< Supporting Information >

Divergent Synthetic Pathway for Pyrimidine-Embedded Medium-Sized Azacycles through *N*-quaternizing Strategy

Yoona Choi[1,†], Heejun Kim[1,†], and Seung Bum Park*[,1,2]

[1]*CRI center for Chemical Proteomics, Department of Chemistry*
[2]*Department of Biophysics and Chemical Biology,*
Seoul National University, Seoul 08826, Korea

sbpark@snu.ac.kr

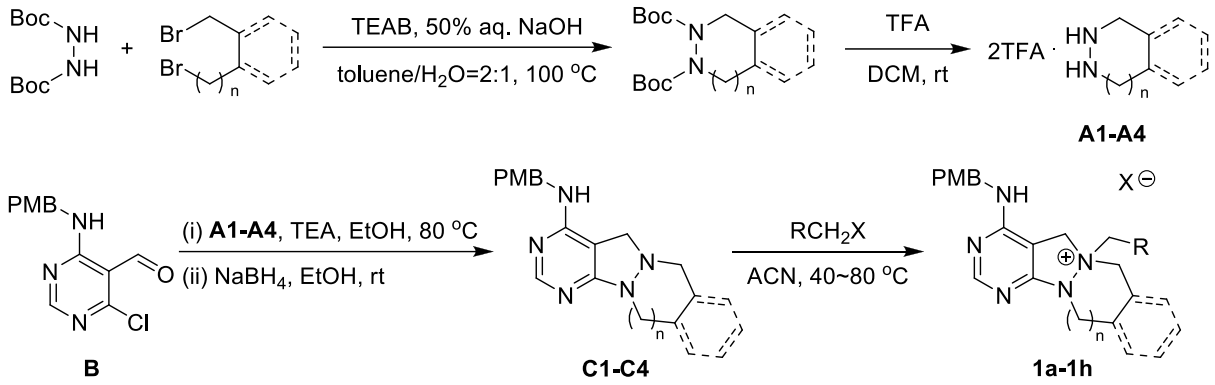
†These authors contributed equally to this work.

I. General information

All commercially available reagents and solvents were purchased from commercial vendors and used without further purification unless noted otherwise. ^{1}H and ^{13}C NMR spectra were obtained on Agilent 400–MR DD2 Magnetic Resonance System (400 MHz, Agilent Technologies) or Varian Inova–500 (500 MHz, Varian Associates). Chemical shifts were measured in parts per million (δ), referenced to tetramethylsilane (TMS) as the internal standard or to the residual solvent peak ($CDCl_3$, ^{1}H: 7.27, ^{13}C: 77.00; MeOH-d_4, ^{1}H: 3.31, ^{13}C: 49.15; acetone-d_6, ^{1}H: 2.05, ^{13}C: 29.92; DMSO-d_6, ^{1}H: 2.50, ^{13}C: 39.50; DCM-d_2, ^{1}H: 5.32, ^{13}C: 54.00). Multiplicities were indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets), brs (broad singlet), and so on. Coupling constants were reported in hertz (Hz). Low-resolution mass spectra (LRMS) were analyzed on LCMS-2020 (Shimazu) using the electrospray ionization (ESI) method. High-resolution mass spectra (HRMS) were analyzed on Compact (Bruker) using the electrospray ionization (ESI) method at the Organic Chemistry Research Center in Sogang University. X-ray crystallographic analysis was performed at Ewha Womans University. The conversion of starting materials was monitored using thin–layer chromatography (TLC) (Merck Kiselgel 60 F_{254} plates), and components were visualized by observation under UV light (254 and 365 nm) or by treating the TLC plates with visualizing agents such as $KMnO_4$, phosphomolybdic acid, and ninhydrin followed by thermal visualization. Products were purified by flash column chromatography on Merck Kieselgel 60 (230–400 mesh). All quantum mechanical calculations were performed in Gaussin09W. The ground state structures of synthesized core skeletons were optimized using density functional theory (DFT) at the B3LYP/6-31G* level. The moment of inertia values of synthesized core skeletons and reported benzannulated medium-sized rings were calculated by PreADMET software for the plotting of principal moment of inertia (PMI).

II. Synthetic procedure and compound characterization

Scheme S1. Synthetic scheme for pyrimidine-containing azacyclic key intermediates **1a**–**1h**.



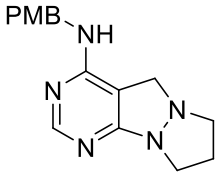
1. General synthetic procedure for the preparation of A1–A4.

To a solution of di-*tert*-butyl hydrazodicarboxylate (2.0 g, 8.6 mmol) and tetraethylammonium bromide (TEAB, 271.4 mg, 1.3 mmol) in toluene (10 mL), 50% aq. NaOH solution (5 mL) and alkyl dibromide (8.8 mmol) were added at room temperature. The resulting mixture was vigorously stirred at 100 °C. After the completion of the reaction was checked by TLC, the resulting solution was quenched with deionized water and saturated aq. NaCl, and the organic material was extracted twice with ethyl acetate (EA). The combined organic extracts were dried over anhydrous Na_2SO_4(s) and filtered. After the solvent was evaporated under reduced pressure, the residue was purified by silica gel flash column chromatography to obtain the desired Boc protected cyclic hydrazines (1.1~2.3 g, 41~94% yields). The resultant was dissolved in dichloromethane (DCM), and trifluoroacetic acid (TFA) was added. The reaction mixture was stirred at room temperature. After the completion of the reaction was checked by TLC, the resulting solution was concentrated under reduced pressure to obtain the desired compounds **A1**–**A4** (1.2~2.5 g, quantitative yields).

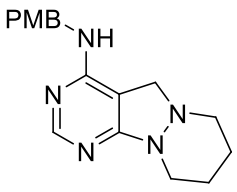
2. General synthetic procedure for the preparation of C1–C4.

Preparation of 4-chloro-6-(4-methoxybenzylamino)pyrimidine-5-carboxaldehyde (**B**) was conducted refer to the reported synthetic procedure.[1]

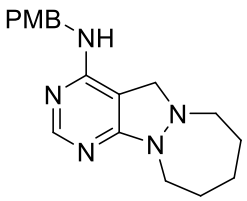
To a solution of **B** (1.0 g, 3.6 mmol) in ethanol (36 mL, 0.1 M), triethylamine (TEA, 2.5 mL, 18.0 mmol) and cyclic hydrazines **A1**–**A4** (4.0 mmol) were added at room temperature. The resulting mixture was stirred at 80 °C. After the complete consumption of starting material was checked by TLC, the reaction mixture was cooled down to room temperature. $NaBH_4$ (408.7 mg, 10.8 mmol) was added to the reaction mixture, and the resulting mixture was stirred at room temperature. When the completion of the reaction was checked by TLC, the resulting mixture was concentrated under reduced pressure, quenched with deionized water and saturated aq. NaCl, and the organic material was extracted three times with EA. The combined organic extracts were dried over anhydrous Na_2SO_4(s) and filtered. After the solvent was evaporated under reduced pressure, the residue was purified by silica gel flash column chromatography to obtain the desired compounds **C1**–**C4**.



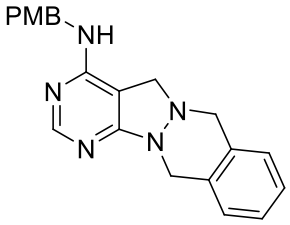
(**C1**) Yield: 66%, 706.7 mg; pale yellow oil; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.13 (s, 1 H), 7.27 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 6.43 (brs., 1 H), 4.61 (d, *J* = 5.5 Hz, 2 H), 4.03 (brs, 2 H), 3.76 (s, 3 H), 3.01 (brs, 4 H), 1.97 (brs, 2 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 170.9, 159.8, 159.6, 158.8, 133.2, 129.6, 114.6, 95.2, 55.5, 52.2, 51.9, 46.0, 44.4, 26.5; LRMS (ESI) *m/z* calcd for $C_{16}H_{20}N_5O$ $[M+H]^+$: 298.17; Found: 298.05.



(**C2**) Yield: 81%, 908.2 mg; pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1 H), 7.24 (d, *J* = 8.2 Hz, 2 H), 6.87 (d, *J* = 8.2 Hz, 2 H), 4.54 (s, 3 H), 3.90 (brs, 3 H), 3.80 (s, 3 H), 2.81 (brs, 2 H), 1.76 (quint, *J* = 5.6 Hz, 2 H), 1.62 (brs, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 158.9, 157.8, 156.4, 131.0, 128.6, 114.1, 93.3, 55.2, 54.5, 54.1, 45.1, 44.7, 24.5, 23.2; LRMS (ESI) *m/z* calcd for $C_{17}H_{22}N_5O$ $[M+H]^+$: 312.18; Found: 312.15.



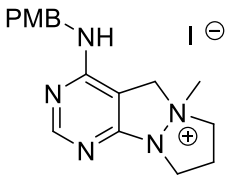
(**C3**) Yield: 68%, 796.8 mg; off-white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (s, 1 H), 7.24 (d, *J* = 8.4 Hz, 2 H), 6.87 (m, *J* = 8.8 Hz, 2 H), 4.56 (d, *J* = 5.4 Hz, 2 H), 4.51 (brs, 1 H), 4.11 (s, 2 H), 3.79 (s, 3 H), 3.52 (t, *J* = 5.9 Hz, 2 H), 2.89 (t, *J* = 5.9 Hz, 2 H), 1.83 (quint, *J* = 4.9 Hz, 2 H), 1.742-1.737 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 159.0, 158.2, 156.5, 130.9, 128.8, 114.0, 94.0, 62.0, 56.3, 55.3, 50.4, 44.6, 29.0, 27.5, 25.0; LRMS (ESI) *m/z* calcd for $C_{18}H_{24}N_5O$ $[M+H]^+$: 326.20; Found: 326.10.



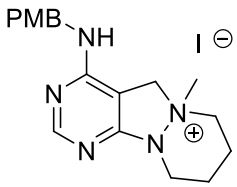
(**C4**) Yield: 36%, 465.9 mg; pale yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1 H), 7.18–7.28 (m, 5 H), 7.09 (d, *J* = 6.9 Hz, 1 H), 6.89 (d, *J* = 8.9 Hz, 2 H), 4.59–4.61 (m, 4 H), 4.13 (brs, 1 H), 4.05 (brs, 2 H), 3.80 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 159.0, 157.9, 156.5, 132.9, 131.5, 130.8, 128.7, 126.8, 126.6, 126.5, 126.4, 114.1, 94.5, 57.0, 55.3, 54.3, 48.7, 44.7; LRMS (ESI) *m/z* calcd for $C_{21}H_{22}N_5O$ $[M+H]^+$: 360.18; Found: 360.10.

3. General synthetic procedure for the preparation of 1a–1h.

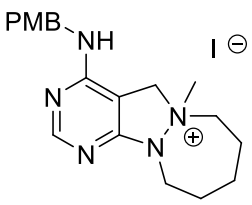
To a solution of pyrimidine-embedded tricyclic/tetracyclic precursor **C1**–**C4** (0.96 mmol) in acetonitrile (ACN, 4.8 mL, 0.2 M), halide partner (2.89 mmol) was added at room temperature. The resulting mixture was stirred at 40~80 °C depending on halide partners. After the complete consumption of starting material was checked by TLC, the reaction mixture was concentrated under reduced pressure to obtain the desired compounds **1a**–**1c** and **1h**. In the case of **1d**–**1g**, further purification was performed by silica-gel flash column chromatography. *tert*-Butyl(2-iodoethoxy)diphenylsilane and *tert*-butyl(3-iodopropoxy)diphenylsilane, for **1d** and **1e** respectively, were synthesized on the basis of the reported synthetic procedure.[2]



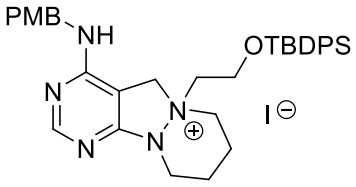
(**1a**) Yield: 99% from **C1**, 419.0 mg; yellow solid; ^{1}H NMR (500 MHz, MeOH-d_4) δ 8.33 (s, 1 H), 7.29 (d, J = 8.3 Hz, 2 H), 8.86 (d, J = 8.8 Hz, 2 H), 5.28 (d, J = 13.7 Hz, 1 H), 4.96 (d, J = 13.7 Hz, 1 H), 4.62 (s, 2 H), 4.13–4.21 (m, 1 H), 4.07–4.11 (m, 1 H), 3.79–3.87 (m, 2 H), 3.76 (s, 3 H), 3.62 (s, 3 H), 2.55–2.64 (m, 1 H), 2.38–2.47 (m, 1 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 165.4, 160.3, 159.8, 158.2, 132.2, 130.2, 114.5, 92.4, 68.5, 65.8, 55.6, 54.5, 49.8, 43.9, 43.8, 25.2; LRMS (ESI) *m/z* calcd for $C_{17}H_{22}N_5O^+$ $[M]^+$: 312.18; Found: 312.10.



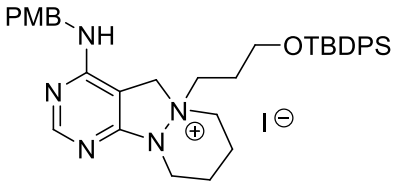
(**1b**) Yield: 99% from **C2**, 432.4 mg; off-white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (s, 1 H), 8.00 (t, J = 5.6 Hz, 1 H), 7.26 (d, J = 8.3 Hz, 2 H), 6.89 (d, J = 8.3 Hz, 2 H), 4.95 (ABq, $\Delta\delta_{AB}$ = 0.07, J_{AB} = 13.7 Hz, 2 H), 4.50–4.60 (m, 2 H), 4.10 (d, J = 15.2 Hz, 1 H), 3.77 (s, 3 H), 3.72 (s, 5 H), 3.66–3.69 (m, 1 H), 2.15–2.26 (m, 1 H), 1.75 (d, J = 14.7 Hz, 1 H), 1.59 (d, J = 13.2 Hz, 1 H), 1.40–1.48 (m, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 158.8, 158.3, 156.6, 131.0, 128.7, 113.7, 89.6, 67.5, 59.4, 55.2, 55.1, 48.4, 48.3, 42.8, 40.6, 18.6, 17.9; LRMS (ESI) *m/z* calcd for $C_{18}H_{24}N_5O^+$ $[M]^+$: 326.20; Found: 326.20.



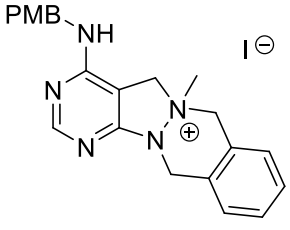
(**1c**) Yield: 99% from **C3**, 445.8 mg; pale yellow solid; ^{1}H NMR (400 MHz, MeOH-d_4) δ 8.24 (s, 1 H), 7.30 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 5.16 (ABq, $\Delta\delta_{AB}$ = 0.07, J_{AB} = 14.1 Hz, 2 H), 4.60 (ABq, $\Delta\delta_{AB}$ = 0.03, J_{AB} = 15.3 Hz, 2 H), 4.26–4.33 (m, 2 H), 4.03 (dd, J = 14.1, 8.6 Hz, 1 H), 3.81–3.87 (m, 1 H), 3.76 (s, 3 H), 3.61 (s, 3 H), 1.96–2.09 (m, 2 H), 1.80–1.87 (m, 4 H), 1.63–1.70 (m, 2 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.7, 160.6, 160.4, 157.8, 132.3, 130.3, 115.1, 88.4, 71.9, 71.0, 57.1, 55.9, 45.0, 44.7, 28.1, 27.1, 24.1; LRMS (ESI) *m/z* calcd for $C_{19}H_{26}N_5O^+$ $[M]^+$: 340.21; Found: 340.15.



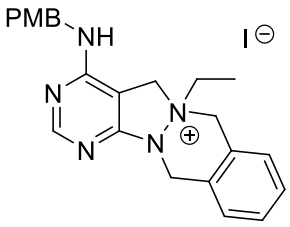
(**1d**) Yield: 72% from **C2**, 500.7 mg; yellow solid; ^{1}H NMR (500 MHz, MeOH-d_4) δ 8.34 (s, 1 H), 7.63 (d, J = 6.4 Hz, 2 H), 7.53 (d, J = 6.8 Hz, 2 H), 7.38–7.46 (m, 4 H), 7.33 (t, J = 7.35 Hz, 2 H), 7.28 (d, J = 8.3 Hz, 2 H), 6.83 (d, J = 8.8 Hz, 2 H), 5.70 (d, J = 13.2 Hz, 1 H), 5.01 (d, J = 13.2 Hz, 1 H), 4.70 (d, J = 14.7 Hz, 1 H), 4.52 (d, J = 15.2 Hz, 1 H), 4.33–4.42 (m, 2 H), 4.18–4.27 (m, 2 H), 4.08 (d, J = 13.2 Hz, 1 H), 3.83–3.94 (m, 2 H), 3.74 (s, 3 H), 3.47–3.53 (m, 1 H), 2.29–2.37 (m, 1 H), 1.88 (d, J = 15.2 Hz, 1 H), 1.61–1.64 (m, 2 H), 0.95 (s, 9 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 160.5, 158.6, 136.8, 136.7, 133.0, 132.9, 132.3, 131.5, 130.3, 129.30, 129.26, 115.0, 90.4, 68.8, 63.2, 61.4, 60.0, 55.91, 55.87, 44.8, 42.8, 29.7, 27.3, 19.9, 19.8; LRMS (ESI) *m/z* calcd for $C_{35}H_{44}N_5O_2Si^+$ $[M]^+$: 594.33; Found: 594.40.



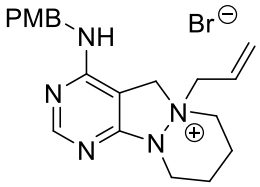
(**1e**) Yield: 72% from **C2**, 510.4 mg; yellow solid; ^{1}H NMR (400 MHz, MeOH-d_4) δ 8.29 (s, 1 H), 7.68 (d, J = 7.4 Hz, 4 H), 7.39–7.44 (m, 6 H), 7.30 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 4.88 (ABq, $\Delta\delta_{AB}$ = 0.04, J_{AB} = 13.7 Hz, 2 H), 4.61 (s, 2 H), 4.15–4.24 (m, 2 H), 4.04–4.11 (m, 1 H), 3.90 (t, J = 5.3 Hz, 2 H), 3.81 (dd, J = 13.3, 2.8 Hz, 1 H), 3.74 (s, 3 H), 3.68–3.72 (m, 1 H), 3.46–3.54 (m, 1 H), 2.18–2.27 (m, 1 H), 1.96–2.14 (m, 2 H), 1.86 (d, J = 15.3 Hz, 1 H), 1.60–1.64 (m, 2 H), 1.07 (s, 9 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 160.6, 160.5, 158.7, 136.8, 134.42, 134.36, 132.2, 131.3, 130.3, 129.2, 115.1, 90.4, 60.3, 61.6, 60.6, 58.0, 55.92, 55.89, 45.0, 42.5, 27.8, 27.6, 20.1, 19.7; LRMS (ESI) *m/z* calcd for $C_{36}H_{46}N_5O_2Si^+$ $[M]^+$: 608.34; Found: 608.30.



(**1f**) Yield: 49% from **C4**, 236.7 mg; light brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1 H), 7.28–7.43 (m, 6 H), 6.78 (d, J = 8.2 Hz, 2 H), 5.74 (d, J = 13.7 Hz, 1 H), 5.51 (dd, J = 19.4, 14.3 Hz, 2 H), 5.35 (d, J = 17.2 Hz, 1 H), 5.00 (d, J=14.5 Hz, 1 H), 4.62–4.68 (m, 3 H), 3.72 (s, 3 H), 3.70 (s, 3 H), 2.55 ppm (brs, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 159.5, 158.7, 157.0, 130.5, 129.8, 129.5, 128.7, 128.2, 126.6, 126.3, 124.2, 113.7, 89.4, 69.6, 61.4, 55.2, 50.4, 43.9, 43.6; LRMS (ESI) *m/z* calcd for $C_{22}H_{24}N_5O^+$ $[M]^+$: 374.20; Found: 374.20.

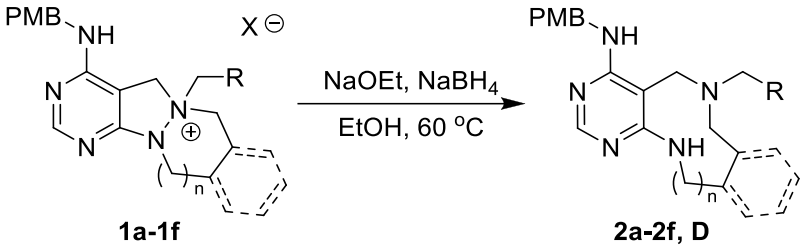


(**1g**) Yield: 62% from **C4**, 307.9 mg; brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1 H), 7.34–7.46 (m, 5 H), 7.29 (d, *J* = 5.5 Hz, 1 H), 6.76 (d, *J* = 8.2 Hz, 2 H), 5.68–5.74 (m, 1 H), 5.38–5.45 (m, 2 H), 5.30 (d, *J* = 14.9 Hz, 1 H), 5.00 (d, *J* = 14.9 Hz, 1 H), 4.61–4.66 (m, 3 H), 4.15–4.24 (m, 1 H), 3.77–3.87 (m, 1 H), 3.69 (s, 3 H), 2.59 (brs, 1 H), 1.50 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 159.5, 158.7, 157.0, 130.5, 129.9, 129.6, 128.8, 128.3, 127.8, 126.2, 124.0, 113.7, 89.3, 66.3, 59.8, 59.1, 55.1, 44.8, 43.6, 9.4; LRMS (ESI) *m/z* calcd for $C_{23}H_{26}N_5O^+$ $[M]^+$: 388.21; Found: 388.20.

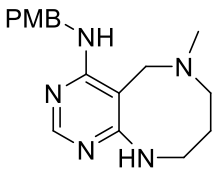


(**1h**) Yield: 99% from **C2**, 412.4 mg; off-white solid; ^{1}H NMR (500 MHz, MeOH-d_4) δ 8.29 (s, 1 H), 7.29 (d, *J* = 8.3 Hz, 2 H), 6.86 (d, *J* = 8.3 Hz, 2 H), 6.02–6.11 (m, 1 H), 5.85 (d, *J* = 16.6 Hz, 1 H), 5.74 (d, *J* = 10.3 Hz, 1 H), 5.01 (d, *J* = 13.2 Hz, 1 H), 4.72–4.80 (m, 3 H), 4.61 (s, 2 H), 4.27 (d, *J* = 14.7 Hz, 1 H), 3.78–3.83 (m, 1 H), 3.75 (s, 3 H), 3.67–3.72 (m, 2 H), 2.34–2.42 (m, 1 H), 1.87 (d, *J* = 15.2 Hz, 1 H), 1.72 (d, *J* = 13.2 Hz, 1 H), 1.59–1.67 (m, 1 H); ^{13}C NMR (100 MHz, MeOH-d_4) δ 163.2, 160.6, 160.4, 158.7, 132.3, 130.2, 129.2, 126.3, 115.0, 90.6, 65.8, 62.8, 59.6, 55.9, 55.8, 44.9, 42.4, 19.9, 19.4; LRMS (ESI) *m/z* calcd for $C_{20}H_{26}N_5O^+$ $[M]^+$: 352.21; Found: 352.10.

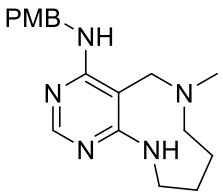
Scheme S2. Synthetic scheme for scaffold I (**2a–2f** and **D**).



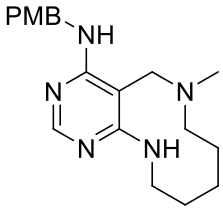
1a-1f **2a-2f, D**



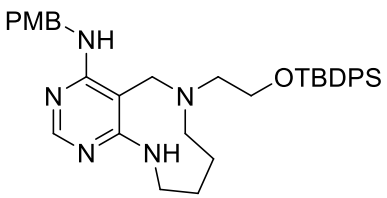
(**2a**) Yield: 69% from **1a**, 34.7 mg; off-white solid; ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.83 (s, 1 H), 7.23 (d, J = 8.2 Hz, 2 H), 6.84 (d, J = 8.6 Hz, 2 H), 4.52 (s, 2 H), 3.95 (s, 2 H), 3.76 (s, 3 H), 3.66 (t, J = 6.3 Hz, 2 H), 2.74 (t, J = 5.1 Hz, 2 H), 2.40 (s, 3 H), 1.96–1.98 (m, 2 H); ^{13}C NMR (100 MHz, MeOH-d_4) δ 164.1, 164.0, 160.3, 157.1, 133.3, 129.8, 114.9, 90.0, 55.8, 50.0, 48.1, 45.5, 43.5, 42.3, 29.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{24}N_5O$ $[M+H]^+$: 314.1975; Found: 314.1976.



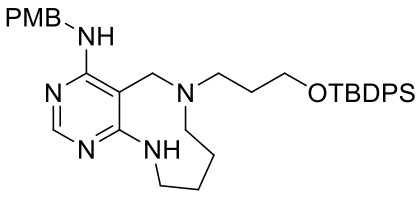
(**2b**) Yield: 84% from **1b**, 44.2 mg; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1 H), 8.17 (brs, 1 H), 7.27 (d, J = 8.2 Hz, 2 H), 6.88 (d, J = 8.2 Hz, 2 H), 4.56–4.60 (m, 3 H), 3.80 (s, 3 H), 3.43 (brs, 2 H), .3.40 (s, 2 H), 2.44 (s, 3 H), 2.28–2.30 (m, 2 H), 1.61–1.63 (m, 2 H), 1.55–1.57 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 160.4, 158.9, 156.5, 131.2, 129.1, 114.0, 95.1, 55.7, 55.2, 53.4, 45.2, 44.8, 44.4, 31.4, 28.1; HRMS (ESI) *m/z* calcd for $C_{18}H_{26}N_5O$ $[M+H]^+$: 328.2132; Found: 328.2130.



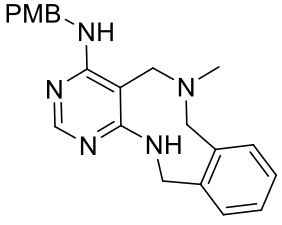
(**2c**) Yield: 56% from **1c**, 30.7 mg; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (brs, 1 H), 8.25 (s, 1 H), 7.27 (d, J = 8.2 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 4.58 (d, J = 5.1 Hz, 2 H), 4.28 (brs, 1 H), 3.80 (s, 3 H), 3.31 (brs, 2 H), 2.32 (s, 3 H), 1.60 (brs, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 159.5, 158.9, 156.3, 131.5, 129.1, 114.0, 91.9, 55.3, 55.2, 53.7, 49.3, 45.0, 43.7, 41.5, 27.0, 26.2, 21.6; HRMS (ESI) *m/z* calcd for $C_{19}H_{28}N_5O$ $[M+H]^+$: 342.2288; Found: 342.2284.



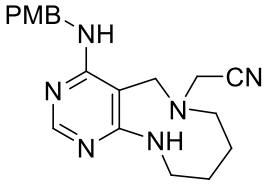
(**2d**) Yield: 71% from **1d**, 67.9 mg; off-white oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1 H), 8.25 (brs, 1 H), 7.65–7.67 (m, 4 H), 7.34–7.42 (m, 6 H), 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.2 Hz, 2 H), 4.57 (d, *J* = 5.1 Hz, 2 H), 4.36 (brs, 1 H), 3.77–3.79 (m, 5 H), 3.41 (brs, 4 H), 2.75 (t, *J* = 5.5 Hz, 2 H), 2.34 (brs, 2 H), 1.60–1.61 (m, 2 H), 1.53 (brs, 2 H), 1.04 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 160.3, 159.0, 156.4, 135.6, 133.3, 131.2, 129.7, 129.2, 127.7, 114.0, 95.2, 61.7, 58.9, 55.3, 54.6, 51.1, 45.3, 44.9, 31.4, 28.8, 26.8, 19.1; HRMS (ESI) *m/z* calcd for $C_{35}H_{46}N_5O_2Si$ $[M+H]^+$: 596.3415; Found: 596.3413.



(**2e**) Yield: 69% from **1e**, 67.6 mg; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1 H), 8.16 (brs, 1 H), 7.66 (d, *J* = 6.3 Hz, 4 H), 7.35–7.43 (m, 6 H), 7.27 (d, *J* = 8.2 Hz, 2 H), 6.88 (d, *J* = 8.2 Hz, 2 H), 4.58 (d, *J* = 4.7 Hz, 2 H), 4.47 (brs, 1 H), 3.79 (s, 3 H), 3.74 (t, *J* = 6.1 Hz, 2 H), 3.35 (brs, 4 H), 2.72 (t, *J* = 7.2 Hz, 2 H), 2.31 (brs, 2 H), 1.76 (quint, *J* = 6.6 Hz, 2 H), 1.58 (brs, 2 H), 1.52 (brs, 2 H), 1.05 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 160.4, 159.0, 156.4, 135.5, 133.7, 131.2, 129.6, 129.2, 127.6, 114.0, 95.2, 61.7, 55.3, 54.7, 54.2, 51.1, 45.4, 44.9, 31.3, 30.8, 29.0, 26.8, 19.2; HRMS (ESI) *m/z* calcd for $C_{36}H_{48}N_5O_2Si$ $[M+H]^+$: 610.3572; Found: 610.3569.

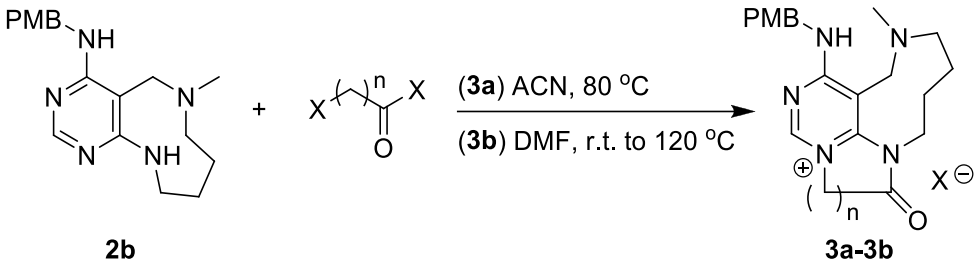


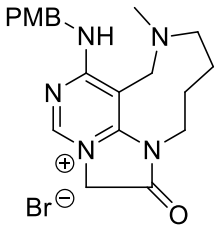
(**2f**) Yield: 14% from **1f**, 8.4 mg; off-white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.75 (s, 1 H), 7.15–7.20 (m, 4 H), 7.07 (d, *J* = 8.3 Hz, 2 H), 6.84 (d, *J* = 8.3 Hz, 2 H), 6.73 (brs, 1 H), 6.62 (brs, 1 H), 4.45 (brs, 4 H), 3.73 (s, 3 H), 3.51 (s, 2 H), 3.40 (s, 2 H), 2.45 (s, 3 H); ^{13}C NMR (100 MHz, DCM-d_2) δ 163.7, 159.2, 156.0, 137.6, 132.5, 131.5, 130.0, 128.8, 128.5, 127.7, 114.2, 98.5, 59.3, 55.8, 48.8, 46.8, 44.3, 30.3; HRMS (ESI) *m/z* calcd for $C_{22}H_{26}N_5O$ $[M+H]^+$: 376.2132; Found: 376.2135.



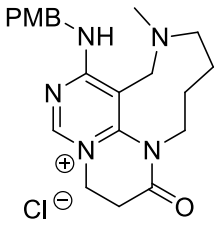
(**D**) Yield: 33% from **1b**, 18.7 mg; yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1 H) 7.27 (d, *J* = 8.5 Hz, 2 H), 7.13 (brs, 1 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 4.66 (t, *J* = 4.8 Hz, 1 H), 4.61 (d, *J* = 5.5 Hz, 2 H), 3.80 (s, 3 H), 3.69 (s, 2 H), 3.60 (s, 2 H), 3.45 (brs, 2 H), 2.52 (t, *J* = 4.0 Hz, 2 H), 1.64–1.69 (m, 2 H), 1.59–1.60 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 160.6, 159.0, 156.9, 131.0, 129.1, 115.2, 114.1, 93.4, 55.3, 55.2, 52.3, 50.5, 45.1, 44.8, 44.3, 31.0, 27.8; LRMS (ESI) *m/z* calcd for $C_{19}H_{25}N_6O$ $[M+H]^+$: 353.21; Found: 353.10.

Scheme S5. Synthetic scheme for scaffold II (**3a**–**3b**).



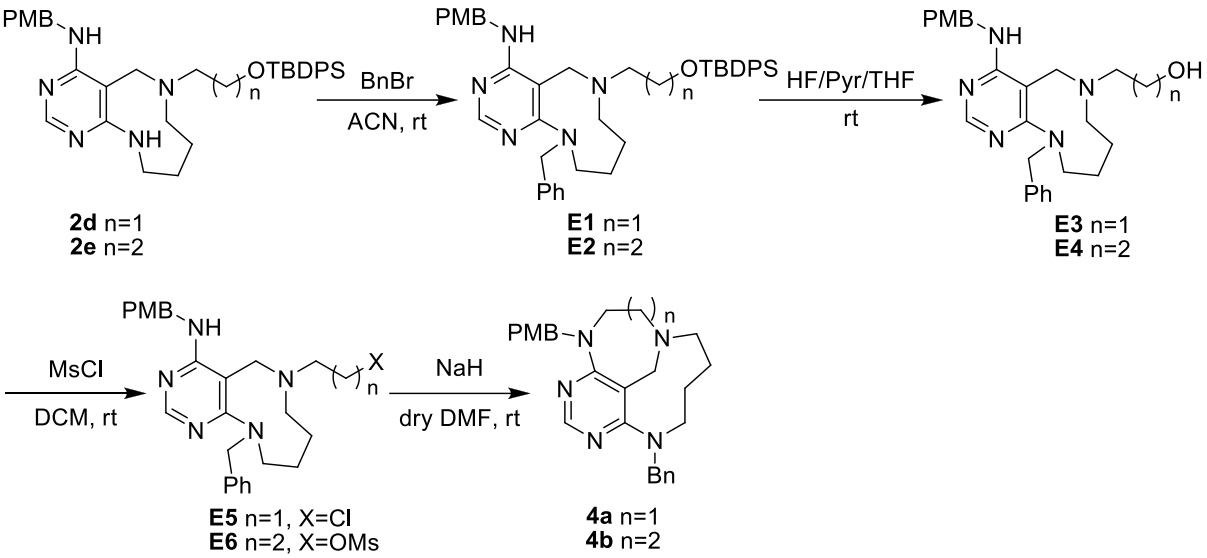


(**3a**) Yield: 80%, 84.1 mg; dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1 H), 7.28 (d, *J* = 8.2 Hz, 2 H), 6.84 (d, *J* = 7.8 Hz, 2 H), 5.35 (s, 2 H), 4.76 (s, 2 H), 4.09 (brs, 2 H), 3.76 (s, 6 H), 3.41 (s, 2 H), 2.78 (s, 2 H), 2.40 (brs, 3 H), 1.82 (brs, 2 H), 1.70 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 163.5, 159.0, 150.5, 148.5, 129.1, 128.7, 114.0, 93.2, 55.2, 53.9, 50.4, 50.3, 47.3, 45.1, 42.5, 42.4, 29.2, 21.4; HRMS (ESI) *m/z* calcd for $C_{20}H_{27}N_5O_2^+$ $[M]^+$: 368.2081; Found: 368.2080.



