Supporting Information for

Acid-Catalyzed [2+2+2] Cycloaddition of Two Cyanamides and One Ynamide: Highly Regioselective Synthesis of 2,4,6-Triaminopyrimidines

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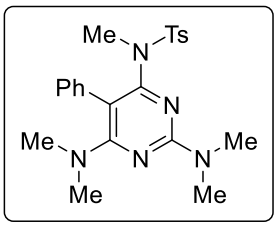
1 General Remarks

NMR spectra were recorded at ambient temperature with a Bruker Avance III 400 instrument at 400.13 MHz (^{1}H NMR) and 100.61 MHz (^{13}C NMR) in $CDCl_3$ or DMSO-d_6. Chemical shifts (δ) are given in ppm relative to resonances of the solvents (^{1}H: δ = 7.26 for residual $CHCl_3$ peak, δ = 2.50 for residual DMSO peak; ^{13}C: δ = 77.2 for $CDCl_3$, δ = 39.5 for DMSO-d_6). Mass-spectra were recorded on Bruker MicroTOF (ESI) and Bruker maXis HRMS-ESI-QTOF instruments. Chromatographic separation was carried out on Macherey–Nagel silica gel 60 M (0.04–0.063 mm). Analytical TLC was performed on unmodified Merck ready-to-use plates (TLC silica gel 60 F254); detection was achieved with a UV lamp. Melting points were measured with Stuart smp30 apparatus. Known ynamides **1** were prepared by the literature procedures.[1,2] Triflic acid was distilled from the mixture with triflic anhydride under dry argon atmosphere. The solvents were purified using standard techniques and stored over activated 4 Å molecular sieves before use. Other reagents were purchased from commercial vendors and were used as received. For known compounds **1a'**,**e**,**g**,**h**, **3a**, **6a**,**d**,**h**,**j**–**l**, the ^{1}H and ^{13}C NMR spectra are consistent with previously reported literature.

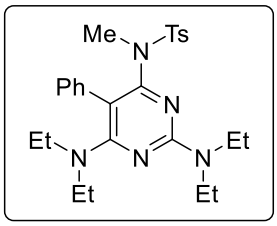
2 Experimental Procedures and Characterization Data

2.1. General Procedure for the TfOH-Catalyzed Synthesis of Pyrimidines 3,6

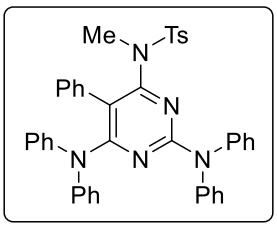
A flame-dried 10 mL round-bottom flask was charged with ynamide (**1**, 0.2 mmol) and cyanamide **2** (0.6 mmol, 3.0 equiv). The flask was fitted with a rubber septum, evacuated under high vacuum, and backfilled with argon. Dry and degassed solution of TfOH (3.0 mg, 0.02 mmol, 10 mol %) in DCE (1 mL) was next added and the reaction mixture was heated at 80 °C for 24 h with stirring. After completion, all volatile components were removed in vacuo and the residue was purified by silica gel chromatography eluting with hexane/EtOAc/Et_3N to afford pyrimidines **3**,**6**.



***N*-(2,6-Bis(dimethylamino)-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3a)**[3]: colorless solid (76.7 mg, 90%); R_f 0.38 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.3 Hz, 2H, Ar), 7.43–7.36 (m, 4H, Ar), 7.30–7.28 (m, 1H, Ar), 7.24 (d, J = 8.1 Hz, 2H, Ar), 2.99 (s, 6H, NMe_2), 2.72 (s, 6H, NMe_2), 2.64 (s, 3H, NMe), 2.44 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.1, 160.4, 160.3, 142.8, 136.9, 136.8, 131.0, 129.1, 128.9, 128.2, 126.7, 107.2, 40.6, 36.9, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{28}H_{32}N_5O_2S^+$: 426.1958; found: 426.1970.

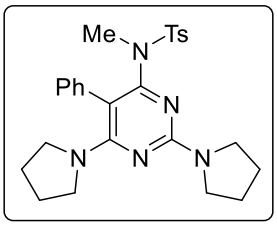


***N*-(2,6-Bis(diethylamino)-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3b)**: colorless solid (68.4 mg, 71%); mp 111.9–113.7 °C (hexane/EtOAc); R_f 0.38 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H, Ar), 7.43 (d, J = 7.0 Hz, 2H, Ar), 7.37 (t, J = 7.5 Hz, 2H, Ar), 7.30–7.28 (m, 1H, Ar), 7.23 (d, J = 8.0 Hz, 2H, Ar), 3.44 (br. s, 4H, $2CH_2$), 3.17 (q, J = 7.0 Hz, 4H, $2CH_2$), 2.61 (s, 3H, NMe), 2.41 (s, 3H, Me), 1.13–1.08 (m, 6H, $2CH_3$), 0.93 (t, J = 7.0 Hz, 6H, $2CH_3$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.2, 160.2, 159.4, 142.7, 137.2, 137.1, 131.0, 128.9, 128.8, 128.2, 126.8, 107.6, 43.9, 41.6, 36.9, 21.6, 13.7, 13.1; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{26}H_{36}N_5O_2S^+$: 482.2584; found: 482.2593.

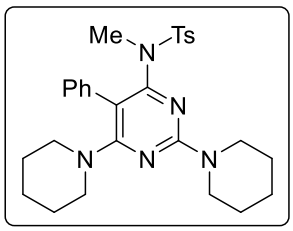


***N*-(2,6-Bis(diphenylamino)-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3c)**: colorless solid (115.8 mg, 86%); mp 191.0–192.4 °C (hexane/EtOAc); R_f 0.39 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.3 Hz, 2H, Ar), 7.17–7.13 (m, 10H, Ar), 7.10–6.91 (m, 13H, Ar), 6.85 (d, J = 7.4 Hz, 4H, Ar), 2.42 (s, 3H, NMe), 2.34 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0, 161.8,

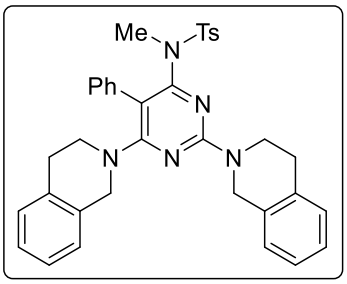
160.2, 145.9, 144.4, 142.9, 135.7, 134.0, 130.7, 129.2, 128.8, 128.7, 127.9, 127.4, 126.8, 126.0, 124.9, 124.2, 116.4, 36.5, 21.7; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd. for $C_{42}H_{36}N_5O_2S^+$: 674.2584; found: 674.2583.



***N*,4-Dimethyl-*N*-(5-phenyl-2,6-di(pyrrolidin-1-yl)pyrimidin-4-yl)-benzenesulfonamide (3d)**: colorless solid (66.9 mg, 70%); mp 156.0–158.0 °C (hexane/EtOAc); R_f 0.50 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.3 Hz, 2H, Ar), 7.42–7.40 (m, 2H, Ar), 7.35 (t, J = 7.2 Hz, 2H, Ar), 7.30–7.26 (m, 1H, Ar), 7.23 (d, J = 8.0 Hz, 2H, Ar), 3.42 (br. s, 4H, 2CH_2), 3.14–3.10 (m, 4H, 2CH_2), 2.61 (s, 3H, Me), 2.41 (s, 3H, Me), 1.93–1.87 (m, 4H, 2CH_2), 1.71–1.65 (m, 4H, 2CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9, 159.9, 159.0, 142.7, 137.0, 136.8, 131.9, 129.2, 128.8, 127.6, 126.8, 106.6, 49.5, 46.4, 36.9, 25.7, 25.6, 21.6; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd. for $C_{26}H_{32}N_5O_2S^+$: 478.2271; found: 478.2280.

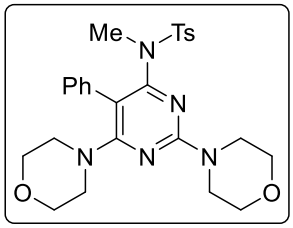


***N*,4-Dimethyl-*N*-(5-phenyl-2,6-di(piperidin-1-yl)pyrimidin-4-yl)benzenesulfonamide (3e)**: colorless solid (79.9 mg, 79%); mp 177.0–178.7 °C (hexane/EtOAc); R_f 0.32 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.62 (d, J = 7.9 Hz, 2H, Ar), 7.42–7.28 (m, 7H, Ar), 3.41 (m, 4H, 2CH_2), 3.09–3.07 (m, 4H, 2CH_2), 2.59 (s, 3H, NMe), 2.38 (s, 3H, Me), 1.59–1.54 (m, 2H, CH_2), 1.46–1.40 (m, 6H, 3CH_2), 1.31–1.25 (m, 4H, 2CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.1, 160.3, 159.7, 142.7, 136.9, 136.6, 130.3, 129.0, 128.8, 128.4, 126.7, 108.5, 48.7, 44.7, 37.0, 26.0, 25.6, 25.1, 24.7, 21.6; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd. for $C_{28}H_{36}N_5O_2S^+$: 506.2584; found: 506.2599.

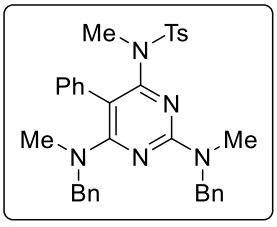


Benzyl-*N*-(2,6-bis(diethylamino)-5-phenylpyrimidin-4-yl)-4-methylbenzenesulfonamide (3f):colorless solid (1.14 g, 75%); mp 167.0–169.0 °C (hexane/EtOAc); R_f 0.50 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 2H, Ar), 7.51 (d, J = 6.9 Hz, 2H, Ar), 7.44 (t, J = 7.5 Hz, 2H, Ar), 7.35 (d, J = 7.2 Hz, 1H, Ar), 7.31 (d, J = 8.0 Hz, 2H, Ar), 7.24–7.17 (m, 3H, Ar), 7.15–7.05 (m, 4H, Ar), 6.99 (dd, J = 5.4, 3.5 Hz, 1H, Ar), 4.67 (br. s, 2H, CH_2), 4.44 (s, 2H, CH_2), 3.88 (br. s, 2H, CH_2), 3.46 (t, J = 5.7 Hz, 2H, CH_2), 2.89 (br. s, 2H, CH_2), 2.71 (s, 3H, Me), 2.65 (t, J = 5.9 Hz, 2H, CH_2), 2.49 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.6, 160.5, 159.5, 142.8, 137.0, 136.3, 135.3, 135.0, 134.61,

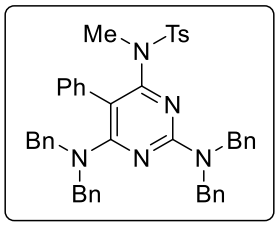
134.60, 130.5, 129.0, 129.0, 128.9, 128.7, 128.6, 127.1, 126.6, 126.5, 126.4, 126.3, 126.2, 126.0, 108.8, 49.7, 46.13, 46.07, 41.3, 37.2, 29.2, 28.4, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{36}H_{36}N_5O_2S^+$: 602.2584; found: 602.2579.



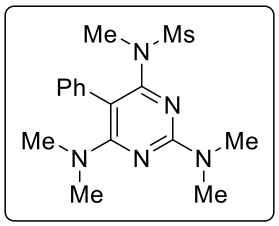
***N*-(2,6-Dimorpholino-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3g)**: colorless solid (81.6 mg, 80%); mp 164.3–166.0 °C (hexane/EtOAc); R_f 0.42 (hexane/EtOAc 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 2H, Ar), 7.46 (d, J = 7.0 Hz, 2H, Ar), 7.41 (t, J = 7.5 Hz, 2H, Ar), 7.30 (t, J = 7.2 Hz, 1H, Ar), 7.23 (d, J = 8.0 Hz, 2H, Ar), 3.67 (t, J = 4.7 Hz, 4H, $2CH_2$), 3.51–3.49 (m, 8H, $4CH_2$), 3.18 (t, J = 4.7 Hz, 4H, $2CH_2$), 2.68 (s, 3H, NMe), 2.41 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.8, 160.7, 159.7, 143.0, 136.8, 135.6, 130.3, 128.9, 128.9, 128.7, 127.3, 109.6, 67.0, 66.6, 48.0, 44.2, 37.2, 21.6; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{26}H_{32}N_5O_4S^+$: 510.2170; found: 510.2182.



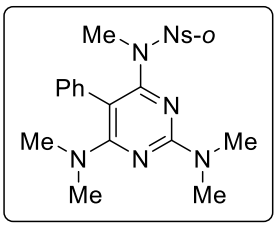
***N*-(2,6-Bis(benzyl(methyl)amino)-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3h)**: colorless oil (108.6 mg, 94%); R_f 0.50 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (br. s, 2H, Ar), 7.45 (d, J = 6.8 Hz, 2H, Ar), 7.37–7.16 (m, 15H, Ar), 4.58 (br. s, 4H, $2CH_2$), 2.93 (br. s, 3H, Me), 2.65 (s, 3H, Me), 2.54 (s, 3H, Me), 2.29 (br. s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.8, 160.9, 160.3, 142.8, 139.2, 138.6, 136.7, 136.6, 131.1, 128.9, 128.5, 128.4, 128.2, 127.6, 127.4, 127.0, 126.9, 107.7, 55.2, 52.2, 39.0, 37.1, 34.6, 21.6; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{34}H_{36}N_5O_2S^+$: 578.2584; found: 578.2594.



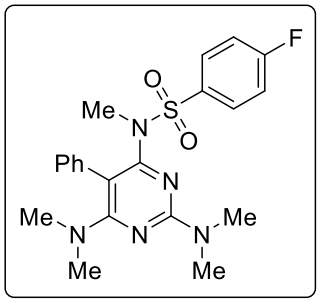
***N*-(2,6-Bis(dibenzylamino)-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3i)** was additionally recrystallized from hexane/EtOAc (4:1): colorless solid (110.9 mg, 76%); mp 129.0–130.0 °C (hexane/EtOAc); R_f 0.45 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.3 Hz, 2H, Ar), 7.45 (d, J = 6.9 Hz, 2H, Ar), 7.32–7.19 (m, 15H, Ar), 7.14–7.13 (m, 4H, Ar), 7.04–7.02 (m, 4H, Ar), 6.86 (d, J = 8.0 Hz, 2H, Ar), 4.68 (br. s, 2H, CH_2), 4.51 (br. s, 2H, CH_2), 4.37 (s, 4H, $2CH_2$), 2.68 (s, 3H, NMe), 2.22 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.2, 161.4, 160.4, 142.8, 138.8, 138.2, 136.6, 136.1, 130.9, 128.9, 128.7, 128.5, 128.4, 128.3, 127.8, 127.5, 127.2, 127.0, 126.9, 109.0, 52.4, 49.0, 37.2, 21.5; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{46}H_{44}N_5O_2S^+$: 730.3210; found: 730.3214.



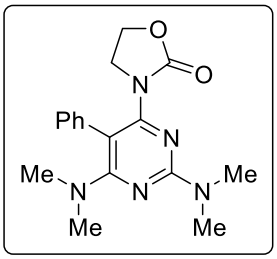
***N*-(2,6-Bis(dimethylamino)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (6a)**[3]: colorless solid (60.9 mg, 87%); R_f 0.30 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37–7.31 (m, 4H, Ph), 7.25–7.21 (m, 1H, Ph), 3.19 (s, 3H, SMe), 3.14 (s, 6H, NMe_2), 2.70 (s, 6H, NMe_2), 2.69 (s, 3H, NMe); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.0, 160.3 (×2), 136.5, 130.8, 128.2, 126.7, 106.3, 40.6, 38.4, 36.9 (×2); **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{16}H_{24}N_5O_2S^+$: 350.1645; found: 350.1649.



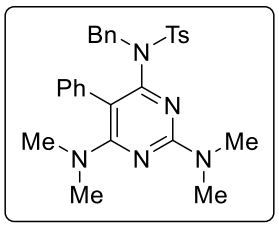
***N*-(2,6-Bis(dibenzylamino)-5-phenylpyrimidin-4-yl)-*N*-methyl-2-nitrobenzenesulfonamide (6b)**: yellow solid (76.7 mg, 84%); mp 133.5–134.5 °C (hexane/EtOAc); R_f 0.40 (hexane/EtOAc 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.55–8.53 (m, 1H, Ar), 7.64–7.59 (m, 2H, Ar), 7.58–7.55 (m, 1H, Ar), 7.42–7.35 (m, 4H, Ar), 7.29–7.27 (m, 1H, Ar), 2.99 (s, 6H, 2Me), 2.73 (s, 6H, 2Me), 2.72 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.1, 160.3, 159.1, 149.2, 136.3, 133.9, 132.9, 132.3, 131.0, 130.9, 128.4, 127.1, 123.6, 106.9, 40.7, 37.4, 36.8; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{21}H_{25}N_6O_4S^+$: 457.1653; found: 457.1659.



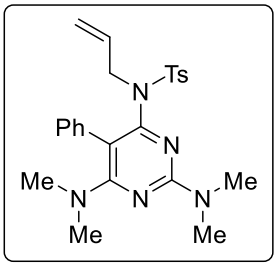
***N*-(2,6-Bis(dimethylamino)-5-phenylpyrimidin-4-yl)-4-fluoro-*N*-methylbenzenesulfonamide (6c)**: colorless solid (68.8 mg, 80%); mp 186.0–188.0 °C (hexane/EtOAc); R_f 0.52 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97–7.93 (m, 2H, Ar), 7.43–7.36 (m, 4H, Ar), 7.30–7.26 (m, 1H, Ar), 7.12 (t, J = 8.6 Hz, 2H, Ar), 2.99 (s, 6H, NMe_2), 2.73 (s, 6H, NMe_2), 2.65 (s, 3H, NMe); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.0, 164.9 (d, J_F = 253.3 Hz), 160.3, 160.0, 136.7, 135.8 (d, J_F = 3.1 Hz), 131.6 (d, J_F = 9.1 Hz), 130.9, 128.2, 126.7, 115.4 (d, J_F = 22.4 Hz), 107.1, 40.5, 37.0, 36.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{21}H_{25}FN_5O_2S^+$: 430.1708; found: 430.1707.



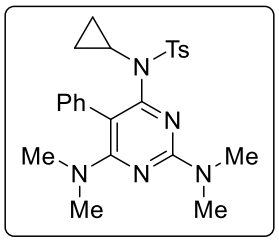
3-(2,6-Bis(dimethylamino)-5-phenylpyrimidin-4-yl)oxazolidin-2-one (6d)[3]: colorless solid (26.6 mg, 38%); R_f 0.42 (hexane/EtOAc 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35–7.30 (m, 4H, Ph), 7.27–7.23 (m, 1H, Ph), 4.17–4.13 (m, 2H, CH_2), 3.63–3.59 (m, 2H, CH_2), 3.15 (s, 6H, NMe_2), 2.72 (s, 6H, NMe_2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.6, 160.2, 157.1, 155.8, 136.8, 130.4, 128.3, 127.0, 106.3, 62.7, 46.3, 40.6, 37.1; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{17}H_{21}N_5NaO_2S^+$: 350.1593 found: 350.1593.



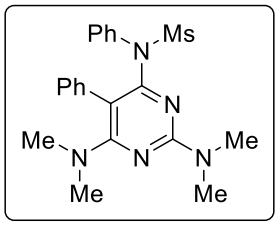
***N*-Benzyl-*N*-(2,6-bis(dimethylamino)-5-phenylpyrimidin-4-yl)-4-methylbenzenesulfonamide (6e)**: yellow solid (66.3 mg, 66%); mp 144.6–146.0 °C (hexane/EtOAc); R_f 0.50 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 2H, Ar), 7.23 (d, J = 8.1 Hz, 2H, Ar), 7.19–7.17 (m, 3H, Ar), 7.09 (t, J = 7.3 Hz, 2H, Ar), 7.00–6.96 (m, 3H, Ar), 6.72 (d, J = 6.8 Hz, 2H, Ar), 4.26 (s, 2H, C$\underline{H}_2$Ph), 3.03 (s, 6H, NMe_2), 2.63 (s, 6H, NMe_2), 2.42 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.3, 159.8, 157.9, 143.1, 136.7, 136.4, 135.0, 131.4, 129.5, 129.4, 128.9, 128.0, 127.7, 127.3, 126.2, 109.6, 53.9, 40.6, 36.8, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{28}H_{32}N_5O_2S^+$: 502.2271; found: 502.2241.



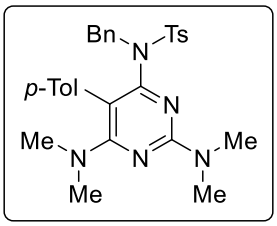
***N*-Allyl-*N*-(2,6-bis(dimethylamino)-5-phenylpyrimidin-4-yl)-4-methylbenzenesulfonamide (6f)**: colorless solid (57.9 mg, 64%); mp 112.4–113.8 °C (hexane/EtOAc); R_f 0.65 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.4 Hz, 2H, Ar), 7.44 (d, J = 7.3 Hz, 2H, Ar), 7.36 (t, J = 7.9 Hz, 2H, Ar), 7.28–7.26 (m, 1H, Ar), 7.23 (d, J = 7.7 Hz, 2H, Ar), 5.29–5.17 (m, 1H, CH), 4.81–4.78 (m, 1H, CH), 4.77–4.76 (m, 1H, CH), 3.64 (d, J = 6.7 Hz, 2H, CH_2), 3.00 (s, 6H, NMe_2), 2.72 (s, 6H, NMe_2), 2.41 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.4, 160.1, 158.4, 142.9, 137.2, 136.9, 132.8, 131.6, 129.3, 128.8, 128.0, 126.6, 118.1, 108.8, 52.9, 40.6, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{24}H_{30}N_5O_2S^+$: 452.2115; found: 452.2117.



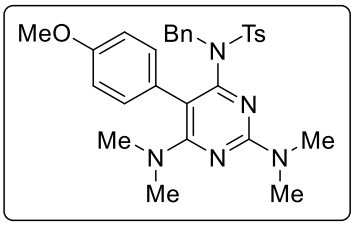
***N*-(2,6-Bis(dimethylamino)-5-phenylpyrimidin-4-yl)-*N*-cyclopropyl-4-methylbenzenesulfonamide (6g)**: colorless solid (80.4 mg, 89%); mp 206.0–208.0 °C (hexane/EtOAc); R_f 0.35 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 2H, Ar), 7.43 (br. s, 2H, Ar), 7.34 (t, J = 7.5 Hz, 2H, Ar), 7.26–7.22 (m, 3H, Ar), 3.03 (s, 6H, 2Me), 2.73 (s, 6H, 2Me), 2.42 (s, 3H, Me), 2.29–2.24 (m, 1H, CH), 0.68–0.61 (m, 1H, CH), 0.48–0.41 (m, 1H, CH), 0.20–0.13 (m, 1H, CH), 0.01–(-0.05) (m, 1H, CH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.4, 160.3, 160.1, 143.0, 137.1, 136.8, 131.3, 129.6, 128.7, 127.9, 126.5, 107.8, 40.6, 36.7, 31.1, 21.7, 7.7, 5.4; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{19}H_{28}N_5O_2S^+$: 390.1958; found: 390.1967.



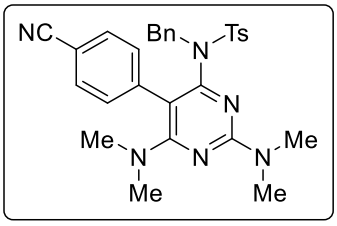
***N*-(2,6-Bis(dimethylamino)-5-phenylpyrimidin-4-yl)-*N*-phenylmethanesulfonamide (6h)**[3]: colorless solid (52.7 mg, 64%); R_f 0.35 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19–7.17 (m, 3H, Ph), 7.11–7.00 (m, 5H, Ph), 6.93–6.90 (m, 2H, Ph), 3.30 (s, 3H, MeS), 3.22 (s, 6H, NMe_2), 2.68 (s, 6H, NMe_2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.6, 159.8 (×2), 139.6, 136.3, 131.4, 128.4, 128.0, 127.7, 127.2, 126.6, 106.9, 40.7, 40.0, 37.3; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{21}H_{25}N_5O_2S^+$: 412.1802; found: 412.1807.



***N*-Benzyl-*N*-(2,6-bis(dimethylamino)-5-(*p*-tolyl)pyrimidin-4-yl)-4-methylbenzenesulfonamide (6i)**: yellow oil (83.6 mg, 81%); R_f 0.44 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 2H, Ar), 7.22 (d, J = 8.0 Hz, 2H, Ar), 7.09 (t, J = 7.4 Hz, 1H, Ar), 7.01–6.96 (m, 4H, Ar), 6.92–6.88 (m, 2H, Ar), 6.74 (d, J = 7.5 Hz, 2H, Ar), 4.24 (s, 2H, CH_2), 3.02 (s, 6H, NMe_2), 2.64 (s, 6H, NMe_2), 2.42 (s, 3H, Me), 2.36 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.5, 160.0, 158.2, 143.0, 136.9, 135.7, 135.2, 133.5, 131.2, 129.5, 129.4, 128.8, 128.5, 127.9, 127.2, 109.4, 53.9, 40.6, 36.7, 21.7, 21.4; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{26}H_{34}N_5O_2S^+$: 516.2428; found: 516.2427.

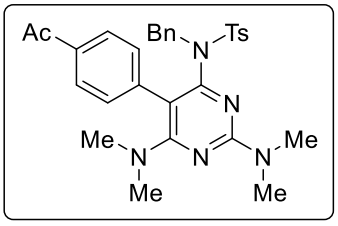


***N*-Benzyl-*N*-(2,6-bis(dimethylamino)-5-(4-methoxyphenyl)-pyrimidin-4-yl)-4-methylbenzenesulfonamide (6j)**[3]: colorless solid (73.4 mg, 69%); R_f 0.40 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.9 Hz, 2H, Ar), 7.23 (d, J = 7.9 Hz, 2H, Ar), 7.09 (t, J = 7.4 Hz, 1H, Ar), 6.99 (t, J = 7.5 Hz, 2H, Ar), 6.90–6.69 (m, 6H, Ar), 4.26 (s, 2H, CH_2), 3.84 (s, 3H, OMe), 3.02 (s, 6H, NMe_2), 2.64 (s, 6H, NMe_2), 2.43 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.6, 159.9, 158.2, 158.1, 143.0, 136.8, 135.2, 132.4, 129.5, 129.4, 128.8, 128.7, 127.9, 127.2, 113.1, 109.1, 55.3, 53.9, 40.5, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{29}H_{34}N_5O_3S^+$: 532.2377; found: 532.2389.

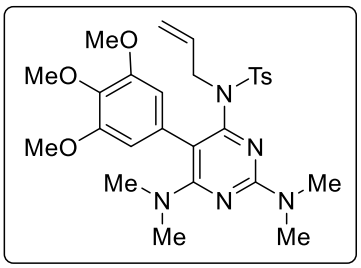


***N*-Benzyl-*N*-(5-(4-cyanophenyl)-2,6-bis(dimethylamino)-pyrimidin-4-yl)-4-methylbenzenesulfonamide (6k)**[3]: colorless solid (66.3 mg, 61%); R_f 0.54 (hexane/EtOAc 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 2H, Ar), 7.39 (d, J = 7.9 Hz, 2H, Ar), 7.28 (d, J = 13.0 Hz, 2H, Ar), 7.12–6.96 (m, 5H,

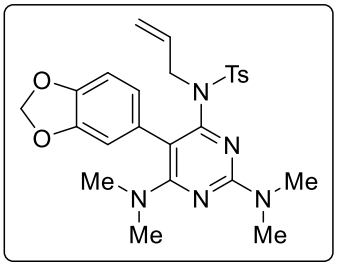
Ar), 6.70 (d, *J* = 7.5 Hz, 2H, Ar), 4.27 (s, 2H, CH_2), 3.01 (s, 6H, NMe_2), 2.60 (s, 6H, NMe_2), 2.44 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.1, 160.3, 158.1, 143.5, 142.2, 136.0, 134.6, 131.7, 131.3, 129.5, 129.3, 129.0, 128.1, 127.5, 119.5, 109.3, 107.9, 54.2, 40.6, 36.6, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{29}H_{31}N_6O_2S^+$: 527.2224; found: 527.2240.



***N*-(5-(4-Acetylphenyl)-2,6-bis(dimethylamino)pyrimidin-4-yl)-*N*-benzyl-4-methylbenzenesulfonamide (6l)**[3]: yellow solid (70.7 mg, 65%); R_f 0.45 (hexane/EtOAc 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 2H, Ar), 7.75 (d, *J* = 8.0 Hz, 2H, Ar), 7.26 (d, *J* = 8.2 Hz, 2H, Ar), 7.11–7.07 (m, 3H, Ar), 6.94 (t, *J* = 7.7 Hz, 2H, Ar), 6.70 (d, *J* = 7.7 Hz, 2H, Ar), 4.26 (s, 2H, CH_2), 3.02 (s, 6H, NMe_2), 2.63 (s, 3H, Me), 2.62 (s, 6H, NMe_2), 2.44 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 165.3, 160.2, 158.0, 143.3, 142.3, 136.3, 134.71, 134.68, 131.4, 129.53, 129.48, 128.9, 128.1, 127.7, 127.4, 108.5, 54.1, 40.6, 36.7, 26.8, 21.7; **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{30}H_{33}N_5NaO_3S^+$: 566.2202; found: 566.2218.

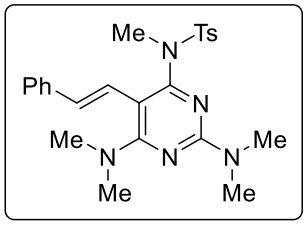


***N*-Allyl-*N*-(2,6-bis(dimethylamino)-5-(3,4,5-trimethoxyphenyl)pyrimidin-4-yl)-4-methylbenzenesulfonamide (6m)**: colorless solid (104.0 mg, 69%); mp 156.0–157.0 °C (hexane/EtOAc); R_f 0.30 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H, Ar), 7.26–7.24 (m, 2H, Ar), 6.76–6.74 (m, 2H, Ar), 5.29–5.17 (m, 1H, CH), 4.80–4.75 (m, 2H, 2CH), 3.91 (s, 3H, OMe), 3.87 (s, 6H, 2OMe), 3.65 (d, *J* = 6.6 Hz, 2H, CH_2), 3.00 (s, 6H, 2Me), 2.78 (s, 6H, 2Me), 2.42 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.1, 160.1, 158.3, 152.8, 143.0, 137.2, 136.9, 133.1, 132.1, 129.3, 128.9, 117.8, 109.9, 109.0, 108.5, 61.2, 56.5, 52.9, 40.5, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{27}H_{36}N_5O_5S^+$: 542.2432; found: 542.2425.

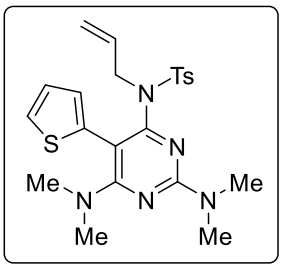


***N*-Allyl-*N*-(5-(benzo[*d*][1,3]dioxol-5-yl)-2,6-bis(dimethylamino)pyrimidin-4-yl)-4-methylbenzenesulfonamide (6n)**: colorless solid (74.3 mg, 75%); mp 177.0–179.0 °C (hexane/EtOAc); R_f 0.45 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 2H, Ar), 7.24 (d, *J* = 8.0 Hz, 2H, Ar), 6.96–6.94 (m, 1H, Ar), 6.91–6.88 (m, 1H, Ar), 6.83–6.81 (m, 1H, Ar), 5.99 (s, 2H, CH_2), 5.37–5.27 (m, 1H, CH), 4.84 (dd, *J* = 6.8, 1.5 Hz, 1H, CH), 4.80 (s, 1H, CH), 3.70 (d, *J* = 6.7 Hz, 2H, CH_2), 2.98 (s, 6H, 2Me), 2.75 (s, 6H, 2Me), 2.41 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.4, 160.0, 158.5, 147.3, 146.3, 143.0, 137.1, 132.8, 130.3,

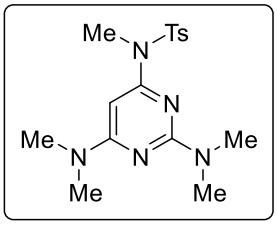
129.3, 128.8, 125.0, 118.3, 112.00, 108.4, 107.9, 101.0, 53.0, 40.6, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{25}H_{30}N_5O_4S^+$: 496.2013; found: 496.2008.



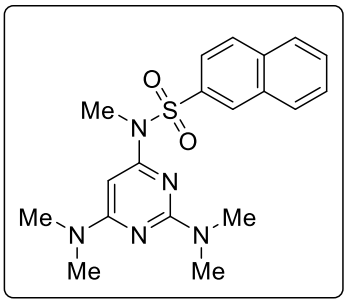
(*E*)-*N*-(2,6-Bis(dimethylamino)-5-styrylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (6o): colorless solid (82.3 mg, 91%); mp 124.0–125.9 °C (hexane/EtOAc); R_f 0.43 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2H, Ar), 7.50 (d, J = 6.7 Hz, 2H, Ar), 7.36–7.29 (m, 3H, Ar), 7.26 (d, J = 8.1 Hz, 2H, Ar), 7.21 (t, J = 7.4 Hz, 1H, Ar), 6.69 (d, J = 16.6 Hz, 1H, CH), 3.03 (s, 6H, NMe_2), 2.99 (s, 3H, Me), 2.97 (s, 6H, NMe_2), 2.42 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.2, 160.0, 159.4, 143.2, 138.7, 135.8, 129.3, 129.0, 128.9, 128.7, 127.0, 126.3, 123.2, 104.0, 41.1, 37.0, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{24}H_{30}N_5O_2S^+$: 452.2115; found: 452.2117.



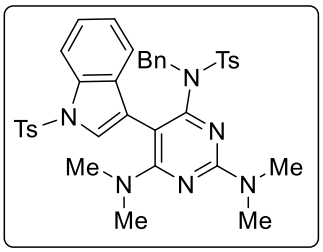
***N*-Allyl-*N*-(2,6-bis(dimethylamino)-5-(thiophen-2-yl)pyrimidin-4-yl)-4-methylbenzenesulfonamide (6p)**: colorless solid (66.8 mg, 73%); mp 146.0–148.0 °C (hexane/EtOAc); R_f 0.35 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 2H, Ar), 7.32 (dd, J = 5.2, 1.2 Hz, 1H, Ar), 7.24 (d, J = 8.1 Hz, 2H, Ar), 7.20 (dd, J = 3.5, 1.2 Hz, 1H, Ar), 7.04 (dd, J = 5.2, 3.5 Hz, 1H, Ar), 5.42–5.32 (m, 1H, CH), 4.85 (dd, J = 8.0, 1.5 Hz, 1H, CH), 4.85 (s, 1H, CH), 3.78 (d, J = 6.7 Hz, 2H, CH_2), 2.97 (s, 6H, 2Me), 2.81 (s, 6H, 2Me), 2.41 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7, 160.0, 159.1, 143.0, 137.8, 136.7, 132.7, 129.6, 129.2, 128.8, 126.7, 125.8, 118.4, 101.6, 52.9, 40.2, 36.6, 21.6; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{22}H_{28}N_5O_2S_2^+$: 458.1679; found: 458.1676.



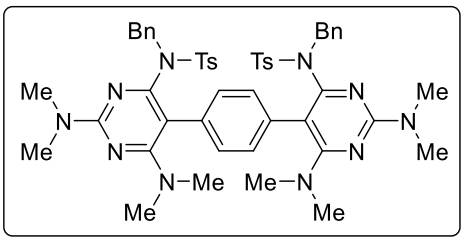
***N*-(2,6-Bis(dimethylamino)pyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (6q)**[3]: colorless solid (42.6 mg, 61%); R_f 0.40 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.3 Hz, 2H, Ar), 7.22 (d, J = 8.0 Hz, 2H, Ar), 6.04 (s, 1H, Ar), 3.35 (s, 3H, NMe), 3.04 (s, 6H, NMe_2), 3.01 (s, 6H, NMe_2), 2.38 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.0, 161.0, 159.8, 143.6, 136.1, 129.5, 127.5, 82.5, 37.3, 36.8, 34.6, 21.6; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{16}H_{24}N_5O_2S^+$: 350.1645; found: 350.1651.



***N*-(2,6-Bis(dimethylamino)pyrimidin-4-yl)-*N*-methyl-naphthalene-2-sulfonamide (6r)**: colorless oil (52.5 mg, 68%); R_f 0.46 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (s, 1H, Ar), 7.92 (d, J = 7.5 Hz, 1H, Ar), 7.87 (d, J = 8.4 Hz, 2H, Ar), 7.72 (dd, J = 8.7, 1.9 Hz, 1H, Ar), 7.61 (dd, J = 7.4, 5.8 Hz, 1H, Ar), 7.58 (dd, J = 7.3, 5.8 Hz, 1H, Ar), 6.06 (s, 1H, Ar), 3.41 (s, 3H, Me), 3.04 (s, 6H, NMe_2), 2.95 (s, 6H, NMe_2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.3, 161.3, 160.1, 136.3, 135.0, 132.1, 129.3, 129.1, 128.9, 128.8, 128.0, 127.5, 122.8, 82.6, 37.2, 36.7, 34.8; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{19}H_{24}N_5O_2S^+$: 386.1645; found: 386.1651.



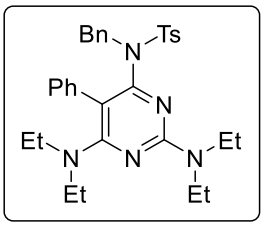
***N*-Benzyl-*N*-(2,6-bis(dimethylamino)-5-(1-tosyl-1*H*-indol-3-yl)pyrimidin-4-yl)-4-methylbenzenesulfonamide (6s)**: colorless solid (90.3 mg, 65%); mp 175.8–176.6 °C (hexane/EtOAc); R_f 0.26 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14–8.12 (m, 3H, Ar), 8.02 (d, J = 8.3 Hz, 1H, Ar), 7.82 (d, J = 7.9 Hz, 2H, Ar), 7.33–7.29 (m, 4H, Ar), 7.19 (t, J = 7.7 Hz, 1H, Ar), 6.84 (t, J = 7.5 Hz, 1H, Ar), 6.54 (t, J = 7.4 Hz, 1H, Ar), 6.31 (br. s, 1H, Ar), 6.14 (br. s, 2H, Ar), 6.03 (br. s, 2H, Ar), 4.22 (dd, J = 107.0, 12.6 Hz, 2H, CH_2), 2.97 (s, 6H, NMe_2), 2.61 (s, 6H, NMe_2), 2.46 (s, 3H, Me), 2.27 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.3, 160.1, 158.5, 144.8, 143.3, 135.9, 135.6, 134.2, 134.1, 131.6, 130.0, 129.3, 129.0, 128.6, 127.8, 127.2, 127.0, 126.7, 124.0, 122.9, 120.1, 118.3, 113.3, 99.9, 53.8, 39.5, 36.6, 21.7, 21.6; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{37}H_{39}N_6O_4S_2^+$: 695.2469; found: 695.2466.



***N*,*N*'-(1,4-phenylenebis(2,6-bis(dimethylamino)pyrimidi-ne-5,4-diyl))bis(N-benzyl-4-methylbenzenesulfonamide) (6t)**: colorless solid (105.5 mg, 57%); mp 284.0–286.0 °C (DCM); R_f 0.35 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 4H, Ar), 7.26–7.22 (m, 6H, Ar), 7.17 (d, J = 7.3 Hz, 2H, Ar), 7.11–6.86 (m, 10H, Ar), 4.27 (s, 4H, $2CH_2$), 3.04 (s, 12H, 4Me), 2.76 (s, 12H, 4Me), 2.42 (s, 6H, 2Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.2, 160.0, 158.1, 142.9, 137.0, 135.1, 134.7, 130.9, 130.0, 129.4, 128.8, 128.1, 127.7, 109.5, 53.9, 40.8, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{50}H_{57}N_{10}O_4S_2^+$: 925.4000; found: 952.4021.

2.2. Gram-Scale Synthesis of 7

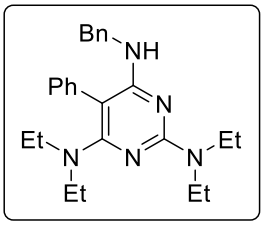
A flame-dried 50 mL round-bottom flask was charged with ynamide **1e** (1.08 g, 3.0 mmol) and *N*,*N'*-diethylcyanamide (**2b**, 0.88 g, 9.0 mmol, 3.0 equiv). The flask was fitted with a rubber septum, evacuated under high vacuum, and backfilled with argon. Dry and degassed solution of TfOH (45.0 mg, 0.3 mmol, 10 mol %) in DCE (10 mL) was next added and the reaction mixture was heated at 80 °C for 24 h with stirring. After completion, the resulting solution was cooled to room temperature, all volatile components were removed in vacuo and the residue was purified by silica gel chromatography eluting with hexane/EtOAc/Et_3N to afford pyrimidine **7**.



***N*-Benzyl-*N*-(2,6-bis(diethylamino)-5-phenylpyrimidin-4-yl)-4-methylbenzenesulfonamide (7)**:colorless solid (1.14 g, 68%); mp 67.5–69.0 °C (hexane/EtOAc); R_f 0.40 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2H, Ar), 7.24–7.20 (m, 5H, Ar), 7.13–6.99 (m, 5H, Ar), 6.74 (d, J = 7.2 Hz, 2H, Ar), 4.26 (s, 2H, Bn), 3.51 (q, J = 7.1 Hz, 4H, $2CH_2$), 3.11 (q, J = 7.0 Hz, 4H, $2CH_2$), 2.43 (s, 3H, Me), 1.16 (t, J = 7.0 Hz, 6H, 2Me), 0.87 (t, J = 7.0 Hz, 6H, 2Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.7, 158.9, 158.0, 142.9, 137.0, 136.8, 135.2, 131.4, 129.3, 129.1, 128.8, 127.9, 127.7, 127.1, 126.2, 109.7, 53.6, 43.9, 41.4, 21.6, 13.8, 12.9; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{32}H_{40}N_5O_2S^+$: 558.2897; found: 558.2900.

2.3. Detosylation of 7

Sodium (2.8 mg, 0.12 mmol, 1.2 equiv) was added to the solution of naphthalene (25.6 mg, 0.20 mmol, 2.0 equiv) in dry THF (3.0 mL). The mixture was stirred at room temperature until deep green color was appeared. Then pyrimidine **7** (55.8 mg, 0.1 mmol) was added and the reaction was heated at 60 °C with stirring for 12 h. When the reaction was quenched by adding 10 ml of water and extracted with DCM (3 × 10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. After filtration, the solvent was removed in vacuo and the residue was purified by silica gel chromatography, eluting with hexane/EtOAc (8/1) to afford pyrimidine **8**.

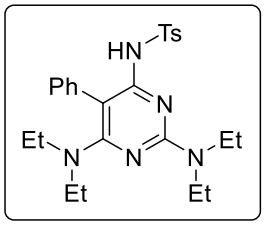


***N*^{4}-Benzyl-*N*^{2},*N*^{2},*N*^{6},*N*^{6}-tetraethyl-5-phenylpyrimidine-2,4,6-triamine (8)**: brownish oil (24.6 mg, 61%); R_f 0.50 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (t, J = 7.5 Hz, 2H, Ph), 7.31–7.29 (m, 2H, Ph), 7.26–7.21 (m, 5H, Ph), 7.20–7.16 (m, 1H, Ph), 4.54 (s, 3H, CH_2+NH), 3.56 (q, J = 7.0 Hz, 4H, $2CH_2$), 3.09 (q, J = 7.0 Hz,

4H, $2CH_2$), 1.13 (t, J = 7.0 Hz, 6H, 2Me), 0.88 (t, J = 6.9 Hz, 6H, 2Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.1, 161.9, 159.1, 141.4, 138.5, 131.8, 129.3, 128.4, 127.2, 126.7, 126.6, 91.7, 45.1, 43.7, 41.6, 13.9, 13.4; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{25}H_{34}N_5^+$: 404.2809; found: 404.2799.

