A cycloaddition route to novel triazole boronic esters

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Supporting Information

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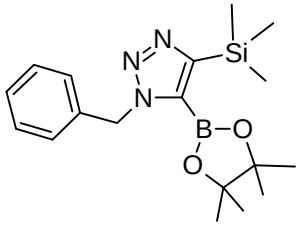
1. General Information

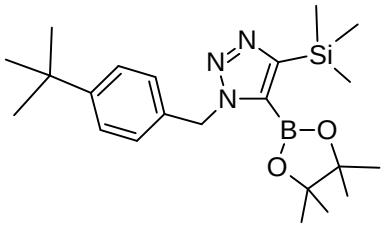
All reactions were conducted in oven or flame-dried glassware under an inert atmosphere of dry nitrogen. Flash chromatography was performed on silica gel (BDH Silica Gel 60 43-60, or Fluorochem Davisil silica gel 43-60). The solvent system used was a gradient of petroleum ether or cyclohexane/ ethyl acetate (90-10), increasing in polarity to ethyl acetate. Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica (0.2 mm, Merck DC-alufolien Kieselgel 60 F254), which were developed using standard visualizing agents: Ultraviolet light or potassium permanganate. $^{1}H/^{13}C$ NMR spectra were recorded on Bruker AC-250 or Av1-250 instruments or AMX-400 or AV1-400 instruments. ^{1}H: Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$:δ7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet), integration, coupling constants (J) in Hz, and assignment. ^{13}C NMR spectra were with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ77.0 ppm). Infrared (FTIR) spectra were recorded on a Perkin Elmer Paragon 100 FTIR spectrophotometer, υ_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m) and weak (w). Samples were recorded as thin films using sodium chloride plates, as a DCM solution or as a KBr disc. Low resolution mass spectra were recorded on Micromass Autospec, operating in E.I., C.I. or FAB mode; or a Perkin-Elmer Turbomass Bench top GC-MS operating in either E.I. or C.I mode. High-resolution mass spectra (HRMS) recorded for accurate mass analysis, were performed on either a MicroMass LCT operating in Electrospray mode (TOF ES+) or a MicroMass Prospec operating in either FAB (FAB+), EI (EI+) or CI (CI+) mode. Melting points were performed on recrsytalised solids and recorded on a Gallenkamp melting point apparatus and are uncorrected. All solvents and reagents were purified using standard, laboratory techniques according to methods published in “Purification of Laboratory Chemicals” by Perrin, Armarego, and Perrin (Pergamon Press, 1966).

2. Synthesis of TMS-triazole boronic esters



2

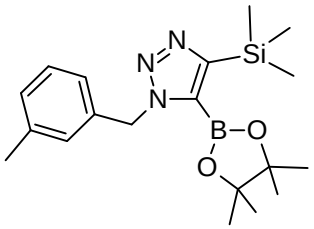
A mixture of benzyl azide (500 mg, 3.80 mmol) and alkyne **1** (1.01 g, 4.50 mmol) in 1,2-dichlorobenzene (15 mL) was heated at 110 °C for 24 h under N_2. The crude product was purified by flash column chromatography on cyclohexane/ethyl acetate (4:1) to give triazole **2** (1.14 g, 84%) as a colourless solid. Mp 64-66 ^{o}C. ^{1}H NMR (250 MHz, $CDCl_3$) δ; 7.29-7.26 (5 H, m), 5.82 (2 H, s), 1.29 (12 H, s), 0.37 (9 H, s). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ; 156.6, 136.9, 128.4, 127.7 (x 2C), 84.7, 53.2, 24.8, -0.8. FTIR 2978 (m), 1503 (m), 1374 (s), 1348 (s), 1321 (s), 1142 (s), 1080 (s), 844 (s), 724 (m). HRMS (EI+) calculated for $C_{18}H_{28}BN_3O_2Si$: 357.2044. Found: 357.2059.



3

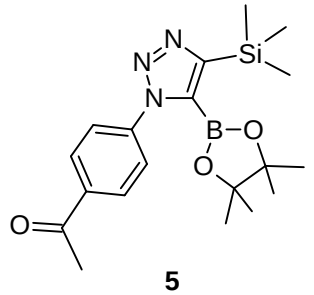
A mixture of 1-(azidomethyl)-4-*tert*-butylbenzene (76 mg, 0.40 mmol) and alkyne **1** (108 mg, 0.48 mmol) in 1,2-dichlorobenzene (1.6 mL) was heated at 110 °C for 24 h under N_2. The crude product was purified by flash column chromatography on cyclohexane/ethyl acetate (4:1) to give triazole **3** (114 mg, 69%) as a colourless solid. Mp 77-79 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.32 (2 H, d, J = 8.0 Hz), 7.24 (2 H, d, J = 8.0 Hz), 5.77 (2 H, s), 1.29 (12 H, s), 0.36 (9 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 156.3, 150.8, 133.8, 127.6, 125.3, 84.6, 52.9, 34.5, 31.3, 24.7, -0.8. FTIR 2962 (m), 1510 (s), 1374 (s), 1344

(m), 1321 (s), 1246 (m), 1140 (s), 1070 (s), 841 (s), 727 (m). HRMS (ESI+) calculated for $C_{22}H_{36}BN_3O_2Si$: 414.2743. Found: 414.2744.



4

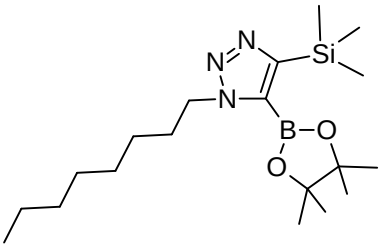
A mixture of 1-(azidomethyl)-3-methylbenzene (147 mg, 1.0 mmol) and alkyne **1** (288 mg, 1.2 mmol) in 1,2-dichlorobenzene (4.0 mL) was heated at 110 °C for 24 h under N_2. The crude product was purified by flash column chromatography on cyclohexane/ethyl acetate (4:1) to give triazole **4** (271 mg, 73%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.20-7.15 (2 H, m), 7.09 (1 H, d, *J* = 8.0 Hz), 7.06 (1 H, d, *J* = 8.0 Hz), 5.76 (2 H, s), 2.30 (3 H, s), 1.29 (12 H, s), 0.36 (9 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 156.4, 138.0, 136.6, 128.6, 128.5, 128.2, 124.9, 84.5, 53.1, 24.7, 21.3, -0.9. FTIR 2978 (w), 1508 (m), 1474 (s), 1323 (s), 1141 (s), 1070 (s), 840 (s), 747 (m). HRMS (ESI+) calculated for $C_{19}H_{30}BN_3O_2Si$: 372.2273. Found: 372.2273.



5

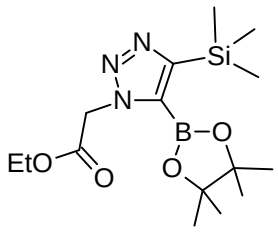
A mixture of 1-(4-azidophenyl)ethanone (48 mg, 0.30 mmol) and alkyne **1** (81 mg, 0.36 mmol) in 1,2-dichlorobenzene (1.2 mL) was heated at 110 °C for 48 h under N_2. The crude product was purified by flash column chromatography on DCM/ethyl acetate (4:1) to give triazole **5** (75 mg, 65%) as a colourless solid. Mp: 91-93 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 8.08 (2 H, d, *J* = 8.0 Hz), 7.66 (2 H, d, *J* = 8.0 Hz), 2.68 (3 H, s), 1.27 (12 H, s), 0.43 (9 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 197.1, 164.7, 141.6, 137.2, 128.8,

125.5, 85.0, 26.8, 24.8, -0.7. FTIR 2924 (m), 1686 (s), 1605 (s), 1343 (s), 1262 (s), 1140 (s), 1051 (m), 843 (s), 762 (m). HRMS (ESI+) calculated for $C_{19}H_{29}BN_3O_3Si$: 386.2066. Found: 386.2069.



6

A mixture of octyl azide (115 mg, 1.0 mmol) and alkyne **1** (288 mg, 1.2 mmol) in 1,2-dichlorobenzene (4 mL) was heated at 110 °C for 48 h under N_2. The crude product was purified by flash column chromatography on cyclohexane/ethyl acetate (4:1) to give triaozle **6** (258 mg, 68%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 4.59 (2 H, t, *J* = 8.0 Hz), 1.86-1.81 (2 H, m), 1.36 (12 H, s), 1.31-1.23 (10 H, m), 0.88 (3 H, t, *J* = 8.0 Hz), 0.37 (9 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 156.1, 84.5, 50.0, 31.8, 31.5, 29.1 (x 2C), 26.6, 24.9, 22.6, 14.1, -0.8. FTIR 2928 (m), 2852 (m), 1508 (s), 1458 (m), 1374 (m), 1319 (s), 1142 (m), 843 (s). HRMS (EI+) calculated for $C_{19}H_{39}BN_3O_2Si$: 380.2905. Found: 380.2907.

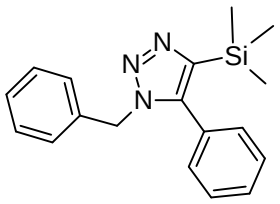


7

A mixture of ethyl azidoacetate (39 mg, 0.3 mmol) and alkyne **1** (81 mg, 0.36 mmol) in 1,2-dichlorobenzene (1.2 mL) was heated at 110 °C for 48 h under N_2. The crude product was purified by flash column chromatography on cyclohexane/ethyl acetate (2:1) to give triazole **7** (79 mg, 75%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 5.39 (2 H, s), 4.20 (2 H, q, *J* = 7.0 Hz), 1.31 (12 H, s), 1.26 (3 H, t, *J* = 7.0 Hz), 0.37 (9 H, s). ^{13}C

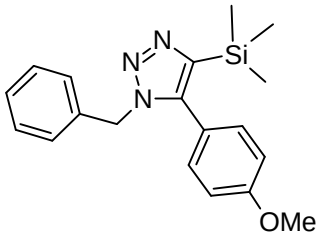
NMR (100.6 MHz, $CDCl_3$) δ; 167.3, 156.4, 84.7, 61.7, 51.1, 24.7, 14.1, -0.9. FTIR 2987(w), 1753 (s), 1464 (m), 1265 (s), 1212 (s), 1023 (m), 744 (m), 700 (s). HRMS (ESI+) calculated for $C_{15}H_{29}BN_3O_4Si$: 354.2015. Found: 354.2018.

3. Functional Group Transformations of TMS- Triazole Boronic Esters



8

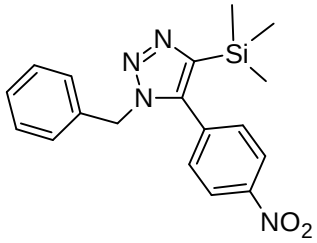
A mixture of triazole boronic ester **2** (860 mg, 2.4 mmol), Pd_2dba_3 (100 mg, 5 mol%), $^tBu_3PH.BF_4$ (80 mg, 12 mol%), K_3PO_4 (1020 mg, 4.8 mmol), iodobenzene (1.00 g, 4.8 mmol) in MeCN (20 mL) was heated at 50 ^oC under N_2 for 16 h, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude product was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **8** (715 mg, 97 %) as a clear colourless solid. Mp 40-42 ^oC. ^1H NMR (250 MHz, $CDCl_3$) δ; 7.46-7.39 (3 H, m), 7.28-7.23 (3 H, m), 7.11-7.07 (2 H, m), 7.03-6.99 (2 H, m), 5.38 (2 H, s), 0.14 (9 H, s). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ; 146.2, 143.6, 135.7, 130.1, 129.4, 128.6, 128.5, 128.0, 127.6 (x 2C), 51.4, -0.9. FTIR 3072 (m), 2958 (s), 2895 (m), 1451 (s), 1412 (s), 1250 (s), 842 (s), 760 (s). HRMS (EI+) calculated for $C_{18}H_{21}N_3Si$: 307.1505. Found: 307.1510.



9

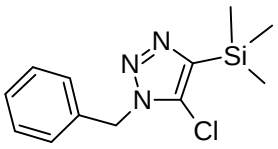
A mixture of triazole boronic ester **2** (43 mg, 0.12 mmol), Pd_2dba_3 (5 mg, 5 mol%), $^tBu_3PH.BF_4$ (4 mg, 12 mol%), K_3PO_4 (51 mg, 0.24 mmol), 1-iodo-4-methoxybenzene (56 mg, 0.24 mmol) in MeCN (1 mL) was heated at 50 ^oC under N_2 for 16 h, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude product

was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **9** (29 mg, 72 %) as a clear colourless solid. Mp 71-72 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.28-7.26 (3 H, m), 7.05-7.03 (2 H, m), 7.01 (2 H, d, *J* = 8.0 Hz), 6.92 (2 H, d, *J* = 8.0 Hz), 5.37 (2 H, s), 3.87 (3 H, s), 0.15 (9 H, s).^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 160.4, 144.9, 143.4, 135.8, 131.3, 128.6, 128.0, 127.6, 120.4, 113.9, 55.3, 51.3, -0.8. FTIR 2965 (m), 1614 (s), 1481 (s), 1291 (s), 1250 (s), 1178 (s), 1034 (m), 843 (s). HRMS (EI+) calculated for $C_{19}H_{23}N_3OSi$: 337.1610. Found: 337.1613.



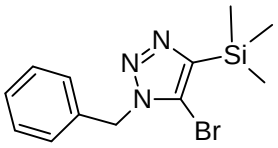
10

A mixture of triazole boronic ester **2** (71 mg, 0.2 mmol), Pd_2dba_3 (9 mg, 5 mol%), $^{t}Bu_3PH.BF_4$ (7 mg, 12 mol%), K_3PO_4 (85 mg, 0.4 mmol), 1-iodo-4-nitrobenzene (100 mg, 0.4 mmol) in MeCN (2 mL) was heated at 50 ^{o}C under N_2 for 16 h, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude product was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **10** (46 mg, 66 %) as a clear colourless solid. Mp 100-102 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 8.23 (2 H, d, *J* = 9.0 Hz), 7.26-7.22 (5 H, m), 6.98-6.93 (2 H, m), 5.41 (2 H, s), 0.14 (9 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 148.4, 145.9, 141.2, 135.7, 135.1, 131.1, 128.9, 128.4, 127.4, 123.6, 51.9, -0.8. FTIR 2928 (m), 1721 (m), 1524 (s), 1341 (s), 1249 (m), 842 (s). HRMS (EI+) calculated for $C_{18}H_{20}N_4O_2Si$: 352.1356. Found: 352.1369.



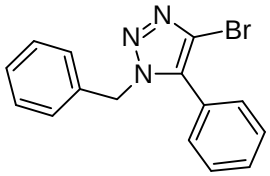
11

A mixture of triazole boronic ester **2** (36 mg, 0.1 mmol) and copper(II) chloride (27 mg, 0.2 mmol) in MeCN (2 mL) was heated at 50 ^{o}C under N_2 for 16 h the reaction was then filtered through celite and concentrated *in vacuo*. The product was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **11** (20 mg, 75%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.39-7.30 (5 H, s), 5.53 (2 H, s), 0.36 (9 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 142.7, 134.2, 131.1, 128.9, 128.5, 127.9, 51.4, -1.6. FTIR 2958 (m), 1727 (w), 1467 (s), 1456 (s), 1250 (s), 840 (s), 721 (s). HRMS (ESI+) calculated for $C_{12}H_{17}{}^{35}ClN_3Si$: 266.0875. Found: 266.0876.



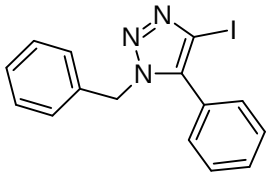
12

A mixture of triazole boronic ester **2** (71 mg, 0.2 mmol) and copper(II) bromide (89 mg, 0.4 mmol) in MeCN (4 mL) was heated at 50 ^{o}C under N_2 for 16 h the reaction was then filtered through celite and concentrated *in vacuo*. The product was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **12** (51 mg, 82%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.37-7.29 (5 H, s), 5.57 (2 H, s), 0.38 (9 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 145.7, 134.3, 128.8, 128.4, 127.8, 117.1, 52.1, -1.5. FTIR 2957 (m), 1453 (s), 1250 (s), 1203 (s), 1026 (m), 837 (s), 720 (s). HRMS (ESI+) calculated for $C_{12}H_{17}N_3Si^{79}Br$: 310.0375. Found: 310.0372.



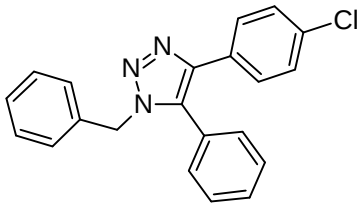
13

A mixture of triazole **8** (123 mg, 0.4 mmol) and NBS (356 mg, 2.0 mmol) in MeCN (10 mL) was heated at reflux under N_2 for 16 h the reaction was then filtered through celite and concentrated *in vacuo*. The product was purified by flash column chromatography on petroleum ether/ethyl acetate (5:1) to give triazole **13** (125 mg, 99%) as a yellow solid. Mp 90-92 ^{o}C. ^{1}H NMR (250 MHz, $CDCl_3$) δ; 7.49-7.46 (3 H, m), 7.29-7.23 (5 H, m), 7.07-7.03 (2 H, m), 5.49 (2 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 136.2, 134.7, 130.1, 129.7, 129.0, 128.9, 128.5, 127.5, 125.4, 120.7, 53.1. FTIR 3068 (m) 3026 (m), 1496 (s), 1450 (s), 1265 (s), 988 (m), 767 (s), 694 (s). HRMS (EI+) calculated for $C_{15}H_{12}N_3{}^{79}Br$: 313.0215. Found: 313.0208.



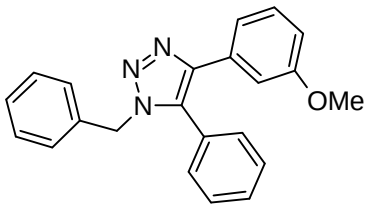
14

A mixture of triazole **8** (200 mg, 0.65 mmol) and NIS (731 mg, 3.25 mmol) in MeCN (15 mL) was heated at reflux under N_2 for 4 days the reaction was then filtered through celite and concentrated *in vacuo*. The product was purified by flash column chromatography on petroleum ether/ethyl acetate (5:1) to give triazole **14** (219 mg, 94%) as a yellow solid. Mp 68-70 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.53-7.45 (3 H, m), 7.30-7.26 (3 H, m), 7.23-7.20 (2 H, m), 7.05-7.03 (2 H, m), 5.51 (2 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 140.4, 134.8, 130.1, 129.9, 129.0, 128.8, 128.4, 127.5, 126.2, 90.4, 53.0. FTIR 3067 (m) 3037 (m), 1476 (s), 1450 (s), 1245 (s), 987 (s), 844 (s), 731 (s), 694 (s). HRMS (EI+) calculated for $C_{15}H_{12}N_3I$: 313.0215. Found: 313.0208.



15

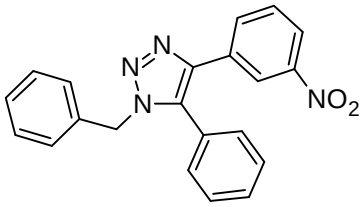
A mixture of triazole **14** (54 mg, 0.15 mmol), Pd_2dba_3 (7 mg, 5 mol%), $^tBu_3PH.BF_4$ (5 mg, 12 mol%), K_3PO_4 (64 mg, 0.30 mmol), 4-chlorobenzene boronic acid pinacol ester (64 mg, 0.30 mmol) in MeCN (2 mL) was heated at 50 ^oC under N_2 for 48 h, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude product was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **15** (39 mg, 75 %) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.52-7.42 (5 H, m), 7.28-7.22 (5 H, m), 7.14 (2 H, dd, *J* = 7.0, 1.5 Hz), 7.04-7.02 (2 H, m), 5.42 (2 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 143.6, 135.2, 134.0, 133.6, 131.6, 130.0, 129.9, 129.4, 129.3, 128.7 (x 2C), 128.2, 127.9, 127.5, 52.1. FTIR 2924 (m) 1455 (s), 1243 (s), 1026 (m), 983 (s), 794 (m), 763 (s). HRMS (ESI+) calculated for $C_{21}H_{16}{}^{35}ClN_3$: 346.1106. Found: 346.1106.



16

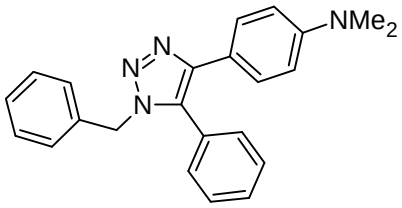
A mixture of triazole **14** (54 mg, 0.15 mmol), Pd_2dba_3 (7 mg, 5 mol%), $^tBu_3PH.BF_4$ (5 mg, 12 mol%), K_3PO_4 (64 mg, 0.30 mmol), 3-methoxylphenyl boronic acid pinacol ester (74 mg, 0.30 mmol) in MeCN (2 mL) was heated at 50 ^oC under N_2 for 48 h, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude product

was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **16** (33 mg, 65 %) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.51-7.41 (3 H, m), 7.27-7.25 (3 H, m), 7.19-7.13 (4 H, m), 7.11-7.08 (1 H, m), 7.04-7.02 (2 H, m), 6.81-6.78 (1 H, m), 5.42 (2 H, s), 3.68 (3 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 175.8, 159.6, 144.4, 135.3, 134.0, 132.2, 130.2, 129.7, 129.5, 129.2, 128.7, 128.2, 127.5, 119.0, 114.3, 111.4, 55.1, 52.1. FTIR 1604 (m), 1584 (m), 1455 (m), 1290 (m), 1238 (s), 1042 (m), 854 (m), 701 (s). HRMS (ESI+) calculated for $C_{22}H_{20}N_3O$: 342.1601. Found: 342.1598.



17

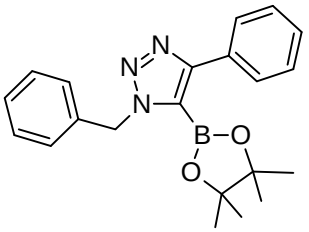
A mixture of triazole **14** (54 mg, 0.15 mmol), Pd_2dba_3 (7 mg, 5 mol%), $^{t}Bu_3PH.BF_4$ (5 mg, 12 mol%), K_3PO_4 (64 mg, 0.30 mmol), 3-nitrophenyl boronic acid pinacol ester (75 mg, 0.30 mmol) in MeCN (2 mL) was heated at 50 ^{o}C under N_2 for 16 h, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude product was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **17** (37 mg, 70 %) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 8.40 (1 H, app t, *J* = 2.0 Hz), 8.08 (1 H, dd, *J* = 8.0, 2.0 Hz), 7.92 (1 H, dd, *J* = 6.5, 1.5 Hz), 7.57-7.53 (1 H, m), 7.50-7.42 (3 H, m), 7.29-7.26 (3 H, m), 7.18-7.15 (2 H, m), 7.05-7.03 (2 H, m), 5.44 (2 H, s, CH_2). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 148.4, 142.4, 134.9 (x 2C), 132.7, 132.2, 130.3, 129.9, 129.6, 129.4, 128.8, 128.4, 127.6, 126.9, 122.3, 121.3, 52.2. FTIR 1616 (m), 1526 (s), 1344 (s), 1122 (m), 1112 (m), 851 (m), 693 (s). HRMS (EI+) calculated for $C_{21}H_{17}N_4O_2$: 357.1346. Found: 357.1344.



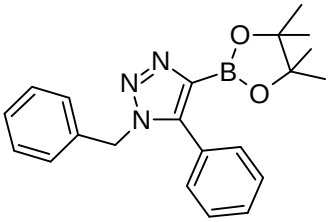
18

A mixture of triazole **14** (54 mg, 0.15 mmol), Pd_2dba_3 (7 mg, 5 mol%), $^tBu_3PH.BF_4$ (5 mg, 12 mol%), K_3PO_4 (64 mg, 0.30 mmol), 4-dimethylaminopnenyl boronic acid pinacol ester (74 mg, 0.30 mmol) in MeCN (2 mL) was heated at 50 ^oC under N_2 for 16 h, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude product was purified by flash column chromatography on petroleum/ethyl acetate (10:1) to give triazole **18** (36 mg, 68 %) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.47-7.39 (5 H, m, Ar), 7.28-7.25 (3 H, m), 7.92 (1 H, d, *J* = 7.0 Hz), 7.17 (2 H, d, *J* = 8.0 Hz), 7.05-7.03 (2 H, m), 6.63 (2 H, d, *J* = 8.0 Hz), 5.44 (2 H, s), 2.93 (6 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 149.9, 145.0, 135.6, 132.4, 130.3, 129.4, 129.0, 128.6, 128.4, 128.0, 127.6, 127.5, 119.0, 112.2, 52.0, 40.4. FTIR 2922 (m), 2851 (m), 1615 (s), 1518 (s), 1356 (m), 1198 (s), 944 (m), 823 (s). HRMS (ESI+) calculated for $C_{23}H_{23}N_4$: 355.1917. Found: 355.1914.

