Supporting Information for

Synthesis of Macrocyclic Tetrazoles for Rapid Photoinduced Bioorthogonal 1,3-Dipolar Cycloaddition Reactions

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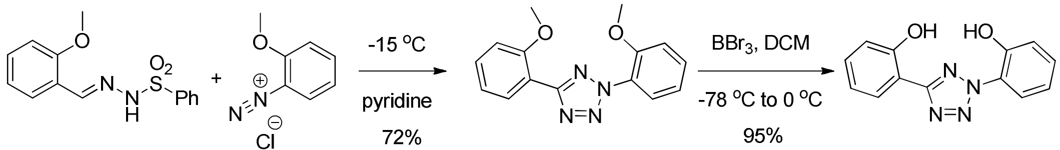
General Information

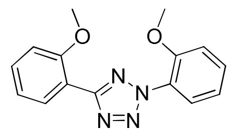
All photo reactions were carried out under the ambient condition using oven-dried quartz test tubes with magnetic stirrers. Solvents and chemicals were purchased from commercial sources and used directly without further purification. Flash chromatography was performed with SiliCycle P60 silica gel (40-63 μm, 60Å). ^{1}H NMR spectra were recorded with Inova-300, -400 or -500 MHz spectrometers, and chemical shifts were reported in ppm using either TMS or deuterated solvents as internal standards (TMS, 0.00; $CDCl_3$, 7.26; C_6D_6, 7.15; DMSO-d_6, 2.50). Multiplicity was reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. ^{13}C NMR spectra were recorded at 75.4 MHz, and chemical shifts were reported in ppm using the deuterated solvents as internal standards ($CDCl_3$, 77.0; DMSO-d_6, 39.5; C_6D_6, 128.0).

Experimental Procedures and Characterization Data

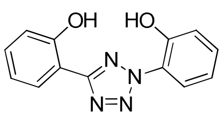
Synthesis of 2,5-bis(*o*-phenolyl)tetrazole (1):



10 **1**


10

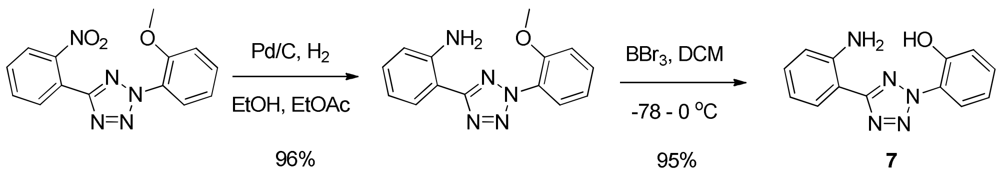
2,5-bis(2-methoxyphenyl)-2*H*-tetrazole (10): Tetrazole **10** was synthesized according to the published procedure[1]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.61 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.54-7.50 (m, 1H), 7.49- 7.45 (m, 1H), 7.13-7.06 (m, 4H), 3.96 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 157.6, 153.7, 131.9, 131.6, 131.0, 127.2, 126.5, 120.7, 120.6, 116.4, 112.7, 111.8, 56.2, 56.1.

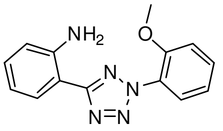

1

A solution of tetrazole **10** (0.846 g, 3 mmol) in 15 mL dichloromethane was cooled to -78 °C with stirring, then added 15 mL BBr_3 solution in DCM (1 M, 15 mmol). The mixture was warmed up to room temperature over 3 h before quenching with

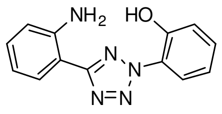
20 mL water under cooling. The solution was basified with 2 N NaOH to pH 10 for 10 min, and then brought back to pH 5 with 2 N HCl. The solution was extracted with DCM (20 mL × 3), and the organic layers were separated, dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by flash chromatography on a silica gel column using a stepwise gradient of 2-15 % ethyl acetate/hexanes to afford the desired product as a crystalline needle (0.724 g, 95% yield): ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 9.67 (b, 1H), 9.53 (b, 1H), 8.23 (d, J = 8.0 Hz, 1H), 8.09 (dd, J = 8.0, 1.5 Hz, 1H), 7.47-7.42 (m, 2H), 7.25 (d, J = 8.0 Hz, 1H), 7.16-7.04 (m, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 162.9, 156.8, 148.4, 133.0, 131.6, 127.5, 122.4, 120.7, 120.6, 120.2, 119.3, 117.9, 110.0; MS (ESI) calcd for $C_{13}H_{11}N_4O_2$ 255.3 [M+H$^+$], found 255.3.

Synthesis of 2-*o*-phenolyl-5-*o*-anilinyltetrazole (7):





A suspension of 2-*o*-methoxyphenyl-5-*o*-nitrophenyltetrzole[1] (3.00 g, 10.1 mmol) and palladium on carbon (50% wet, 10% weight, 300 mg) in 200 mL EtOAc/ EtOH (1:1) was flushed with 1 atm hydrogen gas for 8 h under vigorous stirring. After the reaction was completed as monitored by TLC, the solid was removed via filtration through a thin layer of silica gel and the solvent was evaporated to get the desired compound as a white solid (2.586 g, 96% yield): ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 8.22 (dd, J = 8.0, 1.5 Hz, 1H), 7.60 (dd, J = 7.5, 1.5 Hz, 1H), 7.57-7.53 (m, 1H), 7.28-7.24 (m, 1H), 7.16-7.12 (m, 2H), 6.85-6.81 (m, 2H), 5.51 (b, 2H), 3.88 (s, 3H); MS (ESI) calcd for $C_{14}H_{14}N_5O$ 268.1 [M+H$^+$], found 268.1.



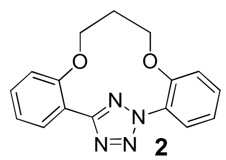
7

A solution of 2-*o*-methoxyphenyl-5-*o*-anilinyltetrazole (1.6 g, 6 mmol) in 15 mL DCM was cooled to -78 °C with stirring, then added 32 mL BBr_3 solution in DCM (1 M, 32 mmol). The mixture was warmed up to room temperature over 3 h before quenching by adding 30 mL water under cooling. The solution was basified with 2 N NaOH to pH 10 for 10 min before brought back to pH 5 with 2 N HCl. The solution was extracted with DCM (50 mL × 3). The organic layers were separated, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by flash chromatography on a silica gel column using a stepwise gradient of 2-10 % ethyl acetate/hexanes to afford the desired product as a crystalline needle (1.443 g, 95% yield): ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 9.70 (b, 1H), 8.22 (dd, J = 8.5, 1.5 Hz, 1H), 8.12 (dd, J = 8.0, 1.5 Hz, 1H), 7.42-7.38 (m, 1H), 7.31-7.28 (m, 1H), 7.24 (dd, J = 8.5, 1.0 Hz, 1H), 7.11-7.08 (m, 1H), 6.88-6.83 (m, 2H), 5.55 (b, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 163.8, 148.3, 146.2, 131.9, 131.0, 128.9, 122.7, 120.5, 119.1, 117.5, 116.8, 108.5; MS (ESI) calcd for $C_{13}H_{12}N_5O$ 254.1 [$M+H^+$], found 254.1.

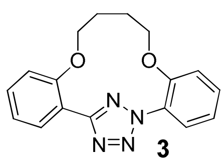
Procedure for the screening of alkali metal bases for macrocyclic ring closure:
A solution of 2,5-bis(o-phenolyl)tetrazole (**1**, 5.0 mg) and 1.1 equiv of dibromoalkane in 5.0 mL acetone was refluxed with stirring overnight in the presence of 3 equiv of different alkali metal bases. Afterwards, the solvent was removed under reduced pressure to give the crude product which was subsequently purified via silica gel flash chromatography.

General procedure for the synthesis of macrocyclic tetrazoles using specific alkali metal base:
A solution of 2,5-bis(o-phenolyl)tetrazole (**1**, 1.0 mmol) and 1.1 equiv of dibromoalkane in 200 mL acetone was refluxed with stirring overnight in the presence of 3 equiv of the indicated alkali metal base. The mixture was filtrated through Celite and the solvent was removed under reduced pressure to give the crude product, which was subsequently purified via silica gel flash chromatography.

General procedure for the photoactivated 1,3-dipolar cycloaddition:
A solution containing 0.1 mmol tetrazole and 10 mmol alkene dipolarophile in 250 mL EtOAc was irradiated with a hand-held 302-nm UV lamp (UVP; UVM-57, 302 nm, 115V, 0.16 AMPS). The solvent and excess reagents were removed under reduced pressure to give the crude product, which was subsequently purified by silica gel flash chromatography.

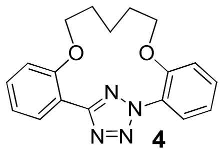

2

1,3-Propane-linked-2,5-bis(*o*-phenolyl)-2*H*-tetrazole (2)
^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.26 (dd, J = 7.5, 1.5 Hz, 1H), 7.98 (dd, J = 8.0, 1.5 Hz, 1H), 7.53 (td, J = 8.5, 1.5 Hz, 1H), 7.48 (td, J = 8.0, 2.0 Hz, 1H), 7.39-7.26 (m, 4H), 4.49 (t, J = 5.0, 2H), 3.85 (t, J = 5.0 Hz, 2H), 2.18 (quint, J = 5.0 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 161.6, 157.6, 152.2, 131.7, 131.3, 131.0, 129.3, 124.7, 124.7, 123.9, 123.9, 123.9, 120.9, 71.7, 69.4, 31.2; HRMS (ESI) calcd for $C_{16}H_{15}N_4O_2$ 295.1195 [$M + H^+$], found 295.1190.


3

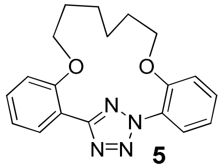
1,4-Butane-linked-2,5-bis(*o*-phenolyl)-2*H*-tetrazole (3)
^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.07 (dd, J = 7.5, 1.5 Hz, 1H), 7.86 (dd, J = 8.0, 1.5 Hz, 1H), 7.50-7.43 (m, 2H), 7.19-7.16 (m, 2H), 7.12 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 8.5 Hz, 1H), 4.17 (t, J = 5.5 Hz, 2H), 4.04 (t, J = 5.5 Hz, 2H), 1.99-1.92 (m,

4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 161.8, 157.7, 152.8, 131.4, 131.4, 129.6, 128.0, 124.9, 121.8, 121.6, 118.7, 117.1, 116.7, 71.9, 70.9, 26.1, 25.5; HRMS (ESI) calcd for $C_{17}H_{17}N_4O_2$ 309.1352 [M + H$^+$], found 309.1346.


4

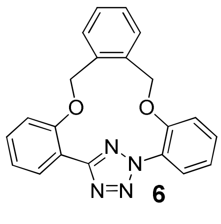
1,5-Pentane-linked-2,5-bis(*o*-phenolyl)-2*H*-tetrazole (4)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.71 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.51-7.43 (m, 2H), 7.17-7.10 (m, 3H), 7.04 (d, *J* = 8.5 Hz, 1H), 4.19 (t, *J* = 5.5 Hz, 2H), 4.12 (t, *J* = 5.5 Hz, 2H), 1.88-1.77 (m, 6H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 162.5, 157.1, 152.5, 131.4, 131.3, 130.1, 127.1, 126.3, 120.7, 120.6, 117.2, 114.4, 113.5, 68.4, 67.3, 27.8, 27.7, 20.5; HRMS (ESI) calcd for $C_{18}H_{19}N_4O_2$ 323.1508 [M + H$^+$], found 323.1503.


5

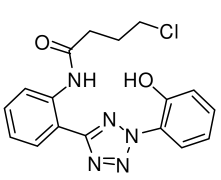
1,6-Hexane-linked-2,5- bis(*o*-phenolyl)-2*H*-tetrazole (5)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.56 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.52 (td, *J* = 7.8, 1.5 Hz, 1H), 7.48 (td, *J* = 7.8, 1.5 Hz, 1H), 7.12-7.07 (m, 4H), 4.15 (t, *J* = 5.0 Hz, 2H), 4.12 (t, *J* = 5.5 Hz, 2H), 1.79-1.72 (m, 4H), 1.65-1.59 (m, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 162.9, 157.2, 153.3, 131.9, 131.4, 130.8, 127.6, 126.5, 120.7, 120.2, 117.3, 113.4, 113.2, 70.3, 69.8, 28.6, 28.1, 27.3, 26.7; HRMS (ESI) calcd for $C_{19}H_{21}N_4O_2$ 337.1665 [M + H$^+$], found 337.1659.

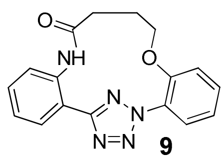

6

***o*-Xylylene-linked-2,5- bis(*o*-phenolyl)-2*H*-tetrazole (6)**

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 7.6, 1.6 Hz, 1H), 8.02 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.63-7.54 (m, 5H), 7.47-7.44 (m, 3H), 7.38-7.27 (m, 2H), 5.45 (s, 2H), 5.24 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 157.2, 151.5, 136.0, 135.3, 132.4, 132.2, 131.7, 131.4, 130.6, 130.4, 129.9, 129.3, 129.1, 124.5, 124.4, 124.2, 124.0, 122.3, 121.0, 75.5, 73.7; HRMS (ESI) calcd for $C_{21}H_{17}N_4O_2$ 357.1346 [M + H$^+$], found 357.1359.

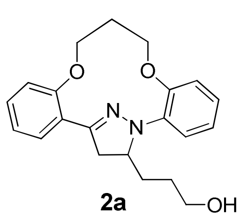

8

4-Chloro-*N*-(2-(2-(2-hydroxyphenyl)-2*H*-tetrazol-5-yl)phenyl)butanamide (8): A mixture of 150 mL saturated $NaHCO_3$ solution and 2-*o*-methoxyphenyl -5-*o*-anilinyltetrazole (**7**) (0.6 g, 2.37 mmol) in 50 mL EtOAc with vigorously stirred at room temperature. To this solution was added a solution of 4-chloro- butanoyl chloride (274.6 μL, 2.84 mmol) in 10 mL EtOAc dropwise, and the stirring was continued for additional 2 hours. The mixture was then extracted with EtOAc (50 mL × 3). The organic layers were separated, dried over sodium sulfate, and concentrated under the reduced pressure. The residue was purified by flash chromatography on a silica gel column using a stepwise gradient of 8-10 % ethyl acetate/hexanes to afford the desired product as a light-yellow solid, which was further purified via recrystallization to give the pure product as a white powder (550 mg, 65% yield): ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 10.69 (b, 1H), 9.50 (b, 1H), 8.69 (d, *J* = 8.5 Hz, 1H), 8.24-8.20 (m, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.26-7.22 (m, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 3.70 (t, *J* = 6.0 Hz, 2H), 2.75 (t, *J* = 7.0 Hz, 2H), 2.28 (quint, *J* = 6.5 Hz 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 170.5, 163.0, 148.4, 137.5, 132.1, 131.6, 128.5, 123.7, 122.4, 121.3, 120.7, 120.6, 119.4, 113.0, 44.3, 35.0, 27.9; MS (ESI) calcd for $C_{17}H_{17}ClN_5O_2$ 358.1 [M+H$^+$], found 358.1.



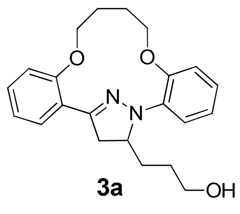
9

1,3-Propane-linked-2-(*o*-oxophenyl)-5-(*o*-*N*-formamidophenyl)-*2H*-tetrazole (9): ^{1}H-NMR (300 MHz, DMSO-d_6) δ 10.59 (s, 1H), 8.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.64-7.46 (m, 5H), 7.17 (d, *J* = 7.2 Hz, 1H), 7.5 (td, *J* = 7.5, 1.2 Hz, 1H), 3.76 (t, *J* = 6.9 Hz, 2H), 2.31(t, *J* = 7.5 Hz, 2H), 2.17-2.07 (m, 2H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ 174.5, 162.7, 152.2, 137.8, 132.6, 131.8, 130.0, 129.6, 128.5, 127.1, 125.3, 124.8, 119.8, 117.9, 50.6, 31.3, 19.0; HRMS (ESI) calcd for $C_{17}H_{16}N_5O_2$ 322.1299 [M + H$^+$], found 322.1300.