2.4. Debenzylation of 7

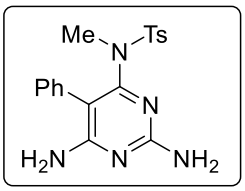
A 50 mL round-bottom flask containing **7** (55.8 mg, 0.1 mmol) and 10% palladium on carbon (10.6 mg, 0.01 mmol, 10 mol %) was fitted with a rubber septum, evacuated under high vacuum and backfilled with hydrogen. Degassed MeOH (5 mL) was next added. The flask was equipped with a hydrogen balloon and the black suspension was heated at 50 °C for 24 h with stirring. After completion, all volatile components were removed in vacuo and the residue was purified by silica gel chromatography eluting with hexane/EtOAc (4/1) to afford pyrimidine **9**.



***N*-(2,6-Bis(diethylamino)-5-phenylpyrimidin-4-yl)-4-methylbenzenesulfonamide (9)**: colorless solid (68.3 mg, 73%); mp 129.0–130.5 °C (hexane/EtOAc); R_f 0.40 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (br. s, 2H, Ar), 7.42–7.20 (m, 7H, Ar), 6.69 (br. s, 1H, NH), 3.42 (br. s, 4H, $2CH_2$), 3.09 (q, J = 7.1 Hz, 4H, $2CH_2$), 2.38 (s, 3H, Me), 1.11 (br. s, 6H, 2Me), 0.87 (t, J = 6.9 Hz, 6H, 2Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9, 155.1, 142.6, 136.1, 131.3, 129.2, 128.6, 127.6, 127.1, 126.6, 124.2, 94.3, 43.8, 41.8, 21.6, 13.5, 13.3; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{25}H_{34}N_5O_2S^+$: 468.2433; found: 468.2428.

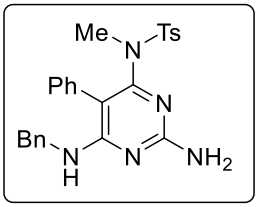
2.5. Debenzylation of 3i

A 50 mL round-bottom flask containing **3i** (73.0 mg, 0.1 mmol) and 10% palladium on carbon (10.6 mg, 0.01 mmol, 10 mol %) was fitted with a rubber septum, evacuated under high vacuum and backfilled with hydrogen. Degassed MeOH (5 mL) was next added. The flask was equipped with a hydrogen balloon and the black suspension was heated at 50 °C for 24 h with stirring. After completion, all volatile components were removed in vacuo and the residue was purified by silica gel chromatography eluting with DCM/MeOH to afford pyrimidines **10** and **10'**.



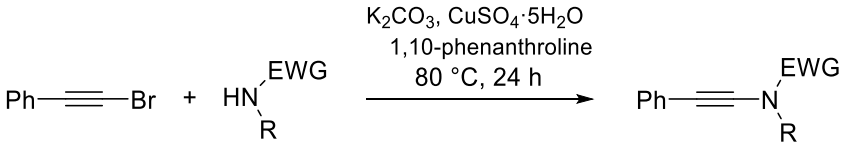
***N*-(2,6-Diamino-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (10)**: colorless oil (43.6 mg, 59%, 88% purity from NMR assay); R_f 0.25 (DCM/MeOH 100:3); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H, Ar), 7.49–7.45 (m, 2H, Ar), 7.42–7.36 (m, 3H, Ar), 7.23 (d, J = 8.1 Hz, 2H, Ar), 4.79 (s, 2H, NH_2), 4.70 (s, 2H, NH_2),

2.74 (s, 3H, NMe), 2.41 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.2, 161.7, 159.4, 143.4, 136.3, 133.3, 130.6, 130.6, 129.3, 129.2, 128.9, 128.1, 107.5, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{18}H_{20}N_5O_2S^+$: 370.1332; found: 370.1324.

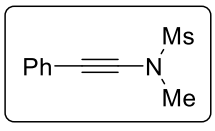


***N*-(2-Amino-6-(benzylamino)-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (10')**: colorless oil (25.7 mg, 28%, 92% purity from NMR assay); R_f 0.30 (DCM/MeOH 100:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H, Ar), 7.48–7.43 (m, 2H, Ar), 7.41–7.35 (m, 3H, Ar), 7.32–7.29 (m, 2H, Ar), 7.26–7.22 (m, 5H, Ar), 5.03 (t, J = 5.9 Hz, 1H, NH), 4.71 (s, 2H, NH_2), 4.59 (d, J = 5.8 Hz, 2H, CH_2), 2.75 (s, 3H, NMe), 2.41 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.2, 161.9, 158.3, 143.3, 139.1, 136.3, 133.2, 130.9, 129.4, 129.1, 128.9, 128.7, 128.1, 127.42, 127.35, 108.3, 45.0, 36.7, 21.7; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{25}H_{26}N_5O_2S^+$: 460.1802; found: 460.1791.

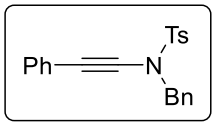
2.6. General Procedure for the Synthesis of Starting Ynamides from (Bromoethynyl)benzene



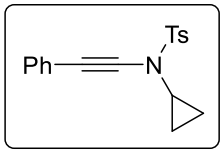
A 50 mL round-bottom flask was charged with amide (1.0 mmol), K_2CO_3 (415 mg, 3.0 mmol, 3.0 equiv), 1,10-phenanthroline monohydrate (59.5 mg, 0.3 mmol, 30 mol %) and $CuSO_4 \cdot 5H_2O$ (49.9 mg, 0.2 mmol, 20 mol %). The flask was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon. Dry and degassed toluene (10 mL) and (bromoethynyl)benzene (199 mg, 1.1 mmol, 1.1 equiv) were next added and the suspension was heated at 80 °C for 12 h with stirring. After completion, all volatile components were removed in vacuo and the residue was purified by silica gel chromatography eluting with hexane/EtOAc to afford ynamides **1**.



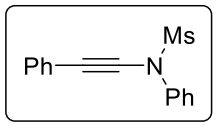
***N*-Methyl-*N*-(phenylethynyl)methanesulfonamide (1a')**:[4] orange solid (159 mg, 76%); mp 55.0–56.2 °C (hexane/EtOAc); R_f 0.21 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43–7.39 (m, 2H, Ar), 7.33–7.28 (m, 3H, Ar), 3.30 (s, 3H, Me), 3.12 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 131.7, 128.5, 128.2, 122.5, 83.2, 69.6, 39.3, 36.9; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{10}H_{11}NNaO_2S^+$: 232.0403; found: 232.0400.



***N*-Benzyl-4-methyl-*N*-(phenylethynyl)benzenesulfonamide (1e)**:[5] yellow solid (213 mg, 59%); mp 76.5–78.8 °C (hexane/EtOAc); R_f 0.41 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, J = 6.5 Hz, 2H, Ar), 7.38–7.32 (m, 7H, Ar), 7.29–7.26 (m, 5H, Ar), 4.61 (s, 2H, CH_2), 2.46 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.8, 134.8, 134.6, 131.3, 129.9, 129.0, 128.7, 128.5, 128.3, 127.9, 127.8, 123.0, 82.8, 71.5, 55.8, 21.8; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{22}H_{20}NO_2S^+$: 384.1029; found: 384.1027.

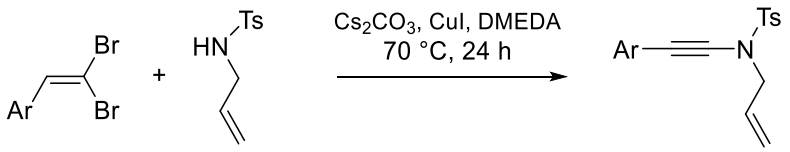


***N*-Cyclopropyl-4-methyl-*N*-(phenylethynyl)benzenesulfonamide (1g)**:[6] yellow solid (261 mg, 84%); mp 67.0–68.0 °C (hexane/EtOAc); R_f 0.45 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 2H, Ar), 7.38–7.35 (m, 4H, Ar), 7.32–7.28 (m, 3H, Ar), 2.84 (tt, J = 7.0, 3.5 Hz, 1H, CH), 2.46 (s, 3H, Me), 0.94–0.90 (m, 2H, CH_2), 0.82–0.77 (m, 2H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.9, 134.1, 131.5, 129.8, 128.4, 128.2, 127.9, 123.0, 82.0, 70.7, 33.1, 21.8, 6.6; **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{18}H_{17}NNaO_2S^+$: 334.0872; found: 334.0876.



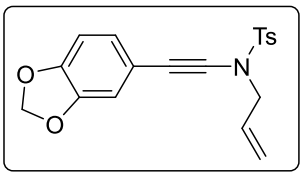
***N*-Phenyl-*N*-(phenylethynyl)methanesulfonamide (1h)**:[7] orange solid (52.0 mg, 19%); mp 76.1–77.0 °C (hexane/EtOAc); R_f 0.33 (hexane/EtOAc 4:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.2 Hz, 2H, Ar), 7.47–7.43 (m, 4H, Ar), 7.40–7.35 (m, 1H, Ar), 7.34–7.30 (m, 3H, Ar), 3.16 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.8, 131.7, 129.6, 128.5, 128.5, 128.4, 125.7, 122.4, 82.1, 71.1, 37.0; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd. for $C_{15}H_{13}NNaO_2S^+$: 294.0559; found: 294.0556.

2.7. General Procedure for the Synthesis of Starting Ynamides from 1,1-Dibromo-1-alkenes

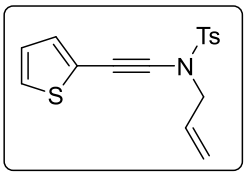


A 50 mL round-bottom flask was charged with *N*-allyl-4-methylbenzenesulfonamide (211 mg, 1.0 mmol), 1,1-dibromo-1-alkene (1.2 mmol, 1.2 equiv.), Cs_2CO_3 (1.30 g, 4.0 mmol, 4.0 equiv), and copper(I) iodide (24 mg, 0.125 mmol, 12.5 mol %). The flask was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon. Dry and degassed DMF (5 mL) and *N*,*N*'-dimethylethylenediamine (22 mg, 0.25 mmol, 25 mol %) were next added and the blue or green suspension was heated at 70 °C for 24 h with stirring. After completion, all volatile components

were removed in vacuo and the residue was purified by silica gel chromatography eluting with hexane/EtOAc to afford enynamides **1**.



***N*-Allyl-*N*-(benzo[*d*][1,3]dioxol-5-ylethynyl)-4-methylbenzenesulfonamide (1n)**: colorless oil (249 mg, 70%); R_f 0.35 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.4 Hz, 2H, Ar), 7.34 (d, J = 8.1 Hz, 2H, Ar), 6.87 (dd, J = 8.0, 1.6 Hz, 1H, Ar), 6.79 (d, J = 1.6, Hz, 1H, Ar), 6.71 (d, J = 8.0 Hz, 1H, Ar), 5.93 (m, 2H, CH_2), 5.82–5.72 (m, 1H, CH), 5.27 (dd, J = 17.0, 1.4 Hz, 1H, CH), 5.22 (dd, J = 10.2, 1.3 Hz, 1H, CH), 4.02 (d, J = 6.4 Hz, 2H, CH_2), 2.44 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.8, 147.4, 144.8, 134.7, 131.0, 129.8, 127.8, 126.4, 120.0, 115.9, 111.9, 108.4, 101.3, 80.7, 70.7, 54.5, 21.7.; **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{19}H_{17}NNaO_4S^+$: 378.0770; found: 378.0774.



***N*-Allyl-4-methyl-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1p)**: brown oil (200 mg, 63%); R_f 0.35 (hexane/EtOAc 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.3 Hz, 2H, Ar), 7.36 (d, J = 8.1 Hz, 2H, Ar), 7.25 (dd, J = 5.2, 1.2 Hz, 1H, Ar), 7.15 (dd, J = 3.6, 1.2 Hz, 1H, Ar), 6.95 (dd, J = 5.2, 3.6 Hz, 1H, Ar), 5.82–5.73 (m, 1H, CH), 5.30–5.25 (m, 1H, CH), 5.24–5.21 (m, 1H, CH), 4.05 (dt, J = 6.3, 1.3 Hz, 2H, CH_2), 2.46 (s, 3H, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.9, 134.7, 133.0, 130.8, 129.9, 127.9, 127.8, 127.0, 122.9, 120.2, 85.9, 64.3, 54.5, 21.7; **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{16}H_{15}NNaO_2S_2^+$: 340.0436; found: 340.0440.

3 References

1 A. Coste, G. Karthikeyan, F. Couty and G. Evano, Copper-Mediated Coupling of 1,1-Dibromo-1-alkenes with Nitrogen Nucleophiles: A General Method for the Synthesis of Ynamides, *Angew. Chemie*, 2009, **121**, 4445–4449.

2 D. P. Zimin, D. V. Dar'in, V. Yu. Kukushkin and A. Yu. Dubovtsev, Oxygen Atom Transfer as Key To Reverse Regioselectivity in the Gold(I)-Catalyzed Generation of Aminooxazoles from Ynamides, *J. Org. Chem.*, 2021, **86**, 1748–1757.

3 A. Y. Dubovtsev, N. V Shcherbakov, D. V Dar'in and V. Y. Kukushkin, The Dichotomy of Gold-catalyzed Interplay between Cyanamides and Ynamides: Controllable Switch from [2+2+2] to [4+2] Cycloaddition, *Adv. Synth. Catal.*, 2020, **362**, 2672–2682.

4 A. Mukherjee, R. B. Dateer, R. Chaudhuri, S. Bhunia, S. N. Karad and R. S. Liu, Gold-catalyzed 1,2-difunctionalizations of aminoalkynes using only N- and O-containing oxidants, *J. Am. Chem. Soc.*, 2011, **133**, 15372–15375.

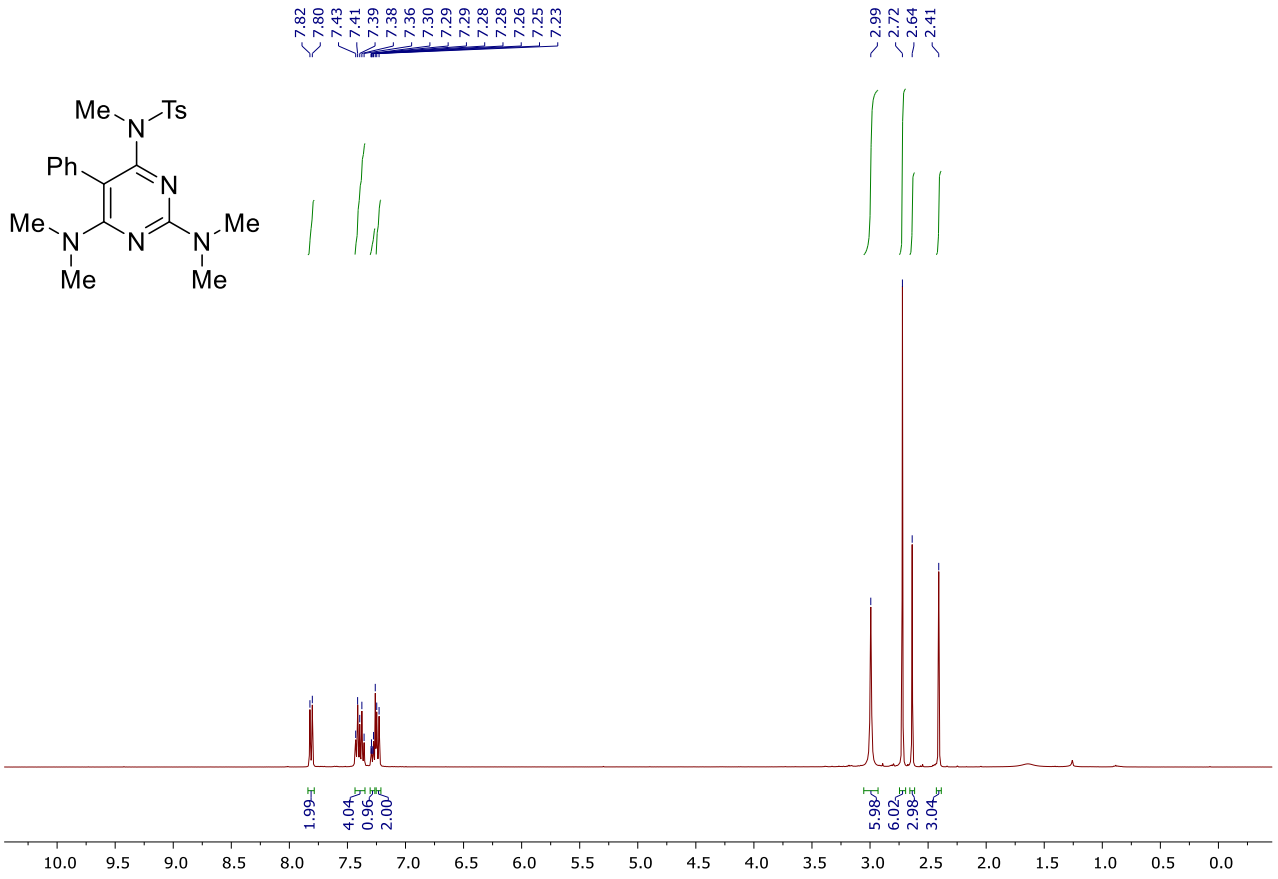
5 C. F. Xu, M. Xu, Y. X. Jia and C. Y. Li, Gold-catalyzed synthesis of benzil derivatives and α-keto imides via oxidation of alkynes, *Org. Lett.*, 2011, **13**, 1556–1559.

6 K. Jouvin, A. Coste, A. Bayle, F. Legrand, G. Karthikeyan, K. Tadiparthi and G. Evano, Copper-Mediated Selective Cross-Coupling of 1,1-Dibromo-1-alkenes and Heteronucleophiles: Development of General Routes to Heterosubstituted Alkynes and Alkenes, *Organometallics*, 2012, **31**, 7933–7947.

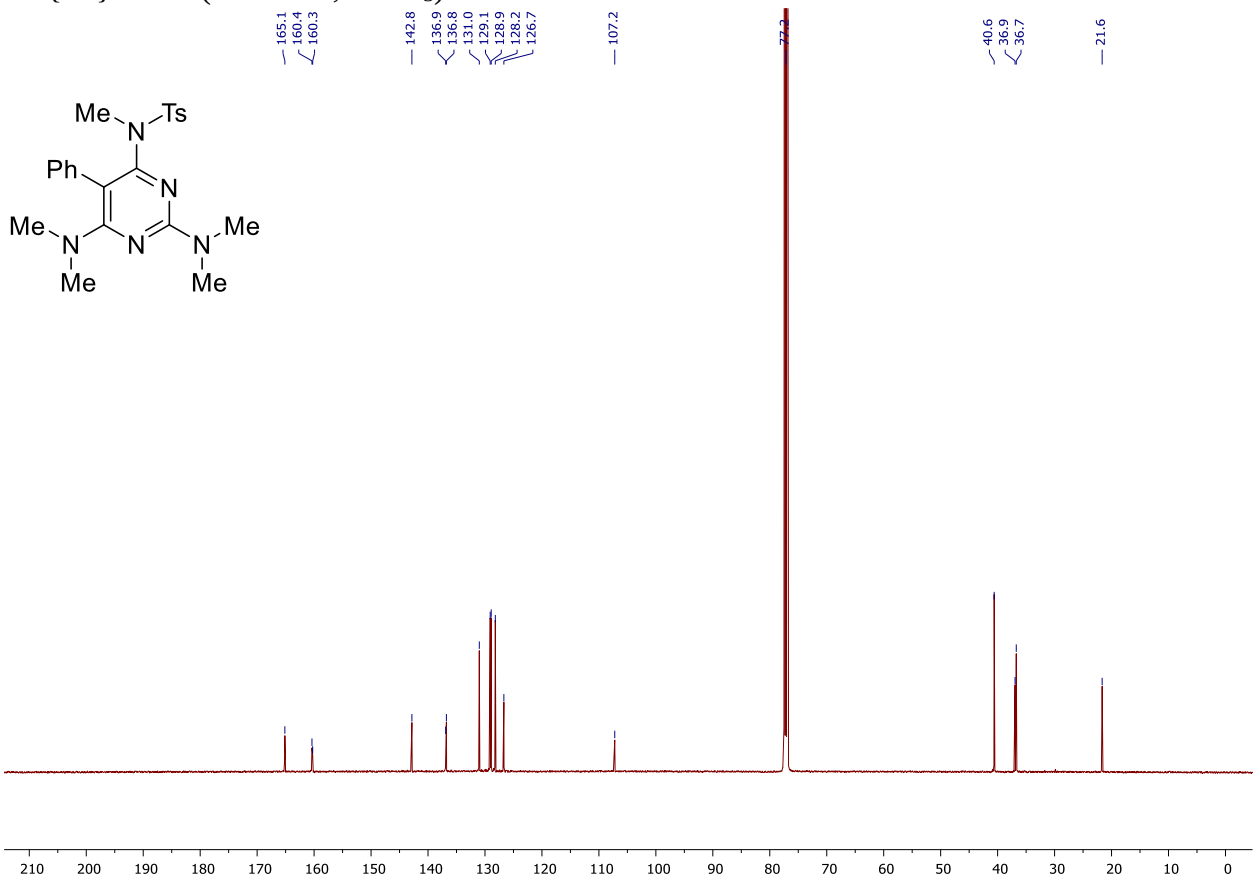
7 L. Zhu, Y. Yu, Z. Mao and X. Huang, Gold-Catalyzed Intermolecular Nitrene Transfer from 2H-Azirines to Ynamides: A Direct Approach to Polysubstituted Pyrroles, *Org. Lett.*, 2014, **17**, 30–33.

4 NMR Spectra

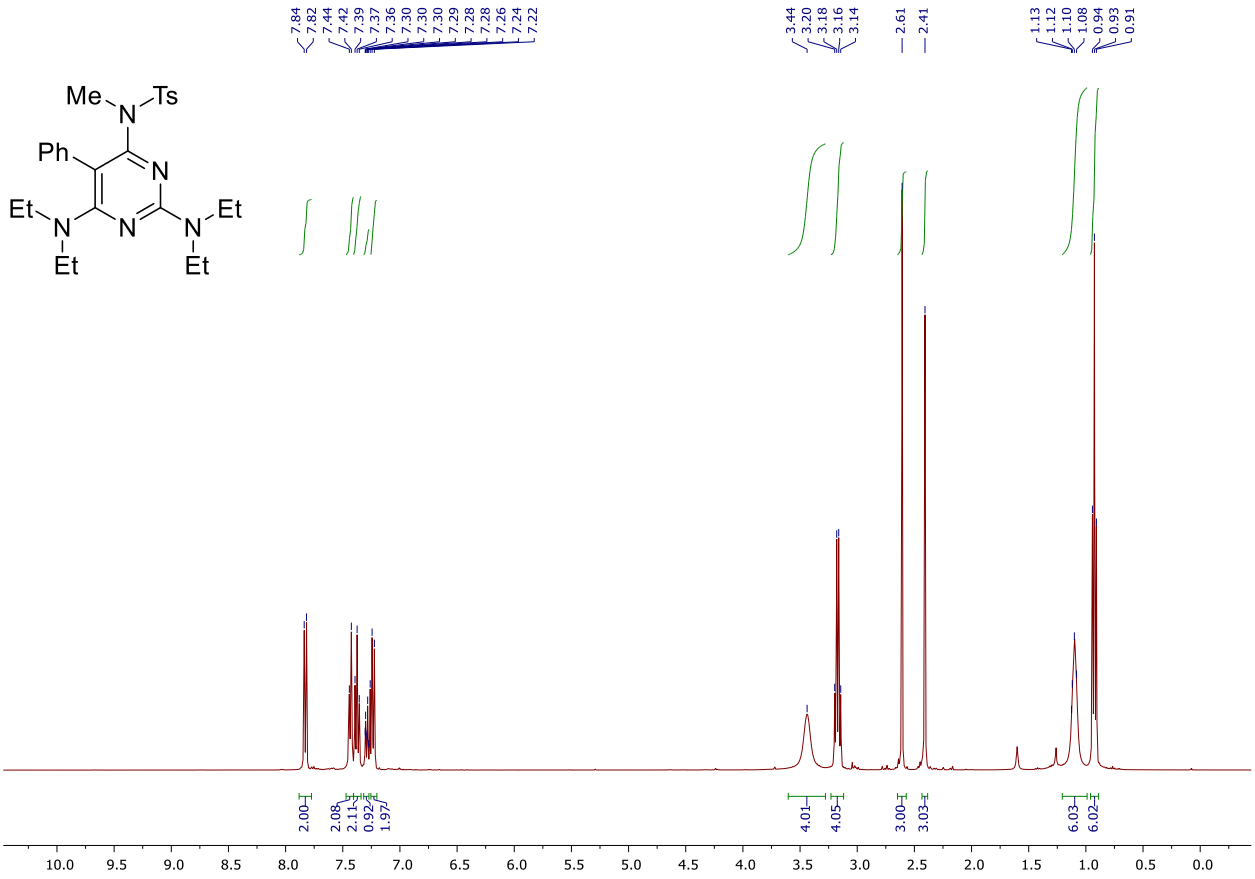
^{1}H NMR (400 MHz, $CDCl_3$) of **3a**



^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3a**



^{1}H NMR (400 MHz, $CDCl_3$) of **3b**



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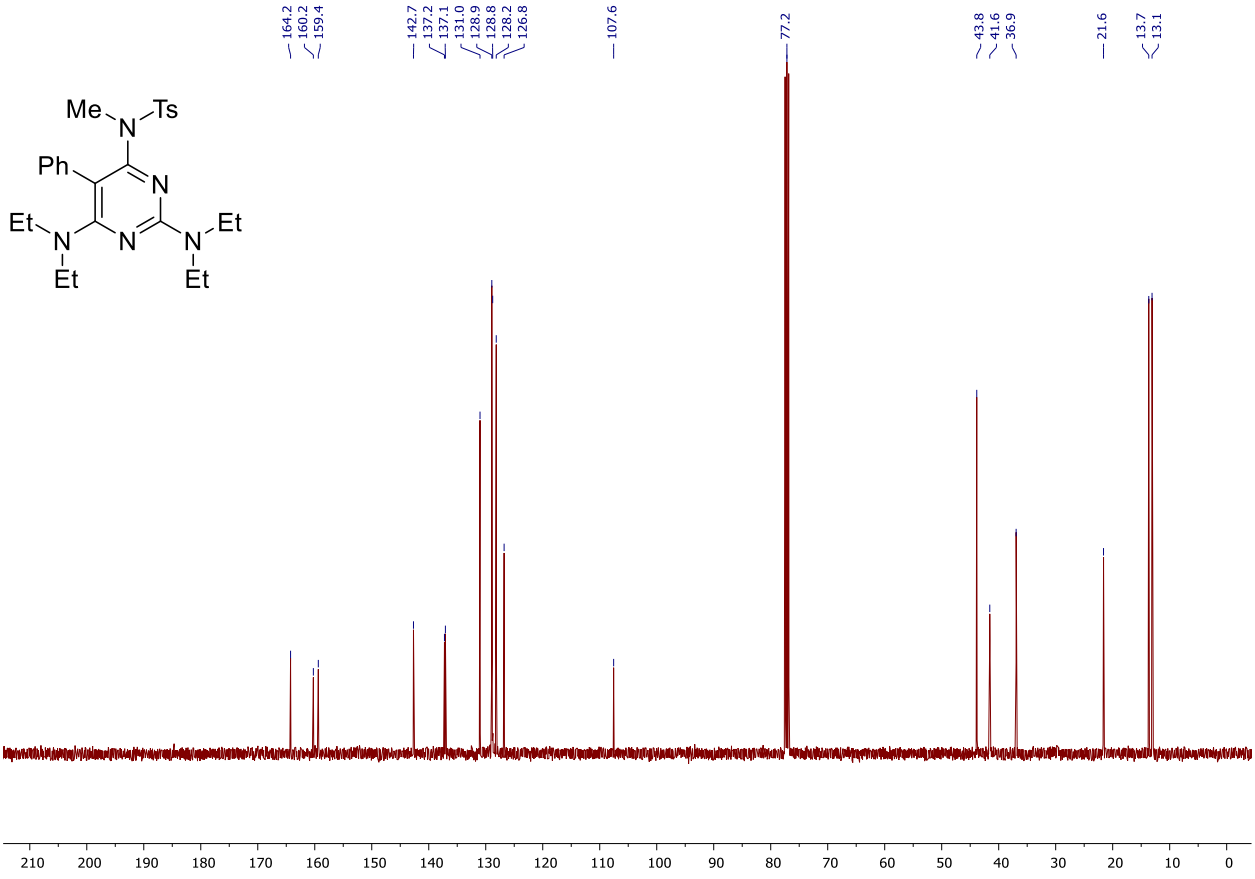
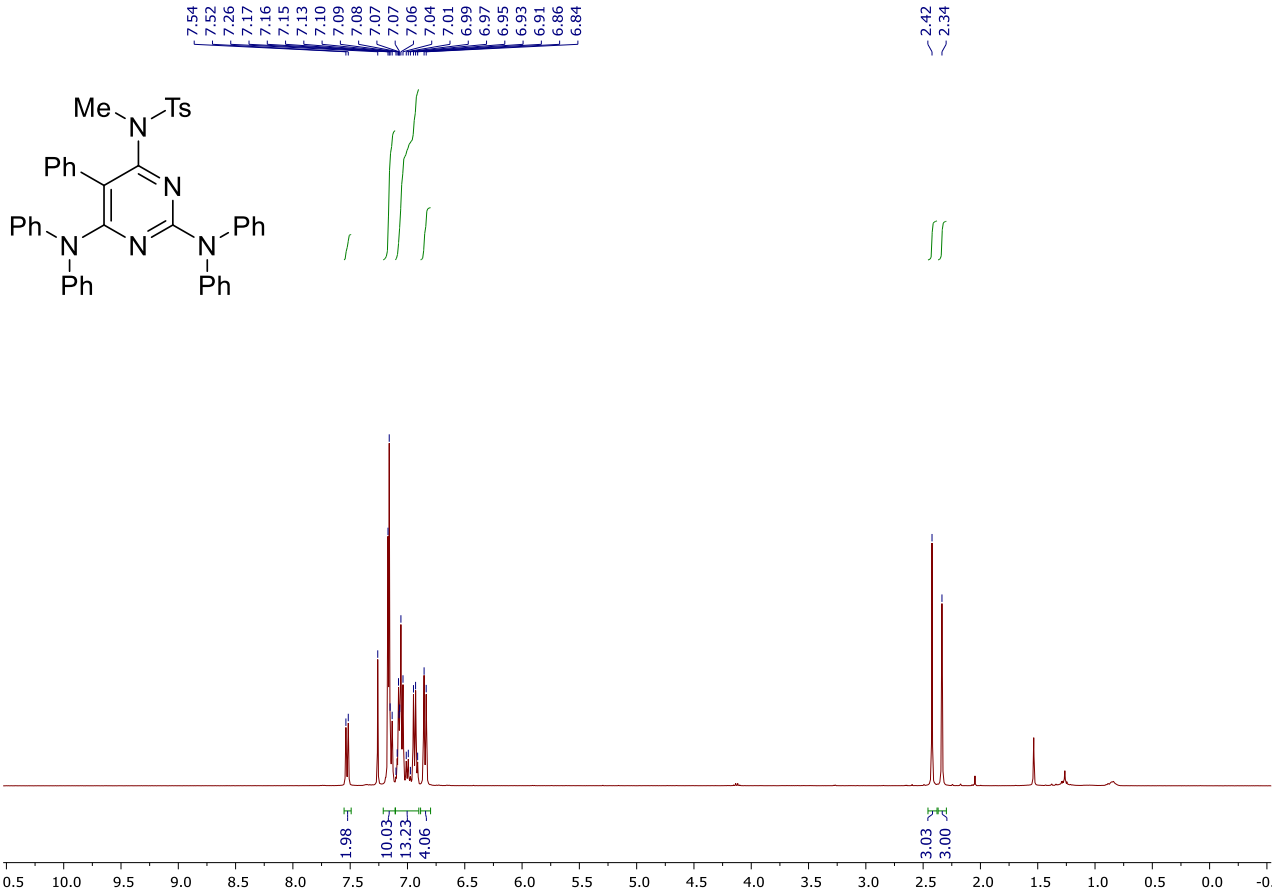


^{1}H NMR (400 MHz, $CDCl_3$) of **3c**



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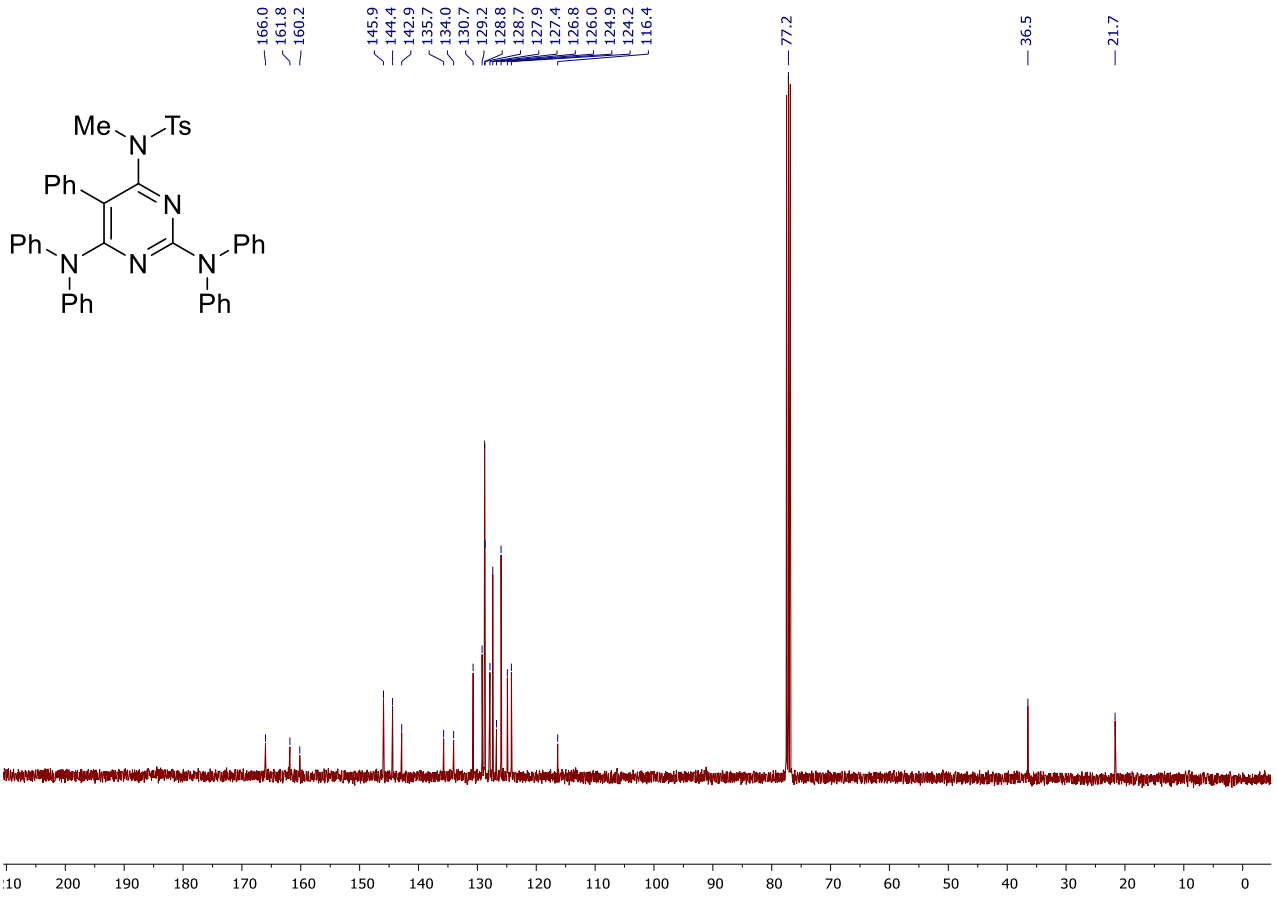
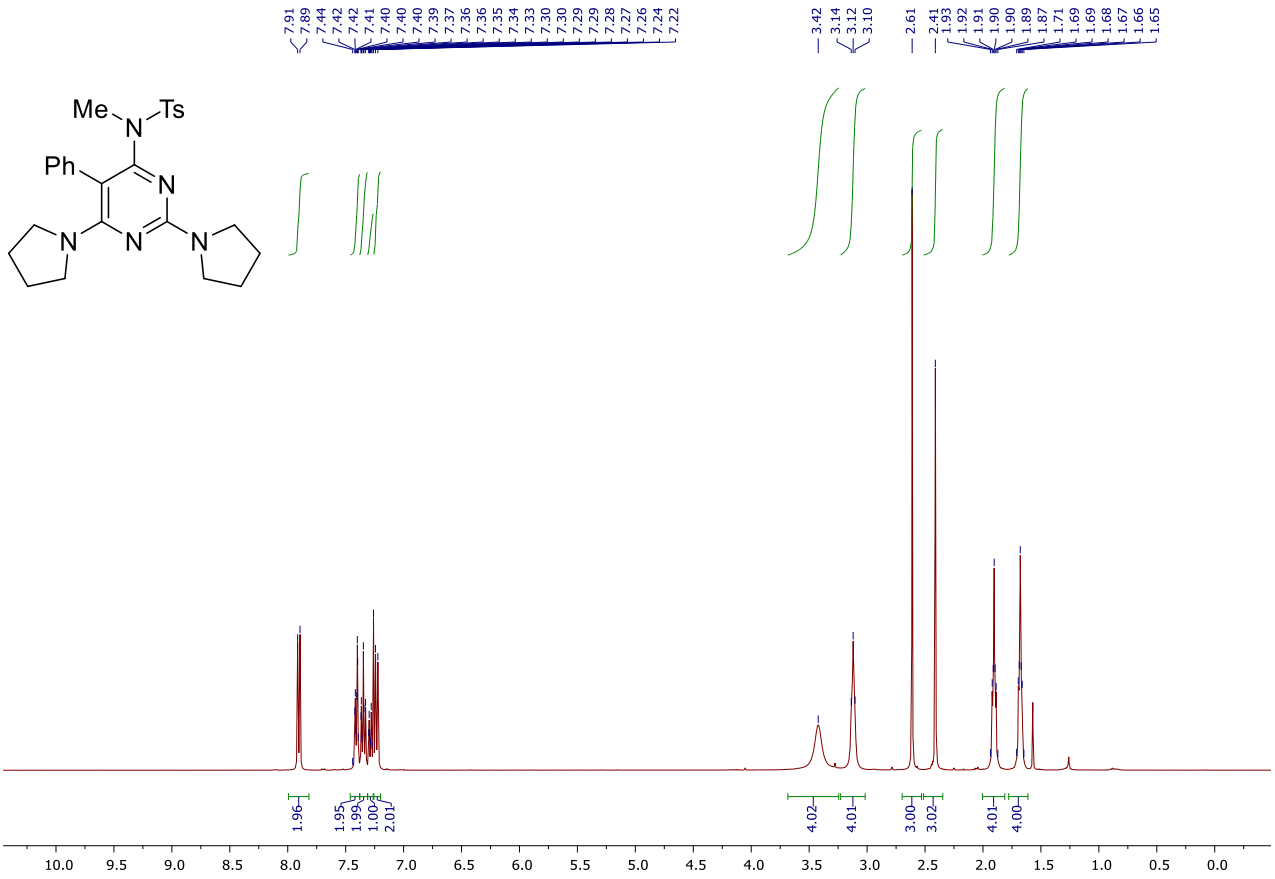
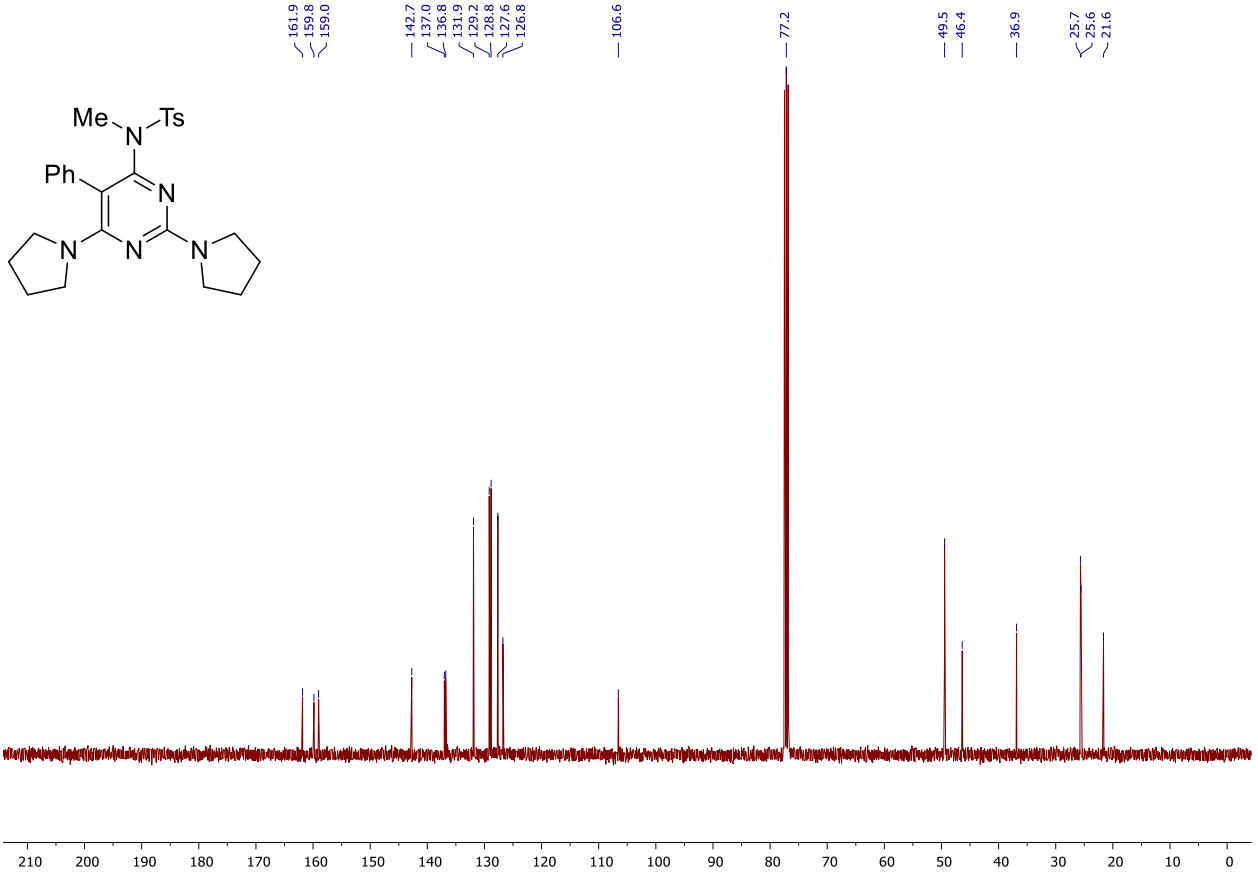