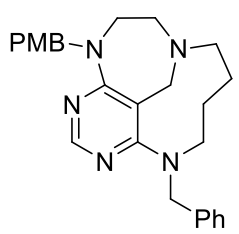
(**3b**) Yield: 67%, 65.6 mg; off-white solid; ^{1}H NMR (500 MHz, MeOH-d_4) δ 8.57 (s, 1 H), 7.30 (d, *J* = 8.3 Hz, 2 H), 6.88 (d, *J* = 8.3 Hz, 3 H), 4.78 (s, 2 H), 4.38 (t, *J* = 5.9 Hz, 2 H), 3.96 (brs, 2 H), 3.76 (s, 3 H), 3.60 (brs, 2 H), 2.89 (t, *J* = 5.9 Hz, 2 H), 2.63–2.66 (m, 2 H), 2.25 (s, 3 H), 1.89 (brs, 2 H), 1.79 (brs, 2 H); ^{13}C NMR (100 MHz, MeOH-d_4) δ 169.6, 165.0, 160.8, 152.2, 149.3, 130.9, 130.3, 115.2, 104.3, 57.0, 55.91, 55.86, 51.3, 46.9, 46.1, 44.0, 32.5, 28.4, 27.4; HRMS (ESI) *m/z* calcd for $C_{21}H_{28}N_5O_2^+$ $[M]^+$: 382.2238; Found: 382.2238.

Scheme S6. Synthetic scheme for scaffold III (**4a**–**4b**).

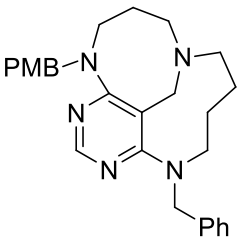


To a solution of **2d**–**2e** (0.73 mmol) in ACN (14.6 mL, 0.05 M), benzyl bromide (130.5 µL, 1.10 mmol) was added at room temperature with stirring. When the completion of the reaction was checked by TLC, the resulting mixture was concentrated under reduced pressure, quenched with deionized water and saturated aq. $NaHCO_3$, and the organic material was extracted three times with EA and three times with DCM. The combined organic extracts were dried over anhydrous Na_2SO_4(s) and filtered. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography to obtain the desired compounds **E1** (84% yield from **2d**, 420.6 mg) and **E2** (87% yield from **2e**, 444.6 mg). **E1** and **E2** (0.26 mmol) were treated with HF/pyridine/tetrahydrofuran (5/5/90) solution (2.6 mL, 0.1 M), and the reaction mixture was stirred at room temperature. When the completion of the reaction was checked by TLC, ethoxytrimethylsilane was added and allowed to quench any excess HF. The resulting mixture was concentrated under reduced pressure, and the residue was purified by silica gel flash column chromatography to obtain the desired compounds **E3** (57% yield from **E1**, 66.3 mg) and **E4** (49% yield from **E2**, 58.8 mg). To a solution of **E3** or **E4** (0.13 mmol) in DCM (2.6 mL, 0.05 M), TEA (36.2 µL, 0.26 mmol) and methanesulfonyl chloride (15.1 µL, 0.20 mmol) were added at room temperature with stirring. When the completion of the reaction was checked by TLC, the resulting mixture was quenched with deionized water and saturated aq. $NaHCO_3$, and the organic material was extracted three times with DCM and three times with EA. The combined organic extracts were dried over anhydrous

Na_2SO_4(s) and filtered. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography to obtain the desired compounds **E5** (22% yield from **E3**, 13.3 mg) and **E6** (57% yield from **E4**, 40.0 mg).

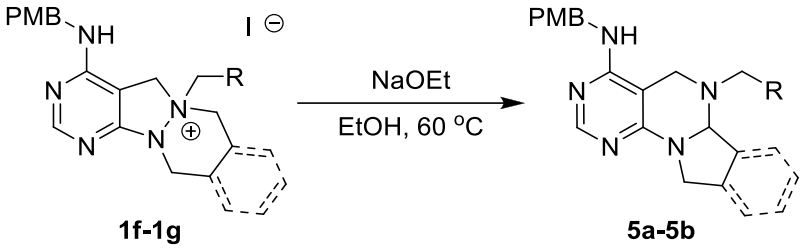


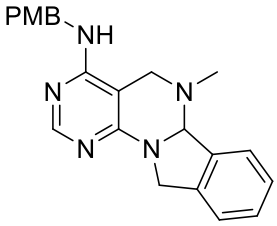
(**4a**) Yield: 80% from **E5**, 17.5 mg; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (s, 1 H), 7.26–7.33 (m, 7 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 5.10 (d, *J* = 14.7 Hz, 1 H), 4.97 (d, *J* = 15.2 Hz, 1 H), 4.42 (d, *J* = 14.7 Hz, 2 H), 3.99 (d, *J* = 14.7 Hz, 1 H), 3.80 (s, 3 H), 3.63 (brs, 2 H), 3.44–3.45 (m, 2 H), 3.10 (dd, *J* = 13.2, 9.3 Hz, 1 H), 2.79–2.85 (m, 2 H), 2.65–2.71(m, 2 H), 1.79–1.83 (m, 1 H), 1.60–1.67 (m, 2 H), 1.44–1.47 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 166.3, 158.7, 154.6, 139.3, 130.9, 129.3, 128.5, 128.3, 127.0, 113.8, 100.5, 55.6, 55.3, 55.2, 54.2, 53.8, 53.6, 53.0, 52.6, 51.7, 28.9, 25.9; HRMS (ESI) *m/z* calcd for $C_{26}H_{32}N_5O$ $[M+H]^+$: 430.2601; Found: 430.2602.



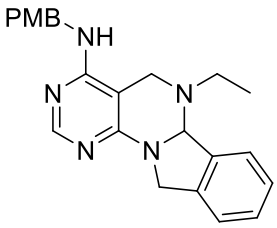
(**4b**) Yield: 40% from **E6**, 9.1 mg; white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1 H), 7.39 (d, *J* = 7.3 Hz, 2 H), 7.26–7.29 (m, 2 H), 7.18–7.21 (m, 3 H), 6.85 (d, *J* = 8.3 Hz, 2 H), 5.01 (d, *J* = 14.7 Hz, 1 H), 4.87 (d, *J* = 15.2 Hz, 1 H), 4.81 (dd, *J* = 13.5, 3.7 Hz, 1 H), 4.75 (d, *J* = 15.2 Hz, 1 H), 4.14 (d, *J* = 14.7 Hz, 1 H), 4.05 (d, *J* = 14.7 Hz, 1 H), 3.79 (s, 3 H), 3.49–3.59 (m, 2 H), 3.11 (dd, *J* = 13.9, 2.7 Hz, 1 H), 2.98 (d, *J* = 14.7 Hz, 1 H), 2.88 (dd, *J* = 11.0, 6.1 Hz, 1 H), 2.70–2.75 (m, 2 H), 2.43–2.48 (m, 1 H), 2.21 (t, *J* = 11.2 Hz, 1 H), 1.93–2.04 (m, 1H), 1.70–1.83 (m, 2 H), 1.45–1.50 (m, 1 H), 1.37–1.40 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 161.3, 158.6, 154.9, 140.4, 131.2, 128.8, 128.5, 128.0, 126.5, 113.8, 105.0, 58.9, 57.3, 57.1, 55.3, 55.2, 55.1, 53.4, 44.9, 28.4, 26.6, 21.4; HRMS (ESI) *m/z* calcd for $C_{27}H_{34}N_5O$ $[M+H]^+$: 444.2758; Found: 444.2758.

Scheme S7. Synthetic scheme for scaffold IV (**5a**–**5b**).



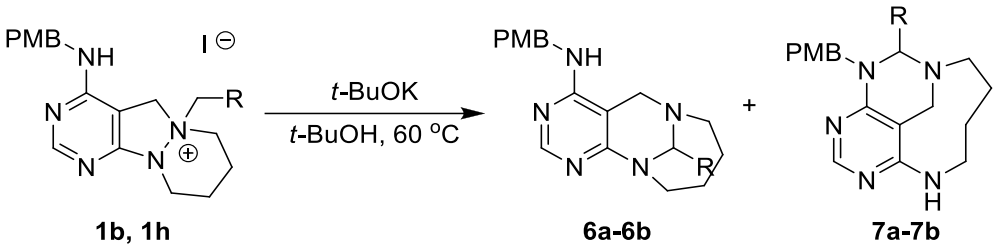


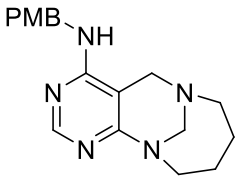
(**5a**) Yield: 47% from **1f**, 26.3 mg; orange solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1 H), 7.37–7.44 (m, 4 H), 7.29 (d, J = 8.3 Hz, 2 H), 6.89 (d, J = 8.3 Hz, 2 H), 5.85 (s, 1 H), 4.87 (ABq, $\Delta\delta_{AB}$ = 0.04, J_{AB} = 14.9 Hz, 2 H), 4.56–4.70 (m, 2 H), 4.21 (brs, 1 H), 4.16 (d, J = 15.7 Hz, 1 H), 3.80 (s, 3 H), 3.50 (d, J = 15.2 Hz, 1 H), 1.93 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 158.2, 156.6, 156.2, 138.0, 136.6, 131.3, 129.1, 128.9, 127.7, 123.7, 123.1, 114.0, 88.0, 80.0, 55.2, 51.9, 50.3, 44.6, 34.4; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}N_5O$ $[M+H]^+$: 374.1975; Found: 374.1976.



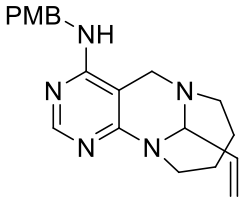
(**5b**) Yield: 40% from **1g**, 23.2 mg; light brown solid; NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1 H), 7.45 (d, J = 6.8 Hz, 1 H), 7.35–7.39 (m, 3 H), 7.26–7.30 (m, 3 H), 6.89 (d, J = 6.4 Hz, 2 H), 5.91 (s, 1 H), 4.84 (ABq, $\Delta\delta_{AB}$ = 0.03, J_{AB} = 14.7 Hz, 2 H), 4.56–4.70 (m, 2 H), 4.27 (brs, 1 H), 4.01 (d, J = 15.7 Hz, 1 H), 3.81 (s, 3 H), 3.71 (d, J = 15.7 Hz, 1 H), 2.15–2.22 (m, 1 H), 1.96–2.04 (m, 1 H), 0.95 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 158.2, 156.7, 156.6, 138.1, 136.7, 131.4, 129.1, 128.9, 127.7, 123.8, 123.2, 114.1, 88.2, 80.8, 55.3, 51.6, 45.6, 44.7, 39.2, 13.7; HRMS (ESI) *m/z* calcd for $C_{23}H_{26}N_5O$ $[M+H]^+$: 388.2132; Found: 388.2133.

Scheme S8. Synthetic scheme for scaffold V (**6a**–**6b**) and scaffold III (**7a**–**7b**).

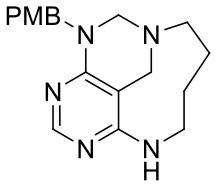




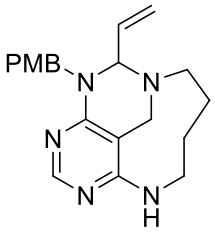
(**6a**) Yield: 67% from **1b**, 50.1 mg; off-white solid; ^{1}H NMR (400 MHz, MeOH-d_4) δ 8.03 (s, 1 H), 7.23 (d, J = 8.2 Hz, 2 H), 6.84 (d, J = 8.6 Hz, 2 H), 4.56 (ABq, $\Delta\delta_{AB}$ = 0.02, J_{AB} = 15.1 Hz, 2 H), 4.41(dd, J = 13.7, 2.0 Hz, 1 H), 4.14–4.20 (m, 2 H), 3.99 (d, J = 16.0 Hz, 1 H), 3.74 (s, 3 H), 3.37 (d, J = 16.4 Hz, 1 H), 3.21–3.26 (m, 1 H), 2.92–2.99 (m, 1 H), 2.40–2.45 (m, 1 H), 1.87–1.92 (m, 1 H), 1.68–1.78 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 159.3, 156.0, 131.0, 129.2, 114.1, 95.6, 66.2, 56.0, 55.3, 50.9, 49.2, 44.6, 31.5, 26.1; HRMS (ESI) *m/z* calcd for $C_{18}H_{24}N_5O$ $[M+H]^+$: 326.1975; Found: 326.1977.



(**6b**) Yield: 47% from **1h**, 38.0 mg; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1 H), 7.28 (d, J = 8.3 Hz, 2 H), 6.88 (d, J = 8.3 Hz, 2 H), 5.81 (ddd, J = 17.1, 10.5, 2.7 Hz, 1 H), 5.27 (d, J = 17.6 Hz, 1 H), 5.17 (d, J = 10.3 Hz, 1 H), 4.75 (brs, 1 H), 4.58 (d, J = 5.4 Hz, 2 H), 4.42–4.48 (m, 1 H), 4.15 (brs, 1 H), 3.88 (d, J = 16.1 Hz, 1 H), 3.80 (s, 3 H), 3.17–3.24 (m, 2 H), 3.00–3.06 (m, 1 H), 2.58–2.63 (m, 1 H), 1.91–1.94 (m, 2 H), 1.60–1.68 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 159.0, 158.6, 156.1, 134.9, 130.9, 129.2, 118.2, 114.0, 95.3, 73.6, 57.1, 55.2, 48.9, 45.6, 44.7, 31.5, 26.1; HRMS (ESI) *m/z* calcd for $C_{20}H_{26}N_5O$ $[M+H]^+$: 352.2132; Found: 352.2133.

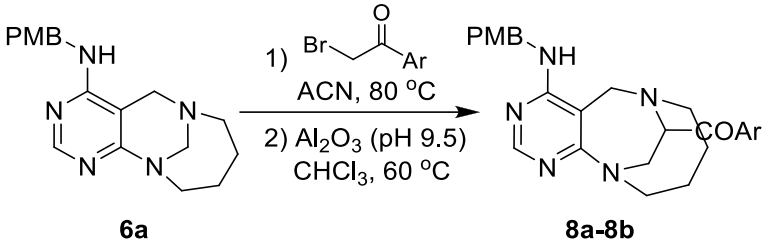


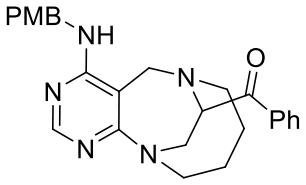
(**7a**) Yield: 10% from **1b**, 7.5 mg; white solid; ^{1}H NMR (400 MHz, MeOH-*d*$_4$) δ 7.91 (s, 1 H), 7.22 (d, *J* = 8.2 Hz, 2 H), 6.89 (d, *J* = 8.2 Hz, 2 H), 4.98 (d, *J* = 14.9 Hz, 1 H), 4.55 (d, *J* = 11.7 Hz, 1 H), 4.43 (d, *J* = 15.6 Hz, 1 H), 4.23 (d, *J* = 15.7 Hz, 1 H), 3.86 (d, *J* = 11.3 Hz, 1 H), 3.78 (s, 3 H), 3.62 (dd, *J* = 15.7, 10.2 Hz, 1 H), 3.52 (d, *J* = 15.3 Hz, 1 H), 3.42 (dd, *J* = 16.2, 6.8 Hz, 1 H), 2.71 (t, *J* = 10.2 Hz, 1 H), 2.23–2.31 (m, 2 H), 1.95–2.02 (m, 1 H), 1.33–1.42 (m, 1 H), 0.98–1.03 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 159.4, 158.8, 155.6, 129.9, 128.8, 113.9, 85.8, 68.3, 55.2, 53.5, 47.4, 47.1, 43.5, 32.3, 27.5; HRMS (ESI) *m/z* calcd for $C_{18}H_{24}N_5O$ $[M+H]^+$: 326.1975; Found: 326.1979.



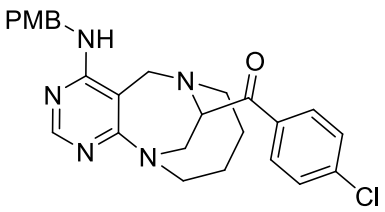
(**7b**) Yield: 33% from **1h**, 26.7 mg; colorless oil; ^{1}H NMR (400 MHz, MeOH_*d*$_4$) δ 7.94 (s, 1 H), 7.16 (d, *J* = 8.4 Hz, 2 H), 6.83 (d, *J* = 8.4 Hz, 2 H), 5.86–5.94 (m, 1 H), 5.61 (d, *J* = 15.2 Hz, 1 H), 5.43 (d, *J* = 10.4 Hz, 1 H), 5.28 (d, *J* = 17.2 Hz, 1 H), 4.28 (d, *J* = 5.2 Hz, 1 H), 3.96 (d, *J* = 16.4 Hz, 1 H), 3.90 (d, *J* = 15.2 Hz, 1 H), 3.75 (s, 3 H), 3.54–3.63 (m, 2 H), 3.39 (dd, *J* = 16.0, 7.2 Hz, 1 H), 2.50 (dd, *J* = 11.0, 9.4 Hz, 1 H), 2.17–2.26 (m, 1 H), 2.01 (dd, *J* = 11.2, 9.6 Hz, 1 H), 1.86–1.94 (m, 1 H), 1.28–1.39 (m, 1 H), 0.87–0.95 (m, 1 H); ^{13}C NMR (400 MHz, MeOH_*d*$_4$) δ 161.5, 161.1, 160.7, 156.2, 156.1, 136.7, 131.3, 130.5, 119.3, 115.1, 87.3, 76.8, 55.9, 55.8, 55.5, 48.0, 47.9, 47.6, 38.6, 33.8, 28.1; HRMS (ESI) *m/z* calcd for $C_{20}H_{26}N_5O$ $[M+H]^+$: 352.2132; Found: 352.2133.

Scheme S9. Synthetic scheme for scaffold VI (**8a**–**8b**).



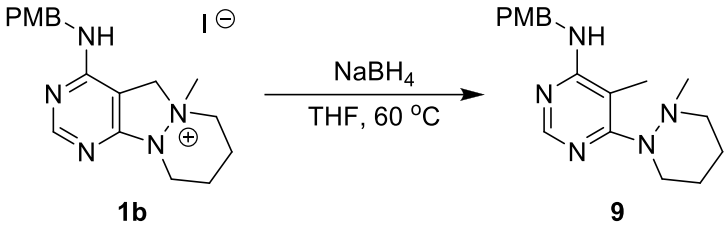


(**8a**) Yield: 44%, 56.6 mg; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1 H), 7.93 (d, *J* = 7.8 Hz, 2 H), 7.57 (t, *J* = 7.3 Hz, 1 H), 7.47 (t, *J* = 7.6 Hz, 2 H), 7.24 (d, *J* = 8.6 Hz, 2 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 4.72 (dd, *J* = 11.3, 6.3 Hz, 1 H), 4.48–4.64 (m, 3 H), 4.11–4.21 (m, 2 H), 3.93 (d, *J* = 17.2 Hz, 1 H), 3.79 (s, 3 H), 3.40–3.48 (m, 2 H), 3.30–3.37 (m, 1 H), 3.05–3.16 (m, 2 H), 1.99–2.04 (m, 2 H), 1.68–1.76 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 165.3, 160.9, 159.0, 155.3, 136.0, 133.0, 130.7, 129.2, 128.5, 128.3, 114.0, 99.6, 61.4, 56.7, 55.3, 51.5, 50.2, 46.3, 45.0, 30.9, 28.5; HRMS (ESI) *m/z* calcd for $C_{26}H_{30}N_5O_2$ $[M+H]^+$: 444.2394; Found: 444.2393.



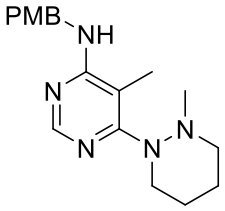
(**8b**) Yield: 44%, 61.0 mg; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1 H), 7.86 (d, *J* = 8.6 Hz, 2 H), 7.43 (d, *J* = 8.6 Hz, 2 H), 7.24 (d, *J* = 8.6 Hz, 2 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 4.47–4.65 (m, 4 H), 4.11–4.20 (m, 2 H), 3.83 (d, *J* = 16.8 Hz, 1 H), 3.78 (s, 3 H), 3.39–3.46 (m, 2 H), 3.27–3.34 (m, 1 H), 3.05–3.13 (m, 2 H), 1.97–2.04 (m, 2 H), 1.68–1.76 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 165.2, 160.9, 159.0, 155.3, 139.3, 134.3, 130.7, 129.8, 129.3, 128.8, 114.0, 99.4, 61.6, 56.7, 55.3, 55.2, 51.4, 50.2, 46.3, 45.0, 30.9, 28.4; HRMS (ESI) *m/z* calcd for $C_{26}H_{29}ClN_5O_2$ $[M+H]^+$: 478.2004; Found: 478.2005.

Scheme S10. Synthetic scheme for compound **9**.



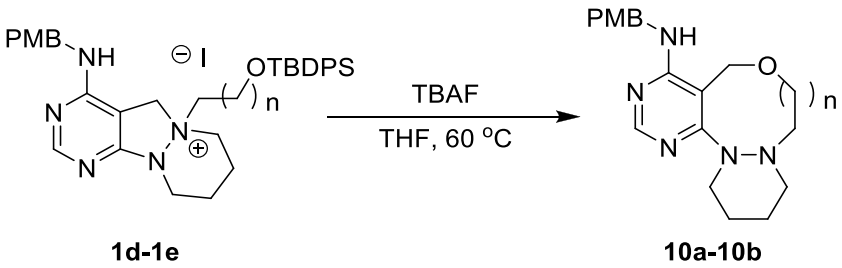
1b **9**

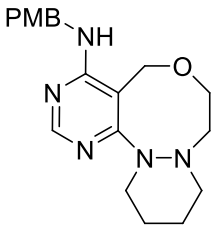
To a solution of **1b** (82.0 mg, 0.18 mmol) in tetrahydrofuran (THF, 1.8 mL, 0.1 M), $NaBH_4$ (34.2 mg, 0.90 mmol) was added at room temperature. The resulting mixture was stirred at 60 °C. When the completion of the reaction was checked by TLC, the reaction mixture was concentrated under reduced pressure, quenched with deionized water and saturated aq. NaCl, and the organic material was extracted three times with EA and three times with DCM. The combined organic extracts were dried over anhydrous Na_2SO_4(s) and filtered. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography to obtain the desired compound **9**.



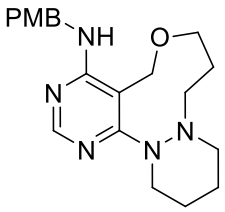
(**9**) Yield: 64%, 37.9 mg; white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (s, 1 H), 7.29 (d, *J* = 8.3 Hz, 2 H), 6.88 (d, *J* = 8.3 Hz, 2 H), 4.60 (s, 3 H), 3.80 (s, 3 H), 3.55 (brs, 2 H), 2.96 (brs, 2 H), 2.53 (s, 3 H), 1.97 (s, 3 H), 1.78–1.80 (m, 2 H), 1.63 (brs, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 161.6, 158.9, 154.0, 131.6, 129.1, 114.0, 98.6, 55.3, 55.2, 52.3, 45.1, 37.0, 36.7, 24.0, 16.9, 12.1; HRMS (ESI) *m/z* calcd for $C_{18}H_{26}N_5O$ $[M+H]^+$: 328.2132; Found: 328.2131.

Scheme S11. Synthetic scheme for scaffold VII (**10a**–**10b**).





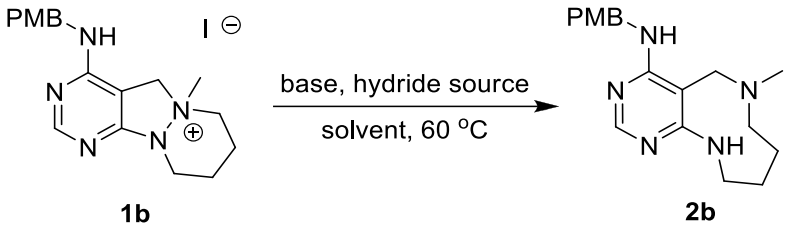
(**10a**) Yield: 78% from **1d**, 61.0 mg; light brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1 H), 7.25 (d, *J* = 8.8 Hz, 3 H), 6.86 (d, *J* = 6.8 Hz, 2 H), 5.12 (brs, 2 H), 4.83 (s, 1 H), 4.55 (s, 2 H), 3.80 (s, 3 H), 3.56 (s, 2 H), 3.19 (brs, 2 H), 3.04 (s, 2 H), 1.79 (s, 2 H), 1.58 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 161.3, 158.8, 155.9, 131.3, 129.1, 113.9, 92.8, 64.3, 63.6, 55.3, 53.3, 52.7, 45.3, 37.0, 24.7, 18.8; HRMS (ESI) *m/z* calcd for $C_{19}H_{26}N_5O_2$ $[M+H]^+$: 356.2081; Found: 356.2083.



(**10b**) Yield: 44% from **1e**, 35.8 mg; light brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 1 H), 7.25 (d, *J* = 9.8 Hz, 2 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 5.48 (d, *J* = 12.2 Hz, 1 H), 5.17 (brs, 1 H), 4-51–4.65 (m, 3 H), 4.42 (d, *J* = 12.2 Hz, 1 H), 3.79 (s, 3 H), 3.72–3.77 (m, 1 H), 3.58–3.62 (m, 1 H), 2.96–3.10 (m, 3 H), 2.82–2.88 (m, 2 H), 1.67–1.89 (m, 5 H), 1.39 (d, *J* = 12.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 160.9, 158.7, 156.0, 131.6, 128.8, 113.9, 94.1, 69.6, 65.3, 55.2, 51.0, 50.9, 44.9, 37.5, 30.7, 23.9, 17.9; HRMS (ESI) *m/z* calcd for $C_{20}H_{28}N_5O_2$ $[M+H]^+$: 370.2238; Found: 370.2239.

III. Optimization of N−N bond cleavage reaction conditions

Table S1. Optimization table of N–N bond cleavage reaction.



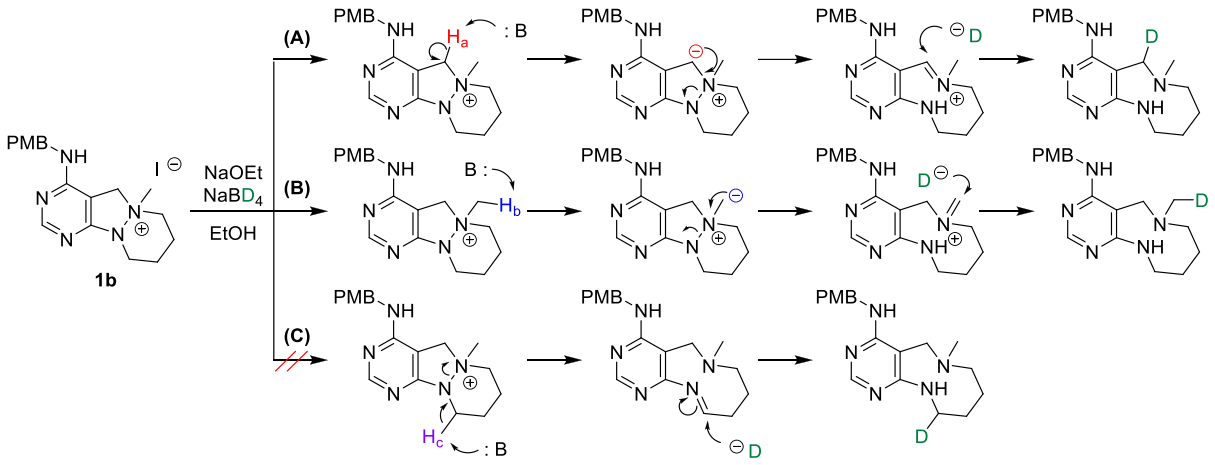
entry	base (equiv.)	hydride source (equiv.)	solvent	yield (%)[a]
1	NaOMe (5.0)	$NaBH_4$ (20.0)	MeOH	38
2	NaOEt (5.0)	$NaBH_4$ (20.0)	EtOH	51
3	*t*-BuOK (5.0)	$NaBH_4$ (20.0)	*t*-BuOH	-[b]
4	Na_2CO_3 (5.0)	$NaBH_4$ (20.0)	MeOH	0
5	TEA (5.0)	$NaBH_4$ (20.0)	MeOH	0
6	DBU (5.0)	$NaBH_4$ (20.0)	MeOH	0
7	NaOMe (5.0)	$NaBH(OAc)_3$ (20.0)	MeOH	0
8	NaOMe (5.0)	$NaBH_3CN$ (20.0)	MeOH	-[b]
9	NaOEt (1.5)	$NaBH_4$ (20.0)	EtOH	87
10	NaOEt (1.5)	$NaBH_4$ (10.0)	EtOH	84
11	NaOEt (1.5)	$NaBH_4$ (6.0)	EtOH	-[b]
12	NaOEt (1.5)	$NaBH_4$ (3.0)	EtOH	-[b]
13	NaOEt (5.0)	-	EtOH	0

[a] isolated yields. [b] messy reaction pattern.

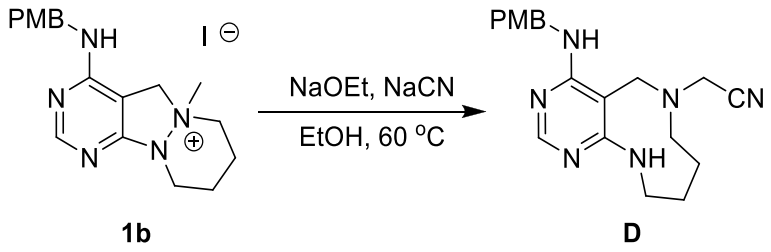
IV. A proposed mechanism of N–N bond cleavage reaction

Scheme S12. Mechanism study to elucidate the N–N bond cleavage reaction.

(a) The expected result of the deuterium-labeling experiment



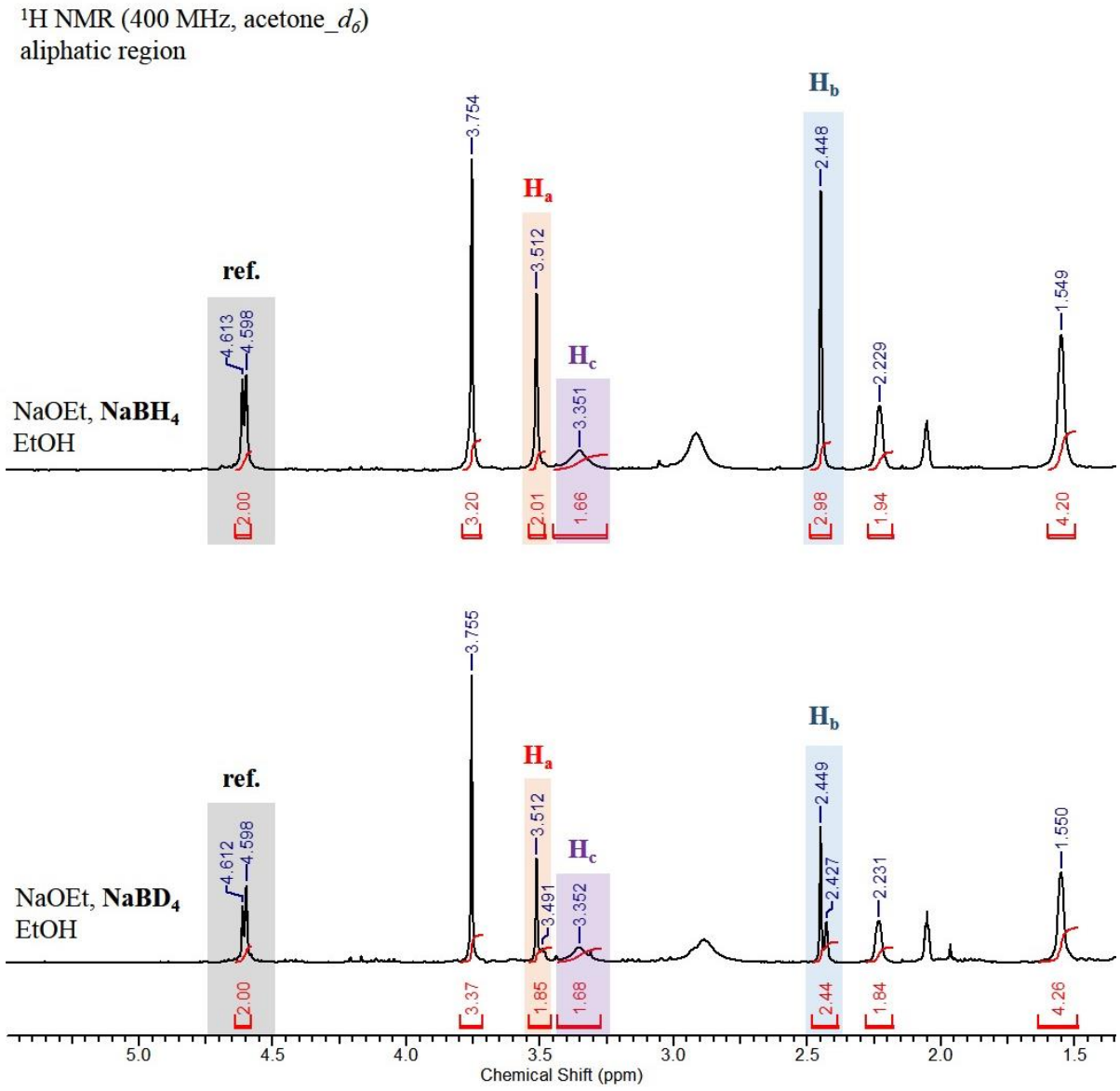
(b) Introduction of cyanide instead of a hydride source



To understand the reaction mechanism of N–N bond cleavage reaction, we performed the deuterium-labeling experiment using $NaBD_4$ (Scheme S12a). Synthetic procedure was identical to Scheme S4 ($NaBD_4$ was used instead of $NaBH_4$.). As shown in Figure S1, the decrease of the number of protons and ^2H-isotope shift supported the deuterium incorporation in H_a (~16% D incorporation) and H_b (~54% D incorporation), and not in H_c. Consequently, the N–N bond cleavage reaction proceeds through both the proposed mechanism (B) (major mechanism) and (A) (minor mechanism), and Hofmann elimination (mechanism (C)) doesn't

occur. Furthermore, we conducted an experiment for the introduction of another nucleophile, cyanide (Scheme S12b). Synthetic procedure was identical to Scheme S4 (NaCN was used instead of $NaBH_4$.). Generation of cyanide-added product **D** as a major product also supported that the N–N bond cleavage reaction mainly proceeds through the proposed mechanism (B).

Figure S1. ^1H NMR spectra of the deuterium-labeling experiment.