4. Other Triazole Boronic Ester and Derivatives

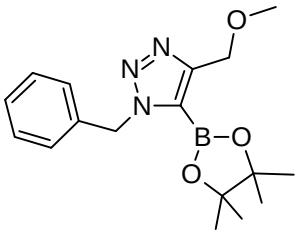


22a

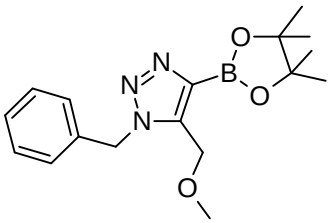


22b

A mixture of benzyl azide (40 mg, 0.3 mmol) and alkyne **19** (82 mg, 0.36 mmol) in 1,2-dichlorobenzene (1.2 mL) was heated at 150 °C for 16 h under N_2. The crude product was purified by flash column chromatography on petroleum ether/ethyl acetate (2:1) to give triazole **22a** (27 mg, 25%) as a colourless oil and triazole **22b** (41 mg, 38%) as a colourless oil. **22a:** ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.95 (2 H, dd, *J* = 8.0, 1.5 Hz), 7.41-7.34 (3 H, m), 7.31-7.25 (3 H, m), 7.20 (2 H, dd, *J* = 8.0, 1.5Hz), 5.85 (2 H, s), 1.21 (12 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 156.0, 136.7, 131.5, 128.5 (x 2C), 128.2, 128.0, 127.9, 127.2, 84.7, 54.0, 24.6. FTIR 2978 (m), 1496 (s), 1455 (s), 1371 (s), 1325 (s), 1221 (m), 1137 (s), 1080 (s), 852 (s), 729 (s). HRMS (ESI+) calculated for $C_{21}H_{25}BN_3O_2$: 362.2034. Found: 362.2035. **22b:** ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.49-7.39 (3 H, m), 7.28-7.25 (5 H, m), 7.05-7.02 (2 H, m), 5.53 (2 H, s), 1.29 (12 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 145.4, 135.6, 129.9, 129.3, 128.7, 128.2, 128.0, 127.2, 127.1, 83.9, 51.4, 24.7. FTIR 2977 (m), 2926 (m), 1496 (m), 1456 (s), 1372 (s), 1332 (s), 1211 (m), 1142 (s), 853 (m), 698 (s). HRMS (ESI+) calculated for $C_{21}H_{25}BN_3O_2$: 362.2034. Found: 362.2036.

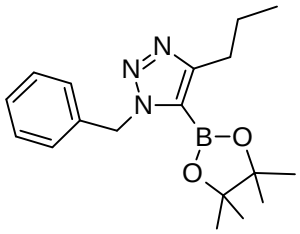


23a

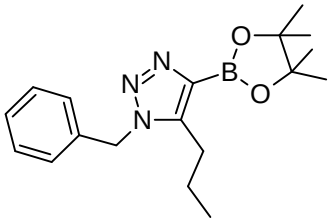


23b

A mixture of benzyl azide (40 mg, 0.30 mmol) and alkyne **20** (59 mg, 0.30 mmol) in 1,2-dichlorobenzene (1.2 mL) was heated at 150 °C for 24 h under N_2 to give an inseperable 40:60 mixture of **23a** and **23b** (98 mg, 99%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.32-7.22 (5 H, m), 5.76 (0.8 H, s), 5.66 (1.2 H, s), 4.69 (0.8 H, s), 4.57 (1.2 H, s), 3.42 (1.2 H, s), 3.25 (1.8 H, s), 1.35 (7.2 H, s), 1.28 (4.8 H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 153.5, 140.7, 136.2, 134.9, 128.7, 128.4, 128.1, 127.9, 127.6, 127.5, 84.6, 84.1, 65.1, 61.7, 58.1, 57.6, 53.6, 51.9, 24.7, 24.6. FTIR 2981 (m), 1561 (m), 1456 (s), 1372 (s), 1333 (s), 1140 (s), 1083 (s), 908 (s), 726 (m). HRMS (ESI+) calculated for $C_{17}H_{25}BN_3O_3$: 330.1984. Found: 330.1981.



24a

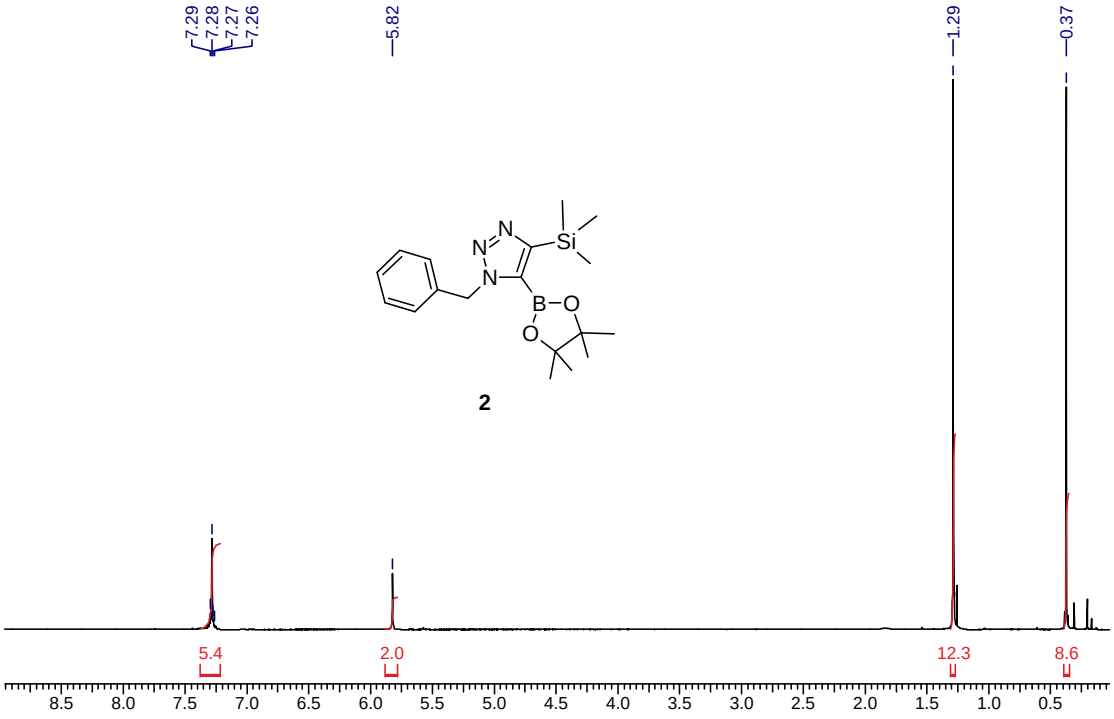


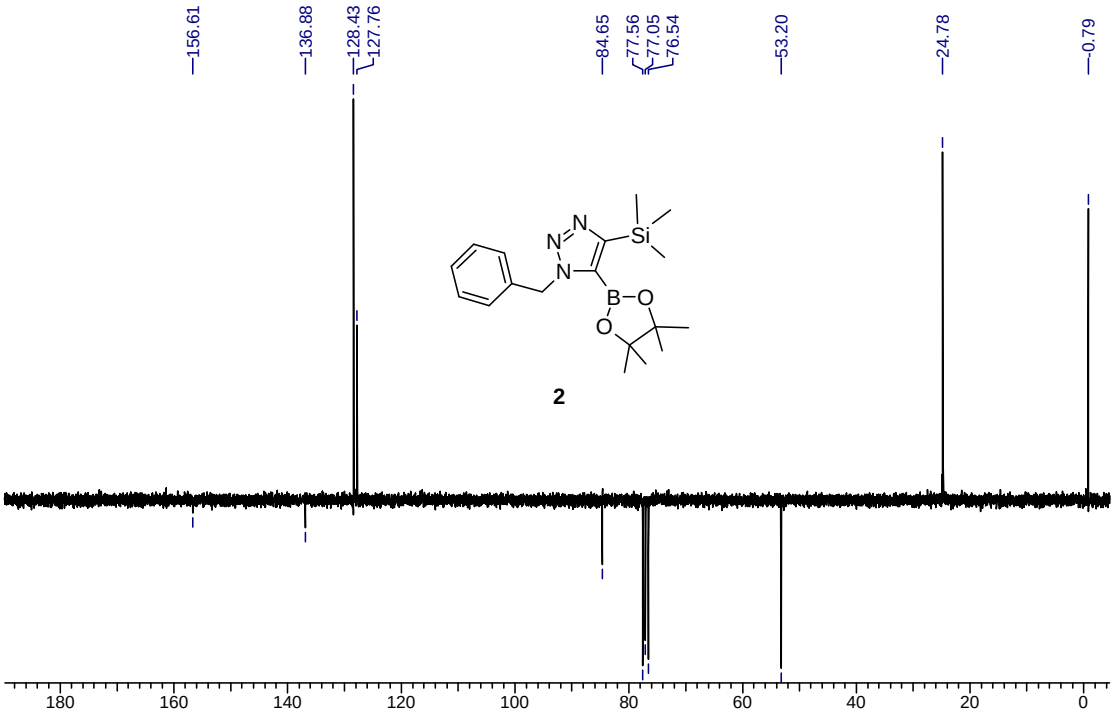
24b

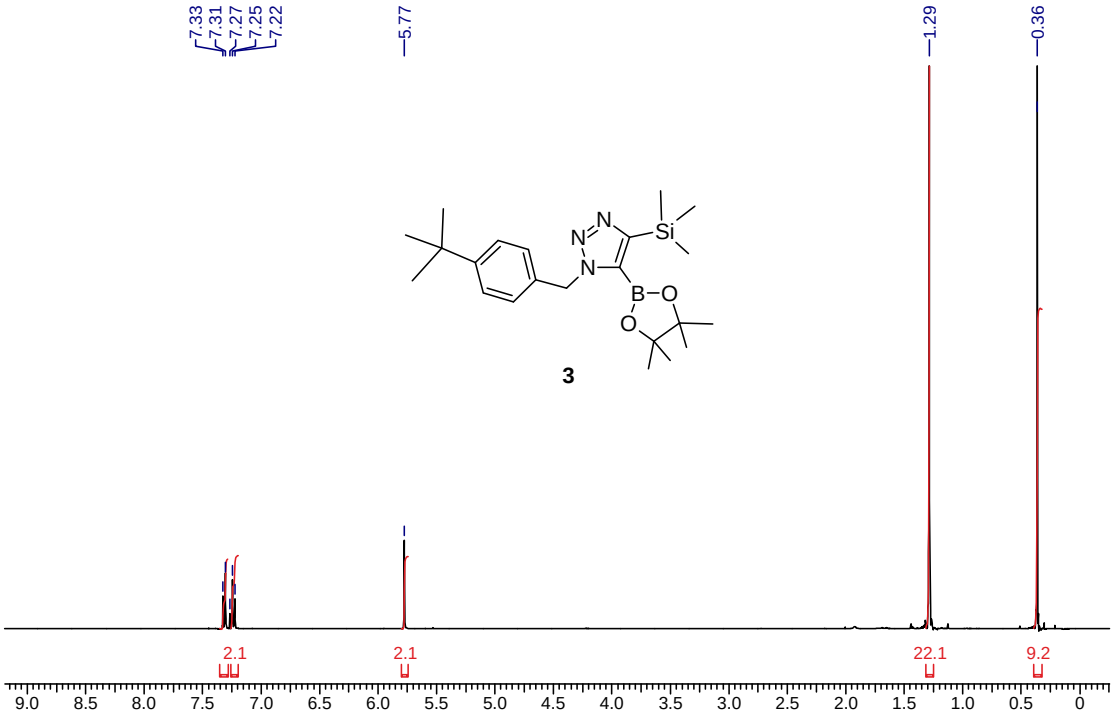
A mixture of benzyl azide (40 mg, 0.30 mmol) and alkyne **21** (58 mg, 0.30 mmol) in 1,2-dichlorobenzene (1.2 mL) was heated at 150 °C for 24 h under N_2 to give an inseperable 40:60 mixture of **24a** and **24b** (96 mg, 98%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ; 7.31-7.20 (3 H, m), 7.13-7.11 (2 H, m), 5.71 (0.8 H, s), 5.51 (1.2 H, s), 2.82 (0.8 H, t, *J*

= 7.0 Hz), 2.70 (1.2 H, t, *J* = 7.0 Hz), 1.68 (1.2 H, m), 1.54 (0.8 H, m), 1.32 (7.2 H, s), 1.23 (4.8 H, s), 0.91 (1.2 H, t, *J* = 7.0 Hz), 0.81 (1.8 H, t, *J* = 7.0 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 136.7, 135.3, 130.4, 128.7, 128.3, 128.0, 127.7, 127.5, 126.9, 84.2, 83.7, 53.5, 51.1, 27.8, 24.8, 24.7, 24.6, 23.4, 22.5, 21.5, 21.4. FTIR 1558 (m), 1454 (s), 1368 (s), 1342 (s), 1137 (s), 1085 (s), 912 (m), 730 (m). HRMS (ESI+) calculated for $C_{18}H_{26}BN_3O_2$: 328.2256. Found: 328.2254.

5. ^{1}H and ^{13}C NMR Spectra







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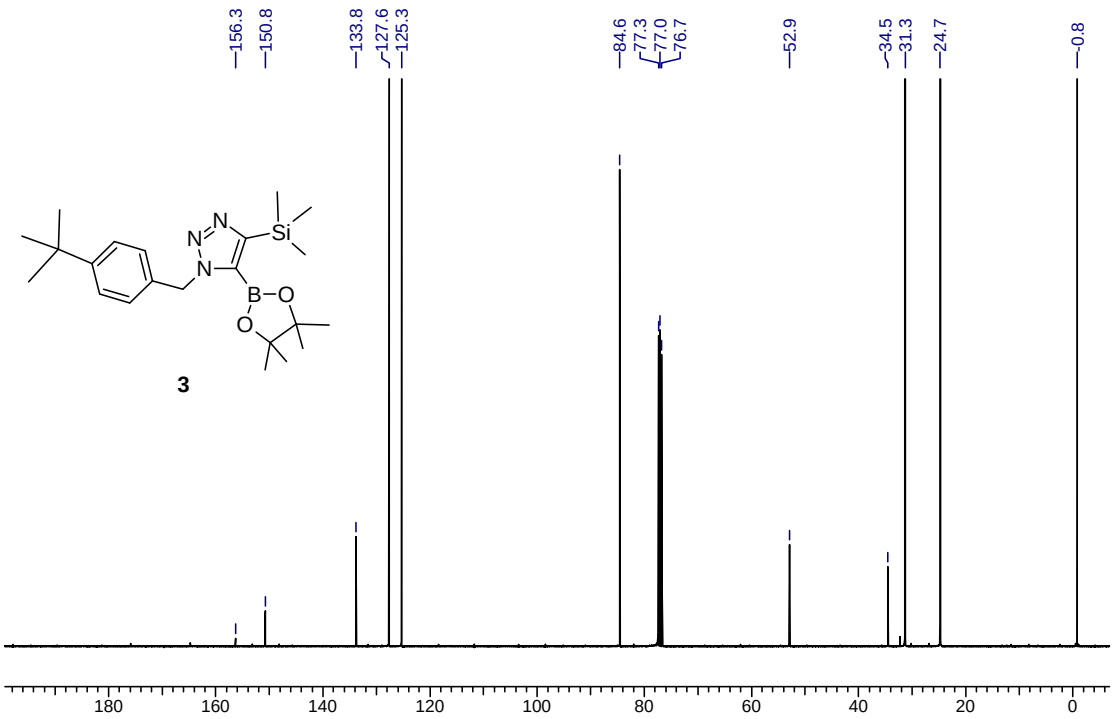

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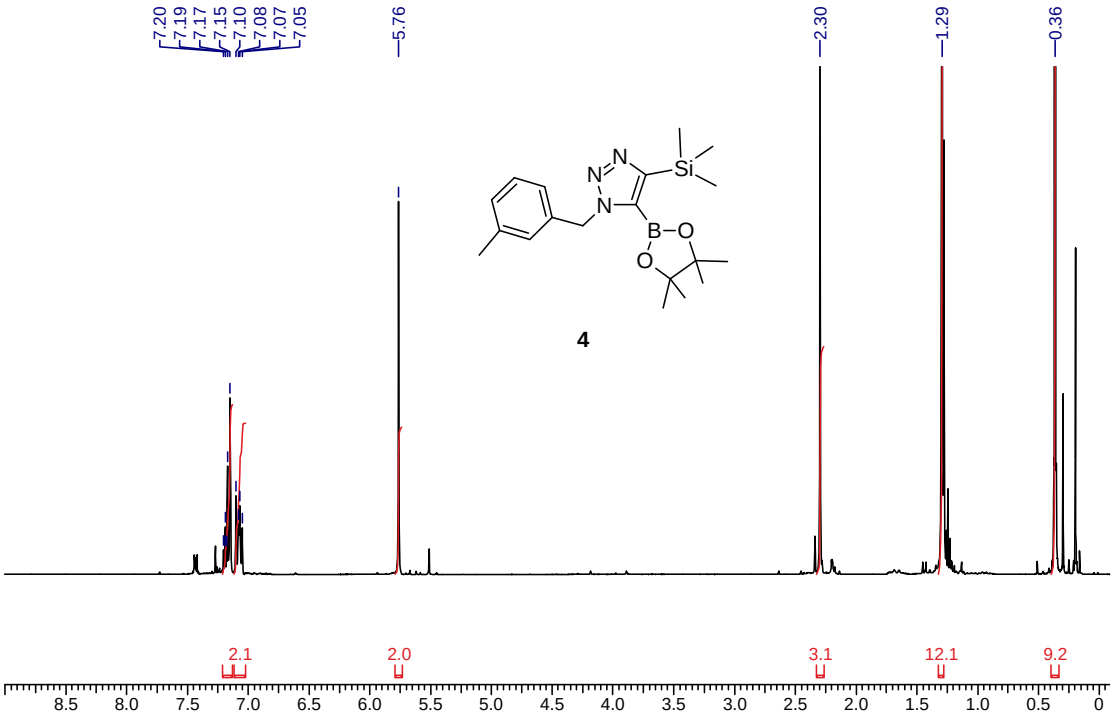

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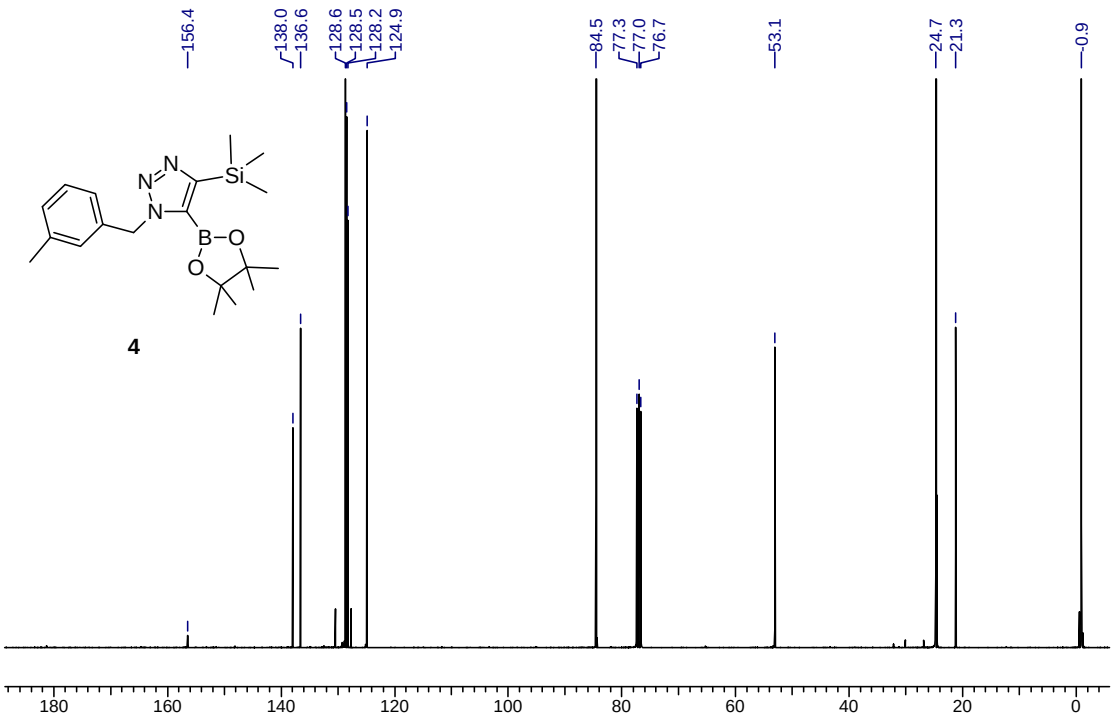

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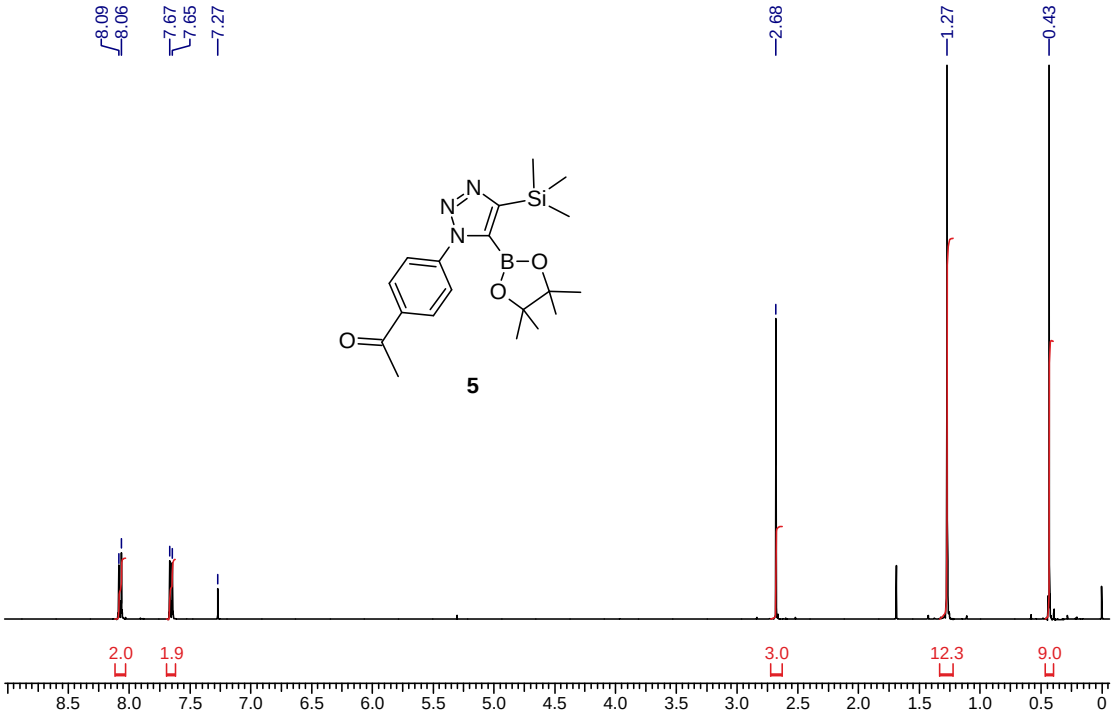

