Pd-Catalyzed Alkene Diamination Reactions of Nitrogen Electrophiles. Synthesis of Cyclic Guanidines and Ureas Bearing Dialkylaminomethyl Groups.

Luke J. Peterson, Janelle K. Kirsch, and John P. Wolfe*

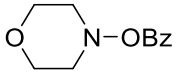
Department of Chemistry, University of Michigan, 920 N. University Avenue, Ann Arbor, Michigan 48109-1055

Supporting Information

General: All reactions were carried out under a nitrogen atmosphere in flame-dried glassware. All reagents, palladium precatalysts, and ligands were purchased from commercial sources and were used without purification unless otherwise noted. The substrates 1-allyl-1,3-dibenzyl-2-cyanoguanidine (**7a**),[1] 1,3-dibenzyl-1-(but-3-en-2-yl)-2-

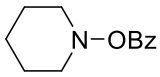
cyanoguanidine (**7c**),[1] *N*-{[allyl(benzyl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (**7b**),[1] *N*-{[benzyl(but-3-en-2-yl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (**7d**),[1] morpholino benzoate (**3a**),[2] piperidin-1-yl benzoate (**3b**),[2] and *tert*-Butyl 4-(benzoyloxy)piperazine-1-carboxylate (**3c**)[3] were prepared according to published procedures. Bulk quantities of cesium carbonate were stored in nitrogen-filled glove box and small amounts were removed within a few days of use. Toluene, THF, dichloromethane and diethyl ether were purified using a GlassContour solvent purification system. Anhydrous dioxane was purchased from Sigma-Aldrich and was used without purification. Structural and stereochemical assignments were made on the basis of 2-D COSY and NOESY experiments. Ratios of diastereomers were determined by ^{1}H NMR analysis. Yields refer to isolated yields of compounds estimated to be ≥95% pure as determined by ^{1}H NMR analysis unless otherwise noted. The yields reported in the supporting information describe the result of a single experiment, whereas yields reported in Tables 2–4 and equation 4 are average yields of two or more experiments. Thus, the yields reported in the supporting information may differ from those shown in Tables 2–4 and equation 4.

Preparation and Characterization of Benzoate Electrophiles

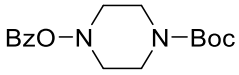


Morpholino benzoate (3a).[2] A flame dried flask was cooled under a stream of nitrogen and charged with morpholine (1.00 g, 11.48 mmol), THF (34 mL), and Na_2HPO_4 (8.149 g, 57.4 mmol). A solution of benzoyl peroxide (2.969 g, 12.26 mmol) in THF (12 mL) was then added slowly, and the reaction was heated to reflux with stirring overnight. The

mixture was then cooled to rt, filtered through celite, and then concentrated *in vacuo*. The crude product was then purified via flash column chromatography on silica gel (EtOAc:Hexanes = 15:85) to yield 1.28 g (54%) of the product as a white solid, mp 81–83 °C (lit[4] mp 82–84 °C). Characterization data for this compound matched the data given in the literature.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.6 Hz, 2 H), 7.56 (t, *J* = 7.2 Hz, 1 H), 7.43 (t, *J* = 7.6 Hz, 2 H), 3.95 (br s, 2 H), 3.89–3.82 (m, 2 H), 3.43 (d, *J* = 10 Hz, 2 H), 3.03 (br s, 2 H).



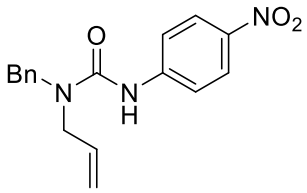
Piperidin-1-yl benzoate (3b).[2] The title compound was prepared from piperidine (1.25 g, 14.7 mmol), Na_2HPO_4 (9.39 g, 66.2 mmol), and benzoyl peroxide (3.91 g, 16.16 mmol) using a procedure analogous to that described above for the preparation of morpholino benzoate. The crude product was purified via flash column chromatography on silica gel (EtOAc:Hexanes = 15:85) to yield 2.06 g (68%) of the product as a white solid, mp 62–64 °C (lit[4] mp 55–59 °C). Characterization data for this compound matched the data given in the literature.[4] ^{1}H NMR (400 MHz, CDCl3) δ 7.99 (d, *J* = 6.8 Hz, 2 H), 7.54 (t, *J* = 7.2 Hz, 1 H), 7.43 (t, *J* = 8.0 Hz, 2 H), 3.48 (br s, 2 H), 2.78–2.70 (m, 2 H), 1.83–1.79 (m, 4 H), 1.67 (br s, 2 H).



***tert*-Butyl 4-(benzoyloxy)piperazine-1-carboxylate (3c)**.[3] The title compound was prepared from 1-Boc-piperizine (2.328 g, 12.5 mmol), Na_2HPO_4 (8.873 g, 62.5 mmol),

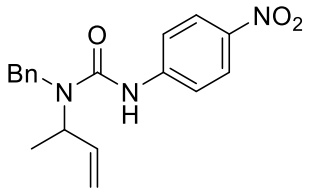
and benzoyl peroxide (3.33 g, 13.75 mmol) using a procedure analogous to that described above for the preparation of morpholino benzoate. The crude product was then purified via flash column chromatography on silica gel (EtOAc:Hexanes = 15:85) to yield 2.50 g (65%) of the product as a white solid, mp 104–106 °C (lit[5] mp 103–105 °C). Characterization data for this compound matched the data given in the literature.[3] ^{1}H NMR (400 MHz, CDCl3) δ 7.98 (d, *J* = 7.2 Hz, 2 H), 7.56 (t, *J* = 7.2 Hz, 1 H), 7.43 (d, *J* = 7.6 Hz, 1 H), 4.02 (br s, 2 H), 3.44–3.25 (m, 4 H), 2.90 (br s, 2 H), 1.40 (s, 9 H).

Preparation and Characterization of Substrates

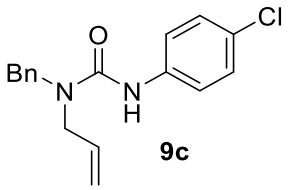


1-Allyl-1-benzyl-3-(4-nitrophenyl)urea (9a). A flame-dried flask was cooled under a stream of nitrogen and charged with *p*-nitrophenyl isocyanate (0.500 g, 3.05 mmol) and dichloromethane (3 mL). *N*-benzylprop-2-en-1-ylamine (0.450 g, 3.05 mmol) was then added, and the reaction mixture was stirred at rt overnight. The reaction mixture was then concentrated *in vacuo*, and the crude product was purified via flash column chromatography on silica gel (10% ethyl acetate in hexanes) to afford 0.845 g (90%) of the title compound as a yellow solid, m.p. 108–110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16–8.13 (m, 2 H), 7.47–7.43 (m, 2 H), 7.41–7.37 (m, 2 H), 7.35–7.31 (m, 3 H), 6.79 (br s, 1 H), 5.93–5.84 (m, 1 H), 5.38–5.34 (m, 2 H), 4.61 (s, 2 H), 4.01 (d, *J* = 5 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 145.3, 142.5, 136.8, 133.4, 129.0, 128.0, 127.5, 125.0, 118.3,

118.0, 50.8, 50.2; IR (film) 3332, 1654 cm^{-1}; MS (ESI^+) 312.1345 (312.1343 calcd for $C_{17}H_{17}N_3O_3$, M + H^+).



1-Benzyl-1-(but-3-en-2-yl)-3-(4-nitrophenyl)urea (9b). The title compound was prepared from *p*-nitrophenyl isocyanate (0.356 g, 2.17 mmol) and *N*-benzylbut-3-en-2-ylamine (0.350 g, 2.17 mmol) using a procedure analogous to that described above for the synthesis of 1-allyl-1-benzyl-3-(4-nitrophenyl)urea. This procedure afforded 0.563 g (80%) of the title compound as a yellow solid, mp 90–92 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.2 Hz, 2 H), 7.42–7.28 (m, 7 H), 6.74 (br s, 1 H), 6.03–5.95 (m, 1 H), 5.32–5.27 (m, 2 H), 4.95 (br s, 1 H), 4.56 (d, *J* = 16.8 Hz, 1 H), 4.39 (d, *J* = 17.2 Hz, 1 H), 1.35 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 145.2, 142.4, 138.7, 137.2, 127.3, 128.2, 126.8, 124.9, 118.2, 116.9, 52.8, 47.8, 16.5; IR (film) 3384, 1653; MS (ESI^+) 326.1502 (326.1499 calcd for $C_{18}H_{19}N_3O_3$, M + H^+).



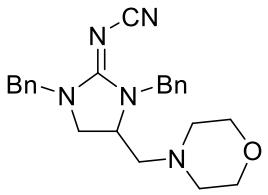
9c

1-Allyl-1-benzyl-3-(4-chlorophenyl)urea (9c). The title compound was prepared from *N*-benzylprop-2-en-1-amine (0.997 g, 6.6 mmol) and 4-chlorophenyl isocyanate (1.44 g, 9.4 mmol) using a procedure analogous to that described above for the synthesis of 1-

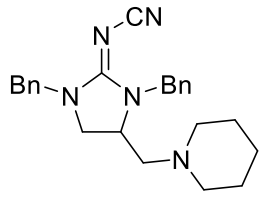
allyl-1-benzyl-3-(4-nitrophenyl)urea. This procedure afforded 1.68 g (85%) the title compound as a peach colored solid, mp 84–85 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.33 (m, 2 H), 7.37–7.27 (m, 3 H), 7.27–7.17 (m, 4 H), 6.45 (s, 1 H), 5.85 (ddt, J = 17.3, 10.5, 5.4 Hz, 1 H), 5.35–5.26 (m, 2 H), 4.58 (s, 2 H), 3.97 (dt, J = 5.6, 1.7 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5, 137.7, 137.4, 133.7, 128.9, 128.8, 127.9, 127.8, 127.5, 120.9, 117.6, 50.6, 50.0. IR (film) 3326, 1637, cm^{-1}. HRMS (ESI^{+}) 301.1114 (301.1102 calcd for $C_{17}H_{17}ClN_2O$ M + 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 $Pd(acac)_2$ (4 mol%), JackiePhos (16 mol%), the *O*-benzoylhydroxylamine derived electrophile (3 equiv), and Cs_2CO_3 (2 equiv). The tube was purged with nitrogen and then a solution of the *N*-protected guanidine or urea substrate (1 equiv) in 1,4-dioxane (0.1 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 ^{1}H NMR analysis of the reaction mixture (ca 16 h). The mixture was then cooled to rt and diluted with diethyl ether (2 mL). The resulting mixture was then filtered through cotton, and this procedure was repeated once more. The solution was then concentrated *in vacuo*, and the crude product was purified via flash column chromatography on silica gel (methanol:dichloromethane = 1:99).

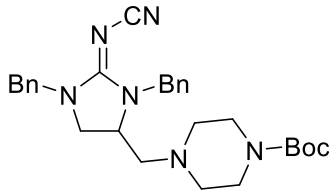


***N*-(1,3-Dibenzyl-4-(morpholinomethyl)imidazolidin-2-ylidene)cyanamide (8a)**. The general procedure was followed for the coupling of 1-allyl-1,3-dibenzyl-2-cyanoguanidine **(7a)** (30.4 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 36 mg (92%) of the title compound as a tan, viscous oil. ^{1}H NMR (500 MHz, C_6D_6) δ 7.29–6.95 (m, 10 H), 5.24 (d, *J* = 15.5 Hz, 1 H), 4.56–4.46 (m, 2 H) 4.05 (d, *J* = 15.5 Hz, 1 H), 3.33–3.24 (m, 4 H), 3.01 (m, 1 H), 2.64 (app t, *J* = 9.5 Hz, 1 H), 2.52 (dd, *J* = 9.6, 7.1 Hz, 1 H), 1.87 (dd, *J* = 12.8, 5.6 Hz, 1 H), 1.77–1.66 (m, 4 H), 1.53 (dd, *J* = 12.8. 6.9 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 135.9, 135.4, 128.9, 128.8, 128.2, 128.1, 128.0, 127.9, 116.5, 66.7, 61.0, 54.1, 51.9, 49.5, 49.3, 47.8; IR (film) 2919, 2171, 1596 cm^{-1}; MS (ESI^{+}) 390.2292 (390.2288 calcd for $C_{23}H_{27}N_5O$, M + H^{+}).

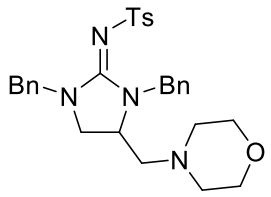


***N*-(1,3-Dibenzyl-4-(piperidin-1-ylmethyl)imidazolidin-2-ylidene)cyanamide (8b)**. The general procedure was followed for the coupling of 1-allyl-1,3-dibenzyl-2-cyanoguanidine **(7a)** (30.4 mg, 0.1 mmol) with piperidin-1-yl benzoate **(3b)** (61.5 mg, 0.3 mmol). This procedure afforded 36 mg (93%) of the title compound as a tan, viscous oil. ^{1}H NMR (500 MHz, C_6D_6) δ 7.26 (d, *J* = 7.5 Hz, 2 H), 7.17–7.03 (m, 8 H), 5.31 (d, *J* = 16 Hz, 1 H), 4.51 (s, 2 H), 4.12 (d, *J* = 15.4 Hz, 1 H), 3.10 (dt, *J* = 13.1, 6.6 Hz, 1 H), 2.66 (t, *J* = 9.5 Hz, 1

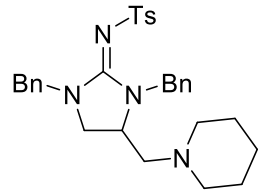
H), 2.57 (dd, *J* = 9.6, 7.1 Hz, 1 H), 1.97 (dd, *J* = 12.7, 5.6 Hz, 1 H), 1.83 (br s, 4 H), 1.61 (dd, *J* = 12.8, 7.1 Hz, 1 H), 1.24 (h, *J* = 5.6 Hz, 4 H), 1.15 (q, *J* = 5.8 Hz, 2 H). ^{13}C NMR (100 MHz, C_6D_6) δ 158.3, 136.8, 136.0, 128.6, 128.5, 128.4, 128.3, 115.9, 61.2, 54.8, 51.9, 49.1, 47.4, 25.8, 24.0; IR (film) 2933, 2171, 1595 cm^{-1}; MS (ESI$^+$) 388.2496 (388.496 calcd for $C_{24}H_{29}N_5$, M + H$^+$).



***tert*-Butyl 4-{[1,3-dibenzyl-2-(cyanoimino)imidazolidin-4-yl]methyl}piperazine-1-carboxylate (8c)**. The general procedure was followed for the coupling of 1-allyl-1,3-dibenzyl-2-cyanoguanidine **(7a)** (30.4 mg, 0.1 mmol) with *tert*-butyl 4-(benzoyloxy)piperazine-1-carboxylate **(3c)** (91.9 mg, 0.3 mmol). This procedure afforded 30 mg (61%) of the title compound as a pale yellow, viscous oil. One peak in the ^{13}C NMR spectrum is missing due to incidental equivalence. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.11 (m, 10 H), 5.28 (d, *J* = 15.6 Hz, 1 H), 4.83–4.61 (m, 2 H), 4.33 (d, *J* = 15.6 Hz, 1 H), 3.58 (dt, *J* = 12.4, 6.3 Hz, 1 H), 3.38 (t, *J* = 9.7 Hz, 1 H), 3.28 (br s, 4 H), 3.09 (dd, *J* = 9.8, 6.5 Hz, 1 H), 2.49 (dd, *J* = 12.9, 5.6 Hz, 1 H), 2.29–2.13 (m, 5 H), 1.42 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.3, 154.5, 135.8, 135., 128.8, 128.2, 128.0, 127.9, 127.8, 116.4, 79.7, 60.6, 53.4, 51.9, 49.4, 49.2, 47.7, 43.2, 28.3; IR (film) 2927, 2170, 1685, 1595 cm^{-1}; MS (ESI$^+$) 489.2970 (489.2973 calcd for $C_{28}H_{36}N_6O_2$, M + H$^+$).

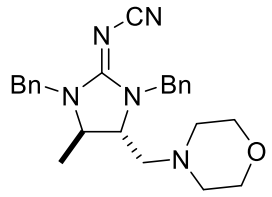


***N*-[1,3-Dibenzyl-4-(morpholinomethyl)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (8d)**. The general procedure was followed for the coupling of *N*-{[allyl(benzyl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (**7b**) (43.3 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 42.5 mg (82%) of the title compound as a tan, viscous oil. ^{1}H NMR (500 MHz, C_6D_6) δ 8.27 (d, *J* = 8.1 Hz, 2 H), 7.29 (d, *J* = 7 Hz, 4 H), 7.19–7.09 (m, 4 H), 7.05 (td, *J* = 7.3, 4.8 Hz, 2 H), 6.82 (d, *J* = 7.9 Hz, 2 H), 5.48 (d, *J* = 15.3 Hz, 1 H), 4.84 (d, *J* = 15.0 Hz, 1 H), 4.68 (d, *J* = 15.0 Hz, 1 H), 4.15 (d, *J* = 15.3 Hz, 1 H), 3.37–3.30 (m, 4 H), 3.14–3.07 (m, 1 H), 2.76 (t, *J* = 9.7 Hz, 1 H), 2.67 (dd, *J* = 9.8, 6.4 Hz, 1 H), 1.91 (dd, *J* = 12.5, 5 Hz, 1 H), 1.89 (s, 3 H), 1.86–1.83 (m, 2 H), 1.79–1.74 (m, 2 H), 1.67 (dd, *J* = 12.8, 6.9 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 142.9, 141.1, 136.2, 135.8, 129.0, 128.8, 128.7, 128.4, 128.1, 127.9, 127.8, 125.8, 66.7, 60.7, 54.1, 51.7, 50.8, 49.1, 48.7, 21.3; iR (film) 2921, 1559 cm^{-1}; MS (ESI^{+}) 519.2422 (519.2424 calcd for $C_{29}H_{34}N_4O_3S$, M + H^{+}).



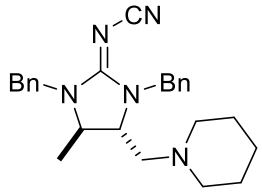
***N*-[1,3-Dibenzyl-4-(piperidin-1-ylmethyl)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (8e)**. The general procedure was followed for the coupling of *N*-{[allyl(benzyl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide (**7b**)

(43.3 mg, 0.1 mmol) with piperidin-1-yl benzoate **(3b)** (61.5 mg, 0.3 mmol). This procedure afforded 39 mg (76%) of the title compound as a tan, viscous oil. One signal in the ^{13}C NMR spectrum is missing due to incidental equivalence. ^{1}H NMR (400 MHz, C_6D_6) δ 8.26 (d, *J* = 8.0 Hz, 2 H), 7.34–7.27 (m, 4 H), 7.14–6.96 (m, 6 H), 6.81 (d, *J* = 8.0 Hz, 2 H), 5.46 (d, *J* = 15.2 Hz, 1 H), 4.82 (d, *J* = 15.0 Hz, 1 H), 4.70 (d, *J* = 15.0 Hz, 1 H), 4.22 (d, *J* = 15.3 Hz, 1 H), 3.22–3.14 (m, 1 H), 2.79 (t, *J* = 9.7 Hz, 1 H), 2.70 (dd, *J* = 9.8, 6.3 Hz, 1 H), 2.04 (dd, *J* = 12.8, 5.5 Hz, 1 H), 1.89 (s, 3 H), 1.88–1.83 (m, 4 H), 1.73 (dd, *J* = 12.8, 7.1 Hz, 1 H), 1.23 (br s, 4 H), 1.17–1.12 (m, 2 H); ^{13}C NMR (100 MHz, C_6D_6) δ 156.2, 144.3, 140.4, 137.1, 136.4, 128.8, 128.6, 128.5, 128.45, 128.41, 127.4 126.2, 61.1, 54.8, 51.7, 50.8, 48.8, 48.7, 25.8, 24.0, 20.7; IR (film) 2932, 1578 cm^{-1}; MS (ESI^+) 517.2633 (517.2632 calcd for $C_{30}H_{36}N_4O_2S$, M + H^+).



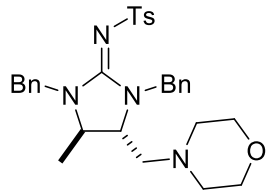
(4*R,5*R**)-*N*-[1,3-Dibenzyl-4-methyl-5-(morpholinomethyl)imidazolidin-2-ylidene]cyanamide (8f)**. The general procedure was followed for the coupling of 1,3-dibenzyl-1-(but-3-en-2-yl)-2-cyanoguanidine **(7c)** (31.8 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.1 mg, 0.3 mmol). This procedure afforded 32.3 mg (80%) of the title compound as a tan, viscous oil. This compound was obtained as a 4:1 mixture of diastereomers as judged by ^{1}H NMR analysis of the crude reaction mixture. After purification the compound was isolated as a 3:1 mixture of diastereomers. ^{1}H NMR data are for the major diastereomer, ^{13}C NMR data are for the mixture. ^{1}H NMR (400 MHz,

C_6D_6) δ 7.22–7.17 (m, 5 H), 7.15–7.02 (m, 5 H), 5.42 (d, *J* = 15.5 Hz, 1 H), 5.35 (d, *J* = 15.5 Hz, 1 H), 4.07 (d, *J* = 16 Hz, 1 H), 3.85 (d, *J* = 16 Hz, 1 H), 3.33–3.27 (m, 4 H), 2.92 (p, *J* = 6.5 Hz, 1 H), 2.72 (q, *J* = 6.0 Hz, 1 H), 1.84 (dd, *J* = 13.0 Hz, 6.0 Hz, 1 H), 1.80–1.72 (m, 4 H), 1.50 (dd, *J* = 13.0, 6.5 Hz, 1 H), 0.57 (d, *J* = 5.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0, 136.0, 135.8, 128.9, 128.8, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 116.7, 66.8, 66.7, 60.7, 59.2, 56.7, 55.1, 54.3, 54.1, 54.0, 53.9, 47.8, 47.7, 56.8, 56.2, 18.6, 12.0; IR (film) 2925, 2170, 1591 cm^{-1}; MS (ESI$^+$) 404.2446 (404.2445 cacld for $C_{24}H_{29}N_5O$, M + H$^+$).

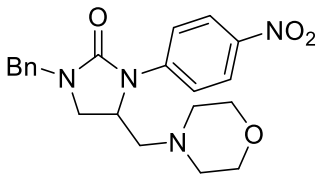


(4*R,5*R**)-*N*-[1,3-Dibenzyl-4-methyl-5-(piperidin-1-ylmethyl)imidazolidin-2-ylidene]cyanamide (8g)**. The general procedure was followed for the coupling of 1,3-dibenzyl-1-(but-3-en-2-yl)-2-cyanoguanidine **(7c)** (31.8 mg, 0.1 mmol) with piperidin-1-yl benzoate **(3b)** (61.5 mg, 0.3 mmol). This procedure afforded 31 mg (76%) of the title compound as a tan, viscous oil. This compound was obtained as a 3:1 mixture of diastereomers as judged by ^{1}H NMR analysis; ^{1}H NMR data are for the major diastereomer, ^{13}C NMR data are for the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 6.8 Hz, 2 H), 7.15–7.00 (m, 8 H), 5.45 (d, *J* = 15.6 Hz, 1 H), 5.30 (d, *J* = 15.6 Hz, 1 H), 4.11 (d, *J* = 15.2 Hz, 1 H), 3.83 (d, *J* = 15.6 Hz, 1 H), 2.96–2.90 (m, 1 H), 2.79 (q, *J* = 6.0 Hz, 1 H), 1.91 (dd, *J* = 13.4, 4.8 Hz, 1 H), 1.83 (br s, 4 H), 1.55 (dd, *J* = 12.4 Hz, 6.4 Hz, 1 H), 1.20 (br s, 4 H), 1.18–1.12 (m, 2 H), 0.57 (d, *J* = 6 Hz, 3 H); ^{13}C NMR (125 MHz,

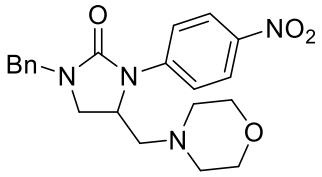
C_6D_6) δ 158.1, 137.1 136.7, 136.5, 136.4, 128.6, 128.56, 128.51, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 116.0, 60.9, 59.3, 56.4, 55.3, 54.8, 54.6, 54.5, 53.6, 47.4, 47.2, 46.5, 45.9, 25.8, 25.7, 24.1, 24.0, 17.8, 11.3; IR (film) 2933, 2173, 1585 cm^{-1}; MS (ESI^+) 402.2650 (402.2652 calcd for $C_{25}H_{31}N_5$, M + H^+)



(4*R*,5*R*)-*N*-[1,3-Dibenzyl-4-methyl-5-(morpholinomethyl)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (8h). The general procedure was followed for the coupling of *N*-{[benzyl(but-3-en-2-yl)amino](benzylamino)methylene}-4-methylbenzenesulfonamide **(7d)** (44.8 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 46 mg (86%) of the title compound as a tan, viscous oil. This compound was obtained as a 3:1 mixture of diastereomers as judged by ^1H NMR analysis; data are for the major diastereomer. Two peaks in the ^{13}C NMR spectrum are missing due to incidental equivalence. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2 H), 7.32–7.11 (m, 12 H), 5.34–5.22 (m, 2 H), 4.23 (d, *J* = 15.2 Hz, 1 H), 4.07 (d, *J* = 15.2 Hz, 1 H), 3.55–3.50 (m, 4 H), 3.31–3.27 (m, 1 H), 3.00 (q, *J* = 4.8 Hz, 1 H), 2.37–2.32 (m, 1 H), 2.23–2.13 (m, 4 H), 2.04 (dd, *J* = 12.8, 7.6 Hz, 1 H), 0.98 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 155.6, 144.2, 140.5, 136.9, 136.7, 128.8, 128.5, 128.48, 128.45, 128.3, 126.2, 66.4, 60.0, 58.8, 54.2, 54.0, 49.1, 48.0, 20.7, 18.2; IR (film) 2925, 1559 cm^{-1}; MS (ESI^+) 533.2580 (533.2581 calcd for $C_{30}H_{36}N_4O_3S$, M + H^+).

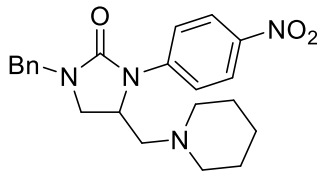


1-Benzyl-4-(morpholinomethyl)-3-(4-nitrophenyl)imidazolidin-2-one (10a). The general procedure was followed for the coupling of 1-allyl-1-benzyl-3-(4-nitrophenyl)urea (**9a**) (31.1 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 46 mg (86%) of the title compound as a yellow solid, mp 108-110 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 8.04 (d, *J* = 9.3 Hz, 2 H), 7.59 (d, *J* = 9.3 Hz, 2 H), 7.15–7.02 (m, 5 H), 4.30–4.19 m, 2 H), 3.44–3.34 (m, 4 H), 2.85 (dd, *J* = 8.9, 2.8 Hz, 1 H), 2.75 (t, *J* = 8.7 Hz, 1 H), 1.98 (dd, *J* = 13.0, 3.1 Hz, 1 H), 1.97–1.88 (m, 2 H), 1.83–1.75 (m, 2 H), 1.71 (dd, *J* = 13.0, 9.3 Hz, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 155.8, 145.0, 142.0, 136.6, 128.6, 128.2, 127.9, 124.6, 116.8, 66.4, 58.7, 53.8, 50.0, 47.5, 45.3; IR (film) 2921, 1709 cm^{-1}; MS (ESI^{+}) 397.1868 (397.1870 calcd for $C_{21}H_{24}N_4O_4$, M + H^{+}).

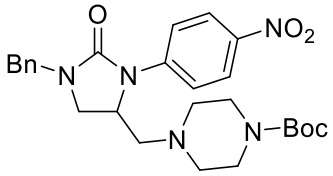


1-Benzyl-4-(morpholinomethyl)-3-(4-nitrophenyl)imidazolidin-2-one (10a).

The general procedure was followed for the coupling of 1-allyl-1-benzyl-3-(4-nitrophenyl)urea (**9a**) (0.3113 g, 1 mmol) with morpholino benzoate **(3a)** (0.6216 g, 3 mmol). This procedure afforded 0.3022 g (76%) of the title compound as a yellow solid. Spectroscopic data matched those reported above.