V. Chemoinformatic analysis

Figure S2. Bioactive benzannulated medium-sized rings used in PMI analysis.[3]

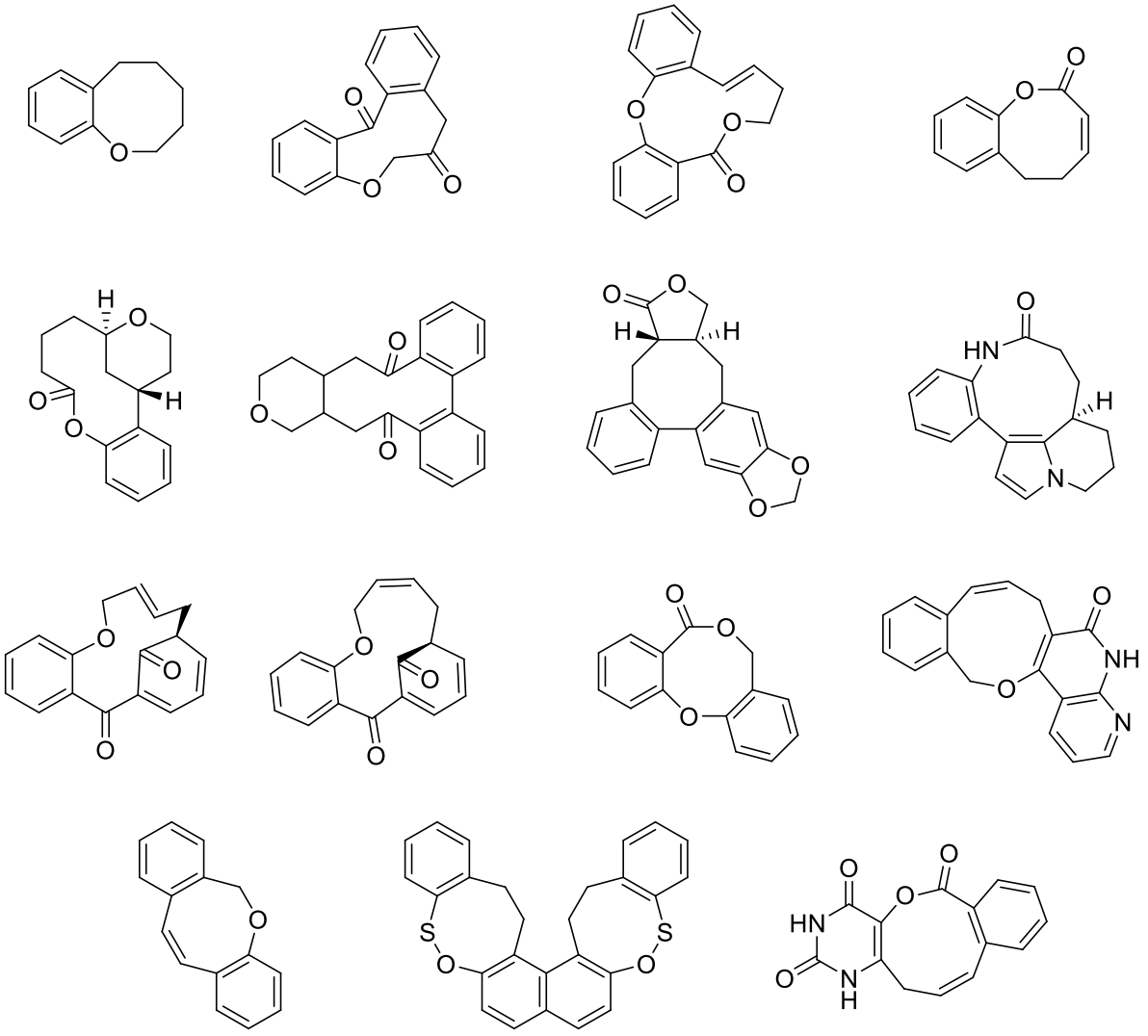
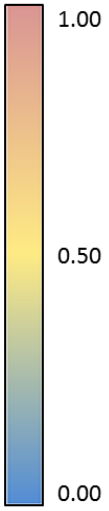


Figure S3. Tanimoto similarity matrix for synthesized 14 core scaffolds.

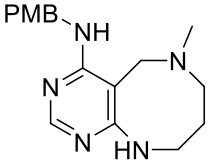
	A	B	C	D	E	F	G	H	I	J	K	L	M	N
A	1.00	0.80	0.77	0.22	0.22	0.20	0.21	0.45	0.19	0.20	0.20	0.20	0.18	0.18
B	0.80	1.00	0.87	0.25	0.24	0.24	0.24	0.44	0.19	0.20	0.23	0.19	0.18	0.18
C	0.77	0.87	1.00	0.25	0.24	0.23	0.23	0.43	0.18	0.19	0.23	0.19	0.18	0.18
D	0.22	0.25	0.25	1.00	0.65	0.13	0.13	0.14	0.11	0.14	0.13	0.14	0.13	0.13
E	0.22	0.24	0.24	0.65	1.00	0.13	0.13	0.14	0.11	0.14	0.12	0.13	0.13	0.13
F	0.20	0.24	0.23	0.13	0.13	1.00	0.77	0.13	0.10	0.18	0.64	0.21	0.12	0.12
G	0.21	0.24	0.23	0.13	0.13	0.77	1.00	0.13	0.10	0.18	0.65	0.21	0.12	0.12
H	0.45	0.44	0.43	0.14	0.14	0.13	0.13	1.00	0.26	0.17	0.13	0.17	0.16	0.16
I	0.19	0.19	0.18	0.11	0.11	0.10	0.10	0.26	1.00	0.23	0.10	0.22	0.20	0.19
J	0.20	0.20	0.19	0.14	0.14	0.18	0.18	0.17	0.23	1.00	0.17	0.59	0.27	0.27
K	0.20	0.23	0.23	0.13	0.12	0.64	0.65	0.13	0.10	0.17	1.00	0.17	0.12	0.12
L	0.20	0.19	0.19	0.14	0.13	0.21	0.21	0.17	0.22	0.59	0.17	1.00	0.27	0.26
M	0.18	0.18	0.18	0.13	0.13	0.12	0.12	0.16	0.20	0.27	0.12	0.27	1.00	0.77
N	0.18	0.18	0.18	0.13	0.13	0.12	0.12	0.16	0.19	0.27	0.12	0.26	0.77	1.00



Tanimoto similarity matrix for our resulting 14 core scaffolds (**A**–**N**) indicates a good level of structural diversity (average is 0.24). Tanimoto similarity coefficients were calculated using Discovery Studio [Accelrys] based on ECFP_6 (extended-connectivity fingerprint) molecular fingerprints. Heat map was generated in Excel [Microsoft] using a three-color scale set to 0.00(blue), 0.50 (yellow), and 1.00 (red). 1.00 represents 100% similarity and 0.00 indicates 0% similarity.

VI. X-ray crystallographic analysis data for 2a and 7a

Figure S3. X-ray crystal structure of **2a**. Deposition number in Cambridge Structural Database: CCDC 1866158.



2a

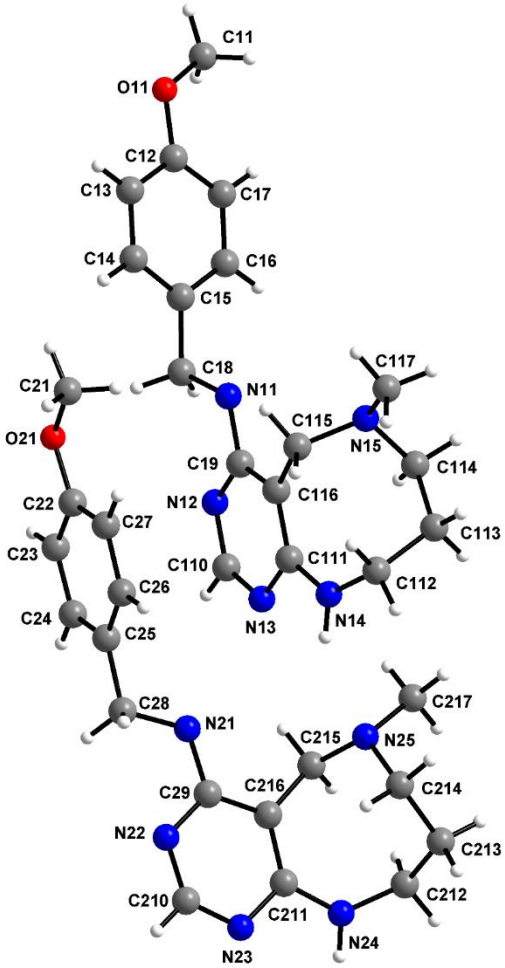


Table S2. Crystal data and structure refinement for **2a**.

Chemical formula	$C_{17}H_{22}N_5O$
Formula weight	312.39
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal size	0.100 x 0.150 x 0.160 mm
Crystal habit	colorless block
Crystal system	triclinic
Space group	P -1
Unit cell dimensions	a = 9.7756(12) Å α = 84.4412(12)° b = 12.9665(16) Å β = 86.9004(12)° c = 12.9912(16) Å γ = 84.1930(12)°
Volume	1628.9(3) $Å^3$
Z	4
Density (calculated)	1.274 g/cm^3
Absorption coefficient	0.083 mm^{-1}
F(000)	668
Theta range for data collection	2.83 to 28.68°
Index ranges	-13<=h<=13, -17<=k<=17, -17<=l<=17
Reflections collected	50448
Independent reflections	8325 [R(int) = 0.0701]
Coverage of independent reflections	99.0%
Absorption correction	multi-scan
Max. and min. transmission	0.9920 and 0.9870
Refinement method	Full-matrix least-squares on F2
Refinement program	SHELXL-2013 (Sheldrick, 2013)
Function minimized	Σ w(Fo2 - Fc2)2
Data / restraints / parameters	8325 / 0 / 419
Goodness-of-fit on F2	1.014
Final R indices	4482 data; I>2σ(I) R1 = 0.0657, wR2 = 0.1432 all data R1 = 0.1345, wR2 = 0.1765
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0665P)^2+0.5658P]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	0.519 and -0.208 $eÅ^{-3}$
R.M.S. deviation from mean	0.041 $eÅ^{-3}$

Table S3. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å ^{2}) for **2a**. U(eq) is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C11	0.4823(4)	0.6103(3)	0.5736(3)	0.0954(12)
C12	0.4407(2)	0.75548(18)	0.6738(2)	0.0490(6)
C13	0.4462(3)	0.7922(2)	0.7689(2)	0.0580(7)
C14	0.4231(3)	0.8972(2)	0.7780(2)	0.0608(7)
C15	0.3928(2)	0.96839(19)	0.6939(2)	0.0546(7)
C16	0.3844(3)	0.9290(2)	0.5999(2)	0.0618(7)
C17	0.4083(3)	0.8232(2)	0.5889(2)	0.0587(7)
C18	0.3760(3)	0.0835(2)	0.7037(3)	0.0773(10)
C19	0.1981(2)	0.22857(17)	0.72046(18)	0.0432(5)
C110	0.2648(3)	0.39021(19)	0.6897(2)	0.0590(7)
C111	0.0408(2)	0.37857(16)	0.74127(17)	0.0395(5)
C112	0.7794(3)	0.40200(19)	0.7691(2)	0.0538(6)
C113	0.7311(3)	0.3490(2)	0.6796(2)	0.0602(7)
C114	0.8227(3)	0.25377(19)	0.64569(19)	0.0524(6)
C115	0.9596(2)	0.20027(16)	0.79891(17)	0.0419(5)
C116	0.0654(2)	0.26971(15)	0.75264(16)	0.0367(5)
C117	0.7522(3)	0.1209(2)	0.7770(3)	0.0735(9)
C21	0.3167(4)	0.0728(2)	0.0190(3)	0.0862(10)
C22	0.3526(2)	0.24969(17)	0.97191(18)	0.0454(6)
C23	0.4411(3)	0.3211(2)	0.9311(2)	0.0619(7)
C24	0.3995(3)	0.4260(2)	0.9254(2)	0.0608(7)
C25	0.2696(3)	0.46287(18)	0.96117(18)	0.0459(6)
C26	0.1841(3)	0.3901(2)	0.0027(2)	0.0581(7)
C27	0.2233(3)	0.2844(2)	0.0077(2)	0.0567(7)
C28	0.2253(3)	0.57730(18)	0.9593(2)	0.0557(7)
C29	0.1262(2)	0.72353(15)	0.84561(16)	0.0344(5)
C210	0.1052(3)	0.88027(17)	0.9104(2)	0.0484(6)
C211	0.0337(2)	0.87712(16)	0.74693(17)	0.0390(5)
C212	0.9058(3)	0.90628(18)	0.5790(2)	0.0530(6)
C213	0.7848(3)	0.84106(19)	0.6042(2)	0.0576(7)
C214	0.8090(2)	0.74317(17)	0.67985(19)	0.0451(6)
C215	0.0626(2)	0.70652(16)	0.66215(16)	0.0365(5)
C216	0.0736(2)	0.77028(15)	0.75125(16)	0.0330(4)
C217	0.9147(3)	0.6213(2)	0.56087(19)	0.0572(7)

	x/a	y/b	z/c	U(eq)
N11	0.2320(2)	0.12331(14)	0.72103(18)	0.0545(6)
N12	0.2998(2)	0.28929(15)	0.68792(18)	0.0562(6)
N13	0.1440(2)	0.44037(14)	0.71250(17)	0.0514(5)
N14	0.9177(2)	0.43509(14)	0.75661(16)	0.0494(5)
N15	0.86701(19)	0.17037(14)	0.72315(15)	0.0454(5)
N21	0.16566(19)	0.61962(13)	0.86095(14)	0.0413(4)
N22	0.1410(2)	0.77899(14)	0.92746(14)	0.0427(5)
N23	0.0537(2)	0.93434(13)	0.82782(16)	0.0473(5)
N24	0.9720(2)	0.93695(14)	0.66709(16)	0.0499(5)
N25	0.92598(18)	0.66735(13)	0.65852(13)	0.0376(4)
O11	0.4711(2)	0.64915(14)	0.67059(17)	0.0725(6)
O21	0.4040(2)	0.14683(13)	0.97493(15)	0.0660(5)

Table S4. Bond lengths (Å) for **2a**.

C11-O11	1.397(4)	C11-H11A	0.96
C11-H11B	0.96	C11-H11C	0.96
C12-C17	1.372(4)	C12-C13	1.372(4)
C12-O11	1.385(3)	C13-C14	1.373(4)
C13-H13	0.93	C14-C15	1.385(4)
C14-H14	0.93	C15-C16	1.377(4)
C15-C18	1.502(3)	C16-C17	1.388(4)
C16-H16	0.93	C17-H17	0.93
C18-N11	1.463(3)	C18-H18A	0.97
C18-H18B	0.97	C19-N12	1.355(3)
C19-N11	1.371(3)	C19-C116	1.409(3)
C110-N12	1.321(3)	C110-N13	1.323(3)
C110-H110	0.93	C111-N14	1.359(3)
C111-N13	1.365(3)	C111-C116	1.403(3)
C112-N14	1.455(3)	C112-C113	1.525(4)
C112-H11D	0.97	C112-H11E	0.97
C113-C114	1.536(4)	C113-H11F	0.97
C113-H11G	0.97	C114-N15	1.453(3)
C114-H11H	0.97	C114-H11I	0.97
C115-N15	1.476(3)	C115-C116	1.502(3)
C115-H11J	0.97	C115-H11K	0.97
C117-N15	1.461(3)	C117-H11L	0.96
C117-H11M	0.96	C117-H11N	0.96
C21-O21	1.409(3)	C21-H21A	0.96
C21-H21B	0.96	C21-H21C	0.96
C22-C27	1.371(3)	C22-O21	1.374(3)
C22-C23	1.380(3)	C23-C24	1.376(3)
C23-H23	0.93	C24-C25	1.383(3)
C24-H24	0.93	C25-C26	1.376(3)
C25-C28	1.501(3)	C26-C27	1.382(3)
C26-H26	0.93	C27-H27	0.93
C28-N21	1.468(3)	C28-H28A	0.97
C28-H28B	0.97	C29-N22	1.362(3)
C29-N21	1.362(2)	C29-C216	1.413(3)
C210-N23	1.318(3)	C210-N22	1.325(3)
C210-H210	0.93	C211-N24	1.363(3)
C211-N23	1.377(3)	C211-C216	1.397(3)

C212-N24	1.452(3)	C212-C213	1.526(3)
C212-H21D	0.97	C212-H21E	0.97
C213-C214	1.535(3)	C213-H21F	0.97
C213-H21G	0.97	C214-N25	1.464(3)
C214-H21H	0.97	C214-H21I	0.97
C215-N25	1.480(3)	C215-C216	1.501(3)
C215-H21J	0.97	C215-H21K	0.97
C217-N25	1.467(3)	C217-H21L	0.96
C217-H21M	0.96	C217-H21N	0.96
N14-H14A	0.86	N24-H24A	0.86

Table S5. Bond angles (°) for **2a**.

O11-C11-H11A	109.5	O11-C11-H11B	109.5
H11A-C11-H11B	109.5	O11-C11-H11C	109.5
H11A-C11-H11C	109.5	H11B-C11-H11C	109.5
C17-C12-C13	120.0(2)	C17-C12-O11	124.0(2)
C13-C12-O11	116.0(2)	C12-C13-C14	119.7(3)
C12-C13-H13	120.2	C14-C13-H13	120.2
C13-C14-C15	122.1(3)	C13-C14-H14	118.9
C15-C14-H14	118.9	C16-C15-C14	116.9(2)
C16-C15-C18	121.5(3)	C14-C15-C18	121.5(3)
C15-C16-C17	121.9(3)	C15-C16-H16	119.0
C17-C16-H16	119.0	C12-C17-C16	119.3(3)
C12-C17-H17	120.3	C16-C17-H17	120.3
N11-C18-C15	112.4(2)	N11-C18-H18A	109.1
C15-C18-H18A	109.1	N11-C18-H18B	109.1
C15-C18-H18B	109.1	H18A-C18-H18B	107.9
N12-C19-N11	115.8(2)	N12-C19-C116	122.8(2)
N11-C19-C116	121.4(2)	N12-C110-N13	129.6(2)
N12-C110-H110	115.2	N13-C110-H110	115.2
N14-C111-N13	112.14(19)	N14-C111-C116	126.3(2)
N13-C111-C116	121.6(2)	N14-C112-C113	116.1(2)
N14-C112-H11D	108.3	C113-C112-H11D	108.3
N14-C112-H11E	108.3	C113-C112-H11E	108.3
H11D-C112-H11E	107.4	C112-C113-C114	116.9(2)
C112-C113-H11F	108.1	C114-C113-H11F	108.1
C112-C113-H11G	108.1	C114-C113-H11G	108.1
H11F-C113-H11G	107.3	N15-C114-C113	119.3(2)
N15-C114-H11H	107.5	C113-C114-H11H	107.5
N15-C114-H11I	107.5	C113-C114-H11I	107.5
H11H-C114-H11I	107.0	N15-C115-C116	114.08(18)
N15-C115-H11J	108.7	C116-C115-H11J	108.7
N15-C115-H11K	108.7	C116-C115-H11K	108.7
H11J-C115-H11K	107.6	C111-C116-C19	115.8(2)
C111-C116-C115	122.80(19)	C19-C116-C115	121.41(19)
N15-C117-H11L	109.5	N15-C117-H11M	109.5
H11L-C117-H11M	109.5	N15-C117-H11N	109.5
H11L-C117-H11N	109.5	H11M-C117-H11N	109.5

O21-C21-H21A	109.5	O21-C21-H21B	109.5
H21A-C21-H21B	109.5	O21-C21-H21C	109.5
H21A-C21-H21C	109.5	H21B-C21-H21C	109.5
C27-C22-O21	124.7(2)	C27-C22-C23	119.4(2)
O21-C22-C23	116.0(2)	C24-C23-C22	120.3(2)
C24-C23-H23	119.9	C22-C23-H23	119.9
C23-C24-C25	121.4(2)	C23-C24-H24	119.3
C25-C24-H24	119.3	C26-C25-C24	117.1(2)
C26-C25-C28	121.1(2)	C24-C25-C28	121.7(2)
C25-C26-C27	122.4(2)	C25-C26-H26	118.8
C27-C26-H26	118.8	C22-C27-C26	119.5(2)
C22-C27-H27	120.3	C26-C27-H27	120.3
N21-C28-C25	112.18(19)	N21-C28-H28A	109.2
C25-C28-H28A	109.2	N21-C28-H28B	109.2
C25-C28-H28B	109.2	H28A-C28-H28B	107.9
N22-C29-N21	115.35(19)	N22-C29-C216	122.46(18)
N21-C29-C216	122.19(18)	N23-C210-N22	129.8(2)
N23-C210-H210	115.1	N22-C210-H210	115.1
N24-C211-N23	112.00(19)	N24-C211-C216	126.5(2)
N23-C211-C216	121.5(2)	N24-C212-C213	116.0(2)
N24-C212-H21D	108.3	C213-C212-H21D	108.3
N24-C212-H21E	108.3	C213-C212-H21E	108.3
H21D-C212-H21E	107.4	C212-C213-C214	117.1(2)
C212-C213-H21F	108.0	C214-C213-H21F	108.0
C212-C213-H21G	108.0	C214-C213-H21G	108.0
H21F-C213-H21G	107.3	N25-C214-C213	118.5(2)
N25-C214-H21H	107.7	C213-C214-H21H	107.7
N25-C214-H21I	107.7	C213-C214-H21I	107.7
H21H-C214-H21I	107.1	N25-C215-C216	113.34(17)
N25-C215-H21J	108.9	C216-C215-H21J	108.9
N25-C215-H21K	108.9	C216-C215-H21K	108.9
H21J-C215-H21K	107.7	C211-C216-C29	116.24(18)
C211-C216-C215	123.16(19)	C29-C216-C215	120.60(18)
N25-C217-H21L	109.5	N25-C217-H21M	109.5
H21L-C217-H21M	109.5	N25-C217-H21N	109.5
H21L-C217-H21N	109.5	H21M-C217-H21N	109.5
C19-N11-C18	119.4(2)	C110-N12-C19	114.5(2)
C110-N13-C111	115.28(19)	C111-N14-C112	130.09(19)

C111-N14-H14A	115.0	C112-N14-H14A	115.0
C114-N15-C117	112.9(2)	C114-N15-C115	114.47(17)
C117-N15-C115	110.0(2)	C29-N21-C28	119.15(18)
C210-N22-C29	114.53(19)	C210-N23-C211	115.28(18)
C211-N24-C212	129.92(19)	C211-N24-H24A	115.0
C212-N24-H24A	115.0	C214-N25-C217	112.27(18)
C214-N25-C215	114.70(16)	C217-N25-C215	110.31(17)
C12-O11-C11	117.7(2)	C22-O21-C21	116.9(2)

Table S6. Anisotropic atomic displacement parameters (Å ^{2}) for **2a**. The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C11	0.097(3)	0.072(2)	0.123(3)	-0.047(2)	0.000(2)	-0.0039(19)
C12	0.0339(12)	0.0448(13)	0.0677(17)	-0.0055(12)	-0.0006(11)	-0.0011(10)
C13	0.0547(16)	0.0623(17)	0.0532(16)	0.0009(13)	0.0022(12)	0.0042(13)
C14	0.0505(16)	0.0692(18)	0.0638(18)	-0.0236(15)	0.0024(13)	0.0028(13)
C15	0.0330(13)	0.0463(14)	0.084(2)	-0.0115(14)	-0.0041(12)	0.0061(11)
C16	0.0520(16)	0.0586(17)	0.0722(19)	0.0061(14)	-0.0192(14)	0.0046(13)
C17	0.0543(16)	0.0615(17)	0.0629(17)	-0.0151(14)	-0.0156(13)	-0.0021(13)
C18	0.0412(15)	0.0500(16)	0.142(3)	-0.0240(17)	-0.0022(17)	0.0053(12)
C19	0.0420(13)	0.0381(12)	0.0512(14)	-0.0086(10)	-0.0084(11)	-0.0041(10)
C110	0.0508(16)	0.0429(14)	0.086(2)	-0.0065(13)	0.0002(14)	-0.0174(12)
C111	0.0455(13)	0.0330(11)	0.0409(12)	-0.0067(9)	-0.0045(10)	-0.0039(10)
C112	0.0483(15)	0.0426(13)	0.0681(17)	-0.0075(12)	0.0048(12)	0.0049(11)
C113	0.0544(16)	0.0535(15)	0.0717(18)	0.0022(13)	-0.0147(14)	-0.0016(13)
C114	0.0503(15)	0.0610(16)	0.0493(14)	-0.0110(12)	-0.0067(12)	-0.0138(12)
C115	0.0465(13)	0.0338(11)	0.0435(13)	-0.0017(10)	0.0036(10)	0.0004(10)
C116	0.0410(12)	0.0327(11)	0.0370(12)	-0.0056(9)	-0.0039(9)	-0.0031(9)
C117	0.0522(17)	0.0552(16)	0.112(3)	-0.0006(16)	0.0180(16)	-0.0165(13)
C21	0.095(3)	0.0413(16)	0.120(3)	0.0044(17)	0.010(2)	-0.0152(16)
C22	0.0474(14)	0.0376(12)	0.0498(14)	0.0024(10)	-0.0045(11)	-0.0019(10)
C23	0.0463(15)	0.0504(15)	0.086(2)	-0.0040(14)	0.0175(14)	-0.0024(12)
C24	0.0558(17)	0.0451(14)	0.080(2)	0.0058(13)	0.0088(14)	-0.0131(12)
C25	0.0508(15)	0.0409(12)	0.0444(13)	0.0037(10)	-0.0113(11)	0.0017(11)
C26	0.0433(14)	0.0553(16)	0.0708(18)	0.0051(13)	0.0046(13)	0.0043(12)
C27	0.0460(15)	0.0500(15)	0.0713(18)	0.0087(13)	0.0053(13)	-0.0090(12)
C28	0.0685(18)	0.0457(14)	0.0521(15)	-0.0014(11)	-0.0185(13)	0.0036(12)
C29	0.0318(11)	0.0312(10)	0.0408(12)	-0.0049(9)	0.0011(9)	-0.0063(9)
C210	0.0556(15)	0.0390(13)	0.0539(15)	-0.0151(11)	-0.0051(12)	-0.0095(11)
C211	0.0360(12)	0.0330(11)	0.0481(13)	-0.0023(10)	-0.0013(10)	-0.0065(9)
C212	0.0593(16)	0.0411(13)	0.0565(16)	0.0105(11)	-0.0148(12)	-0.0025(11)
C213	0.0487(15)	0.0469(14)	0.0770(19)	0.0013(13)	-0.0195(13)	-0.0012(12)
C214	0.0338(12)	0.0451(13)	0.0569(15)	-0.0036(11)	-0.0012(11)	-0.0074(10)
C215	0.0377(12)	0.0342(11)	0.0373(12)	-0.0030(9)	0.0000(9)	-0.0041(9)
C216	0.0298(11)	0.0297(10)	0.0395(12)	-0.0025(9)	-0.0005(9)	-0.0042(8)
C217	0.0716(18)	0.0563(15)	0.0482(15)	-0.0139(12)	-0.0099(13)	-0.0163(13)
N11	0.0387(11)	0.0357(10)	0.0894(16)	-0.0147(10)	-0.0059(11)	0.0058(9)

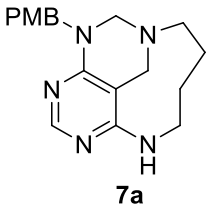
	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N12	0.0421(12)	0.0435(12)	0.0848(16)	-0.0104(11)	-0.0014(11)	-0.0092(9)
N13	0.0518(13)	0.0343(10)	0.0697(14)	-0.0077(9)	-0.0046(11)	-0.0089(9)
N14	0.0509(12)	0.0317(10)	0.0658(14)	-0.0117(9)	-0.0006(10)	0.0012(9)
N15	0.0408(11)	0.0382(10)	0.0583(12)	-0.0073(9)	0.0038(9)	-0.0099(8)
N21	0.0478(11)	0.0320(9)	0.0427(11)	0.0020(8)	-0.0090(9)	0.0018(8)
N22	0.0484(11)	0.0362(10)	0.0453(11)	-0.0093(8)	-0.0065(9)	-0.0056(8)
N23	0.0548(12)	0.0291(9)	0.0597(13)	-0.0077(9)	-0.0091(10)	-0.0052(9)
N24	0.0571(13)	0.0289(9)	0.0635(13)	0.0040(9)	-0.0162(10)	-0.0046(9)
N25	0.0402(10)	0.0344(9)	0.0395(10)	-0.0070(8)	-0.0012(8)	-0.0074(8)
O11	0.0690(13)	0.0513(11)	0.0970(16)	-0.0140(11)	0.0027(11)	-0.0019(10)
O21	0.0689(13)	0.0382(9)	0.0876(14)	0.0014(9)	0.0058(10)	-0.0012(9)

Table S7. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å ^{2}) for **2a**.

	x/a	y/b	z/c	U(eq)
H11A	0.3943	-0.3792	0.5427	0.143
H11B	0.5122	-0.4627	0.5814	0.143
H11C	0.5481	-0.3538	0.5299	0.143
H13	0.4654	-0.2538	0.8269	0.07
H14	0.4280	-0.0787	0.8427	0.073
H16	0.3621	-0.0254	0.5422	0.074
H17	0.4023	-0.2015	0.5246	0.07
H18A	0.4285	0.0982	0.7610	0.093
H18B	0.4132	0.1194	0.6410	0.093
H110	0.3357	0.4323	0.6723	0.071
H11D	-0.2846	0.4626	0.7799	0.065
H11E	-0.2253	0.3544	0.8313	0.065
H11F	-0.2782	0.4003	0.6203	0.072
H11G	-0.3598	0.3277	0.6988	0.072
H11H	-0.2262	0.2235	0.5948	0.063
H11I	-0.0953	0.2787	0.6105	0.063
H11J	0.0066	0.1376	0.8326	0.05
H11K	-0.0955	0.2356	0.8517	0.05
H11L	-0.2977	0.1684	0.8210	0.11
H11M	-0.2131	0.0593	0.8182	0.11
H11N	-0.3080	0.1025	0.7272	0.11
H21A	0.2898	0.0870	1.0888	0.129
H21B	0.3645	0.0043	1.0192	0.129
H21C	0.2362	0.0765	0.9790	0.129
H23	0.5294	0.2982	0.9073	0.074
H24	0.4599	0.4731	0.8970	0.073
H26	0.0967	0.4129	1.0284	0.07
H27	0.1624	0.2371	1.0352	0.068
H28A	0.1579	0.5892	1.0155	0.067
H28B	0.3042	0.6139	0.9704	0.067
H210	0.1184	0.9191	0.9649	0.058
H21D	-0.0255	0.8672	0.5377	0.064
H21E	-0.1263	0.9688	0.5365	0.064
H21F	-0.2441	0.8199	0.5398	0.069
H21G	-0.2911	0.8854	0.6324	0.069

	x/a	y/b	z/c	U(eq)
H21H	-0.1807	0.7656	0.7479	0.054
H21I	-0.2737	0.7072	0.6839	0.054
H21J	0.0811	0.7486	0.5980	0.044
H21K	0.1324	0.6477	0.6670	0.044
H21L	-0.1686	0.5875	0.5635	0.086
H21M	-0.0077	0.5713	0.5506	0.086
H21N	-0.0872	0.6751	0.5046	0.086
H14A	-0.0777	0.5006	0.7594	0.059
H24A	-0.0277	1.0030	0.6693	0.06

Figure S4. X-ray crystal structure of **7a**. Deposition number in Cambridge Structural Database: CCDC 1866157.



7a

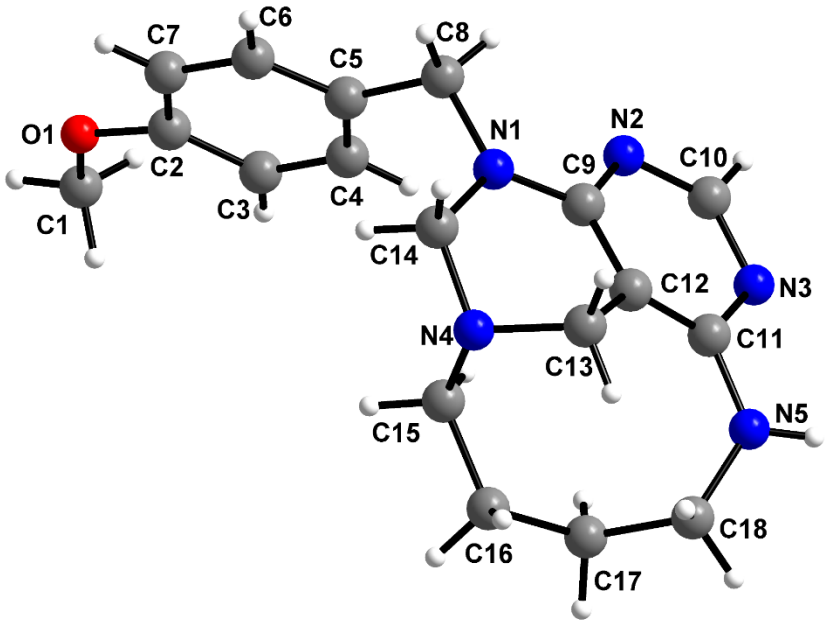


Table S8. Crystal data and structure refinement for **7a**.

Chemical formula	$C_{18}H_{23}N_5O$	
Formula weight	325.41	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal size	0.200 x 0.200 x 0.240 mm	
Crystal habit	colorless block	
Crystal system	monoclinic	
Space group	P 1 2_1/n 1	
Unit cell dimensions	a = 8.8828(6) Å	a = 8.8828(6) Å
	b = 19.2484(13) Å	b = 19.2484(13) Å
	c = 10.8095(7) Å	c = 10.8095(7) Å
Volume	1695.3(2) Å ^{3}	1695.3(2) Å ^{3}
Z	4	
Density (calculated)	1.275 g/cm^3	
Absorption coefficient	0.083 mm^{-1}	
F(000)	696	
Theta range for data collection	2.12 to 28.46°	
Index ranges	-11<=h<=11, -25<=k<=25, -14<=l<=14	
Reflections collected	58559	
Independent reflections	4271 [R(int) = 0.0430]	
Coverage of independent reflections	99.8%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9840 and 0.9800	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	4271 / 0 / 218	
Goodness-of-fit on F2	1.007	
Final R indices	2783 data; I>2σ(I)	R1 = 0.0479, wR2 = 0.1151
	all data	R1 = 0.0824, wR2 = 0.1365
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0544P)^2+0.4518P]$ where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	0.264 and -0.256 eÅ $^{-3}$	
R.M.S. deviation from mean	0.031 eÅ $^{-3}$	

Table S9. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å ^{2}) for **7a**. U(eq) is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C1	0.9322(3)	0.53666(13)	0.6828(2)	0.1014(9)
C2	0.1392(2)	0.48546(9)	0.87647(19)	0.0646(5)
C3	0.0815(2)	0.41919(9)	0.83958(19)	0.0604(5)
C4	0.1663(2)	0.36354(9)	0.91544(18)	0.0571(4)
C5	0.3091(2)	0.37189(9)	0.02939(17)	0.0526(4)
C6	0.3613(3)	0.43905(11)	0.0665(2)	0.0834(7)
C7	0.2786(3)	0.49497(11)	0.9911(2)	0.0938(8)
C8	0.4055(2)	0.31040(10)	0.10779(18)	0.0594(4)
C9	0.25907(19)	0.20102(8)	0.10969(15)	0.0475(4)
C10	0.2229(2)	0.11722(9)	0.95582(17)	0.0565(4)
C11	0.1005(2)	0.10107(8)	0.10316(15)	0.0484(4)
C12	0.18125(19)	0.15928(8)	0.17309(14)	0.0465(4)
C13	0.1855(2)	0.18571(9)	0.30550(15)	0.0538(4)
C14	0.2689(3)	0.29642(10)	0.26626(19)	0.0673(5)
C15	0.9785(2)	0.27072(9)	0.18705(19)	0.0613(5)
C16	0.8450(2)	0.22781(10)	0.2061(2)	0.0658(5)
C17	0.7904(2)	0.15896(10)	0.12897(18)	0.0611(4)
C18	0.8771(2)	0.09021(9)	0.18902(17)	0.0588(4)
N1	0.31221(18)	0.26539(7)	0.15956(14)	0.0560(4)
N2	0.28392(17)	0.17966(7)	0.99998(13)	0.0541(3)
N3	0.12932(18)	0.07701(7)	0.99502(14)	0.0560(4)
N4	0.14333(18)	0.25941(7)	0.29235(13)	0.0573(4)
N5	0.99179(19)	0.06305(7)	0.13487(15)	0.0618(4)
O1	0.0706(2)	0.54421(7)	0.80459(16)	0.0946(5)

Table S10. Bond lengths (Å) for **7a**.