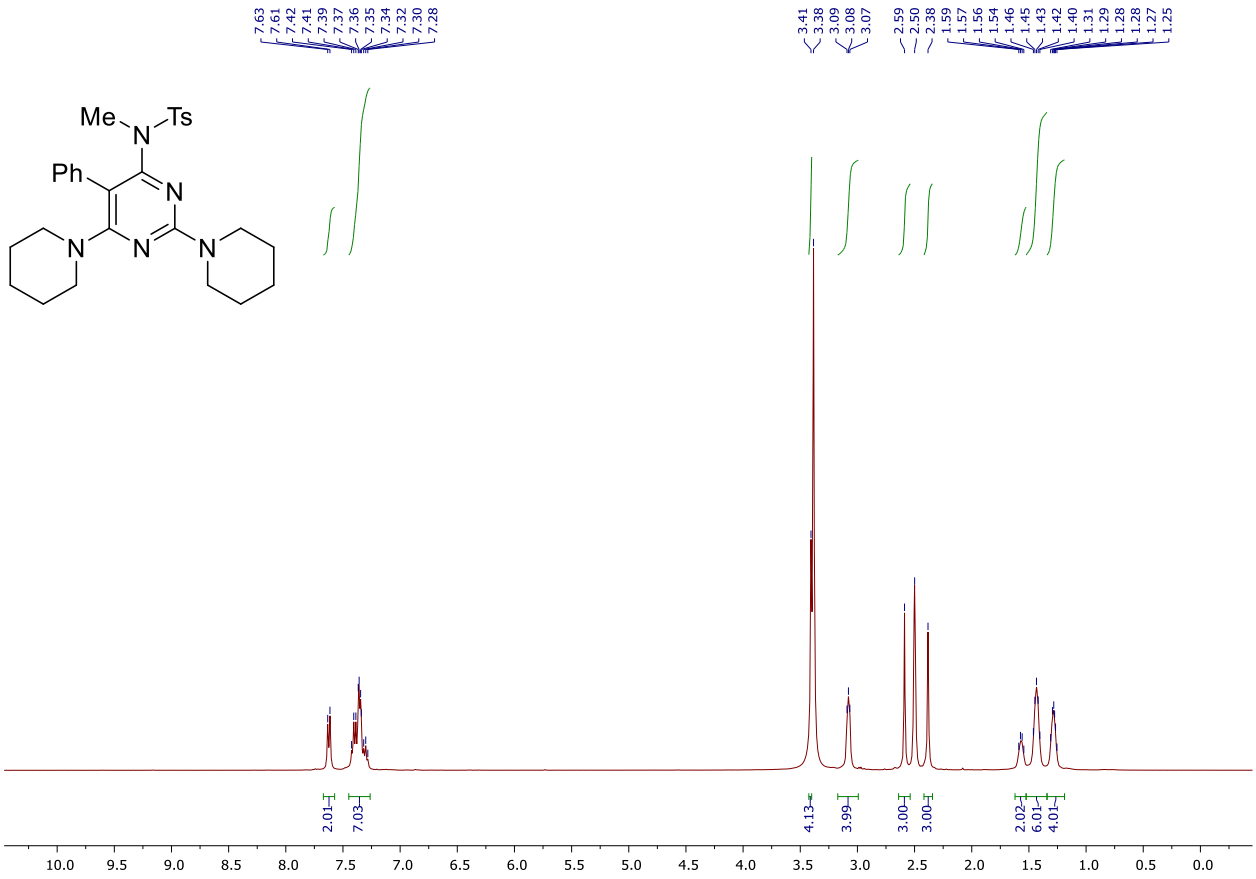
^{1}H NMR (400 MHz, $CDCl_3$) of **3d**



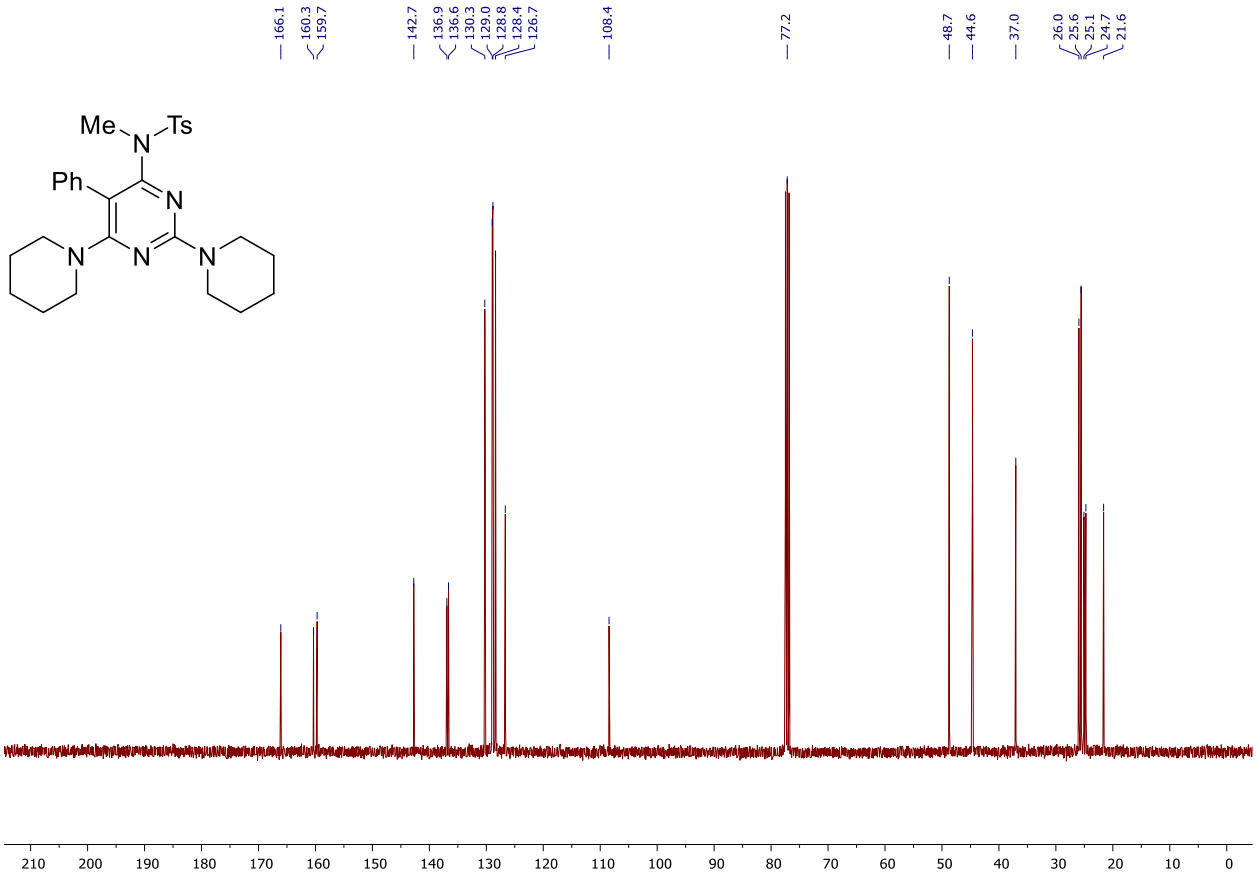
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3d**



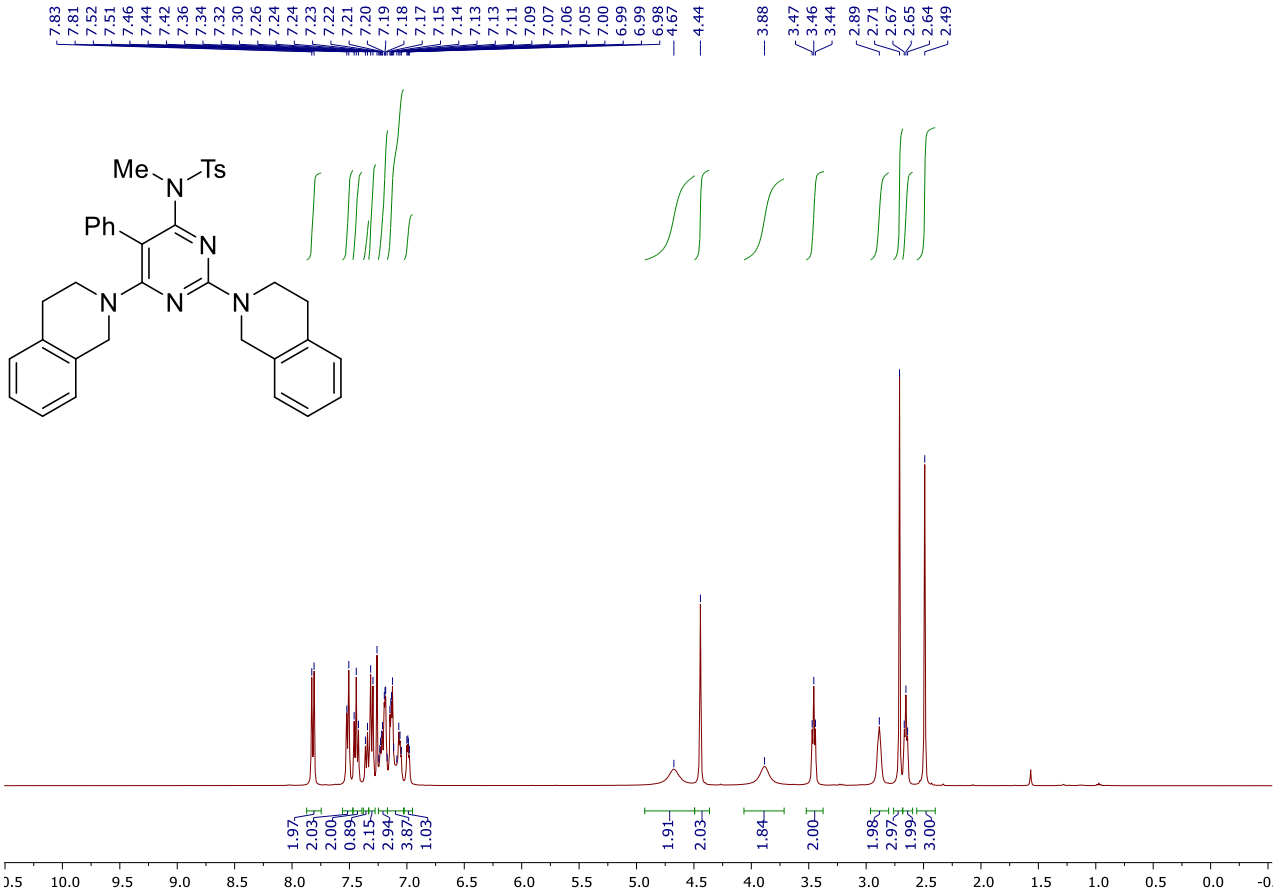
^{1}H NMR (400 MHz, DMSO-d_6) of **3e**



^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3e**



^{1}H NMR (400 MHz, $CDCl_3$) of **3f**



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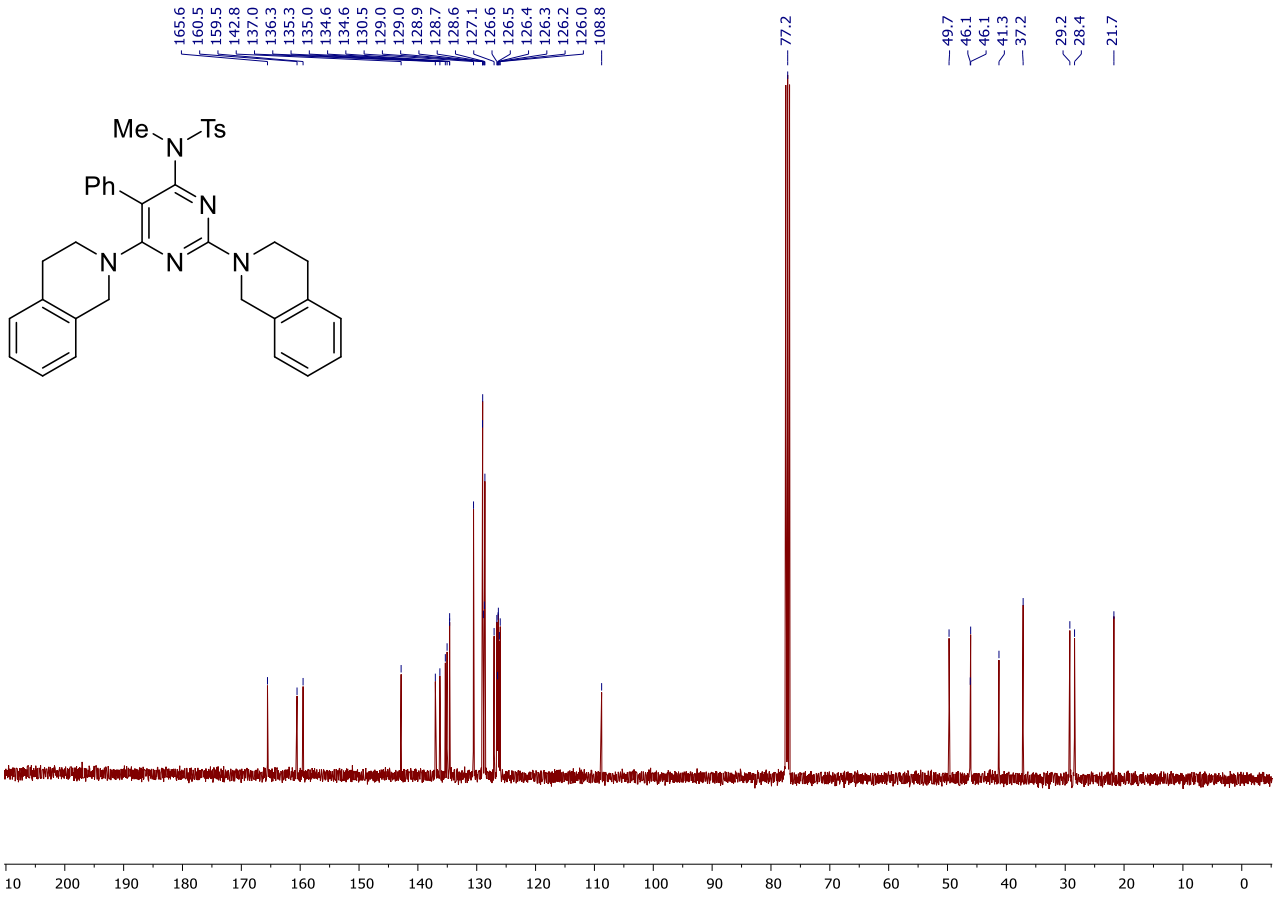

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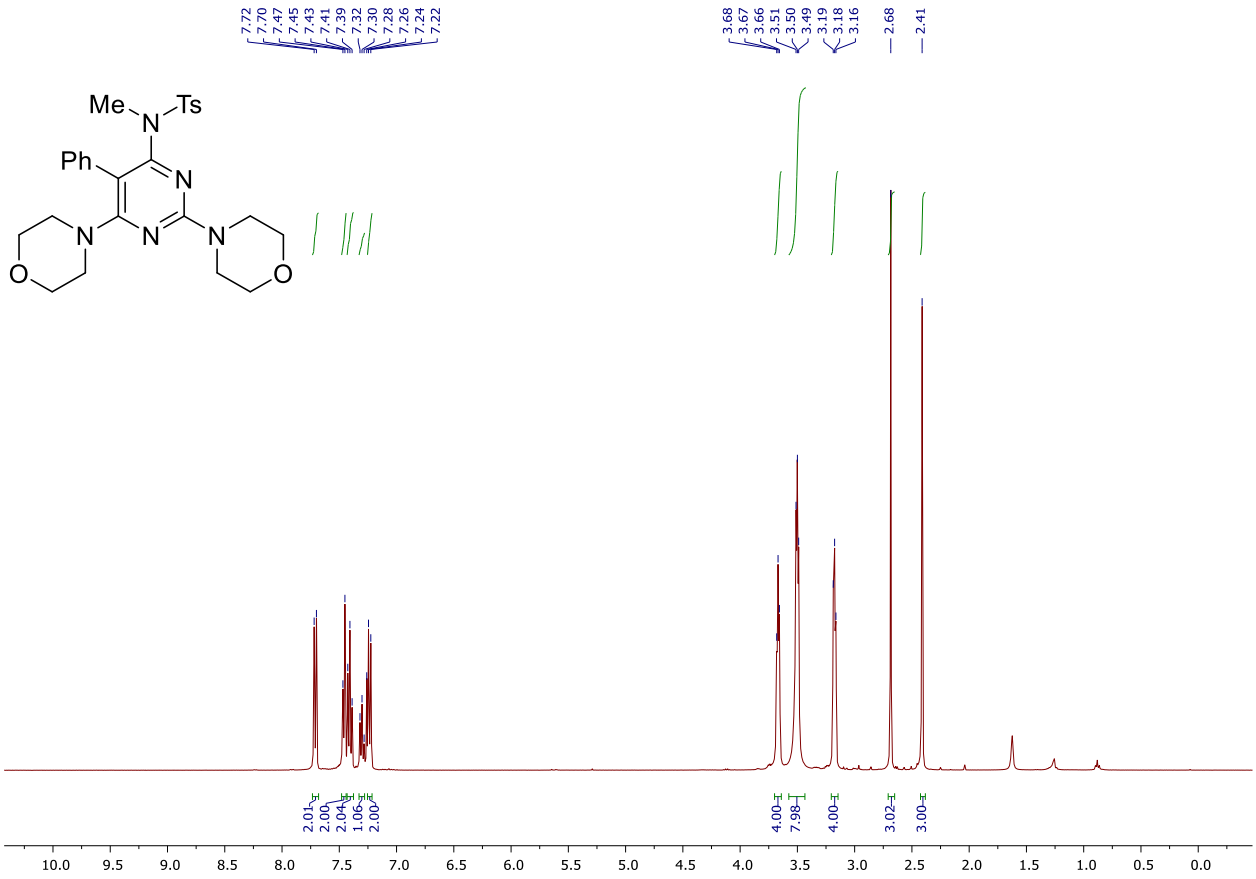

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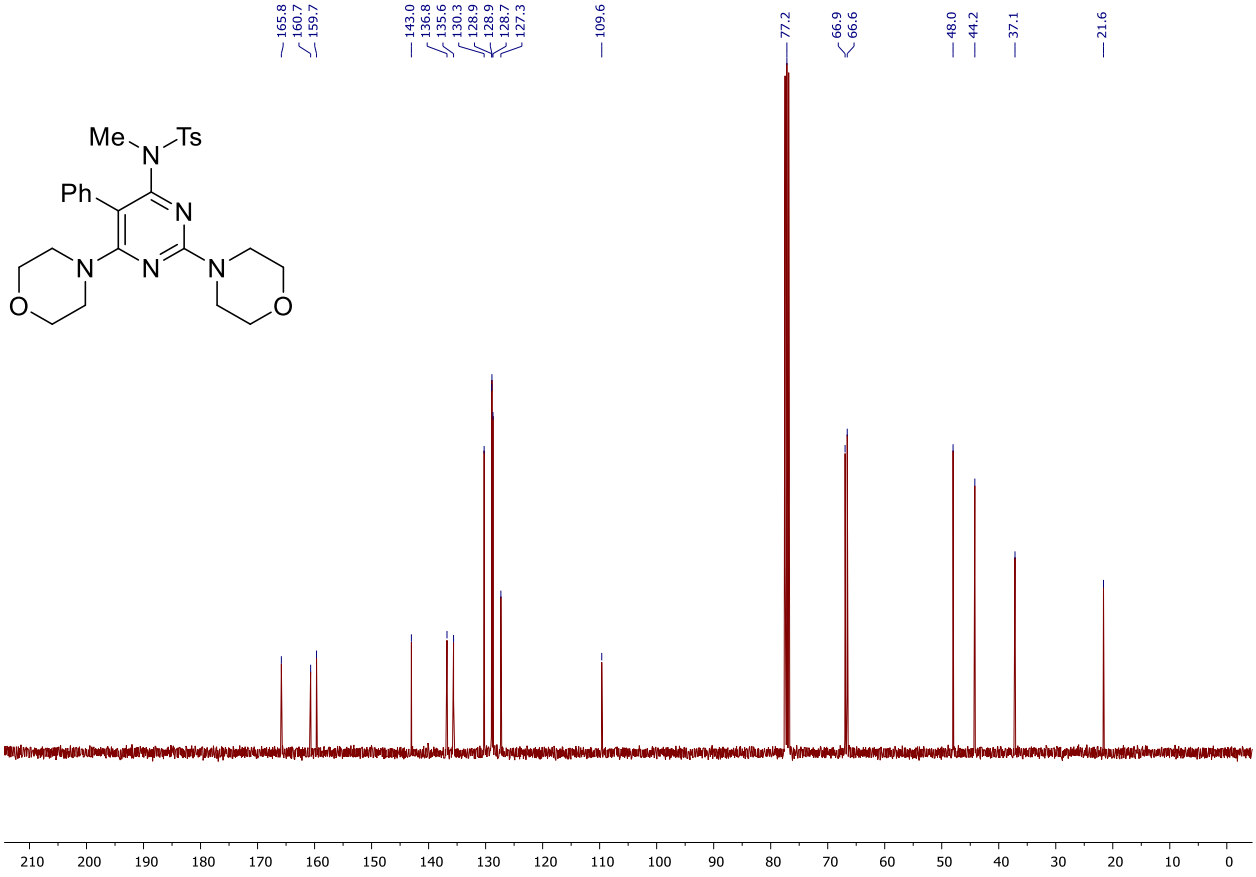
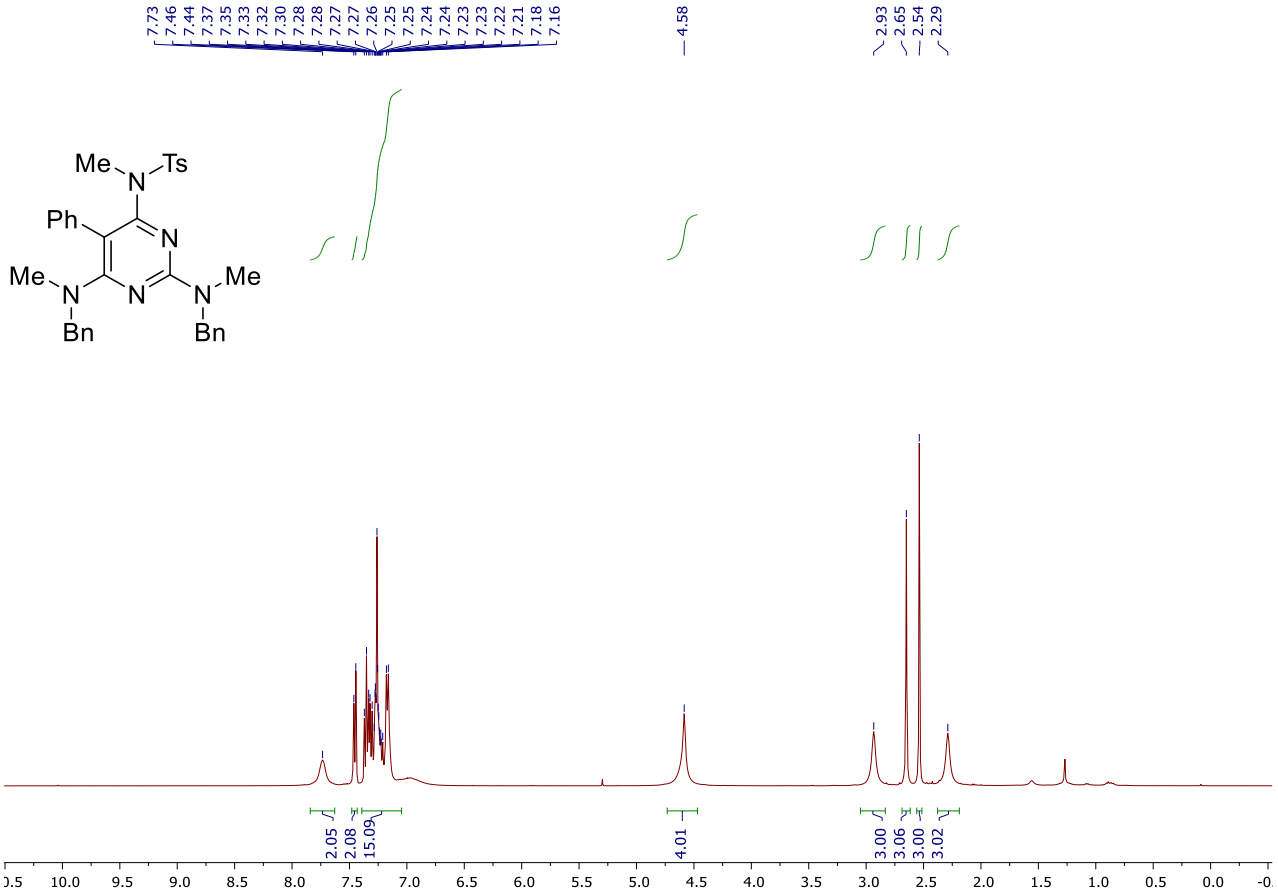


^{1}H NMR (400 MHz, $CDCl_3$) of **3h**



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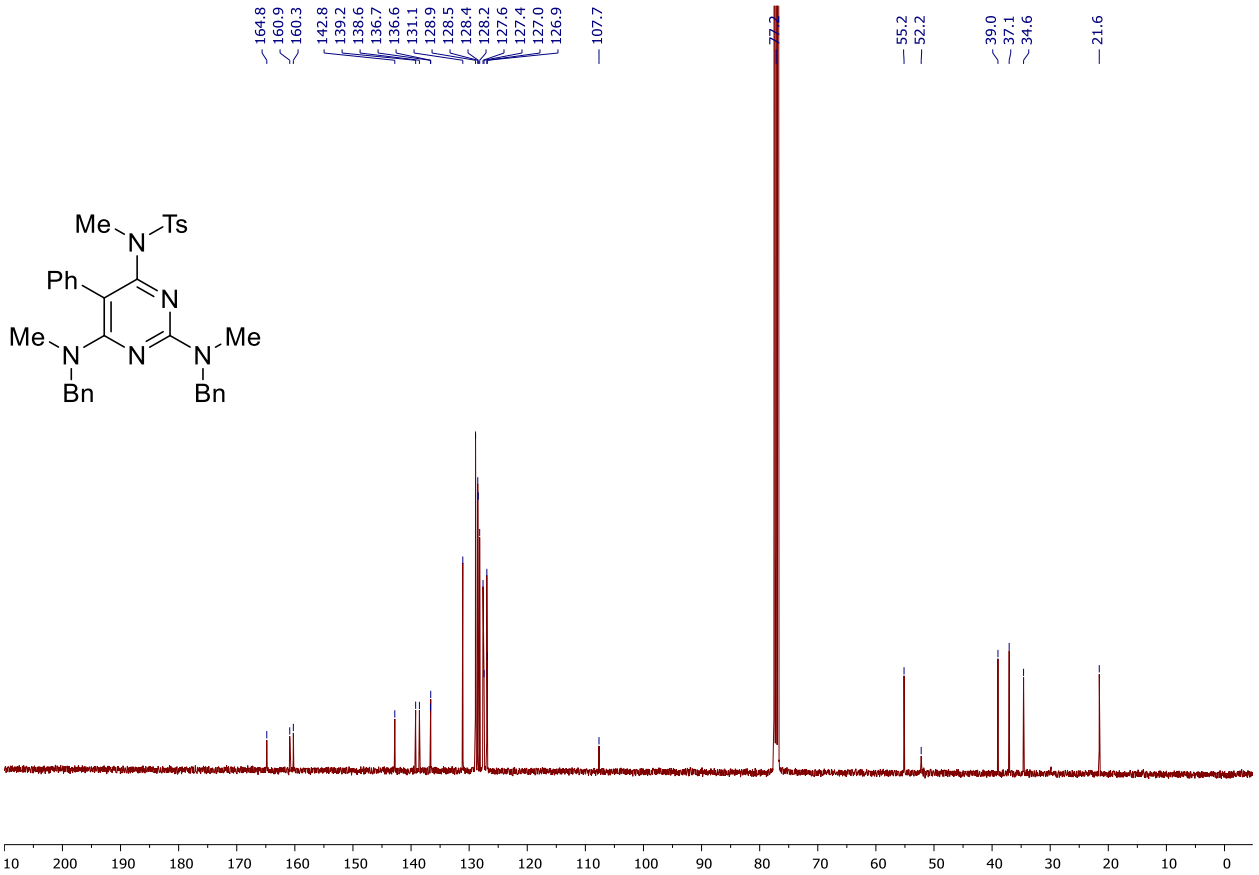
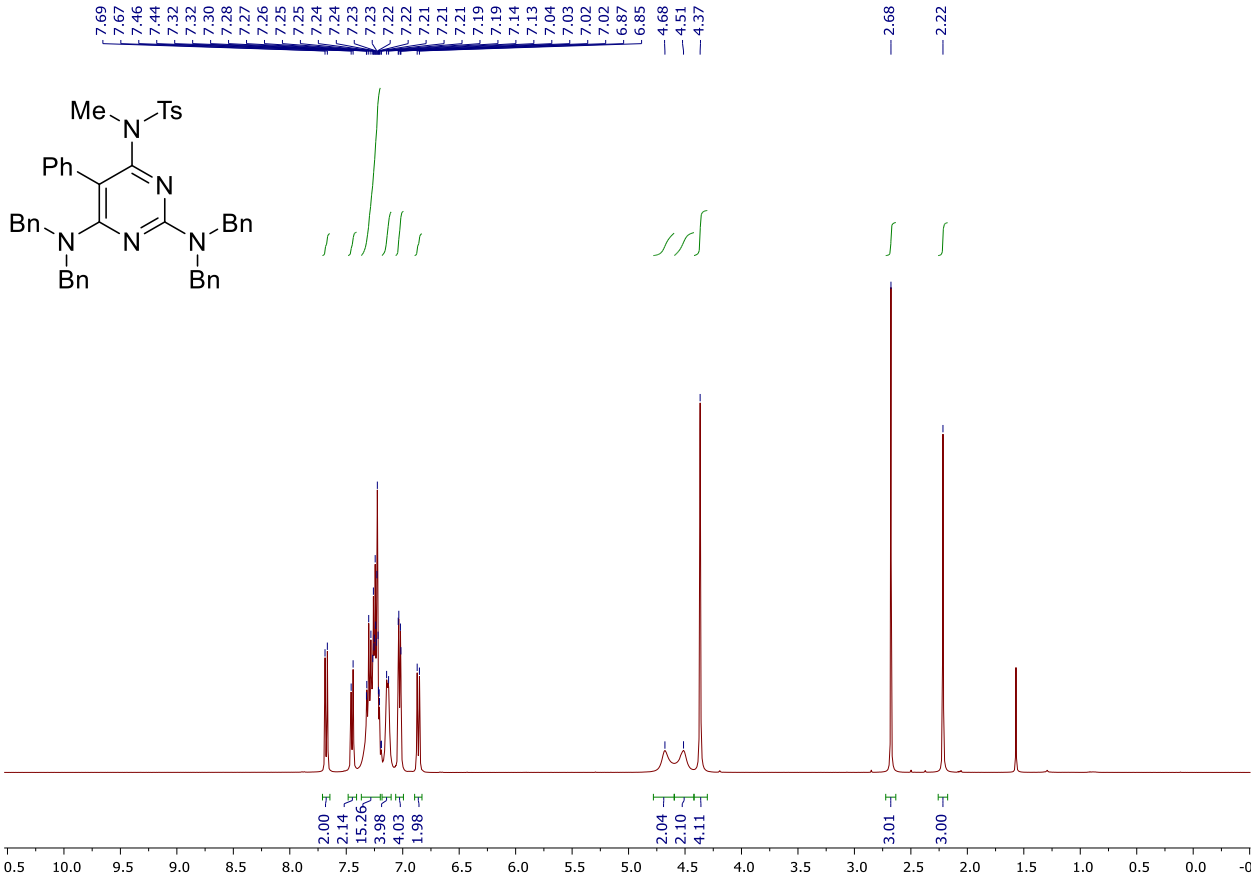


^{1}H NMR (400 MHz, $CDCl_3$) of **3i**



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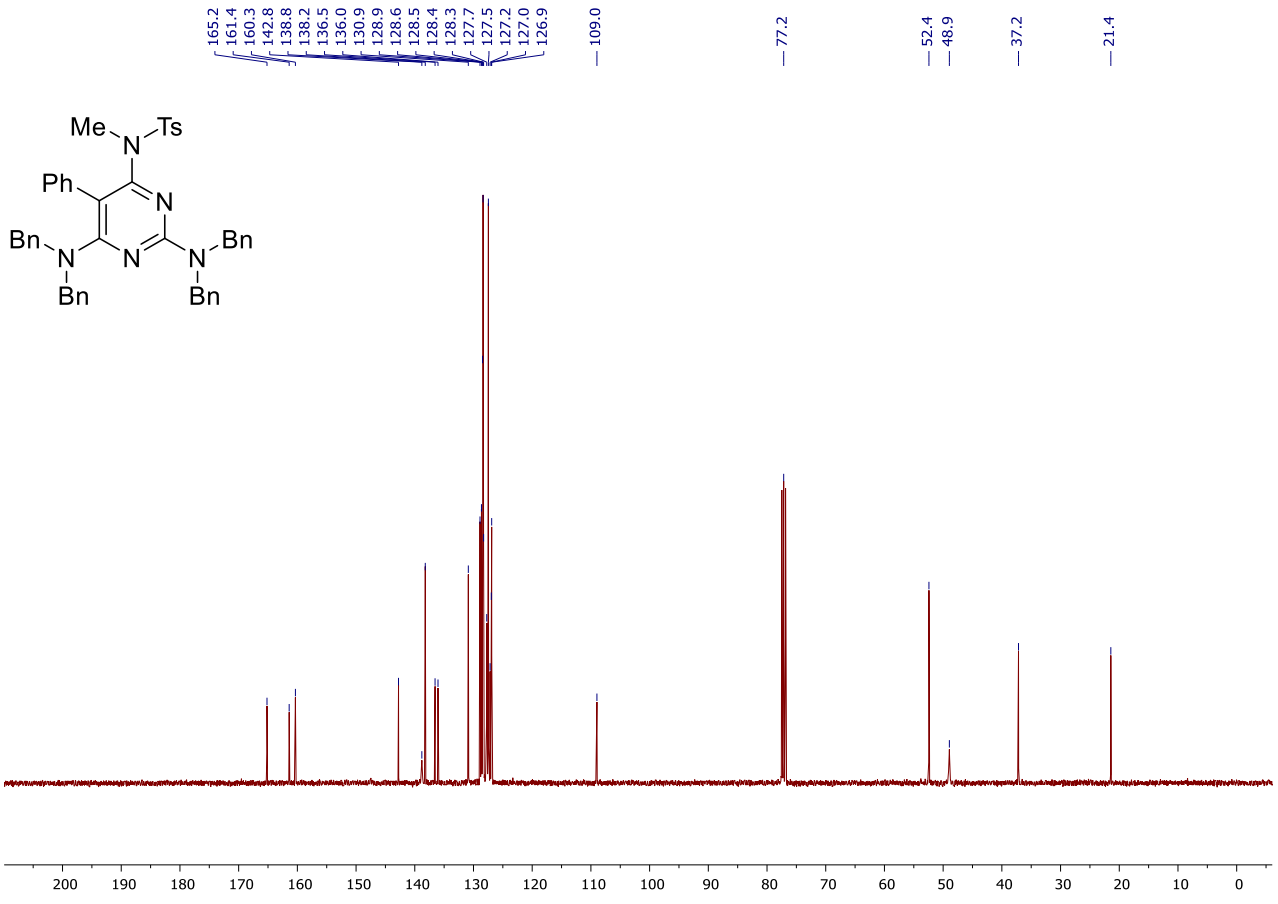
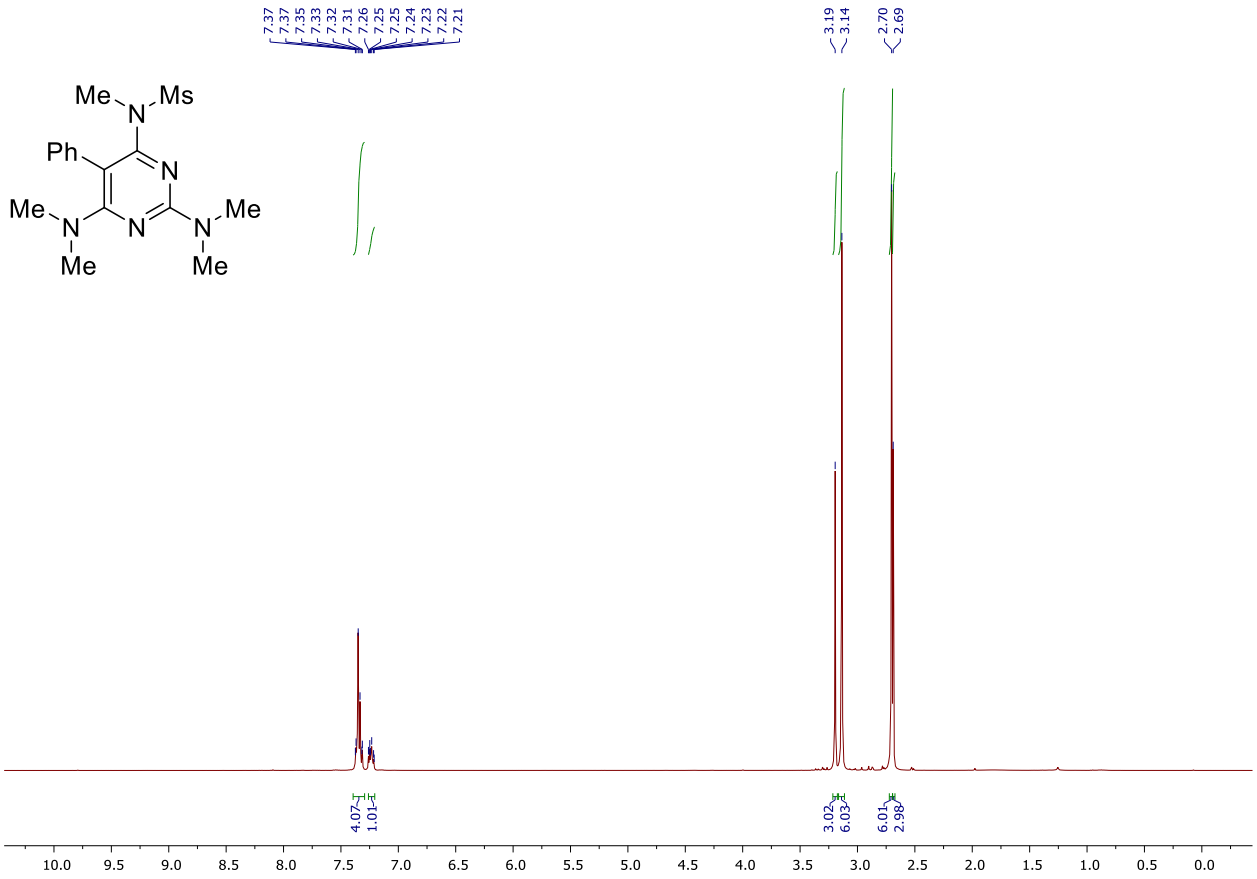


^{1}H NMR (400 MHz, $CDCl_3$) of **6a**



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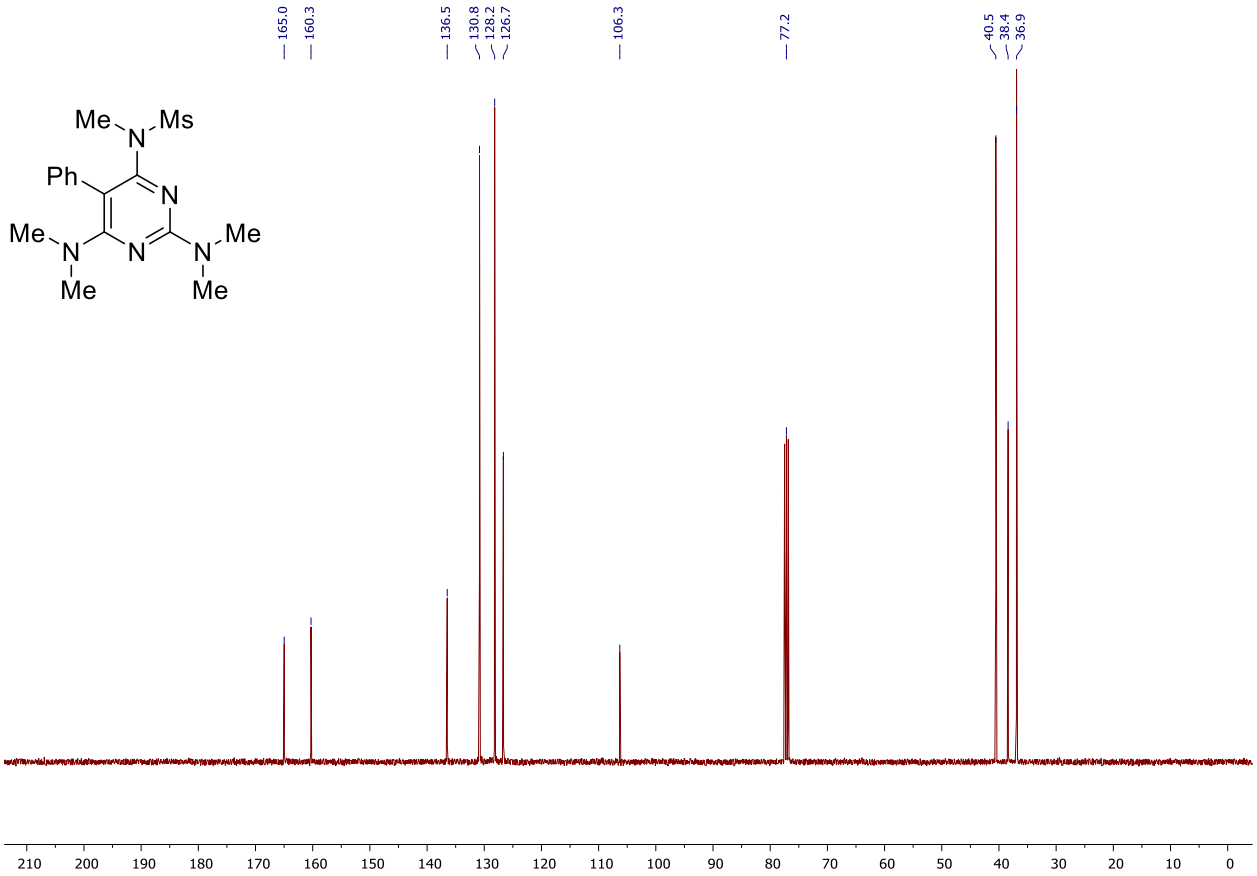
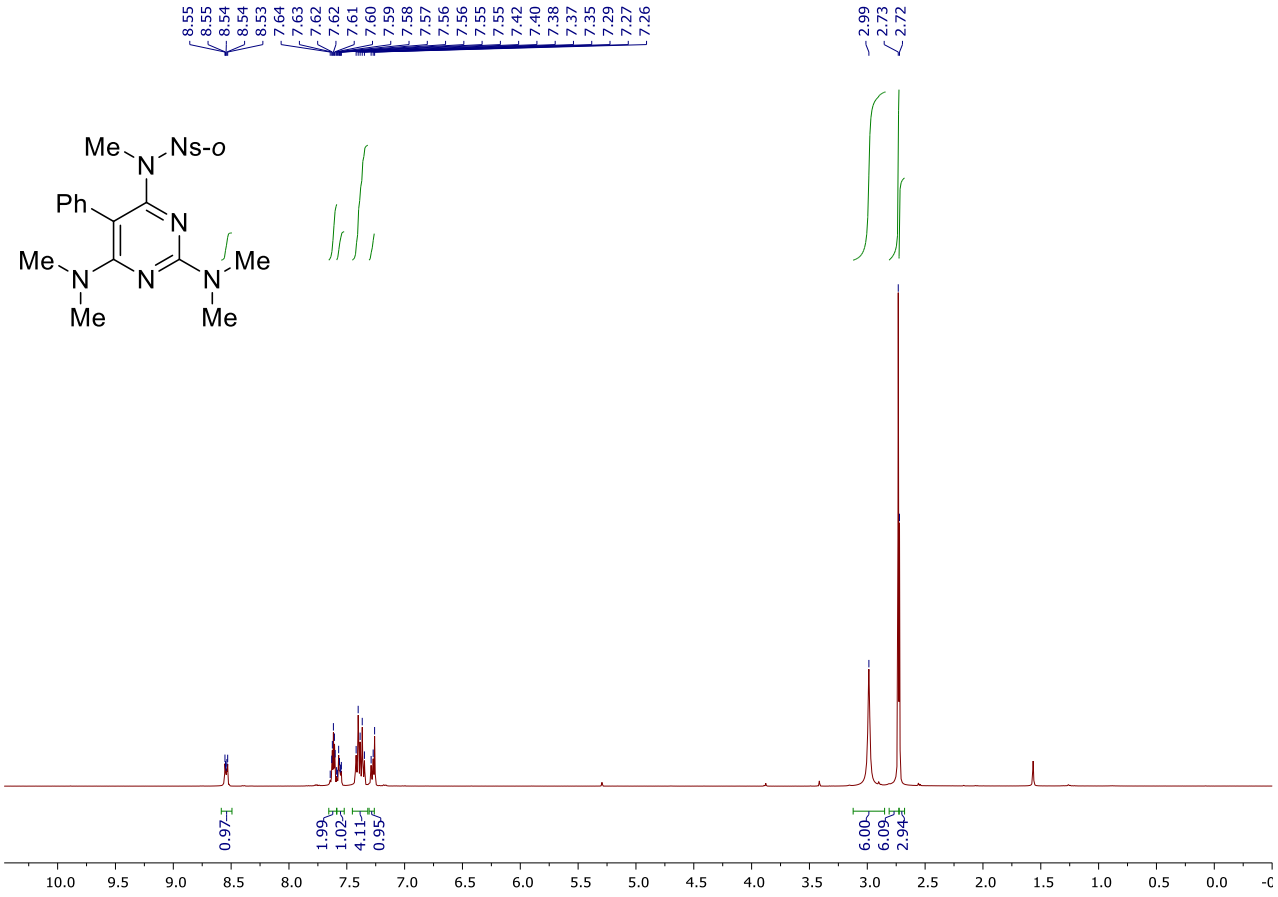


