mmol). This procedure afforded 76.2 mg (70%) of the title compound as a pale yellow solid, m.p. 151–153 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, J = 8.4 Hz, 2 H), 7.39–7.10 (m, 14 H), 6.89 (d, J = 8.4 Hz, 2 H), 5.33 (d, J = 15.4 Hz, 1 H), 4.80 (d, J = 15.0 Hz, 1 H), 4.40 (d, J = 15.0 Hz, 1 H), 4.19 (d, J = 15.4 Hz, 1 H), 3.65 (tt, J = 9.5, 4.8 Hz, 1 H), 3.23 (t, J = 9.9 Hz, 1 H), 2.93 (dd, J = 10.3, 5.1 Hz, 1 H), 2.83 (dd, J = 13.7, 4.5 Hz, 1 H), 2.53 (dd, J = 13.7, 8.1 Hz, 1 H), 2.36 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.1, 142.8, 141.2, 135.8, 135.5, 133.7, 133.0, 130.6, 129.0, 128.9, 128.7, 128.2, 128.0, 127.9, 125.8, 55.1, 50.5, 49.0, 48.3, 37.4, 21.3 (two carbon signals are absent due to incidental equivalence); IR (film) 2923, 1561 cm^{-1} ; MS (ESI+) 544.1814 (544.1820 calcd for $\text{C}_{31}\text{H}_{30}\text{ClN}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

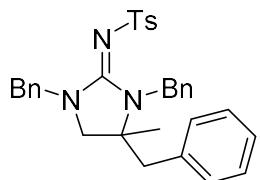


***N*-[1,3-Dibenzyl-4-(naphthalen-2-ylmethyl)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (9c).** The general procedure B was employed for the coupling of naphthalen-2-yl trifluoromethanesulfonate (139 mg, 0.50 mmol) with *N*-{[allyl(benzyl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7a**) (145.7 mg, 0.34 mmol). This procedure afforded 151.6 mg (80%) of the title compound as a pale yellow solid, m.p. 149–152 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, J = 8.4 Hz, 2 H), 7.82–7.75 (m, 1 H), 7.69 (dd, J = 9.0, 2.6 Hz, 2 H), 7.48–7.43 (m, 2 H), 7.40–7.30 (m, 3 H), 7.0–7.19 (m, 6 H), 7.17 (d, J = 8.0 Hz, 2 H), 7.14–7.08 (m, 2 H), 6.98 (dd, J = 8.4, 1.7 Hz, 1 H), 5.34 (d, J = 15.4 Hz, 1 H), 4.83 (d, J = 15.0 Hz, 1 H), 4.42 (d, J = 15.1 Hz, 1 H), 4.26 (d, J = 15.4 Hz, 1 H), 3.78 (tt, J = 9.3, 4.7 Hz, 1 H), 3.22 (t, J = 9.9 Hz, 1 H), 3.21–2.99 (m, 2 H), 2.68 (dd, J = 13.6, 8.7 Hz, 1 H), 2.35 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.2, 142.9, 141.1, 136.0, 135.7, 133.3, 132.8, 132.3, 128.9, 129.0, 128.9, 128.7, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 127.1, 126.3, 125.9, 125.8, 55.3, 50.6, 48.8, 48.4, 38.2, 21.3; IR (film) 2921, 1559 cm^{-1} ; MS (ESI+) 560.2358 (560.2366 calcd for $\text{C}_{35}\text{H}_{33}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).



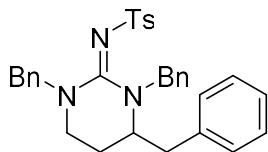
***N*-[1,3-dibenzyl-4-(2-methylbenzyl)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (9d).**

The general procedure B was employed for the coupling of *o*-tolyl trifluoromethanesulfonate (108.1 mg, 0.45 mmol) with *N*-{[allyl(benzyl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7a**) (130 mg, 0.30 mmol). This procedure afforded 122 mg of the title compound as a pale yellow solid, m.p. 130–133 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 8 Hz, 2 H), 7.35–7.24 (m, 8 H), 7.18 (d, *J* = 7.6 Hz, 4 H), 7.09–6.97 (m, 3 H), 6.64 (d, *J* = 7.6 Hz, 1 H), 5.26 (d, *J* = 15.2 Hz, 1 H), 4.90 (d, *J* = 14.8 Hz, 1 H), 4.51 (d, *J* = 15.2 Hz, 1 H), 4.09 (d, *J* = 15.2 Hz, 1 H), 3.65 (tt, 9.6, 4.9 Hz, 1 H), 3.21 (t, 9.8 Hz, 1 H), 3.00 (m, 2 H), 2.42 (dd, *J* = 13.6, 9.6 Hz, 1 H), 2.34 (s, 3 H), 1.95 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 156.2, 142.9, 141.2, 136.3, 136.0, 135.9, 134.0, 130.6, 130.0, 129.0, 128.8, 128.5, 128.2, 128.0, 127.9, 127.1, 126.2, 125.8, 54.1, 50.8, 48.9, 48.8, 36.0, 21.4, 19.2 (one carbon signal is absent due to incidental equivalence); IR (film) 2922, 1562 cm⁻¹; MS (ESI+) 524.2365 (524.2366 calcd for C₃₂H₃₃N₃O₂S, M + H⁺).



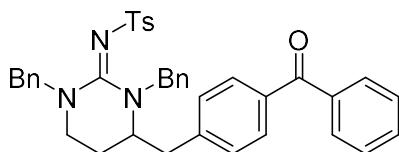
4-Methyl-*N*-(1,3,4-tribenzyl-4-methylimidazolidin-2-ylidene)benzenesulfonamide (9e). The general procedure B was employed for the coupling of phenyl trifluoromethanesulfonate (67.9 mg, 0.30 mmol) with *N*-{[benzyl(2-methylallyl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7b**) (89.5 mg, 0.20) except using 1 mL benzotrifluoride (0.1 M) as solvent. This procedure afforded 89.8 mg (86%) of the title compound as a pale yellow solid, m.p. 129–131 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.73 (d, *J* = 7.9 Hz, 2 H), 7.39–7.31 (m, 5 H), 7.31–7.15 (m, 8 H), 7.11 (d, *J* = 7.9 Hz, 2 H), 6.74 (dd, *J* = 7.3, 1.9 Hz, 2 H), 5.02 (d, *J* = 14.8 Hz, 1 H), 4.75 (d, *J* = 16.0 Hz, 1 H), 4.64 (d, *J* = 14.9 Hz, 1 H), 4.31 (d, *J* = 16.0 Hz, 1 H), 3.32 (d, *J* = 10.3 Hz, 1 H), 2.93 (d, *J* = 10.3 Hz, 1 H), 2.61 (q, *J* = 13.4 Hz, 2 H), 2.33 (s, 3 H), 1.11 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 155.5, 142.8, 141.0, 138.3, 133.0, 135.1, 130.1, 129.0,

128.9, 128.8, 128.5, 128.4, 127.9, 127.4, 27.2, 127.1, 125.8, 61.0, 55.1, 51.7, 45.0, 43.4, 24.0, 21.3; IR (film) 2927, 1564 cm^{-1} ; MS (ESI+) 524.2362 (524.2366 calcd for $\text{C}_{32}\text{H}_{33}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).



4-Methyl-N-[1,3,4-tribenzyltetrahydropyrimidin-2(1H)-ylidene]benzenesulfonamide (9f).

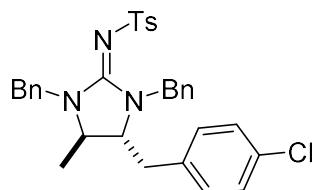
The general procedure B was employed for the coupling of phenyl trifluoromethanesulfonate (101.8 mg, 0.45 mmol) with *N*-(benzyl(but-3-en-1-yl)amino)(benzylamino)methylene)-4-methylbenzenesulfonamide (**7c**) (134.3 mg, 0.30 mmol). This procedure afforded 133.2 mg (85%) of the title compound as a pale yellow solid, m.p. 141–143 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, J = 8.4 Hz, 2 H), 7.40–7.16 (m, 11 H), 7.12 (dd, J = 7.5, 1.9 Hz, 2 H), 7.07 (d, J = 8.0 Hz, 2 H), 6.94 (d, J = 8.4 Hz, 2 H), 5.40 (d, J = 15.2 Hz, 1 H), 5.19 (d, J = 14.8 Hz, 1 H), 4.52 (d, J = 14.8 Hz, 1 H), 3.95 (d, J = 15.2 Hz, 1 H), 3.48–3.37 (m, 1 H), 3.23–3.11 (m, 2 H), 2.91 (dd, J = 13.6, 6.2 Hz, 1 H), 2.48 (dd, J = 13.6, 8.8 Hz, 1 H), 2.27 (s, 3 H), 1.67–1.47 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.1, 143.5, 140.5, 137.0, 136.3, 136.2, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 128.0, 127.8, 126.9, 125.5, 56.1, 54.9, 54.3, 42.2, 38.0, 24.4, 21.3; IR (film) 3028, 1537 cm^{-1} ; MS (ESI+) 524.2360 (524.2366 calcd for $\text{C}_{32}\text{H}_{33}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).



***N*-[4-(4-Benzoylbenzyl)-1,3-dibenzyltetrahydropyrimidin-2-[1H]-ylidene]-4-**

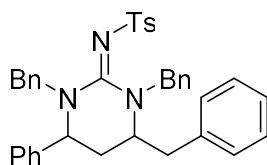
methylbenzenesulfonamide (9g). The general procedure B was employed for the coupling of 4-benzoylphenyl trifluoromethanesulfonate (148.6 mg, 0.45 mmol) with *N*-(benzyl(but-3-en-1-yl)amino)(benzylamino)methylene)-4-methylbenzenesulfonamide (**7c**) (134.3 mg, 0.30 mmol). This procedure afforded 183.0 mg (96%) of the title compound as a pale yellow solid, m.p. 70–73 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.84–7.76 (m, 2 H), 7.76–7.65 (m, 4 H), 7.56 (t, J = 7.7 Hz, 2 H), 7.39–7.20 (m, 8 H), 7.19–7.11 (m, 2 H), 7.07 (dd, J = 8.3, 2.6 Hz, 4 H), 5.41 (d, J = 15.1 Hz, 1 H), 5.15 (d, J = 14.8 Hz, 1 H), 4.50 (d, J = 14.8 Hz, 1 H), 4.01 (d, J = 15.2 Hz, 1 H), 3.51–3.41 (m, 1 H), 3.25–3.10 (m, 2 H), 2.98 (dd, J = 13.6, 6.3 Hz, 1 H), 2.56 (dd, J = 13.5, 8.5 Hz, 1 H), 2.26 (s, 3 H), 1.71–1.49 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 196.1, 155.2, 143.4, 141.9, 140.7, 137.4, 136.3, 136.2, 136.1, 132.5, 130.6, 129., 129.0, 128.9, 128.8, 128.5, 128.3,

128.2, 128.1, 128.0, 125.5, 56.0, 54.7, 54.6, 42.1, 38.1, 24.7, 21.3; IR (film) 2922, 1536 cm^{-1} ; MS (ESI+) 628.2622 (628.2628 calcd for $\text{C}_{39}\text{H}_{37}\text{N}_3\text{O}_3\text{S}$, $\text{M} + \text{H}^+$).



***N*-[1,3-Dibenzyl-4-(4-chlorobenzyl)-5-methylimidazolidin-2-ylidene]-4-methylbenzenesulfonamide (9h).**

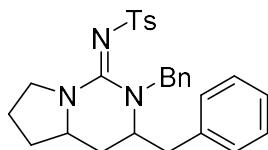
The general procedure B was employed for the coupling of 4-chlorophenyl trifluoromethanesulfonate (117.3 mg, 0.45 mmol) with *N*-{[benzyl(but-3-en-2-yl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7d**) (134.3 mg, 0.30 mmol). This procedure afforded 106 mg (63%) of the title compound as a pale yellow solid, m.p. 47–50 °C. This compound was obtained as a 3:1 mixture of diastereomers as judged by ^1H NMR analysis; ^1H data are for the major diastereomer, ^{13}C data are for the mixture. ^1H NMR (400 MHz, C_6D_6) δ 8.21 (d, J = 8.4 Hz, 2 H), 7.15–7.05 (m, 6 H), 7.04–6.98 (m, 4 H), 6.94–6.90 (m, 2 H), 6.80–6.75 (m, 2 H), 6.37 (d, J = 8.4 Hz, 2 H), 5.72 (d, J = 15.6 Hz, 1 H), 5.29 (d, J = 15.3 Hz, 1 H), 3.85 (d, J = 15.4 Hz, 1 H), 3.69 (d, J = 15.3 Hz, 1 H), 2.79 (dt, J = 7.6, 4.4 Hz, 1 H), 2.71 (qd, J = 6.2, 3.7 Hz, 1 H), 2.40 (dd, J = 14.0, 7.8 Hz, 1 H), 2.18–1.96 (m, 1 H), 1.82 (s, 3 H), 0.33 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.1, 155.1, 143.0, 141.2, 141.1, 136.2, 136.0, 135.9, 135.8, 135.4, 133.8, 132.9, 132.8, 130.8, 130.6, 129.1, 129.0, 128.9, 128.9, 128.8, 128.7, 128.7, 128.5, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 125.8, 125.7, 62.3, 59.3, 54.2, 53.6, 20.4, 19.3, 47.8, 47.0, 37.2, 33.5, 21.4, 18.6, 12.4; IR (film) 2924, 1557 cm^{-1} ; MS (ESI+) 558.1977 (558.1977 calcd for $\text{C}_{32}\text{H}_{32}\text{ClN}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).



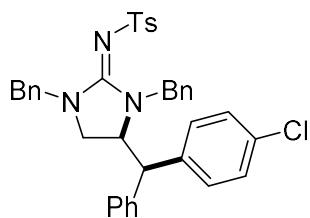
***4-Methyl-N*-[1,3,4-tribenzyl-6-phenyltetrahydropyrimidin-2(1*H*)-ylidene]benzenesulfonamide (9i).**

The general procedure B was employed for the coupling of phenyl trifluoromethanesulfonate (101.8 mg, 0.45 mmol) with *N*-{[benzyl(1-phenylbut-3-en-1-yl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7e**) (157 mg, 0.30 mmol). This procedure afforded 150.7 mg (84%) of the title compound as a pale yellow solid, m.p. 76–80 °C. This compound was obtained as a 2:1 mixture of diastereomers as judged by ^1H NMR

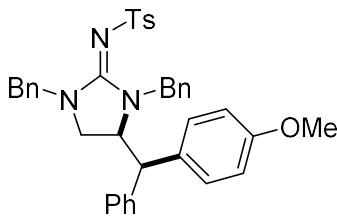
analysis; data are for the mixture. ^1H NMR (500 MHz, CDCl_3) δ 7.91–7.87 (m, 4 H), 7.51–7.14 (m, 33 H), 7.14–7.03 (m, 7 H), 6.90–6.84 (m, 2 H), 6.53–6.43 (m, 2 H), 5.89 (d, J = 15.3 Hz, 1 H), 5.84 (d, J = 14.8 Hz, 1 H), 5.71 (d, J = 15.4 Hz, 1 H), 5.23 (d, J = 15.0 Hz, 1 H), 4.47 (dd, J = 6.4, 4.5 Hz, 1 H), 4.27 (dd, J = 11.7, 6.7 Hz, 1 H), 4.09 (d, J = 15.5 Hz, 1 H), 3.98 (d, J = 14.8 Hz, 1 H), 3.92 (d, J = 15.3 Hz, 1 H), 3.83 (d, J = 15.0 Hz, 1 H), 3.53–3.43 (m, 1 H), 3.36 (tq, J = 7.6, 4.1, 3.5 Hz, 1 H), 3.00 (dd, J = 13.6, 4.6 Hz, 1 H), 2.74 (dd, J = 13.5, 7.2 Hz, 1 H), 2.43 (dd, J = 13.6, 8.2 Hz, 1 H), 2.37 (s, 3 H), 2.33–2.28 (m, 1 H), 2.27 (s, 3 H), 1.95 (dt, J = 14.1, 4.2 Hz, 1 H), 1.86–1.78 (m, 2 H), 1.71–1.62 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.9, 155.6, 143.7, 143.4, 140.7, 139.2, 137.0, 136.8, 136.6, 136.0, 135.99, 129.4, 129.3, 129.2, 129.1, 129.0, 128.94, 128.87, 128.85, 128.79, 128.71, 128.6, 128.5, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.0, 126.9, 126.8, 126.7, 125.6, 56.8, 56.4, 55.2, 54.5, 54.4, 54.0, 52.7, 38.1, 36.0, 31.4, 21.4, 21.3; IR (film) cm^{-1} ; MS (ESI+) 600.2673 (600.2679 calcd for $\text{C}_{38}\text{H}_{37}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).



***N*-[2,3-Dibenzylhexahydropyrrolo(1,2-c)pyrimidin-1(2H)-ylidene]4-methylbenzenesulfonamide (9j).** The general procedure B was employed for the coupling of phenyl trifluoromethanesulfonate (101.8 mg, 0.45 mmol) with 2-allyl-*N*-benzyl-*N'*-tosylpyrrolidine-1-carboximidamide (**7f**) (119.3 mg, 0.30 mmol). This procedure afforded 141 mg (99%) of the title compound as a pale yellow solid, m.p. 55–57 °C. This compound was obtained as a 2:1 mixture of diastereomers as judged by ^1H NMR analysis; data are for the mixture. ^1H NMR (400 MHz, CDCl_3) δ 7.79–7.73 (m, 4 H), 7.40–7.17 (m, 15 H), 7.17–7.09 (m, 5 H), 7.09–7.03 (m, 1 H), 6.93–6.87 (m, 3 H), 5.34 (d, J = 15.6 Hz, 1 H), 5.15 (d, J = 15.3 Hz, 1 H), 4.25 (d, J = 15.6 Hz, 1 H), 4.21–4.06 (m, 2 H), 4.01 (dt, J = 11.8, 7.2 Hz, 1 H), 3.88–3.68 (m, 2 H), 3.55–3.45 (m, 1 H), 3.40–3.28 (m, 2 H), 3.10 (dd, J = 13.7, 5.3 Hz, 1 H), 2.65 (dd, J = 13.7, 9.5 Hz, 1 H), 2.44–2.35 (m, 1 H), 2.33 (s, 6 H), 2.25–2.16 (m, 1 H), 2.16–2.06 (m, 1 H), 2.03–1.72 (m, 8 H), 1.63–1.47 (m, 2 H), 1.40 (q, J = 12.3, 11.9 Hz, 1 H), 1.20 (td, J = 12.9, 5.4 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 154.2, 144.1, 143.7, 140.6, 140.3, 137.2, 137.0, 136.9, 129.1, 128.9, 128.89, 128.87, 128.79, 128.65, 128.6, 127.9, 127.8, 127.63, 127.6, 127.0, 126.8, 125.5, 125.4, 55.2, 55.0, 54.5, 53.6, 51.5, 51.48, 51.5, 51.2, 39.7, 39.1, 35.5, 32.5, 31.5, 28.8, 23.1, 23.08, 21.3; IR (film) 2922, 1538 cm^{-1} ; MS (ESI+) 474.2204 (474.2210 calcd for $\text{C}_{28}\text{H}_{31}\text{N}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).

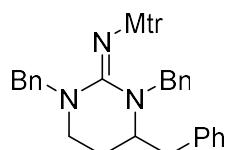


(4S,4'R)-N-{1,3-Dibenzyl-4-[(4-chlorophenyl)(phenyl)methyl]imidazolidin-2-ylidene}-4-methylbenzenesulfonamide (9k). The general procedure B was employed for the coupling of 4-chlorophenyltrifluoromethanesulfonate (78.2 mg, 0.30 mmol) with *N*-{[benzyl(cinnamyl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7g**) (101.9 mg, 0.20 mmol). This procedure afforded 94 mg (76%) of the title compound as a pale yellow solid, m.p. 70–75 °C. This compound was obtained as a >20:1 mixture of diastereomers as judged by ¹H NMR analysis; data are for the major diastereomer. ¹H NMR (500 MHz, CDCl₃) δ 7.86–7.80 (m, 2 H), 7.37–7.23 (m, 9 H), 7.20–7.05 (m, 8 H), 7.03–6.96 (m, 2 H), 6.91–6.83 (m, 2 H), 5.23 (d, *J* = 15.7 Hz, 1 H), 4.69 (d, *J* = 15.0 Hz, 1 H), 4.34 (d, *J* = 15.0 Hz, 1 H), 4.15–4.10 (m, 1 H), 3.96 (d, *J* = 8 Hz, 1 H), 3.44 (t, *J* = 10.1 Hz, 1 H), 3.32 (d, *J* = 15.7 Hz, 1 H), 2.96 (dd, *J* = 10.6, 3.6 Hz, 1 H), 2.34 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 156.8, 142.8, 141.2, 139.8, 138.1, 136.3, 135.5, 133.1, 129.9, 129.0, 128.8, 128.7, 128.6, 128.3, 127.9, 127.8, 127.6, 125.8, 57.3, 54.1, 50.4, 50.3, 48.3, 21.4; IR (film) 2922, 1564 cm⁻¹; MS (ESI+) 620.2128 (620.2133 calcd for C₃₇H₃₄CIN₃O₂S, M + H⁺).



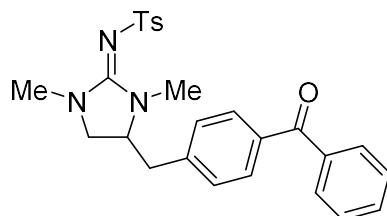
(4S,4'R)-N-{1,3-Dibenzyl-4-[(4-methoxyphenyl)(phenyl)methyl]imidazolidin-2-ylidene}-4-methylbenzenesulfonamide (9l). The general procedure B was employed for the coupling of 4-methoxyphenyltrifluoromethanesulfonate (77 mg, 0.30 mmol) with *N*-{[benzyl(cinnamyl)amino][benzylamino]methylene}-4-methylbenzenesulfonamide (**7g**) (101.9 mg, 0.20 mmol). This procedure afforded 101 mg (82%) of the title compound as a pale yellow solid, m.p. 65–69 °C. This compound was obtained as a 10:1 mixture of diastereomers as judged by ¹H NMR analysis; data are for the major diastereomer. ¹H NMR (500 MHz, CDCl₃) δ 7.83 (d, *J* = 8.3 Hz, 2 H), 7.35–7.20 (m, 9 H), 7.20–7.08 (m, 6 H), 7.00–6.94 (m, 2 H), 6.86 (d, *J* = 8.8 Hz, 2

H), 6.73 (d, J = 8.8 Hz, 2 H), 5.17 (d, J = 16 Hz, 1 H), 4.64 (d, J = 15 Hz, 1 H), 4.44 (d, J = 15.0 Hz, 1 H), 4.10 (ddd, J = 9.6, 8.3, 3.6 Hz, 1 H), 3.91 (d, J = 8.5 Hz, 1 H), 3.74 (s, 3 H), 3.42 (t, J = 10 Hz, 1 H), 3.2 (d, J = 15.5 Hz, 1 H), 2.99 (dd, J = 10.6, 3.7 Hz, 1 H), 2.34 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.5, 17.0, 142.9, 141.1, 140.7, 136.5, 135.7, 131.8, 129.4, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 127.9, 127.8, 127.7, 127.3, 125.8, 114.1, 57.6, 55.2, 54.4, 50.4, 50.2, 48.7, 21.3; IR (film) 3027, 2248, 1561 cm^{-1} ; MS (ESI+) 616.2624 (616.2628 calcd for $\text{C}_{38}\text{H}_{37}\text{N}_3\text{O}_3\text{S}$, M + H^+).



(Z)-4-methoxy-2,3,6-trimethyl-N-[1,3,4-tribenzyltetrahydropyrimidin-2(1H)-ylidene]benzenesulfonamide (21).

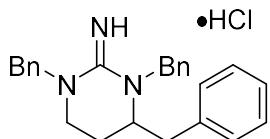
The general procedure B was employed for the coupling of phenyltrifluoromethanesulfonate (68 mg, 0.30 mmol) with (*E*)-*N*-{[benzyl(but-3-en-1-yl)amino]{benzylamino}methylene]-4-methoxy-2,3,6-trimethylbenzenesulfonamide (**20**) (101.1 mg, 0.20 mmol). This procedure afforded 110 mg (95%) of the title compound as a pale yellow solid, m.p. 62–65 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.40–7.17 (m, 11 H), 7.12 (d, J = 6.5 Hz, 2 H), 6.95 (d, J = 6.5 Hz, 2 H), 6.41 (s, 1 H), 5.34 (d, J = 15.1 Hz, 1 H), 5.05 (d, J = 14.8 Hz, 1 H), 4.55 (d, J = 14.8 Hz, 1 H), 4.06 (d, J = 15.2 Hz, 1 H), 3.75 (s, 3 H), 3.50–3.37 (m, 1 H), 3.25–3.14 (m, 2 H), 2.96 (dd, J = 13.6, 5.8 Hz, 1 H), 2.73 (s, 3 H), 2.67 (s, 3 H), 2.50 (dd, J = 13.6, 9.1 Hz, 1 H), 2.06 (s, 3 H), 1.68–1.50 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.4, 155.0, 137.4, 137.1, 137.0, 136.7, 136.5, 135.0, 129.0, 128.8, 128.6, 128.5, 125.4, 128.1, 127.8, 127.7, 126.9, 124.2, 111.5, 55.8, 55.3, 55.1, 54.4, 42.2, 38.1, 24.4, 24.2, 18.5, 11.9; IR (film) 2936, 1494, 1113 cm^{-1} ; MS (ESI+) 582.283 (582.2785 calcd for $\text{C}_{35}\text{H}_{39}\text{N}_3\text{O}_3\text{S}$, M + H^+).



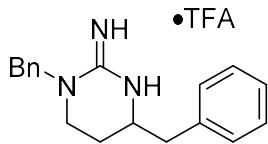
***N*-[4-(4-Benzoylbenzyl)-1,3-dimethylimidazolidin-2-ylidene]-4-methylbenzenesulfonamide (24).** The general procedure B was employed for the coupling of 4-benzoylphenyl trifluoromethanesulfonate (148.6 mg, 0.45 mmol) with *N*-{[allyl(methyl)amino](methylamino)methylene]-4-methylbenzenesulfonamide (**23**) (84.4 mg,

0.3 mmol). This procedure afforded 96 mg (69%) of the title compound as a pale yellow solid, m.p. 53–56 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 8.4 Hz, 2 H), 7.78–7.76 (m, 4 H), 7.60–7.57 (m, 1 H), 7.47 (t, *J* = 7.6 Hz, 2 H), 7.29 (d, *J* = 8.4 Hz, 2 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 3.95–3.85 (m, 1 H), 3.51 (t, *J* = 9.7 Hz, 1 H), 3.19–3.13 (m, 2 H), 3.05 (s, 3 H), 2.95 (s, 3 H), 2.92–2.80 (m, 1 H), 2.37 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 196.1, 157.1, 142.9, 141.2, 140.5, 137.4, 136.6, 132.5, 130.6, 129.9, 129.2, 128.9, 128.3, 125.7, 59.4, 52.8, 38.7, 34.4, 33.2, 21.4; IR (film) 2922.5, 1652.6, 1568.5 cm⁻¹; MS (ESI+) 462.1848 (462.1846 calcd for C₂₆H₂₇N₃O₃S, M + H⁺).

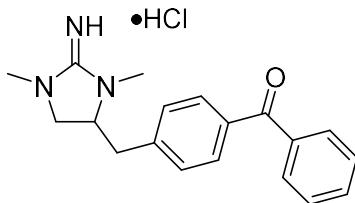
Deprotection of Cyclic Guanidine Products



1,3,4-Tribenzyltetrahydropyrimidin-2(1H)-imine hydrochloride (19): A scintillation vial containing *N*-[1,3,4-tribenzyltetrahydropyrimidin-2(1H)-ylidene]cyanamide (**7f**) (57 mg, 0.145 mmol) was charged with a stir bar and purged with nitrogen. Concentrated hydrochloric acid (1.5 mL) was added via syringe, and the mixture was heated to 90 °C overnight. The reaction mixture was then cooled to rt, and was extracted with dichloromethane (3 x 3 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate then dried, filtered, and concentrated *in vacuo* to afford the title compound as a light brown foam (95%), m.p. 48–52 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.41–7.12 (m, 13 H), 6.98 (d, *J* = 7.2 Hz, 2 H), 6.30 (s, br, 2 H), 5.27 (d, *J* = 16.0 Hz, 1 H), 5.05 (d, *J* = 15.9 Hz, 1 H), 4.54 (d, *J* = 15.9 Hz, 1 H), 4.12 (d, *J* = 16.0 Hz, 1 H), 3.50–3.39 (m, 1 H), 3.36–3.29 (m, 1 H), 3.18–3.12 (m, 1 H), 2.93 (dd, *J* = 13.5, 5.6 Hz, 1 H), 2.57 (dd, *J* = 13.5, 9.2 Hz, 1 H), 1.83–1.75 (m, 1 H), 1.67–1.61 (m, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 155.9, 137.5, 137.0, 136.8, 129.0, 128.8, 128.7, 127.6, 127.58, 127.55, 126.8, 56.0, 54.2, 52.9, 24.6, 38.2, 24.8 (two carbon signals are absent due to incidental equivalence); IR (film) 3062, 1572 cm⁻¹; MS (ESI+) 370.2277 (370.2278 calcd for C₃₂H₃₃N₃O₂S, M + H⁺).



1,4-Dibenzyltetrahydropyrimidin-2(1H)-imine 2,2,2-trifluoroacetate (22). A sample of (Z)-4-methoxy-2,3,6-trimethyl-N-[1,3,4-tribenzyltetrahydropyrimidin-2(1H)-ylidene]benzenesulfonamide (**21**) (53 mg, 0.092 mmol) was dissolved in trifluoroacetic acid (5 mL). Methanesulfonic acid (0.27 mL, 4.2 mmol) was added slowly, followed by thioanisole (65 μ L, 0.55 mmol). The reaction solution was stirred at 50 °C for 24 hours. After cooling to rt the trifluoroacetic acid was azeotroped off with toluene (3 x 5 mL). The crude material was dissolved in DCM (10 mL) and washed with sat. sodium bicarbonate solution. The organic layer was dried, filtered, and concentrated *in vacuo* to afford crude product. Purification via flash column chromatography afforded 17 mg (47%) of the desired product as a tan, viscous oil. 1 H NMR (500 MHz, CDCl_3) δ 8.82 (s, 1 H), 7.39 (s, 2 H), 7.37–7.27 (m, 5 H), 7.26–7.13 (m, 5 H), 4.75–4.52 (m, 2 H), 3.65–3.60 (m, 1 H), 3.29–3.20 (m, 2 H), 3.14 (dd, J = 13.5, 4.3 Hz, 1 H), 2.70 (dd, J = 13.5, 9.3 Hz, 1 H), 2.05 (s, br, 1 H), 1.86–1.82 (m, 1 H), 1.66–1.60 (m, 1 H); 13 C NMR (125 MHz, CDCl_3) δ 154.3, 136.0, 134.1, 129.4, 129.2, 128.7, 128.4, 127.4, 127.0, 53.3, 50.5, 44.9, 41.2, 25.4; IR (film) 3144, 1630, 1593 cm^{-1} ; MS (ESI+) 280.1817 (280.1808 calcd for $\text{C}_{18}\text{H}_{21}\text{N}_3$, $\text{M} + \text{H}^+$).



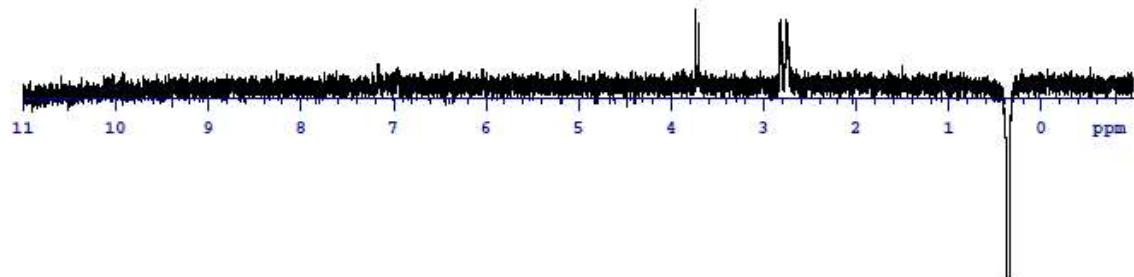
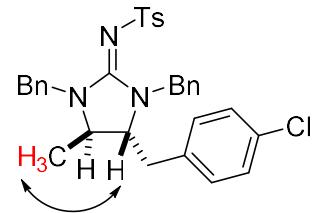
{4-[(2-Imino-1,3-dimethylimidazolidin-4-yl)methyl]phenyl}(phenyl)methanone hydrochloride (25). A sample of *N*-[4-(4-benzoylbenzyl)-1,3-dimethylimidazolidin-2-ylidene]-4-methylbenzenesulfonamide (**24**) (95 mg, 0.206 mmol) was dissolved in trifluoroacetic acid (13 mL). Methanesulfonic acid (0.6 mL, 9.5 mmol) was added slowly, followed by thioanisole (146 μ L, 1.24 mmol). The reaction solution was stirred at rt for 16 hours. The trifluoroacetic acid was

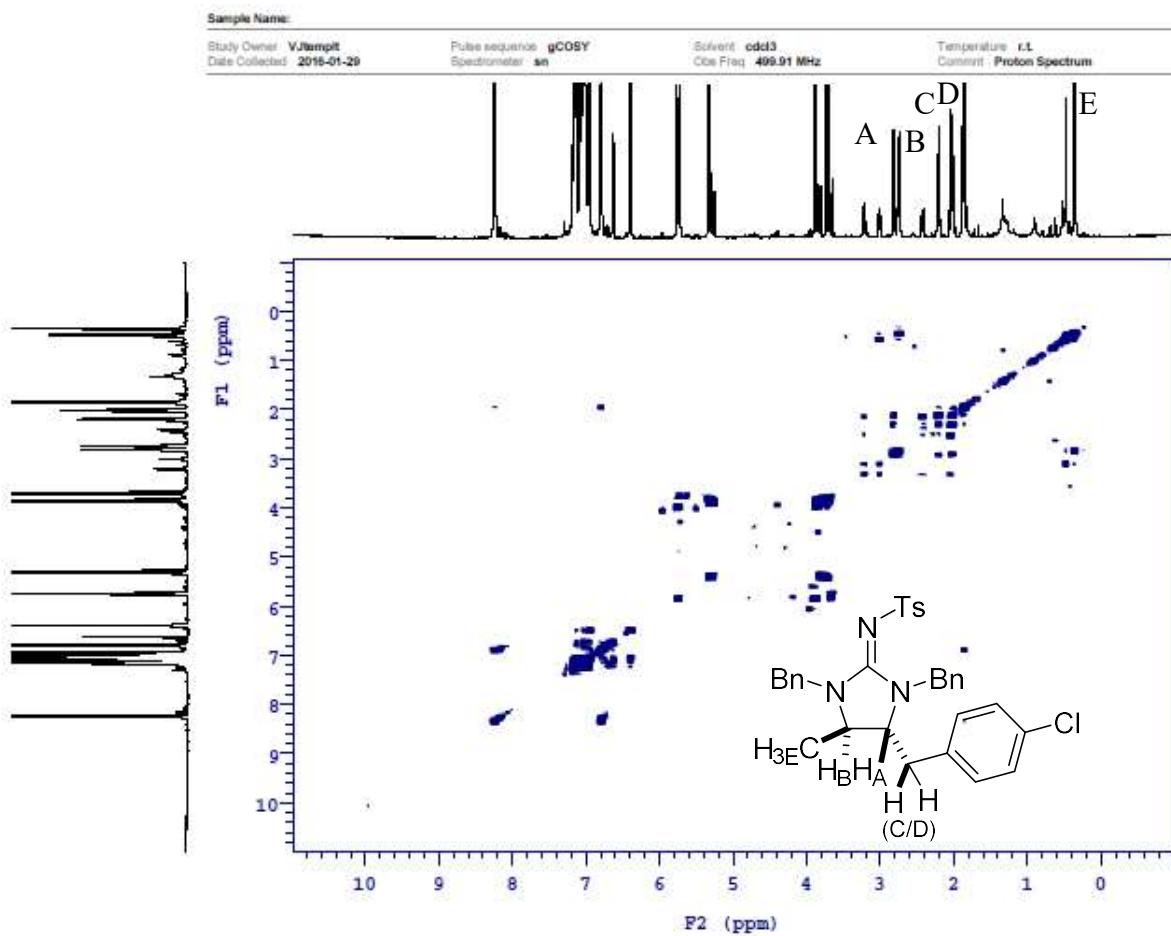
azeotroped off with toluene (3 x 5 mL). The crude material was dissolved in DCM (10 mL) and washed with HCl (6 M), followed by sat. sodium bicarbonate solution. The organic layer was dried, filtered, and concentrated *in vacuo* to afford crude product. Purification via flash column chromatography (methanol:dichloromethane = 9:91) afforded 50 mg (70%) of the desired product as a tan solid, m.p. 252–255 °C. ¹H NMR (400 MHz, CD₃OD) δ 7.76–7.72 (m, 4 H), 7.65–7.62 (m, 1 H), 7.52 (t, *J* = 7.6 Hz, 2 H), 7.43 (d, *J* = 7.9 Hz, 2 H), 4.20–4.12 (m, 1 H), 3.64 (t, *J* = 9.6 Hz, 1 H), 3.37 (dd, *J* = 9.8, 6.0 Hz, 1 H), 3.29 (s, 3 H), 3.21 (dd, *J* = 13.7, 4.4 Hz, 1 H), 3.01 (s, 3 H), 2.96 (dd, *J* = 13.6, 7.8 Hz, 1 H), 2.81 (s, 3 H); ¹³C NMR (125 MHz, CD₃OD) δ 196.6, 158.1, 141.1, 137.4, 136.3, 132.5, 130.1, 129.5, 129.3, 128.1, 59.9, 52.5, 37.0, 30.7, 29.8; IR (film) 3376, 1684 cm⁻¹; MS (ESI+) 308.1760 (308.1757 calcd for C₁₉H₂₁N₃O, M + H⁺).

Assignment of relative stereochemistry for 9h

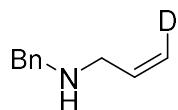
The relative stereochemistry of 9h was assigned using COSY and 1D NOESY analysis. The coupling found in the 1D NOESY can be seen below.

Sample Name:				
Study Owner	lukepet	Pulse sequence	NOESY1D	Temperature
Data Collected	2018-01-29	Spectrometer	80	31.1
				Comment
				Proton Spectrum



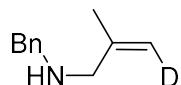


Synthesis of deuterated substrates and products

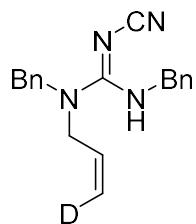


(Z)-N-benzylprop-2-en-3-d-1-amine (S13): A flame dried flask was cooled under a stream of nitrogen and charged with *N*-benzylprop-2-en-1-ylamine (1.00 g, 6.84 mmol) and diethyl ether (12 mL). The solution was cooled to -42 °C, and then *n*-butyl lithium (8.2 mmol, 2.5 M) was added slowly. After 30 minutes *tert*-butyl lithium (15 mmol, 1.7 M) was added slowly. After stirring at -42 °C for 30 minutes the reaction was transferred to an ice-water bath and allowed to stir for 1 hour. The reaction was then cooled to -78 °C, and deuterium oxide was added (2.5 mL, 136.8 mmol). After stirring overnight the reaction was cooled on an ice-water bath, and then quenched with water (15 mL). The mixture was extracted with diethyl ether (2 x 20 mL) and separated. The combined organic layers were then dried, filtered, and evaporated. The crude

product was purified via flash column chromatography on silica gel (ethyl acetate/hexanes) to afford 0.568 g (56%) of the title compound as a pale yellow oil, with 84% deuterium incorporation as determined by ^1H NMR. ^1H NMR (400 MHz, CDCl_3) δ 7.31 (d, J = 4.5 Hz, 4 H), 7.2–7.18 (m, 1 H), 6.03–5.79 (m, 1 H), 5.22–5.15 (m, 1 H), 5.12–5.06 (m, 1 H), 3.78 (s, 3 H), 3.27 (d, 6 Hz, 2 H).

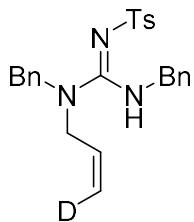


(Z)-N-benzyl-2-methylprop-2-en-3-d-1-amine (S14). A flame dried flask was cooled under a stream of nitrogen and charged with *N*-benzylbut-3-en-2-ylamine (**S5**) (1.00 g, 6.62 mmol) and diethyl ether (13 mL). The solution was cooled to -42 °C, and then n-butyl lithium (7.95 mmol, 2.5 M) was added slowly. After 30 minutes tert-butyl lithium (14.59 mmol, 1.7 M) was added slowly. After stirring at -42 °C for 30 minutes the reaction was transferred to an ice-water bath and allowed to stir for 1 hour. The reaction was then cooled to -78 °C, and deuterium oxide was added (2.4 mL, 132.4 mmol). After stirring overnight the reaction was cooled on an ice-water bath, and then quenched with water (15 mL). The mixture was extracted with diethyl ether (2 x 20 mL) and separated. The combined organic layers were then dried, filtered, and evaporated. The crude product was purified via flash column chromatography on silica gel (ethyl acetate/hexanes) to afford 0.60 g (56%) of the title compound as a pale yellow oil, with 83% deuterium incorporation as determined by ^1H NMR. ^1H NMR (CDCl_3) δ 7.39–7.28 (m, 4 H), 7.28–7.18 (m, 1 H), 4.90 (s, 1 H), 4.84 (s, 1 H), 3.76 (s, 2 H), 3.18 (s, 2 H), 1.76 (s, 3 H).



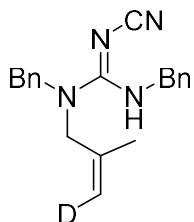
1-[(Z)-allyl-3-d]-1,3-dibenzyl-2-cyanoguanidine (10): A round bottom flask was charged with methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.196 g, 0.96 mmol), ethanol (10 mL), and mercuric oxide (0.312 g, 1.44 mmol), then purged with nitrogen. Triethylamine (0.5 mL, 3.84 mmol) was added followed by (Z)-*N*-benzylprop-2-en-3-d-1-amine (**S13**) (0.170 g, 1.15 mmol). The reaction mixture was then stirred at rt for 72 h. The mixture was filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate/hexanes

to yield 0.153 g (52%) of the title compound as a clear, viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.41–7.28 (m, 6 H), 7.24–7.18 (m, 4 H), 5.80–5.72 (m, 1 H), 5.23 (d, J = 10.4 Hz, 1 H), 5.15 (d, J = 17.2 Hz, 1 H), 4.98 (br, 1 H), 4.74 (d, J = 5.2 Hz, 2 H), 4.58 (s, 2 H), 3.95 (d, J = 5.2 Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.0, 137.1, 135.8, 129.0, 128.9, 128.0, 127.9, 127.7, 127.3, 118.2 (t, J = 23.5 Hz, 117.2, 52.2, 51.4, 47.5; IR (film) 3249, 2162, 1536 cm^{-1} ; MS (ESI+) 306.1827 (306.1823 calcd for $\text{C}_{19}\text{H}_{19}\text{DN}_4$, $\text{M} + \text{H}^+$).

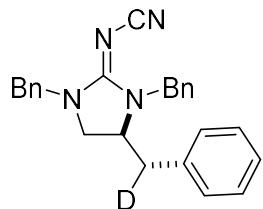


***N*-[(Z)-allyl-3-d](benzyl)amino-benzylaminomethylene-4-methylbenzenesulfonamide**

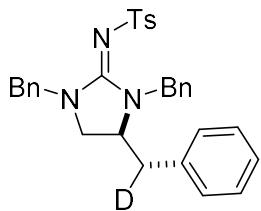
(11): A round bottom flask was charged with dimethyl tosylcarbonimidodithioate (**S3**) (0.569 g, 1.70 mmol), ethanol (17 mL), and mercuric oxide (0.548 g, 2.53 mmol), then purged with nitrogen. Triethylamine (0.95 mL, 6.75 mmol) was added followed by (Z)-*N*-benzylprop-2-en-3-d-1-amine (**S13**) (0.300 g, 2.0 mmol). The reaction mixture was then stirred at rt for 72 h. The mixture was filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate/hexanes) to yield 0.363 g (49%) of the title compound as a white solid, m.p. 79–81 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.59 (d, J = 8.4 Hz, 2 H), 7.33–7.20 (m, 6 H), 7.18–7.06 (m, 6 H), 6.96 (br, 1 H), 5.75–5.67 (m, 1 H), 5.16 (d, J = 10.4 Hz, 1 H), 5.08 (d, J = 17.3 Hz, 1 H), 4.47 (s, 2 H), 4.37 (d, J = 5.9 Hz, 2 H), 2.37 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.9, 141.7, 141.0, 136.9, 136.4, 132.3, 129.1, 128.9, 128.7, 128.0, 127.61, 127.6, 127.58, 127.4, 126.0, 118.6 (t, J = 25 Hz), 51.8, 51.75, 49.7; IR (film) 3322, 1564 cm^{-1} ; MS (ESI+) 435.1965 (435.1960 calcd for $\text{C}_{25}\text{H}_{26}\text{DN}_3\text{O}_2\text{S}$, $\text{M} + \text{H}^+$).



1,3-dibenzyl-2-cyano-1-[(Z)-2-methylallyl-3-d]guanidine (12). A round bottom flask was charged with methyl *N*-benzyl-*N'*-cyanocarbamimidothioate (**S1**) (0.60 g, 2.91 mmol), ethanol (30 mL), and mercuric oxide (0.95 g, 4.37 mmol), then purged with nitrogen. Triethylamine (1.6 mL, 11.64 mmol) was added followed by (Z)-*N*-benzyl-2-methylprop-2-en-3-d-1-amine (**S14**) (0.57 g, 3.49 mmol). The reaction mixture was then stirred at rt for 72 h. The mixture was filtered through celite. The celite was rinsed with acetone, and the solution was concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel (ethyl acetate/hexanes) to yield 0.39 g (42%) of the title compound as a clear, viscous oil. ¹H NMR (400 MHz, CDCl₃) δ 7.38–7.24 (m, 6 H), 7.24–7.18 (m, 4 H), 5.09 (s, br, 1 H), 4.93 (s, 1 H), 4.80 (s, 1 H), 4.77 (d, *J* = 5.3 Hz, 2 H), 4.60 (s, 2 H), 3.80 (s, 2 H), 1.65 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 159.2, 139.5, 137.1, 135.9, 129.0, 128.9, 128.8, 128.1, 128.0, 127.7, 127.5, 117.1, 112.6 (t, *J* = 33.1 Hz), 54.2, 52.5, 47.7, 19.8; IR (film) 3256, 2162, 1539 cm⁻¹; MS (ESI+) 320.1986 (320.1980 calcd for C₂₀H₂₁DN₄, M + H⁺).