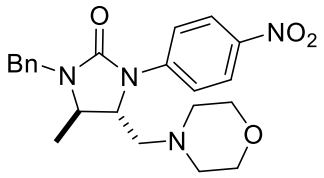


1-Benzyl-3-(4-nitrophenyl)-4-(piperidin-1-ylmethyl)imidazolidin-2-one (10b). The general procedure was followed for the coupling of 1-allyl-1-benzyl-3-(4-nitrophenyl)urea (**9a**) (31.1 mg, 0.1 mmol) with piperidin-1-yl benzoate (**3b**) (61.5 mg, 0.3 mmol). This procedure afforded 32.2 mg (82%) of the title compound as a yellow solid, mp 92-95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 9.3 Hz, 2 H), 7.75 (d, *J* = 9.3 Hz, 2 H), 7.41–7.26 (m, 5 H), 4.50–4.45 (m, 2 H), 4.30 (t, *J* = 8.8 Hz, 1 H), 3.46 (t, *J* = 8.8 Hz, 1 H), 3.33 (dd, *J* = 9.2, 2.8 Hz, 1 H), 2.54 (dd, *J* = 13.0, 3.2 Hz, 1 H), 2.43 (br s, 2 H), 2.37–2.20 (m, 3 H), 1.52–1.45 (m, 4 H), 1.40–1.35 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 145.5, 141.8, 136.2, 128.8, 128.2, 127.7, 124.9, 117.1, 59.8, 55.3, 51.4, 47.8, 46.2, 25.9, 23.9; IR (film) 2932, 1710 cm^{-1}; MS (ESI$^+$) 395.2074 (395.2078 calcd for $C_{22}H_{26}N_4O_3$, M + H$^+$).

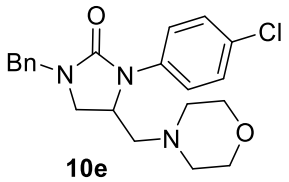


***tert*-Butyl 4-{[1-benzyl-3-(4-nitrophenyl)-2-oxoimidazolidin-4-yl]methyl}piperazine-1-carboxylate (10c)**. The general procedure was followed for the coupling of 1-allyl-1-benzyl-3-(4-nitrophenyl)urea (**9a**) (31.1 mg, 0.1 mmol) with *tert*-butyl 4-(benzoyloxy)piperazine-1-carboxylate **(3c)** (91.9 mg, 0.3 mmol). This procedure afforded 21 mg (42%) of the title compound as a yellow solid, mp 98-102 °C. ^{1}H NMR (500 MHz, C_6D_6) δ 8.04 (d, *J* = 9.1 Hz, 2 H), 7.57 (d, *J* = 9.0 Hz, 2 H), 7.14–7.03 (m, 5 H), 4.28–4.18

(m, 2 H), 3.41–3.35 (m, 1 H), 3.22 (br s, 4 H), 2.79 (dd, *J* = 8.9, 2.7 Hz, 1 H), 2.71 (t, *J* = 8.7 Hz, 1 H), 1.91–1.83 (m, 3 H), 1.81–1.72 (m, 2 H), 1.67 (dd, *J* = 13.1, 9.2 Hz, 1 H), 1.46 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6) δ 155.8, 154.0, 145.0, 142.0, 136.6, 128.6, 128.2, 127.9, 124.6, 116.7, 79.1, 58.2, 53.1, 50.2, 47.5, 45.2, 28.1, 28.0; IR (film) 2927, 1693 cm^{-1}; MS (ESI$^+$) 496.2548 (496.2554 calcd for $C_{26}H_{33}N_5O_5$, M + H$^+$).

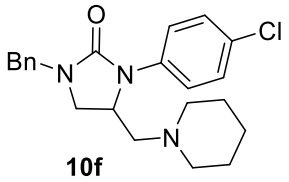


(4*R,5*R**)-1-Benzyl-5-methyl-4-(morpholinomethyl)-3-(4-nitrophenyl)imidazolidin-2-one (10d)**. The general procedure was followed for the coupling of 1-benzyl-1-(but-3-en-2-yl)-3-(4-nitrophenyl)urea (**9b**) (32.5 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 13 mg (34%) of the title compound as a viscous yellow oil. This compound was obtained as a 2:1 mixture of diastereomers as judged by ^{1}H NMR analysis; ^{1}H NMR data are for the major diastereomer; ^{13}C NMR data are for the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21–8.18 (m, 2 H), 7.75–7.68 (m, 2 H), 7.37–7.24 (m, 5 H), 4.93 (d, *J* = 15.2 Hz, 1 H), 4.06 (d, *J* = 15.2 Hz, 1 H), 3.89–3.86 (m, 1 H), 3.57–3.51 (m, 5 H), 2.55–2.36 (m, 4 H), 2.29–2.23 (m, 2 H), 1.25 (d, *J* = 6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 155.6, 145.5, 145.3, 142.3, 141.9, 136.7, 136.4, 128.8, 128.7, 128.2, 128.1, 127.8, 127.7, 125.0, 124.7, 118.9, 117.3, 66.9, 66.7, 58.8, 58.7, 55.5, 54.2, 54.0, 53.7, 51.9, 51.1, 45.1, 45.0, 18.9, 13.0; IR (film) 2923, 1708 cm^{-1} ; MS (ESI$^+$) 411.2027 (411.2027 calcd for $C_{22}H_{26}N_4O_4$, M + H$^+$).



10e

1-Benzyl-3-(4-chlorophenyl)-4-(morpholinomethyl)imidazolidin-2-one (10e). The general procedure was followed for the coupling of 1-allyl-1-benzyl-3-(4-chlorophenyl)urea (**9c**) (30.1 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 17.5 mg (45%) of the title compound as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.8 Hz, 2 H), 7.38–7.27 (m, 7 H), 4.46 (s, 2 H), 4.27 (tt, *J* = 8.6, 3.8 Hz, 1 H), 3.66–3.54 (m, 4 H), 3.45 (t, *J* = 8.9 Hz, 1 H), 3.29 (dd, *J* = 9.0, 4.1 Hz, 1 H), 2.55 (dd, *J* = 12.9, 3.3 Hz, 1 H), 2.50–2.23 (m, 5 H);^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 137.7, 136.7, 128.9, 128.7, 128.3, 128.2, 127.6, 121.1, 66.8, 59.6, 54.2, 51.1, 47.9, 46.4; IR (film) 2917, 1700 cm^{-1}; MS (ESI^{+}) 386.1634 (386.1635 calcd for $C_{21}H_{24}ClN_3O_2$, M + H^{+}).



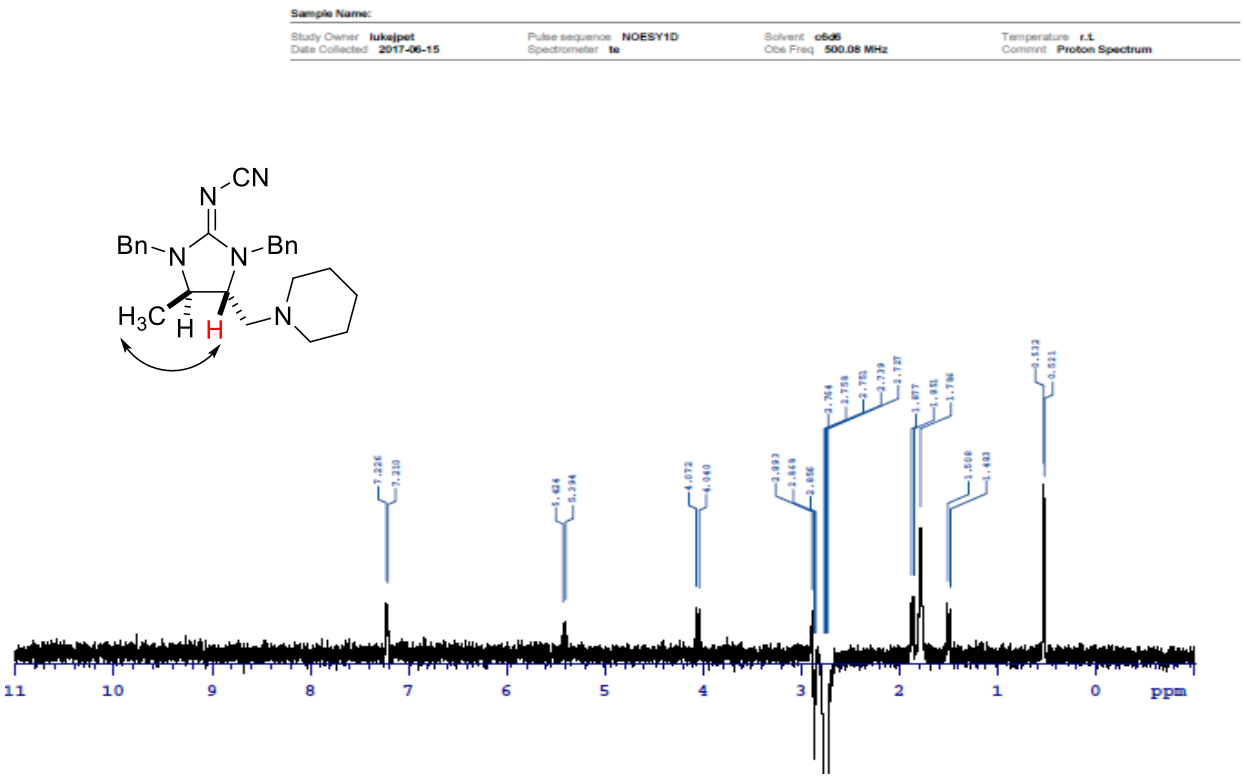
10f

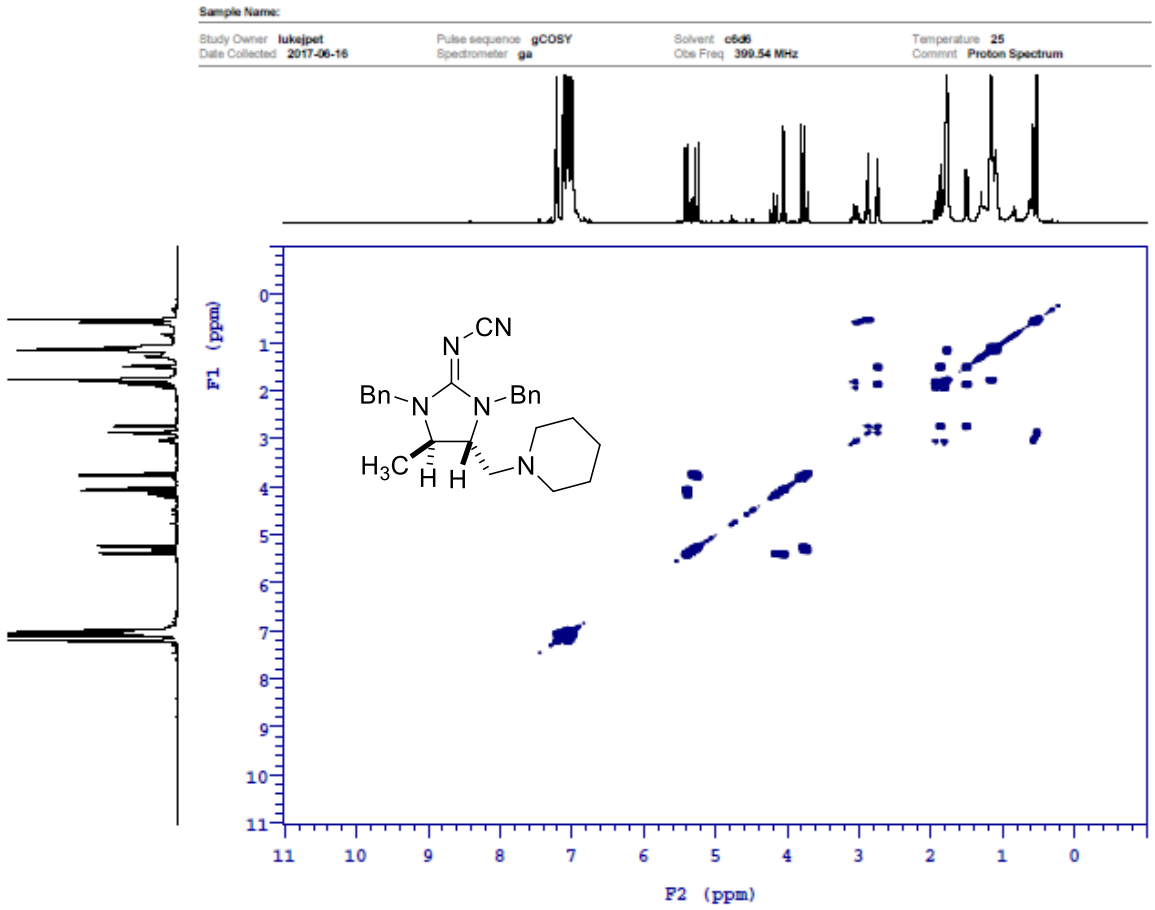
1-Benzyl-3-(4-chlorophenyl)-4-(piperidin-1-ylmethyl)imidazolidin-2-one (10f). The general procedure was followed for the coupling of 1-allyl-1-benzyl-3-(4-chlorophenyl)urea (**9c**) (30.1 mg, 0.1 mmol) with piperidin-1-yl benzoate **(3b)** (61.5 mg, 0.3 mmol). This procedure afforded 7.0 mg (18%) of the title compound as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.6 Hz, 2 H), 7.38–7.27 (m, 7 H), 4.55–4.37 (m, 2 H), 4.24 (td, *J* = 8.9, 4.5 Hz, 1 H), 3.44 (t, *J* = 8.8 Hz, 1 H), 3.28 (dd, *J* = 9.1, 4.0 Hz, 1 H),

2.51 (dd, *J* = 12.9, 3.1 Hz, 1 H), 2.42 (br m, 2 H), 2.35–2.20 (m, 3 H), 1.55–1.43 (m, 4 H), 1.37 (p, *J* = 6.2 Hz, 2 H);^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 138.0, 137.0, 129.0, 128.8, 128.4, 128.2, 127.7, 121.1, 60.3, 55.5, 51.6, 48.0, 46.9, 26.1, 24.2; IR (film) 2934, 1703 cm^{-1}; MS (ESI$^+$) 384.1847 (384.1837 calcd for $C_{22}H_{26}ClN_3O$, M + H$^+$).

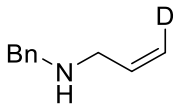
Assignment of relative stereochemistry for 8f-h and 10d.

The relative stereochemistry of **8g** was assigned using 2D COSY and 1D NOESY analysis, based on the low energy conformations described above. The key NMR signals are shown below. Structurally related products **8f**, **8h**, and **10d** were assigned based on analogy to **8g**



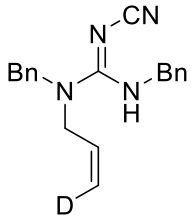


Synthesis of deuterated substrates and products



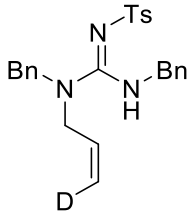
(Z)-*N*-Benzylprop-2-en-3-d-1-amine (S1). A flame dried flask was cooled under a stream of nitrogen and charged with *N*-benzylprop-2-en-1-ylamine (1.00 g, 6.84 mmol) and diethyl ether (12 mL). The solution was cooled to -42 °C, and then *n*-butyllithium (8.2 mmol, 2.5 M in hexanes) was added slowly. After 30 min *tert*-butyl lithium (15 mmol, 1.7 M in pentane) was added slowly. After stirring at -42 °C for 30 min 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 using 30% ethyl acetate in hexanes as the eluant to afford 0.568 g (56%) of the title compound as a pale yellow oil, with 84% deuterium incorporation as determined by ^{1}H NMR analysis. ^{1}H 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).

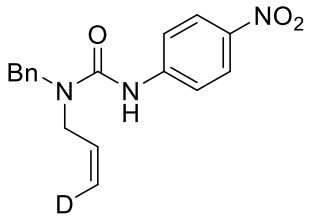


(*Z*)-1-[Allyl-3-*d*]-1,3-dibenzyl-2-cyanoguanidine (*d*-7a).[1] A round bottom flask was charged with methyl *N*-benzyl-*N*'-cyanocarbamimidothioate[1] (0.196 g, 0.96 mmol), ethanol (10 mL), and mercuric oxide (0.312 g, 1.44 mmol), then purged with nitrogen. Triethylamine (0.5 mL, 3.84 mmol) was added followed by (*Z*)-*N*-benzylprop-2-en-3-d-1-amine **(S1)** (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 (methanol:dichloromethane = 1:99) to yield 0.153 g (52%) of the title compound as a clear, viscous oil. ^{1}H 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,

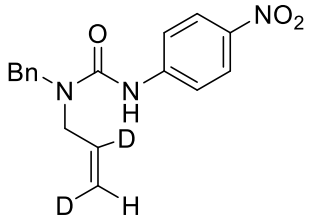
127.3, 118.2 (t, J = 23.5 Hz, 117.2, 52.2, 51.4, 47.5; IR (film) 3249, 2162, 1536 cm^{-1}; MS (ESI^+) 306.1827 (306.1823 calcd for $C_{19}H_{19}DN_4$, M + H^+).



(*Z*)-*N*-{[Allyl-3-d](benzyl)amino}-benzylaminomethylene-4-methylbenzenesulfonamide (*d*-7b).[1] A round bottom flask was charged with dimethyl tosylcarbonimidodithioate[1] (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 **(S1)** (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 (methanol:dichloromethane = 1:99) 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 s, 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 $C_{25}H_{26}DN_3O_2S$, M + H^+).



(*Z*)-1-(Allyl-3-d)-1-benzyl-3-(4-nitrophenyl)urea (*d*-9a). The title compound was prepared from *p*-nitrophenyl isocyanate (0.244 g, 1.48 mmol) and (*Z*)-*N*-benzylprop-2-en-3-d-1-amine (**S1**) (0.220 mg, 1.48 mmol) using a procedure analogous to that described above for the synthesis of 1-allyl-1-benzyl-3-(4-nitrophenyl)urea. This procedure afforded 0.245 g (53%) of the title compound as a yellow solid, mp 108–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 9.2 Hz, 2 H), 7.12–7.04 (m, 7 H), 6.17 (s, 1 H), 5.37–5.30 (m, 1 H), 4.83–4.76 (m, 2 H), 4.17 (s, 2 H), 3.34 (d, J = 4.8 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8, 145.3, 142.5, 136.9, 133.3, 129.1, 128.0, 127.5, 125.0, 118.3, 117.8 (t, J = 23.6 Hz), 50.9, 50.2; IR (film) 3346, 1652 cm^{-1}; MS (ESI^{+}) 313.1405 (313.1405 calcd for $C_{17}H_{16}N_3O_3$, M + H^{+}).



(*Z*)-1-(Allyl-2,3-d_2)-1-benzyl-3-(4-nitrophenyl)urea (15). A round-bottom flask equipped with a stirbar was charged with benzylamine (11.8 mL, 108 mmol) and cooled to 0 ºC. Propargyl bromide (2 mL, 18 mmol, 80 wt% in toluene) was added dropwise and the mixture was warmed to rt and stirred overnight. The mixture was then concentrated *in* vacuo and the crude product was purified via flash column chromatography on silica gel (10% ethyl acetate in hexanes) to afford 2.11 g (81%) of N-benzylprop-2-yn-1-amine as

a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.30 (m, 3 H), 7.28–7.26 (m, 2 H), 3.89 (s, 2 H), 3.44 (d, *J* = 2.4 Hz, 2 H), 2.26 (t, *J* = 2.4 Hz, 1 H), 1.50 (s, 1 H).

A round-bottom flask equipped with a stirbar was charged with di-*tert*-butyl dicarbonate (0.5786 g, 2.65 mmol) and THF (0.5 mL). The mixture was cooled to 0 °C and a solution of *N*-benzylprop-2-yn-1-amine (0.35 g, 2.41 mmol) in THF (0.7 mL) was added dropwise. The mixture was warmed to rt and stirred overnight, then THF (5 mL) and 1 M NaOH (5 mL) were added and the resulting mixture was stirred vigorously at rt for 24 h. The mixture was then diluted with ether and transferred to a separatory funnel. The layers were separated, the aqueous layer was extracted with ether (3 x 10 mL) and the combined organic layers were washed with saturated aqueous ammonium chloride (1 x 25 mL) and brine (1 x 25 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated *in vacuo* to afford *tert*-butyl benzyl(prop-2-yn-1-yl)carbamate as a clear oil (0.4743 g, 80%) that was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.30 (m, 2 H), 7.30–7.24 (m, 3 H), 4.55 (s, 2 H), 3.97 (d, *J* = 53.8 Hz, 2 H), 2.21 (s, 1 H), 1.49 (s, 9 H).

A flame dried flask was cooled under a stream of nitrogen and charged with THF (2 mL) and *n*-butyllithium (0.4 mL, 0.90 mmol, 1.1 equiv, 2.5 M in THF). The solution was cooled to –78 °C and a solution of *tert*-butyl benzyl(prop-2-yn-1-yl)carbamate (0.2 g, 0.815 mmol) in THF (2 mL) was added dropwise. The resulting mixture was stirred at –78 °C for 20 min, then warmed to 0 °C and quenched with D_2O (0.15 mL, 10 equiv). The mixture was diluted with ether and transferred to a separatory funnel. The layers were separated, the aqueous layer was extracted with ether (3 x 10 mL) and the combined organic layers were washed with brine (1 x 25 mL). The organic layer was dried over anhydrous sodium

sulfate and concentrated *in vacuo*, and the crude product was purified via flash column chromatography on silica gel (2% ethyl acetate in hexanes) to afford 0.1522 g (76%) of *tert*-butyl benzyl(prop-2-yn-1-yl-3-*d*)carbamate as a clear oil. This material was judged to have ca 95% deuterium incorporation at the terminal alkyne position, plus ca 25% deuterium incorporation at the benzylic position as judged by ^{1}H NMR analysis. The doubly deuterated material was not separated, and was carried forward through the synthesis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.30 (m, 2 H), 7.30–7.23 (m, 3 H), 4.54 (s, 2 H), 4.04 (s, br, 1 H), 3.90 (s, br, 1 H), 1.49 (s, 9 H).

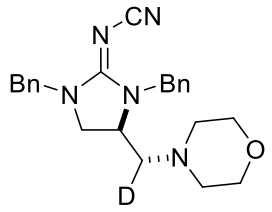
A flame dried flask was cooled under a stream of nitrogen and charged with zirconocene dichloride (0.3654 g, 1.25 mmol, 2.8 equiv) and THF (1.5 mL). The mixture was stirred vigorously, and then a solution of *tert*-butyl benzyl(prop-2-yn-1-yl-3-*d*)carbamate (0.110 g, 0.466 mmol) in THF (1 mL) was added. A solution of $LiAlD(O\textit{t}Bu)_3$ (0.32g, 2.8 equiv) in THF (0.5 mL) was added quickly, and the resulting mixture was stirred at rt for 30 min. Water (0.22 mL, 12 mmol, 26.8 equiv) was added dropwise, and the resulting mixture was stirred at rt for 2 h. The solution was then filtered through celite, rinsed with ethyl acetate and concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel using 2% ethyl acetate in hexanes as the eluant to afford 0.0913 g (82%) of (*Z*)-*tert*-butyl-(allyl-2,3-d_2)(benzyl)carbamate as a clear oil. This material was judged to have ca 95% deuterium incorporation at both the internal alkene position and at the terminal alkene position, and was obtained as one stereoisomer (>20:1 dr) as judged by ^{1}H NMR analysis. This material also contained ca 25% d-incorporation at the benzylic position (carried through from the previous intermediate). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, J = 7.4 Hz, 2 H), 7.28–7.20 (m, 3 H),

5.12 (s, 1 H), 4.40 (s, 2 H), 3.84 (br s, 1 H), 3.72 (br s, 1 H), 1.47 (s, 9 H); ^{1}H NMR (500 MHz, C_6D_6) δ 7.28–7.03 (m, 5 H), 4.92 (s, 1 H), 4.43 (br s, 1 H), 4.24 (br s, 1 H), 3.83 (br s, 1 H), 3.56 (br s, 1 H), 1.44 (s, 9 H).

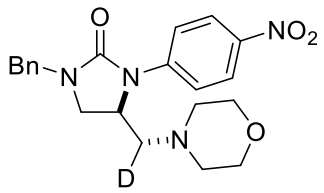
A 25 mL vial was charged with (*Z*)-*tert*-butyl-(allyl-2,3-d_2)(benzyl)carbamate (0.0913 g, 0.37 mmol) and dichloromethane (0.37 mL, 1 M) and the solution was cooled to 0 ºC. Trifluoroacetic acid (0.37 mL, 1 M) was added dropwise and the solution was warmed to rt and stirred overnight. Toluene (2 mL) was added, and the resulting solution was concentrated *in vacuo*. Additional toluene (2 mL) was added, the mixture was concentrated again, and this process was repeated two additional times. This afforded the trifluoroacetate salt of (*Z*)-*N*-benzylprop-2-en-2,3-d_2-1-ylamine as a crude oil that was carried on to the next step without purification.

A round-bottom flask equipped with a stirbar was charged with dichloromethane (2 mL) and 4-nitrophenyl isocyanate (0.06 g, 0.37 mmol, 1 equiv). A solution of the crude (*Z*)-*N*-benzylprop-2-en-2,3-d_2-1-ylamine trifluroacetate salt (from the previous step) in dichloromethane (1.7 mL) was added, then triethylamine (0.2 mL, 0.44 mmol, 3.9 equiv) was added dropwise and the resulting solution was stirred at rt overnight. The mixture was then concentrated *in vacuo*, and the crude product was purified via flash column chromatography on silica gel using 10% ethyl acetate in hexanes as the eluant to afford 0.112 g (98%) of the title compound as a yellow solid, mp 105–107 °C. This material was determined to contain ca 95% deuterium incorporation at each of the alkene positions, along with ca 25% deuterium incorporation at the benzylic position (carried through from earlier intermediates) by ^{1}H NMR, ^{2}D NMR, and MS analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.9 Hz, 2 H), 7.45 (d, *J* = 8.8 Hz, 2 H), 7.39 (t, *J* = 7.5 Hz, 2 H), 7.34 (d, *J* =

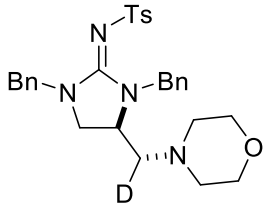
7.1 Hz, 3 H), 6.79 (s, 1 H), 5.33 (s, 1 H), 4.61 (m, 2 H), 4.01 (s, 2 H); Note: the unusual multiplicity for the peak at δ 4.61 is due the ~25% deuterium incorporation at the benzylic position. ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 145.4, 142.8, 137.0, 133.2 (t, *J* = 24.0 Hz), 129.2, 128.2, 127.7, 125.2, 118.5, 117.8 (t, *J* = 23.5 Hz), 51.0, 50.0; IR (film) 3347, 1657, 1610 cm^{-1}; MS (ESI$^+$) 314.1468 (314.1468 calcd for $C_{17}H_{15}D_2N_3O_3$, M + H$^+$).



(4*S,4'*R**)-*N*-(1,3-Dibenzyl-4-(morpholinomethyl-*d*)imidazolidin-2-ylidene)cyanamide (*d*-8a)**. The general procedure was followed for the coupling of (*Z*)-1-[allyl-3-*d*]-1,3-dibenzyl-2-cyanoguanidine **(*d*-7a)** (30.5 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 26 mg (67%) of the title compound as a tan, viscous oil. This compound was obtained as a 3:1 mixture of diastereomers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (500 MHz, C_6D_6) δ 7.17–7.12 (m, 4 H), 7.11–6.98 (m, 6 H), 5.25 (d, *J* = 15.5 Hz, 1 H), 4.52 (q, *J* = 15.1 Hz, 2 H), 4.08–4.02 (m, 1 H), 3.29 (br s, 4 H), 3.01 (q, *J* = 7.4 Hz, 1 H), 2.65 (dd, *J* = 11.5, 7.3 Hz, 1 H), 2.54 (q, *J* = 8.2 Hz, 1 H), 1.89–1.84 (m, 1 H), 1.78–1.68 (m, 4 H), 1.58–1.51 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 135.9, 135.4, 128.9, 128.8, 128.2, 128.1, 128.0, 127.9, 66.7, 60.5 (t, *J* = 21.9 Hz), 54.0, 51.8, 49.5, 49.3, 47.8; IR (film) 2924, 2169, 1583 cm^{-1}; MS (ESI$^+$) 391.2355 (391.2351 calcd for $C_{23}H_{26}DN_5O$, M + H$^+$).