C1-O1	1.406(3)	C1-H1A	0.96
C1-H1B	0.96	C1-H1C	0.96
C2-O1	1.370(2)	C2-C7	1.371(3)
C2-C3	1.373(2)	C3-C4	1.377(2)
C3-H3	0.93	C4-C5	1.381(2)
C4-H4	0.93	C5-C6	1.378(2)
C5-C8	1.508(2)	C6-C7	1.373(3)
C6-H6	0.93	C7-H7	0.93
C8-N1	1.456(2)	C8-H8A	0.97
C8-H8B	0.97	C9-N2	1.354(2)
C9-N1	1.359(2)	C9-C12	1.404(2)
C10-N3	1.323(2)	C10-N2	1.327(2)
C10-H10	0.93	C11-N5	1.360(2)
C11-N3	1.3730(19)	C11-C12	1.382(2)
C12-C13	1.505(2)	C13-N4	1.460(2)
C13-H13A	0.97	C13-H13B	0.97
C14-N4	1.443(2)	C14-N1	1.479(2)
C14-H14A	0.97	C14-H14B	0.97
C15-N4	1.469(2)	C15-C16	1.525(3)
C15-H15A	0.97	C15-H15B	0.97
C16-C17	1.538(3)	C16-H16A	0.97
C16-H16B	0.97	C17-C18	1.539(2)
C17-H17A	0.97	C17-H17B	0.97
C18-N5	1.459(2)	C18-H18A	0.97
C18-H18B	0.97	N5-H5	0.86

Table S11. Bond angles (°) for **7a**.

O1-C1-H1A	109.5	O1-C1-H1B	109.5
H1A-C1-H1B	109.5	O1-C1-H1C	109.5
H1A-C1-H1C	109.5	H1B-C1-H1C	109.5
O1-C2-C7	116.10(16)	O1-C2-C3	124.88(17)
C7-C2-C3	118.99(18)	C2-C3-C4	119.83(16)
C2-C3-H3	120.1	C4-C3-H3	120.1
C3-C4-C5	122.08(15)	C3-C4-H4	119.0
C5-C4-H4	119.0	C6-C5-C4	116.87(17)
C6-C5-C8	121.50(16)	C4-C5-C8	121.62(15)
C7-C6-C5	121.59(18)	C7-C6-H6	119.2
C5-C6-H6	119.2	C2-C7-C6	120.59(18)
C2-C7-H7	119.7	C6-C7-H7	119.7
N1-C8-C5	113.59(14)	N1-C8-H8A	108.8
C5-C8-H8A	108.8	N1-C8-H8B	108.8
C5-C8-H8B	108.8	H8A-C8-H8B	107.7
N2-C9-N1	118.19(15)	N2-C9-C12	122.53(15)
N1-C9-C12	119.28(14)	N3-C10-N2	129.30(15)
N3-C10-H10	115.3	N2-C10-H10	115.3
N5-C11-N3	115.15(15)	N5-C11-C12	124.38(14)
N3-C11-C12	120.47(15)	C11-C12-C9	116.51(14)
C11-C12-C13	127.24(15)	C9-C12-C13	116.11(14)
N4-C13-C12	109.12(12)	N4-C13-H13A	109.9
C12-C13-H13A	109.9	N4-C13-H13B	109.9
C12-C13-H13B	109.9	H13A-C13-H13B	108.3
N4-C14-N1	114.48(14)	N4-C14-H14A	108.6
N1-C14-H14A	108.6	N4-C14-H14B	108.6
N1-C14-H14B	108.6	H14A-C14-H14B	107.6
N4-C15-C16	113.81(15)	N4-C15-H15A	108.8
C16-C15-H15A	108.8	N4-C15-H15B	108.8
C16-C15-H15B	108.8	H15A-C15-H15B	107.7
C15-C16-C17	119.21(15)	C15-C16-H16A	107.5
C17-C16-H16A	107.5	C15-C16-H16B	107.5
C17-C16-H16B	107.5	H16A-C16-H16B	107.0
C16-C17-C18	121.05(15)	C16-C17-H17A	107.1

C18-C17-H17A	107.1	C16-C17-H17B	107.1
C18-C17-H17B	107.1	H17A-C17-H17B	106.8
N5-C18-C17	116.80(14)	N5-C18-H18A	108.1
C17-C18-H18A	108.1	N5-C18-H18B	108.1
C17-C18-H18B	108.1	H18A-C18-H18B	107.3
C9-N1-C8	123.44(14)	C9-N1-C14	121.36(14)
C8-N1-C14	115.08(14)	C10-N2-C9	113.87(14)
C10-N3-C11	115.43(14)	C14-N4-C13	108.08(14)
C14-N4-C15	112.63(15)	C13-N4-C15	110.94(13)
C11-N5-C18	125.99(14)	C11-N5-H5	117.0
C18-N5-H5	117.0	C2-O1-C1	118.11(16)

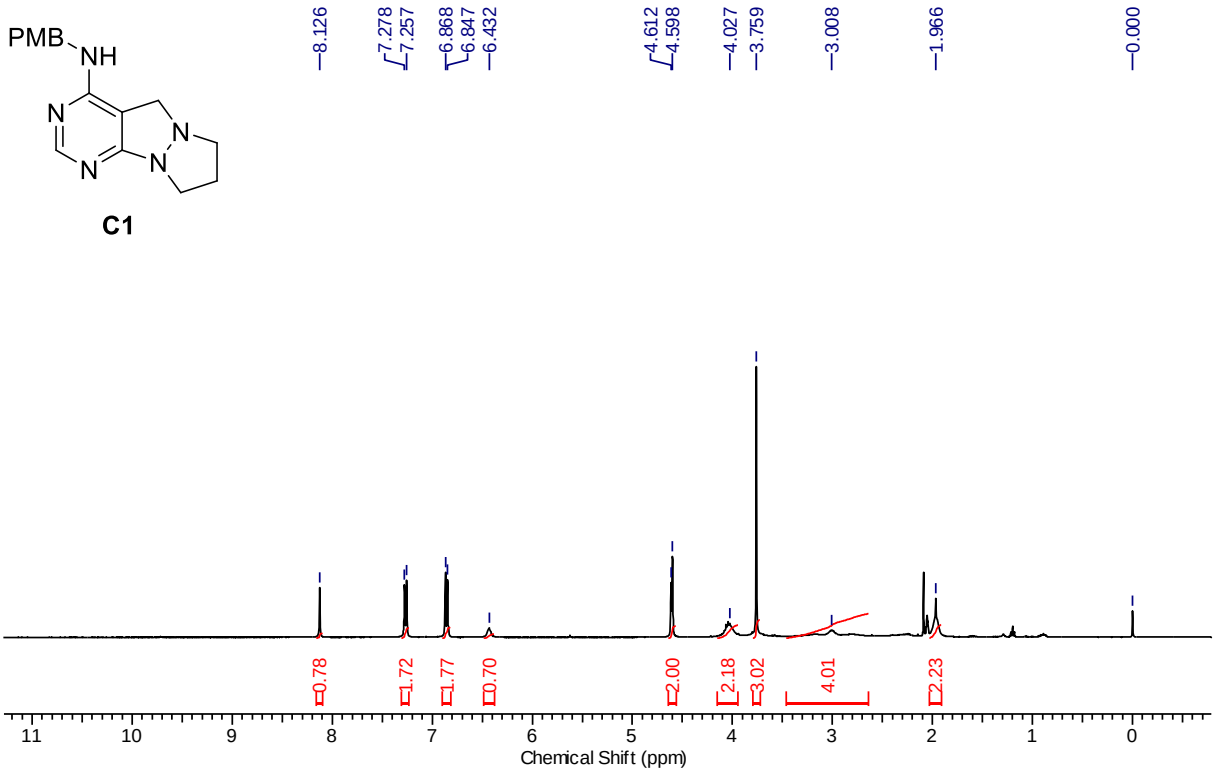
Table S12. Anisotropic atomic displacement parameters (Å ^{2}) for **7a**. The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$.

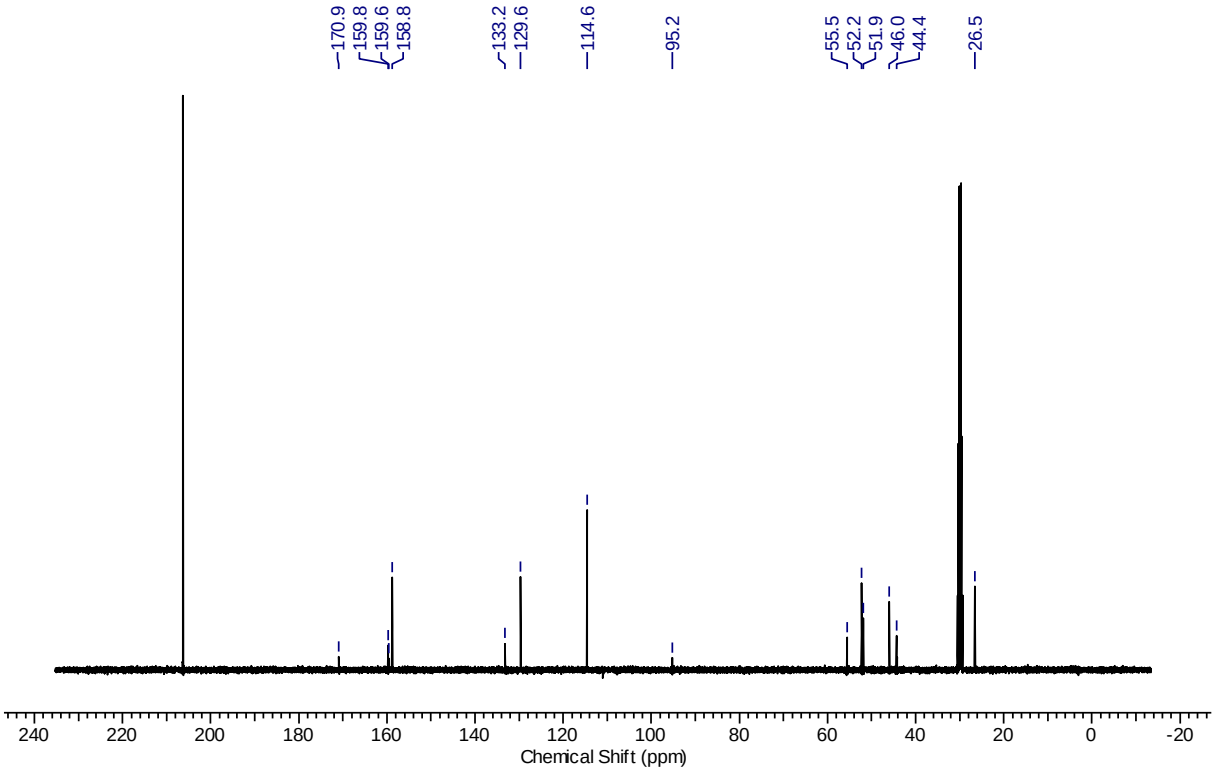
	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.1011(18)	0.0746(14)	0.0911(16)	-0.0077(12)	-0.0012(14)	0.0197(13)
C2	0.0651(11)	0.0499(10)	0.0676(11)	-0.0110(9)	0.0148(9)	-0.0056(8)
C3	0.0465(9)	0.0562(10)	0.0673(11)	-0.0129(8)	0.0108(8)	-0.0073(8)
C4	0.0493(9)	0.0484(9)	0.0704(11)	-0.0139(8)	0.0204(8)	-0.0123(7)
C5	0.0493(9)	0.0549(9)	0.0536(9)	-0.0087(7)	0.0203(7)	-0.0104(7)
C6	0.0828(14)	0.0632(12)	0.0690(12)	-0.0125(10)	-0.0068(11)	-0.0197(11)
C7	0.1047(17)	0.0512(11)	0.0849(15)	-0.0157(11)	-0.0051(13)	-0.0210(11)
C8	0.0497(9)	0.0656(11)	0.0591(10)	-0.0055(8)	0.0174(8)	-0.0069(8)
C9	0.0473(8)	0.0497(9)	0.0414(8)	0.0008(7)	0.0134(7)	0.0091(7)
C10	0.0673(11)	0.0569(10)	0.0499(9)	-0.0042(8)	0.0283(8)	0.0128(9)
C11	0.0563(9)	0.0438(8)	0.0440(8)	0.0036(6)	0.0187(7)	0.0130(7)
C12	0.0493(8)	0.0481(8)	0.0381(7)	0.0035(6)	0.0130(6)	0.0116(7)
C13	0.0562(10)	0.0630(10)	0.0356(7)	0.0010(7)	0.0112(7)	0.0049(8)
C14	0.0828(13)	0.0675(11)	0.0553(10)	-0.0194(9)	0.0314(10)	-0.0137(10)
C15	0.0743(12)	0.0483(9)	0.0626(10)	-0.0018(8)	0.0285(9)	0.0135(8)
C16	0.0634(11)	0.0702(12)	0.0671(11)	-0.0055(9)	0.0295(9)	0.0152(9)
C17	0.0568(10)	0.0724(12)	0.0526(10)	0.0001(8)	0.0203(8)	0.0023(9)
C18	0.0676(11)	0.0612(10)	0.0520(9)	-0.0003(8)	0.0286(8)	-0.0040(9)
N1	0.0635(9)	0.0560(8)	0.0505(8)	-0.0071(6)	0.0248(7)	-0.0050(7)
N2	0.0593(8)	0.0571(8)	0.0492(7)	-0.0024(6)	0.0251(7)	0.0063(7)
N3	0.0691(9)	0.0477(8)	0.0550(8)	-0.0054(6)	0.0288(7)	0.0077(7)
N4	0.0674(9)	0.0590(8)	0.0460(7)	-0.0131(6)	0.0231(7)	-0.0030(7)
N5	0.0802(10)	0.0460(8)	0.0685(9)	-0.0036(7)	0.0395(8)	-0.0005(7)
O1	0.1024(12)	0.0523(8)	0.0908(10)	-0.0048(7)	-0.0019(9)	-0.0010(8)

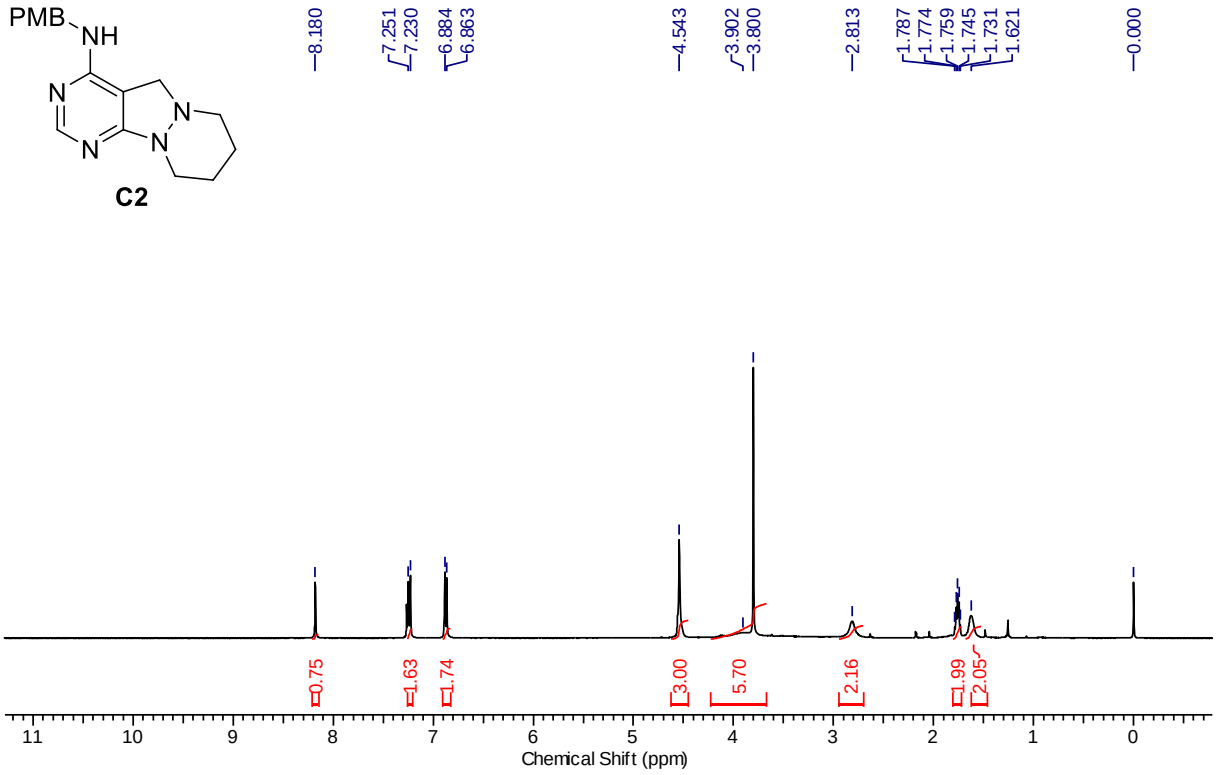
Table S13. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å ^{2}) for **7a**.

	x/a	y/b	z/c	U(eq)
H1A	-0.0431	0.5048	-0.3749	0.152
H1B	-0.0970	0.5810	-0.3610	0.152
H1C	-0.1579	0.5190	-0.2989	0.152
H3	-0.0146	0.4119	-0.2365	0.073
H4	0.1261	0.3189	-0.1109	0.069
H6	0.4548	0.4467	0.1446	0.1
H7	0.3175	0.5397	0.0181	0.113
H8A	0.4430	0.2833	0.0499	0.071
H8B	0.5017	0.3272	0.1829	0.071
H10	0.2498	0.0991	-0.1125	0.068
H13A	0.1078	0.1600	0.3303	0.065
H13B	0.2942	0.1791	0.3757	0.065
H14A	0.3670	0.2985	0.3491	0.081
H14B	0.2321	0.3437	0.2407	0.081
H15A	-0.0198	0.2594	0.1001	0.074
H15B	-0.0489	0.3196	0.1857	0.074
H16A	-0.2514	0.2571	0.1821	0.079
H16B	-0.1179	0.2175	0.3015	0.079
H17A	-0.2022	0.1649	0.0424	0.073
H17B	-0.3249	0.1529	0.1107	0.073
H18A	-0.0639	0.0966	0.2854	0.071
H18B	-0.2065	0.0552	0.1761	0.071
H5	-0.0095	0.0189	0.1218	0.074

VII. ^{1}H and ^{13}C NMR spectra






PMB
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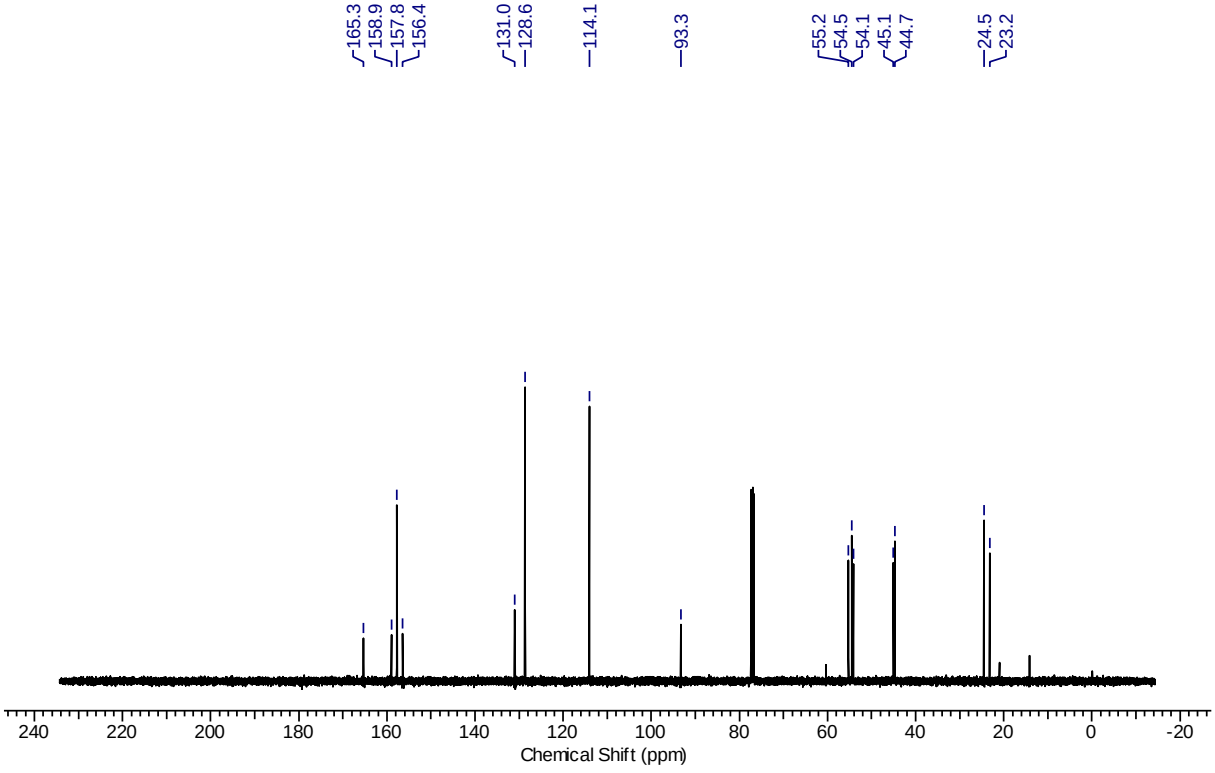
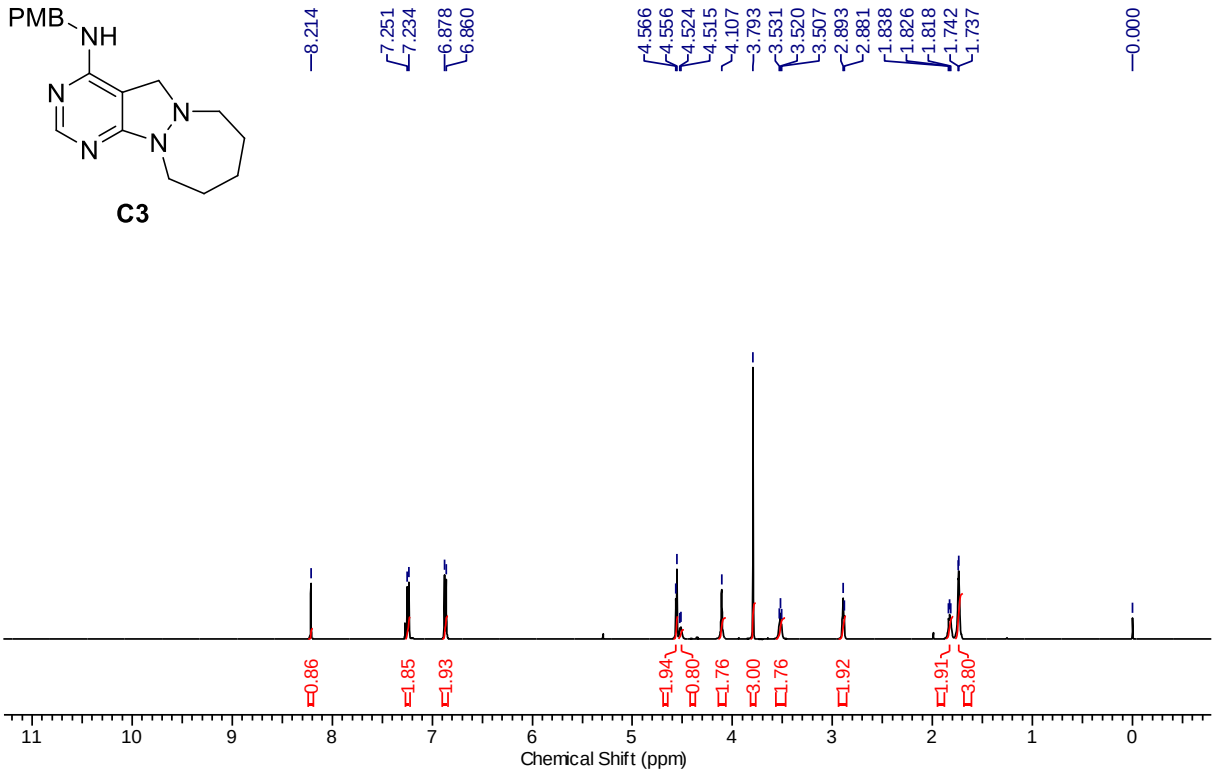
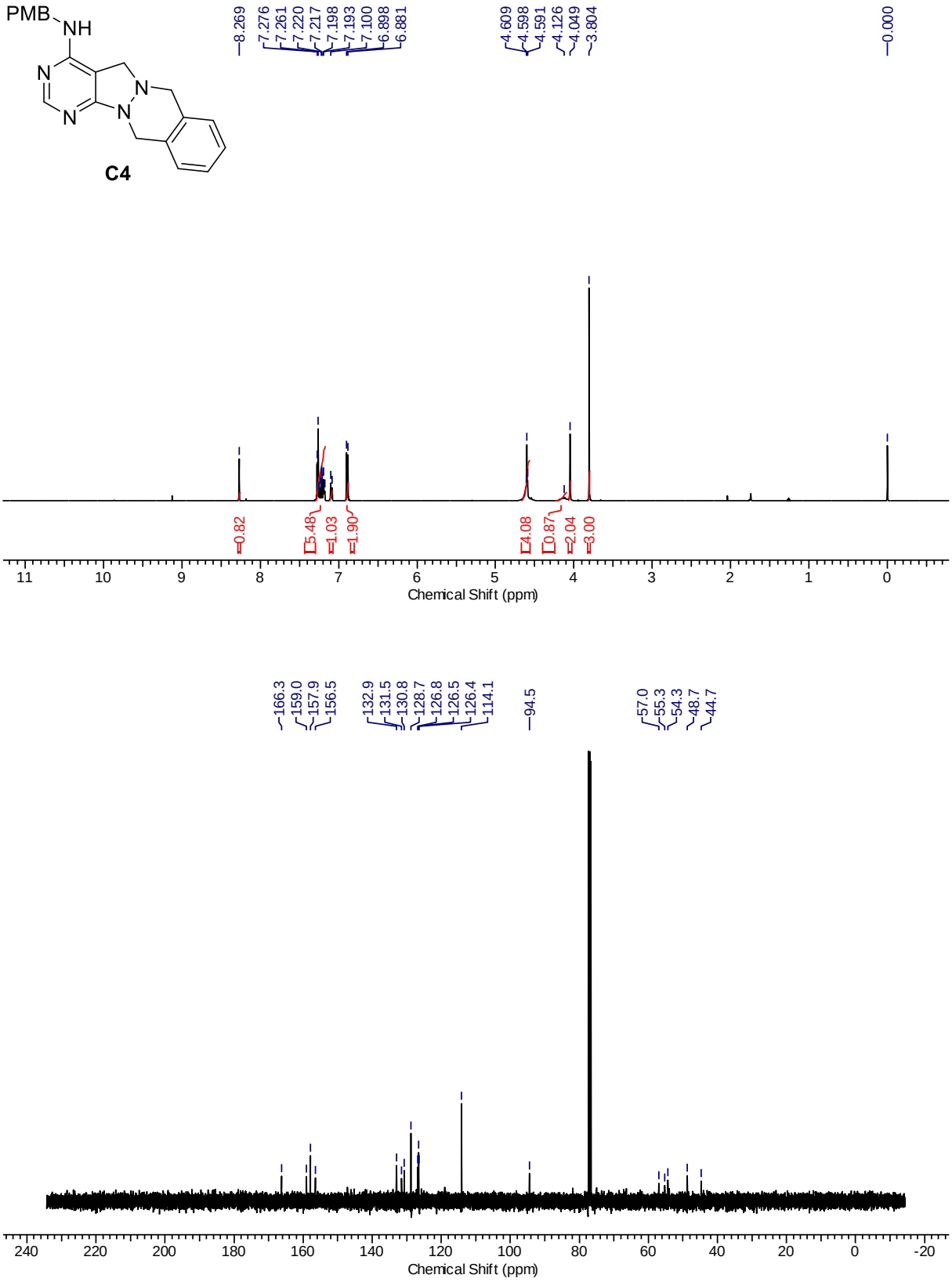
N
N
N
C2
8.180
7.251
7.230
6.884
6.863
4.543
3.902
3.800
2.813
1.787
1.774
1.759
1.745
1.731
1.621
0.000
0.75
1.63
1.74
3.00
5.70
2.16
1.99
2.05
Chemical Shift (ppm)


165.3
158.9
157.8
156.4
131.0
128.6
114.1
93.3
55.2
54.5
54.1
45.1
44.7
24.5
23.2
Chemical Shift (ppm)


PMB
NH
N
N
N
N
C3
8.214
7.251
7.234
6.878
6.860
4.566
4.556
4.524
4.515
4.107
3.793
3.531
3.520
3.507
2.893
2.881
1.838
1.826
1.818
1.742
1.737
0.000
0.86
1.85
1.93
1.94
0.80
1.76
3.00
1.76
1.92
1.91
3.80
Chemical Shift (ppm)
166.9
159.0
158.2
156.5
130.9
128.8
114.0
94.0
62.0
56.3
55.3
50.4
44.6
29.0
27.5
25.0
Chemical Shift (ppm)