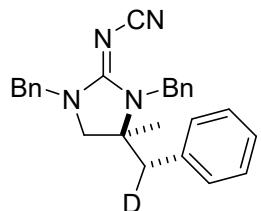


***N*-(\pm)-1,3-dibenzyl-4-[(\pm)-phenylmethyl-d]imidazolidin-2-ylidene}cyanamide (13):** The general procedure A was employed for the coupling of bromobenzene (35.3 mg, 0.225 mmol) with 1-((Z)-allyl-3-d)-1,3-dibenzyl-2-cyanoguanidine (**10**) (45.8 mg, 0.15 mmol). This procedure afforded 33.3 mg (58%) of the title compound as a white, viscous oil. This compound was obtained as a 9:1 mixture of diastereomers as judged by ¹H NMR analysis; data are for the mixture. ¹H NMR (400 MHz, CDCl₃) δ 7.39–7.25 (m, 8 H), 7.25–7.15 (m, 5 H), 6.95–6.84 (m, 2 H), 5.36 (d, *J* = 15.6 Hz, 1 H), 4.79–4.51 (m, 2 H), 4.19 (d, *J* = 15.6 Hz, 1 H), 3.78–3.60 (m, 1 H), 3.19 (t, *J* = 9.6 Hz, 1 H), 3.05–2.90 (m, 2 H), 2.54 (dd, *J* = 13.4, 8.8 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 158.2, 135.7, 135.34, 135.2, 129.1, 129.0, 128.88, 128.82, 128.2, 128.13, 128.11, 128.0, 127.2, 116.5, 55.8, 49.5, 47.3, 38.2, 37.8 (t, *J* = 19.3 Hz); IR (film) 2169, 1596 cm⁻¹; MS (ESI+) 382.2132 (382.2136 calcd for C₂₅H₂₃DN₄, M + H⁺).



***N*-{(\pm)-1,3-dibenzyl-4-[(\pm)-phenylmethyl-d]imidazolidin-2-ylidene}-4-methylbenzenesulfonamide (14):**

methylbenzenesulfonamide (14): The general procedure B was employed for the coupling of phenyl trifluoromethanesulfonate (101.8 mg, 0.45 mmol) with *N*-{[(Z)-allyl-3-d](benzyl)amino}-benzylaminomethylene-4-methylbenzenesulfonamide (**11**) (134.3 mg, 0.30 mmol). This procedure afforded 140 mg (92%) of the title compound as a pale yellow solid, m.p. 106–108 °C. This compound was obtained as a >20:1 mixture of diastereomers as judged by ¹H NMR analysis; data are for the mixture. ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, *J* = 8.4 Hz, 2 H), 7.36–7.26 (m, 5 H), 7.25–7.14 (m, 10 H), 6.87–6.80 (m, 2 H), 5.27 (d, *J* = 15.3 Hz, 1 H), 4.75 (d, *J* = 15.0 Hz, 1 H), 4.51 (d, *J* = 15.1 Hz, 1 H), 4.15 (d, *J* = 15.4 Hz, 1 H), 3.64 (dt, 9.7, 4.9 Hz, 1 H), 3.20 (t, *J* = 9.9 Hz, 1 H), 3.02–2.85 (m, 2 H), 2.49 (dd, *J* = 13.8, 8.3 Hz, 1 H), 2.34 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 156.2, 143.0, 141.1, 135.9, 135.7, 135.5, 129.2, 128.9, 128.8, 128.74, 128.72, 128.3, 128.27, 127.9, 127.8, 127.0, 125.8, 55.4, 50.8, 48.76, 48.71, 37.9 (t, *J* = 19 Hz); IR (film) 1563 cm⁻¹, MS (ESI+) 511.2271 (511.2273 calcd for C₃₁H₃₀DN₃O₂S, M + H⁺).



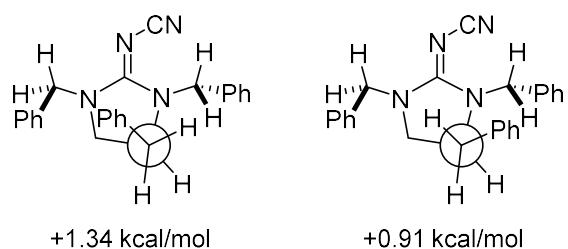
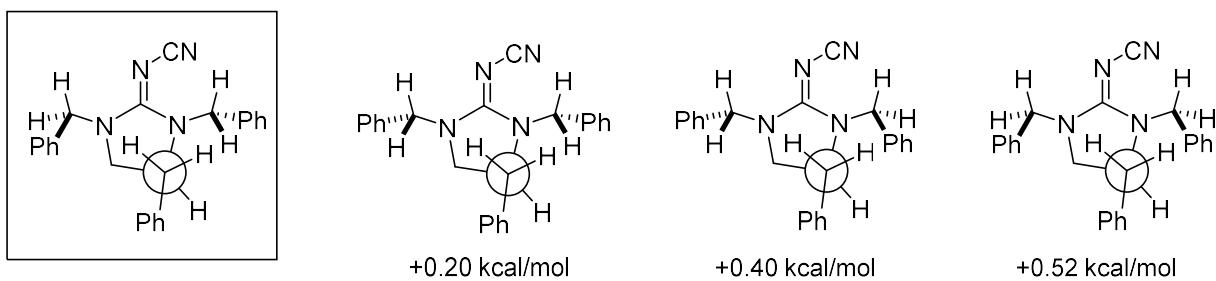
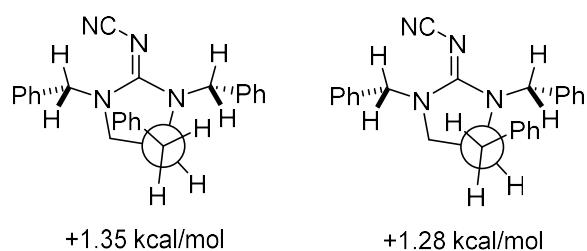
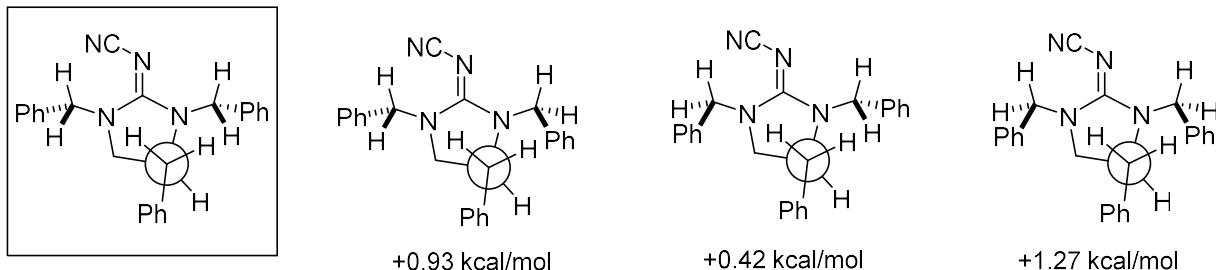
***N*-(4S)-1,3-dibenzyl-4-methyl-4-(phenylmethyl-d)imidazolidin-2-ylidene]cyanamide (15).**

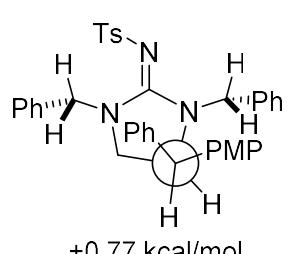
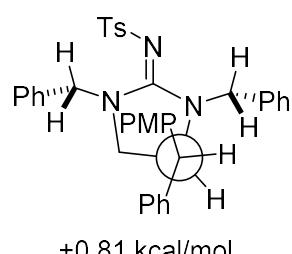
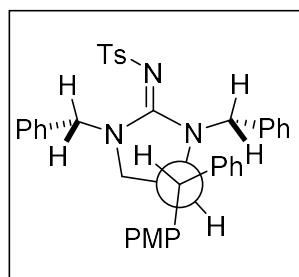
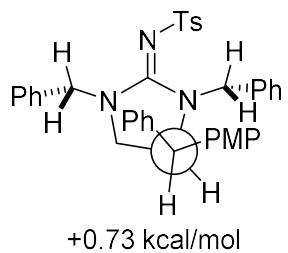
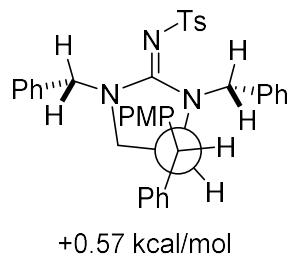
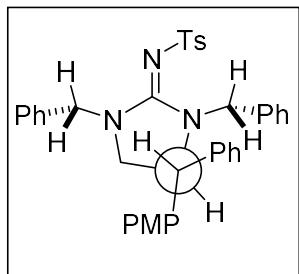
The general procedure A was employed for the coupling of bromobenzene (35.3 mg, 0.225 mmol) with 1,3-dibenzyl-2-cyano-1-[(Z)-2-methylallyl-3-d]guanidine (**12**) (64 mg, 0.2 mmol). This procedure afforded 63 mg (80%) of the title compound as a white, viscous oil. This compound was obtained as a 15.5:1 mixture of diastereomers as judged by ¹H NMR analysis; data are for the mixture. ¹H NMR (CDCl₃) δ 7.39–7.30 (m, 6 H), 7.28–7.22 (m, 4 H), 7.20 (dd, *J* = 7.7, 1.8 Hz, 2 H), 6.93–6.86 (m, 2 H), 5.00 (d, *J* = 16.2 Hz, 1 H), 4.69–4.52 (m, 2 H), 4.41 (d, *J* = 16.2 Hz, 1 H), 3.29 (d, *J* = 9.8 Hz, 1 H), 2.91 (d, *J* = 9.8 Hz, 1 H), 2.77 (d, *J* = 13.7 Hz, 1 H), 2.59 (d, *J* = 12.2 Hz, 1 H), 1.16 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 157.4, 138.2, 135.4, 135.0, 129.9,

128.9, 128.8, 128.7, 128.6, 128.4, 128.0, 127.5, 127.4, 127.3, 62.3, 55.6, 49.4, 44.7, 43.5, 43.2 (t, $J = 20$ Hz), 24.5; IR (film) 2167, 1593 cm^{-1} ; MS (ESI+) 396.2300 (296.2293 calcd for $\text{C}_{26}\text{H}_{25}\text{DN}_4$, $\text{M} + \text{H}^+$).

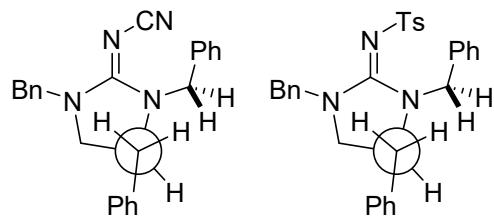
Computational Details

All geometries were optimized using the spin-restricted B3LYP^[5] density functional and the 6-31G* basis set. All density functional calculations were performed using Spartan'14^[6]. The calculations are meant to be used for qualitative purposes only.

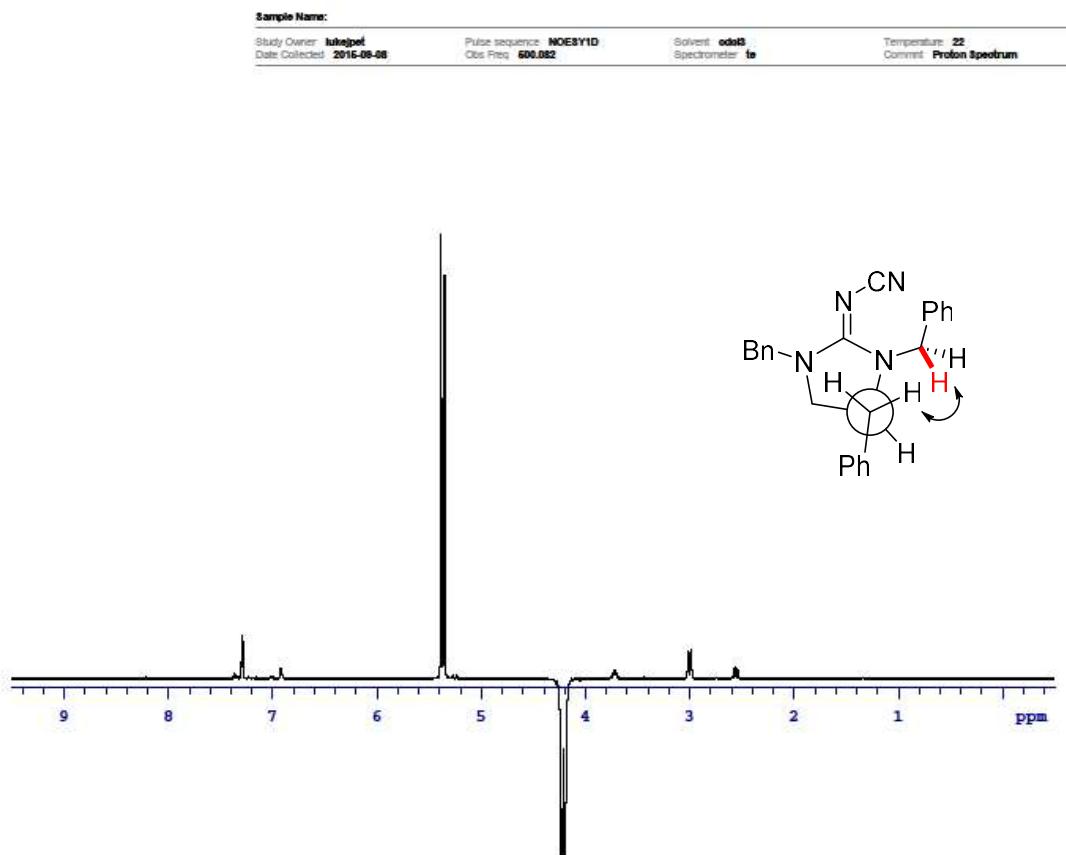


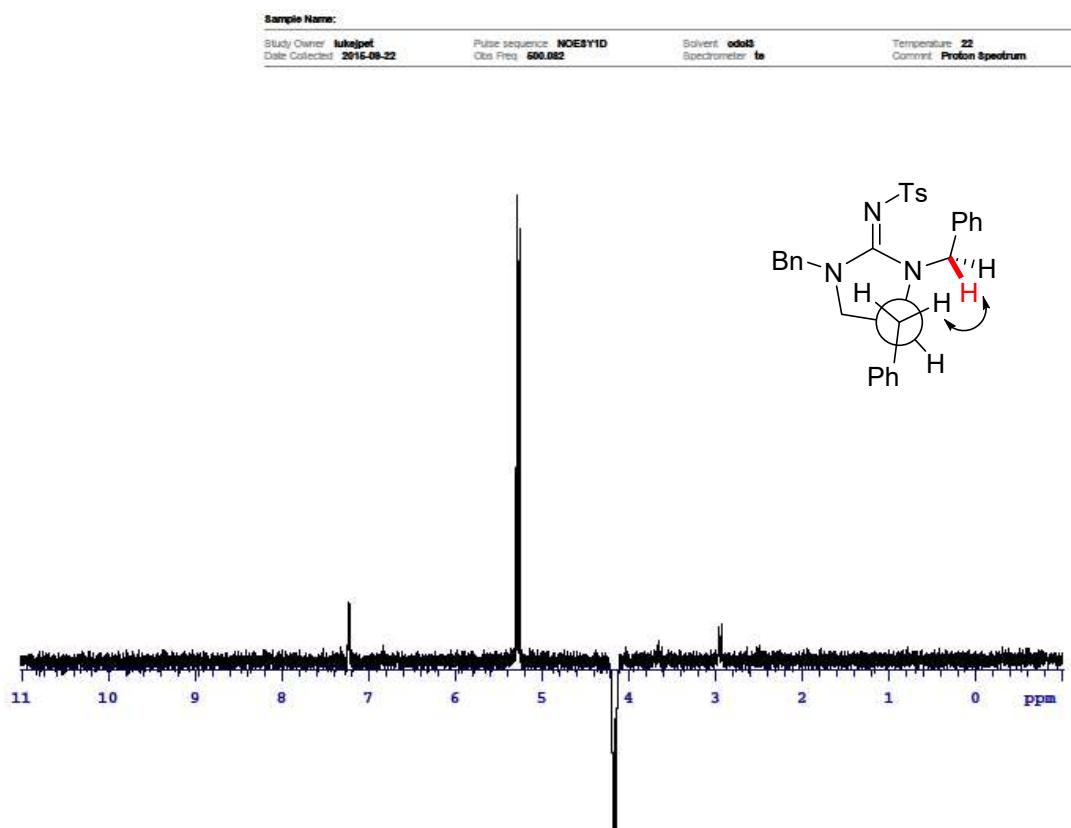
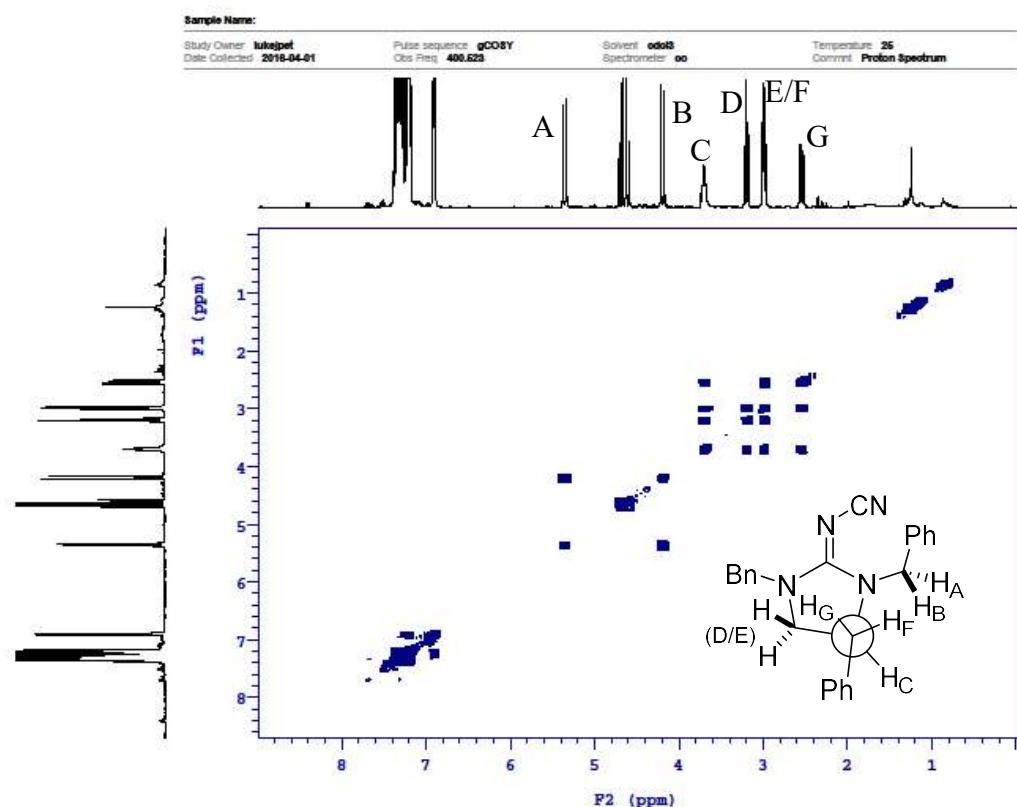


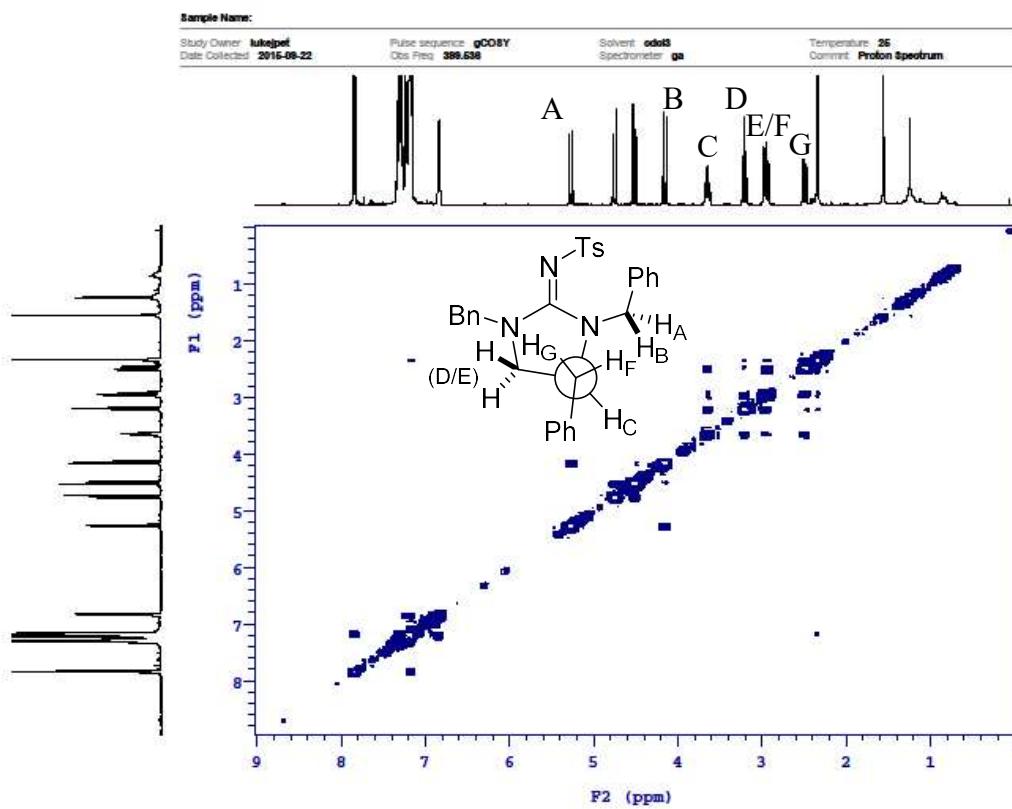
Deuterium Labeling Studies



In order to determine the relative stereochemical configuration of the deuterium labelled compounds **13** and **14**, the hypothesized ground state energy conformations shown above were used in conjunction with 1D ^1H nOe analysis of the all-proteo analogs of these compounds. The key nOe signals are shown below.







The configuration of the deuterated products was then assigned by examining which signal was absent from the ^1H NMR.

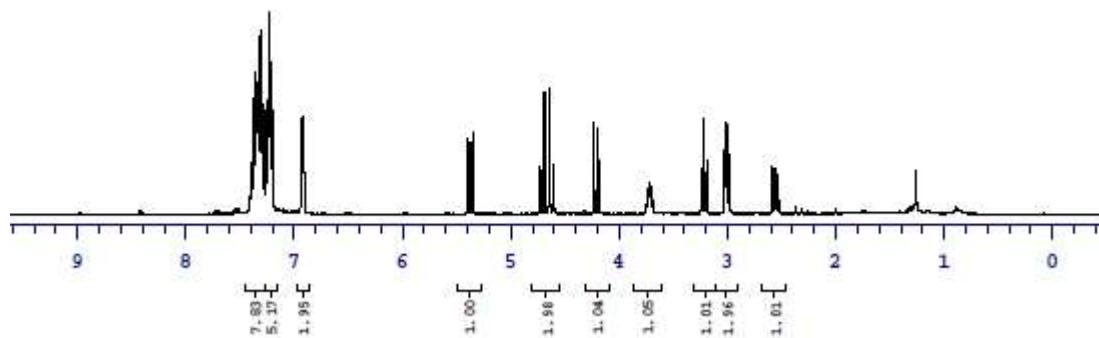
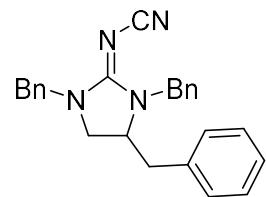
logies

Sample Name: Date collected: 2015-10-07

Pulse sequence: PROTON
Solvent: *cdcl3*

Temperature 25
Operator **lukejpet**

Study owner lukejpet
Printed from za.chem.lsu

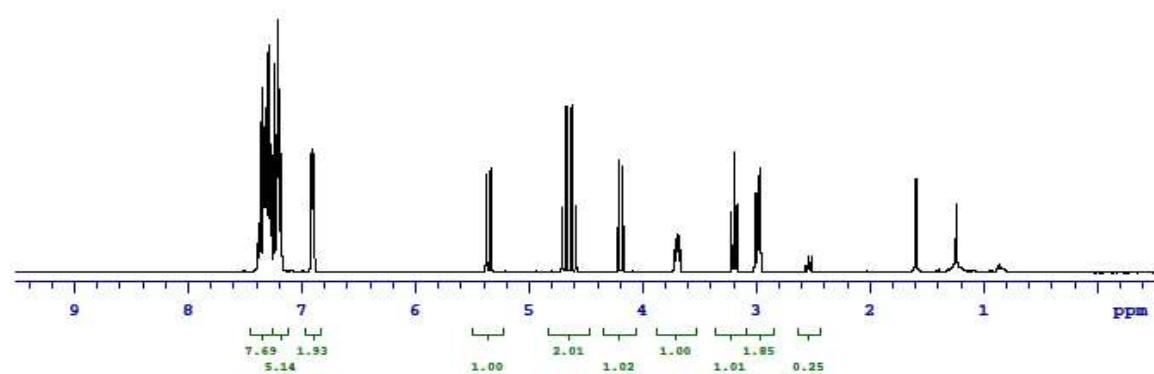
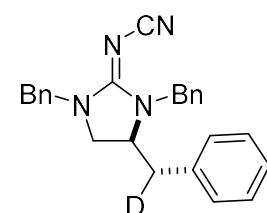


Sample Name
Date collected 2015-09-07

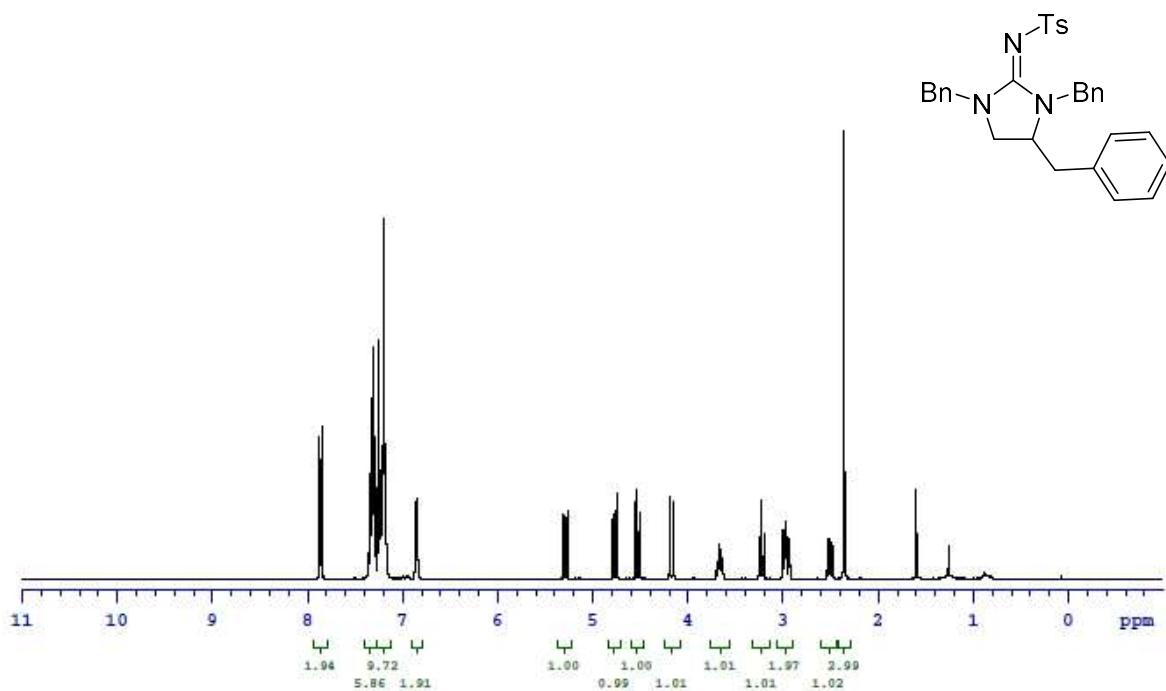
Pulse sequence **PROTON**
Solvent **cdcl3**

Temperature 26
Operator Lukaspet

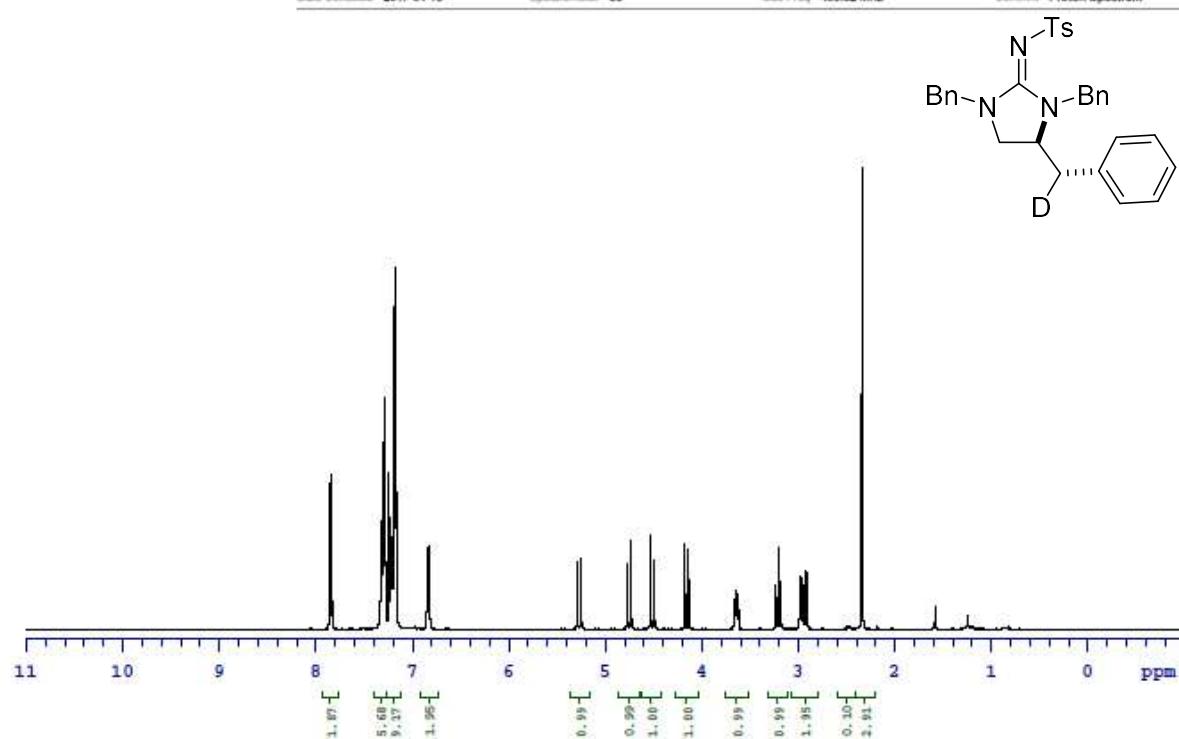
Study owner **lukejpet**
Printed from <http://chem-lsa.umich.edu/vnmrj-500>



Sample Name:	luoji	Positive sequence:	PROTON	Temperature:	25	Study owner:	luoji
Date collected:	2015-10-23	Robert:	0013	Operator:	Jurij	Edited by:	luoji

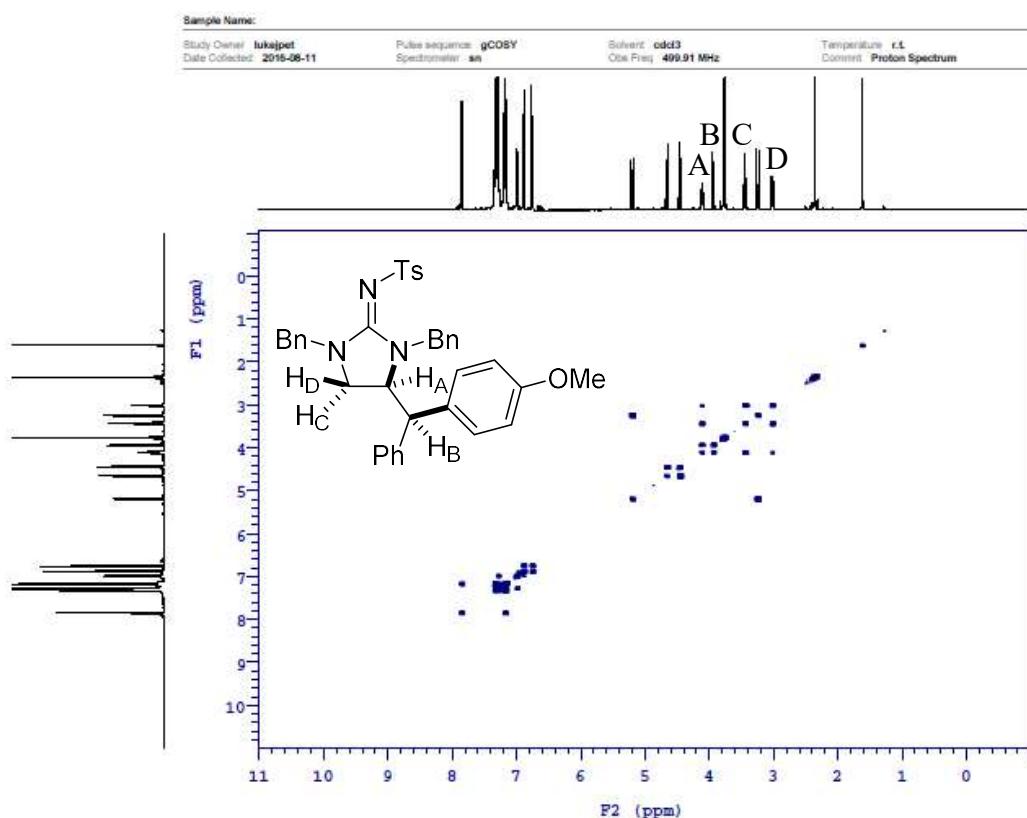


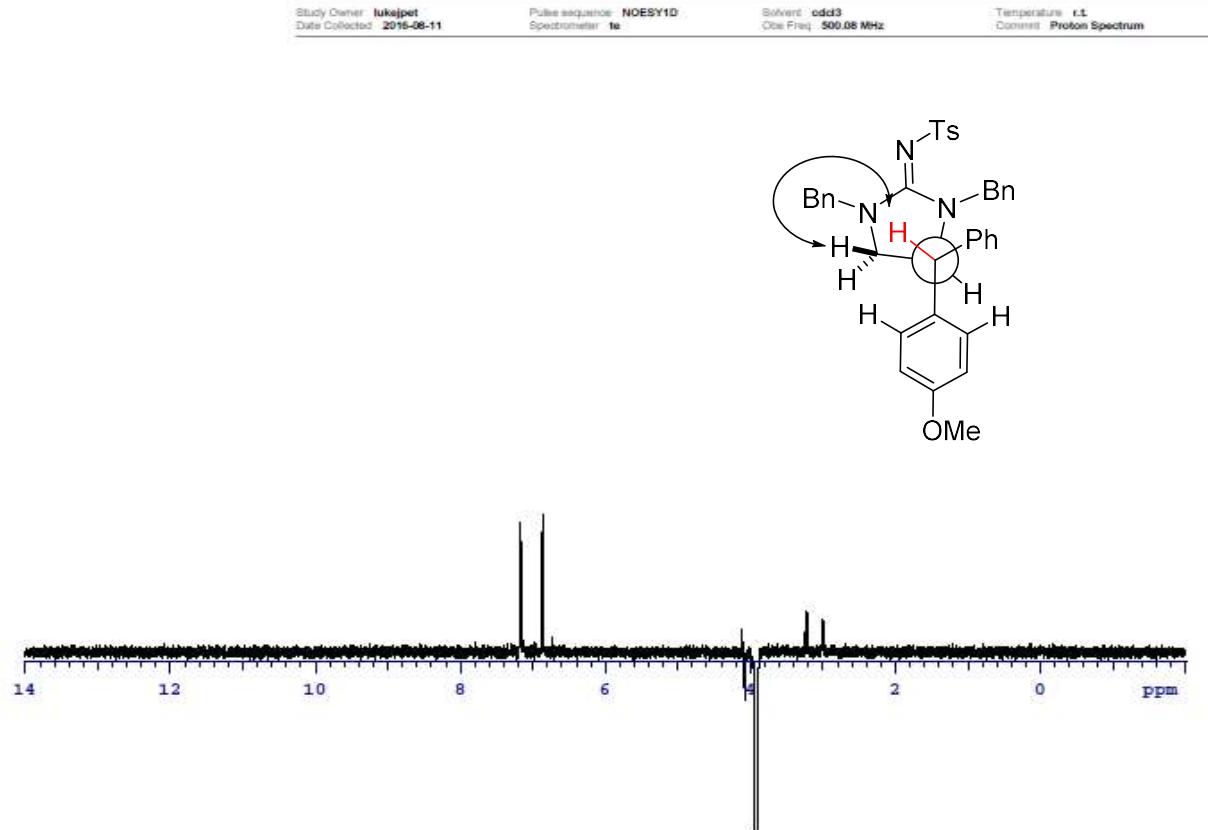
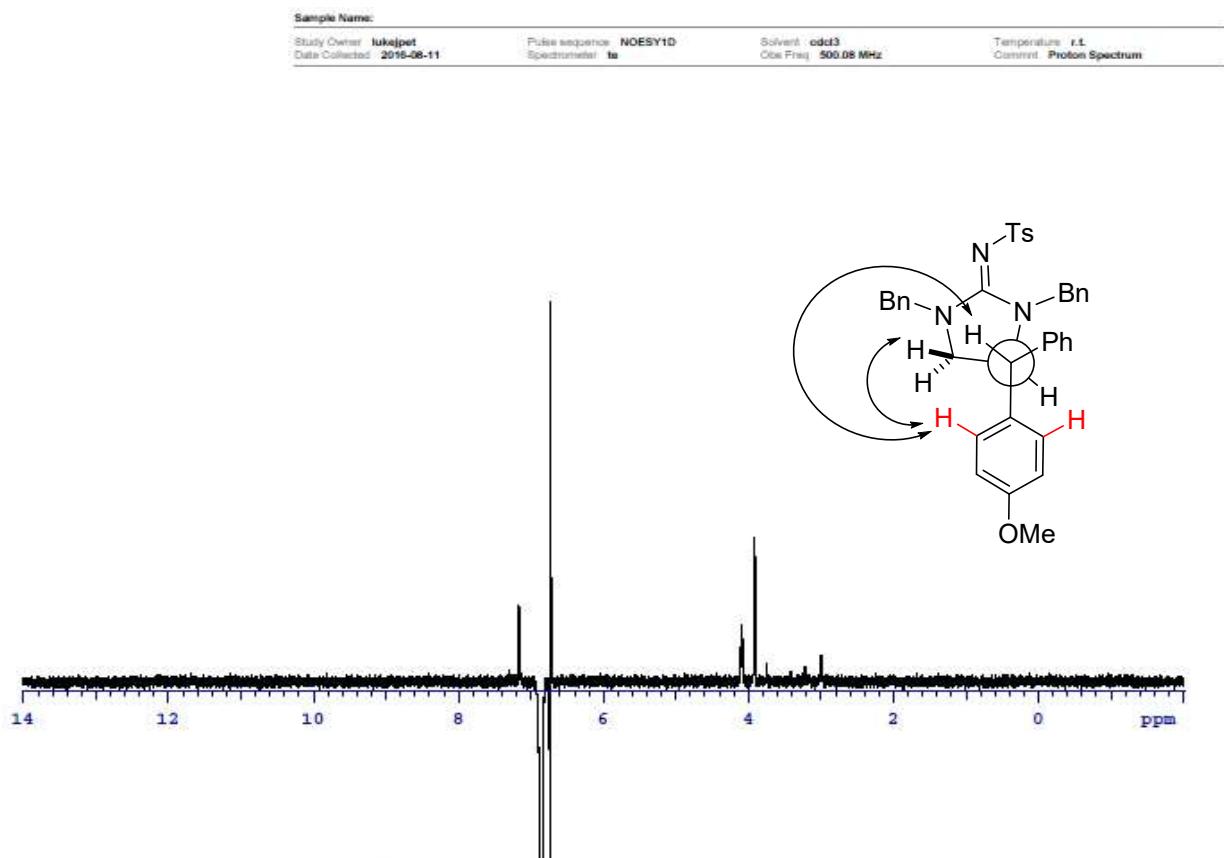
Sample Name: **lukajpet** Pulse sequence: **PROTON** Solvent: **cd3d** Temperature: **r.t.**
Study Owner: **lukajpet** Date Collected: **2017-04-18** Spectrometer: **400** Cope Event: **400.52 MHz** Compton: **Proton Spectrum**



Assignment of Stereochemistry for **8n**, **9k**, and **9l**.

The stereochemistry for compound **9l** was determined through use of 1D ^1H nOe analysis. The key nOe signals are shown below. The stereochemistry for compounds **8n** and **9k** were assumed based on the results for compound **9l**.





References

[1] Frantz, D. E.; Weaver, D. G.; Carey, J. P.; Kress, M. H.; Dolling, U. H. *Org. Lett.* **2002**, *4*, 4717–4718.

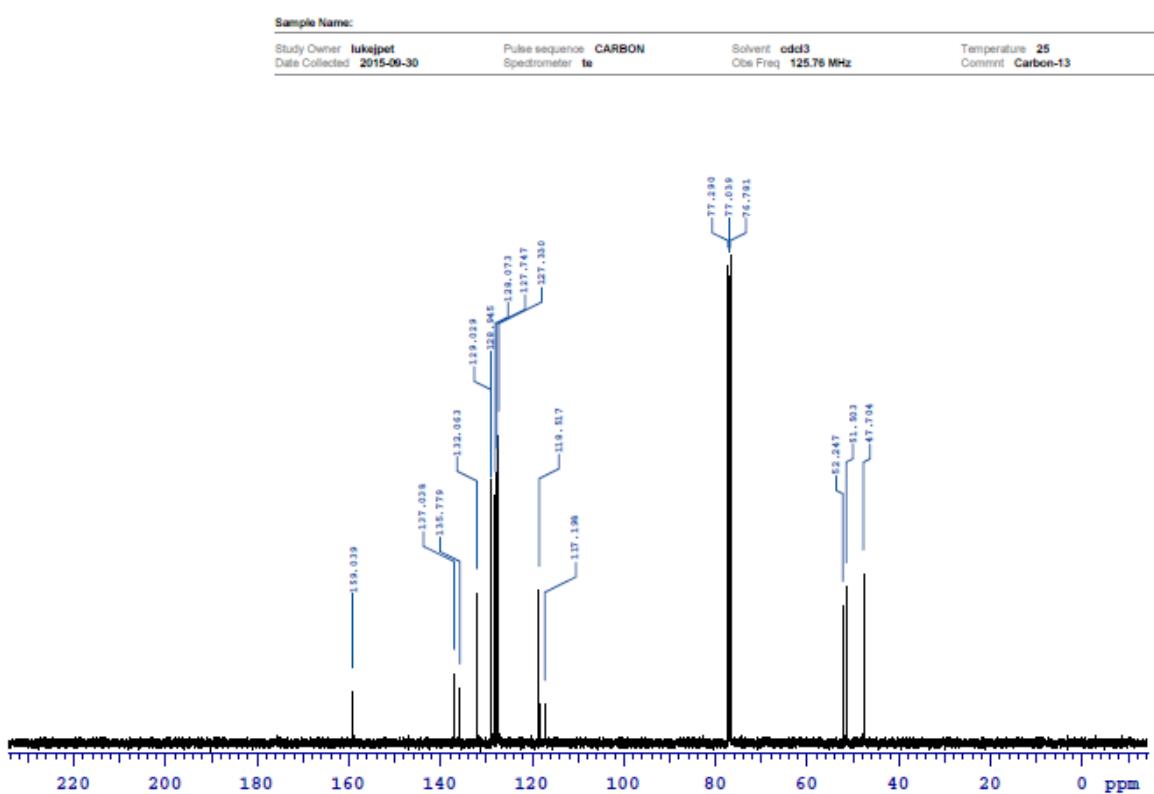
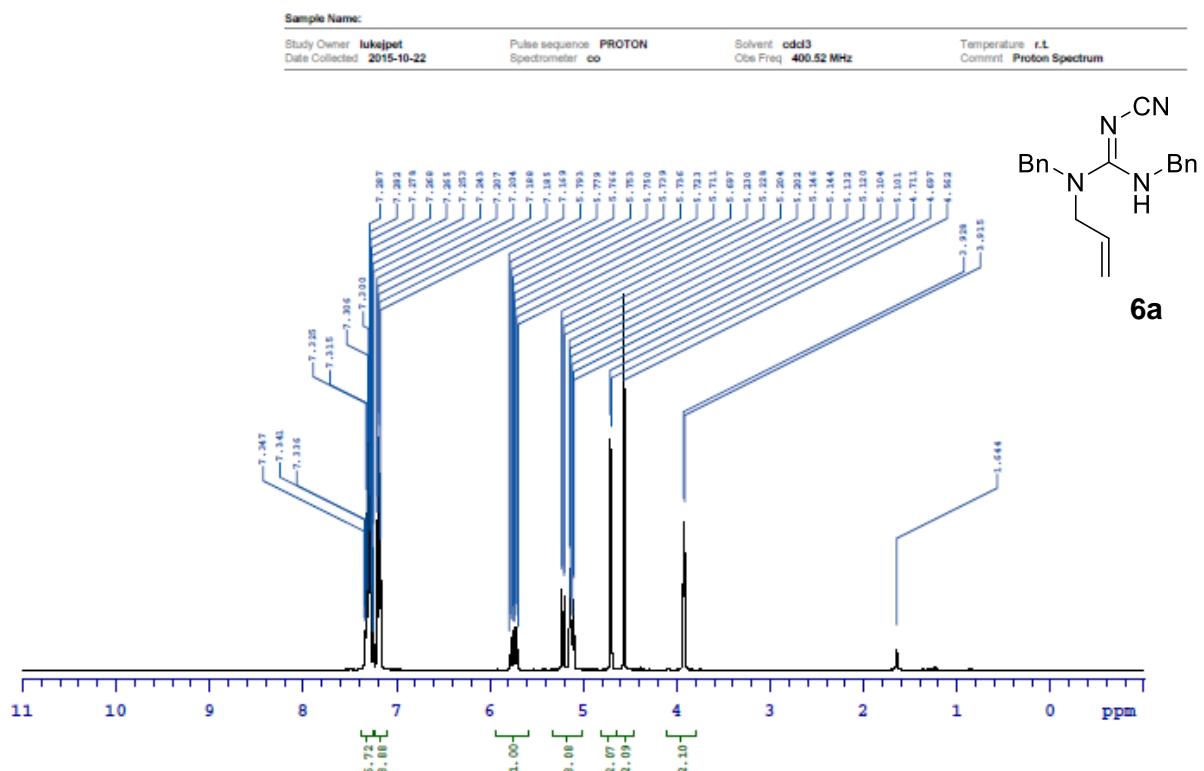
[2] Fritz, J. A.; Wolfe, J. P. *Tetrahedron* **2008**, *64*, 6838–6852.