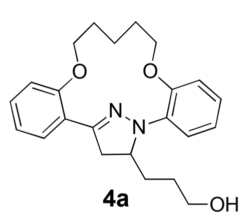
2a

1,3-Propane-linked-3-(1,3-bis(2-oxophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)propan-1-ol (2a): ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.28-7.22 (m, 2H), 7.17-7.12 (m, 3H), 7.05-7.02 (m, 1H), 6.97-6.94 (m, 2H), 4.36-4.29 (m, 2H), 4.28-4.25 (m, 1H), 4.19-4.15 (m, 1H), 3.95-3.91 (m, 1H), 3.61 (t, *J* = 6.5 Hz, 2H), 3.37 (dd, *J* = 16.0, 11.0 Hz, 1H), 2.94 (dd, *J* = 16.0, 8.5 Hz, 1H), 2.19-2.15 (m, 2H), 1.90-1.84 (m, 1H), 1.71-1.54 (m, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 156.8, 151.5, 144.2, 137.3, 128.9, 128.3, 126.6, 124.0, 124.0, 123.8, 123.8, 122.7, 119.9, 70.7, 69.1, 62.5, 61.6, 38.9, 31.4, 28.6, 28.4; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_3$ 353.1865 [M + H$^+$], found 353.1860.



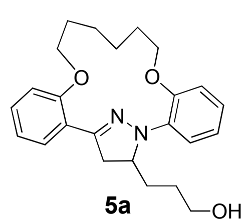
3a

1,4-Butane-linked-3-(1,3-bis(2-oxophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl) propan-1-ol (3a): ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31-7.29 (m, 1H), 7.28-7.26 (m, 1H), 7.15-7.13 (m, 1H), 7.11-7.06 (m, 1H), 7.03-6.99 (m, 2H), 6.95-6.91 (m, 2H), 4.16-4.13 (m, 3H), 4.03-3.98 (m, 1H), 3.61 (t, *J* = 6.0 Hz, 2H), 3.54 (dd, *J* = 16.4, 10.8 Hz, 1H), 2.79 (dd, *J* = 16.4, 9.6 Hz, 1H), 2.13-1.89 (m, 4H), 1.84-1.81 (m, 1H), 1.71-1.57 (m, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 157.7, 154.9, 148.9, 136.1, 129.4, 128.8, 125.8, 125.7, 125.1, 121.8, 121.2, 117.3, 116.3, 72.5, 70.4, 64.1, 62.7, 41.6, 30.2, 29.1, 26.9, 26.8; HRMS (ESI) calcd for $C_{22}H_{27}N_2O_3$ 367.2022 [M + H$^+$], found 367.2016.



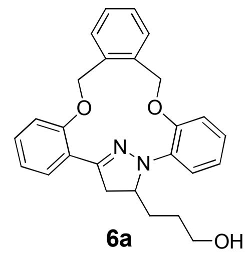
4a

1,5-Pentane-linked-3-(1,3-bis(2-oxophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl) propan-1-ol (4a): ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.40 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.31-7.27 (m, 2H), 7.20 (td, *J* = 8.0, 1.6 Hz, 1H), 6.97-6.87 (m, 4H), 4.40-4.35 (m, 1H), 4.19-4.11 (m, 1H), 4.07-3.95 (m, 2H), 3.89 (td, *J* = 8.8, 2.4 Hz, 1H), 3.72 (dd, *J* = 16.4, 10.4 Hz, 1H), 3.64 (t, *J* = 6.4 Hz, 2H), 2.71 (dd, *J* = 16.4, 12.8 Hz, 1H), 1.99-1.91 (m, 2H), 1.90-1.79 (m, 2H), 1.74-1.56 (m, 7H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 157.6, 156.7, 151.7, 135.1, 129.6, 129.4, 129.0, 127.9, 124.7, 121.1, 119.8, 114.0, 112.2, 67.4, 66.4, 65.9, 62.8, 42.0, 30.5, 29.6, 27.0, 26.9, 21.1; HRMS (ESI) calcd for $C_{23}H_{29}N_2O_3$ 381.2178 [M + H$^+$], found 381.2173.



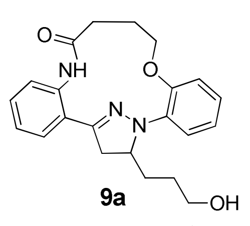
5a

1,6-Hexane-linked-3-(1,3-bis(2-oxophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl) propan-1-ol (5a): ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.49 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.33 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.27 (td, *J* = 8.0, 2.0 Hz, 1H), 7.22 (td, *J* = 8.0, 2.0 Hz, 1H), 6.93-6.86 (m, 4H), 4.28-4.25 (m, 1H), 4.16-4.11 (m, 2H), 4.04-4.01 (m, 1H), 3.89-3.84 (m, 1H), 3.82 (dd, *J* = 16.4, 10.4 Hz, 1H), 3.60 (t, *J* = 6.4 Hz, 2H), 2.61 (dd, *J* = 16.4, 13.2 Hz, 1H), 1.85-1.77 (m, 4H), 1.75-1.54 (m, 8H), 1.45-1.39 (m, 1H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 157.6, 156.8, 151.3, 135.3, 130.9, 129.9, 129.6, 128.5, 123.7, 120.3, 120.2, 113.5, 111.4, 70.3, 68.2, 66.0, 62.8, 41.8, 30.6, 30.2, 29.7, 29.6, 27.5, 27.1; HRMS (ESI) calcd for $C_{24}H_{31}N_2O_3$ 395.2335 [M + H$^+$], found 395.2329.



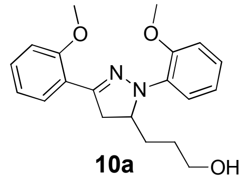
6a

***o*-Xylylene-linked-3-(1,3-bis(2-oxophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl) propan-1-ol (6a)**: ^{1}H-NMR (500 MHz, CDCl$_3$) δ 7.55 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.47 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.38-7.26 (m, 7H), 7.12-7.07 (m, 2H), 7.04-7.00 (m, 1H), 5.41 (dd, *J* = 9.5, 4.5 Hz, 2H), 5.11 (dd, *J* = 14.5, 9.5 Hz, 2H), 4.25-4.19 (m, 1H), 3.61 (t, *J* = 6.0 Hz, 2H), 3.36 (dd, *J* = 16.0, 10.5 Hz, 1H), 2.83 (dd, *J* = 16.0, 10.0 Hz, 1H), 1.93-1.86 (m, 1H), 1.71-1.54 (m, 4H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 156.5, 153.1, 147.0, 137.4, 136.4, 136.2, 131.6, 130.8, 129.2, 128.8, 128.5, 128.5, 126.3, 124.5, 123.1, 122.8, 122.4, 120.6, 120.5, 73.3, 72.6, 62.6, 62.4, 40.2, 29.6, 29.0; HRMS (EI) calcd for $C_{26}H_{26}N_2O_3$ 414.1943 [M$^+$], found 414.1938.



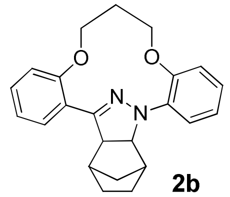
9a

1,3-Propane-linked-3-(1-(2-oxophenyl)-3-(2-*N*-formamidophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)propan-1-ol (9a): ^{1}H-NMR (500 MHz, CDCl$_3$) δ 11.98 (b, 1H), 8.61 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.32-7.28 (m, 1H), 7.25 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.07 (td, *J* = 7.5, 1.0 Hz, 1H), 6.98-6.92 (m, 3H), 6.85 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.54-4.48 (m, 1H), 4.08-4.06 (m, 2H), 3.67-3.64 (m, 2H), 3.50 (dd, *J* = 16.5, 11.5 Hz, 1H), 2.97 (dd, J = 16.5, 7.0 Hz, 1H), 2.71-2.67 (m, 1H), 2.61-2.58 (m, 1H), 2.28-2.23 (m, 2H), 1.97-1.92 (m, 1H), 1.71-1.60 (m, 4H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 172.9, 171.1, 149.6, 146.3, 137.6, 132.6, 128.7, 127.1, 122.5, 121.4, 120.4, 119.6, 116.4, 114.6, 69.4, 62.4, 60.2, 37.8, 36.4, 28.3, 28.0, 25.6; HRMS (ESI) calcd for $C_{22}H_{26}N_3O_3$ 380.1969 [M + H$^+$], found 380.1972.



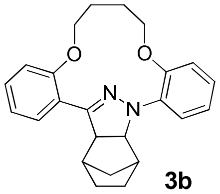
10a

3-(1,3-bis(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)propan-1-ol (10a): ^{1}H-NMR (500 MHz, CDCl$_3$) δ 7.87 (dd, J = 7.6, 1.6 Hz, 1H), 7.55 (dd, J = 8.0, 2.0 Hz, 1H), 7.32-7.28 (m, 1H), 7.02-6.89 (m, 5H), 4.72-4.65 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.51 (t, J = 6.4 Hz, 2H), 3.45 (dd, J = 17.2, 10.8 Hz, 1H), 3.22 (dd, J = 17.2, 3.6 Hz, 1H), 1.58 (br, 1H), 1.51-1.38 (m, 2H), 1.36-1.28 (m, 2H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 157.5, 149.7, 148.6, 135.0, 129.6, 128.9, 122.7, 122.7, 121.3, 121.2, 120.7, 111.6, 111.4, 62.6, 62.5, 55.7, 55.4, 40.7, 28.2, 27.6; HRMS (EI) calcd for $C_{20}H_{24}N_2O_3$ 340.1787 [M$^+$], found 340.1781.



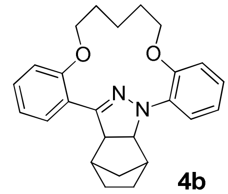
2b

1,3-Propane-linked-1,3-bis(2-oxophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoindazole (2b): ^{1}H-NMR (500 MHz, CDCl$_3$) δ 7.41 (dd, J = 8.5, 2.0 Hz, 1H), 7.24-7.21 (m, 1H), 7.17-7.12 (m, 3H), 7.06-7.03 (m, 1H), 6.87 (dd, J = 8.0, 1.5 Hz, 1H), 6.81 (td, J = 8.0, 1.5 Hz, 1H), 4.32-4.27 (m, 2H), 4.23-4.20 (m, 2H), 4.00-3.96 (m, 1H), 3.52 (d, J = 9.5 Hz,1H), 2.71-2.68 (m, 1H), 2.63-2.58 (m, 1H), 2.11-2.14 (m, 2H), 1.61-1.56 (m, 3H), 1.46-1.43 (m, 1H), 1.36-1.31 (m, 1H), 1.14-1.11 (m, 1H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 156.9, 148.3, 145.4, 136.8, 128.3, 128.1, 126.2, 124.9, 124.2, 124.2, 124.0, 120.0, 115.8, 70.4, 69.3, 67.7, 54.8, 40.9, 40.4, 33.1, 31.9, 27.8, 24.4; HRMS (EI) calcd for $C_{23}H_{24}N_2O_2$ 360.1838 [M$^+$], found 360.1832.

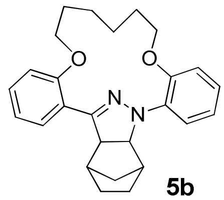


3b

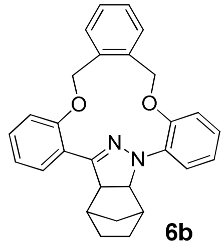
1,4-Butane-linked-1,3-bis(2-oxophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoindazole (3b): ^{1}H-NMR (500 MHz, CDCl$_3$) δ 7.34 (d, J = 7.5 Hz, 1H), 7.29-7.21 (m, 1H), 7.08-7.03 (m, 1H), 7.03-6.92 (m, 5H), 4.21-4.10 (m, 3H), 4.09-4.02 (m, 2H), 3.75-3.55 (m, 1H), 2.62-2.52 (m, 1H), 2.45-2.36 (m, 1H), 2.13-2.07 (m, 1H), 2.06-1.93 (m, 3H), 1.67 (d, J = 10.0 Hz, 1H), 1.58-1.47 (m, 2H), 1.42-1.34 (m, 1H), 1.29-1.21 (m, 1H), 1.18-1.13 (m, 1H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 157.7, 152.7, 149.6, 129.0, 128.9, 123.3, 121.8, 121.7, 121.6, 121.5, 117.8, 117.7, 116.4, 72.1, 70.8, 70.5, 57.5, 42.0, 39.8, 33.3, 28.0, 27.6, 26.5, 24.4; HRMS (EI) calcd for $C_{24}H_{26}N_2O_2$ 374.1994 [M$^+$], found 374.1989.


4b

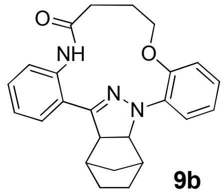
1,5-Pentane-linked-1,3-bis(2-oxophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoindazole (4b): ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.32 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.28-7.24 (m, 1H), 7.17 (td, *J* = 8.0, 2.0 Hz, 1H), 6.93-6.91 (m, 2H), 6.88 (td, *J* = 8.0, 1.0 Hz, 1H), 6.84 (dd, *J* = 8.0, 1.0 Hz, 1H), 4.42-4.38 (m, 1H), 3.97-3.89 (m, 4H), 3.84-3.82 (m, 1H), 2.40 (d, *J* = 4.0 Hz, 1H), 2.23 (d, *J* = 3.5 Hz, 1H), 1.92-1.84 (m, 2H), 1.82-1.72 (m, 3H), 1.71-1.66 (m, 1H), 1.53-1.42 (m, 2H), 1.32-1.25 (m, 2H), 1.22-1.20 (m, 1H), 1.14-1.09 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 157.3, 156.9, 153.3, 136.1, 130.1, 129.3, 129.2, 127.6, 124.7, 121.1, 119.7, 114.1, 112.0, 73.7, 67.3, 66.8, 58.9, 43.5, 39.7, 33.4, 28.6, 27.2, 27.1, 24.2, 21.4; HRMS (EI) calcd for $C_{25}H_{28}N_2O_2$ 388.2151 [M^+], found 388.2145.


5b

1,5-Pentane-linked-1,3-bis(2-oxophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoindazole (5b): ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.37 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.28-7.18 (m, 2H), 6.93-6.86 (m, 4H), 4.29-4.24 (m, 1H), 4.13-4.07 (m, 1H), 4.03-3.91 (m, 3H), 3.83 (d, *J* = 9.6 Hz, 1H), 2.34 (d, *J* = 4.4 Hz, 1H), 2.16 (d, *J* = 3.6 Hz, 1H), 1.92-1.64 (m, 8H), 1.53-1.38 (m, 3H), 1.31-1.24 (m, 1H), 1.19-1.15 (m, 1H), 1.13-1.07 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 157.7, 156.5, 152.7, 136.4, 130.9, 130.5, 129.3, 128.2, 123.5, 120.3, 120.2, 113.2, 111.4, 73.4, 70.4, 68.4, 58.7, 43.5, 39.7, 33.3, 30.3, 29.9, 28.6, 27.3, 26.7, 24.2; HRMS (ESI) calcd for $C_{26}H_{30}N_2O_2$ 402.2302 [M^+], found 402.2292.

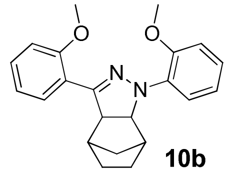

6b

***o*-Xylylene-linked-1,3-bis(2-oxophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoindazole (6b)**: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.54-750 (m, 2H), 7.44 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.42-7.39 (m, 2H), 7.32-7.23 (m, 3H), 7.17-7.14 (m, 1H), 7.09-7.05 (m, 1H), 6.98 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.92 (td, *J* = 7.5, 1.5 Hz, 1H), 5.36 (d, *J* = 9.5 Hz, 1H), 5.24 (dd, *J* = 20.5, 9.5 Hz, 2H), 5.17 (d, *J* = 9.5 Hz, 1H), 4.27 (d, *J* = 10.0 Hz, 1H), 3.58 (d, *J* = 9.5 Hz, 1H), 2.68-2.63 (m, 1H), 2.59-2.48 (m, 1H), 1.67-1.61 (m, 1H), 1.60-1.55 (m, 2H), 1.44-1.38 (m, 1H), 1.35-1.30 (m, 1H), 1.18-1.13 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 157.2, 149.6, 147.7, 137.2, 137.0, 131.7, 131.2, 128.9, 128.7, 128.6, 128.6, 126.2, 123.8, 123.8, 123.7, 122.7, 121.2, 117.3, 75.6, 74.5, 68.1, 55.5, 41.4, 40.3, 33.3, 28.0, 24.3; HRMS (EI) calcd for $C_{28}H_{26}N_2O_2$ 422.1994 [M^+], found 422.1989.