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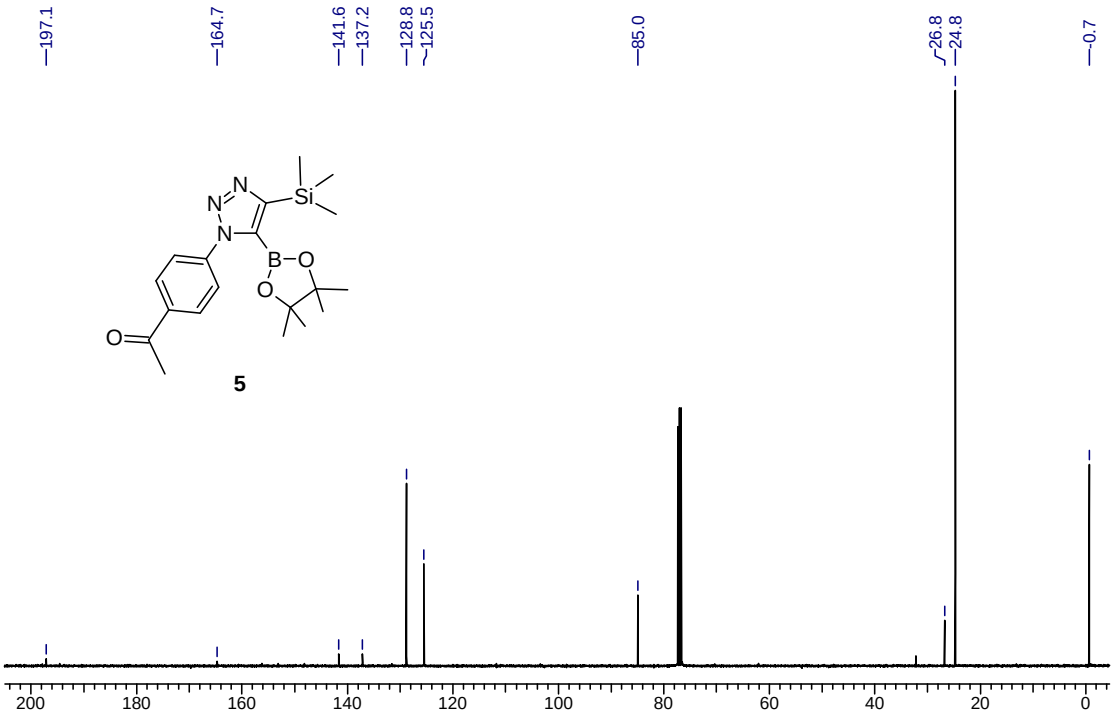

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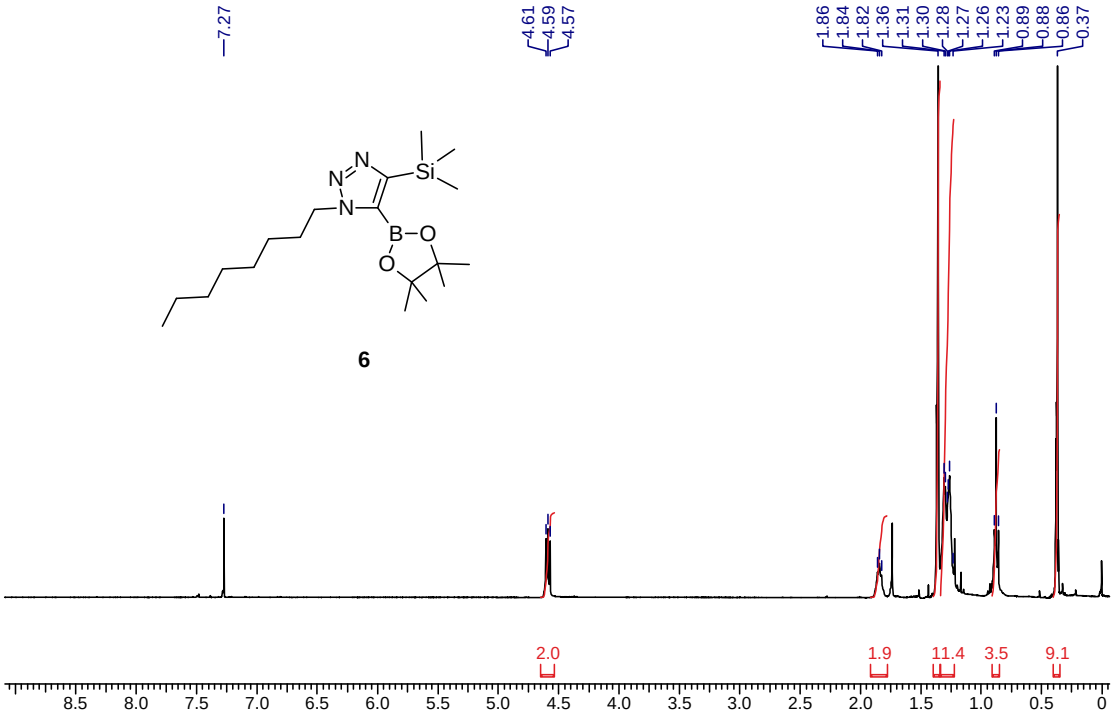
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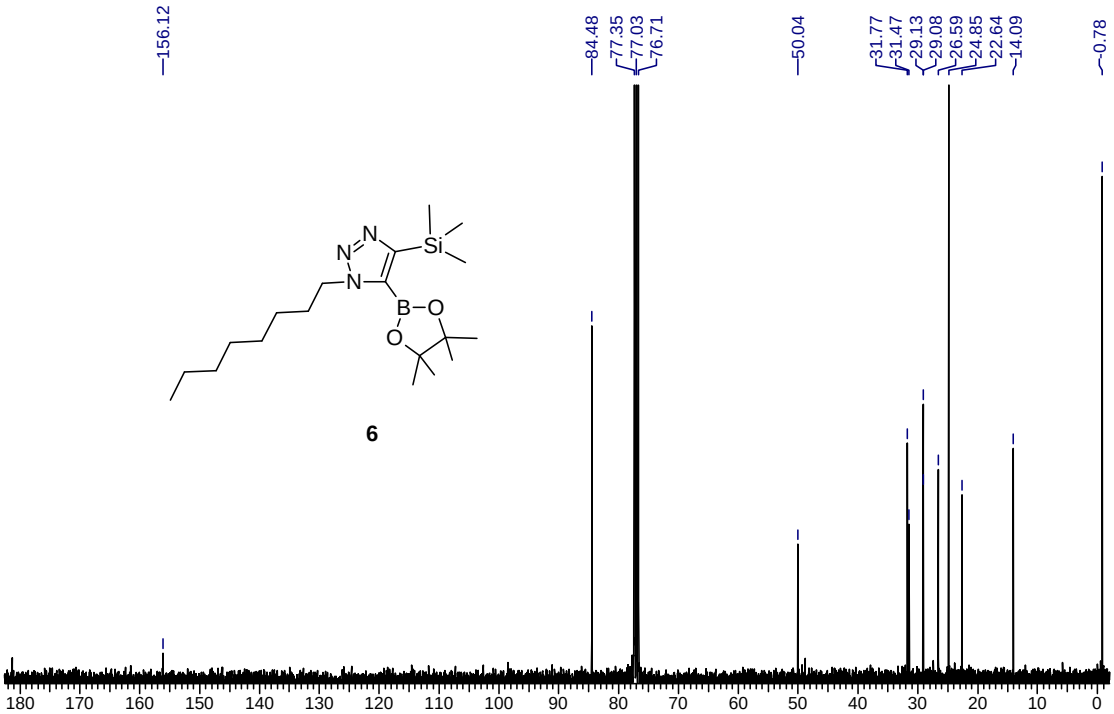
1.27
1.26
1.23
0.89
0.88
0.86
0.37
2.0
1.9
11.4
3.5
9.1
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0

6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22.64
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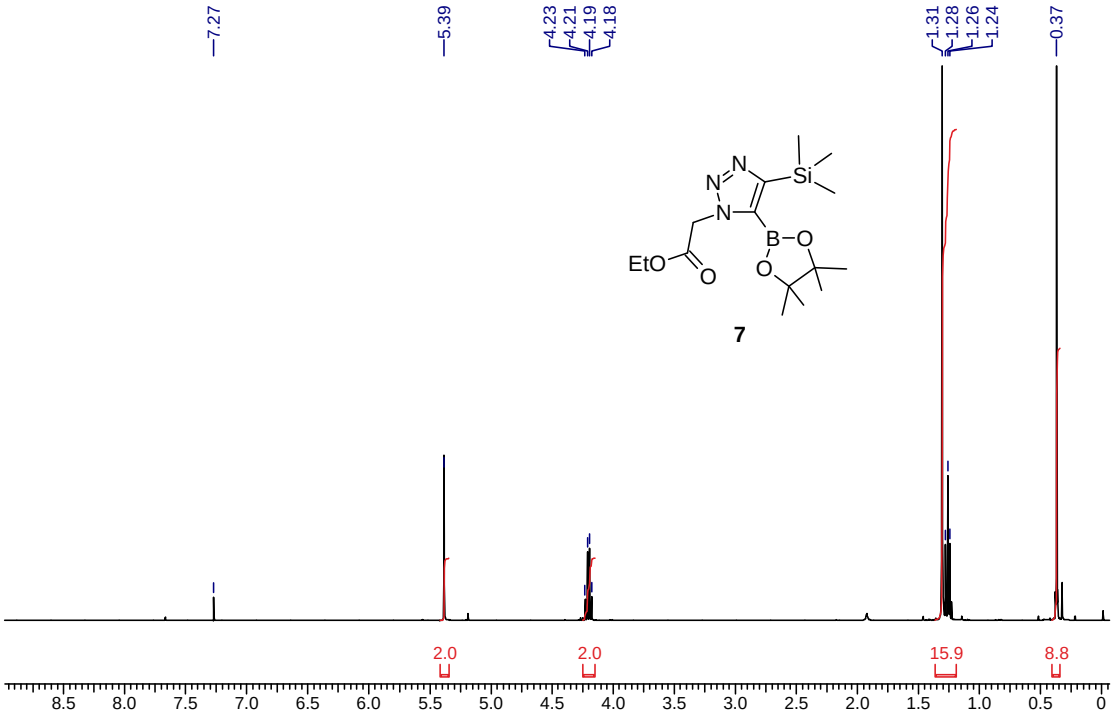
6



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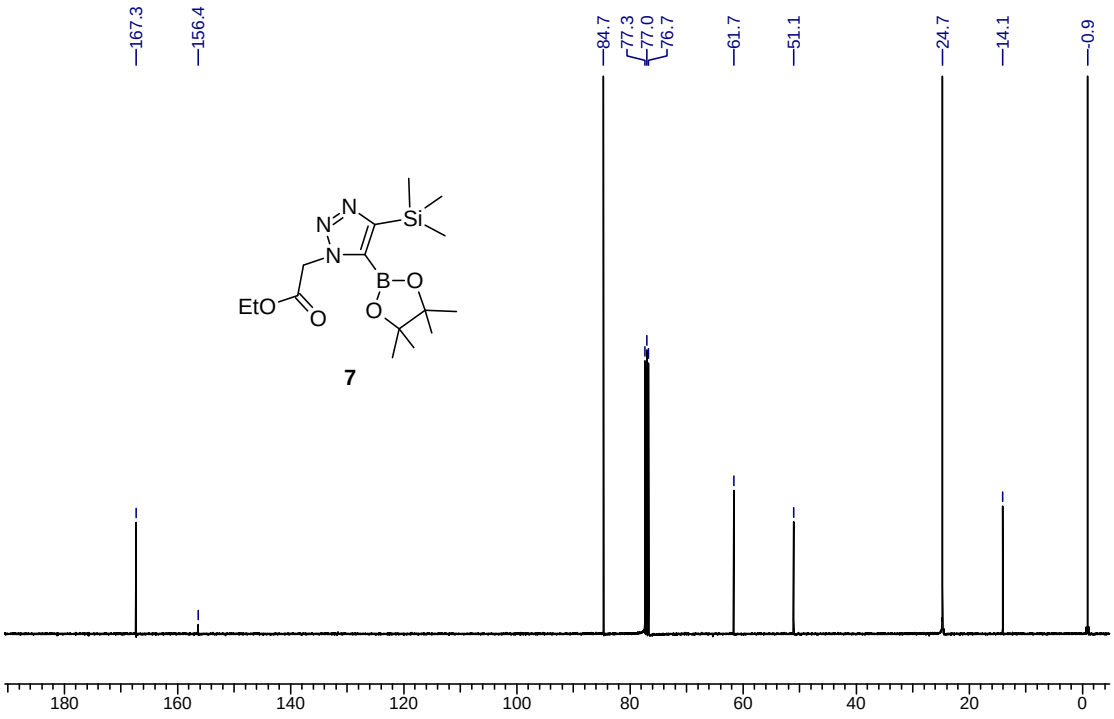

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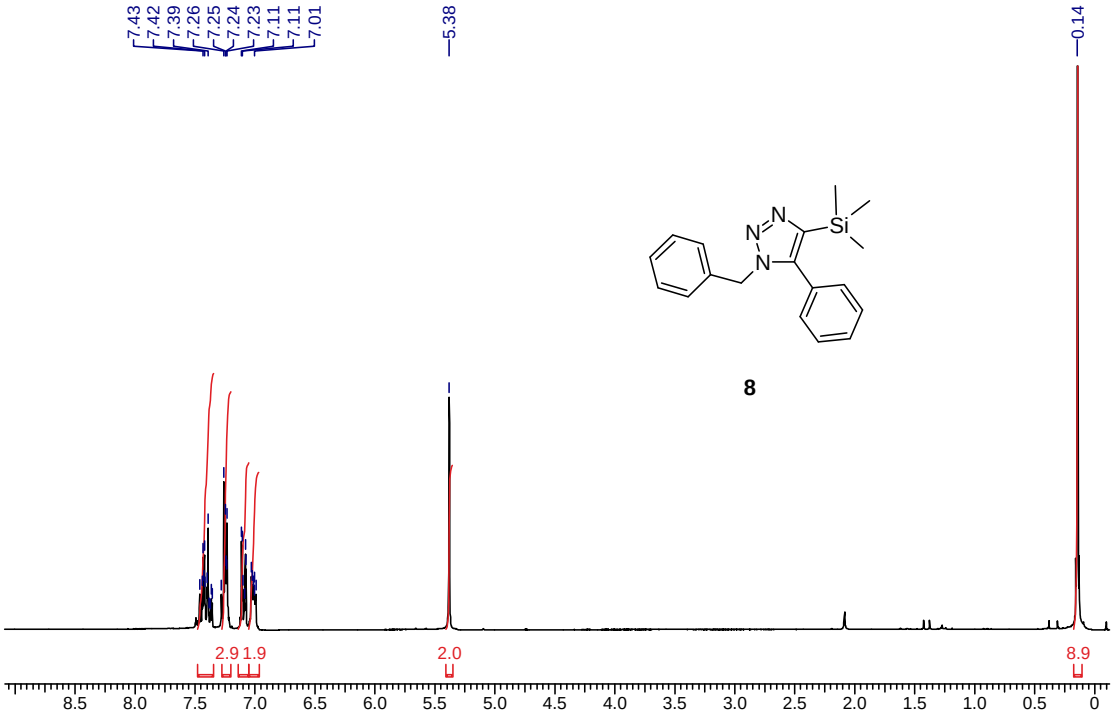
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N
Si
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8.5
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0

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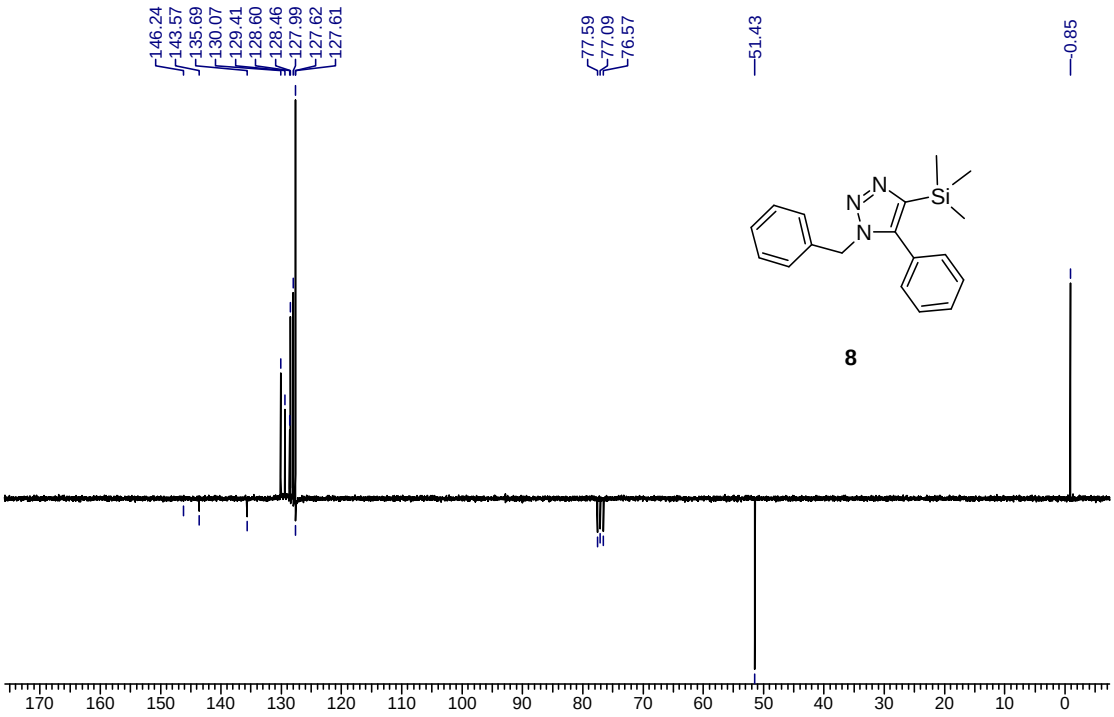
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100
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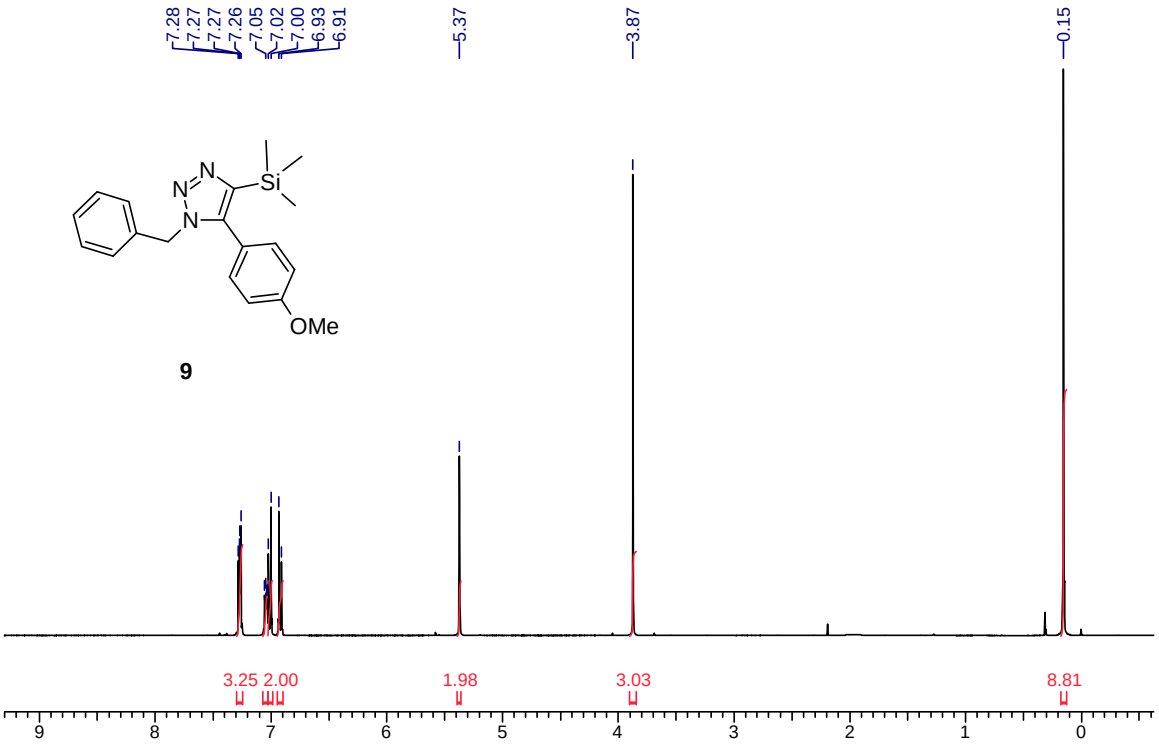
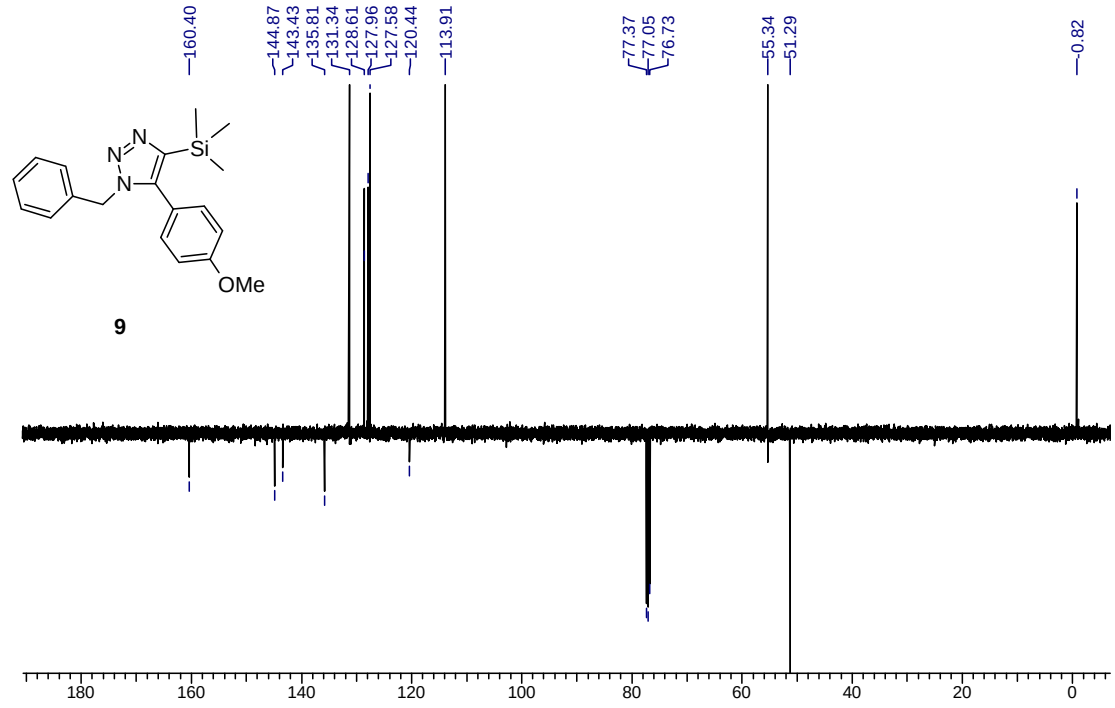
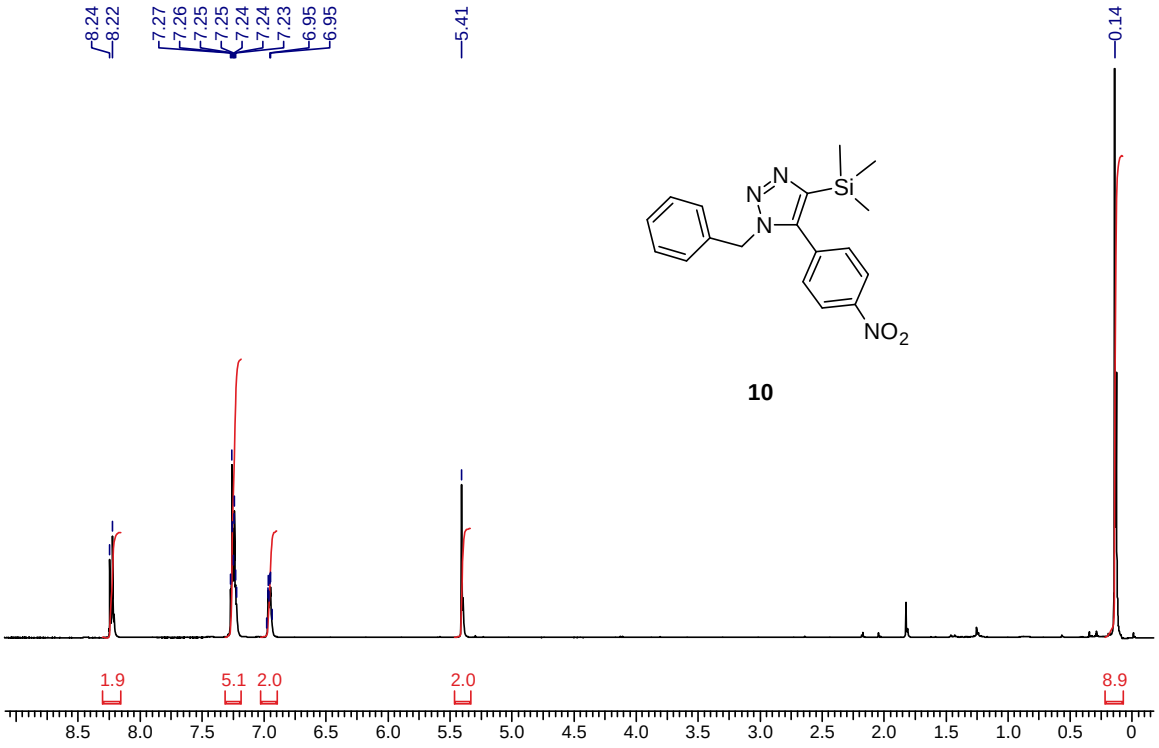
20
10
0

