Synthesis of Cyclic Guanidines via Pd-Catalyzed Alkene Carboamination

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Supporting Information

Experimental procedures and characterization data for new compounds in Tables 1–3 and Equations 1–2.

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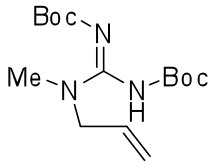
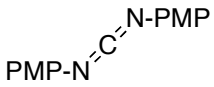
General: All reactions were carried out under a nitrogen atmosphere in flame-dried glassware unless otherwise noted. Tris(dibenzylidene)acetone dipalladium and Nixantphos were purchased from Strem Chemical Co. and used without purification. All other reagents were obtained from commercial sources and were used as obtained unless otherwise noted. (*Z*)-1-bromobutene[1] was prepared according to a slight modification of a literature procedure; the preparation was conducted at rt instead of using microwave heating. *N*-methylbut-2-en-1-ylamine was prepared as a 7:1 mixture of *E*:*Z* alkene isomers according to a published procedure.[2] Sodium *tert*-butoxide was kept in a glove box and removed only prior to use. Toluene, THF, diethyl ether and dichloromethane were purified using a GlassContour solvent purification system. 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 isolated yields reported in Tables 1–3 and Equation 1 are averages of yields for two or more experiments. Thus, the yields reported in the supporting information may differ from those shown in Tables 1–3 and Equation 1.

Preparation and Characterization of Guanidine Substrates



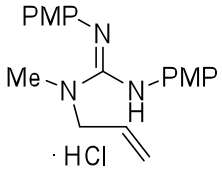
***N*^{1}-Allyl-*N*^{2},*N*^{3}-Bis(*tert*-butoxycarbonyl)-*N*^{1}-methylguanidine (3)**. The title compound was prepared using the general guanylation procedure reported by Lipton.[3] A flame-dried flask equipped with a stirbar was cooled under a stream of N_2, and charged with *N*,*N*'-bis-Boc-thiourea (1.79 g, 6.45 mmol), dichloromethane (65 mL), *N*-methylallylamine (518 µL, 5.4 mmol), triethylamine (1.66 mL, 11.9 mmol), and *N*-methyl-2-chloropyridinium iodide (1.64 g, 6.42 mmol). The resulting solution was stirred overnight (16 h) at rt. Water was added to the reaction flask, the mixture was stirred at rt for 5 min, then was transferred to a separatory funnel. The layers were separated and the organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford 660 mg (39%) of the title compound as a white solid: mp = 71–74 °C. This compound was found to exist as a mixture of rotamers as judged by ^{1}H and ^{13}C NMR analysis; data are for the mixture. ^{1}H NMR (700 MHz, $CDCl_3$) δ 10.05 (s, 1 H), 5.86–5.81 (m, 1 H), 5.26–5.21 (m, 2 H), 4.08 (s, br, 2 H), 2.96 (s, 3 H), 1.49 (s, 18 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 182.0, 162.6, 155.9, 151.2, 132.7, 118.5, 84.2, 81.9, 79.4, 53.4, 36.4, 28.1, 27.9; IR (film) 3286, 3175, 1748, 1612 cm^{-1}. MS (ESI) 314.2073 (314.2074 calcd for $C_{15}H_{27}N_3O_4$, M + H$^+$).



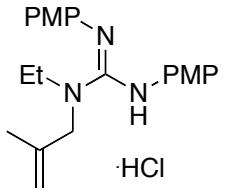
***N*,*N*'-Methanediylidene-bis-(4-methoxyaniline) (S1).** The title compound was prepared using a procedure published by Coppola.[4] A flame-dried flask was cooled under a stream of N_2, charged with 1,3-bis(4-methoxyphenyl)thiourea (5.67 g, 19.6 mmol), 4-dimethylaminopyridine (96.0 mg, 0.786 mmol), methanesulfonyl chloride (1.7 mL, 21.6 mmol), triethylamine (8.2 mL, 58.9 mmol), and dichloromethane (196 mL, 0.1 M). The resulting solution was stirred at 0 °C for 5 min. The solution was then filtered through a plug of silica gel, and the silica gel was washed with 300 mL of a 1:1 mixture of ethyl acetate and hexanes. The filtrate was concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford 3.98 g (80%) of the title compound as a white solid. Spectroscopic properties were identical to those

previously reported:[5] mp = 48–50 °C (lit.[5] mp = 48–50 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.8 Hz, 4 H), 6.85 (d, *J* = 8.8 Hz, 4 H), 3.80 (s, 6 H).

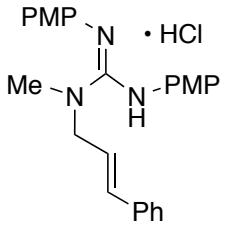
General Procedure for Synthesis of Bis(4-methoxyphenyl)guanidine Substrates. The bis(4-methoxyphenyl)guanidine derivatives were synthesized using a modification of a procedure published by Xi.[6] A flame dried round-bottom flask equipped with a stirbar was cooled under a stream of N_2, and charged with *N*,*N*'-methanediylidene-bis-(4-methoxyaniline) (1.0 equiv), the appropriate amine (1.2 equiv), zinc chloride (1 equiv), dichloromethane (0.025 M), and diethyl ether (0.25 M). The resulting mixture was stirred overnight at rt, then was filtered through a plug of celite, and the celite plug was washed with dichloromethane (150 mL). The filtrate was washed with 1M aqueous HCl (5 mL/mmol) and saturated aqueous sodium chloride (5 mL/mmol). The organic layer was then concentrated *in vacuo* and the resulting crude product was purified by flash chromatography on silica gel.



1-Allyl-2,3-bis(4-methoxyphenyl)-1-methylguanidine hydrochloride (4). The title compound was prepared from *N*,*N*'-methanediylidene-bis-(4-methoxyaniline) (1.68 g, 6.61 mmol) and *N*-methylallylamine (0.8 mL, 7.93 mmol) according to the general procedure. This procedure afforded 1.43 g (60%) of the title compound as a white foam solid: mp = 77–79 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 2 H), 7.00 (d, *J* = 9.0 Hz, 4 H), 6.55 (d, *J* = 8.0 Hz, 4 H), 5.88–5.78 (m, 1 H), 5.31–5.21 (m, 2 H), 4.13 (s, 2 H), 3.64 (s, 6 H), 3.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 154.2, 131.4, 129.7, 123.7, 120.3, 114.1, 55.4, 55.3, 38.1; IR (film) 3203, 1625 cm^{-1}. MS (ESI) 326.1863 (326.1866 calcd for $C_{19}H_{24}N_3O_2$, M^+).

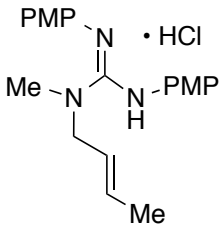


1-Ethyl-2,3-bis(4-methoxyphenyl)-1-(2-methylallyl)guanidine hydrochloride (9). The title compound was prepared from *N*,*N*'-methanediylidene-bis-(4-methoxyaniline) (2.06 g, 8.09 mmol) and *N*-ethyl-2-methylallylamine (1.28 mL, 9.7 mmol) according to the general procedure except the *N*-ethyl-2-methylallylamine was filtered through a plug of silica gel prior to addition, and the silica plug was eluted with 5 mL of dichloromethane, which was added to the reaction mixture. This procedure afforded 2.43 g (73%) of the title compound as a white foam solid: mp = 68 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (d, *J* = 8.0 Hz, 4 H), 6.56 (d, *J* = 8.0 Hz, 4 H), 4.99 (s, 1 H), 4.92 (s, 1 H), 4.09 (s, 2 H), 3.66 (s, 6 H), 3.63–3.58 (m, 2 H), 1.74 (s, 3 H), 1.17 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 156.8, 153.9, 139.7, 129.9, 123.6, 114.5, 114.0, 55.9, 55.3, 45.4, 20.3, 13.2; IR (film) 3040, 1619 cm^{-1}. MS (ESI) 354.2180 (354.2176 calcd for $C_{21}H_{28}N_3O_2$, M^+).

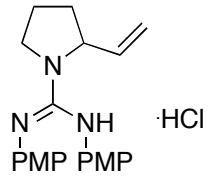


1-Cinnamyl-2,3-bis(4-methoxyphenyl)-1-methylguanidine hydrochloride (10a). The title compound was prepared from commercially available cinnamyl bromide via a two-step procedure. A round-bottom flask equipped with a stirbar was charged with cinnamyl bromide (5.9 g, 30 mmol) and ethanol (30 mL) and cooled to 0 °C. Methylamine (37.5 mL, 300 mmol, 33% solution in ethanol) was slowly added to the reaction flask over the course of 10 min. The reaction mixture was allowed to warm rt and was stirred overnight. The reaction mixture was concentrated, dissolved in dichloromethane (100 mL), and transferred to a separatory funnel. 1 M HCl (20 mL) was added to the separatory funnel and the layers were separated. The organic layer was washed again with 1 M HCl (20 mL). The combined aqueous layers were transferred to a round-bottom flask and dichloromethane (50mL) was added. The biphasic mixture was basified with NH_4OH to pH > 12, and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated

in vacuo. The crude *N*-methylcinnamylamine was then coupled with *N*,*N*'-methanediylidene-bis-(4-methoxyaniline) (4.3 g, 17.0 mmol) according to the general procedure described above. This procedure afforded 1.82 g (27%) of the title compound as a off-white solid: mp = 84–89 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, br, 2 H), 7.33–7.20 (m, 5 H), 7.18 (d, *J* = 9.0 Hz, 4 H), 6.75 (d, *J* = 8.5 Hz, 4 H), 6.49 (d, *J* = 16.5 Hz, 1 H), 6.02–5.97 (m, 1 H), 4.15 (s, br, 2 H), 3.67 (s, 6 H), 2.99 (s, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 157.6, 154.8, 135.8, 135.6, 129.3, 128.6, 128.1, 126.7, 124.4, 121.6, 114.7, 55.4, 54.9, 37.7; IR (film) 3256, 3205, 1627 cm^{-1}. MS (ESI) 402.2176 (402.2176 calcd for $C_{25}H_{28}N_3O_2$, M^+).

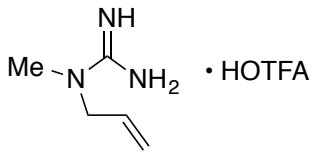


1-(But-2-en-1-yl)-2,3-bis(4-methoxyphenyl)-1-methylguanidine hydrochloride (10b). The title compound was prepared from *N*,*N*'-methanediylidene-bis-(4-methoxyaniline) (778 mg, 3.06 mmol) and *N*-methylbut-2-en-1-amine (employed as a 7:1 mixture of *E*:*Z* alkene isomers and as a 20% solution in EtOH) (260 mg, 3.06 mmol, 1.0 equiv,) according to the general procedure. After purification by flash column chromatography, 448 mg (39%) of the title compound was obtained as a pale brown solid (mp: 58–63 °C) and as a 7:1 mixture of *E*:*Z* alkene isomers as determined by ^{1}H NMR analysis. The ^{1}H data contains dichloromethane which was difficult to remove *in vacuo*. The data is for the mixture. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (s, 2 H), 7.17–7.13 (m, 4 H), 6.81–6.78 (m, 4 H), 5.73–5.66 (m, 1 H), 5.37–5.32 (m, 1 H), 3.93 (d, *J* = 5 Hz, 2 H), 3.73 (s, 6 H), 2.92 (s, 3 H), 1.69 (d, *J* = 5.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 157.4, 154.5, 133.0, 131.2, 129.3, 125.0, 124.3, 123.1, 114.7, 114.7, 55.5, 55.5, 54.7, 37.6, 17.8; IR (film) 3247, 2954, 1627 cm^{-1}. MS (ESI) 340.2019 (340.2020 calcd for $C_{20}H_{25}N_3O_2$, M^+).



(±)-*N*,*N*'-Bis(4-methoxyphenyl)-2-vinylpyrrolidine-1-carboximidamide hydrochloride (11). The title compound was prepared from commercially available *N*-Boc-2-vinylpyrrolidine via a

two-step procedure. A round-bottom flask equipped with a stirbar was charged with *N*-Boc-2-vinylpyrrolidine (2.5 mL, 12.5 mmol) and dichloromethane (25 mL). Trifluoroacetic acid (12.5 mL, 1.0 M) was added to the flask and the mixture was stirred at rt for 1 h until the starting material had been completely consumed as judged by TLC analysis. The solution was diluted with water, basified with NH_4OH to pH > 12, and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude amine was then coupled with *N*,*N*'-methanediylidene-bis-(4-methoxyaniline) (3.2 g, 12.5 mmol) according to the general procedure described above. This procedure afforded 464 mg (10%) of the title compound as a pale yellow solid: mp = 58–62 °C. ^{1}H NMR (700 MHz, CD_3OD) δ 7.00 (d, *J* = 9.1 Hz, 4 H), 6.82 (d, *J* = 9.1 Hz, 4 H), 5.90–5.85 (m, 1 H), 5.27–5.22 (m, 2 H), 4.58–4.55 (m, 1 H), 3.73 (s, 6 H), 3.67–3.63 (m, 1 H), 3.58–3.54 (m, 1 H), 2.30–2.26 (m, 1 H), 2.08–2.04 (m, 1 H), 2.01–1.95 (m, 1 H), 1.87–1.82 (m, 1 H); ^{13}C NMR (175 MHz, CD_3OD) δ 159.4, 153.8, 137.6, 130.7, 125.9, 118.4, 115.6, 63.5, 56.0, 51.4, 33.7, 25.0; IR (film) 3204, 1629 cm^{-1}. MS (ESI) 352.2020 (352.2020 calcd for $C_{21}H_{26}N_3O_2$, M^+).

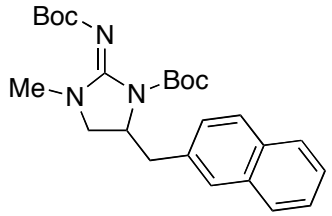


1-Allyl-1-methylguanidinium trifluoroacetate (28). A round-bottom flask equipped with a stirbar was charged with **3** (196 mg, 0.63 mmol) and dichloromethane (2.4 mL). Trifluoroacetic acid (0.9 mL) was added to the flask and the reaction mixture was stirred overnight at rt, and the solution was then concentrated *in vacuo*. Toluene (4 mL) was added and the resulting solution was concentrated *in vacuo*. The addition of toluene and subsequent concentration was repeated (3x) to remove all excess trifluoroacetic acid, at which time the compound was obtained as a crystalline white solid: mp = 159–164 °C. This procedure afforded 85 mg (60%) of the title compound. This material also contained ca. 10% of an unidentified side product. ^{1}H NMR (500 MHz, CD_3OD) δ 5.83–5.75 (m, 1 H), 5.26–5.17 (m, 2 H), 3.95 (d, 2 H), 2.99 (s, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 159.4, 132.8, 118.9, 45.4, 37.3; IR (film) 3312, 3150, 1663 cm^{-1}. MS (ESI) 114.1028 (114.1026 calcd for $C_5H_{11}N_3$, M^+).

Preparation and Characterization of Cyclic Guanidine Products

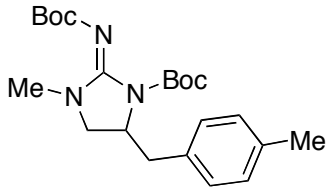
General Procedure for the Pd-Catalyzed Synthesis of Cyclic Guanidines. A flame-dried Schlenk tube was cooled under vacuum and charged with the appropriate guanidine substrate (1.0 equiv), $Pd_2(dba)_3$ (0.02 equiv), Nixantphos (0.08 equiv), and NaO*t*Bu (2.4 equiv). The flask was evacuated and backfilled with N_2. Toluene (0.1 M) was added via syringe and the resulting mixture was stirred at rt for 2 min. The appropriate aryl or alkenyl bromide (1.5 equiv) was added and the tube was heated to 107 °C and stirred overnight (~16 h). The mixture was cooled to room temperature and 1 M HCl (10 mL/mmol substrate) and dichloromethane (25 mL/mmol substrate) were added. The layers were separated and the aqueous layer was extracted with dichloromethane (10 mL/mmol). The organic layers were combined and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel.

General Procedure for the Asymmetric Pd-Catalyzed Synthesis of Enantioenriched Cyclic Guanidines. A flame-dried Schlenk tube was cooled under vacuum and charged with the guanidine substrate **9** (1.0 equiv), $Pd_2(dba)_3$ (0.02 equiv), the appropriate ligand (0.08 equiv for monodenate ligands, and 0.16 equiv for bidendate ligands), and NaO*t*Bu (2.4 equiv). The flask was evacuated and backfilled with N_2. Toluene (0.1 M) was added via syringe and the resulting mixture was stirred at rt for 2 min. 4-bromotoluene (1.5 equiv) was added and the tube was heated to 107 °C and stirred overnight (~16 h). The mixture was cooled to room temperature and 1 M HCl (10 mL/mmol substrate) and dichloromethane (25 mL/mmol substrate) were added. The layers were separated and the aqueous layer was extracted with dichloromethane (10 mL/mmol). The organic layers were combined and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel.

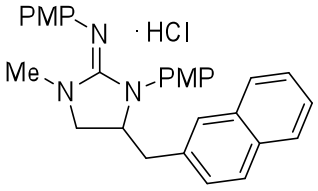


***tert*-Butyl-2-[(*tert*-butoxycarbonyl)imino]-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidine-1-carboxylate (5).** The general procedure was employed for the coupling of **3** (94 mg, 0.3 mmol) and 2-bromonaphthalene (93 mg, 0.45 mmol) using a catalyst composed of Pd_2dba_3 (5.5 mg, 0.006 mmol) and Nixantphos (13 mg, 0.024 mmol). Saturated aqueous NH_4Cl was used during the workup instead of 1 M HCl. This procedure afforded 43 mg

(33%) of the title compound as an off-white solid: mp = 56–58 °C. This compound was found to exist as a mixture of rotamers as judged by ^{1}H and ^{13}C NMR analysis; data are for the mixture. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.81–7.79 (m, 3 H), 7.70 (s, 1 H), 7.48–7.43 (m, 2 H), 7.36 (dd, *J* = 1.4, 8.4 Hz, 1 H), 4.47–4.44 (m, 1 H), 3.44–3.40 (m, 1 H), 3.35 (dd, *J* = 4.9, 14.0 Hz, 1 H), 3.07 (dd, *J* = 2.1, 9.8 Hz, 1 H), 2.93 (dd, *J* = 9.1, 14.0 Hz, 1 H), 2.83 (s, 3 H), 1.54 (s, 9 H), 1.45 (s, 9 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.6, 151.5, 149.8, 133.9, 133.5, 132.4, 128.4, 128.2, 127.6, 127.6, 127.5, 126.2, 125.8, 82.5, 78.7, 56.7, 49.9, 40.2, 32.1, 28.3, 28.1; IR (film) 1748, 1629 cm^{-1}. MS (ESI) 440.2538 (440.2544 calcd for $C_{25}H_{33}N_3O_4$, M + H$^+$).

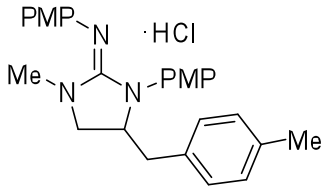


***tert*-Butyl 2-[(*tert*-butoxycarbonyl)imino]-3-methyl-5-(4-methylbenzyl)imidazolidine-1-carboxylate (6).** The general procedure was employed for the coupling of **3** (63 mg, 0.2 mmol) and 4-bromotoluene (51 mg, 0.3 mmol) using a catalyst composed of Pd_2dba_3 (3.7 mg, 0.004 mmol) and Nixantphos (8.8 mg, 0.016 mmol). Saturated aqueous NH_4Cl was used during the workup instead of 1 M HCl. This procedure afforded 21 mg (26%) of the title compound as a pale yellow oil. This compound was found to exist as a mixture of rotamers as judged by ^{1}H and ^{13}C NMR analysis; data are for the mixture. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.7 Hz, 2 H), 7.09 (d, *J* = 7.7 Hz, 2 H), 4.29–4.26 (m, 1 H), 3.25–3.21 (m, 2 H), 3.04 (dd, *J* = 2.8, 9.1 Hz, 1 H), 2.76 (s, 3 H), 2.65 (dd, *J* = 9.8, 13.3 Hz, 1 H), 2.32 (s, 3 H), 1.57 (s, 9 H), 1.45 (s, 9 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 165.5, 154.1, 150.6, 136.5, 133.3, 129.4, 129.2, 82.3, 53.2, 47.7, 39.0, 30.5, 28.2, 21.0; IR (film) 1750, 1627 cm^{-1}. MS (ESI) 404.2545 (404.2544 calcd for $C_{22}H_{33}N_3O_4$, M + H$^+$).

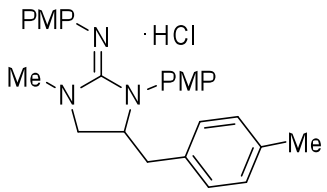


***N*,3-Bis(4-methoxyphenyl)-1-methyl-4-(naphthalen-2-ylmethyl)imidazolidin-2-imine hydrochloride (7):** The general procedure was employed for the coupling of **4** (54 mg, 0.15

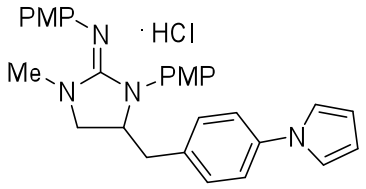
mmol) and 2-bromonaphthalene (47 mg, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 42 mg (57%) of the title compound as a pale yellow-brown foam solid: mp = 67–68 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80–7.77 (m, 3 H), 7.60 (s, 1 H), 7.50–7.46 (m, 2 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 7.04–7.02 (m, 2 H), 6.97–6.94 (m, 2 H), 6.63–6.60 (m, 2 H), 6.52–6.49 (m, 2 H), 4.50–4.44 (m, 1 H), 3.83–3.79 (m, 1 H), 3.70–3.68 (m, 3 H), 3.39–3.36 (m, 3 H), 3.61–3.59 (m, 1 H), 3.39–3.62 (m, 3 H), 3.23–3.19 (m, 1 H), 3.04 (dd, *J* = 10.0, 13.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 157.7, 156.5, 133.4, 132.5, 132.4, 132.4, 132.3, 129.5, 128.8, 128.0, 127.7, 127.5, 126.9, 126.6, 126.6, 126.1, 114.6, 113.8, 63.8, 55.5, 55.4, 54.0, 39.5, 35.7; IR (film) 3050, 1632 cm^{-1}. MS (ESI) 452.2328 (452.2333 calcd for $C_{29}H_{30}N_3O_2$, M^+).



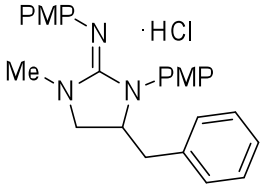
***N*,3-Bis(4-methoxyphenyl)-1-methyl-4-(4-methylbenzyl)imidazolidin-2-imine hydrochloride (8):** The general procedure was employed for the coupling of **4** (54 mg, 0.15 mmol) and 4-iodotoluene (49 mg, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 42 mg (62%) of the title compound as a pale yellow-brown foam solid: mp = 73–75 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.5 Hz, 2 H), 7.11–7.06 (m, 4 H), 7.02 (d, *J* = 8.0 Hz, 2 H), 6.67 (d, *J* = 9.0 Hz, 2 H), 6.56 (d, *J* = 9.0 Hz, 2 H), 4.49–4.42 (m, 1 H), 3.90–3.86 (m, 1 H), 3.72 (s, 3 H), 3.66 (s, 3 H), 3.60 (dd, *J* = 7.5, 10.0 Hz, 1 H), 3.23 (s, 3 H), 2.96 (dd, *J* = 4.5, 13.5 Hz, 1 H), 2.91 (dd, *J* = 10.0, 13.5 Hz, 1 H), 2.30 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 158.2, 156.1, 137.0, 131.8, 129.6, 129.2, 129.0, 128.7, 127.7, 126.9, 114.8, 113.9, 63.6, 55.6, 55.5, 54.2, 38.4, 36.2, 21.0; IR (film) 3133, 1631 cm^{-1}. MS (ESI) 416.2340 (416.2333 calcd for $C_{26}H_{30}N_3O_2$, M^+).



***N*,3-Bis(4-methoxyphenyl)-1-methyl-4-(4-methylbenzyl)imidazolidin-2-imine hydrochloride (8):** The general procedure was employed for the coupling of **4** (54 mg, 0.15 mmol) and 4-bromotoluene (39 mg, 0.225 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 50 mg (73%) of the title compound as a pale yellow-brown foam solid. Spectroscopic data were identical to those provided above.