9b

1,3-Propane-linked-1-(2-oxophenyl)-3-(2-*N*-formamidophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoindazole (9b): ^{1}H-NMR (400 MHz, CDCl$_3$) δ 11.93 (b, 1H), 8.64 (dd, J = 8.4, 0.8 Hz, 1H), 7.36 (dd, J = 7.6, 1.6 Hz, 1H), 7.30-7.26 (m, 1H), 7.07 (td, J = 7.6, 1.2 Hz, 1H), 6.99-6.95 (m, 2H), 6.85-6.78 (m, 2H), 4.29 (d, J = 9.6 Hz, 1H), 4.08-4.04 (m, 1H), 4.02-3.99 (m, 1H), 3.54 (d, J = 9.6 Hz, 1H), 2.78-2.74 (m, 1H), 2.74-2.69 (m, 1H), 2.69-2.64 (m, 1H), 2.63-2.56 (m, 1H), 2.25-2.18 (m, 2H), 1.69-1.59 (m, 2H), 1.52-1.45 (m, 2H), 1.42-1.33 (m, 1H), 1.18-1.13 (m, 1H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 173.0, 148.3, 148.0, 137.9, 132.8, 128.3, 127.0, 122.3, 121.8, 120.5, 119.8, 118.9, 115.7, 114.1, 69.7, 67.8, 54.1, 40.8, 40.6, 36.0, 33.2, 27.9, 25.6, 24.2; HRMS (EI) calcd for $C_{24}H_{25}N_3O_2$ 387.1947 [M$^+$], found 387.1941.



10b

1,3-bis(2-methoxyphenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoindazole (10b): ^{1}H-NMR (500 MHz, CDCl$_3$) δ 7.86-7.85 (m, 1H), 7.51-7.36 (m, 1H), 7.35-7.25 (m, 1H), 7.03-6.88 (m, 5H), 4.42-4.22 (m, 1H), 3.88 (s, 6H), 3.92-3.65 (m, 1H), 2.46-2.38 (m, 1H), 2.29-2.21 (m, 1H), 1.63-1.58 (m, 1H), 1.39-1.31 (m, 2H), 1.28-1.19 (m, 2H), 1.03-0.95 (m, 1H); ^{13}C-NMR (75 MHz, CDCl$_3$) δ 157.1, 151.4, 149.0, 129.5, 129.5, 121.7, 121.3, 121.2, 121.2, 120.7, 119.6, 119.5, 111.5, 70.1, 57.9, 55.6, 55.5, 41.9, 39.6, 32.4, 27.7, 25.0; HRMS (EI) calcd for $C_{22}H_{24}N_2O_2$ 348.1838 [M$^+$], found 348.1832.

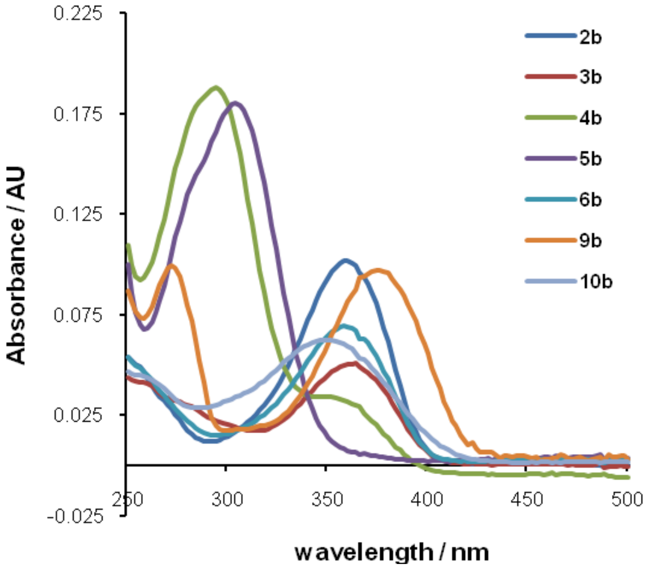


Figure S1. UV-Vis spectra of the norbornene-derived pyrazolines: Compounds were dissolved in a mixed ACN/PBS buffer (1: 1) solvent to derive the final concentrations of 5 µM for **2b**, **3b**, **6b**, **9b**-**10b**, and 20 µM for **4b**, **5b**.

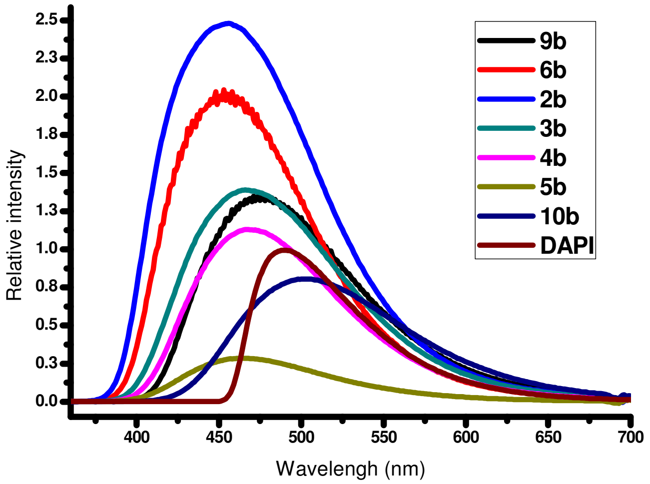


Figure S2. Normalized fluorescence spectra of the norbornene-derived pyrazolines: Compounds were dissolved in a mixed ACN/PBS buffer (1:1) solvent to derive final concentrations of 5 µM for **2b**, **3b**, **6b**, **9b**-**10b**, and 20 µM for **4b**, **5b**. The pyrazolines fluorescent intensities were normalized against DAPI.

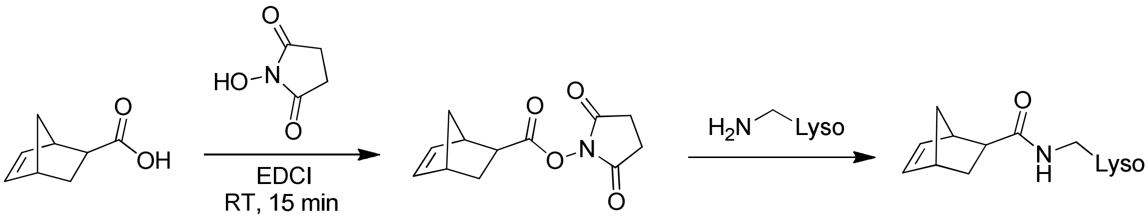
Quantum yield determination

The fluorescence spectra were measured for **2b-6b**, **9b**, and **10b** with excitation wavelength of 348 nm. The relative quantum yields were calculated by comparing the wavelength-integrated intensities of the norbornene-derived pyrazoline sample to that of DAPI standard using the following equation[2]:

$$\Phi_F = \Phi_{st} \frac{I_F}{I_{st}} \frac{OD_{st}}{OD_F} \frac{n_F^2}{n_{st}^2}$$

where *Φ* is the quantum yield, *I* is the integrated intensity, *n* is the refractive index, and *OD* is the optical density. The subscript *st* refers to the reference fluorophore (DAPI).

Labeling of chicken lysozyme with 5-norbornene-2-carboxylic acid



To a 600-µL solution of 5-norbornene-2-carboxylic acid (25 mM in DMF) was added *N*-hydroxysuccinimide (5.6 mg, 75 mM) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (4.4 mg, 38 mM). The reaction mixture was vortexed for 15 min to afford the activated norbornene. A 50-µL aliquot of the reaction mixture was added to 450 µL of a buffered solution of chicken egg white lysozyme (125 µM in 100 mM NaH_2PO_4, 25 mM NaOAc, pH 8.5) and the mixture was rocked on a rotating shaker for 3h at room temperature. Afterwards, excess amount of small molecules was removed by protein spin columns (Pierce). The protein fraction was found to contain mainly singly- (Lyso-Nor) and doubly-labeled lysozyme (Lyso-d-Nor) as well as unreacted lysozyme (Lyso) in a 3:3:2 ratio, estimated on the basis of the extracted ion intensities in an LC-ESI/MS analysis. The identities of the major fractions were confirmed by the deconvoluted intact masses: Lyso calcd 14304 Da, found 14305.2 ± 0.9 Da; Lyso-Nor, calcd 14424 Da, found 14425.4 ± 0.5; Lyso-d-Nor, calcd 14544 Da, found 14545 ± 1 Da.

Photoinduced cycloaddition of Lyso-norbornene with macrocyclic tetrazoles

To a 20-µL solution of either Lyso or Lyso-Nor (10 µM) in PBS buffer, pH 7.4, in a 96-well microtiter plate was added 1 µL of the various tetrazoles (4 mM in DMSO, final concentration is 200 µM). The mixtures were irradiated with a handheld 302-nm UV lamp for 1 min before quenching by addition of 5 µL of 6× SDS sample buffer, boiled for 5 min at 95 ^{o}C, loaded onto a NuPAGE 12% Bis-Tris gel (Invitrogen), and then subjected to protein electrophoresis. The Lyso-Pyr cycloadducts in the gel were visualized by illuminating the gel with a handheld 365-nm UV lamp and the resulting image was captured by a digital camera. After the image acquisition, the same gel was stained with Coomassie blue to confirm the size and equal loading of proteins. The cycloaddition was specific to the norbornene-labeled lysozyme and the 302-nm UV irradiation was needed for reaction to proceed as indicated in the control experiment (Figure S3).

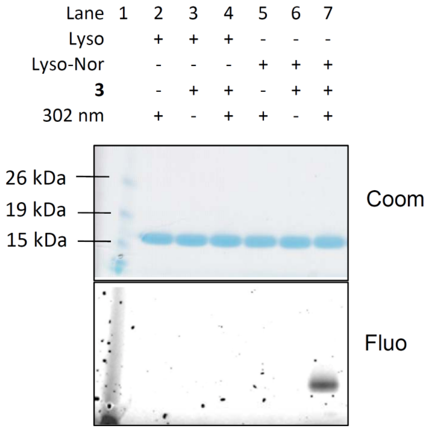


Figure S3. Cycloaddition reaction of Lyso-Norbornene with the macrocyclic tetrazole **3**: top panel, Coomassie blue staining of the SDS-PAGE gel; bottom panel, inverted fluorescence imaging of the same gel with λ_{ex} = 365 nm.

Reference:

(1) Ito, S.; Tanaka, Y.; Kakehi, A.; Kondo, K. *Bull. Chem. Soc. Jpn*. **1976**, *49*, 1920.

(2) (a) Du, H.; Fuh, R. A. J.; Corkan, Li, A.; Lindsey, J. S. *Photochem. Photobiol.* **1998**, *68*, 141. (b) Hard, T.; Fan, P.; and Kearns, D. R. *Photochem. Photobiol.* **1990**, *51*, 77. (c) Williams, A. T. R.; Winfield, S. A.; and Miller, J. N. *Analyst* **1983**, *108*, 1067.

Table S1. Crystal data and structure refinement for tetrazole **6**.

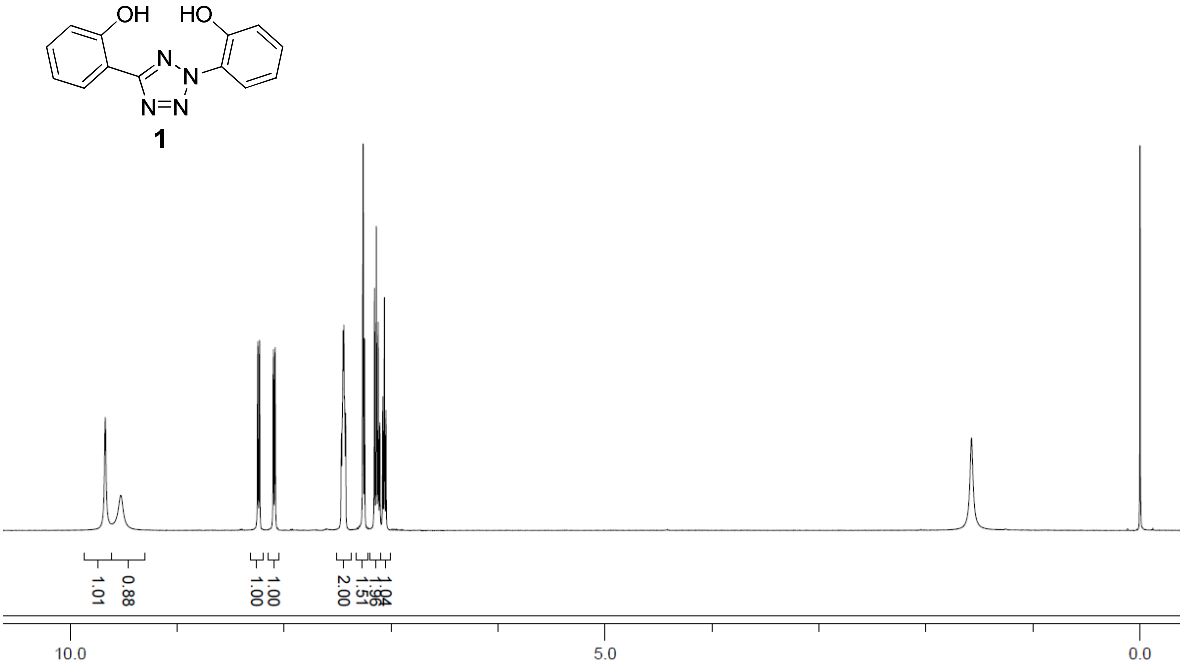
Identification code	tetrazole **6**	
Empirical formula	C21 H16 N4 O2	
Formula weight	356.38	
Temperature	100.0(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 9.1339(7) Å	α = 90°
	b = 11.9708(9) Å	β = 100.414(2)°
	c = 15.7136(12) Å	γ = 90°
Volume	1689.8(2) Å^3	
Z	4	
Density (calculated)	1.401 Mg/m^3	
Absorption coefficient	0.093 mm^{-1}	
F(000)	744	
Crystal color, morphology	colorless, block	
Crystal size	0.36 x 0.32 x 0.24 mm^3	
Theta range for data collection	2.15 to 37.78°	
Index ranges	$-15 \leq h \leq 15$, $-20 \leq k \leq 20$, $-26 \leq l \leq 26$	
Reflections collected	46895	
Independent reflections	9002 [R(int) = 0.0361]	
Observed reflections	6877	
Completeness to theta = 37.78°	99.2%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9779 and 0.9671	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9002 / 4 / 253	
Goodness-of-fit on F^2	1.029	
Final R indices [I>2sigma(I)]	$R1$ = 0.0486, $wR2$ = 0.1291	
R indices (all data)	$R1$ = 0.0672, $wR2$ = 0.1419	
Largest diff. peak and hole	0.600 and -0.206 e.Å^{-3}	

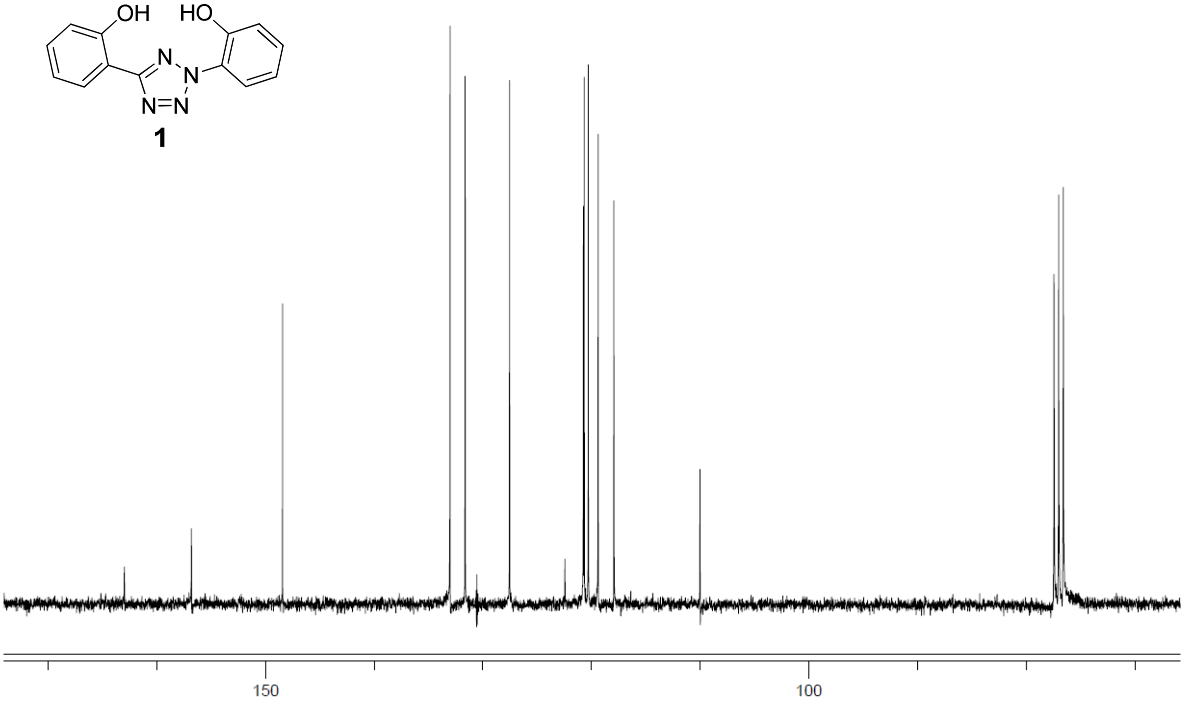
Table S2. Crystal data and structure refinement for tetrazole **9**.