^{1}H NMR (400 MHz, $CDCl_3$) of **6b**



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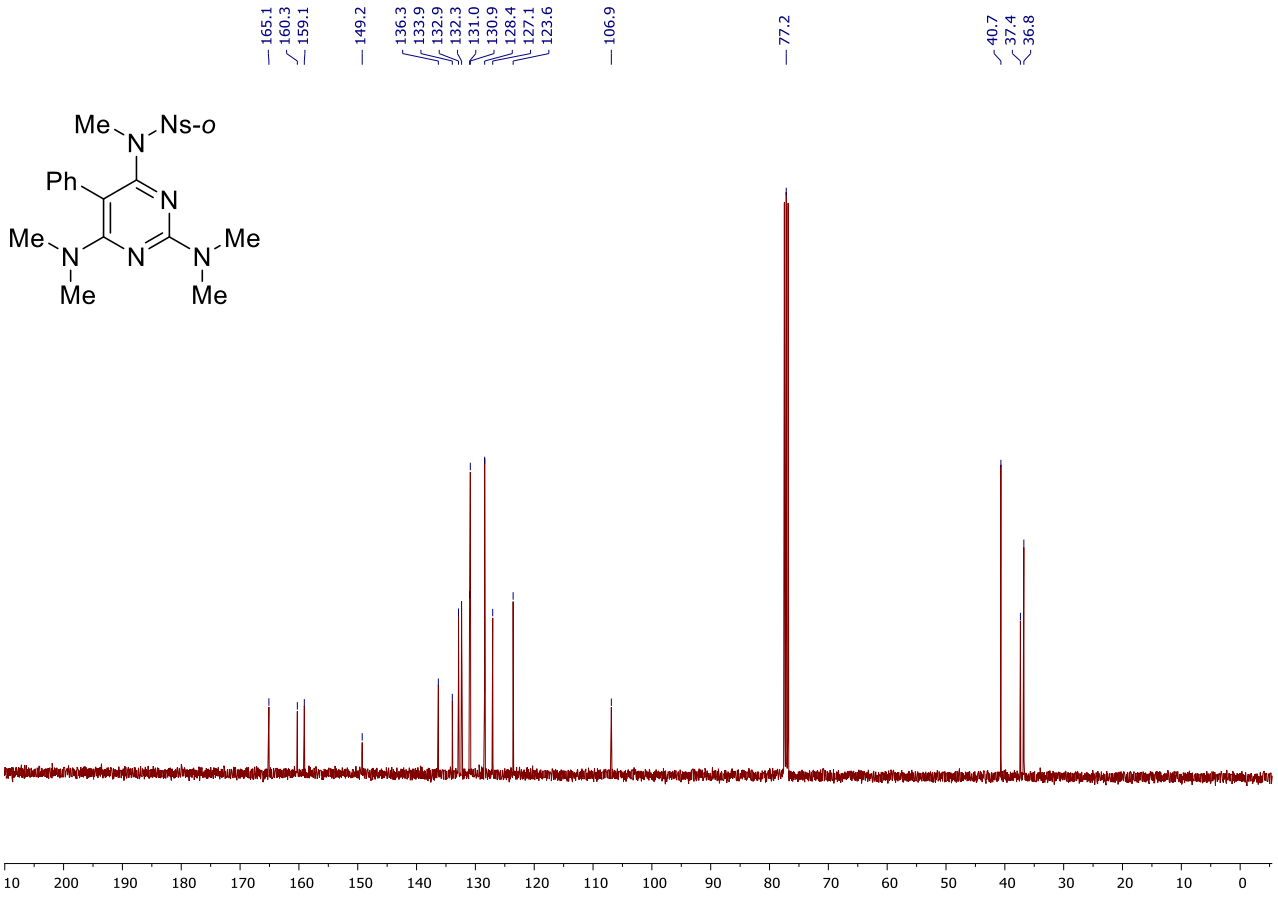
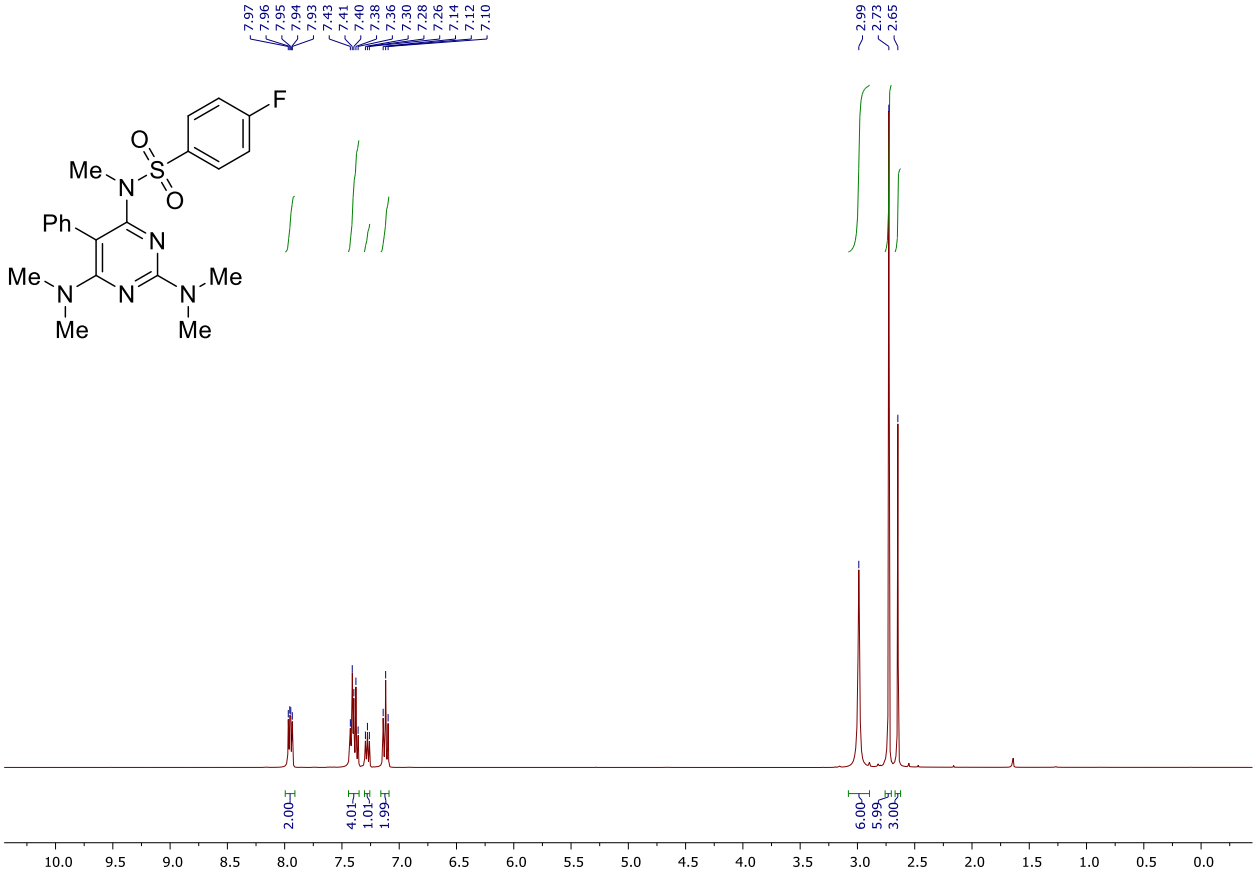


^{1}H NMR (400 MHz, $CDCl_3$) of **6c**



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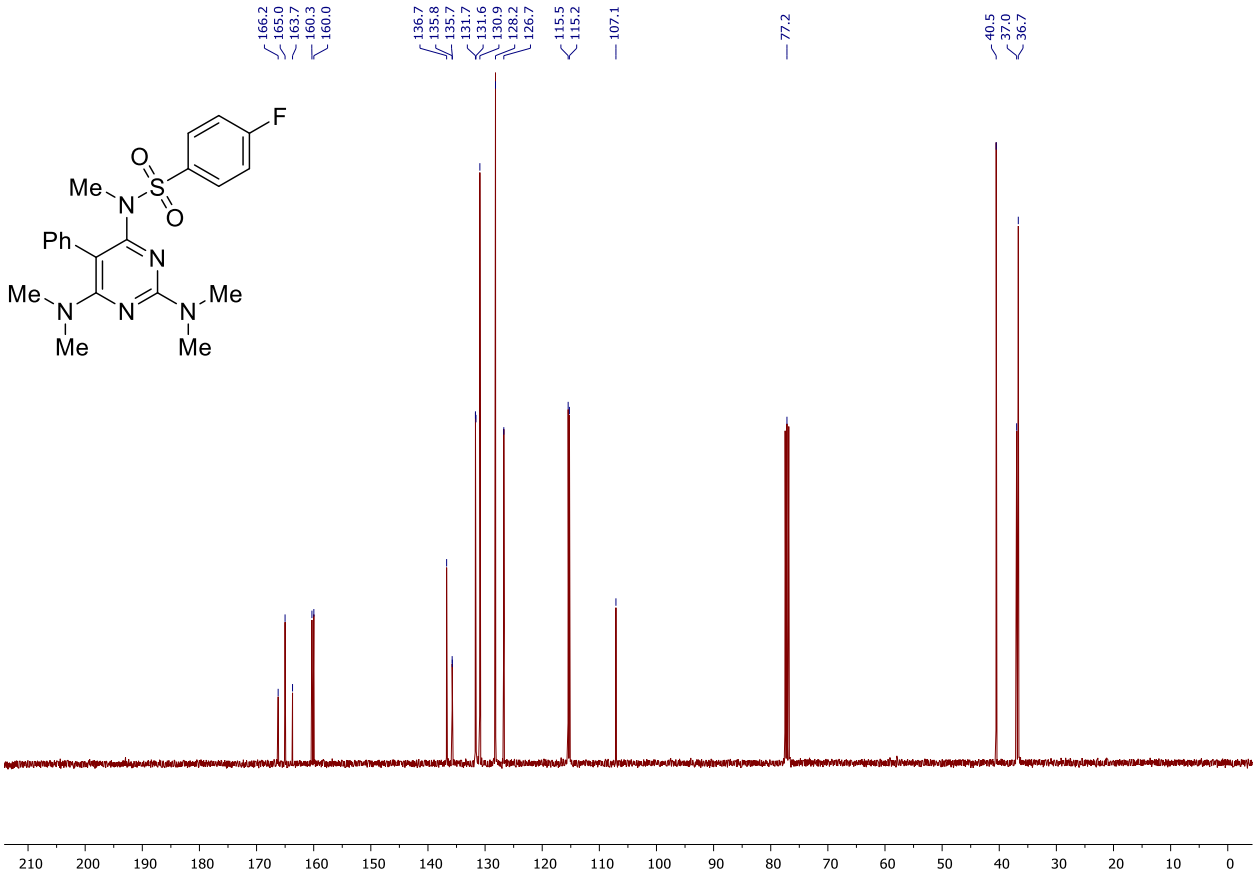

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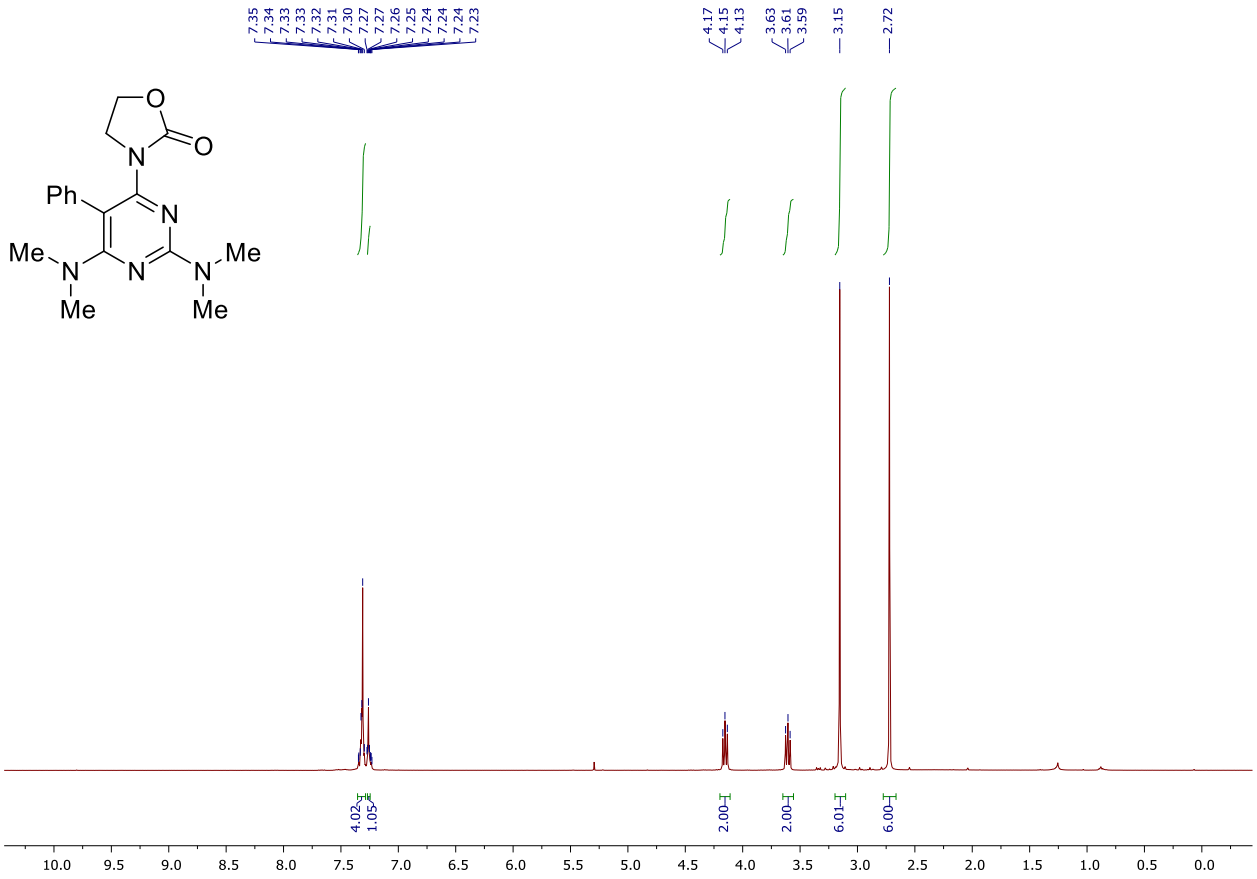

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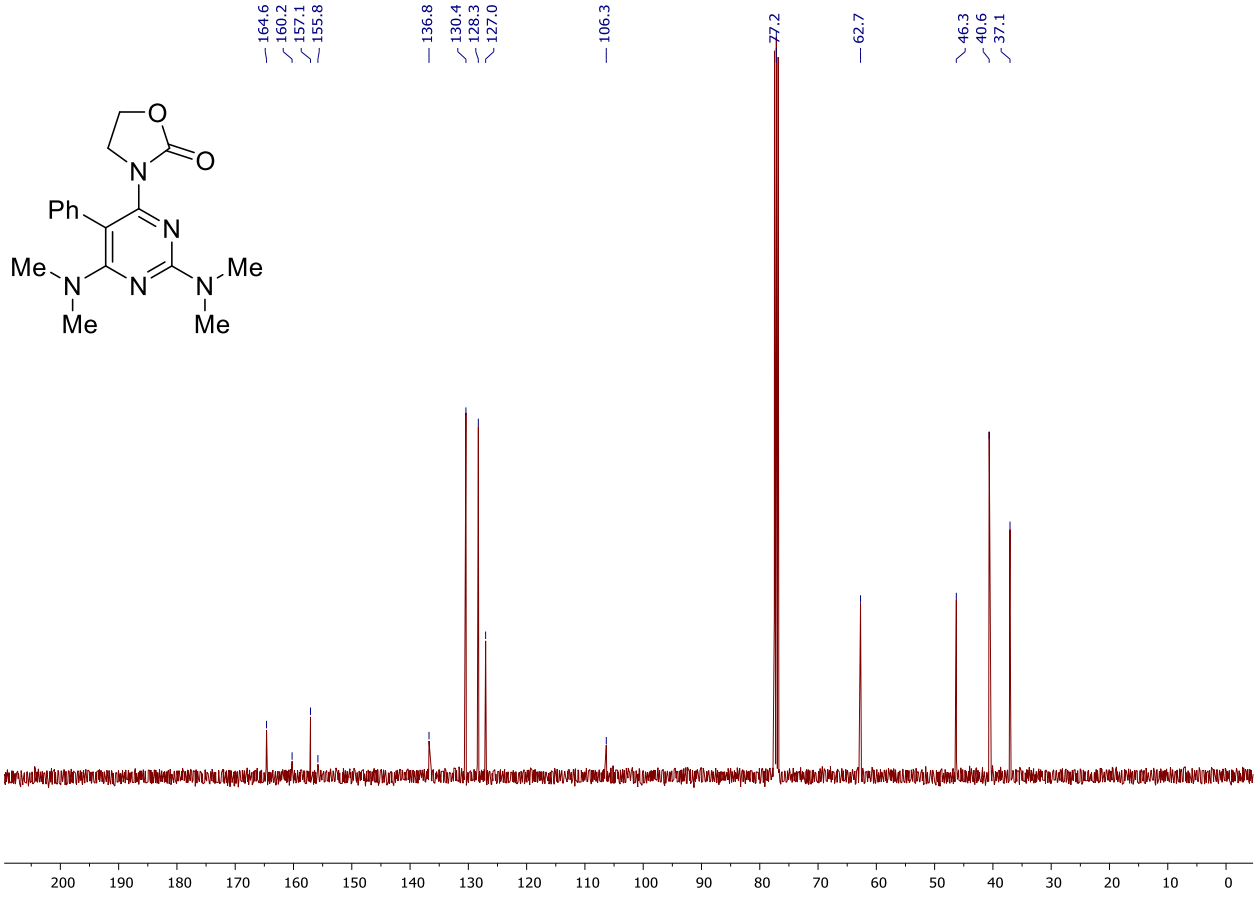

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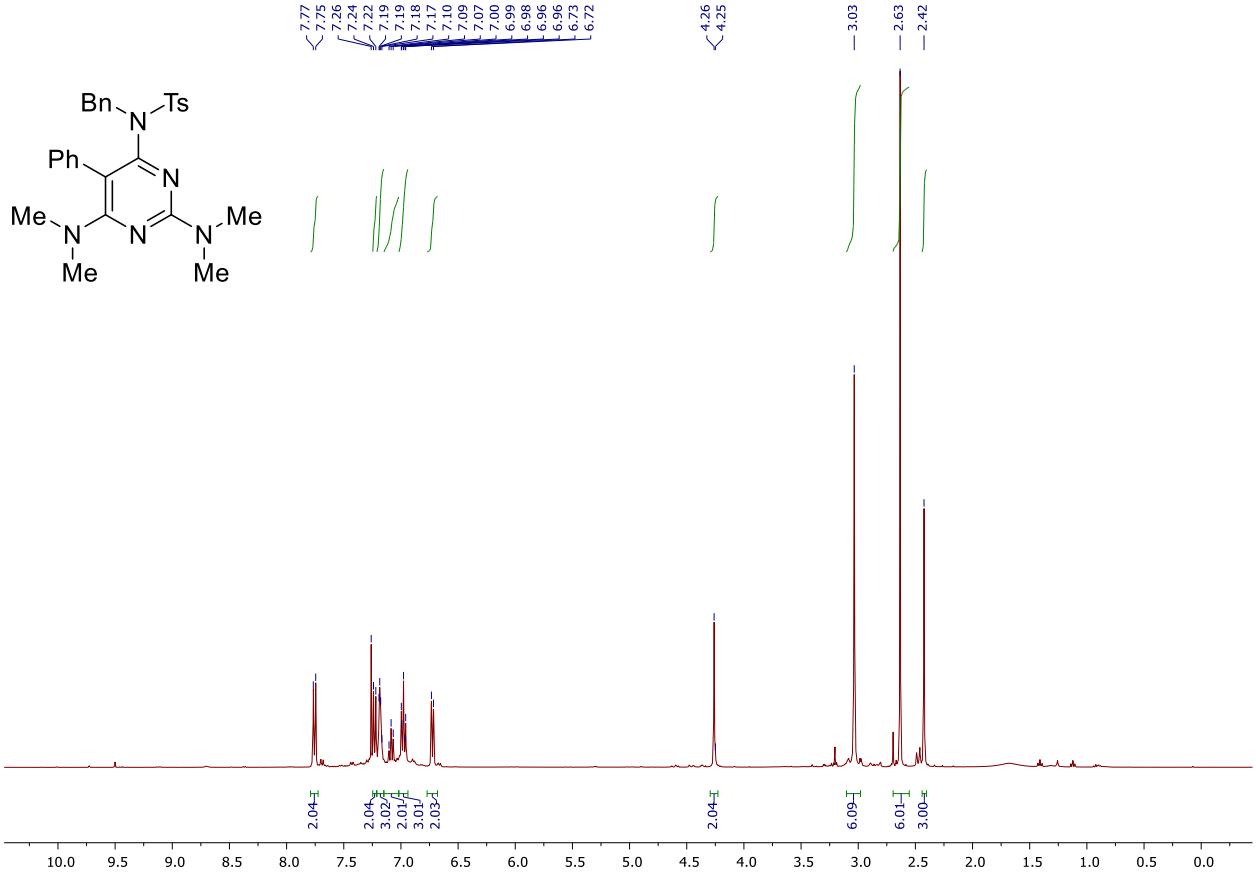

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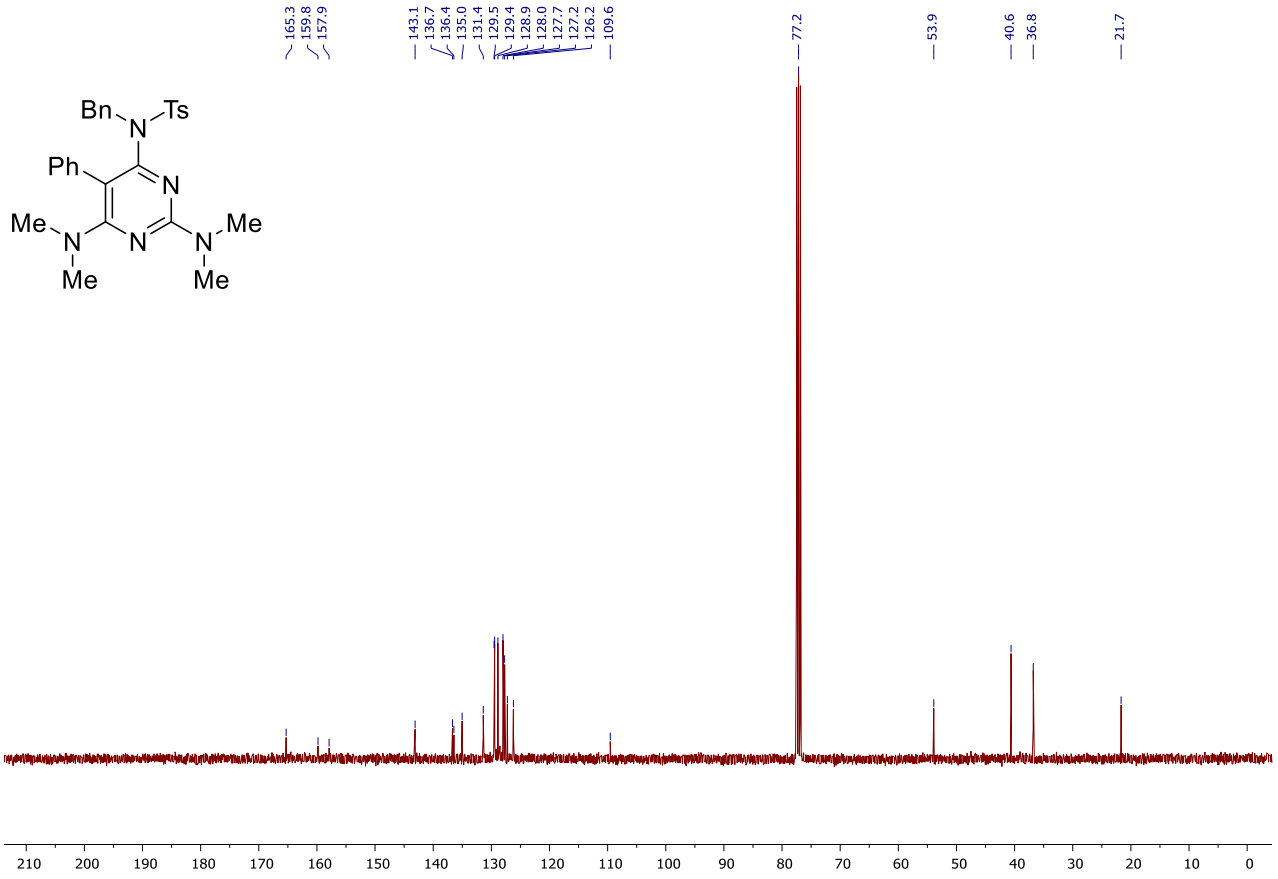

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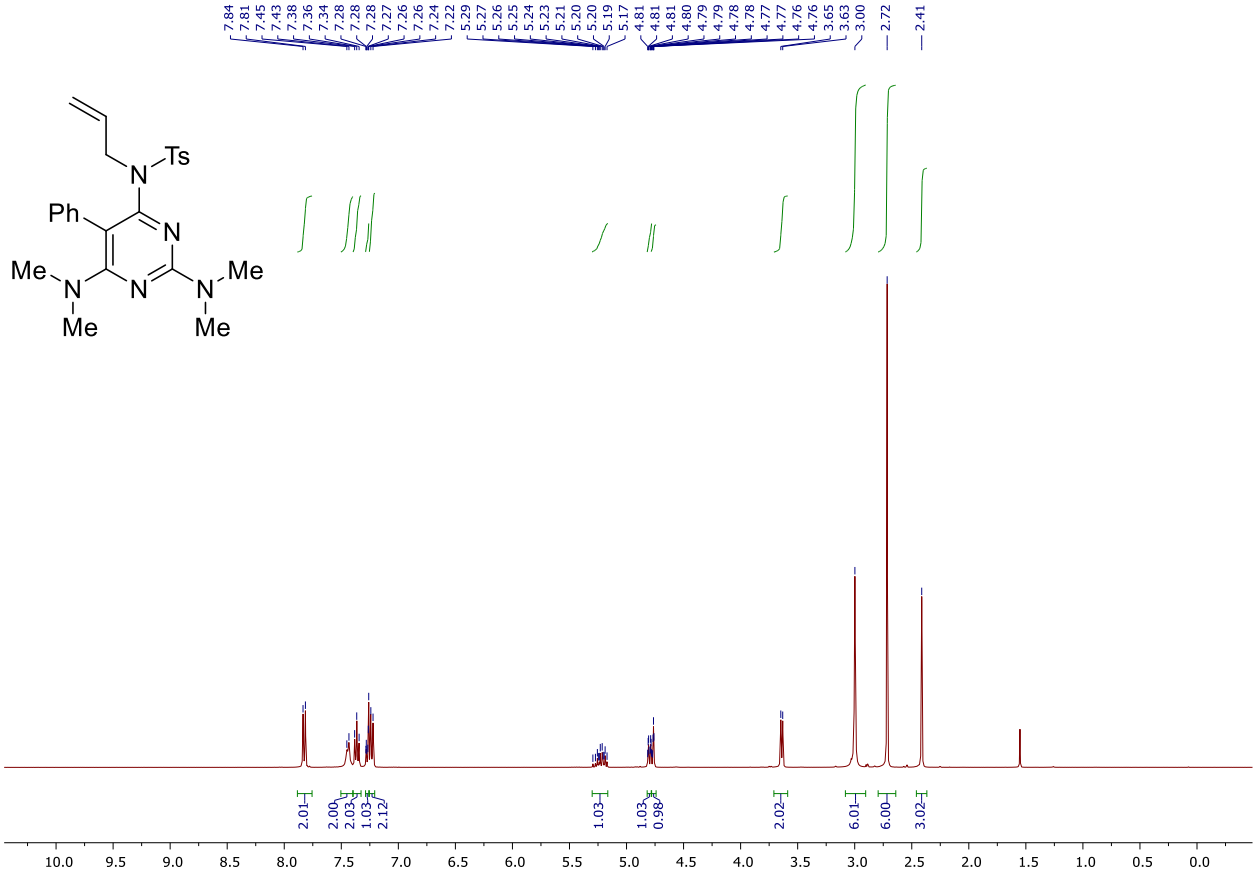

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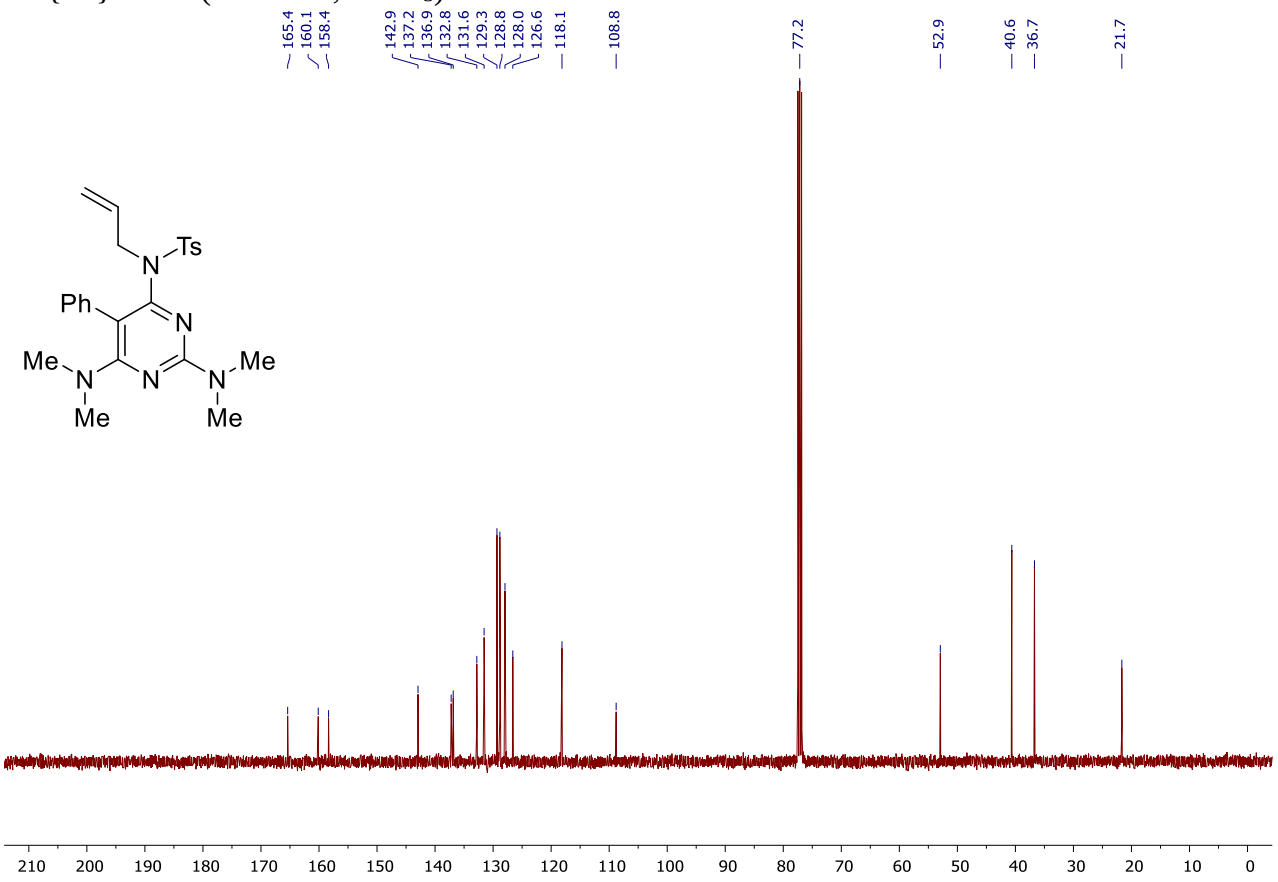

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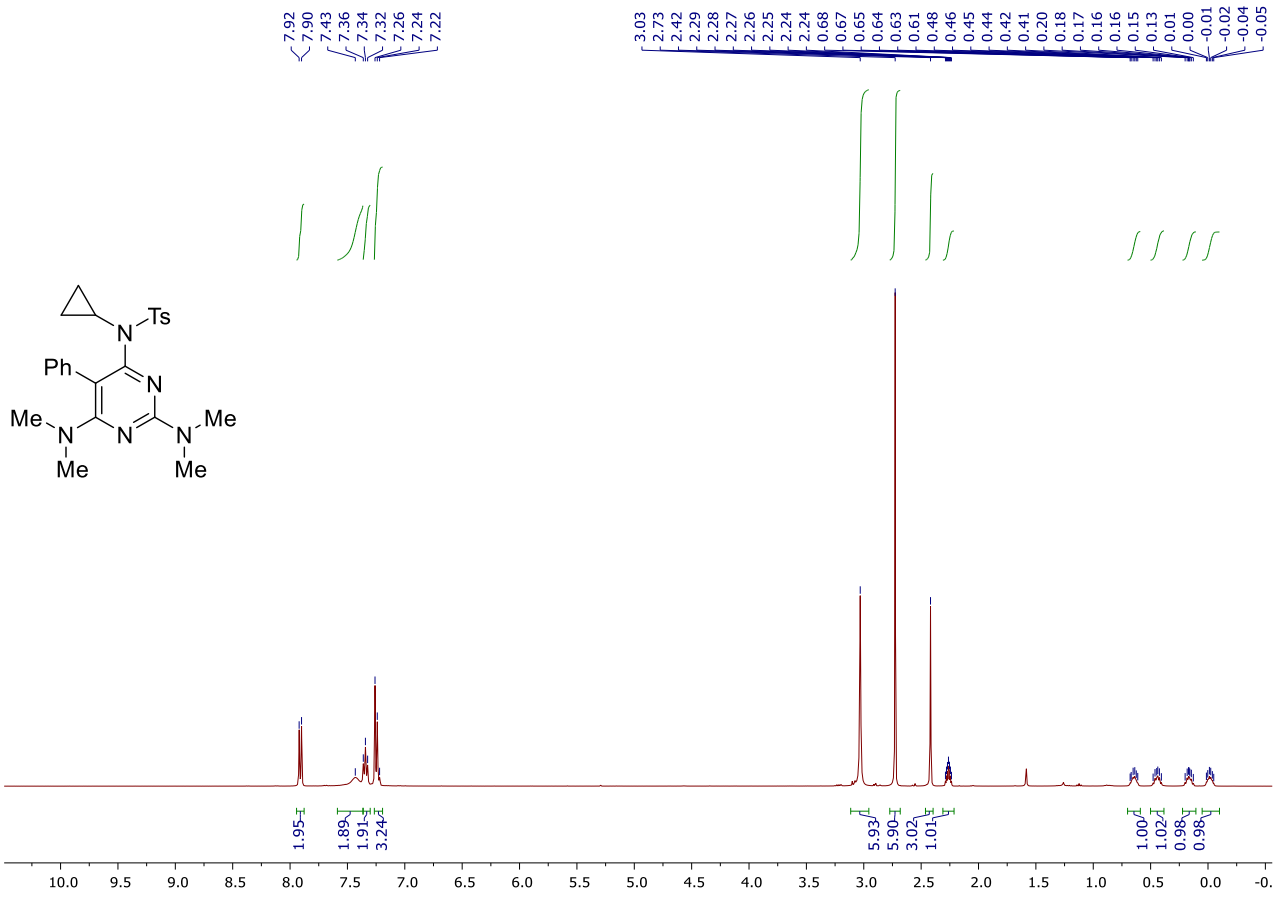
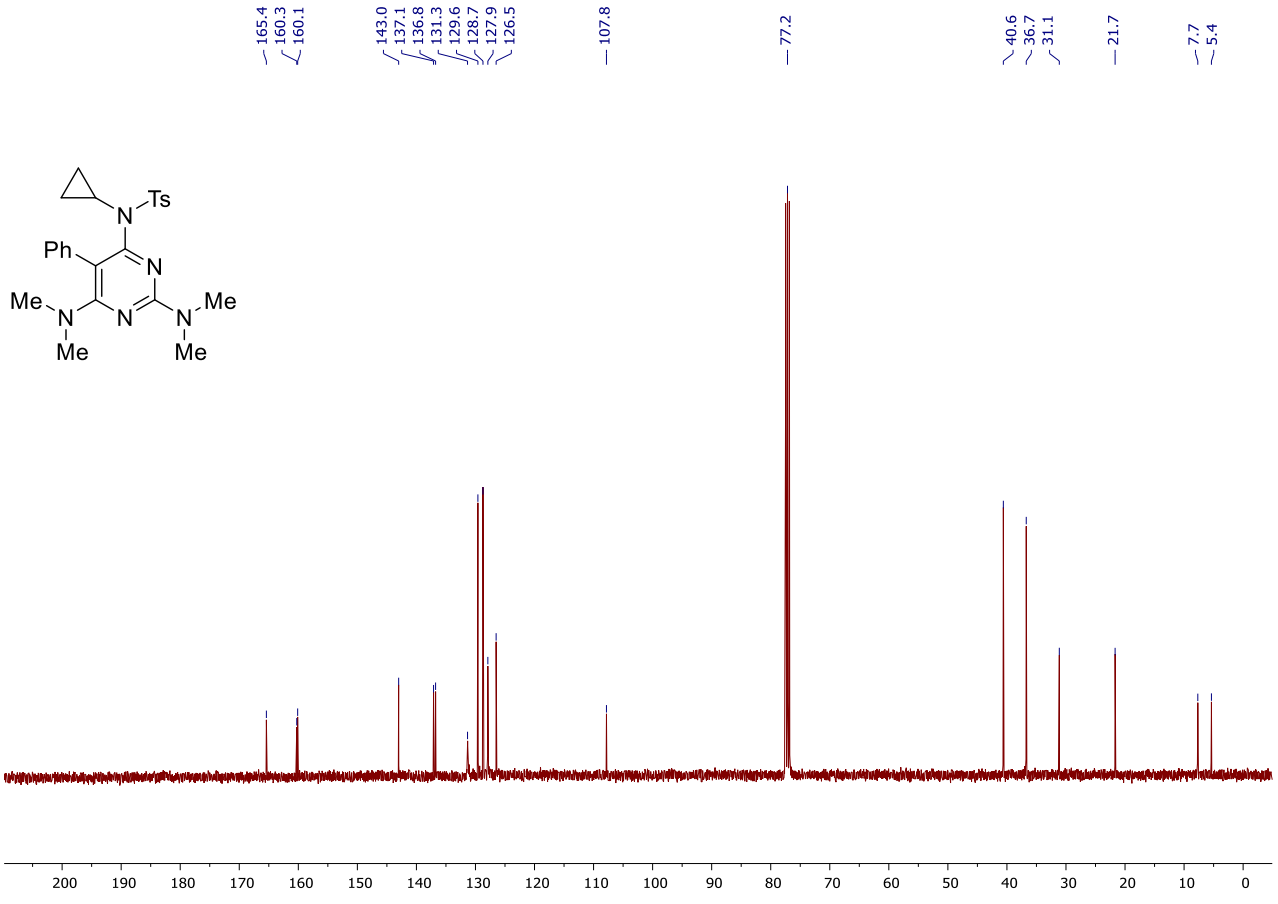


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6g**



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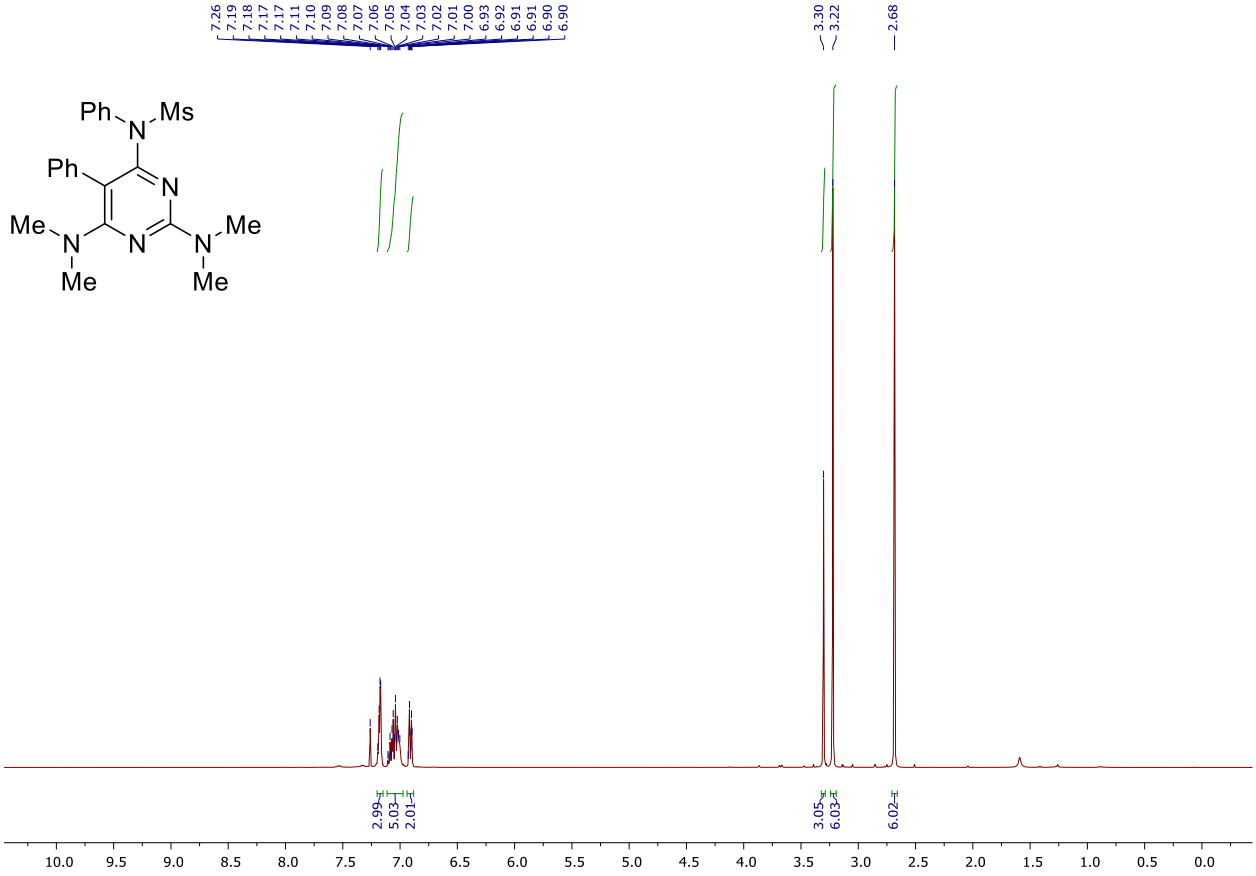