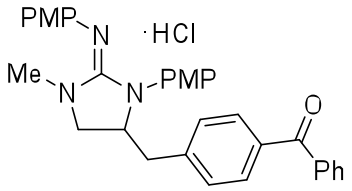


4-[4-(1*H*-Pyrrol-1-yl]benzyl)-*N*,3-bis(4-methoxyphenyl)-1-methylimidazolidin-2-imine hydrochloride (12): The general procedure was employed for the coupling of **4** (54 mg, 0.15 mmol) and 1-(4-iodophenyl)pyrrole (61 mg, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 48 mg (63%) of the title compound as a pale yellow-brown foam solid: mp = 70–71 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.0 Hz, 2 H), 7.21–7.17 (m, 4 H), 7.14 (d, *J* = 8.5 Hz, 2 H), 7.04 (t, *J* = 2.5 Hz, 2 H), 6.69 (d, *J* = 9.0 Hz, 2 H), 6.58 (d, *J* = 9.0 Hz, 2 H), 6.33 (t, *J* = 3.0 Hz, 2 H), 4.58–4.51 (m, 1 H), 3.95–3.91 (m, 1 H), 3.72 (s, 3 H), 3.70–3.68 (m, 1 H), 3.67 (s, 3 H), 3.22 (s, 3 H), 3.06–3.04 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 158.2, 156.2, 139.8, 132.4, 130.3, 129.3, 128.6, 127.7, 127.0, 120.7, 119.2, 114.8, 113.9, 110.6, 63.5, 55.6, 55.5, 54.3, 38.2, 36.0; IR (film) 3058, 1635 cm^{-1}. MS (ESI) 467.2450 (467.2442 calcd for $C_{29}H_{31}N_4O_2$, M^+).

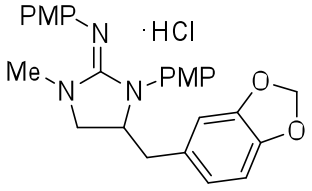


4-Benzyl-*N*,3-bis(4-methoxyphenyl)-1-methylimidazolidin-2-imine hydrochloride (13): The general procedure was employed for the coupling of **4** (54 mg, 0.15 mmol) and bromobenzene (24 μL, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 48 mg (73%) of the title compound as a pale yellow-brown foam solid: mp = 58–59 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.0

Hz, 2 H), 7.27–7.26 (m, 1 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 6.98 (d, *J* = 9.0 Hz, 2 H), 6.92 (d, *J* = 9.0 Hz, 2 H), 6.61 (d, *J* = 8.5 Hz, 2 H), 6.50 (d, *J* = 9.0 Hz, 2 H), 4.34–4.27 (m, 1 H), 3.83–3.78 (m, 1 H), 3.69 (s, 3 H), 3.65 (s, 3 H), 3.51 (dd, *J* = 3.5, 13.5 Hz, 1 H), 3.40 (s, 3 H), 3.06 (dd, *J* = 3.5, 13.5 Hz, 1 H), 2.85 (dd, *J* = 10.0, 14.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 157.5, 156.5, 135.0, 129.9, 129.1, 129.0, 128.6, 128.3, 127.5, 126.5, 114.5, 113.8, 63.9, 55.5, 55.5, 53.8, 39.5, 35.4; IR (film) 3003, 1640 cm^{-1}. MS (ESI) 402.2177 (402.2176 calcd for $C_{25}H_{28}N_3O_2$, M^+).

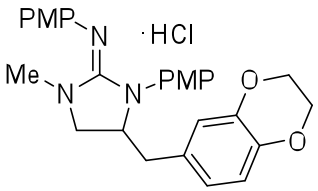


[4-{3-(4-Methoxyphenyl)-2-[(4-methoxyphenyl)imino]-1-methylimidazolidin-4-ylmethyl}phenyl](phenyl)methanone hydrochloride (14): The general procedure was employed for the coupling of **4** (54 mg, 0.15 mmol) and 4-iodobenzophenone (69 mg, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 56 mg (69%) of the title compound as a pale yellow-brown foam solid: mp = 70–71 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 1 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.67 (d, *J* = 7.0 Hz, 2 H), 7.59 (t, *J* = 8.0 Hz, 1 H), 7.48 (t, *J* = 7.5 Hz, 2 H), 7.30 (d, *J* = 8.5 Hz, 2 H), 7.20 (d, 7.5 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 6.67 (d, *J* = 7.5 Hz, 2 H), 6.57 (d, *J* = 7.5 Hz, 2 H), 4.72–4.65 (m, 1 H), 4.02–3.98 (m, 1 H), 3.76–3.73 (m, 1 H), 3.70 (s, 3 H), 3.65 (s, 3 H), 3.23 (s, 3 H), 3.21–3.17 (m, 1 H), 3.10 (dd, *J* = 4.5, 13.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 159.5, 158.3, 156.1, 140.2, 137.3, 136.3, 132.6, 130.5, 129.9, 129.5, 129.2, 128.3, 128.2, 128.0, 126.6, 114.8, 113.9, 63.1, 55.6, 55.5, 54.4, 38.8, 36.1; IR (film) 3135, 1655, 1630 cm^{-1}. MS (ESI) 506.2437 (506.2438 calcd for $C_{32}H_{32}N_3O_3$, M^+).

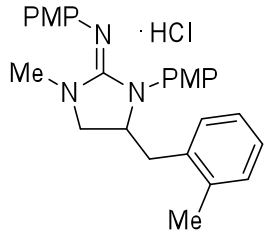


4-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-*N*,3-bis(4-methoxyphenyl)-1-methylimidazolidin-2-imine hydrochloride (15): The general procedure was employed for the coupling of **4** (54 mg,

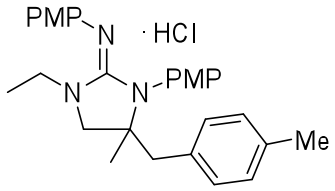
0.15 mmol) and 4-bromo-1,2-(methylenedioxy)benzene (27 μL, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 59 mg (81%) of the title compound as a pale yellow-brown foam solid: mp = 66–68 °C. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.01 (d, *J* = 9.1 Hz, 2 H), 6.92 (d, *J* = 9.1 Hz, 2 H), 6.73 (d, *J* = 7.7 Hz, 1 H), 6.61–6.58 (m, 4 H), 6.51 (d, *J* = 9.1 Hz, 2 H), 5.93 (s, 2 H), 4.31–4.26 (m, 1 H), 3.84–3.81 (m, 1 H), 3.70 (s, 3 H), 3.65 (s, 3 H), 3.53 (dd, *J* = 7.0, 9.8 Hz, 1 H), 3.39 (s, 3 H), 2.95 (dd, *J* = 4.2, 13.3 Hz, 1 H), 3.78 (dd, *J* = 9.8, 14.0 Hz, 1 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.1, 157.7, 156.4, 148.1, 146.8, 129.6, 128.7, 128.4, 127.8, 126.8, 122.2, 114.5, 113.7, 109.2, 108.6, 101.1, 63.9, 55.5, 55.4, 53.8, 38.9, 35.6; IR (film) 3005, 1640 cm^{-1}. MS (ESI) 446.2077 (446.2074 calcd for $C_{26}H_{28}N_3O_4$, M^+).



4-[(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)methyl]-*N*,3-bis(4-methoxyphenyl)-1-methylimidazolidin-2-imine hydrochloride (16): The general procedure was employed for the coupling of **4** (54 mg, 0.15 mmol) and 6-bromo-1,4-benzodioxane (30 μL, 0.225 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 67 mg (90%) of the title compound as a pale yellow-brown foam solid: mp = 76–77 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (d, *J* = 9.0 Hz, 2 H), 6.88 (d, *J* = 9.0 Hz, 2 H), 6.78 (d, *J* = 8.0 Hz, 1 H), 6.61–6.57 (m, 4 H), 6.49 (d, *J* = 8.5 Hz, 2 H), 4.29–4.24 (m, 1 H), 4.23 (s, 4 H), 3.84–3.80 (m, 1 H), 3.69 (s, 3 H), 3.64 (s, 3 H), 3.49 (dd, *J* = 7.0, 10.5 Hz, 1 H), 3.39 (s, 3 H), 2.92 (dd, *J* = 4.5, 13.5 Hz, 1 H), 2.72 (dd, *J* = 9.5, 14.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 157.5, 156.4, 143.7, 142.9, 129.9, 128.5, 128.3, 127.9, 126.5, 122.0, 117.7, 117.7, 114.5, 113.7, 64.4, 64.3, 63.9, 55.5, 55.4, 53.7, 38.5, 35.3; IR (film) 3000, 1639 cm^{-1}. MS (ESI) 460.2226 (460.2231 calcd for $C_{27}H_{30}N_3O_4$, M^+).

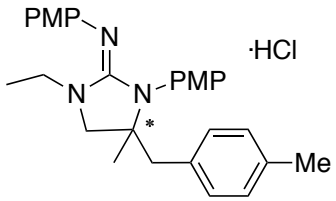


***N*,3-Bis(4-methoxyphenyl)-1-methyl-4-(2-methylbenzyl)imidazolidin-2-imine hydrochloride (17):** The general procedure was employed for the coupling of **4** (54 mg, 0.15 mmol) and 2-bromotoluene (27 μL, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 52 mg (76%) of the title compound as a pale yellow-brown foam solid. The material contained ca. 8% of an unsaturated cyclic guanidine resulting from oxidation of the title compound (tentatively assigned as the 2-aminoimidazole derivative (*E*)-*N*,3-bis(4-methoxyphenyl)-1-methyl-4-(2-methylbenzyl)-1,3-dihydro-2*H*-imidazol-2-imine hydrochloride). mp = 78–79 °C. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.15–7.11 (m, 3 H), 7.08–7.07 (m, 1 H), 7.00 (d, *J* = 9.1 Hz, 2 H), 6.90 (d, *J* = 8.4 Hz, 2 H), 6.60 (d, *J* = 9.1 Hz, 2 H), 6.49 (d, *J* = 9.1 Hz, 2 H), 4.33–4.29 (m, 1 H), 3.81–3.78 (m, 1 H), 3.69 (s, 3 H), 3.64 (s, 3 H), 3.54 (dd, *J* = 7.7, 10.5 Hz, 1 H), 3.42 (s, 3 H), 3.06 (dd, *J* = 4.2, 14.0 Hz, 1 H), 2.81 (dd, *J* = 10.5, 14.0 Hz, 1 H), 2.10 (s, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.0, 157.5, 156.4, 136.3, 133.4, 130.8, 129.6, 129.6, 128.6, 128.2, 127.5, 126.6, 126.4, 114.5, 113.7, 62.6, 55.5, 55.4, 54.1, 36.8, 35.5, 19.3; IR (film) 3002, 1630 cm^{-1}. MS (ESI) 416.2328 (416.2333 calcd for $C_{26}H_{30}N_3O_2$, M^+).

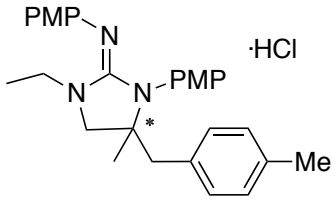


1-Ethyl-*N*,3-bis(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-imine hydrochloride (18): The general procedure was employed for the coupling of **9** (59 mg, 0.15 mmol) and 4-bromotoluene (35 mg, 0.23 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 71 mg (99%) of the title compound as a pale yellow-brown foam solid: mp = 61–62 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.0 Hz, 2 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 6.90–6.87 (m, 4 H), 6.61 (d, *J* = 8.5 Hz, 2 H), 6.50 (d, *J* = 8.5 Hz, 2 H), 4.02–3.95 (m, 1 H), 3.87–3.80 (m, 2 H), 3.70 (s, 3 H), 3.65

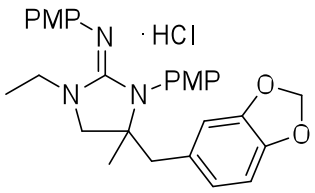
(s, 3 H), 3.35 (d, *J* = 10.5 Hz, 1 H), 2.98 (d, *J* = 13.5 Hz, 1 H), 2.75 (d, *J* = 13.5 Hz, 1 H), 2.36 (s, 3 H), 1.26–1.20 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 157.3, 155.2, 137.6, 131.5, 130.2, 130.0, 129.5, 128.7, 127.0, 126.2, 114.3, 113.7, 65.7, 55.9, 55.5, 55.5, 45.1, 42.0, 25.3, 21.1, 12.3; IR (film) 2971, 1630 cm^{-1}. MS (ESI) 444.2645 (444.2646 calcd for $C_{28}H_{34}N_3O_2$, M^+).



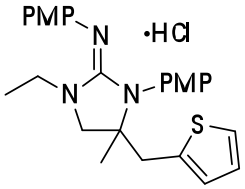
(+)-1-Ethyl-*N*,3-bis(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-imine hydrochloride (18; prepared using (*S*)-Phanephos as ligand): The general procedure for the asymmetric synthesis of cyclic guanidine products was employed for the coupling of **9** (58.5 mg, 0.15 mmol) and 4-bromotoluene (39 mg, 0.225 mmol) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and (*S*)-Phanephos (6.9 mg, 0.012 mmol) except the reaction was run for 36 hrs in order to ensure complete conversion. This procedure afforded 65.0 mg (84%) of the title compound as a pale yellow-brown foam solid: $[\alpha]^{23}_D$ +18.0 (*c* 1.3, CH_2Cl_2). Spectroscopic data were identical to those provided above. The enantiomeric purity was determined to be 61:39 er as assessed by converting this compound to the corresponding Mosher amide (see below for details).



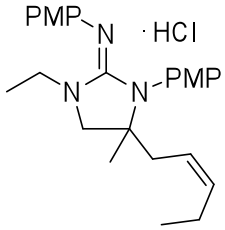
(–)-1-Ethyl-*N*,3-bis(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-imine hydrochloride (18; prepared using (*S*)-BINAP as ligand): The general procedure for the asymmetric synthesis of cyclic guanidine products was employed for the coupling of **9** (39 mg, 0.1 mmol) and 4-bromotoluene (26 mg, 0.15 mmol) using a catalyst composed of Pd_2dba_3 (1.8 mg, 0.002 mmol), and (*S*)-BINAP (5.0 mg, 0.008 mmol). This procedure afforded 48 mg (99%) of the title compound as a pale yellow-brown foam solid: $[\alpha]^{23}_D$ –5.9 (*c* 0.9, CH_2Cl_2). Spectroscopic data were identical to those provided above. The enantiomeric purity was determined to be 48:52 er as assessed by converting this compound to the corresponding Mosher amide (see below for details).



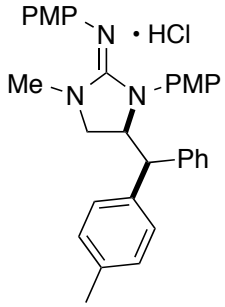
4-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-1-ethyl-*N*,3-bis(4-methoxyphenyl)-4-methylimidazolidin-2-imine hydrochloride (19): The general procedure was employed for the coupling of **9** (59 mg, 0.15 mmol) and 4-bromo-1,2-(methylenedioxy)benzene (27 μL, 0.225 mmol), using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 76 mg (99%) of the title compound as a pale yellow-brown foam solid: mp = 66–67 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93–6.83 (m, 4 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 6.71–6.68 (m, 2 H), 6.62 (s, br, 2 H), 6.51 (d, *J* = 8.5 Hz, 2 H), 5.98 (s, 2 H), 4.01–3.94 (m, 1 H), 3.88 (d, *J* = 10.0 Hz, 1 H), 3.84–3.77 (m, 1 H), 3.71 (s, 3 H), 3.66 (s, 3 H), 3.42 (d, *J* = 10.5 Hz, 1 H), 2.96 (d, *J* = 13.5 Hz, 1 H), 2.69 (d, *J* = 13.5 Hz, 1 H), 1.26–1.19 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 157.6, 155.3, 148.0, 147.2, 129.8, 128.1, 128.0, 126.7, 126.7, 123.6, 114.4, 113.7, 110.4, 108.5, 101.3, 65.8, 55.9, 55.5, 55.5, 45.0, 42.1, 25.3, 12.3; IR (film) 2972, 1627 cm^{-1}. MS (ESI) 474.2379 (474.2387 calcd for $C_{28}H_{32}N_3O_4$, M^+).



1-Ethyl-*N*,3-bis(4-methoxyphenyl)-4-methyl-4-(thiophen-2-ylmethyl)imidazolidin-2-imine hydrochloride (20): The general procedure was employed for the coupling of **9** (59 mg, 0.15 mmol) and 2-bromothiophene (22 μL, 0.225 mmol), using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol). This procedure afforded 70 mg (99%) of the title compound as a pale yellow-brown foam solid: mp = 63–65 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.30 (m, 1 H), 7.06–6.97 (m, 6 H), 6.62 (d, *J* = 8.5 Hz, 2 H), 6.49 (d, *J* = 9.5 Hz, 2 H), 3.98–3.87 (m, 2 H), 3.69–3.60 (m, 8 H), 3.24 (d, *J* = 15.5 Hz, 1 H), 3.05 (d, *J* = 15.0 Hz, 1 H), 1.27 (s, 3 H), 1.10 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 157.4, 155.2, 136.3, 130.3, 128.4, 128.1, 127.2, 126.7, 126.4, 125.5, 114.4, 113.7, 65.3, 55.9, 55.5, 55.4, 41.9, 39.9, 26.0, 11.9; IR (film) 3041, 1630 cm^{-1}. MS (ESI) 436.2057 (436.2053 calcd for $C_{25}H_{29}N_3O_2S$, M^+).

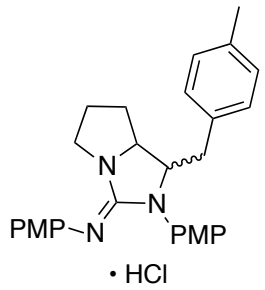


(*Z*)-1-Ethyl-*N*,3-bis(4-methoxyphenyl)-4-methyl-4-(pent-2-en-1-yl)imidazolidin-2-imine hydrochloride (21): The general procedure (using modified stoichiometries of reactants) was used for the coupling of **9** (59 mg, 0.15 mmol) and 1-bromobutene (300 µL, 0.60 mmol, 4.0 equiv, 2 M solution in toluene) using a catalyst composed of Pd_2dba_3 (2.7 mg, 0.003 mmol), and Nixantphos (6.6 mg, 0.012 mmol) in the presence of NaO*t*Bu (64.9 mg, 0.60 mmol, 4.5 equiv). This procedure afforded 57 mg (86%) of the title compound as a pale yellow-brown oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.99 (s, br, 1 H), 6.92 (d, *J* = 8.4 Hz, 2 H), 6.76 (s, br, 1 H), 6.65–6.53 (m, br, 2 H), 6.49 (d, *J* = 9.1 Hz, 2 H), 5.74–5.70 (m, 1 H), 5.39–5.35 (m, 1 H), 4.10–4.05 (m, 1 H), 3.92–3.86 (m, 1 H), 3.71–3.67 (m, 1 H), 3.68 (s, 3 H), 3.64 (s, 3 H), 3.59 (d, *J* = 9.8 Hz, 1 H), 2.42 (dd, *J* = 6.3, 14.7 Hz, 1 H), 2.28 (dd, *J* = 7.7, 15.4 Hz, 1 H), 2.10–2.06 (m, 2 H), 1.34 (t, *J* = 7.0 Hz, 3 H), 1.25 (s, 3 H), 1.01 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.2, 157.3, 155.0, 137.3, 130.5, 129.7, 128.1, 126.3, 120.7, 114.2, 113.7, 65.3, 56.2, 55.4, 55.4, 42.2, 37.1, 25.6, 21.0, 13.9, 12.3; IR (film) 3006, 1627 cm^{-1}. MS (ESI) 408.2643 (408.2646 calcd for $C_{25}H_{34}N_3O_2$, M^+).



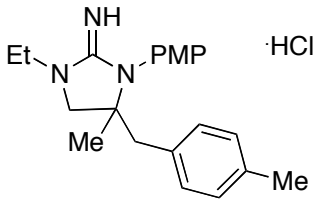
(±)-(*S,*S**)-*N*,3-Bis(4-methoxyphenyl)-1-methyl-4-(phenyl(*p*-tolyl)methyl)imidazolidin-2-imine hydrochloride (22a)**. The general procedure was employed for the coupling of **10** (132 mg, 0.3 mmol) and 4-bromotoluene (76 mg, 0.45 mmol), using a catalyst composed of Pd_2dba_3 (5.5 mg, 0.006 mmol), and Nixantphos (13.2 mg, 0.024 mmol). This procedure afforded 35 mg (22%) of the title compound as a pale yellow-brown solid: mp = 91–93 °C. This compound was judged to be a single diastereomer (> 20:1 dr) by ^{1}H NMR analysis. ^{1}H NMR (700 MHz, $CDCl_3$) δ 11.33 (s, br, 1 H), 7.38–7.36 (m, 2 H), 7.31–7.29 (m, 1 H), 7.25–7.24 (m, 2 H), 7.04 (d, *J* = 7.7 Hz, 2 H), 6.99 (d, *J* = 8.4 Hz, 2 H), 6.76 (d, *J* = 9.1 Hz, 2 H), 6.46 (d, *J* = 9.1 Hz, 2 H), 6.40 (s, 4

H), 4.65–4.62 (m, 1 H), 4.35 (d, *J* = 8.4 Hz, 1 H), 4.15–4.12 (m, 1 H), 3.64 (s, 3 H), 3.63 (s, 3 H), 3.51 (dd, *J* = 4.9, 11.2 Hz, 1 H), 3.27 (s, 3 H), 2.28 (s, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 158.9, 158.1, 157.7, 139.3, 137.3, 136.6, 132.0, 129.6, 129.2, 128.6, 128.5, 128.2, 128.2, 127.9, 126.3, 114.1, 113.7, 66.7, 55.4, 54.8, 53.3, 35.2, 21.0 (one carbon signal is absent due to incidental equivalence); IR (film) 3105, 1641 cm^{-1}. MS (ESI) 492.2652 (492.2646 calcd for $C_{32}H_{34}N_3O_2$, M^+).



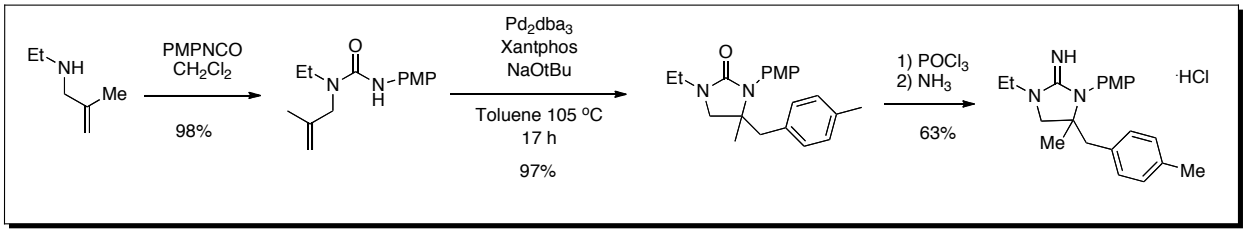
(±)-*N*,2,Bis-(4-methoxyphenyl)-1-(4-methylbenzyl)tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazol-3(2*H*)-imine hydrochloride (23). The general procedure was employed for the coupling of **11** (77.6 mg, 0.2 mmol) and 4-bromotoluene (52 mg, 0.3 mmol), using a catalyst composed of Pd_2dba_3 (3.6 mg, 0.004 mmol), and Nixantphos (8.8 mg, 0.016 mmol). This procedure afforded a crude mixture that was determined to be a 1.5:1 mixture of diastereomers by ^{1}H NMR analysis. After purification by flash column chromatography 53 mg (60%) of the title compound was obtained as a pale brown solid and as a 2:1 mixture of diastereomers as determined by ^{1}H NMR analysis. The data is for the mixture except the ^{1}H NMR data, which is only for the major isomer: mp = 58–61 °C. ^{1}H NMR (700 MHz, $CDCl_3$) δ 10.94, (s, br, 1 H), 7.21–7.14 (m, 4 H), 7.12–7.08 (m, 2 H), 6.97 (d, *J* = 8.4 Hz, 2 H), 6.84–6.80 (m, 2 H), 6.68–6.67 (m, 2 H), 4.50–4.47 (m, 1 H), 3.95–3.92 (m, 1 H), 3.77 (s, 3 H), 3.71 (s, 3 H), 3.45–3.44 (m, 1 H), 3.35–3.32 (m, br, 1 H), 2.98 (dd, *J* = 3.5, 13.3 Hz, 1 H), 2.53 (dd, *J* = 11.2, 14.0 Hz, 1 H), 2.31 (s, 3 H), 2.07–2.03 (m, 1 H), 1.87–1.79 (m, 1 H), 1.62–1.58 (m, 2 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.6, 159.5, 157.8, 157.7, 137.0, 136.8, 132.4, 131.7, 129.7, 129.5, 129.4, 128.8, 128.4, 128.0, 126.6, 126.0, 125.4, 115.1, 115.1, 114.1, 68.4, 66.2, 64.9, 64.6, 55.5, 55.4, 49.3, 48.7, 38.2, 35.2, 31.2, 26.7, 26.2, 25.8, 21.0, 20.0; IR (film) 1625 cm^{-1}. MS (ESI) 442.2484 (442.2489 calcd for $C_{28}H_{32}N_3O_2$, M^+).