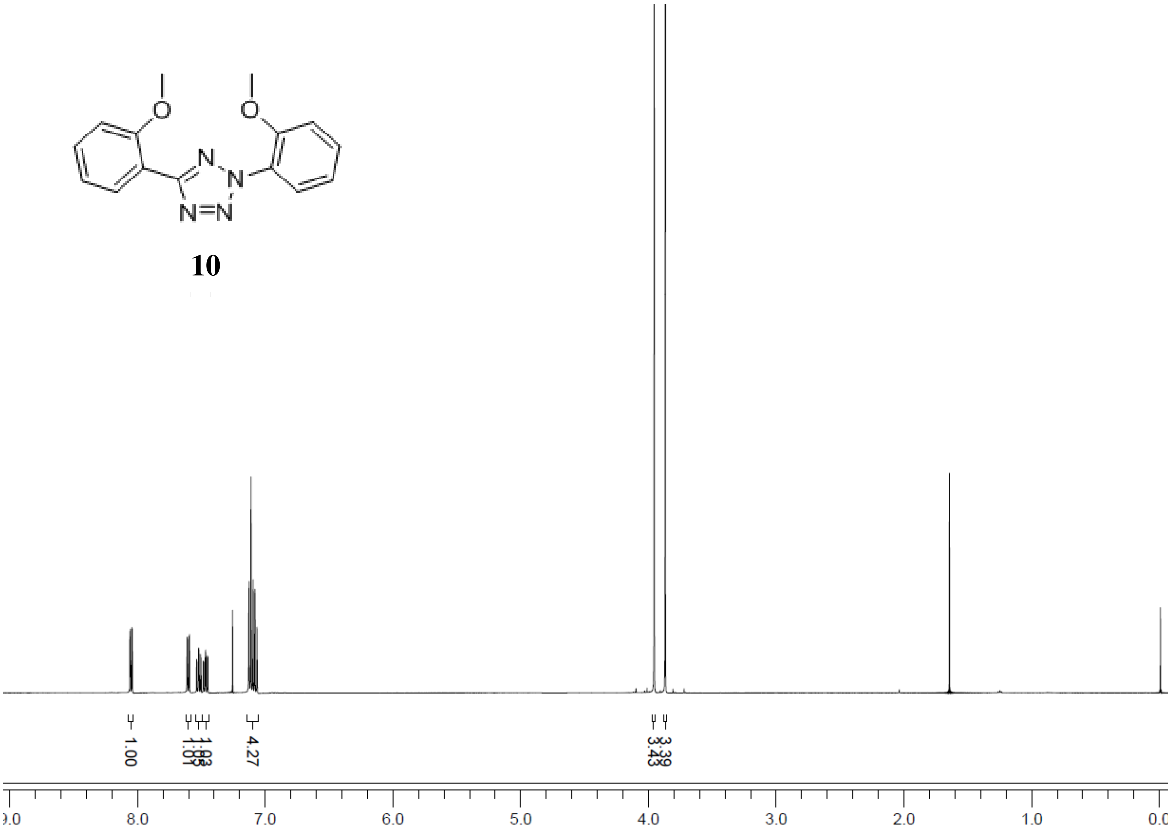
Identification code	tetrazole **9**	
Empirical formula	C17 H15 N5 O2	
Formula weight	321.34	
Temperature	100.0(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 9.8666(9) Å	$\alpha = 90°$
	b = 8.8649(8) Å	$\beta = 91.391(2)°$
	c = 16.9787(15) Å	$\gamma = 90°$
Volume	1484.6(2) $Å^3$	
Z	4	
Density (calculated)	1.438 Mg/m^3	
Absorption coefficient	0.099 mm^{-1}	
F(000)	672	
Crystal color, morphology	colorless, block	
Crystal size	0.28 x 0.24 x 0.20 mm^3	
Theta range for data collection	2.06 to 37.78°	
Index ranges	$-16 \leq h \leq 17$, $-15 \leq k \leq 15$, $-29 \leq l \leq 29$	
Reflections collected	53010	
Independent reflections	7940 [R(int) = 0.0366]	
Observed reflections	6550	
Completeness to theta = 37.78°	99.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9804 and 0.9728	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7940 / 0 / 221	
Goodness-of-fit on F^2	1.052	
Final R indices [I>2sigma(I)]	$R1 = 0.0413$, $wR2 = 0.1126$	
R indices (all data)	$R1 = 0.0508$, $wR2 = 0.1207$	
Largest diff. peak and hole	0.627 and -0.237 e.$Å^{-3}$	

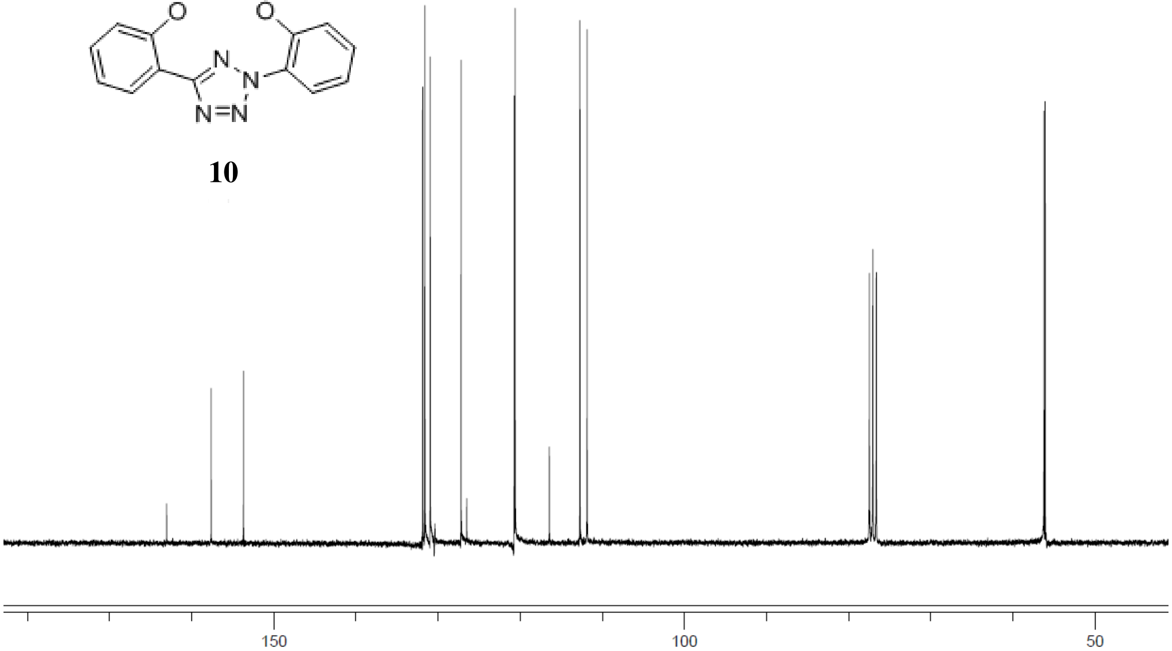
Table S3. Crystal data and structure refinement for pyrazoline **3b**.

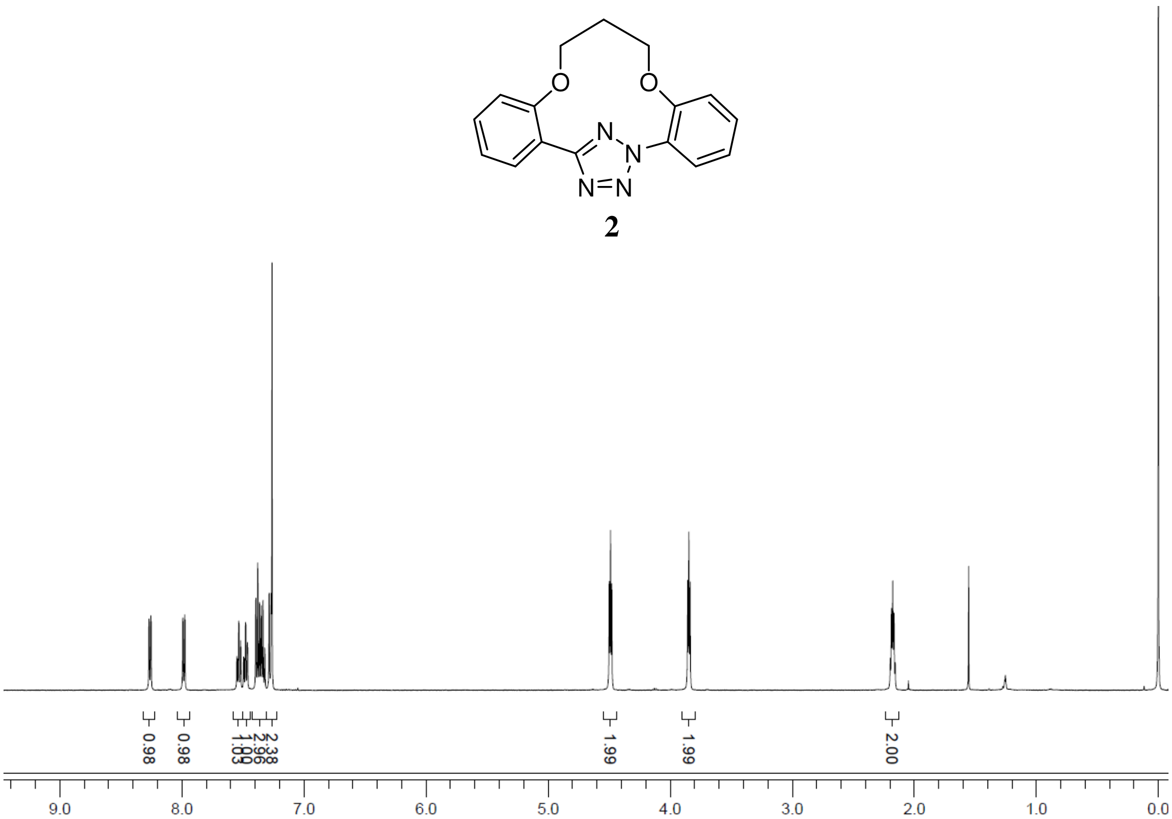
Identification code	pyrazoline **3b**	
Empirical formula	C24 H26 N2 O2	
Formula weight	374.47	
Temperature	100.0(1) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*-1	
Unit cell dimensions	*a* = 9.714(3) Å	α = 114.021(5)°
	b = 10.750(3) Å	β = 103.164(5)°
	c = 10.944(3) Å	γ = 103.862(5)°
Volume	942.8(4) Å^3	
Z	2	
Density (calculated)	1.319 Mg/m^3	
Absorption coefficient	0.084 mm^{-1}	
F(000)	400	
Crystal color, morphology	pale yellow, plate	
Crystal size	0.28 x 0.20 x 0.08 mm^3	
Theta range for data collection	2.19 to 33.73°	
Index ranges	$-15 \leq h \leq 15$, $-16 \leq k \leq 16$, $-17 \leq l \leq 17$	
Reflections collected	18818	
Independent reflections	7448 [*R*(int) = 0.0482]	
Observed reflections	4578	
Completeness to theta = 33.73°	98.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9933 and 0.9768	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7448 / 0 / 357	
Goodness-of-fit on F^2	1.022	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0565, *wR*2 = 0.1354	
R indices (all data)	*R*1 = 0.1026, *wR*2 = 0.1591	
Largest diff. peak and hole	0.444 and -0.333 e.Å^{-3}	


OH
HO
N
N
N
N
1
1.01
0.88
1.00
1.00
2.00
1.51
1.96
1.04
10.0
5.0
0.0


OH
HO
N
N
N
N
1
150
100


10
1.00
1.01
1.03
4.27
3.43
3.39
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


10
150
100
50



2

0.98
0.98
1.03
1.09
2.96
2.38
1.99
1.99
2.00
9.0
8.0
7.0
6.0
5.0
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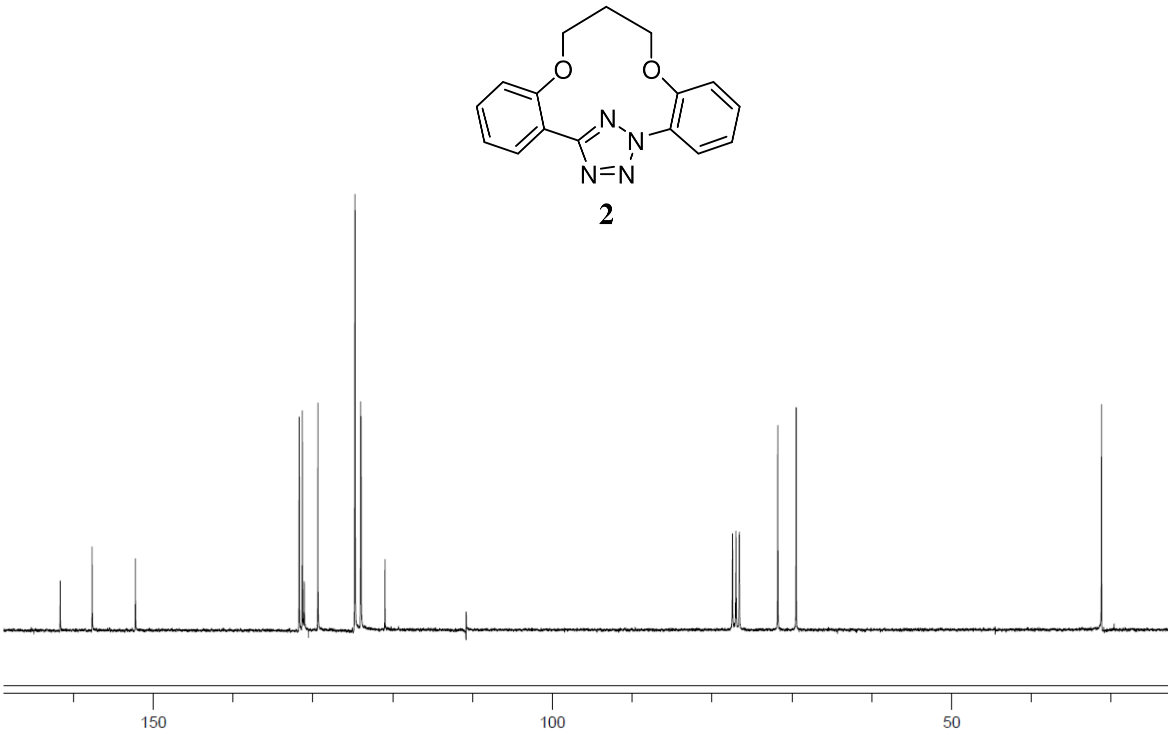
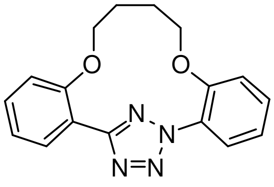
3.0
2.0
1.0
0.0