8







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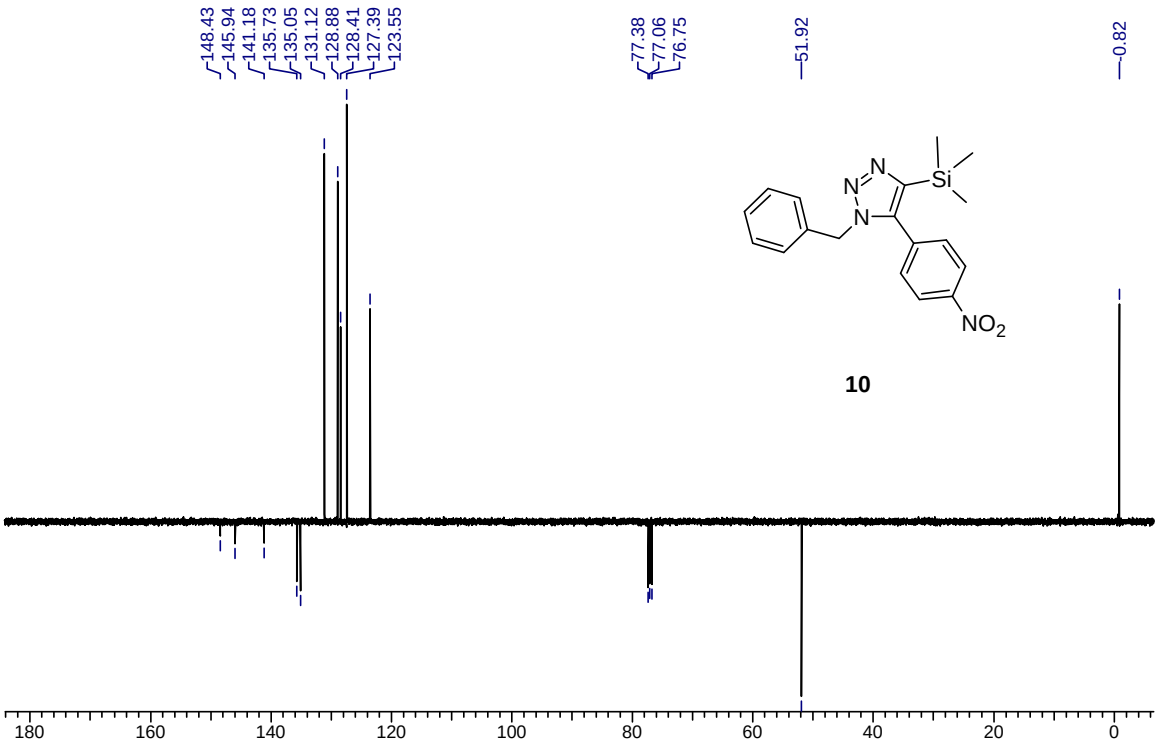

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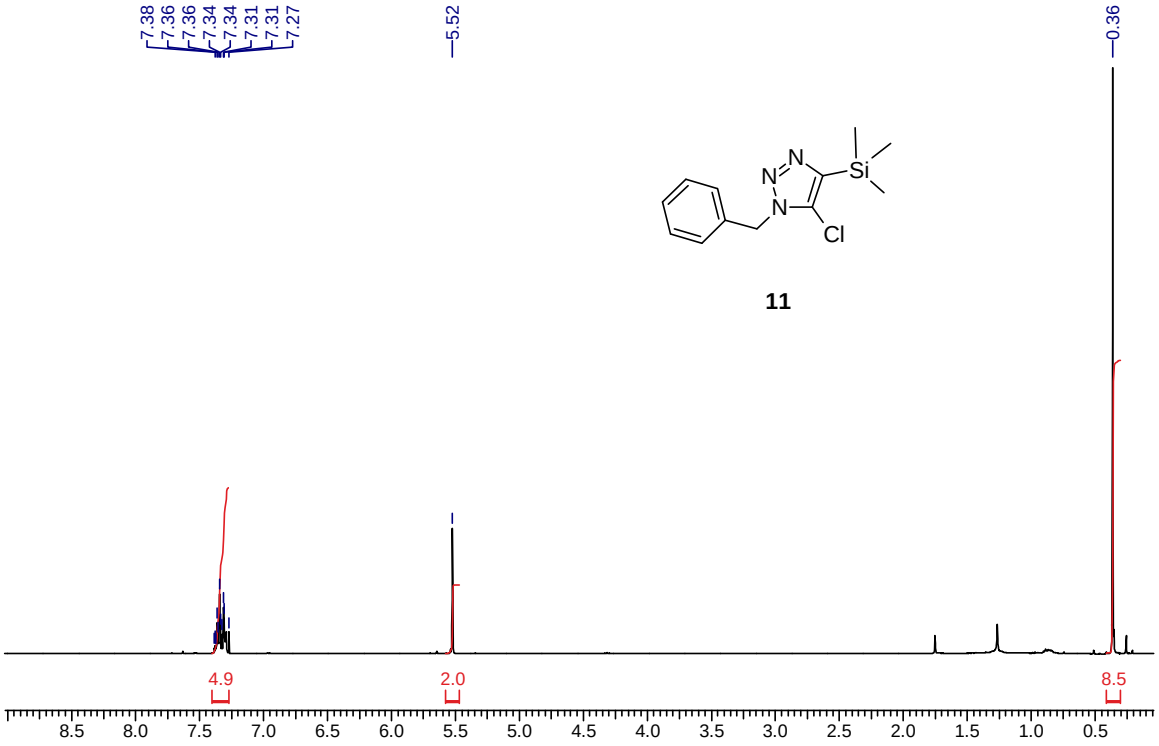
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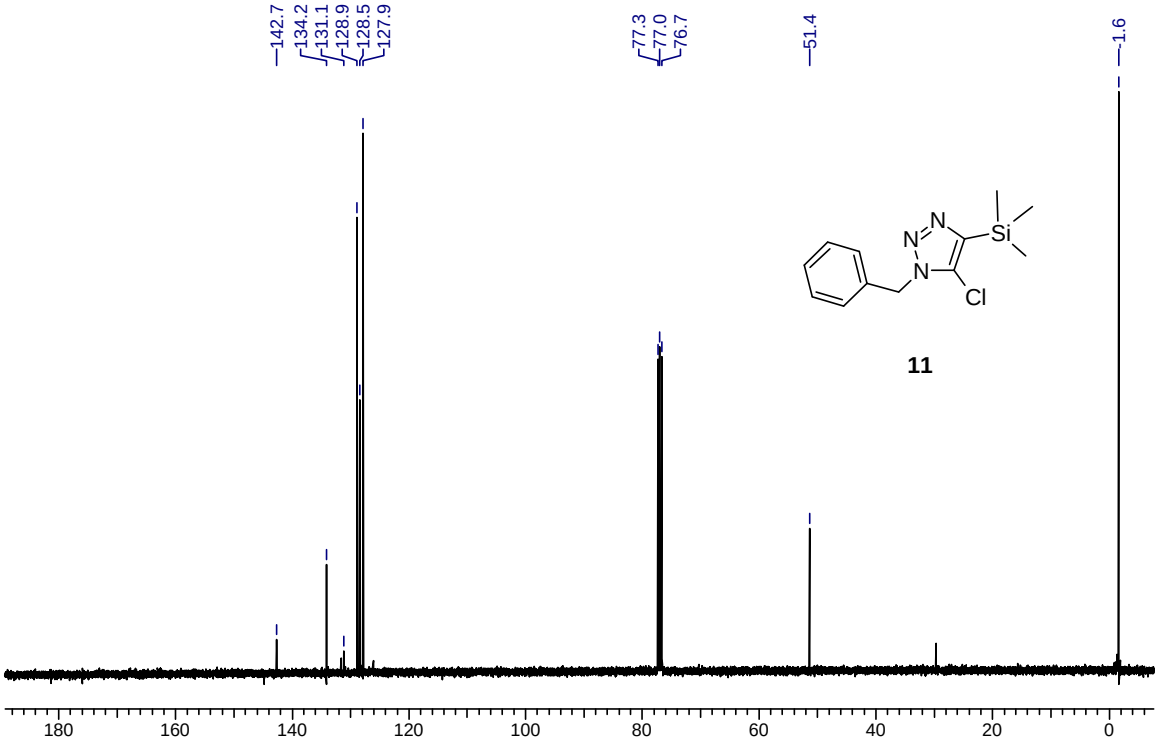
11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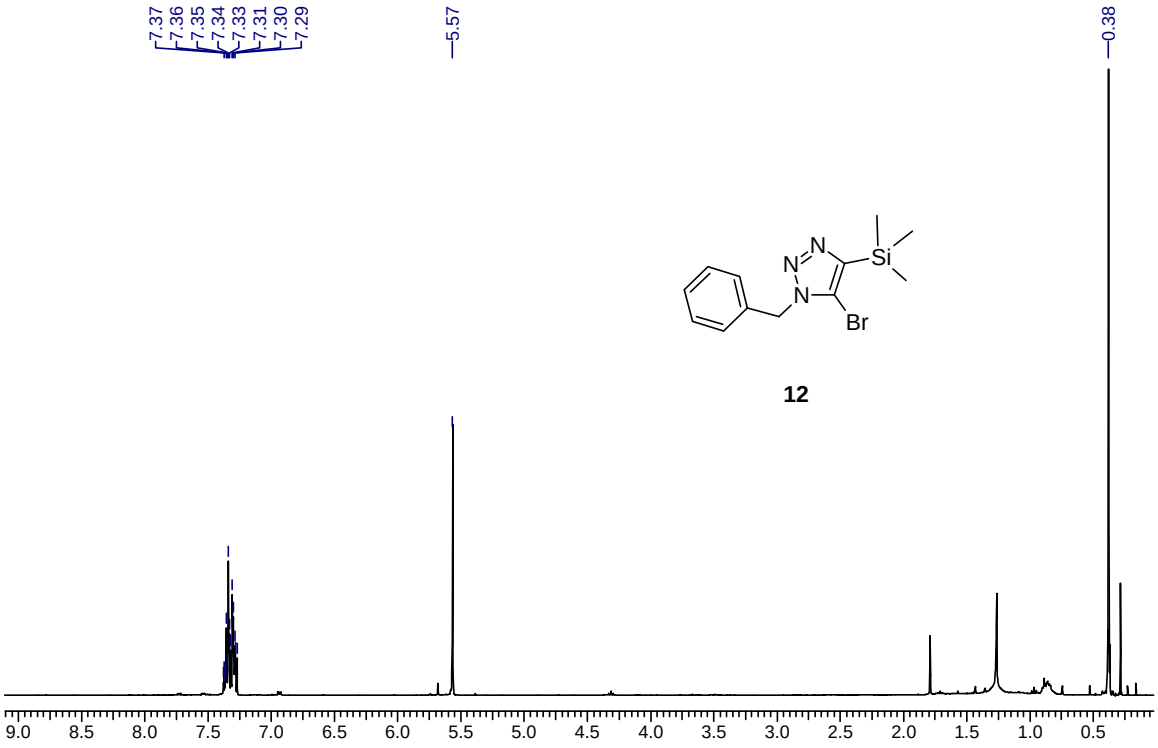
0

11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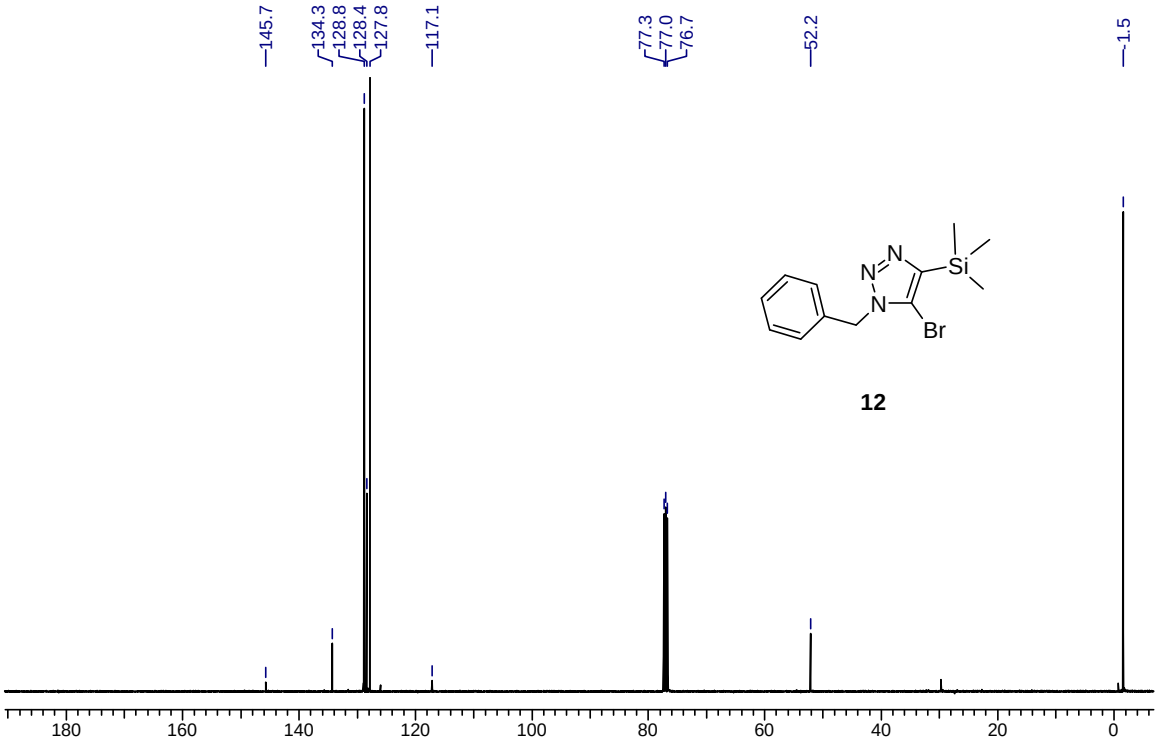
12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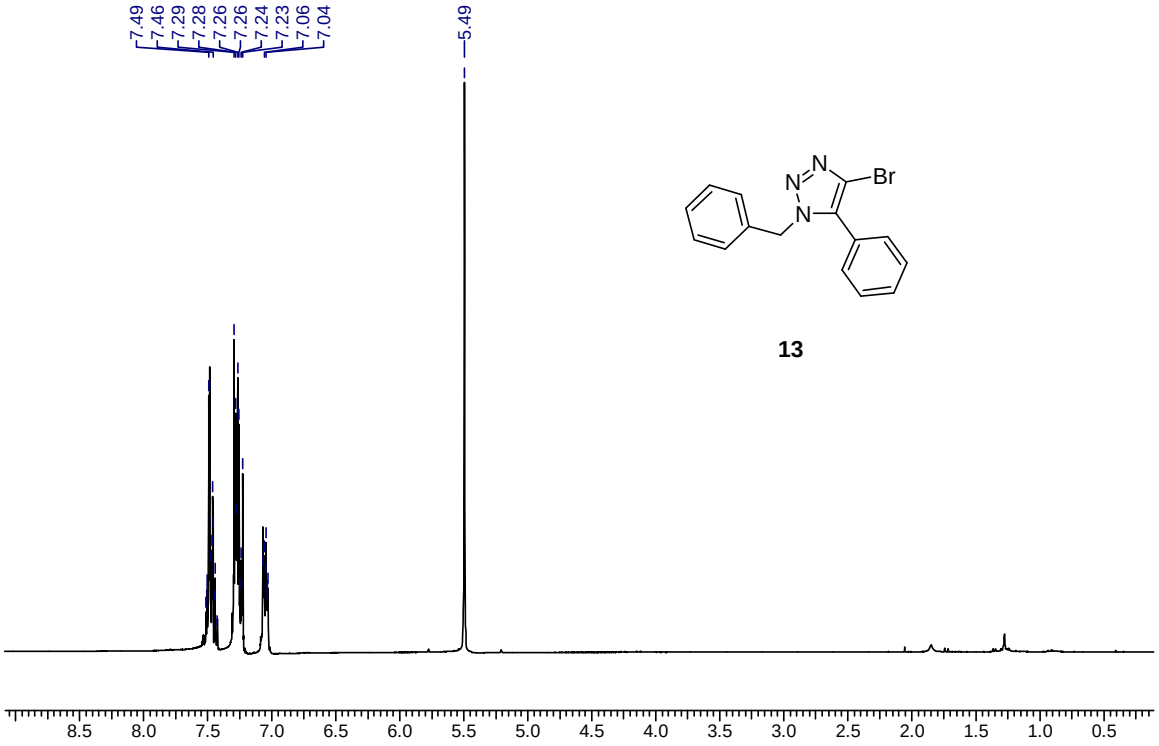
0

12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7.26
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7.23
7.06
7.04
5.49
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N
N
Br
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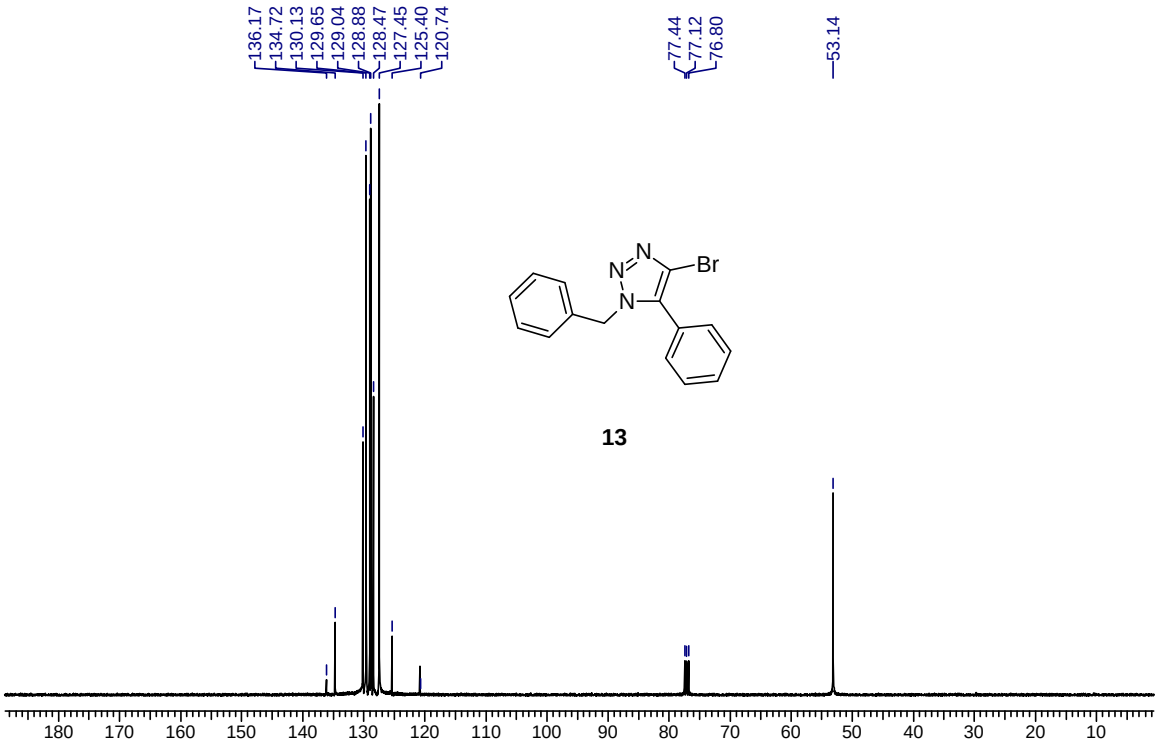
13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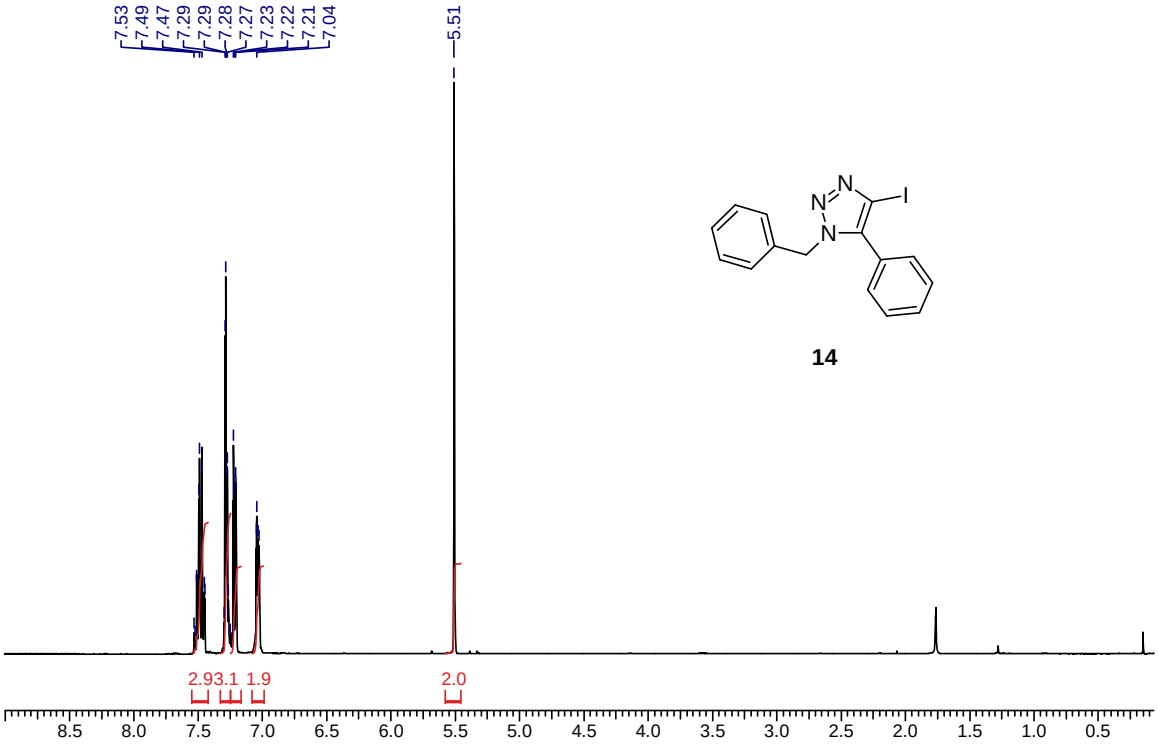
13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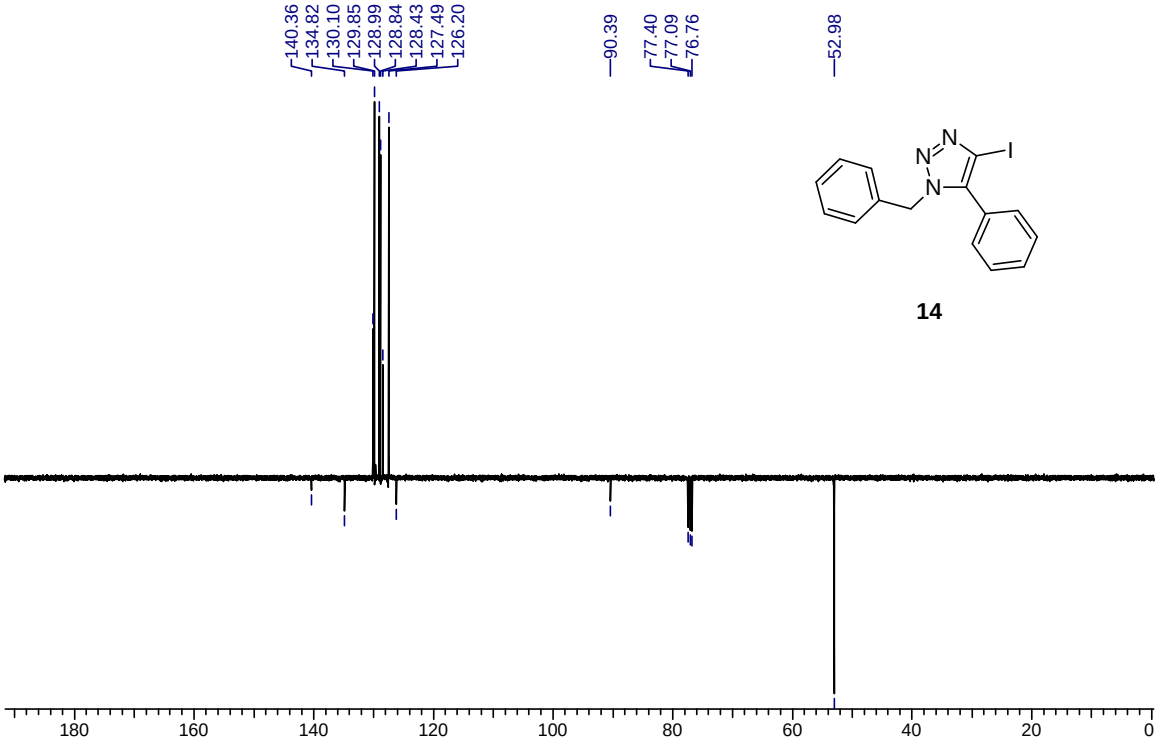
14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120
100
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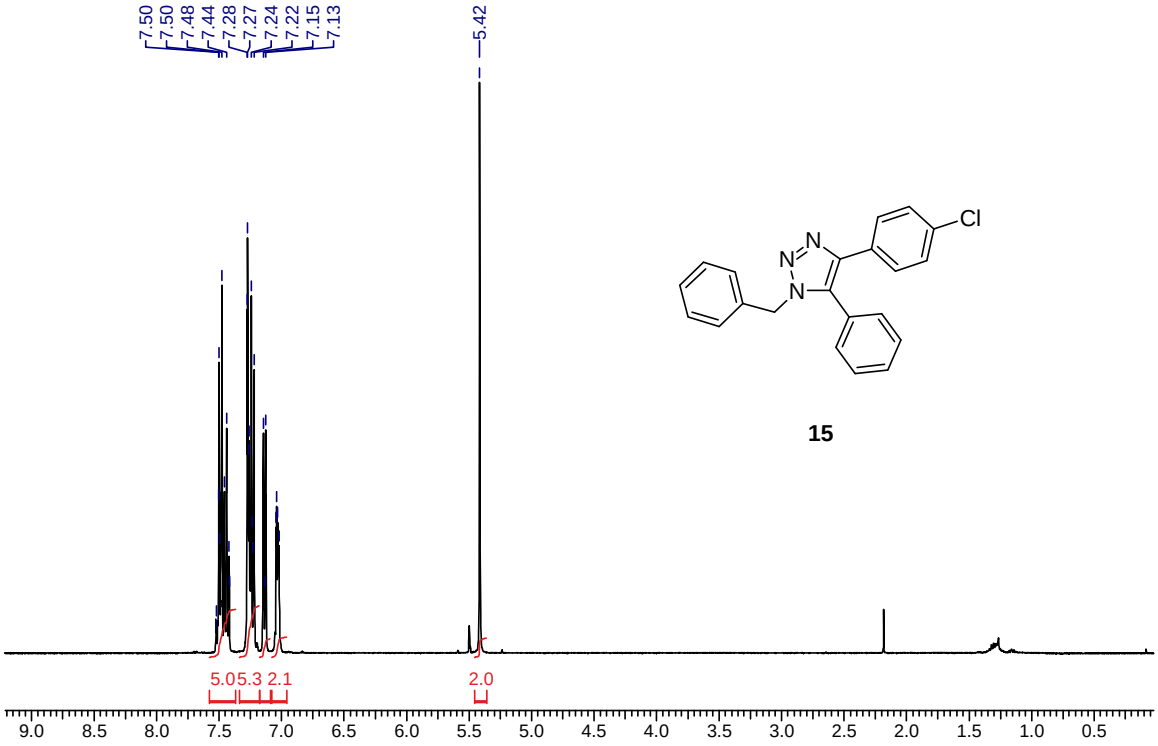
60
40
20
0