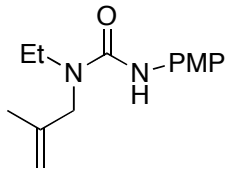
Deprotection of Cyclic Guanidine Product 18



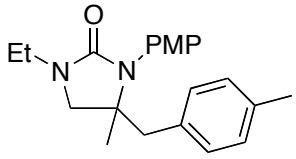
1-Ethyl-3-(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-imine hydrochloride (27). A Schlenk tube was charged with a stirbar, **18** (48 mg, 0.1 mmol) and CH_3CN (1 mL). A solution of ceric ammonium nitrate (329 mg, 0.6 mmol) in H_2O (6 mL) was added to the reaction flask and the mixture was stirred at rt for 5 min. The mixture was then heated at 50 ^oC for 12 h before being cooled to rt, at which time dichloromethane (15 mL) was added. The mixture was transferred to a separatory funnel and the layers were separated. The organic layer was washed with saturated Na_2SO_3 (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford 14.6 mg (39%) of the title compound as white solid: mp = 223–226 $^\circ C$. ^1H NMR (700 MHz, $CDCl_3$) δ 7.19 (s, br 2 H), 7.13 (d, J = 7.7 Hz, 2 H), 7.03 (d, *J* = 9.1 Hz, 2 H), 6.98 (d, *J* = 7.7 Hz, 2 H), 3.91–3.88 (m, 1 H), 3.88 (s, 3 H), 3.84–3.81 (m, 1 H), 3.77 (d, *J* = 9.8 Hz, 1 H), 3.18 (d, *J* = 9.8 Hz, 1 H), 2.94 (d, *J* = 13.3 Hz, 1 H), 2.70 (d, *J* = 13.3 Hz, 1 H), 2.33 (s, 3 H), 1.31 (s, 3 H) 1.25 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.1, 155.9, 137.5, 131.4 (br, 1 C), 131.3, 129.9, 129.6, 123.5, 115.8, 65.8, 55.7, 55.6, 43.7, 41.3, 23.9, 21.0, 12.2; IR (film) 3250, 1658 cm^{-1}. MS (ESI) 338.2228 (338.2227 calcd for $C_{21}H_{28}N_3O$, M^+).

Structural Assignment of Deprotected Cyclic Guanidine Product 27.

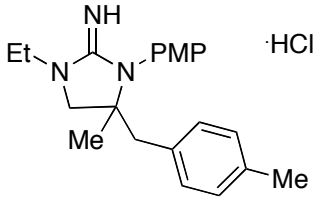




1-Ethyl-3-(4-methoxyphenyl)-1-(2-methylallyl)urea (S2). A flame-dried flask equipped with a stirbar was charged with *N*-ethyl-2-methylallylamine (1.3 mL, 10 mmol) and dichloromethane (100 mL). 4-methoxyphenyl isocyanate (1.55 mL, 12 mmol) was added to the flask and the mixture was stirred at rt for 1 h. The crude reaction mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel to afford 2.43 mg (98%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.5 Hz, 2 H), 6.82 (d, *J* = 8.5 Hz, 2 H), 6.30, (s, 1 H), 5.02 (s, br, 2 H), 3.83 (s, br, 2 H), 3.77 (s, 3 H), 3.42 (q, *J* = 7.0 Hz, 2 H), 1.79 (s, 3 H), 1.20 (t, *J* = 7.0 Hz, 3 H).



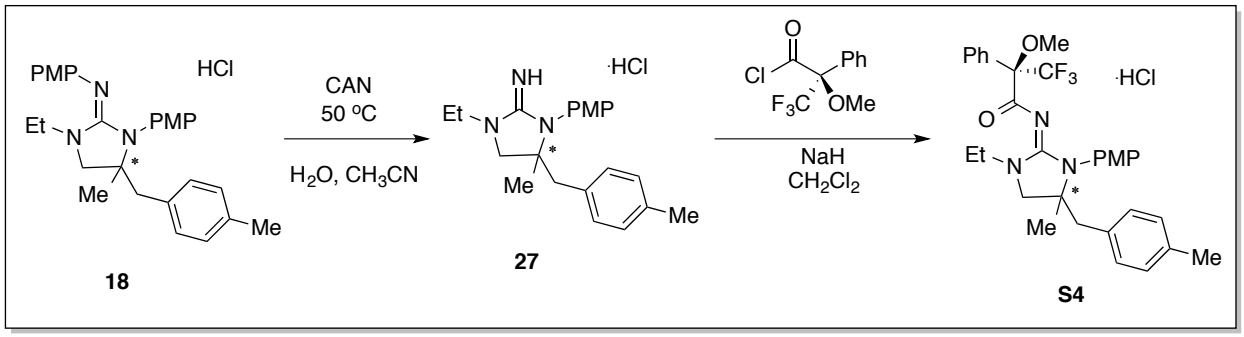
1-Ethyl-3-(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-one (S3): A flame-dried Schlenk tube was cooled under vacuum and charged with Pd_2dba_3 (110 mg, 0.12 mmol), xantphos (139 mg, 0.24 mmol)**,** NaO*t*Bu (865 mg, 9.0 mmol), and 4-bromotoluene (1.5 g, 9.0 mmol). A solution of **S2** (1.5 g, 6.0 mmol) in toluene (30 mL) was added via syringe and the tube was heated to 105 ^{o}C for 3 h. The mixture was cooled to rt and saturated aqueous NH_4Cl (15 mL) and ethyl acetate (25 mL) were added. The layers were separated and the organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford 1.96 mg (97%) of the title compound as a orange yellow oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.18 (d, *J* = 9.1 Hz, 2 H), 7.08 (d, *J* = 7.7 Hz, 2 H), 6.99 (d, *J* = 8.4 Hz, 2 H), 6.92 (d, *J* = 9.1 Hz, 2 H), 3.82 (s, 3 H), 3.46 (d, *J* = 8.4 Hz, 1 H), 3.37–3.32 (m, 1 H), 3.27–3.22 (m, 1 H), 2.92 (d, *J* = 13.3 Hz, 1 H), 2.84 (d, *J* = 9.1 Hz, 1 H), 2.65 (d, *J* = 13.3 Hz, 1 H), 2.31 (s, 3 H), 1.22 (s, 3 H), 1.11 (t, *J* = 7.0 Hz, 3 H);



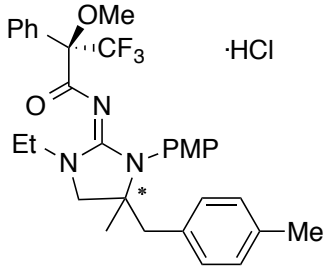
1-Ethyl-3-(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-imine hydrochloride (27). A flame-dried flask was cooled under a stream of N_2 and charged with **S3** (100 mg, 0.3 mmol) and toluene (2 mL). $POCl_3$ (0.6 mL) was added and the mixture was stirred at 100 ^oC until the starting material had been consumed as judged by ESI^+ MS analysis (ca. 2 hr). The reaction mixture was cooled to rt and concentrated *in vacuo*. The crude product was dissolved in acetonitrile (10 mL) and a solution of ammonia in ethanol (15 mL, 2 M in ethanol) was added. The mixture was stirred at rt until the starting material had been consumed as judged by ESI^+ MS analysis (ca. 1 hr). The reaction mixture was concentrated and dissolved in dichloromethane (5 mL). Water (5 mL) was added and the mixture was transferred to a separatory funnel. The layers were separated and the organic layer was washed with 1 M HCl (10 mL) and saturated aqueous sodium chloride (2 x 10 mL). The combined aqueous layers were extracted with dichloromethane (3 x 10 mL). The combined organics layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford 70 mg (63%) of the title compound as a white solid. The spectroscopic properties of this compound were identical to that of compound **27** described above that was prepared by deprotection of **18**.

Stereochemical Analysis of Enantioenriched Cyclic Guanidine Product 18.

In order to assess the enantiomeric purity of cyclic guanidine products **18** prepared from (*S*)-Phanephos and (*S*)-BINAP, the carboamination products were converted to the corresponding Mosher amides **S4** via the two-step procedure illustrated below. The enantiomeric ratio of **18** was assigned based on the diastereomeric ratio of crude **S4** as determined by ^1H NMR analysis.

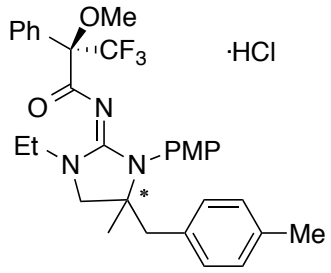


18 **27** **S4**



(2*R*)-*N*-(1-Ethyl-3-(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-ylidene)-3,3,3-trifluoro-2-methoxy-2-phenylpropanamide hydrochloride (S4 prepared from (+)-18 that was generated using (*S*)-Phanephos as ligand). The chiral guanidine **(+)-18** prepared using (*S*)-Phanephos as the ligand (51.5 mg, 0.11 mmol) was deprotected with ceric ammonium nitrate (361 mg, 0.66 mmol) according to the procedure detailed above. After flash chromatography, this procedure afforded 8.0 mg (20%) of enantioenriched **27** as a brown solid. The spectroscopic properties of this compound were identical to that of racemic **27** described above. The purified nonracemic material **27** (8.0 mg, 0.02 mmol) was dissolved in dichloromethane (1 mL) and stirred at rt. NaH (2.5 mg, 0.06 mmol, 60% dispersion in mineral oil) was added and the mixture was allowed to stir at rt for 10 min. Neat (*S*)-(+)-α-Methoxy-α-trifluoromethylphenylacetyl chloride (6 µL, 0.03 mmol) was added via syringe and the mixture was stirred at rt until the starting material had been consumed as judged by ESI^+ MS analysis of an aliquot removed from the reaction mixture (ca. 1 hr). Brine (2 mL) was added and the biphasic mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with dichloromethane (2 x 4 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. This procedure afforded a crude mixture that was determined to be a 61:39 mixture of diastereomers by ^1H NMR analysis. The crude material was purified by flash chromatography on silica gel to afford 8.9 mg (77%) of the title compound as a pale brown foamy-oil and as a 57:43 mixture of diastereomers (note that product er was assigned based on dr of the crude product, as some separation of diastereomers likely occurred during purification). Data are for the mixture of isomers. ^1H NMR (500 MHz, $CDCl_3$) δ 7.44–7.40 (m, 3.5 H), 7.29–7.24 (m, 3.75 H), 7.23–7.16 (m, 5 H), 7.12–7.10 (m, 3.5 H), 7.05–7.02 (m, 3.5 H), 6.89–6.87 (m, 3.5 H), 3.83 (s, 5.25 H), 3.77 (d, *J* = 10.0 Hz, 0.75 H), 3.73 (d, *J* = 10.0 Hz, 1 H), 3.35–3.25 (m, 2.75 H), 3.24 (s, 3 H), 3.22 (s, 2.25 H), 3.20–3.18 (m, 0.75 H), 3.16 (d, *J* = 10.0 Hz, 1 H), 3.10 (d, *J* = 10.5 Hz, 0.75 H), 3.07–3.03 (m, 1.75 H), 2.75 (d, *J* = 13.5 Hz, 1 H), 2.69 (d, *J* = 13.5 Hz, 0.75 H), 2.32 (s, 5.25 H), 1.31 (s, 2.25 H), 1.28 (s, 3 H), 1.12–1.08 (m, 5.25 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 167.8, 164.4, 164.3, 159.7, 159.6, 136.9, 136.9, 135.8, 135.7, 132.2, 132.2, 131.6, 131.6, 130.2,

130.1, 129.3, 129.3, 127.9, 127.6, 127.5, 127.5, 127.4, 125.7, 123.4, 114.1, 64.5, 64.5, 55.5, 55.0, 54.7, 54.3, 44.3, 43.9, 40.2, 40.1, 24.5, 24.4, 21.0, 12.4, 12.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –69.56, –69.58; IR (film) 2925, 1653, 1559 cm^{-1}. MS (ESI) 554.2625 (554.2625 calcd for $C_{31}H_{34}F_3N_3O_3$, M^+).



(2*R*)-*N*-(1-Ethyl-3-(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-ylidene)-3,3,3-trifluoro-2-methoxy-2-phenylpropanamide hydrochloride (S4 prepared from (–)-18 that was generated using (*S*)-BINAP as ligand). The chiral guanidine **(–)-18** prepared using (*S*)-BINAP as the ligand (48 mg, 0.1 mmol) was deprotected with ceric ammonium nitrate (329 mg, 0.6 mmol) according to the procedure detailed above. After flash chromatography, this procedure afforded 14.4 mg (39%) of enantioenriched **27** as a brown solid. The spectroscopic properties of this compound were identical to that of compound racemic **27** described above. The purified nonracemic material **27** (14.4 mg, 0.04 mmol) was dissolved in dichloromethane (1 mL) and stirred at rt. NaH (4.8 mg, 0.12 mmol, 60% dispersion in mineral oil) was added and the mixture was allowed to stir at rt for 10 min. Neat (*S*)-(+)-α-Methoxy-α-trifluoromethylphenylacetyl chloride (11 µL, 0.06 mmol) was added via syringe and the mixture was stirred at rt until the starting material had been consumed as judged by ESI^+ MS analysis of an aliquot removed from the reaction mixture (ca. 1 hr). Brine (2 mL) was added and the biphasic mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with dichloromethane (2 x 4 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. This procedure afforded a crude mixture that was determined to be a 48:52 mixture of diastereomers by ^{1}H NMR analysis. The crude material was purified by flash chromatography on silica gel to afford 10.8 mg (48%) of the title compound as a pale brown foamy-oil and as a 51:49 mixture of diastereomers. Spectroscopic data were identical to those described above (although integration ratios differed due to the differences in product distribution.

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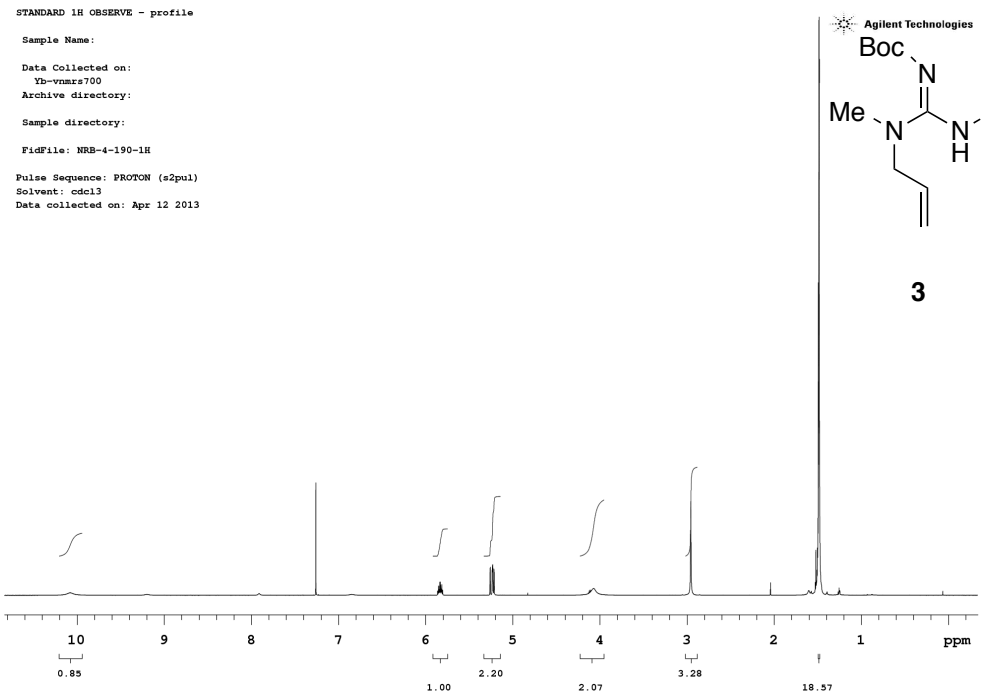
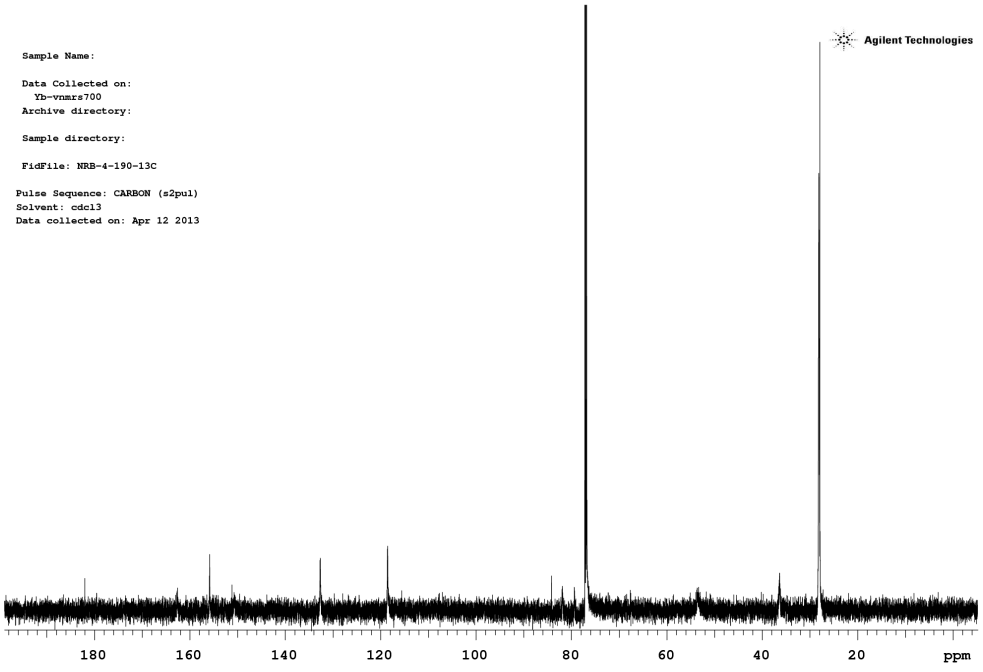
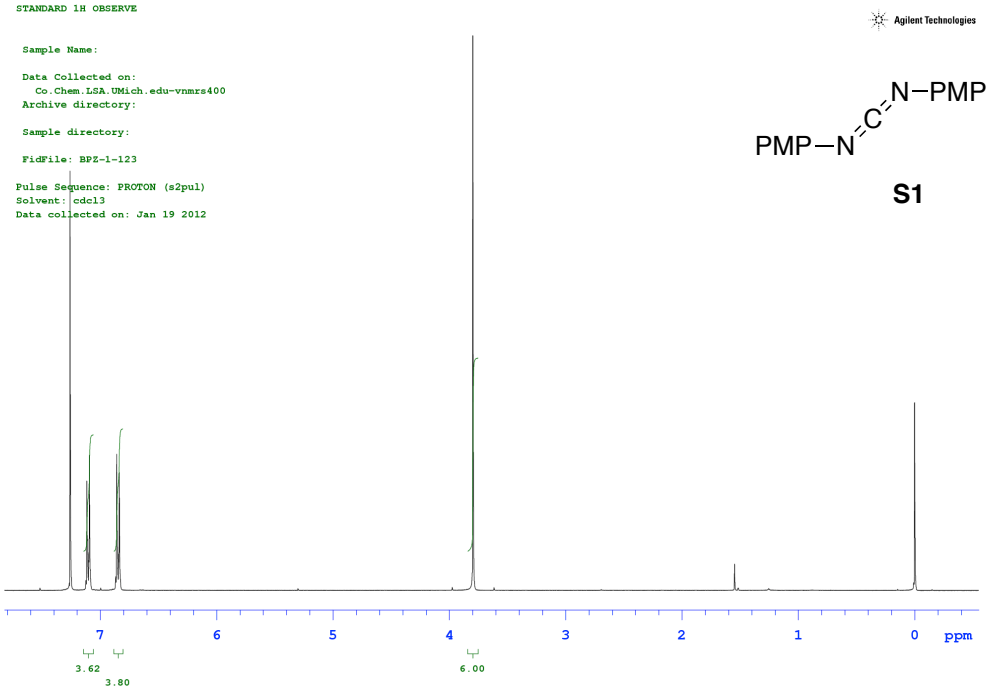
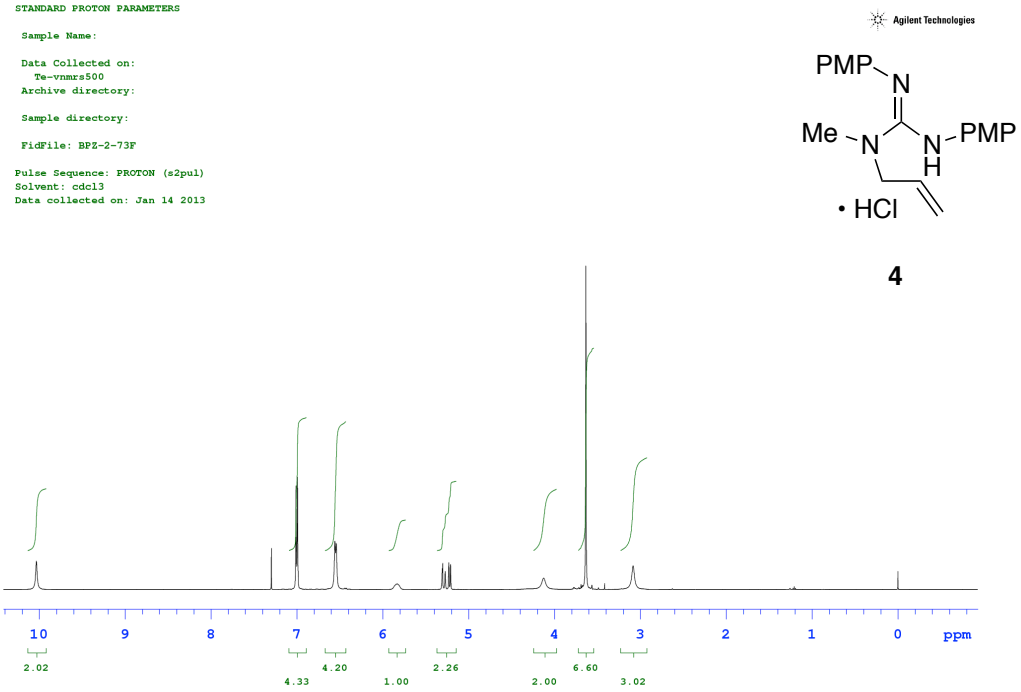
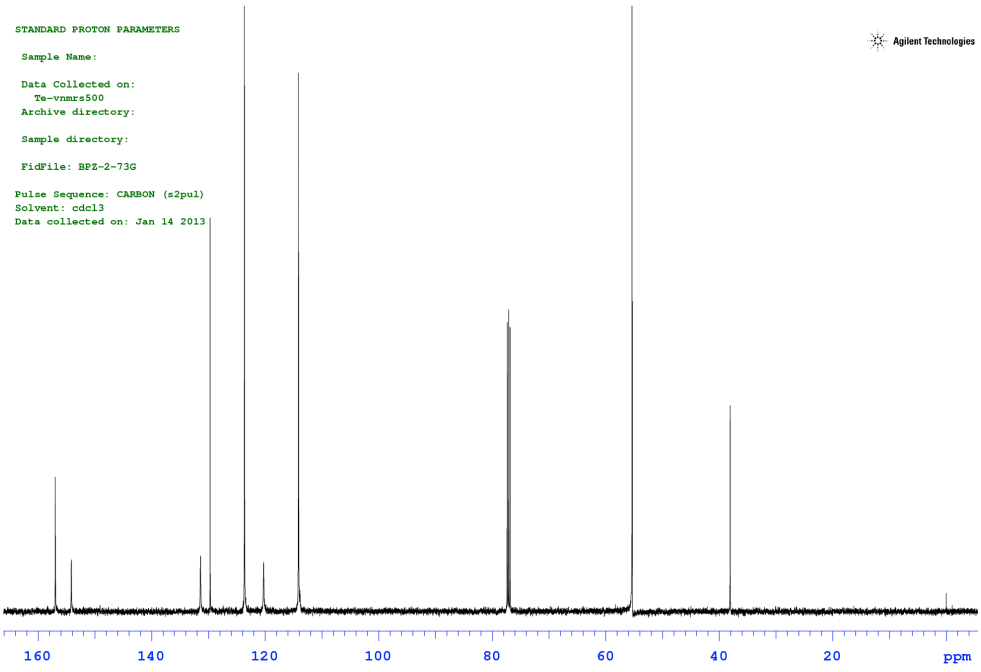