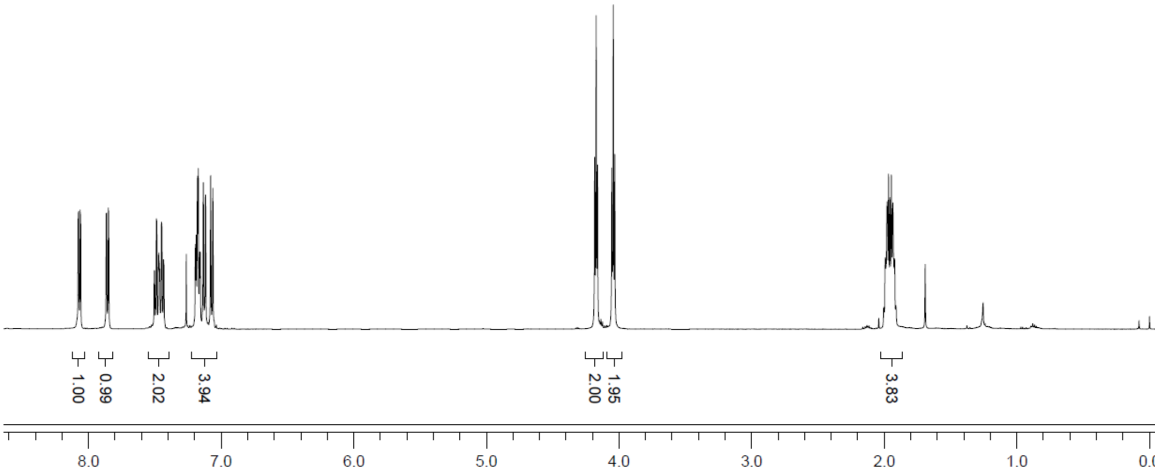


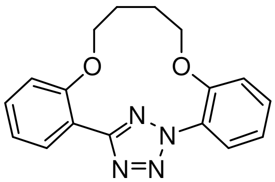
2

150
100
50

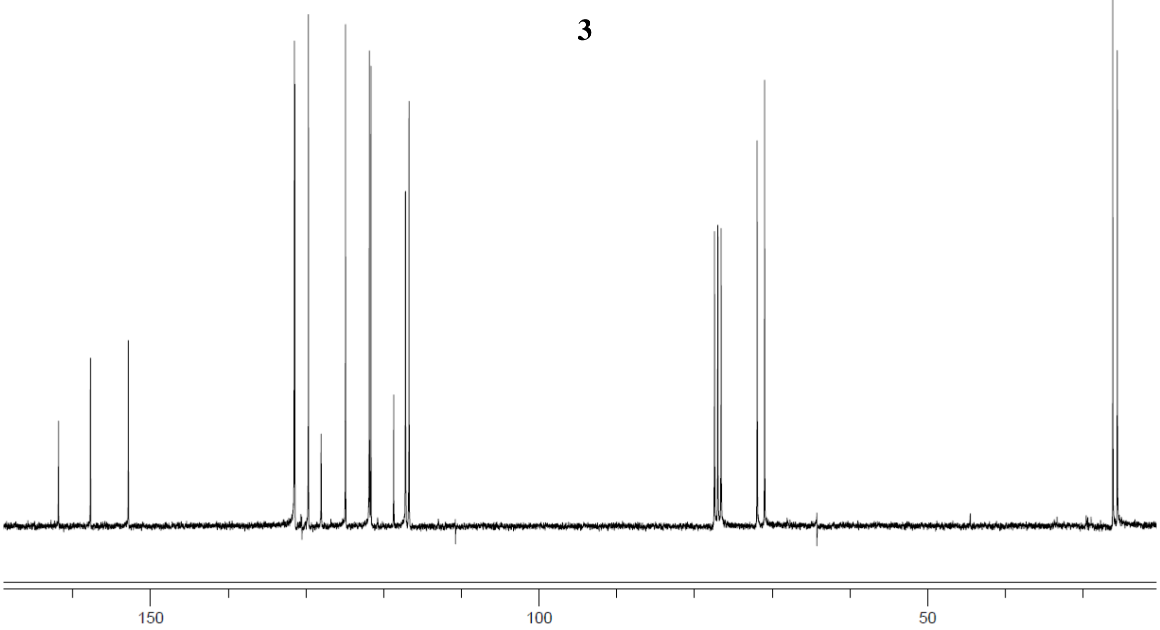


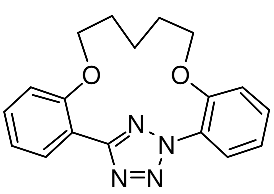
3



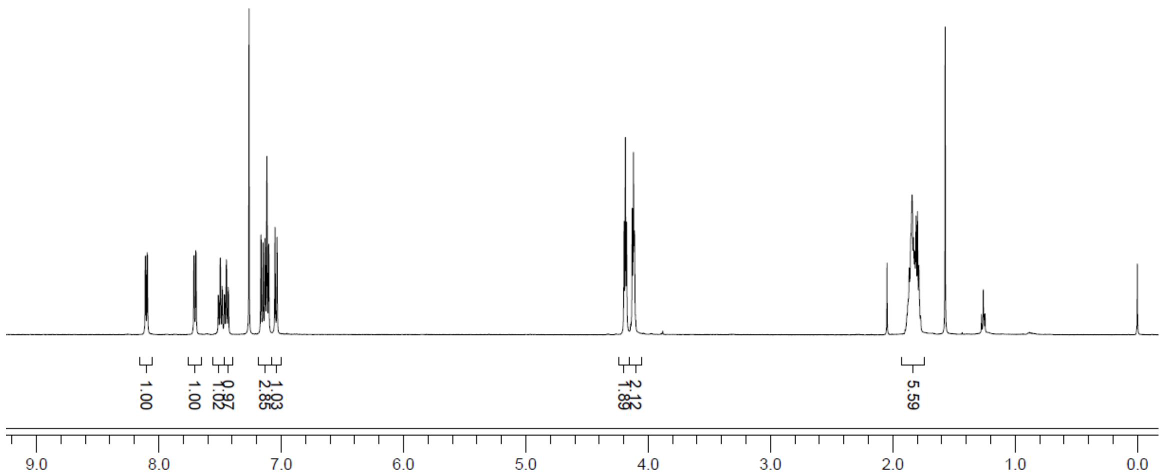


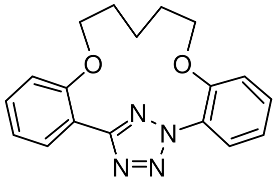
3



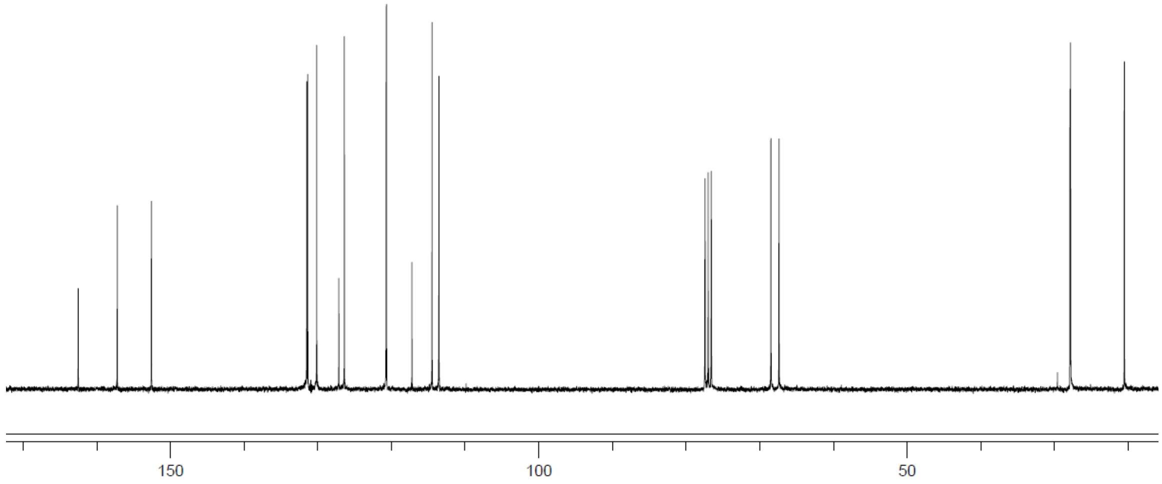


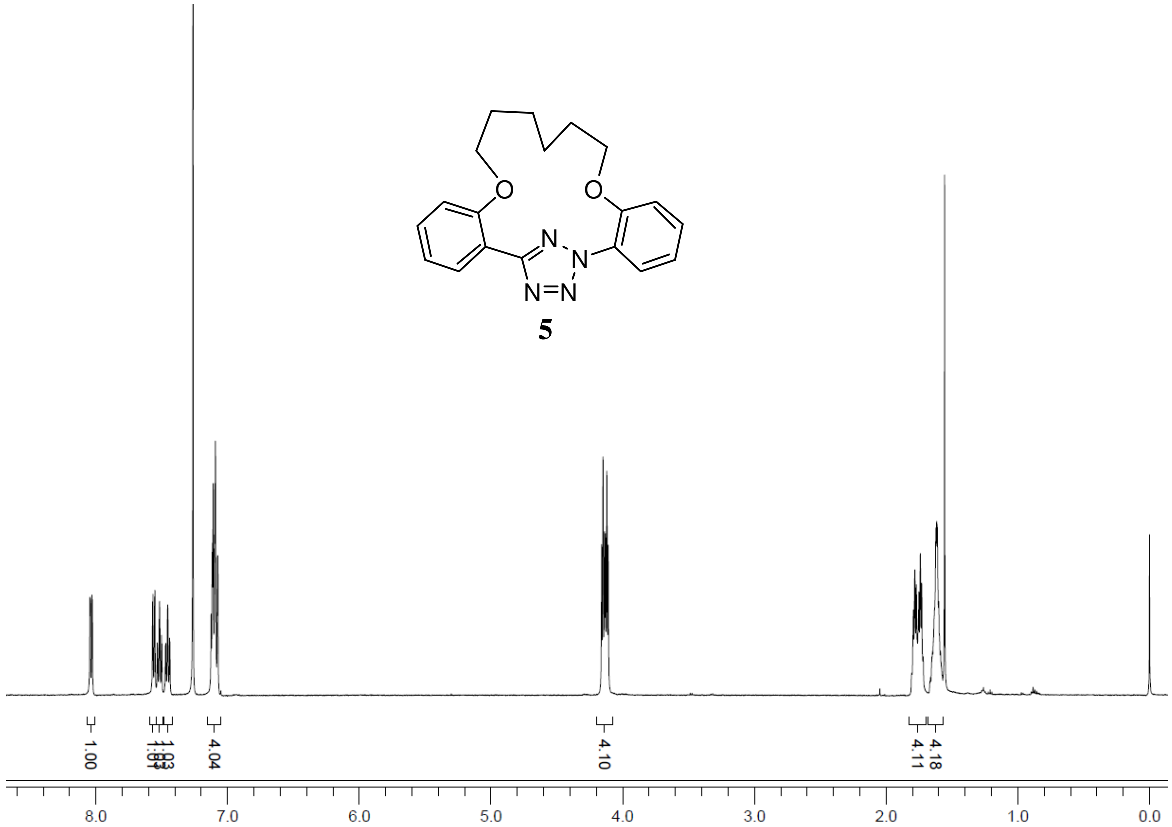
4

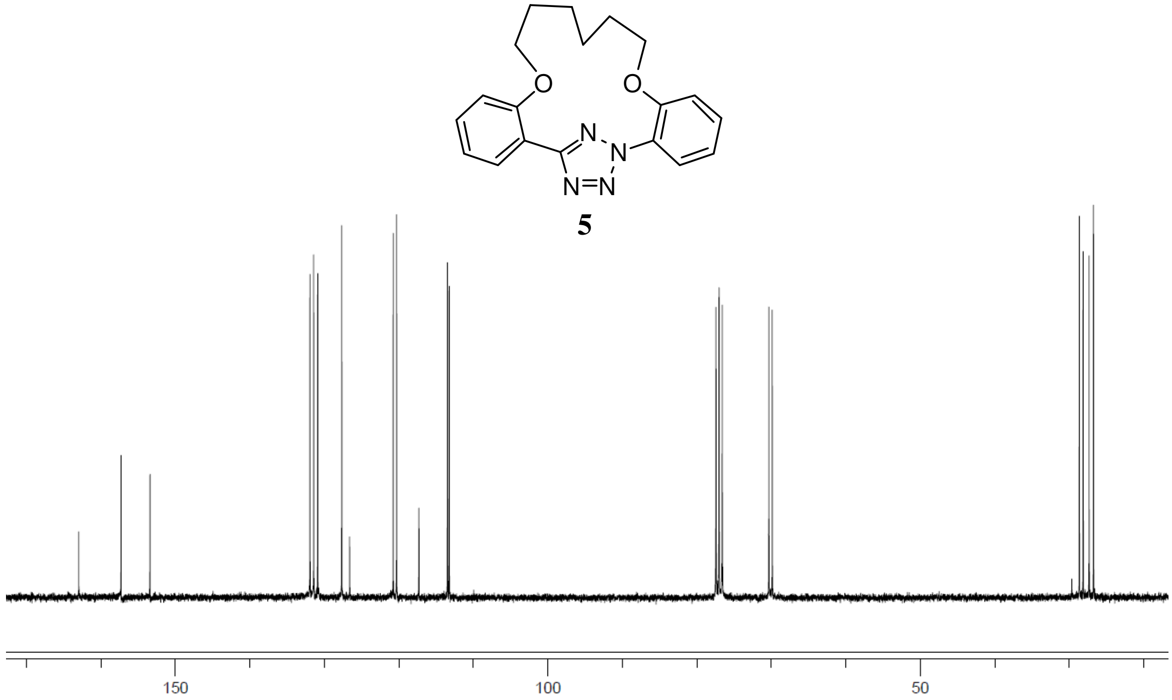

1.00
1.00
1.02
0.97
2.85
1.03
1.89
2.12
5.59
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