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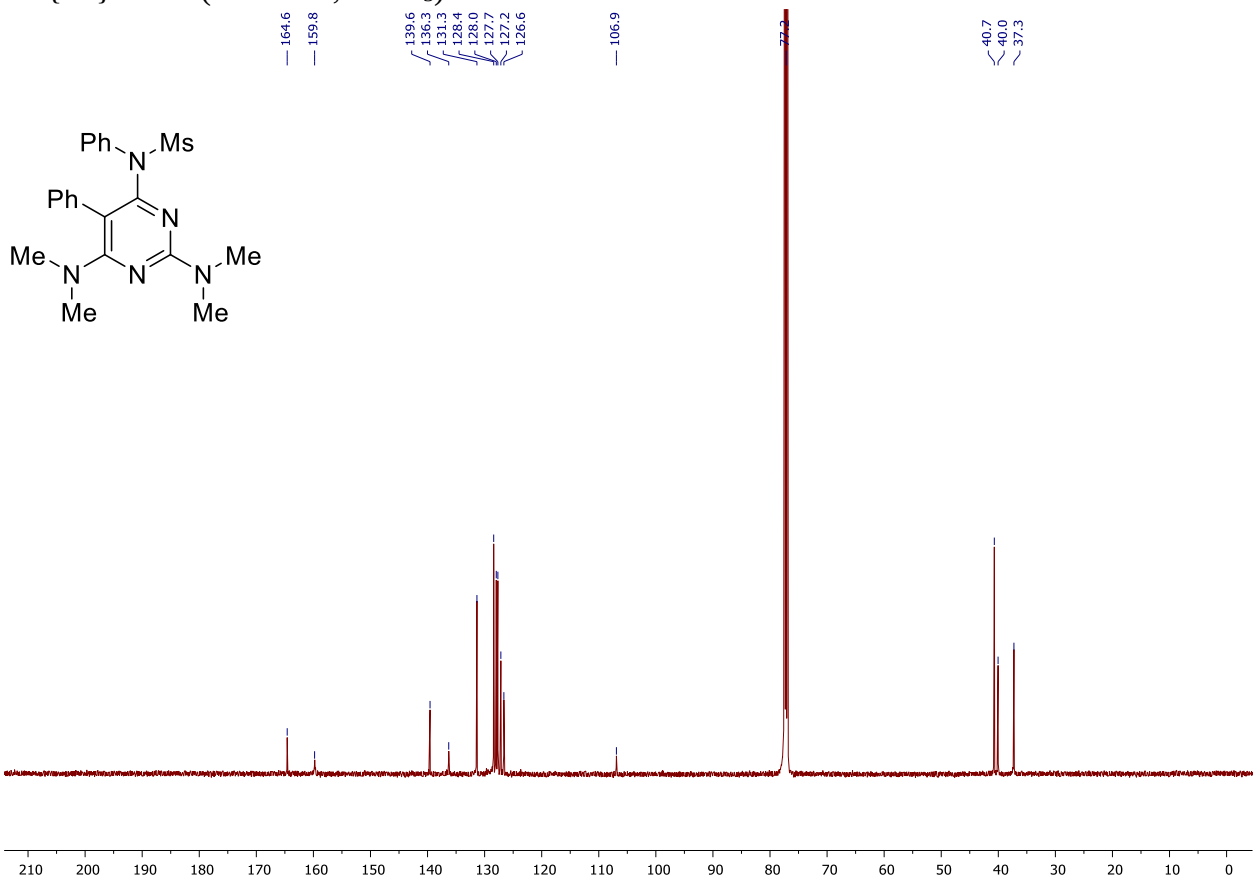

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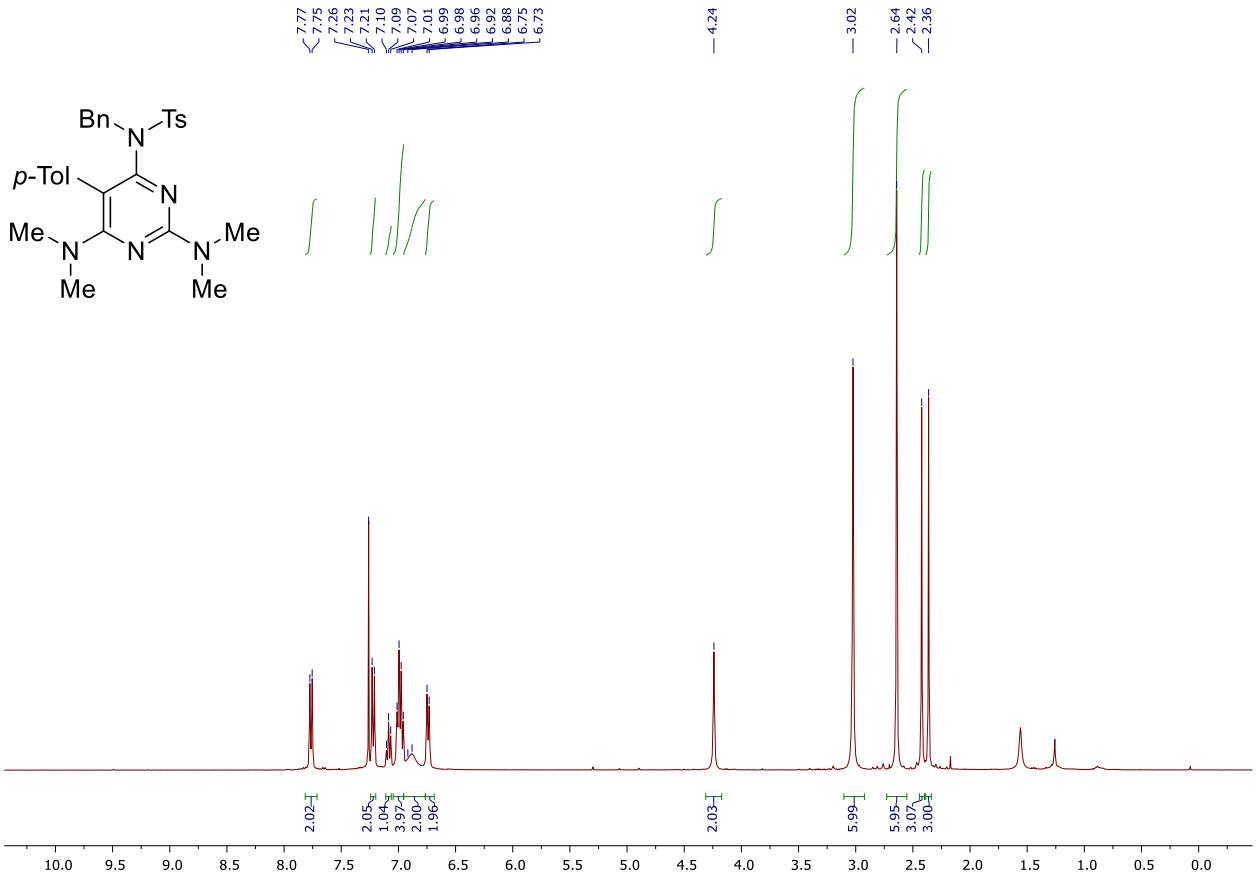

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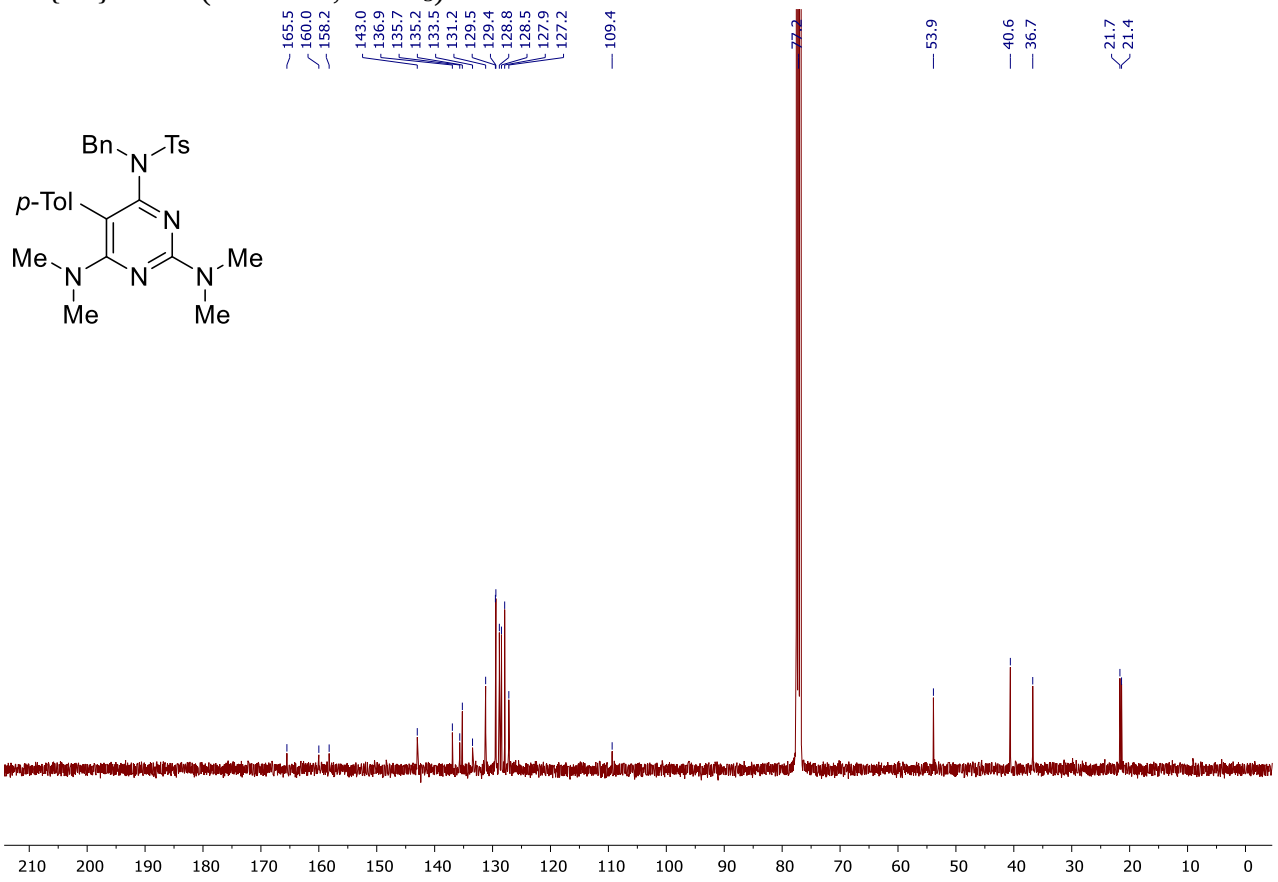

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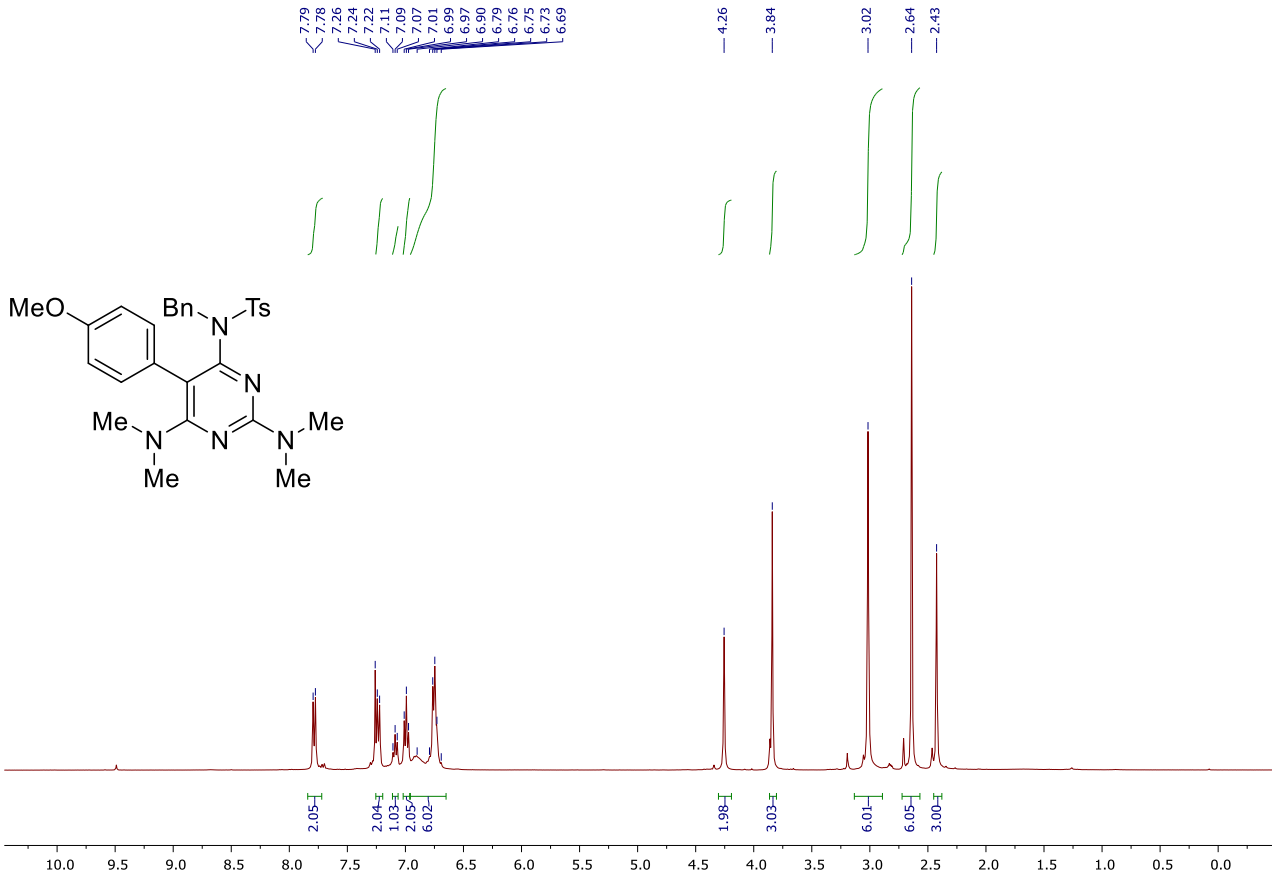

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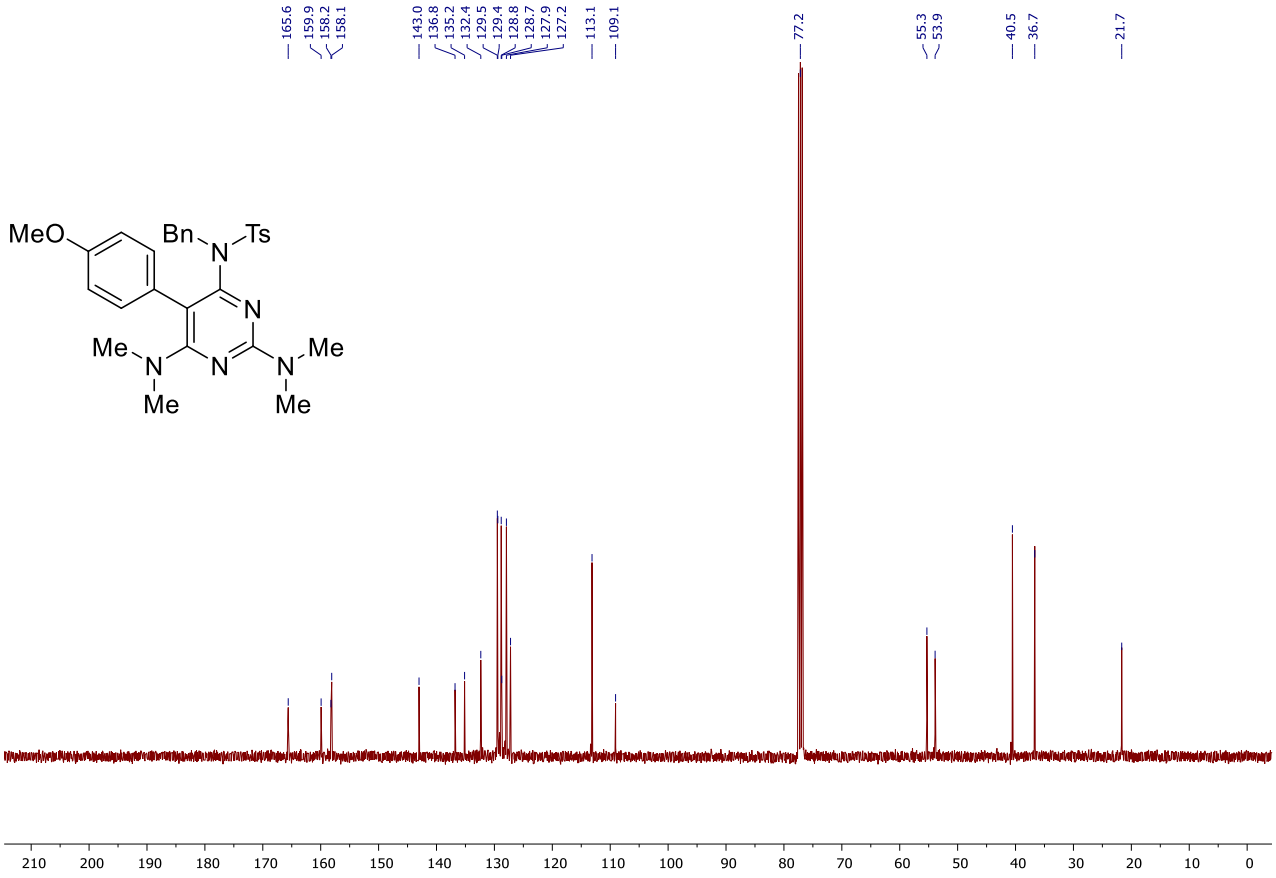

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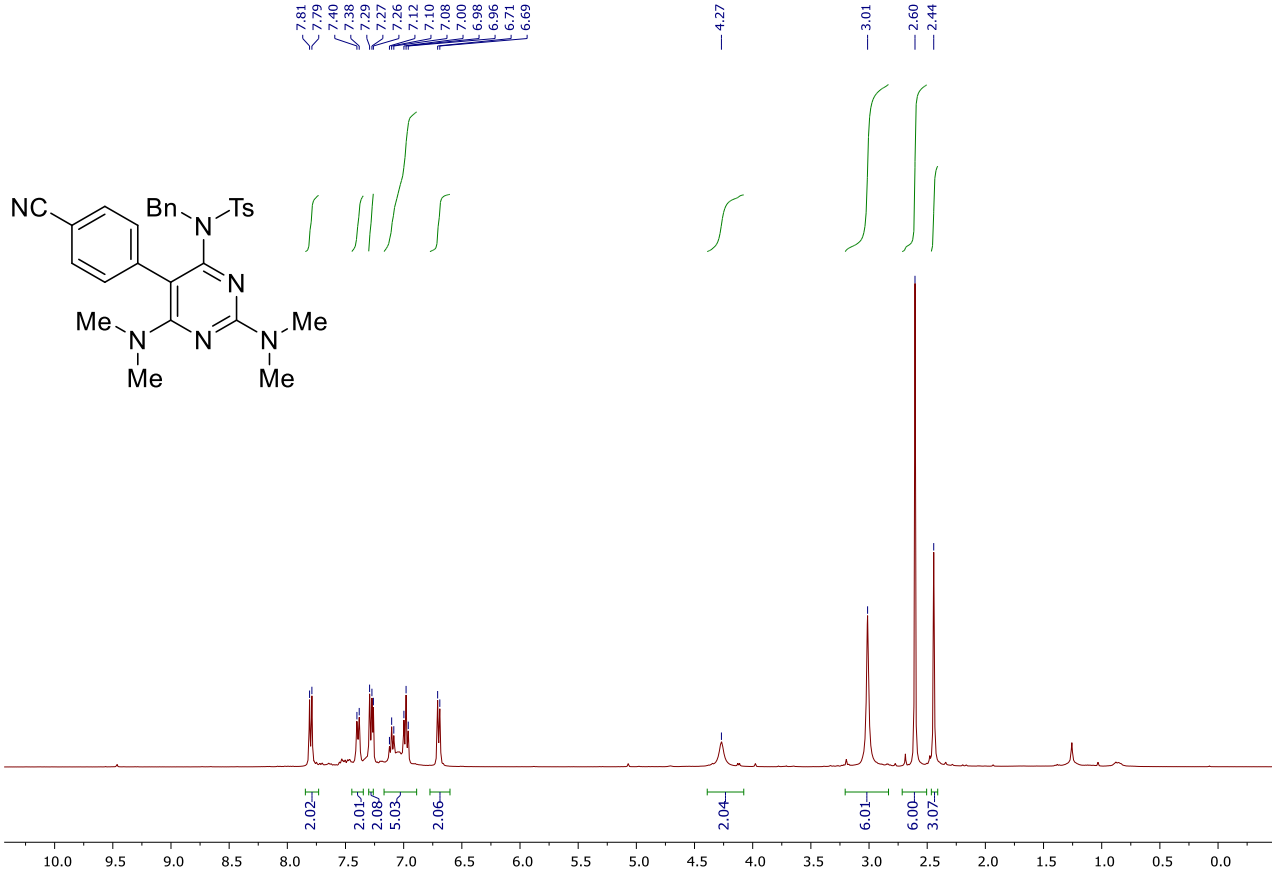

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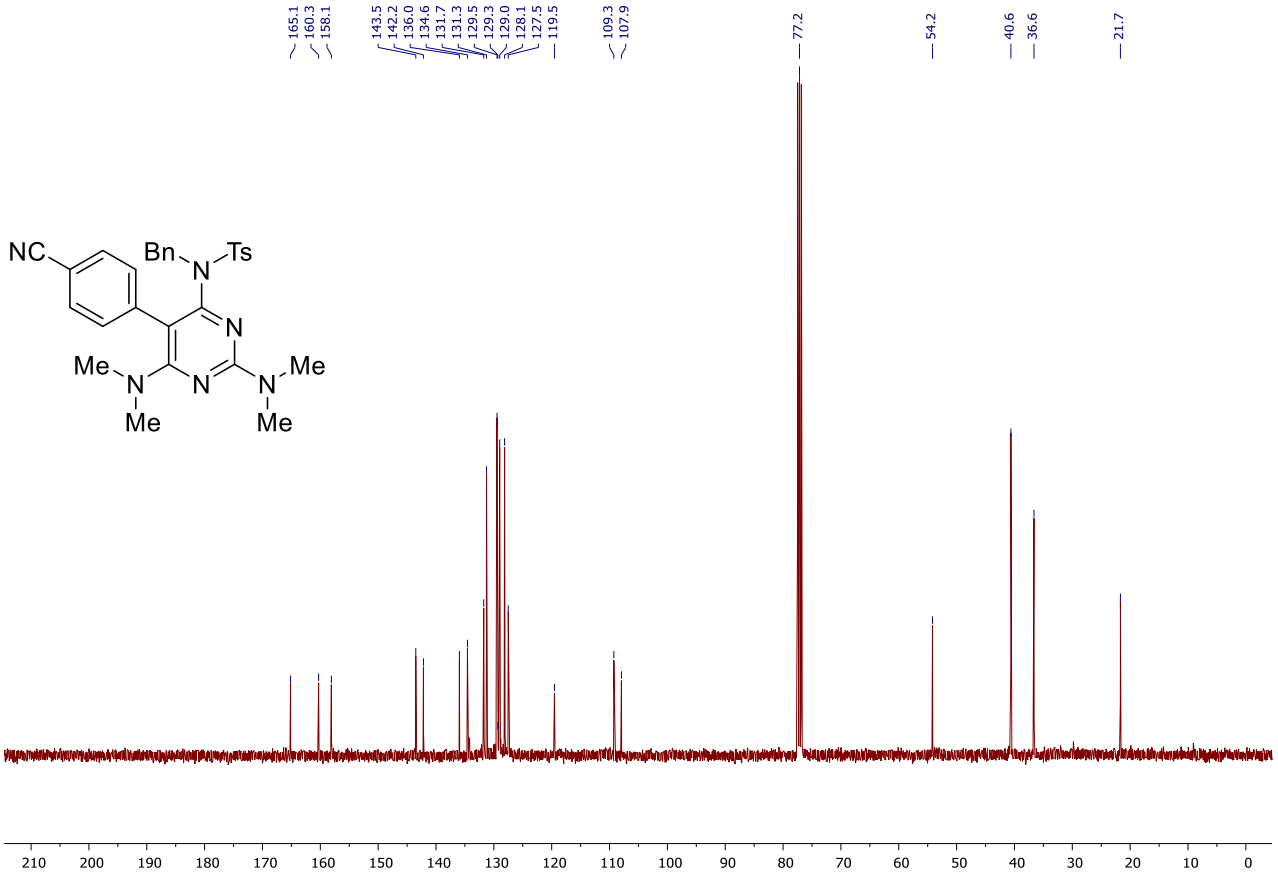

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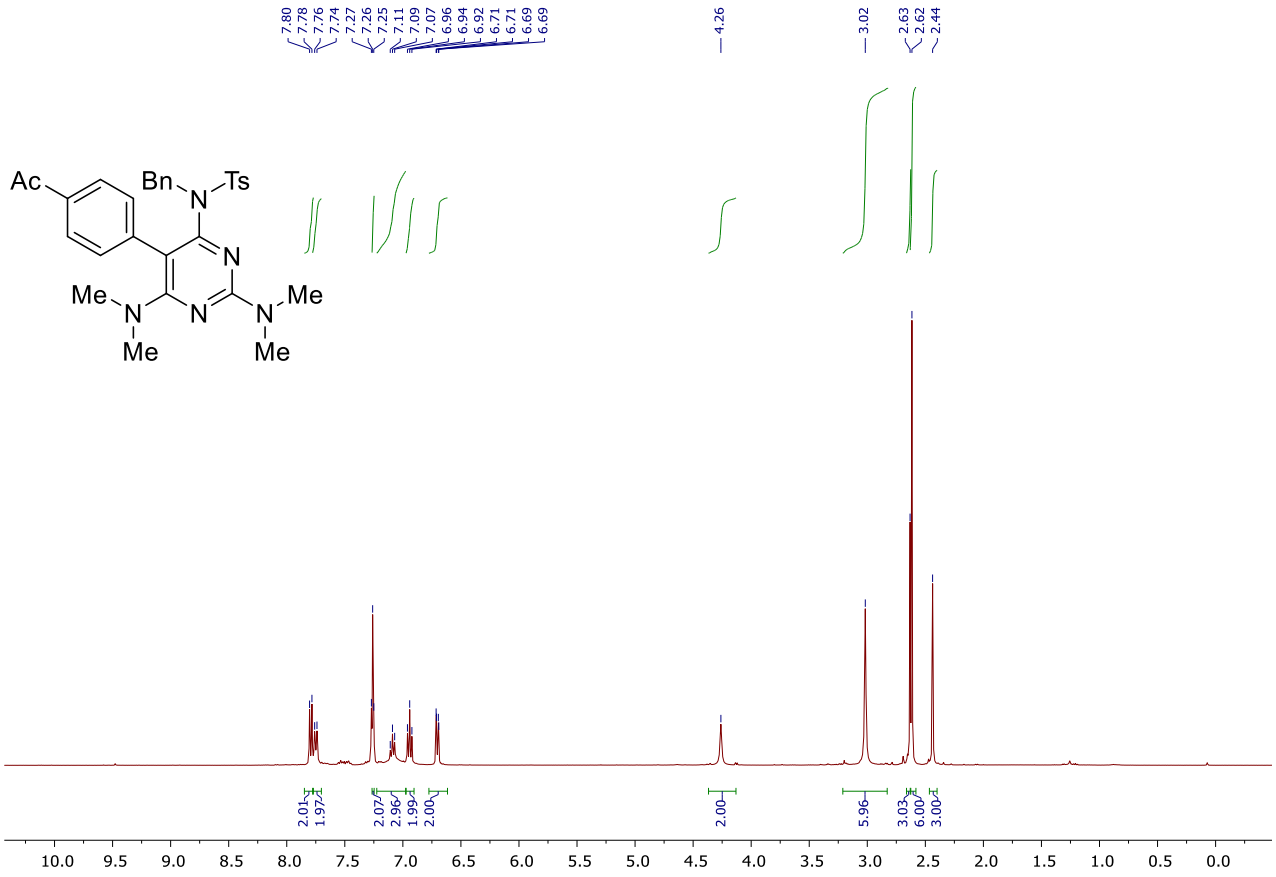

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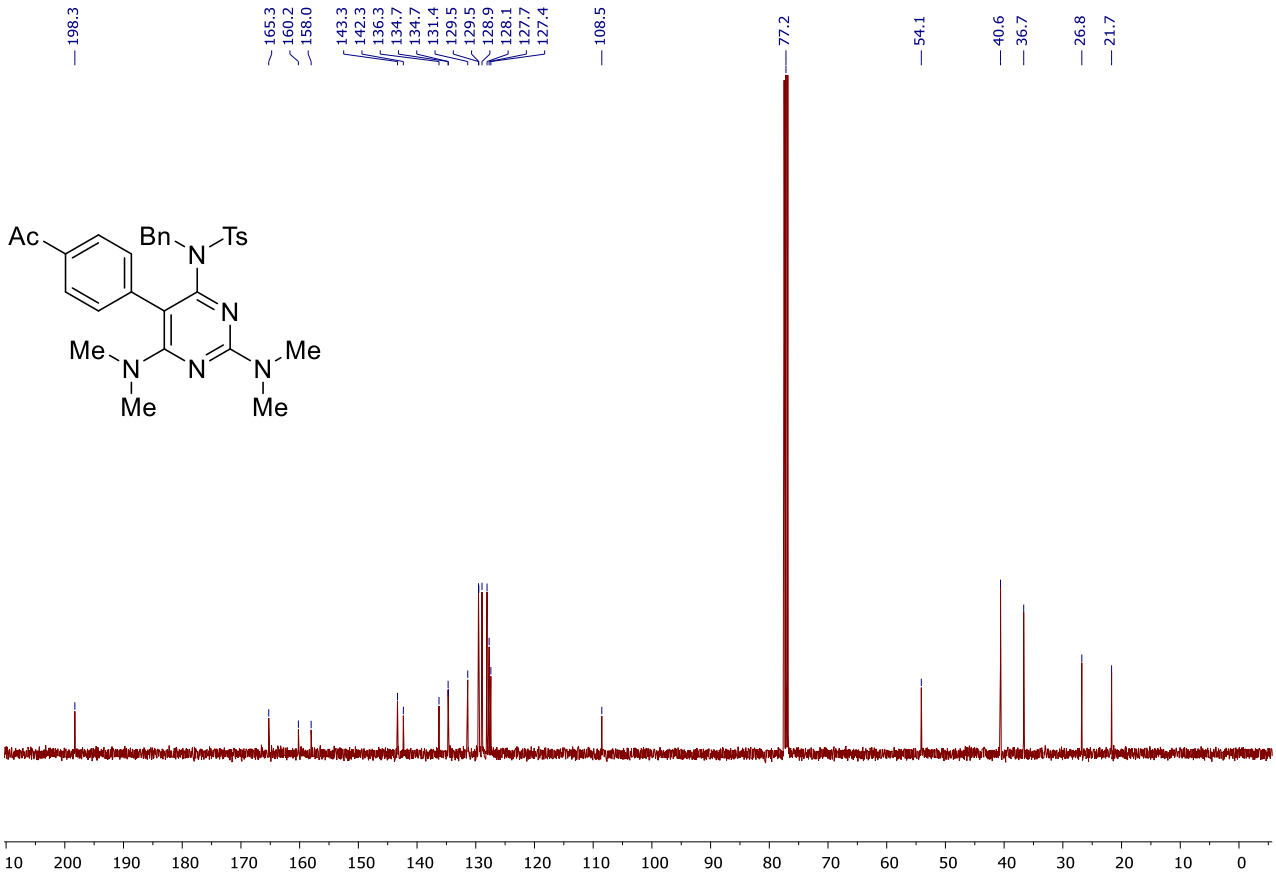
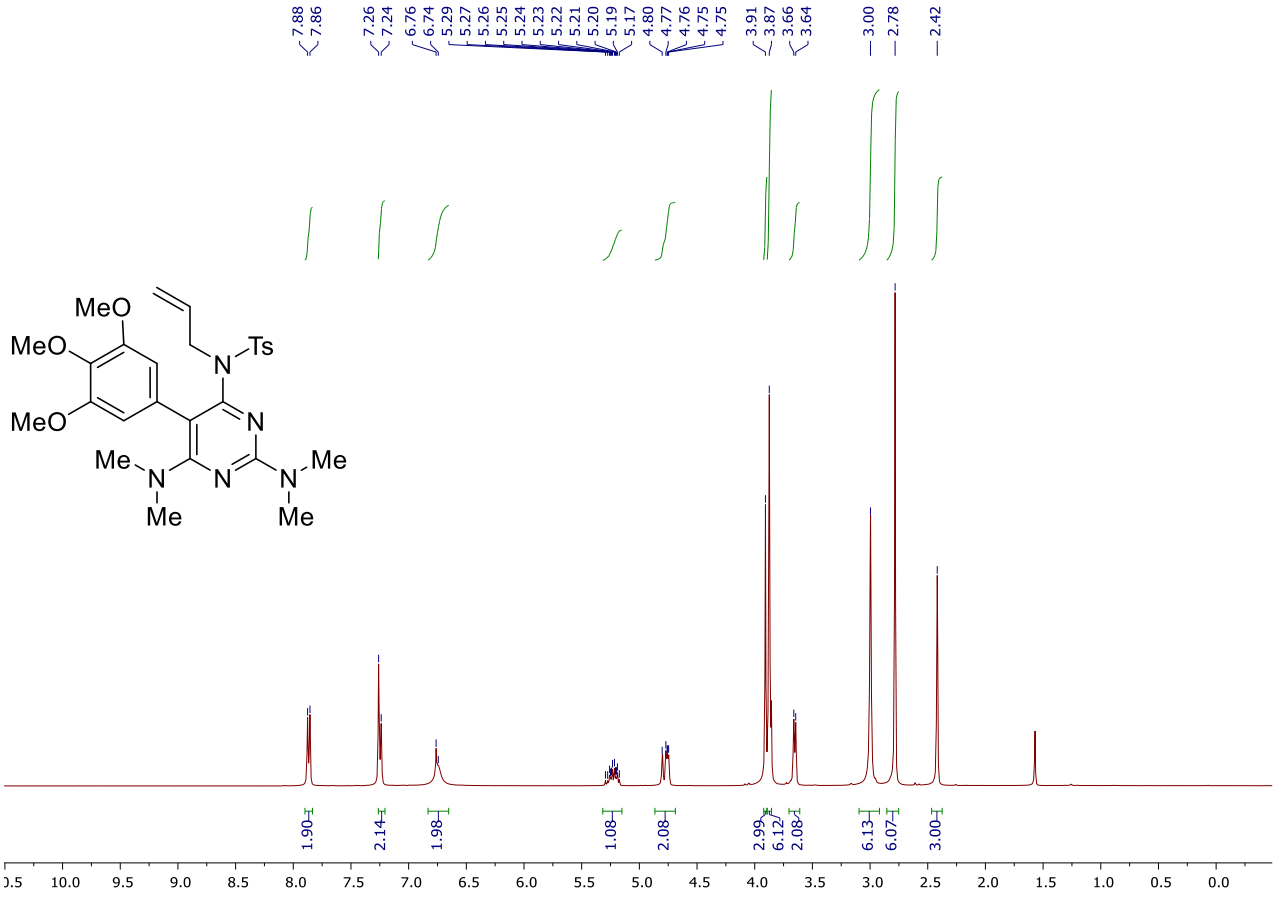
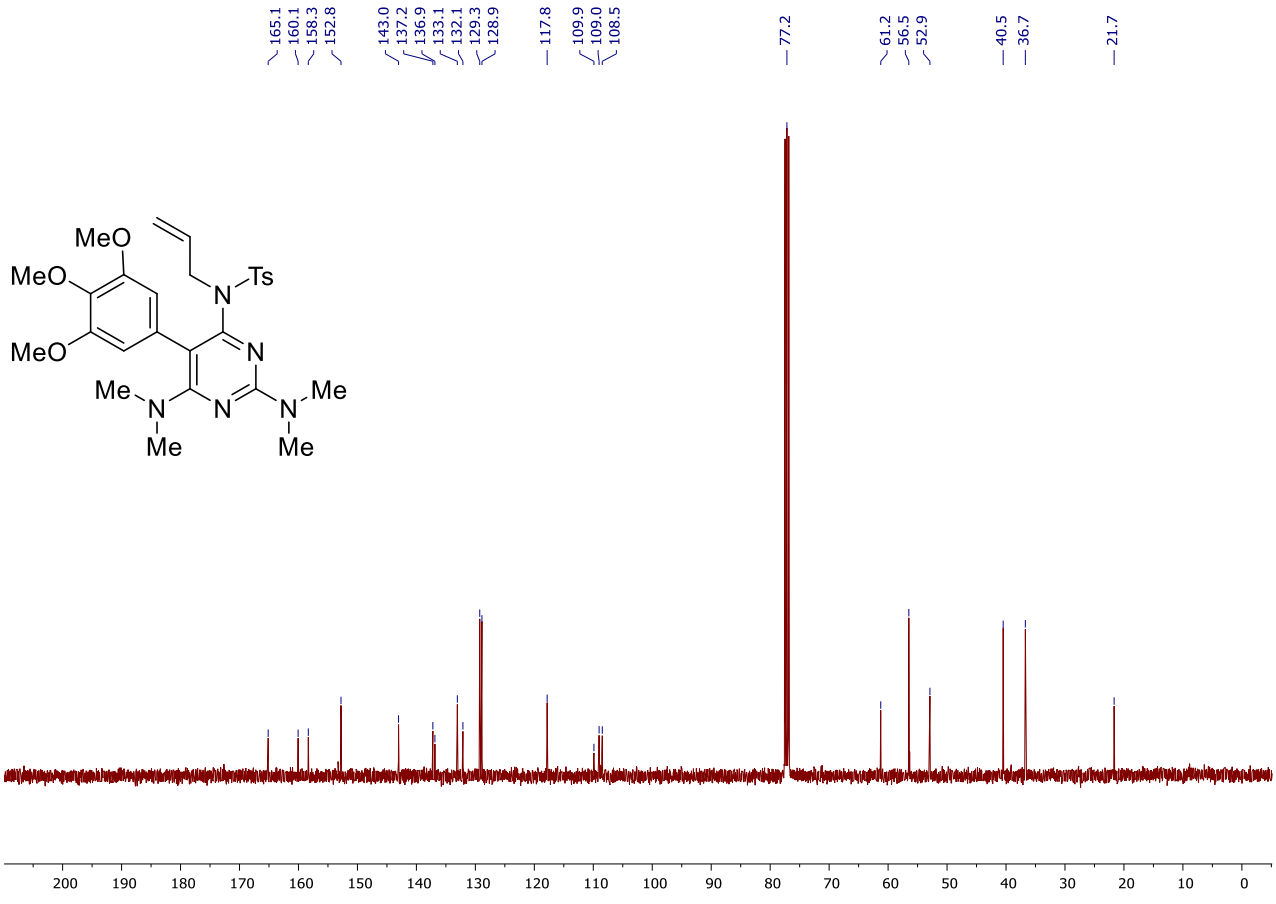


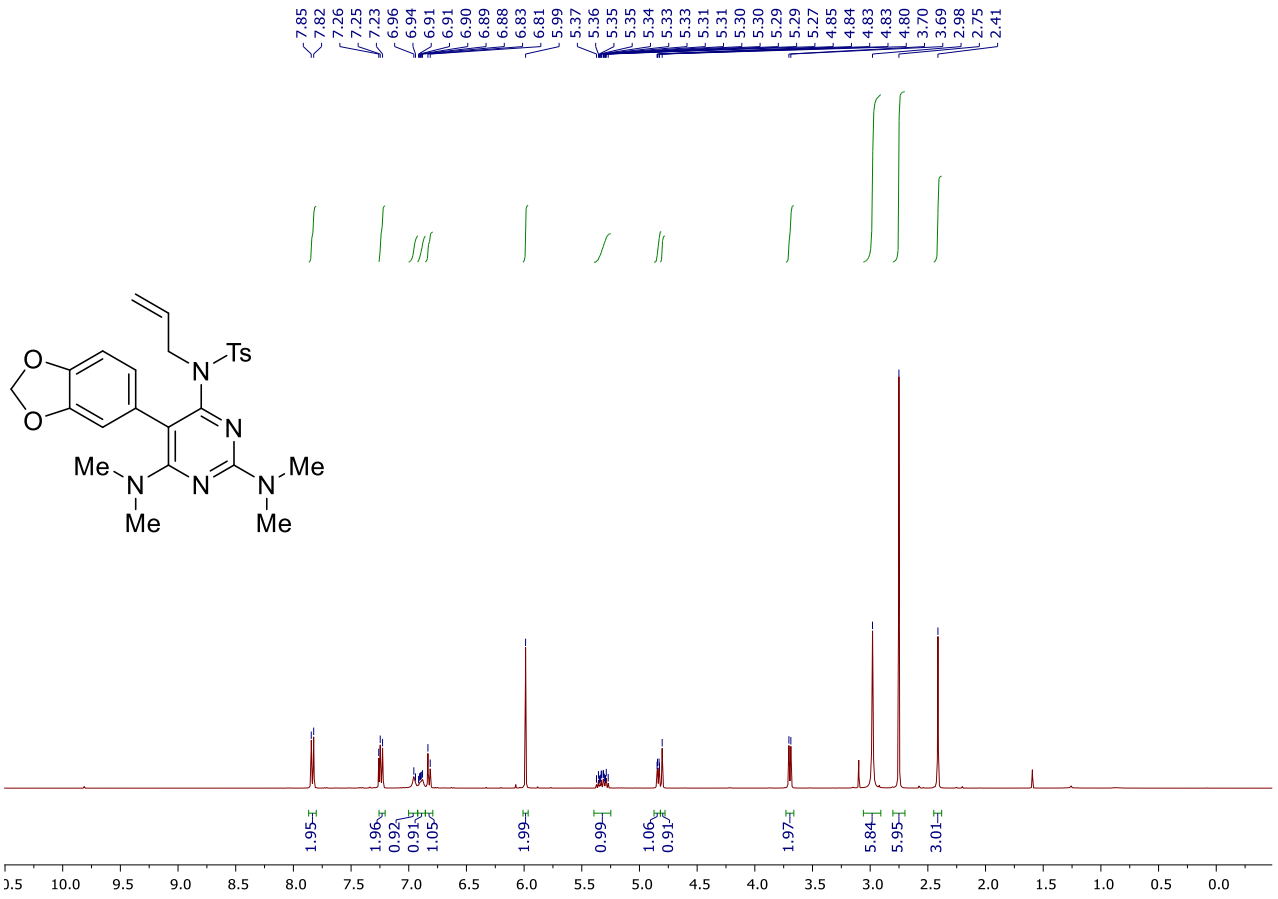
^{1}H NMR (400 MHz, $CDCl_3$) of **6m**



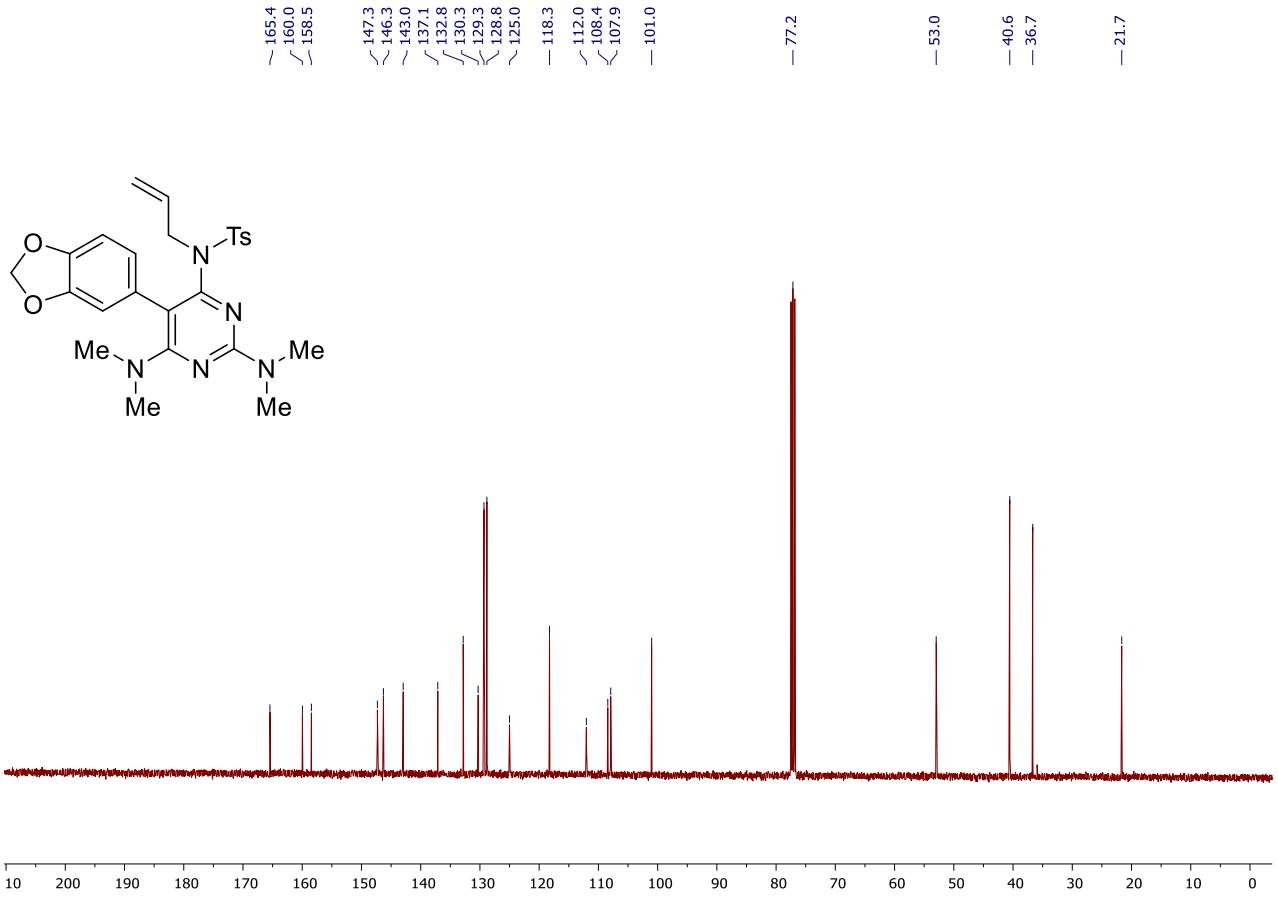
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6m**