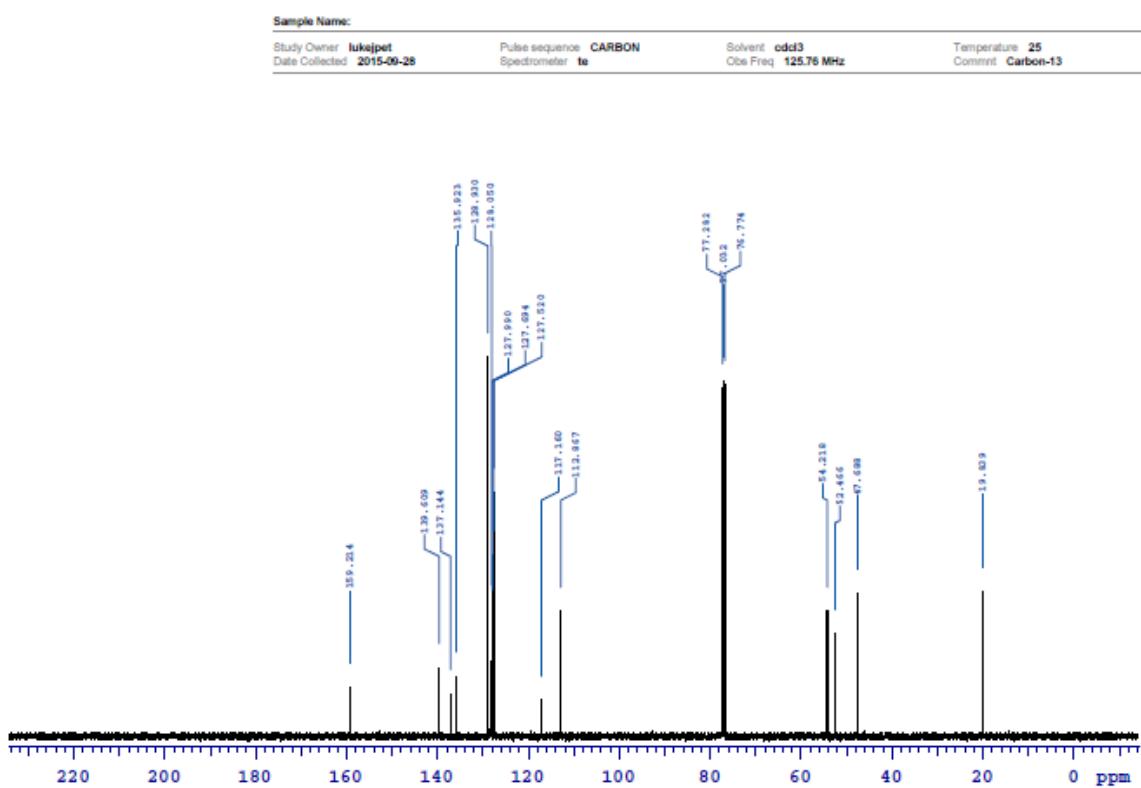
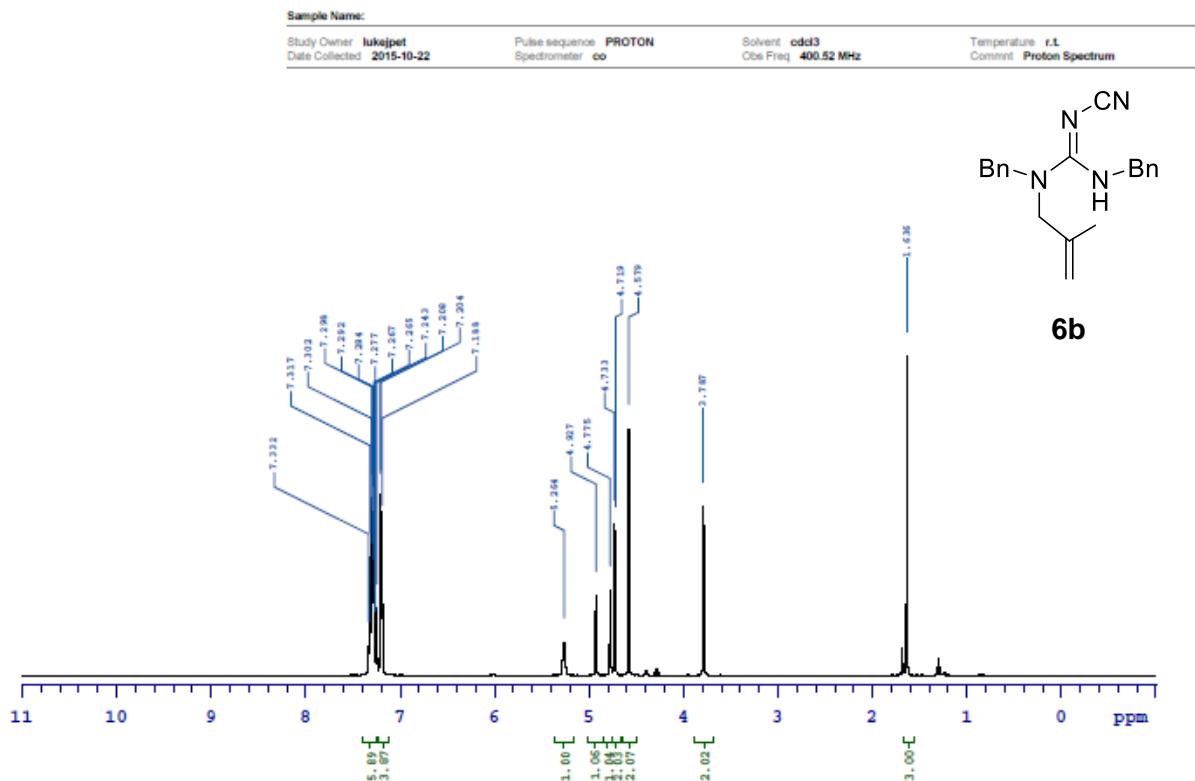
[3] Dieter, R. K.; Oba, G.; Chandupatla, K. R.; Topping, C. M.; Lu, K.; Watson, R. T. *J. Org. Chem.* **2004**, *69*, 3076–3086.

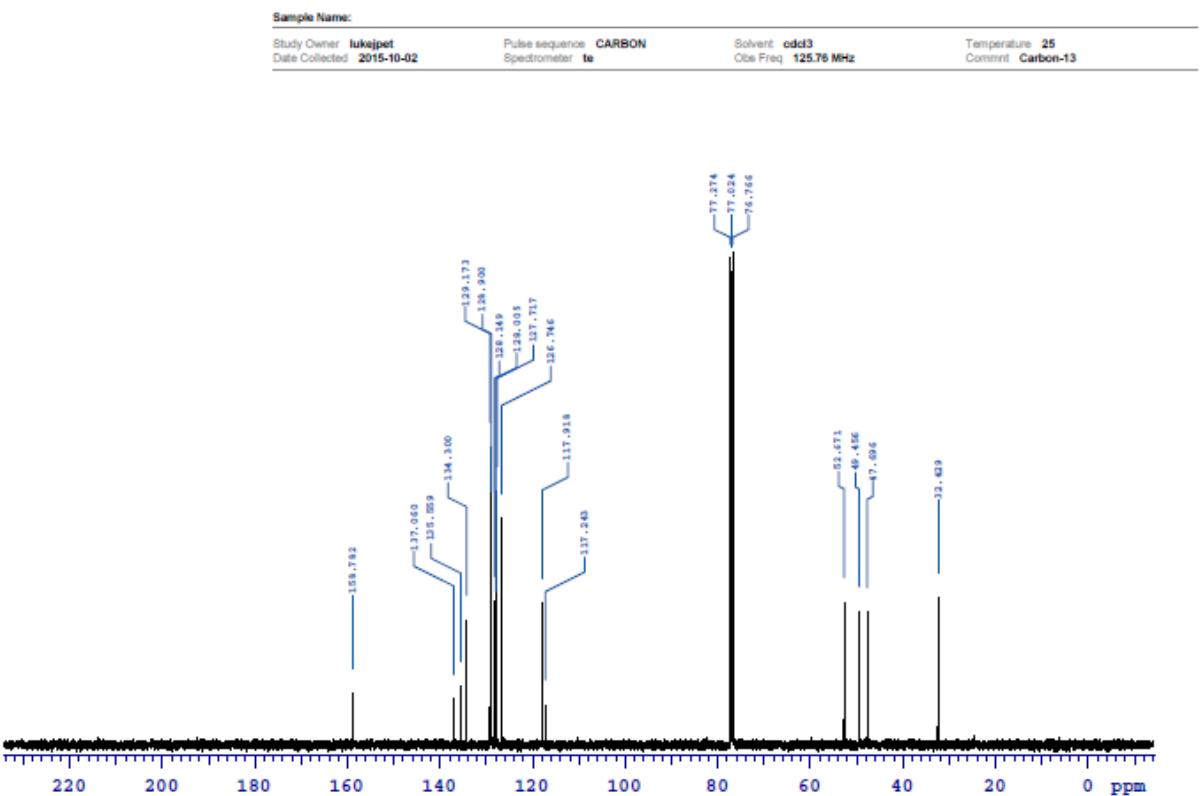
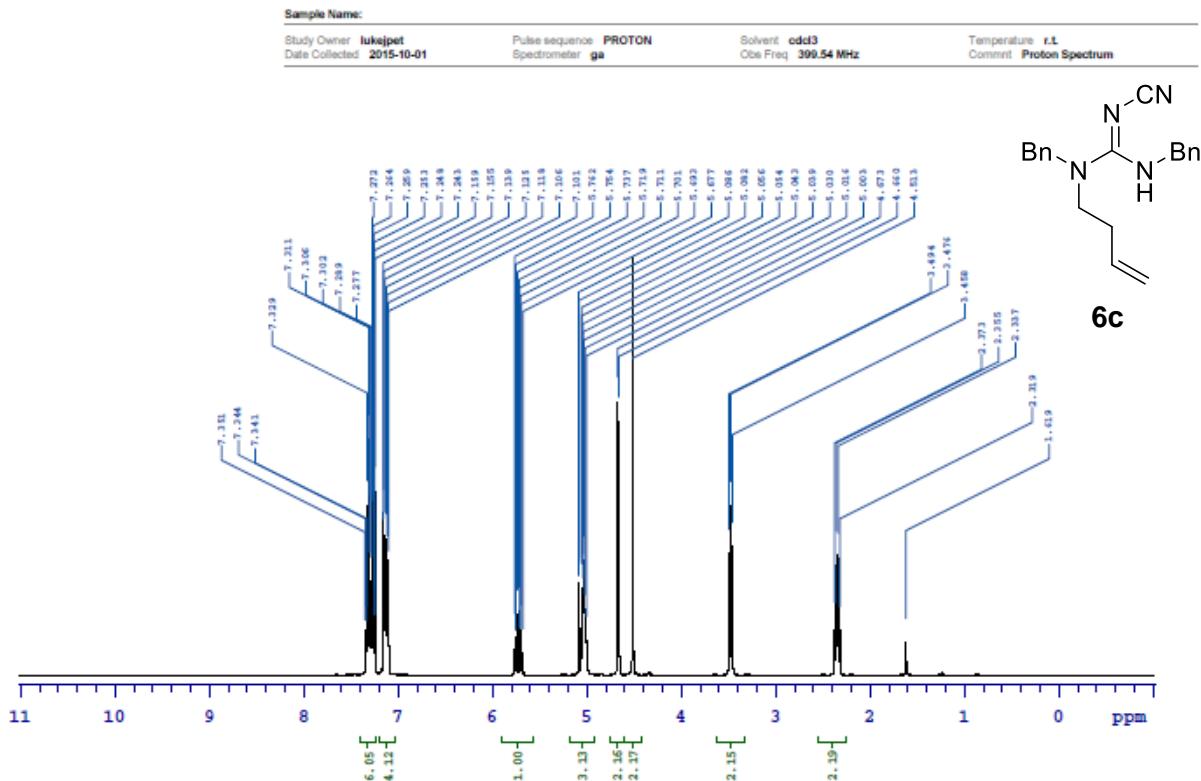
[4] Veenstra, S. J.; Schmid, P. *Tetrahedron Lett.* **1997**, *38*, 997–1000.

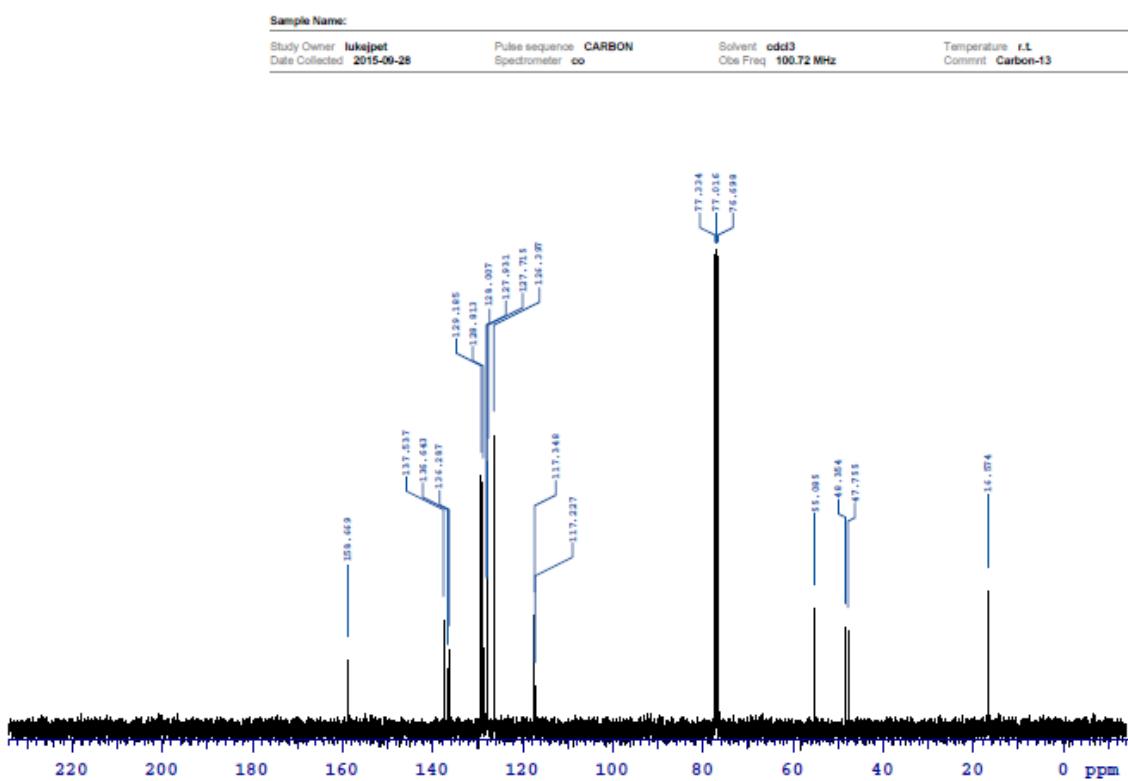
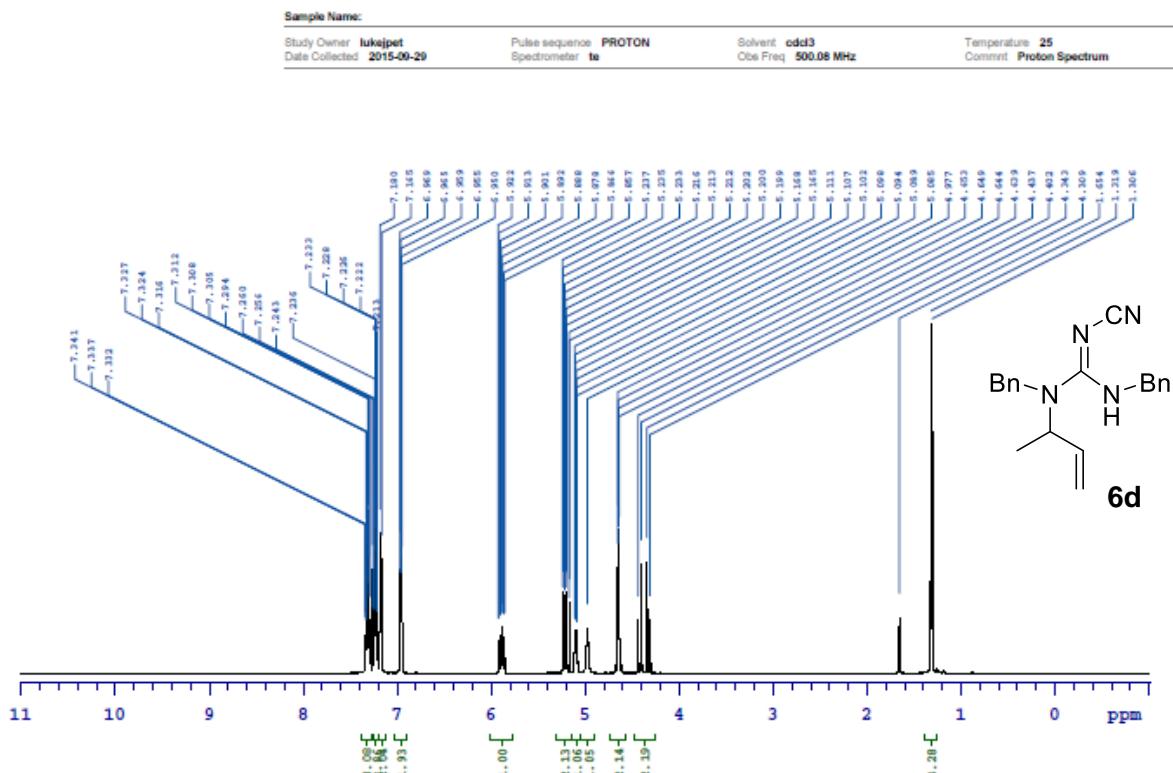
[5] a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. b) Lee, C.; Yang, W.; Parr, R.G. *Phys. Rev.* **1988**, *37*, 785–789. c) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200–1211. d) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627.

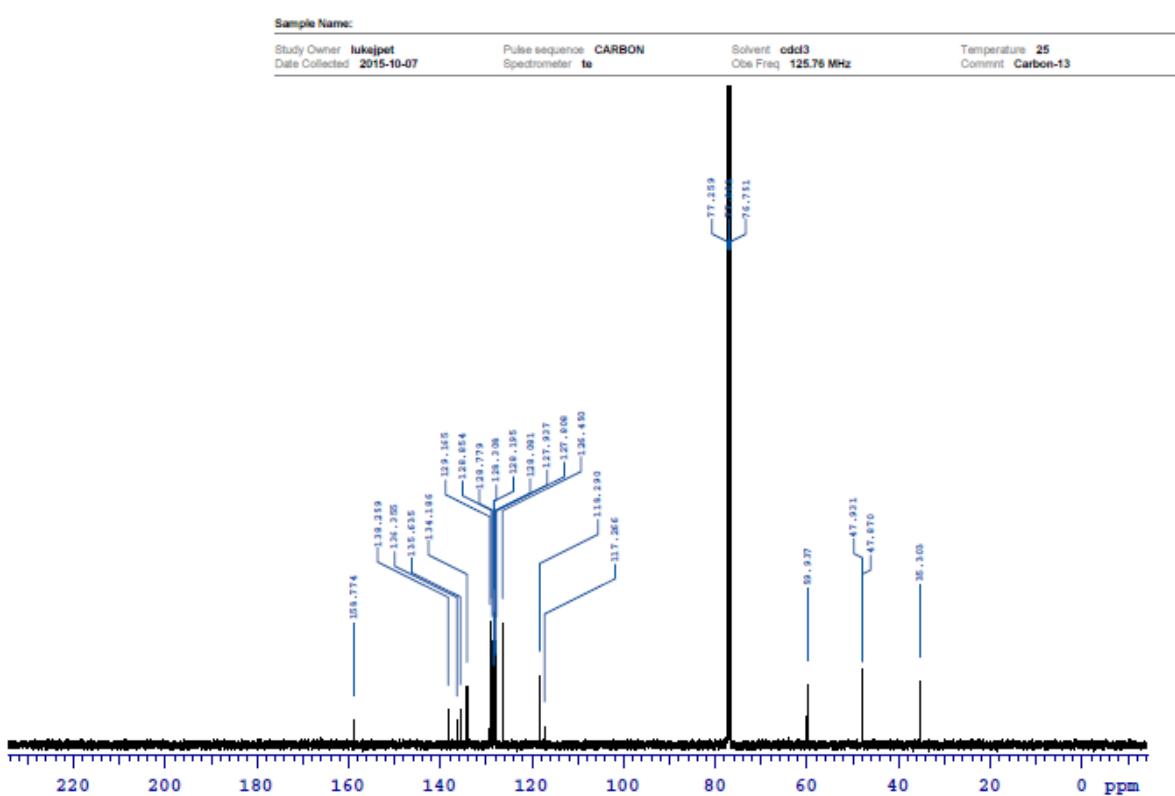
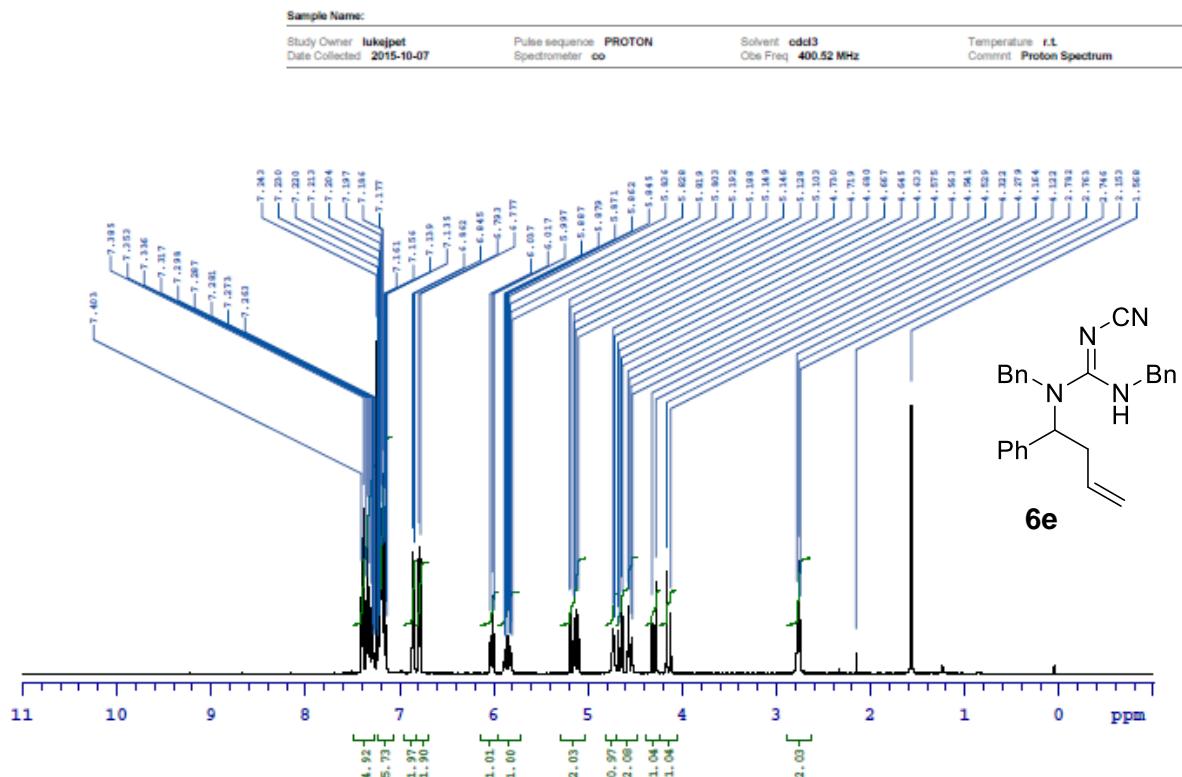
[6] Shao, Y.; Molnar, L. F.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; Levchenko, S. V.; O'Neill, D. P.; DiStasio Jr., R. A.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Van Voorhis, T.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Dachsel, H.; Doerksen, R. J.; Dreuw, A.; Dunietz, B. D.; Dutoi, A. D.; Furlani, T. R.; Gwaltney, S. R.; Heyden, A.; Hirata, S.; Hsu, C-P.; Kedziora, G.; Khaliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W. Z.; Lotan, I.; Nair, N.; Peters, B.; Proynov, E. I.; Pieniazek, P. A.; Rhee, Y. M.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; Woodcock III, H. L.; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; Schaefer, H. F.; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3172. Spartan'14; Wavefunction, Inc.: Irvine, CA, 2014.

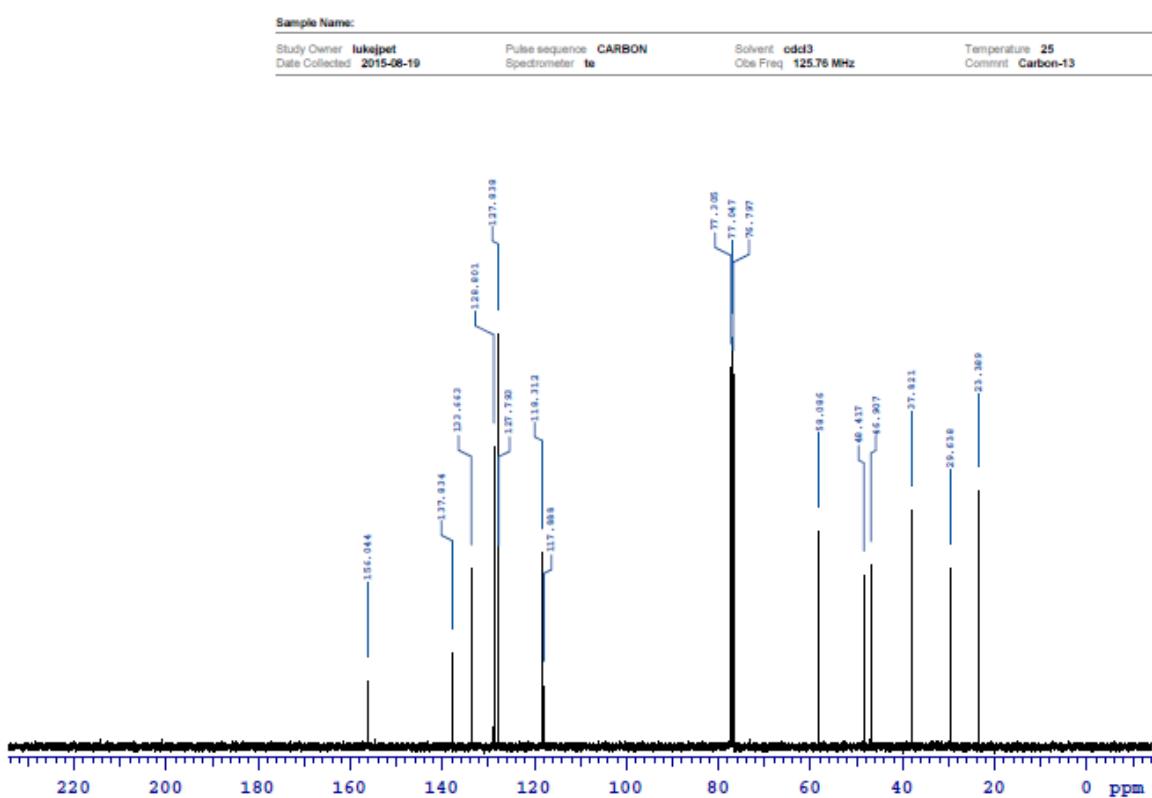
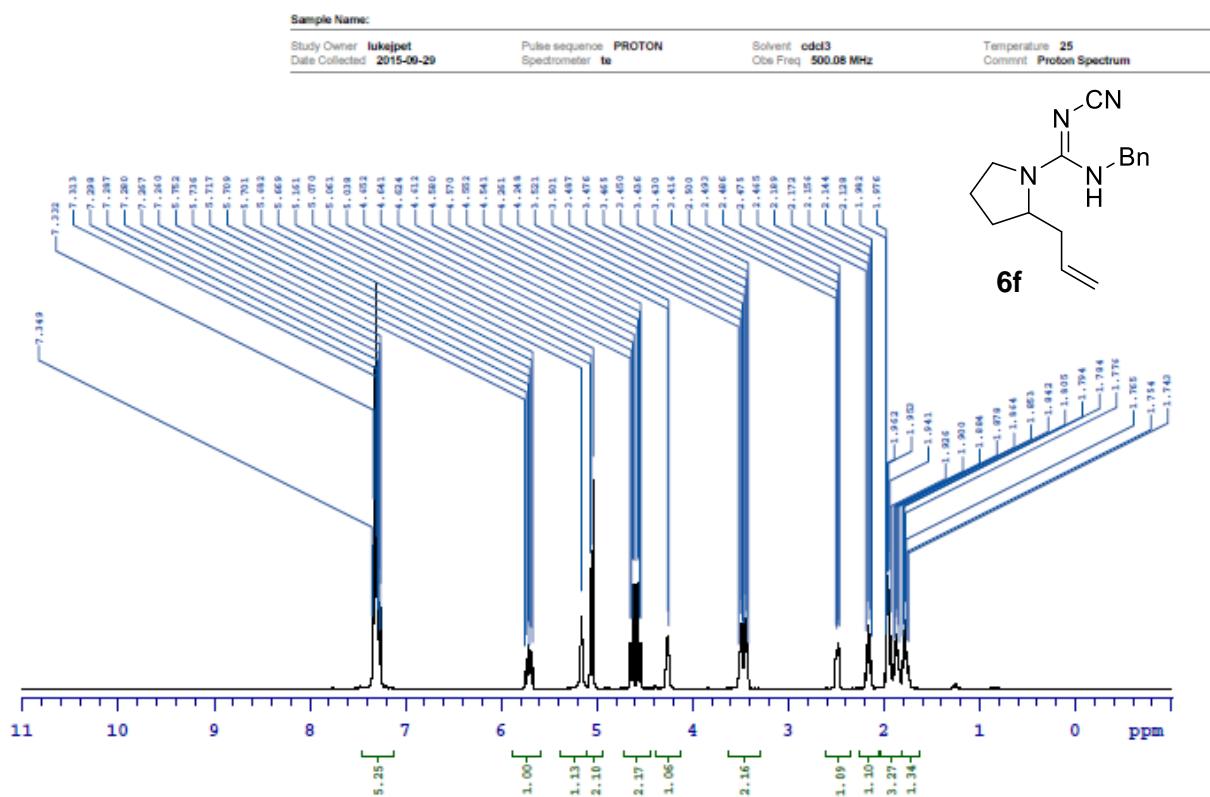


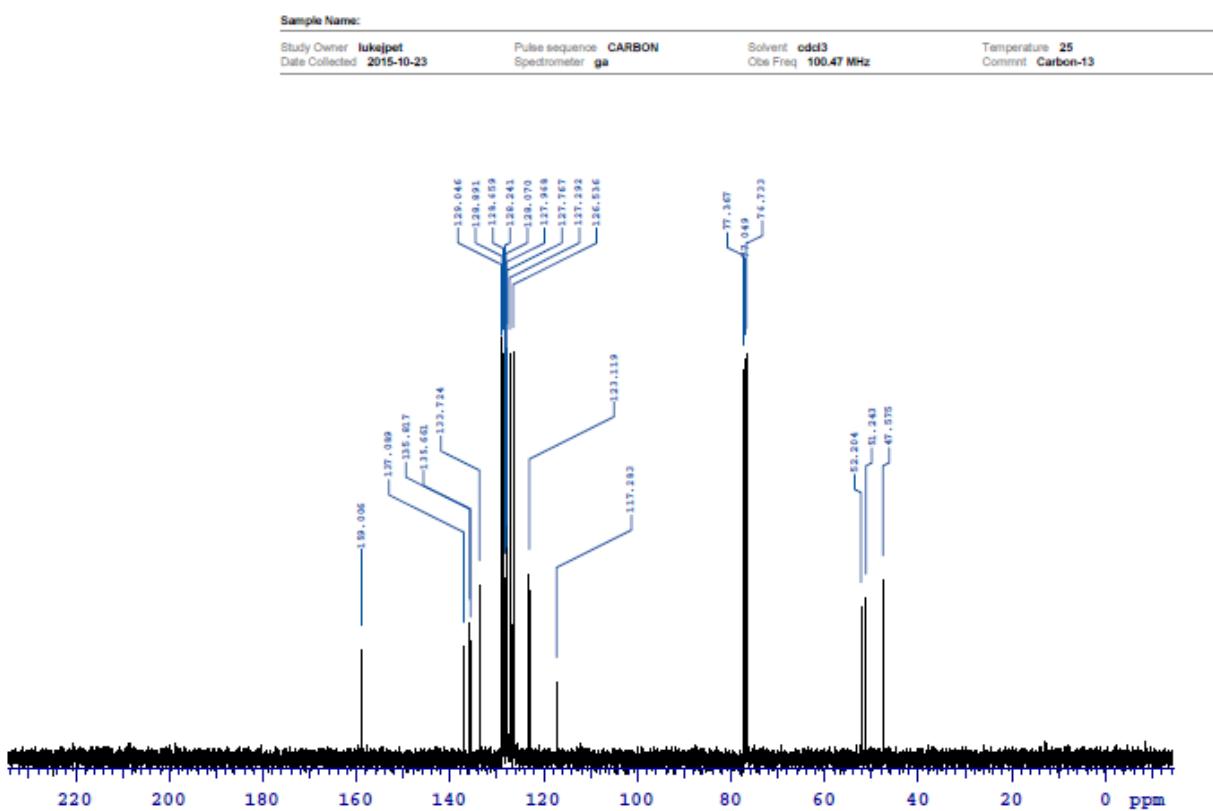
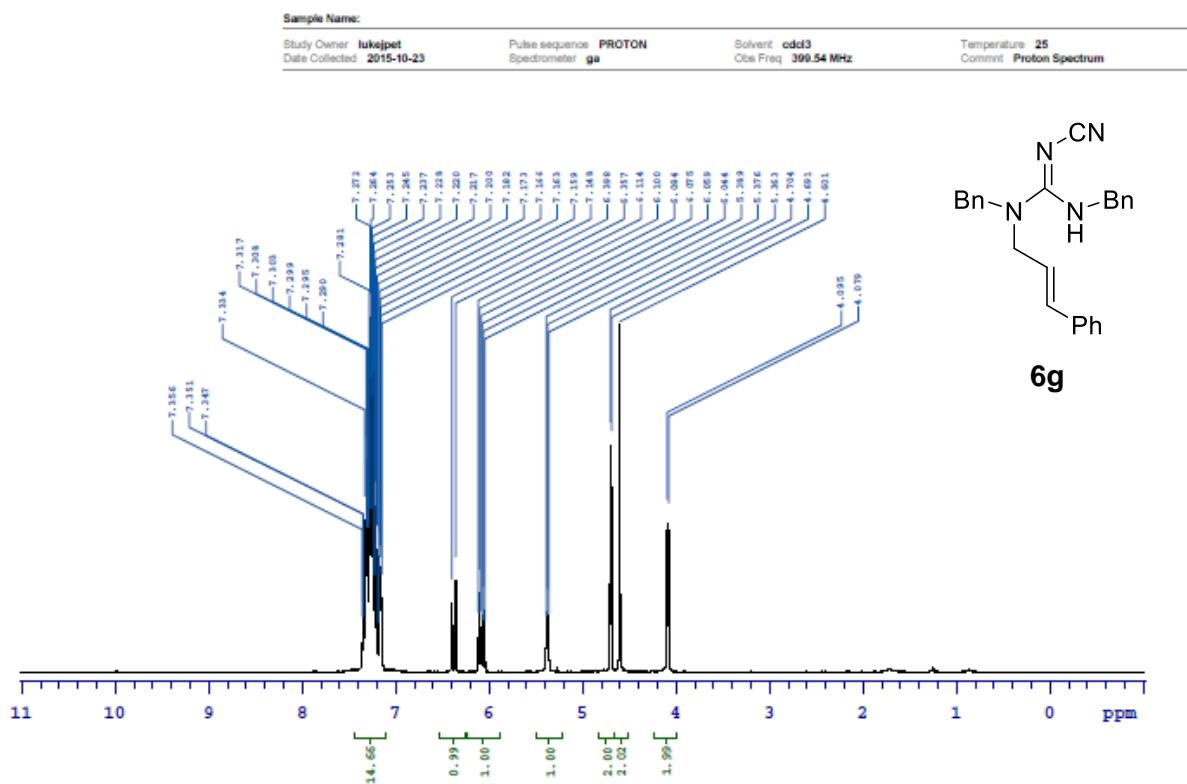


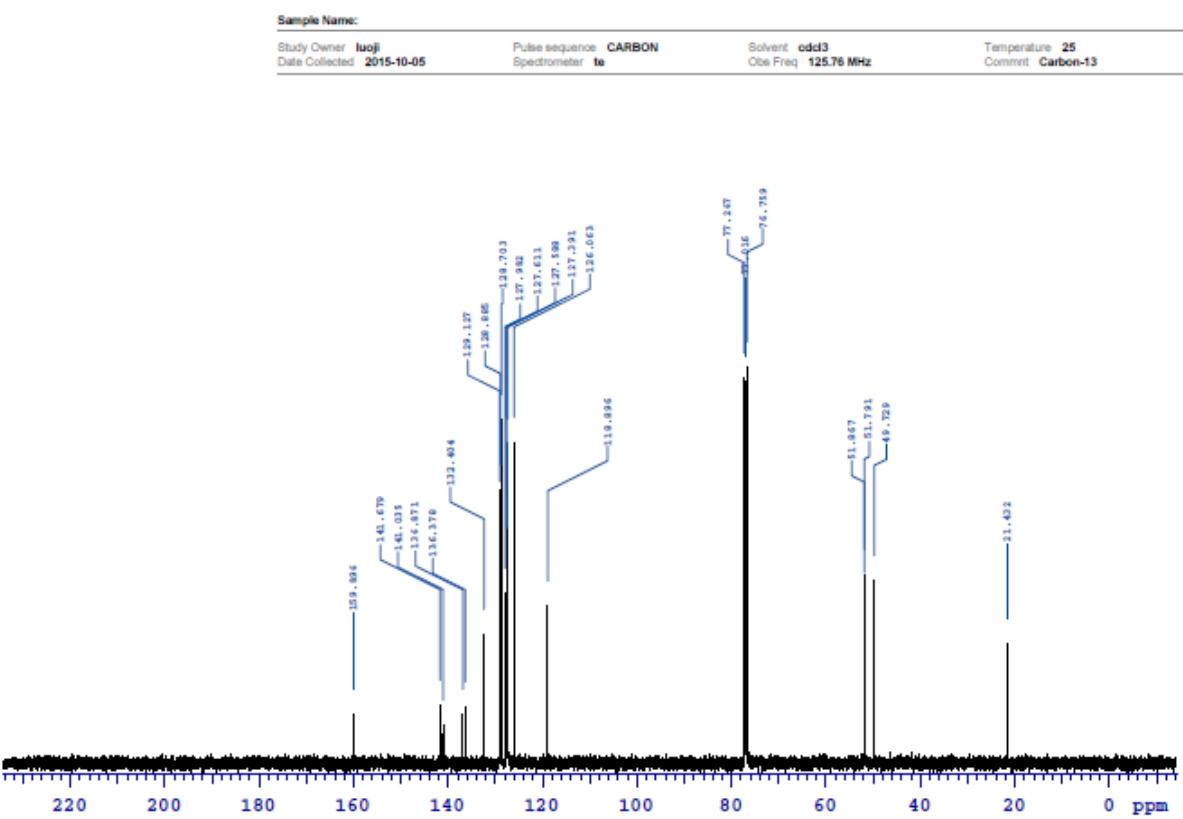
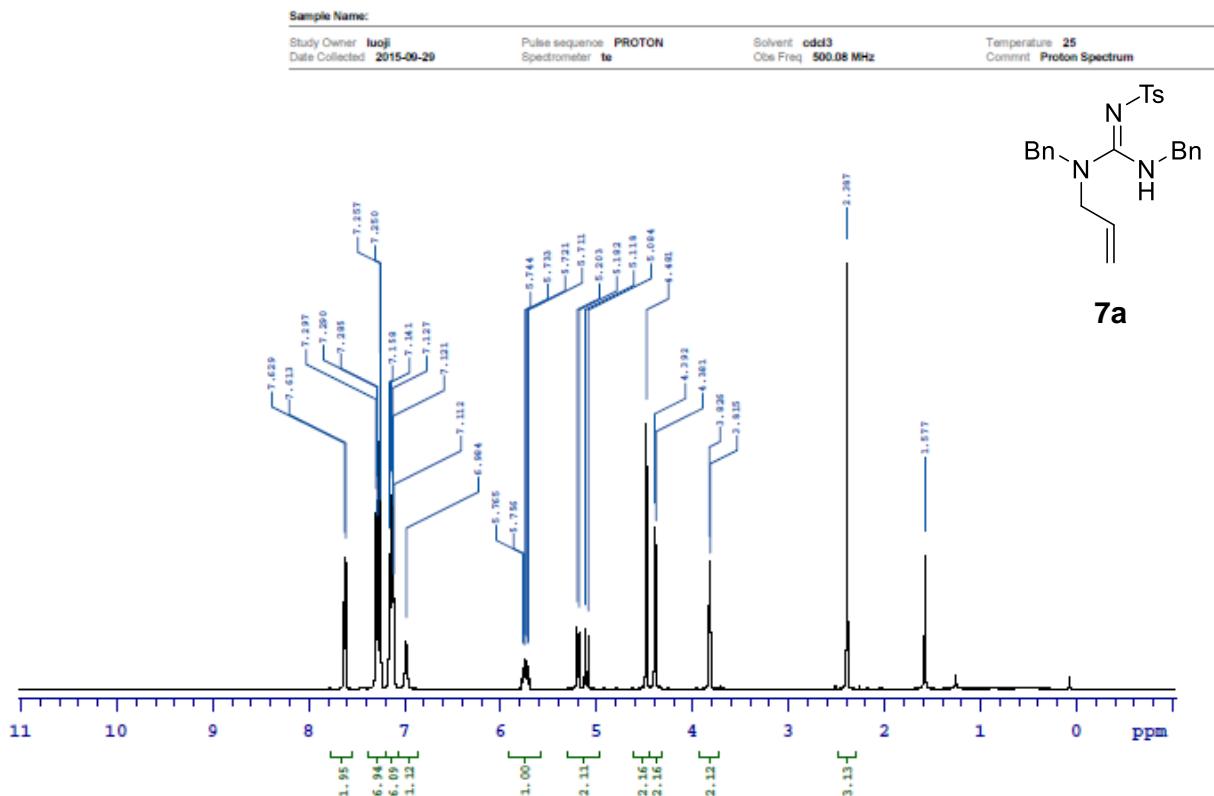


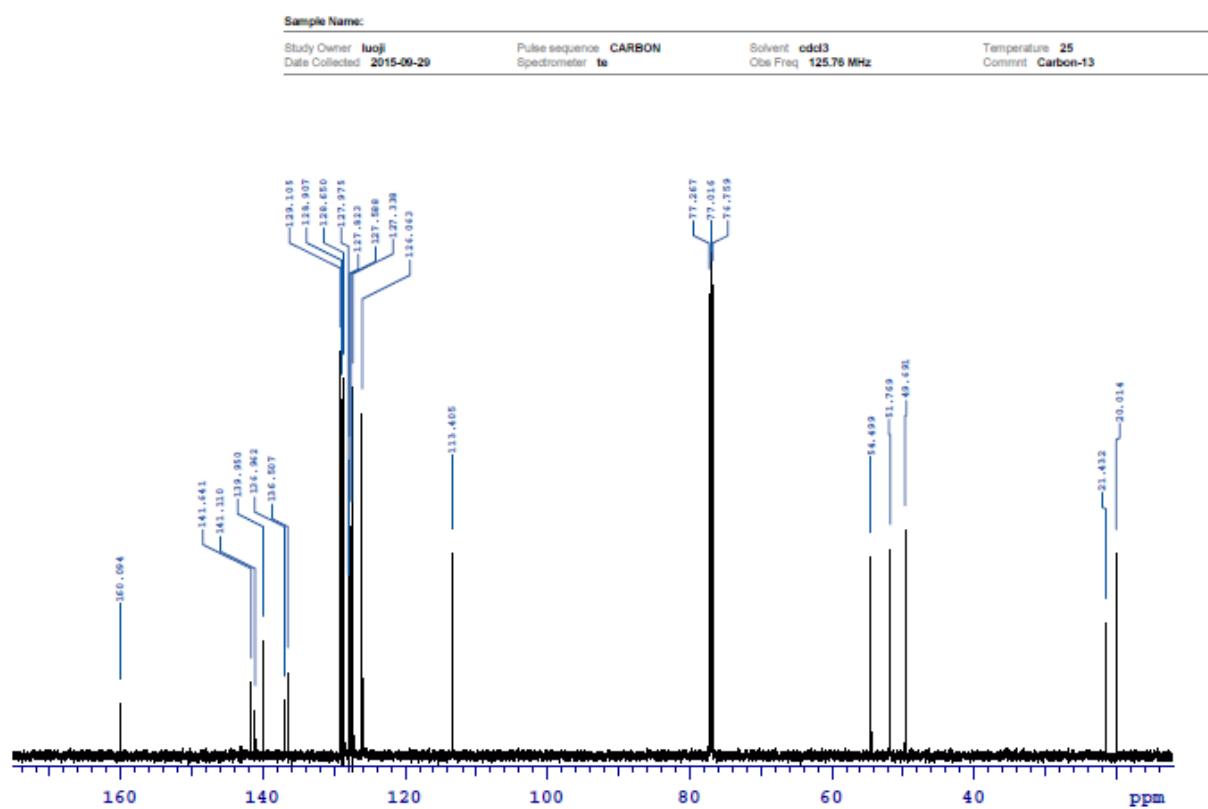
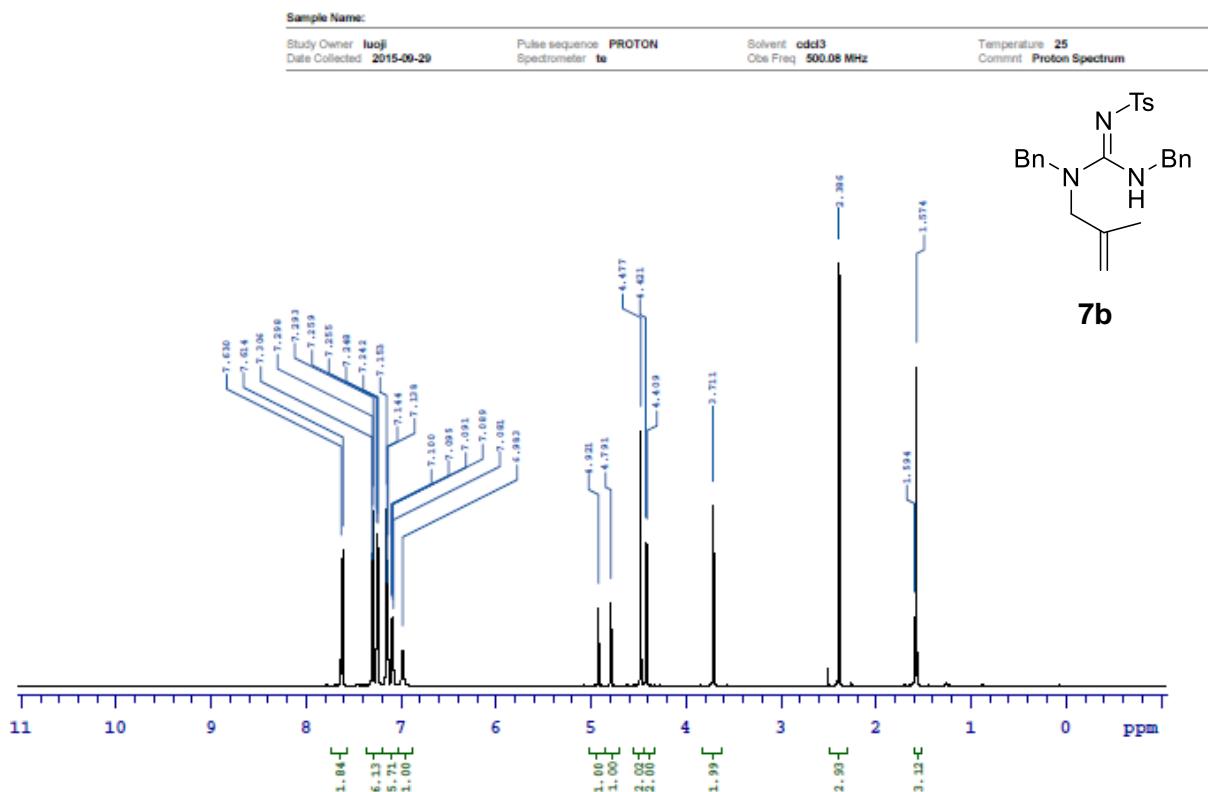