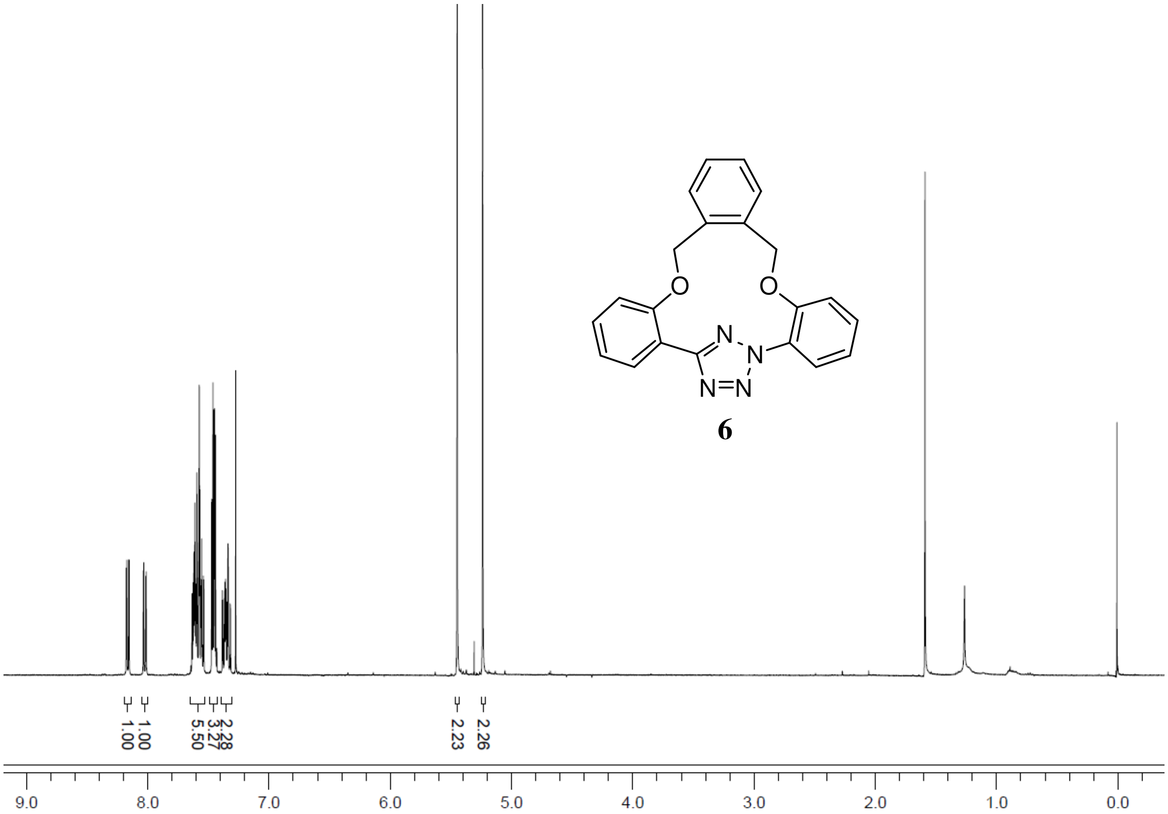


4

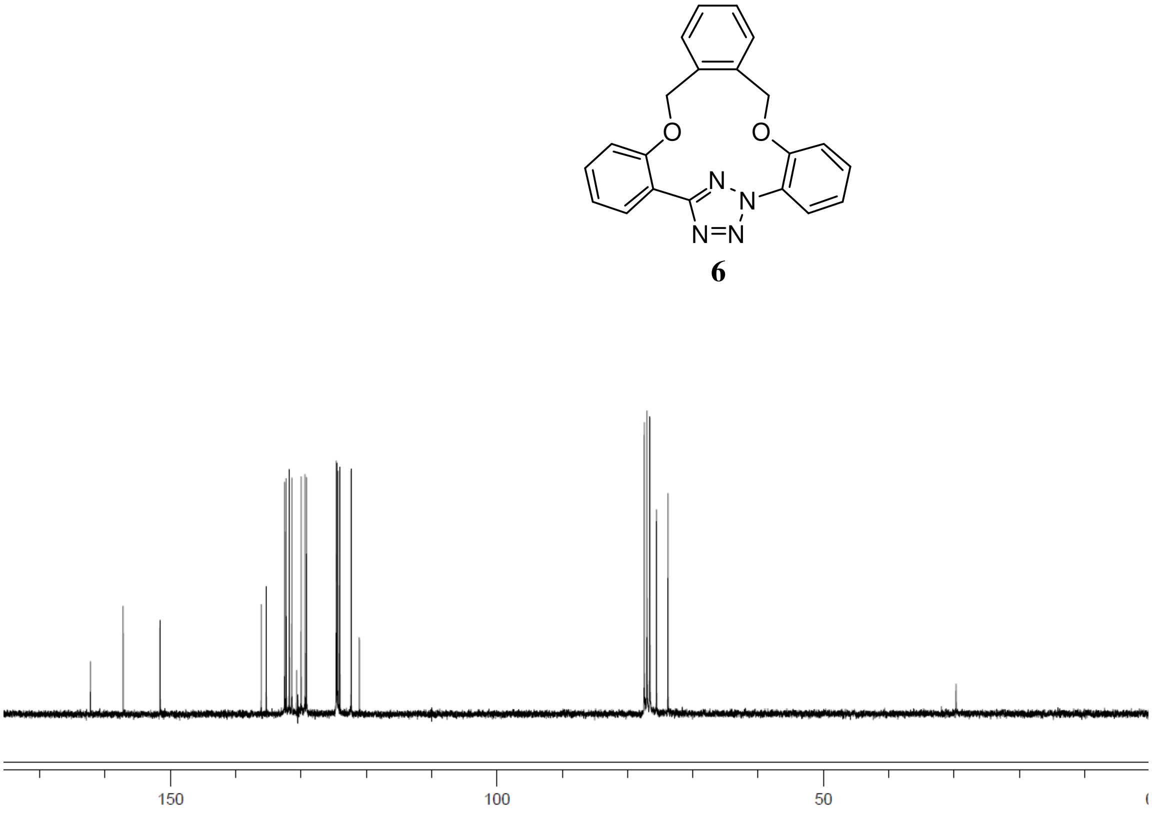

150
100
50


O
O
N
N
N=N
5
1.00
1.01
1.03
4.04
4.10
4.11
4.18
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

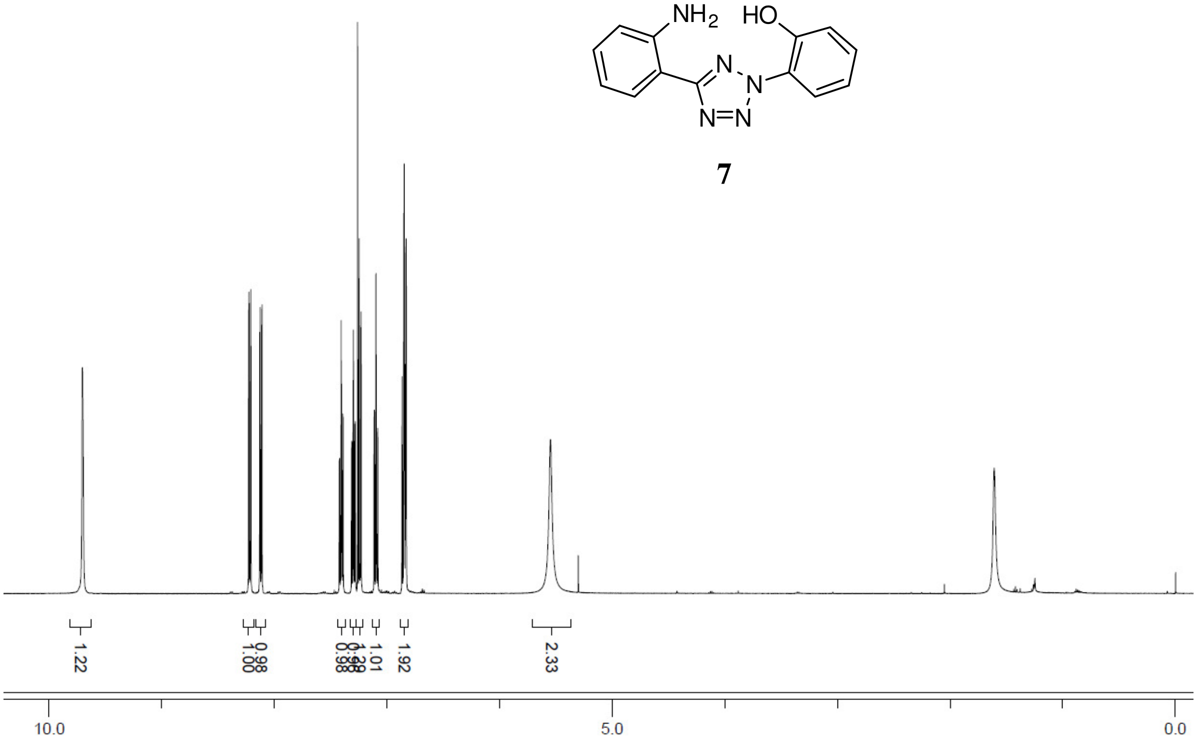

O
O
N
N
N=N
5
150
100
50

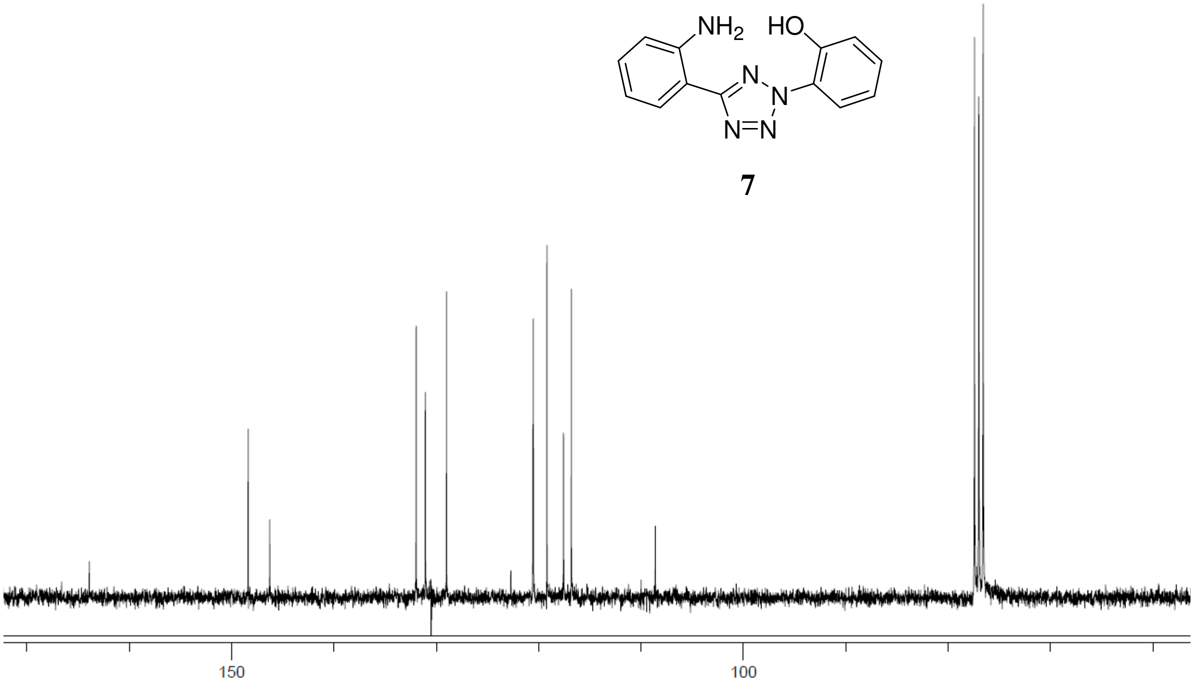

O
O
N
N
N=N
1.00
1.00
5.50
3.27
2.28
2.23
2.26
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