STANDARD 1H OBSERVE - profile
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-4-190-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013
Agilent Technologies
Boc
N
Me
N
N
Boc
H
3
10
9
8
7
6
5
4
3
2
1
ppm
0.85
1.00
2.20
2.07
3.28
18.57


Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-4-190-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013
Agilent Technologies
180
160
140
120
100
80
60
40
20
ppm


STANDARD 1H OBSERVE
Agilent Technologies
Sample Name:
Data Collected on:
Co.Chem.LSA.UMich.edu-vnmrs400
Archive directory:
Sample directory:
FidFile: BPZ-1-123
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 19 2012
N–PMP
PMP–N
C
S1
7
6
5
4
3
2
1
0
ppm
3.62
3.80
6.00


STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-73F
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 14 2013
Agilent Technologies
PMP
N
Me
N
N
PMP
H
• HCl
10
9
8
7
6
5
4
3
2
1
0
ppm
2.02
4.33
4.20
1.00
2.26
2.00
6.60
3.02

4


STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-73G
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 14 2013
Agilent Technologies
160
140
120
100
80
60
40
20
ppm

STANDARD PROTON PARAMETERS

Sample Name:

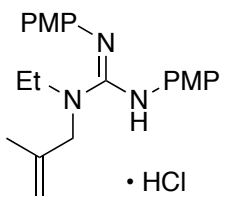
Data Collected on:
Te-vnmrs500
Archive directory:

Sample directory:

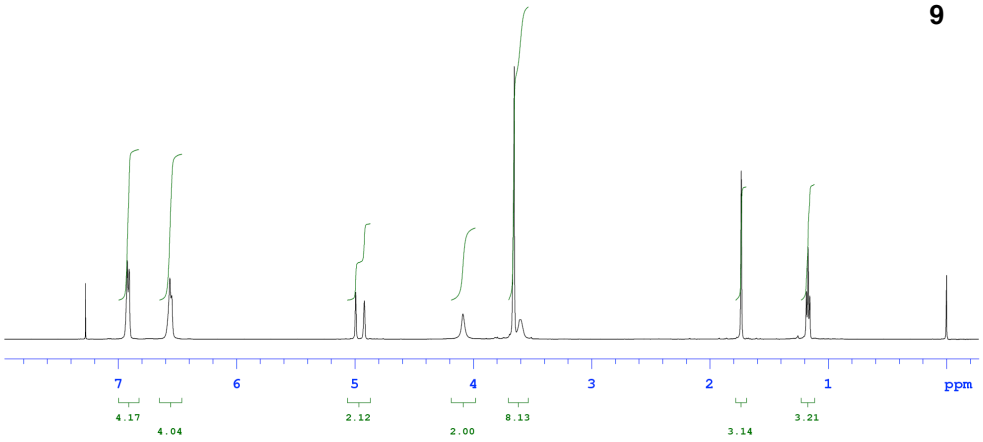
FidFile: BPZ-2-95

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 26 2013

Agilent Technologies



9



Agilent Technologies

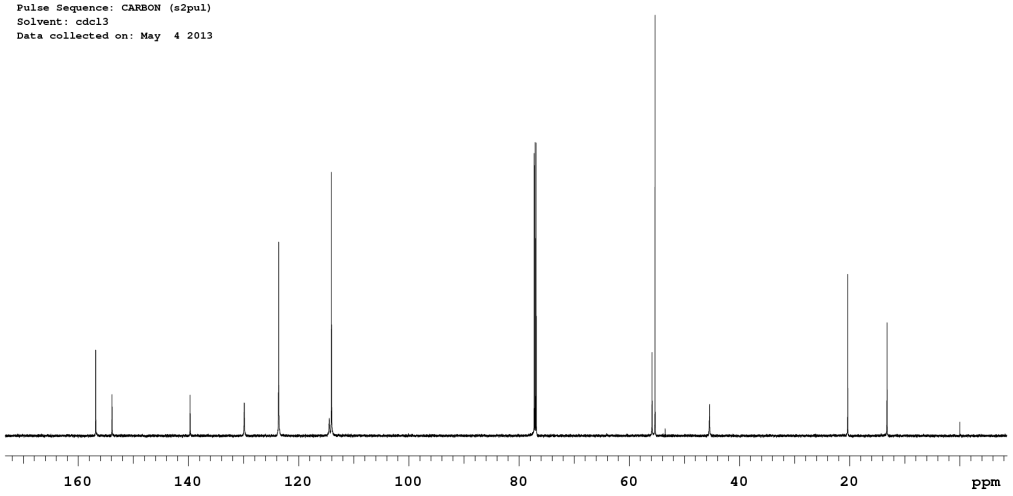
Sample Name:

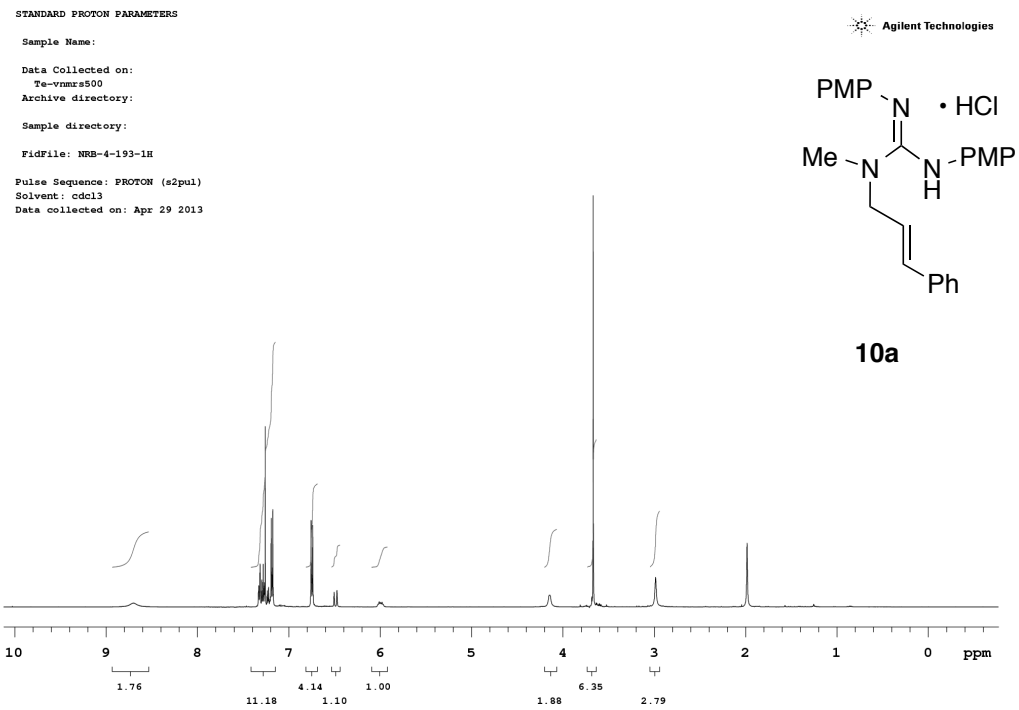
Data Collected on:
Yb-vnmrs700
Archive directory:

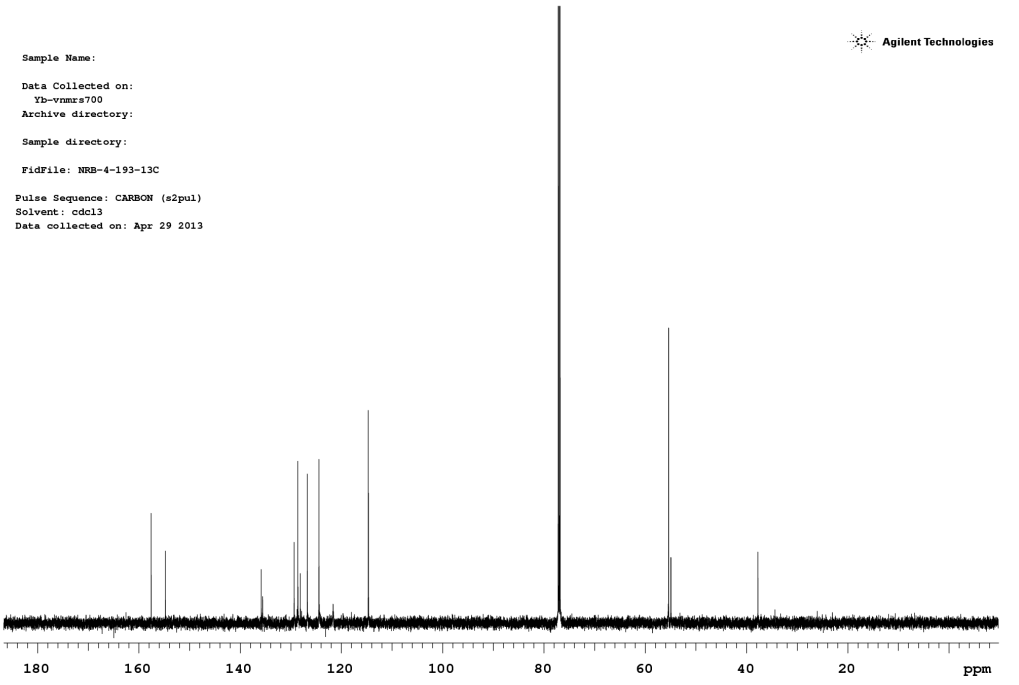
Sample directory:

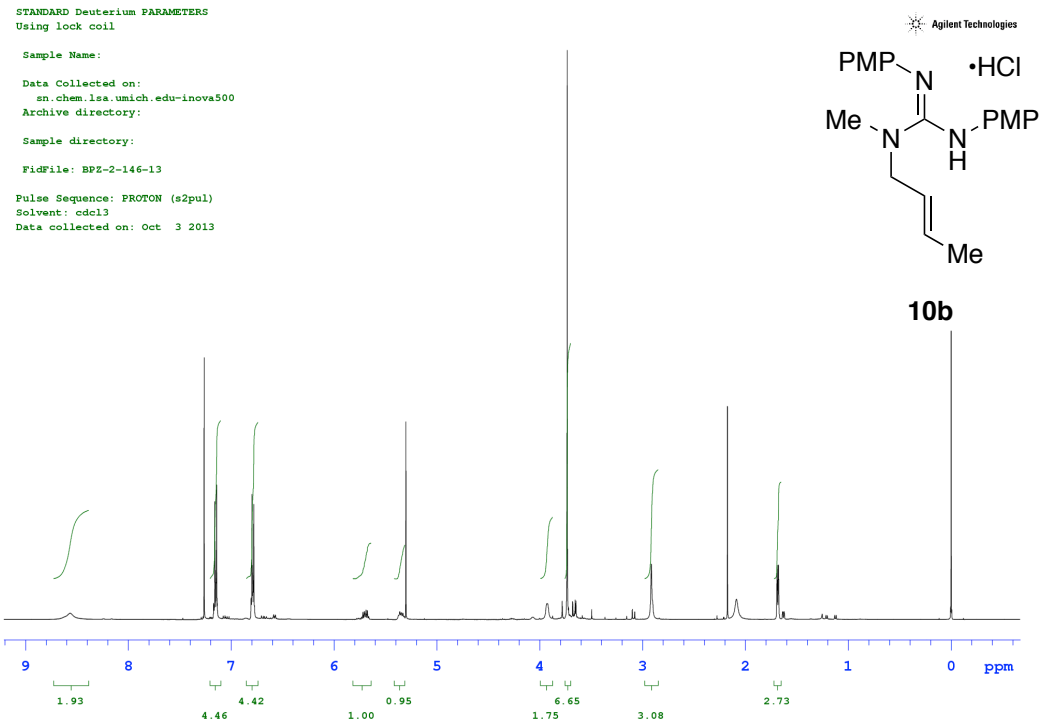
FidFile: BPZ-2-95CC

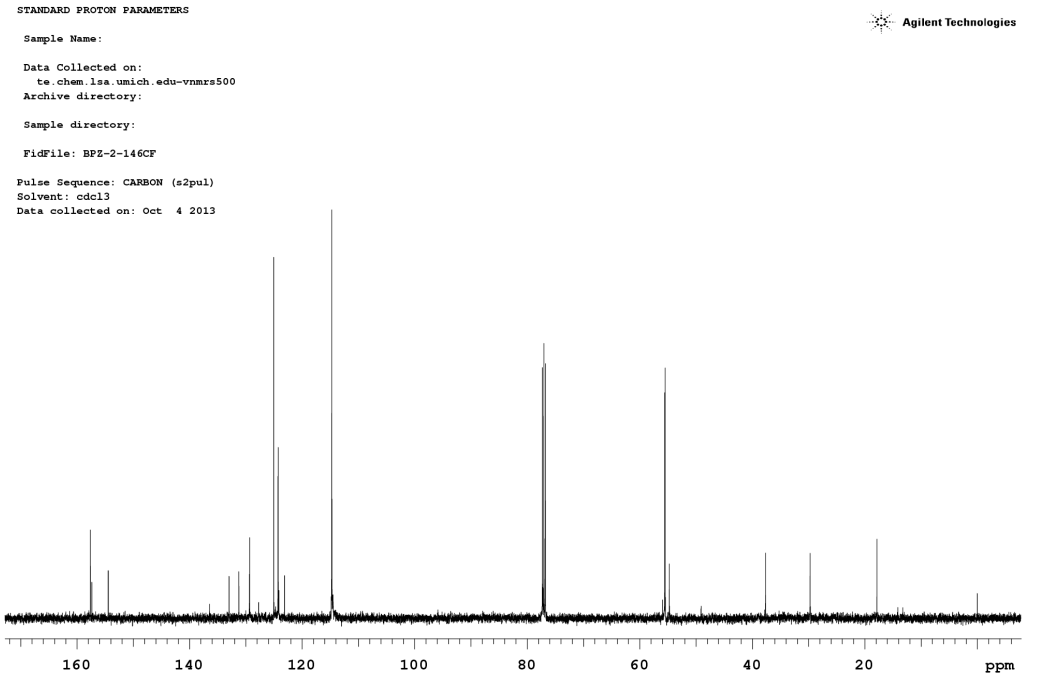
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 4 2013

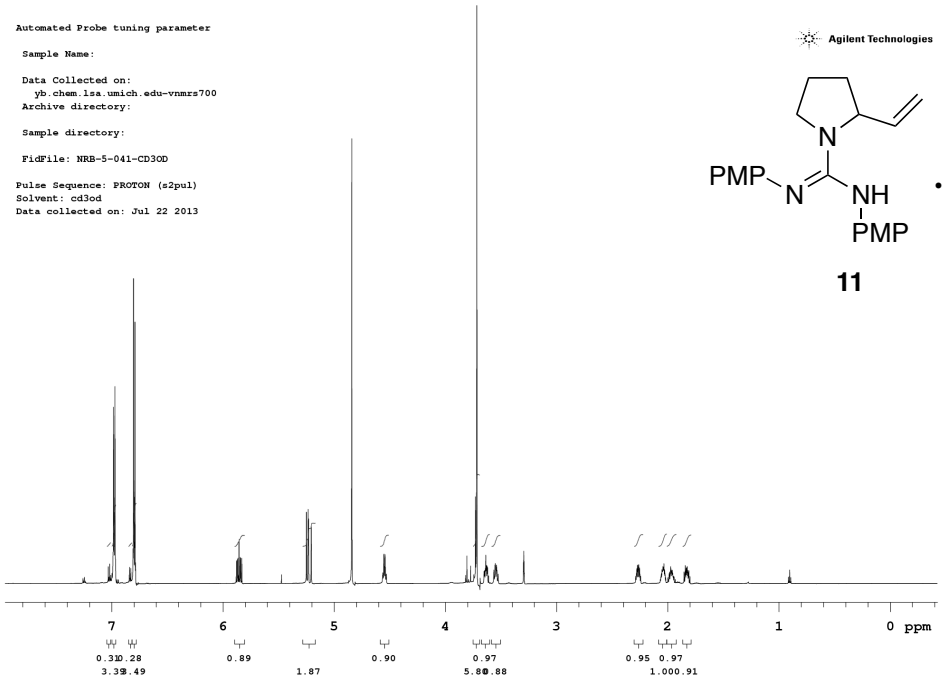


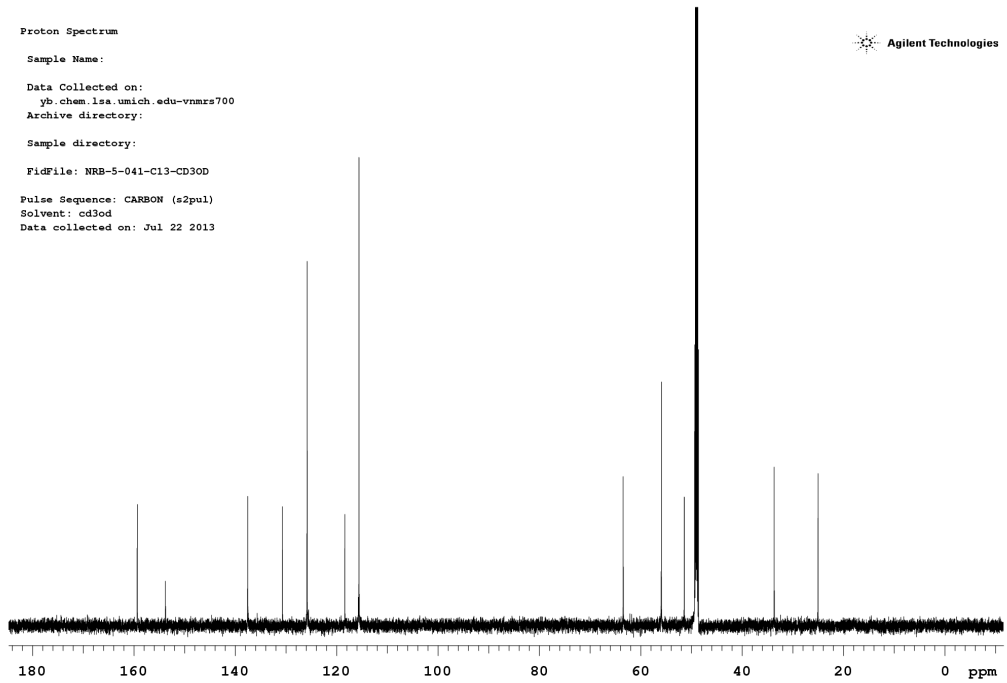

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: NRB-4-193-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 29 2013
Agilent Technologies
PMP
N
• HCl
Me
N
N
H
PMP
Ph
10a
10
9
8
7
6
5
4
3
2
1
0
ppm
1.76
11.18
4.14
1.10
1.00
1.88
6.35
2.79

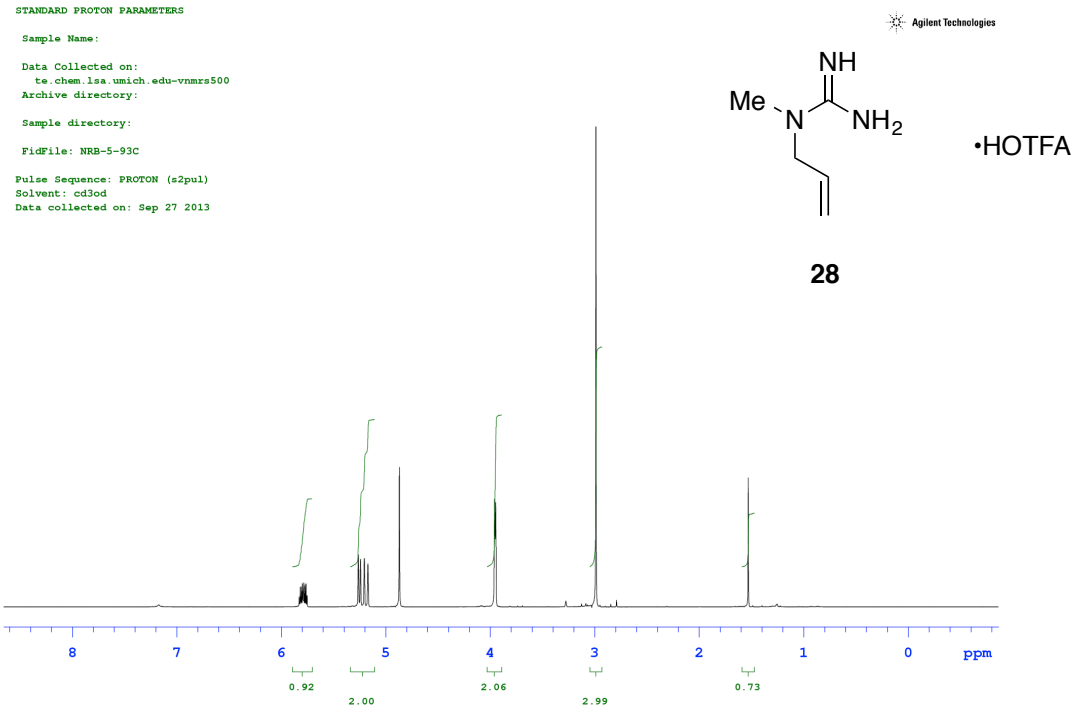

Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-4-193-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 29 2013
Agilent Technologies
180
160
140
120
100
80
60
40
20
ppm

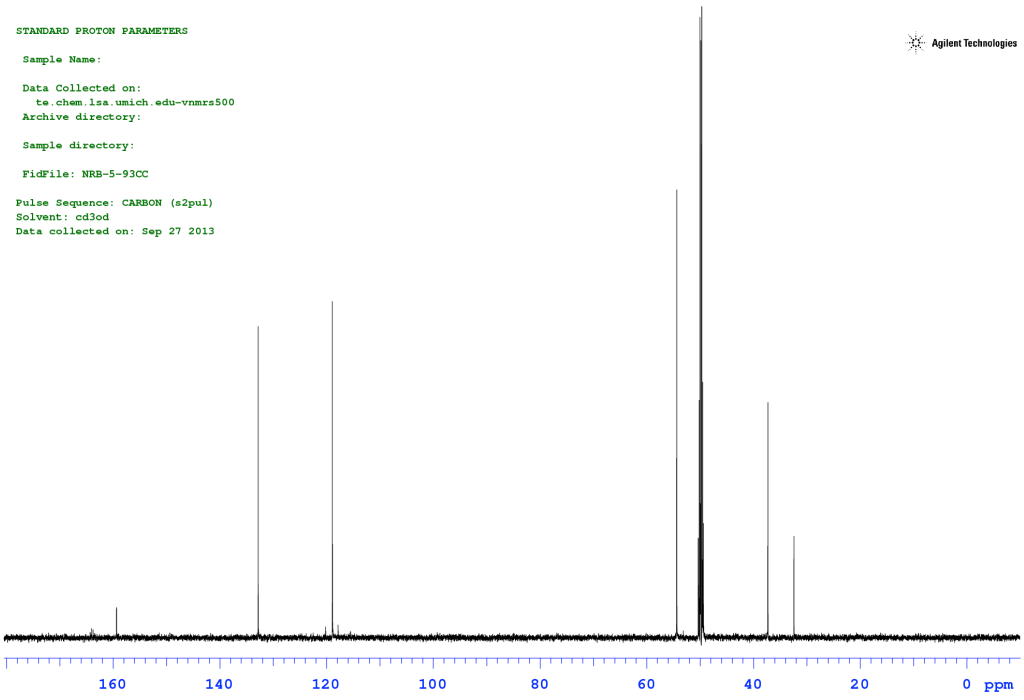

STANDARD Deuterium PARAMETERS
Using lock coil
Sample Name:
Data Collected on:
sn.chem.lsa.umich.edu-inova500
Archive directory:
Sample directory:
FidFile: BPZ-2-146-13
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 3 2013
Agilent Technologies
PMP
N
•HCl
Me
N
N
PMP
H
Me
10b
9
8
7
6
5
4
3
2
1
0
ppm
1.93
4.46
4.42
1.00
0.95
1.75
6.65
3.08
2.73