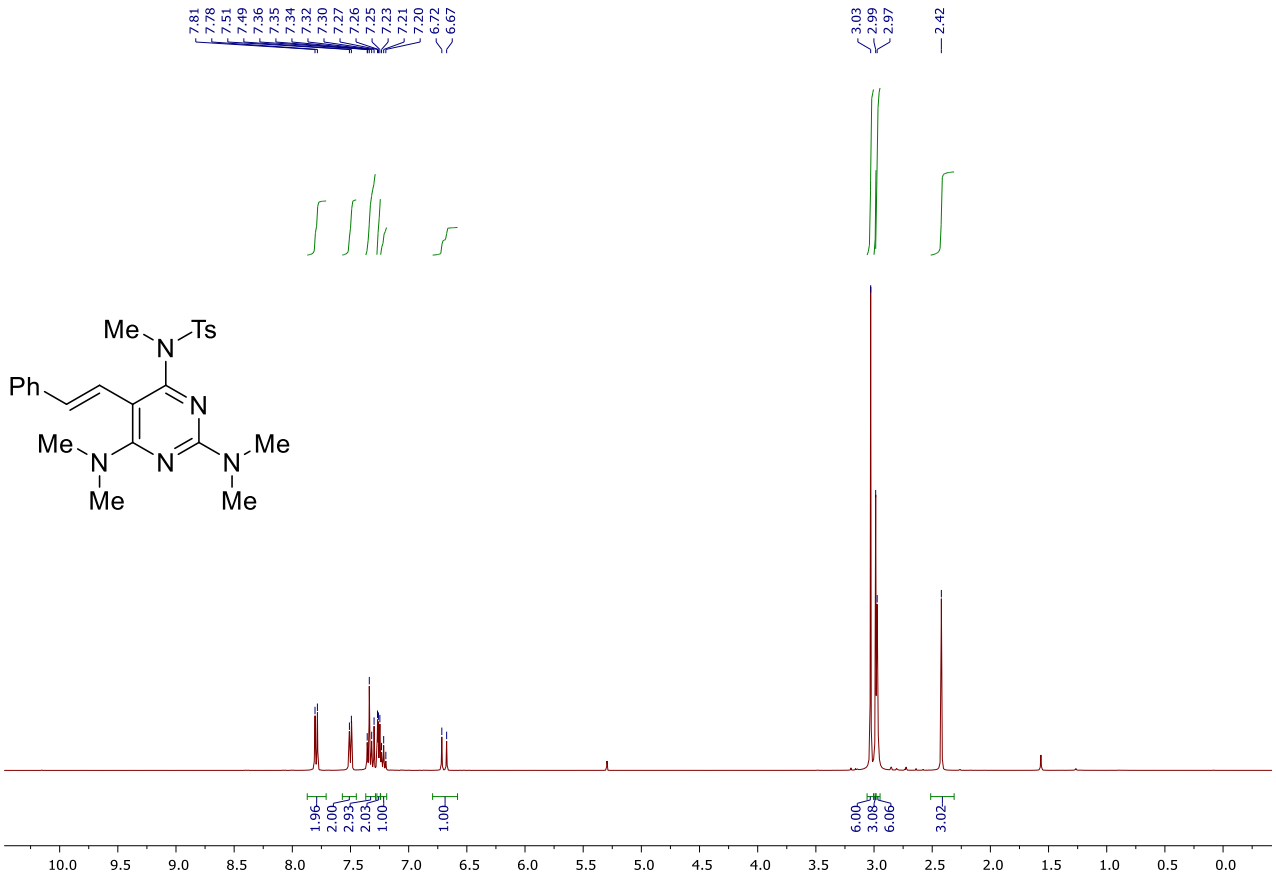
^{1}H NMR (400 MHz, $CDCl_3$) of **6n**



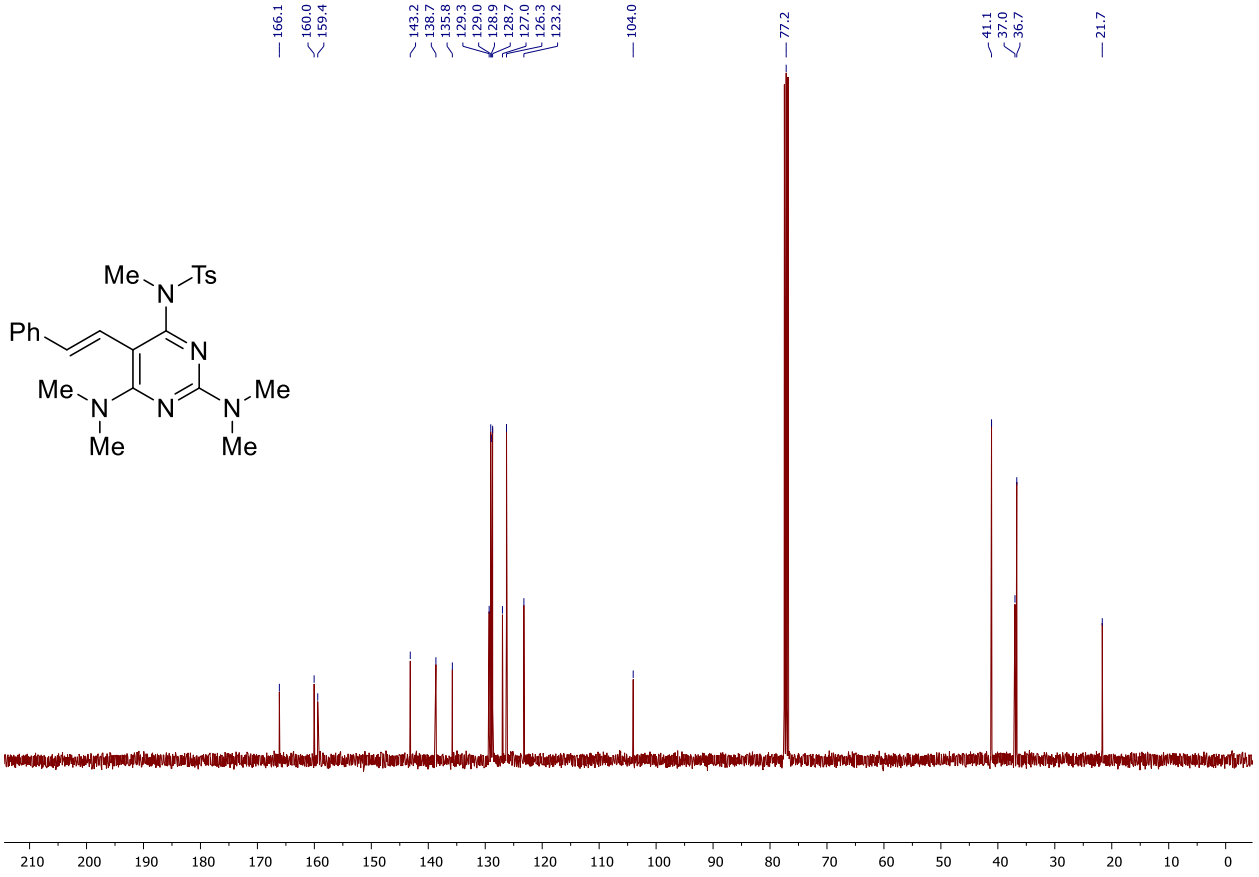
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6n**



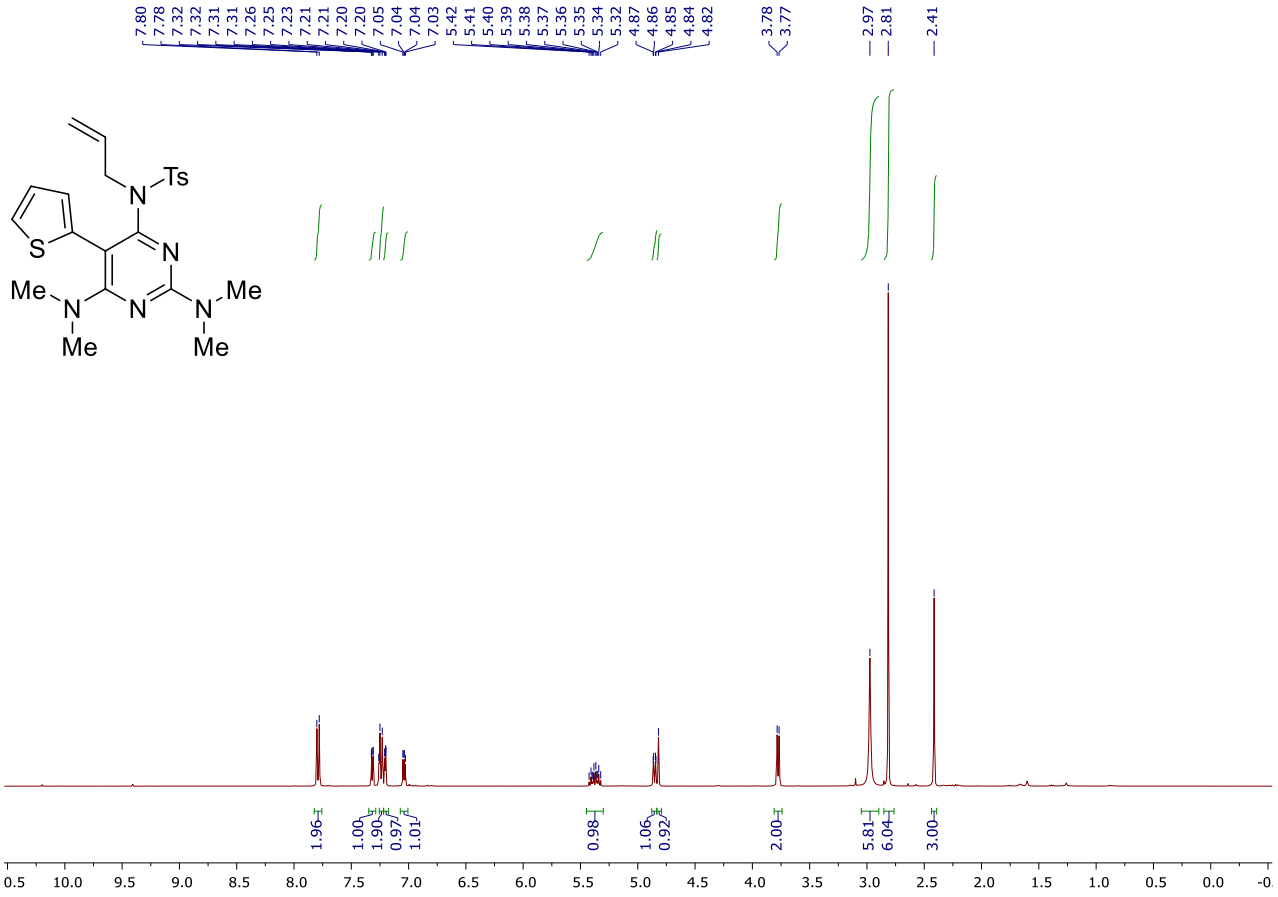
^{1}H NMR (400 MHz, $CDCl_3$) of **6o**



^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6o**



^{1}H NMR (400 MHz, $CDCl_3$) of **6p**



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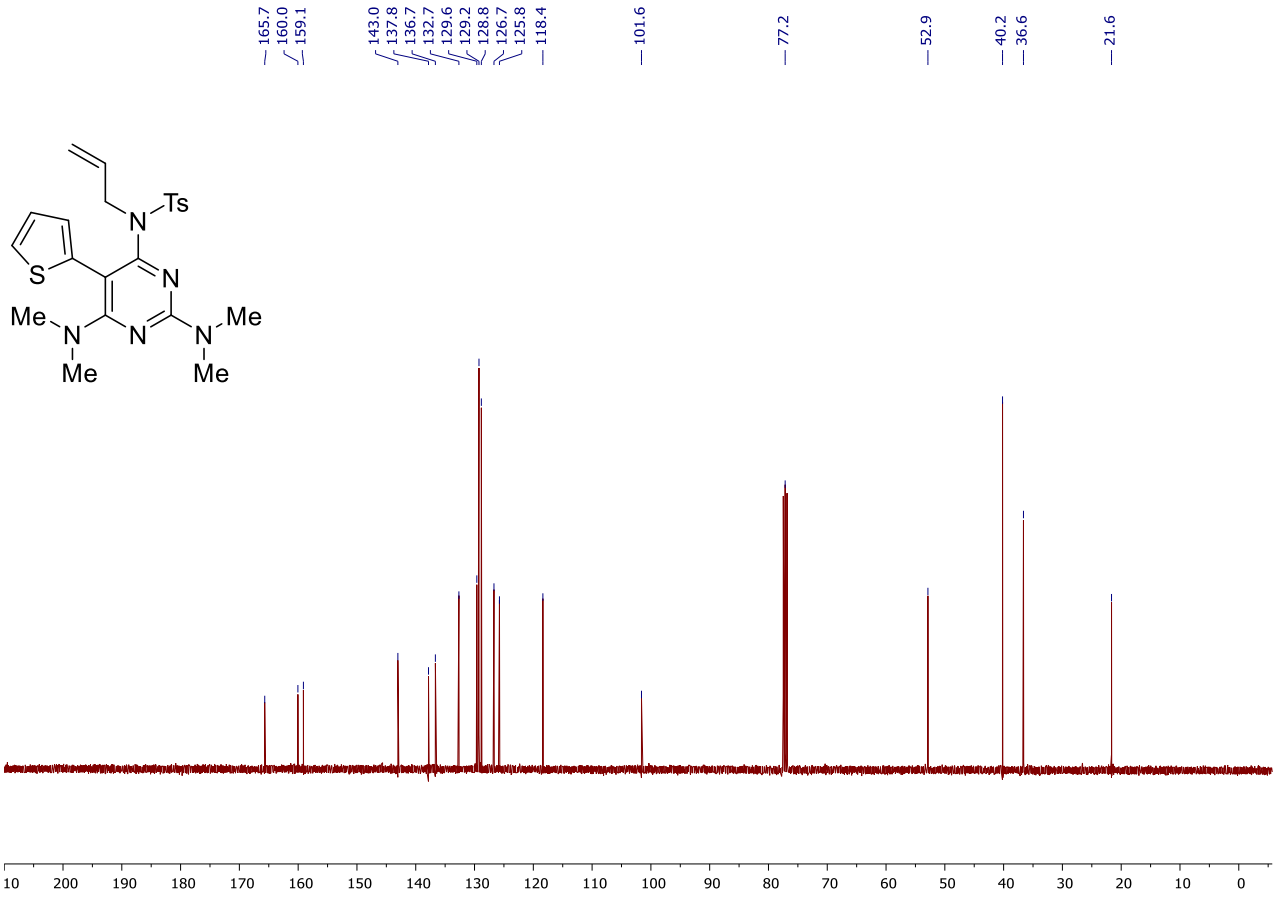
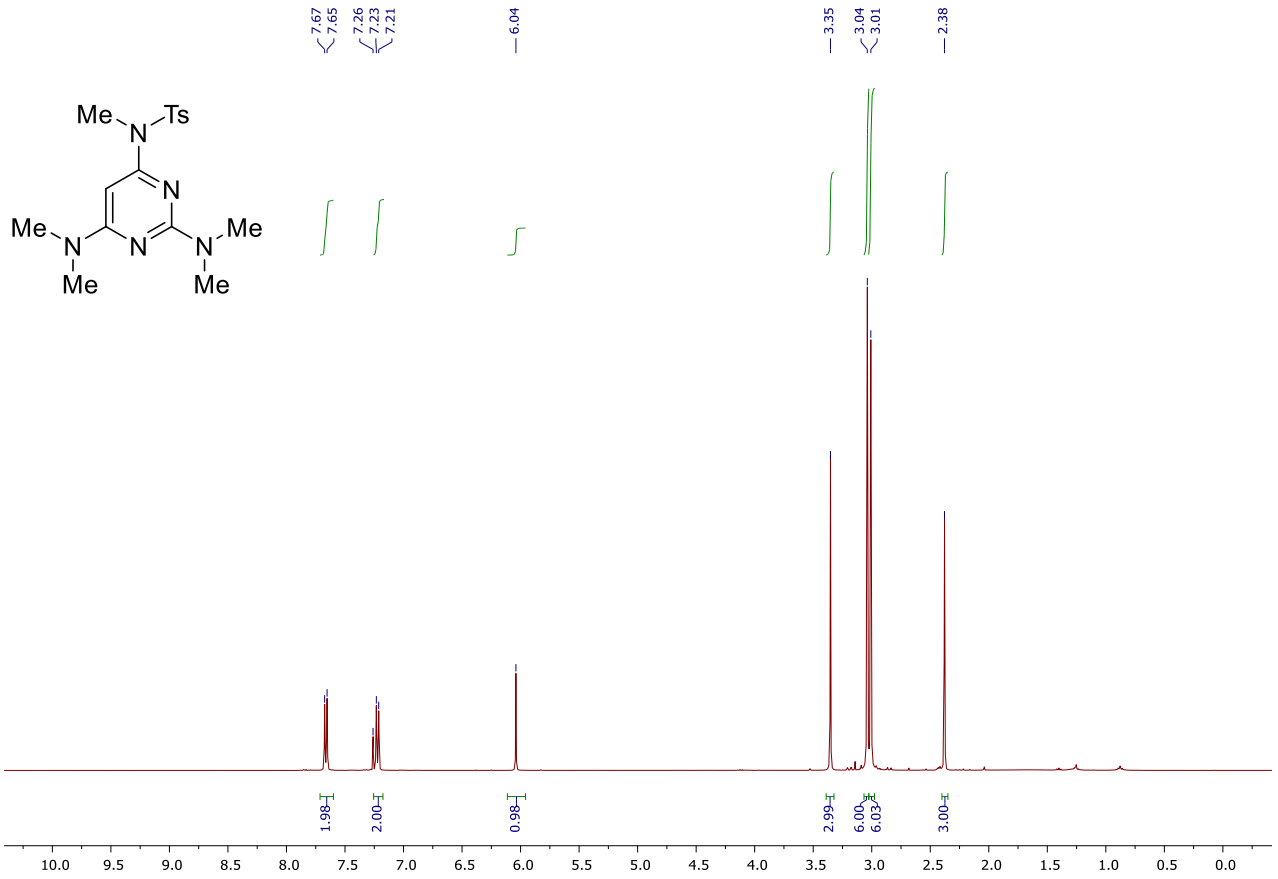
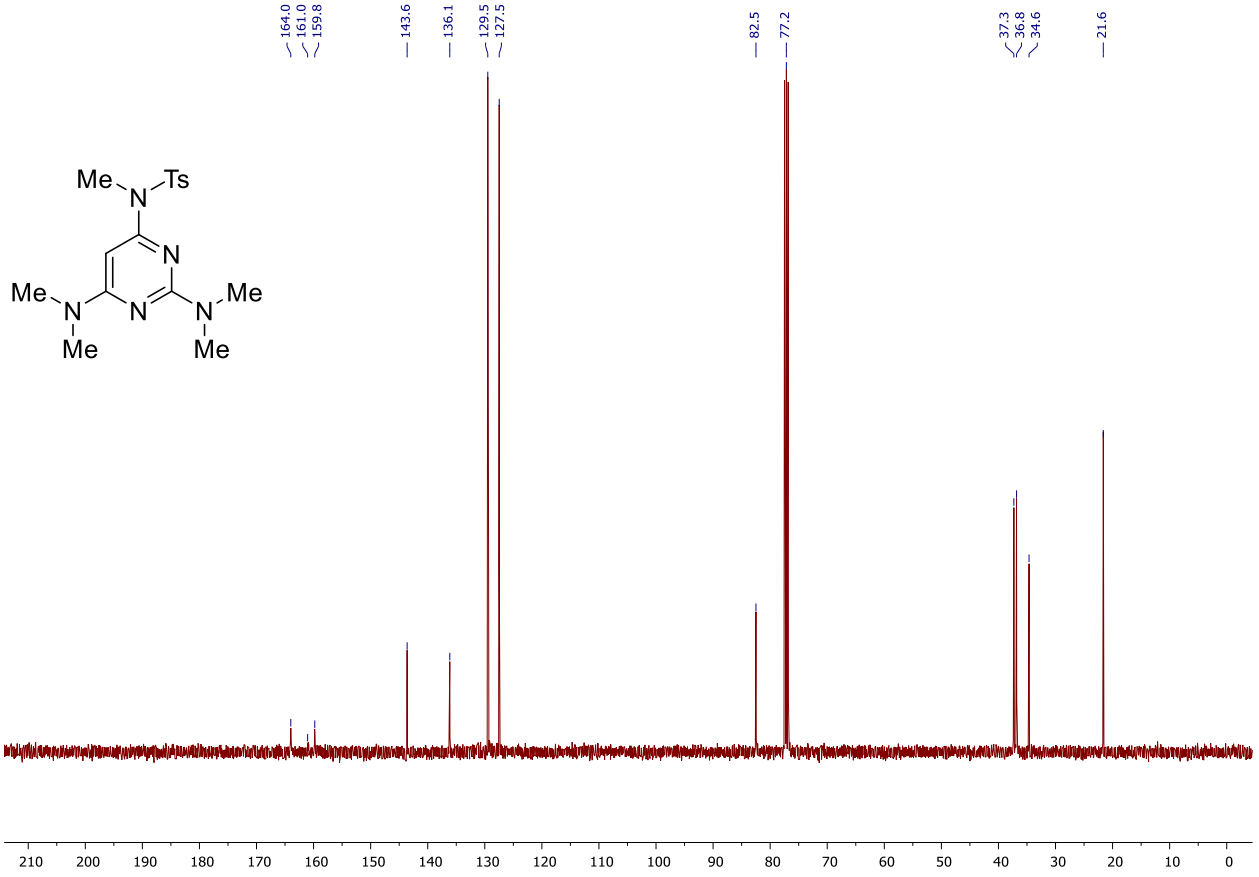


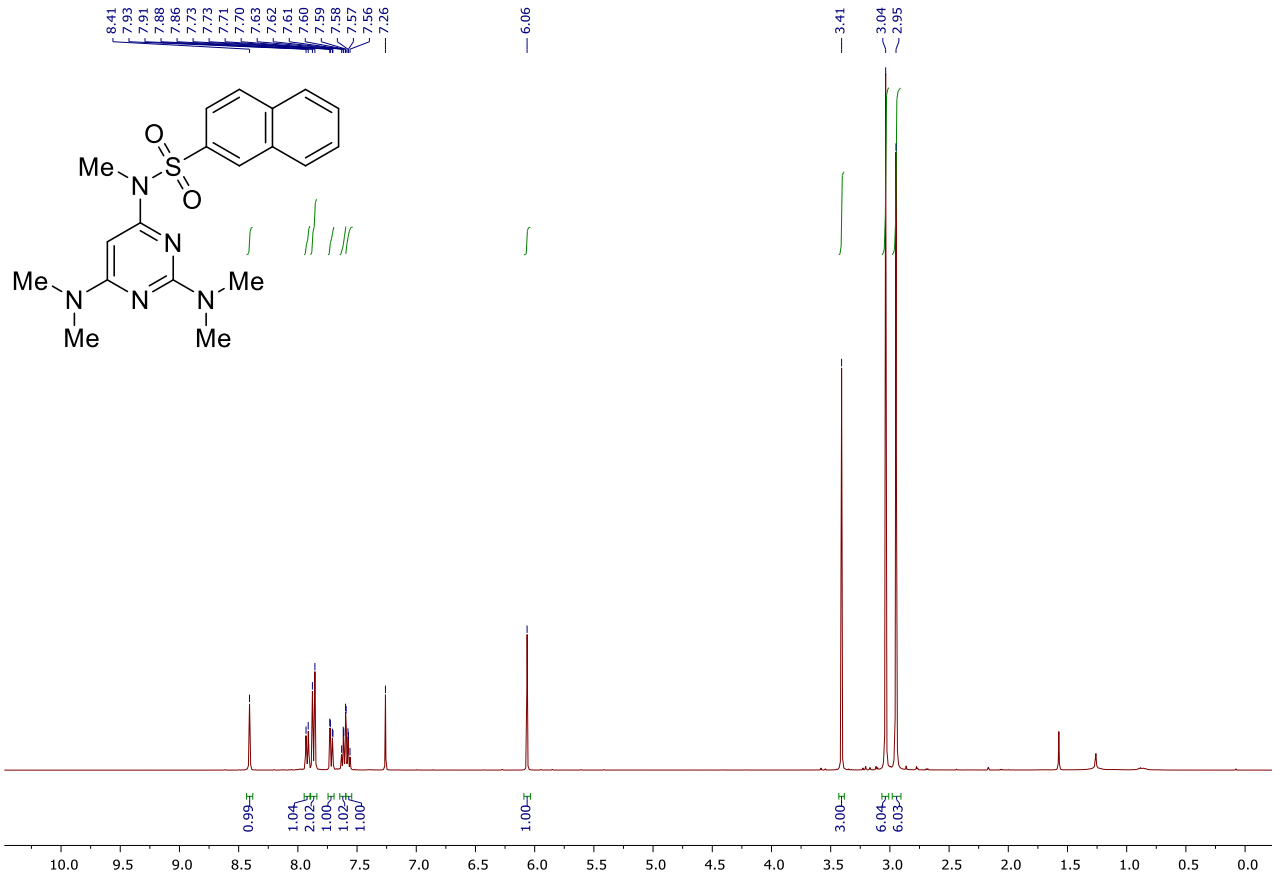
^{1}H NMR (400 MHz, $CDCl_3$) of **6q**



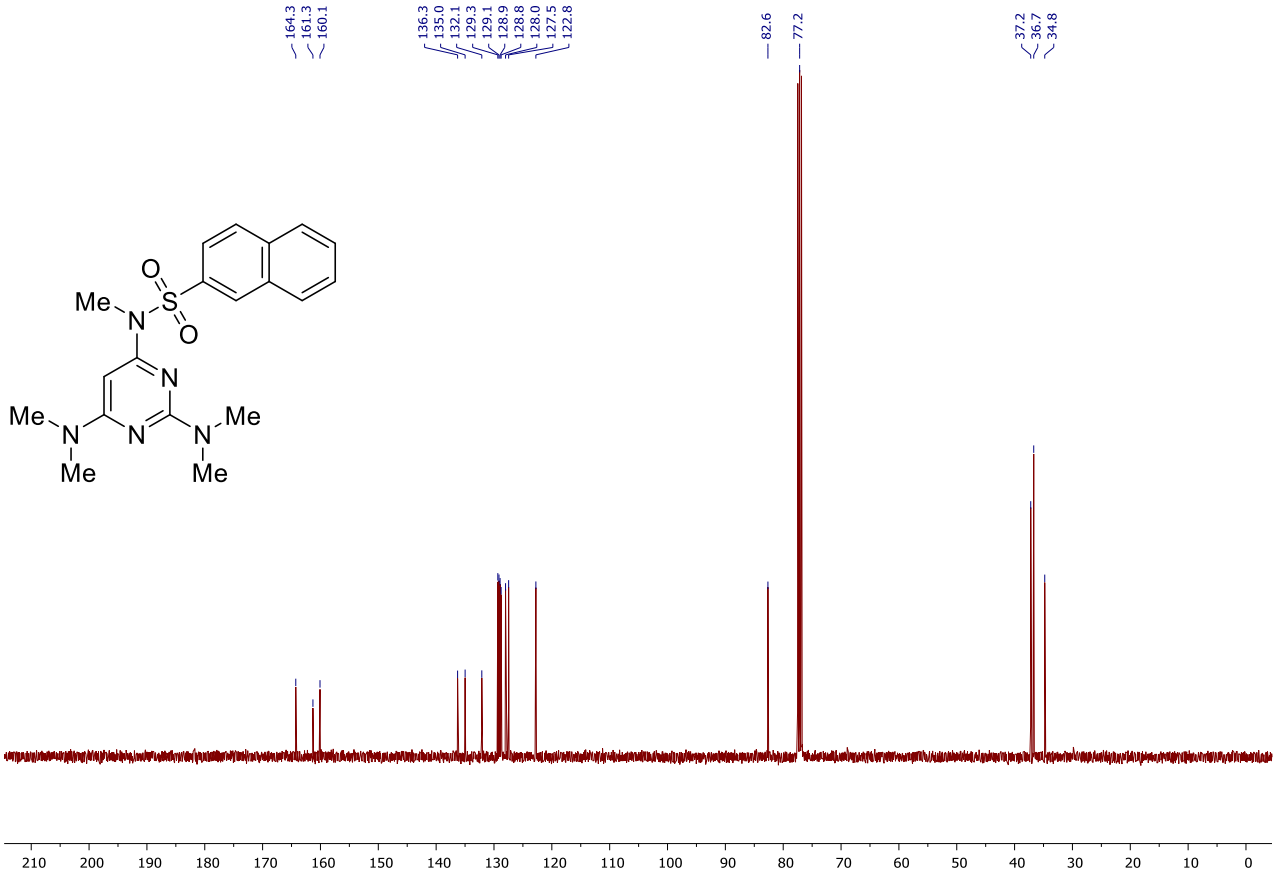
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6q**



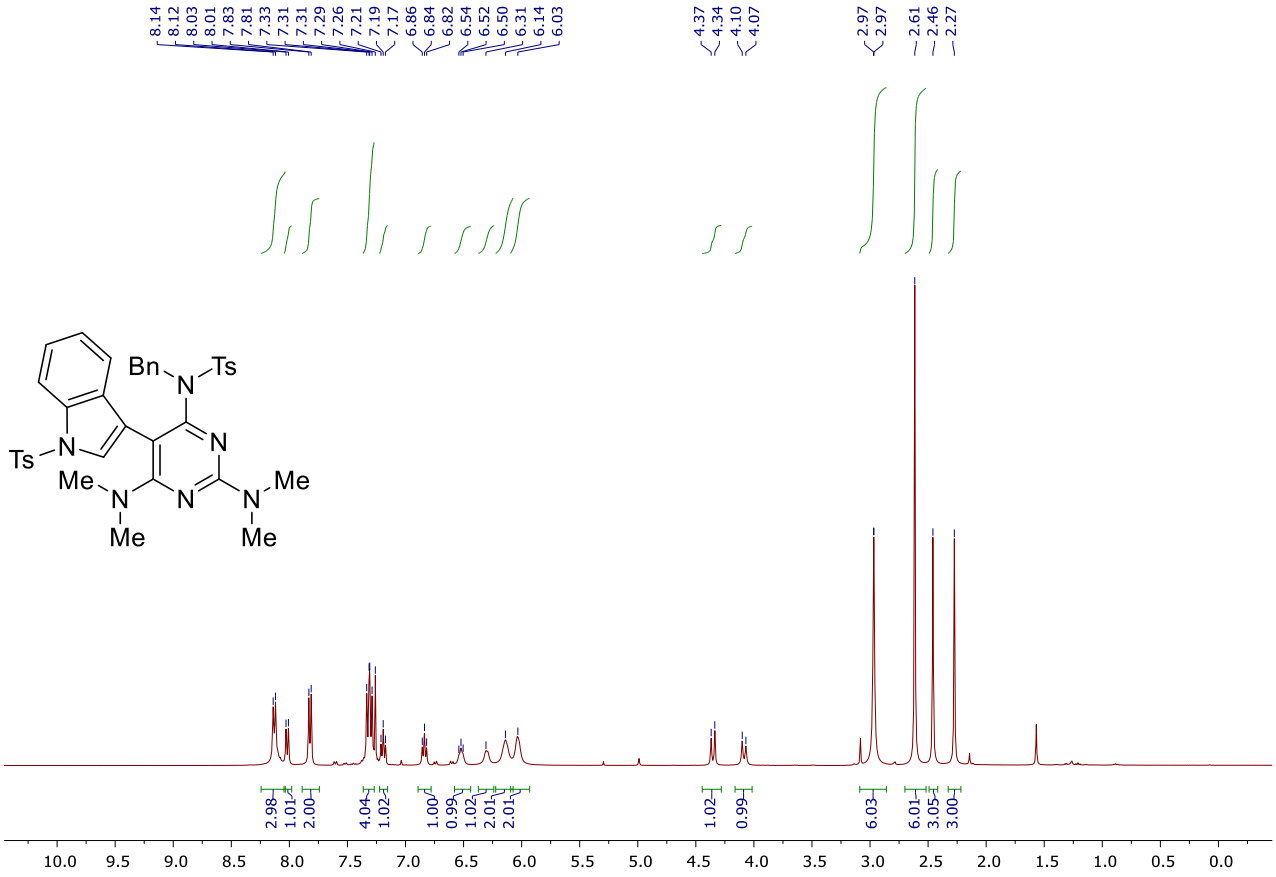
^{1}H NMR (400 MHz, $CDCl_3$) of **6r**



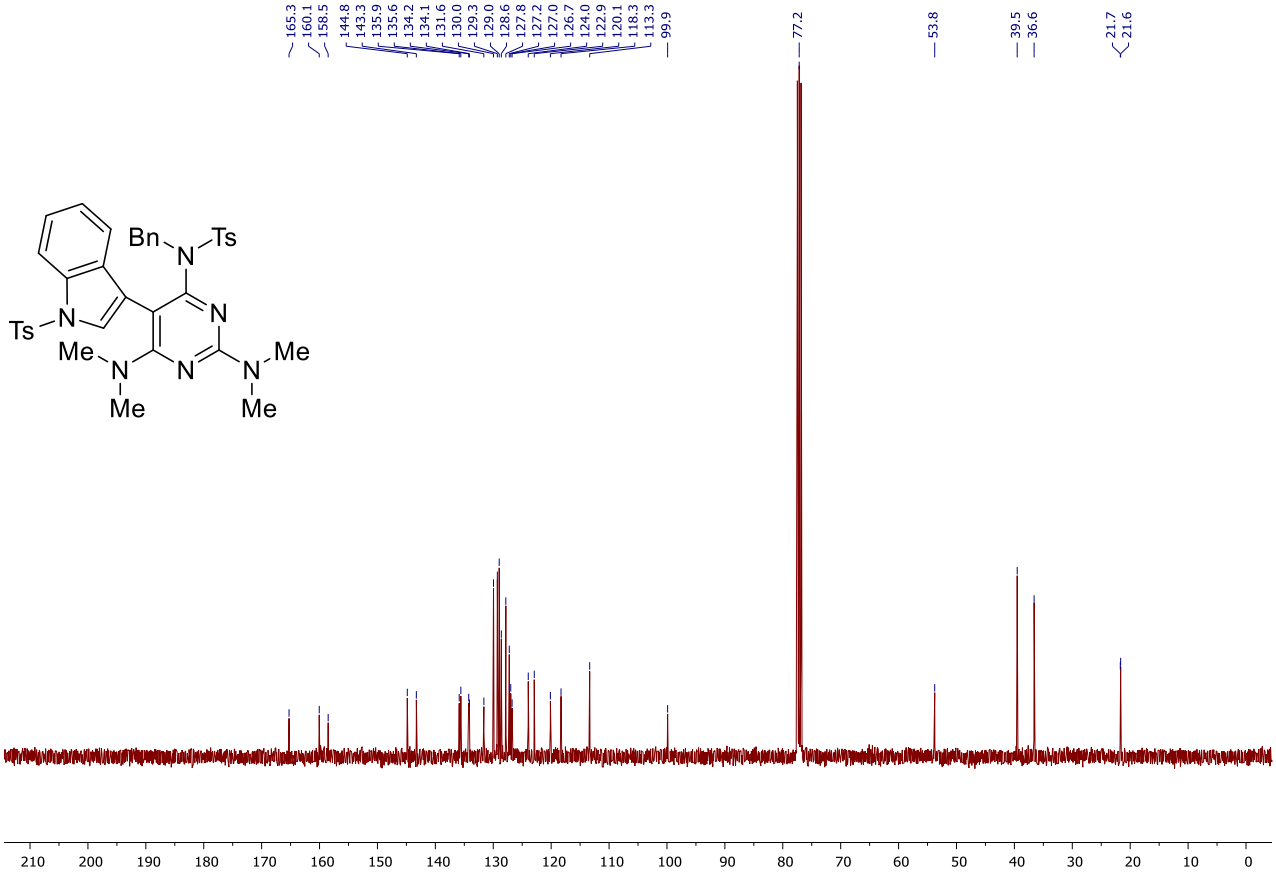
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6r**



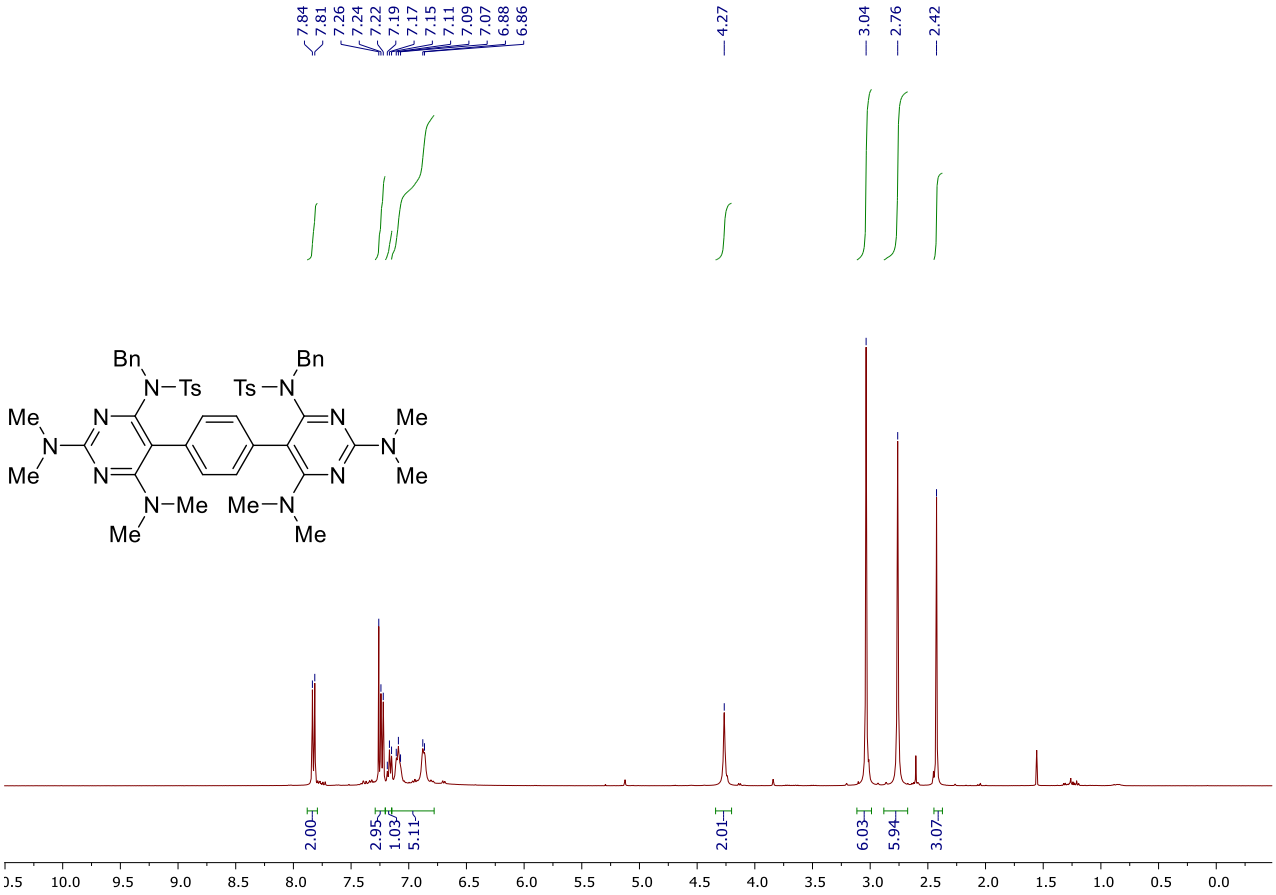
^{1}H NMR (400 MHz, $CDCl_3$) of **6s**



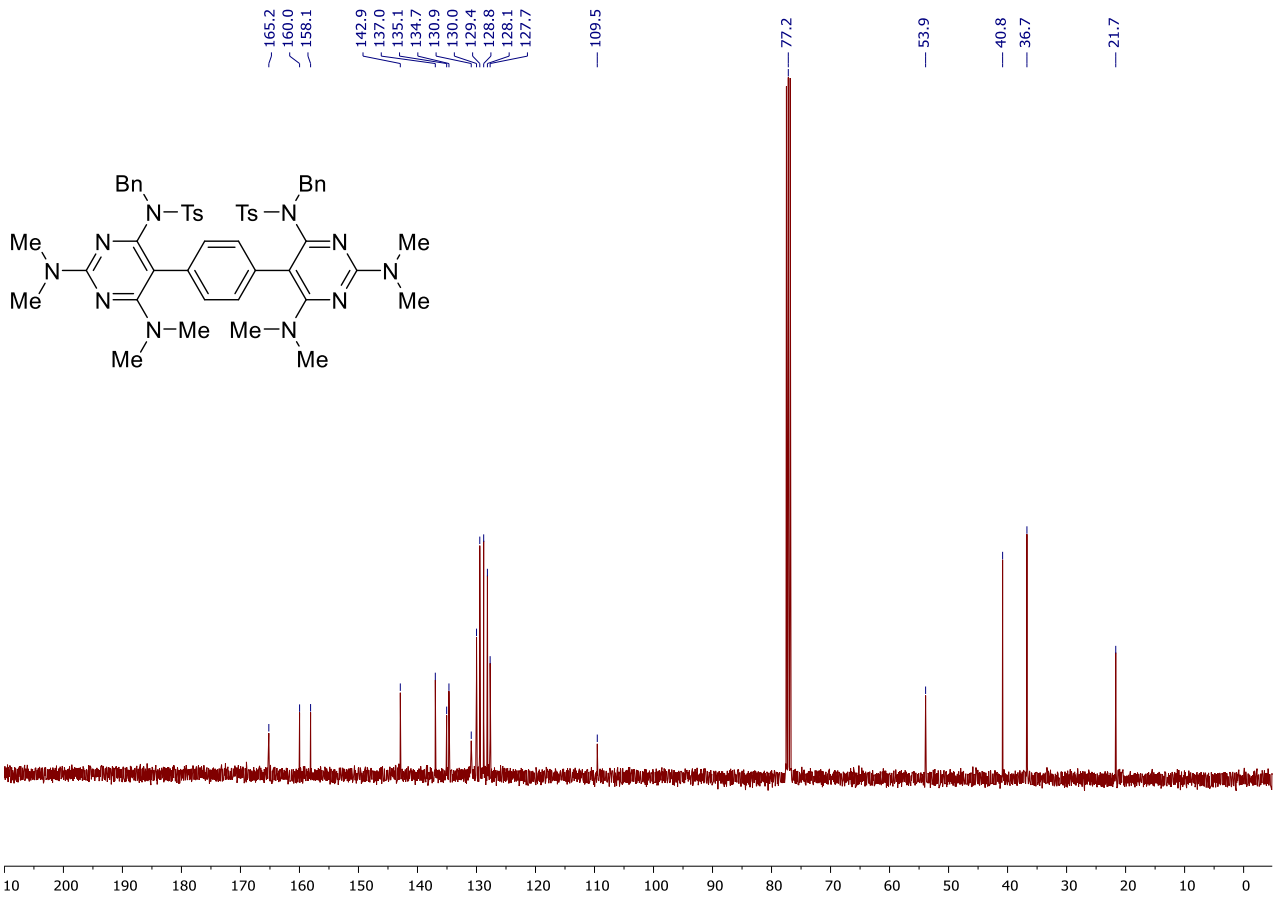
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6s**