14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7.22
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7.13
5.42
5.0 5.3 2.1
2.0
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
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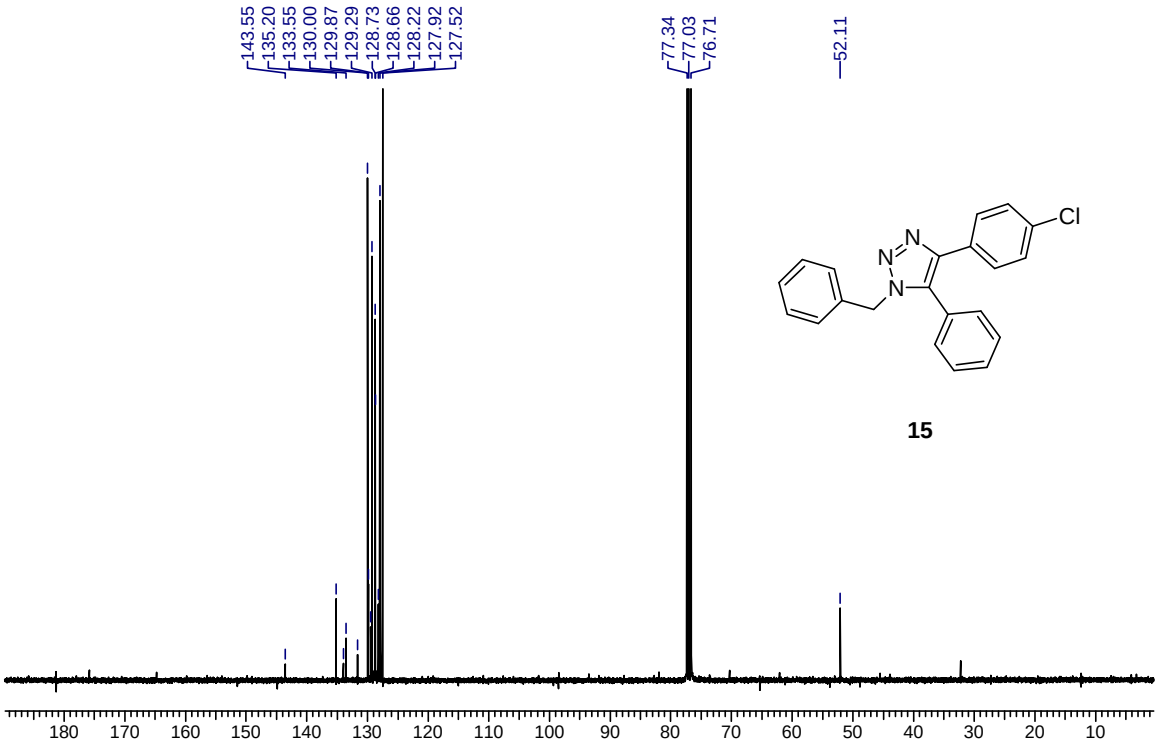
Cl

15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76.71
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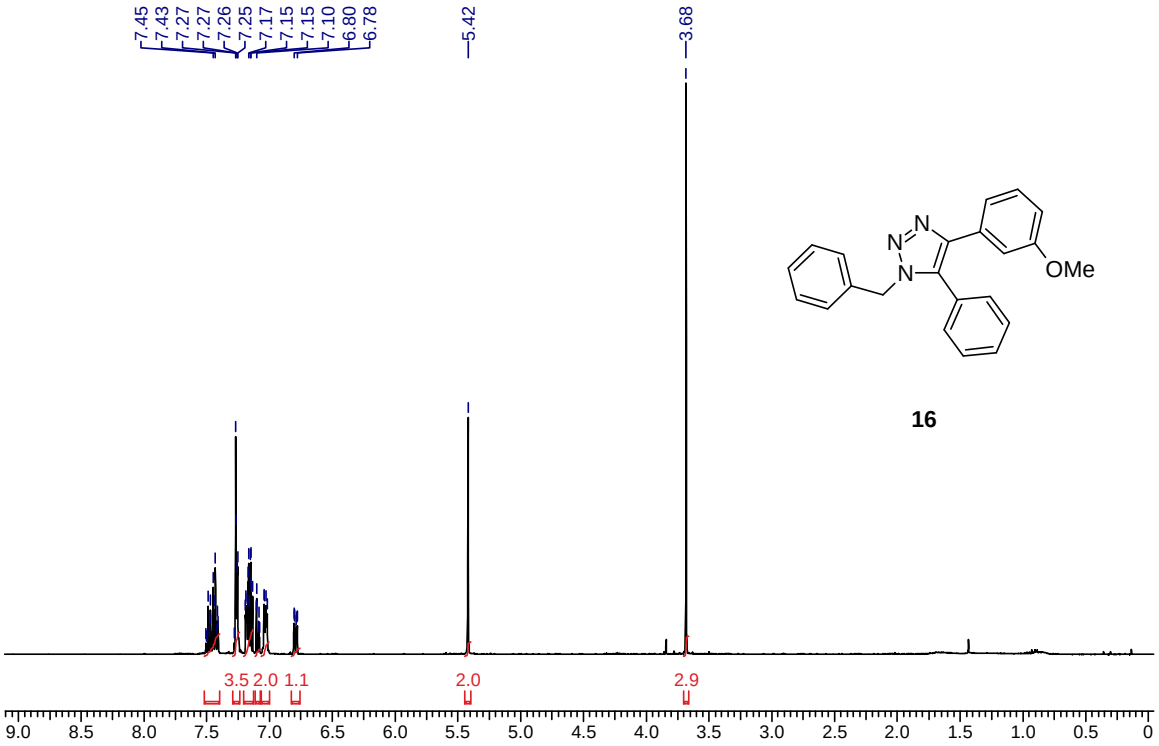
Cl

15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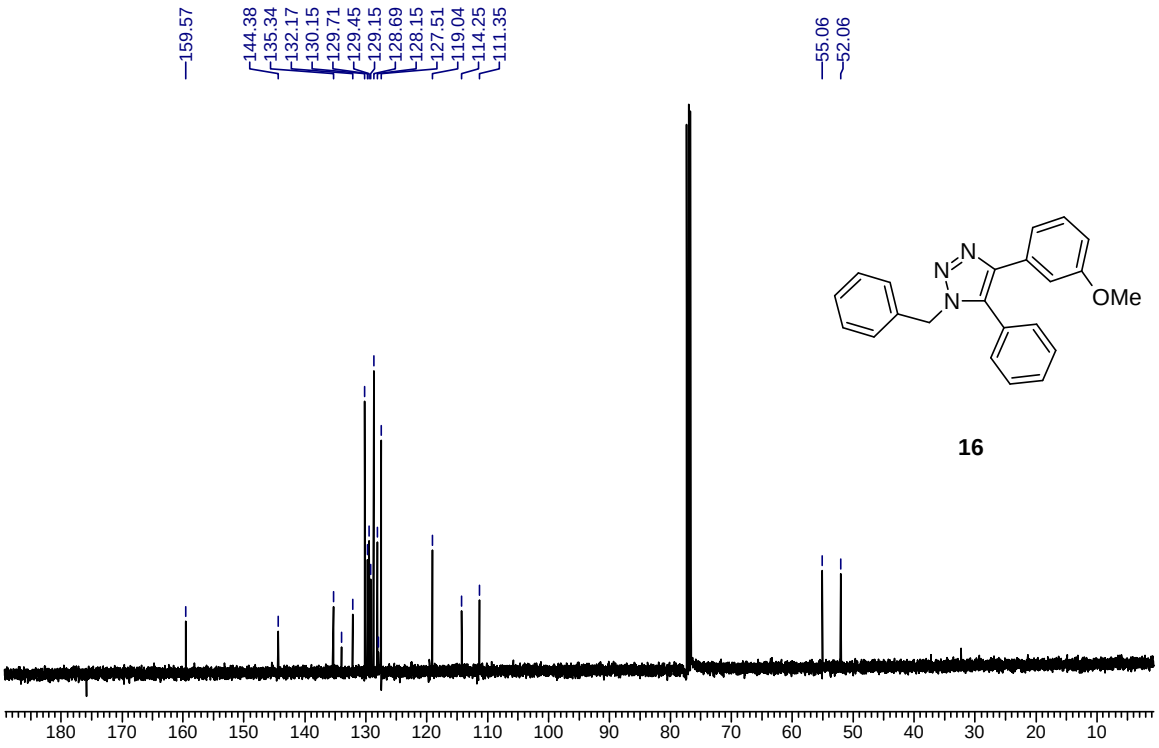
OMe
16
3.5 2.0 1.1
2.0
2.9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OMe
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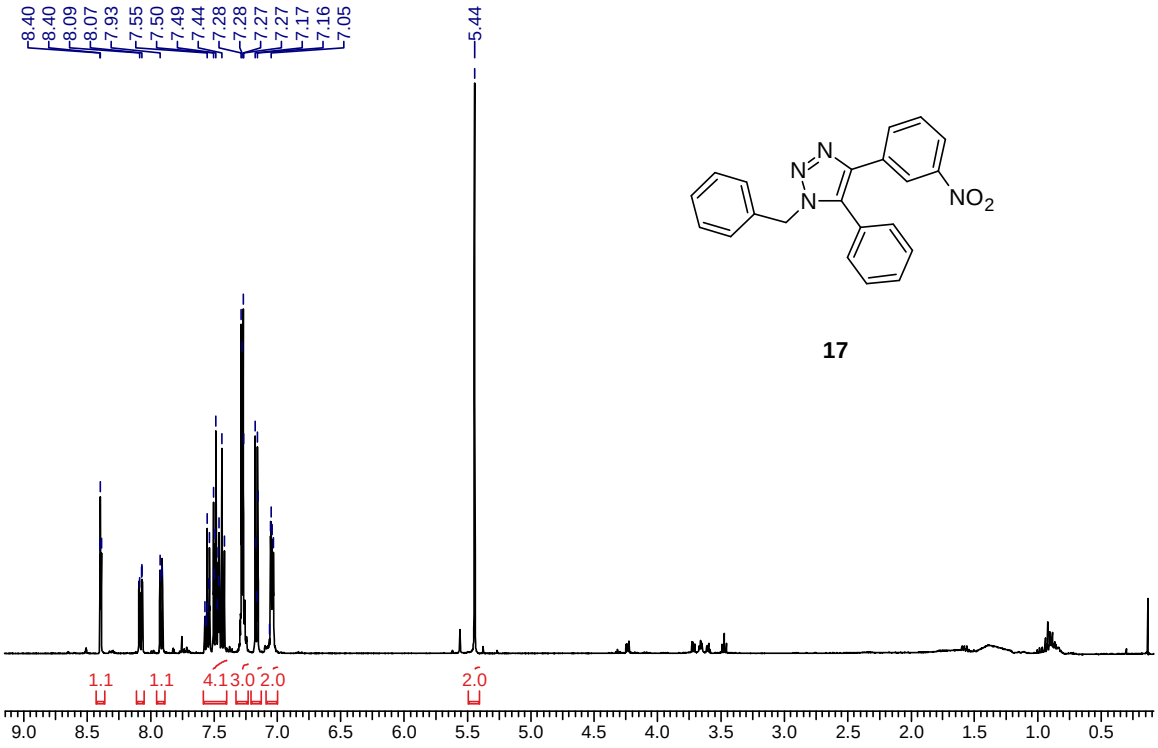
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7.05
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1.1
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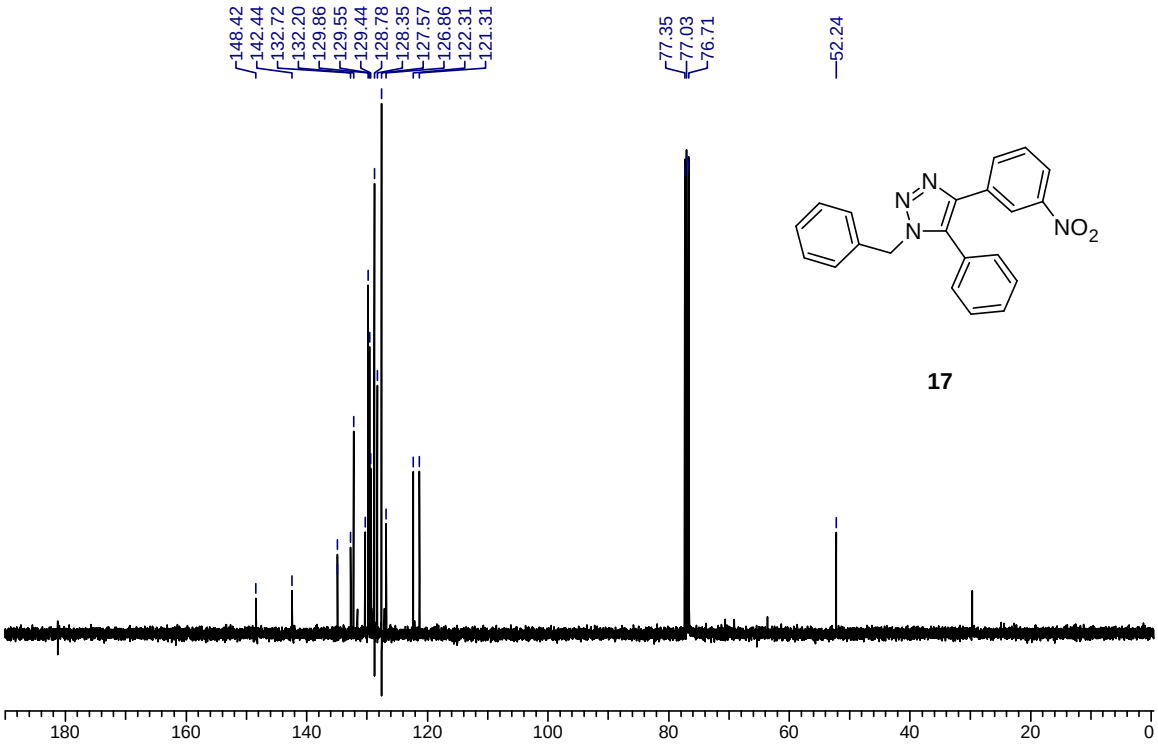
17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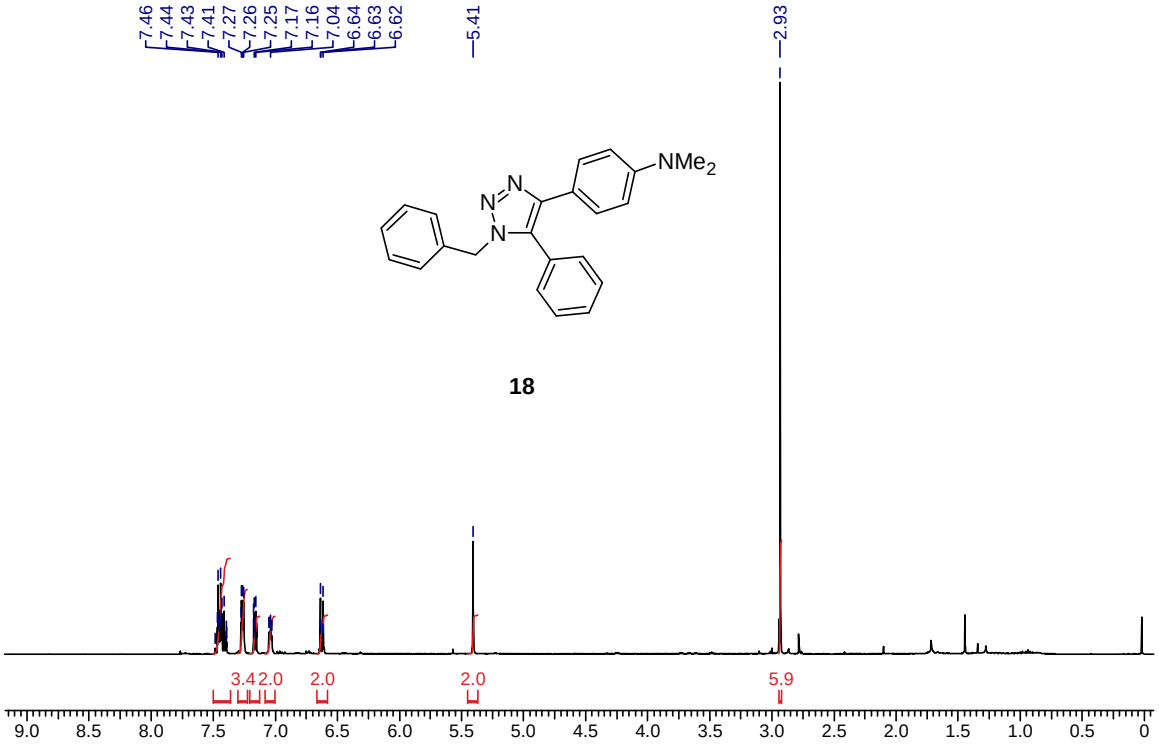
N
N
NO2