PMB
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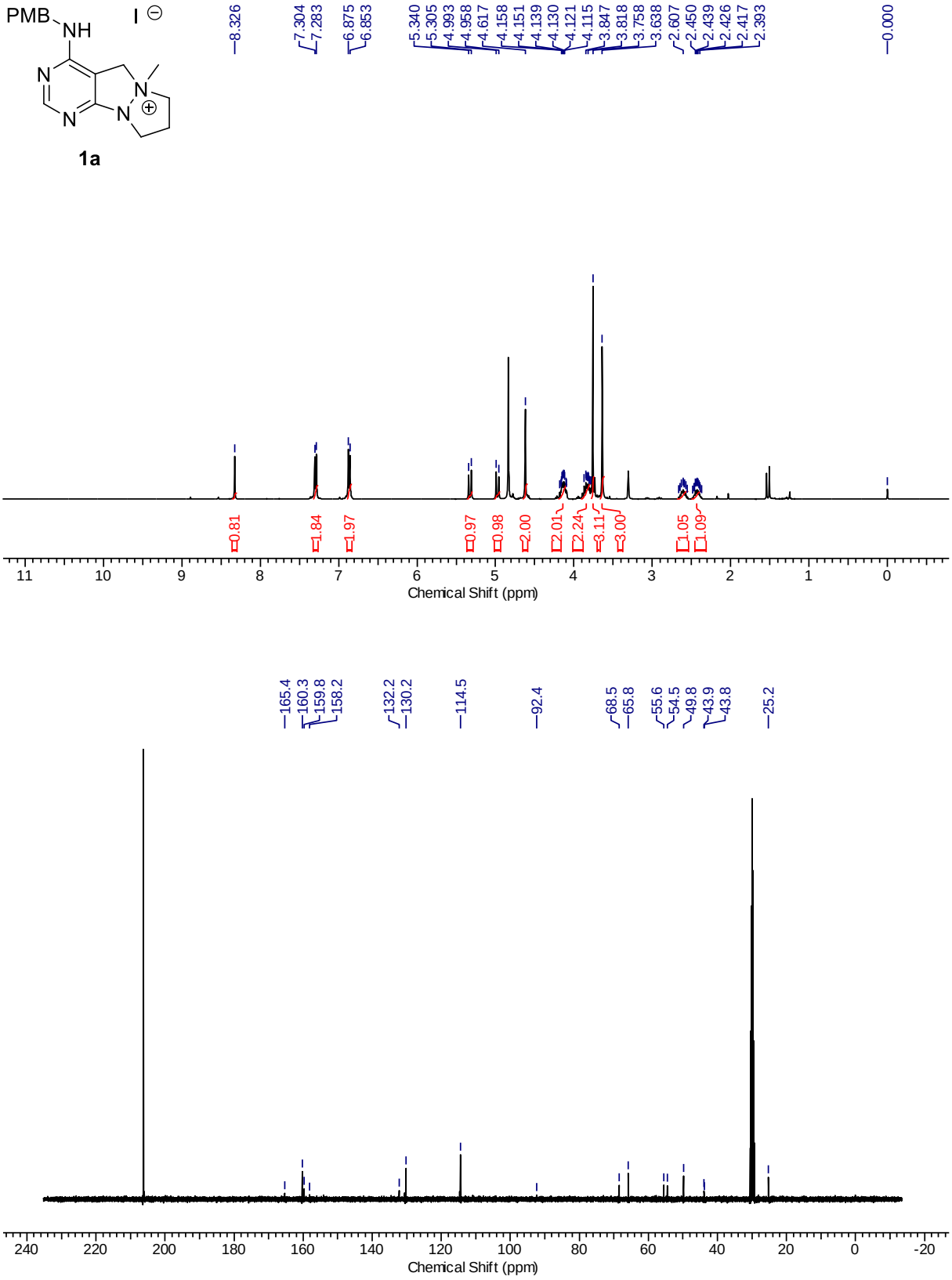
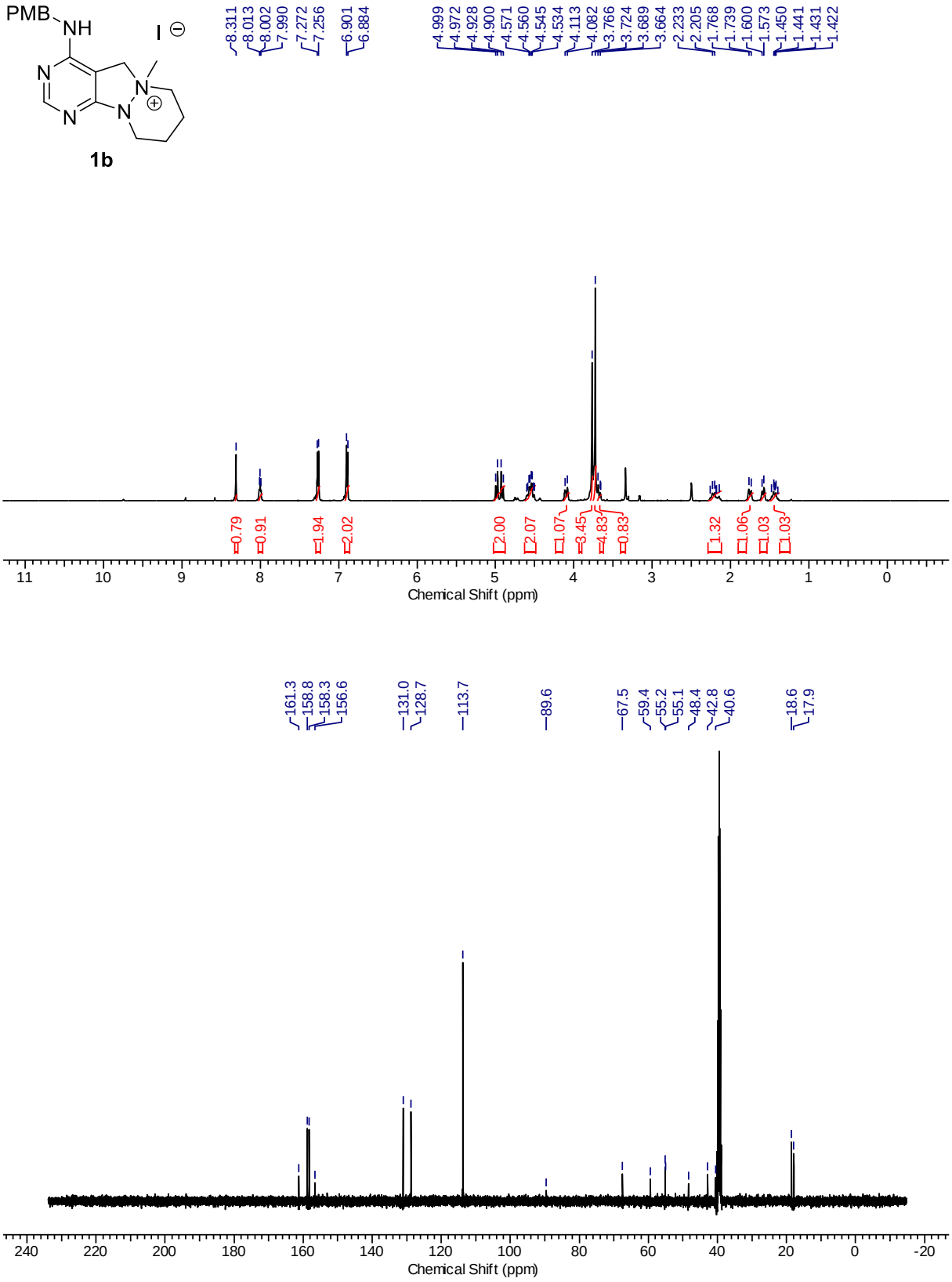
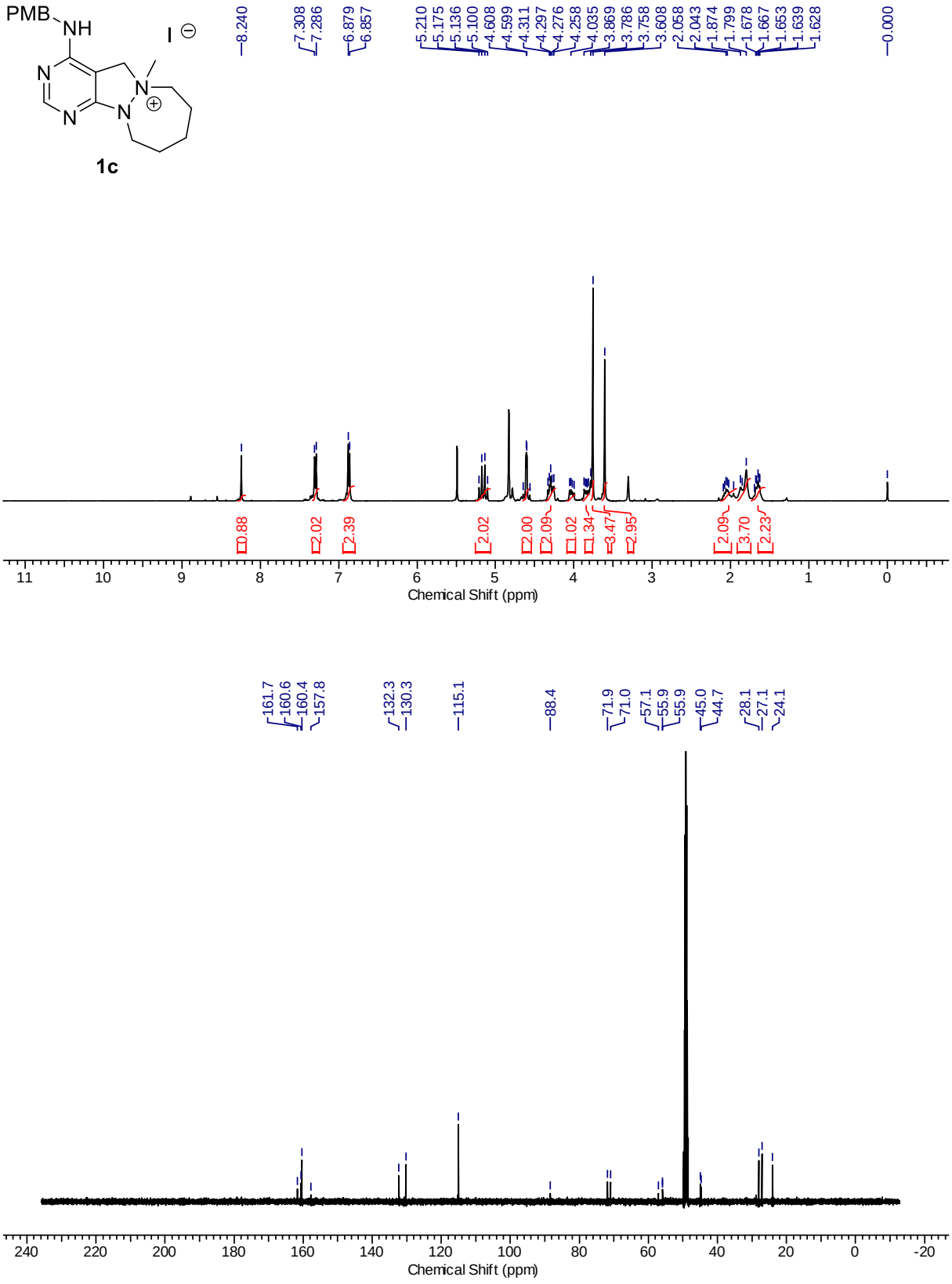
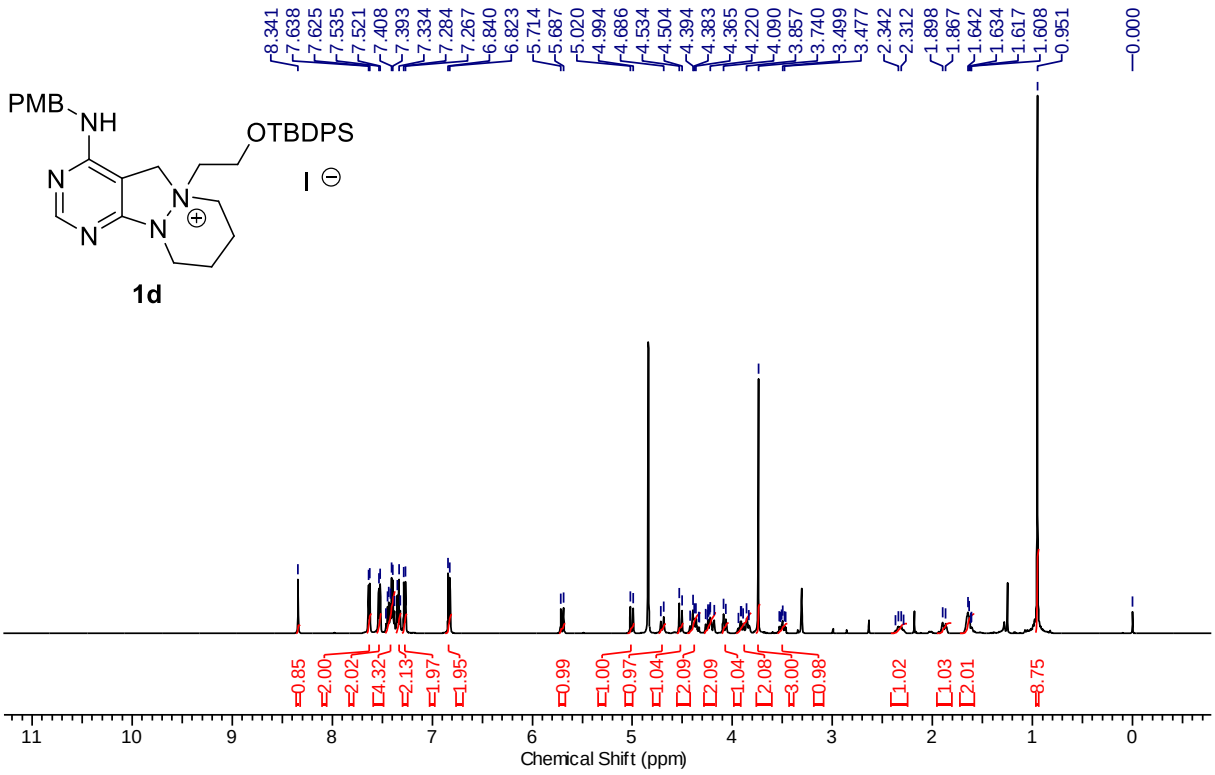
N
N
N
C4
8.269
7.276
7.261
7.220
7.217
7.198
7.193
7.100
6.898
6.881
4.609
4.598
4.591
4.126
4.049
3.804
0.000
0.82
5.48
1.03
1.90
4.08
0.87
2.04
3.00
Chemical Shift (ppm)
166.3
159.0
157.9
156.5
132.9
131.5
130.8
128.7
126.8
126.5
126.4
114.1
94.5
57.0
55.3
54.3
48.7
44.7
Chemical Shift (ppm)


PMB
NH
I
N
N
N
N
1a
8.326
7.304
7.283
6.875
6.853
5.340
5.305
4.993
4.958
4.617
4.158
4.151
4.139
4.130
4.121
4.115
3.847
3.818
3.758
3.638
2.607
2.450
2.439
2.426
2.417
2.393
0.000
0.81
1.84
1.97
0.97
0.98
2.00
2.01
2.24
3.11
3.00
1.05
1.09
Chemical Shift (ppm)
165.4
160.3
159.8
158.2
132.2
130.2
114.5
92.4
68.5
65.8
55.6
54.5
49.8
43.9
43.8
25.2
Chemical Shift (ppm)


PMB
NH
I
N
N
N
1b
8.311
8.013
8.002
7.990
7.272
7.256
6.901
6.884
4.999
4.972
4.928
4.900
4.571
4.560
4.545
4.534
4.113
4.082
3.766
3.724
3.689
3.664
2.233
2.205
1.768
1.739
1.600
1.573
1.450
1.441
1.431
1.422
0.79
0.91
1.94
2.02
2.00
2.07
1.07
3.45
4.83
0.83
1.32
1.06
1.03
1.03
Chemical Shift (ppm)
161.3
158.8
158.3
156.6
131.0
128.7
113.7
89.6
67.5
59.4
55.2
55.1
48.4
42.8
40.6
18.6
17.9
Chemical Shift (ppm)


PMB
NH
I
N
N
N
N
1c
8.240
7.308
7.286
6.879
6.857
5.210
5.175
5.136
5.100
4.608
4.599
4.311
4.297
4.276
4.258
4.035
3.869
3.786
3.758
3.608
2.058
2.043
1.874
1.799
1.678
1.667
1.653
1.639
1.628
0.000
0.88
2.02
2.39
2.02
2.00
2.09
1.02
1.34
3.47
2.95
2.09
3.70
2.23
Chemical Shift (ppm)
161.7
160.6
160.4
157.8
132.3
130.3
115.1
88.4
71.9
71.0
57.1
55.9
55.9
45.0
44.7
28.1
27.1
24.1
Chemical Shift (ppm)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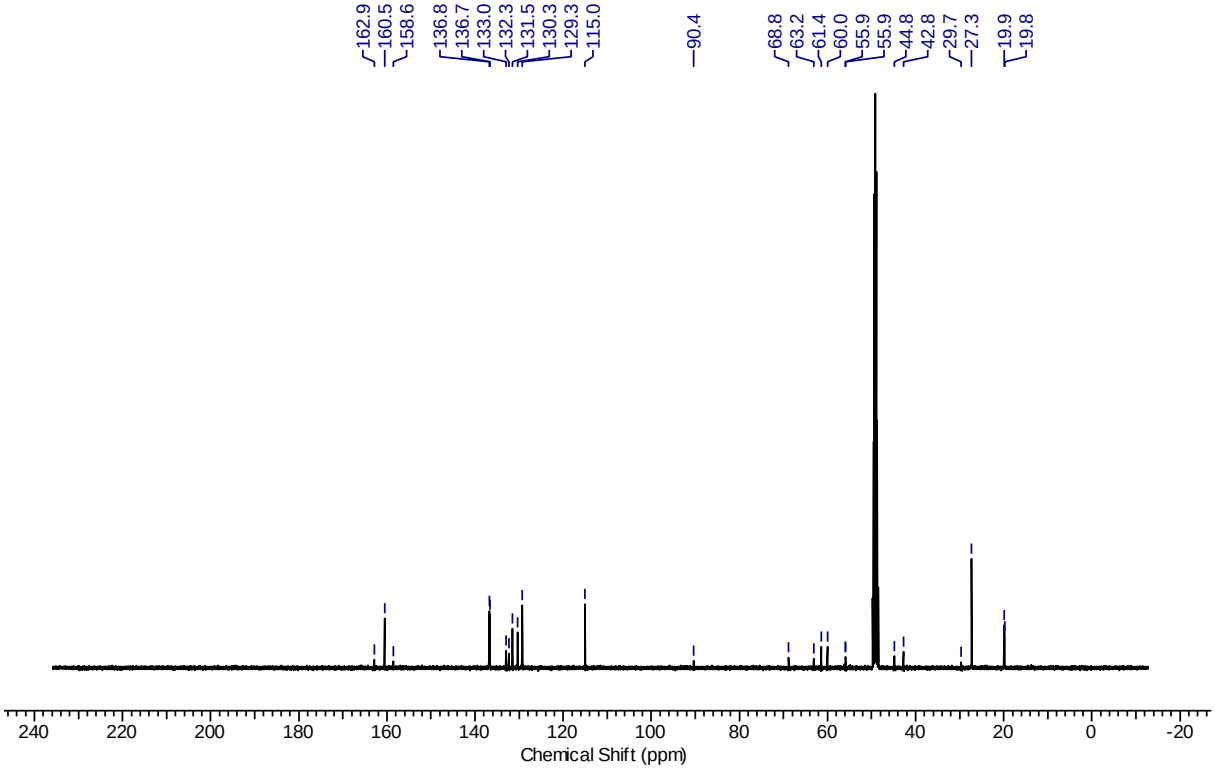
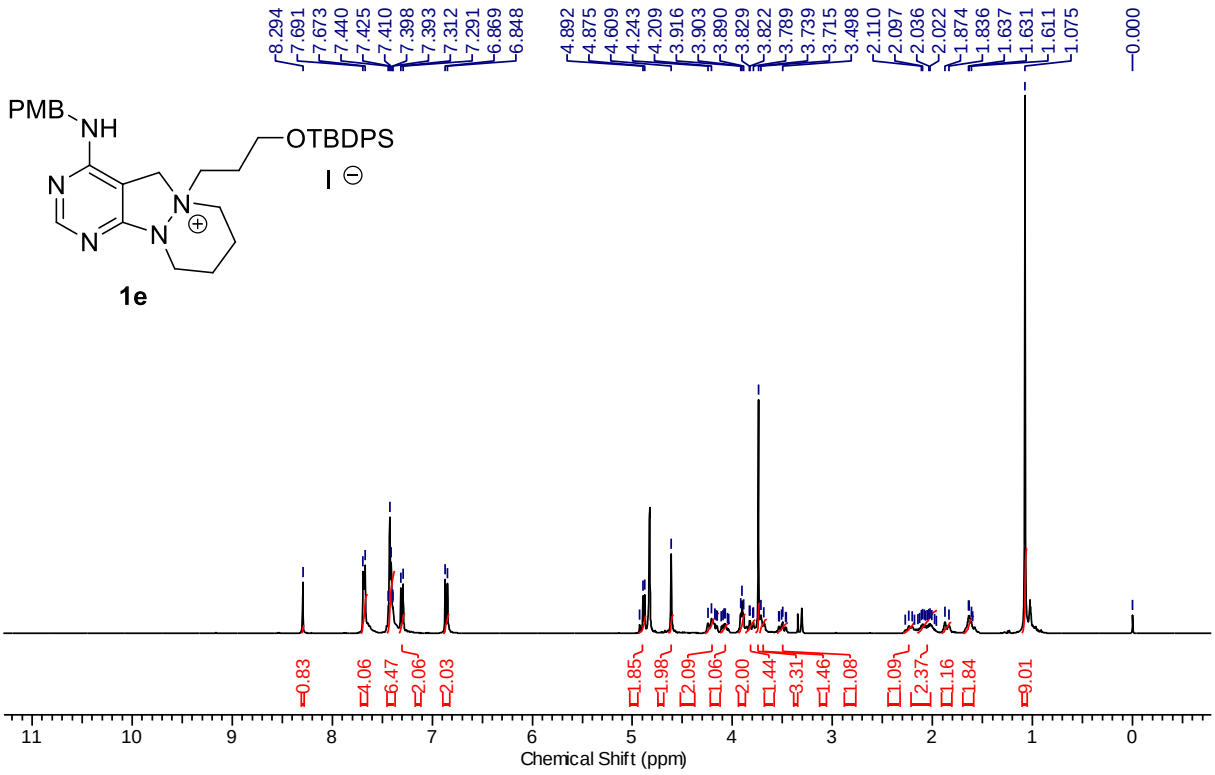
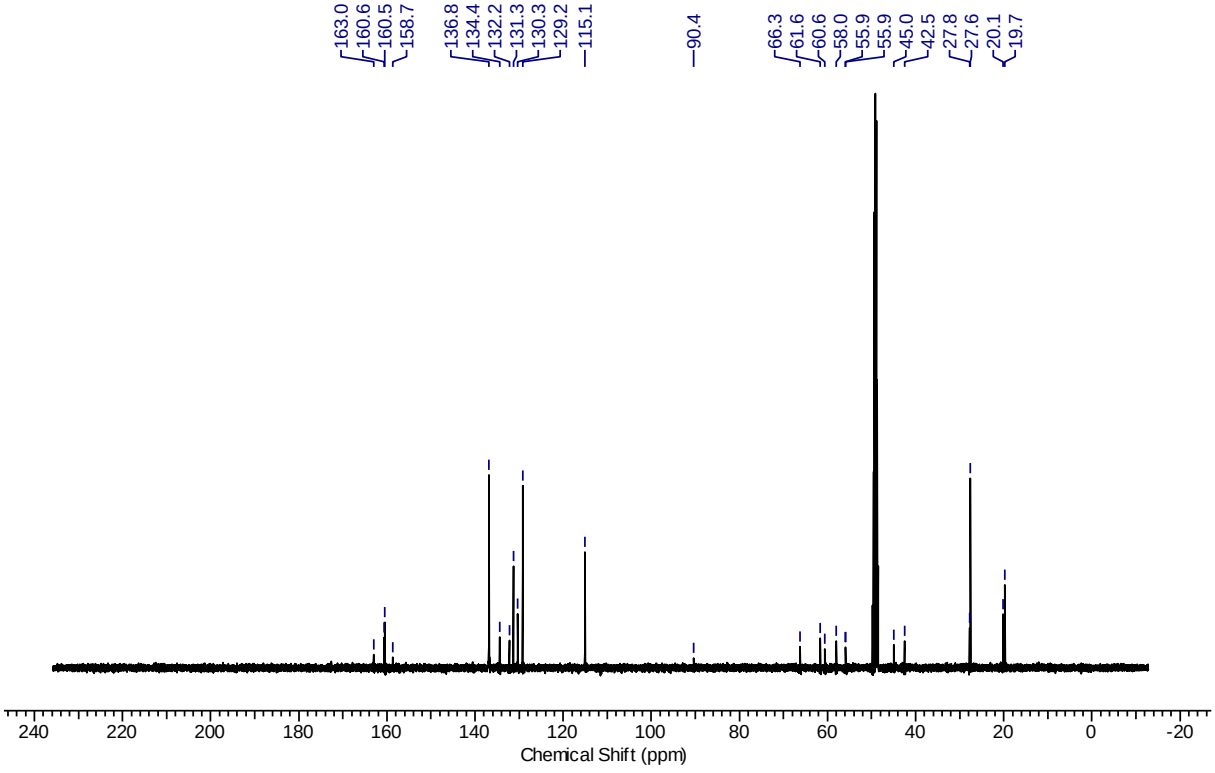
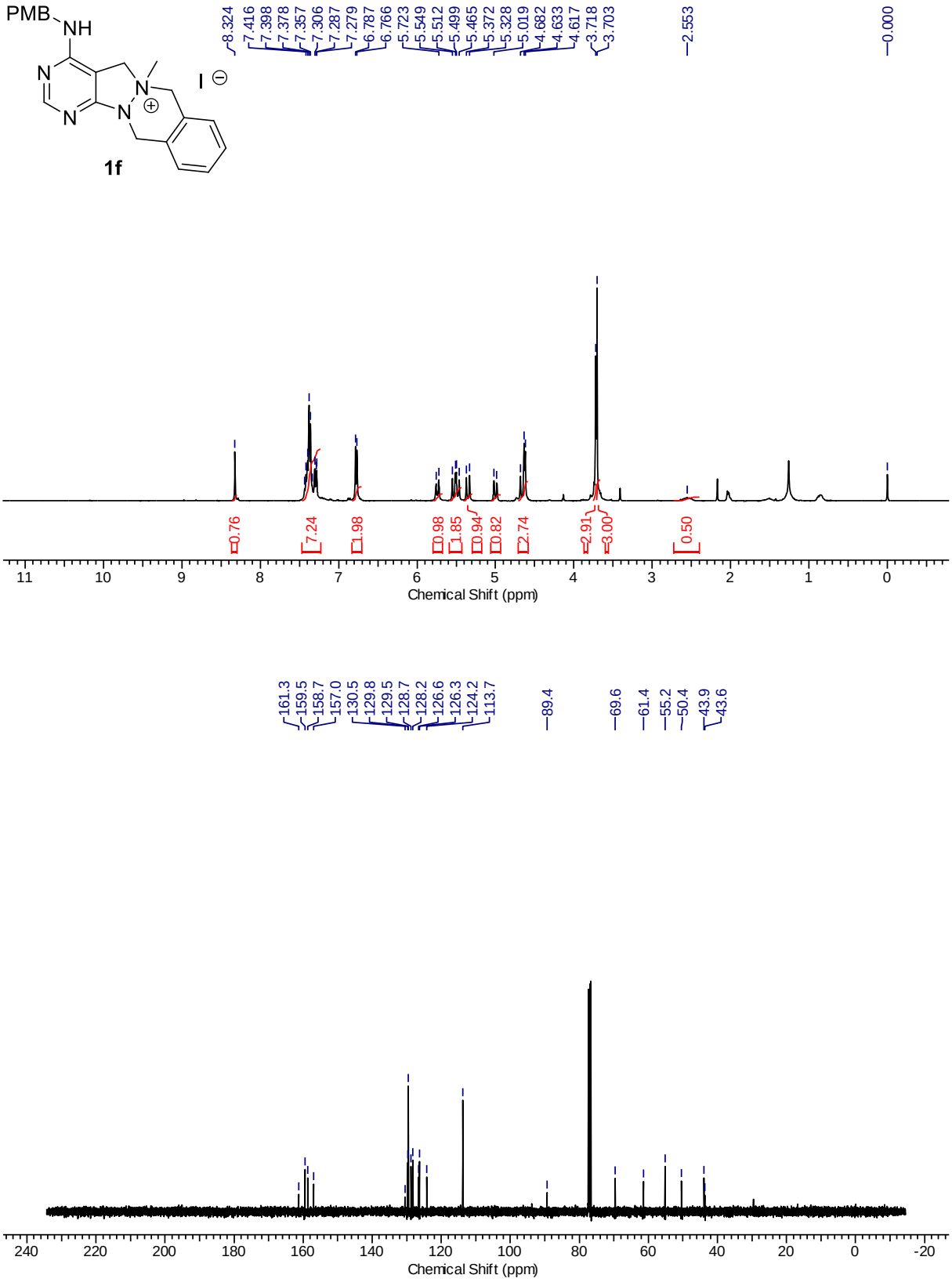
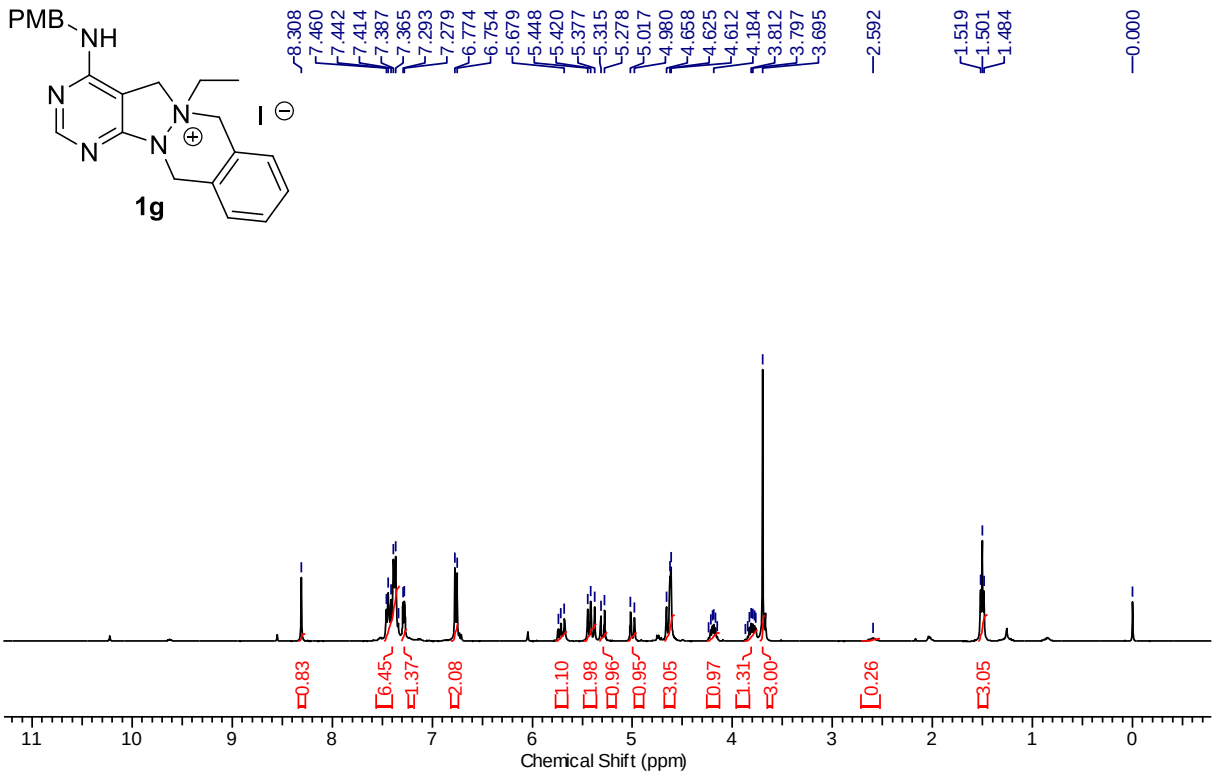
7.638
7.625
7.535
7.521
7.408
7.393
7.334
7.284
7.267
6.840
6.823
5.714
5.687
5.020
4.994
4.686
4.534
4.504
4.394
4.383
4.365
4.220
4.090
3.857
3.740
3.499
3.477
2.342
2.312
1.898
1.867
1.642
1.634
1.617
1.608
0.951
0.000
PMB
NH
OTBDPS
I
1d
0.85
2.00
2.02
4.32
2.13
1.97
1.95
0.99
1.00
0.97
1.04
2.09
2.09
1.04
2.08
3.00
0.98
1.02
1.03
2.01
8.75
Chemical Shift (ppm)


162.9
160.5
158.6
136.8
136.7
133.0
132.3
131.5
130.3
129.3
115.0
90.4
68.8
63.2
61.4
60.0
55.9
55.9
44.8
42.8
29.7
27.3
19.9
19.8
Chemical Shift (ppm)


8.294
7.691
7.673
7.440
7.425
7.410
7.398
7.393
7.312
7.291
6.869
6.848
4.892
4.875
4.609
4.243
4.209
3.916
3.903
3.890
3.829
3.822
3.789
3.739
3.715
3.498
2.110
2.097
2.036
2.022
1.874
1.836
1.637
1.631
1.611
1.075
0.000
PMB
NH
OTBDPS
I
1e
0.83
4.06
6.47
2.06
2.03
1.85
1.98
2.09
1.06
2.00
1.44
3.31
1.46
1.08
1.09
2.37
1.16
1.84
9.01
Chemical Shift (ppm)


163.0
160.6
160.5
158.7
136.8
134.4
132.2
131.3
130.3
129.2
115.1
90.4
66.3
61.6
60.6
58.0
55.9
55.9
45.0
42.5
27.8
27.6
20.1
19.7
Chemical Shift (ppm)


PMB
NH
N
N
N
N
I
1f
8.324
7.416
7.398
7.378
7.357
7.306
7.287
7.279
6.787
6.766
5.723
5.549
5.512
5.499
5.465
5.372
5.328
5.019
4.682
4.633
4.617
3.718
3.703
2.553
0.000
0.76
7.24
1.98
0.98
1.85
0.94
0.82
2.74
2.91
3.00
0.50
Chemical Shift (ppm)
161.3
159.5
158.7
157.0
130.5
129.8
129.5
128.7
128.2
126.6
126.3
124.2
113.7
89.4
69.6
61.4
55.2
50.4
43.9
43.6
Chemical Shift (ppm)


PMB
NH
N
N
N
N
I
1g
8.308
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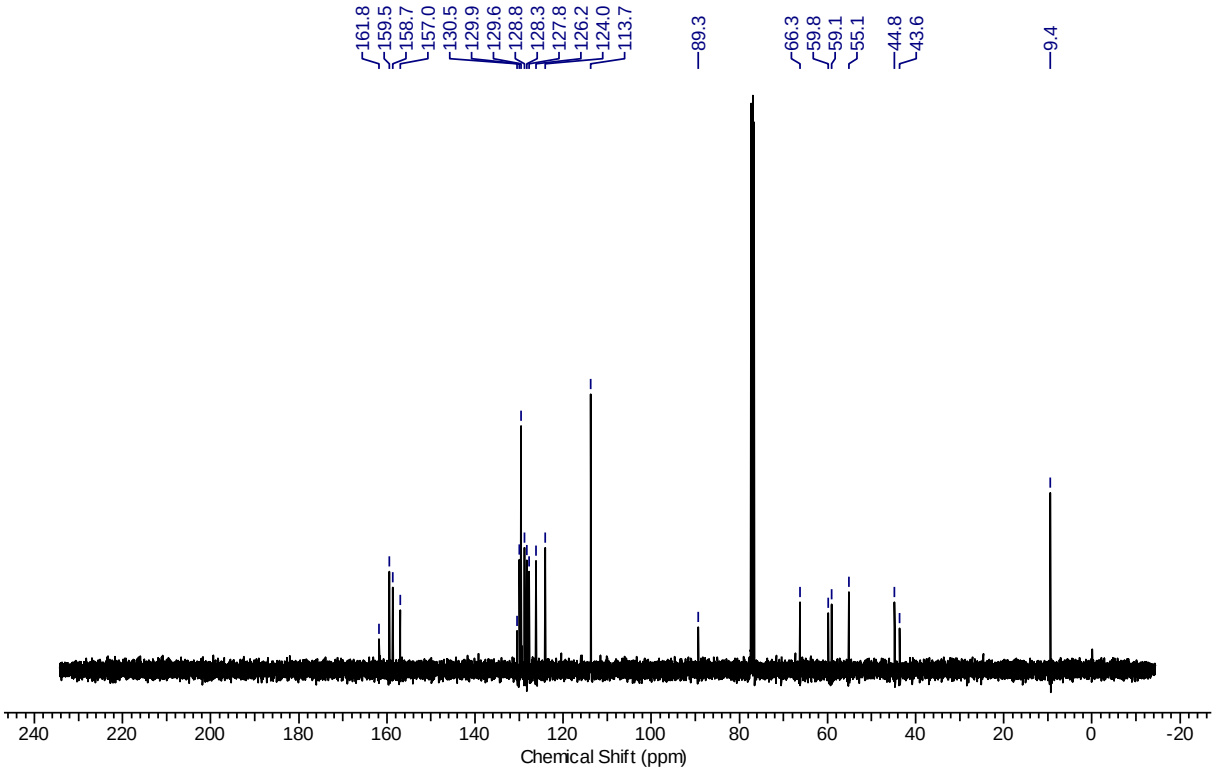
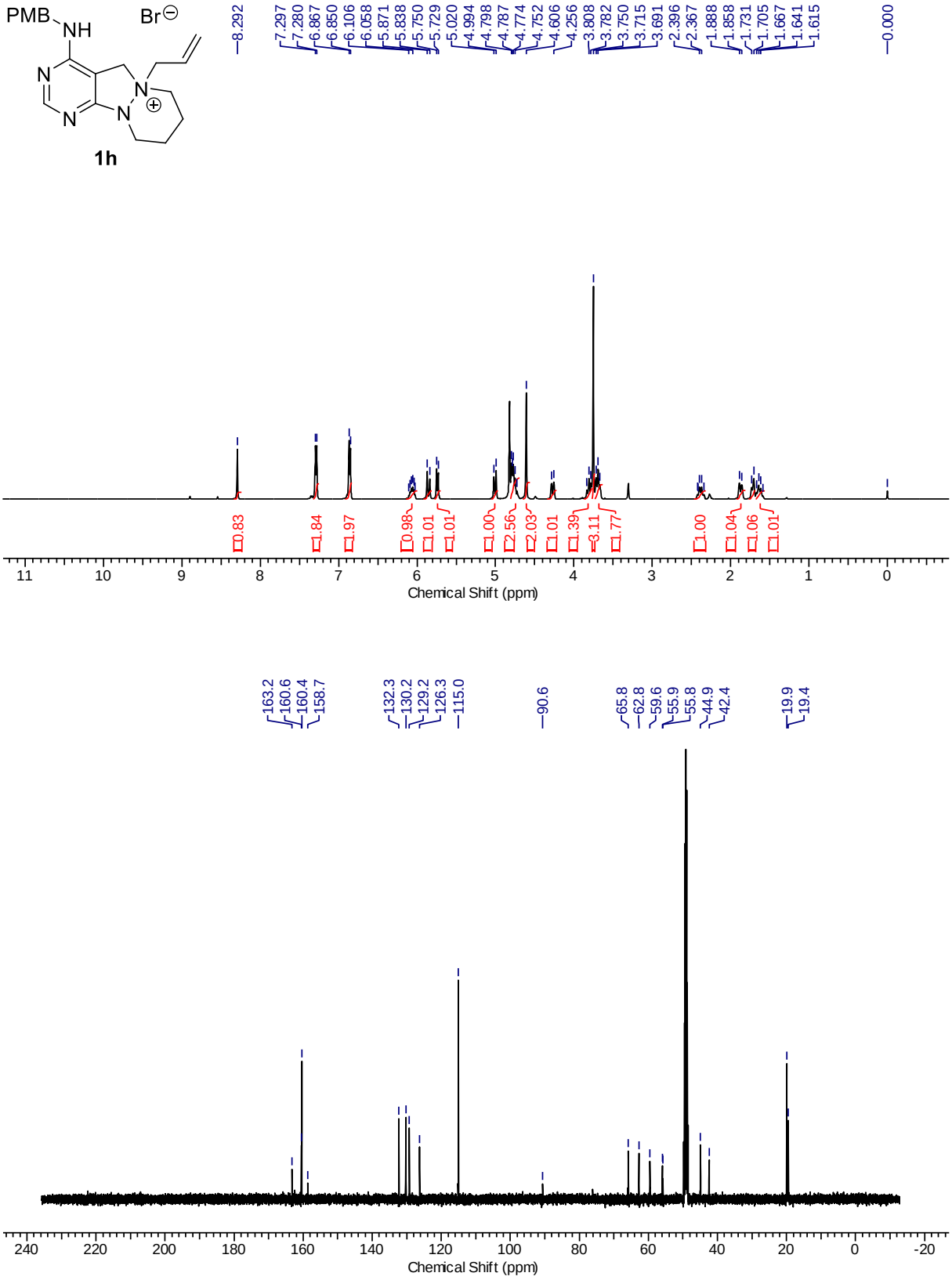
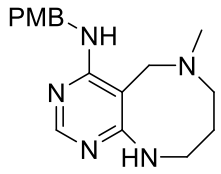
7.442
7.414
7.387
7.365
7.293
7.279
6.774
6.754
5.679
5.448
5.420
5.377
5.315
5.278
5.017
4.980
4.658
4.625
4.612
4.184
3.812
3.797
3.695
2.592
1.519
1.501
1.484
0.000
0.83
6.45
1.37
2.08
1.10
1.98
0.96
0.95
3.05
0.97
1.31
3.00
0.26
3.05
Chemical Shift (ppm)