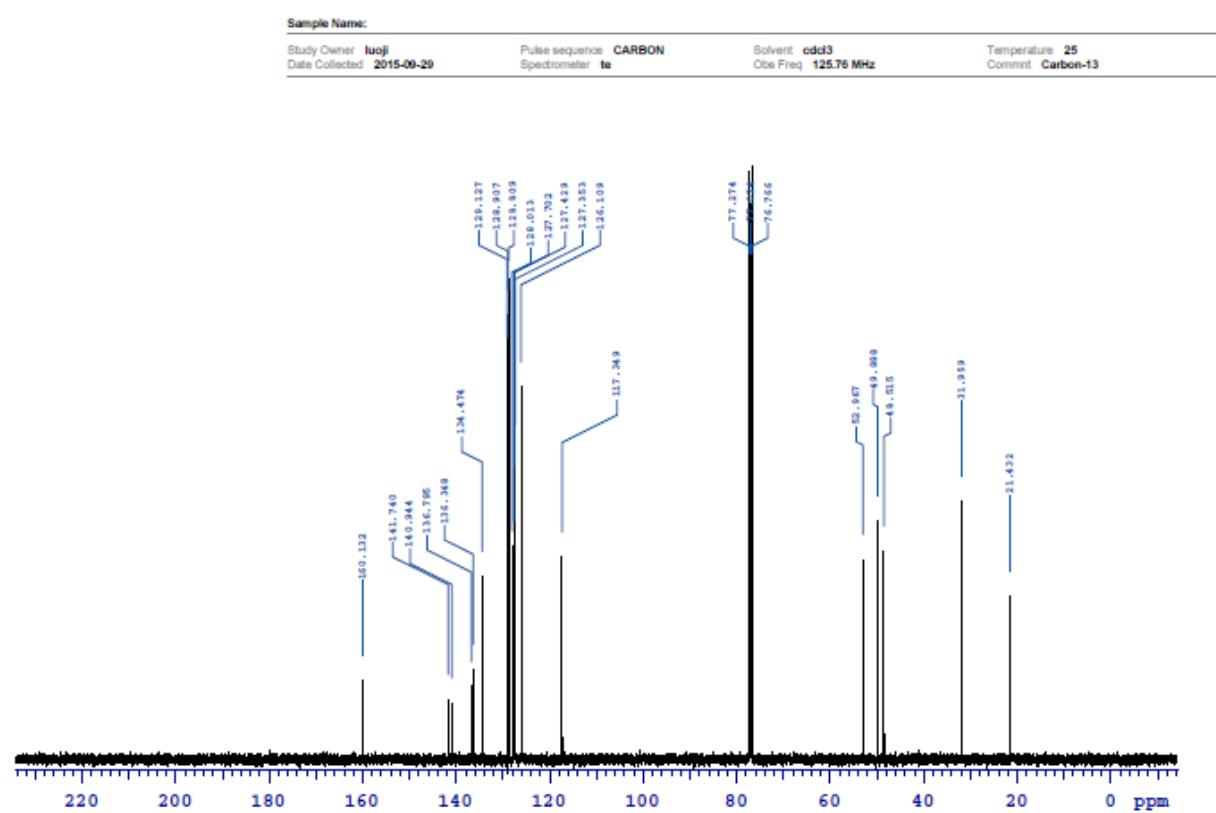
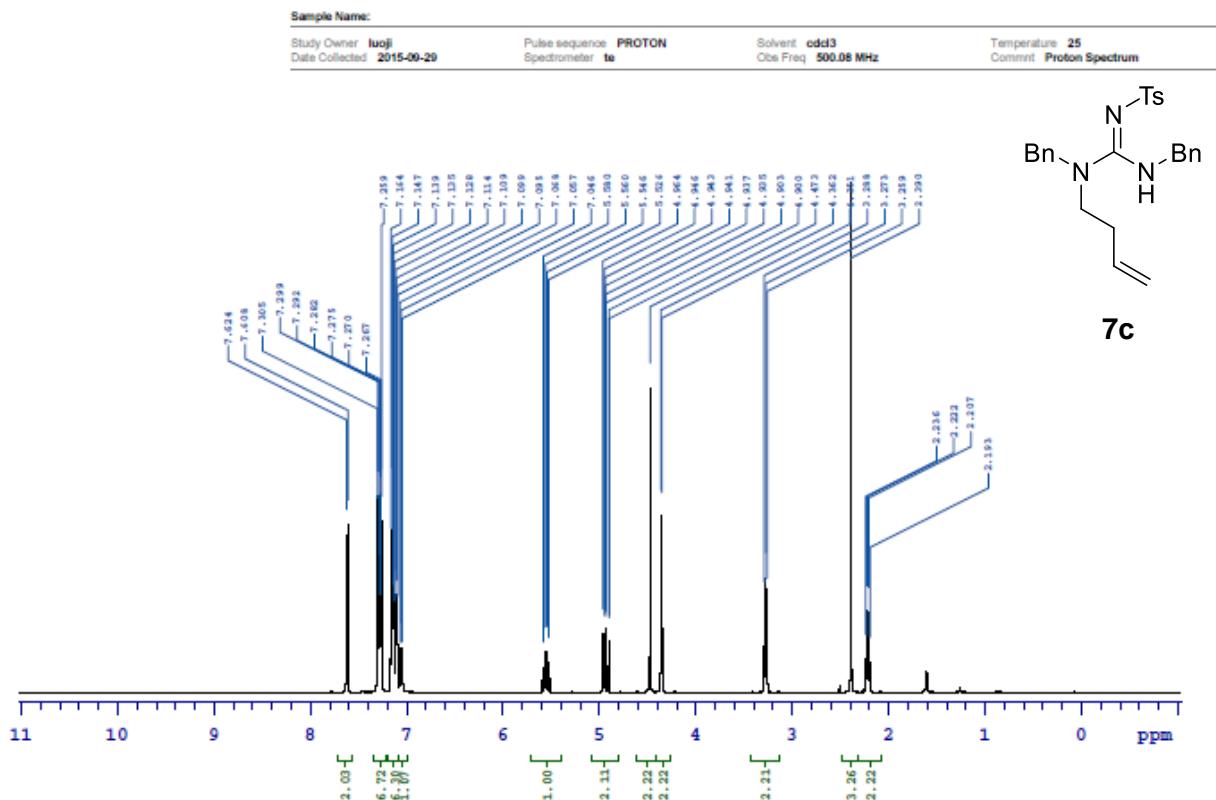


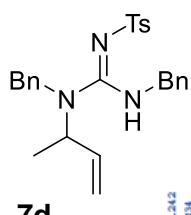












7d

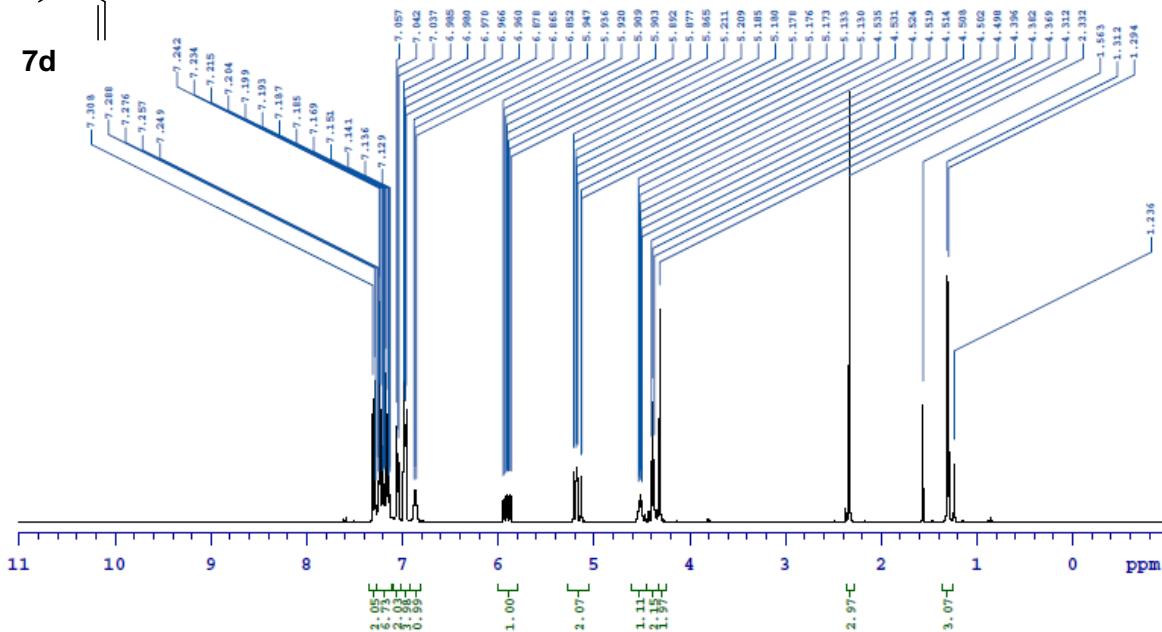
Sample Name:

Study Owner lukejpet
Date Collected 2017-04-13

Pulse sequence **PROTON**
Spectrometer **CO**

Solvent **cdcl3**
Obs Freq **400.52 MHz**

Temperature r.t.
Comment **Proton Spectrum**



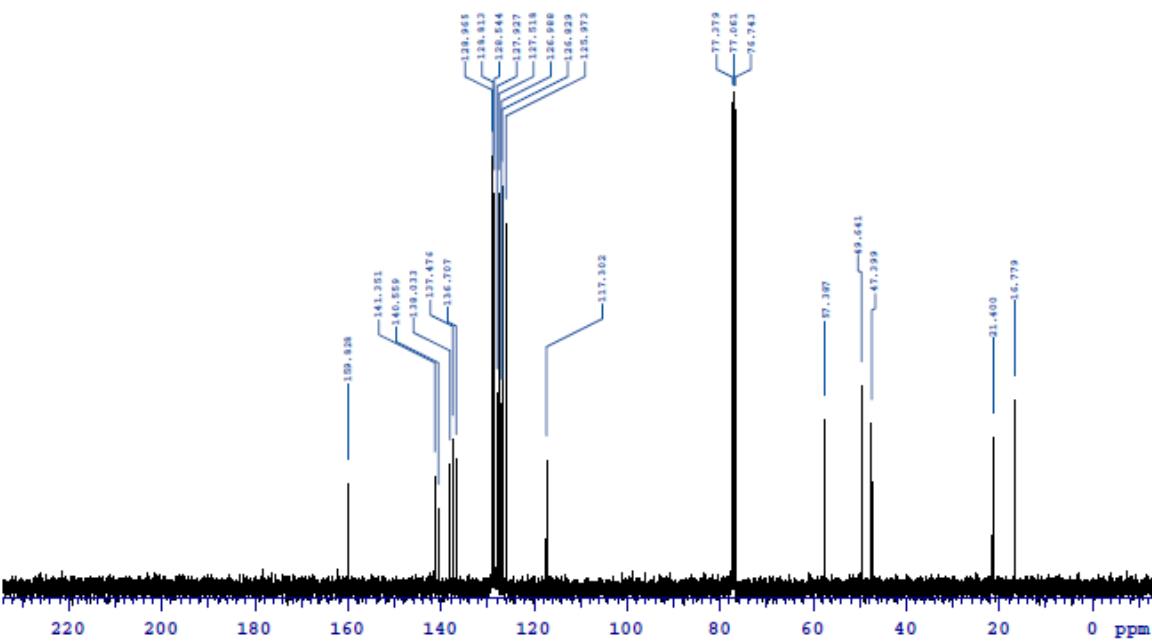
Sample Name:

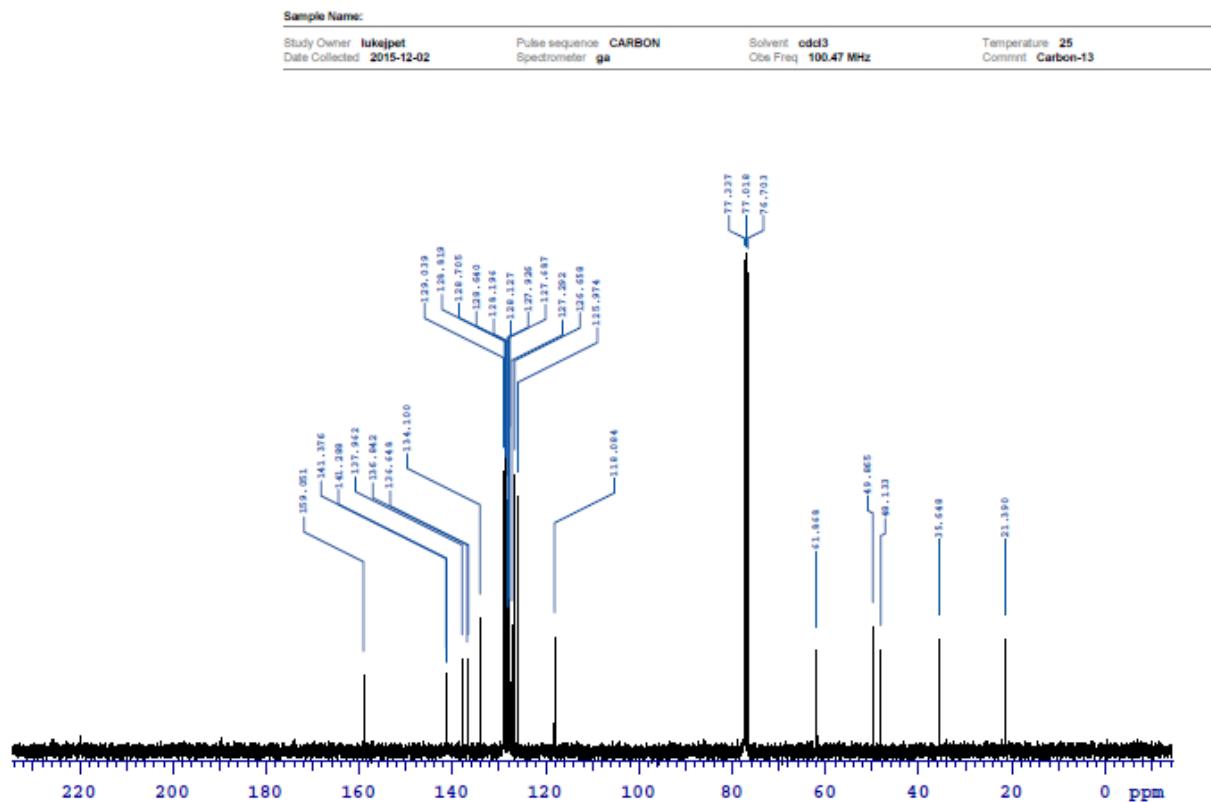
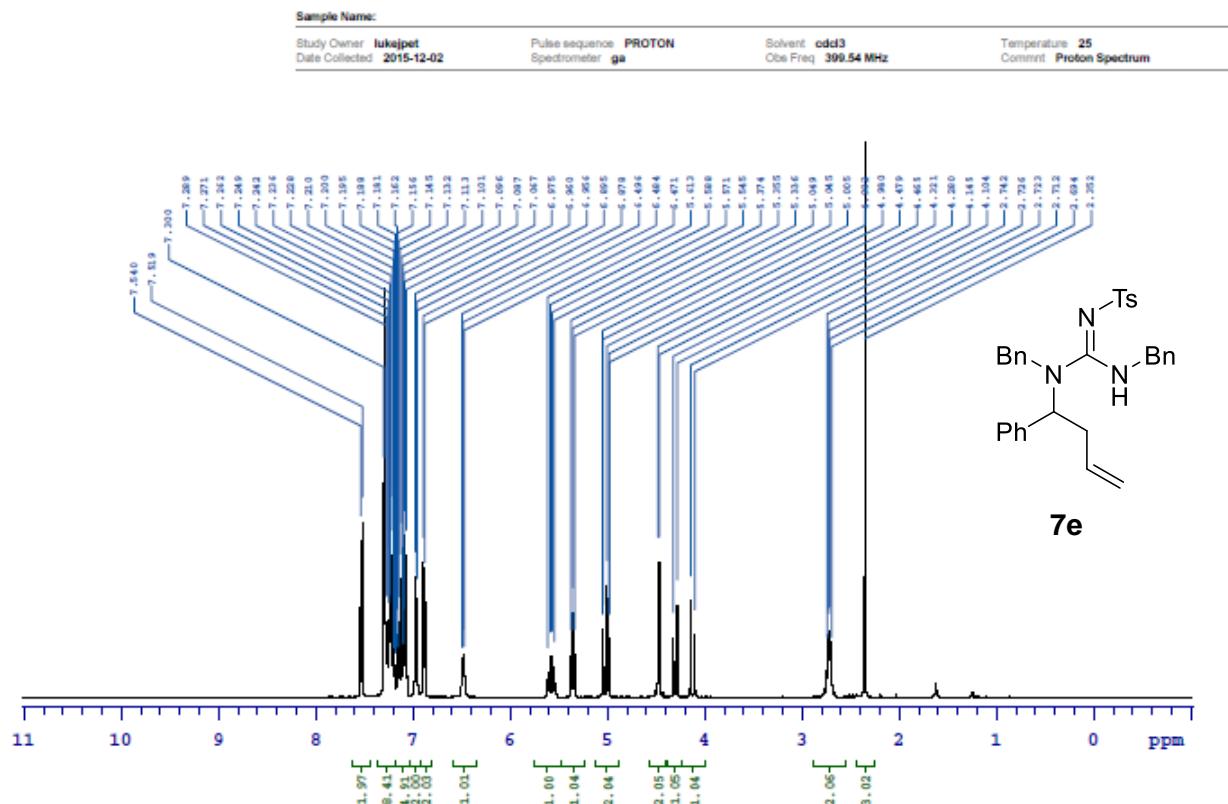
Study Owner lukejpet
Date Collected 2015-12-10

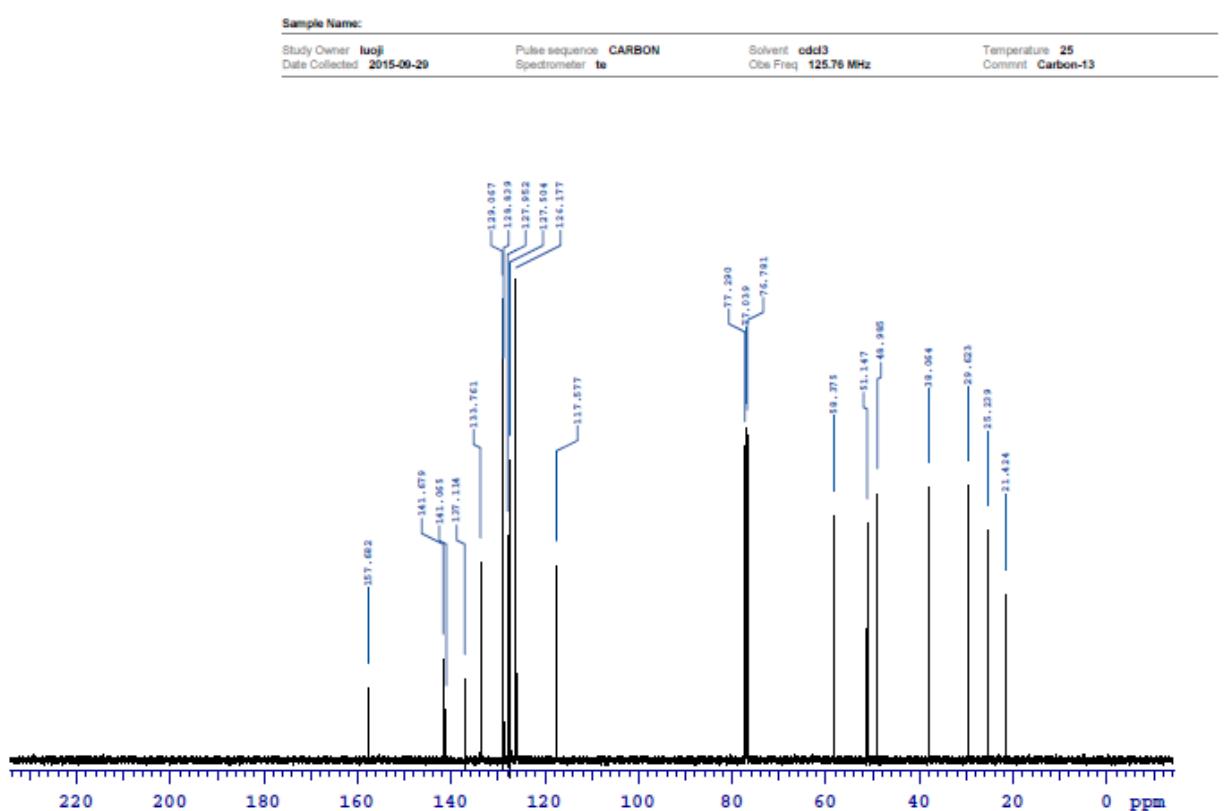
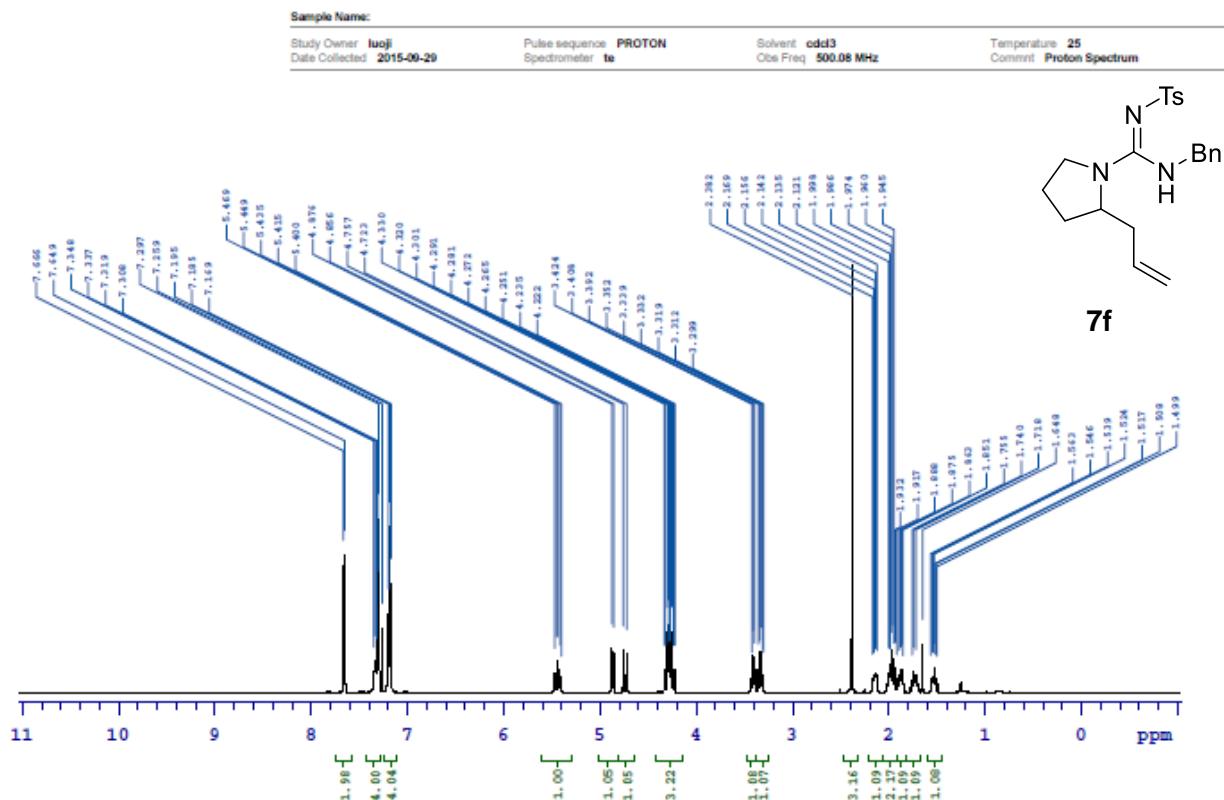
Pulse sequence **CARBON**
Spectrometer **99**

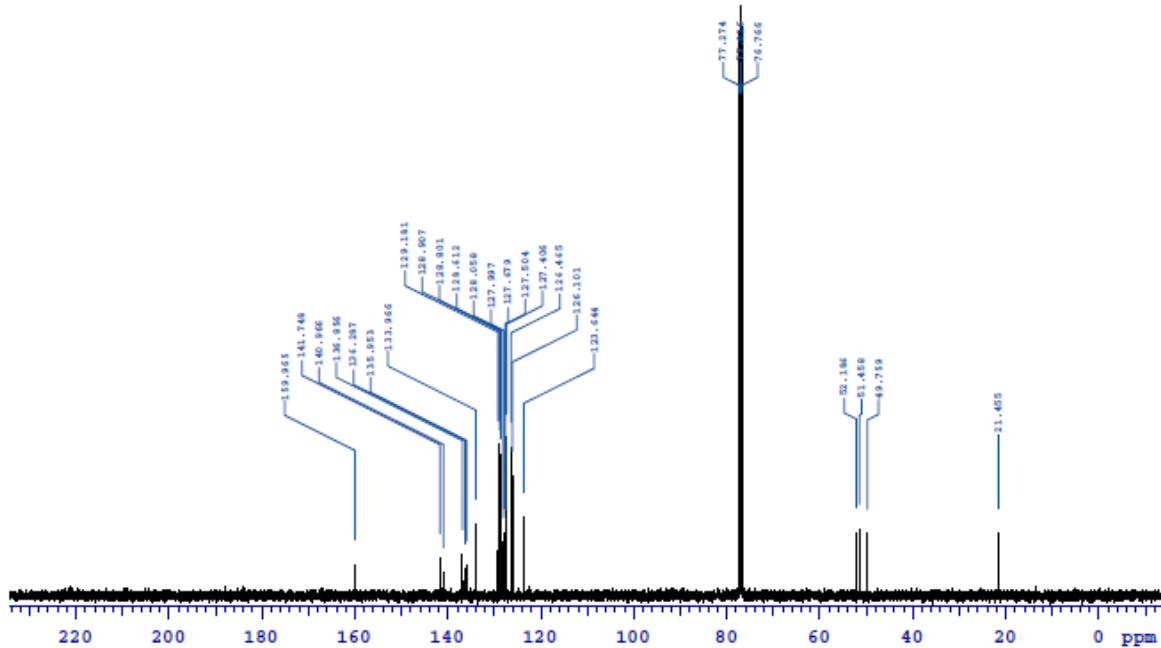
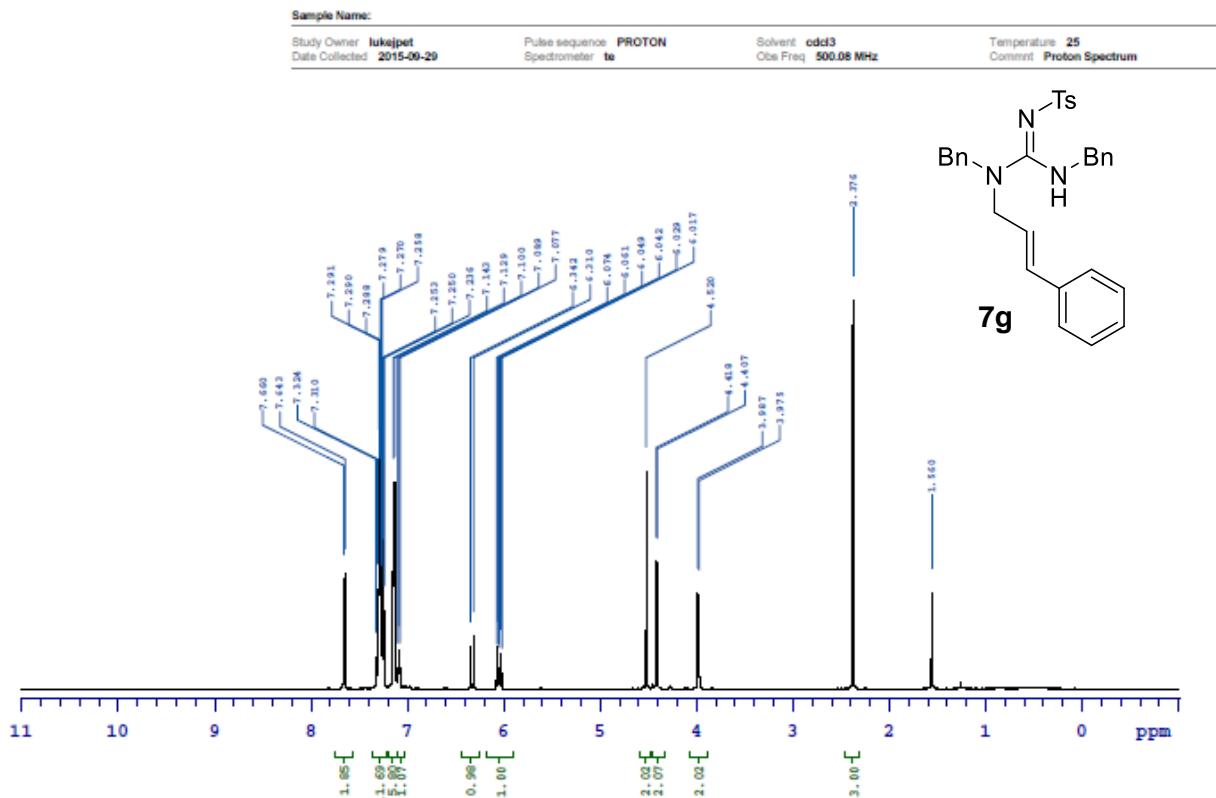
Solvent **cdcl3**
Observe Freq. **100.72 MHz**

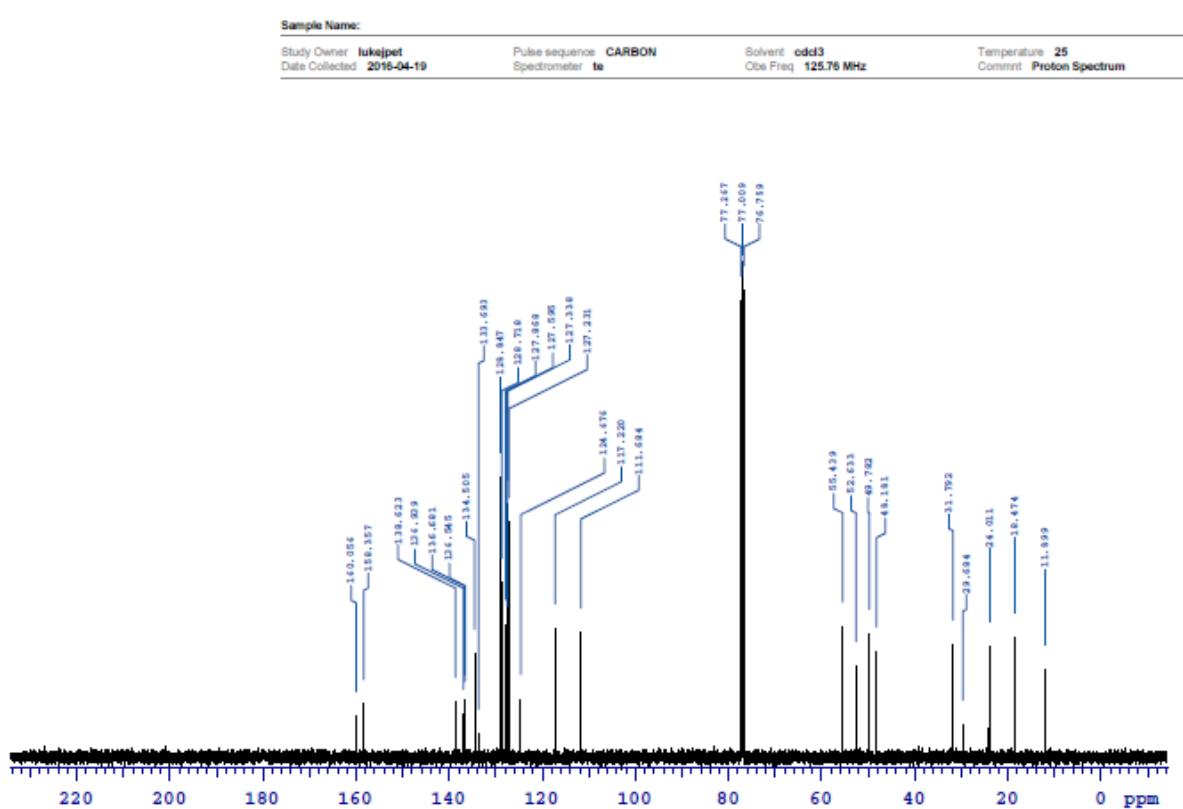
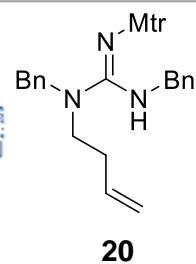
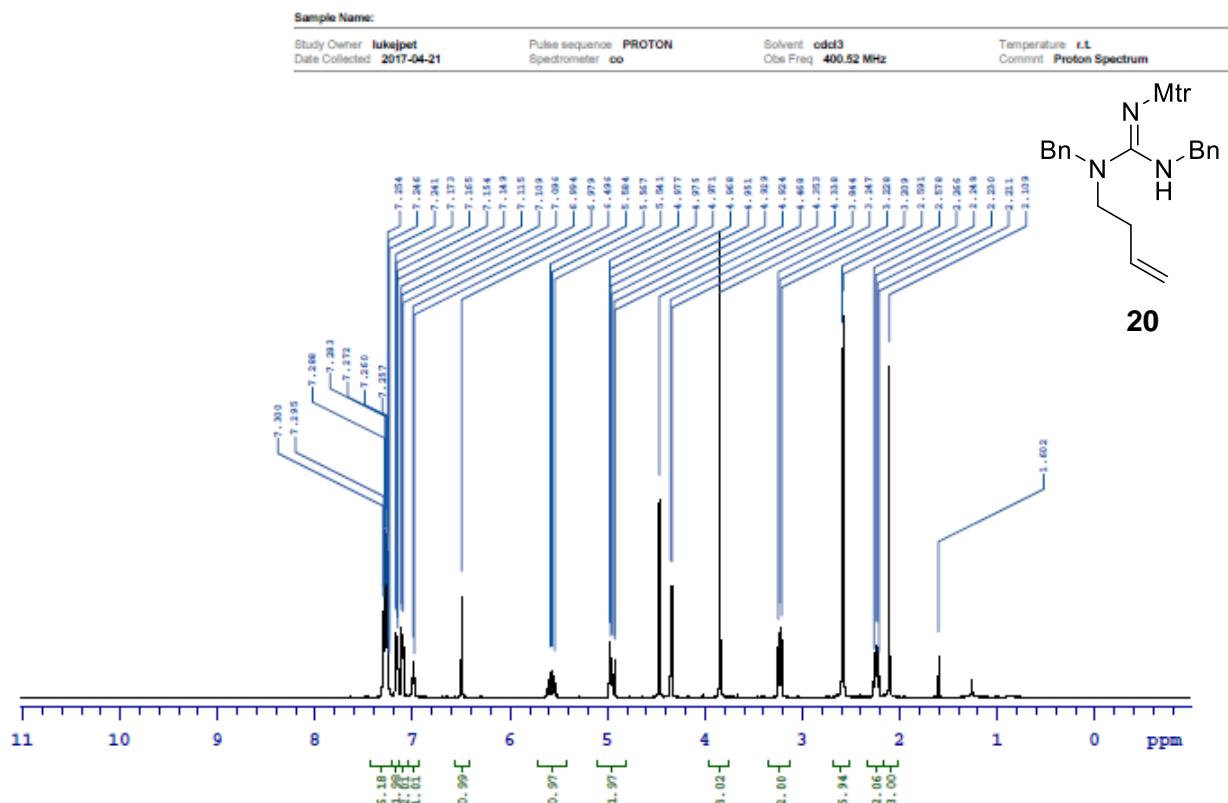
Temperature **1.1**
Comment **Carbon-13**



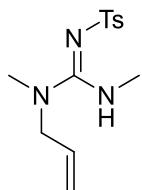




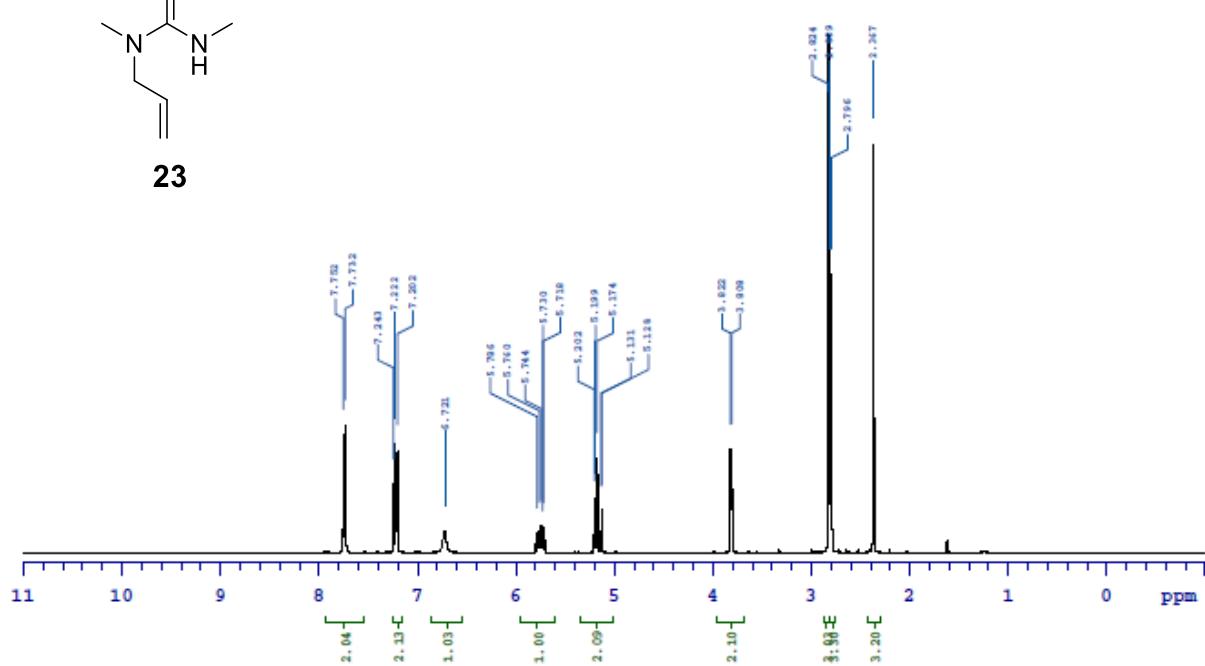




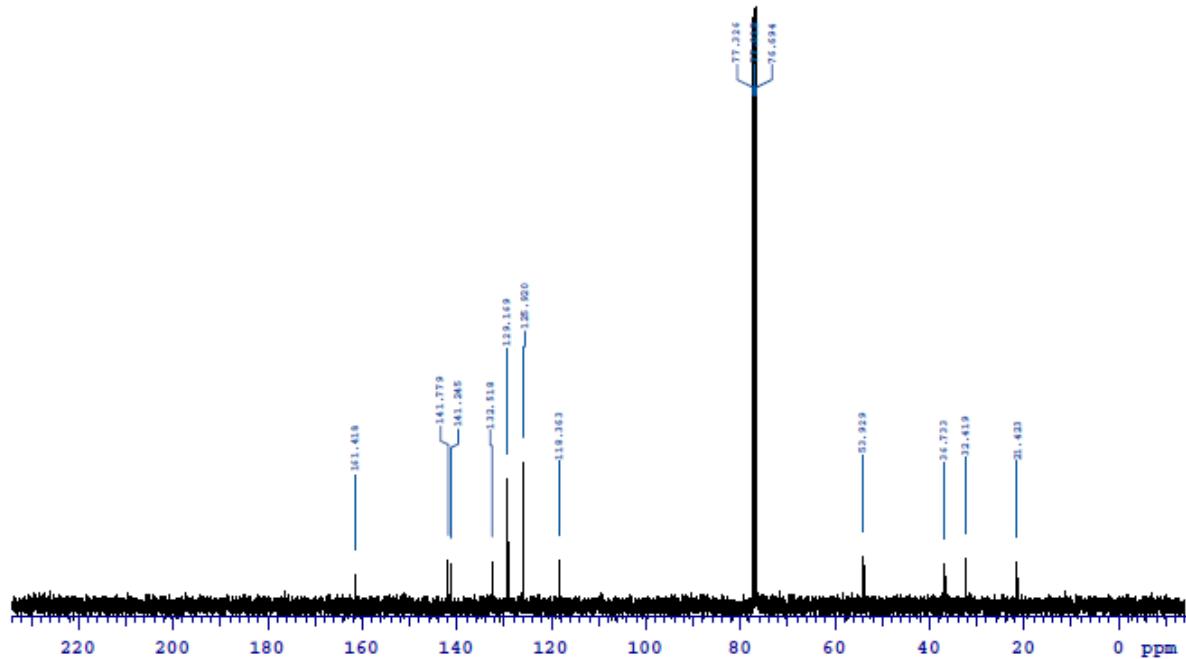
Sample Name:	Study Owner: lukejpet	Pulse sequence: PROTON	Solvent: cdd3	Temperature: r.t.
Date Collected: 2017-05-07	Spectrometer: ∞	Obs Freq: 400.52 MHz	Comment: Proton Spectrum	

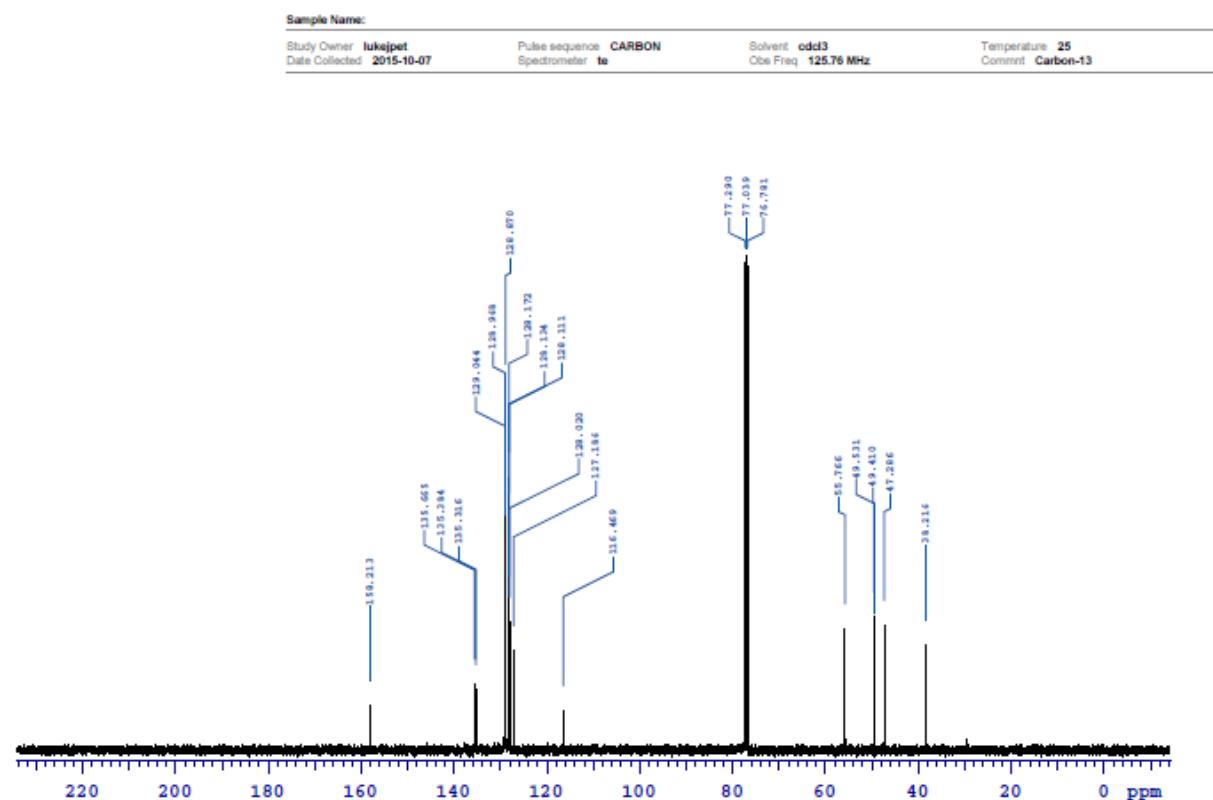
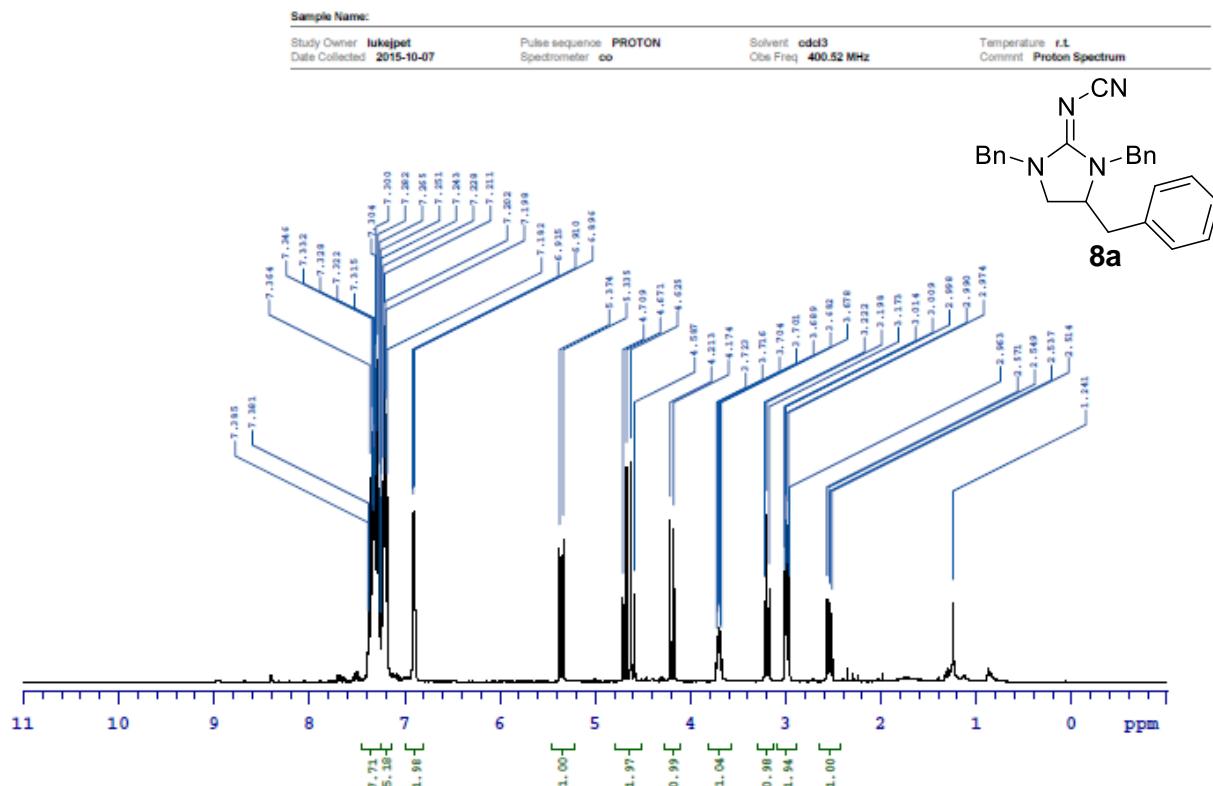