17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5.41
2.93
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N
N
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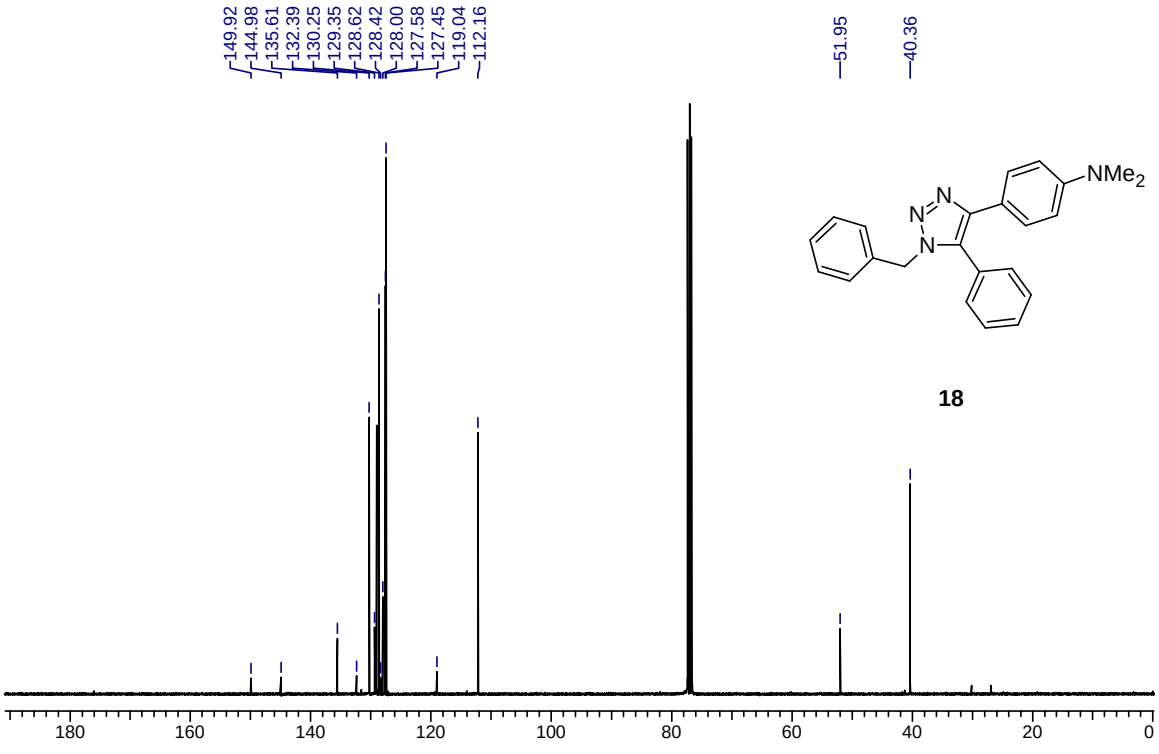
18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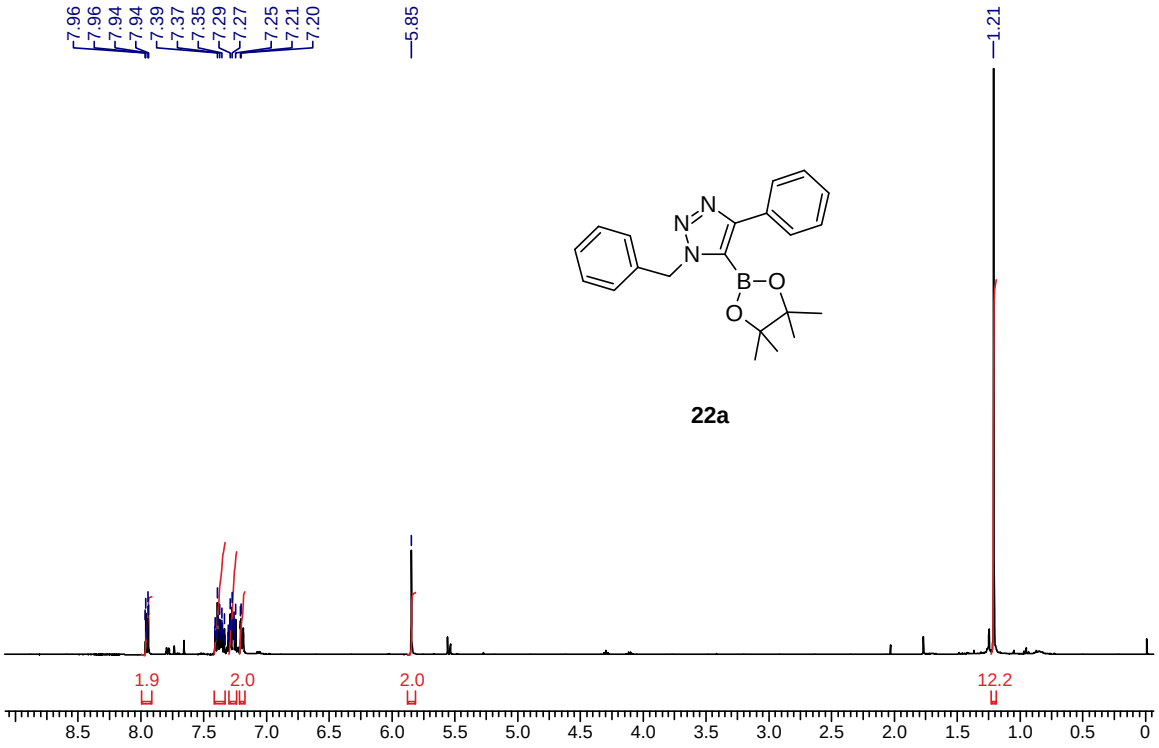
18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N
N
B–O
O
1.9
2.0
2.0
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8.0
7.5
7.0
6.5
6.0
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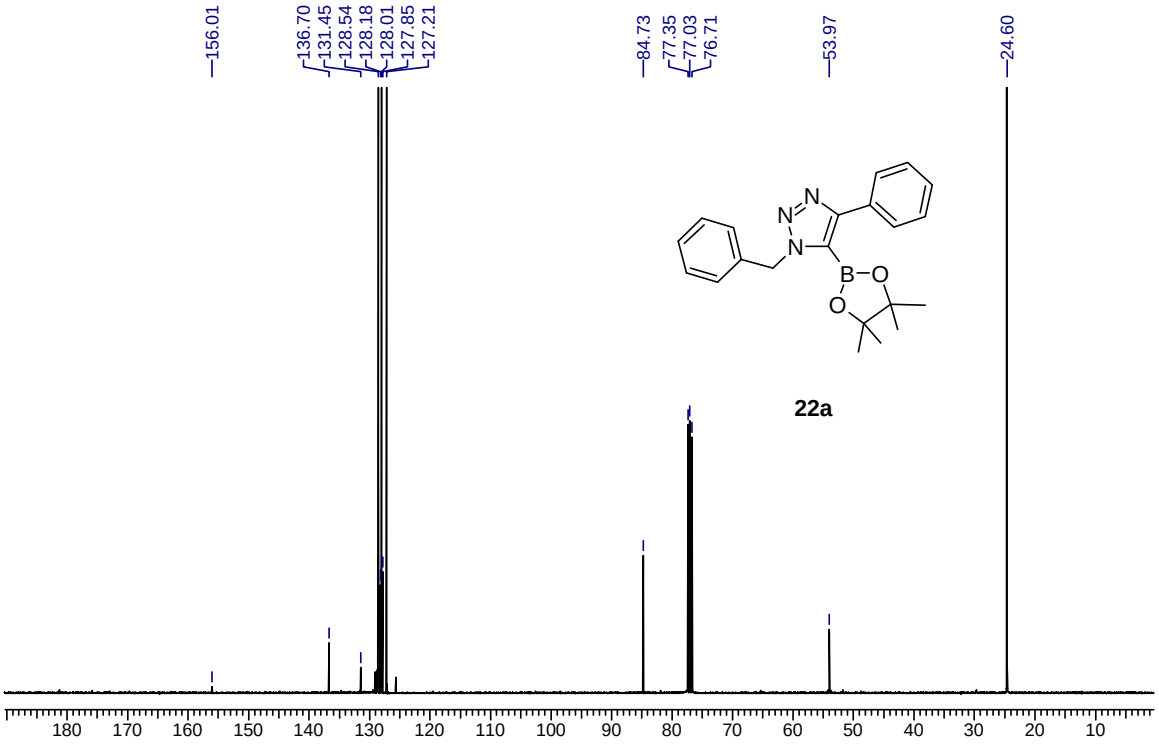
22a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N
N
B–O
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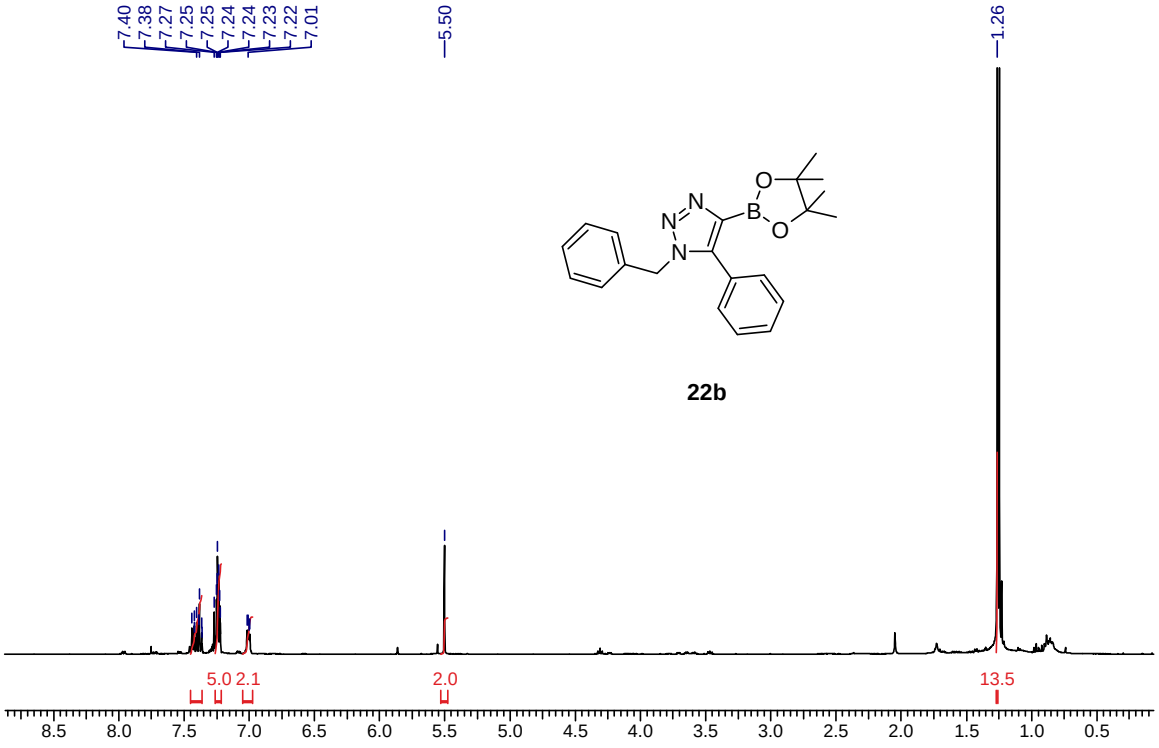
20
10

22a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8.0
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7.0
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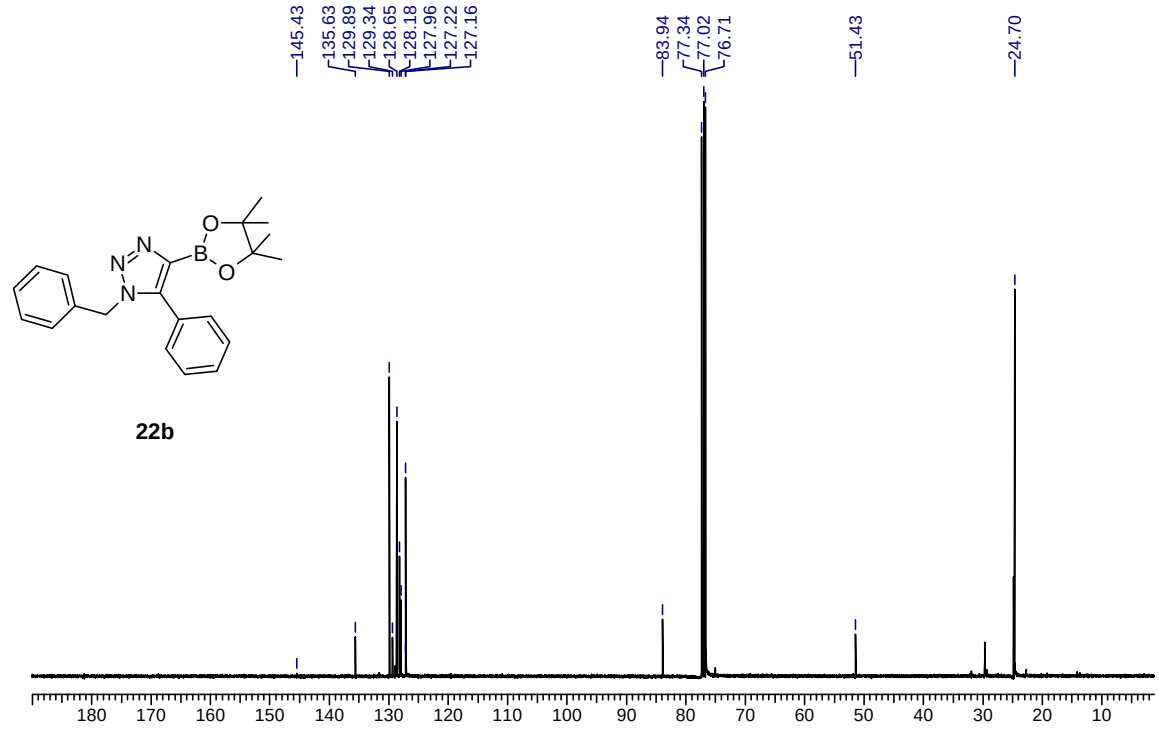
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51.43
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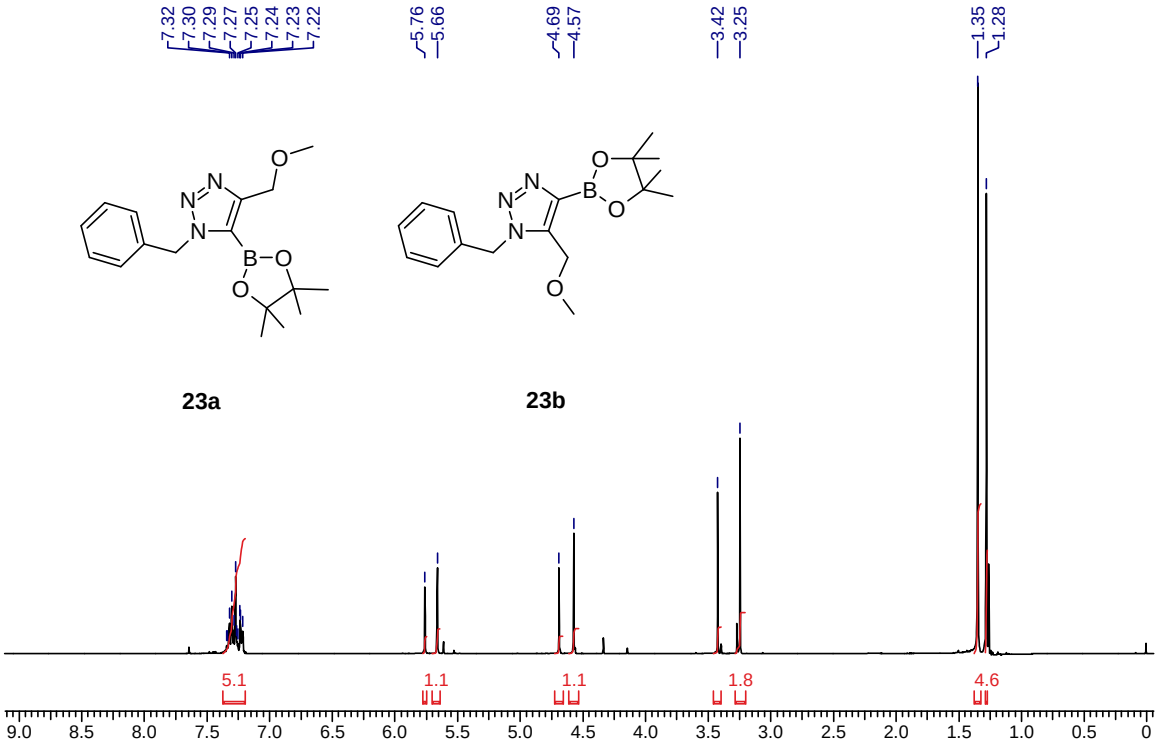
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23b
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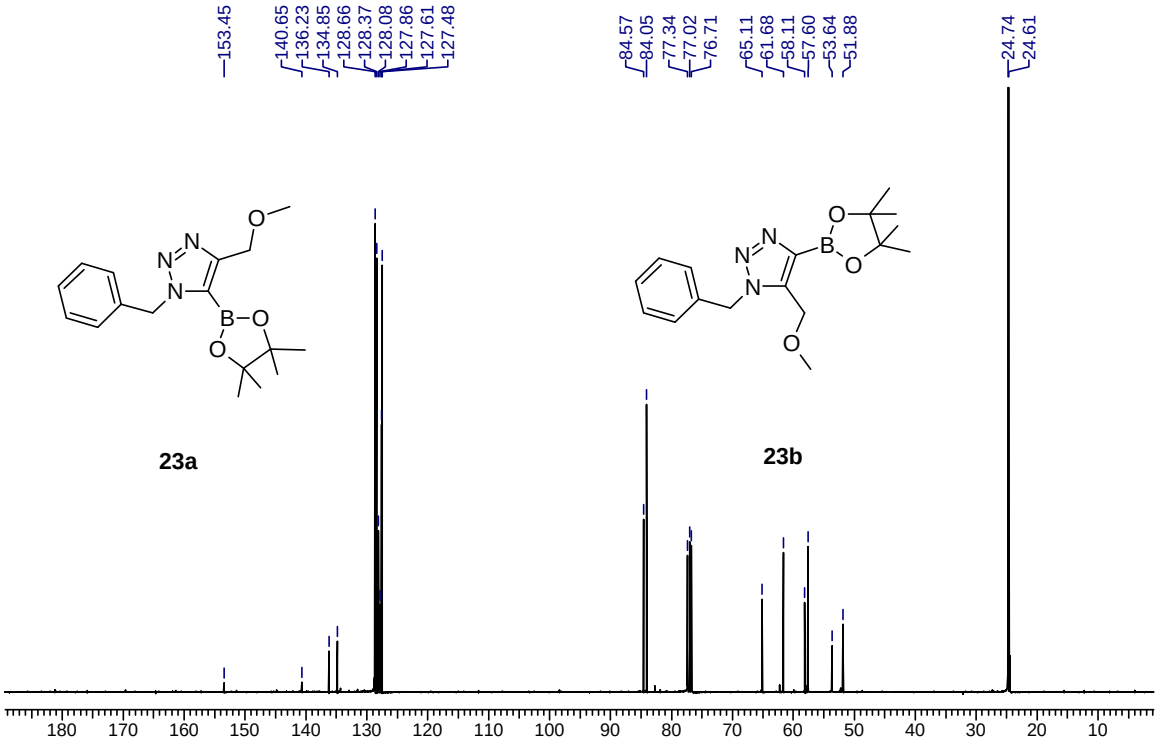
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65.11
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51.88
24.74
24.61
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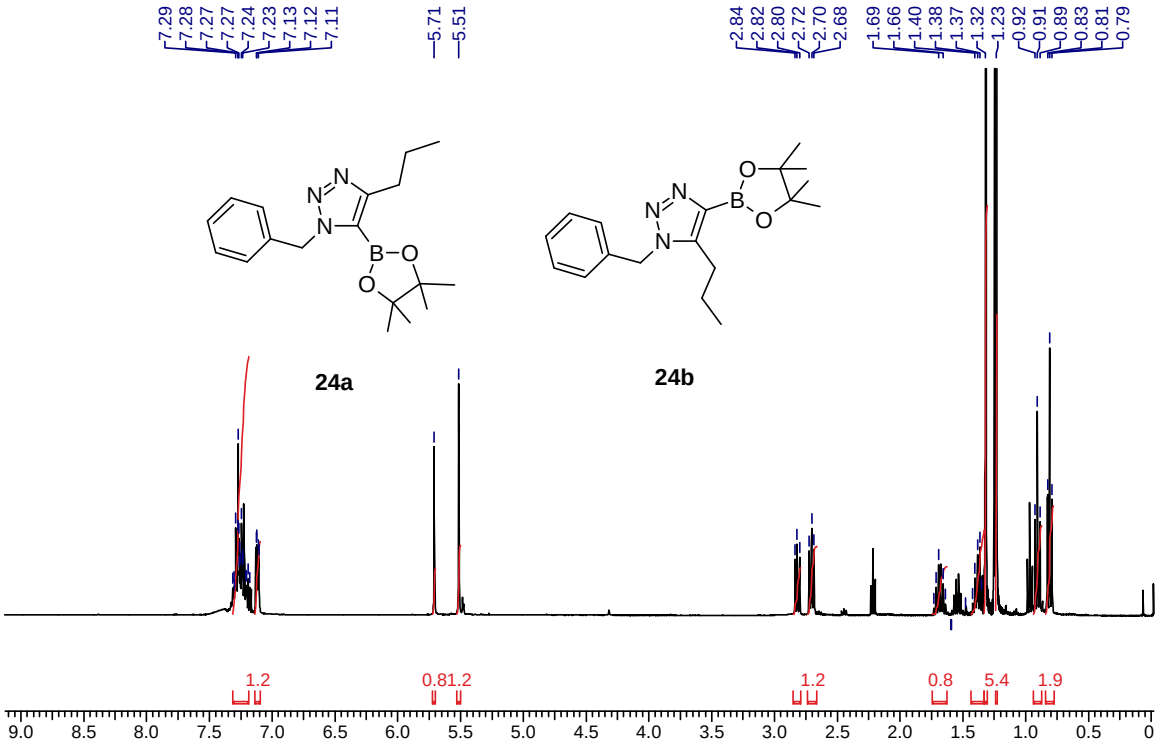
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2.68
1.69
1.66
1.40
1.38
1.37
1.32
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24b
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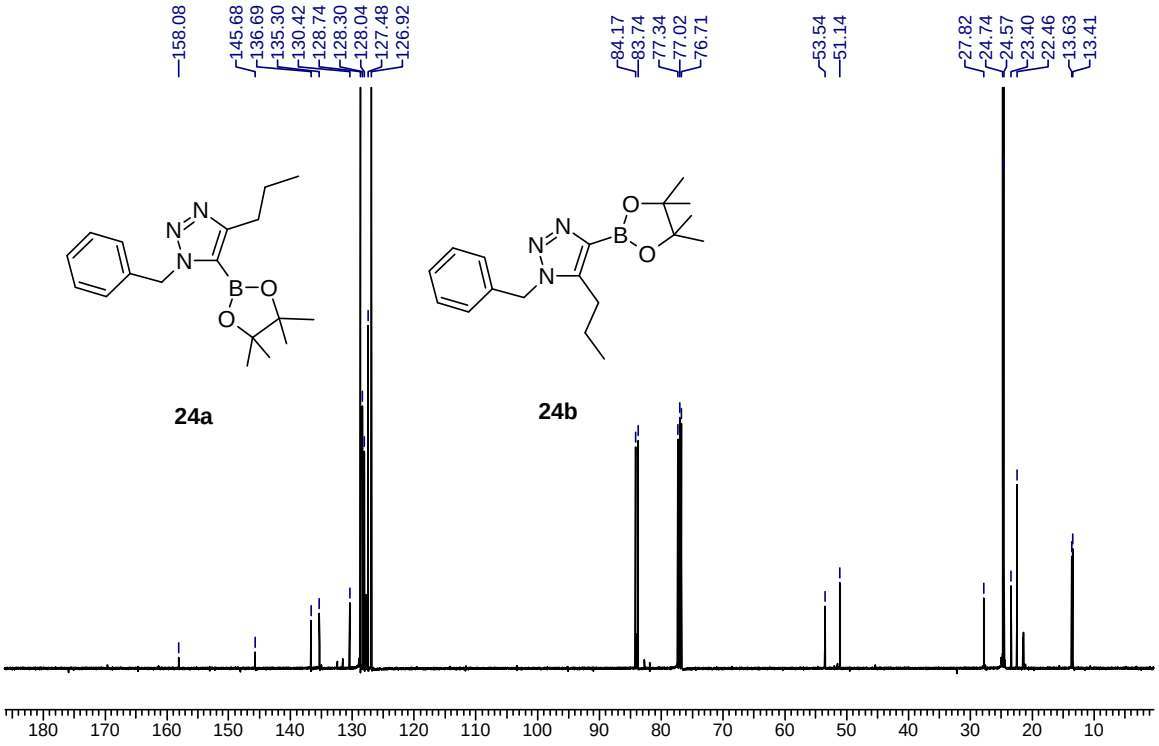
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76.71
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51.14
27.82
24.74
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24a
24b
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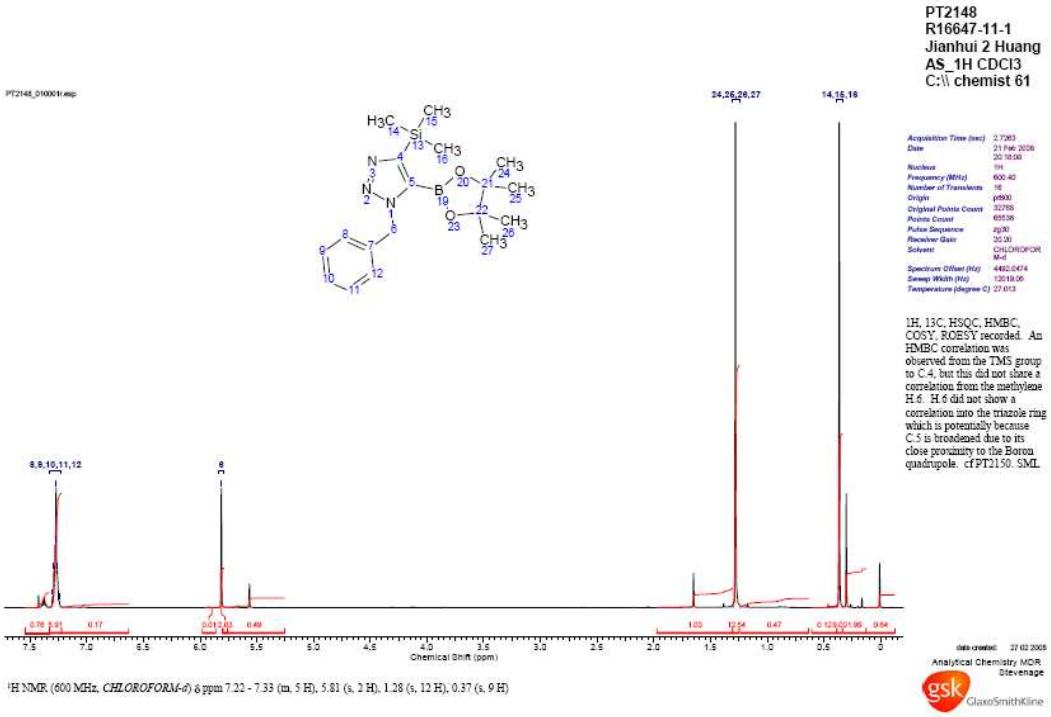
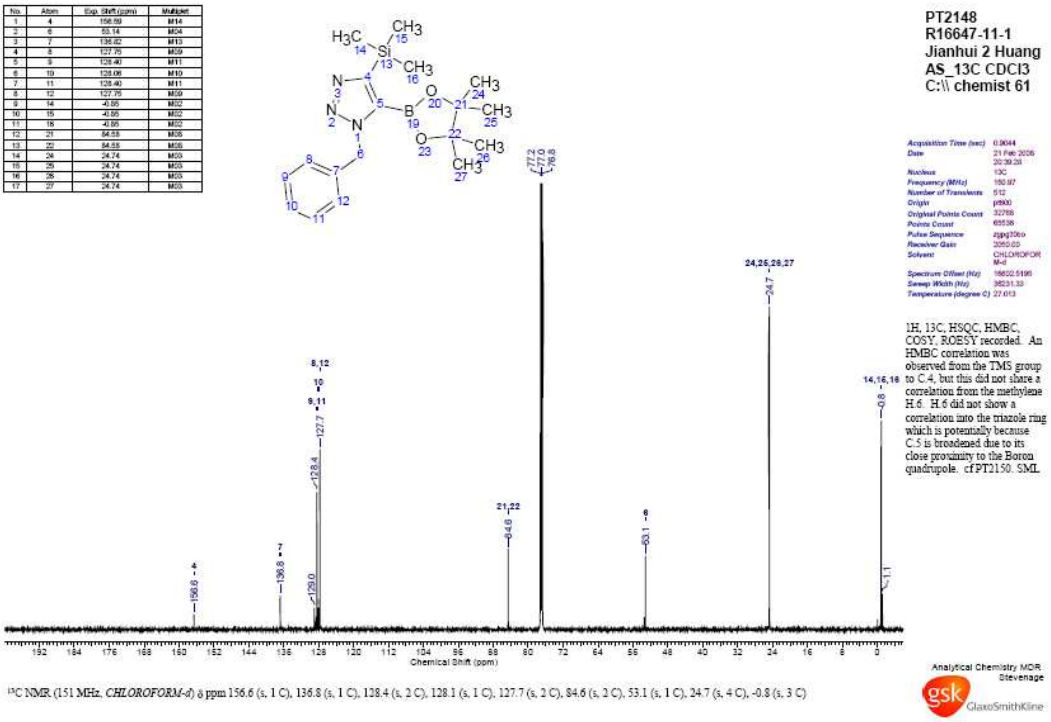
6. Regiochemistry Assignment