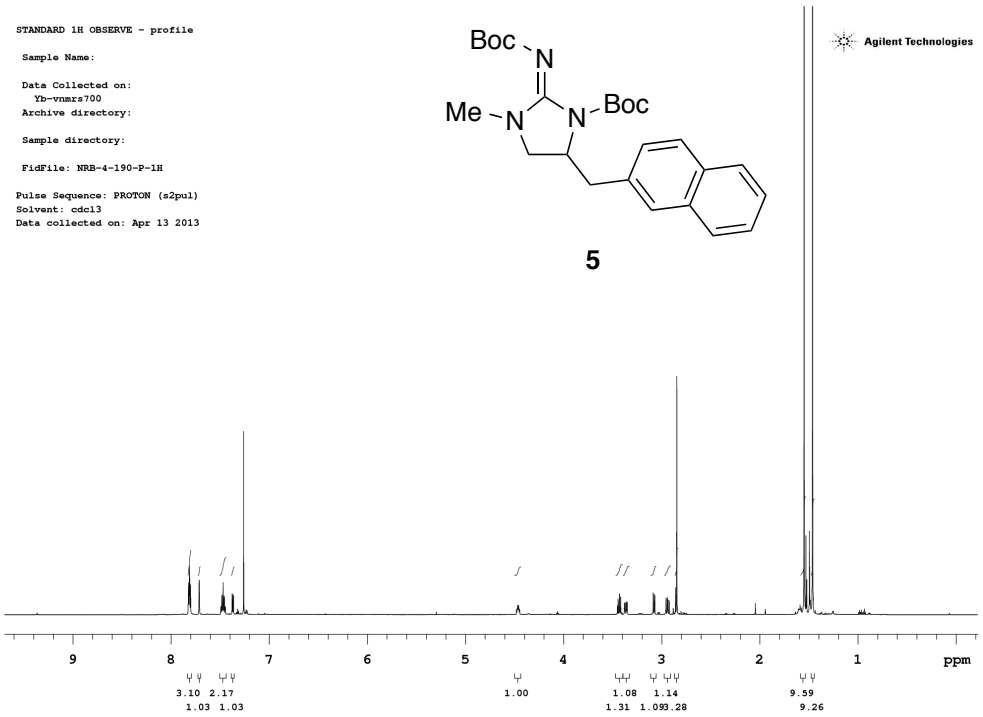

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
te.chem.lsa.umich.edu-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-146CF
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2013
Agilent Technologies
160
140
120
100
80
60
40
20
ppm

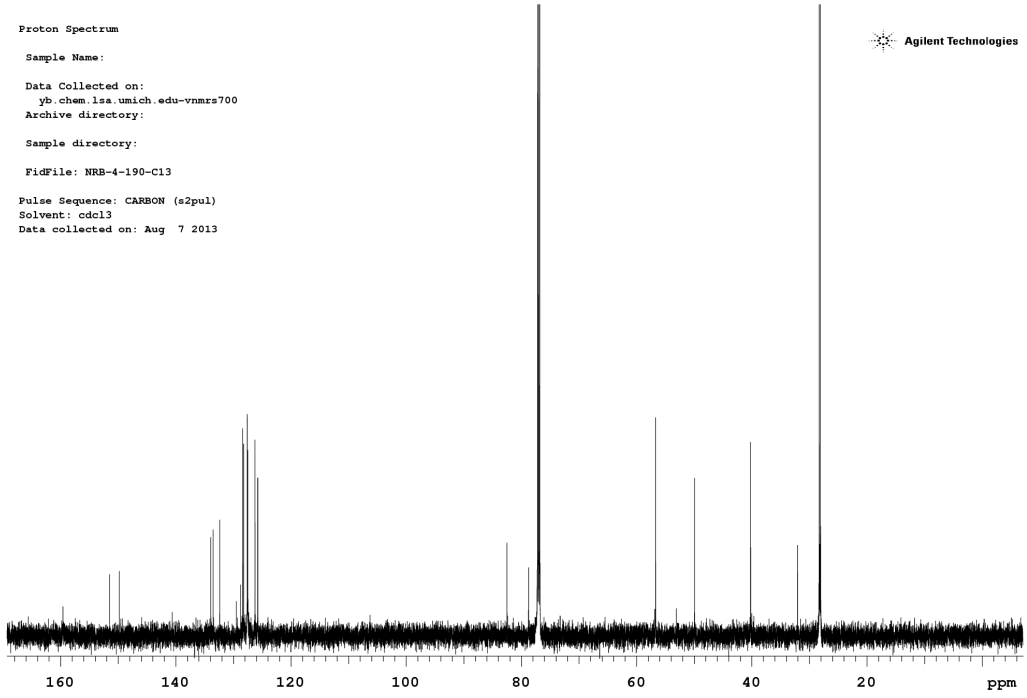

Automated Probe tuning parameter
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-041-CD3OD
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Jul 22 2013
Agilent Technologies
PMP
N
N
NH
PMP
• HCl
11
7
6
5
4
3
2
1
0 ppm
0.31
0.28
0.89
1.87
0.90
0.97
0.95
0.97
3.39
3.49
5.80
0.88
1.000.91

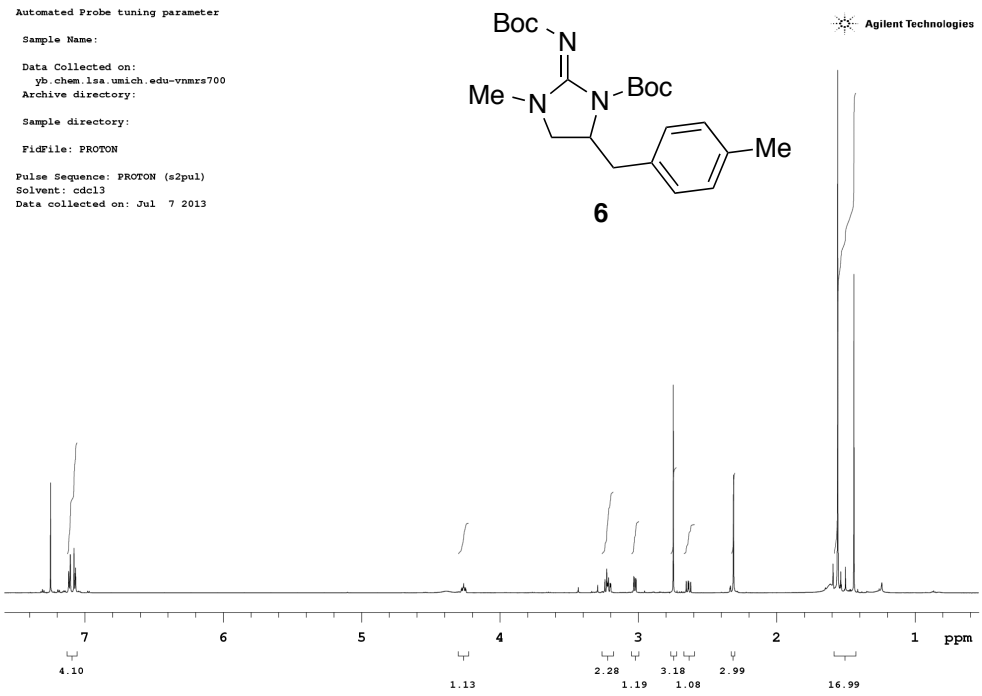

Proton Spectrum
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-041-C13-CD3OD
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Jul 22 2013
Agilent Technologies
180
160
140
120
100
80
60
40
20
0 ppm

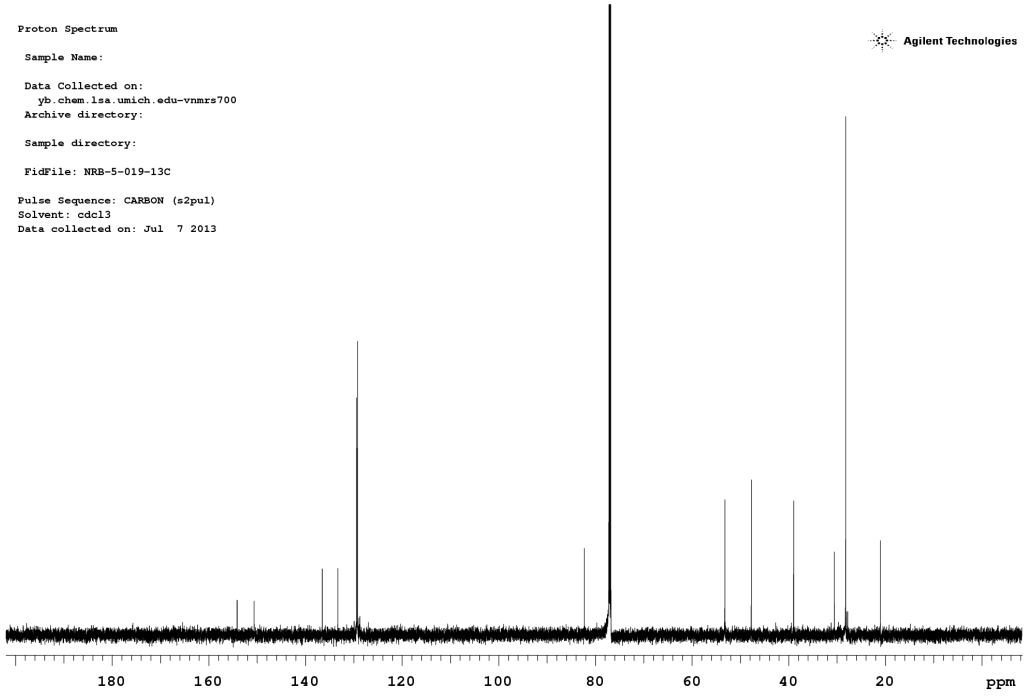

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
te.chem.lsa.umich.edu-vnmrs500
Archive directory:
Sample directory:
FidFile: NRB-5-93C
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Sep 27 2013
Agilent Technologies
NH
Me
N
NH2
•HOTFA
28
8
7
6
5
4
3
2
1
0
ppm
0.92
2.00
2.06
2.99
0.73


STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
te.chem.lsa.umich.edu-vnmrs500
Archive directory:
Sample directory:
FidFile: NRB-5-93CC
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Sep 27 2013
Agilent Technologies
160
140
120
100
80
60
40
20
0
ppm


STANDARD 1H OBSERVE - profile
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-4-190-P-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 13 2013
Agilent Technologies
Boc
N
Me
N
N
Boc
5
9
8
7
6
5
4
3
2
1
ppm
3.10
2.17
1.03
1.03
1.00
1.08
1.14
1.31
1.09
3.28
9.59
9.26


Proton Spectrum
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-4-190-C13
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 7 2013
Agilent Technologies
160
140
120
100
80
60
40
20
ppm


Automated Probe tuning parameter
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 7 2013
Agilent Technologies
Boc
N
Me
N
N
Boc
Me
6
7
6
5
4
3
2
1
ppm
4.10
1.13
2.28
1.19
3.18
1.08
2.99
16.99


Proton Spectrum
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-019-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 7 2013
Agilent Technologies
180
160
140
120
100
80
60
40
20
ppm

STANDARD PROTON PARAMETERS

Sample Name:

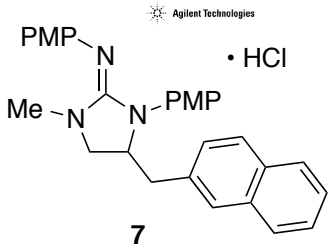
Data Collected on:
Te-vnmrs500
Archive directory:

Sample directory:

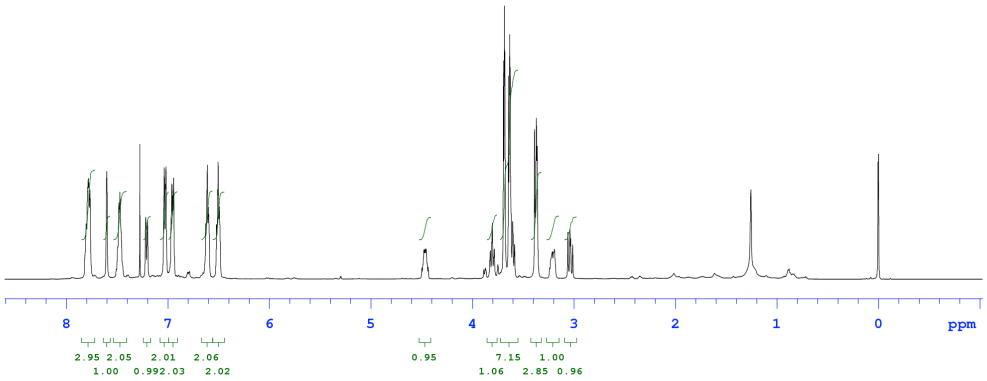
FidFile: BPZ-2-98A

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 1 2013

Agilent Technologies



7



STANDARD PROTON PARAMETERS

Sample Name:

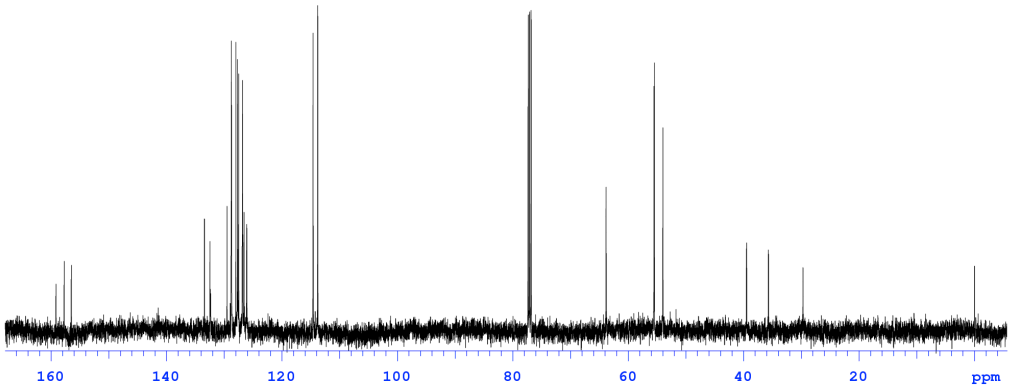
Data Collected on:
Te-vnmrs500
Archive directory:

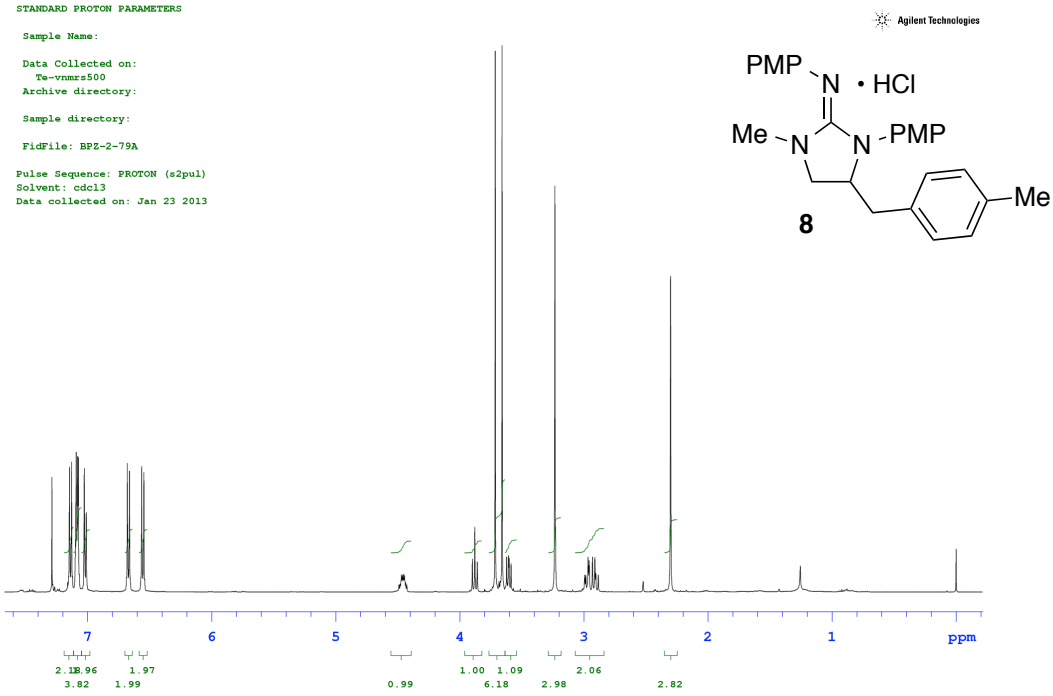
Sample directory:

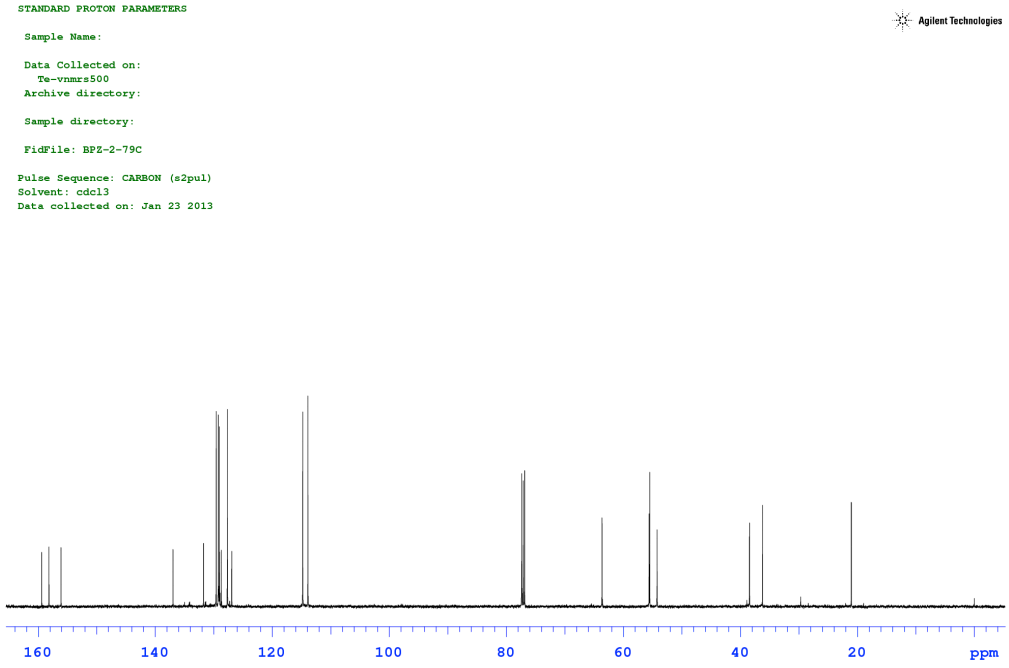
FidFile: BPZ-2-98C

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 1 2013

Agilent Technologies




STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-79A
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2013
Agilent Technologies
PMP
N
• HCl
Me
N
N
PMP
Me
8
7
6
5
4
3
2
1
ppm
2.13
3.96
1.97
3.82
1.99
0.99
1.00
1.09
6.18
2.98
2.06
2.82


STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-79C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2013
Agilent Technologies
160
140
120
100
80
60
40
20
ppm

STANDARD PROTON PARAMETERS

Sample Name:

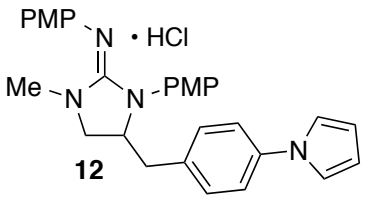
Data Collected on:
Te-vnmrs500
Archive directory:

Sample directory:

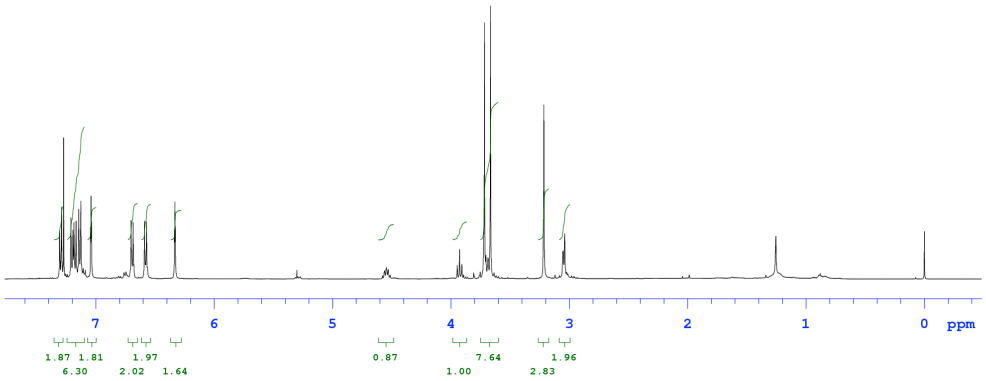
FidFile: BPZ-2-82B

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 30 2013

Agilent Technologies



12



STANDARD PROTON PARAMETERS

Sample Name:

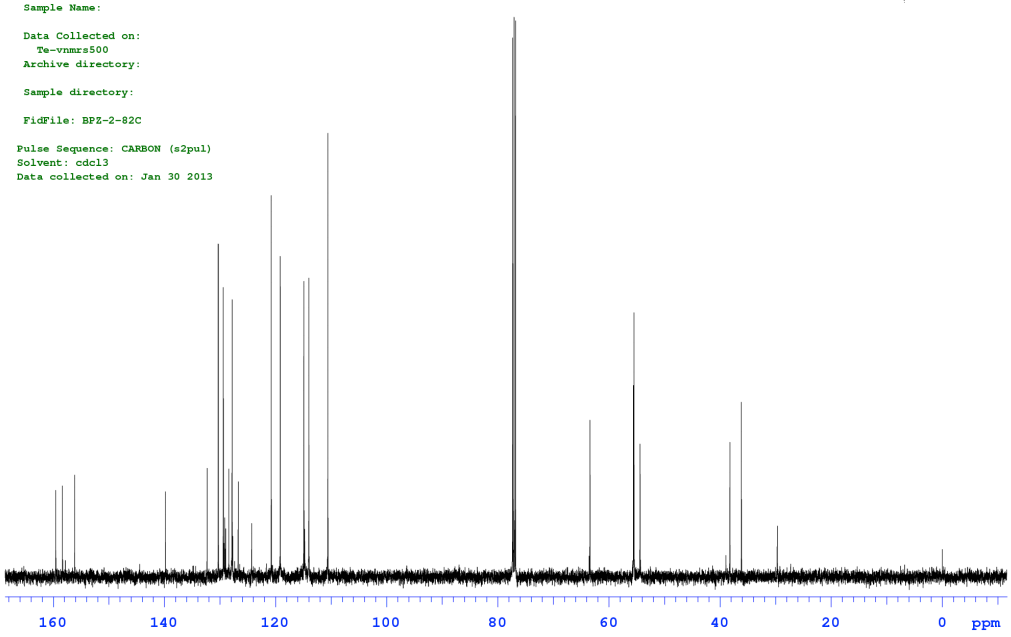
Data Collected on:
Te-vnmrs500
Archive directory:

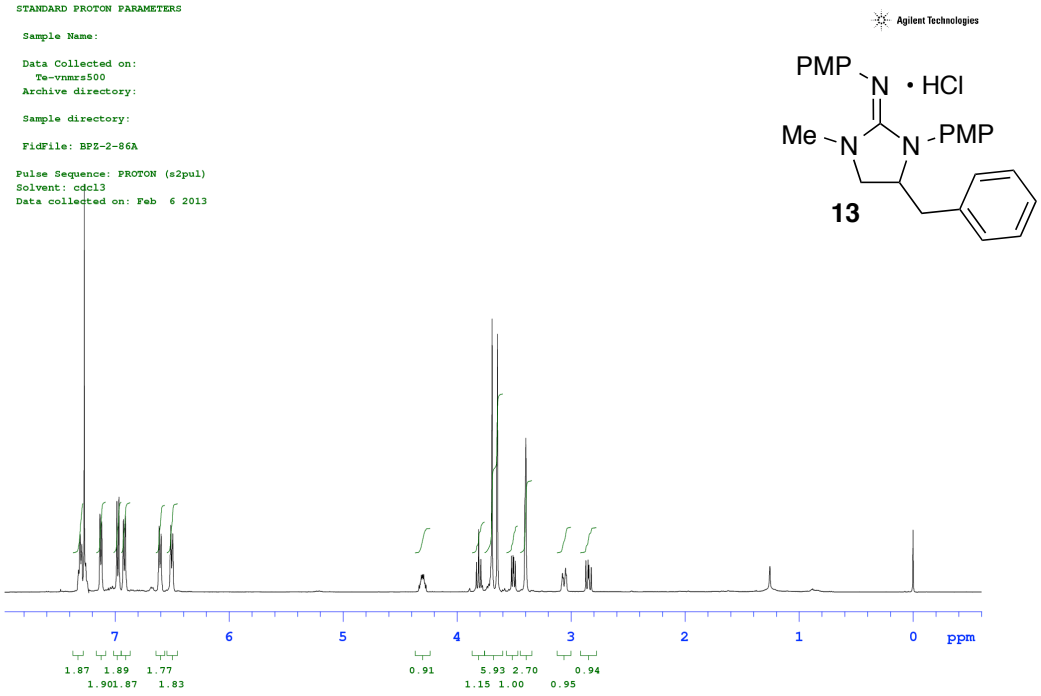
Sample directory:

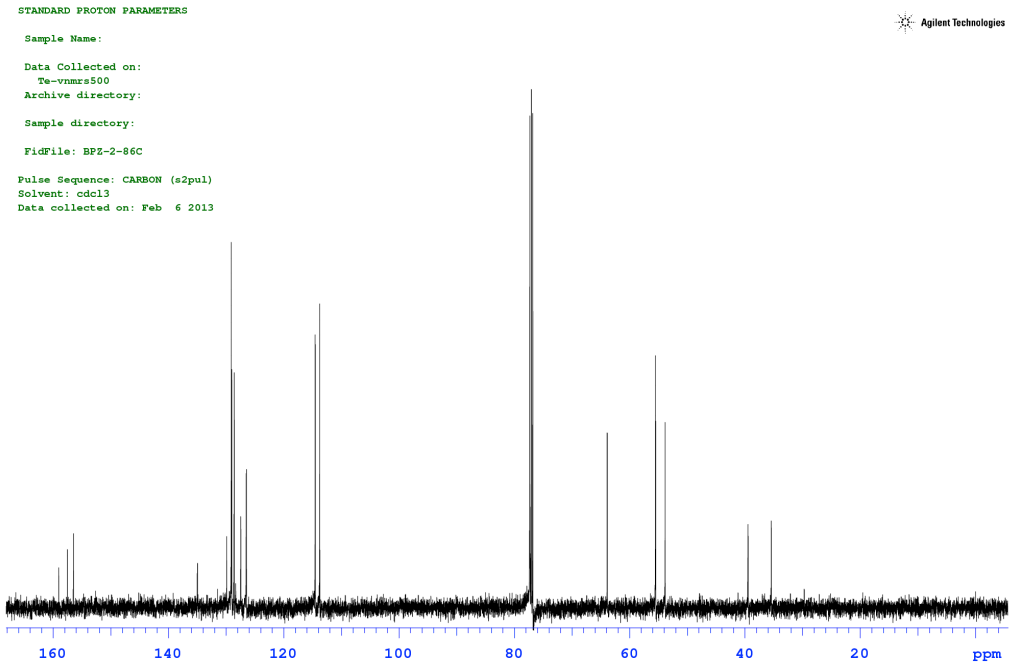
FidFile: BPZ-2-82C

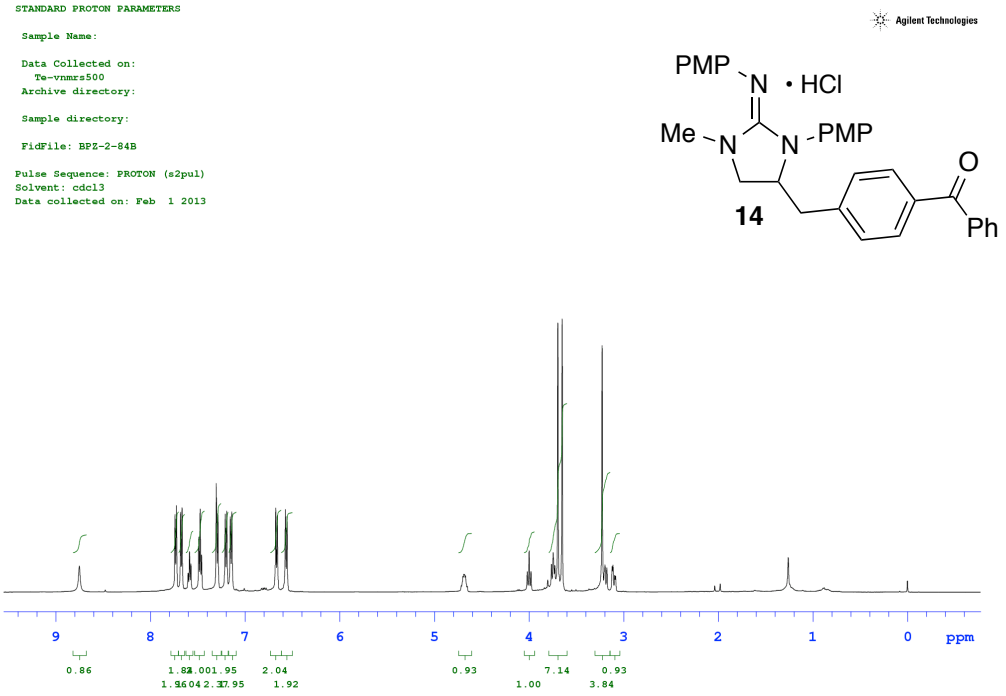
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 30 2013

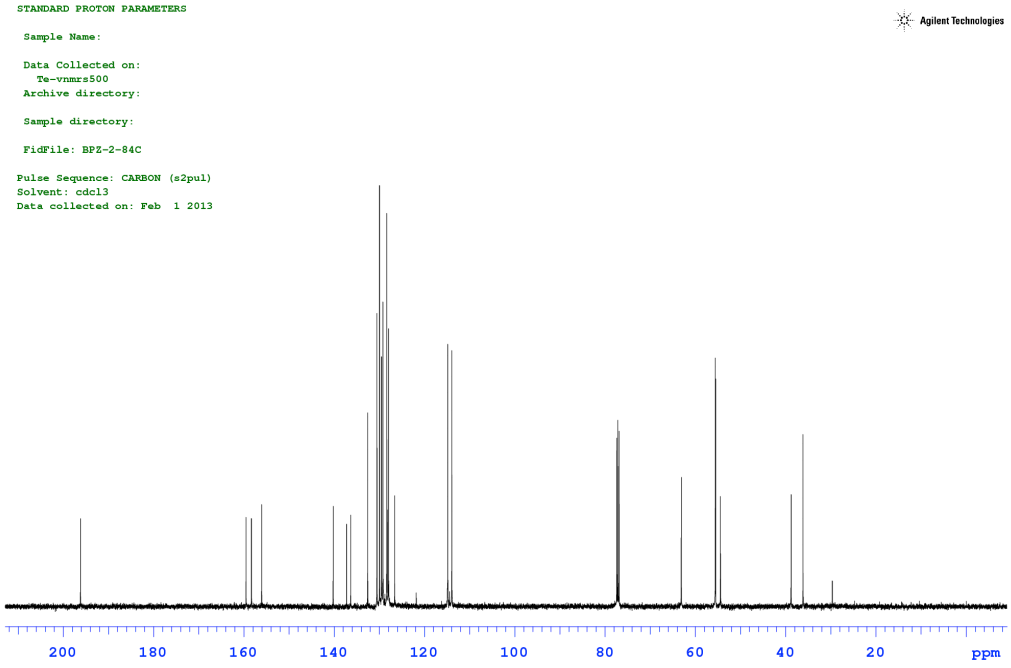
Agilent Technologies

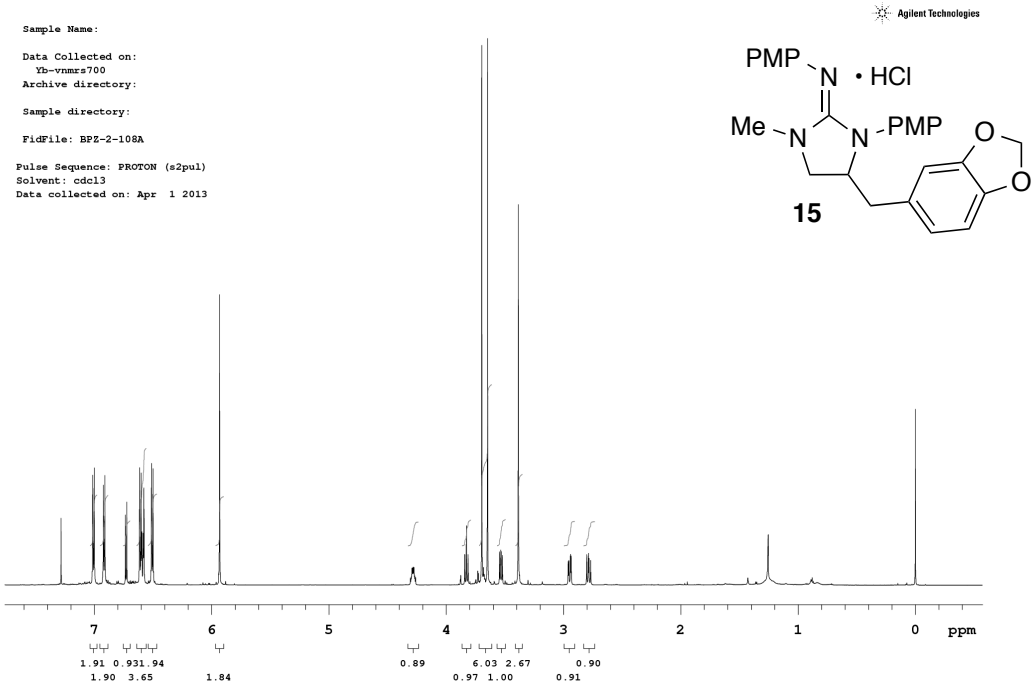


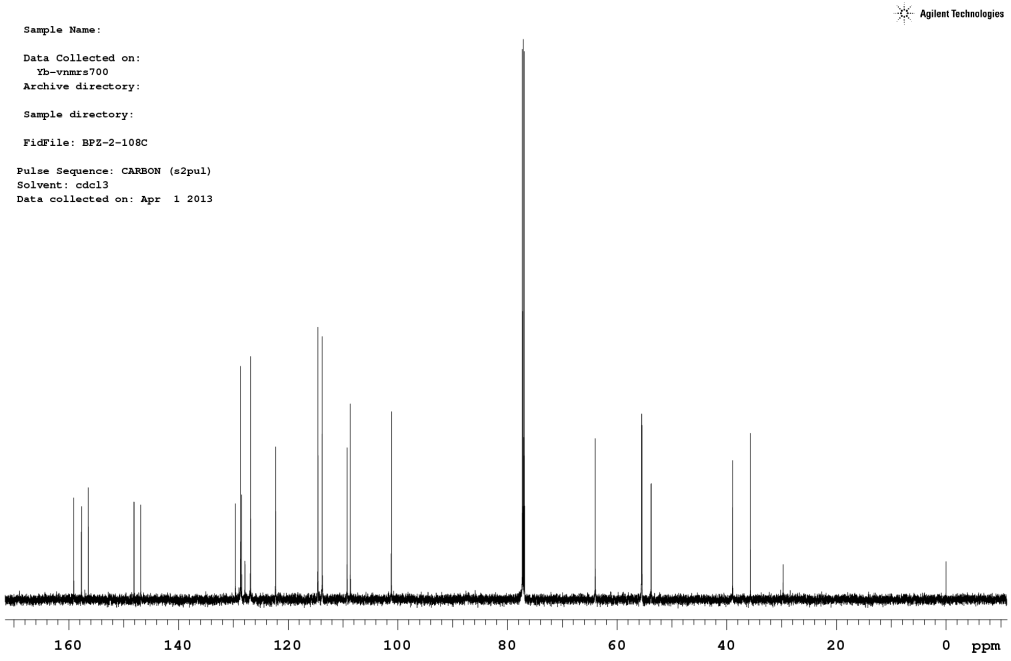

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-86A
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 6 2013
Agilent Technologies
PMP
N
• HCl
Me
N
N
PMP
13
7
6
5
4
3
2
1
0
ppm
1.87
1.89
1.77
1.90
1.87
1.83
0.91
5.93
2.70
1.15
1.00
0.94
0.95

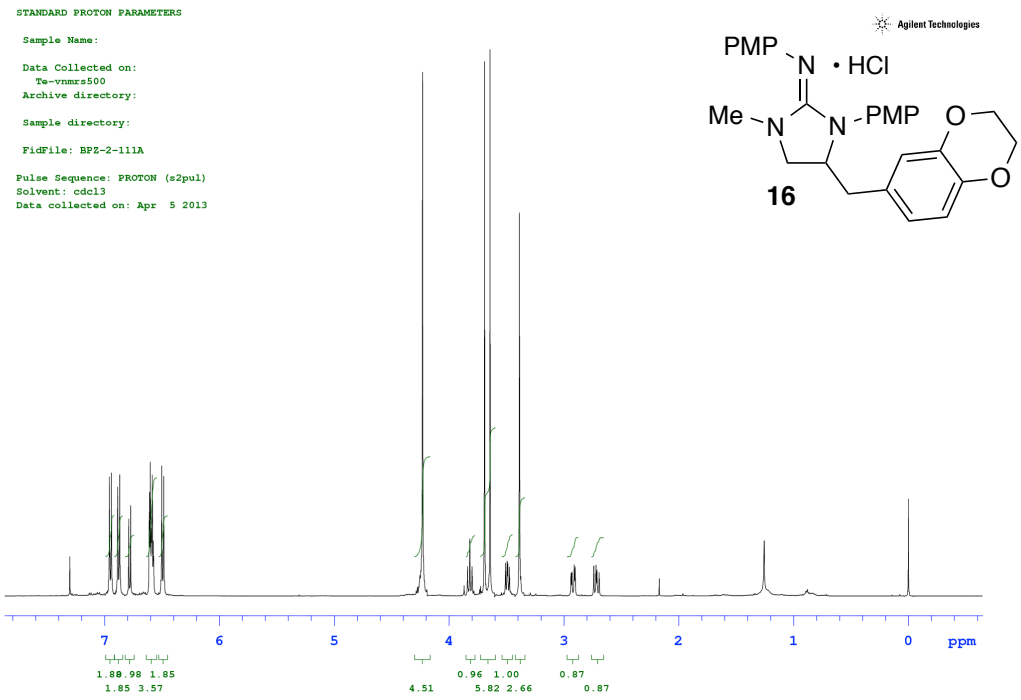

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-86C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 6 2013
Agilent Technologies
160
140
120
100
80
60
40
20
ppm

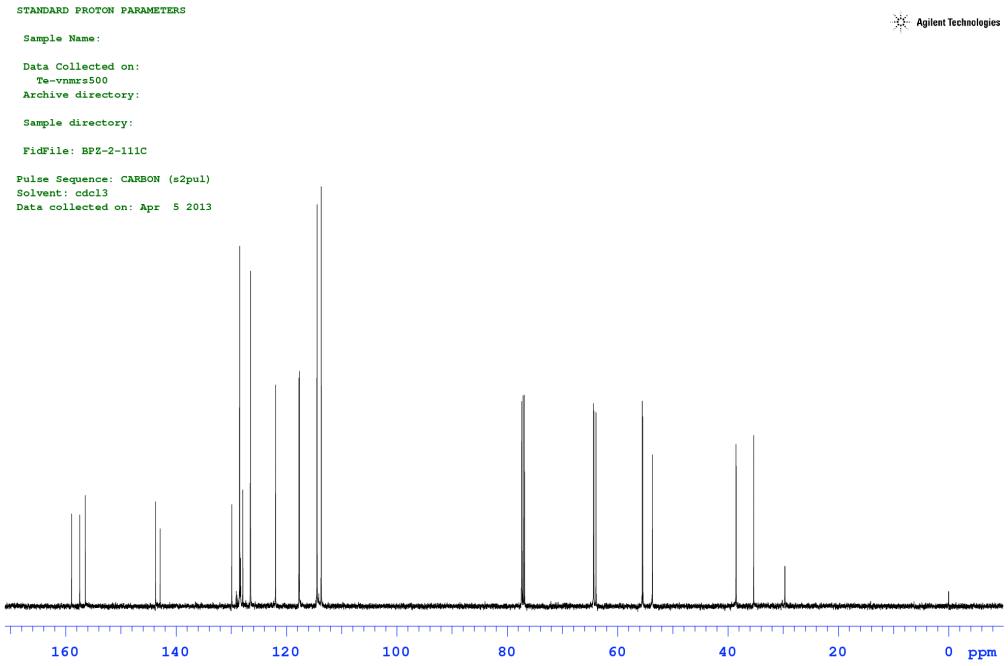

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-84B
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 1 2013
Agilent Technologies
PMP
N
• HCl
Me
N
N
PMP
O
Ph
14
9
8
7
6
5
4
3
2
1
0
ppm
0.86
1.82
1.00
1.95
2.04
1.92
0.93
7.14
1.00
0.93
3.84

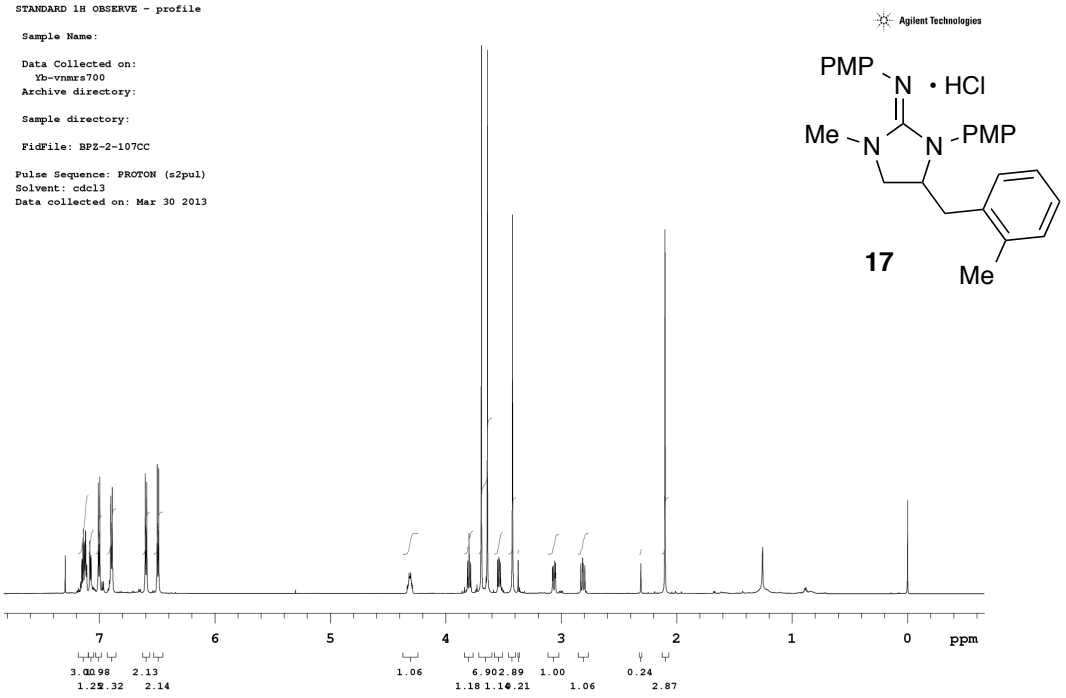

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-84C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 1 2013
Agilent Technologies
200
180
160
140
120
100
80
60
40
20
ppm

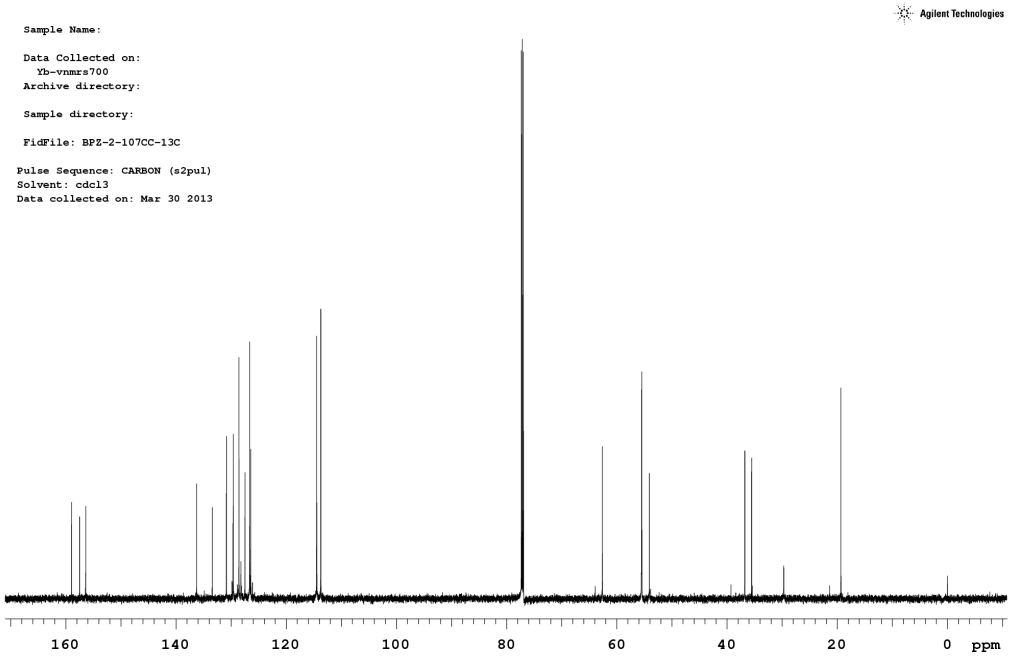

Agilent Technologies
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: BPZ-2-108A
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 1 2013
PMP
N
• HCl
Me
N
N
PMP
O
O
15
7
6
5
4
3
2
1
0
ppm
1.91 0.931.94
1.90 3.65
1.84
0.89
6.03 2.67
0.97 1.00
0.90
0.91

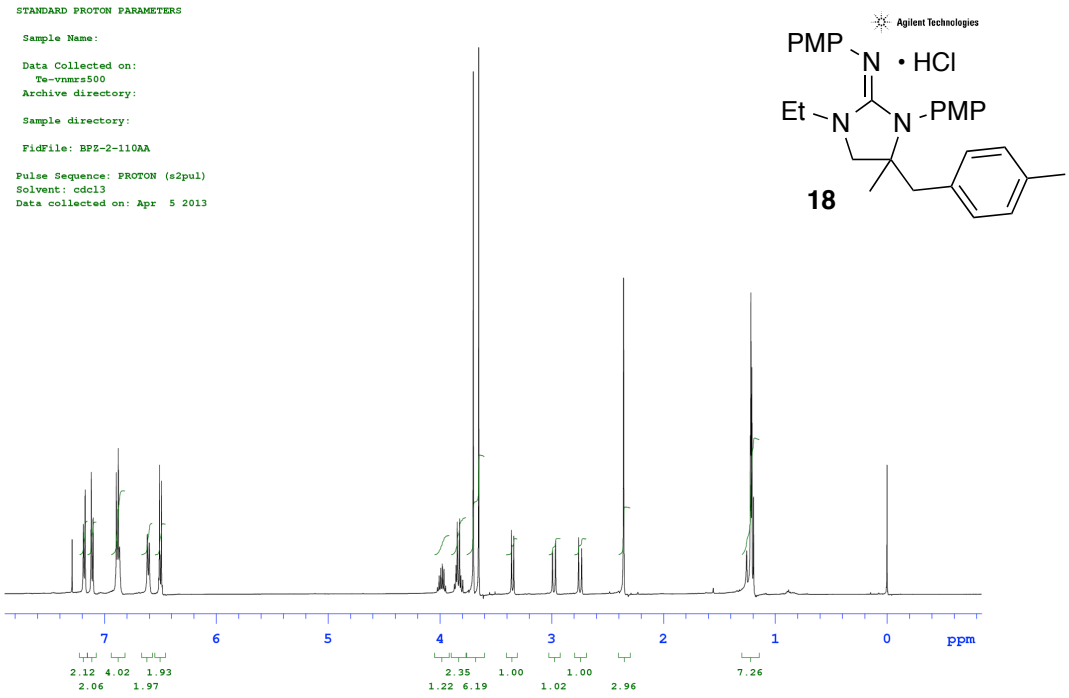

Agilent Technologies
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: BPZ-2-108C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 1 2013
160
140
120
100
80
60
40
20
0
ppm

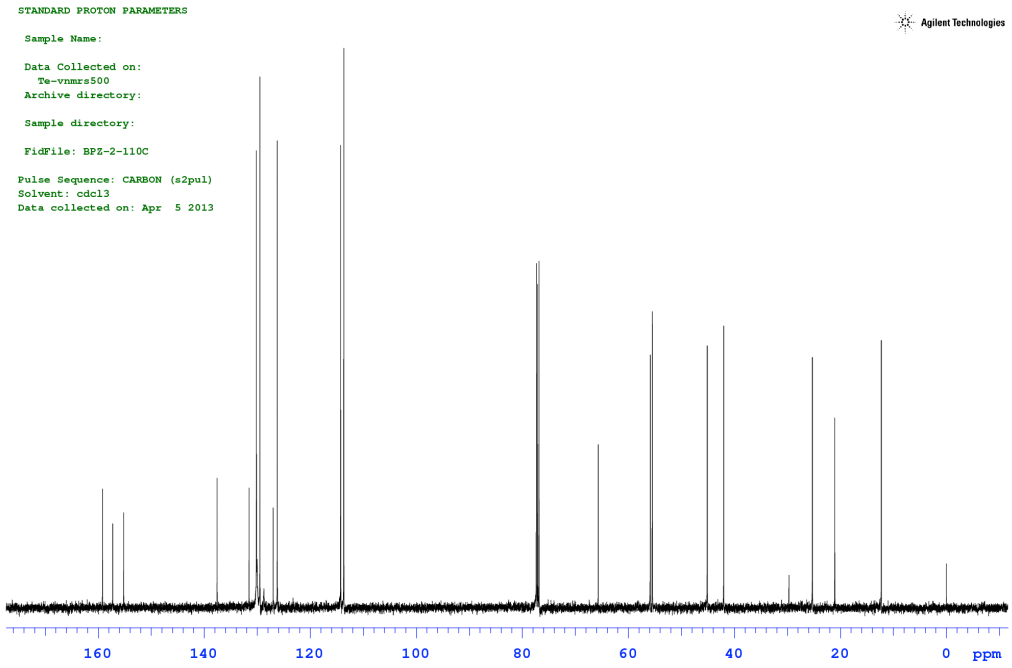

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-111A
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 5 2013
Agilent Technologies
PMP
N
• HCl
Me
N
N
PMP
O
O
16
7
6
5
4
3
2
1
0
ppm
1.88 .98 1.85
1.85 3.57
4.51
0.96 1.00
5.82 2.66
0.87
0.87