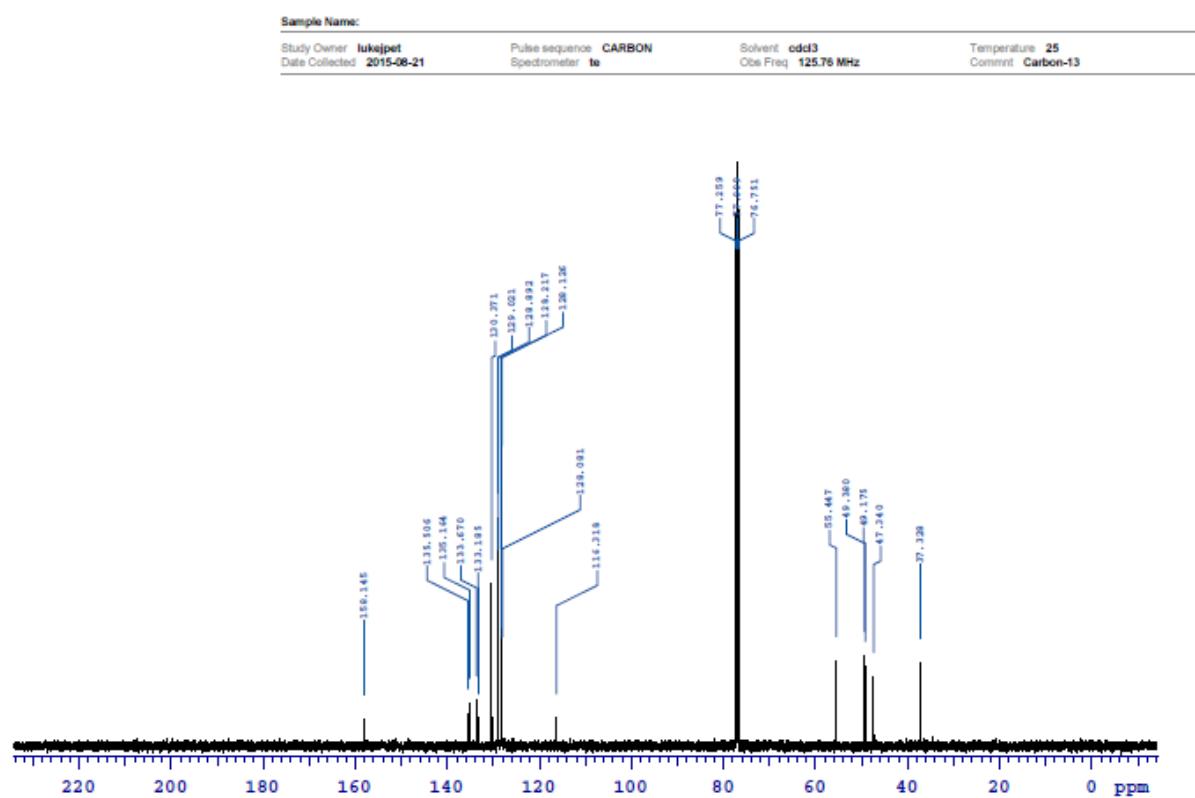
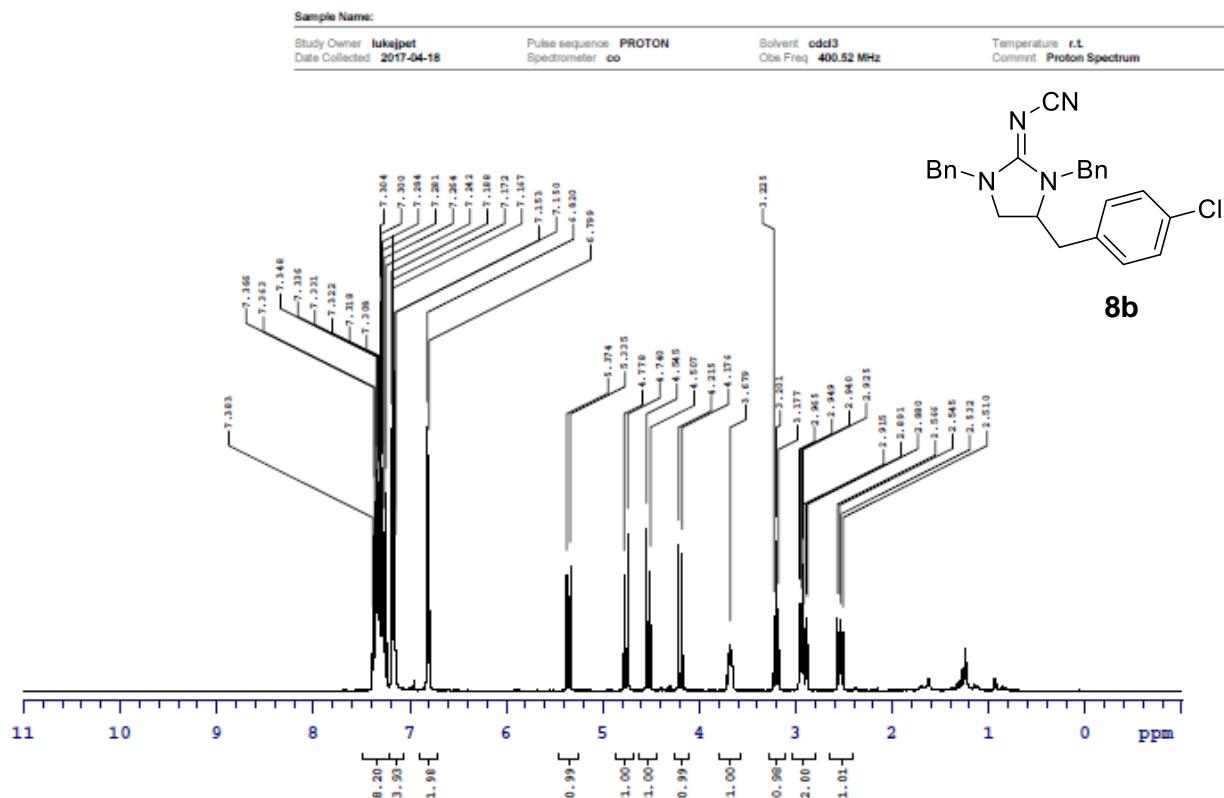
23

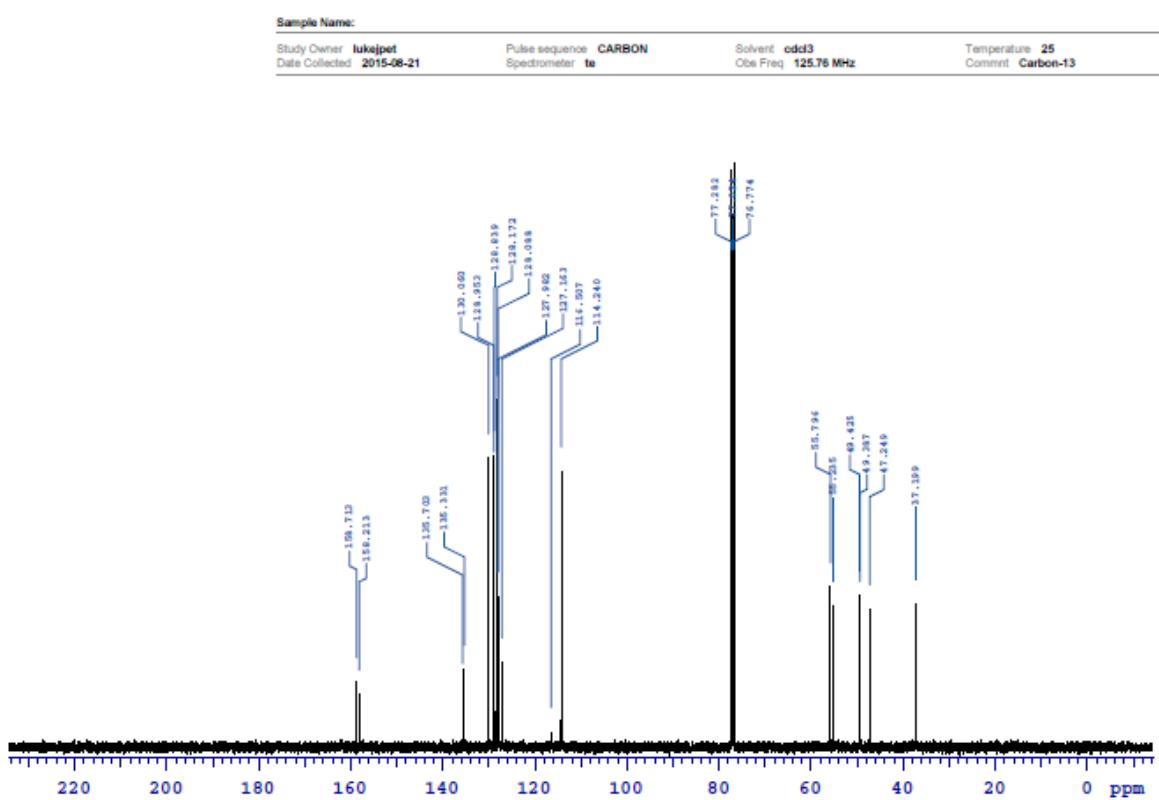
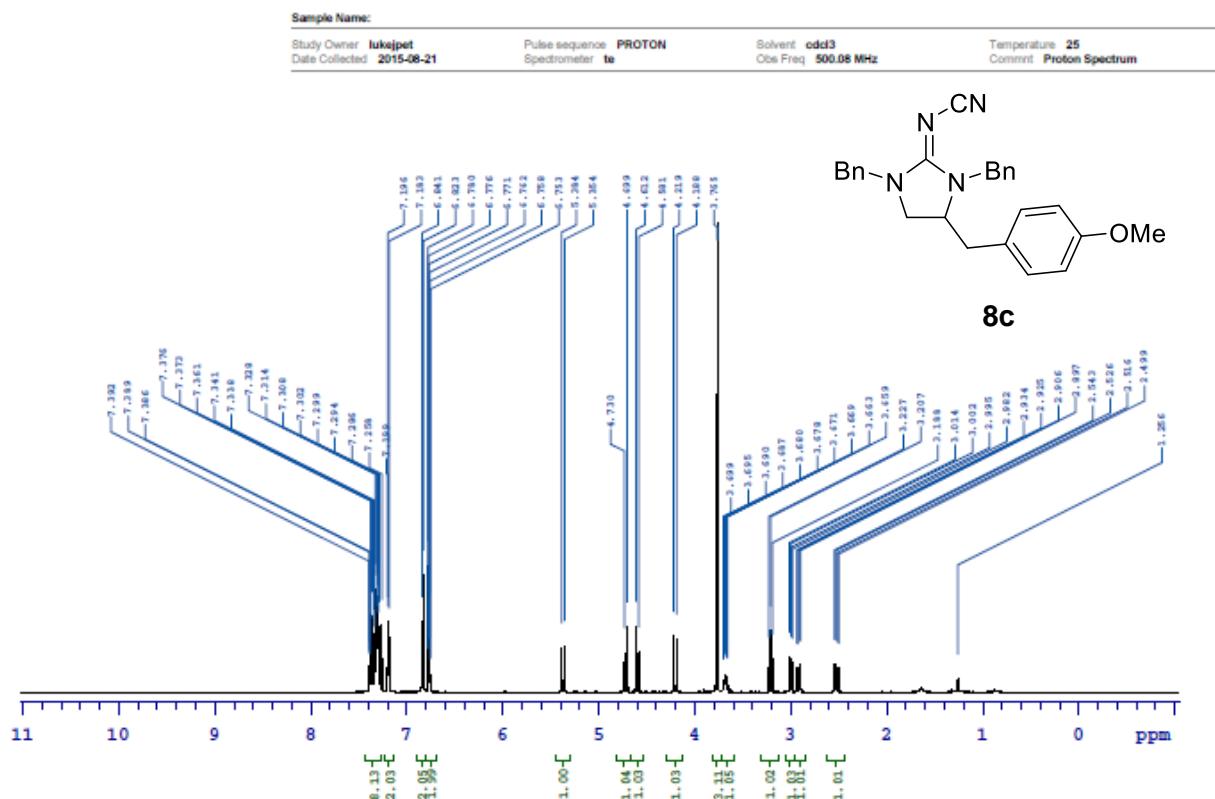


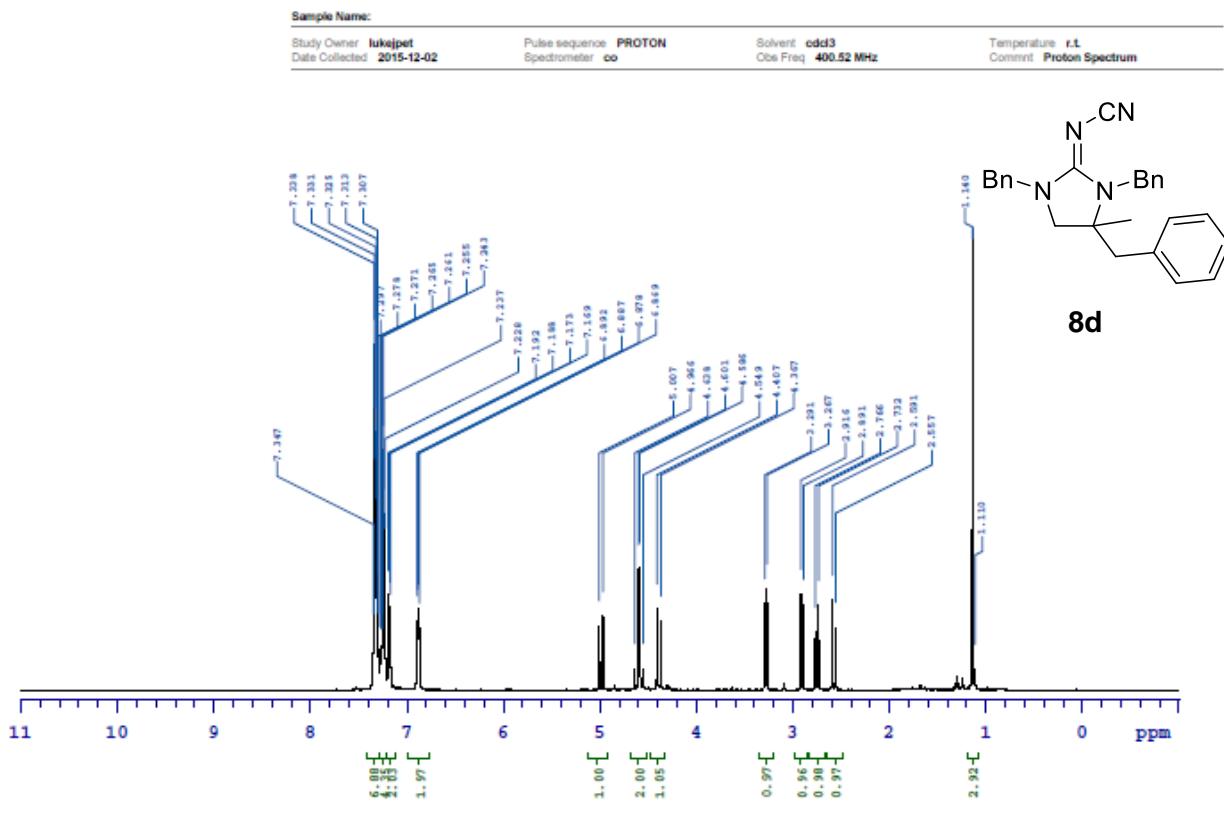
Sample Name:	Study Owner: lukejpet	Pulse sequence: CARBON	Solvent: cdd3	Temperature: r.t.
Date Collected: 2017-05-07	Spectrometer: ∞	Obs Freq: 100.72 MHz	Comment: Carbon-13	

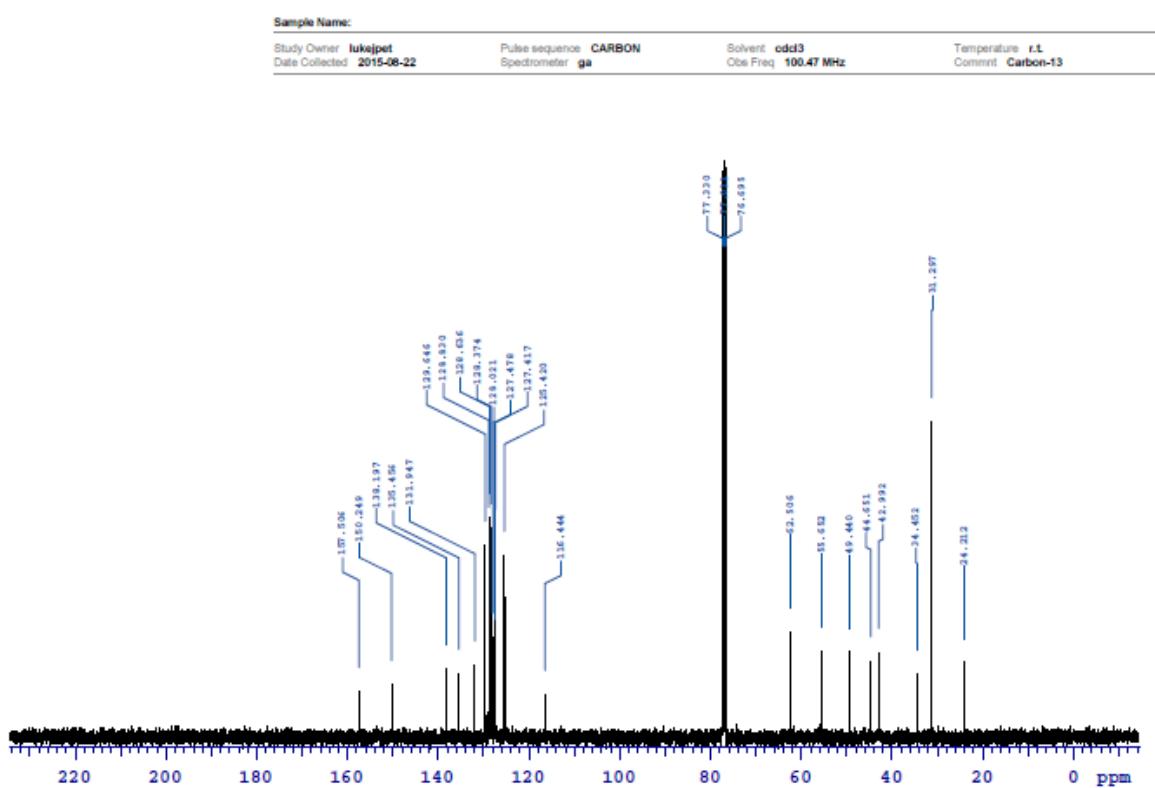
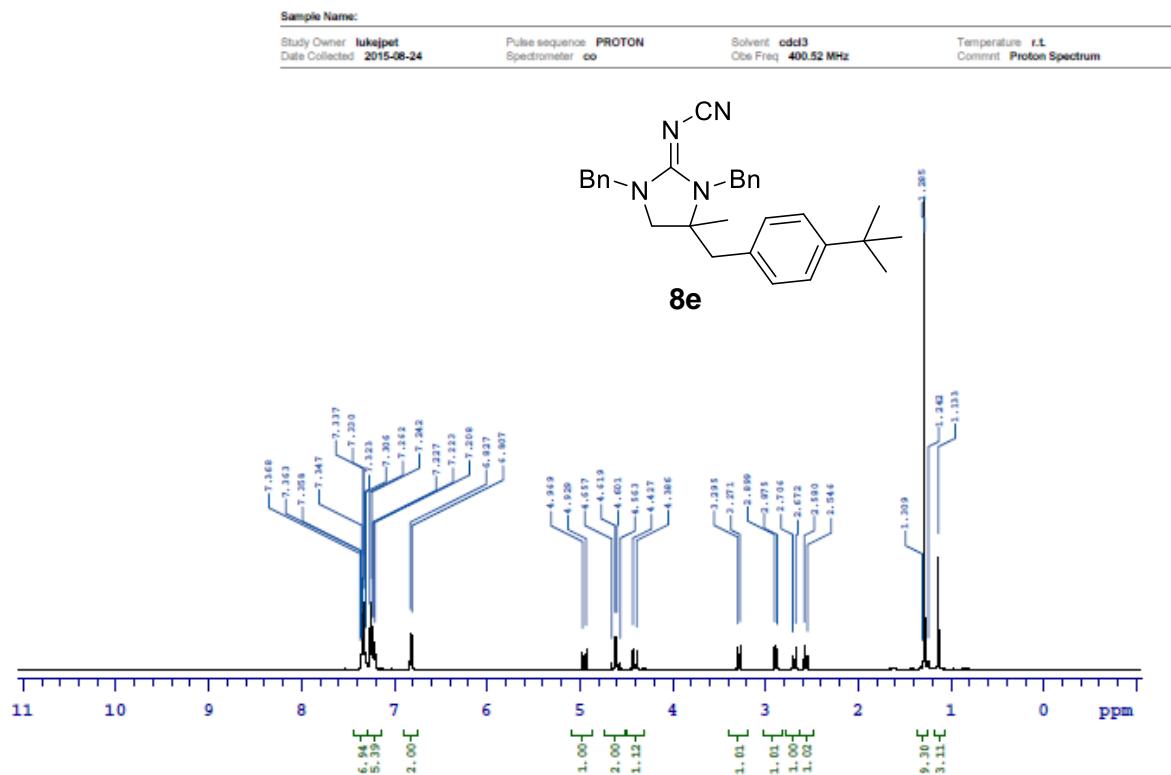


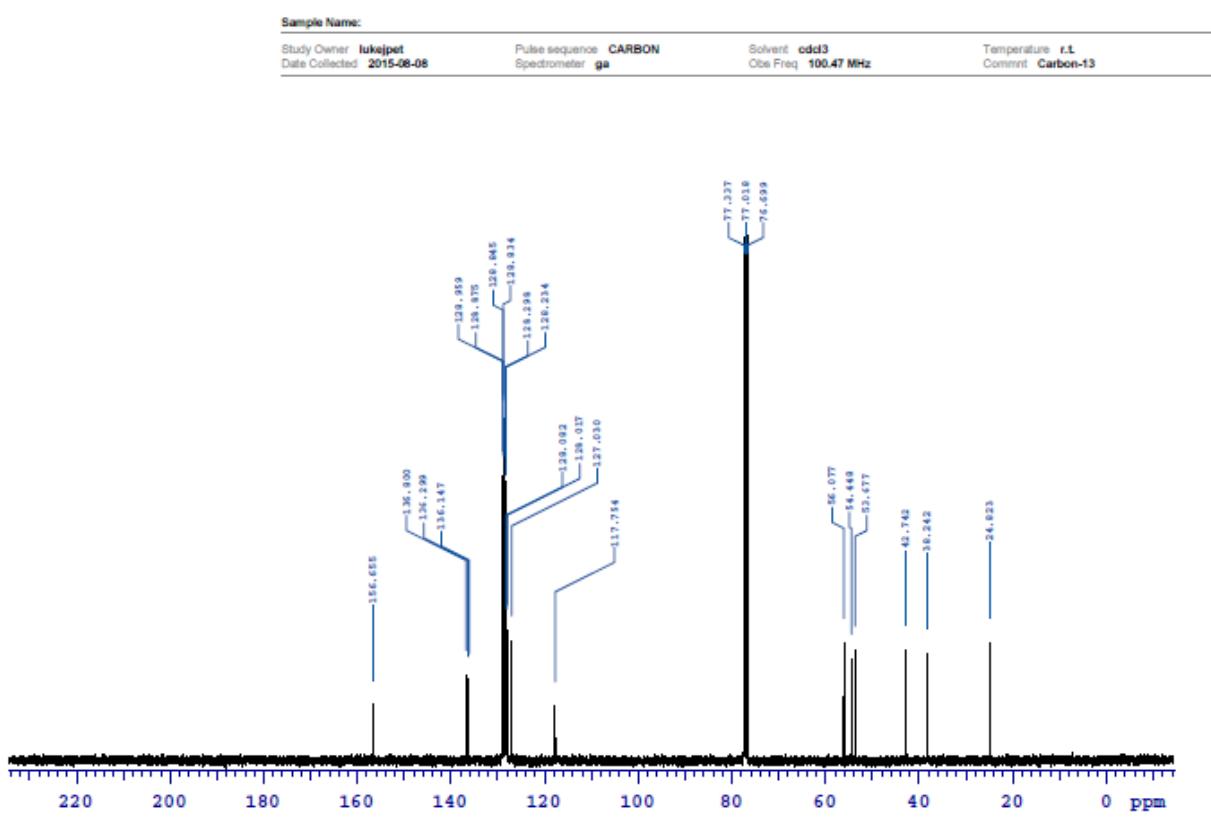
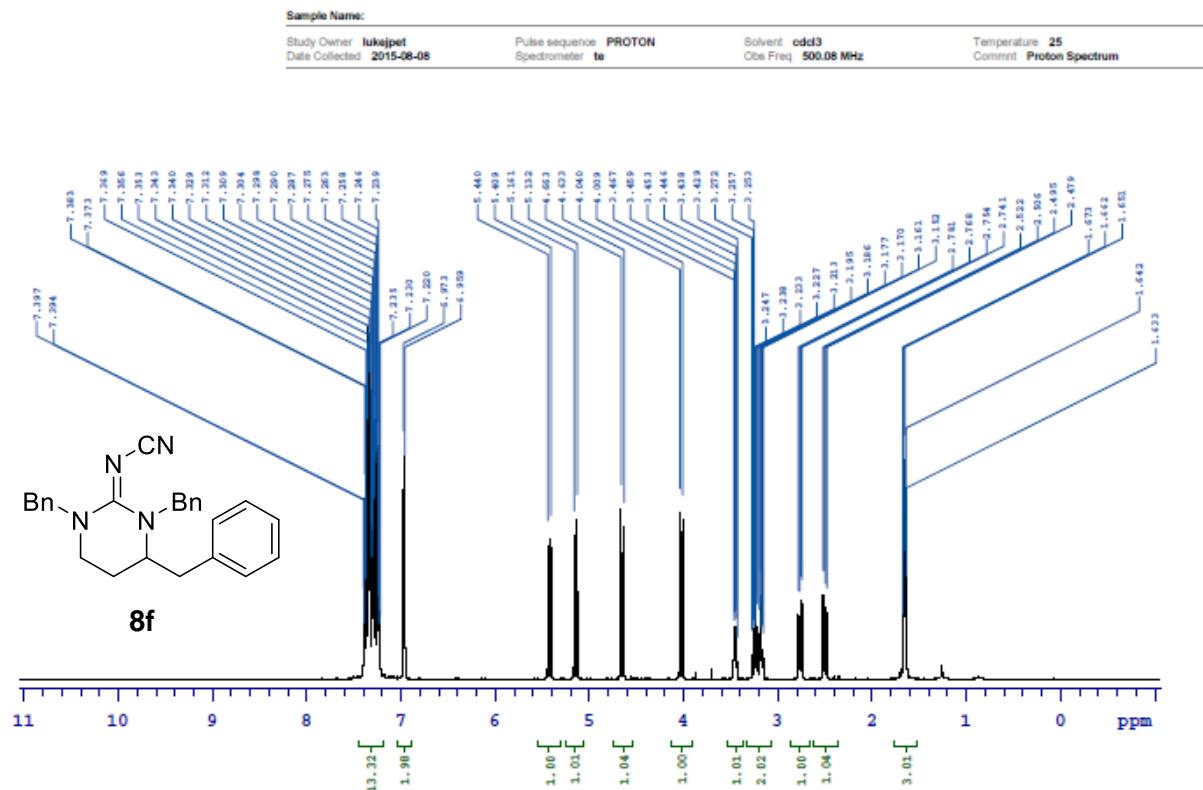


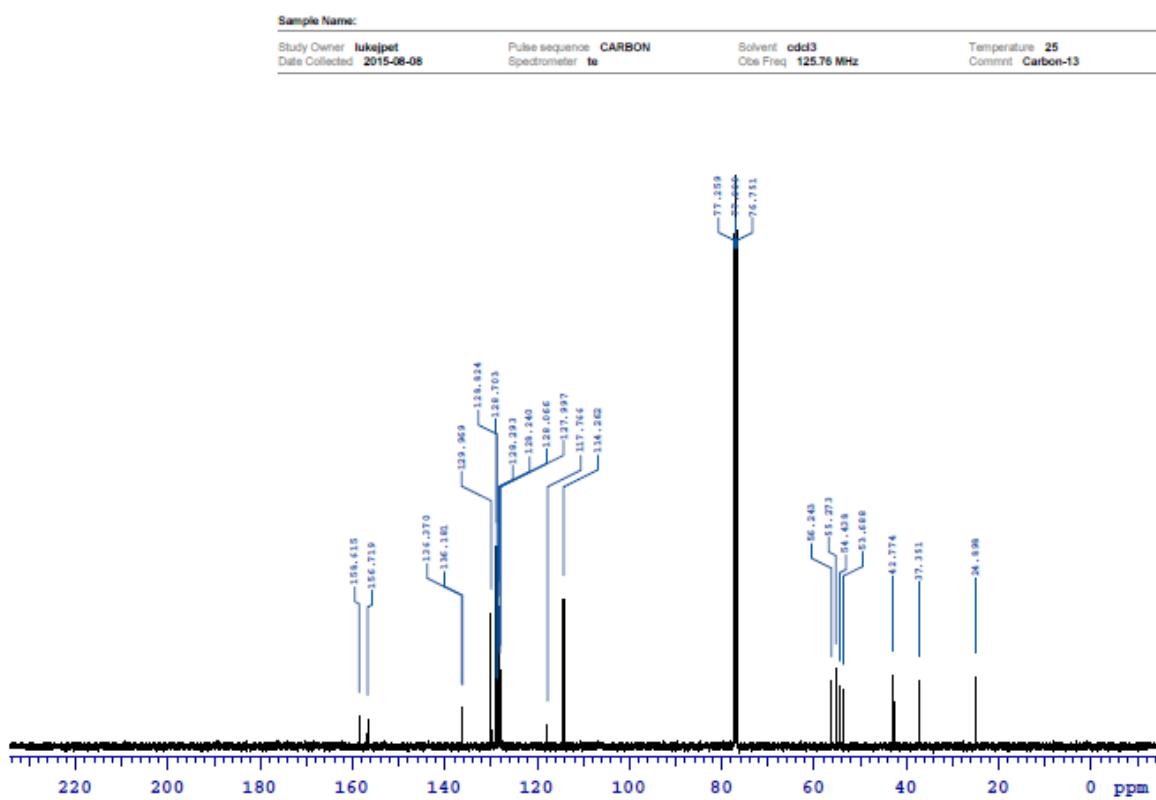
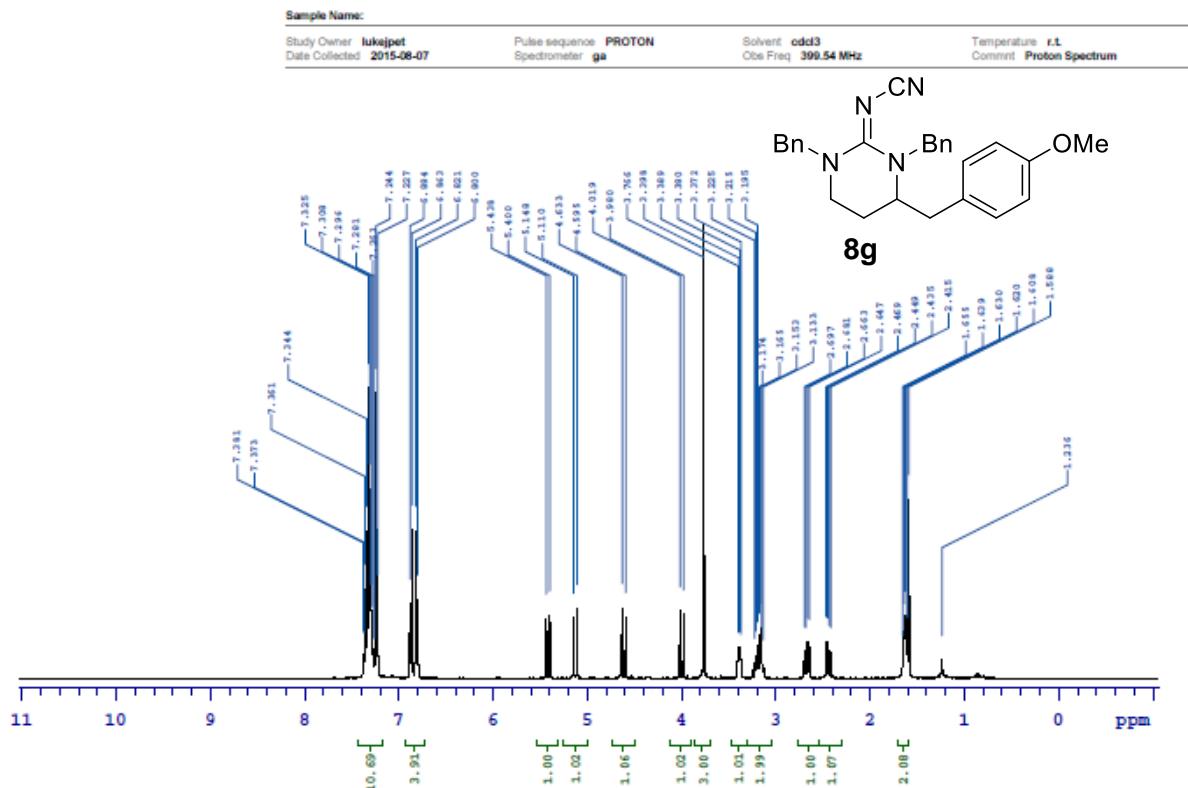


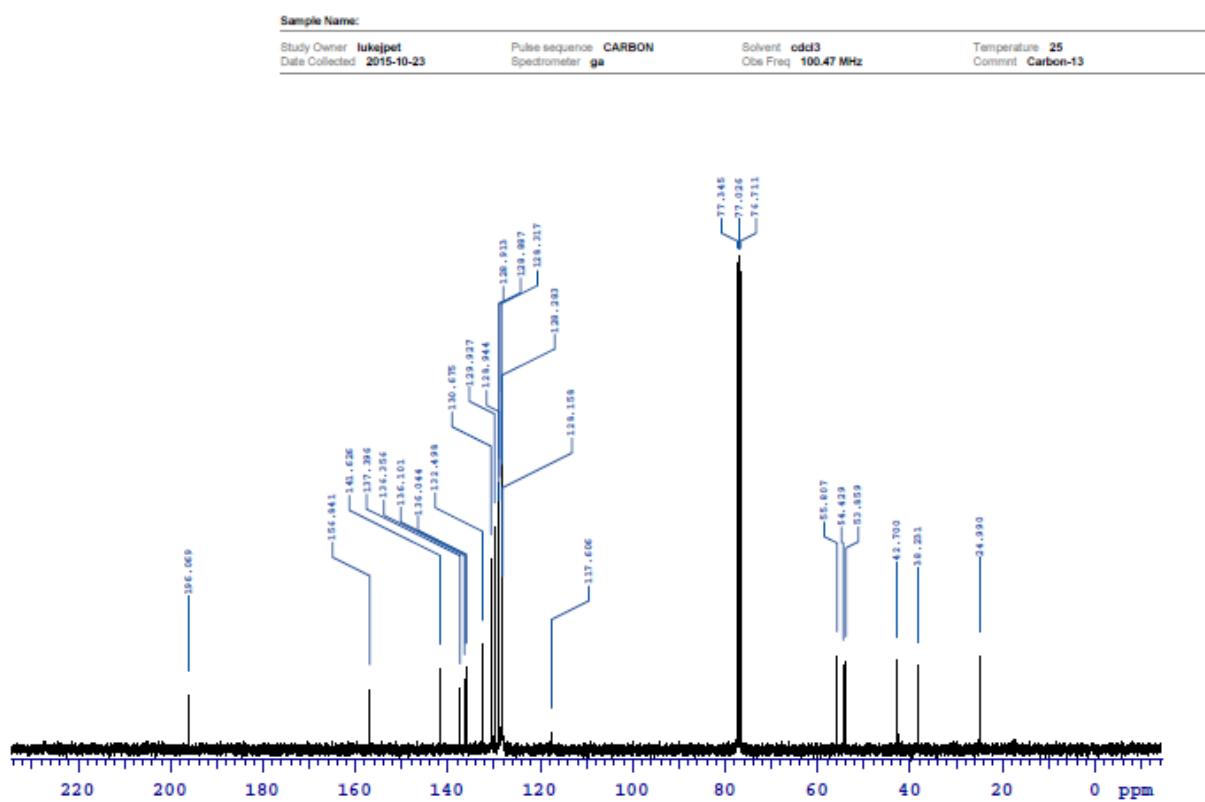
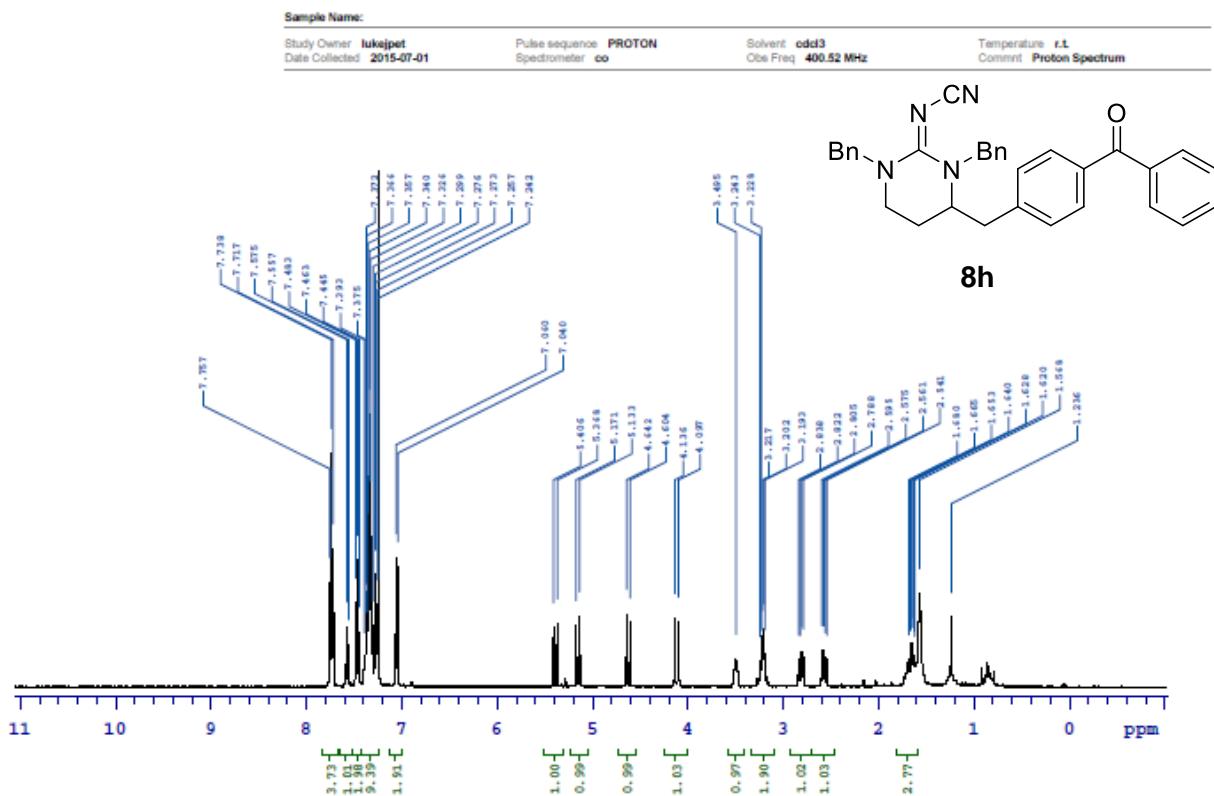












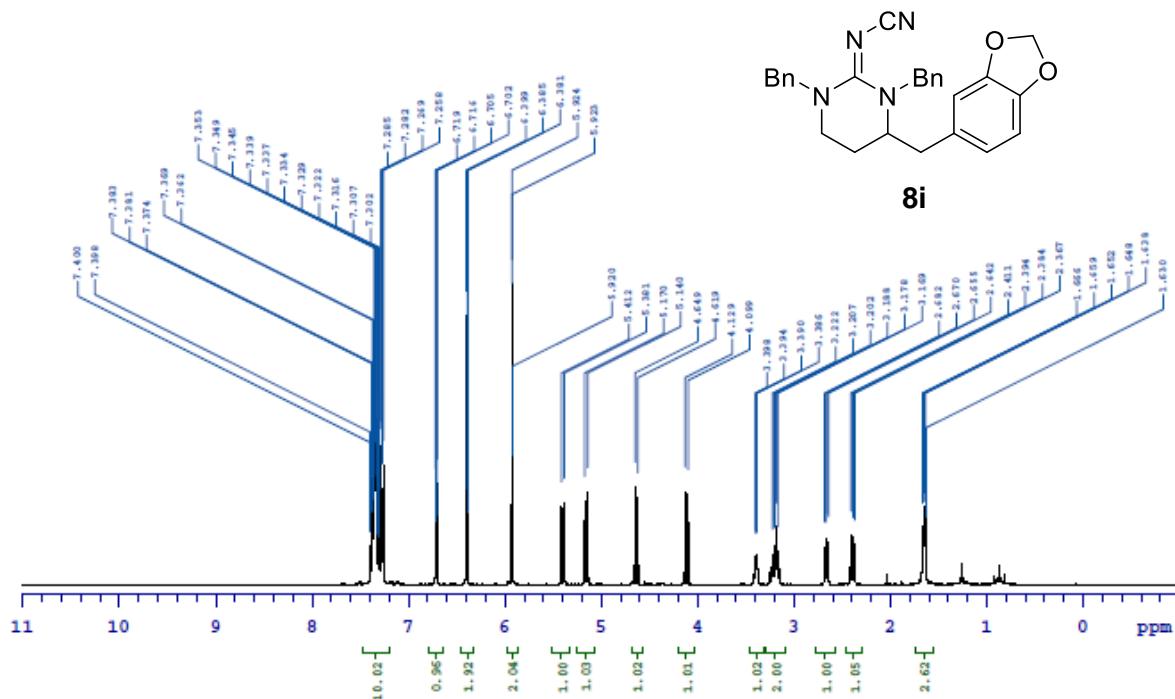
Sample Name:

Study Owner lukejpet
Date Collected 2015-10-09

Pulse sequence **PROTON**

Solvent **cdcl3**
Obs Freq **500.08 MHz**

Temperature 25
Comment Proton Spectrum



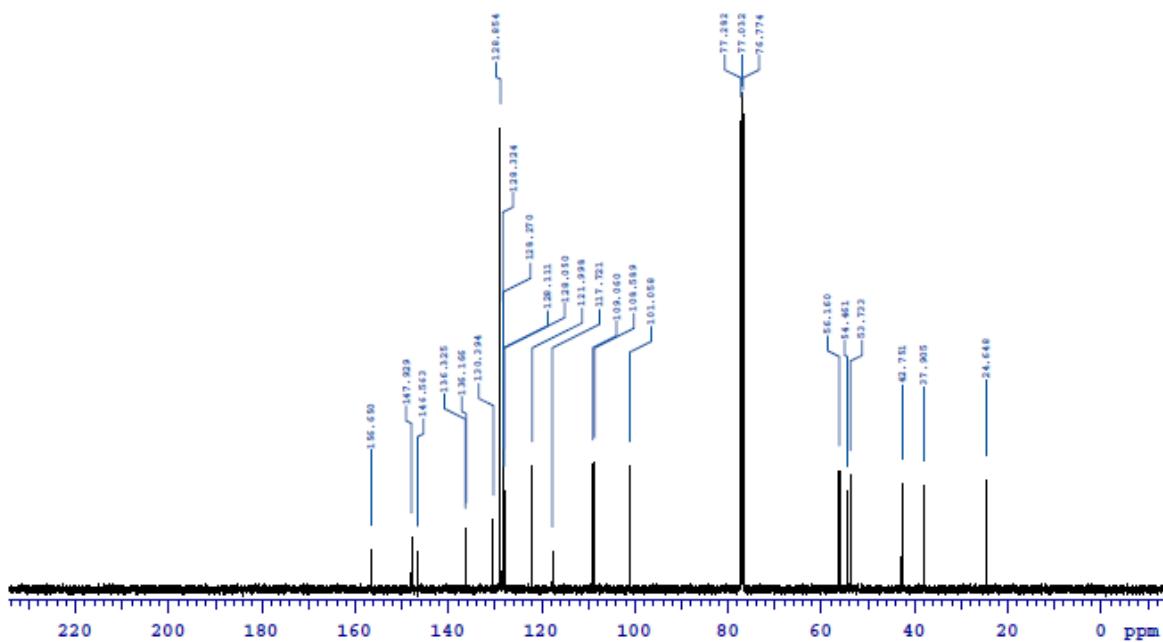
Sample Name:

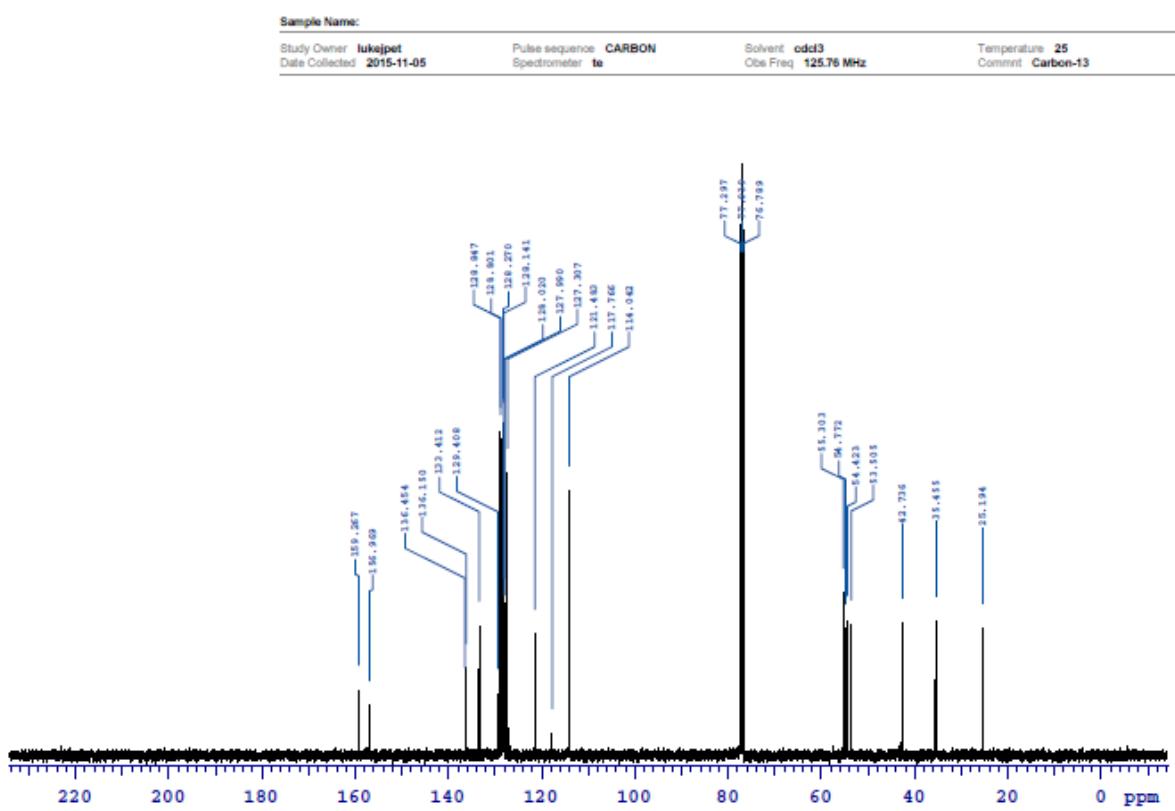
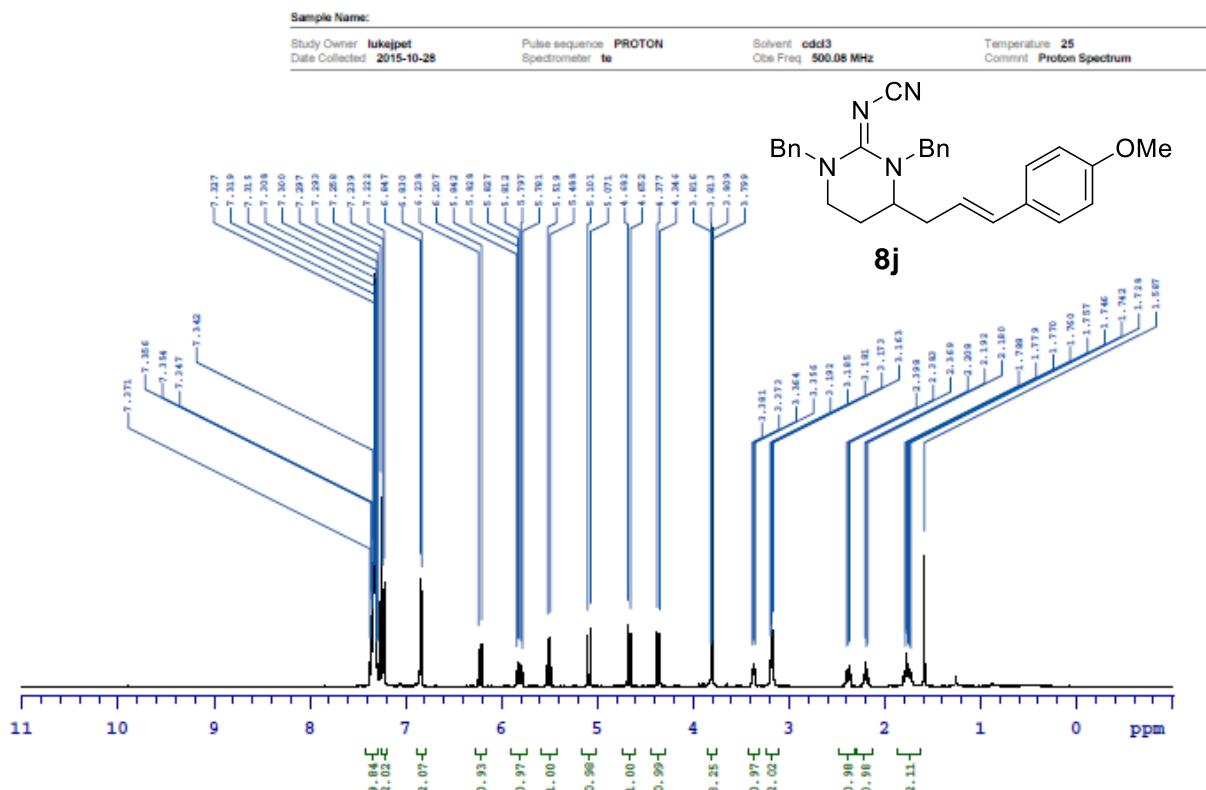
Study Owner lukejpet
Date Collected 2015-10-09

Pulse sequence: **CARBON**

Solvent: **cdcl3**
Obs Freq: **125.76 MHz**

Temperature 25
Comment Carbon-13





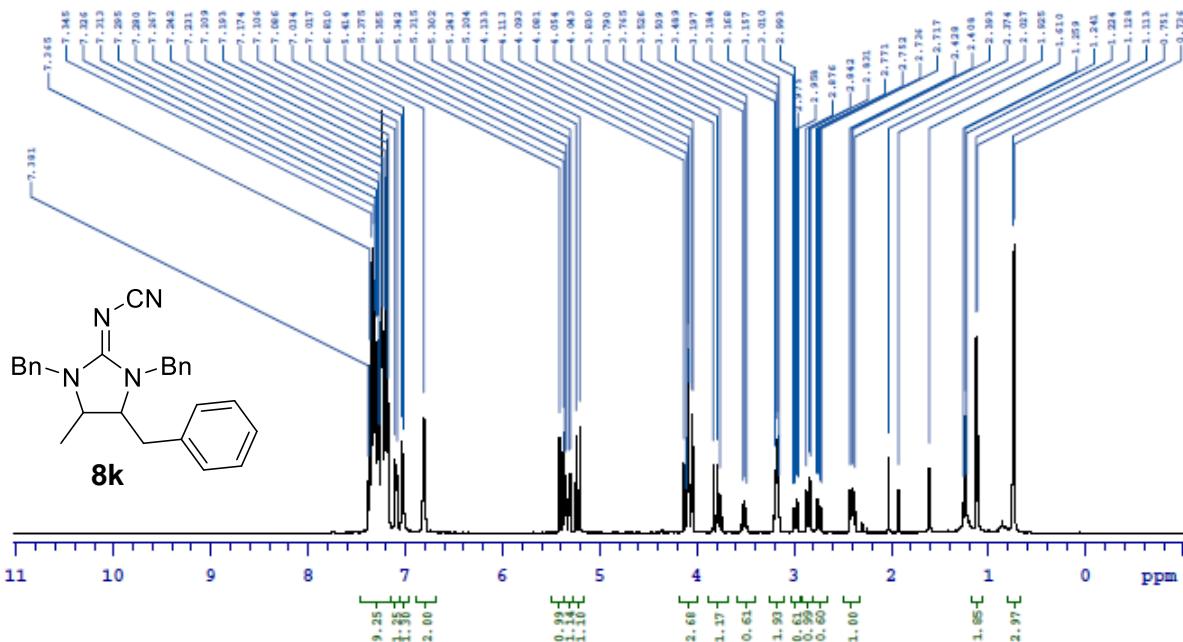
Sample Name:

Study Owner lukejpet
Date Collected 2015-10-21

Pulse sequence **PROTON**
Spectrometer **60**

Solvent **cdcl3**
Obs Freq **400.52 MHz**

Temperature **25.0**
Commit **Proton Spectrum**



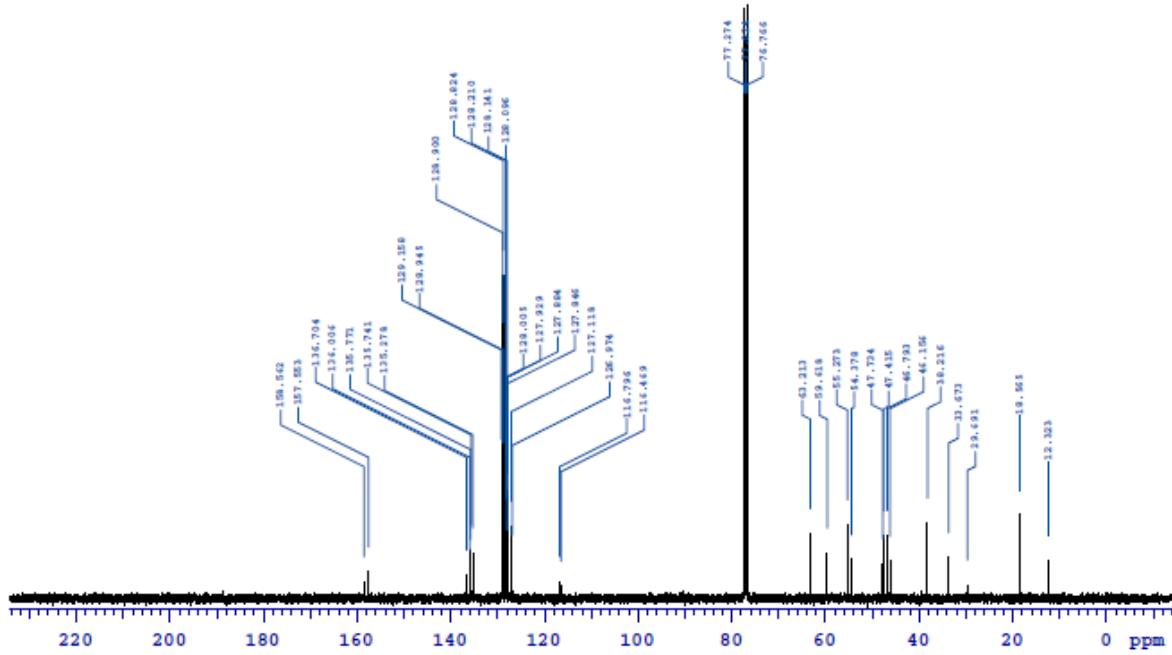
Sample Name:

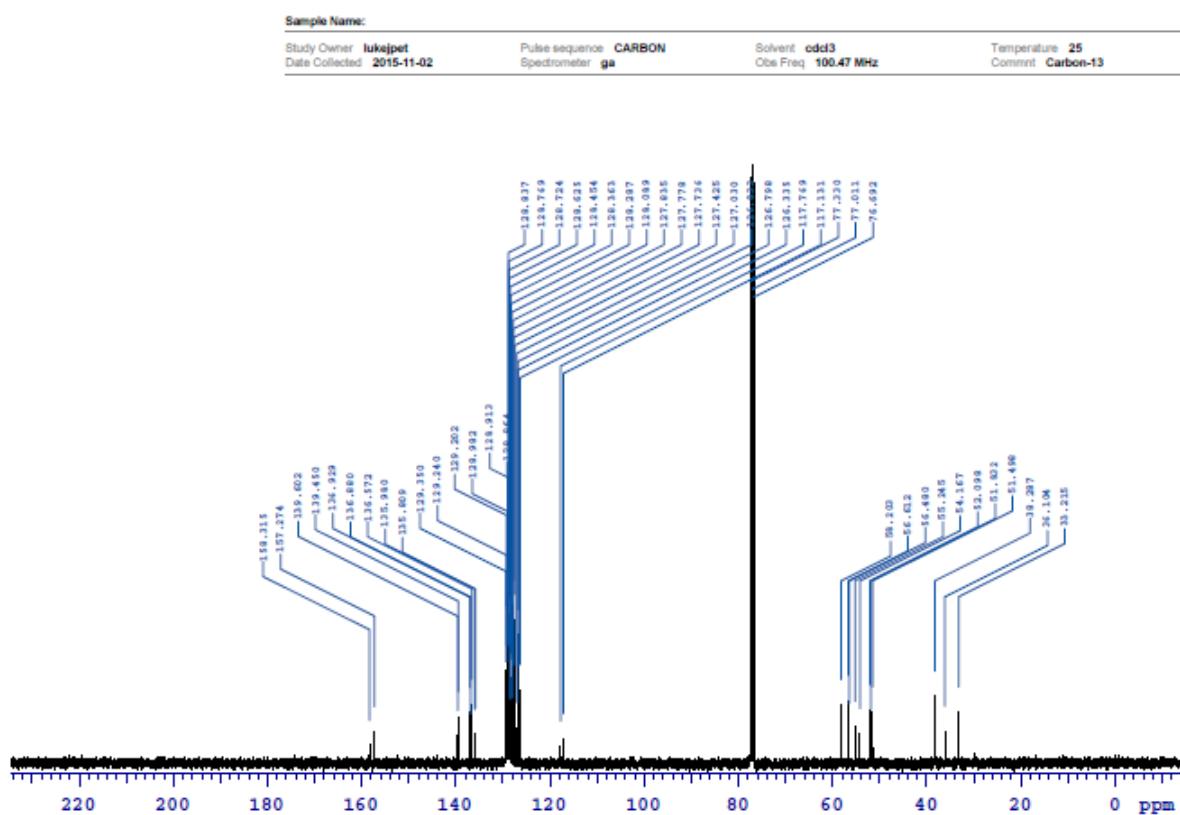
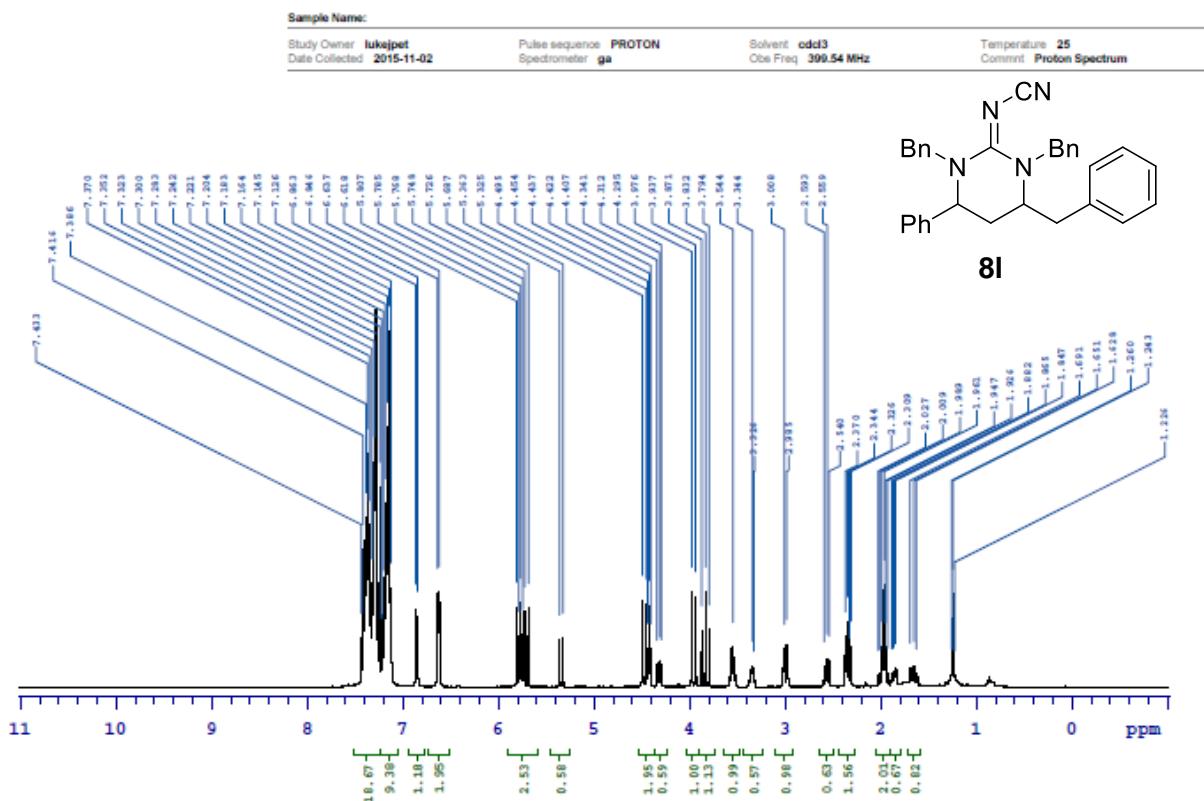
Study Owner luke|pet

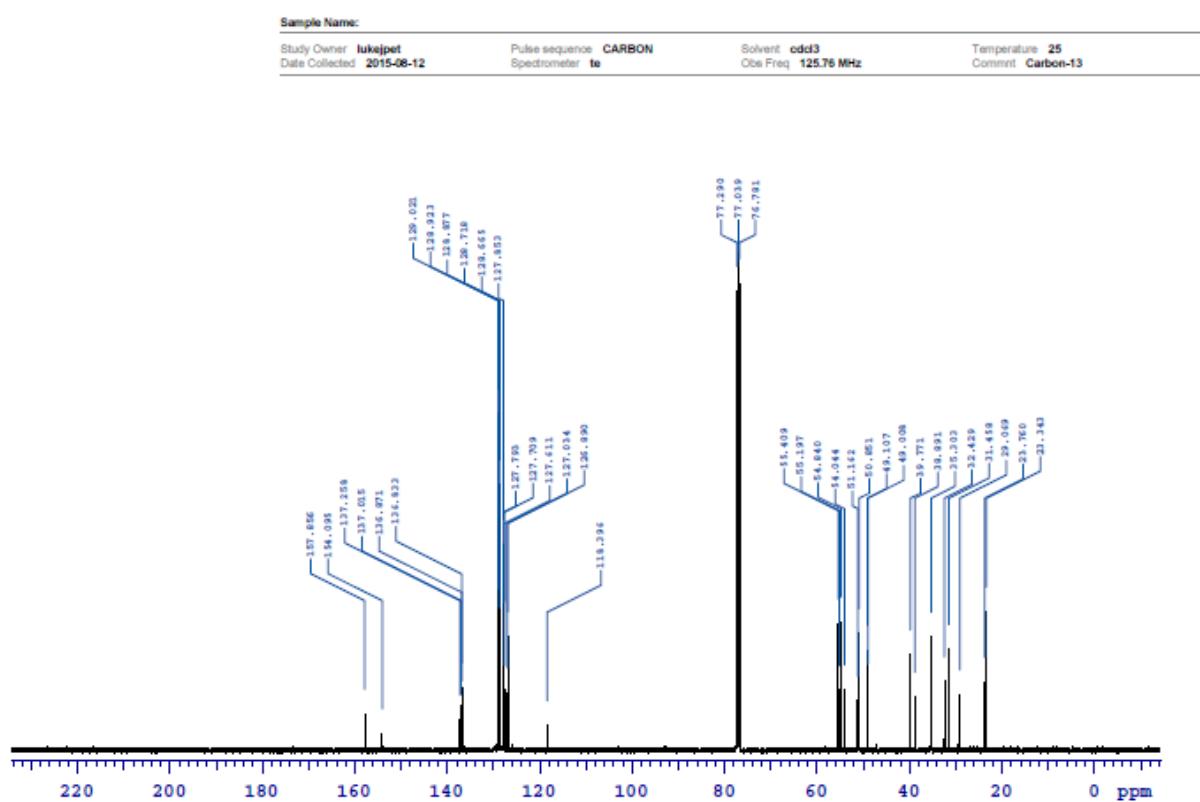
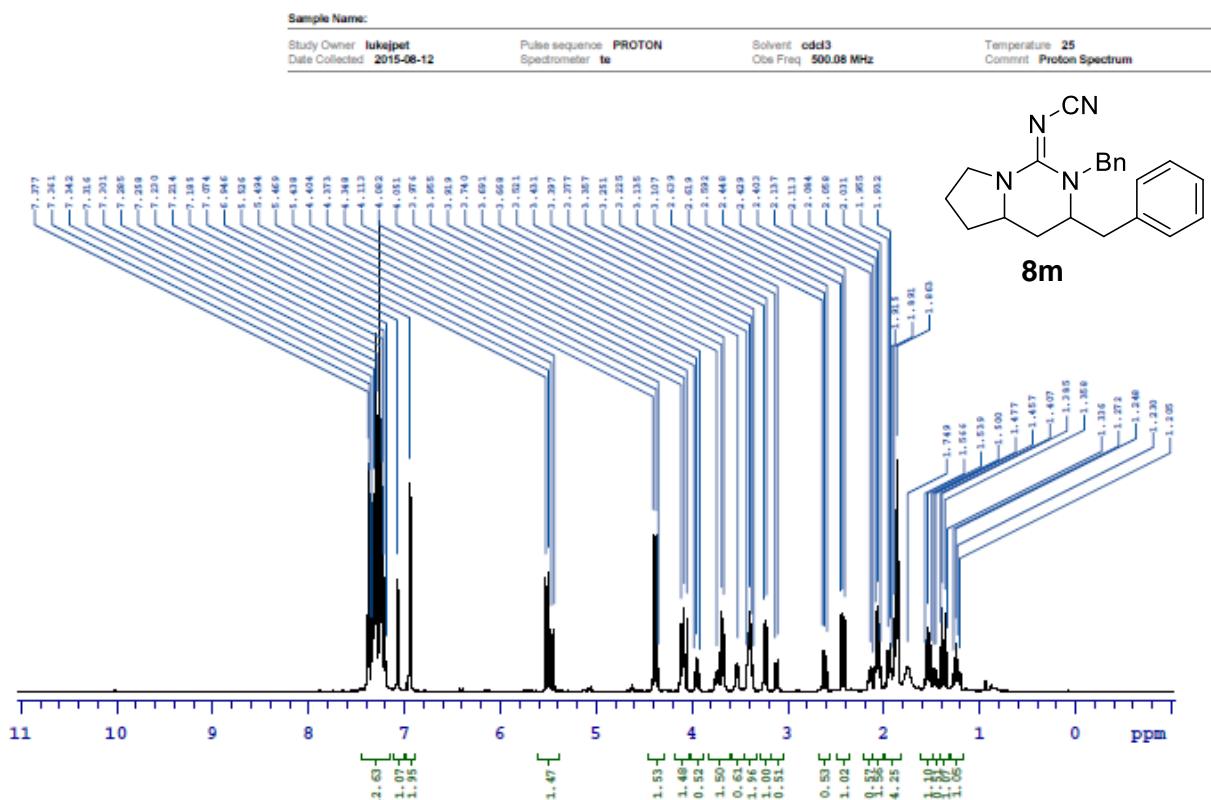
Pulse sequence **CARBON**
Spectrometer **13**

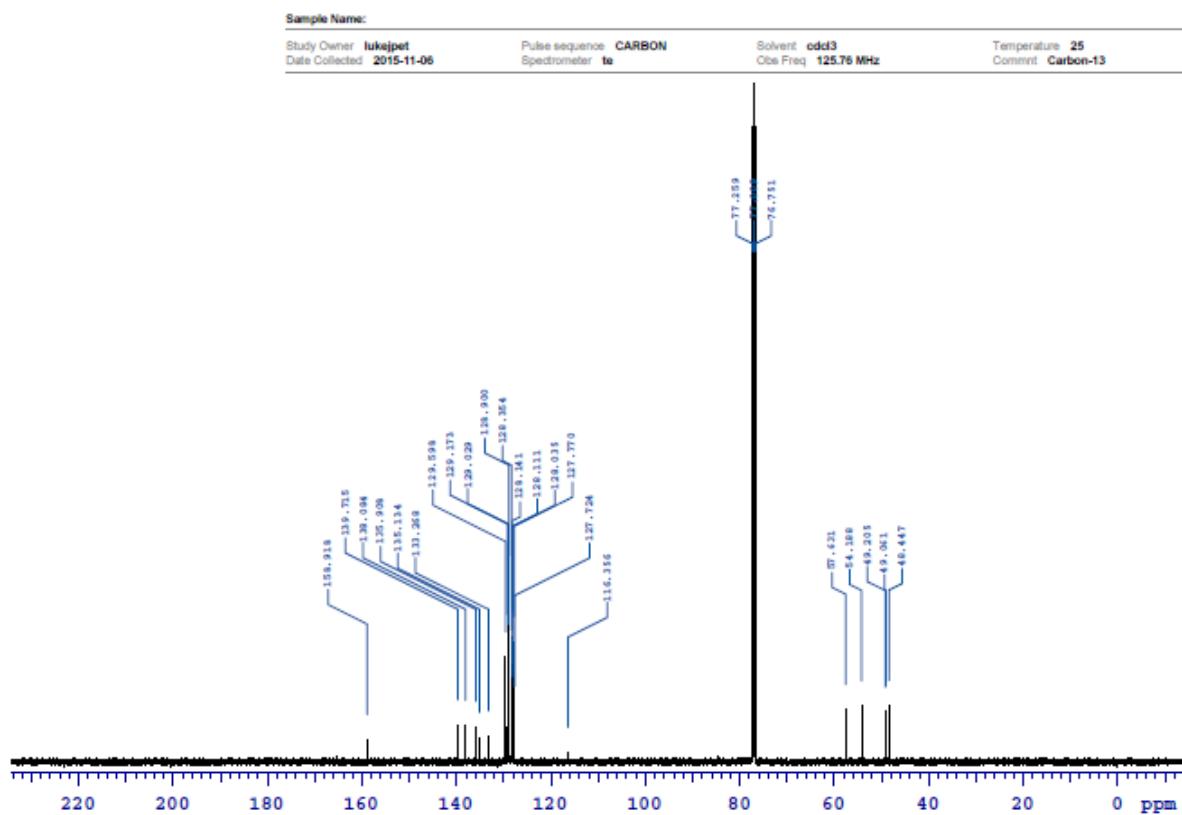
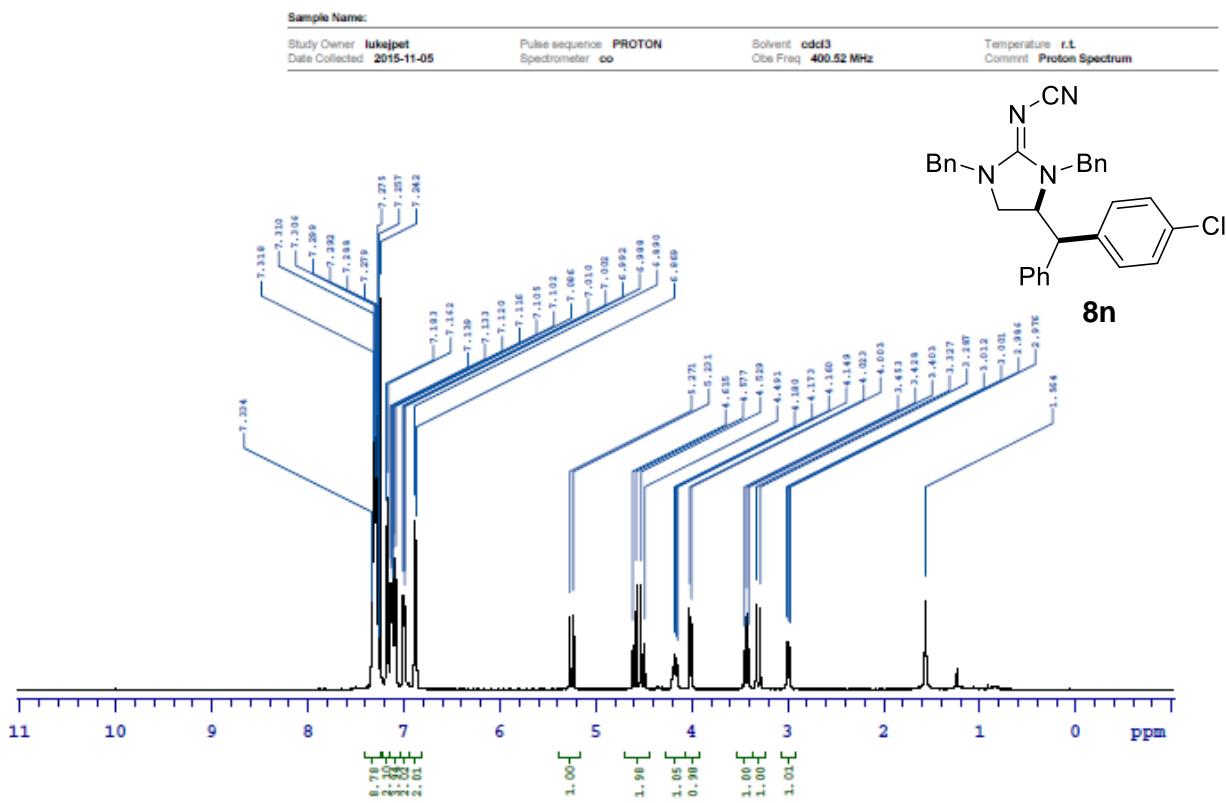
Solvent: **cdcl3**

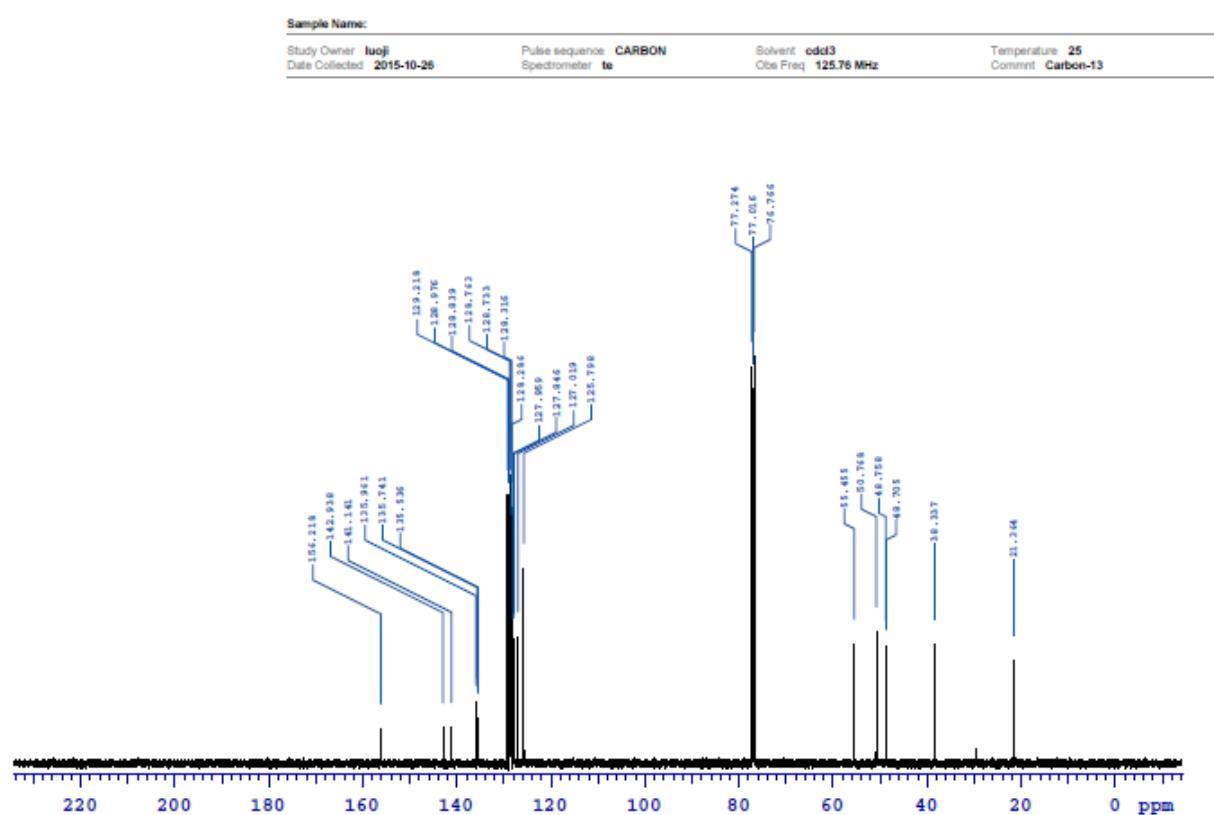
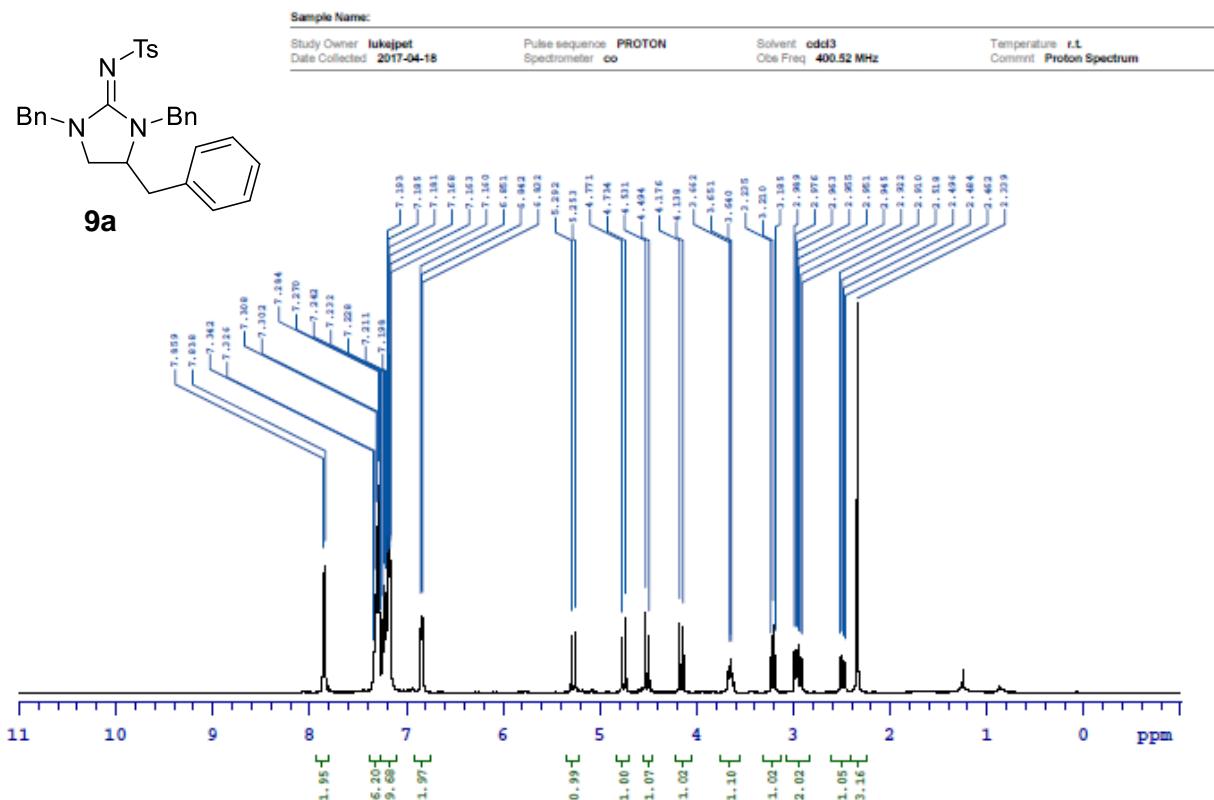
Temperature 25

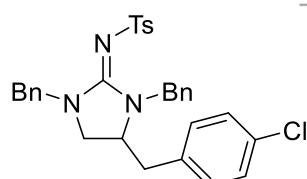




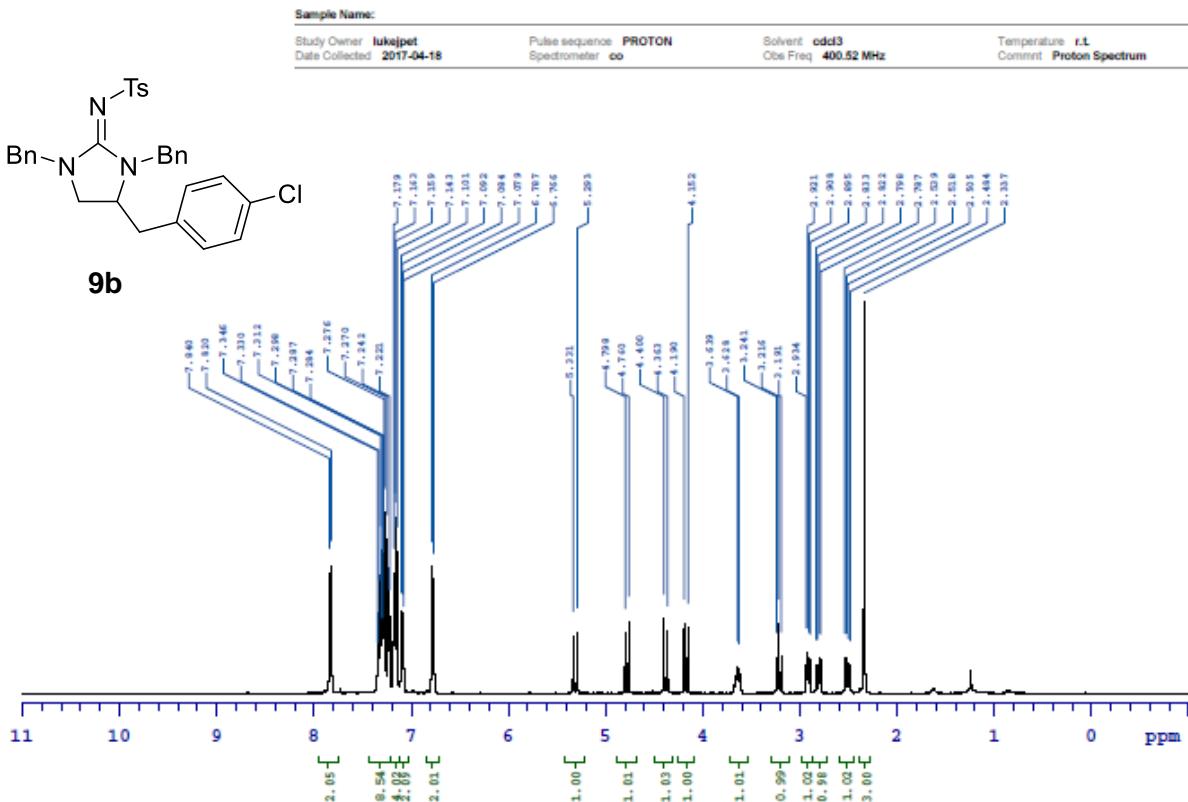








9b

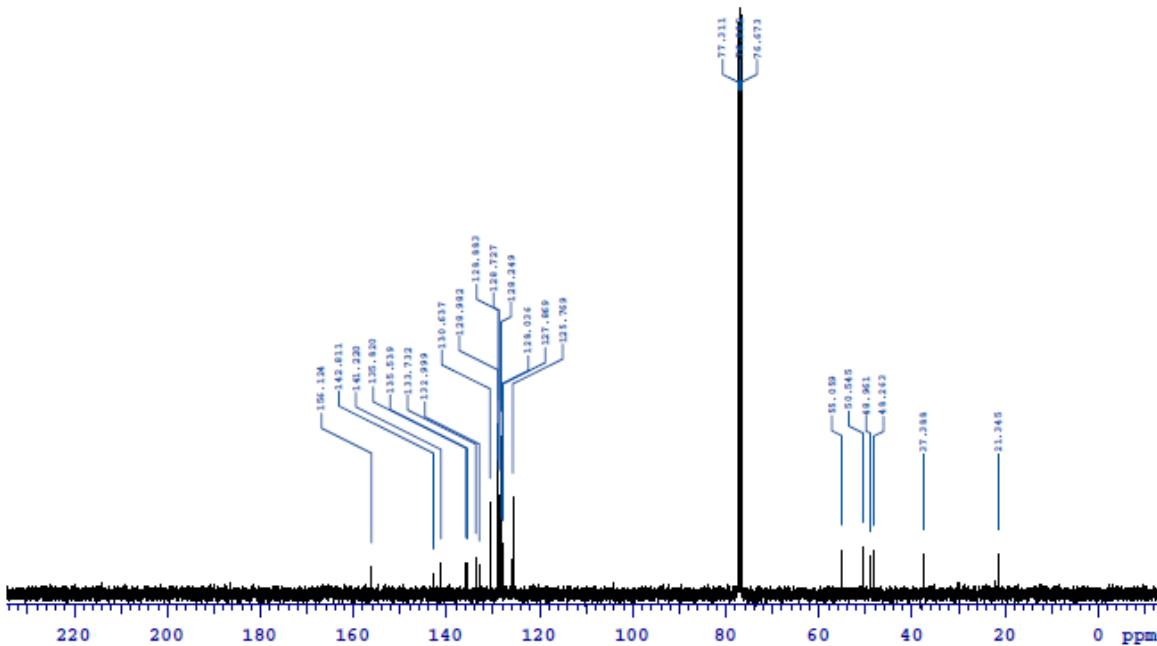


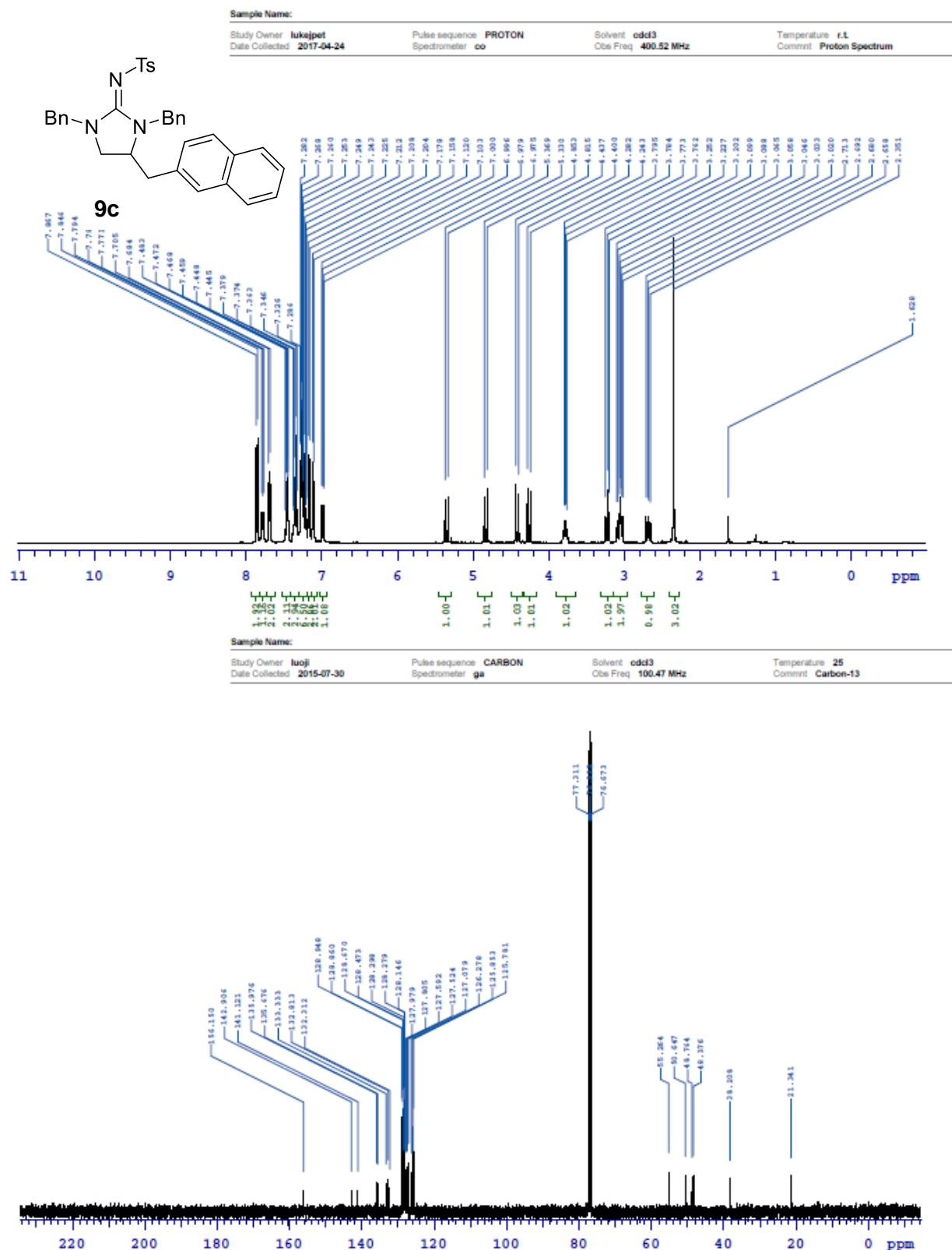
Study Owner **luoji**
Date Collected **2015-07-29**

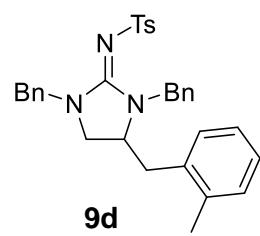
Pulse sequence **CARBON**
Spectrometer **ga**

Solvent **cdcl3**
Obs Freq **100.47 MHz**

Temperature **25**
Commit **Carbon-13**







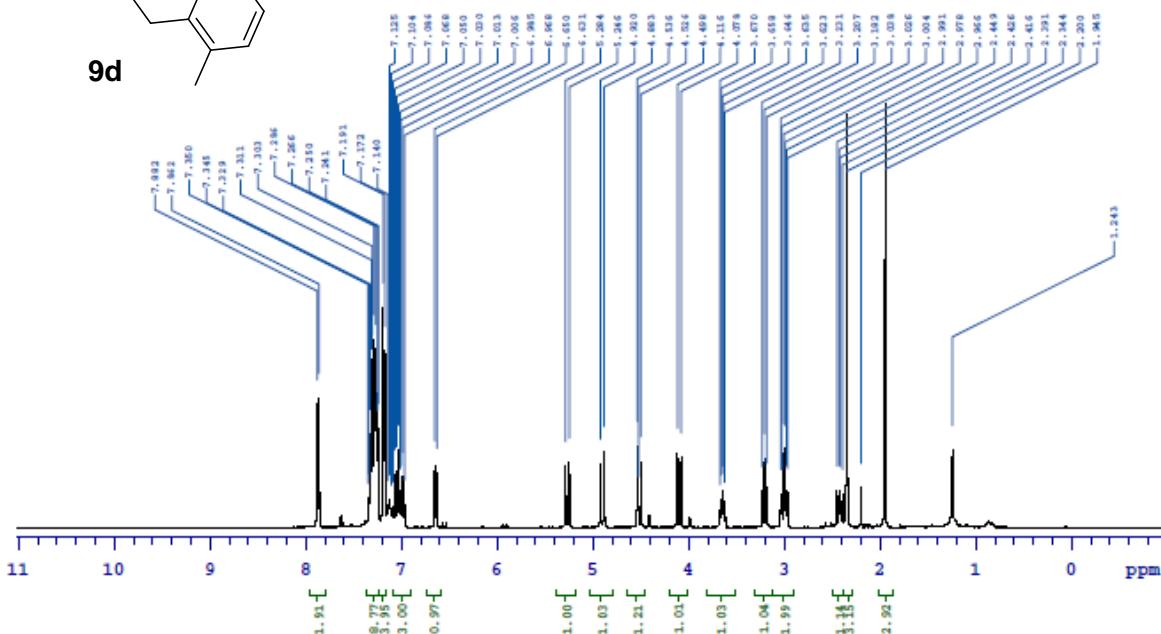
Sample Name:

Study Owner lukejpet
Date Collected 2017-03-21

Pulse sequence **PROTON**
Spectrometer **ga**

Solvent **cdcl3**
Obs Freq **399.54** MHz

Temperature 25
Commit Proton Spectrum



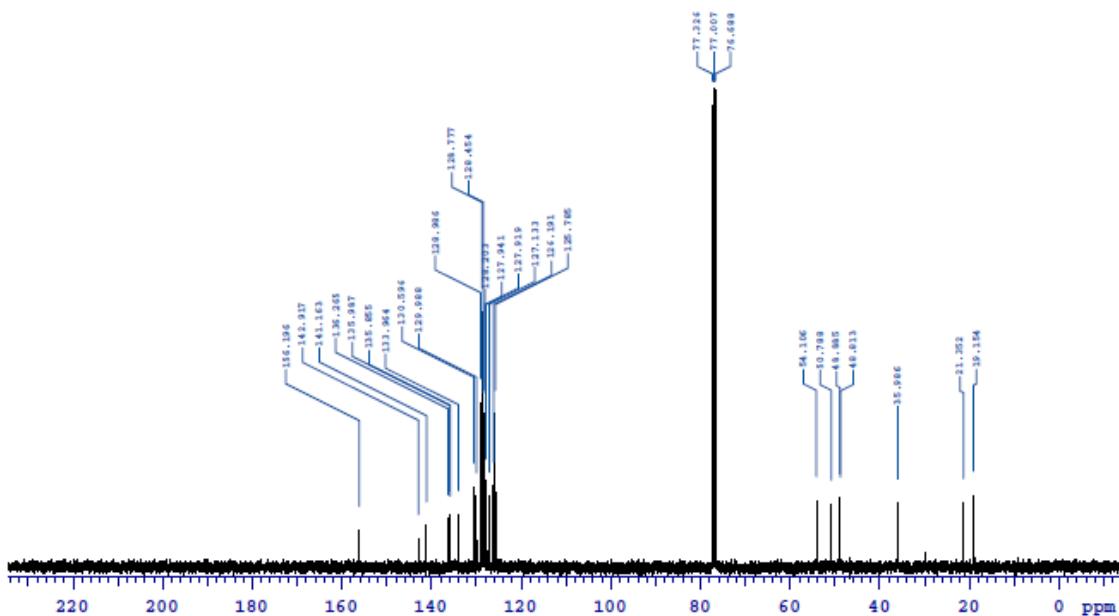
Sample Name:

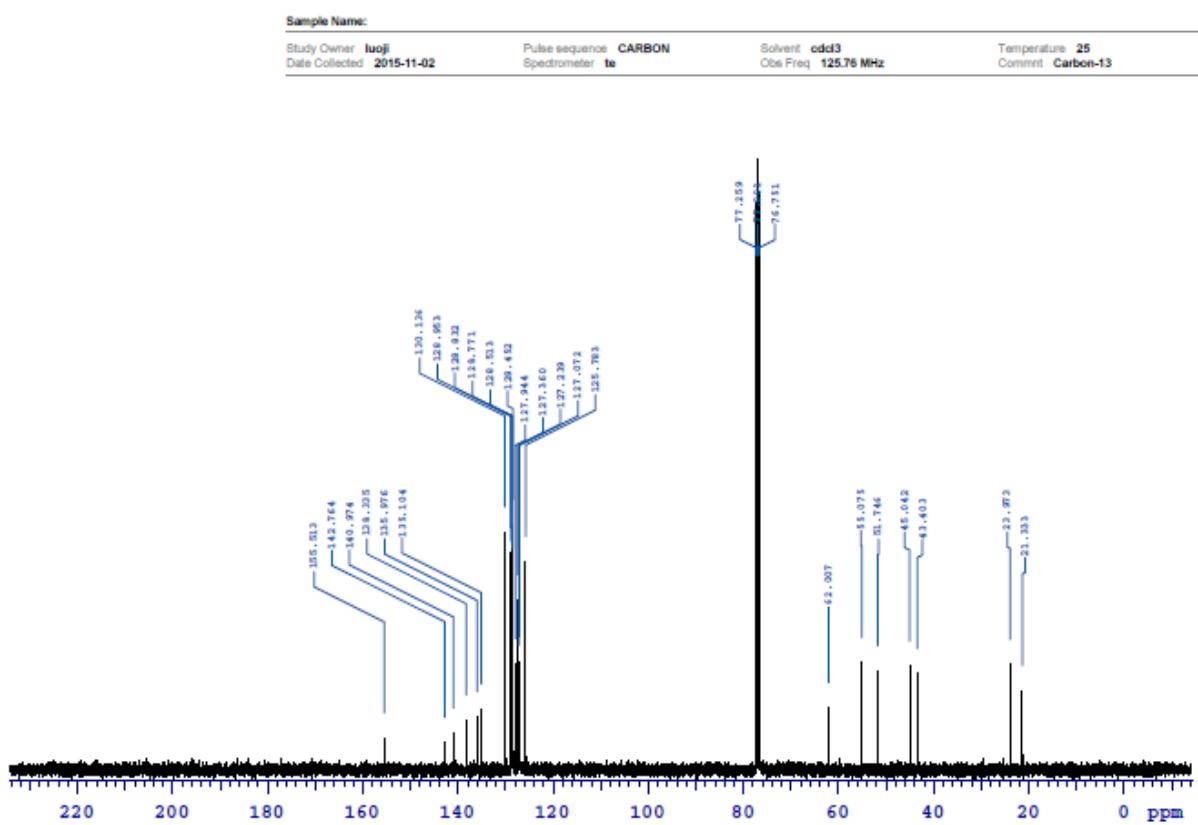
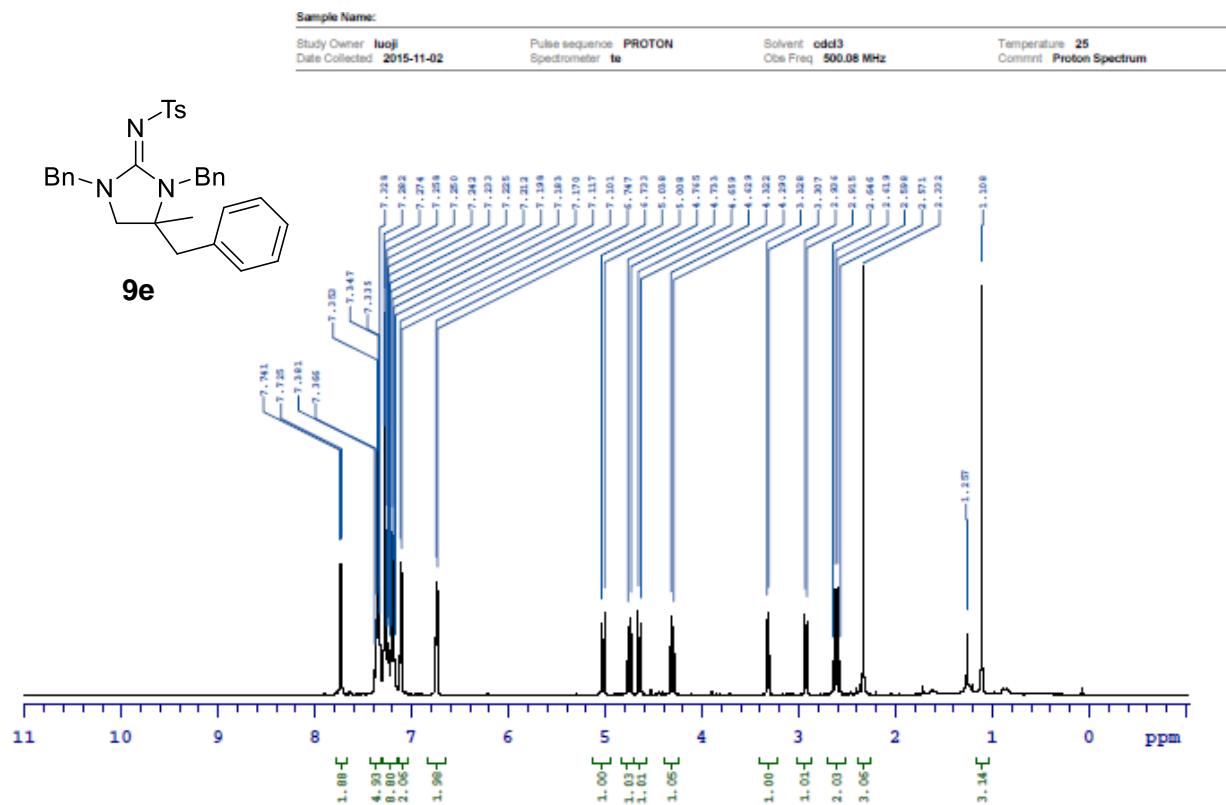
Study Owner lukejpet
Date Collected 2017-03-21

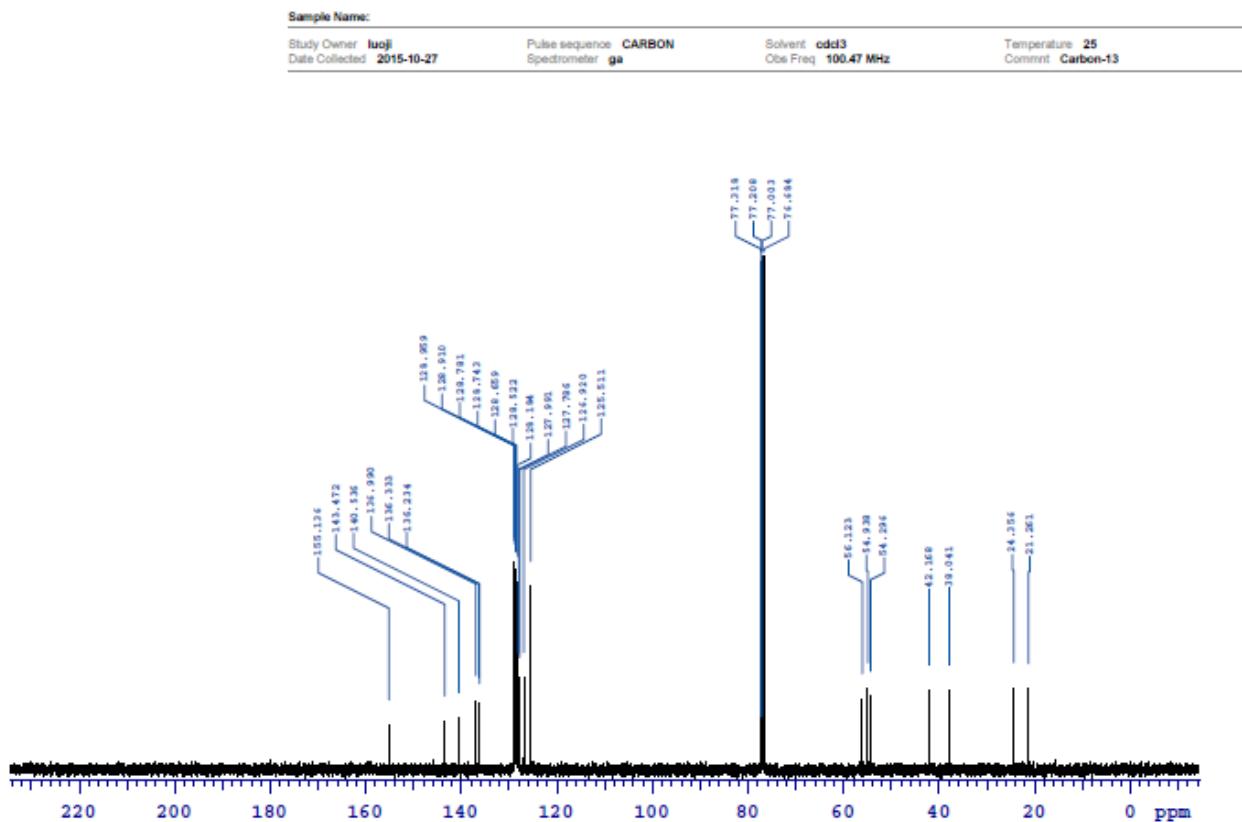
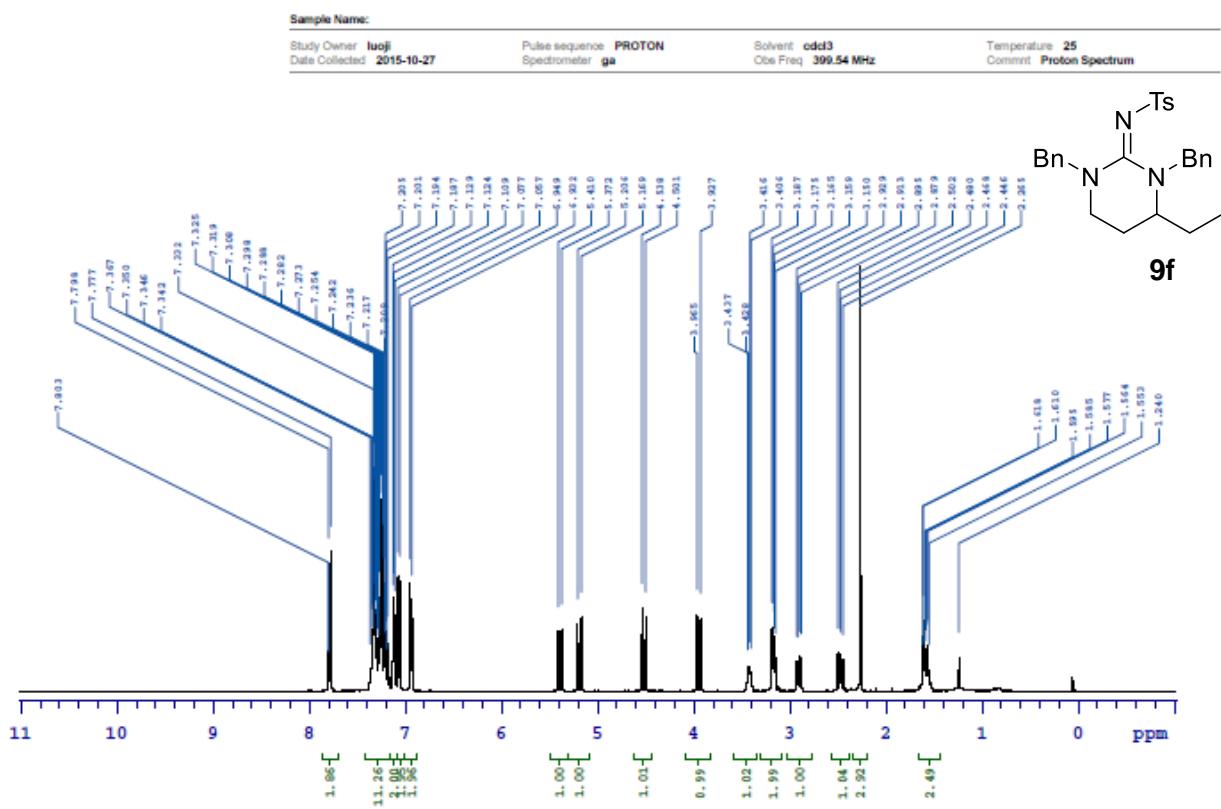
Pulse sequence **CARBON**
Spectrometer **ga**

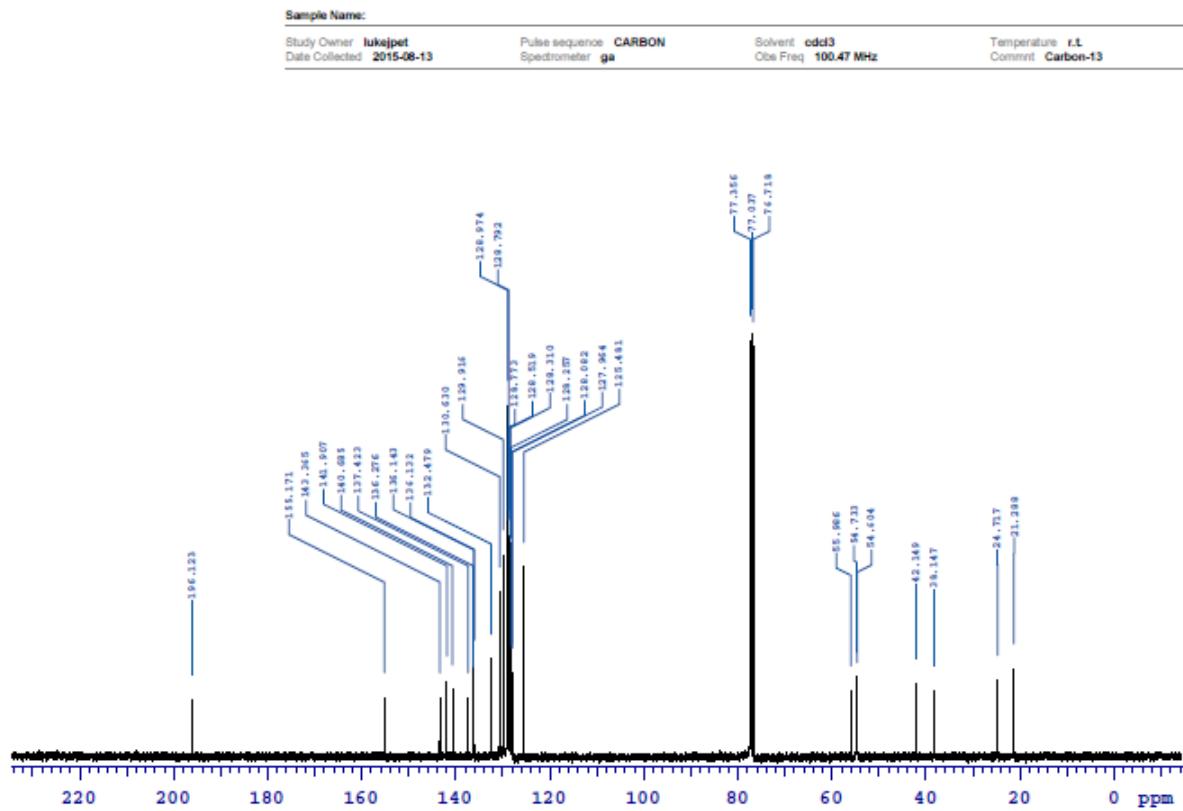
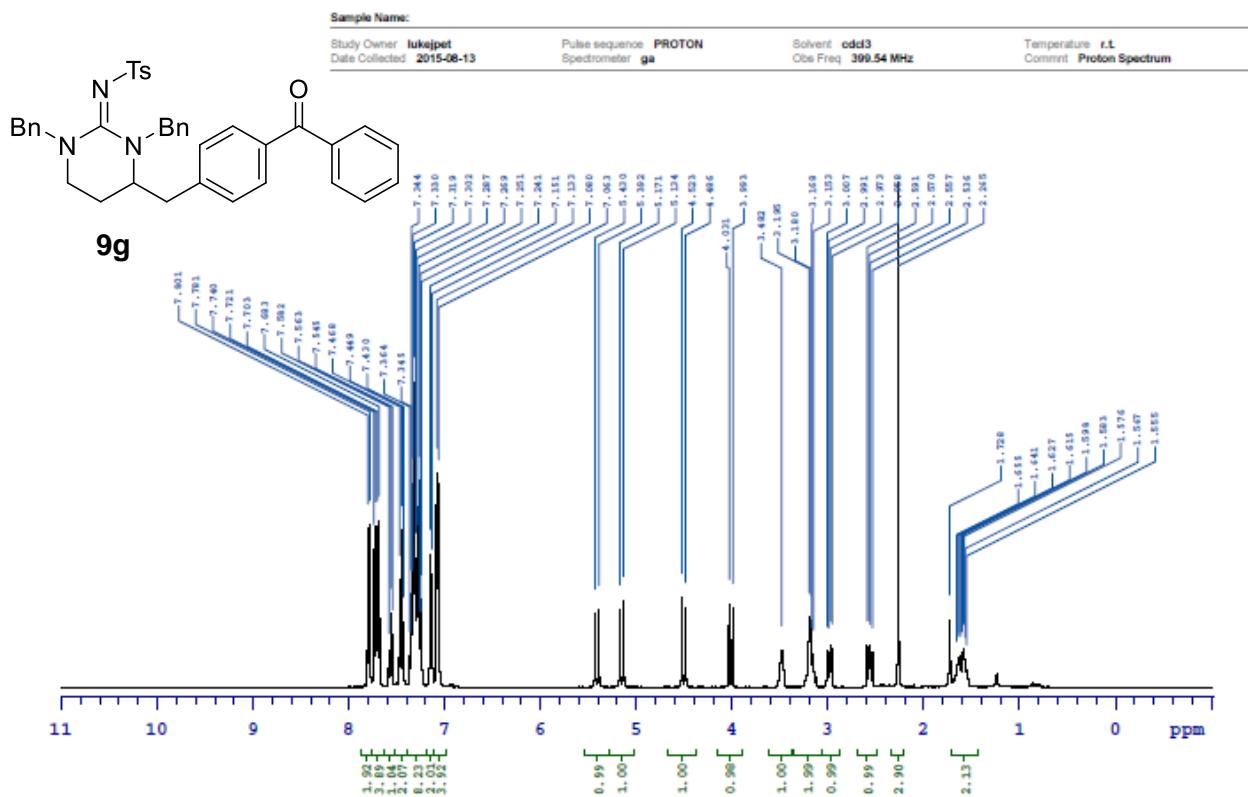
Solvent: **cdcl3**
Obs Freq: **100.47 MHz**

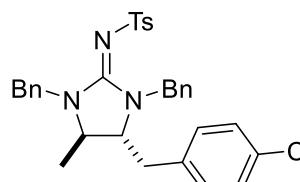
Temperature 25
Comment Carbon-13











Sample Name:

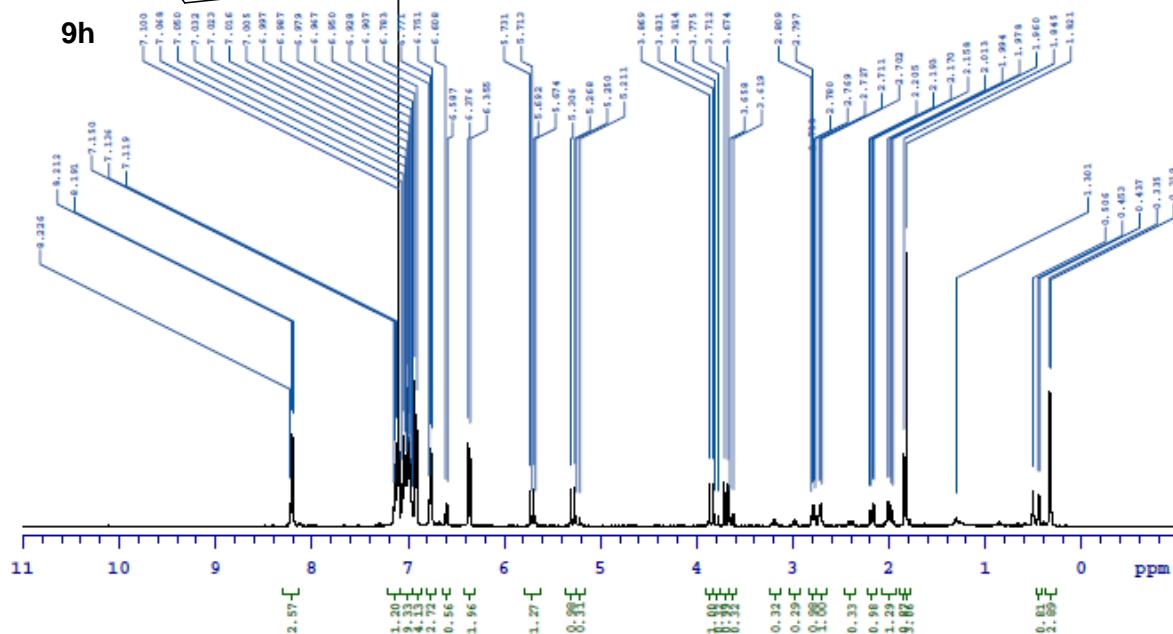
Study Owner lukejpet
Date Collected 2016-02-04

Pulse sequence PROTON
Spectrometer 69

Solvent **c6d6**
Obs Freq **400.52 MHz**

Temperature **r.t.**
Comment **Proton Spectrum**

9h



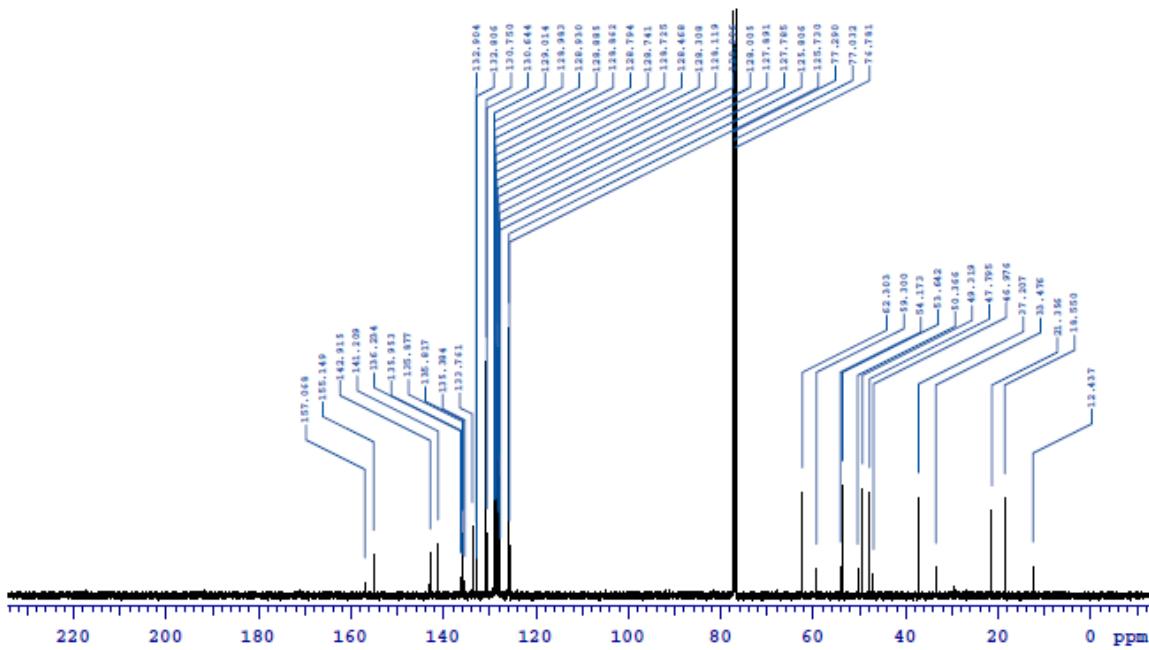
Sample Name:

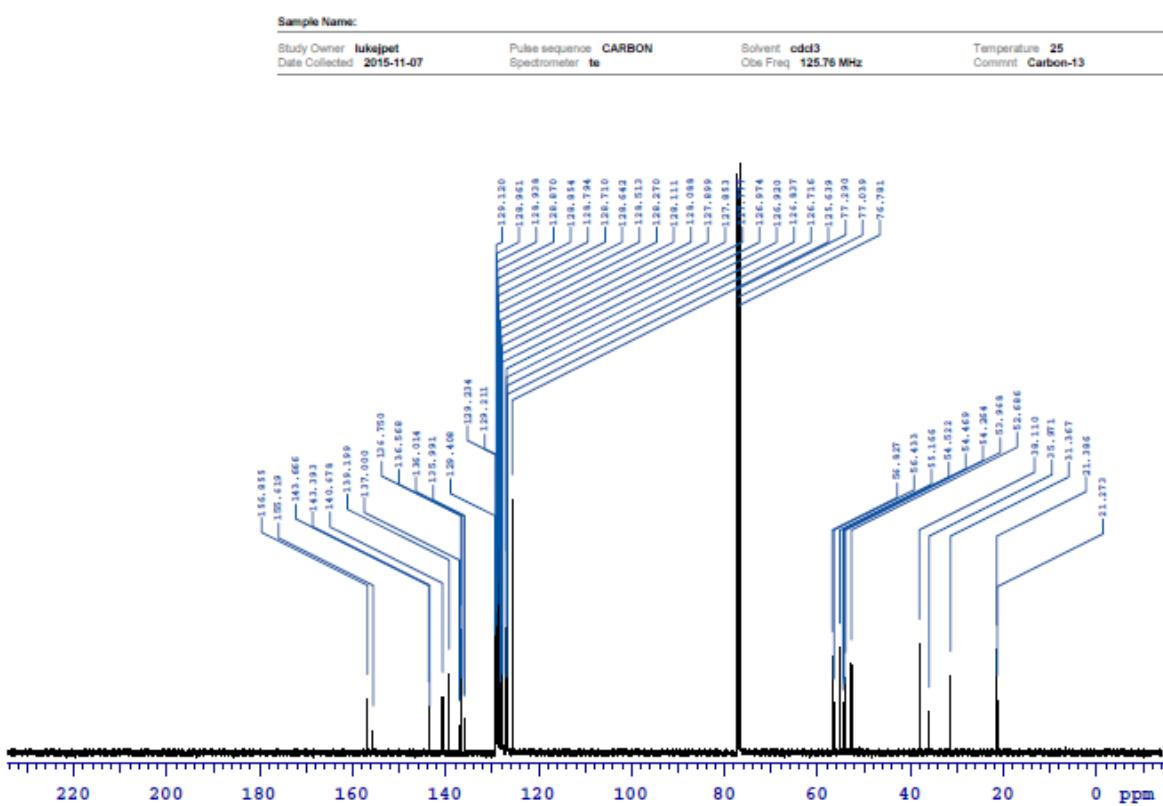
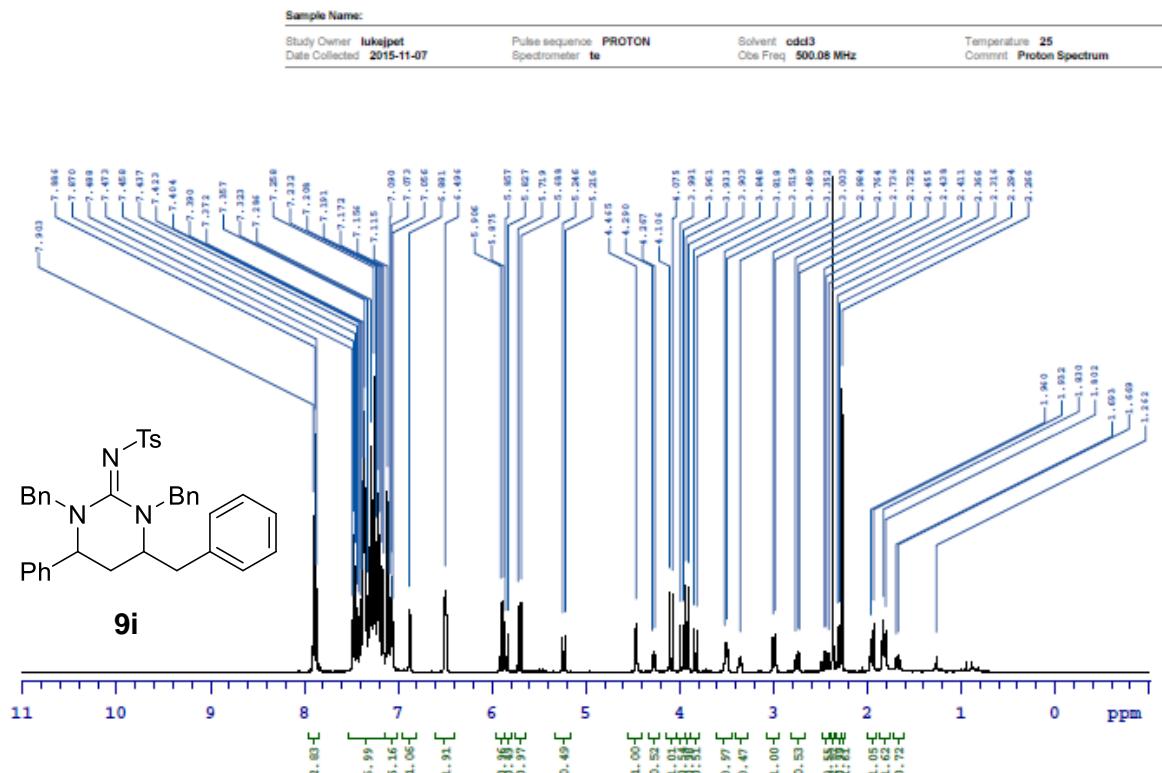
Study Owner lukejpet
Date Collected 2015-12

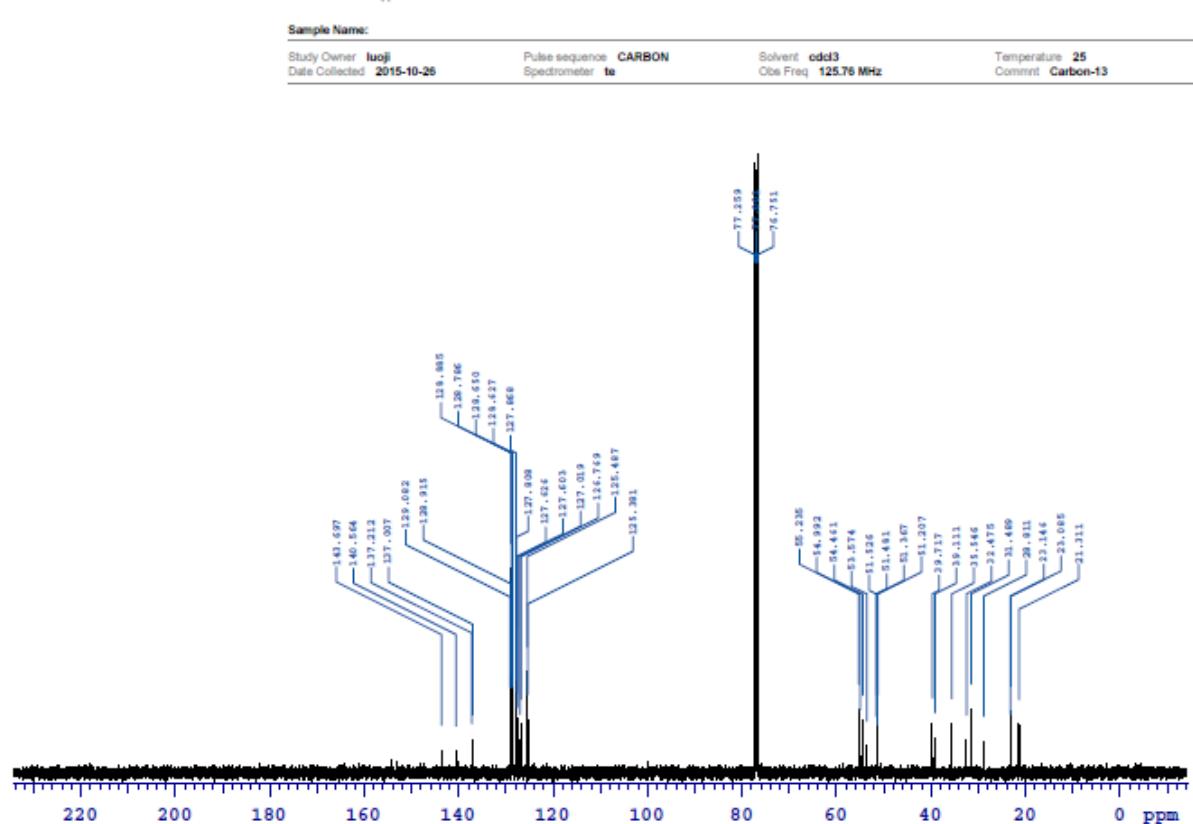
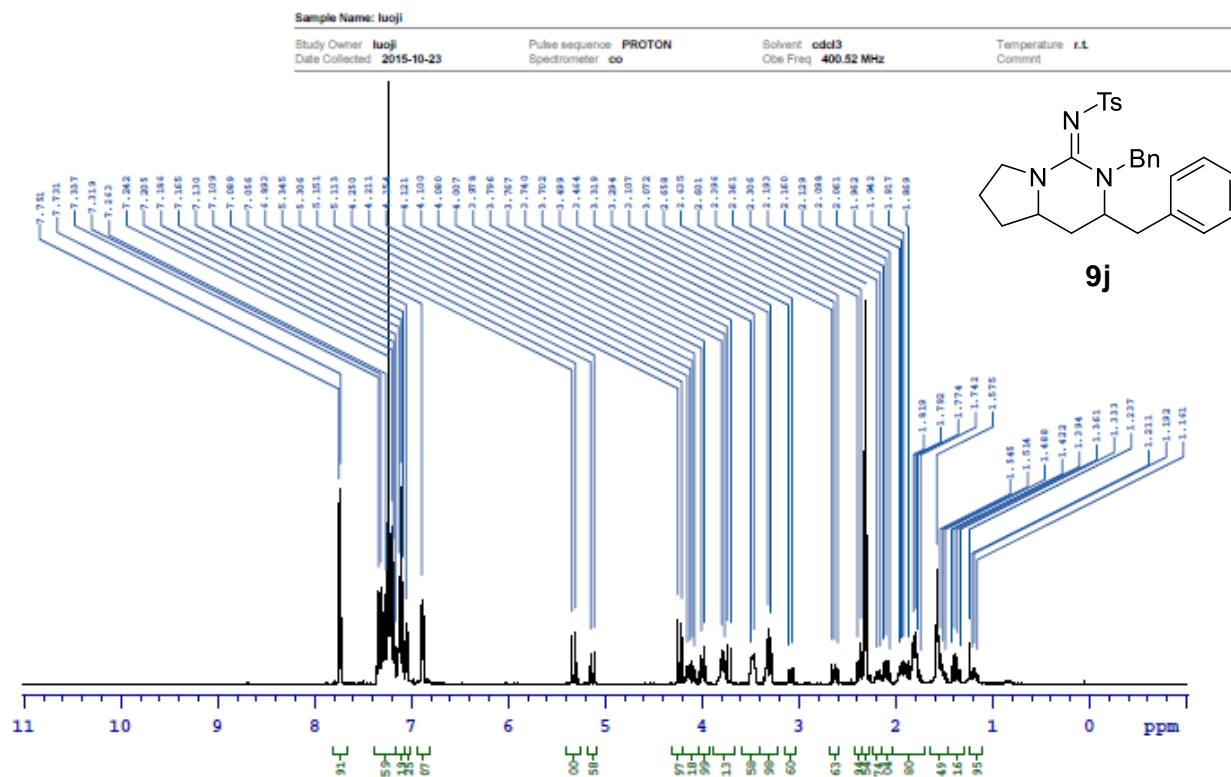
Pulse sequence **CARBON**
Spectrometer **13C**

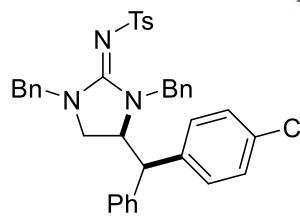
Solvent **ddm3**
Obs Freq **125.76 MHz**

Temperature 23
Commit Carbon-13

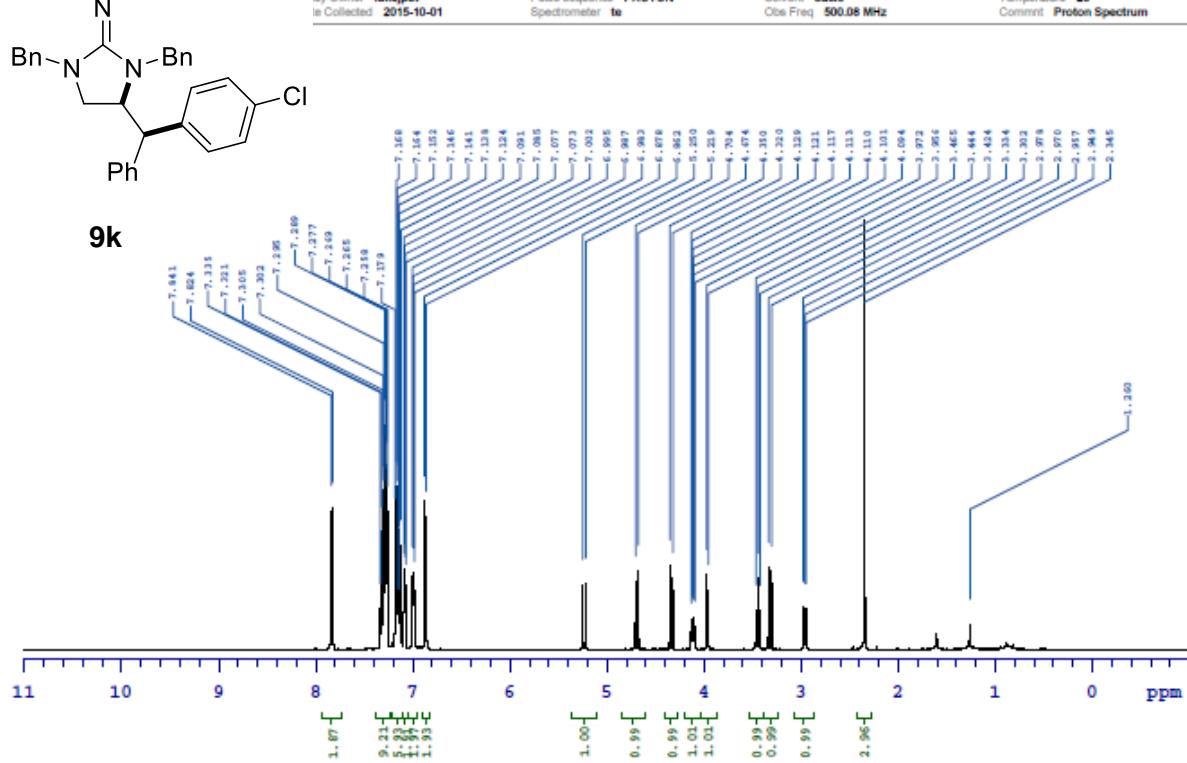








9k



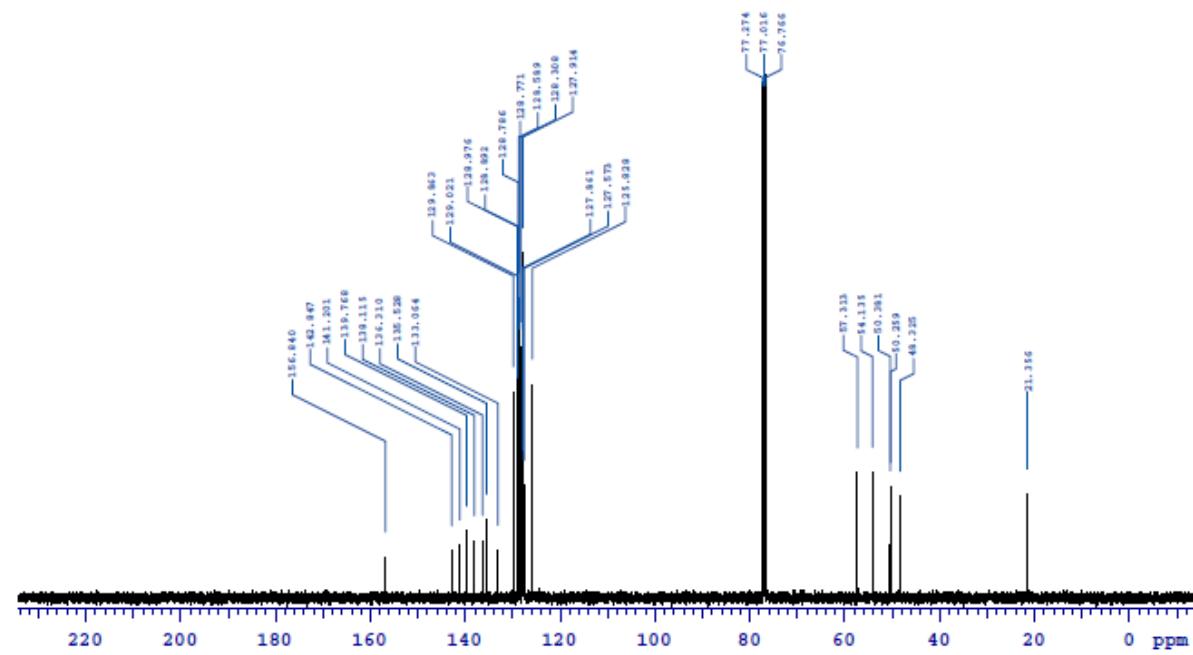
Sample Name:

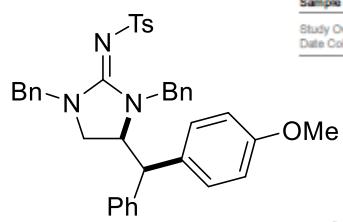
Study Owner lukejpet
Date Collected 2015-10-01

Pulse sequence **CARBON**

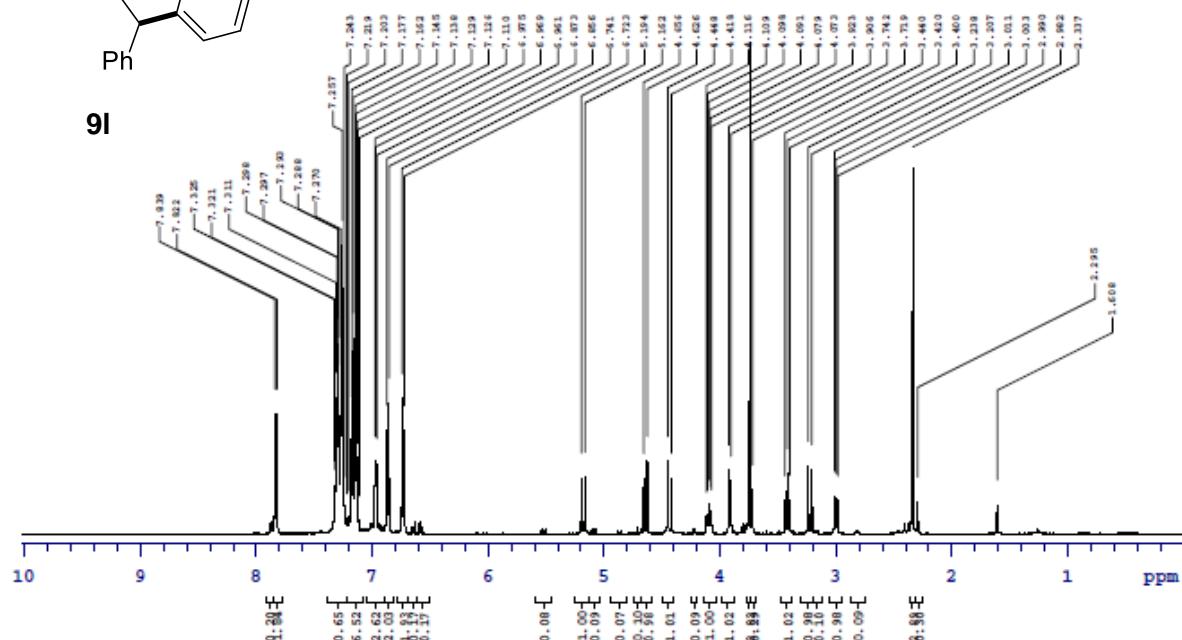
Solvent [cdcl3](#)
Obs Freq **125.76 MHz**

Temperature 25
Commit Carbon-13





91



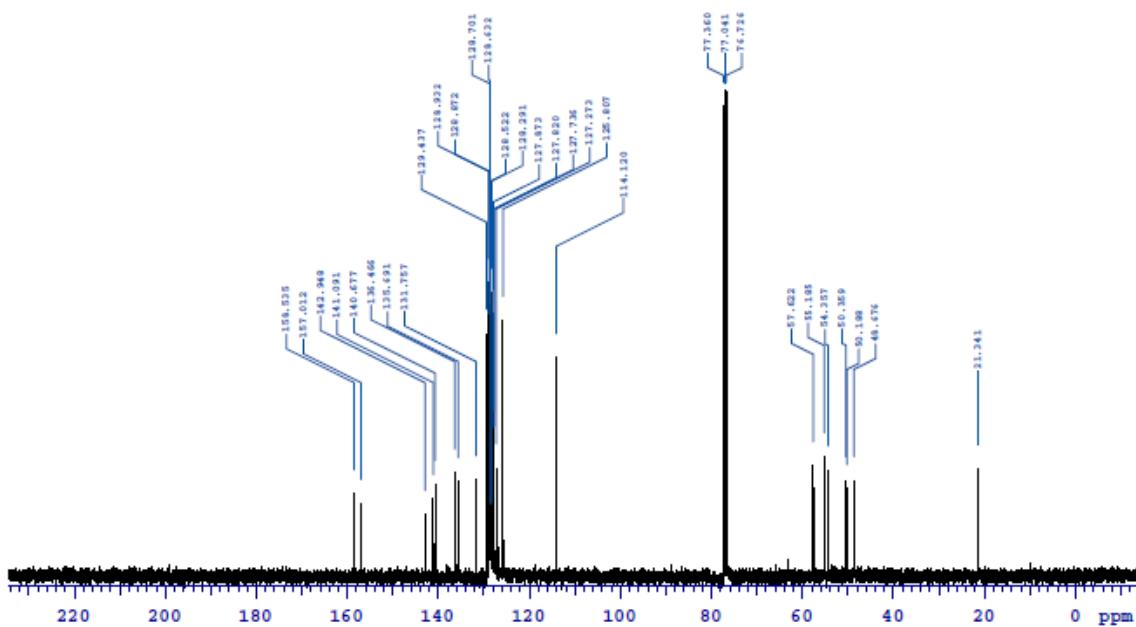
Sample Name:

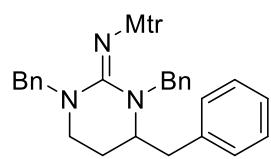
Study Owner lukejpet
Date Collected 2016-09-01