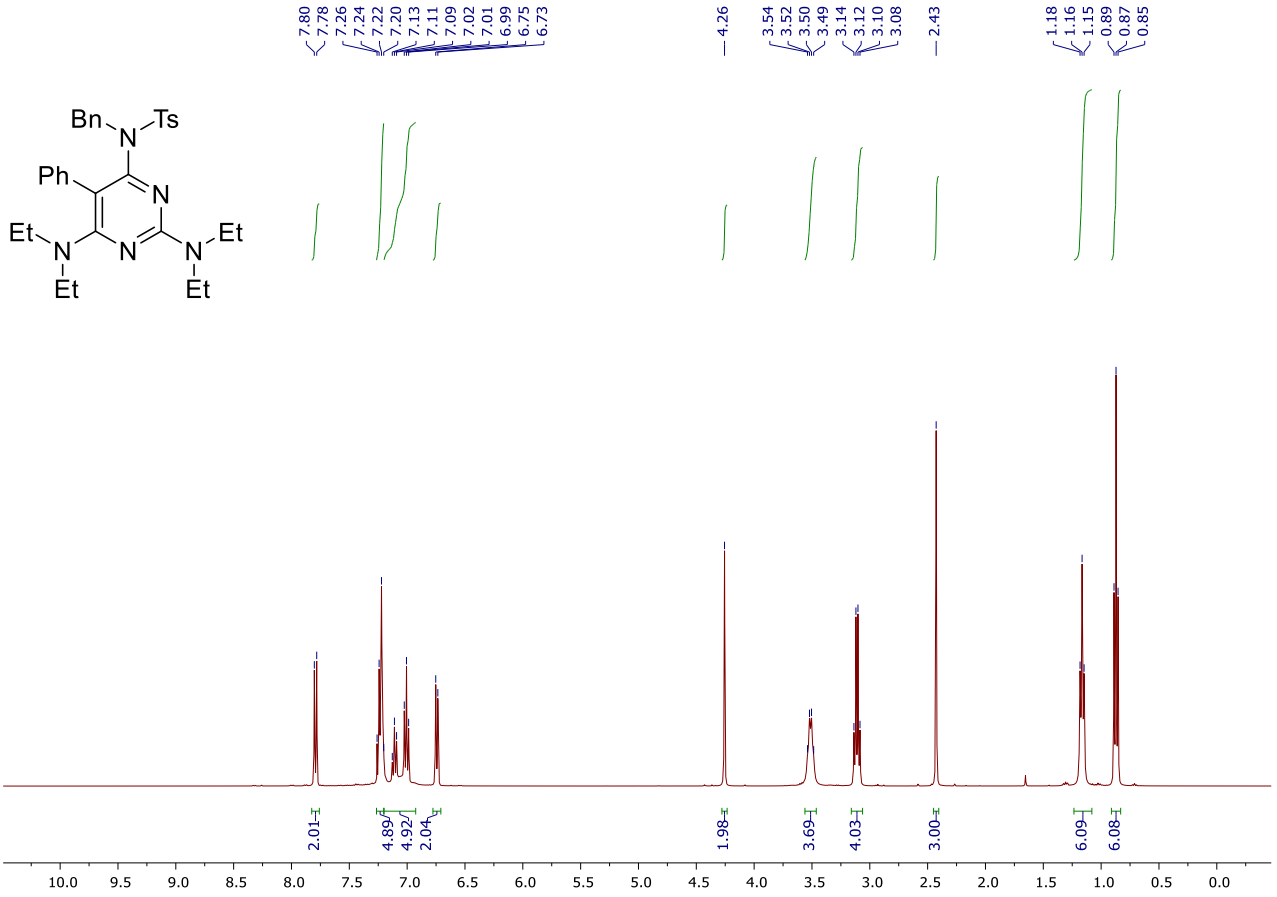
^{1}H NMR (400 MHz, $CDCl_3$) of **6t**



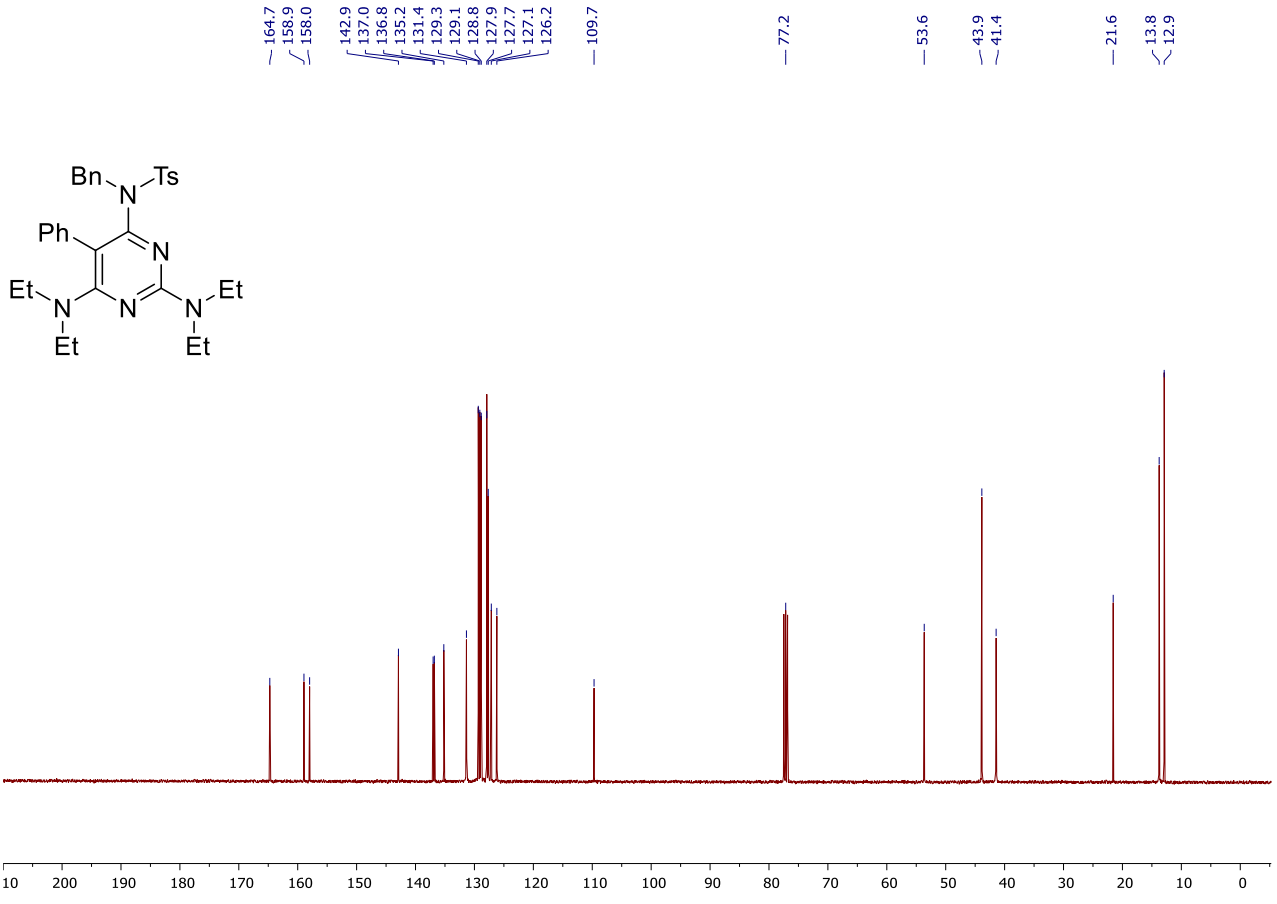
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **6t**



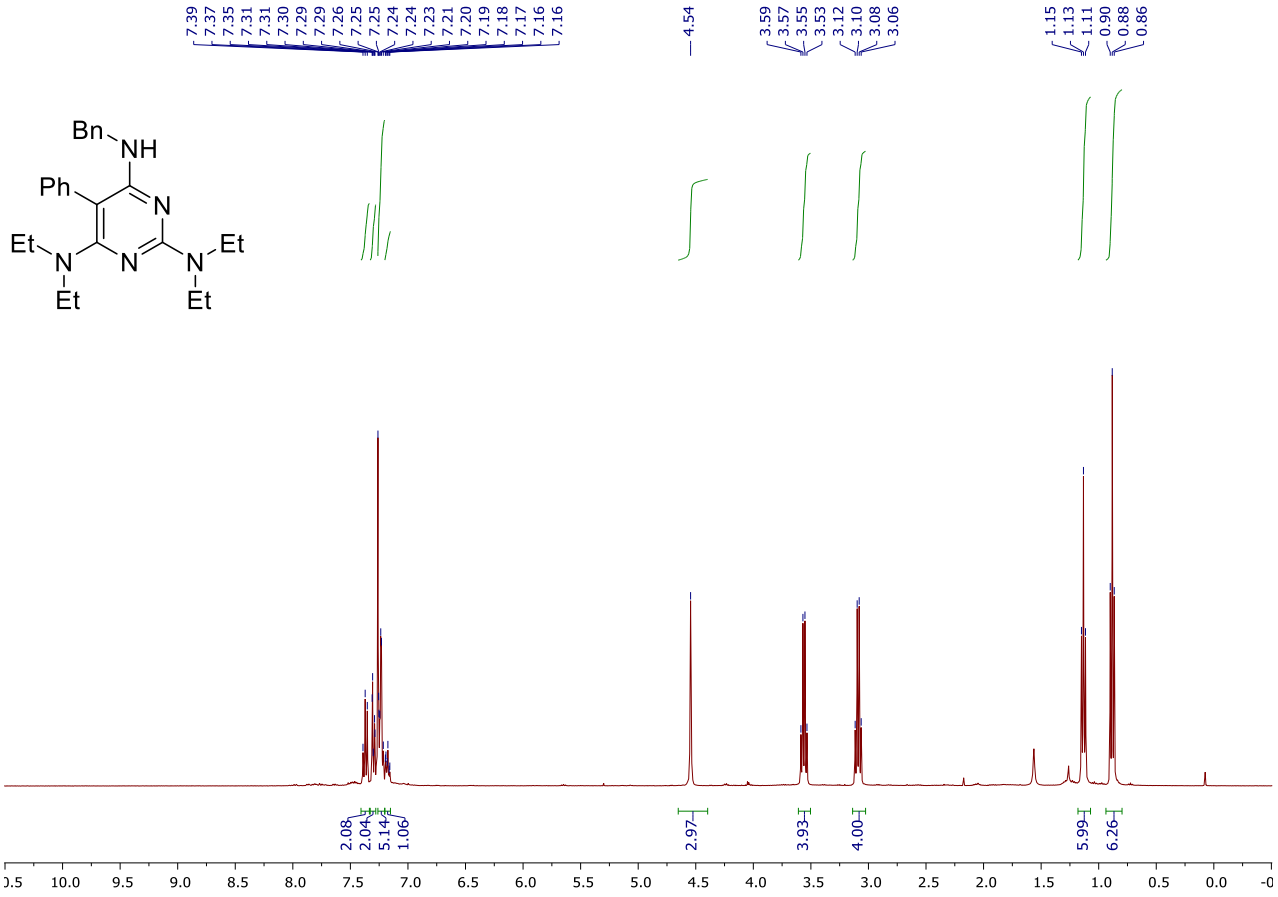
^{1}H NMR (400 MHz, $CDCl_3$) of **7**



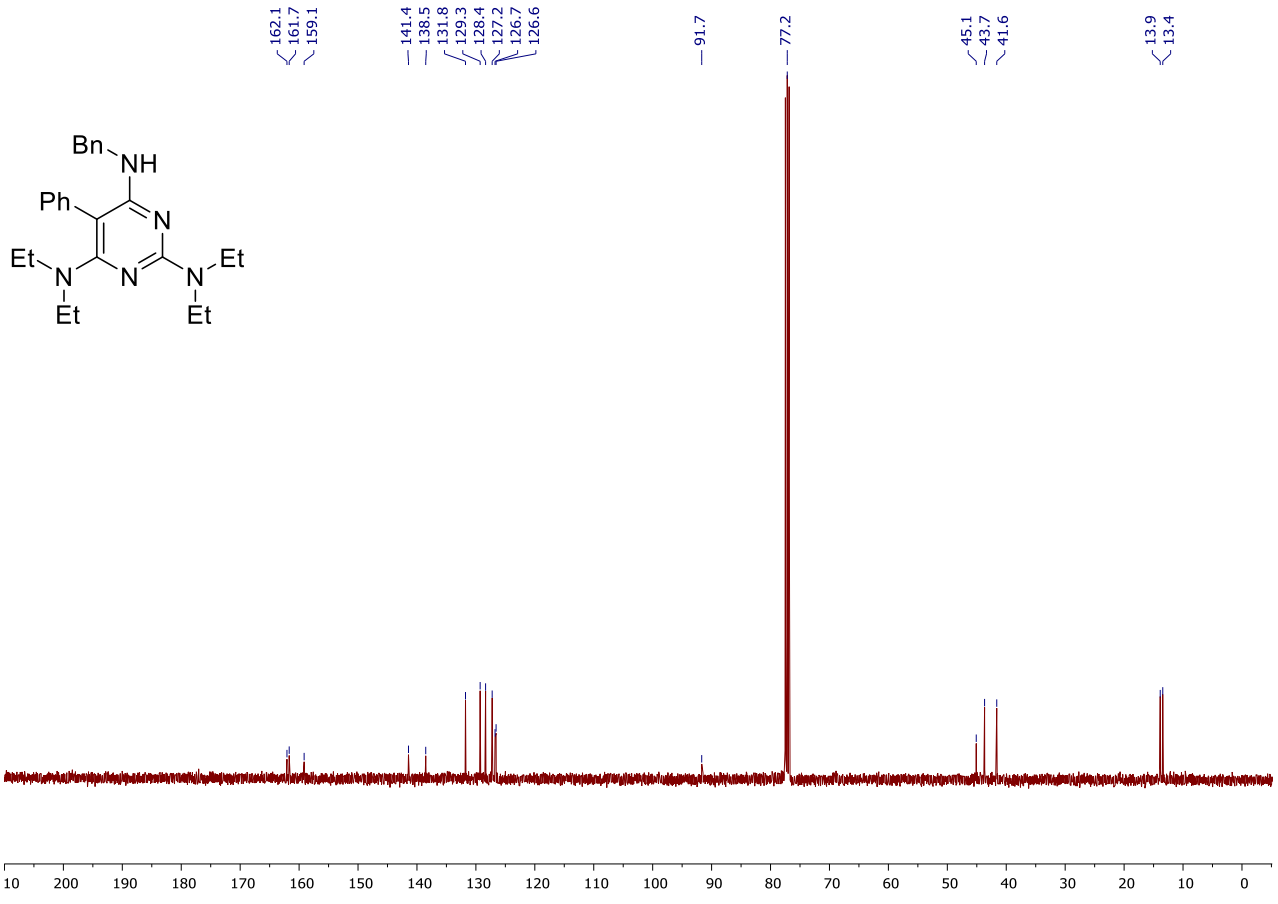
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **7**



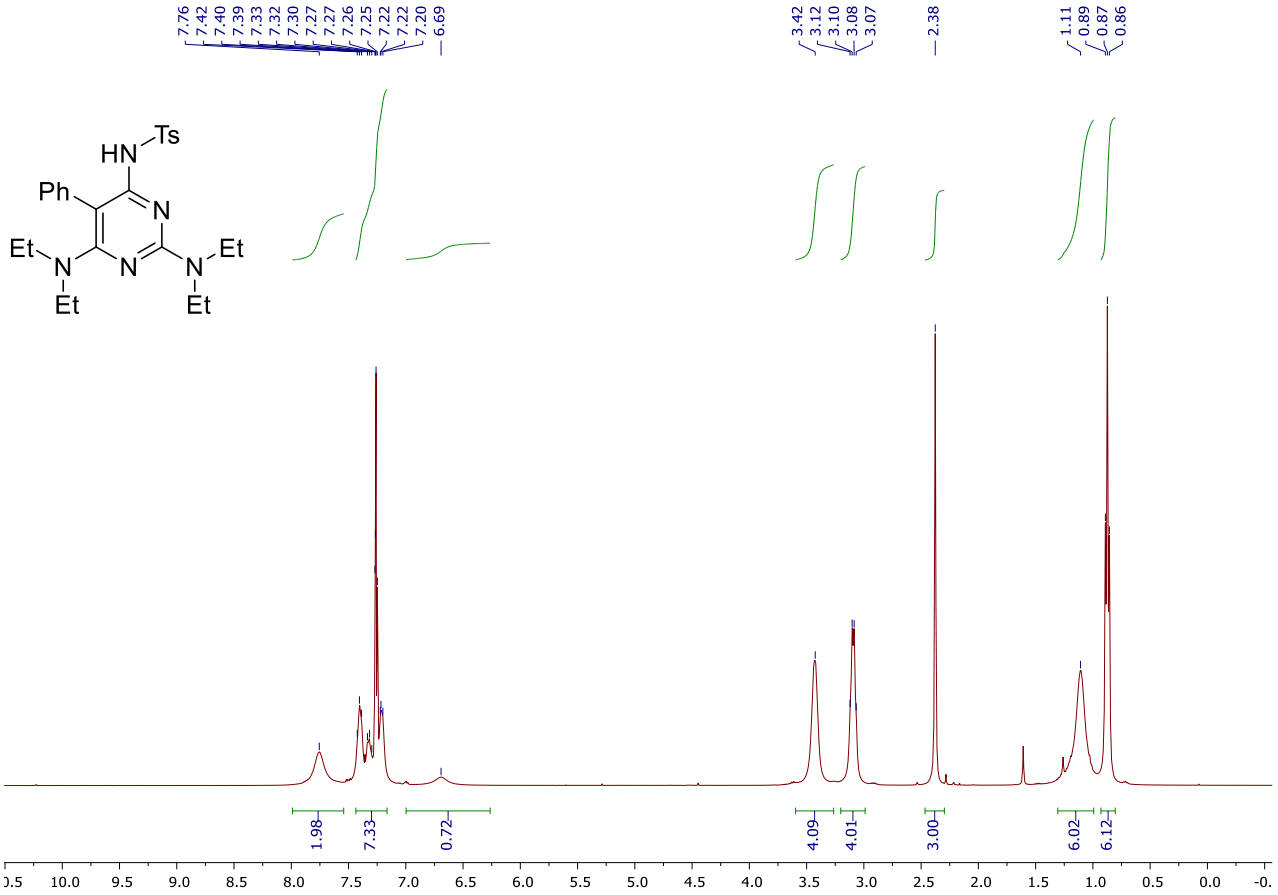
^{1}H NMR (400 MHz, $CDCl_3$) of **8**



^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **8**



^{1}H NMR (400 MHz, $CDCl_3$) of **9**



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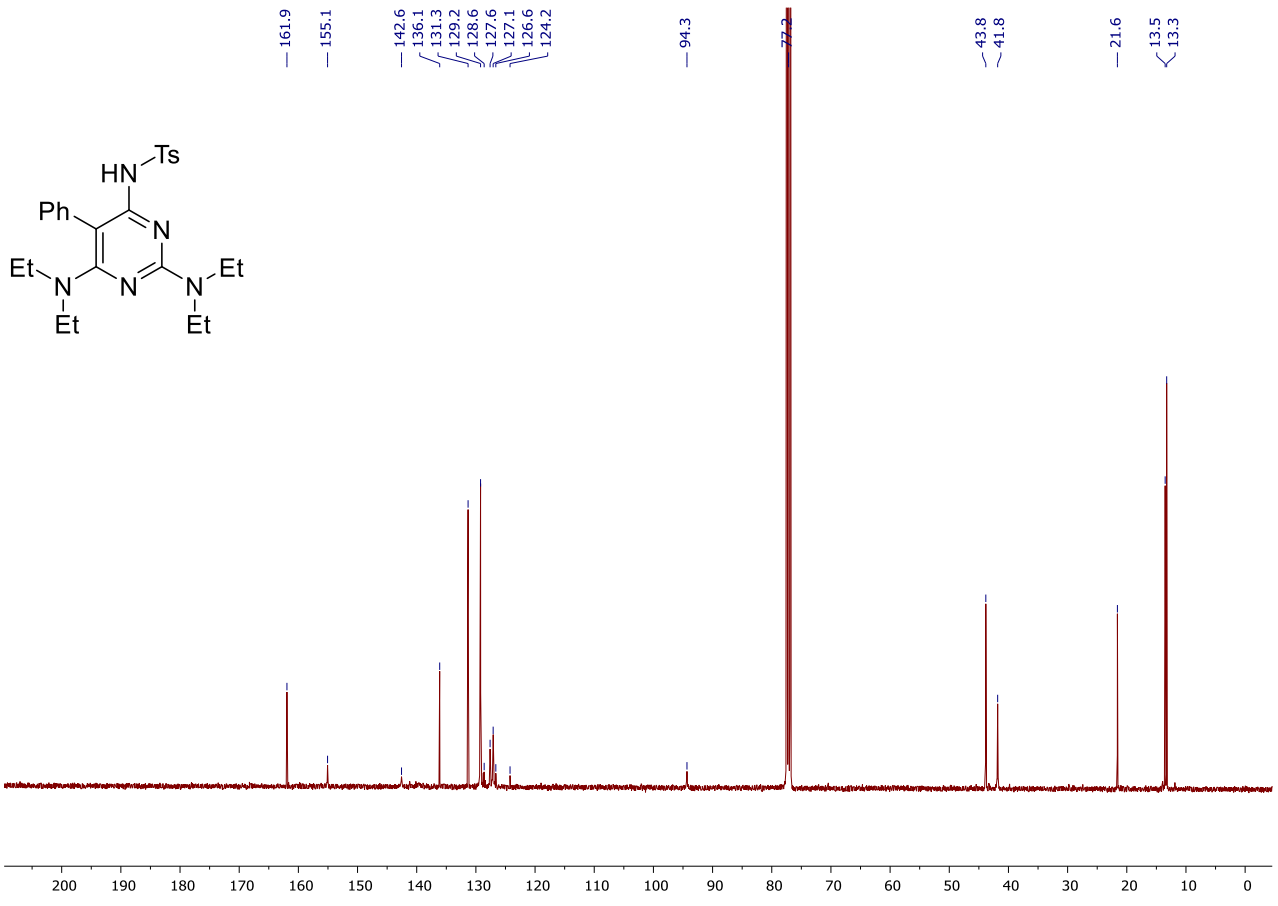
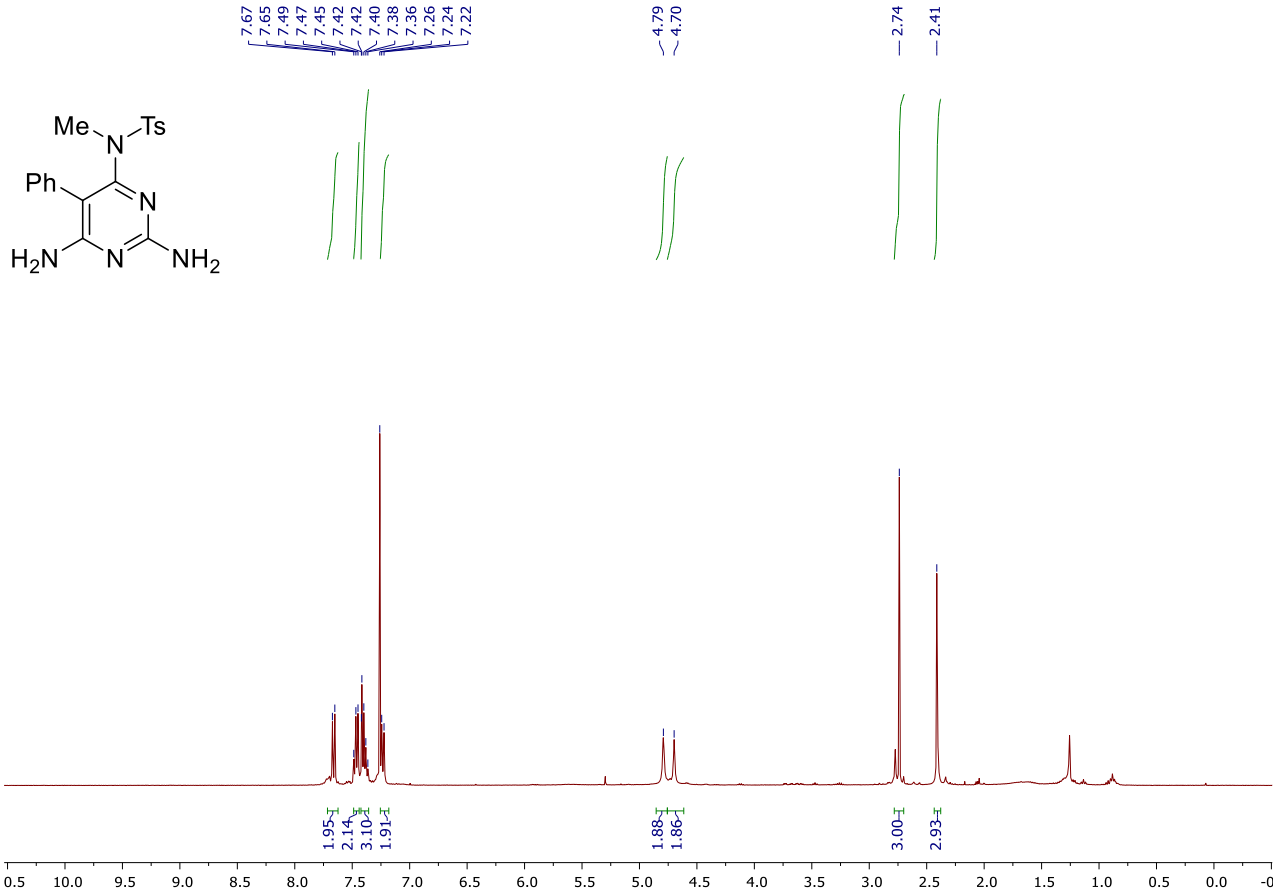
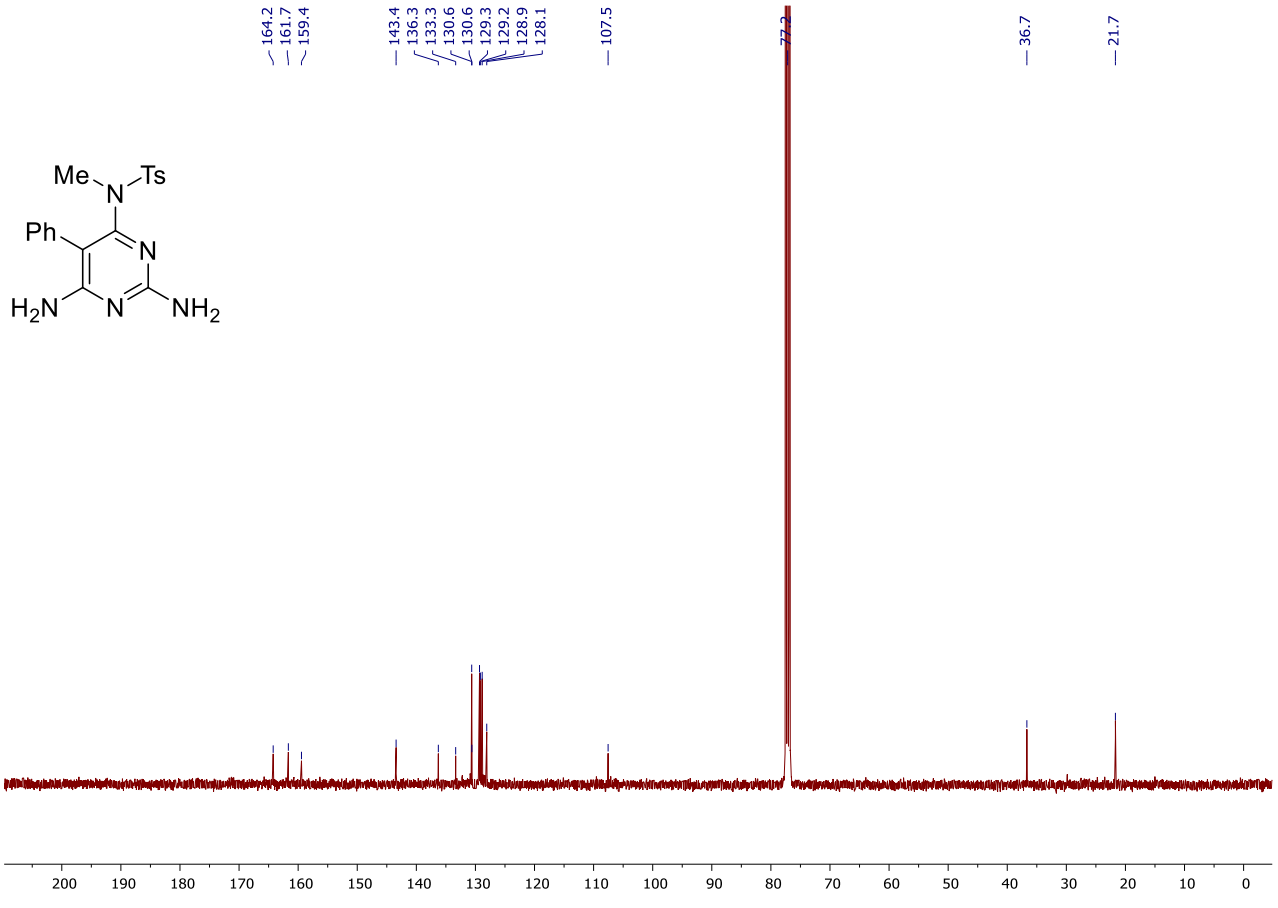


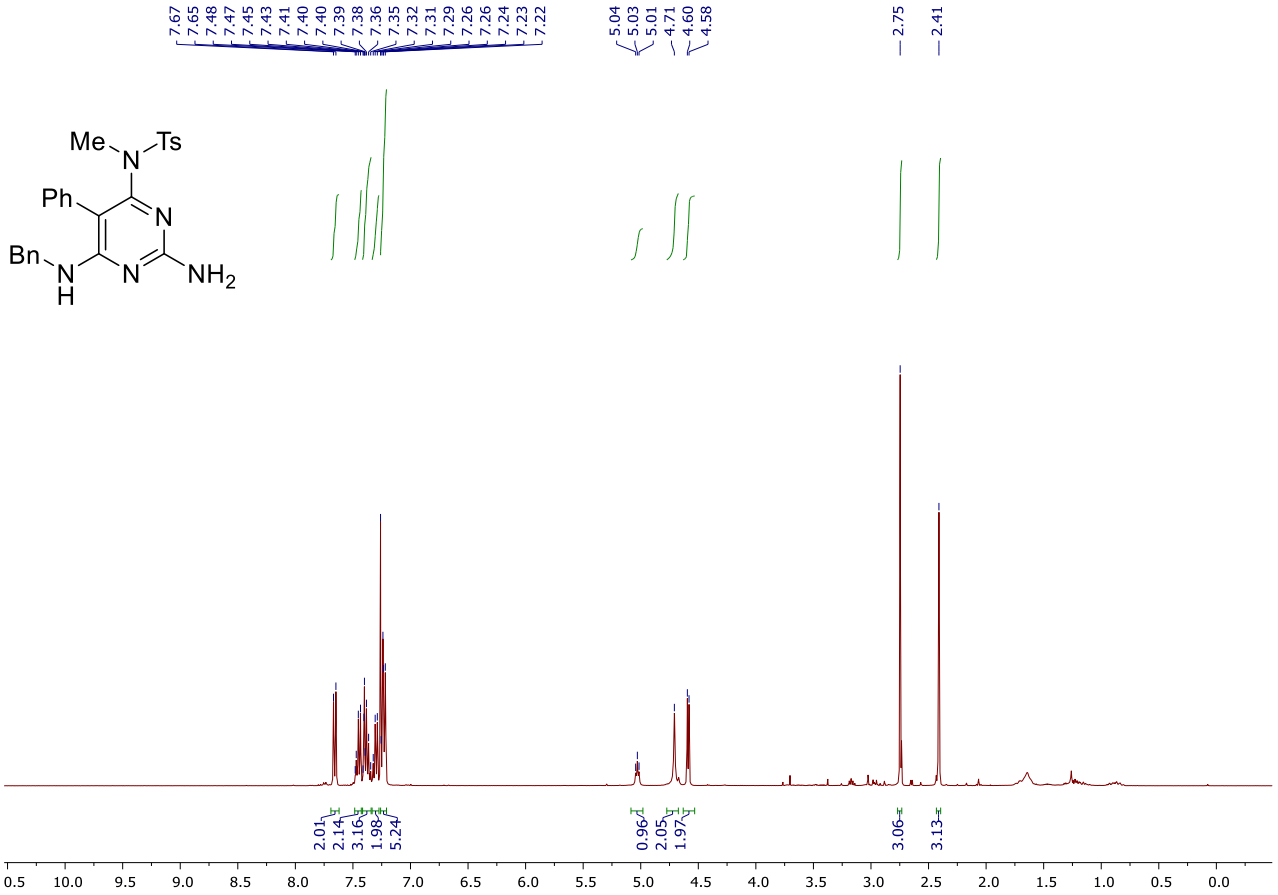
^{1}H NMR (400 MHz, $CDCl_3$) of **10**



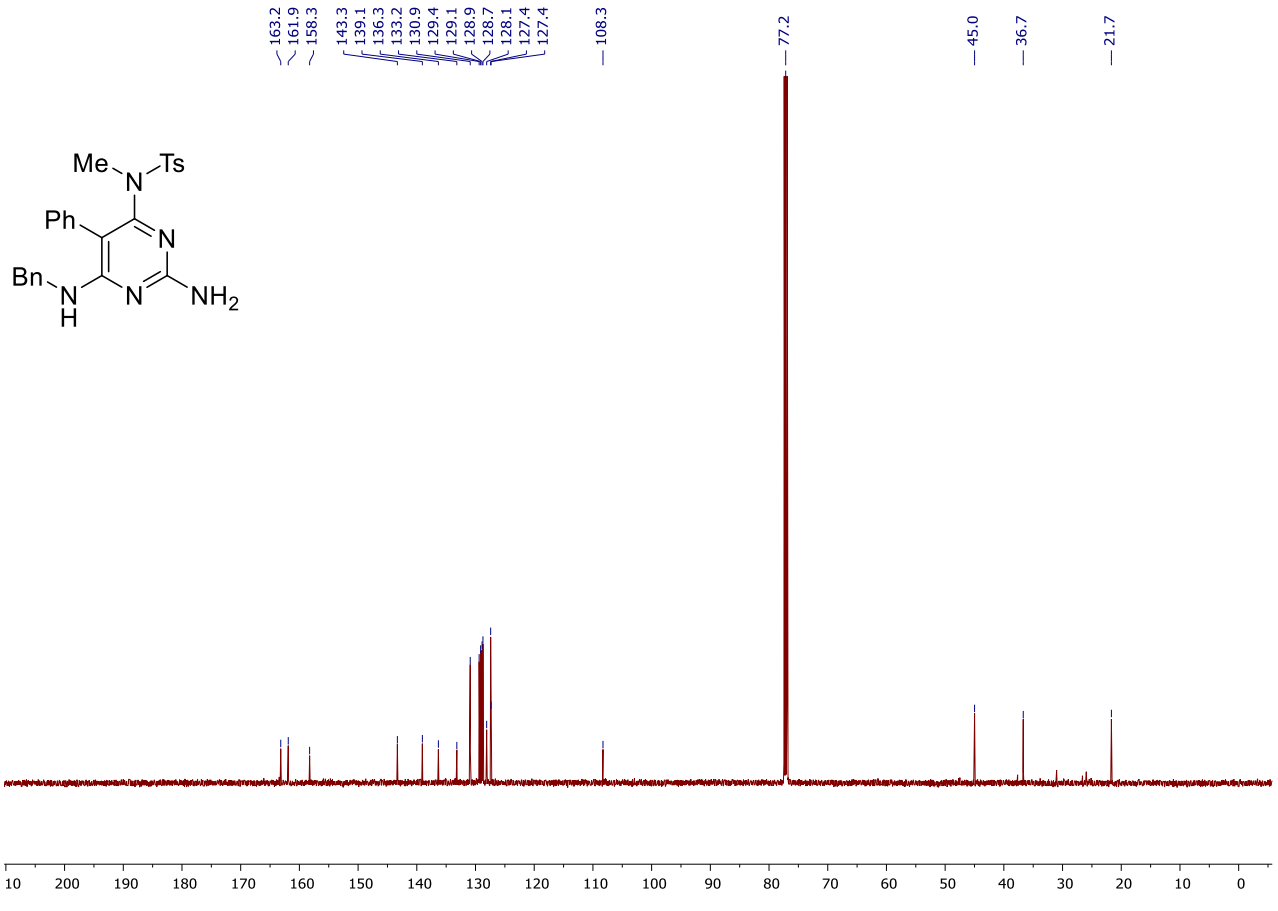
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **10**



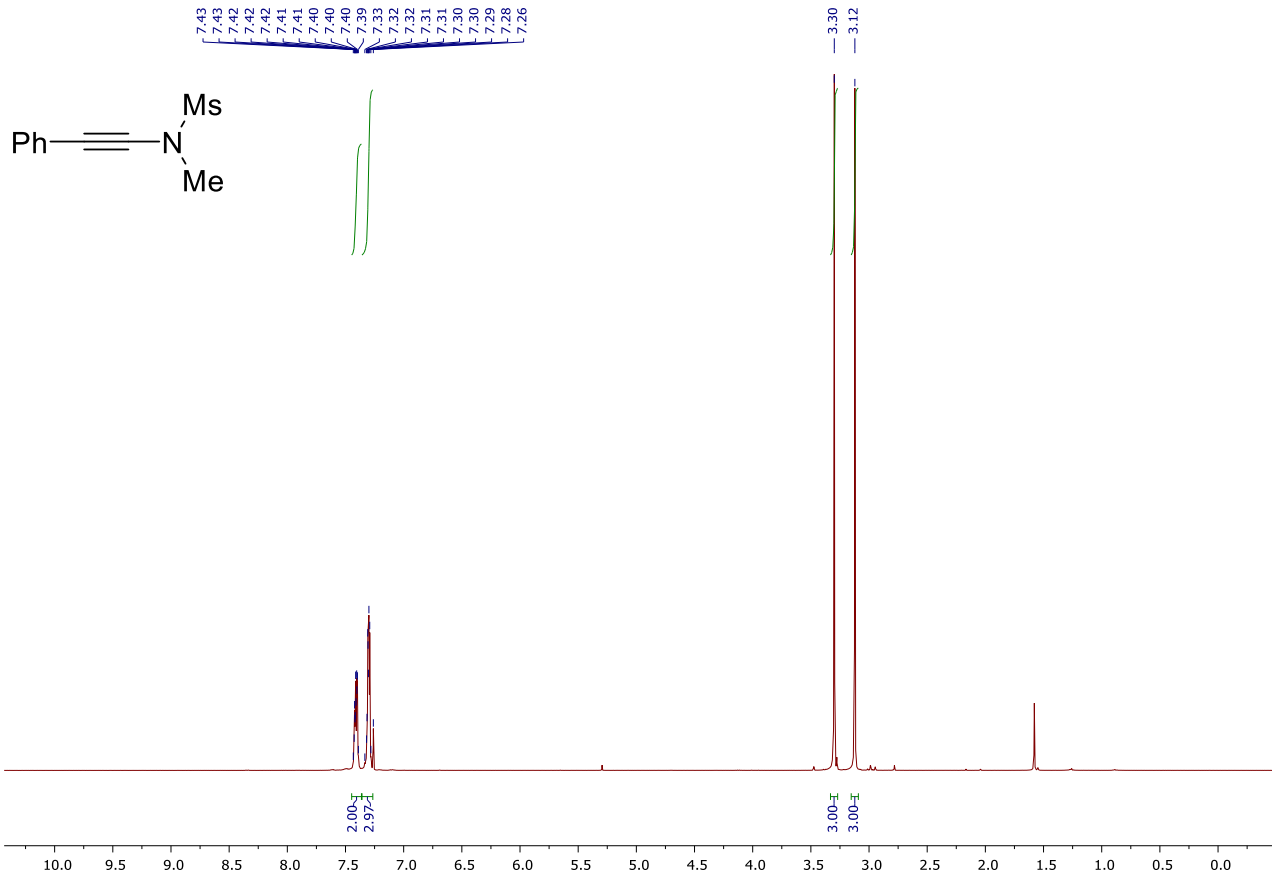
^{1}H NMR (400 MHz, $CDCl_3$) of **10'**