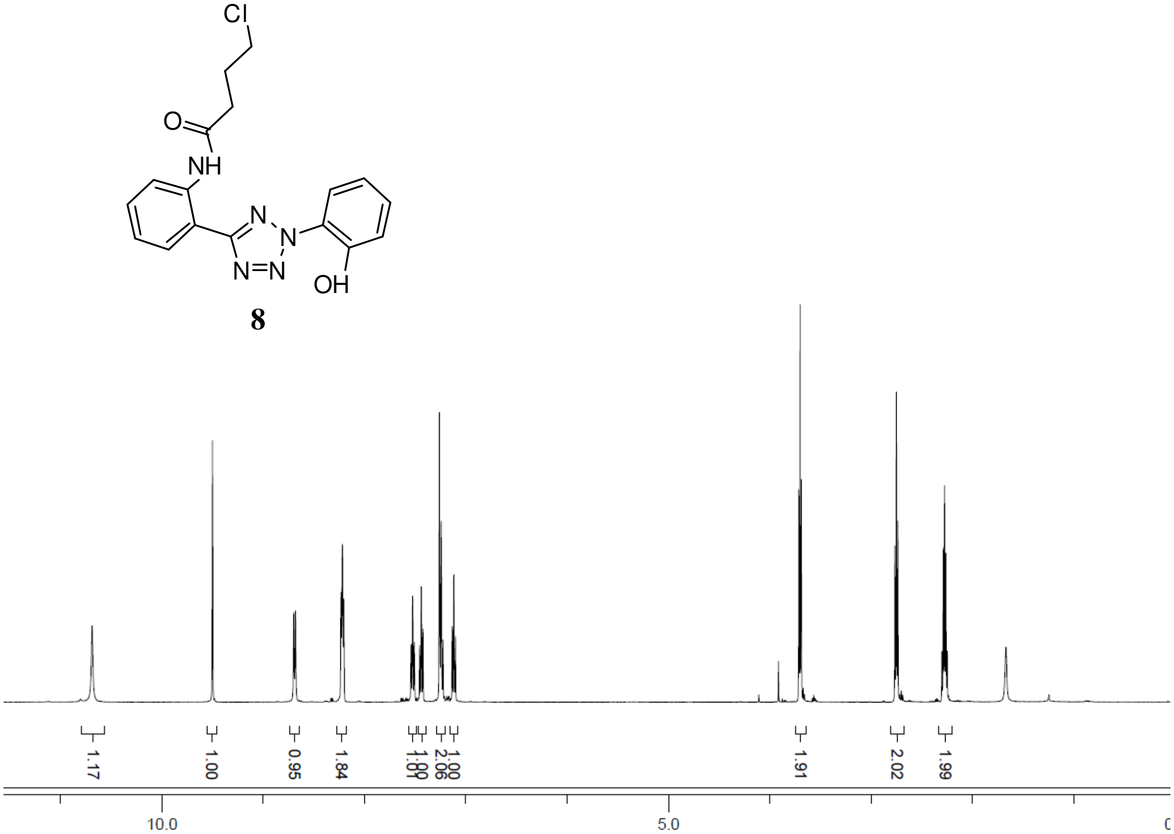
6


O
O
N
N
N=N
150
100
50

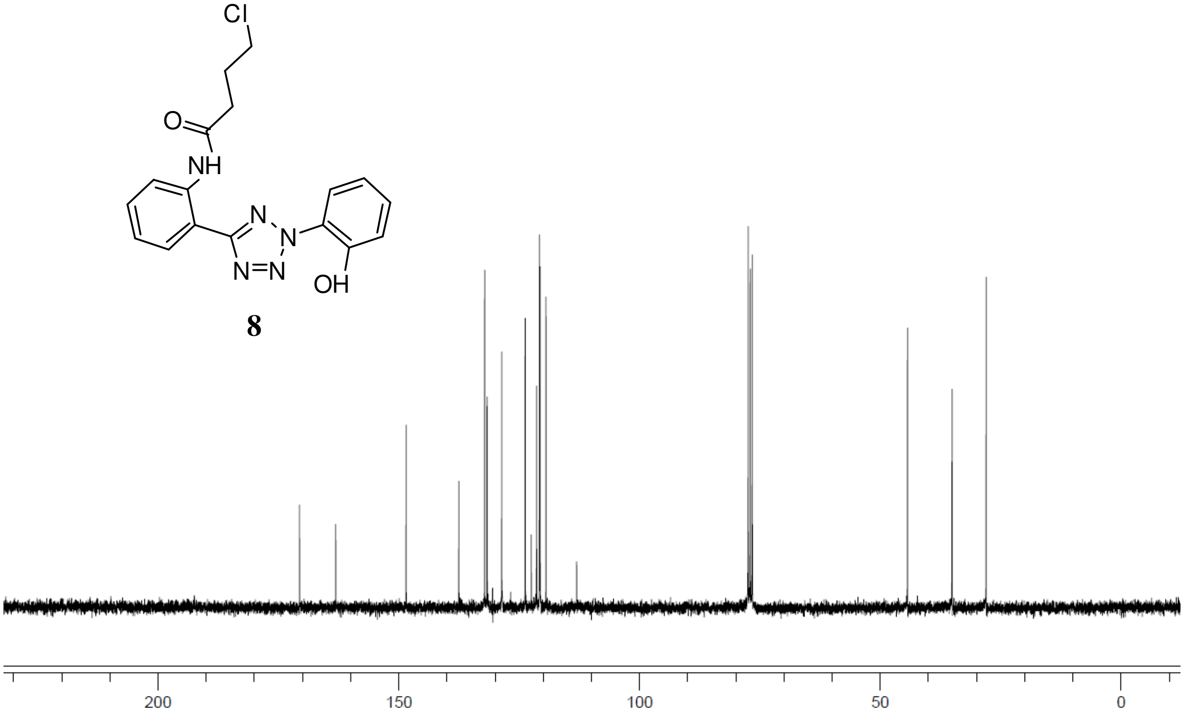
6


NH2
HO
N
N
N=N
7
1.22
1.00
0.98
0.98
0.98
1.29
1.01
1.92
2.33
10.0
5.0
0.0

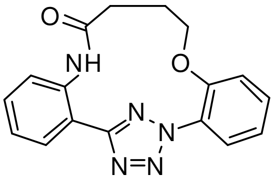

NH2
HO
N
N
N=N
7
150
100


Cl
O
NH
N
N
N=N
OH
1.17
1.00
0.95
1.84
1.01
1.00
2.06
1.00
1.91
2.02
1.99
10.0
5.0

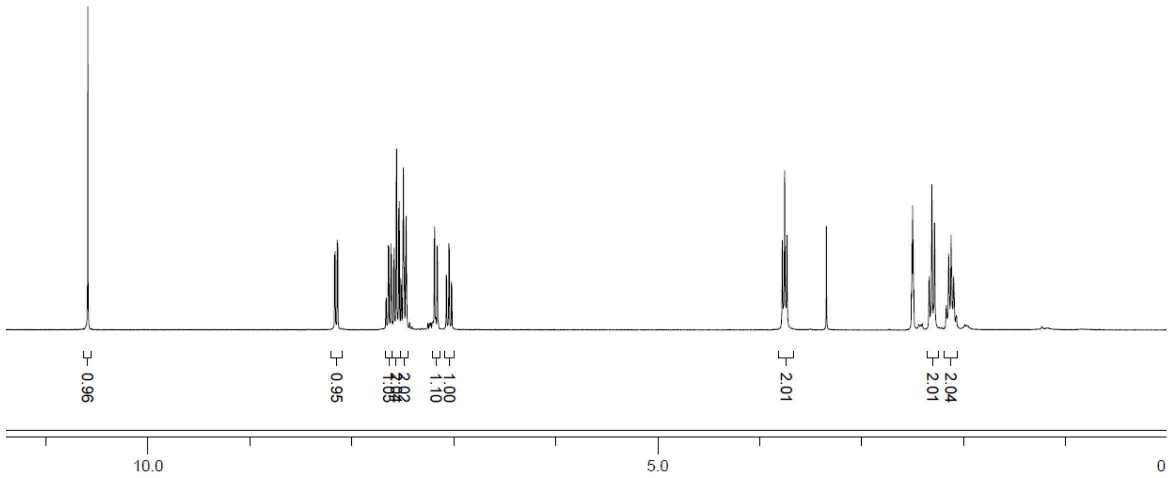
8

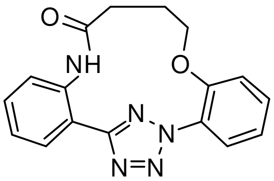

Cl
O
NH
N
N
N=N
OH
200
150
100
50
0

8

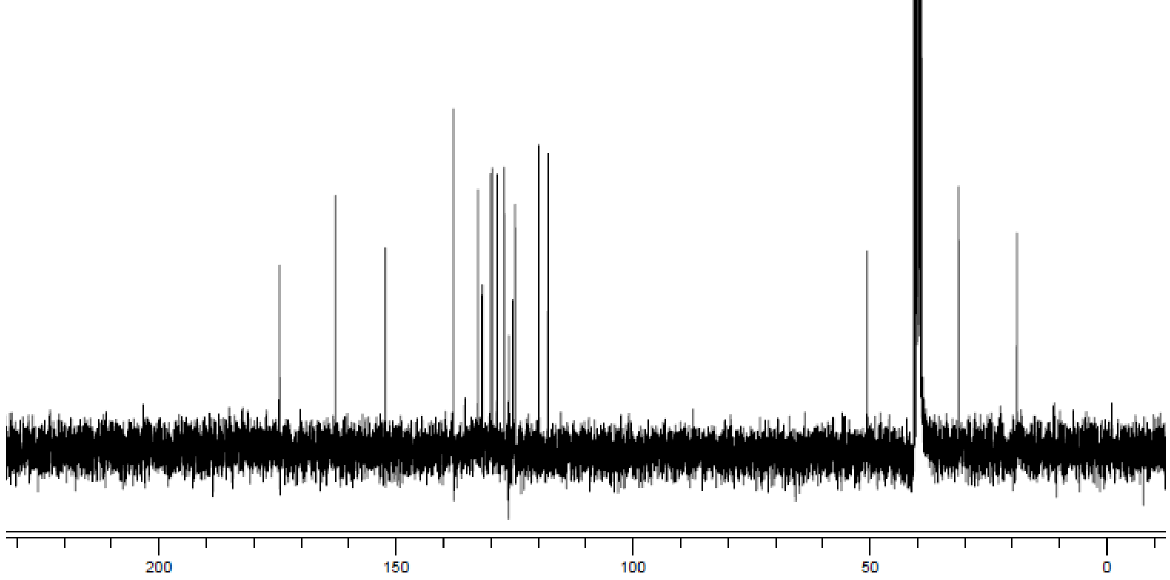

O
NH
O
N
N
N=N

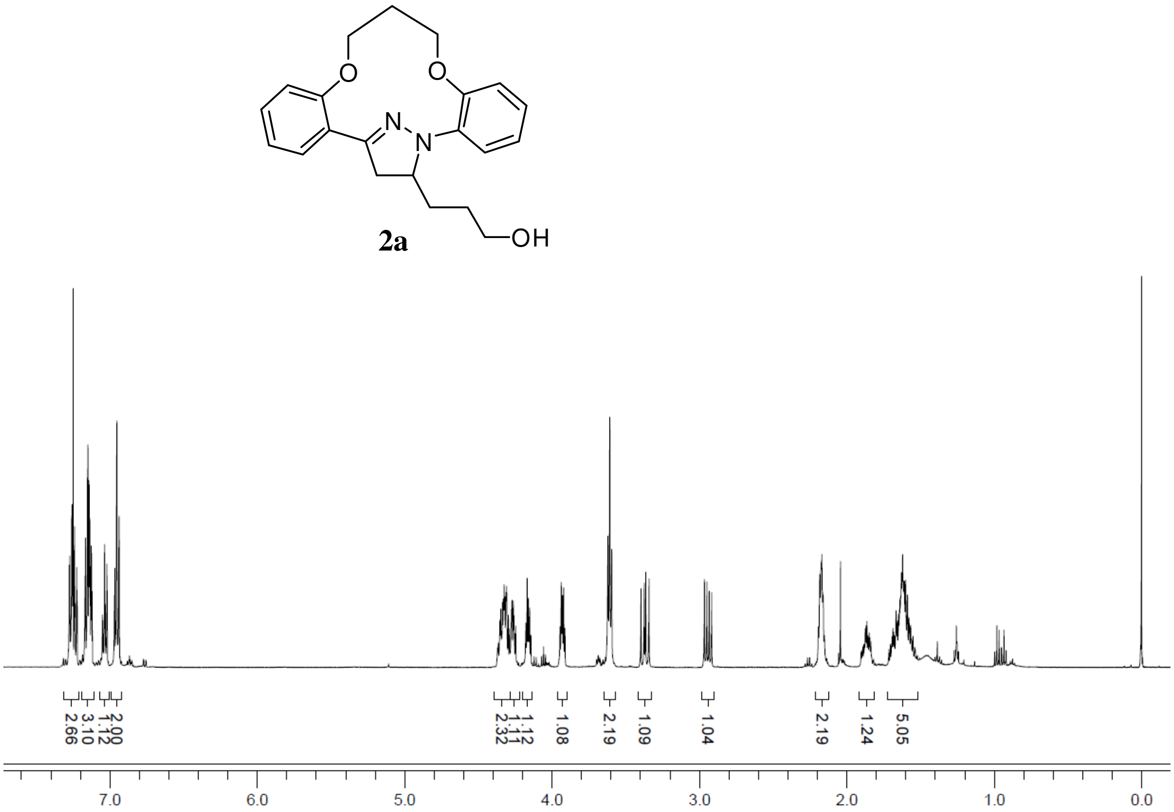
9

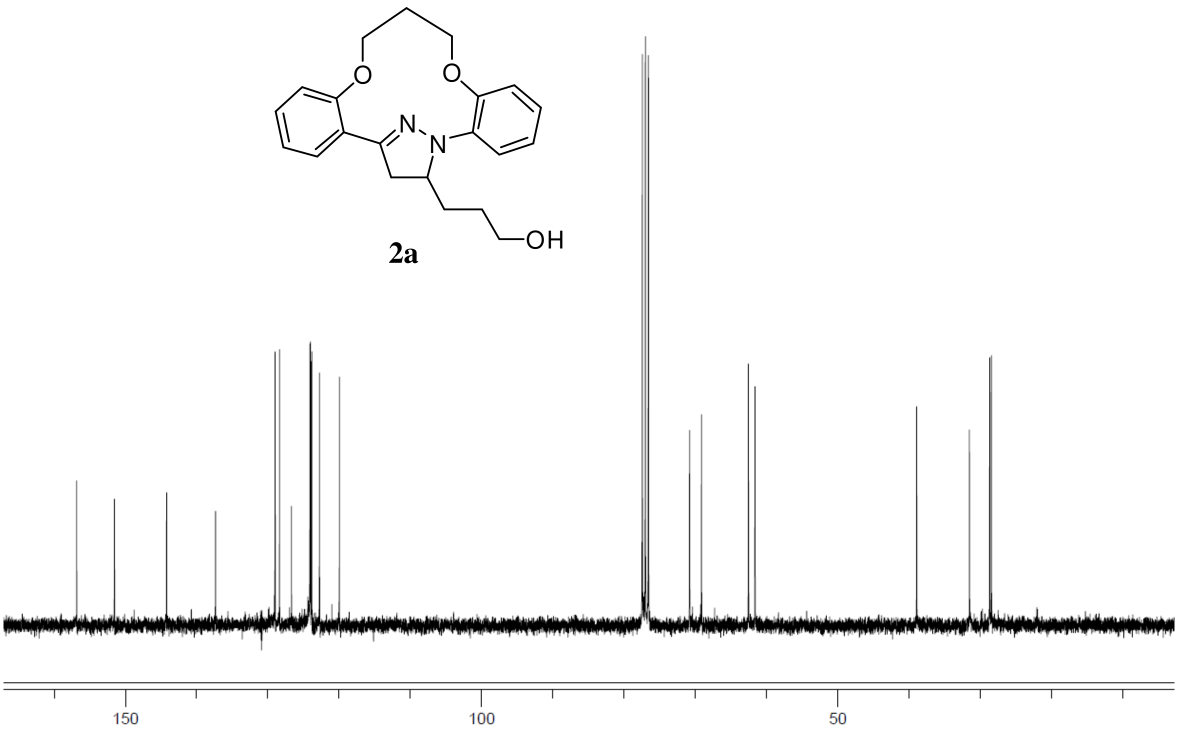

0.96
0.95
1.05
1.04
2.02
1.10
1.00
2.01
2.01
2.04
10.0
5.0
0

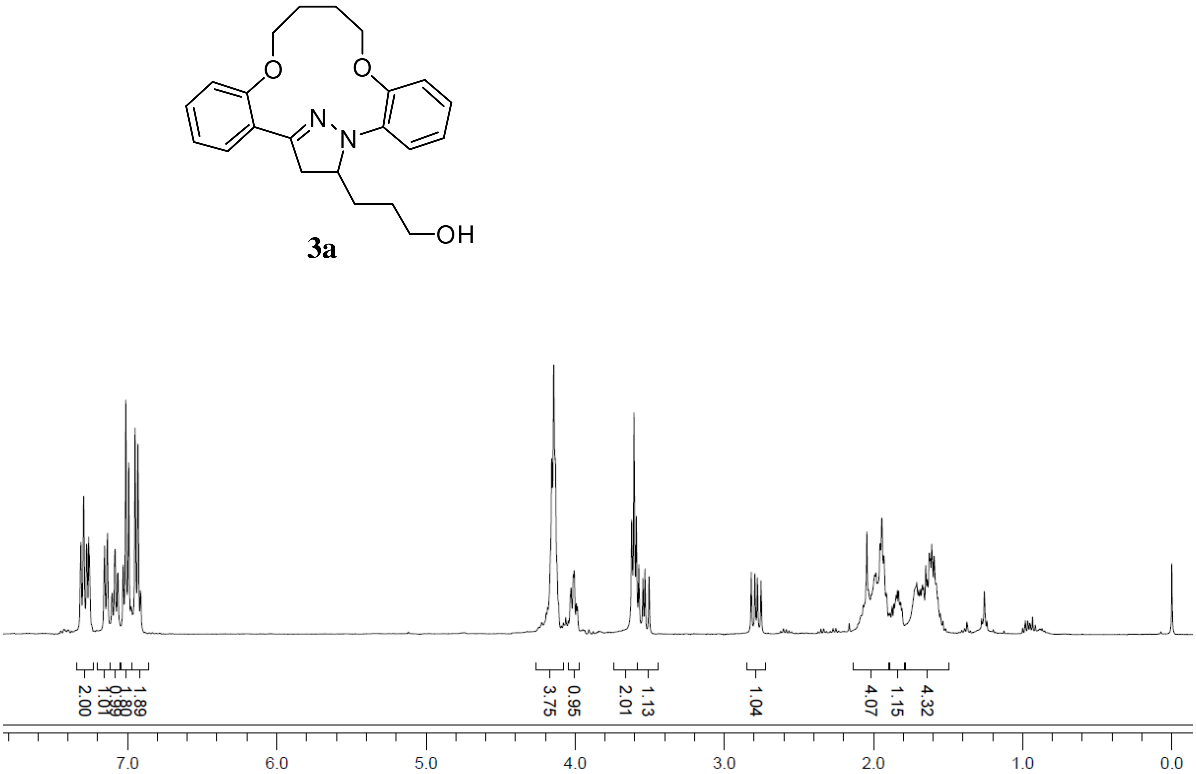

O
NH
O
N
N
N=N

9


200
150
100
50
0

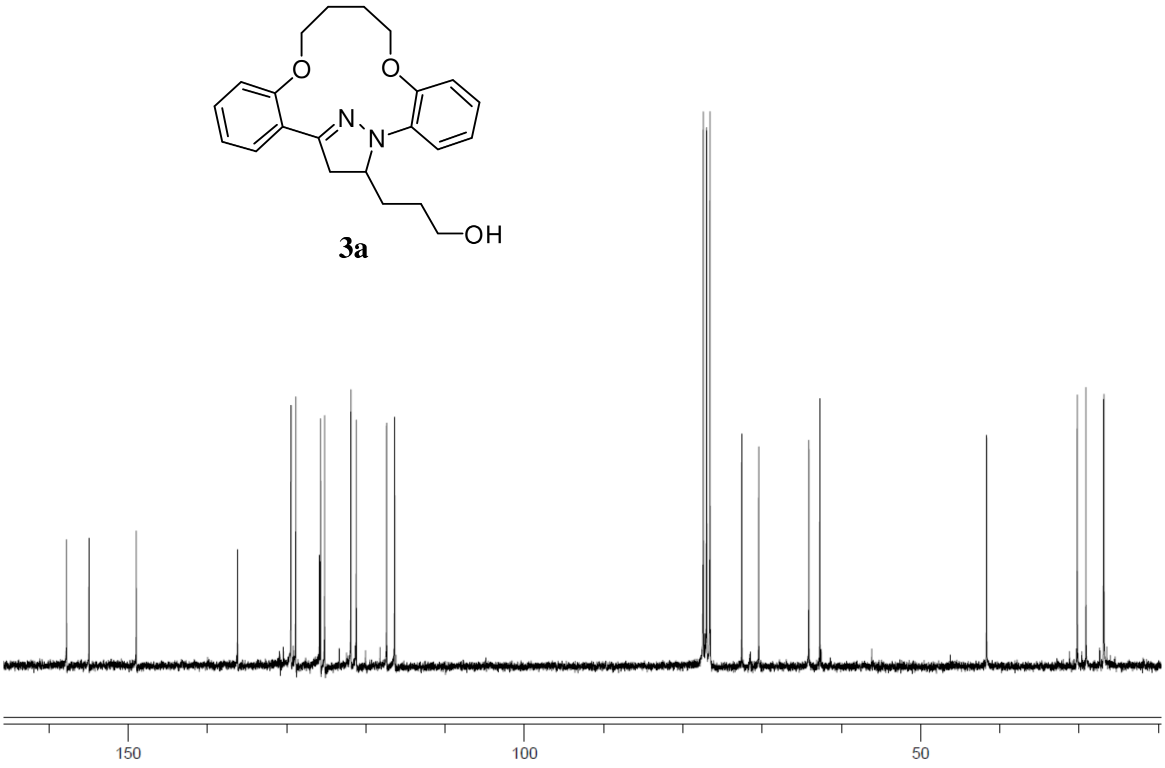

2a
OH
2.66
3.10
1.12
2.00
2.32
1.11
1.12
1.08
2.19
1.09
1.04
2.19
1.24
5.05
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