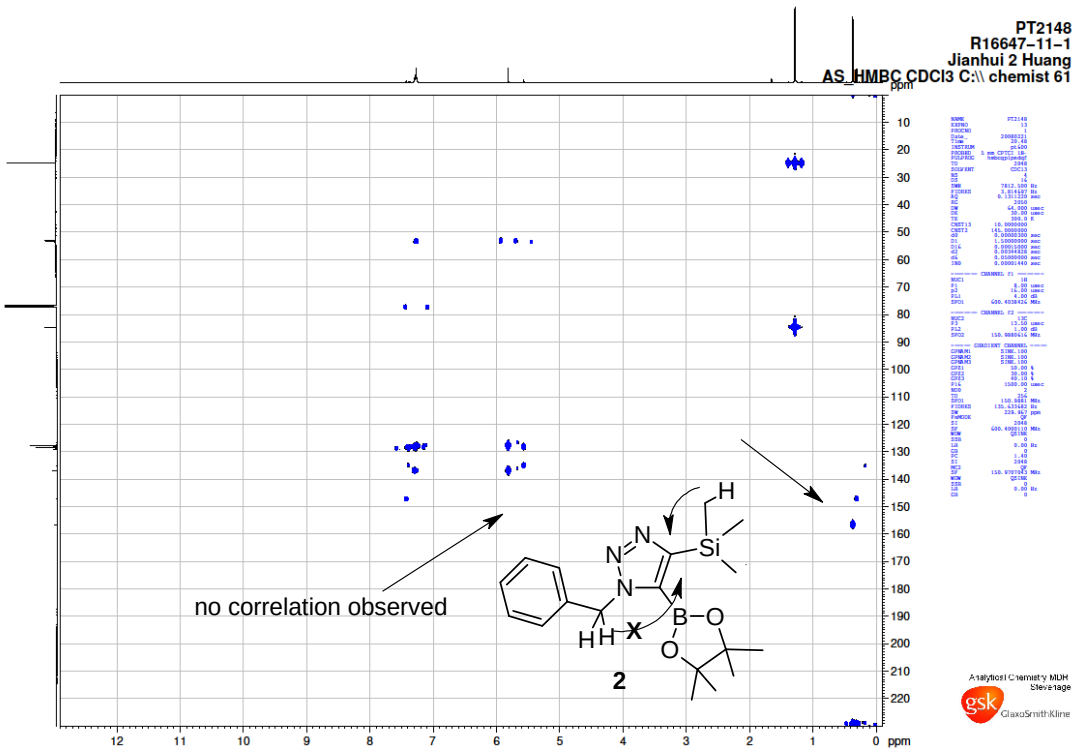


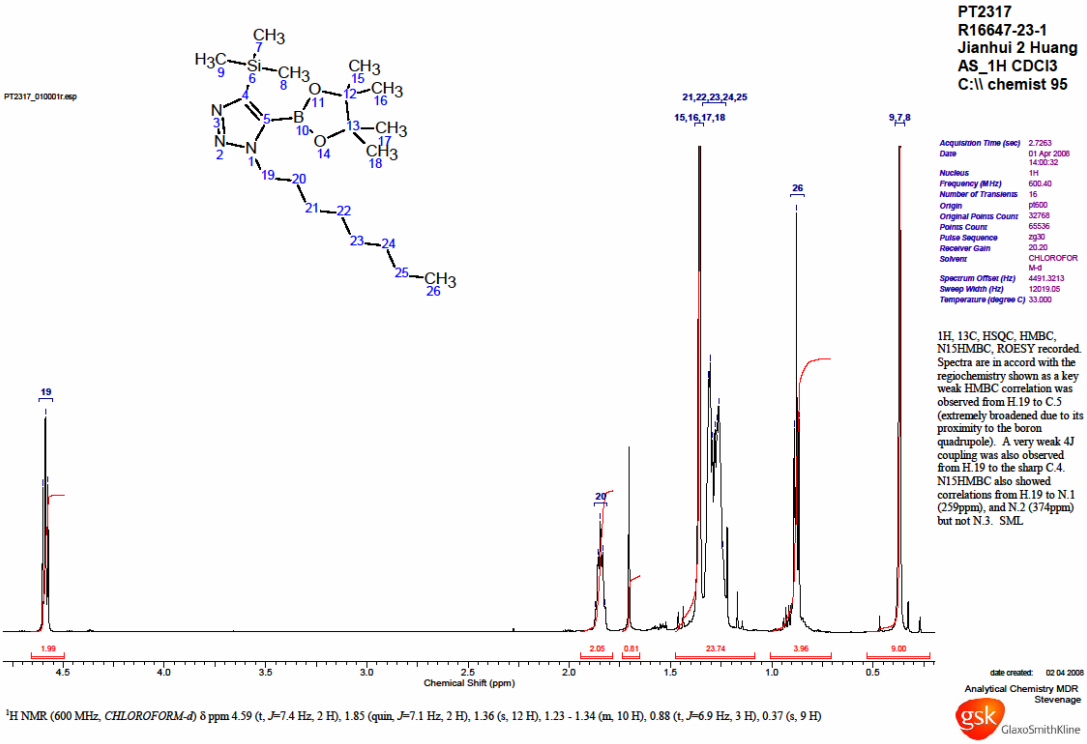
^{1}H NMR (600 MHz, *CHLOROFORM-d*) δ ppm 7.22 - 7.33 (m, 5 H), 5.81 (s, 2 H), 1.28 (s, 12 H), 0.37 (s, 9 H)

No.	Atom	Exp. Shift (ppm)	Multiplet
1	4	156.59	M14
2	6	53.14	M04
3	7	136.82	M13
4	8	127.76	M09
5	9	128.40	M11
6	10	128.06	M10
7	11	128.40	M11
8	12	127.76	M09
9	14	-0.85	M02
10	15	-0.85	M02
11	16	-0.85	M02
12	21	84.59	M06
13	22	84.59	M06
14	24	24.74	M03
15	25	24.74	M03
16	26	24.74	M03
17	27	24.74	M03



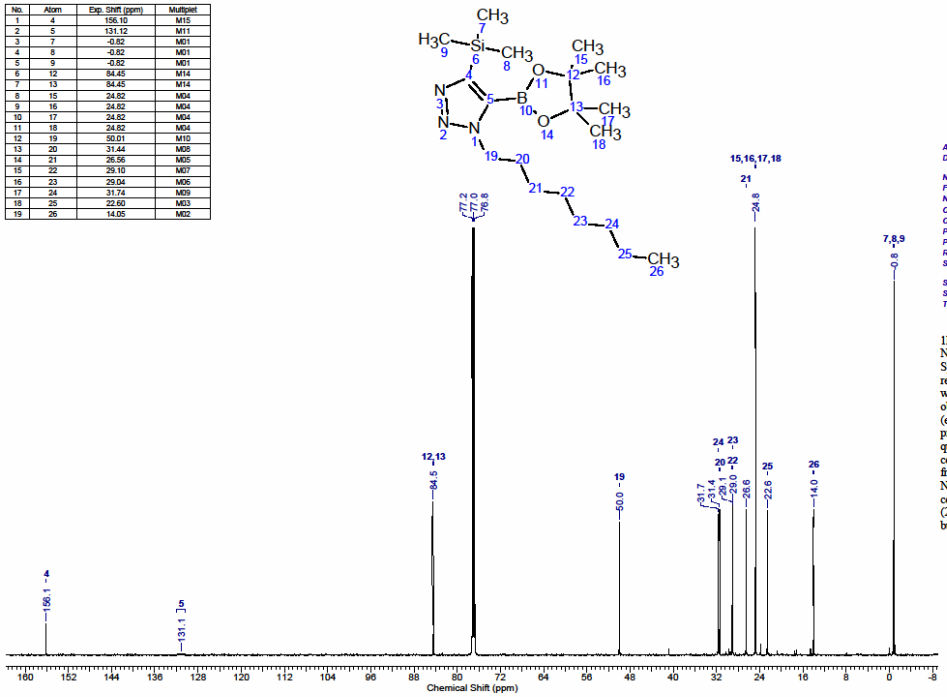
^{13}C NMR (151 MHz, *CHLOROFORM-d*) δ ppm 156.6 (s, 1 C), 136.8 (s, 1 C), 128.4 (s, 2 C), 128.1 (s, 1 C), 127.7 (s, 2 C), 84.6 (s, 2 C), 53.1 (s, 1 C), 24.7 (s, 4 C), -0.8 (s, 3 C)



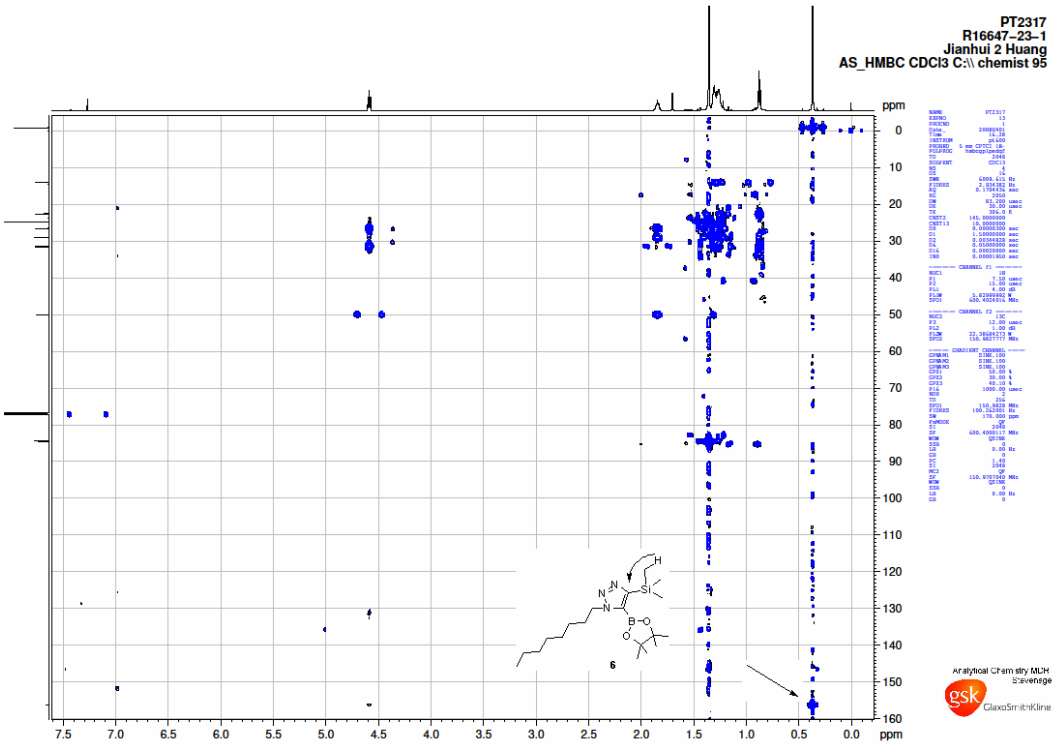


^{1}H NMR (600 MHz, *CHLOROFORM-d*) δ ppm 4.59 (t, *J*=7.4 Hz, 2 H), 1.85 (quin, *J*=7.1 Hz, 2 H), 1.36 (s, 12 H), 1.23 - 1.34 (m, 10 H), 0.88 (t, *J*=6.9 Hz, 3 H), 0.37 (s, 9 H)

No.	Atom	Exp. Shift (ppm)	Multiplet
1	4	156.10	M15
2	5	131.12	M11
3	7	-0.82	M01
4	8	-0.82	M01
5	9	-0.82	M01
6	12	84.45	M14
7	13	84.45	M14
8	15	24.82	M04
9	16	24.82	M04
10	17	24.82	M04
11	18	24.82	M04
12	19	50.01	M10
13	20	31.44	M08
14	21	26.56	M05
15	22	29.10	M07
16	23	29.04	M06
17	24	31.74	M09
18	25	22.60	M03
19	26	14.05	M02



^{13}C NMR (151 MHz, *CHLOROFORM-d*) δ ppm 156.1 (s, 1 C), 131.1 (br. s., 1 C), 84.5 (s, 2 C), 50.0 (s, 1 C), 31.7 (s, 1 C), 31.4 (s, 1 C), 29.1 (s, 1 C), 29.0 (s, 1 C), 26.6 (s, 1 C), 24.8 (s, 4 C), 22.6 (s, 1 C), 14.0 (s, 1 C), -0.8 (s, 3 C)

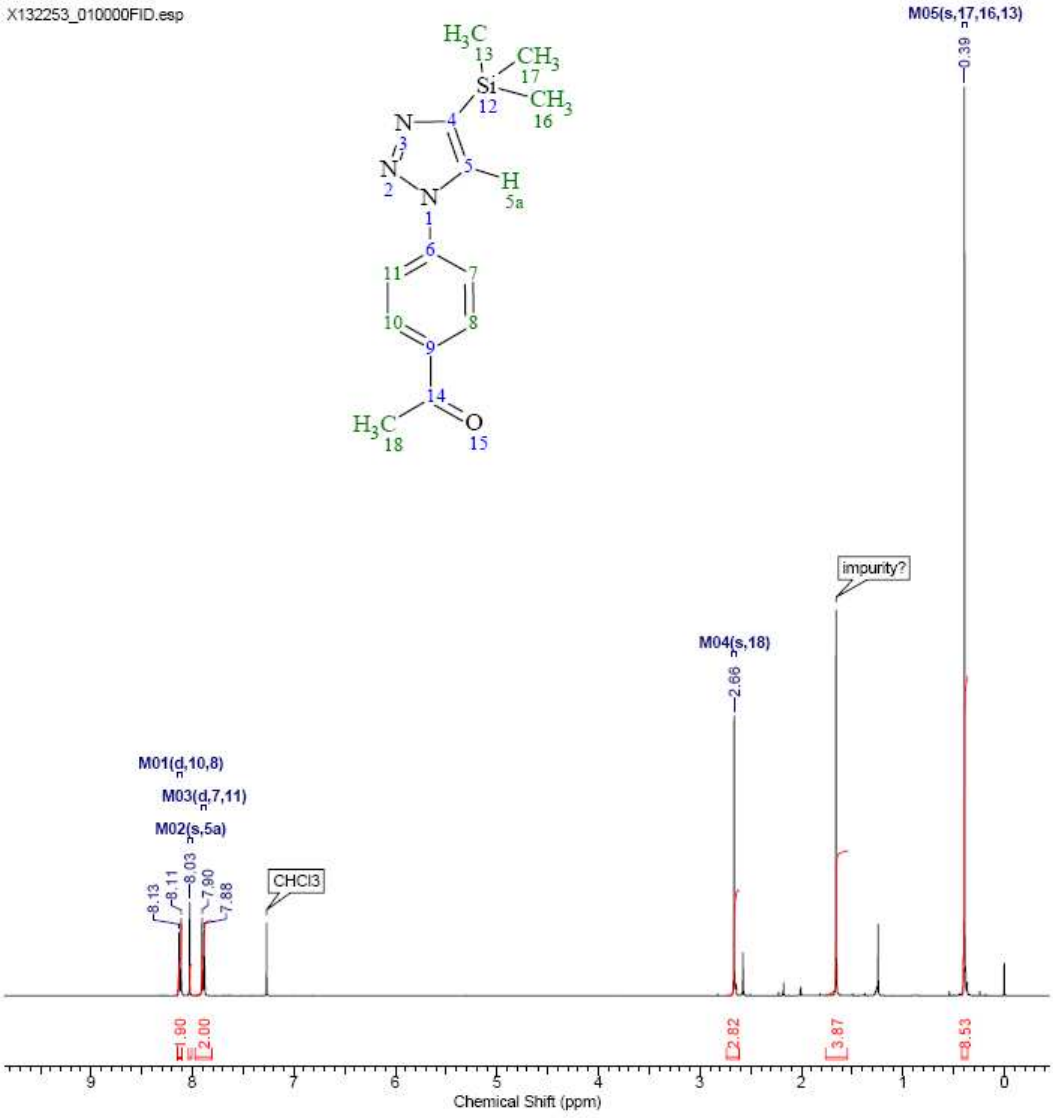


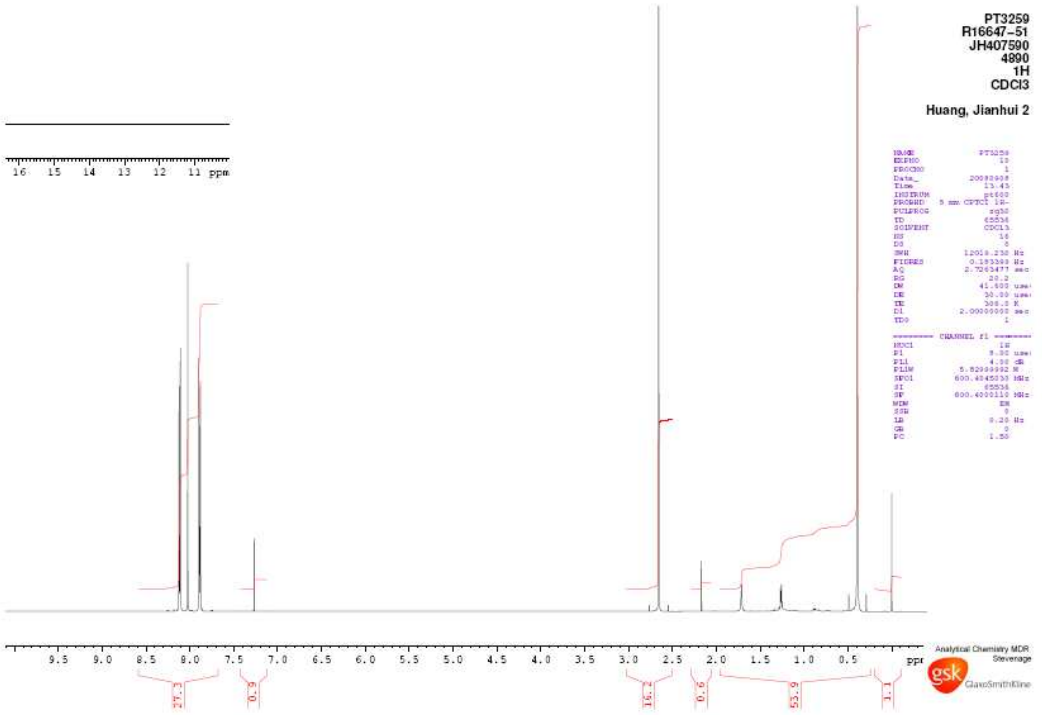
08/09/2008 14:48:40

Acquisition Time (sec)	1.9923	*Comment*	X132253 R16647-51 DEBPIN J Huang 1H CDCl3 Position: 58 ..		
Date	21 May 2008 21:58:24			*Date Stamp*	21 May 2008 21:58:24
File Name	C:\DATA\CHEMIST\NMR\X132253\10\FID			*Frequency (MHz)*	400.13
Nucleus	1H	*Number of Transients*	16	*Origin*	spect
Original Points Count	16384	*Owner*	root	*Points Count*	32768
Pulse Sequence	zg30	*Receiver Gain*	322.50	*SW(cyclical) (Hz)*	8223.68
Solvent	CHLOROFORM-d			*Spectrum Offset (Hz)*	2465.4834
Sweep Width (Hz)	8223.43	*Temperature (degree C)*	27.000		

User Notes HMBC from SiMe's & 5a(127ppm) to 4(148.5ppm).
ROE(NOE) between 5a and 7/11 supports regiochemistry depicted.