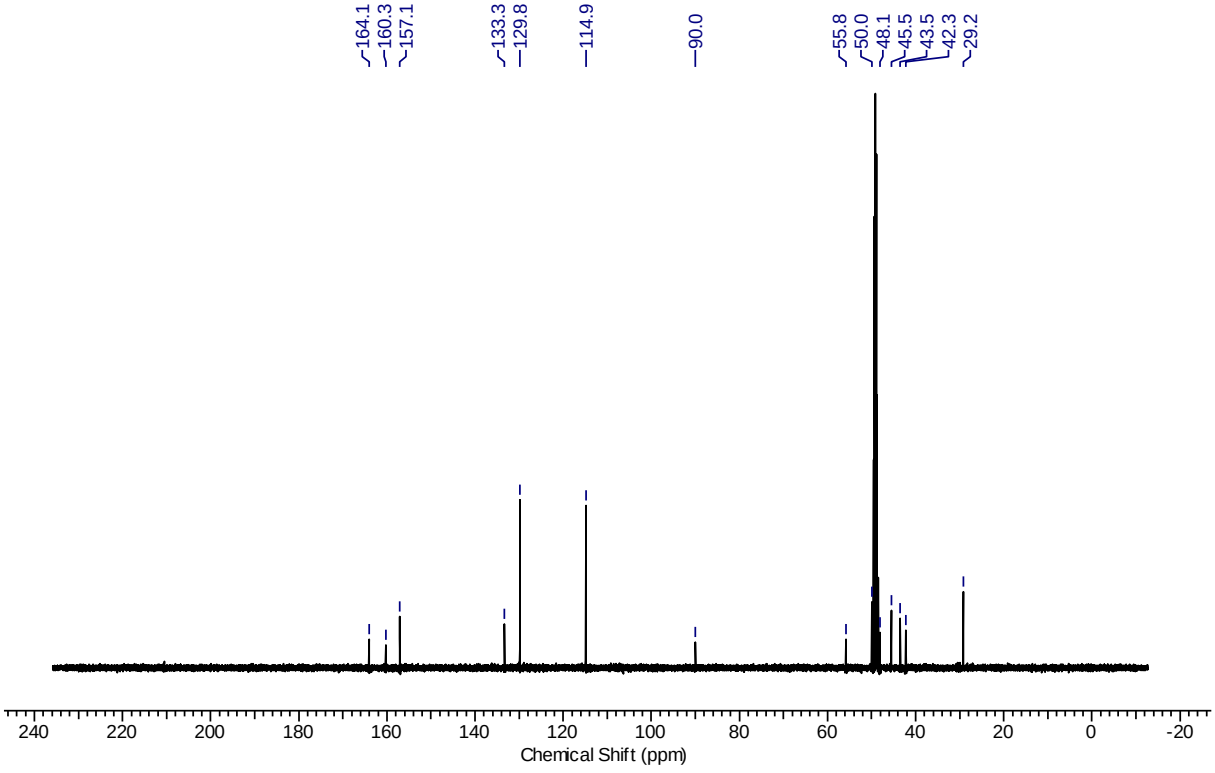

161.8
159.5
158.7
157.0
130.5
129.9
129.6
128.8
128.3
127.8
126.2
124.0
113.7
89.3
66.3
59.8
59.1
55.1
44.8
43.6
9.4
Chemical Shift (ppm)

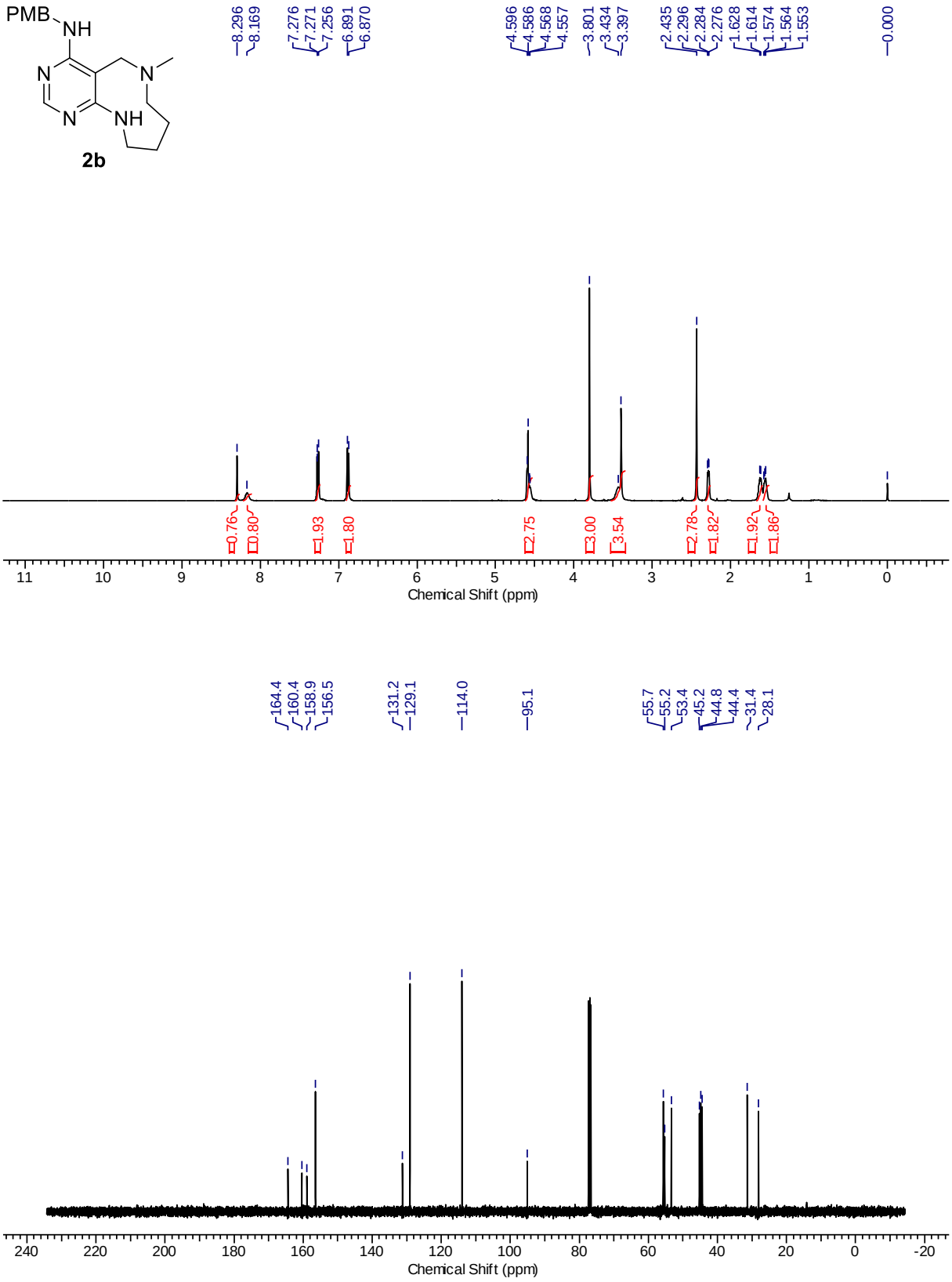

PMB
NH
Br
N
N
N
N
1h
8.292
7.297
7.280
6.867
6.850
6.106
6.058
5.871
5.838
5.750
5.729
5.020
4.994
4.798
4.787
4.774
4.752
4.606
4.256
3.808
3.782
3.750
3.715
3.691
2.396
2.367
1.888
1.858
1.731
1.705
1.667
1.641
1.615
0.000
0.83
1.84
1.97
0.98
1.01
1.01
1.00
2.56
2.03
1.01
1.39
3.11
1.77
1.00
1.04
1.06
1.01
Chemical Shift (ppm)
163.2
160.6
160.4
158.7
132.3
130.2
129.2
126.3
115.0
90.6
65.8
62.8
59.6
55.9
55.8
44.9
42.4
19.9
19.4
Chemical Shift (ppm)

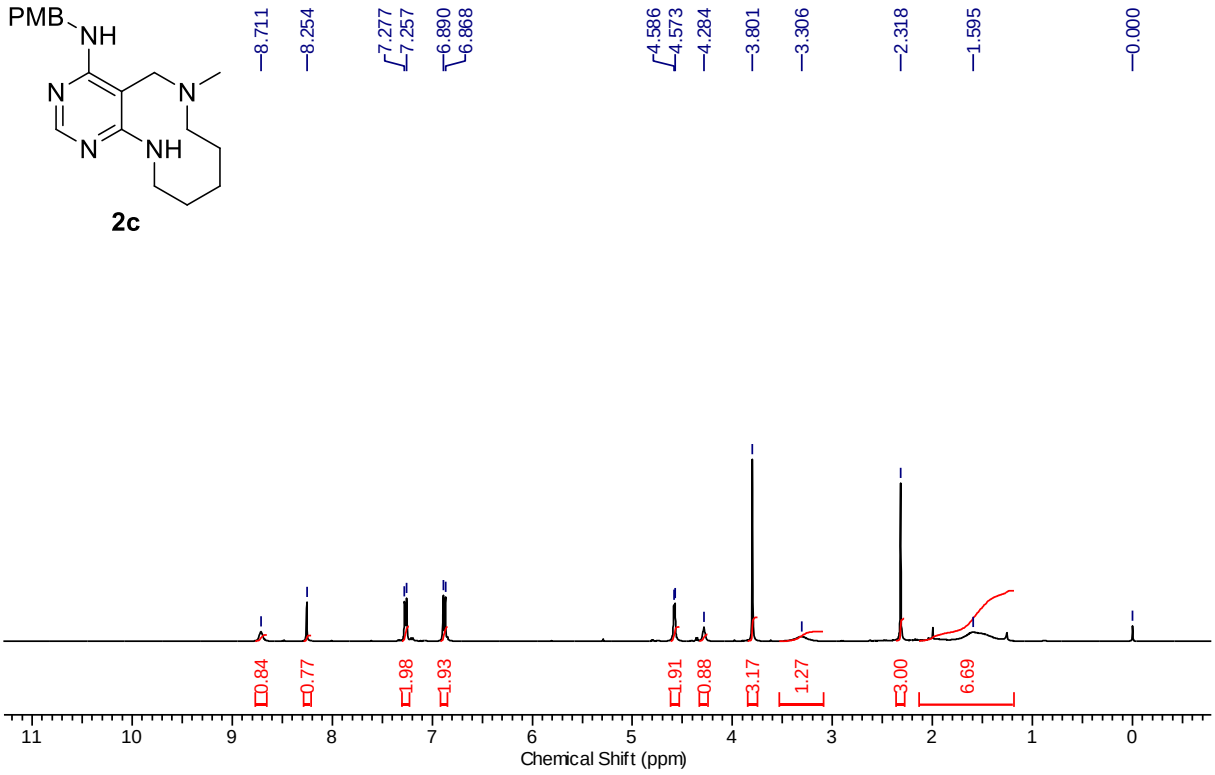

PMB
NH
N
N
N
HN

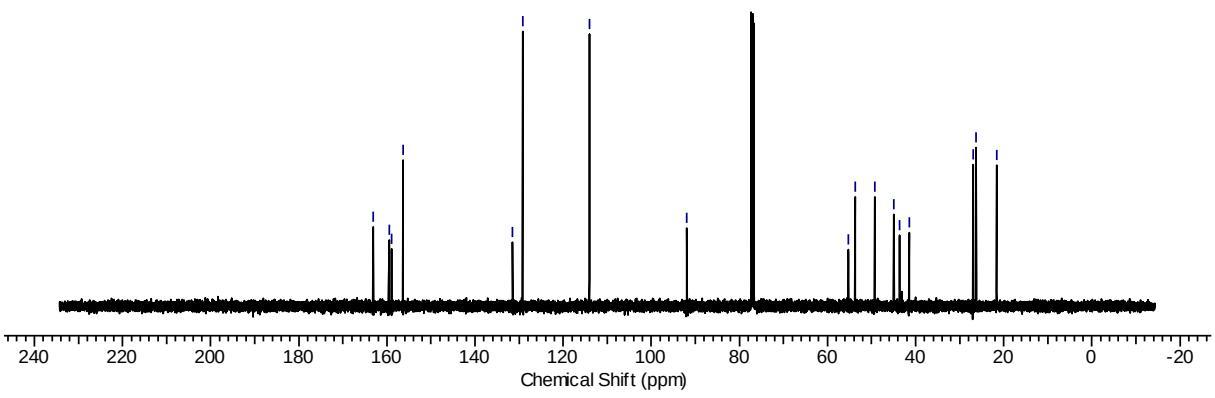
2a

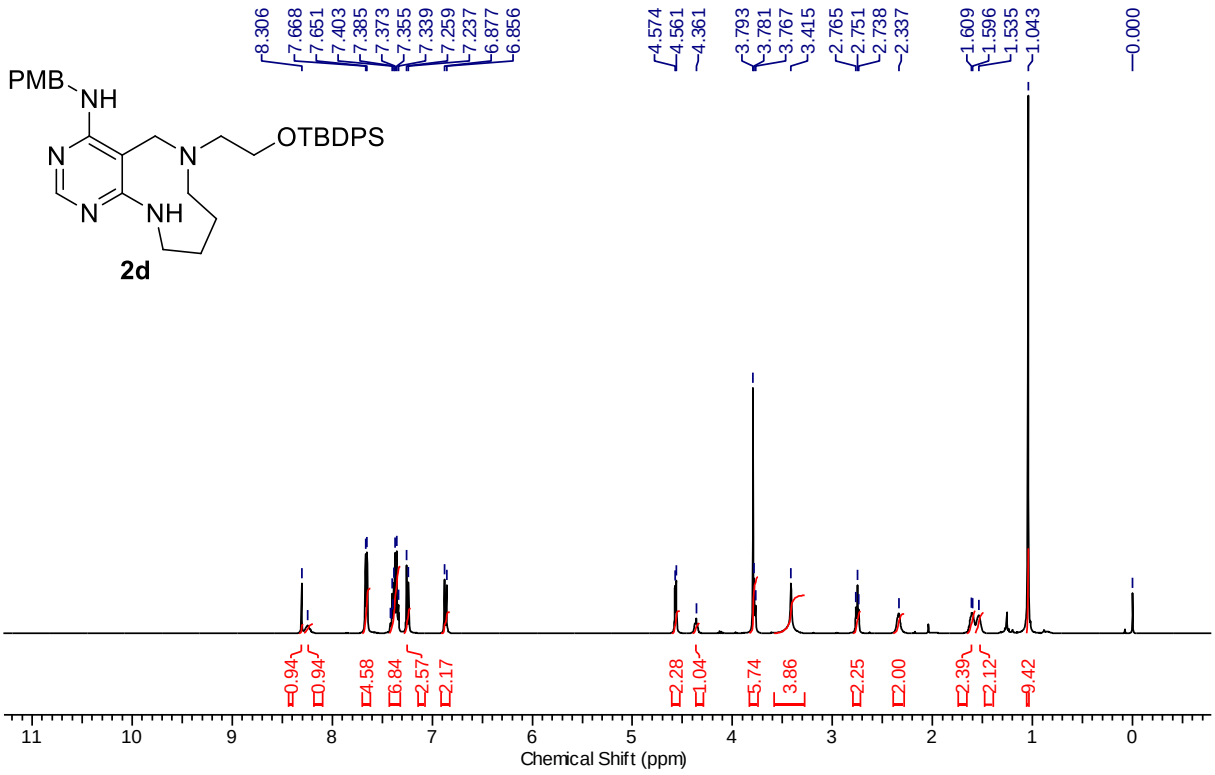
7.828
7.243
7.222
6.854
6.833
4.518
3.946
3.755
3.672
3.656
3.641
2.750
2.738
2.725
2.398
1.984
1.970
1.956
0.83
1.92
1.95
2.08
2.03
3.00
1.96
1.97
3.16
2.13
Chemical Shift (ppm)

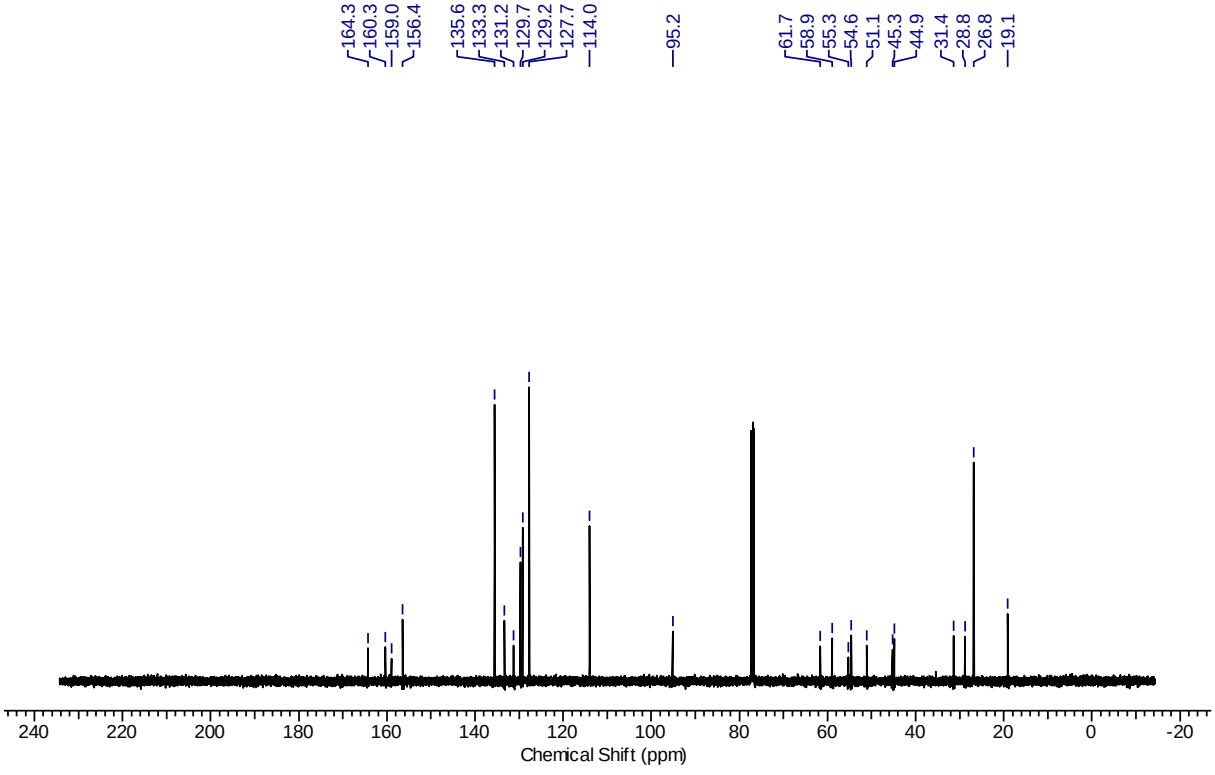

164.1
160.3
157.1
133.3
129.8
114.9
90.0
55.8
50.0
48.1
45.5
43.5
42.3
29.2
Chemical Shift (ppm)

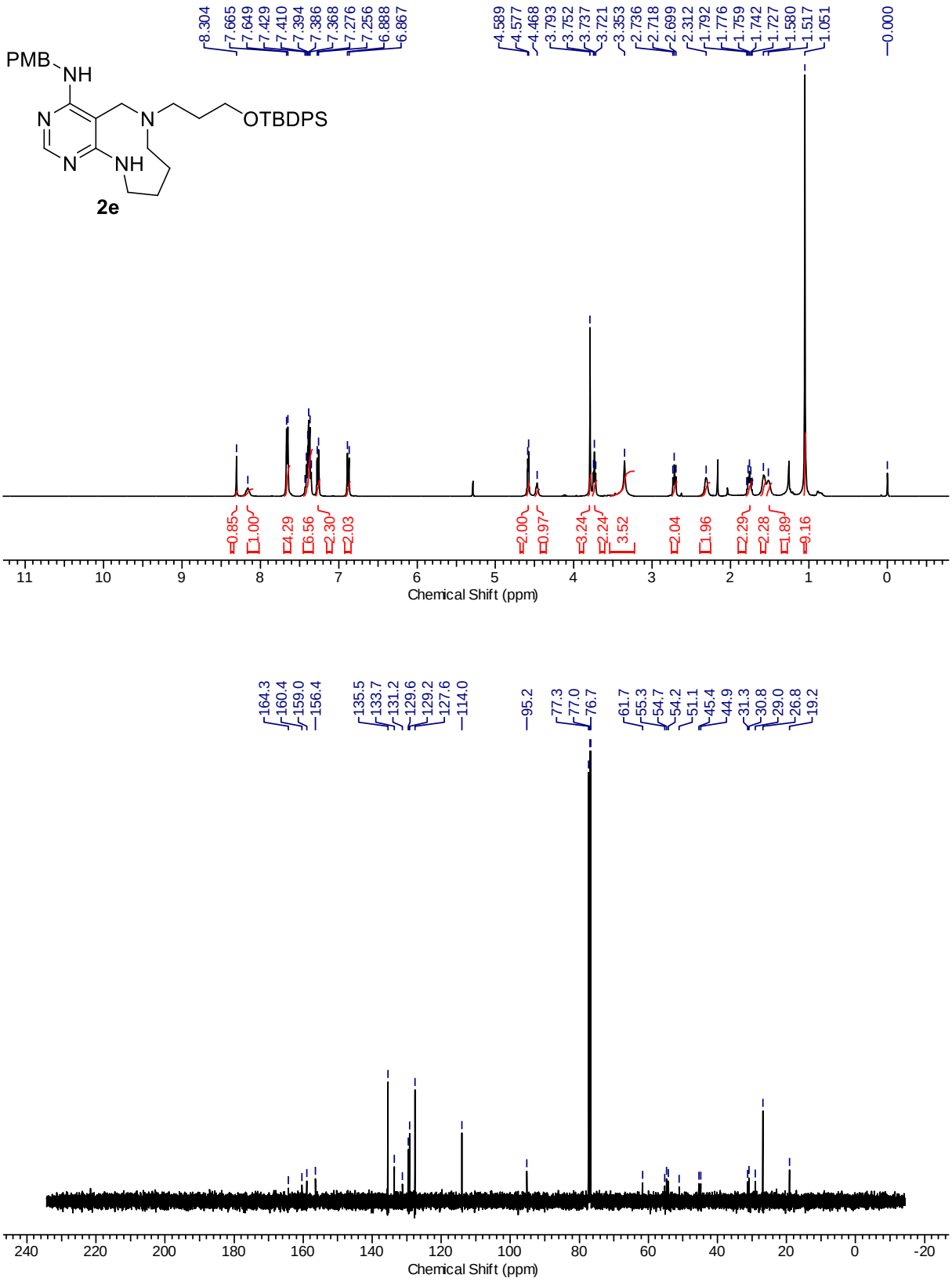

PMB
NH
N
N
N
NH
2b
8.296
8.169
7.276
7.271
7.256
6.891
6.870
4.596
4.586
4.568
4.557
3.801
3.434
3.397
2.435
2.296
2.284
2.276
1.628
1.614
1.574
1.564
1.553
0.000
0.76
0.80
1.93
1.80
2.75
3.00
3.54
2.78
1.82
1.92
1.86
Chemical Shift (ppm)
164.4
160.4
158.9
156.5
131.2
129.1
114.0
95.1
55.7
55.2
53.4
45.2
44.8
44.4
31.4
28.1
Chemical Shift (ppm)

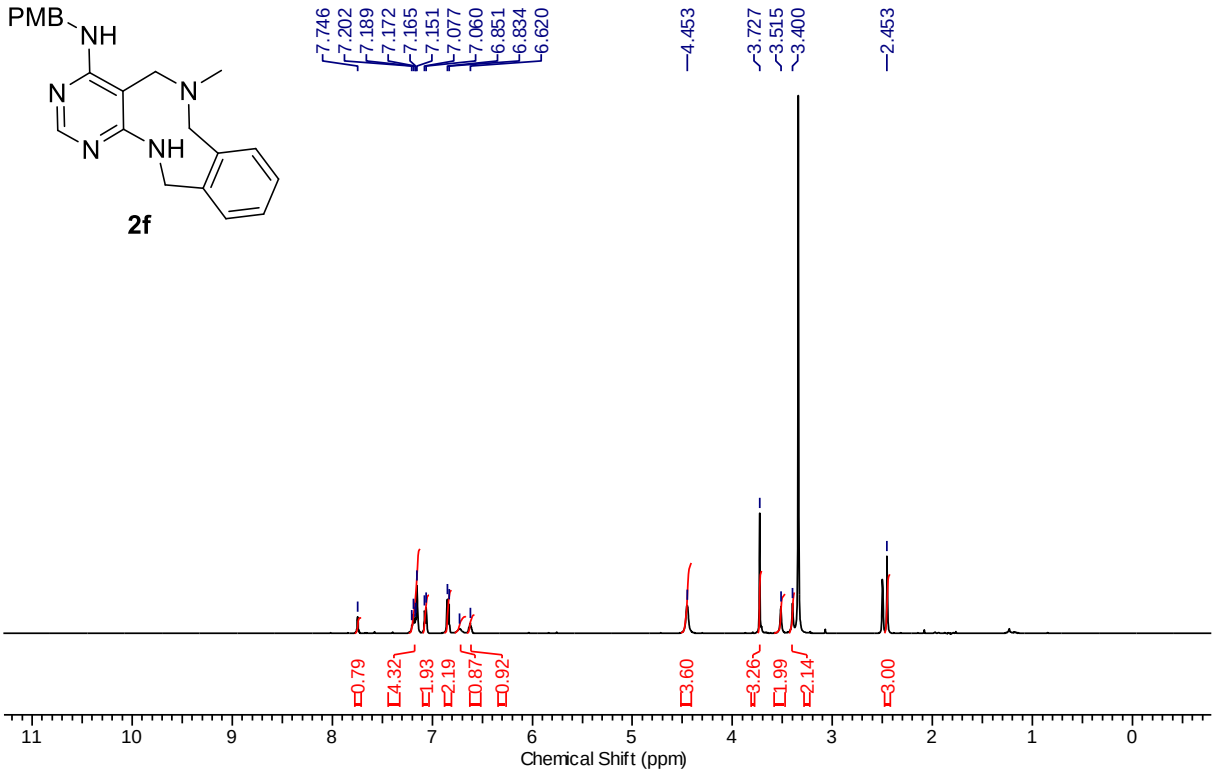

PMB
NH
N
N
N
NH
2c
8.711
8.254
7.277
7.257
6.890
6.868
4.586
4.573
4.284
3.801
3.306
2.318
1.595
0.000
0.84
0.77
1.98
1.93
1.91
0.88
3.17
1.27
3.00
6.69
Chemical Shift (ppm)

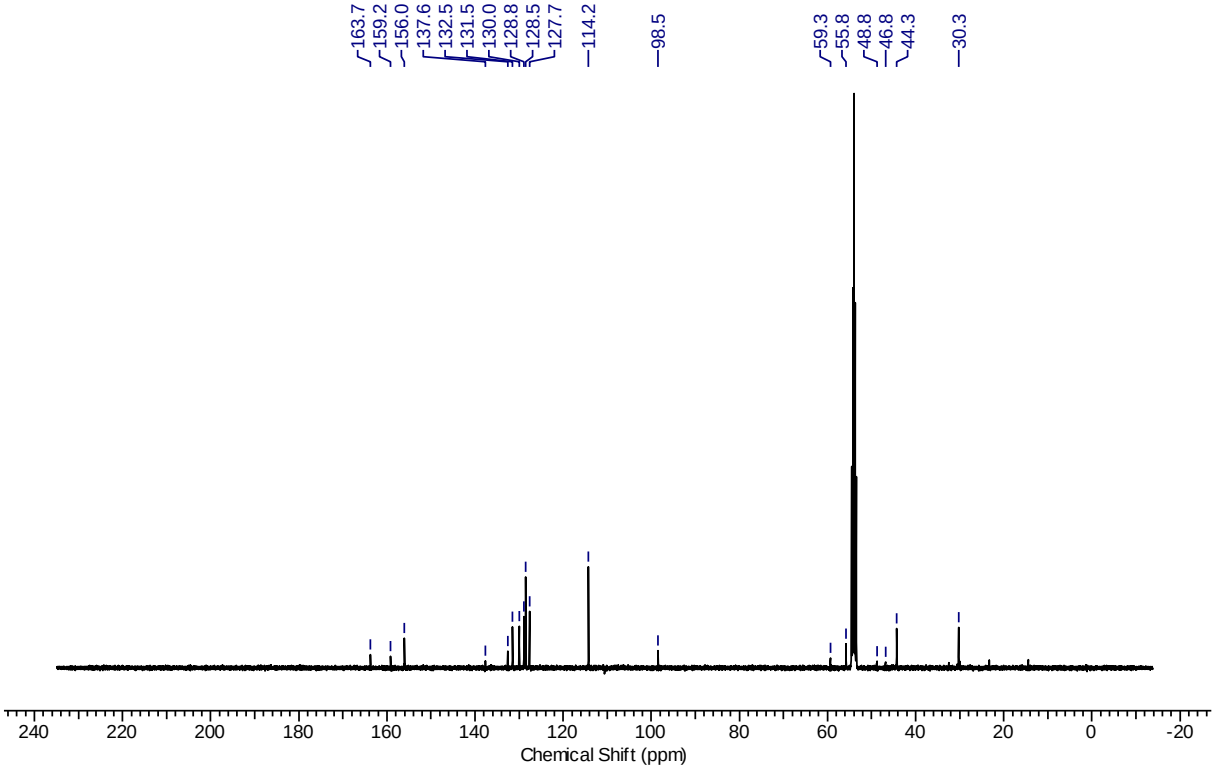

163.1
159.5
158.9
156.3
131.5
129.1
114.0
91.9
55.2
53.7
49.3
45.0
43.7
41.5
27.0
26.2
21.6
Chemical Shift (ppm)

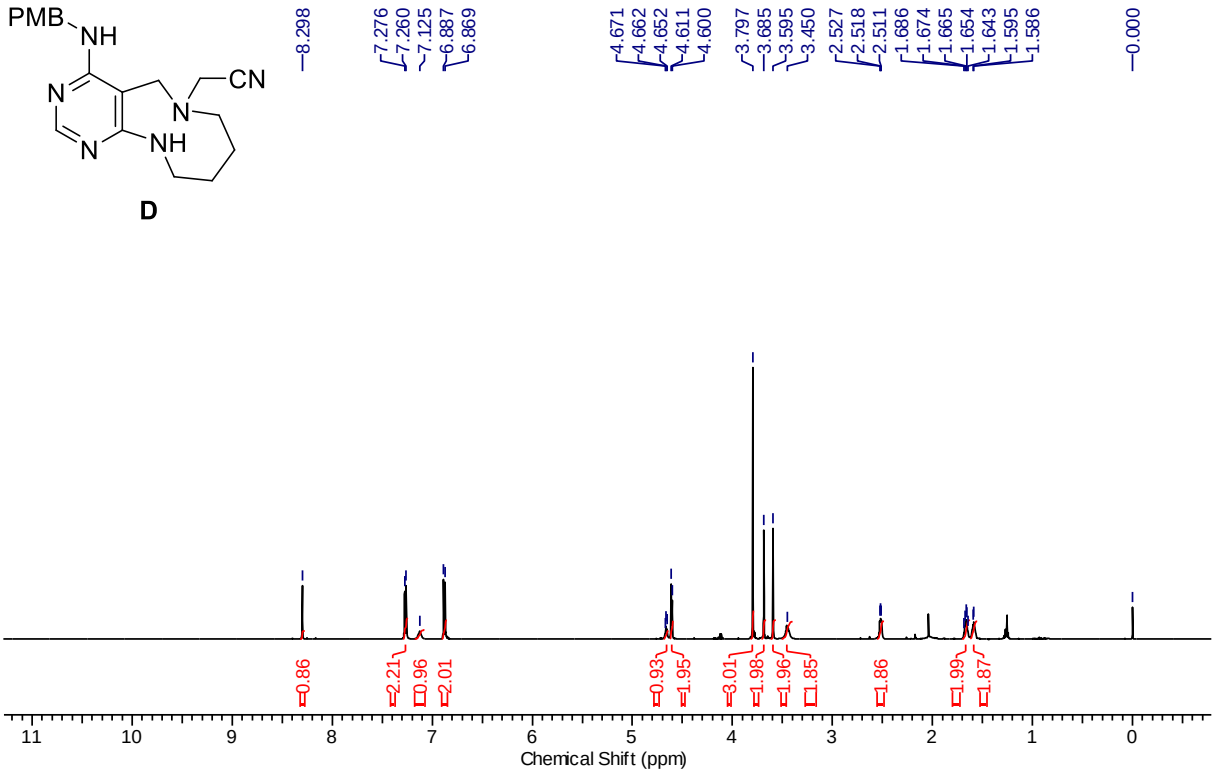

PMB
NH
N
N
N
NH
OTBDPS
2d
8.306
7.668
7.651
7.403
7.385
7.373
7.355
7.339
7.259
7.237
6.877
6.856
4.574
4.561
4.361
3.793
3.781
3.767
3.415
2.765
2.751
2.738
2.337
1.609
1.596
1.535
1.043
0.000
0.94
0.94
4.58
6.84
2.57
2.17
2.28
1.04
5.74
3.86
2.25
2.00
2.39
2.12
9.42
Chemical Shift (ppm)