Pulse sequence **CARBON**
Spectrometer **98**

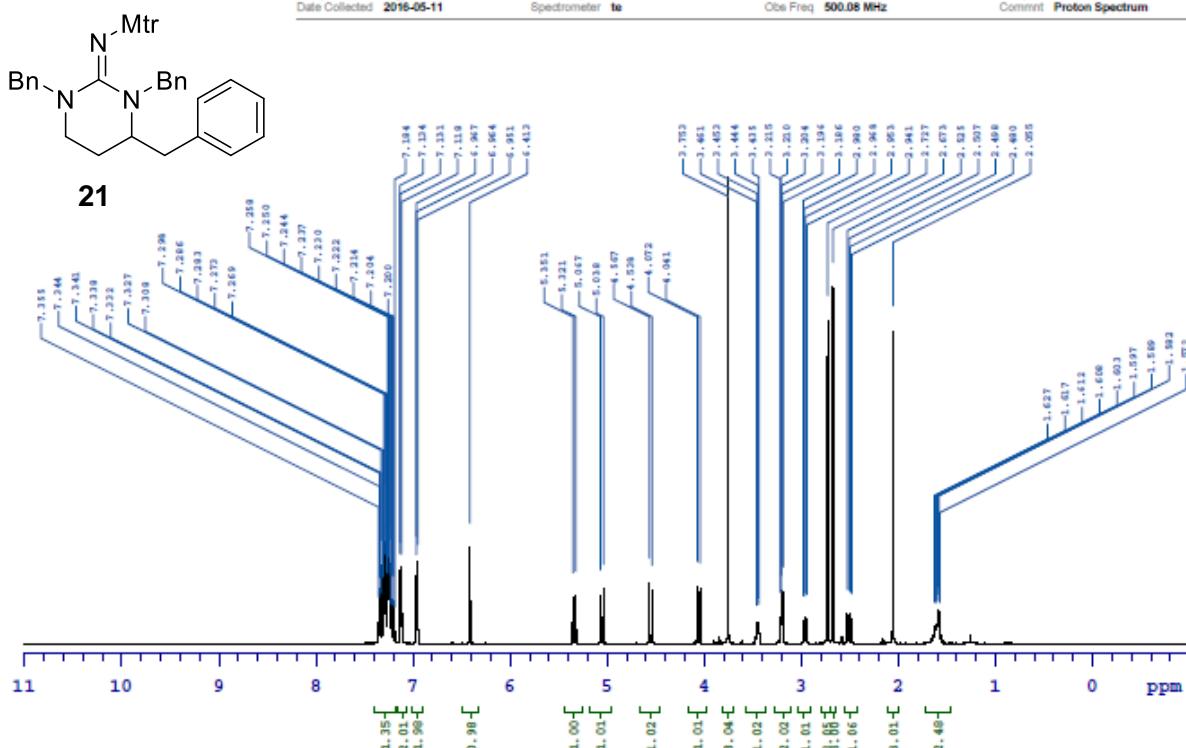
Solvent **cdcl3**
Obs Freq **100.47 MHz**

Temperature **25**
Comment **Carbon-13**





21



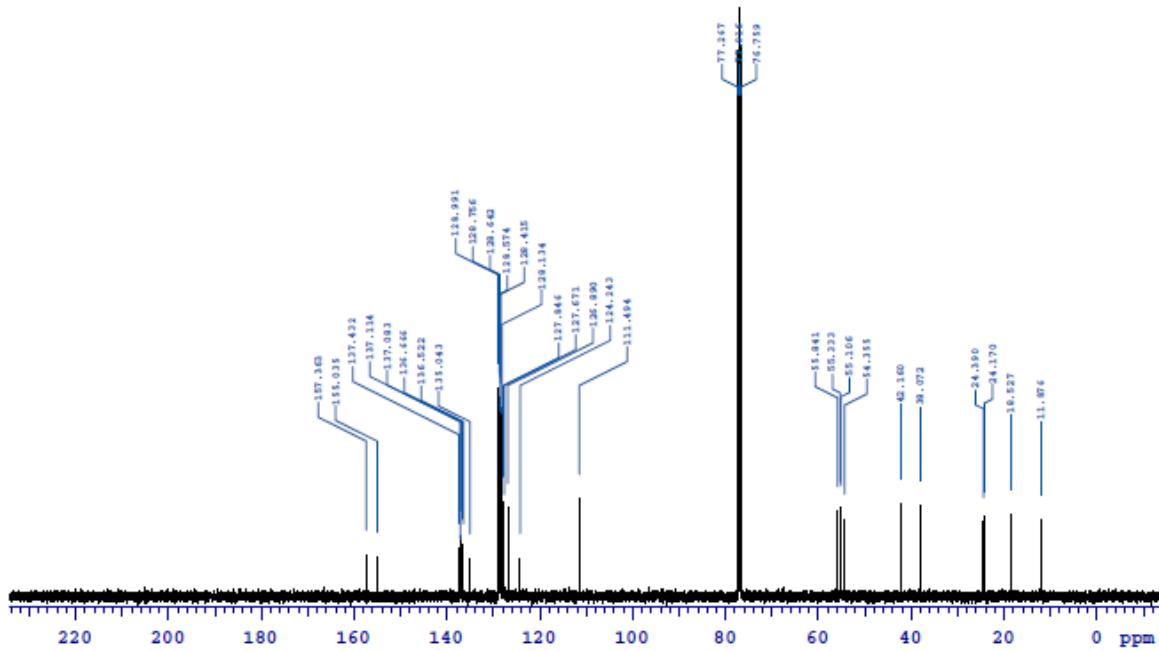
Sample Name:

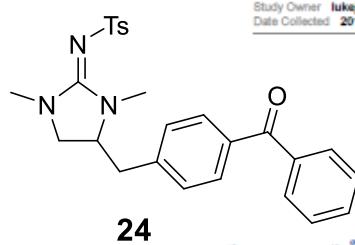
Study Owner lukejpet
Date Collected 2016-05-11

Pulse sequence: **CARBON**

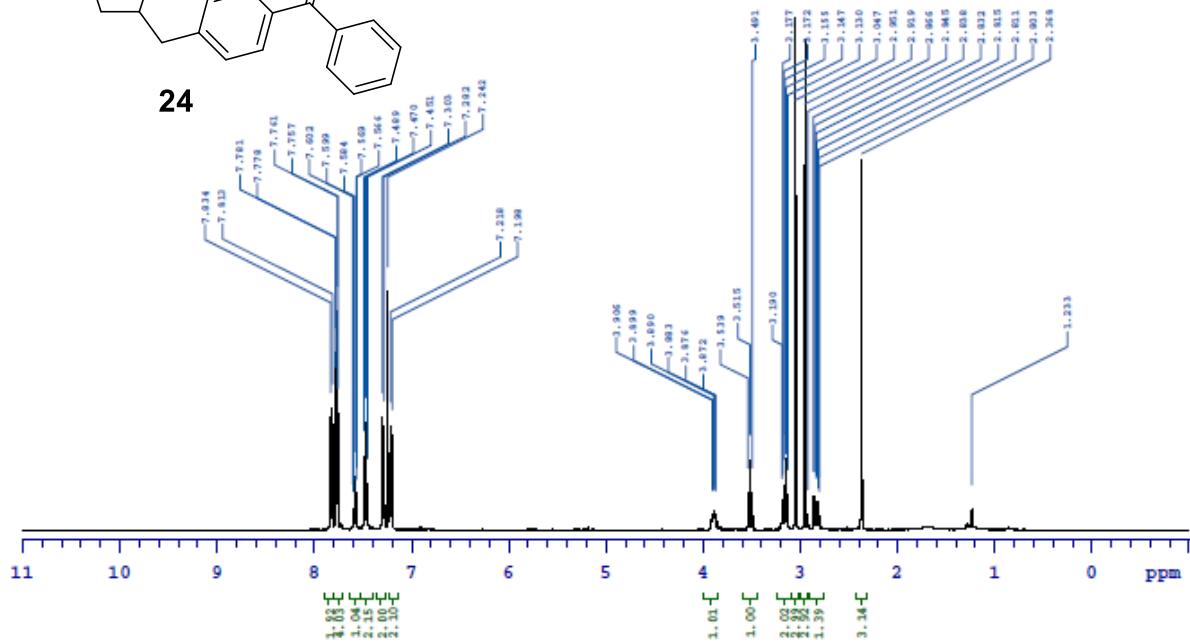
Solvent **cdcl3**
Obs Freq **125.76 MHz**

Temperature 25
Commit Proton Spectrum





24



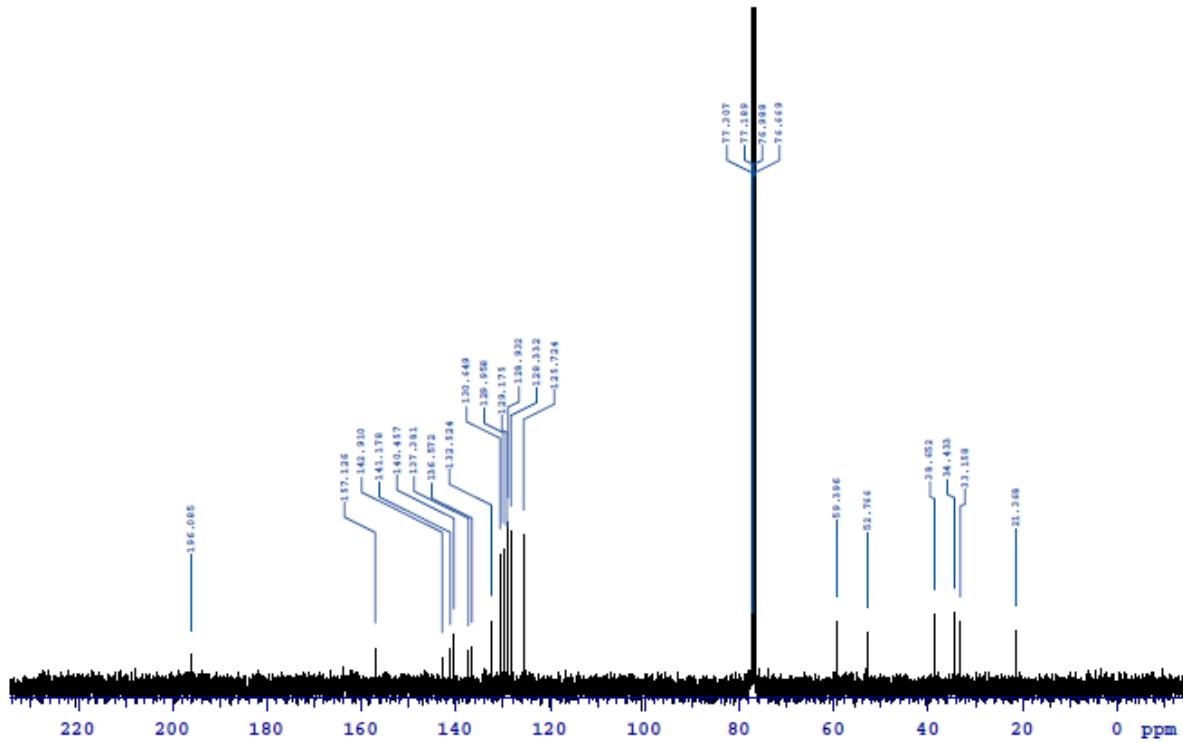
Sample Name:

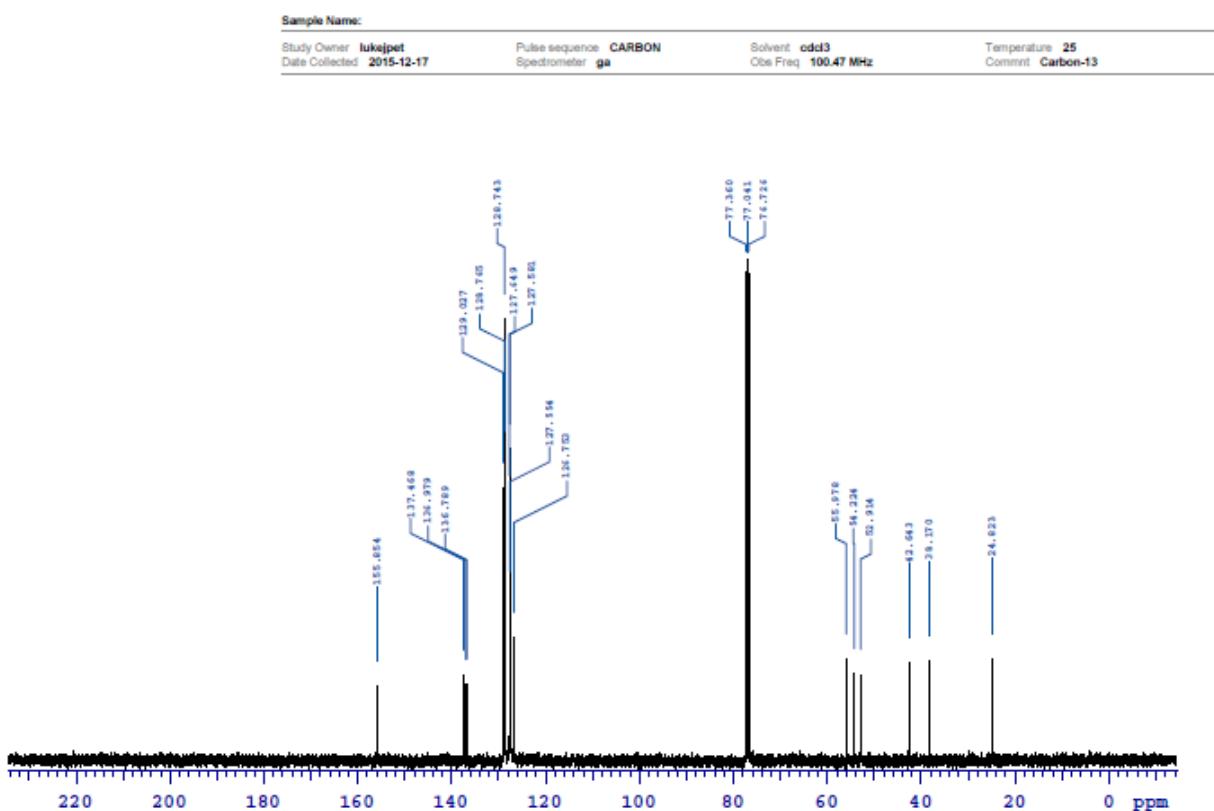
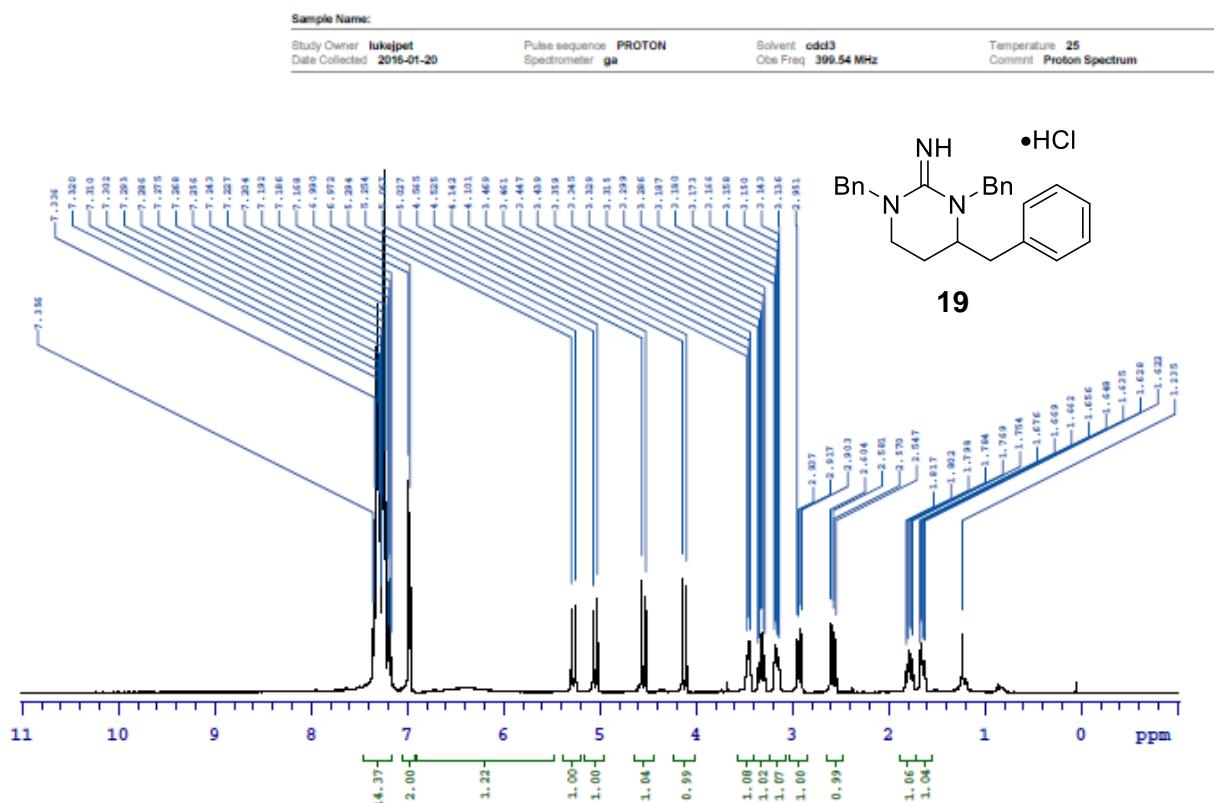
Study Owner lukejpet
Date Collected 2017-05-11

Pulse sequence **CARBON**
Spectrometer **ga**

Solvent **cdcl3**
Obs Freq **100.47 MHz**

Temperature 25
Comment Carbon-13





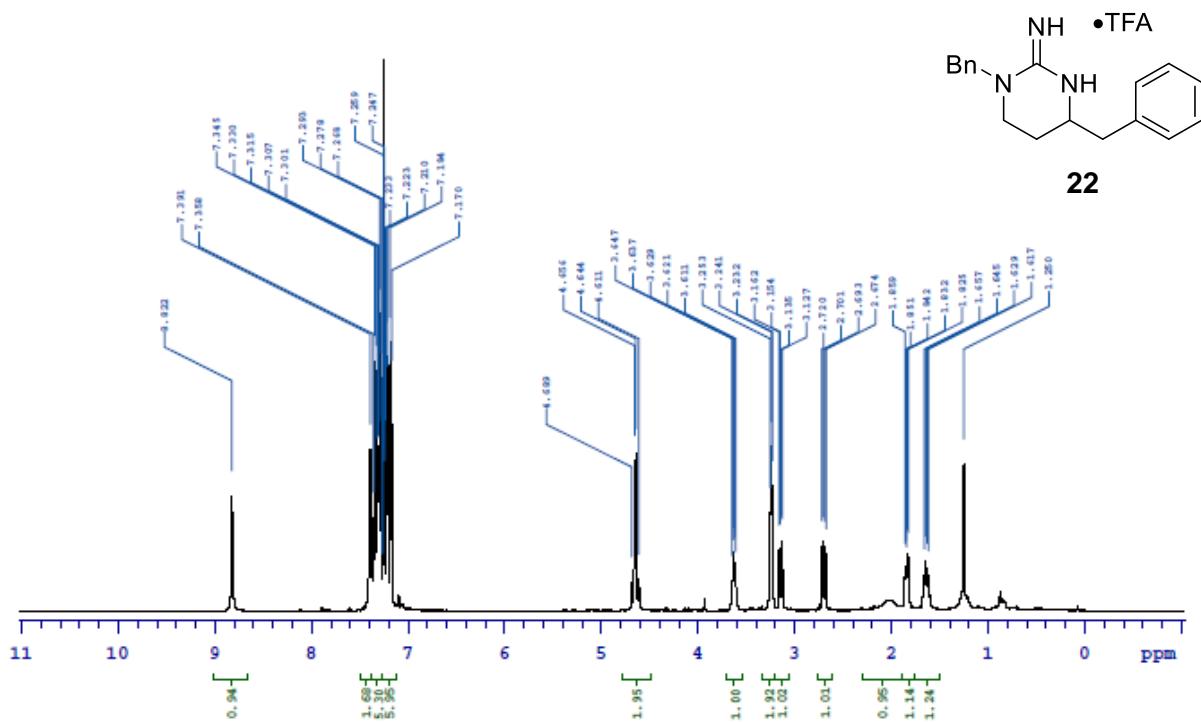
Sample Name:

Study Owner lukejpet
Date Collected 2016-07-25

Pulse sequence **PROTON**
Spectrometer **10**

Solvent **cdcl3**
Obs Freq **500.08 MHz**

Temperature 24
Comment [Proton Spectrum](#)



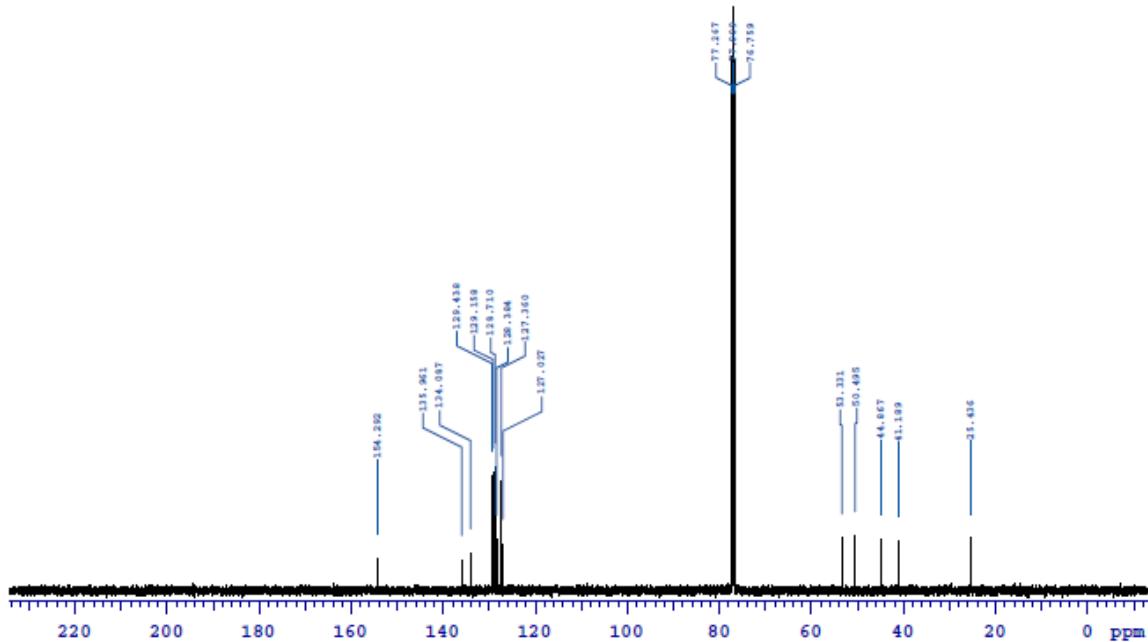
Sample Name:

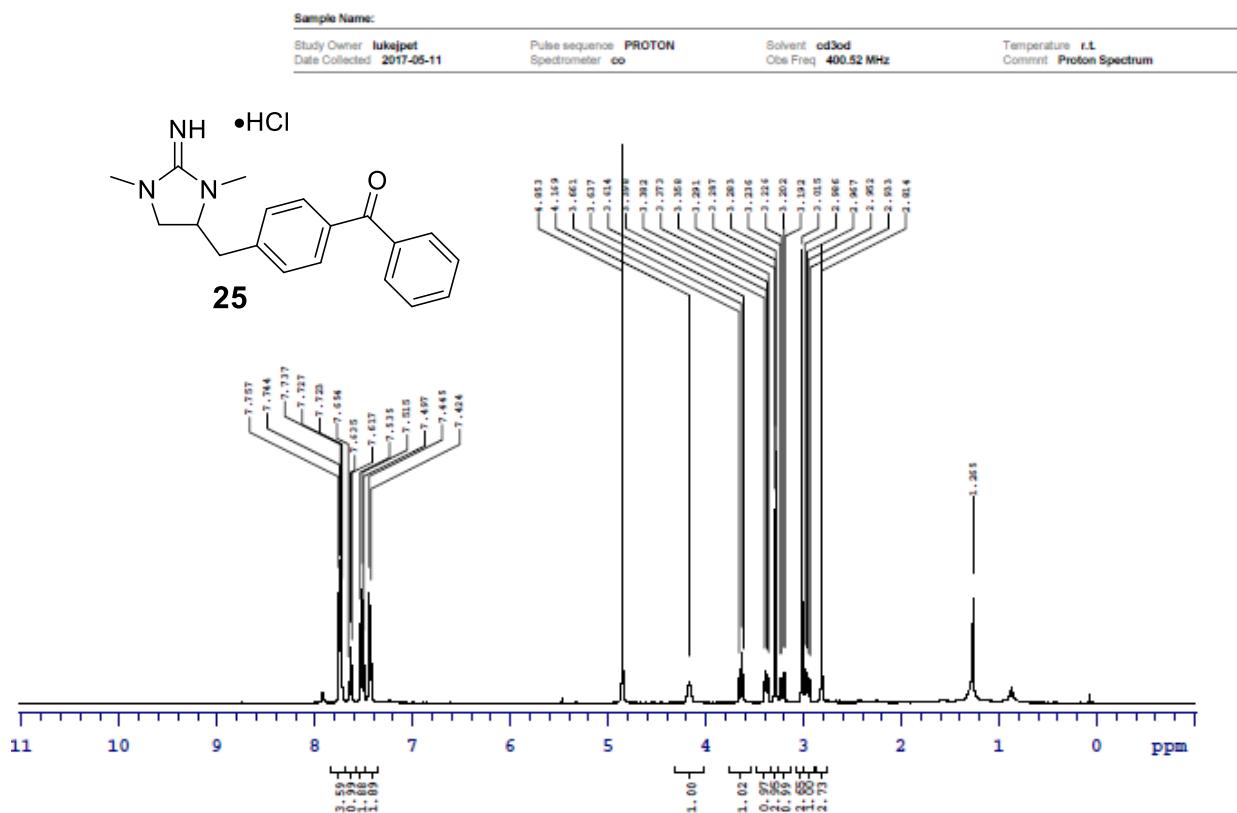
Study Owner lukejpet
Date Collected 2016-07-25

Pulse sequence **CARBON**

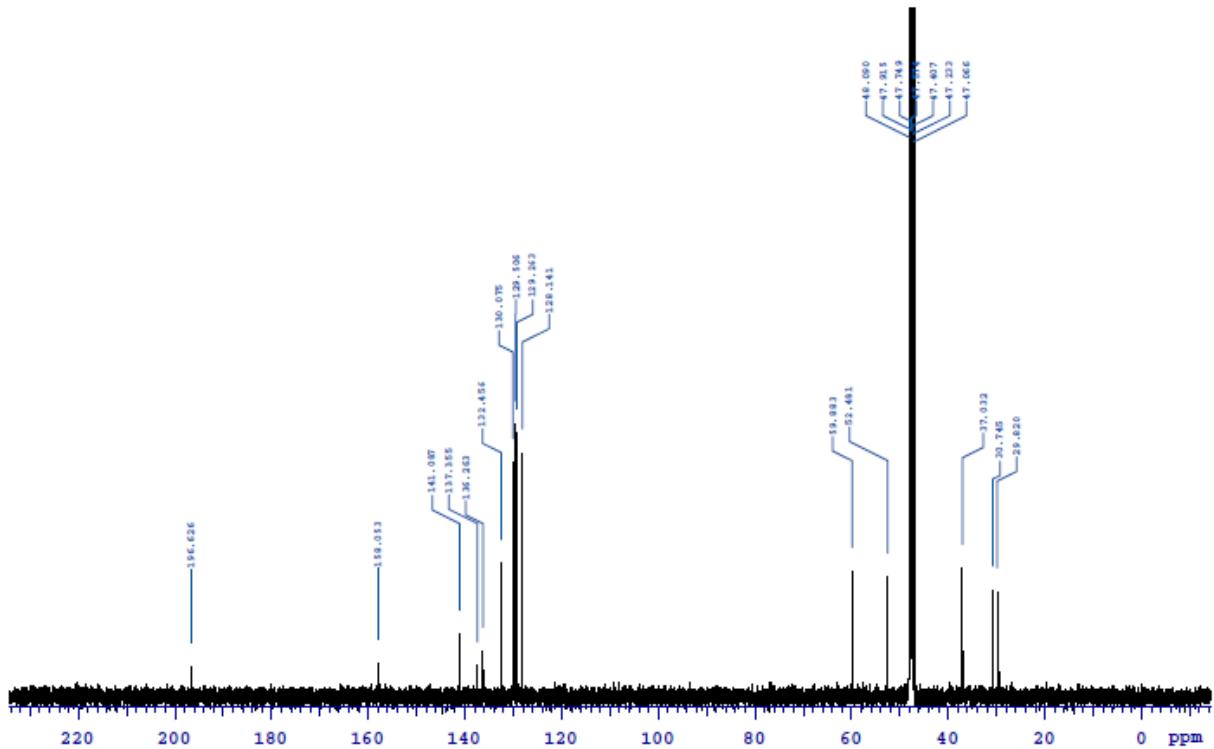
Solvent **edcl3**

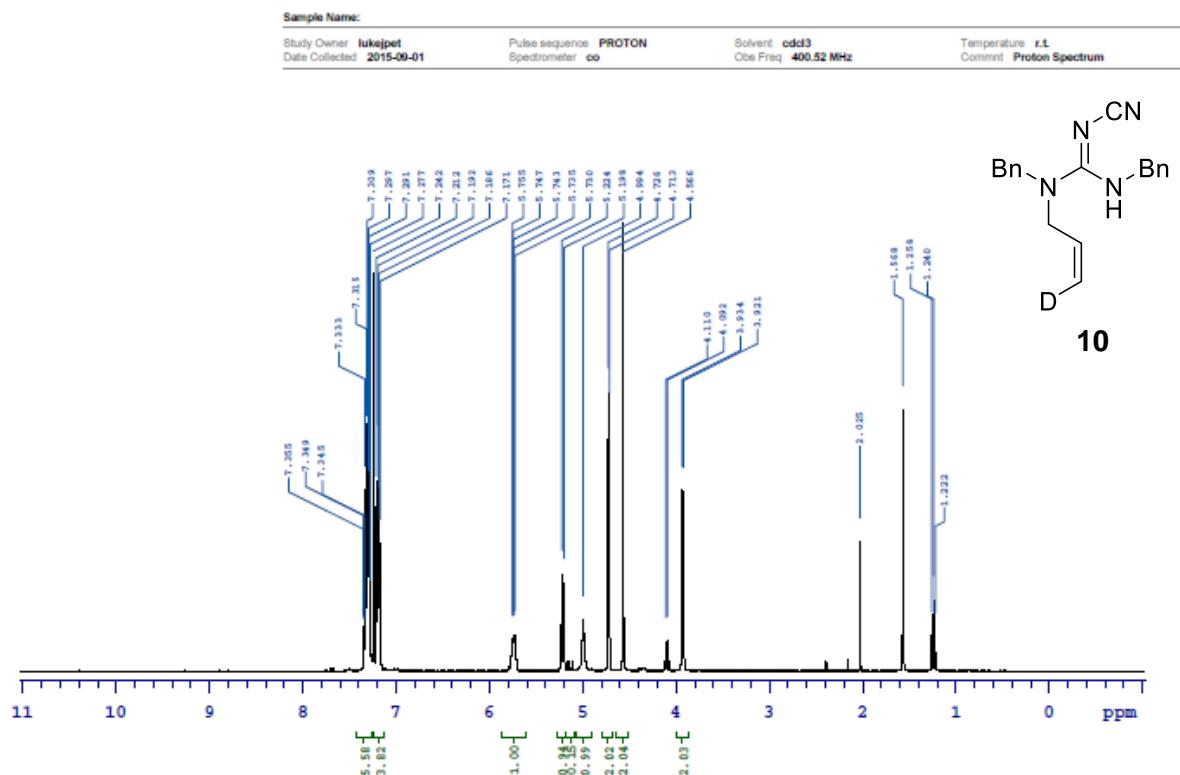
Temperature 24
Comment Proton Spectrum

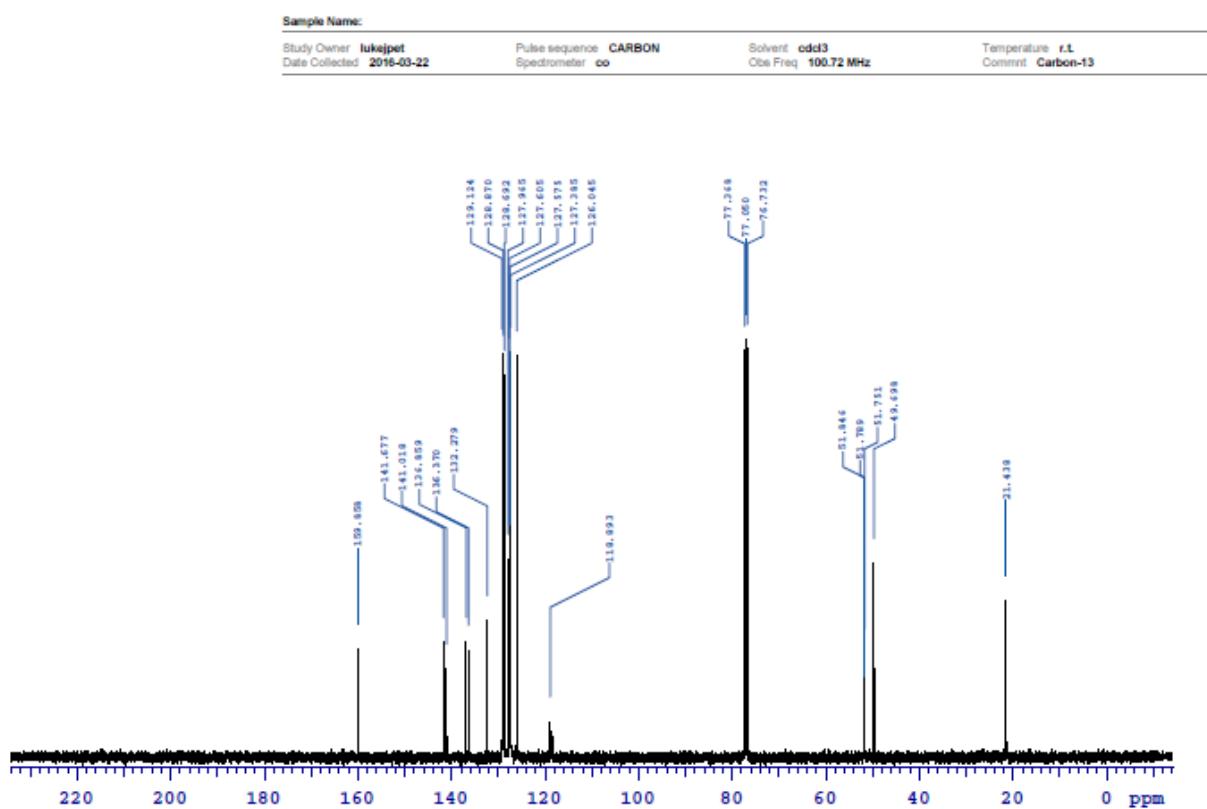
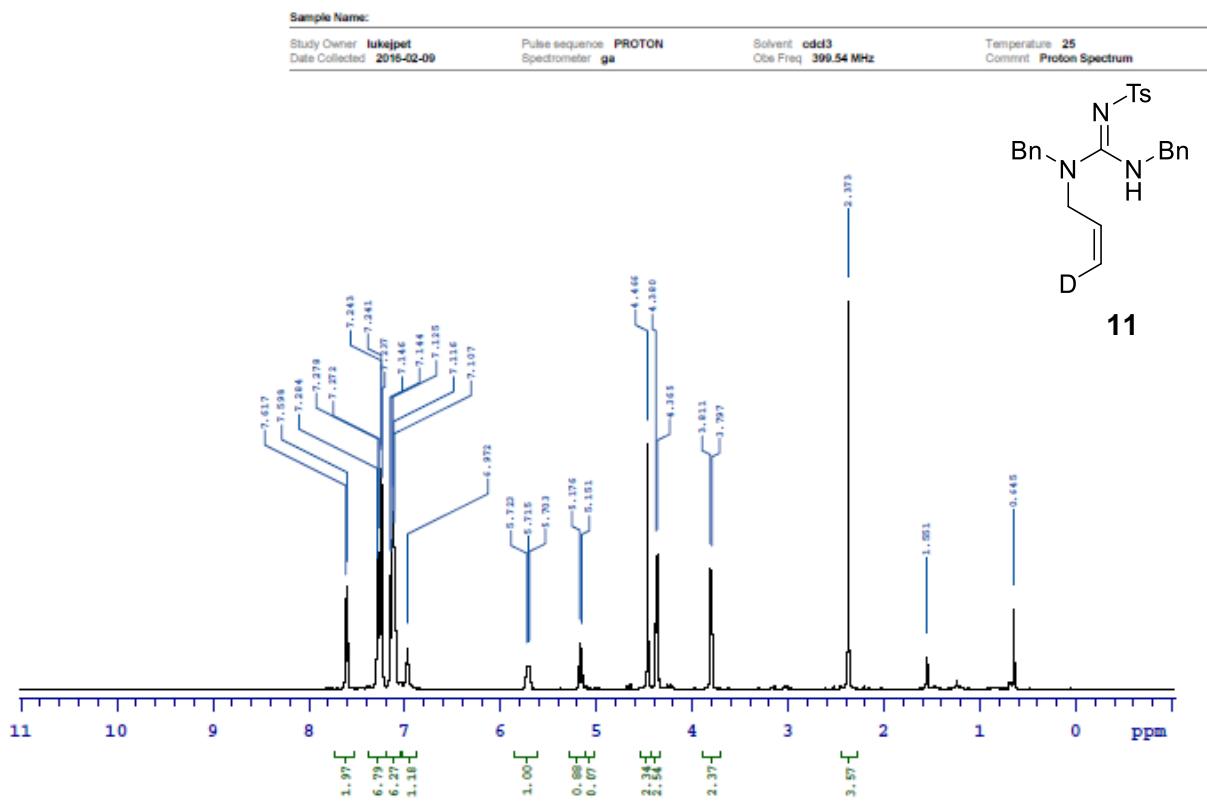


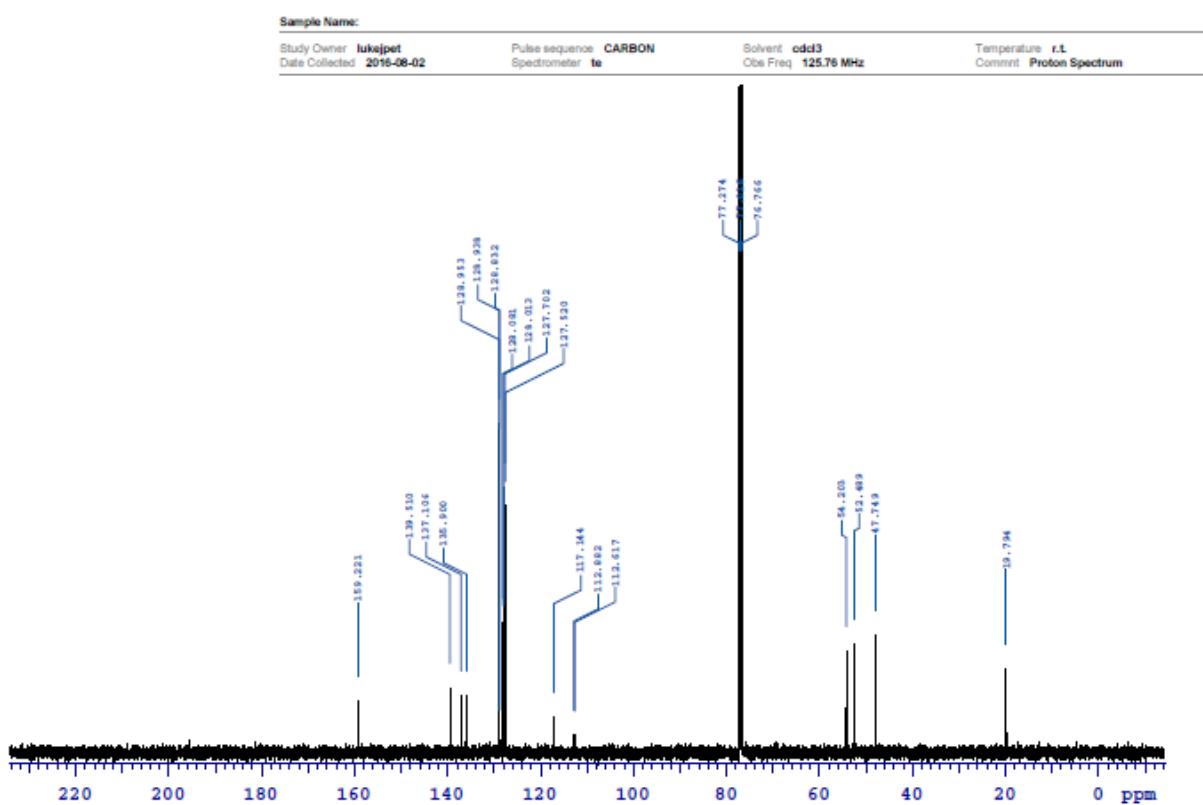
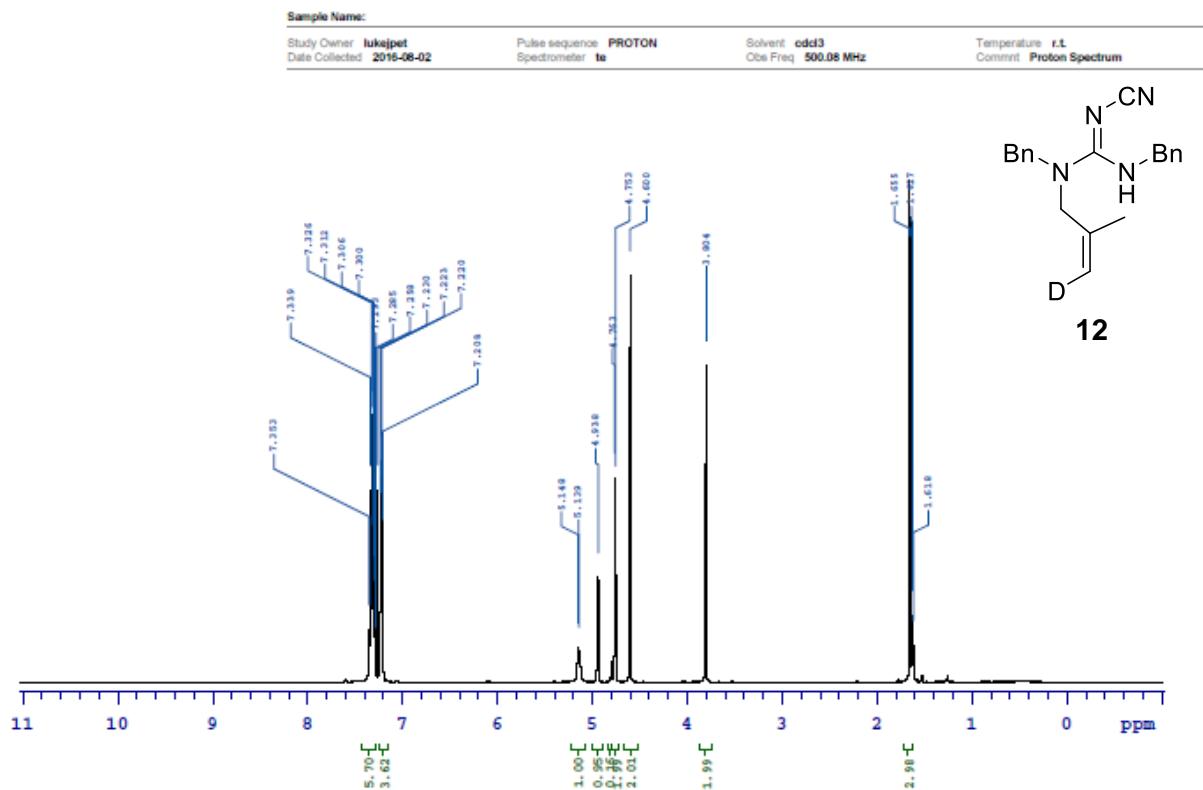


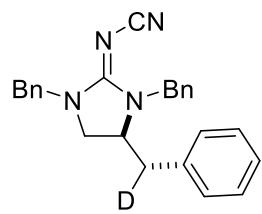
Agilent Technologies



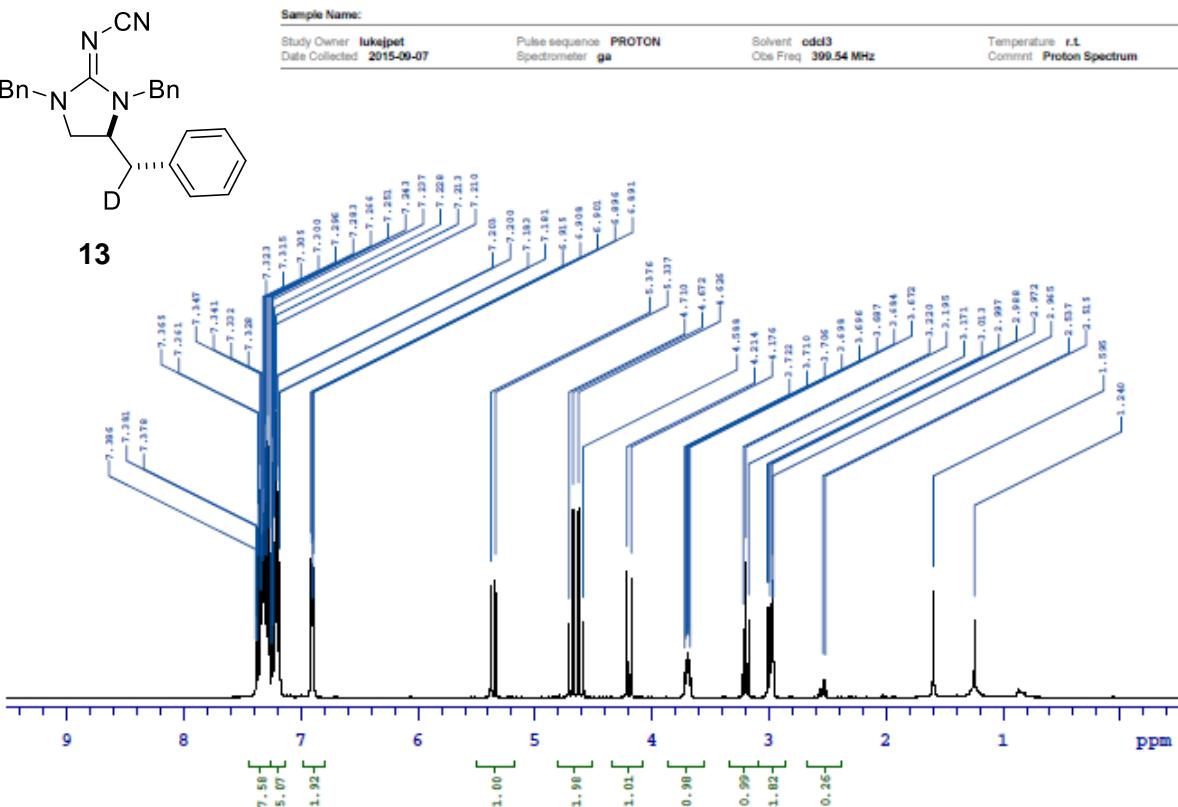








13



Sample Name:

Study Owner lukejpet
Date Collected 2015-09-07

Pulse sequence **CARBON**
Spectrometer **60**

Solvent: **c6d6**
Obs Freq: **100.72 MHz**

Temperature **11**
Commit **Carbon-13**