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.12 (1 H, d, *J*=8.5 Hz), 8.03 (1 H, s), 7.89 (1 H, d, *J*=8.8 Hz), 2.66 (2 H, s), 0.39 (6 H, s)

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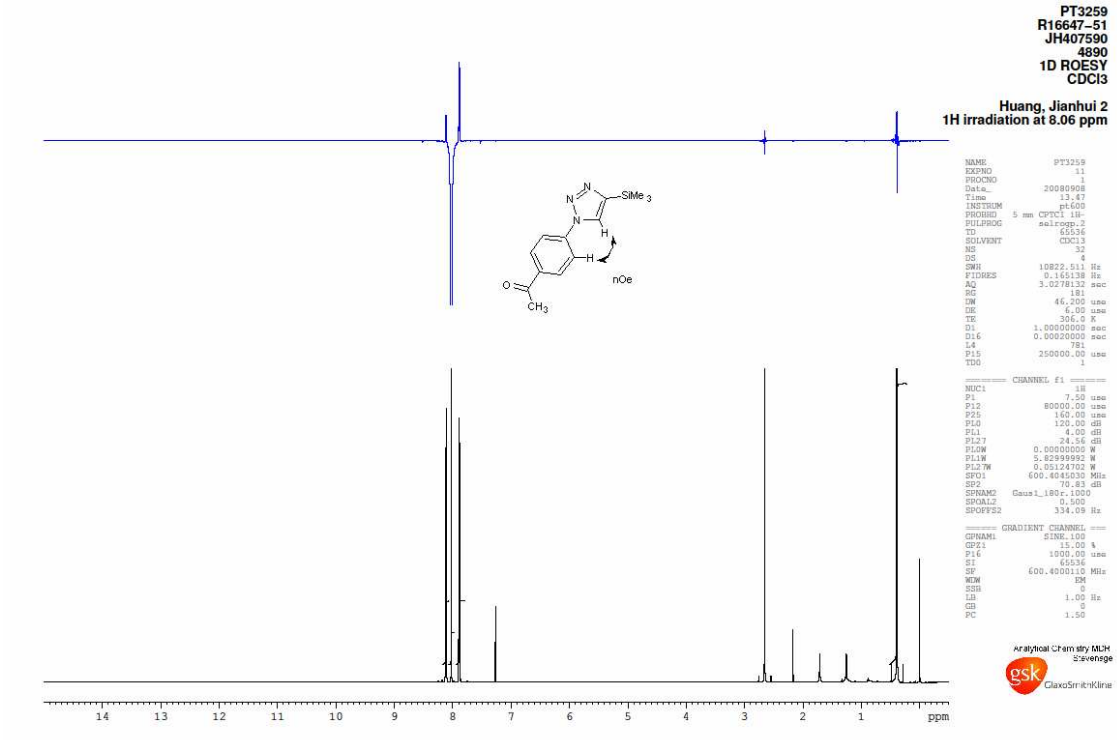
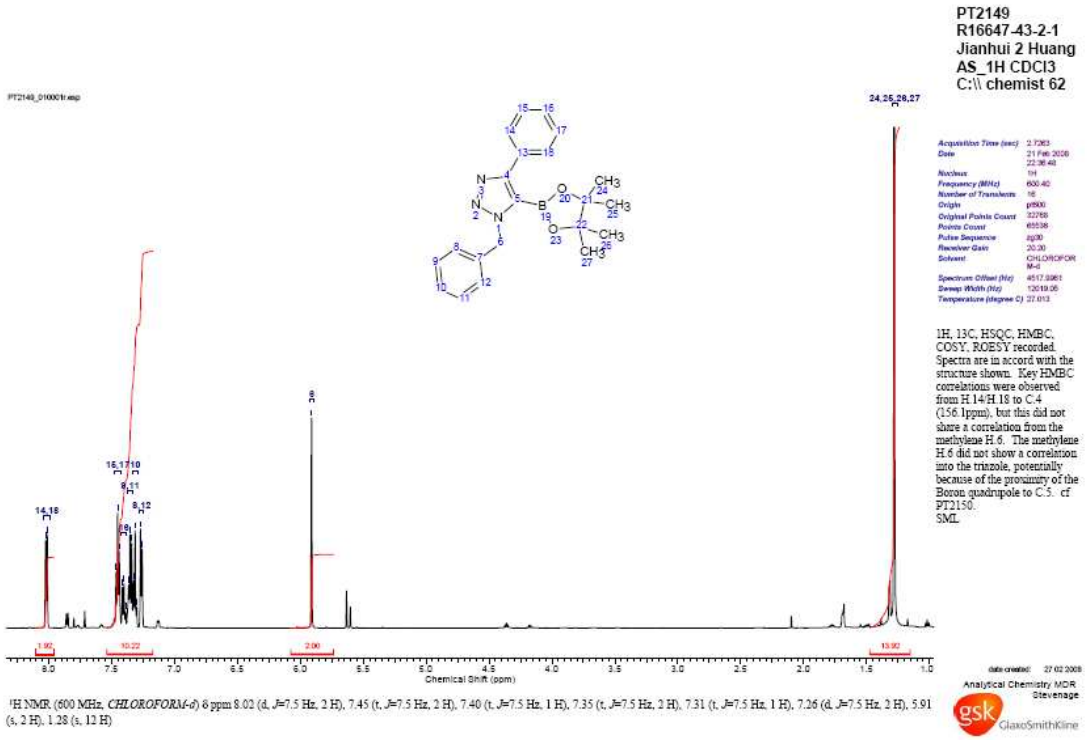
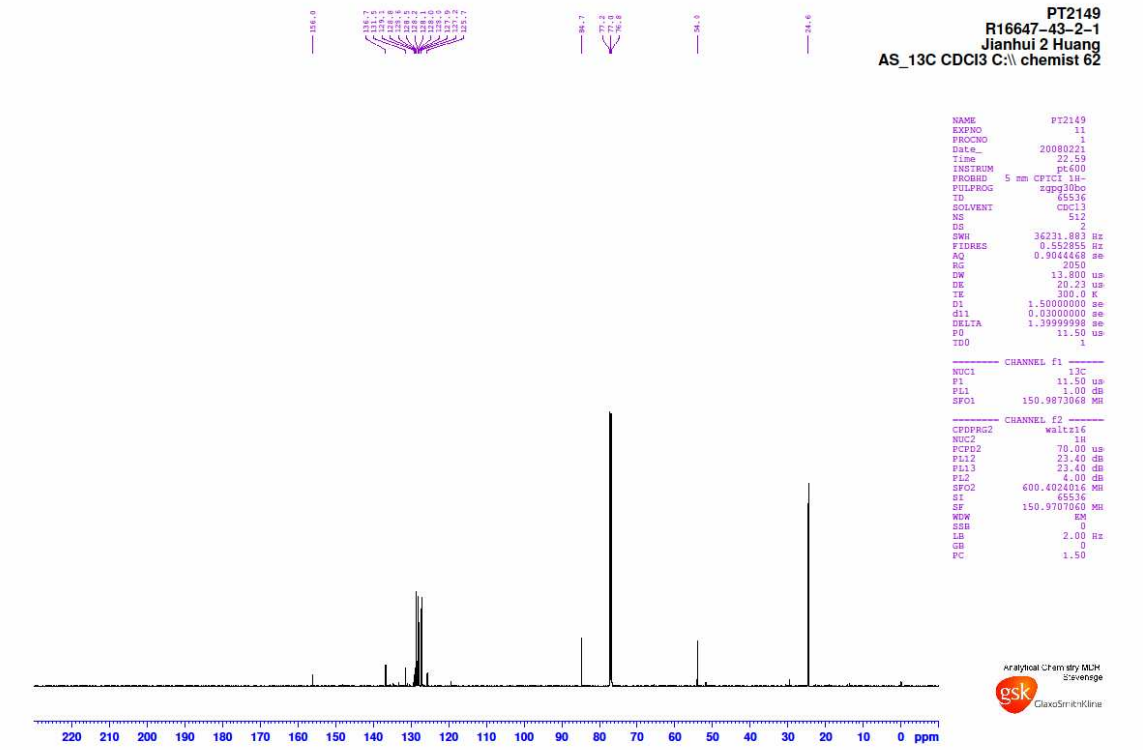
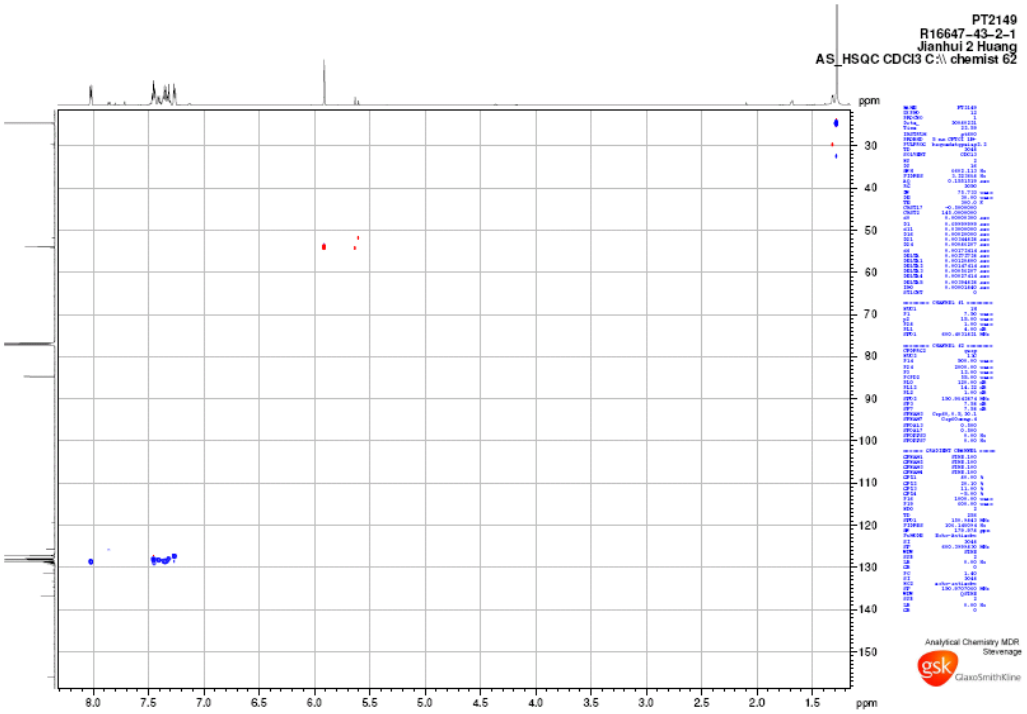
JH407590
4890
1H
CDCl3
Huang, Jianhui 2
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

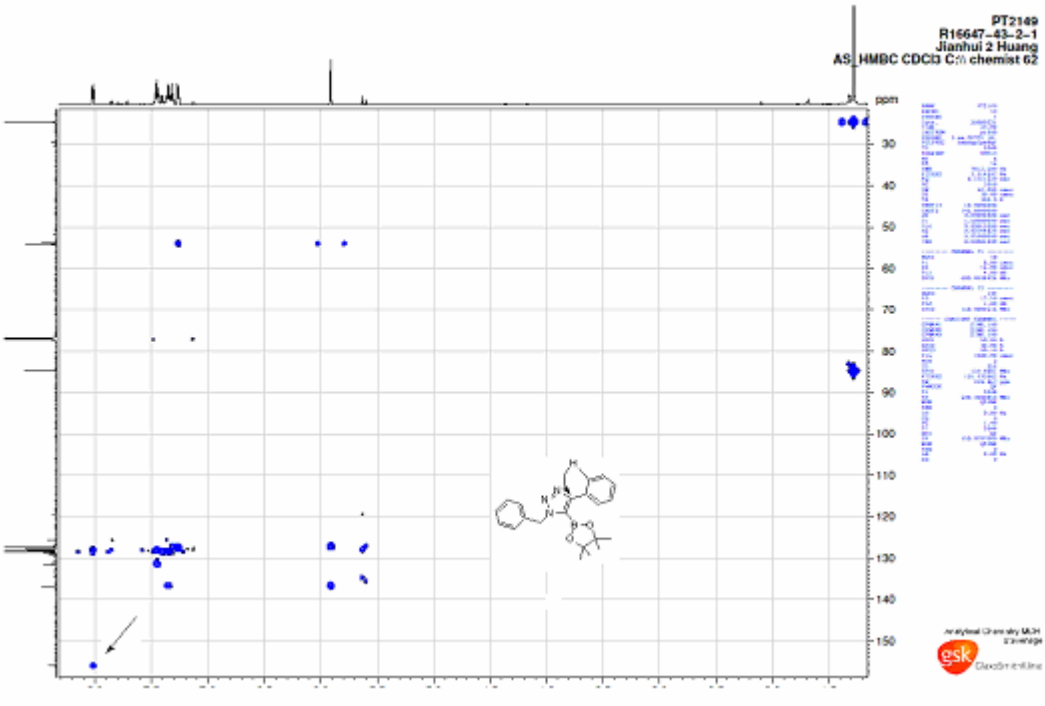

PT3259
R16647-51
JH407590
4890
1D ROESY
CDCl3
Huang, Jianhui 2
1H irradiation at 8.06 ppm
SiMe3
nOe
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline



^{1}H NMR (600 MHz, *CHLOROFORM-d*) δ ppm 8.02 (d, *J*=7.5 Hz, 2 H), 7.45 (t, *J*=7.5 Hz, 2 H), 7.40 (t, *J*=7.5 Hz, 1 H), 7.35 (t, *J*=7.5 Hz, 2 H), 7.31 (t, *J*=7.5 Hz, 1 H), 7.26 (d, *J*=7.5 Hz, 2 H), 5.91 (s, 2 H), 1.28 (s, 12 H)




PT2149
R16647-43-2-1
Jianhui 2 Huang
AS_HSQC CDCl3 C:\ chemist 62
ppm
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline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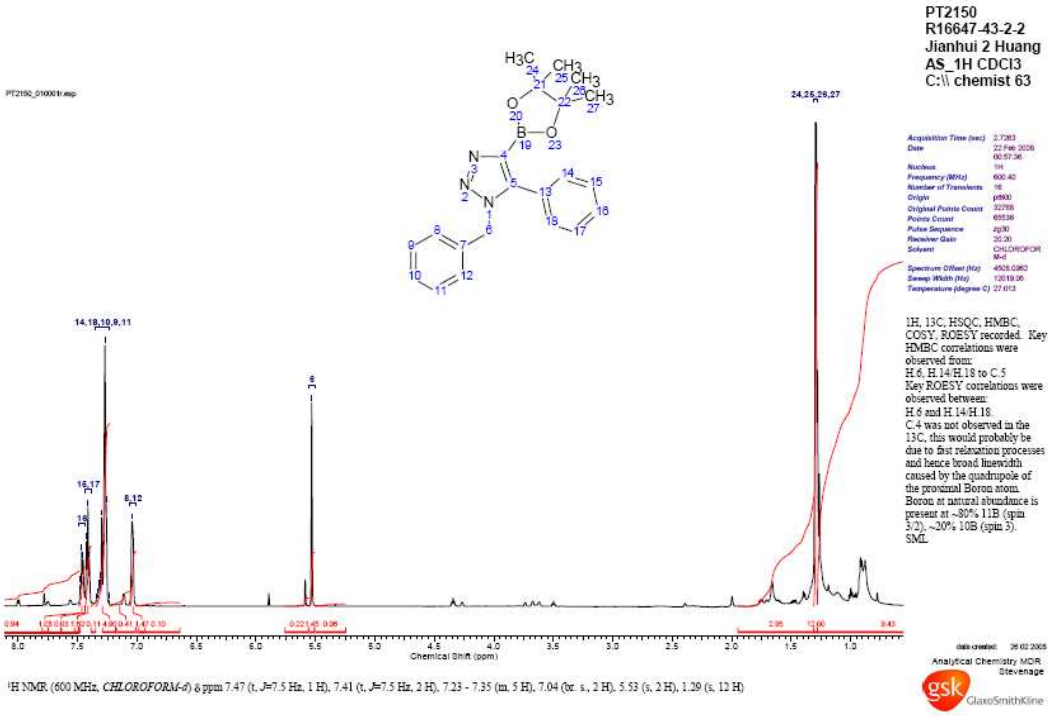
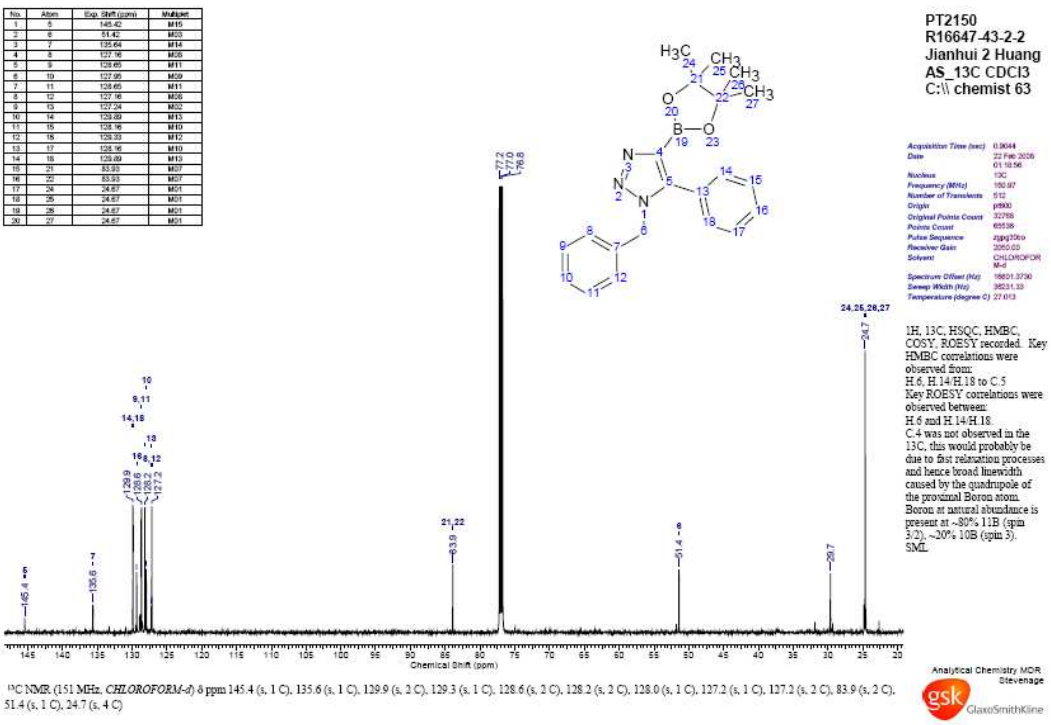
R16647-43-2-1
Jianhui 2 Huang
AS_HMBC CDCl3 C:\ chemist 62
ppm

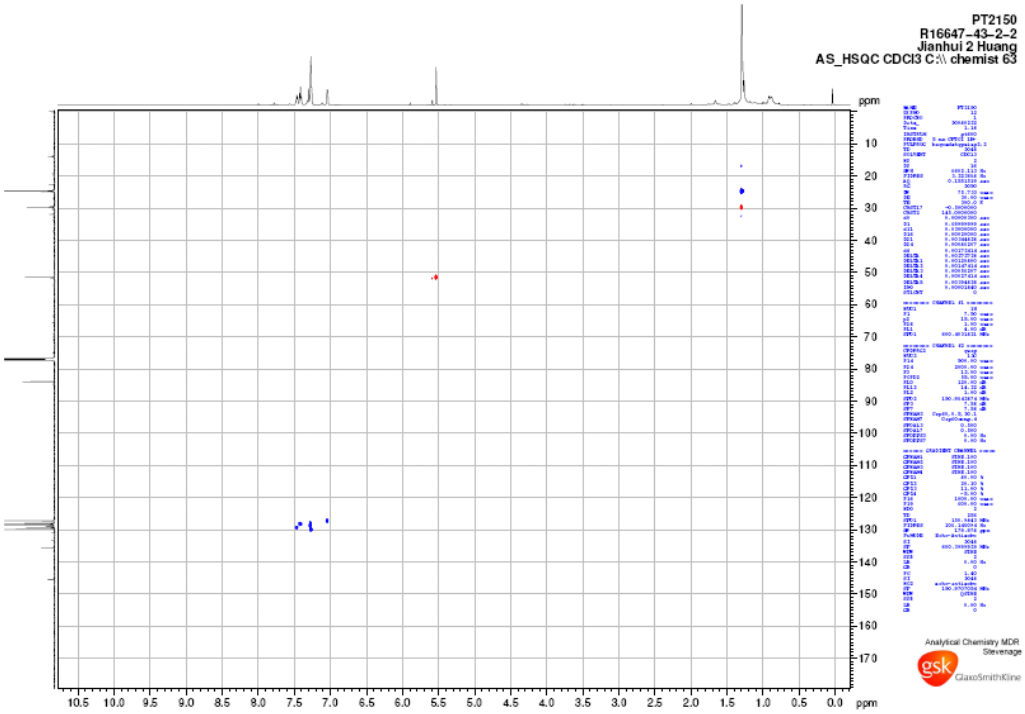


^{1}H NMR (600 MHz, *CHLOROFORM-d*) δ ppm 7.47 (t, *J*=7.5 Hz, 1 H), 7.41 (t, *J*=7.5 Hz, 2 H), 7.23 - 7.35 (m, 5 H), 7.04 (br. s., 2 H), 5.53 (s, 2 H), 1.29 (s, 12 H)

No.	Atom	Exp. Shift (ppm)	Multiplet
1	5	145.40	M15
2	6	51.42	M03
3	7	135.64	M14
4	8	127.16	M06
5	9	128.65	M11
6	10	127.95	M09
7	11	128.65	M11
8	12	127.16	M06
9	13	127.24	M02
10	14	129.89	M13
11	15	128.16	M10
12	16	128.33	M12
13	17	128.16	M10
14	18	129.89	M13
15	21	83.93	M07
16	22	83.93	M07
17	24	24.67	M01
18	25	24.67	M01
19	26	24.67	M01
20	27	24.67	M01



^{13}C NMR (151 MHz, *CHLOROFORM-d*) δ ppm 145.4 (s, 1 C), 135.6 (s, 1 C), 129.9 (s, 2 C), 129.3 (s, 1 C), 128.6 (s, 2 C), 128.2 (s, 2 C), 128.0 (s, 1 C), 127.2 (s, 1 C), 127.2 (s, 2 C), 83.9 (s, 2 C), 51.4 (s, 1 C), 24.7 (s, 4 C)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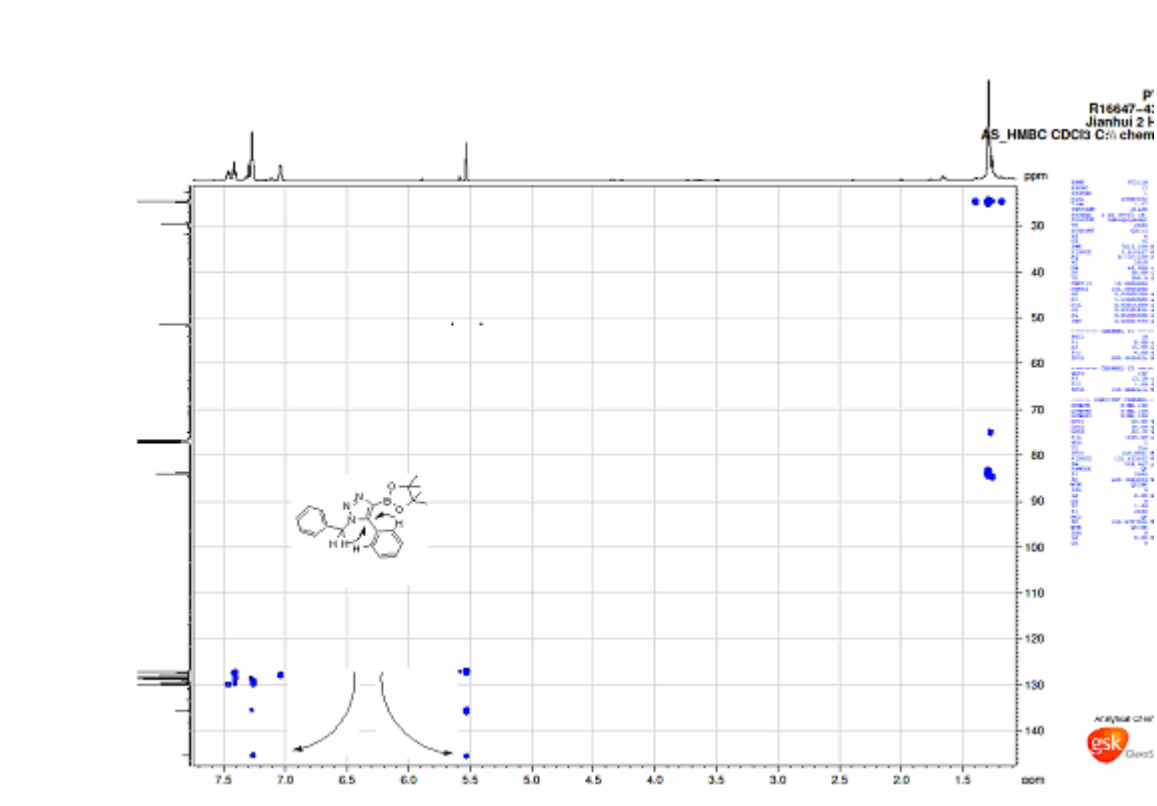
R16647-43-2-2
Jianhui 2 Huang
AS_HSQC CDCl3 C:\ chemist 63
ppm
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline


ppm