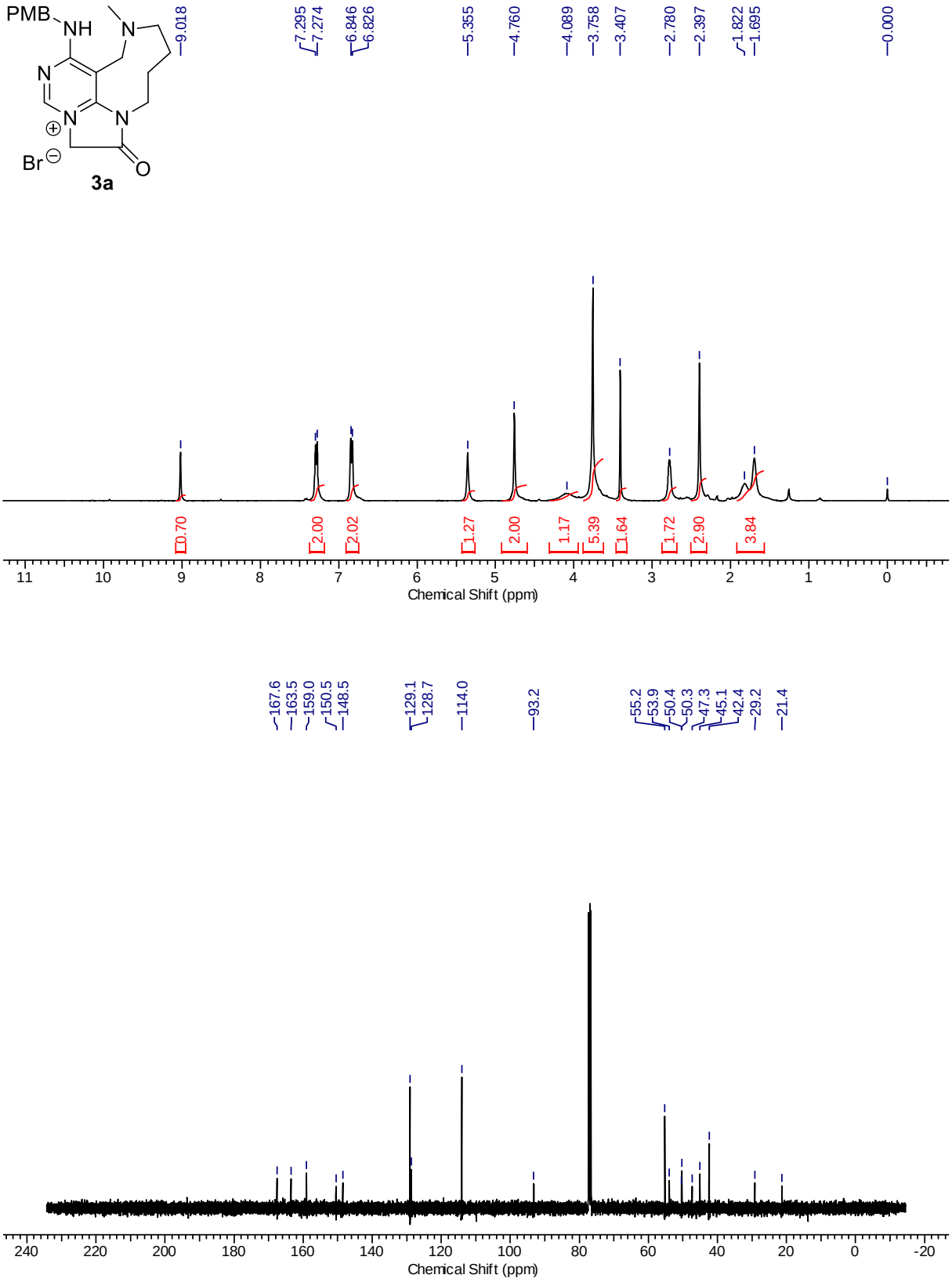

164.3
160.3
159.0
156.4
135.6
133.3
131.2
129.7
129.2
127.7
114.0
95.2
61.7
58.9
55.3
54.6
51.1
45.3
44.9
31.4
28.8
26.8
19.1
Chemical Shift (ppm)

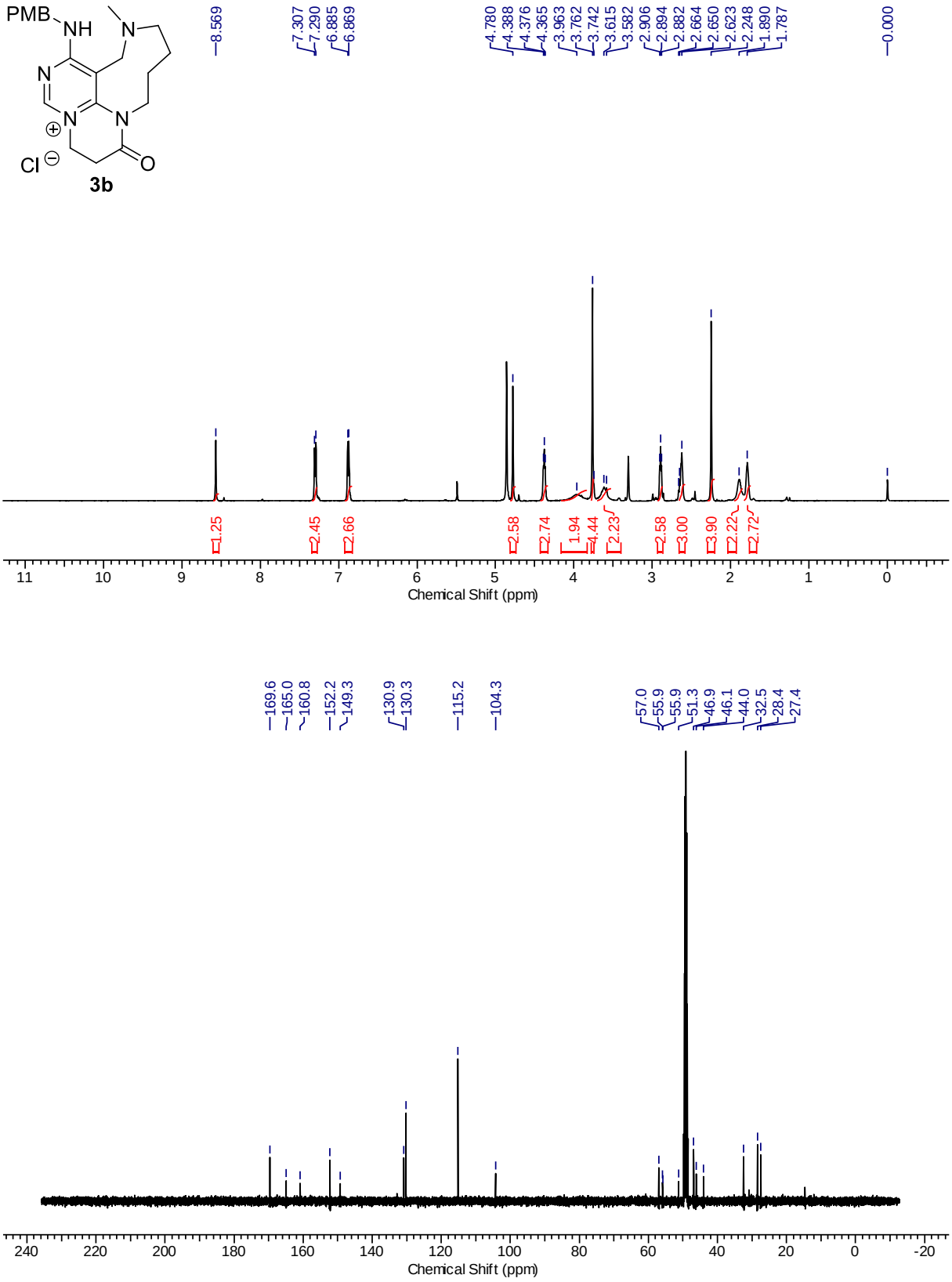

PMB
NH
N
N
N
NH
OTBDPS
2e
8.304
7.665
7.649
7.429
7.410
7.394
7.386
7.368
7.276
7.256
6.888
6.867
4.589
4.577
4.468
3.793
3.752
3.737
3.721
3.353
2.736
2.718
2.699
2.312
1.792
1.776
1.759
1.742
1.727
1.580
1.517
1.051
0.000
0.85
1.00
4.29
6.56
2.30
2.03
2.00
0.97
3.24
2.24
3.52
2.04
1.96
2.29
2.28
1.89
9.16
Chemical Shift (ppm)
164.3
160.4
159.0
156.4
135.5
133.7
131.2
129.6
129.2
127.6
114.0
95.2
77.3
77.0
76.7
61.7
55.3
54.7
54.2
51.1
45.4
44.9
31.3
30.8
29.0
26.8
19.2
Chemical Shift (ppm)

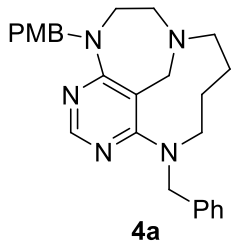

PMB
NH
N
N
N
NH
2f
7.746
7.202
7.189
7.172
7.165
7.151
7.077
7.060
6.851
6.834
6.620
4.453
3.727
3.515
3.400
2.453
0.79
4.32
1.93
2.19
0.87
0.92
3.60
3.26
1.99
2.14
3.00
Chemical Shift (ppm)


163.7
159.2
156.0
137.6
132.5
131.5
130.0
128.8
128.5
127.7
114.2
98.5
59.3
55.8
48.8
46.8
44.3
30.3
Chemical Shift (ppm)


PMB
NH
N
N
N
NH
CN
D
8.298
7.276
7.260
7.125
6.887
6.869
4.671
4.662
4.652
4.611
4.600
3.797
3.685
3.595
3.450
2.527
2.518
2.511
1.686
1.674
1.665
1.654
1.643
1.595
1.586
0.000
0.86
2.21
0.96
2.01
0.93
1.95
3.01
1.98
1.96
1.85
1.86
1.99
1.87
Chemical Shift (ppm)
164.0
160.6
159.0
156.9
131.0
129.1
115.2
114.1
93.4
55.3
52.3
50.5
45.1
44.8
44.3
31.0
27.8
Chemical Shift (ppm)

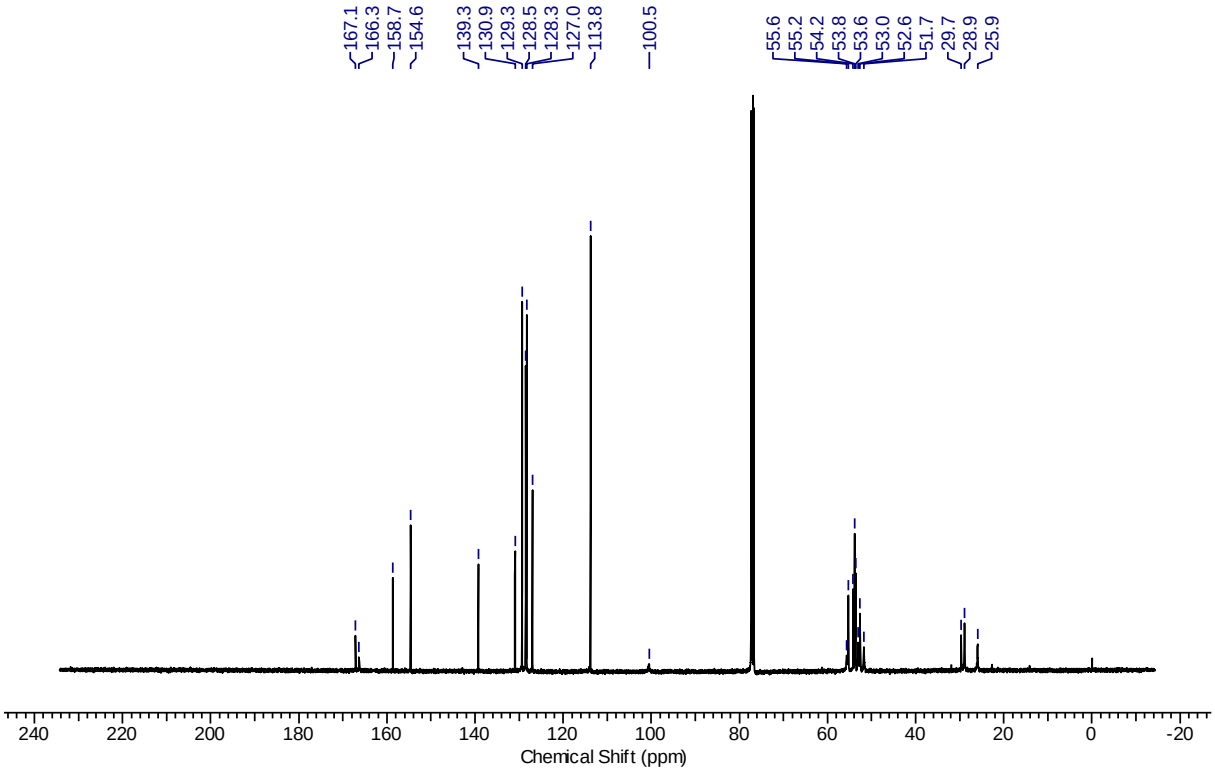

PMB
NH
N
N
N
N
Br
O
3a
9.018
7.295
7.274
6.846
6.826
5.355
4.760
4.089
3.758
3.407
2.780
2.397
1.822
1.695
0.000
0.70
2.00
2.02
1.27
2.00
1.17
5.39
1.64
1.72
2.90
3.84
Chemical Shift (ppm)
167.6
163.5
159.0
150.5
148.5
129.1
128.7
114.0
93.2
55.2
53.9
50.4
50.3
47.3
45.1
42.4
29.2
21.4
Chemical Shift (ppm)

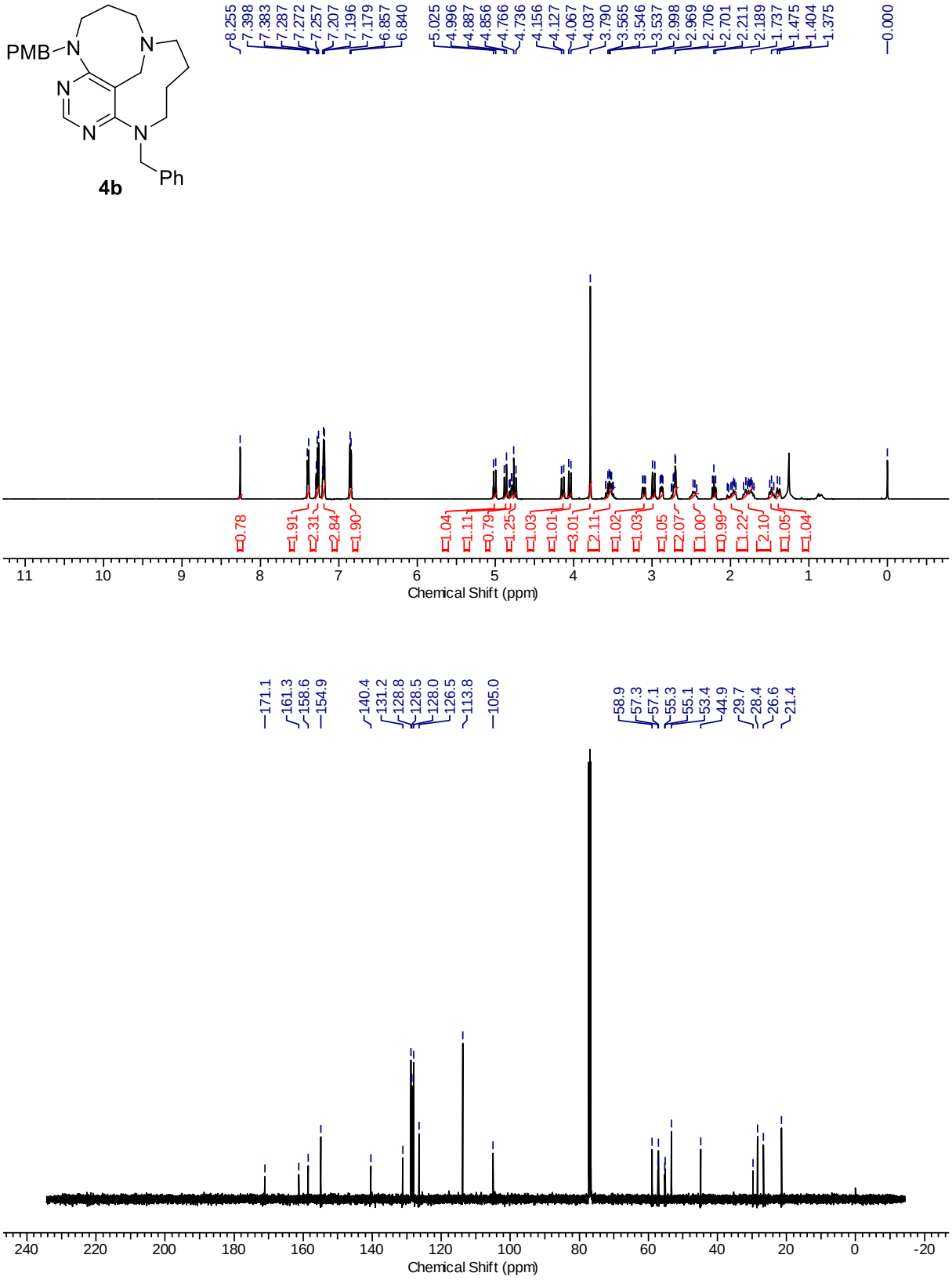

PMB
NH
N
N
N
N
O
Cl
3b
8.569
7.307
7.290
6.885
6.869
4.780
4.388
4.376
4.365
3.963
3.762
3.742
3.615
3.582
2.906
2.894
2.882
2.664
2.650
2.623
2.248
1.890
1.787
0.000
1.25
2.45
2.66
2.58
2.74
1.94
4.44
2.23
2.58
3.00
3.90
2.22
2.72
Chemical Shift (ppm)
169.6
165.0
160.8
152.2
149.3
130.9
130.3
115.2
104.3
57.0
55.9
55.9
51.3
46.9
46.1
44.0
32.5
28.4
27.4
Chemical Shift (ppm)

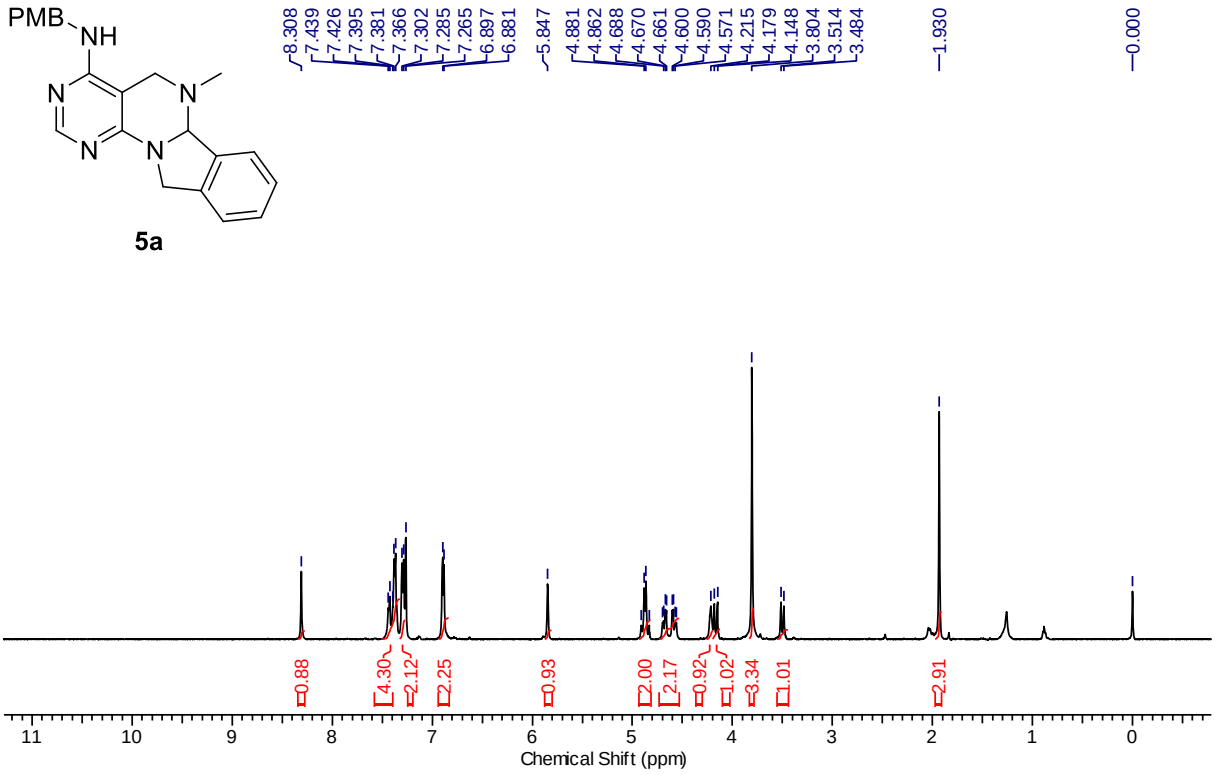

PMB
N
N
N
N
N
Ph

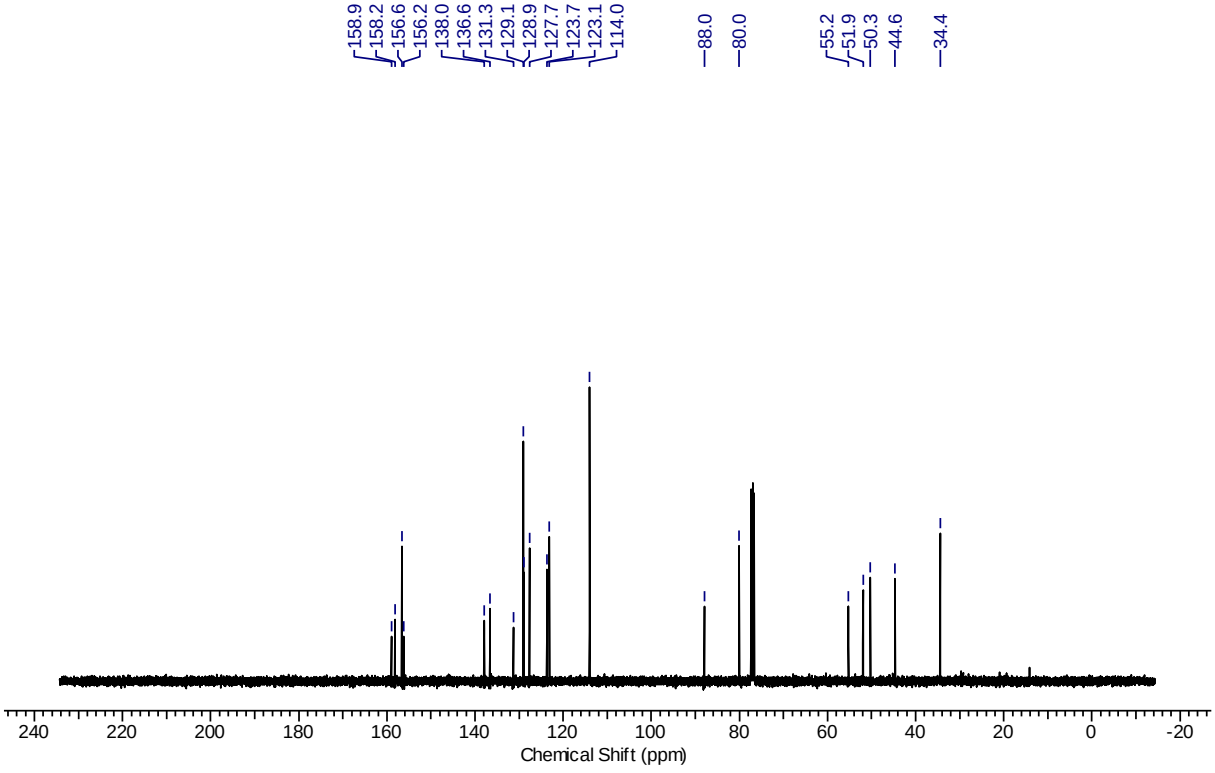
4a

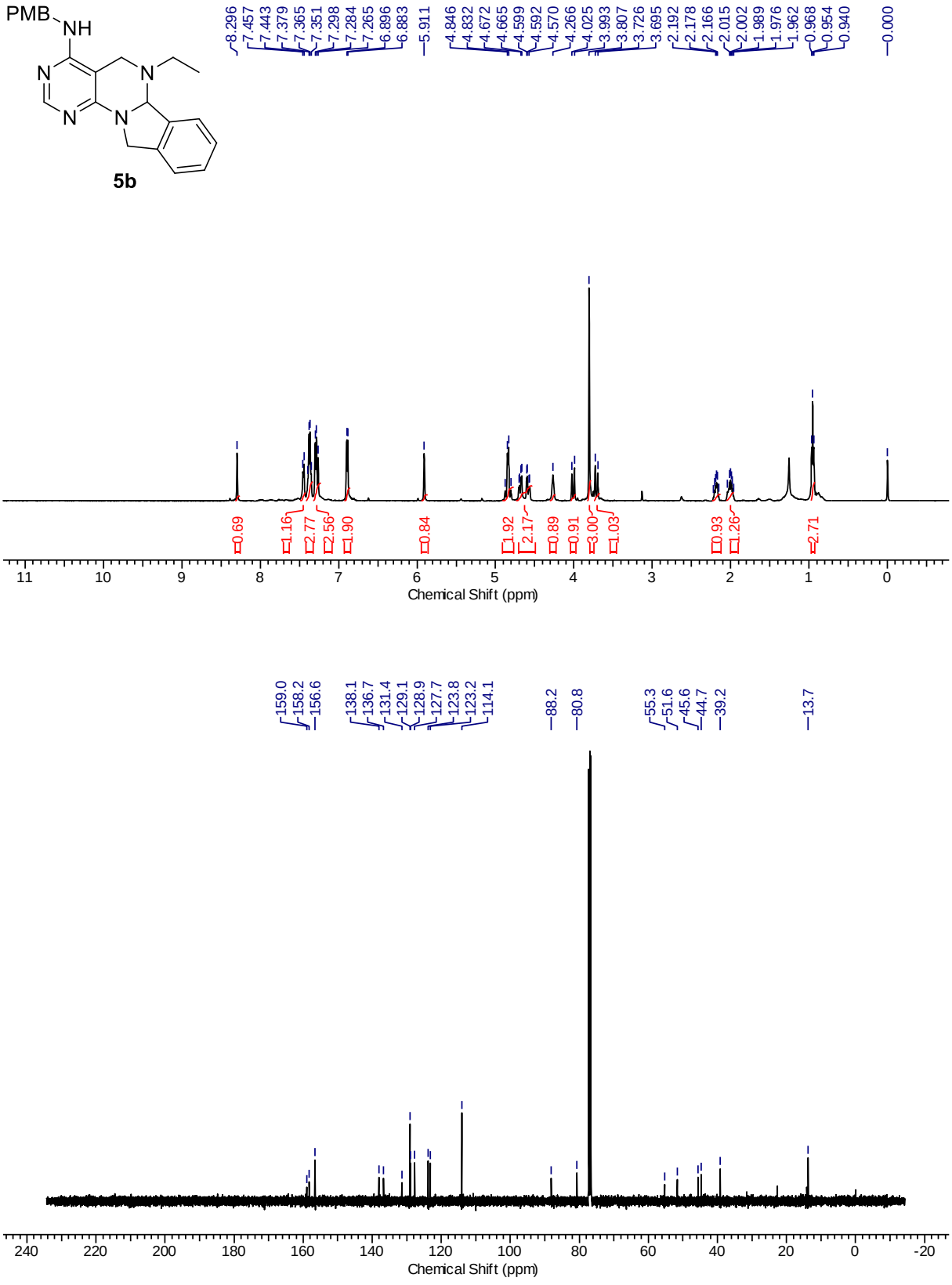
8.243
7.330
7.324
7.303
7.292
7.275
7.260
6.883
6.866
5.116
5.087
4.981
4.950
4.436
4.407
4.007
3.978
3.804
3.634
3.452
3.436
3.108
3.100
2.816
2.788
2.694
2.674
1.802
1.647
1.622
1.596
1.473
1.466
0.000
0.76
7.01
1.85
0.98
0.96
1.95
0.98
3.00
2.02
1.84
0.99
1.98
1.97
1.00
2.07
1.02
Chemical Shift (ppm)

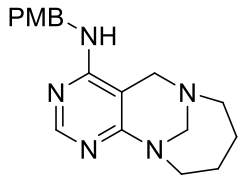

167.1
166.3
158.7
154.6
139.3
130.9
129.3
128.5
128.3
127.0
113.8
100.5
55.6
55.2
54.2
53.8
53.6
53.0
52.6
51.7
29.7
28.9
25.9
Chemical Shift (ppm)


PMB
N
N
N
N
N
Ph
4b
8.255
7.398
7.383
7.287
7.272
7.257
7.207
7.196
7.179
6.857
6.840
5.025
4.996
4.887
4.856
4.766
4.736
4.156
4.127
4.067
4.037
3.790
3.565
3.546
3.537
2.998
2.969
2.706
2.701
2.211
2.189
1.737
1.475
1.404
1.375
0.000
0.78
1.91
2.31
2.84
1.90
1.04
1.11
0.79
1.25
1.03
1.01
3.01
2.11
1.02
1.03
1.05
2.07
1.00
0.99
1.22
2.10
1.05
1.04
Chemical Shift (ppm)
171.1
161.3
158.6
154.9
140.4
131.2
128.8
128.5
128.0
126.5
113.8
105.0
58.9
57.3
57.1
55.3
55.1
53.4
44.9
29.7
28.4
26.6
21.4
Chemical Shift (ppm)


PMB
NH
N
N
N
N
5a
8.308
7.439
7.426
7.395
7.381
7.366
7.302
7.285
7.265
6.897
6.881
5.847
4.881
4.862
4.688
4.670
4.661
4.600
4.590
4.571
4.215
4.179
4.148
3.804
3.514
3.484
1.930
0.000
0.88
4.30
2.12
2.25
0.93
2.00
2.17
0.92
1.02
3.34
1.01
2.91
Chemical Shift (ppm)

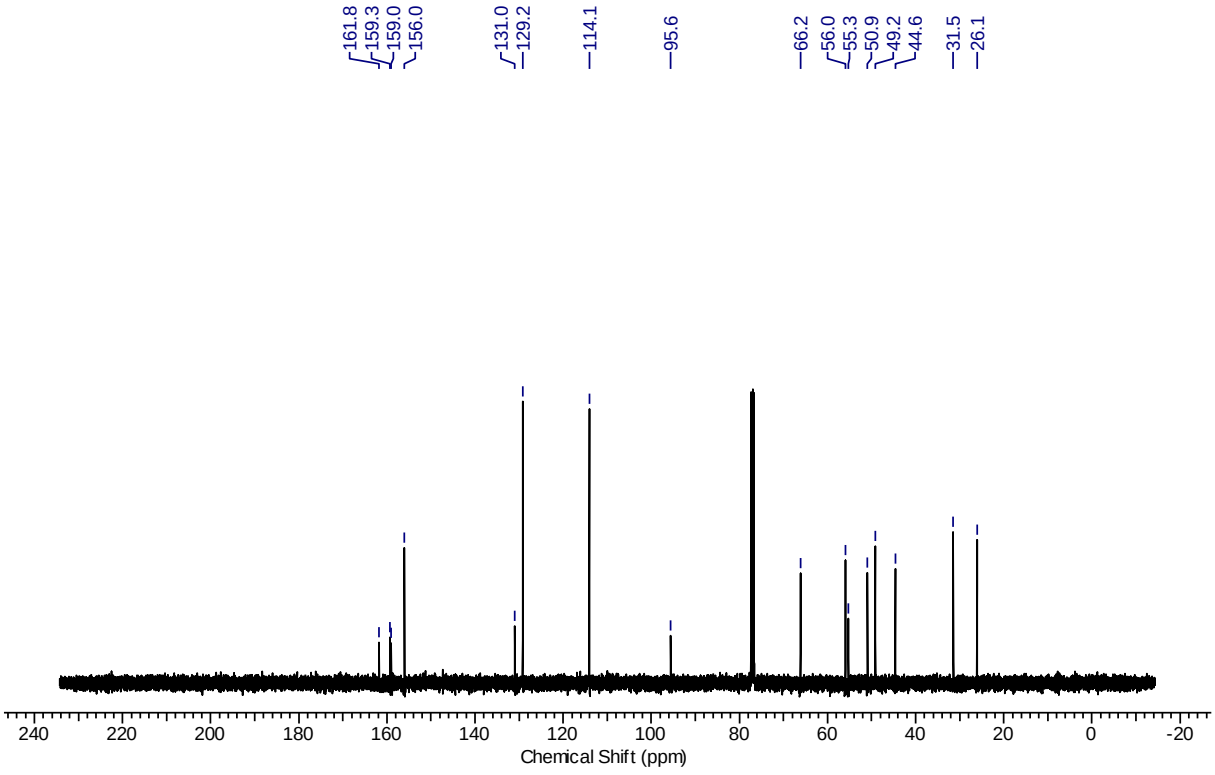

158.9
158.2
156.6
156.2
138.0
136.6
131.3
129.1
128.9
127.7
123.7
123.1
114.0
88.0
80.0
55.2
51.9
50.3
44.6
34.4
Chemical Shift (ppm)

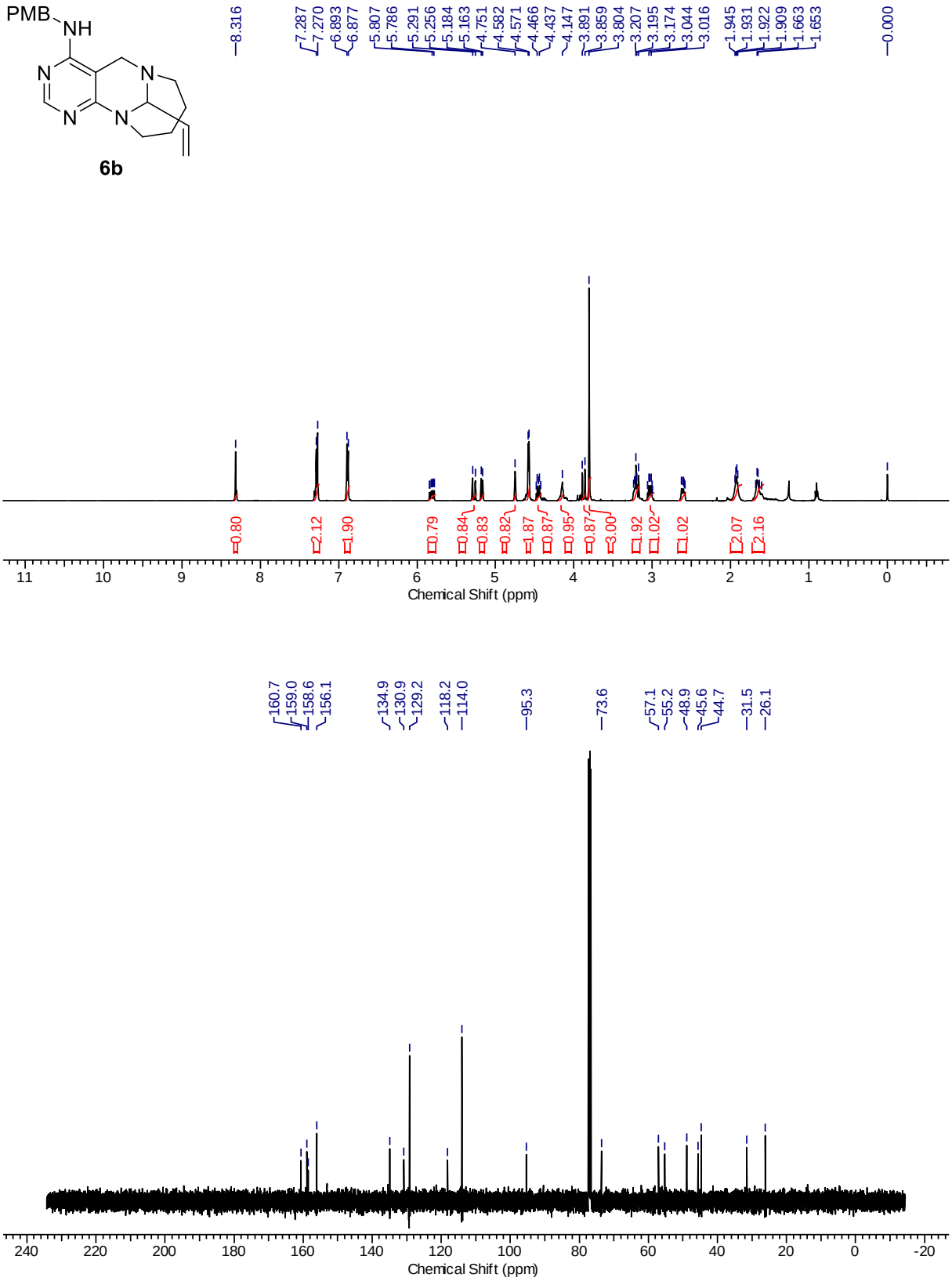

PMB
NH
N
N
N
N
5b
8.296
7.457
7.443
7.379
7.365
7.351
7.298
7.284
7.265
6.896
6.883
5.911
4.846
4.832
4.672
4.665
4.599
4.592
4.570
4.266
4.025
3.993
3.807
3.726
3.695
2.192
2.178
2.166
2.015
2.002
1.989
1.976
1.962
0.968
0.954
0.940
0.000
0.69
1.16
2.77
2.56
1.90
0.84
1.92
2.17
0.89
0.91
3.00
1.03
0.93
1.26
2.71
Chemical Shift (ppm)
159.0
158.2
156.6
138.1
136.7
131.4
129.1
128.9
127.7
123.8
123.2
114.1
88.2
80.8
55.3
51.6
45.6
44.7
39.2
13.7
Chemical Shift (ppm)