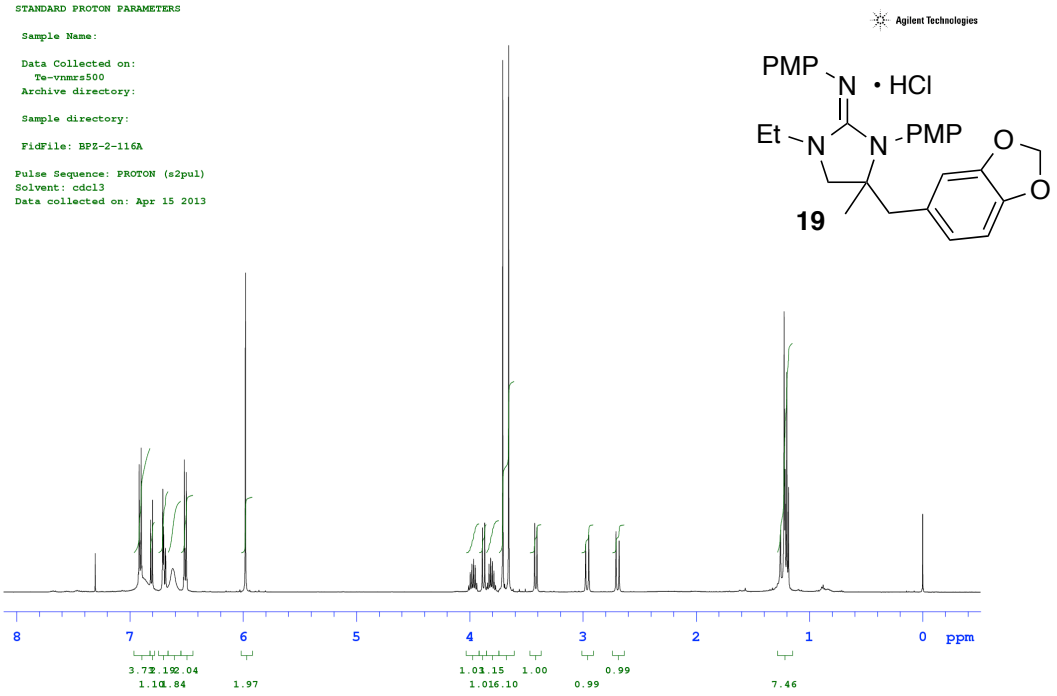

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-111C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 5 2013
Agilent Technologies
160
140
120
100
80
60
40
20
0
ppm

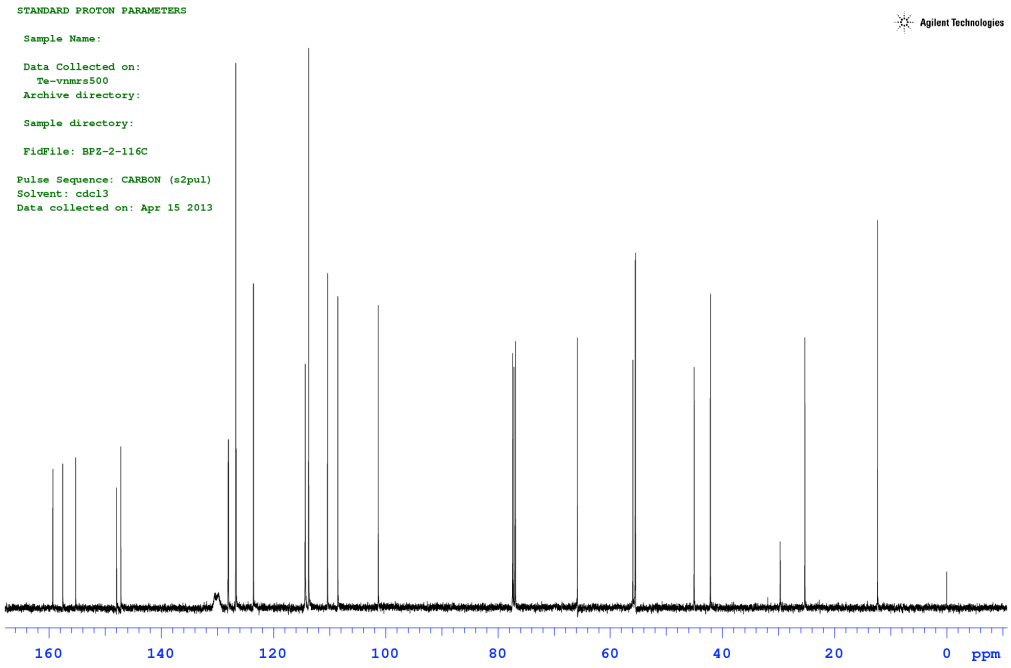

STANDARD 1H OBSERVE - profile
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: BPZ-2-107CC
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 30 2013
Agilent Technologies
PMP
N
• HCl
Me
N
N
PMP
17
Me
7
6
5
4
3
2
1
0
ppm
3.00
0.98
2.13
1.06
6.90
2.89
1.00
0.24
1.25
2.32
2.14
1.18
1.14
0.21
1.06
2.87

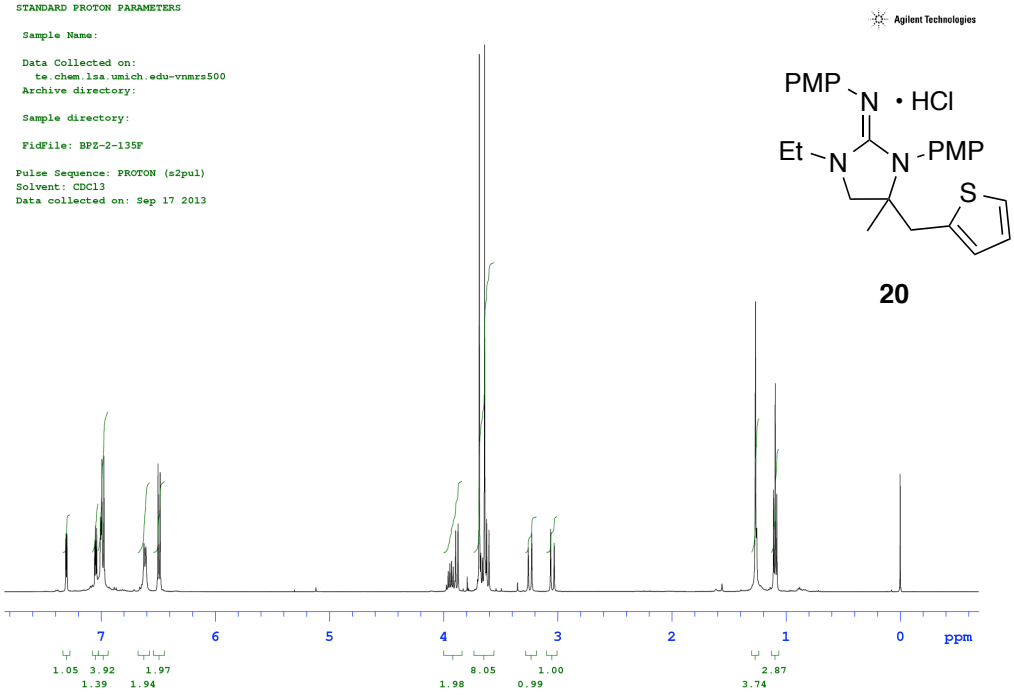

Agilent Technologies
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: BPZ-2-107CC-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 30 2013
160
140
120
100
80
60
40
20
0
ppm

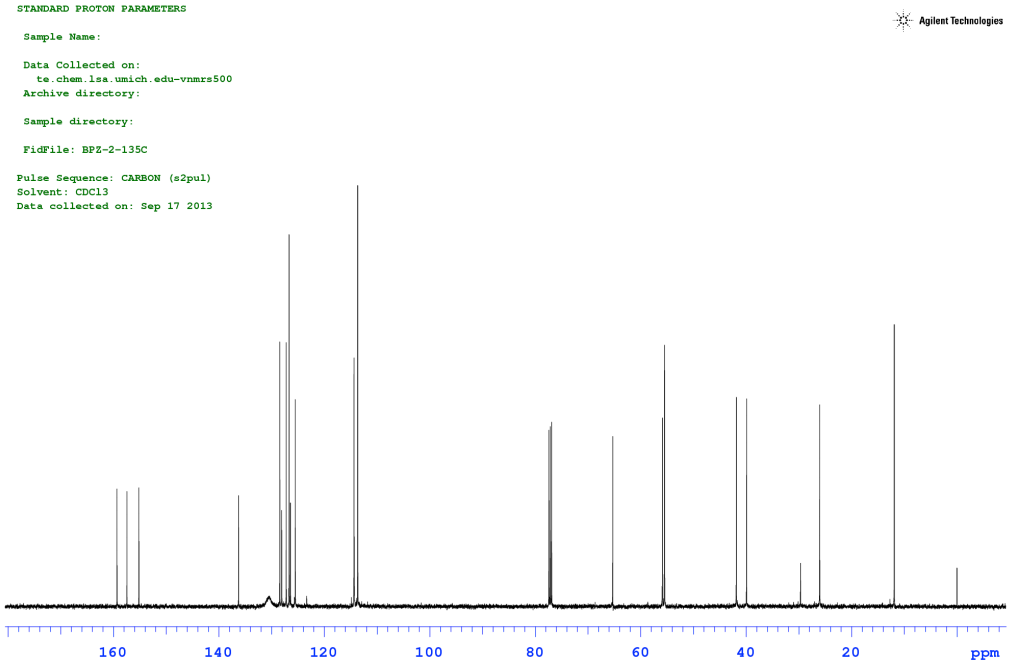

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-110AA
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 5 2013
Agilent Technologies
PMP
N
• HCl
Et
N
N
PMP
18
7
6
5
4
3
2
1
0
ppm
2.12 4.02 1.93
2.06 1.97
2.35 1.00 1.00
1.22 6.19 1.02 2.96
7.26

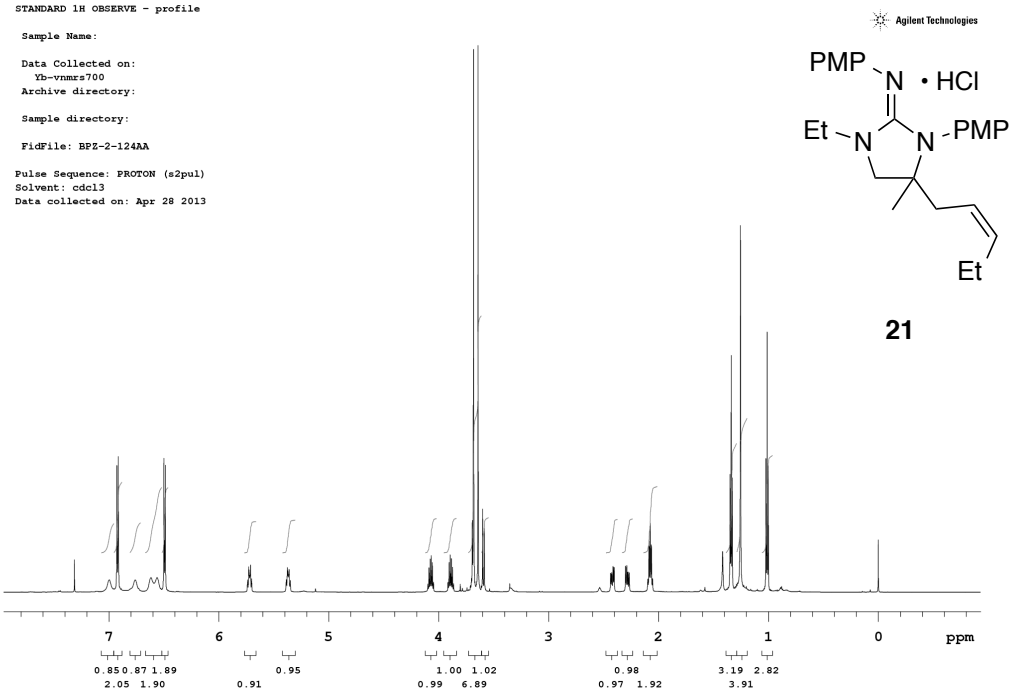

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-110C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 5 2013
Agilent Technologies
160
140
120
100
80
60
40
20
0
ppm

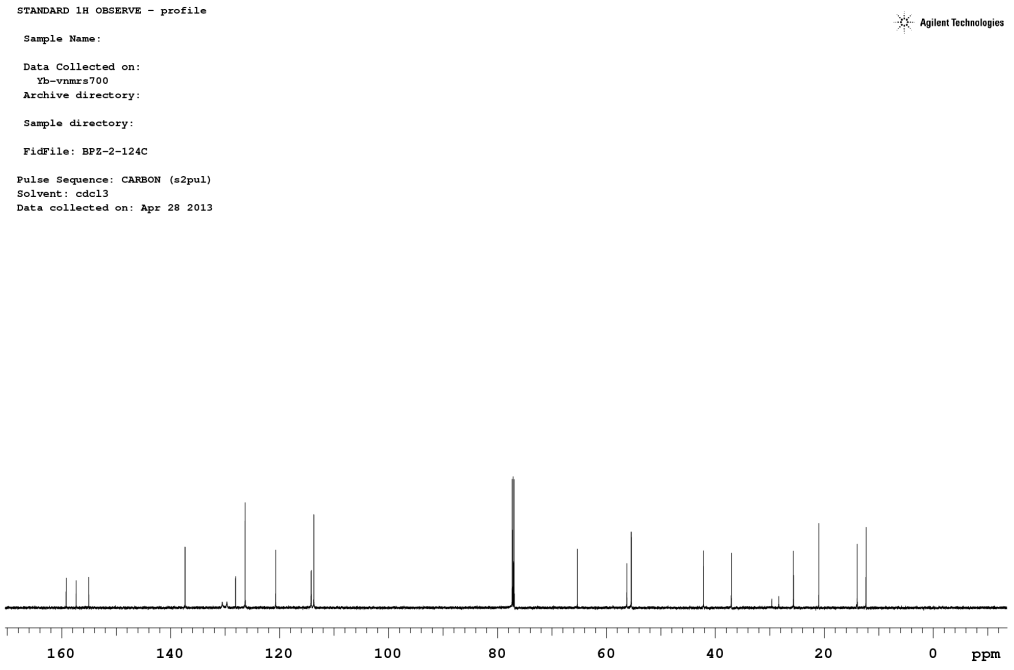

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-116A
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 15 2013
Agilent Technologies
PMP
N
• HCl
Et
N
N
PMP
O
O
19
8
7
6
5
4
3
2
1
0
ppm
3.72
2.19
2.04
1.10
1.84
1.97
1.03
1.15
1.00
0.99
1.01
6.10
0.99
7.46

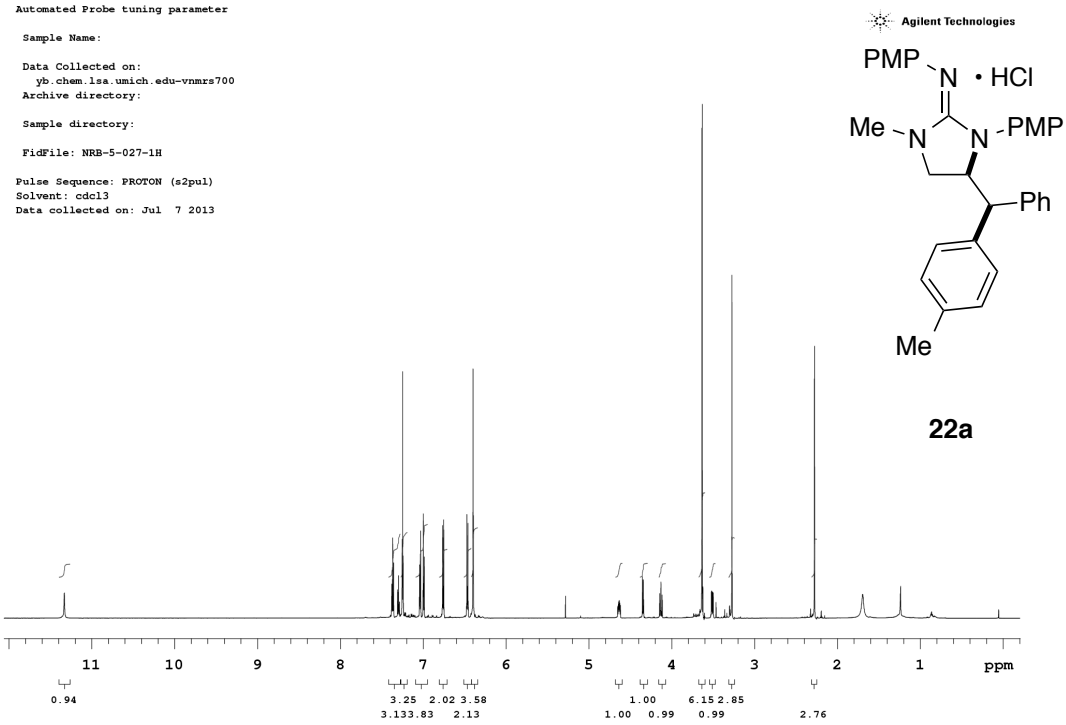

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
Te-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-116C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 15 2013
Agilent Technologies
160
140
120
100
80
60
40
20
0
ppm

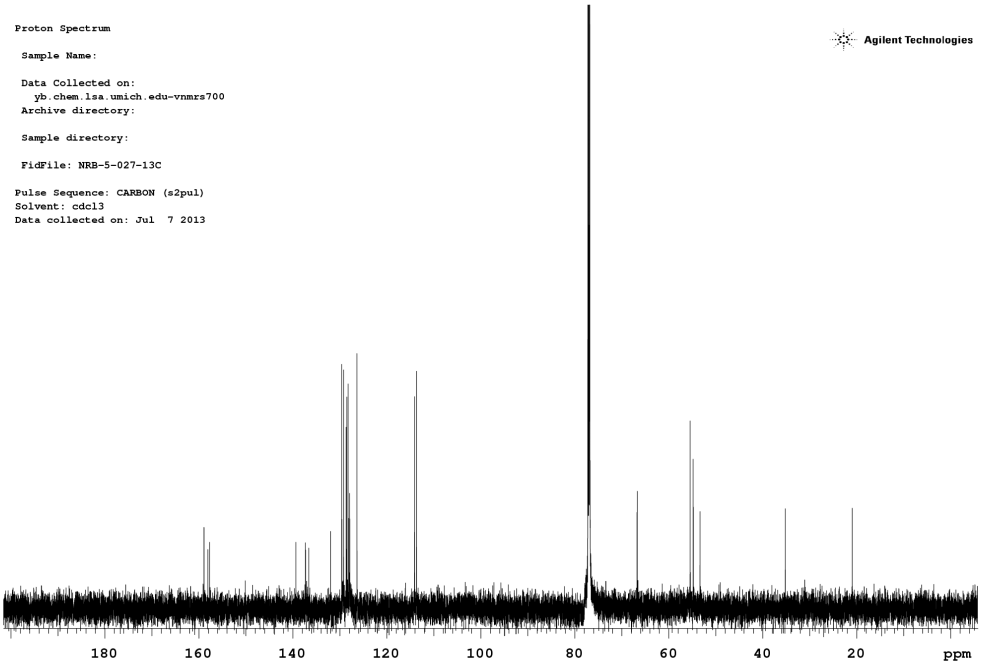

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
te.chem.lsa.umich.edu-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-135F
Pulse Sequence: PROTON (s2pul)
Solvent: CDCl3
Data collected on: Sep 17 2013
Agilent Technologies
PMP
N
• HCl
Et
N
N
PMP
S
20
7
6
5
4
3
2
1
0
ppm
1.05
3.92
1.97
1.39
1.94
8.05
1.00
1.98
0.99
2.87
3.74

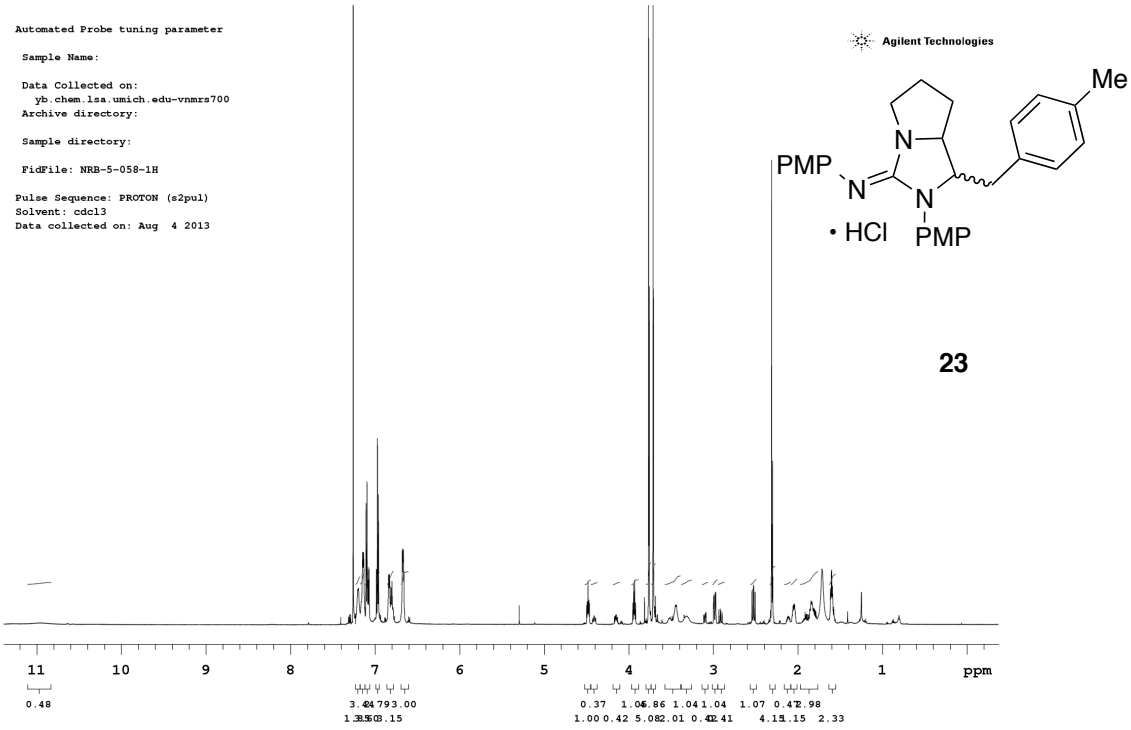

STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
te.chem.lsa.umich.edu-vnmrs500
Archive directory:
Sample directory:
FidFile: BPZ-2-135C
Pulse Sequence: CARBON (s2pul)
Solvent: CDCl3
Data collected on: Sep 17 2013
Agilent Technologies
160
140
120
100
80
60
40
20
ppm