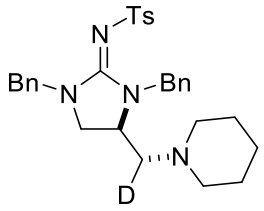


(4*S,4'*R**)-1-Benzyl-4-(morpholinomethyl-*d*)-3-(4-nitrophenyl)imidazolidin-2-one (*d*-10a).** The general procedure was followed for the coupling of (*Z*)-1-(allyl-3-*d*)-1-benzyl-3-phenylurea **(*d*-8a)** (31.2 mg, 0.1 mmol) with morpholino benzoate **(3a)** (62.2 mg, 0.3 mmol). This procedure afforded 28 mg (70%) of the title compound as a yellow solid, m.p. 102-104 °C. This compound was obtained as a 6:1 mixture of diastereomers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (400 MHz, C_6D_6) δ 8.04 (d, *J* = 9.3 Hz, 2 H), 7.61 (d, *J* = 9.3 Hz, 2 H), 7.14–7.02 (m, 5 H), 4.31–4.19 (m, 2 H), 3.52–3.24 (m, 5 H), 2.85 (dd, *J* = 8.9, 2.8 Hz, 1 H), 2.75 (t, *J* = 8.7 Hz, 1 H), 1.95–1.88 (m, 3 H), 1.83–1.79 (m, 2 H), 1.72 (dd, *J* = 13.7, 9.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 145.2, 142.0, 136.1, 128.8, 128.3, 127.9, 124.9, 117.4, 66.7, 58.9 (t, *J* = 19.0 Hz), 54.2, 50.8, 47.8, 45.9; IR (film) 2922, 1710 cm^{-1}; MS (ESI^{+}) 398.1929 (398.1933 calcd for $C_{21}H_{23}DN_4O_4$, M + H^{+}).



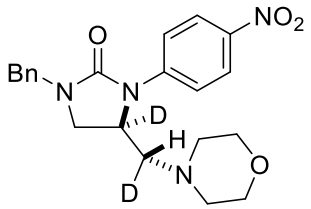
(4*S,4'*R**)-*N*-[1,3-dibenzyl-4-(morpholinomethyl-*d*)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (*d*-8d)**. The general procedure was followed for the coupling of (*Z*)-*N*-{[allyl-3-*d*](benzyl)amino}benzylaminomethylene-4-methylbenzenesulfonamide **(*d*-7b)** (43.5 mg, 0.1 mmol) with morpholino benzoate **(3a)**

(62.2 mg, 0.3 mmol). This procedure afforded 39 mg (75%) of the title compound as a tan, viscous oil. This compound was obtained as a 6:1 mixture of diastereomers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (400 MHz, C_6D_6) δ 8.26 (d, *J* = 8.2 Hz, 2 H), 7.28 (d, *J* = 6.8 Hz, 4 H), 7.20–6.98 (m, 6 H), 6.81 (d, *J* = 8.1 Hz, 2 H), 5.47 (d, *J* = 15.4 Hz, 1 H), 4.83 (d, *J* = 15.0 Hz, 1 H), 4.66 (d, *J* = 14.9 Hz, 1 H), 4.12 (d, *J* = 15.3 Hz, 1 H), 3.33 (br s, 4 H), 3.15–3.05 (m, 1 H), 2.75 (t, *J* = 9.7 Hz, 1 H), 2.66 (d, *J* = 7.3 Hz, 1 H), 1.92–1.87 (m, 4 H), 1.84–1.70 (m, 4 H), 1.77–1.72 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 142.9, 141.2, 136.1, 135.7, 129.9, 128.8, 128.7, 128.6, 128.4, 128.1, 127.9, 127.8, 125.8, 66.7, 60.2 (t, *J* = 19 Hz), 54.1, 51.6, 50.8, 49.0, 48.7, 21.4; IR (film) 2922, 1559 cm^{-1}; MS (ESI$^+$) 520.2482 (520.2487 cacld for $C_{29}H_{33}DN_4O_3S$, M + H$^+$).



(4*S,4'*R**)-*N*-[1,3-Dibenzyl-4-(-piperidin-1-ylmethyl-*d*)imidazolidin-2-ylidene]-4-methylbenzenesulfonamide (*d*-8e)**.The general procedure was followed for the coupling of (*Z*)-*N*-{[allyl-3-d](benzyl)amino}-benzylaminomethylene-4-methylbenzenesulfonamide **(*d*-7b)** (43.5 mg, 0.1 mmol) with piperidin-1-yl benzoate **(3b)** (61.5 mg, 0.3 mmol). This procedure afforded 40 mg (77%) of the title compound as a tan, viscous oil. This compound was obtained as a 7:1 mixture of diastereomers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (500 MHz, C_6D_6) δ 8.26 (d, *J* = 8.0 Hz, 2 H), 7.33 (d, *J* = 7.5 Hz, 2 H), 7.28 (d, *J* = 7.5 Hz, 2 H), 7.15–7.07 (m, 4 H), 7.05–7.00 (m, 2 H), 6.82 (d, *J* = 8 Hz, 2 H), 5.46 (d, *J* = 15 Hz, 1 H), 4.82 (d, *J* = 14.5 Hz, 1 H), 4.65 (d, *J* = 15.5 Hz, 1 H), 4.22 (d, *J* = 15 Hz, 1 H), 3.19 (q, *J* = 9.5 Hz, 1 H), 2.80 (t, *J* =

9.5 Hz, 1 H), 2.72 (dd, *J* = 16.5 Hz, 6.5 Hz, 1 H), 2.05–2.00 (m, 1 H), 1.89 (s, 3 H), 1.86 (br s, 4 H), 1.76–1.71 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 156.2, 144.3, 140.4, 137.1, 136.5, 128.8, 128.6, 128.7, 128.6, 128.5, 128.4, 127.5, 126.2, 60.7 (t, *J* = 22 Hz), 54.8, 51.7, 50.8, 48.8, 48.7, 25.8, 24.1, 20.7; IR (film) 2931, 1559 cm^{-1}; MS (ESI$^+$) 518.2692 (518.2695 calcd for $C_{30}H_{35}DN_4O_2S$, M + H$^+$).

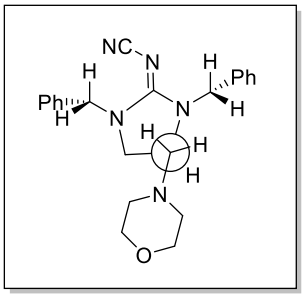


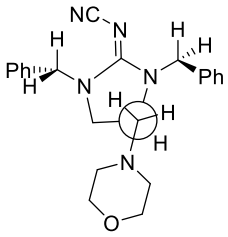
(4*S,4'*R**)-1-Benzyl-4-(morpholinomethyl-*d*)-3-(4-nitrophenyl)imidazolidin-2-one-4-*d* (16)**. A flame dried Schlenk tube was cooled under a stream of nitrogen and charged with (*Z*)-1-(allyl-2,3-d_2)-1-benzyl-3-(4-nitrophenyl)urea **(15)** (0.0313 g, 0.1 mmol), $Pd(acac)_2$ (0.0012g, 0.004 mmol), JackiePhos (0.0127 g, 0.016 mmol), morpholino benzoate **(3a)** (0.0622g, 0.3 mmol), Cs_2CO_3 (0.0652 g, 0.2mmol), and dioxane (1mL, 0.1 M). The solution was heated to 100 ºC for 16 h, then was cooled to rt, filtered through cotton, rinsed with diethyl ether, and concentrated *in vacuo*. The crude product was purified via flash column chromatography on silica gel using 40% ethyl acetate in hexanes as the eluant to afford 25.4 mg (64%) of the title compound as a yellow solid, mp 105–106 °C. This material was obtained as a 6:1 mixture of diastereomers as judged by ^{1}H NMR analysis; data are for the major isomer. Note: this material also contains ca 25% deuterium incorporation at the benzylic position, which was carried over from the starting material, based on ^{1}H and ^{2}D NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 9.4 Hz, 2 H), 7.75 (d, *J* = 8.8 Hz, 2 H), 7.40–7.29 (m, 5 H), 4.58–4.40 (m, 2 H), 3.62 (q, *J* = 9.4 Hz, 4 H), 3.49 (d, *J* = 9.1 Hz, 1 H), 3.36 (d, *J* = 9.3 Hz, 1 H), 2.59 (s, 1 H), 2.50 (d, *J*

= 8.0 Hz, 2 H), 2.37 (q, *J* = 9.7, 8.8 Hz, 2 H; ^{1}H NMR (500 MHz, C_6D_6) δ 8.05 (d, *J* = 9.3 Hz, 2 H), 7.60 (d, *J* = 9.2 Hz, 2 H), 7.21–7.02 (m, 5 H), 4.36–4.09 (m, 2 H), 3.35–3.49 (m, 4 H), 2.84 (d, *J* = 8.8 Hz, 1 H), 2.73 (d, *J* = 8.8 Hz, 1 H), 1.98–1.88 (m, 3 H), 1.81 (ddd, *J* = 10.5, 6.1, 3.1 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 145.4, 142.2, 136.3, 129.0, 128.4, 128.0, 125.1, 117.5, 66.9, 59.0 (t, *J* = 20.3 Hz), 54.3, 50.7 (t, *J* = 20.9 Hz), 48.0, 45.9; IR (film) 2924, 2853, 1710 cm^{-1}; MS (ESI^+) 399.1995 (399.1996 calcd for $C_{21}H_{22}D_2N_4O_4$, $M + H^+$).

Computational Details – Energy minimization for assignment of stereochemistry of deuterated products by nOe.

All geometries were optimized using the spin-restricted B3LYP[6] density functional and the 6-31G* basis set. All density functional calculations were performed using Spartan'16.[7] The calculations are meant to be used for qualitative purposes only.





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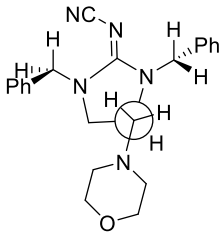

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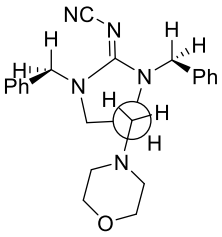

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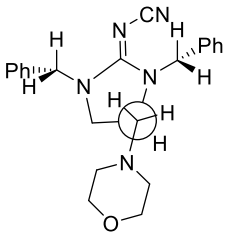
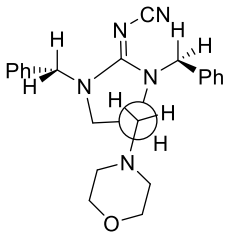
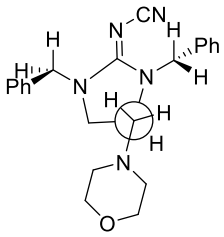


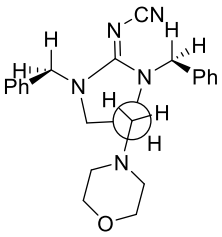
+0.5485 kcal/mol



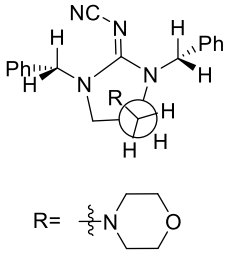
+0.5453kcal/mol



+0.6049 kcal/mol

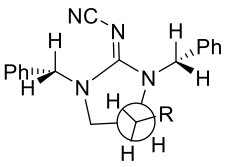


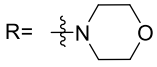
+3.1426 kcal/mol



R=

+2.4002 kcal/mol

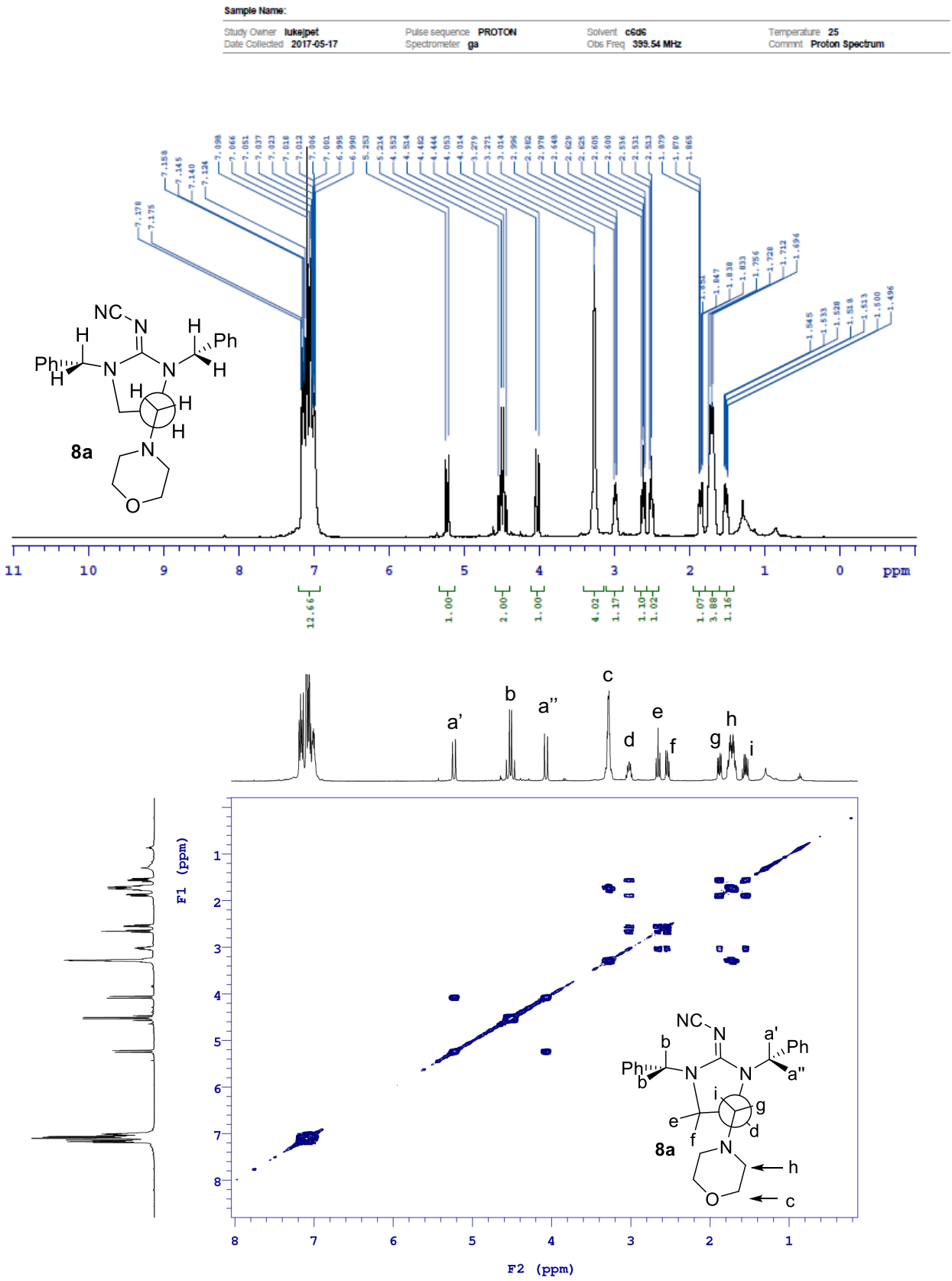


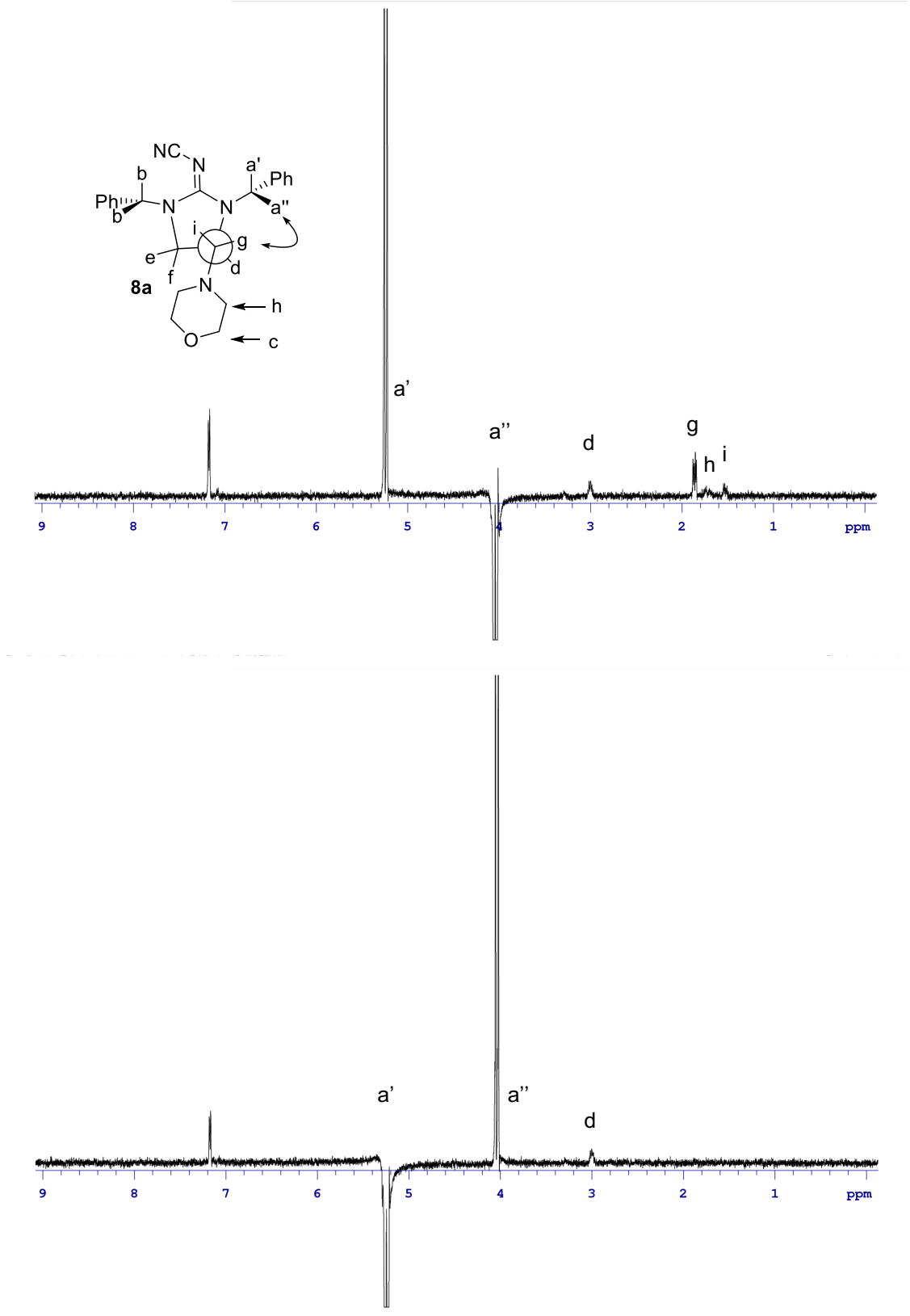
R= 

+0.5842 kcal/mol

Deuterium Labelling Studies – Assignment of product stereochemistry

In order to determine the relative stereochemical configuration of the deuterated products ***d*-8a**, ***d*-8d**, ***d*-8e**, and ***d*-10a**, the calculated ground state energy conformations[1] shown above were used in conjunction with 2D COSY and 1D ^{1}H nOe analysis of the all-proteo analogs of these compounds. The low energy conformation is shown in the box on the previous page, and is copied on the ^{1}H NMR, COSY, and 1D nOe spectra of **8a** shown on the following pages. Irradiation of the signal corresponding to H atom a'' led to a strong nOe correlation to H g, and a weak correlation to H i (plus a strong correlation to the germinal H atom a'). In contrast, irradiation of H atom a' resulted only in nOe correlations to H d and H a''. The stereochemistry of the deuterated compounds was then assigned on the basis of which signal (H g vs. H i) was missing from the ^{1}H NMR spectra of the deuterated products.


Sample Name:
Study Owner lukejpet
Date Collected 2017-05-17
Pulse sequence PROTON
Spectrometer ga
Solvent c6d6
Obs Freq 399.54 MHz
Temperature 25
Commnt Proton Spectrum
8a
ppm
a'
b
a''
c
d
e
f
g
h
i
F1 (ppm)
F2 (ppm)


NC
N
a'
Ph
b
Ph
b
N
N
a''
i
g
e
f
d
N
h
O
c
8a
a'
a''
d
g
h
i
9
8
7
6
5
4
3
2
1
ppm
a'
a''
d
9
8
7
6
5
4
3
2
1
ppm

References

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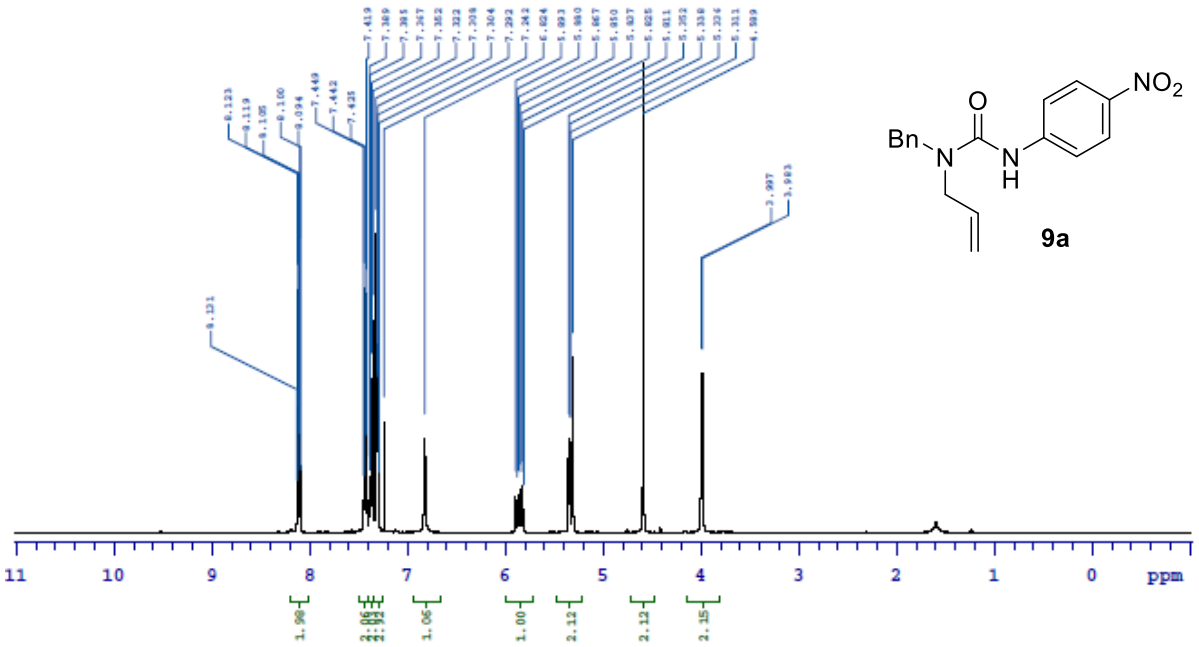
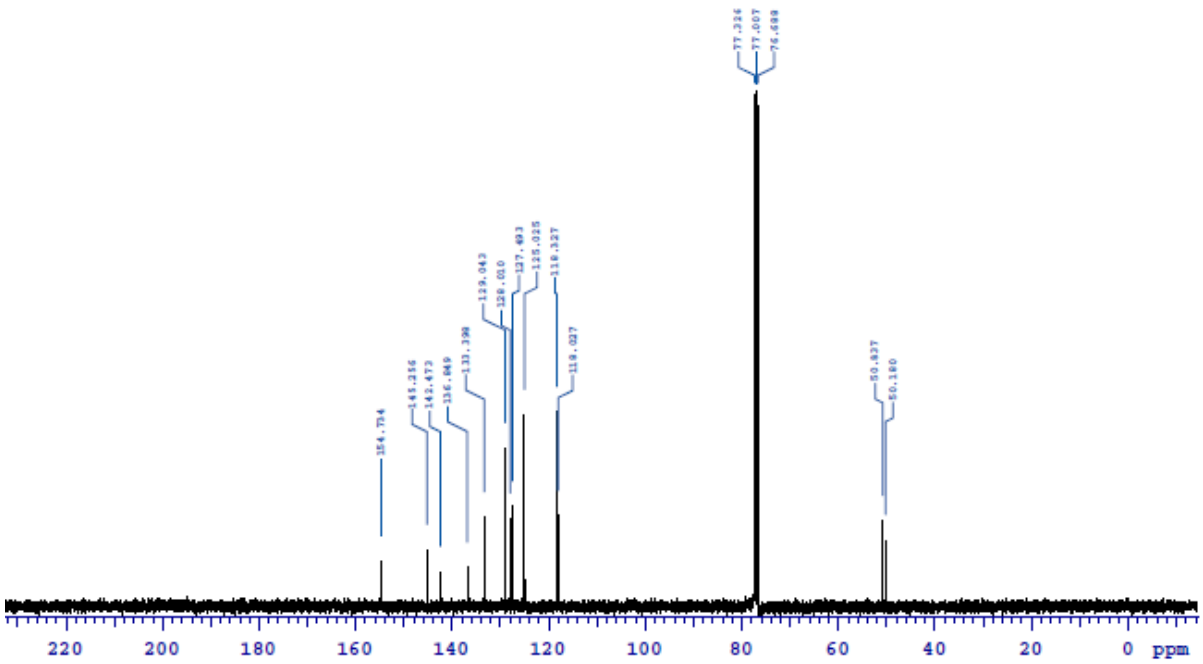
Sample Name:

Study Owner lukejpet	Pulse sequence PROTON	Solvent cdcl3	Temperature 25
Date Collected 2017-07-18	Spectrometer ga	Obs Freq 399.54 MHz	Commnt Proton Spectrum



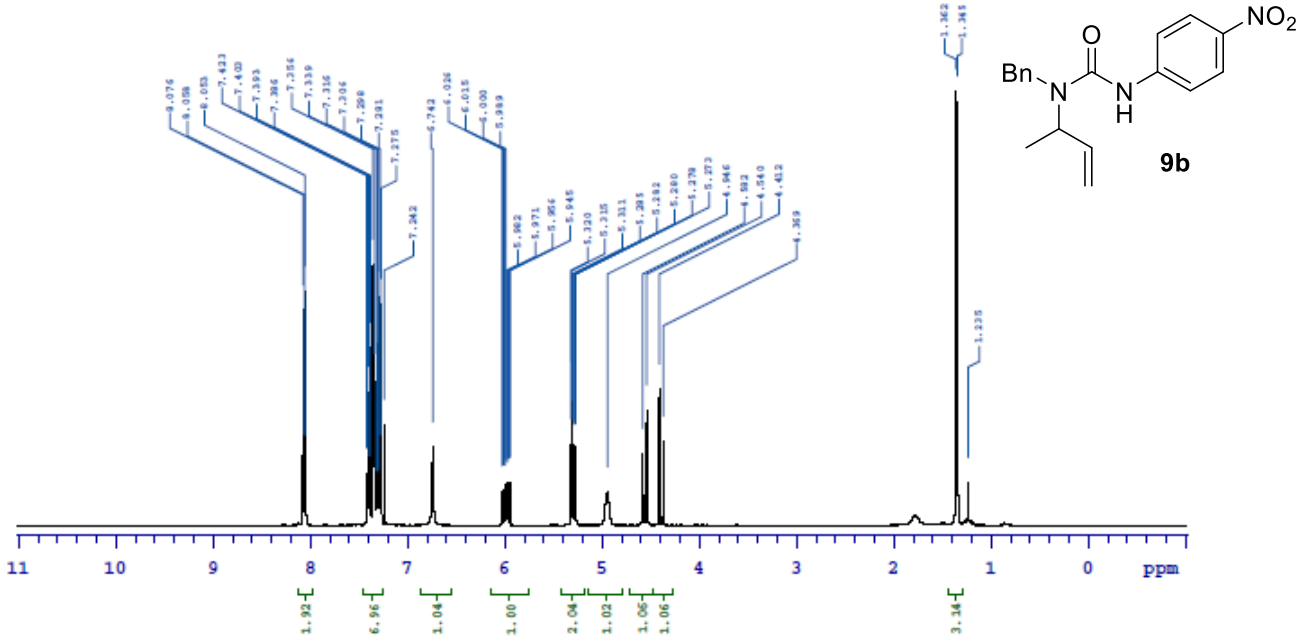
Sample Name:

Study Owner lukejpet	Pulse sequence CARBON	Solvent cdcl3	Temperature 25
Date Collected 2017-07-18	Spectrometer ga	Obs Freq 100.47 MHz	Commnt Carbon-13



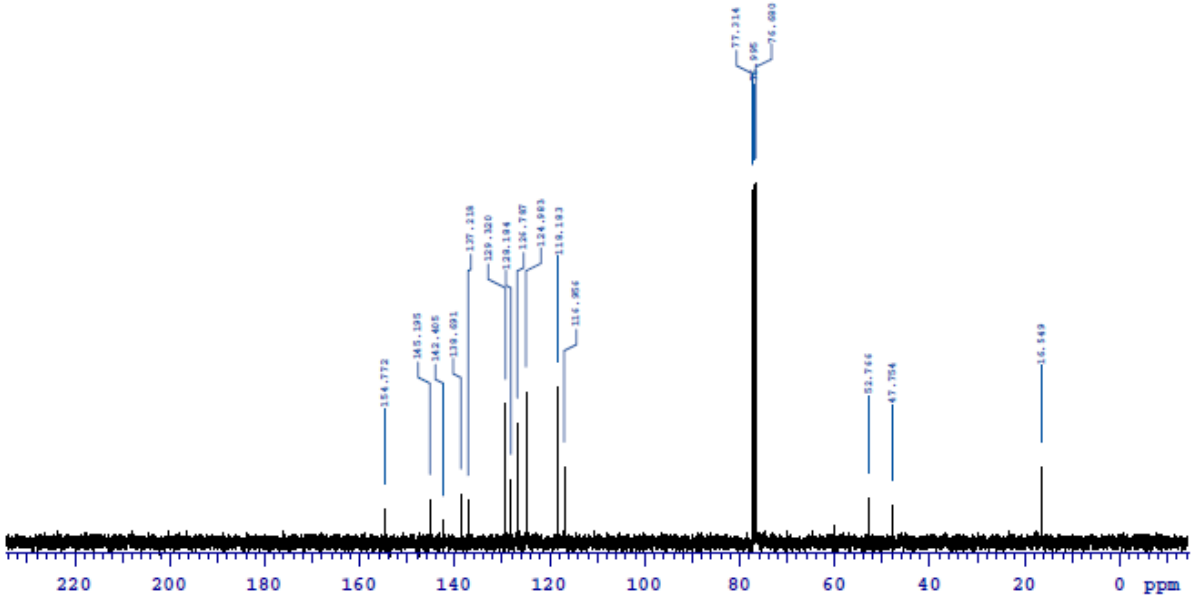
Sample Name:

Study Owner lukejpet	Pulse sequence PROTON	Solvent cdcl3	Temperature 25
Date Collected 2017-07-31	Spectrometer ga	Obs Freq 399.54 MHz	Commnt Proton Spectrum



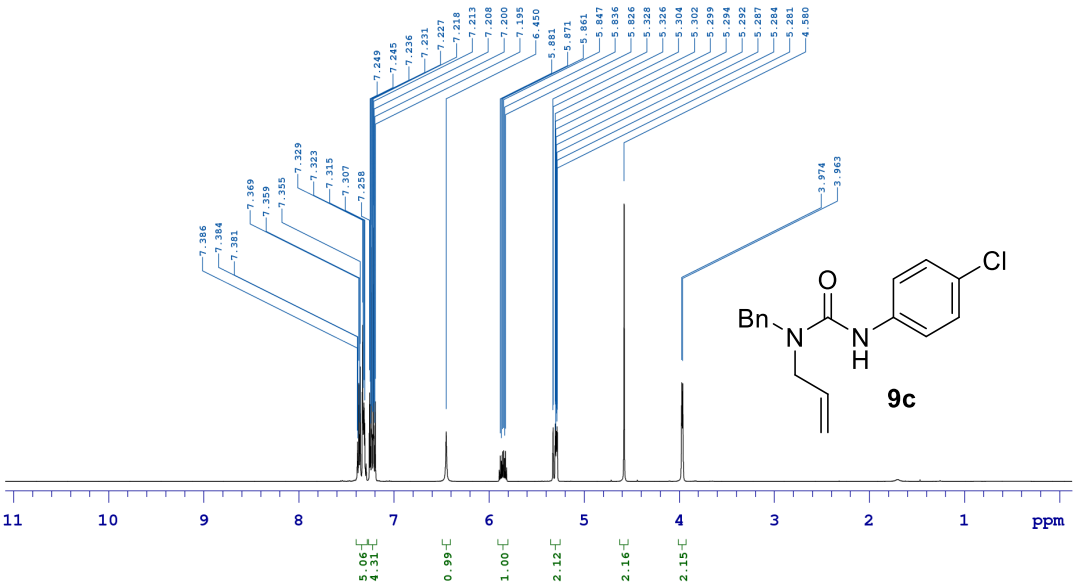
Sample Name:

Study Owner lukejpet	Pulse sequence CARBON	Solvent cdcl3	Temperature 25
Date Collected 2017-07-31	Spectrometer ga	Obs Freq 100.47 MHz	Commnt Carbon-13



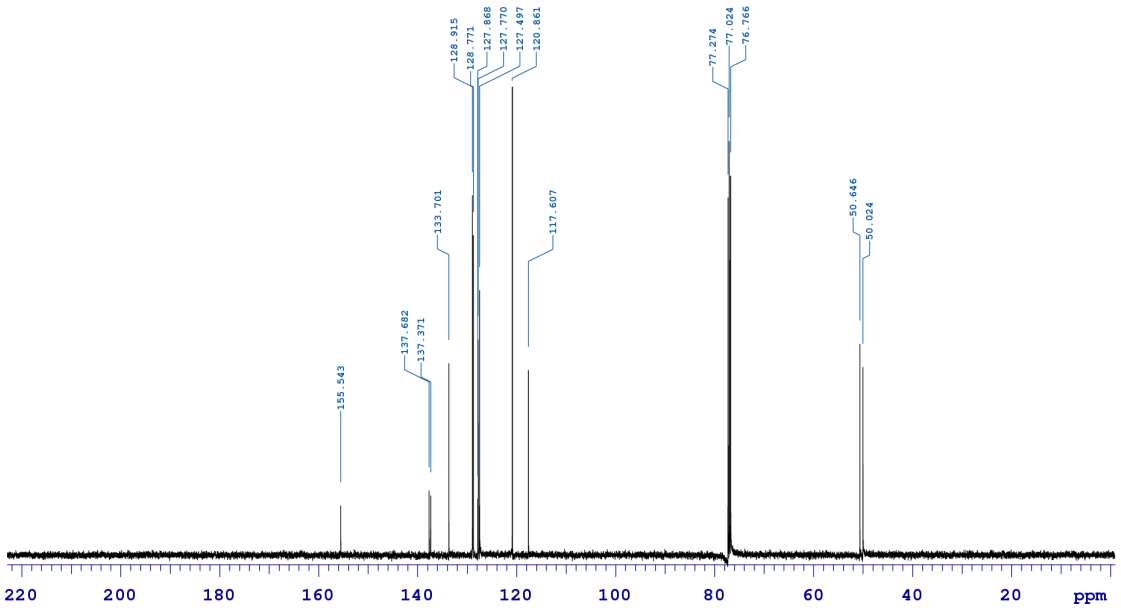
Sample Name:

Study Owner **VJtempIt**	Pulse sequence **PROTON**	Solvent **cdcl3**	Temperature **r.t.**
Date Collected **2016-08-26**	Spectrometer **te**	Obs Freq **500.08 MHz**	Commnt **Proton Spectrum**



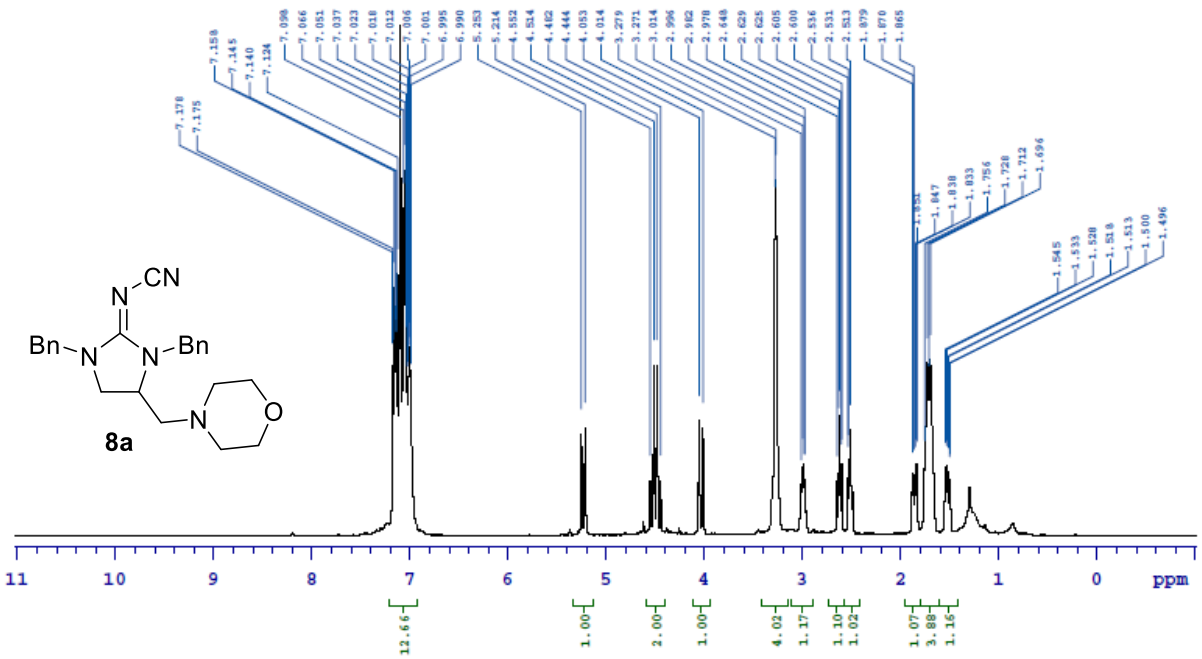
Sample Name:

Study Owner **VJtempIt**	Pulse sequence **CARBON**	Solvent **cdcl3**	Temperature **r.t.**
Date Collected **2016-08-26**	Spectrometer **te**	Obs Freq **125.76 MHz**	Commnt **Proton Spectrum**



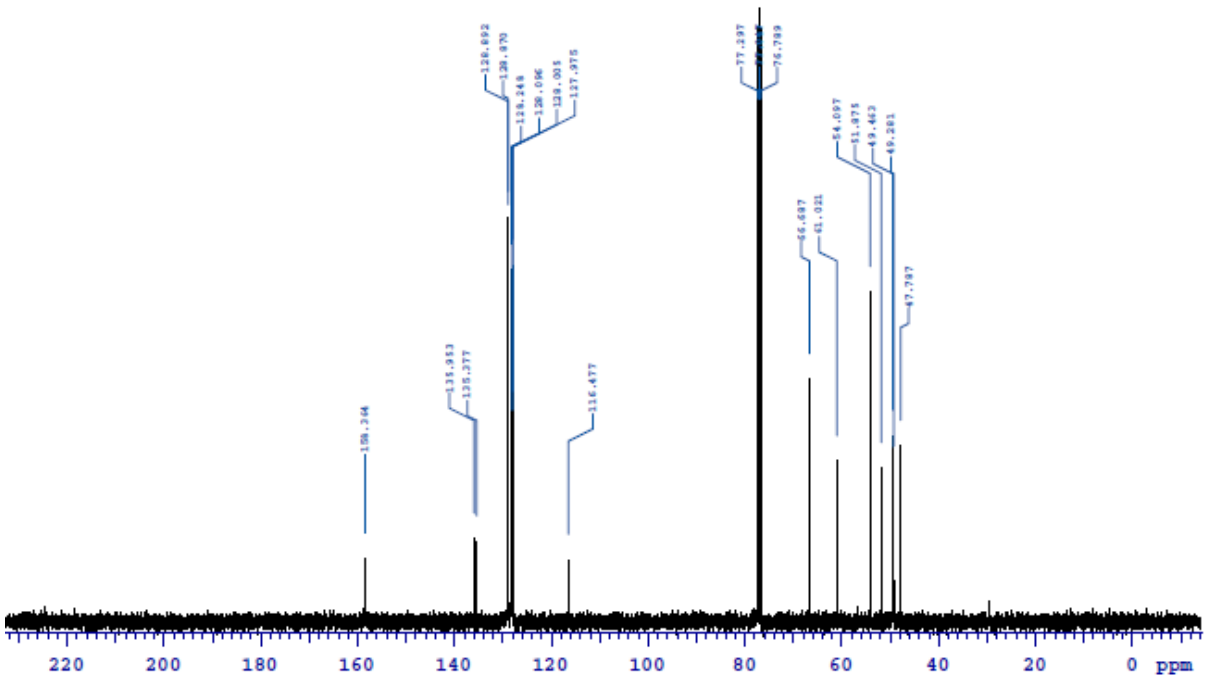
Sample Name:

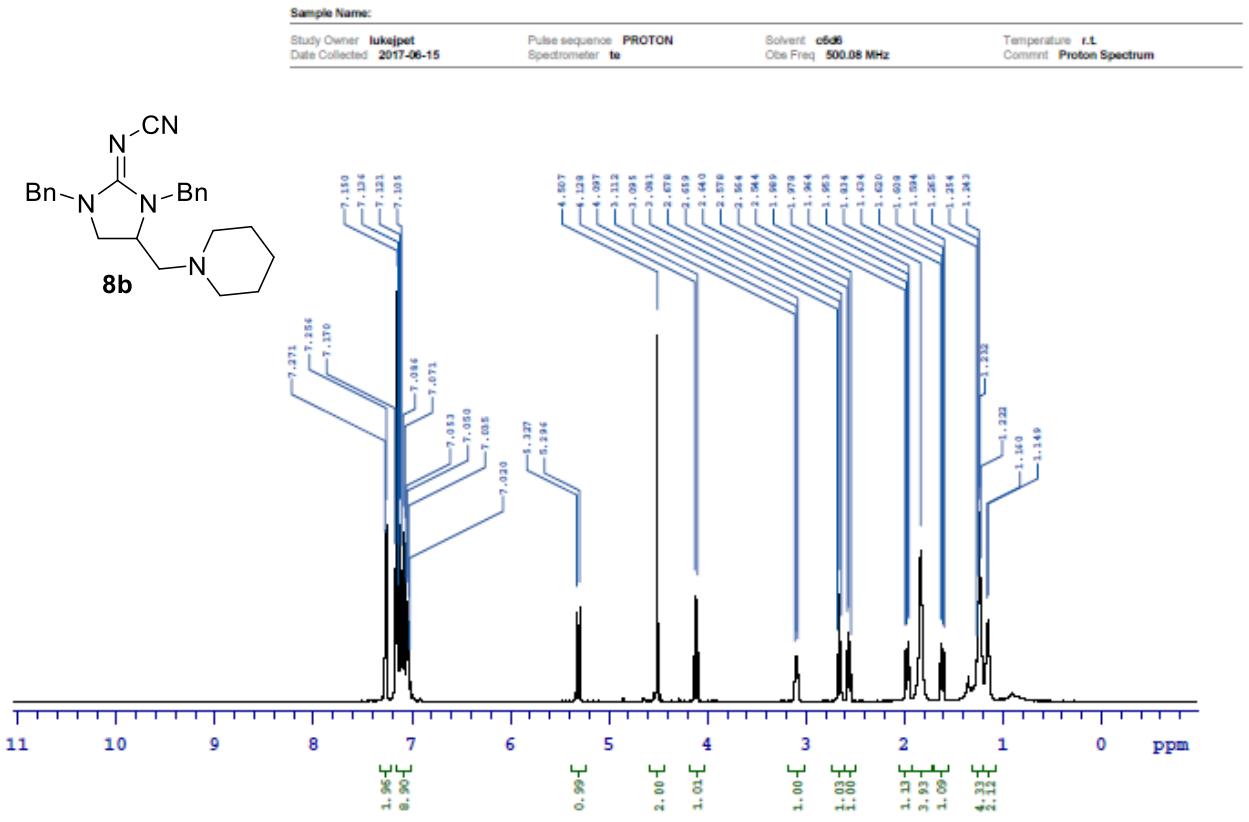
Study Owner	lukejpet	Pulse sequence	PROTON	Solvent	cdcl3	Temperature	25
Date Collected	2017-05-17	Spectrometer	ga	Obs Freq	399.54 MHz	Commnt	Proton Spectrum

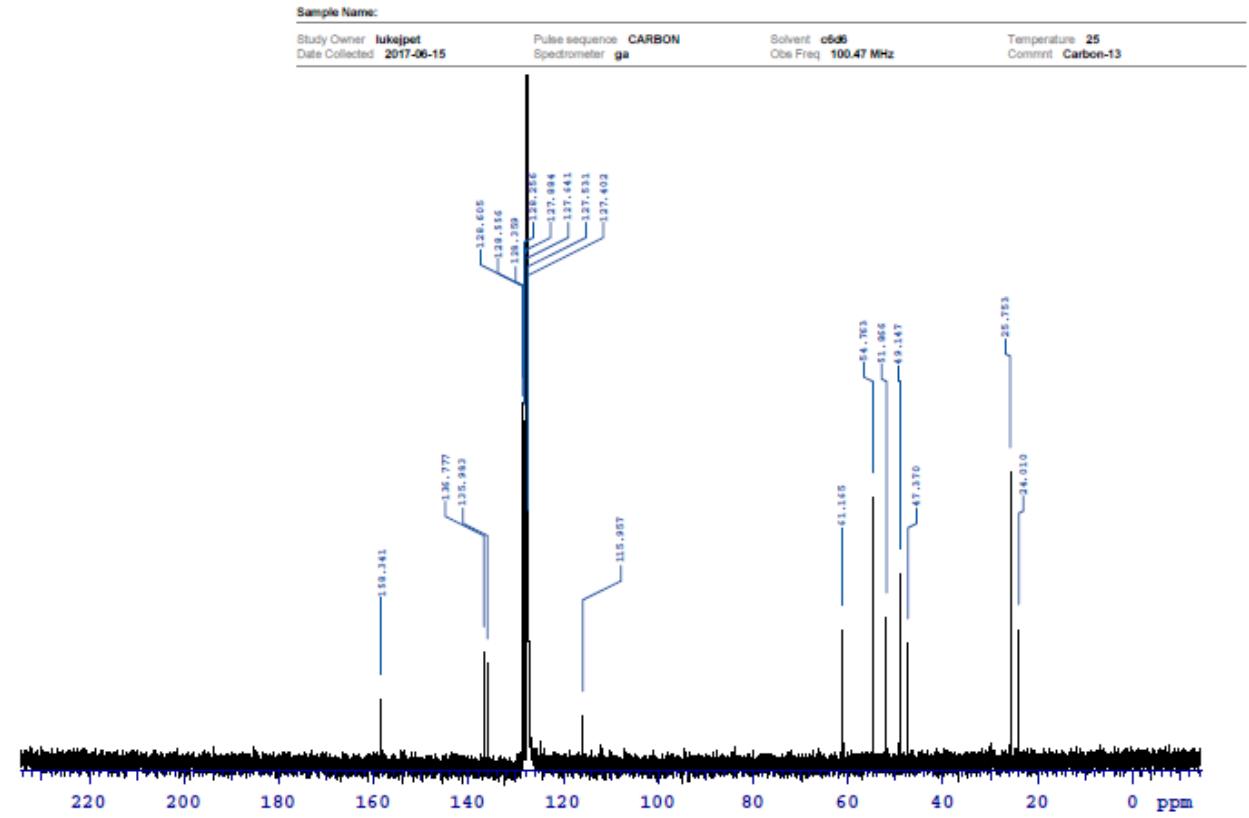


Sample Name:

Study Owner	lukejpet	Pulse sequence	CARBON	Solvent	cdcl3	Temperature	25
Date Collected	2017-02-20	Spectrometer	te	Obs Freq	125.76 MHz	Commnt	Proton Spectrum

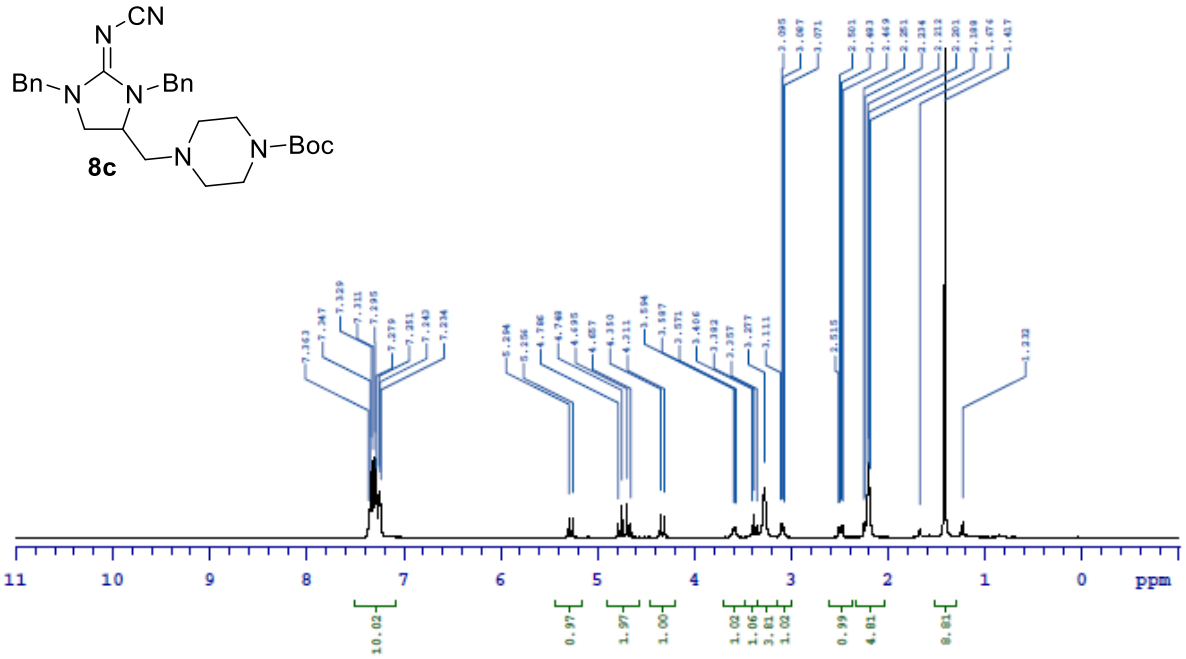



Sample Name:
Study Owner lukejpet
Date Collected 2017-06-15
Pulse sequence PROTON
Spectrometer te
Solvent c6d6
Obs Freq 500.08 MHz
Temperature r.t.
Commnt Proton Spectrum
N
CN
Bn
N
N
Bn
N
8b
11
10
9
8
7
6
5
4
3
2
1
0
ppm


Sample Name:
Study Owner lukejpet
Date Collected 2017-06-15
Pulse sequence CARBON
Spectrometer ga
Solvent c6d6
Obs Freq 100.47 MHz
Temperature 25
Commnt Carbon-13
220
200
180
160
140
120
100
80
60
40
20
0
ppm

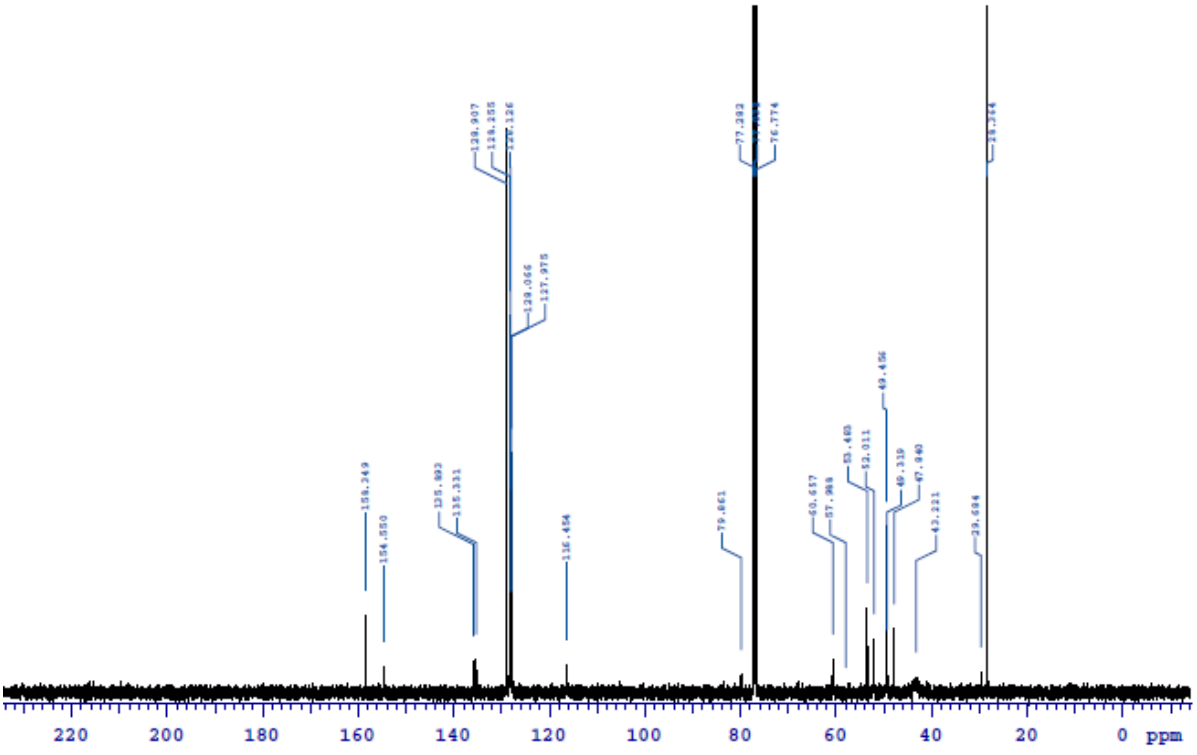
Sample Name:

Study Owner lukejpet	Pulse sequence PROTON	Solvent cdcl3	Temperature r.t.
Date Collected 2017-06-08	Spectrometer co	Obs Freq 400.52 MHz	Commnt Proton Spectrum



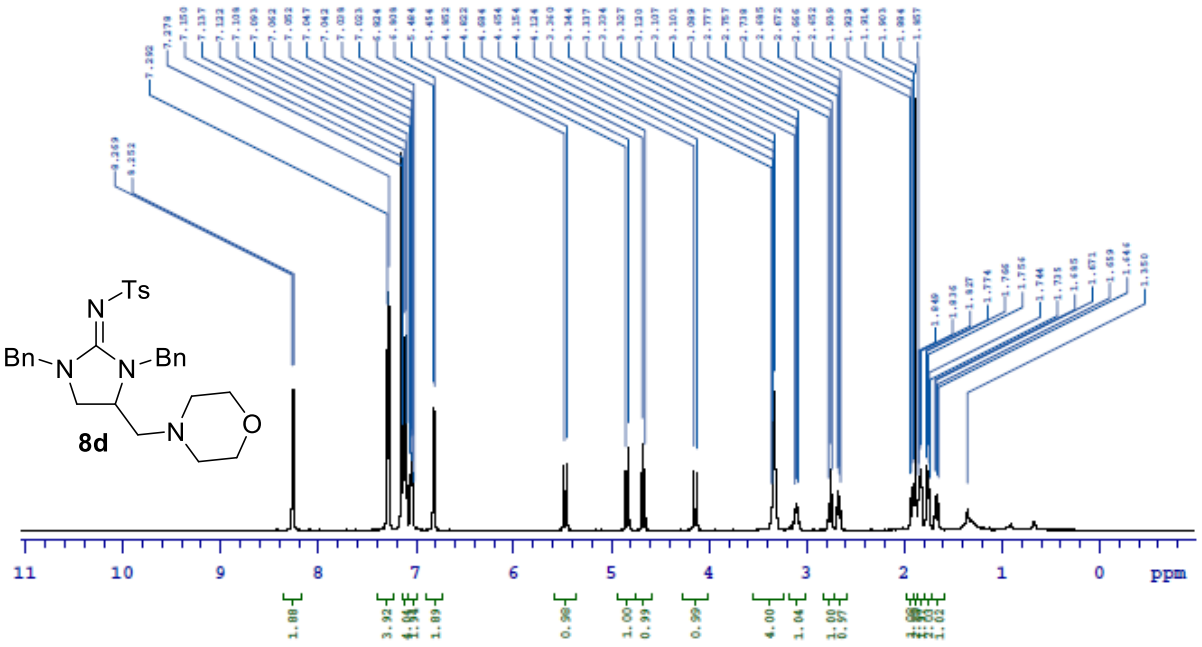
Sample Name:

Study Owner lukejpet	Pulse sequence CARBON	Solvent cdcl3	Temperature r.t.
Date Collected 2017-06-29	Spectrometer te	Obs Freq 125.76 MHz	Commnt Proton Spectrum



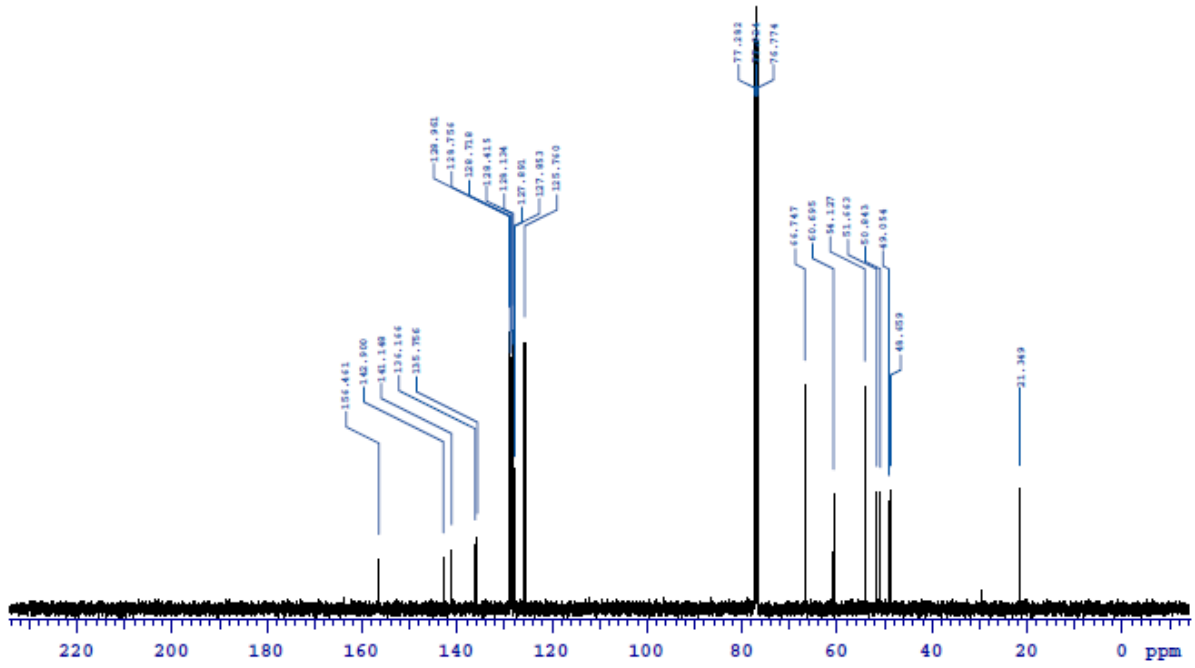
Sample Name:

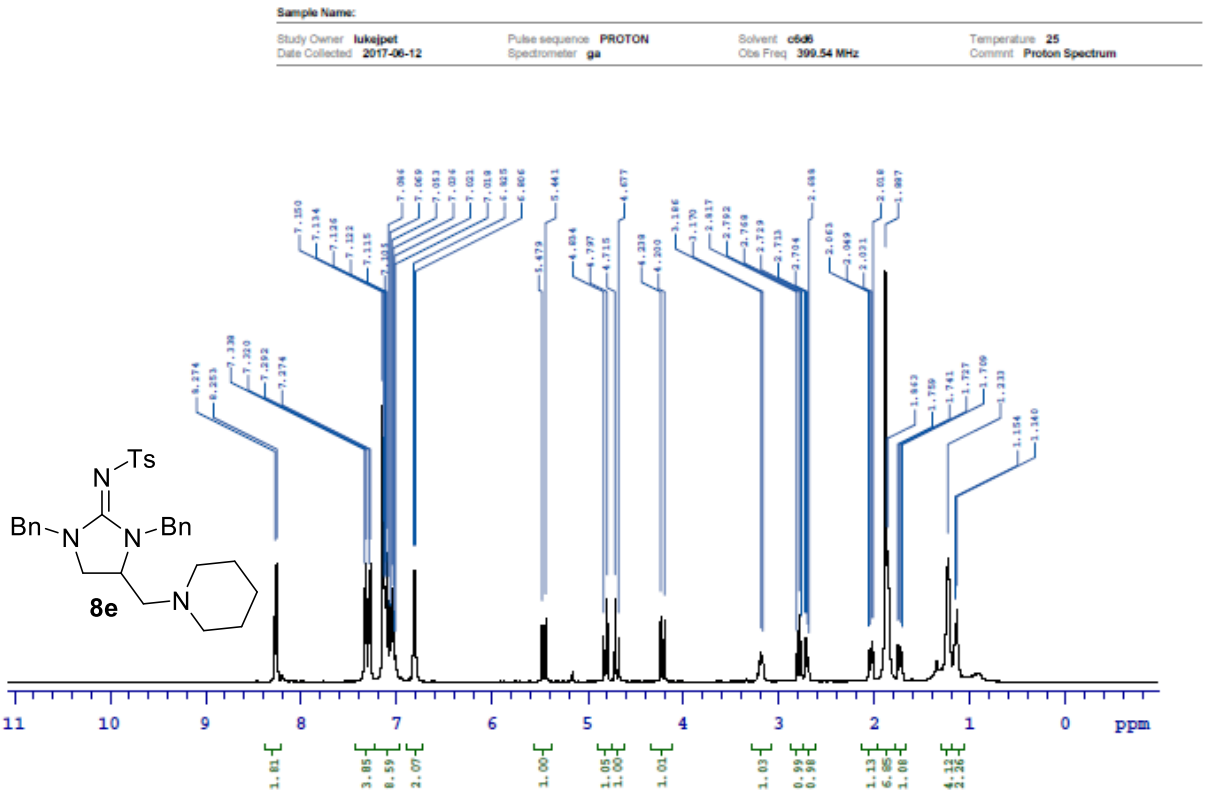
Study Owner lukejpet	Pulse sequence PROTON	Solvent c6d6	Temperature 25
Date Collected 2017-02-20	Spectrometer te	Obs Freq 500.08 MHz	Commnt Proton Spectrum

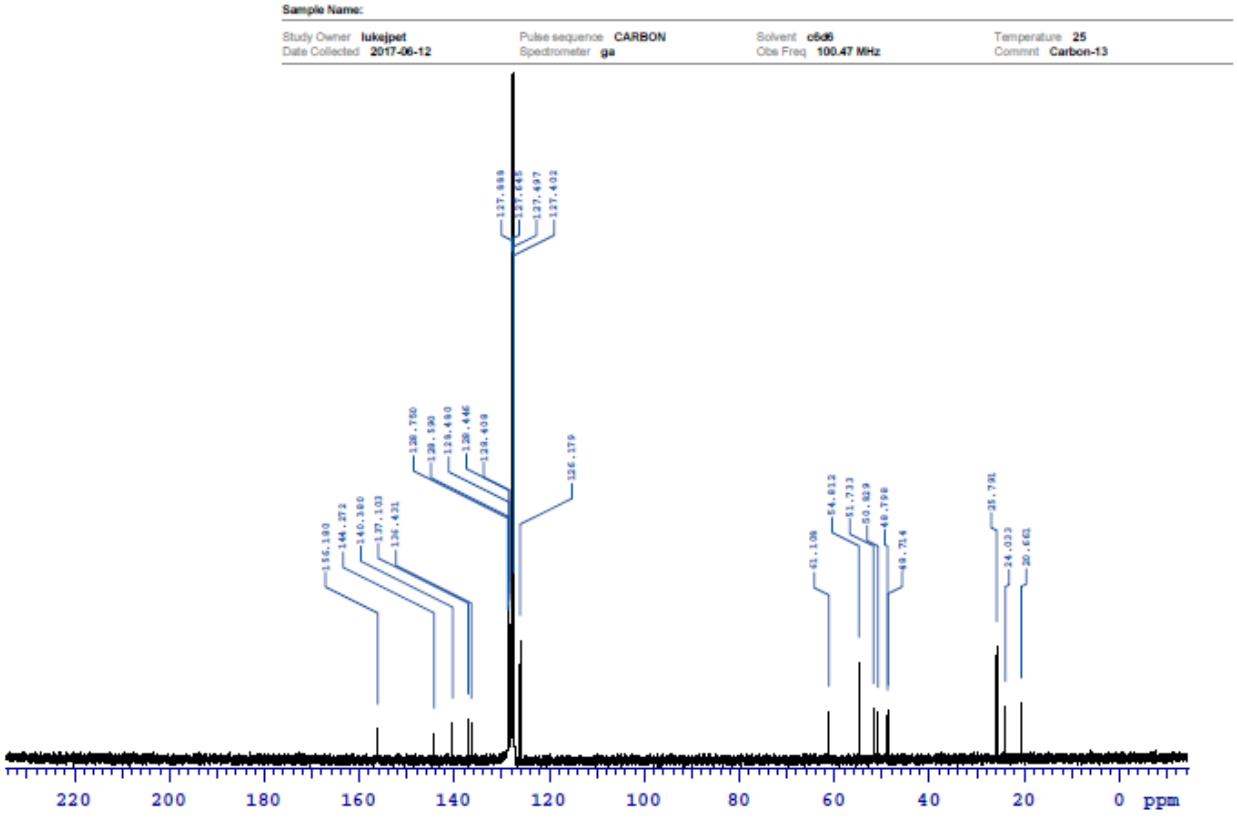


Sample Name:

Study Owner lukejpet	Pulse sequence CARBON	Solvent cdcl3	Temperature 25
Date Collected 2017-02-20	Spectrometer te	Obs Freq 125.76 MHz	Commnt Proton Spectrum

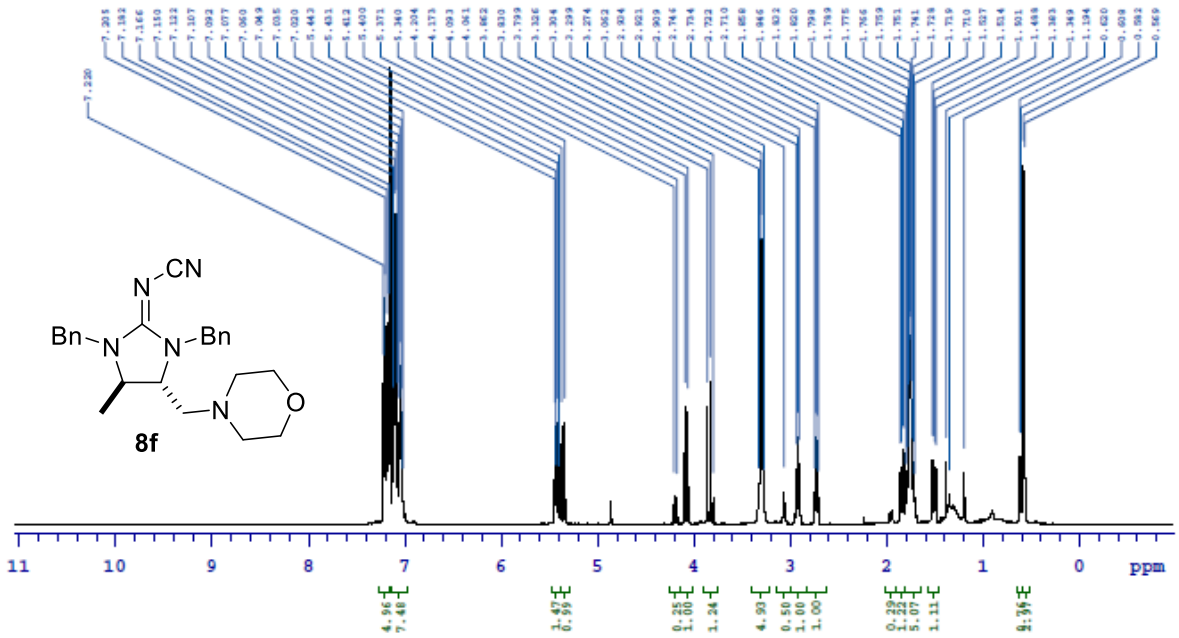



Sample Name:
Study Owner lukejpet
Date Collected 2017-06-12
Pulse sequence PROTON
Spectrometer ga
Solvent c6d6
Obs Freq 399.54 MHz
Temperature 25
Commnt Proton Spectrum
Ts
N
Bn
N
N
Bn
N
8e
11
10
9
8
7
6
5
4
3
2
1
0
ppm


Sample Name:
Study Owner lukejpet
Date Collected 2017-06-12
Pulse sequence CARBON
Spectrometer ga
Solvent c6d6
Obs Freq 100.47 MHz
Temperature 25
Commnt Carbon-13
220
200
180
160
140
120
100
80
60
40
20
0
ppm

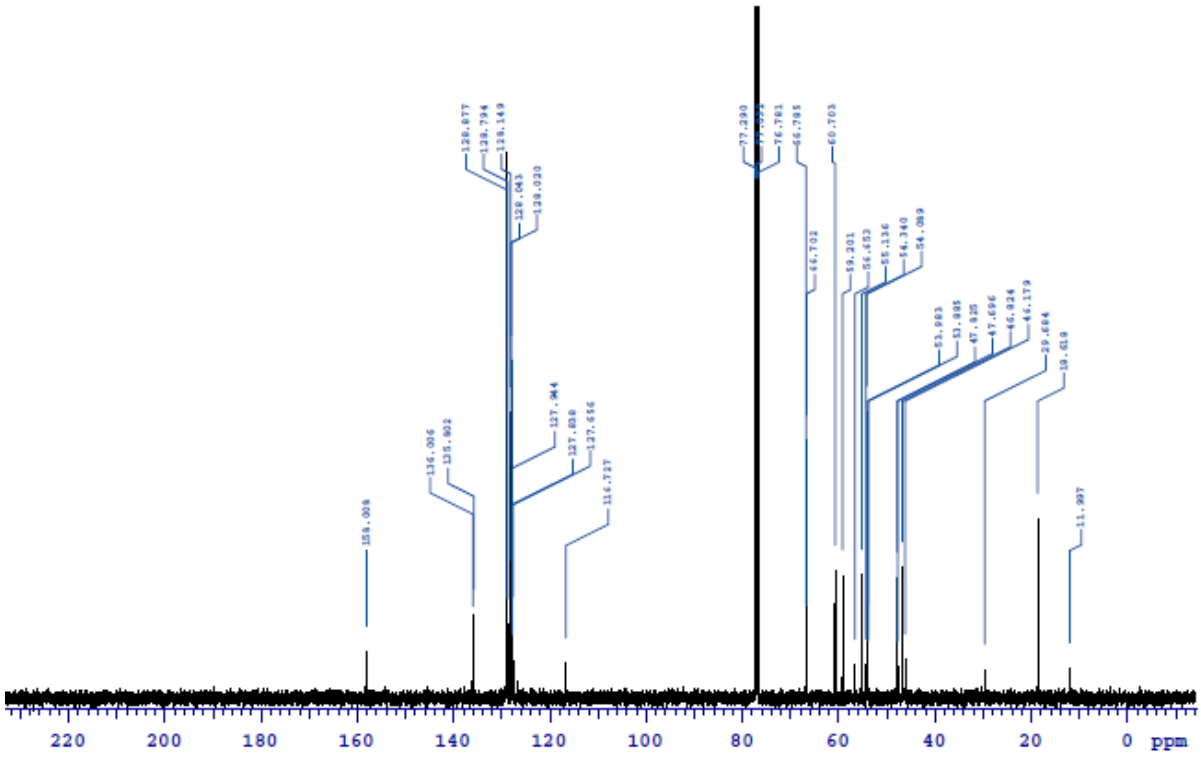
Sample Name:

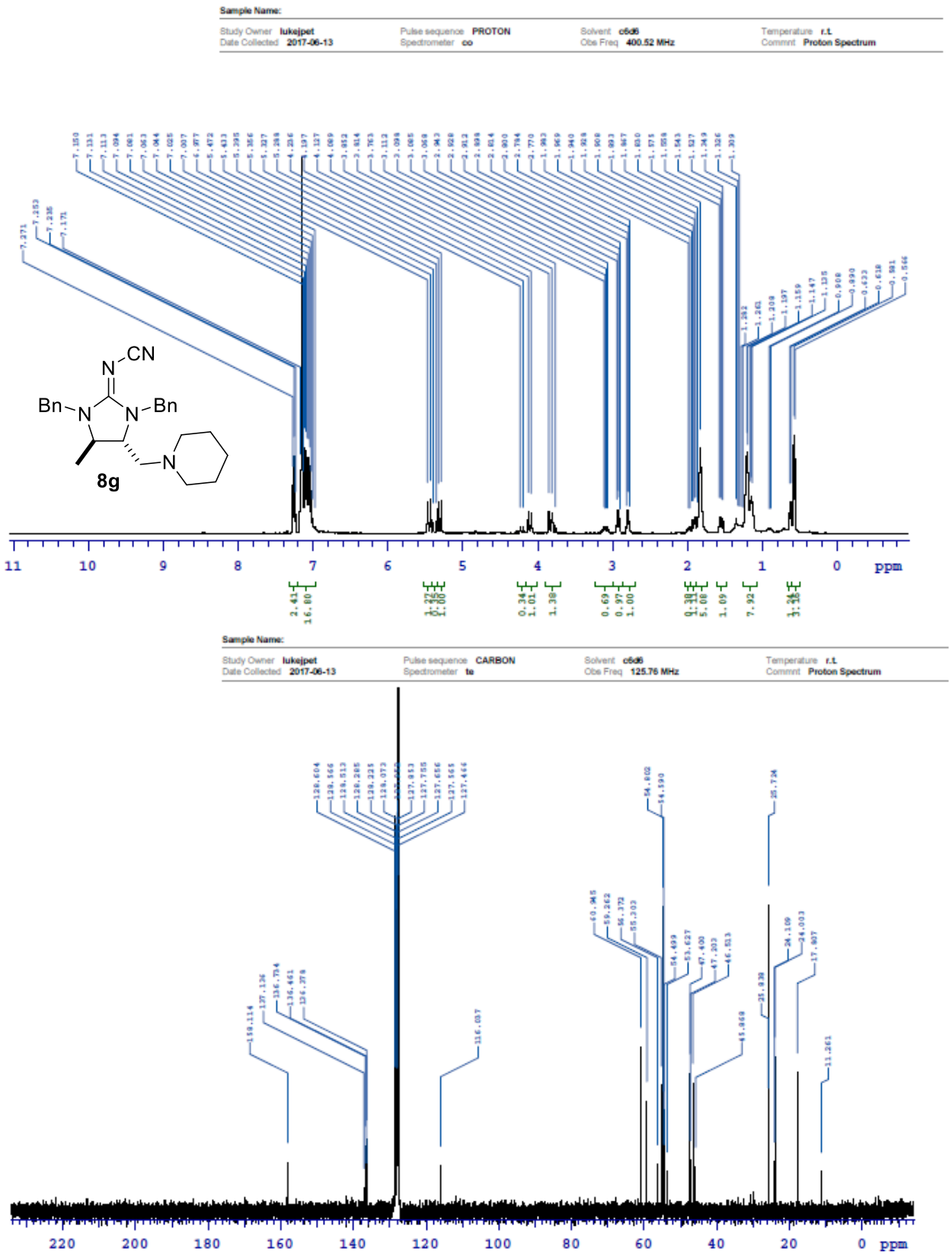
Study Owner lukejpet	Pulse sequence PROTON	Solvent c6d6	Temperature 25
Date Collected 2017-06-27	Spectrometer te	Obs Freq 500.08 MHz	Commnt Proton Spectrum



Sample Name:

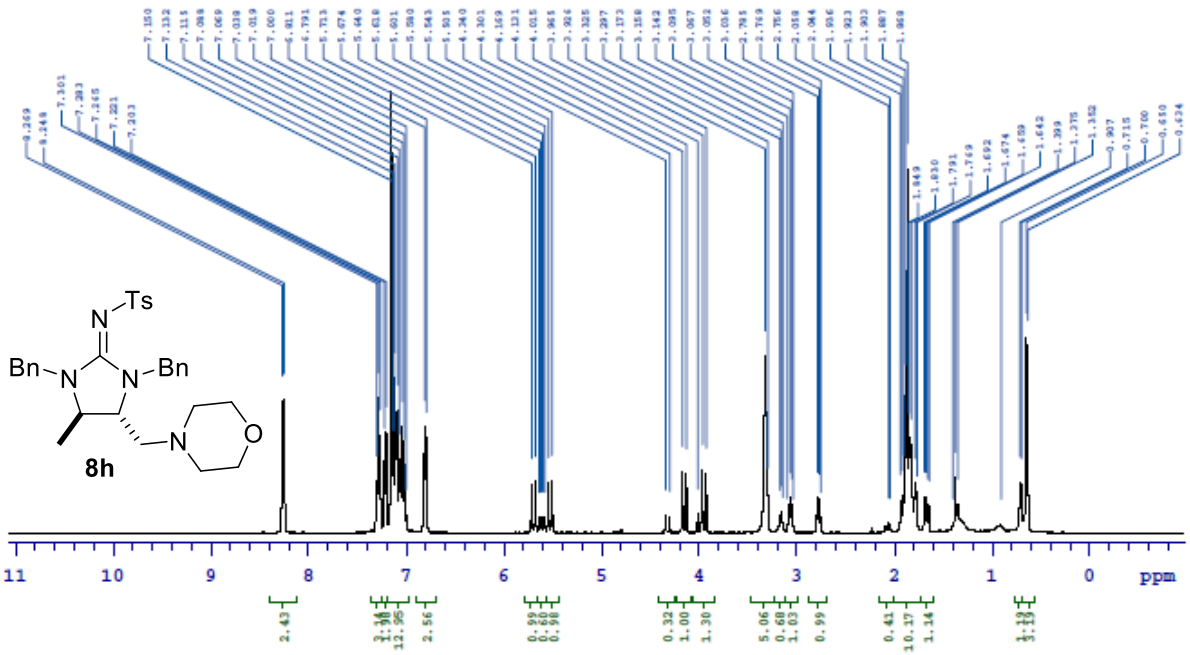
Study Owner lukejpet	Pulse sequence CARBON	Solvent cdcl3	Temperature r.t.
Date Collected 2017-06-29	Spectrometer te	Obs Freq 125.76 MHz	Commnt Proton Spectrum




Sample Name:
Study Owner lukejpet
Date Collected 2017-06-13
Pulse sequence PROTON
Spectrometer co
Solvent c6d6
Obs Freq 400.52 MHz
Temperature r.t.
Commnt Proton Spectrum
N
CN
Bn
N
N
Bn
N
8g
11
10
9
8
7
6
5
4
3
2
1
0
ppm
Sample Name:
Study Owner lukejpet
Date Collected 2017-06-13
Pulse sequence CARBON
Spectrometer te
Solvent c6d6
Obs Freq 125.76 MHz
Temperature r.t.
Commnt Proton Spectrum
220
200
180
160
140
120
100
80
60
40
20
0
ppm

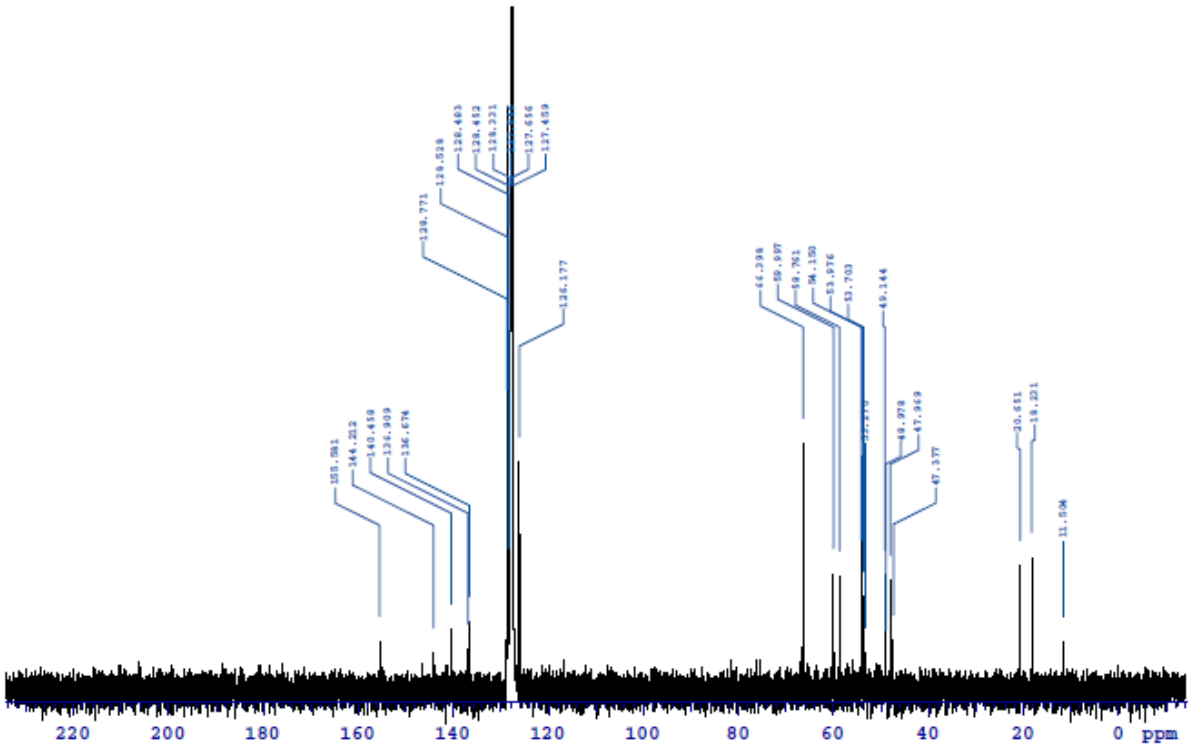
Sample Name:

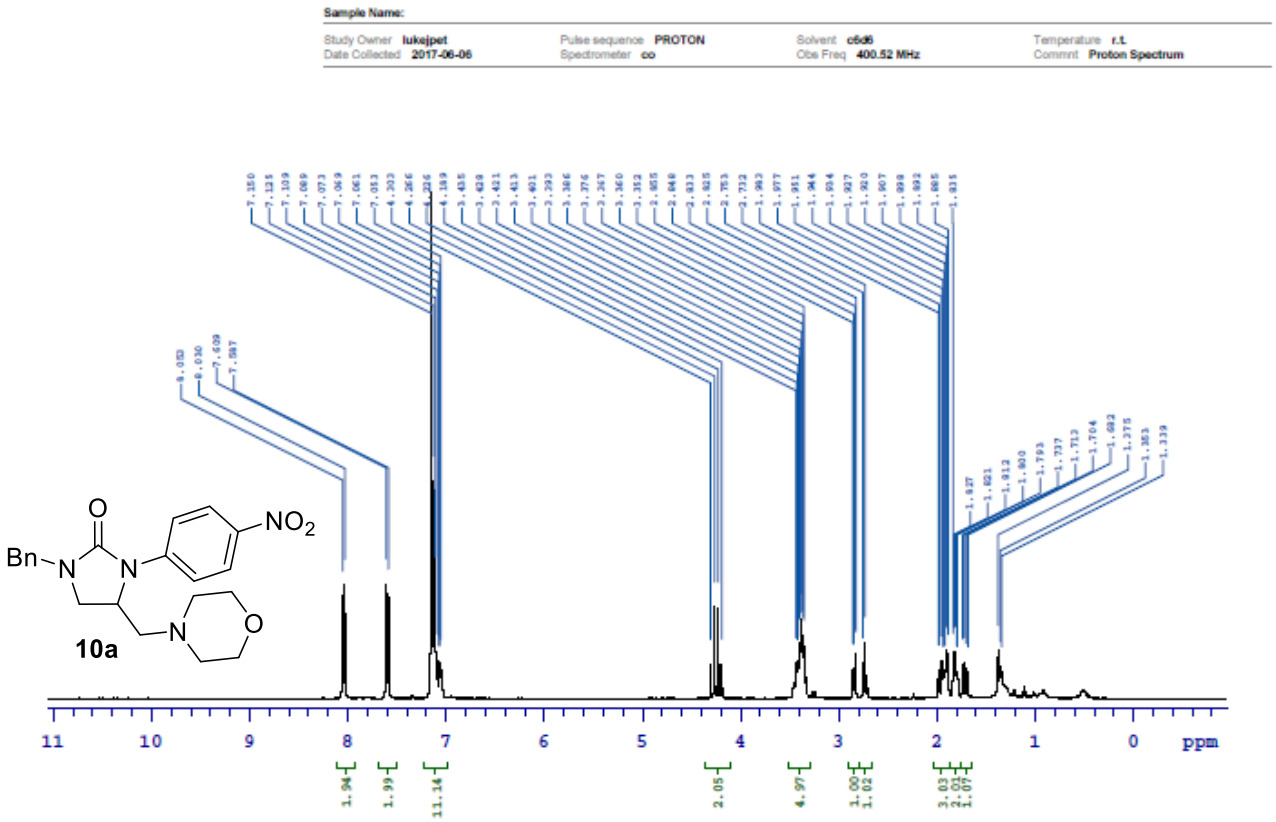
Study Owner lukejpet	Pulse sequence PROTON	Solvent c6d6	Temperature 25
Date Collected 2017-06-28	Spectrometer ga	Obs Freq 399.54 MHz	Commnt Proton Spectrum

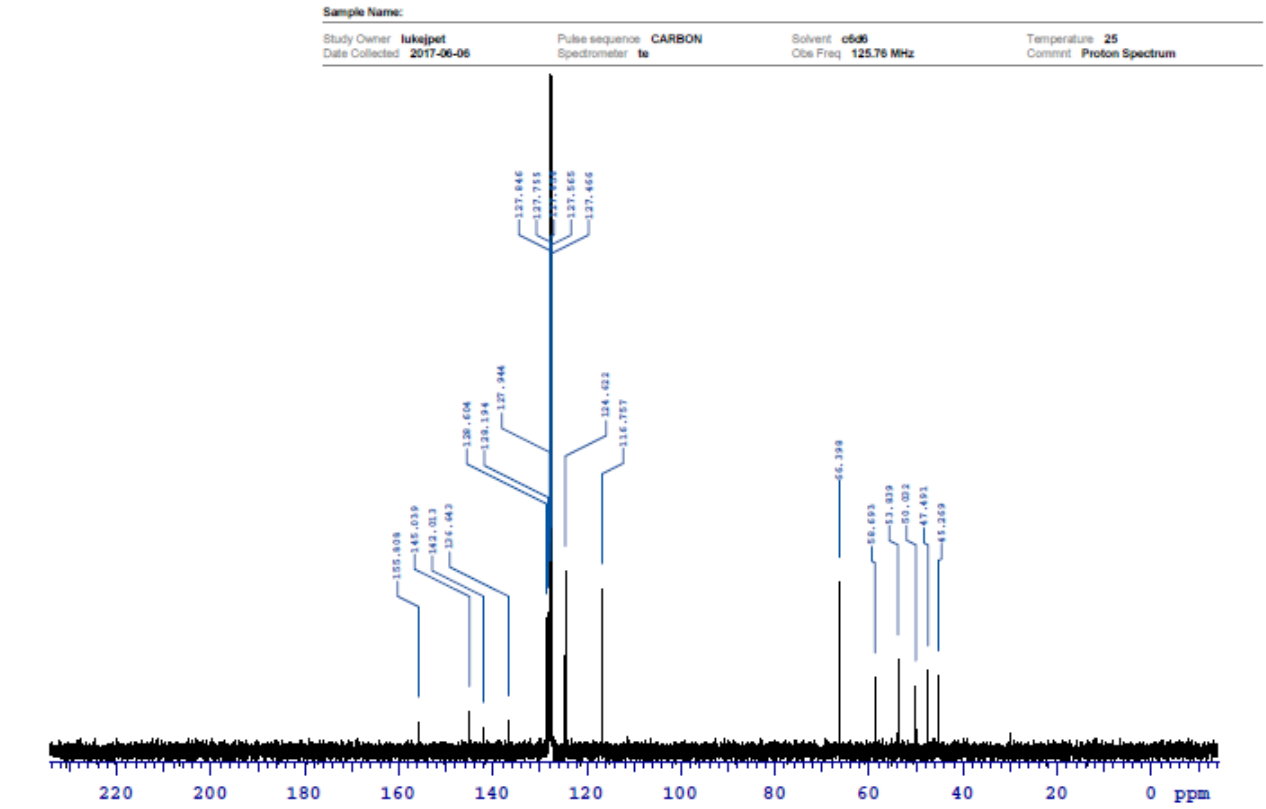


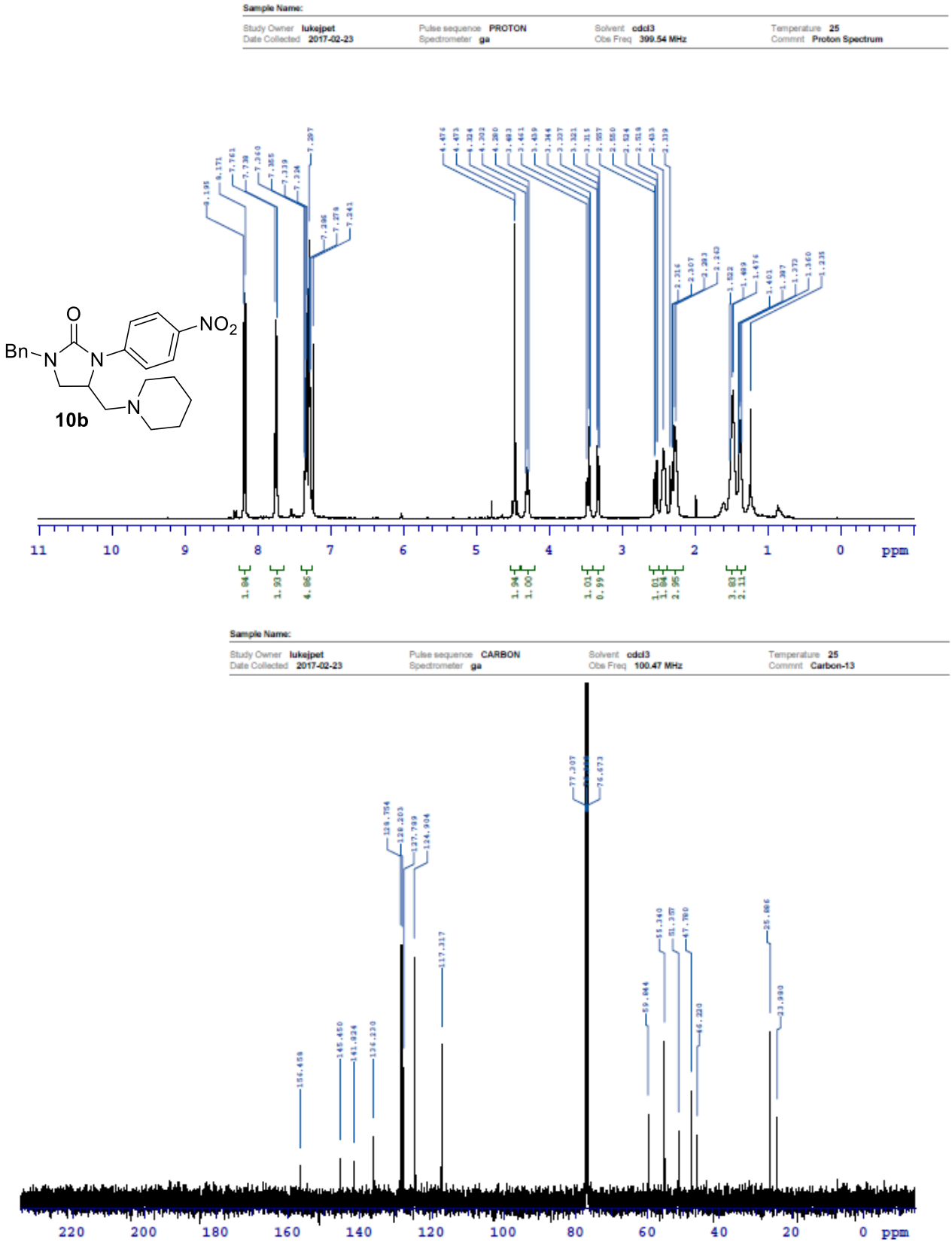
Sample Name:

Study Owner lukejpet	Pulse sequence CARBON	Solvent c6d6	Temperature 25
Date Collected 2017-06-28	Spectrometer te	Obs Freq 125.76 MHz	Commnt Proton Spectrum



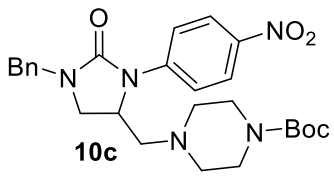

Sample Name:
Study Owner lukejpet
Date Collected 2017-06-06
Pulse sequence PROTON
Spectrometer co
Solvent c6d6
Obs Freq 400.52 MHz
Temperature r.t.
Commnt Proton Spectrum
Bn
N
O
N
NO2
N
O
10a
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.94
1.99
11.14
2.05
4.97
1.00
1.02
3.03
2.01
1.09


Sample Name:
Study Owner lukejpet
Date Collected 2017-06-06
Pulse sequence CARBON
Spectrometer te
Solvent c6d6
Obs Freq 125.76 MHz
Temperature 25
Commnt Proton Spectrum
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Sample Name:
Study Owner lukejpet
Date Collected 2017-02-23
Pulse sequence PROTON
Spectrometer ga
Solvent cdcl3
Obs Freq 399.54 MHz
Temperature 25
Commnt Proton Spectrum
Bn
N
O
N
NO2
N
10b
11 10 9 8 7 6 5 4 3 2 1 0 ppm
Sample Name:
Study Owner lukejpet
Date Collected 2017-02-23
Pulse sequence CARBON
Spectrometer ga
Solvent cdcl3
Obs Freq 100.47 MHz
Temperature 25
Commnt Carbon-13
220 200 180 160 140 120 100 80 60 40 20 0 ppm

Sample Name:

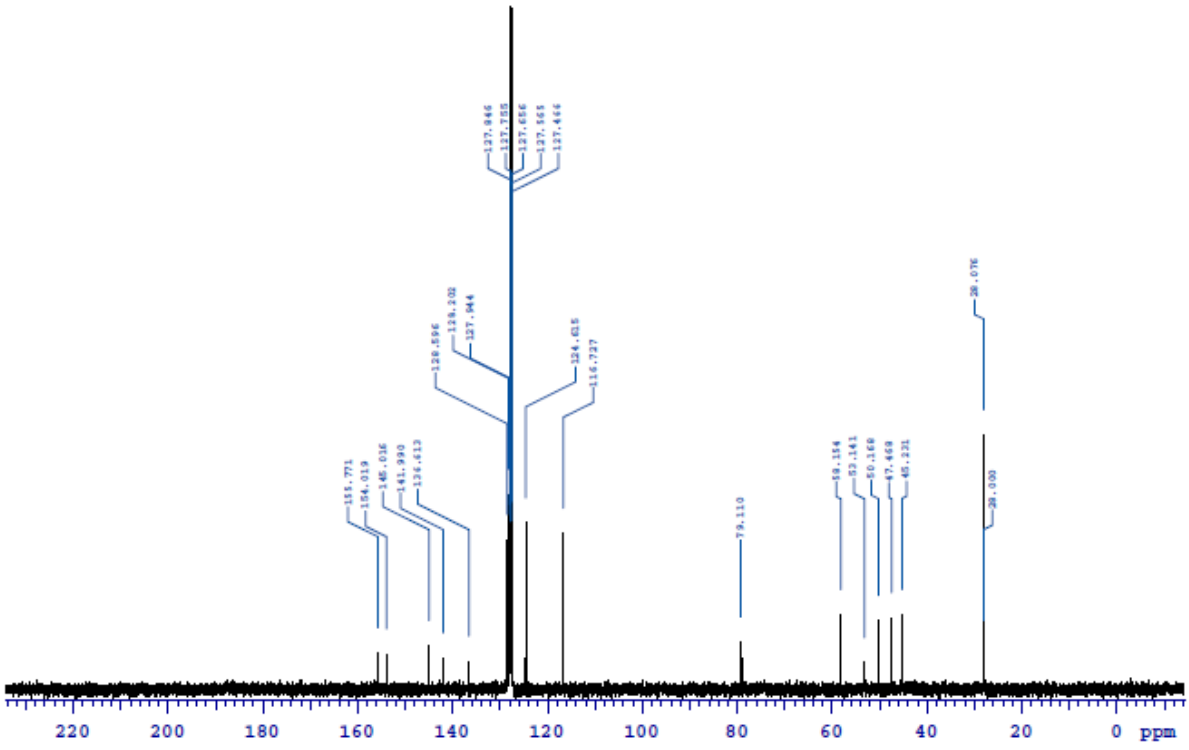
Study Owner lukejpet	Pulse sequence PROTON	Solvent c6d6	Temperature 25
Date Collected 2017-06-12	Spectrometer te	Obs Freq 500.08 MHz	Commnt Proton Spectrum

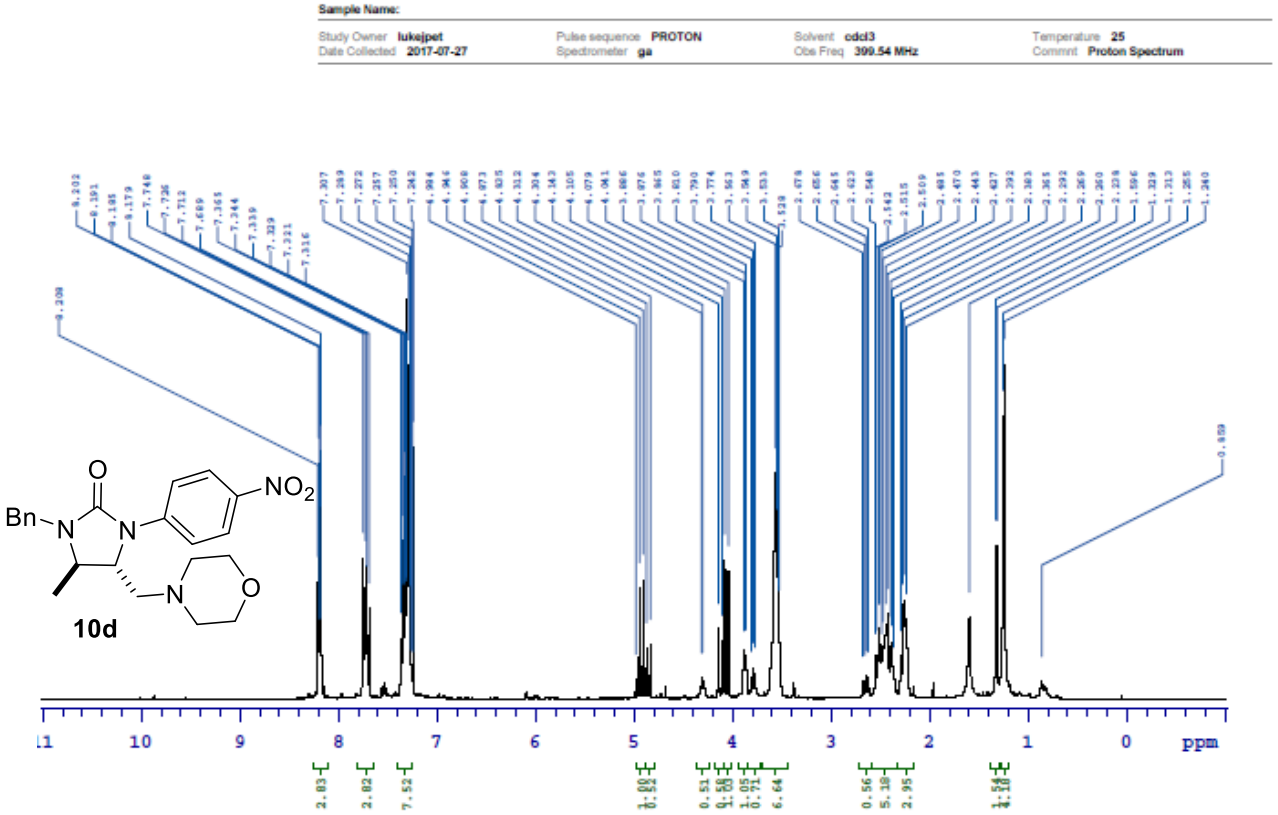


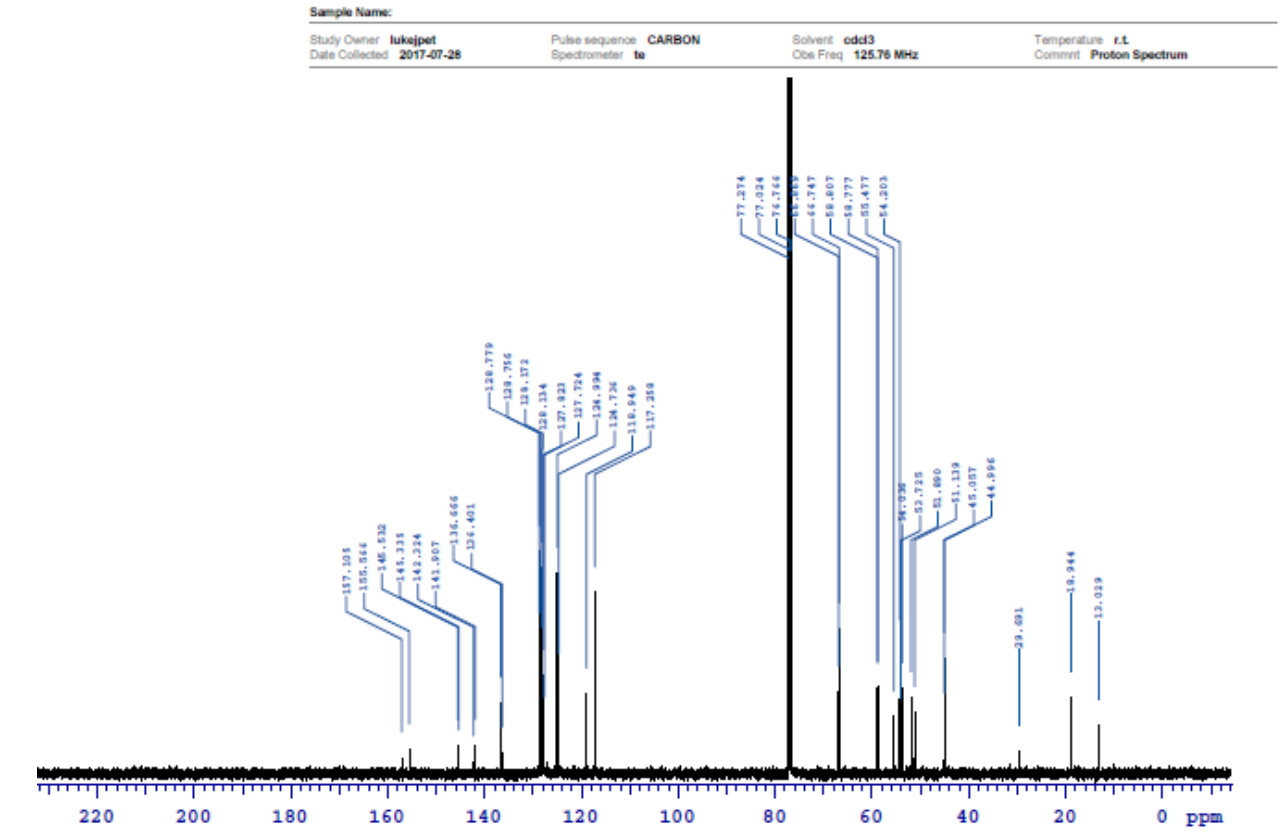
10c

Sample Name:

Study Owner lukejpet	Pulse sequence CARBON	Solvent c6d6	Temperature 25
Date Collected 2017-06-12	Spectrometer te	Obs Freq 125.76 MHz	Commnt Proton Spectrum

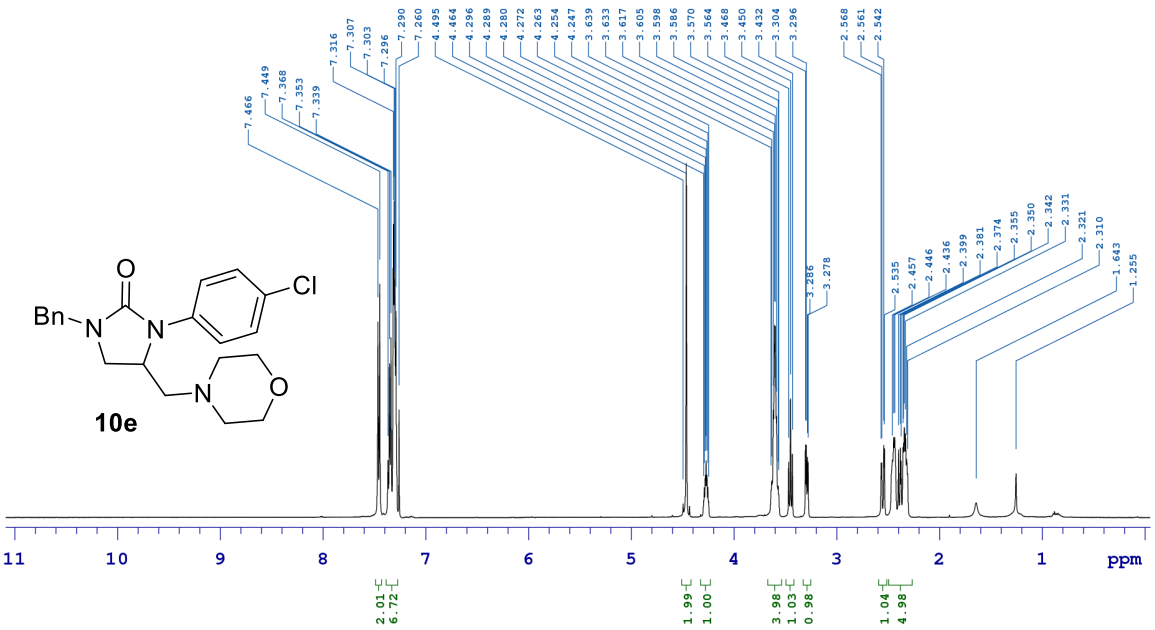



Sample Name:
Study Owner lukejpet
Date Collected 2017-07-27
Pulse sequence PROTON
Spectrometer ga
Solvent cdcl3
Obs Freq 399.54 MHz
Temperature 25
Commnt Proton Spectrum
Bn
N
O
N
NO2
N
O
10d
ppm


Sample Name:
Study Owner lukejpet
Date Collected 2017-07-28
Pulse sequence CARBON
Spectrometer te
Solvent cdcl3
Obs Freq 125.76 MHz
Temperature r.t.
Commnt Proton Spectrum
ppm

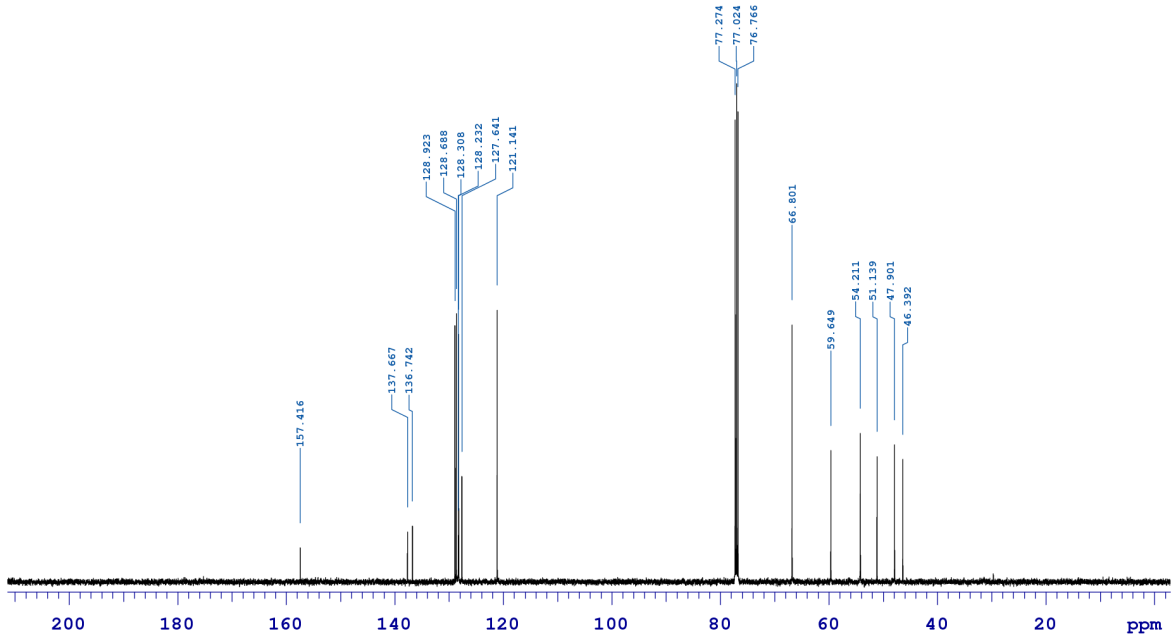
Sample Name:

Study Owner **jakirsch**	Pulse sequence **PROTON**	Solvent **cdcl3**	Temperature **23**
Date Collected **2018-05-21**	Spectrometer **te**	Obs Freq **500.08 MHz**	Commnt **STANDARD PHOSPHORUS PARAMETERS**



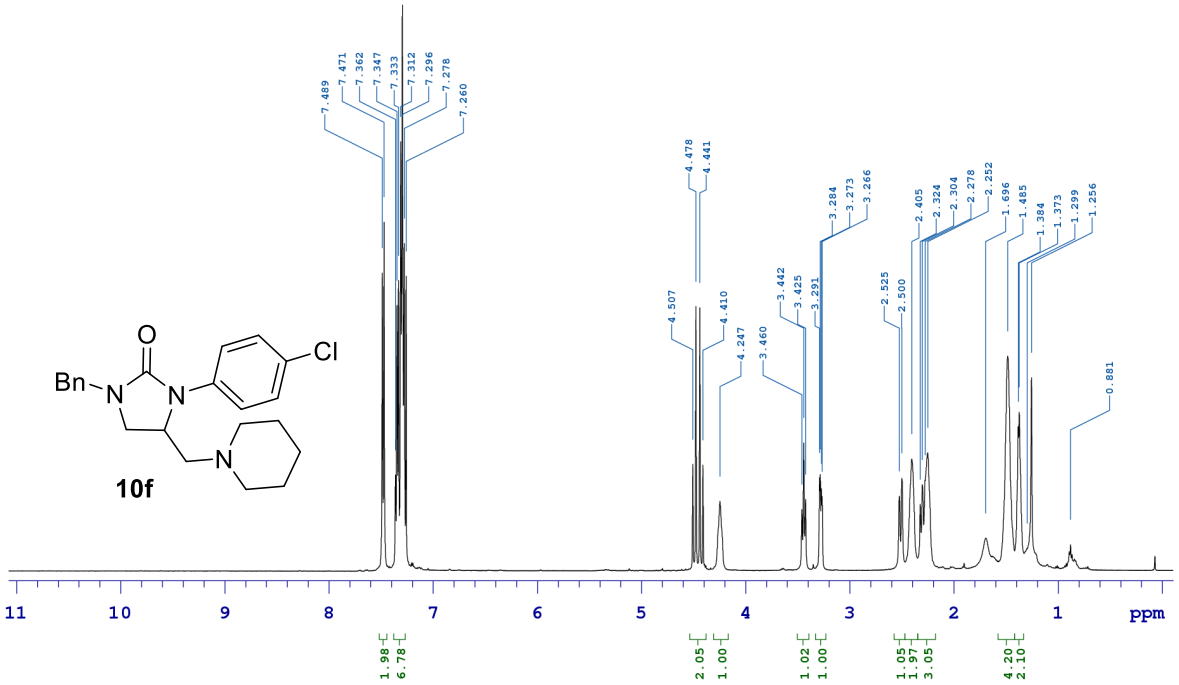
Sample Name:

Study Owner **jakirsch**	Pulse sequence **CARBON**	Solvent **cdcl3**	Temperature **23**
Date Collected **2018-05-21**	Spectrometer **te**	Obs Freq **125.76 MHz**	Commnt **STANDARD PHOSPHORUS PARAMETERS**



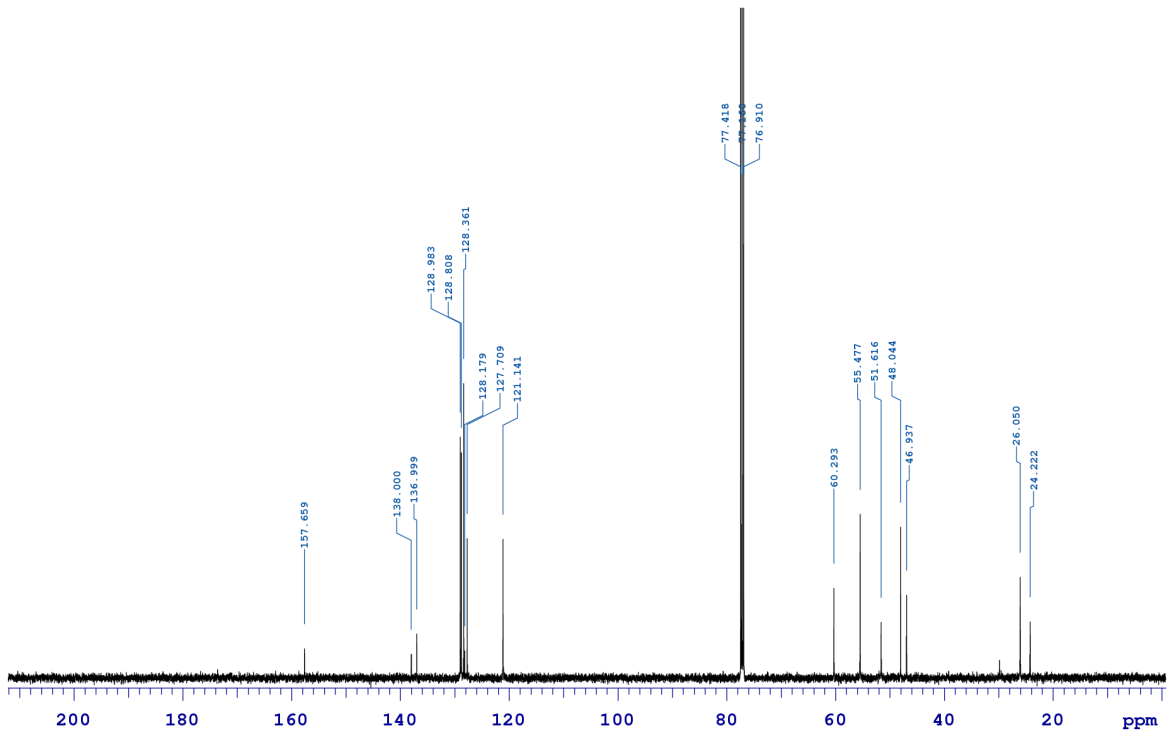
Sample Name:

Study Owner **jakirsch**	Pulse sequence **PROTON**	Solvent **cdcl3**	Temperature **25**
Date Collected **2018-05-29**	Spectrometer **te**	Obs Freq **500.08 MHz**	Commnt **STANDARD PHOSPHORUS PARAMETERS**



Sample Name:

Study Owner **jakirsch**	Pulse sequence **CARBON**	Solvent **cdcl3**	Temperature **25**
Date Collected **2018-05-29**	Spectrometer **te**	Obs Freq **125.76 MHz**	Commnt **STANDARD PHOSPHORUS PARAMETERS**



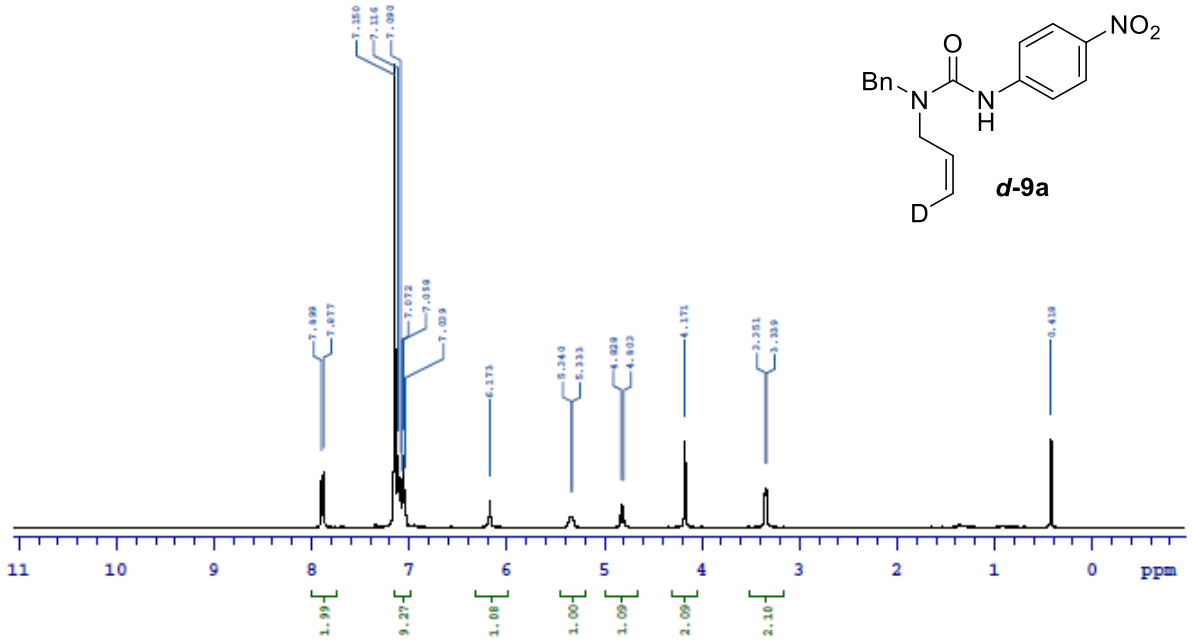
Sample Name:

Study Owner lukejpet
Date Collected 2017-02-28

Pulse sequence PROTON
Spectrometer co

Solvent c6d6
Obs Freq 400.52 MHz

Temperature r.t.
Commnt Proton Spectrum



***d*-9a**

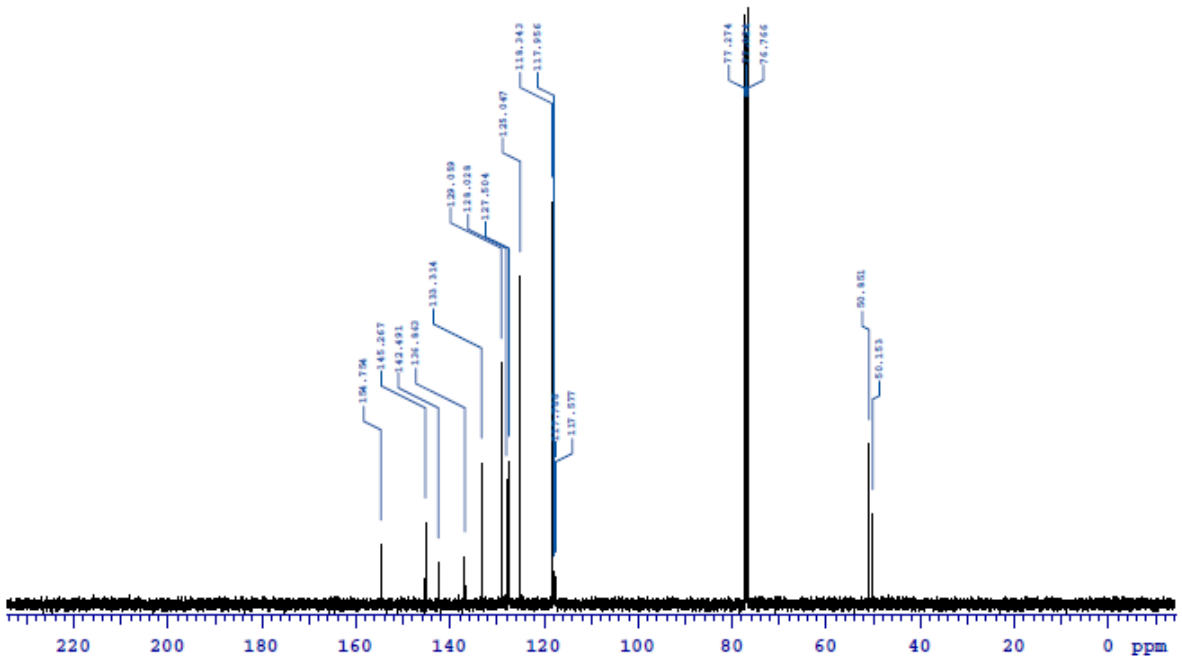
Sample Name:

Study Owner lukejpet
Date Collected 2017-06-29

Pulse sequence CARBON
Spectrometer te

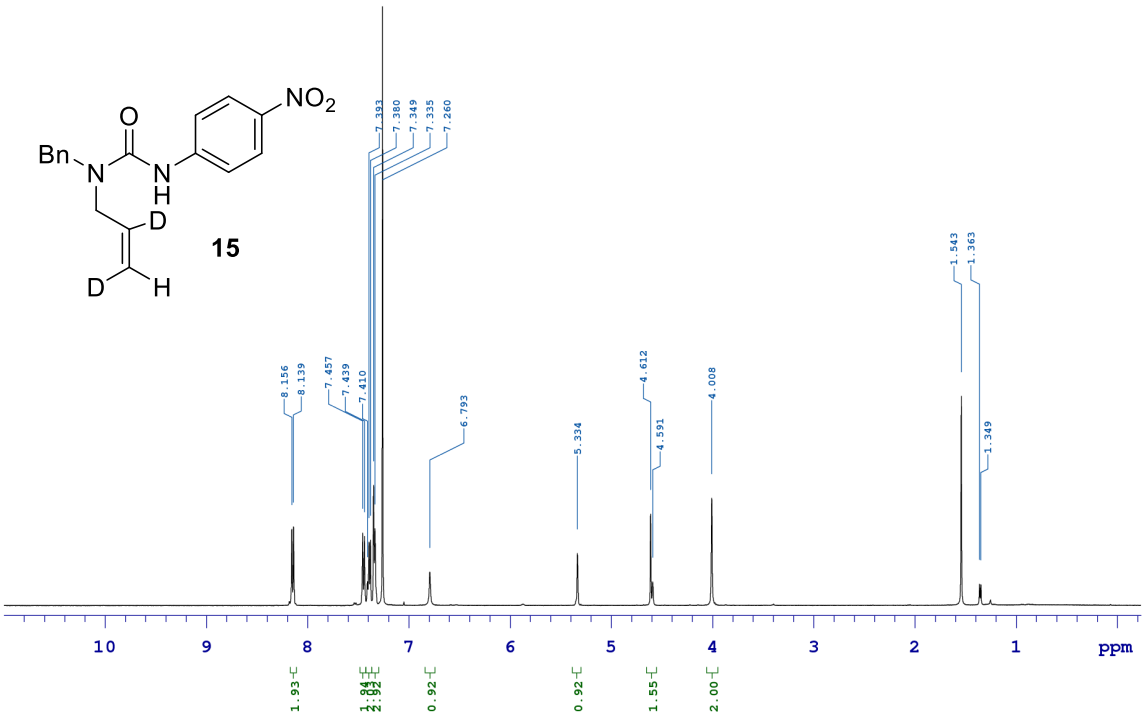
Solvent cdcl3
Obs Freq 125.76 MHz

Temperature r.t.
Commnt Proton Spectrum



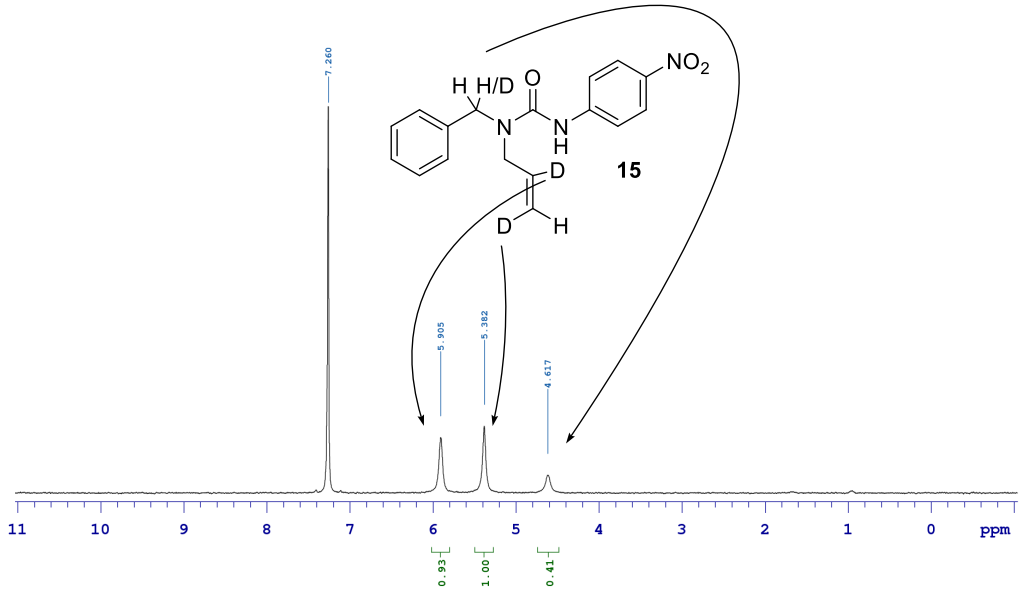
Sample Name:

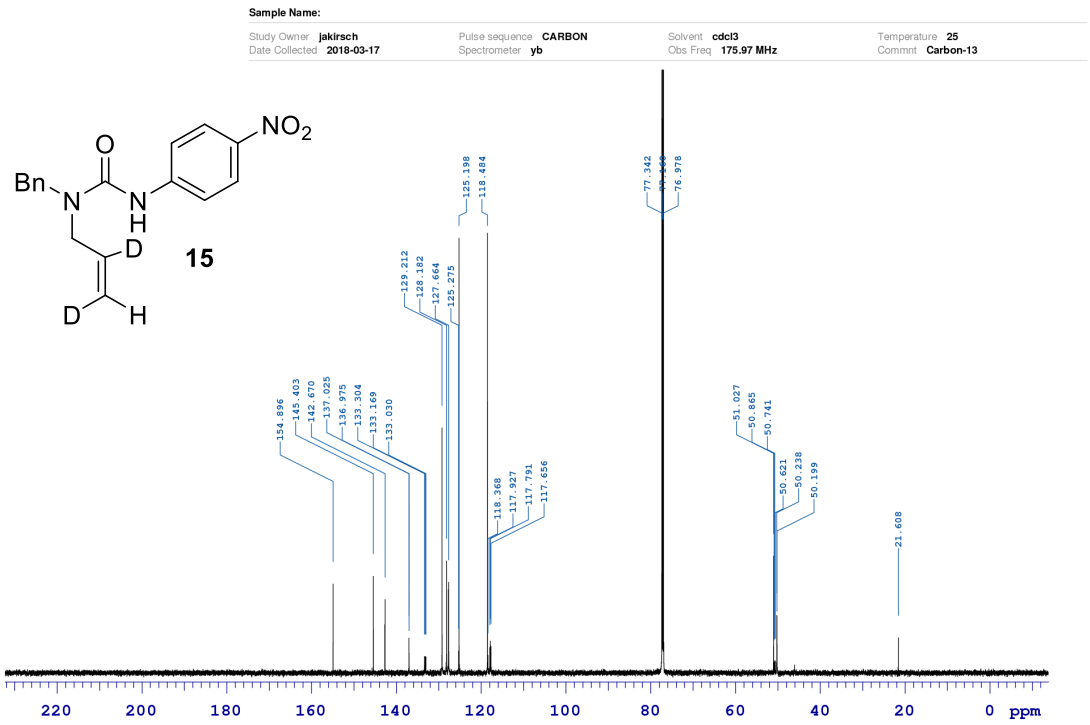
Study Owner jakirsch	Pulse sequence PROTON	Solvent cdcl3	Temperature r.t.
Date Collected 2018-02-12	Spectrometer te	Obs Freq 500.08 MHz	Commnt STANDARD PHOSPHORUS PARAMETERS



Sample Name:

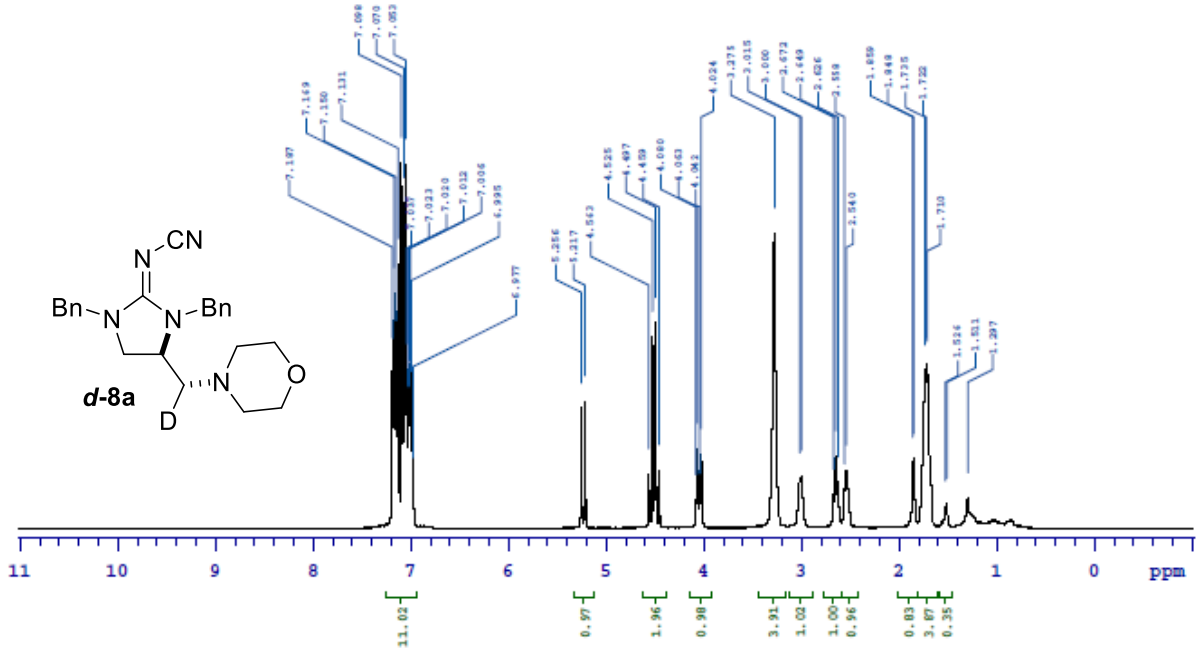
Study Owner jakirsch	Pulse sequence s2pul	Solvent cdcl3	Temperature 25
Date Collected 2018-03-14	Spectrometer yb	Obs Freq 107.42 MHz	Commnt Deuterium (using lock channel)




Sample Name:
Study Owner jakirsch
Date Collected 2018-03-17
Pulse sequence CARBON
Spectrometer yb
Solvent cdcl3
Obs Freq 175.97 MHz
Temperature 25
Commnt Carbon-13
Bn
N
O
N
H
D
D
H
NO2
15
154.896
145.403
142.670
137.025
136.975
133.304
133.169
133.030
129.212
128.182
127.664
125.275
125.198
118.484
118.368
117.927
117.791
117.656
77.342
76.978
51.027
50.865
50.741
50.621
50.238
50.199
21.608
220
200
180
160
140
120
100
80
60
40
20
0
ppm

Sample Name:

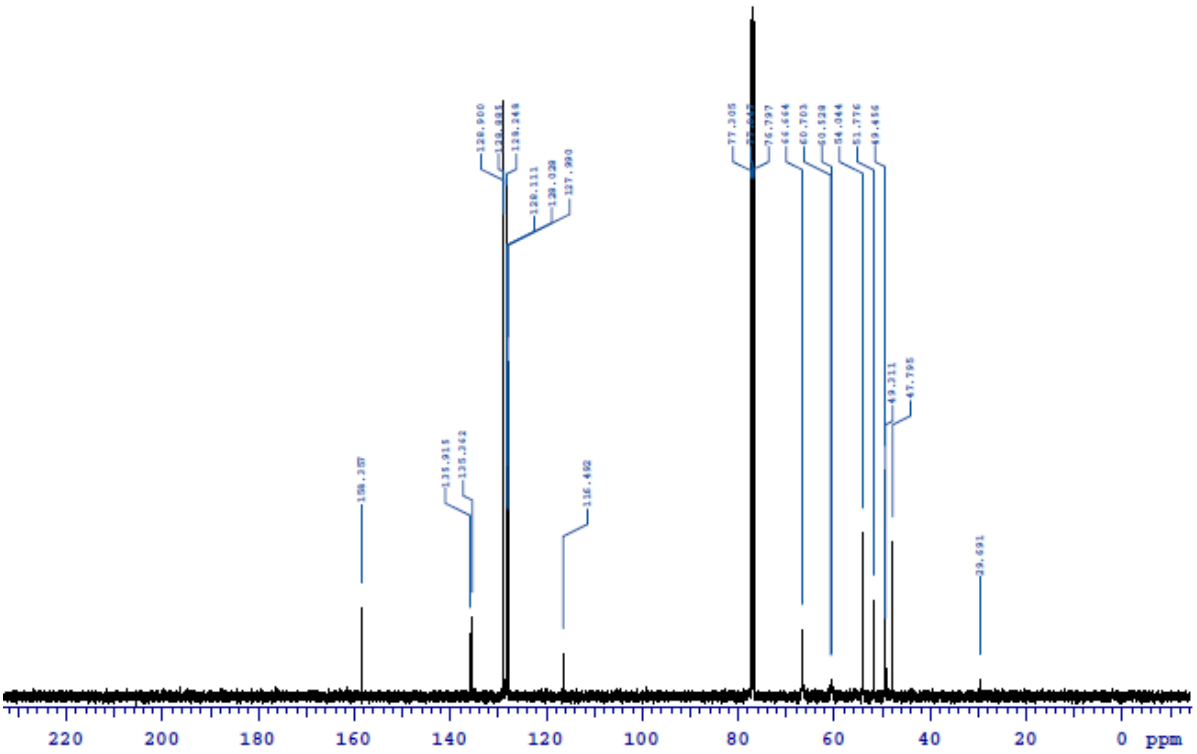
Study Owner lukejpet	Pulse sequence PROTON	Solvent c6d6	Temperature 25
Date Collected 2017-05-17	Spectrometer ga	Obs Freq 399.54 MHz	Commnt Proton Spectrum



d-8a

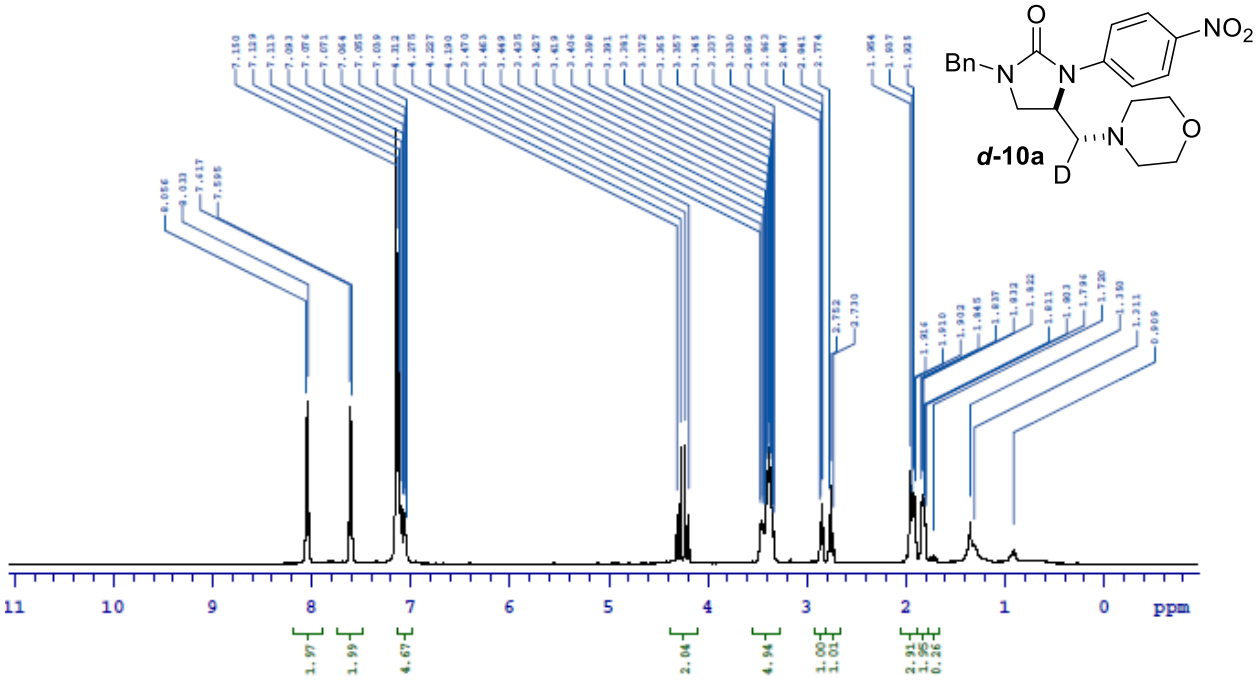
Sample Name:

Study Owner lukejpet	Pulse sequence CARBON	Solvent cdcl3	Temperature r.t.
Date Collected 2017-06-29	Spectrometer te	Obs Freq 125.76 MHz	Commnt Proton Spectrum



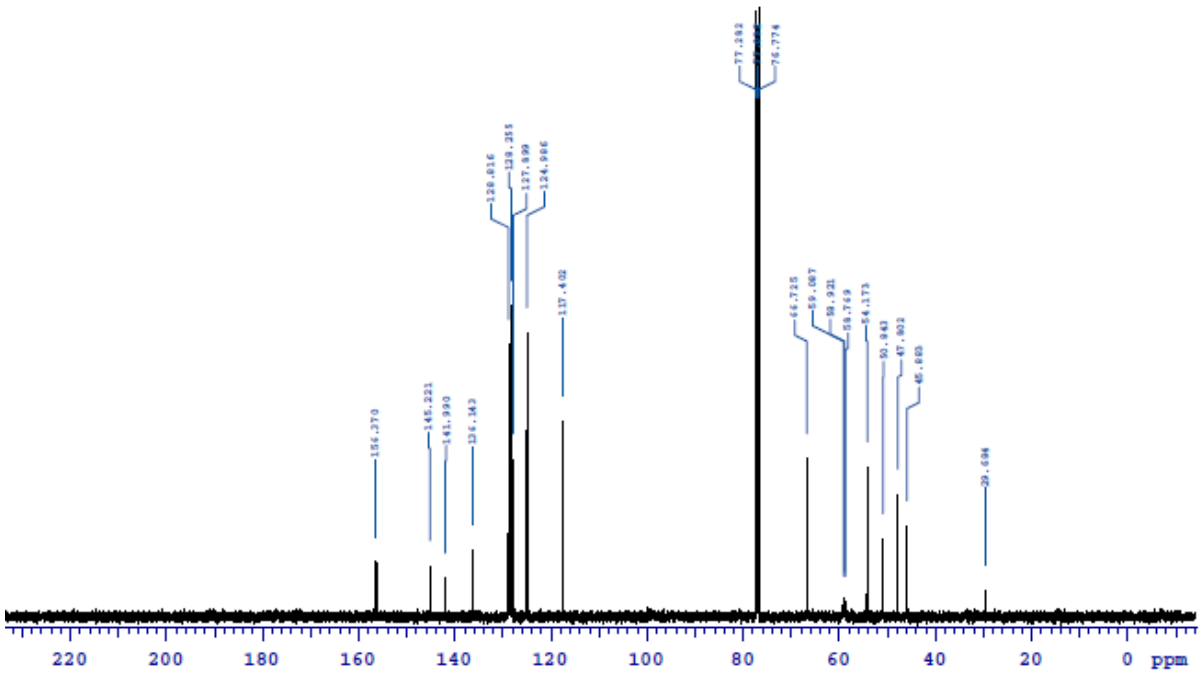
Sample Name:

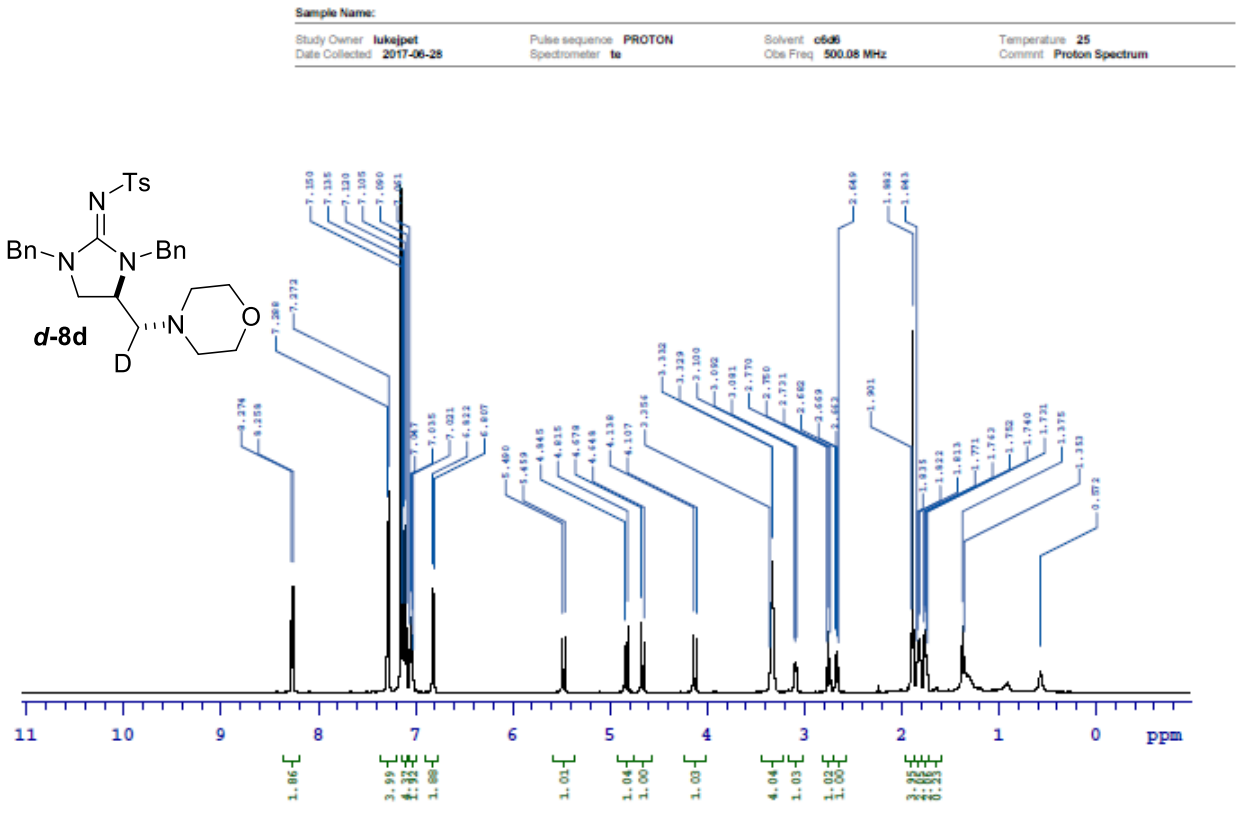
Study Owner lukejpet	Pulse sequence PROTON	Solvent c6d6	Temperature r.t.
Date Collected 2017-06-13	Spectrometer co	Obs Freq 400.52 MHz	Commnt Proton Spectrum

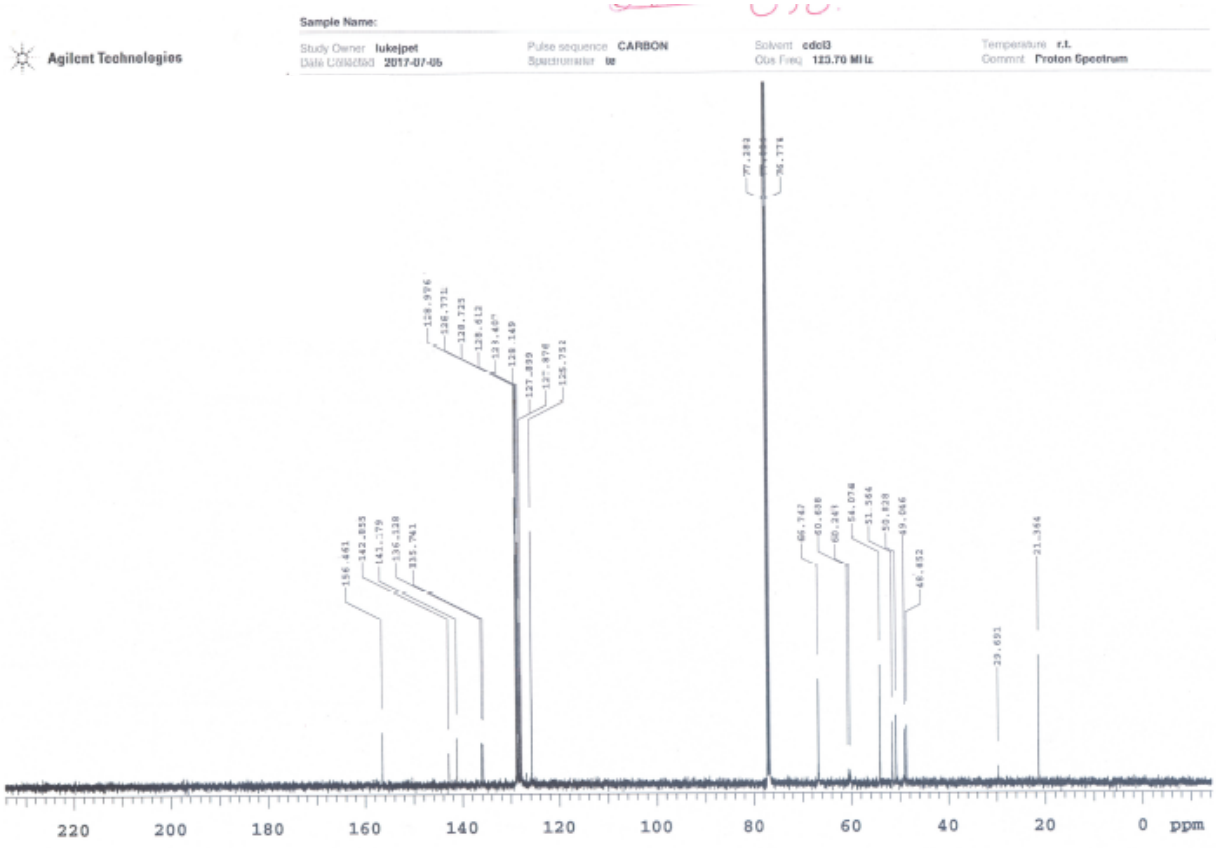


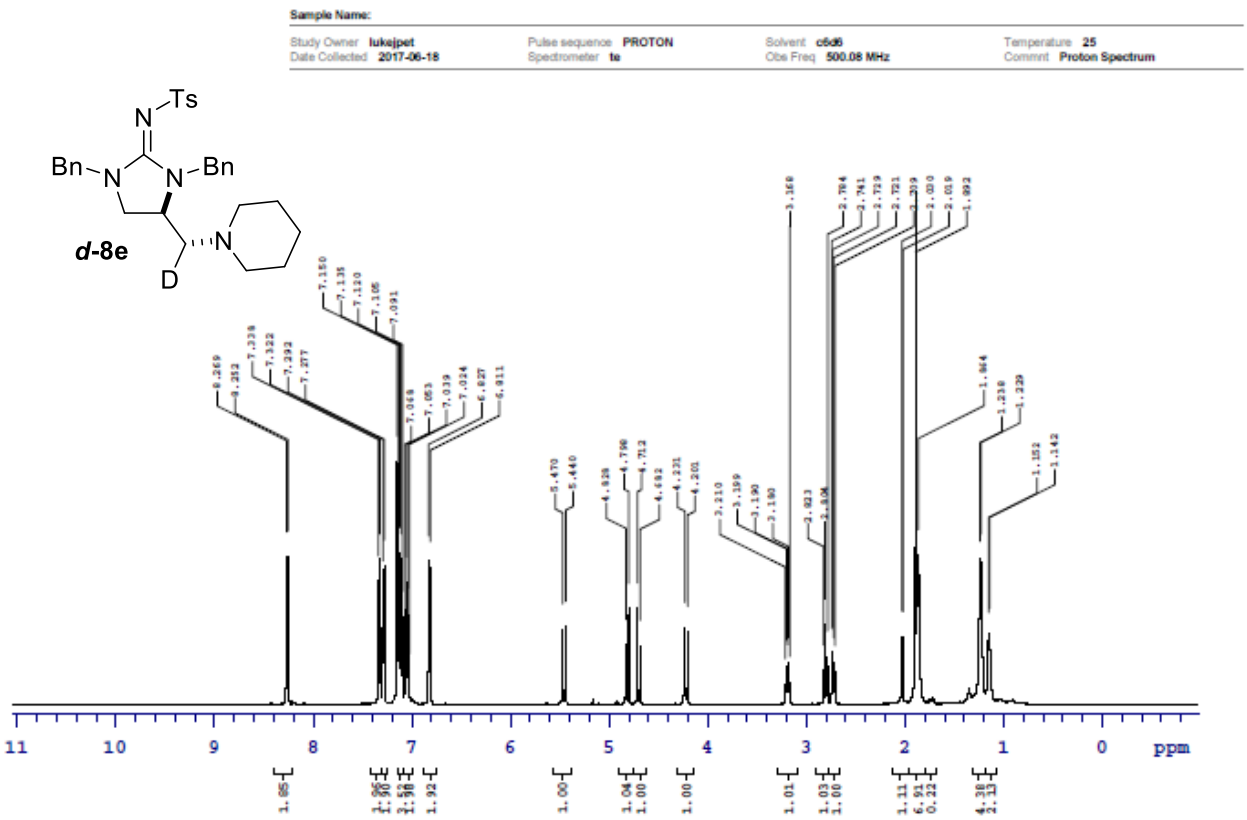
Sample Name:

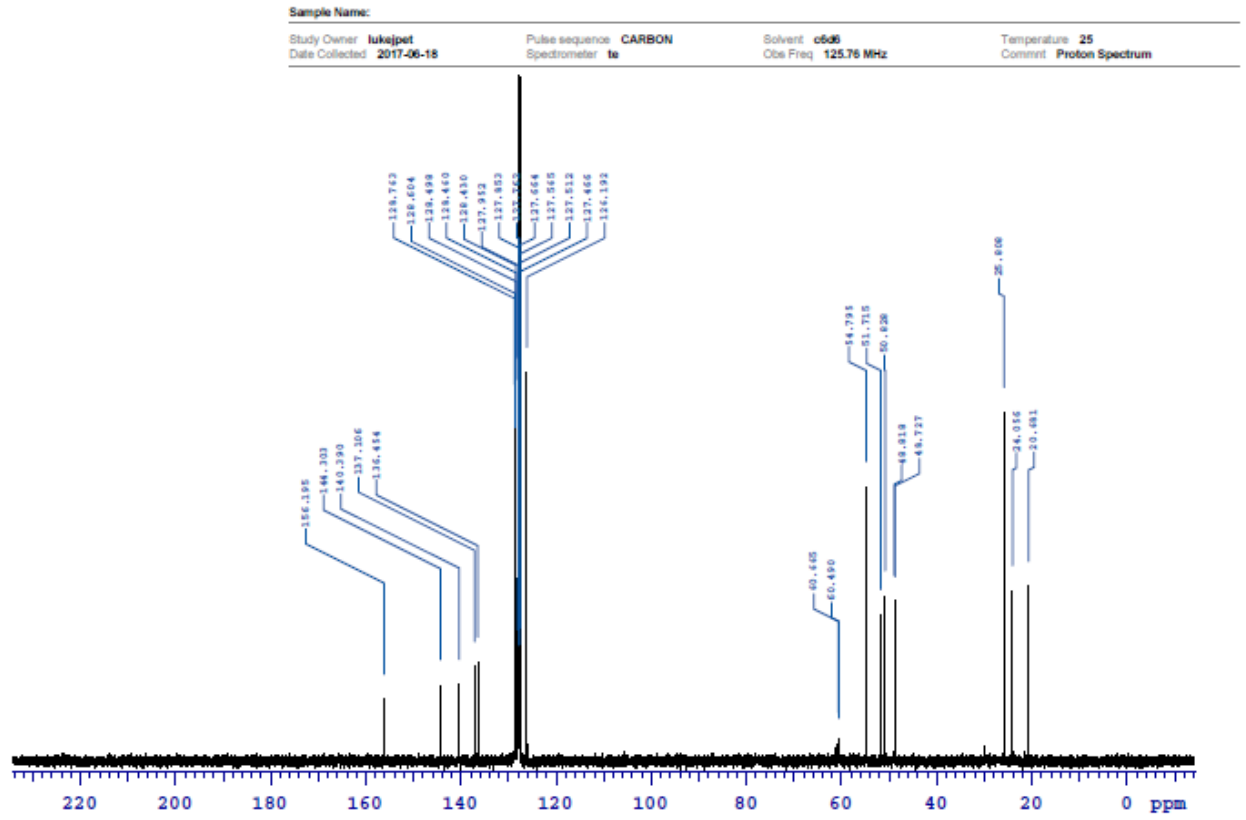
Study Owner lukejpet	Pulse sequence CARBON	Solvent cdcl3	Temperature r.t.
Date Collected 2017-06-29	Spectrometer te	Obs Freq 125.76 MHz	Commnt Proton Spectrum

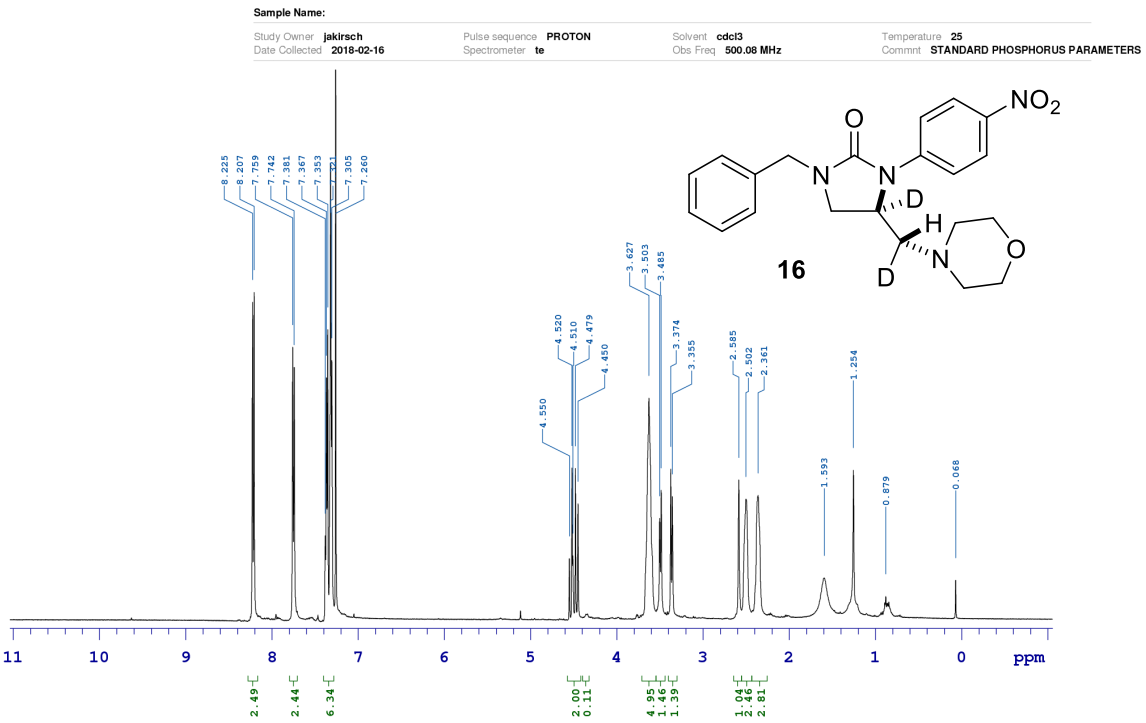


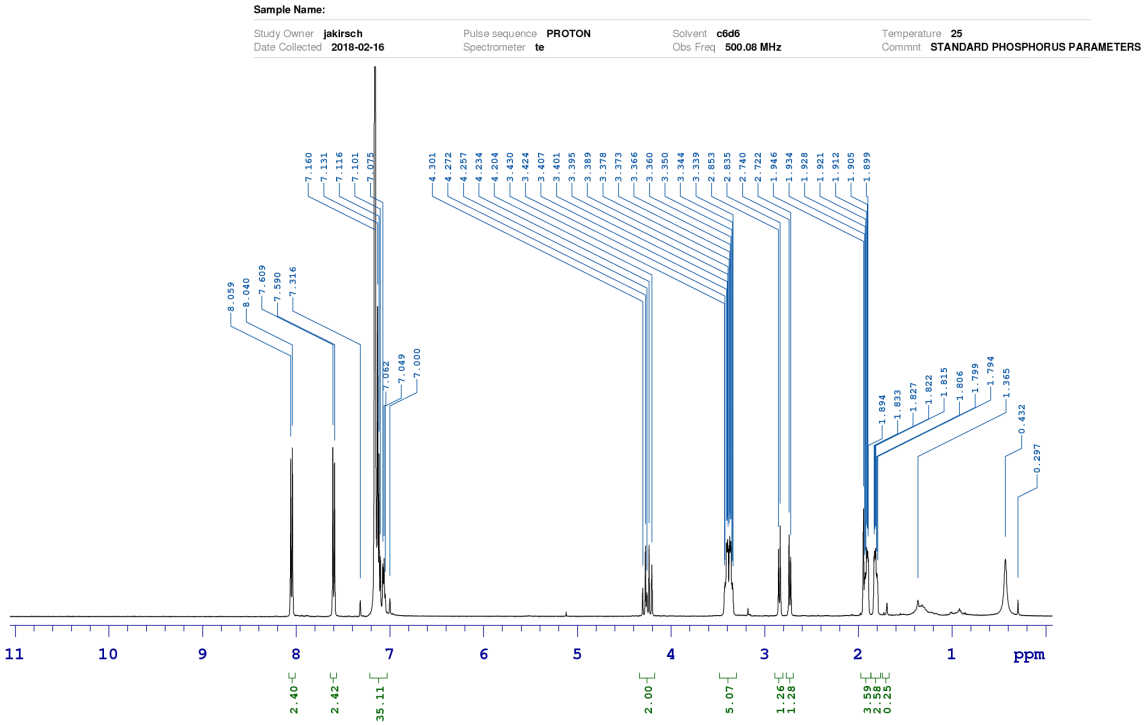

Sample Name:
Study Owner lukejpet
Date Collected 2017-06-28
Pulse sequence PROTON
Spectrometer te
Solvent c6d6
Obs Freq 500.08 MHz
Temperature 25
Commnt Proton Spectrum
Ts
N
Bn
N
N
Bn
N
O
D
d-8d
ppm

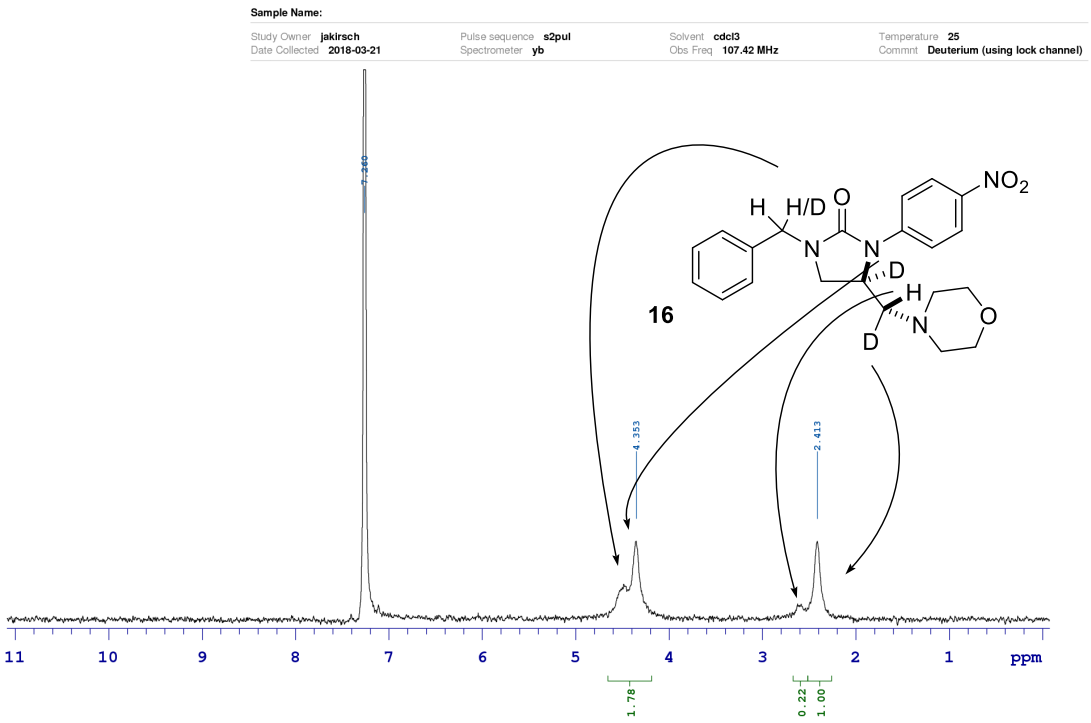

Agilent Technologies
Sample Name:
Study Owner lukejpet
Date Collected 2017-07-05
Pulse sequence CARBON
Spectrometer te
Solvent cdcl3
Obs Freq 123.76 MHz
Temperature r.t.
Commnt Proton Spectrum
ppm

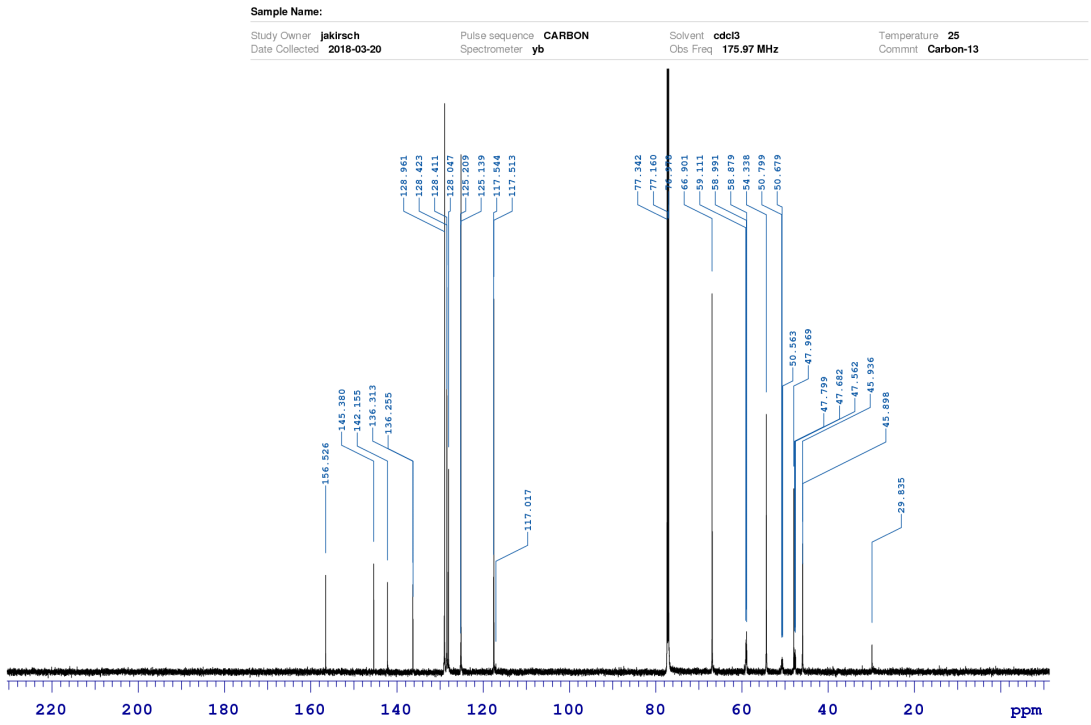

Sample Name:
Study Owner lukejpet
Date Collected 2017-06-18
Pulse sequence PROTON
Spectrometer te
Solvent c6d6
Obs Freq 500.08 MHz
Temperature 25
Commnt Proton Spectrum
Ts
N
Bn
N
N
Bn
N
D
d-8e
ppm


Sample Name:
Study Owner lukejpet
Date Collected 2017-06-18
Pulse sequence CARBON
Spectrometer te
Solvent c6d6
Obs Freq 125.76 MHz
Temperature 25
Commnt Proton Spectrum
ppm


Sample Name:
Study Owner jakirsch
Date Collected 2018-02-16
Pulse sequence PROTON
Spectrometer te
Solvent cdcl3
Obs Freq 500.08 MHz
Temperature 25
Commnt STANDARD PHOSPHORUS PARAMETERS
NO2
O
N
N
D
H
N
O
D
16
8.225
8.207
7.759
7.742
7.381
7.367
7.353
7.321
7.305
7.260
4.550
4.520
4.510
4.479
4.450
3.627
3.503
3.485
3.374
3.355
2.585
2.502
2.361
1.593
1.254
0.879
0.068
11 10 9 8 7 6 5 4 3 2 1 0 ppm
2.49
2.44
6.34
2.00
0.11
4.95
1.46
1.39
1.04
2.46
2.81


Sample Name:
Study Owner jakirsch
Date Collected 2018-02-16
Pulse sequence PROTON
Spectrometer te
Solvent c6d6
Obs Freq 500.08 MHz
Temperature 25
Commnt STANDARD PHOSPHORUS PARAMETERS
8.059
8.040
7.609
7.590
7.316
7.160
7.131
7.116
7.101
7.075
7.062
7.049
7.000
4.301
4.272
4.257
4.234
4.204
3.430
3.424
3.407
3.401
3.395
3.389
3.378
3.373
3.366
3.360
3.350
3.344
3.339
2.853
2.835
2.740
2.722
1.946
1.934
1.928
1.921
1.912
1.905
1.899
1.894
1.833
1.827
1.822
1.815
1.806
1.799
1.794
1.365
0.432
0.297
11 10 9 8 7 6 5 4 3 2 1 ppm
2.40
2.42
35.11
2.00
5.07
1.26
1.28
3.59
2.38
0.25


Sample Name:
Study Owner jakirsch
Date Collected 2018-03-21
Pulse sequence s2pul
Spectrometer yb
Solvent cdcl3
Obs Freq 107.42 MHz
Temperature 25
Commnt Deuterium (using lock channel)
7.260
4.353
2.413
16
NO2
H
H/D
O
N
N
D
H
N
O
D
11
10
9
8
7
6
5
4
3
2
1
ppm
1.78
0.22
1.00


Sample Name:
Study Owner jakirsch
Date Collected 2018-03-20
Pulse sequence CARBON
Spectrometer yb
Solvent cdcl3
Obs Freq 175.97 MHz
Temperature 25
Commnt Carbon-13
156.526
145.380
142.155
136.313
136.255
128.961
128.423
128.411
128.047
125.209
125.139
117.544
117.513
117.017
77.342
77.160
66.901
59.111
58.991
58.879
54.338
50.799
50.679
50.563
47.969
47.799
47.682
47.562
45.936
45.898
29.835
220
200
180
160
140
120
100
80
60
40
20
ppm