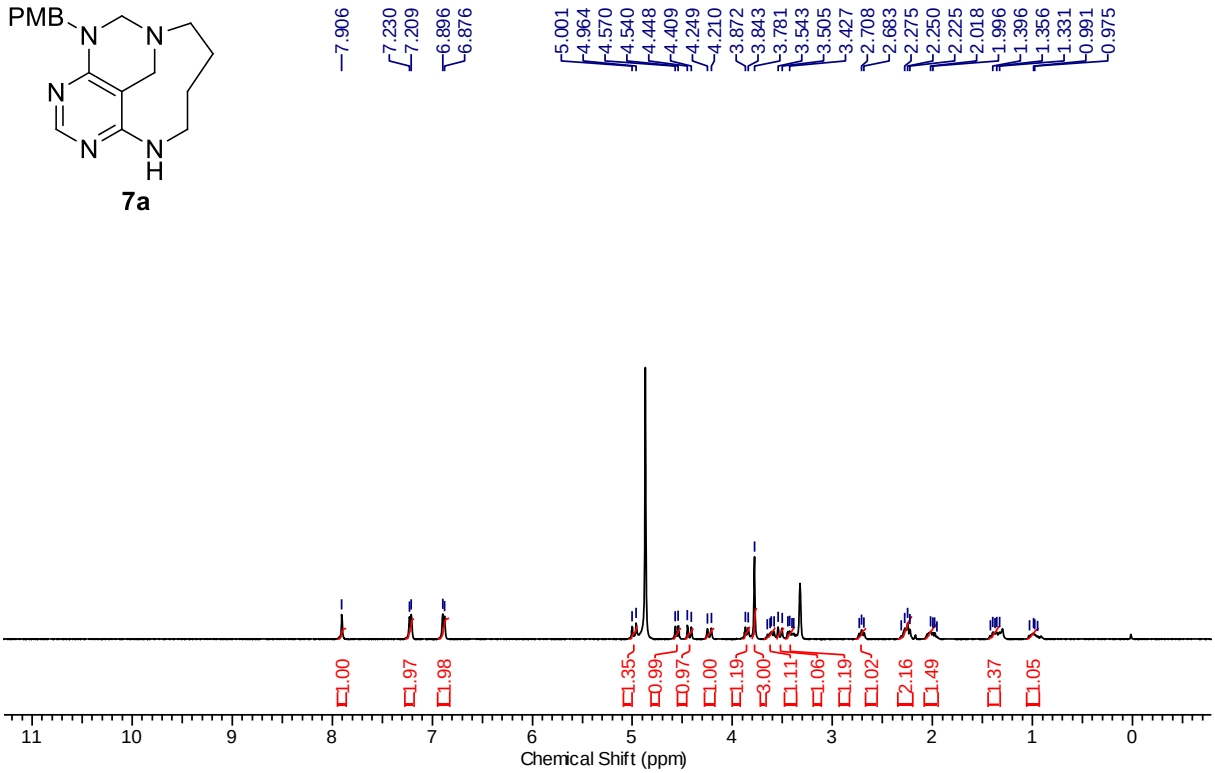

PMB
NH
N
N
N
N

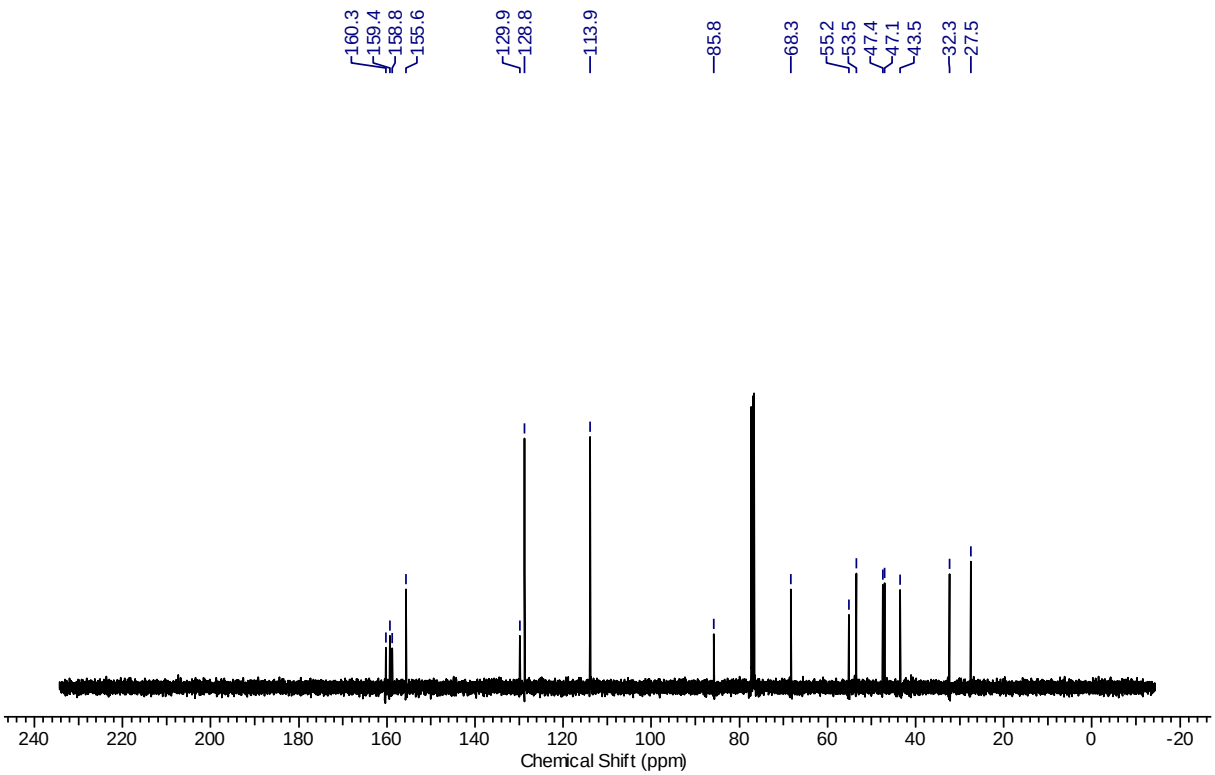
6a

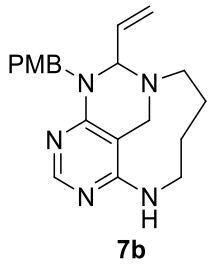
8.032
7.238
7.217
6.852
6.831
4.562
4.556
4.357
4.352
4.322
4.317
4.204
4.169
4.007
3.967
3.745
3.388
3.346
2.399
1.896
1.768
1.750
1.739
1.719
1.705
1.694
0.000
0.78
1.79
1.87
2.00
0.93
1.90
0.93
2.83
1.05
0.99
0.94
1.01
1.01
3.05
Chemical Shift (ppm)


161.8
159.3
159.0
156.0
131.0
129.2
114.1
95.6
66.2
56.0
55.3
50.9
49.2
44.6
31.5
26.1
Chemical Shift (ppm)


PMB
NH
N
N
N
N
6b
8.316
7.287
7.270
6.893
6.877
5.807
5.786
5.291
5.256
5.184
5.163
4.751
4.582
4.571
4.466
4.437
4.147
3.891
3.859
3.804
3.207
3.195
3.174
3.044
3.016
1.945
1.931
1.922
1.909
1.663
1.653
0.000
0.80
2.12
1.90
0.79
0.84
0.83
0.82
1.87
0.87
0.95
0.87
3.00
1.92
1.02
1.02
2.07
2.16
Chemical Shift (ppm)
160.7
159.0
158.6
156.1
134.9
130.9
129.2
118.2
114.0
95.3
73.6
57.1
55.2
48.9
45.6
44.7
31.5
26.1
Chemical Shift (ppm)

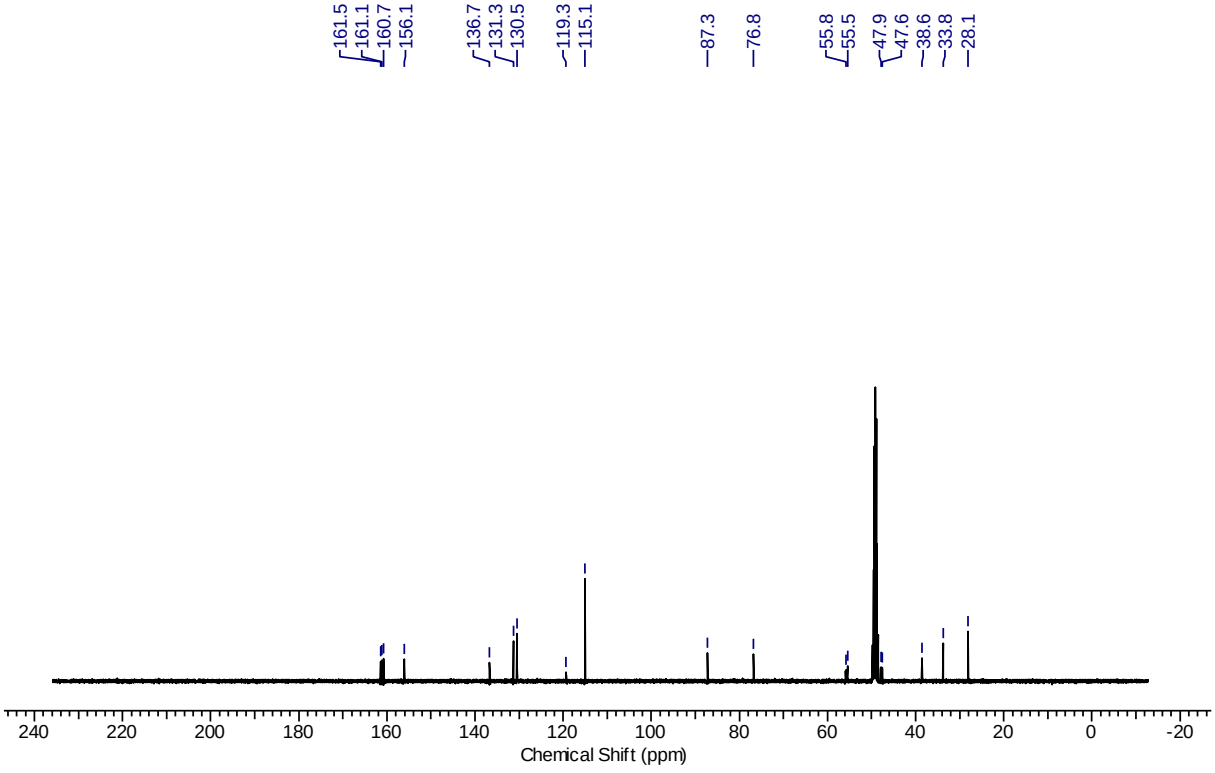

PMB
N
N
N
N
H
7a
7.906
7.230
7.209
6.896
6.876
5.001
4.964
4.570
4.540
4.448
4.409
4.249
4.210
3.872
3.843
3.781
3.543
3.505
3.427
2.708
2.683
2.275
2.250
2.225
2.018
1.996
1.396
1.356
1.331
0.991
0.975
1.00
1.97
1.98
1.35
0.99
0.97
1.00
1.19
3.00
1.11
1.06
1.19
1.02
2.16
1.49
1.37
1.05
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

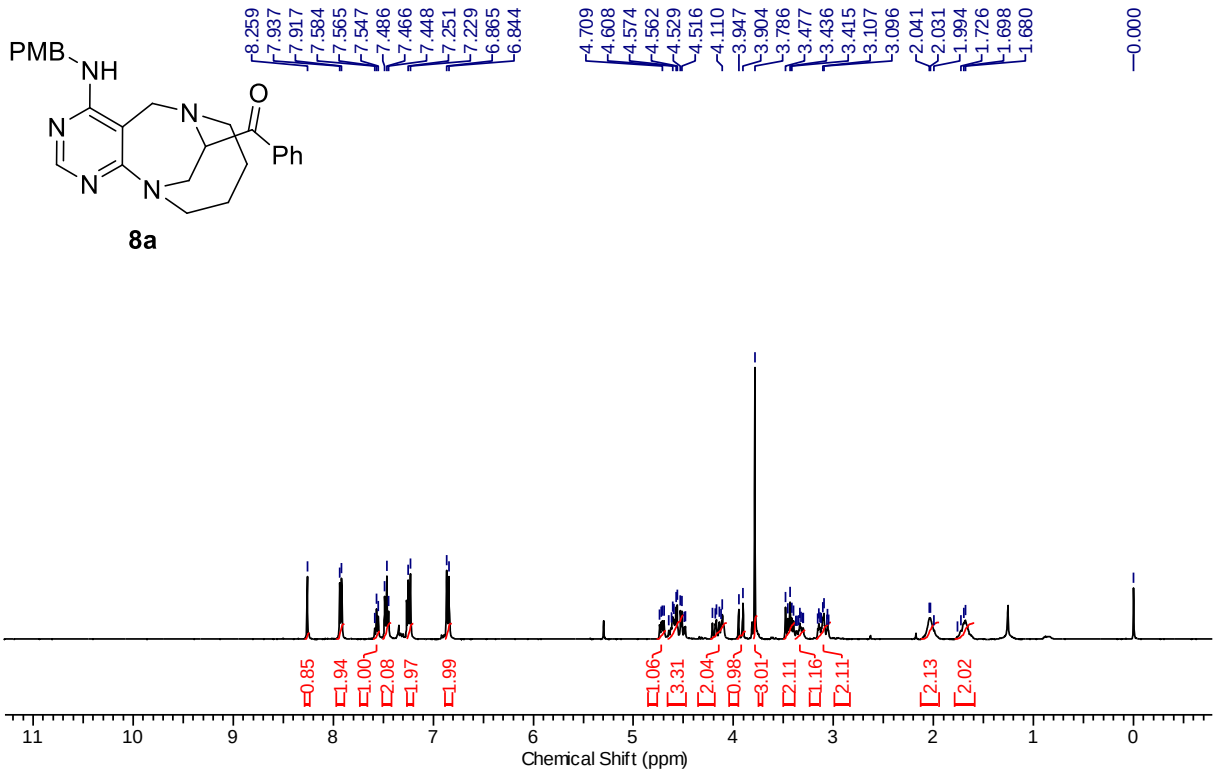

160.3
159.4
158.8
155.6
129.9
128.8
113.9
85.8
68.3
55.2
53.5
47.4
47.1
43.5
32.3
27.5
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

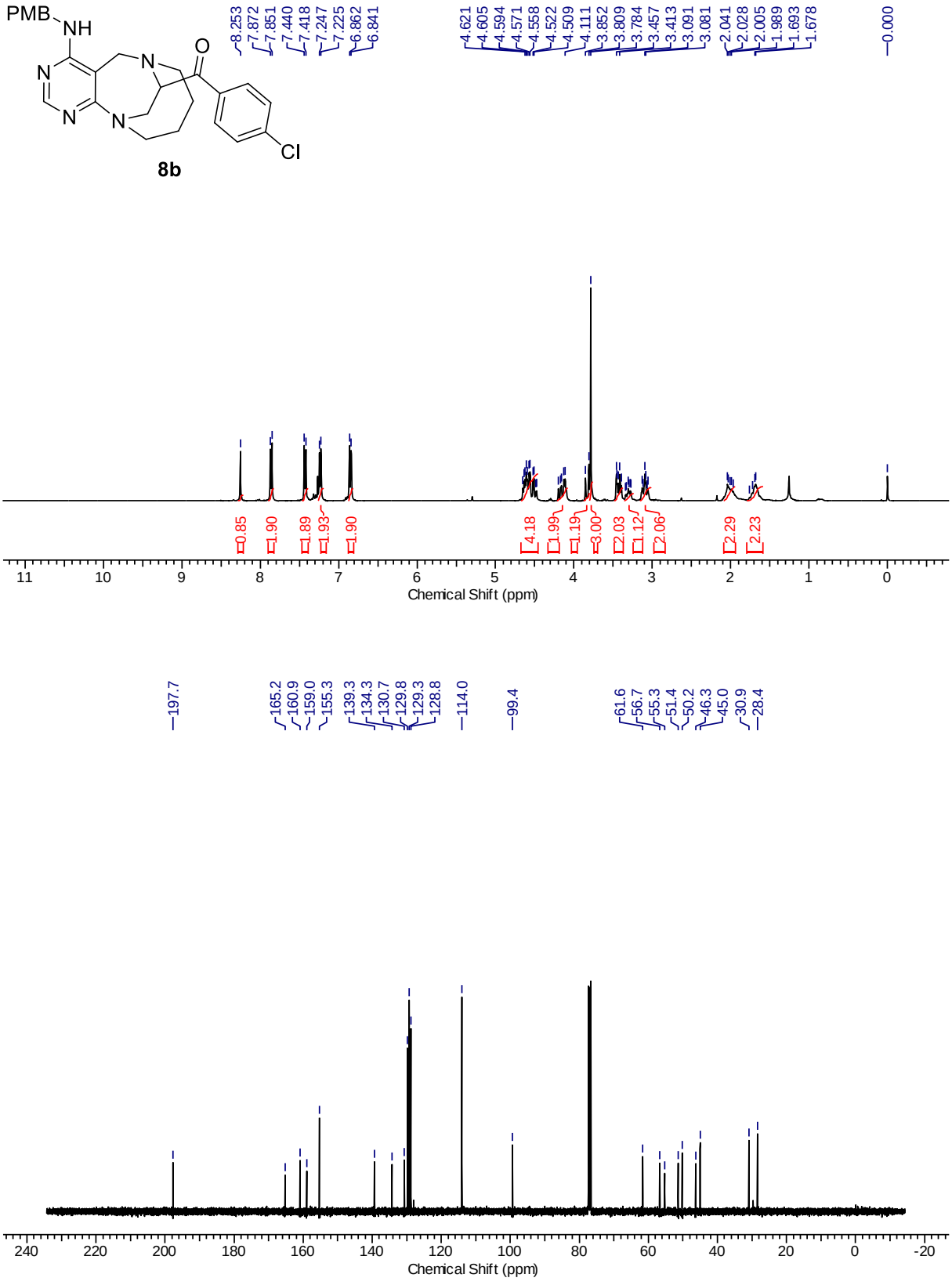

PMB
N
N
N
N
N
H

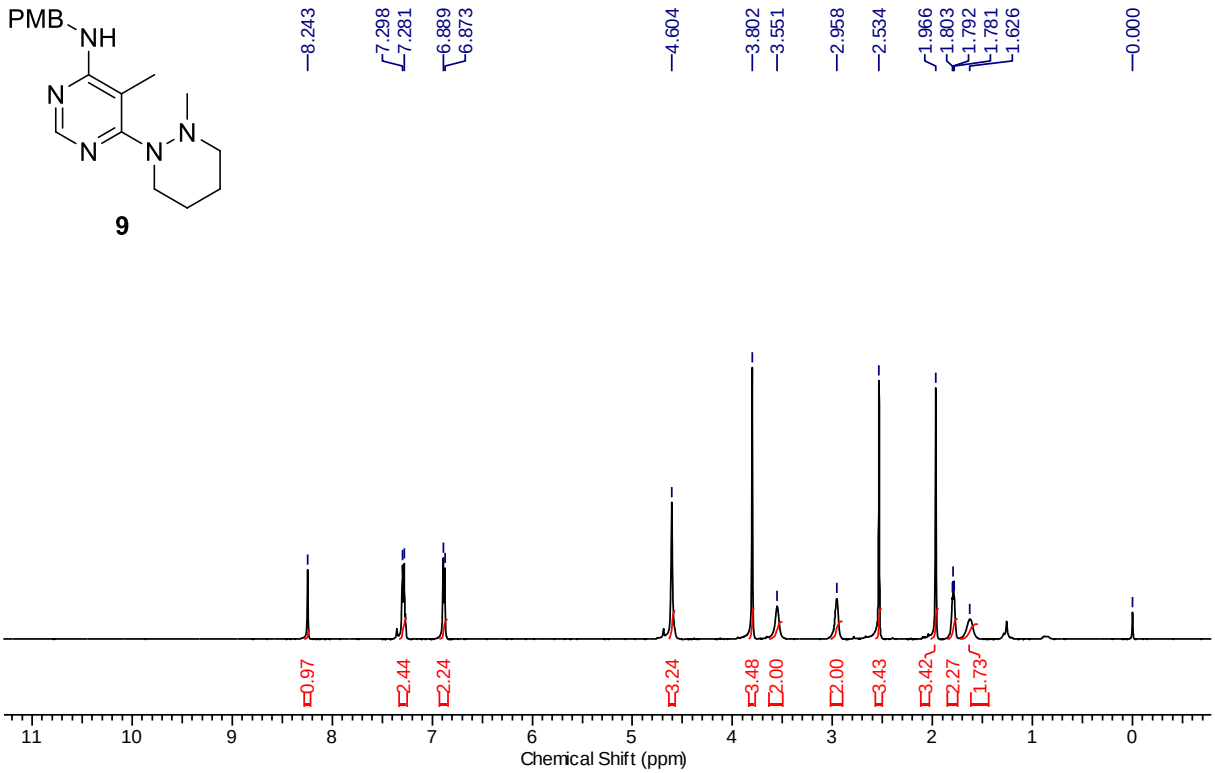
7b

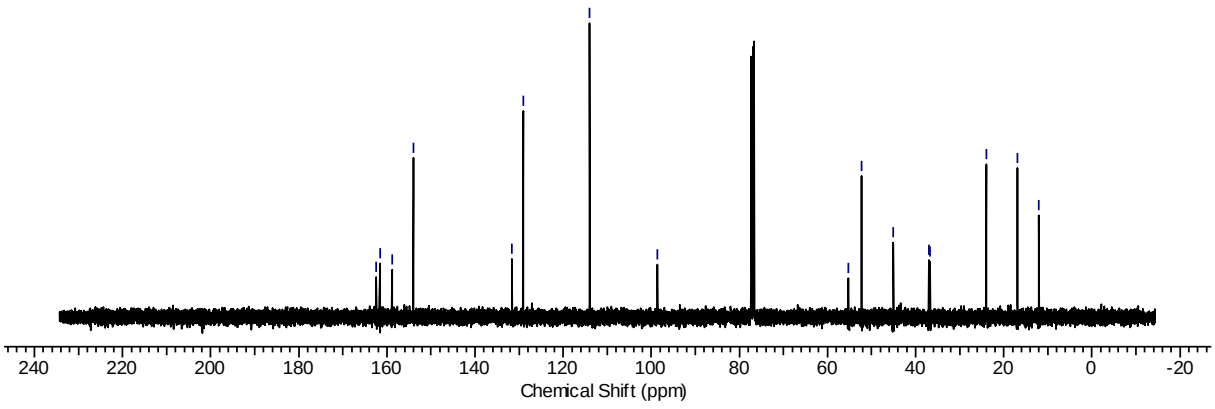
7.942
7.171
7.150
6.845
6.824
5.944
5.875
5.624
5.586
5.440
5.414
5.299
5.256
4.288
4.275
3.978
3.937
3.923
3.885
3.748
3.577
3.562
3.538
3.418
3.310
2.503
2.499
2.475
2.033
2.009
1.981
1.360
1.320
1.295
0.934
0.909
0.81
1.84
1.92
0.95
0.95
0.94
0.97
0.96
1.06
1.01
3.00
2.07
1.01
0.96
0.97
1.08
1.03
1.38
1.20
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

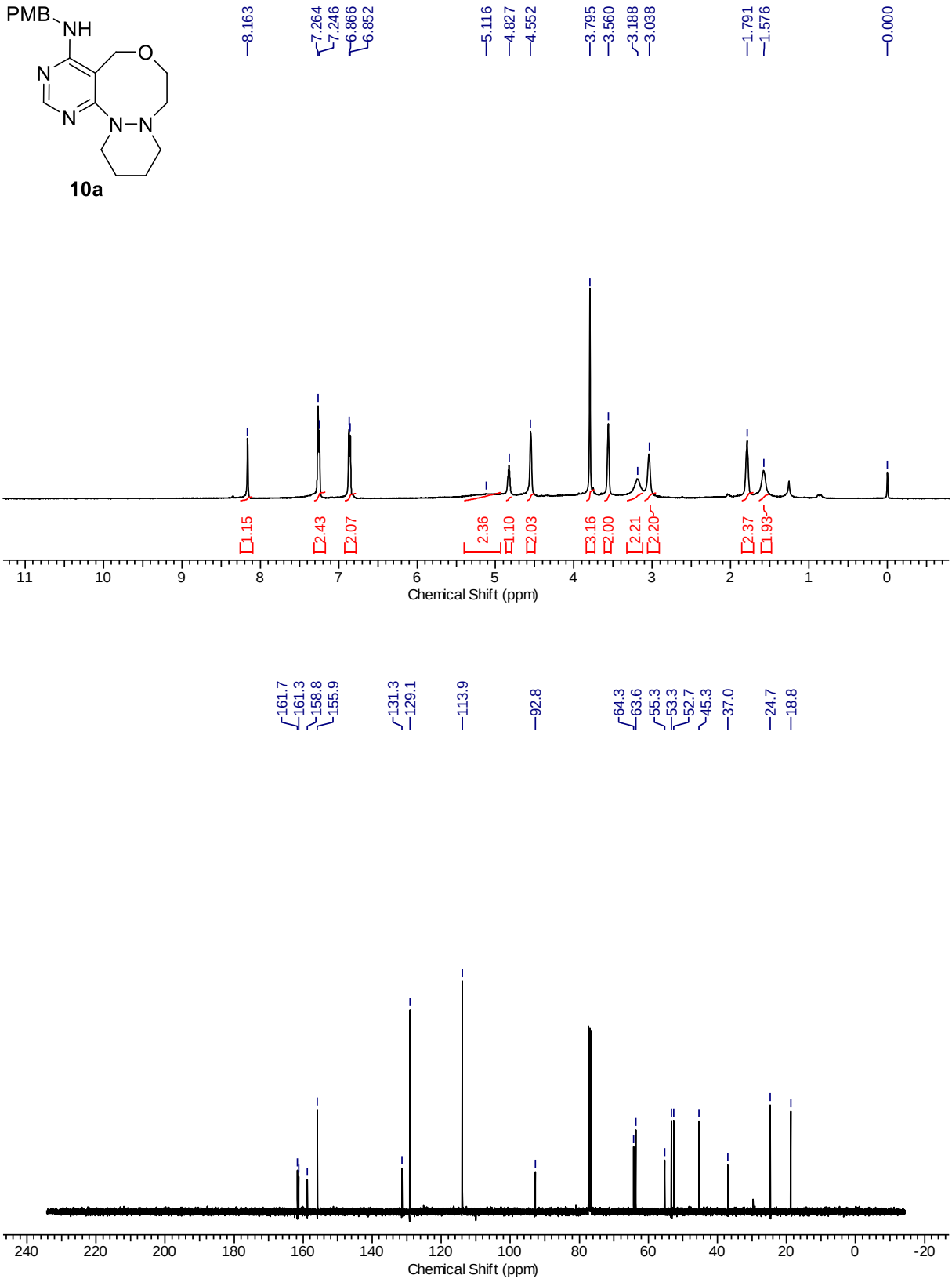

161.5
161.1
160.7
156.1
136.7
131.3
130.5
119.3
115.1
87.3
76.8
55.8
55.5
47.9
47.6
38.6
33.8
28.1
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

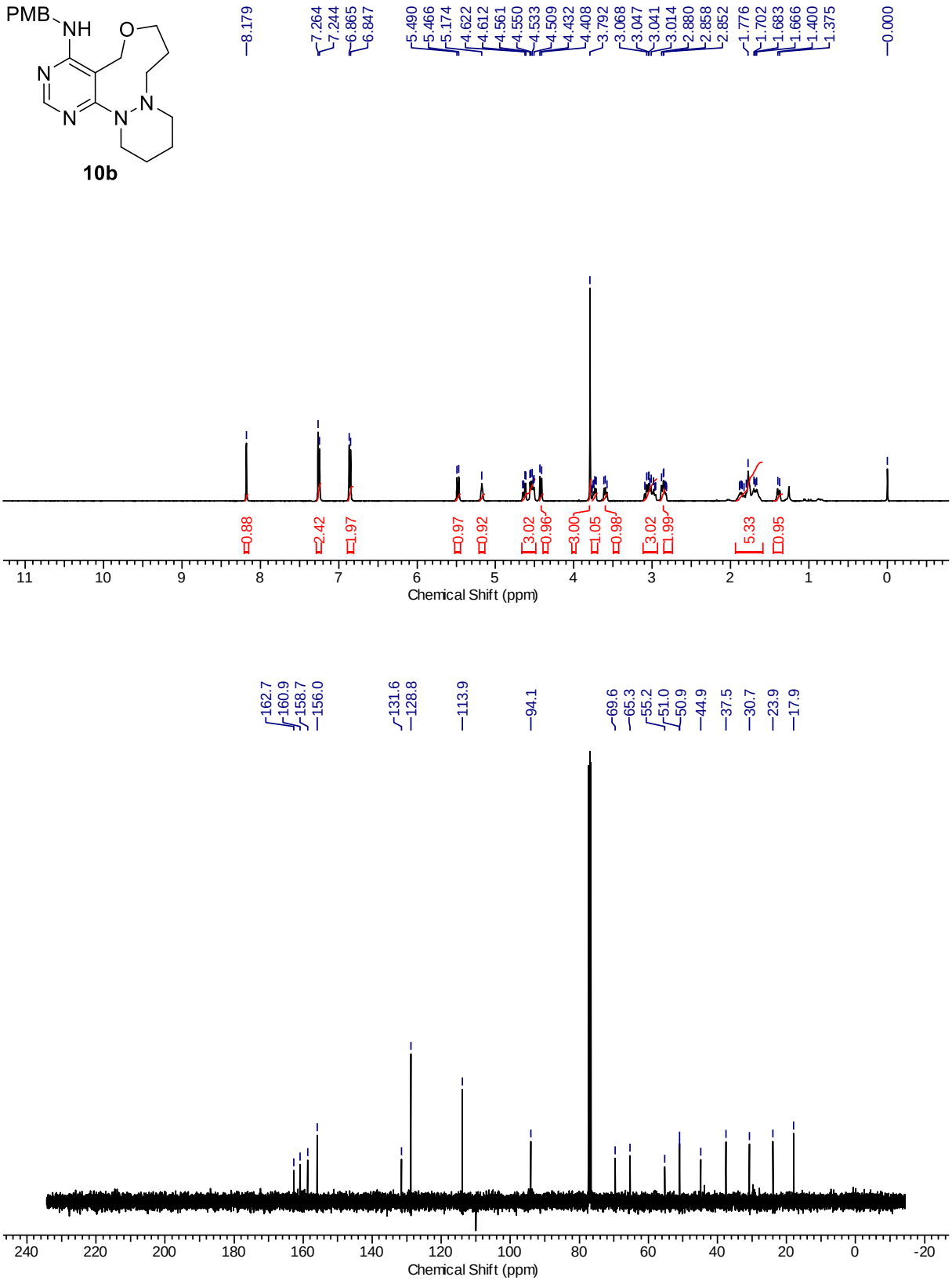

PMB
NH
N
N
N
N
O
Ph
8a
8.259
7.937
7.917
7.584
7.565
7.547
7.486
7.466
7.448
7.251
7.229
6.865
6.844
4.709
4.608
4.574
4.562
4.529
4.516
4.110
3.947
3.904
3.786
3.477
3.436
3.415
3.107
3.096
2.041
2.031
1.994
1.726
1.698
1.680
0.000
0.85
1.94
1.00
2.08
1.97
1.99
1.06
3.31
2.04
0.98
3.01
2.11
1.16
2.11
2.13
2.02
Chemical Shift (ppm)
198.8
165.3
160.9
159.0
155.3
136.0
133.0
130.7
129.2
128.5
128.3
114.0
99.6
61.4
56.7
55.3
51.5
50.2
46.3
45.0
30.9
28.5
Chemical Shift (ppm)


PMB
NH
N
N
N
N
O
Cl
8b
8.253
7.872
7.851
7.440
7.418
7.247
7.225
6.862
6.841
4.621
4.605
4.594
4.571
4.558
4.522
4.509
4.111
3.852
3.809
3.784
3.457
3.413
3.091
3.081
2.041
2.028
2.005
1.989
1.693
1.678
0.000
0.85
1.90
1.89
1.93
1.90
4.18
1.99
1.19
3.00
2.03
1.12
2.06
2.29
2.23
Chemical Shift (ppm)
197.7
165.2
160.9
159.0
155.3
139.3
134.3
130.7
129.8
129.3
128.8
114.0
99.4
61.6
56.7
55.3
51.4
50.2
46.3
45.0
30.9
28.4
Chemical Shift (ppm)


PMB
NH
N
N
N
N
9
8.243
7.298
7.281
6.889
6.873
4.604
3.802
3.551
2.958
2.534
1.966
1.803
1.792
1.781
1.626
0.000
0.97
2.44
2.24
3.24
3.48
2.00
2.00
3.43
3.42
2.27
1.73
Chemical Shift (ppm)


162.4
161.6
158.9
154.0
131.6
129.1
114.0
98.6
55.2
52.3
45.1
37.0
36.7
24.0
16.9
12.1
Chemical Shift (ppm)


PMB
NH
O
N
N
N–N
10a
8.163
7.264
7.246
6.866
6.852
5.116
4.827
4.552
3.795
3.560
3.188
3.038
1.791
1.576
0.000
1.15
2.43
2.07
2.36
1.10
2.03
3.16
2.00
2.21
2.20
2.37
1.93
Chemical Shift (ppm)
161.7
161.3
158.8
155.9
131.3
129.1
113.9
92.8
64.3
63.6
55.3
53.3
52.7
45.3
37.0
24.7
18.8
Chemical Shift (ppm)


PMB
NH
O
N
N
N
N
10b
8.179
7.264
7.244
6.865
6.847
5.490
5.466
5.174
4.622
4.612
4.561
4.550
4.533
4.509
4.432
4.408
3.792
3.068
3.047
3.041
3.014
2.880
2.858
2.852
1.776
1.702
1.683
1.666
1.400
1.375
0.000
0.88
2.42
1.97
0.97
0.92
3.02
0.96
3.00
1.05
0.98
3.02
1.99
5.33
0.95
Chemical Shift (ppm)
162.7
160.9
158.7
156.0
131.6
128.8
113.9
94.1
69.6
65.3
55.2
51.0
50.9
44.9
37.5
30.7
23.9
17.9
Chemical Shift (ppm)

VIII. References

[1] Y. Choi, H. Kim, Y. -H. Shin, S. B. Park, *Chem. Commun.* **2015**, *51*, 13040–13043.

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