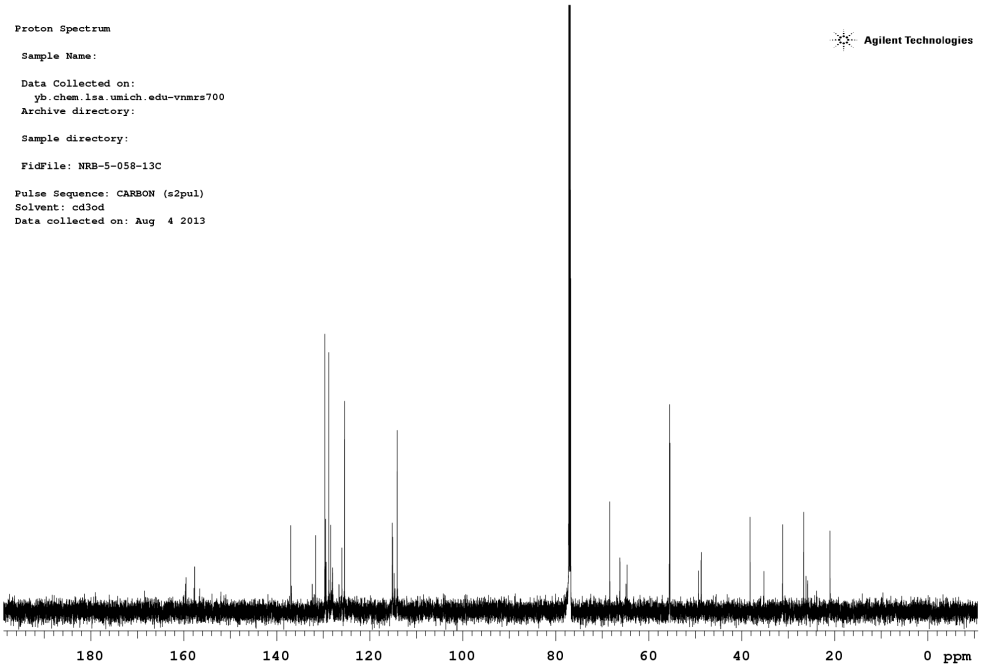

STANDARD 1H OBSERVE - profile
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: BPZ-2-124AA
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 28 2013
Agilent Technologies
PMP
N
• HCl
Et
N
N
PMP
Et
21
7
6
5
4
3
2
1
0
ppm
0.85 0.87 1.89
2.05 1.90
0.91
0.95
1.00 1.02
0.99 6.89
0.98
0.97 1.92
3.19 2.82
3.91

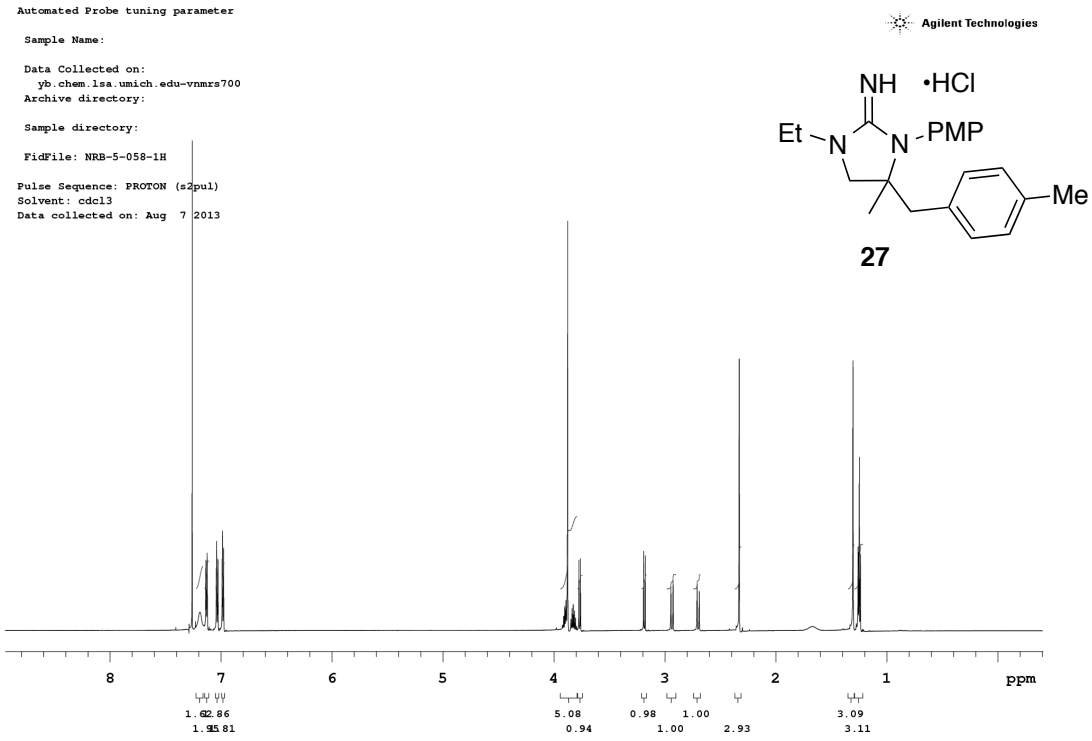

STANDARD 1H OBSERVE - profile
Sample Name:
Data Collected on:
Yb-vnmrs700
Archive directory:
Sample directory:
FidFile: BPZ-2-124C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 28 2013
Agilent Technologies
160
140
120
100
80
60
40
20
0
ppm

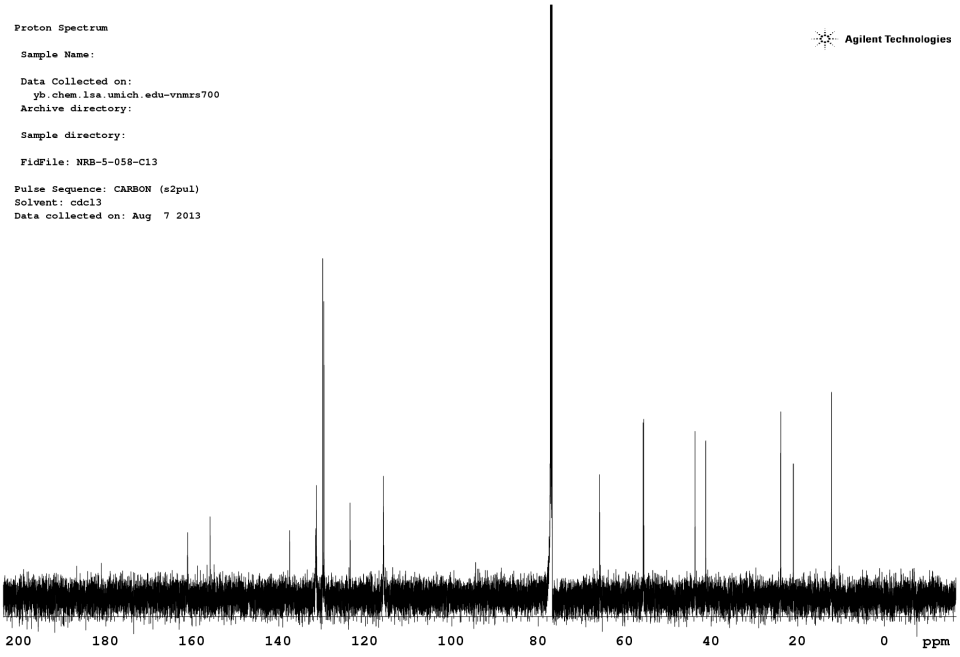

Automated Probe tuning parameter
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-027-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 7 2013
Agilent Technologies
PMP
N
• HCl
Me
N
N
PMP
Ph
Me
22a
11
10
9
8
7
6
5
4
3
2
1
ppm
0.94
3.25
2.02
3.58
1.00
6.15
2.85
3.13
3.83
2.13
1.00
0.99
0.99
2.76

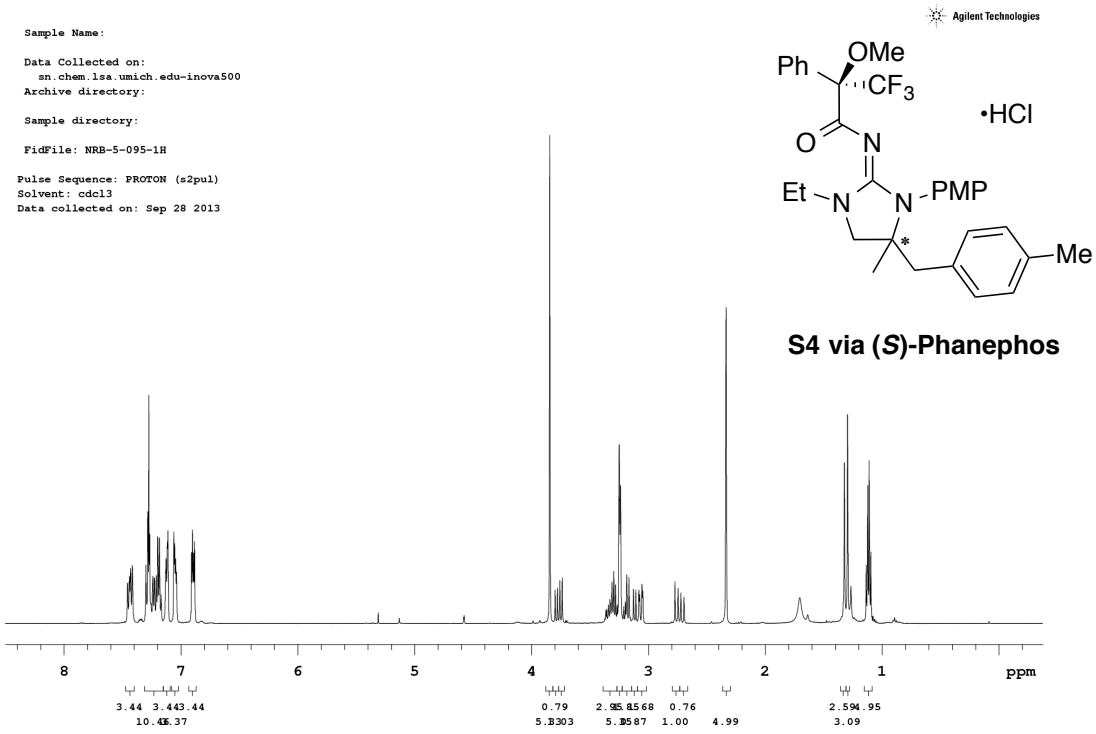

Proton Spectrum
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-027-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 7 2013
Agilent Technologies
180
160
140
120
100
80
60
40
20
ppm

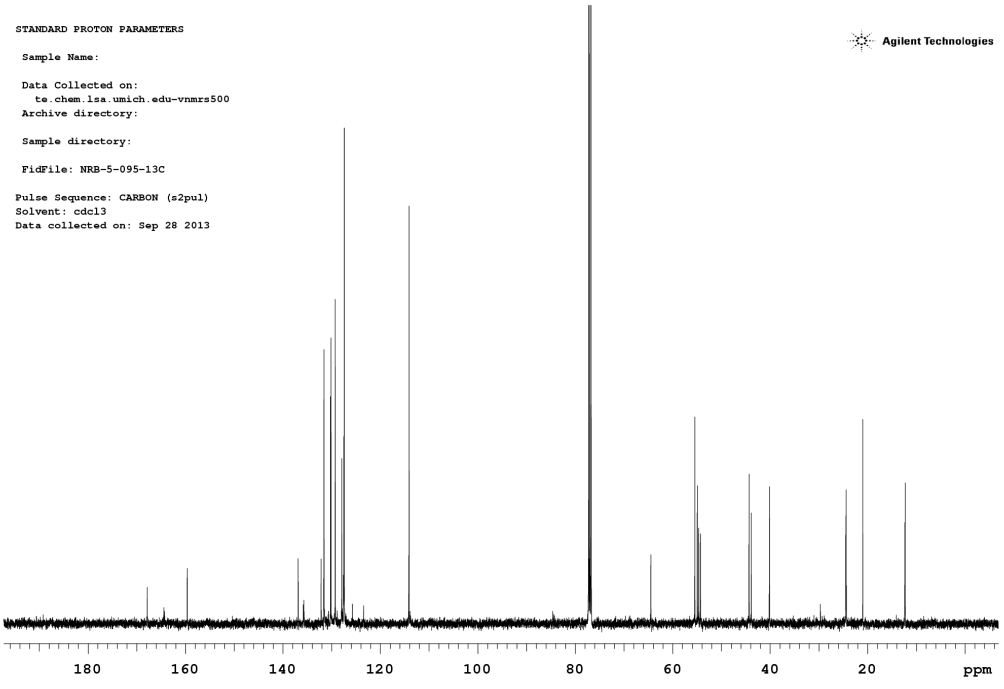

Automated Probe tuning parameter
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-058-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 4 2013
Agilent Technologies
Me
PMP
N
N
N
PMP
• HCl
23
11
10
9
8
7
6
5
4
3
2
1
ppm
0.48
3.00
0.37
1.00
1.04
0.42
6.86
5.08
1.04
2.01
1.04
0.41
1.07
4.15
0.47
1.15
2.98
2.33

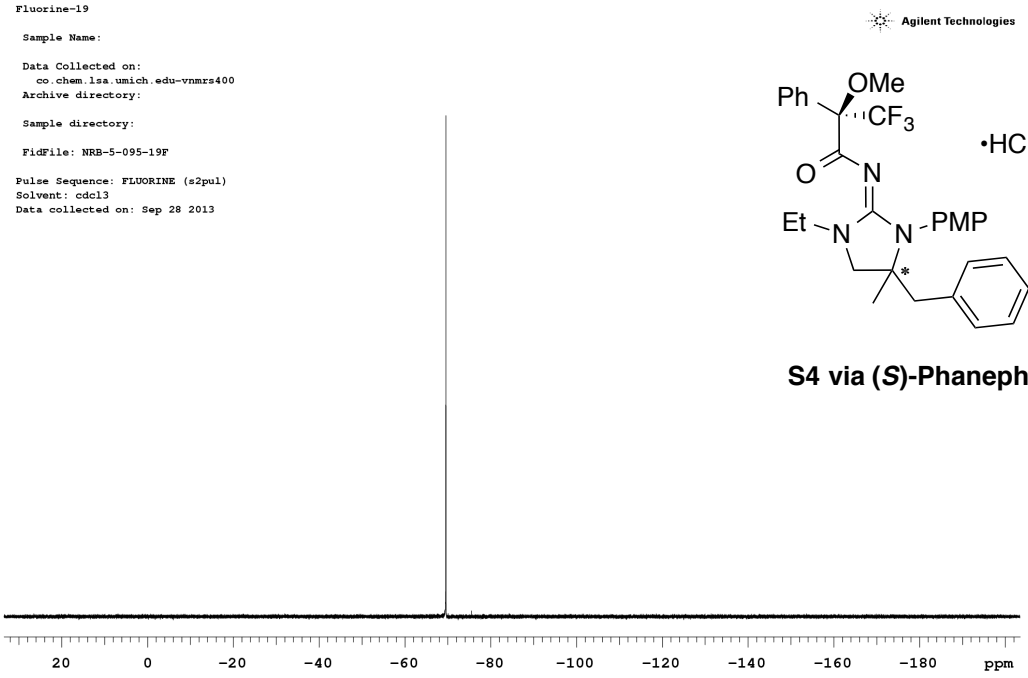

Proton Spectrum
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-058-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Aug 4 2013
Agilent Technologies
180
160
140
120
100
80
60
40
20
0
ppm


Automated Probe tuning parameter
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-058-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 7 2013
Agilent Technologies
NH •HCl
Et N N PMP
Me
27
8 7 6 5 4 3 2 1 ppm
1.62 2.86
1.91 5.81
5.08 0.98 1.00 3.09
0.94 1.00 2.93 3.11

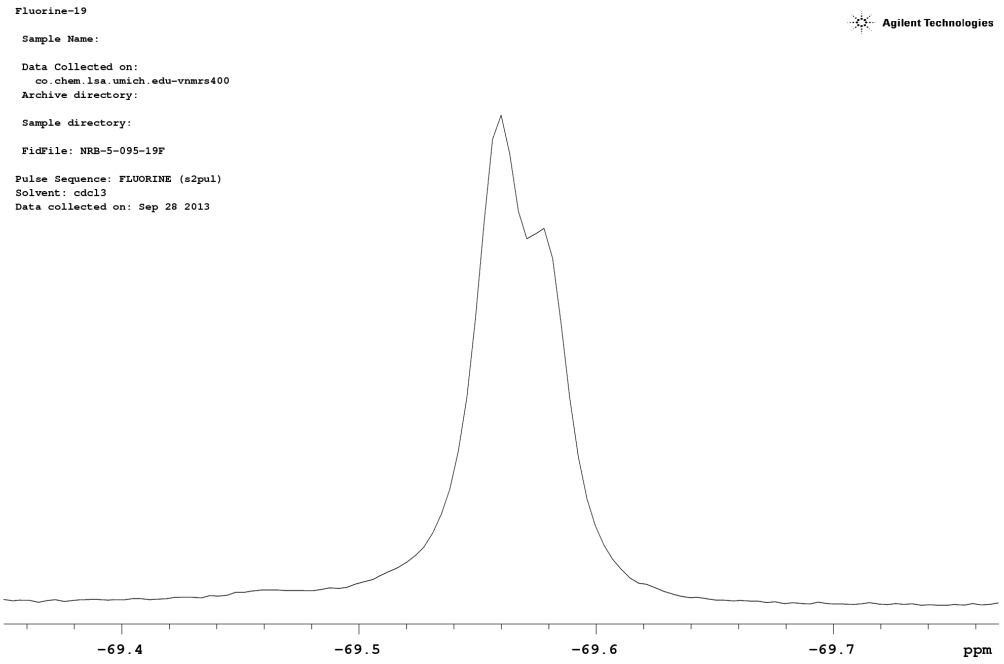

Proton Spectrum
Sample Name:
Data Collected on:
yb.chem.lsa.umich.edu-vnmrs700
Archive directory:
Sample directory:
FidFile: NRB-5-058-C13
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 7 2013
Agilent Technologies
200 180 160 140 120 100 80 60 40 20 0 ppm

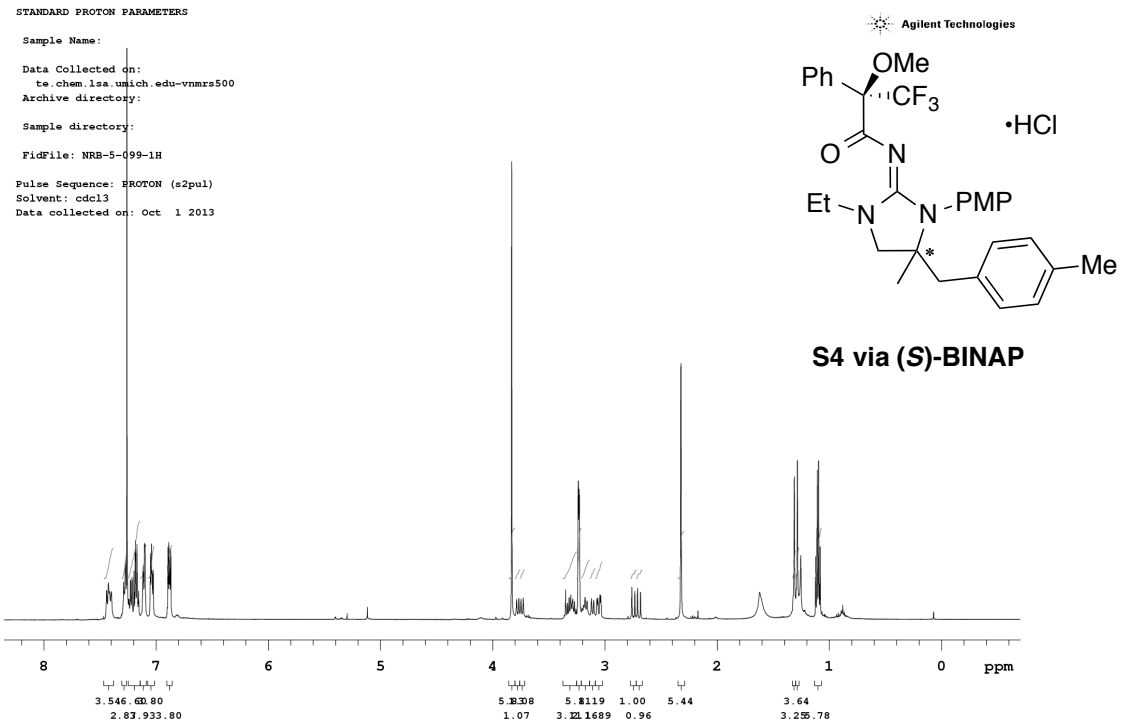

Agilent Technologies
Sample Name:
Data Collected on:
sn.chem.lsa.umich.edu-inova500
Archive directory:
Sample directory:
FidFile: NRB-5-095-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 28 2013
Ph
OMe
CF3
•HCl
O
N
Et
N
N
PMP
*
Me
S4 via (S)-Phanephos
8
7
6
5
4
3
2
1
ppm
3.44
3.44
3.44
0.79
2.95
5.56
0.76
4.99
2.59
4.95
3.09


STANDARD PROTON PARAMETERS
Sample Name:
Data Collected on:
te.chem.lsa.umich.edu-vnmrs500
Archive directory:
Sample directory:
FidFile: NRB-5-095-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 28 2013
Agilent Technologies
180
160
140
120
100
80
60
40
20
ppm

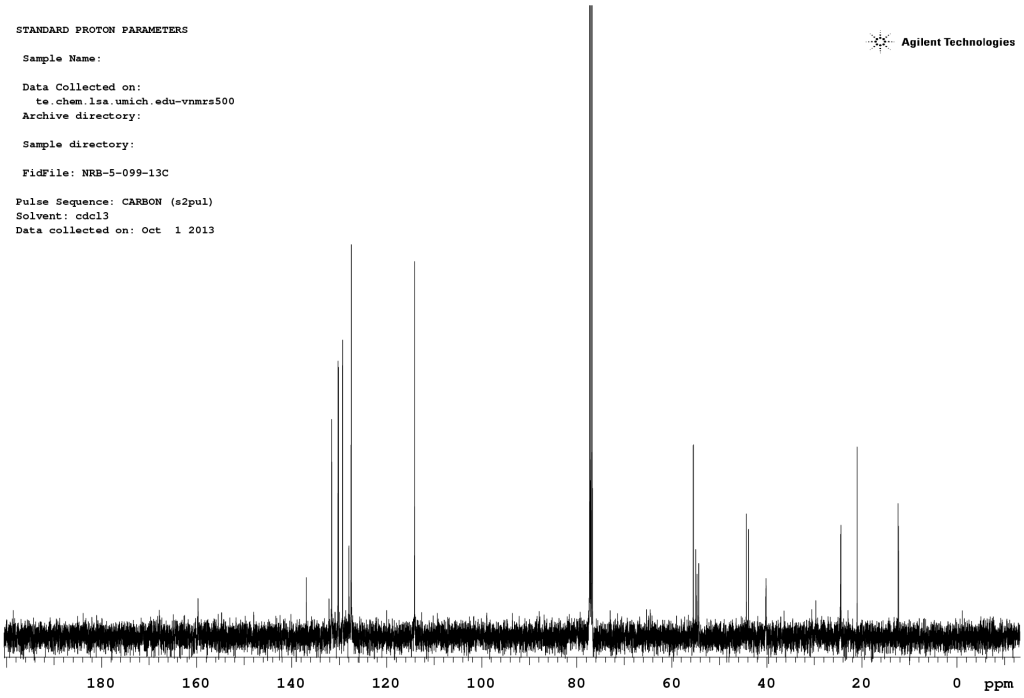


S4 via (*S*)-Phanephos





S4 via (*S*)-BINAP



Fluorine-19

Sample Name:

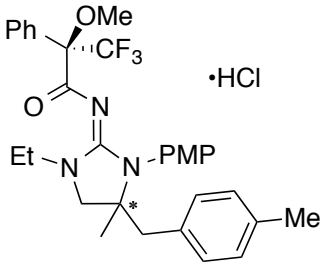
Data Collected on:
co.chem.lsa.umich.edu-vnmrs400
Archive directory:

Sample directory:

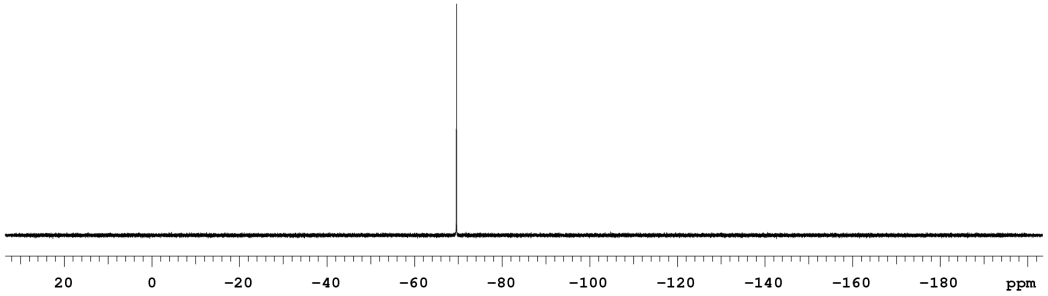
FidFile: NRB-5-099-19F

Pulse Sequence: FLUORINE (s2pul)
Solvent: cdcl3
Data collected on: Oct 1 2013

Agilent Technologies



S4 via (*S*)-BINAP



Fluorine-19

Sample Name:

Data Collected on:
co.chem.lsa.umich.edu-vnmrs400
Archive directory:

Sample directory:

FidFile: NRB-5-099-19F

Pulse Sequence: FLUORINE (s2pul)
Solvent: cdcl3
Data collected on: Oct 1 2013

Agilent Technologies