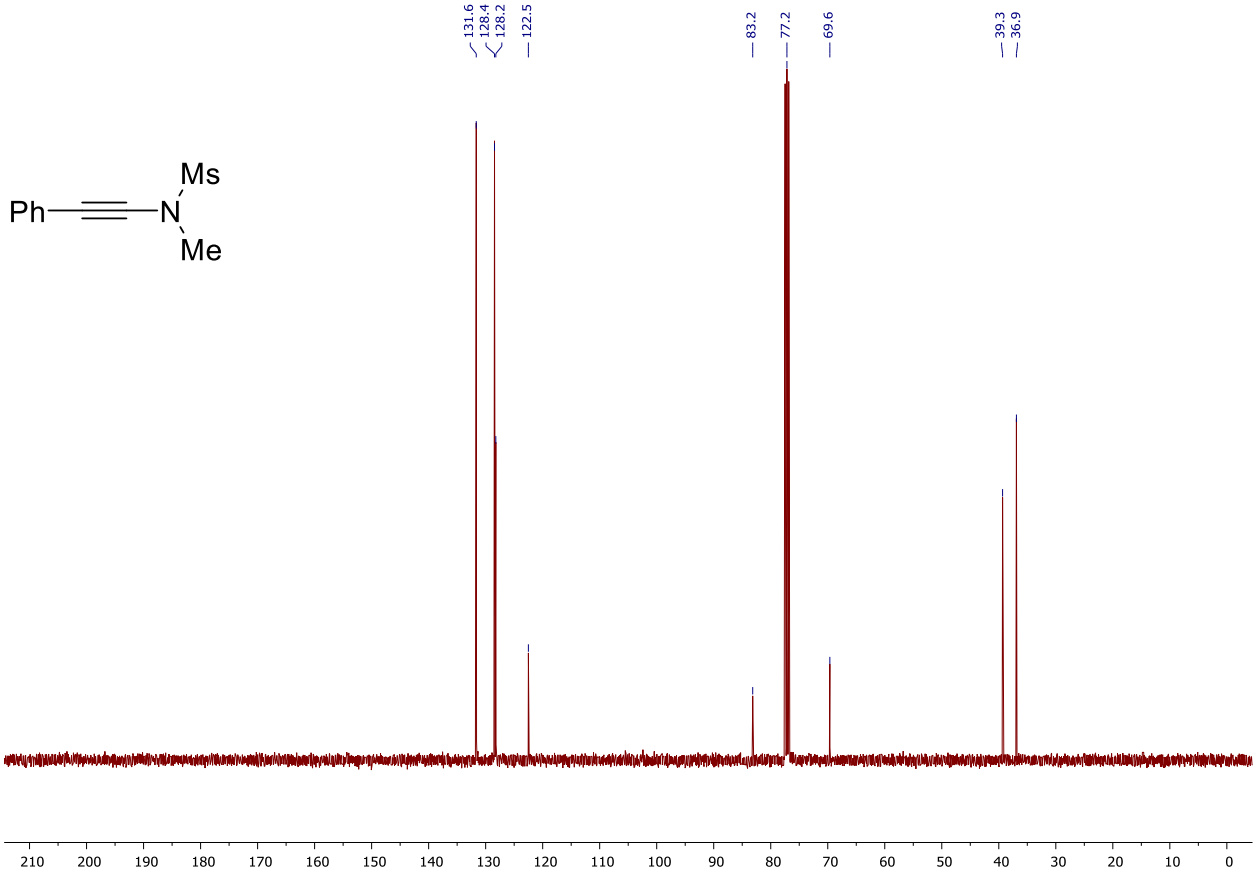
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **10'**



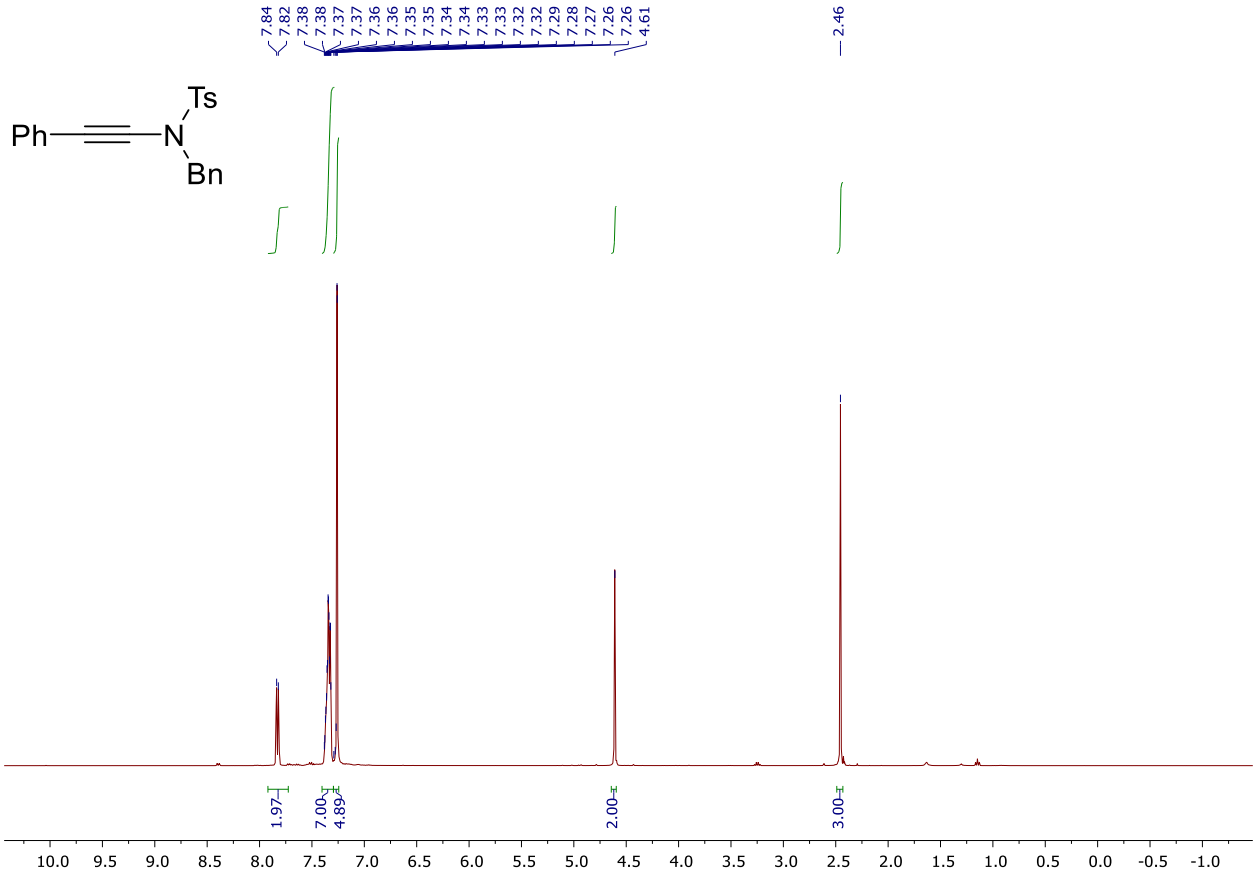
^{1}H NMR (400 MHz, $CDCl_3$) of **1a'**



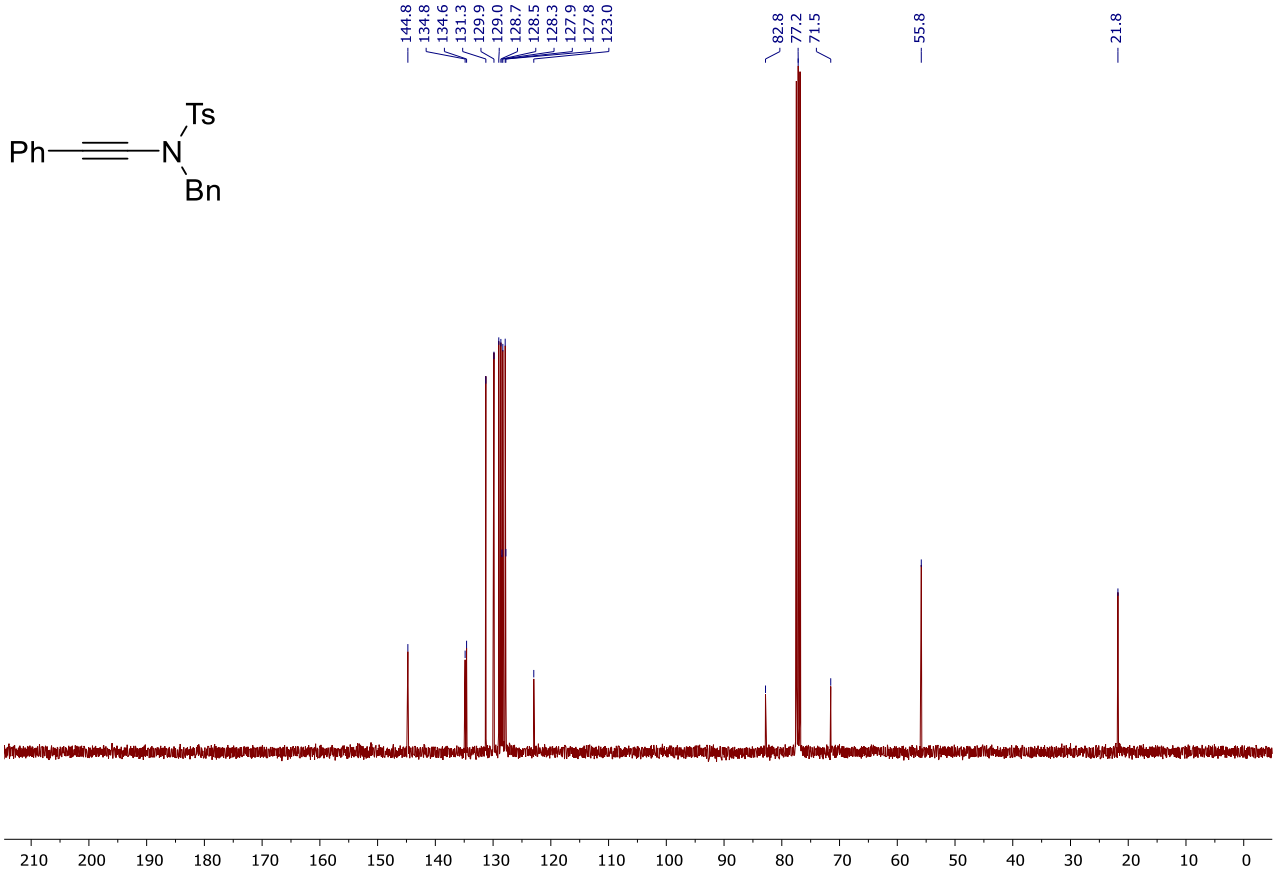
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **1a'**



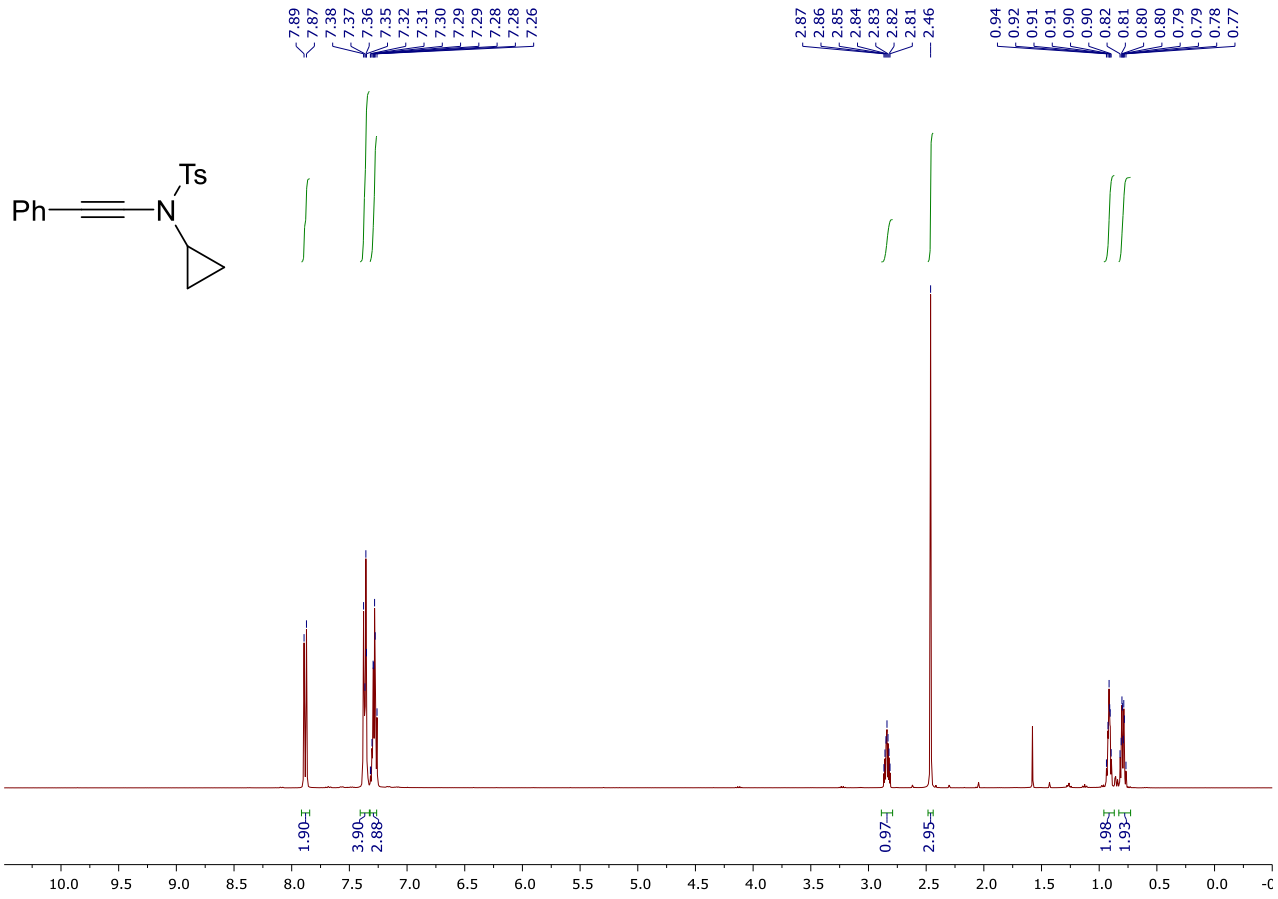
^{1}H NMR (400 MHz, $CDCl_3$) of **1e**



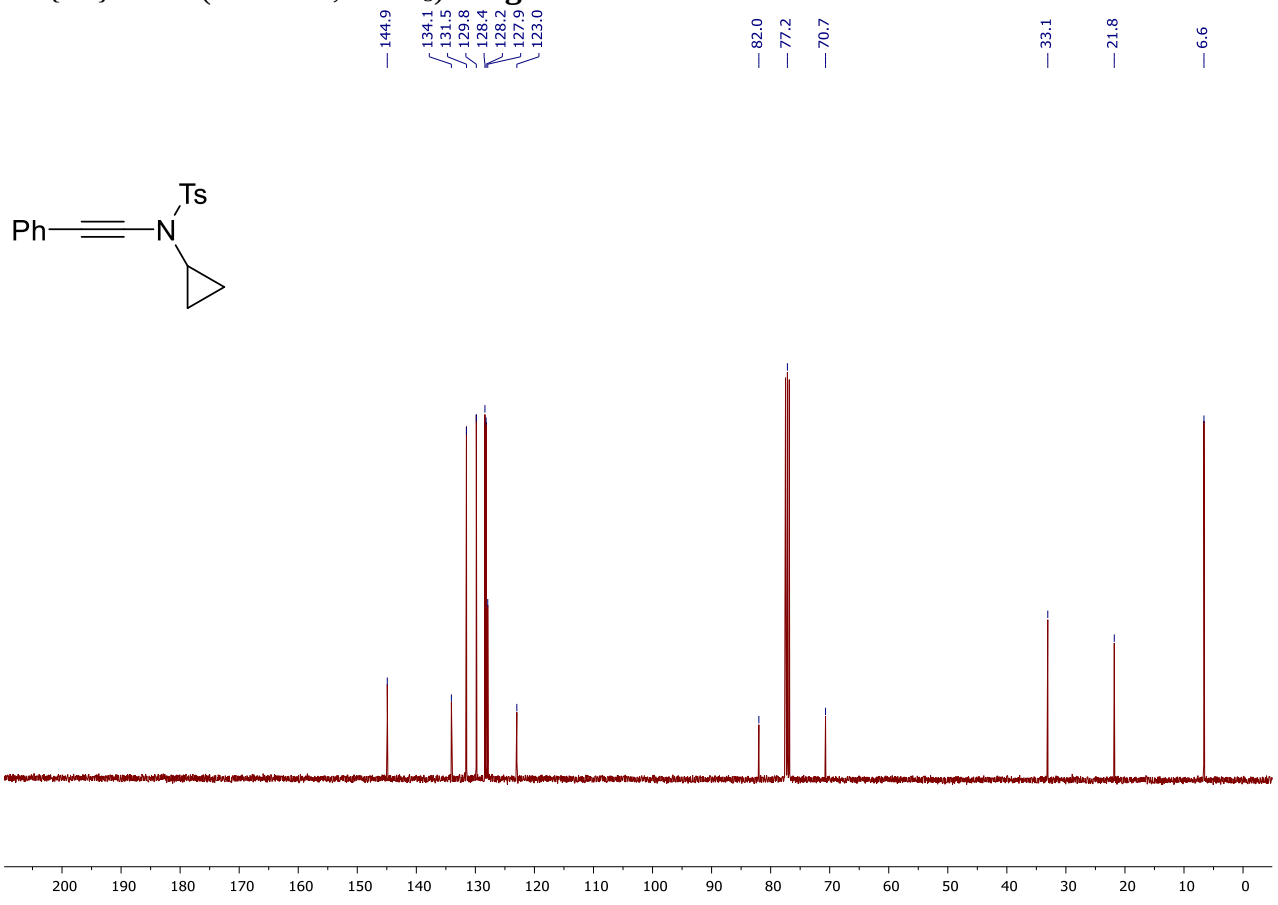
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **1e**



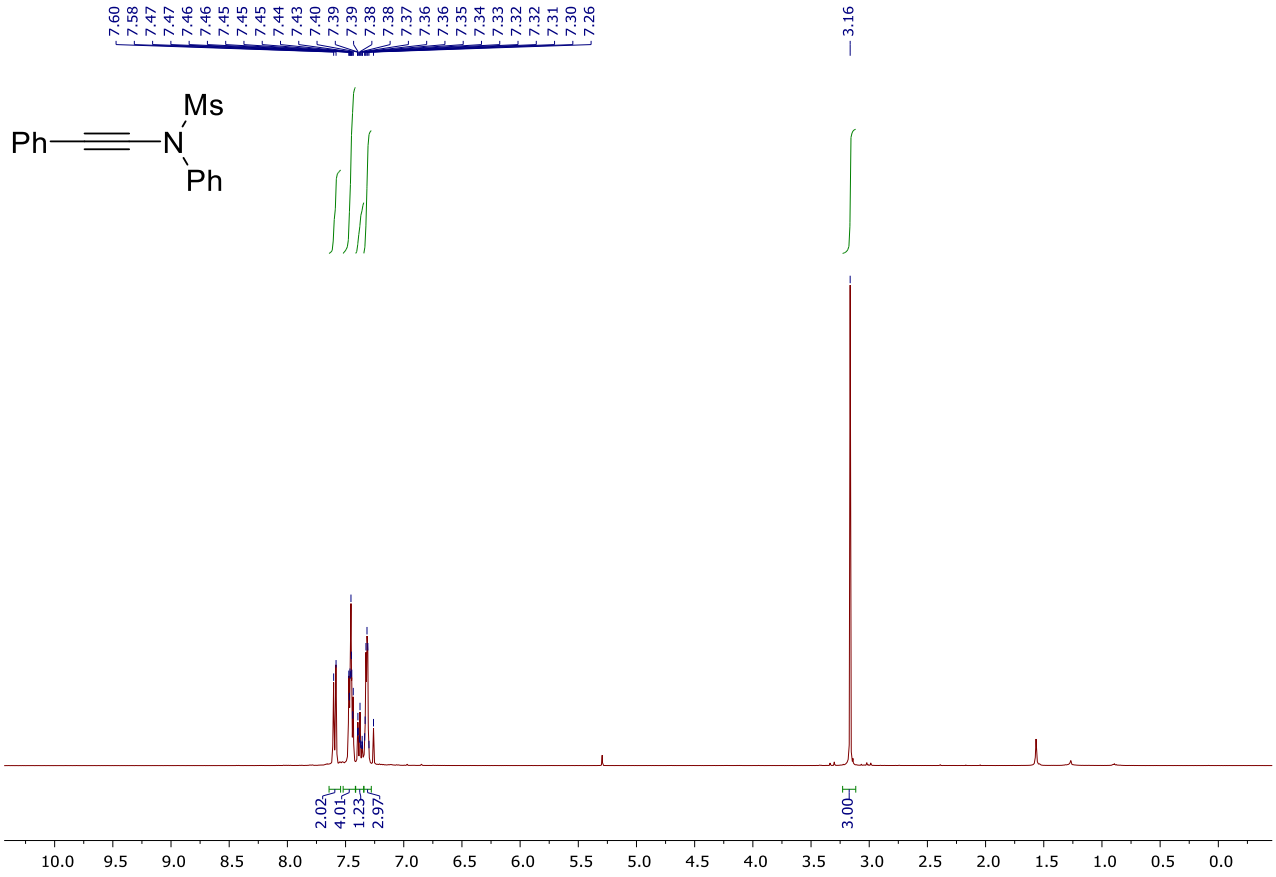
^{1}H NMR (400 MHz, $CDCl_3$) of **1g**



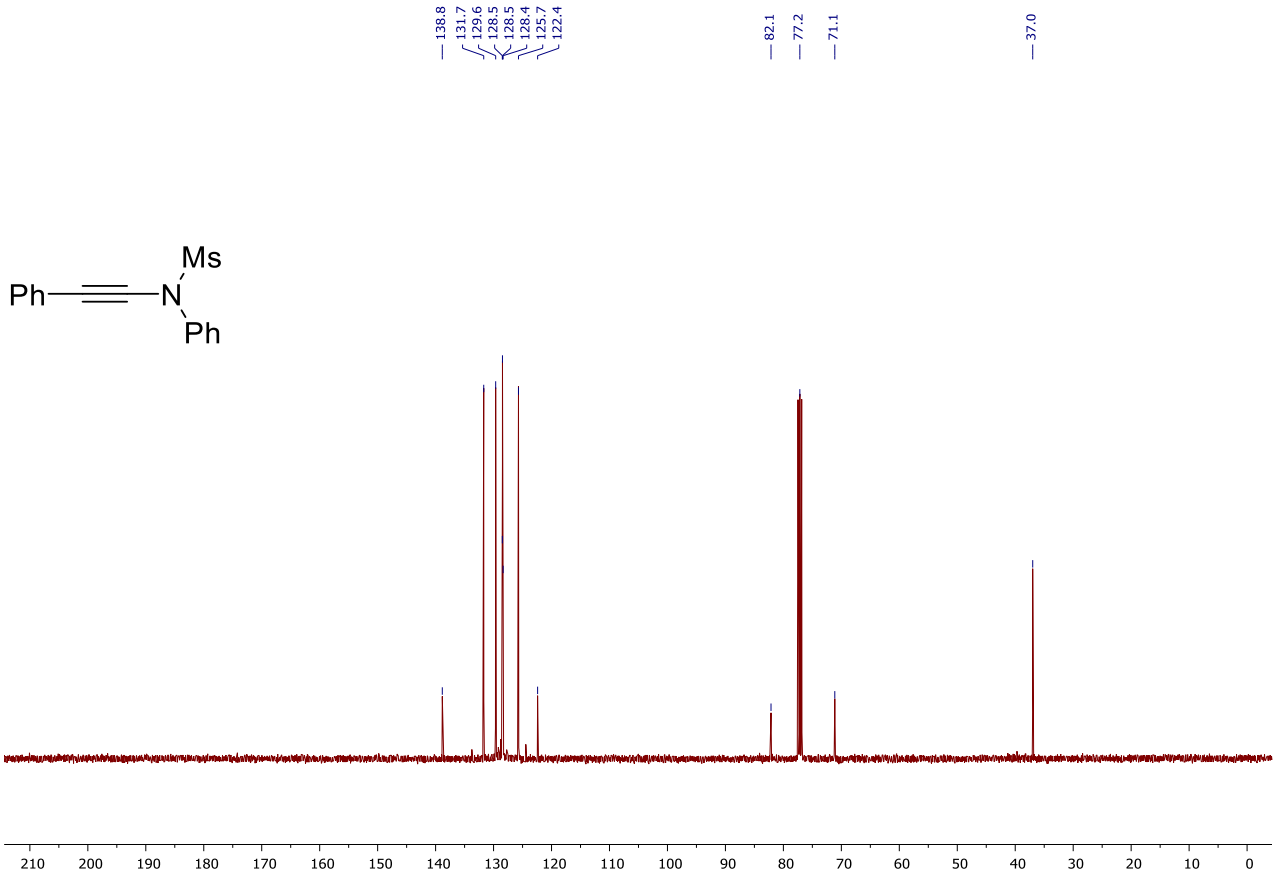
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **1g**



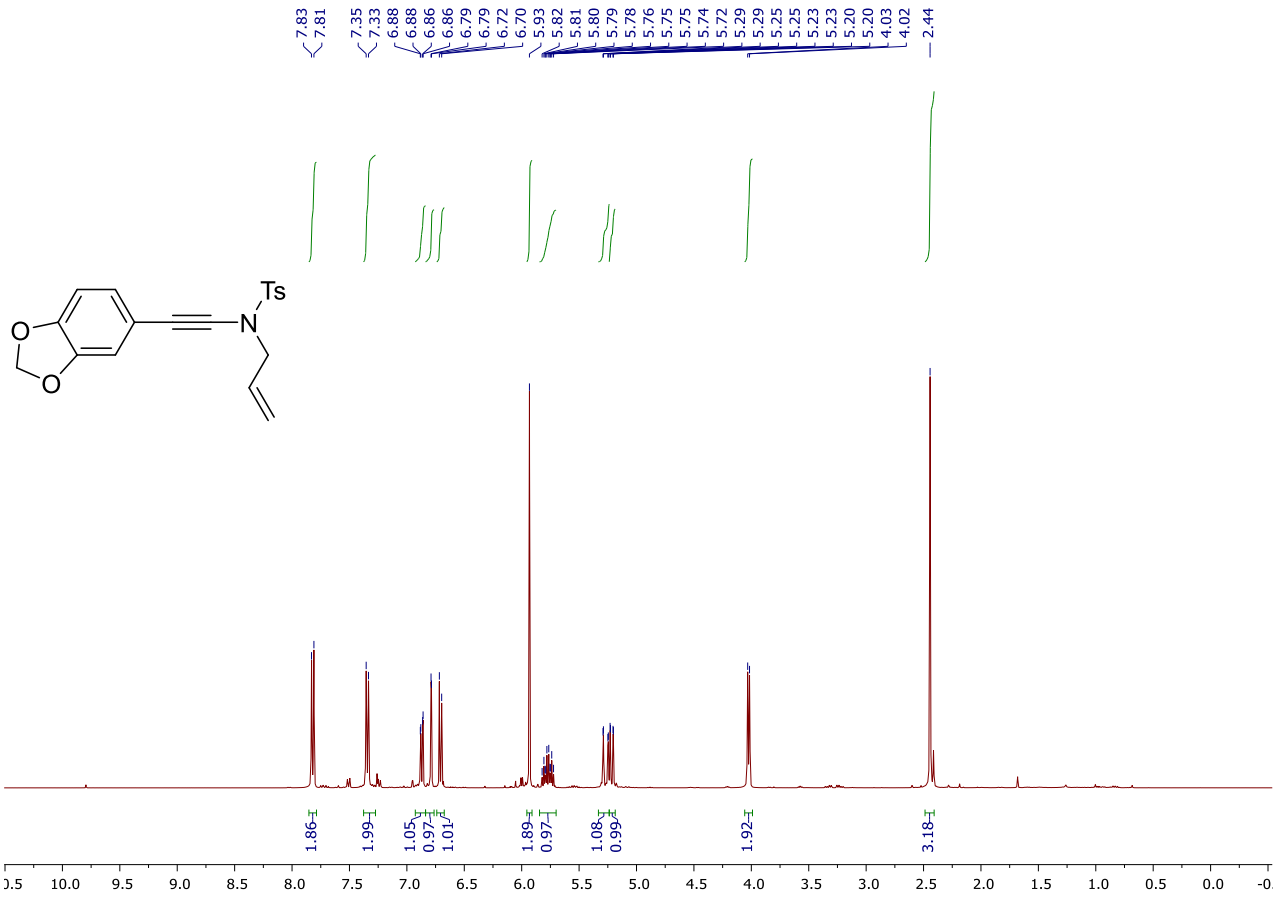
^{1}H NMR (400 MHz, $CDCl_3$) of **1h**



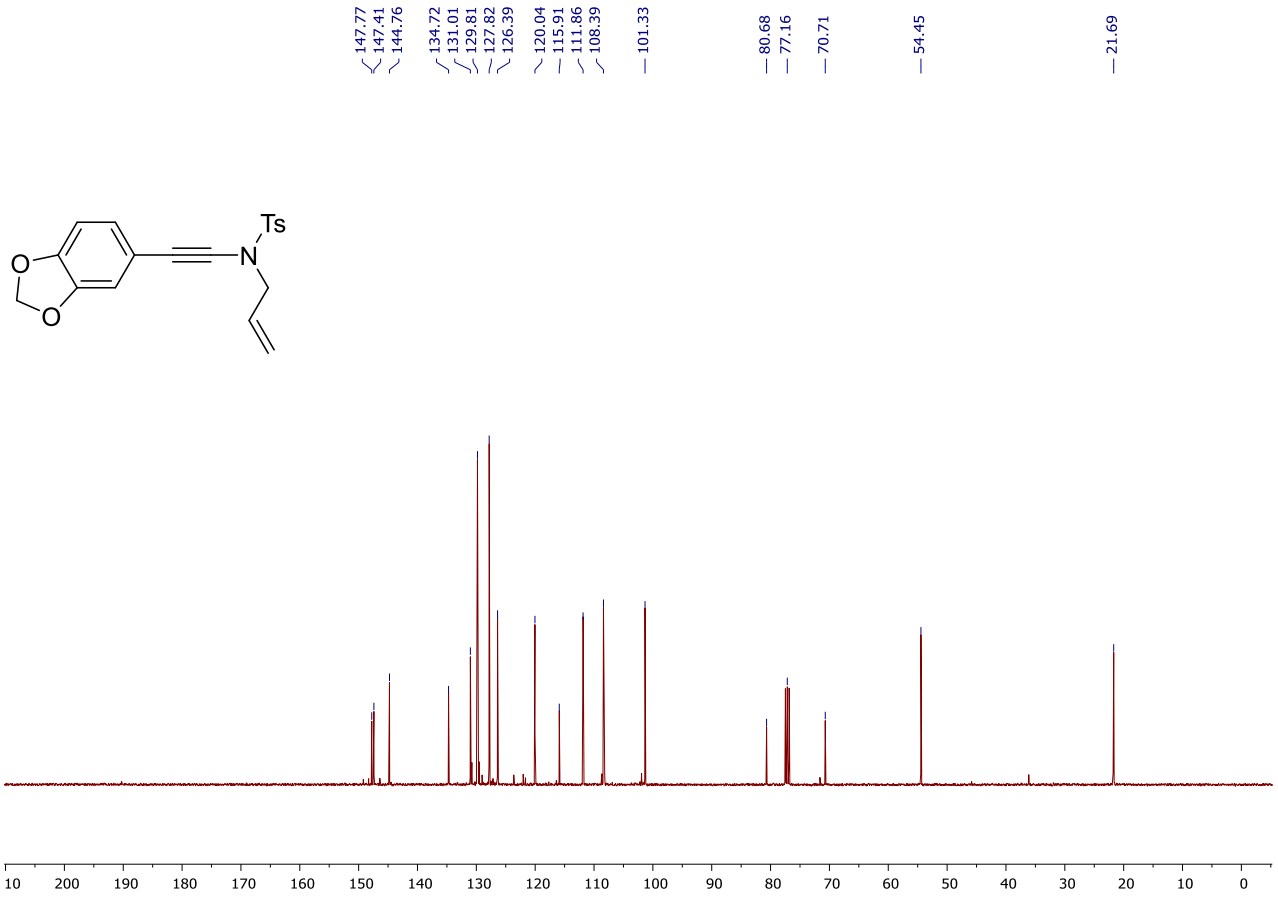
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **1h**



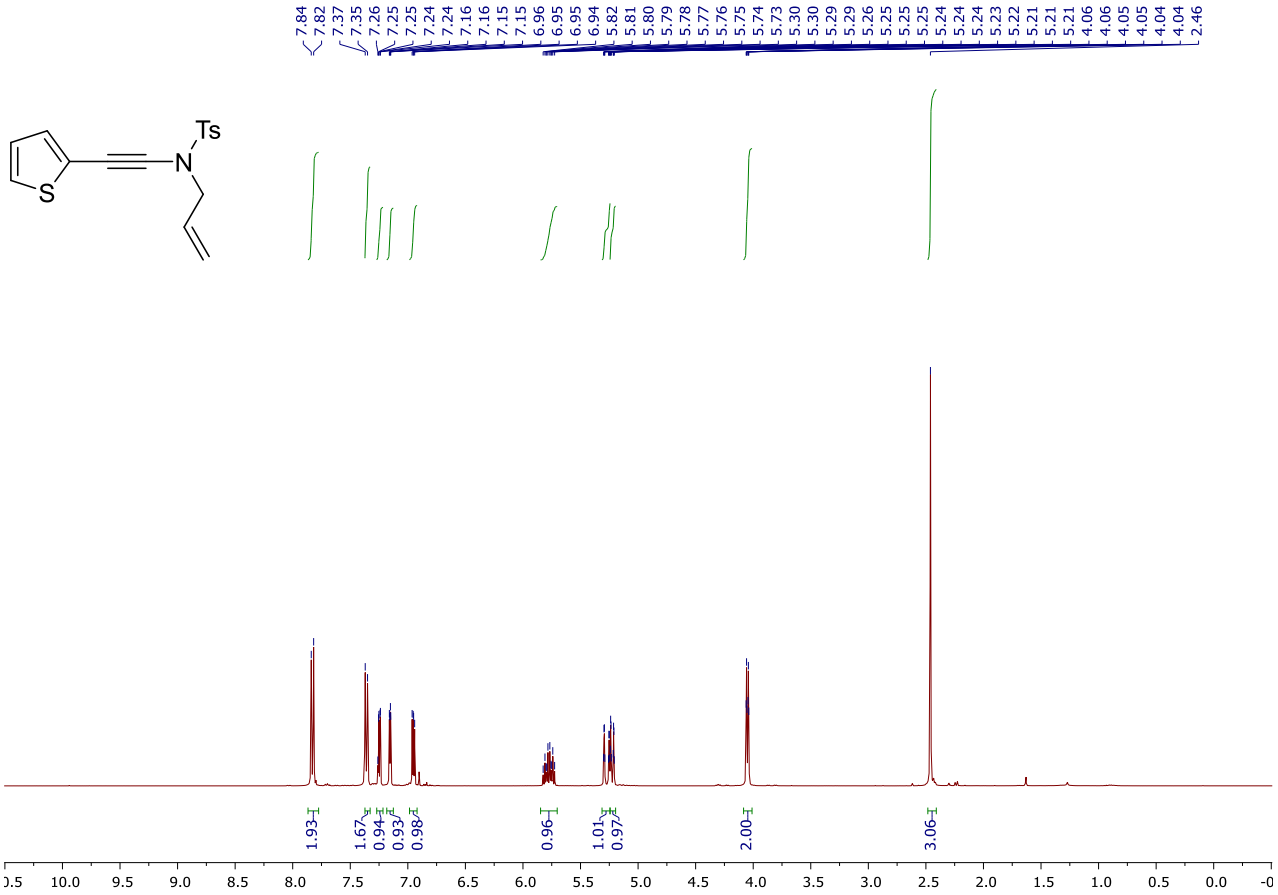
^{1}H NMR (400 MHz, $CDCl_3$) of **1n**



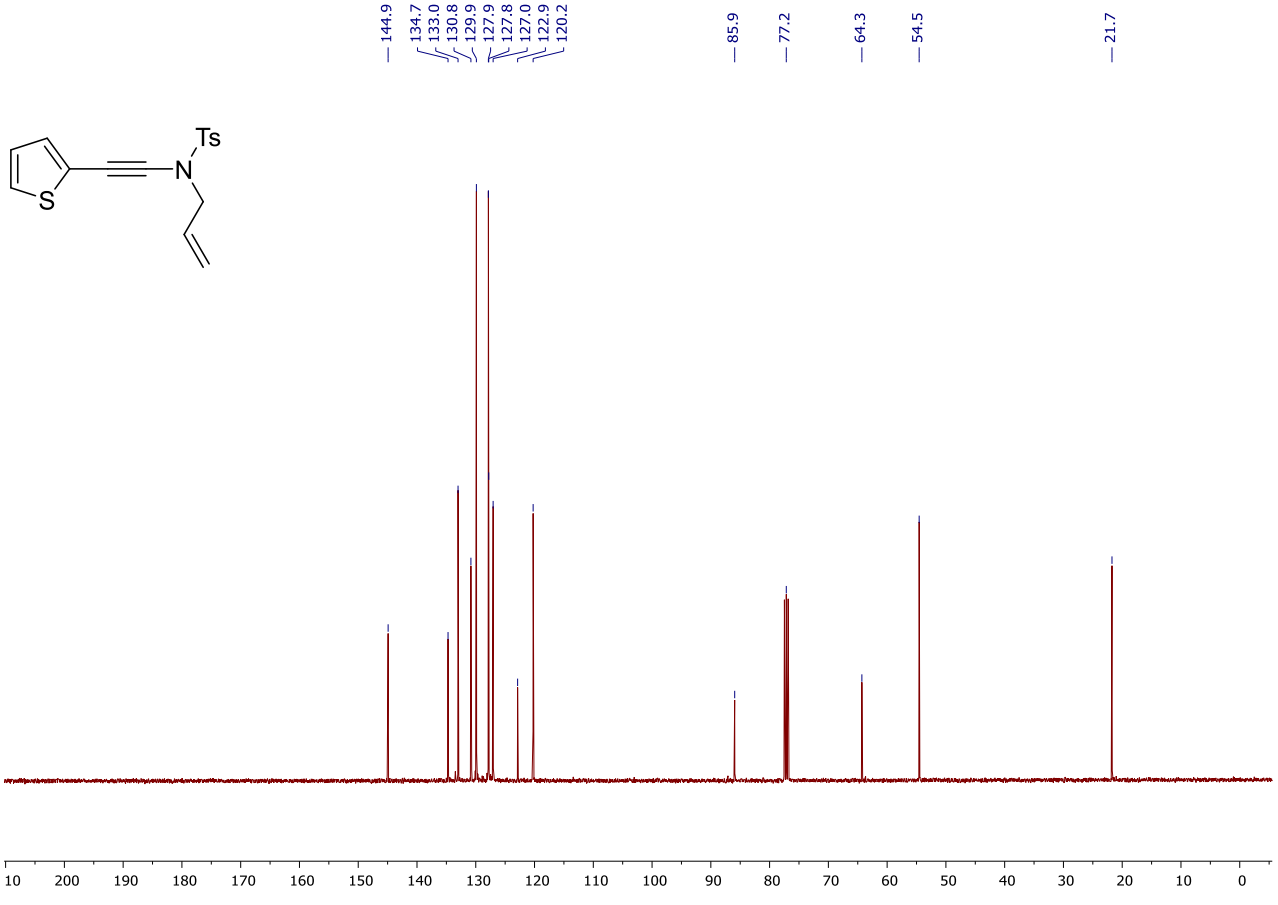
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **1n**



^{1}H NMR (400 MHz, $CDCl_3$) of **1p**



^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **1p**



5. Computational Details

The full geometry optimization of all model structures was carried out at the DFT level of theory using the Becke's three-parameter hybrid exchange functional in combination with the gradient-corrected correlation functional of Lee, Yang, and Parr (B3LYP) [(a) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648-5652; (b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785-789] with the help of Gaussian-09 program package [M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, in Gaussian 09, Revision C.01, Gaussian, Inc., Wallingford, CT, 2010]. The quasi-relativistic pseudopotential MWB60 [D. Andrae, U. Häußermann, M. Dolg, H. Stoll, H. Preuß, *Theor. Chim. Acta* **1990**, *77*, 123-141] that described 60 core electrons and appropriate contracted basis set were used for the gold atom and standard 6-31G* basis sets were used for other atoms. No symmetry restrictions have been applied during the geometry optimization procedure. The Hessian matrices were calculated analytically for all optimized model structures to prove the location of correct minima or saddle points on the potential energy surface (no imaginary frequencies or only one imaginary frequency, respectively) and to estimate the thermodynamic parameters, the latter being calculated at 25 °C (Tables S1 and S2). The nature of all transition states was studied by the analysis of vectors associated with the imaginary frequency and by the calculations of the intrinsic reaction coordinates (IRC) using the Gonzalez−Schlegel method [(a) C. Gonzalez, H. B. Schlegel, *J. Chem. Phys.* **1991**, *95*, 5853-5860; (b) C. Gonzalez, H. B. Schlegel, *J. Chem. Phys.* **1989**, *90*, 2154-2161; (c) C. Gonzalez, H. B. Schlegel, *J. Phys. Chem.* **1990**, *94*, 5523-5227]. The Cartesian atomic coordinates for all optimized equilibrium model structures are given in the attached xyz-files.

Table S1. Calculated total energies, enthalpies, Gibbs free energies (in Hartree), and entropies (in cal/mol•K) for optimized equilibrium model structures (E, H, G, and S, respectively).

Model structure	E	H	G	S
E_H	-1218.77009455	-1218.446780	-1218.520831	155.854
F_H	-1218.77158717	-1218.448315	-1218.522090	155.273
TS_H	-1218.74329468	-1218.421583	-1218.491125	146.363
G_H	-1218.78842112	-1218.463793	-1218.531117	141.695
E_Ph3PAu	-2390.32383202	-2389.716483	-2389.840917	261.893
F_Ph3PAu	-2390.32244371	-2389.715017	-2389.838179	259.216
TS_Ph3PAu	-2390.30428122	-2389.698233	-2389.816746	249.432
C_Ph3PAu	-2390.33574049	-2389.726927	-2389.843915	246.223
E_IPrAu	-2514.09483625	-2513.174837	-2513.327487	321.279
F_IPrAu	-2514.09460348	-2513.174538	-2513.327028	320.942
TS_IPrAu	-2514.07588328	-2513.156971	-2513.304221	309.915
G_IPrAu	-2514.10414615	-2513.182633	-2513.328831	307.700
E_AuPMe3	-1815.12166486	-1814.684238	-1814.784050	210.071
F_AuPMe3	-1815.12096567	-1814.683598	-1814.781664	206.398
TS_AuPMe3	-1815.10158273	-1814.665457	-1814.759684	198.317
G_AuPMe3	-1815.13508296	-1814.696257	-1814.788005	193.100

Table S2. Calculated values of total activation and reaction energies (E_a and ΔE), enthalpies and Gibbs free energies of activation ($\Delta H^{\neq}$ and $\Delta G^{\neq}$) and reaction (ΔH and ΔG) in kcal/mol.

Transformation	E_a	$\Delta H^{\neq}$	$\Delta G^{\neq}$	ΔE	ΔH	ΔG
E_H → F_H				-0.9	-1.0	-0.8
E_H → G_H	16.8	15.8	18.6	-11.5	-10.7	-6.5
E_Ph3PAu → F_Ph3PAu				0.9	0.9	1.7
E_Ph3PAu → G_Ph3PAu	12.3	11.5	15.2	-7.5	-6.6	-1.9
E_IPrAu → F_IPrAu				0.1	0.2	0.3
E_IPrAu → G_IPrAu	11.9	11.2	14.6	-5.8	-4.9	-0.8
E_AuPMe3 → F_AuPMe3				0.4	0.4	1.5
E_AuPMe3 → G_AuPMe3	12.6	11.8	15.3	-8.4	-7.5	-2.5

Table S3. Calculated total energies, enthalpies, Gibbs free energies (in Hartree), and entropies (in cal/mol•K) for optimized equilibrium model structures (E, H, G, and S, respectively).

Model structure	E	H	G	S
E_H	-1446.19034410	-1445.766300	-1445.860068	197.352
TS_to_(E+2a)_H	-1446.18069208	-1445.757444	-1445.847221	188.951
(E+2a)_H	-1446.18228274	-1445.757468	-1445.845555	185.394
E_IPrAu	-2741.51024333	-2740.489138	-2740.662589	365.058
TS_to_(E+2a)_IPrAu	-2741.48648860	-2740.466499	-2740.632456	349.287
(E+2a)_IPrAu	-2741.49229285	-2740.470997	-2740.636142	347.576

Table S4. Calculated values of total activation and reaction energies (E_a and ΔE), enthalpies and Gibbs free energies of activation ($\Delta H^{\neq}$ and $\Delta G^{\neq}$) and reaction (ΔH and ΔG) in kcal/mol.

Transformation	E_a	$\Delta H^{\neq}$	$\Delta G^{\neq}$	ΔE	ΔH	ΔG
E _H → (E+2a)_H	6.1	5.6	8.1	5.1	5.5	9.1
E_IPrAu → TS_to_(E+2a)_IPrAu	14.9	14.2	18.9	11.3	11.4	16.6