2a
OH
150
100
50



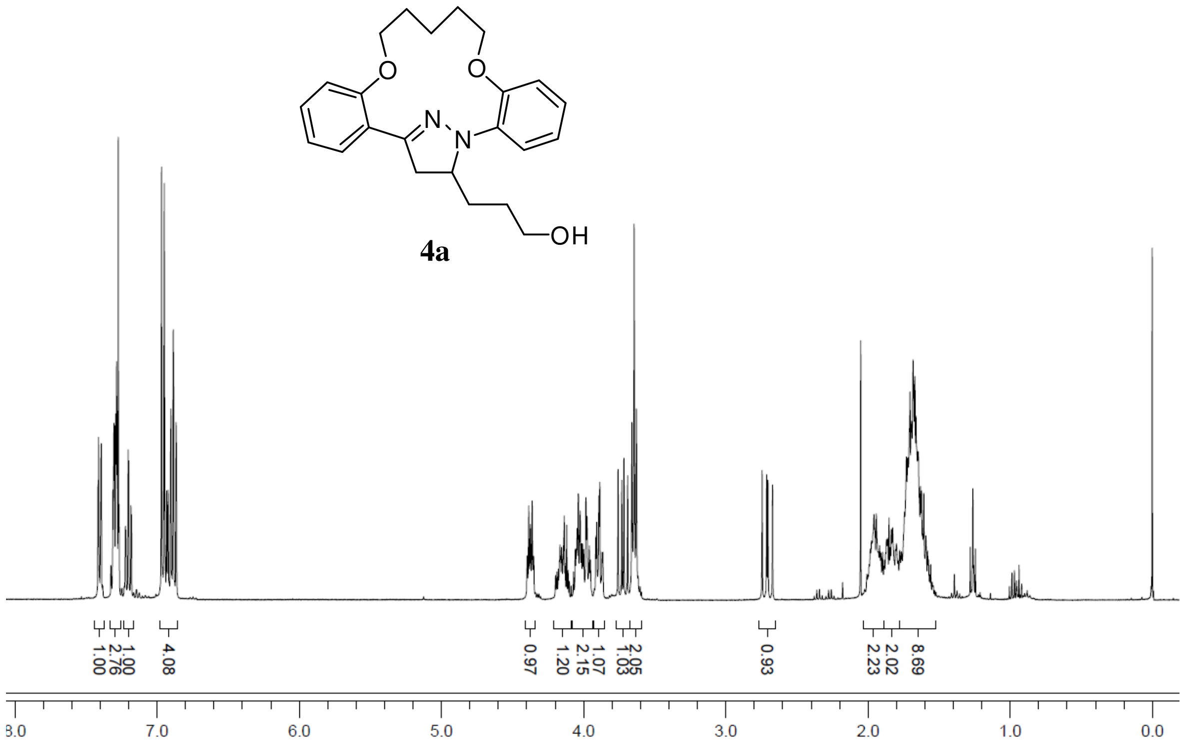
N
N
O
O
OH
2.00
1.01
0.99
1.89
3.75
0.95
2.01
1.13
1.04
4.07
1.15
4.32
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

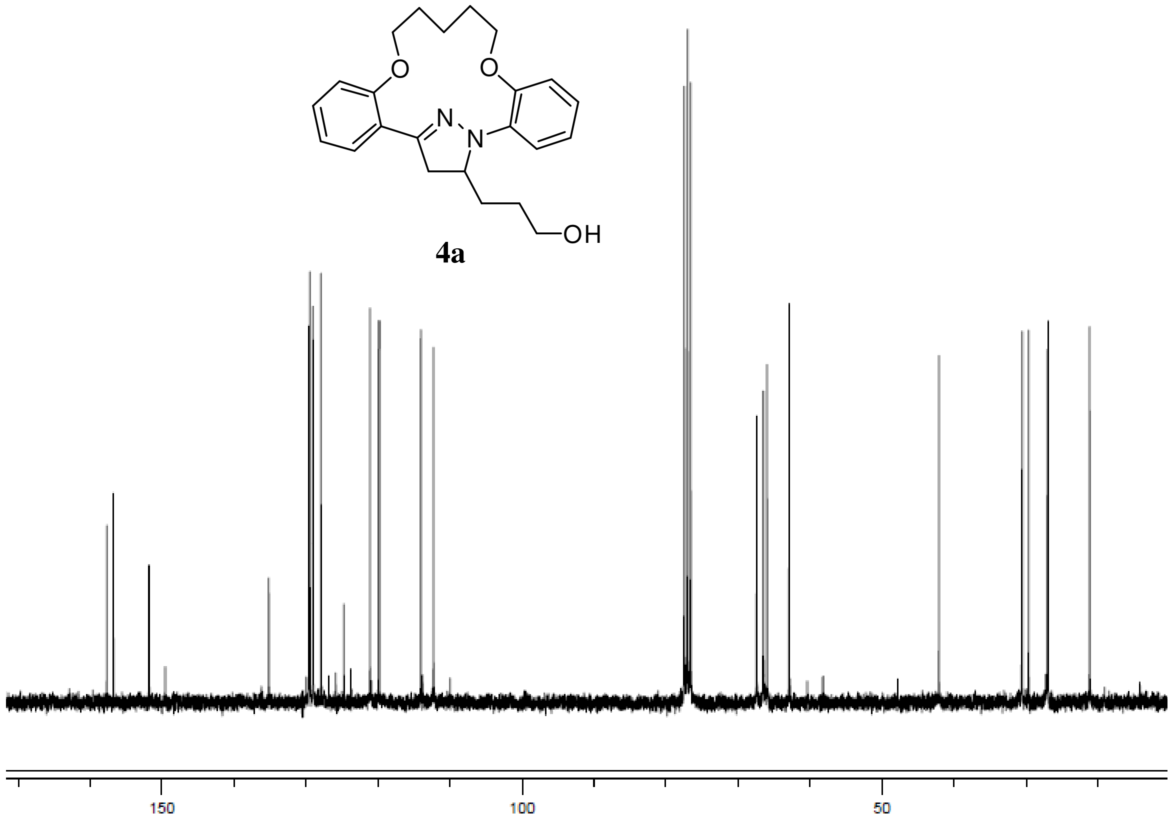
3a

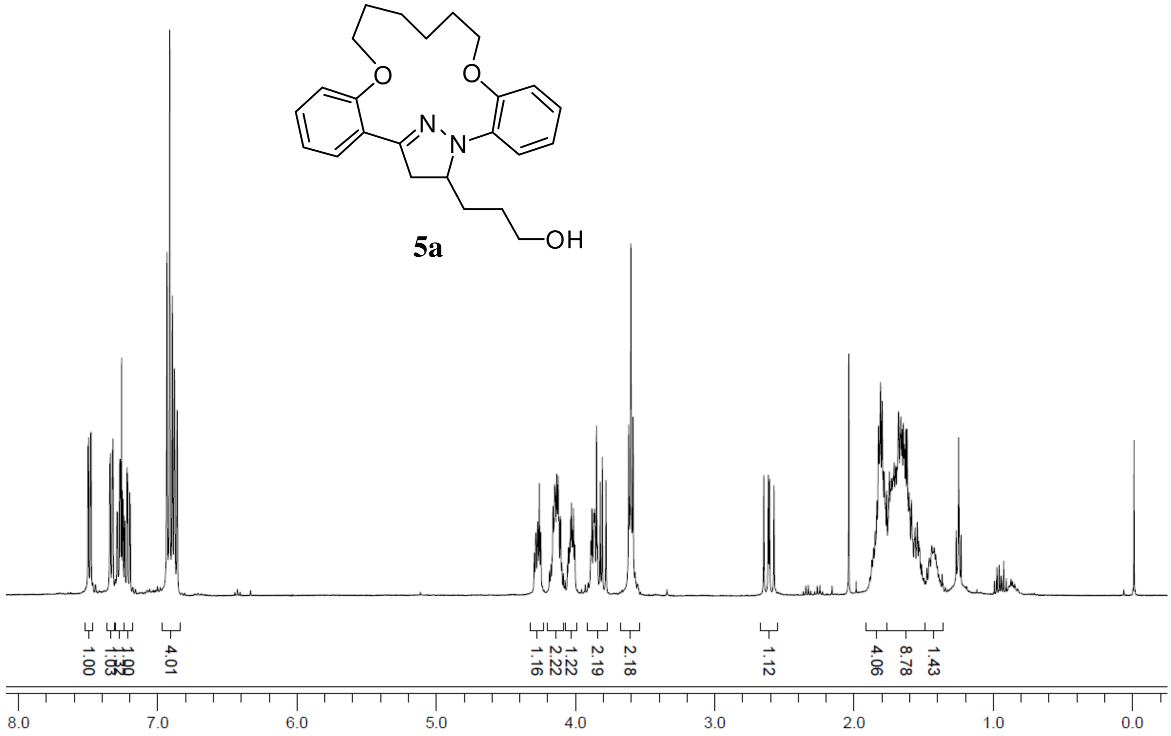


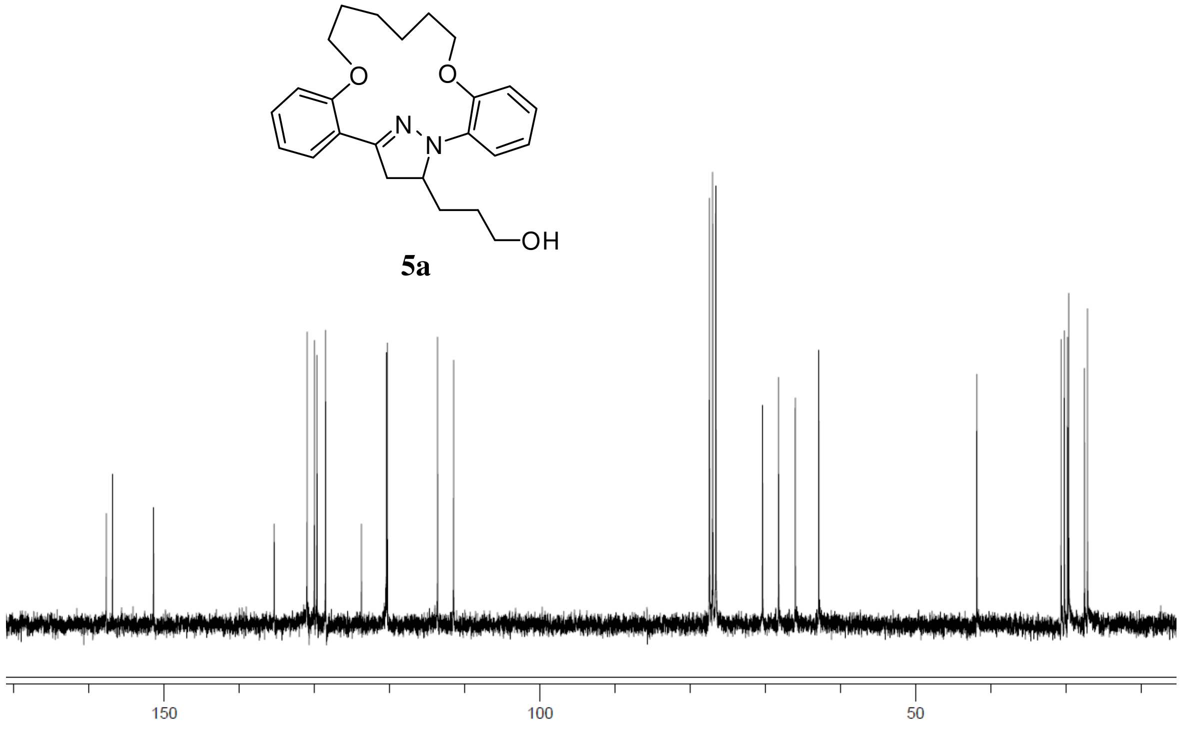
N
N
O
O
OH
150
100
50

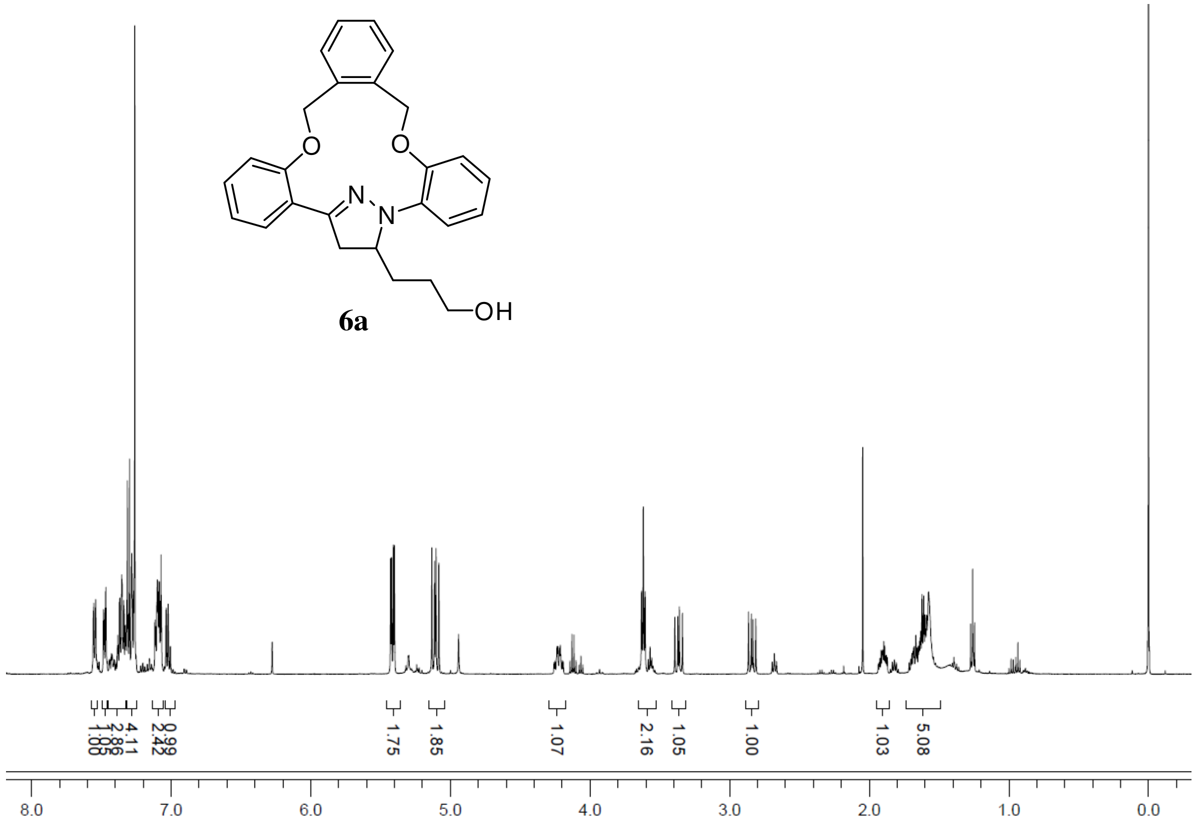
3a

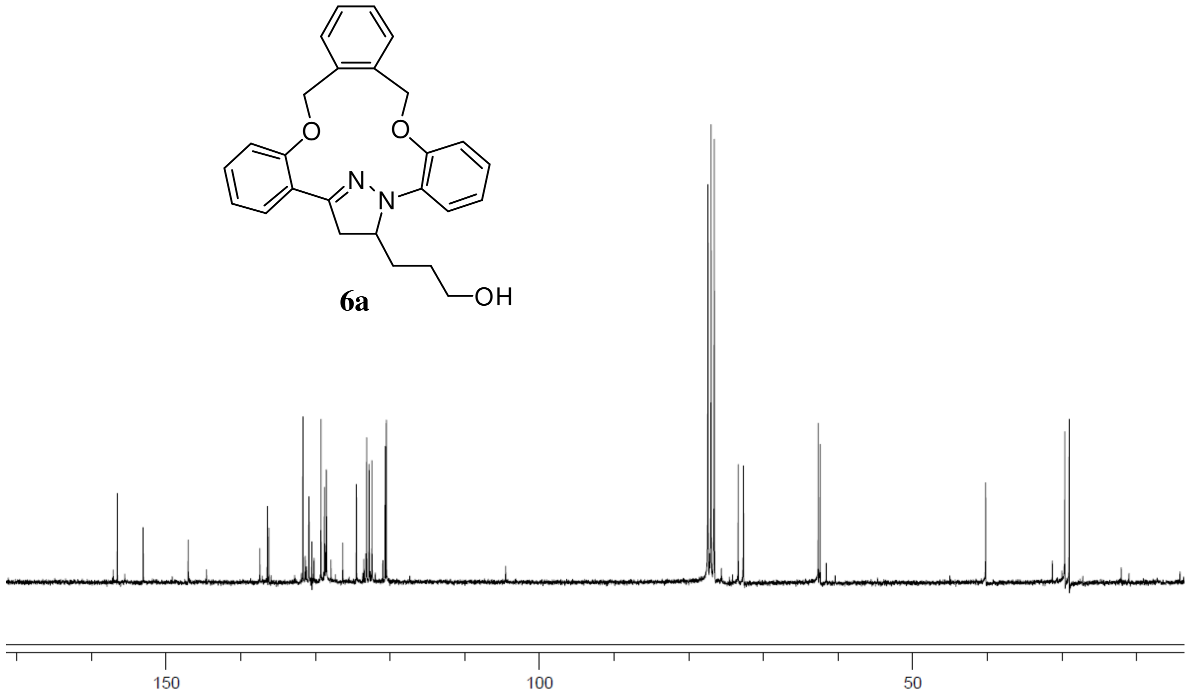

4a
O
O
N
N
OH
1.00
2.76
1.00
4.08
0.97
1.20
2.15
1.07
1.03
2.05
0.93
2.23
2.02
8.69
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

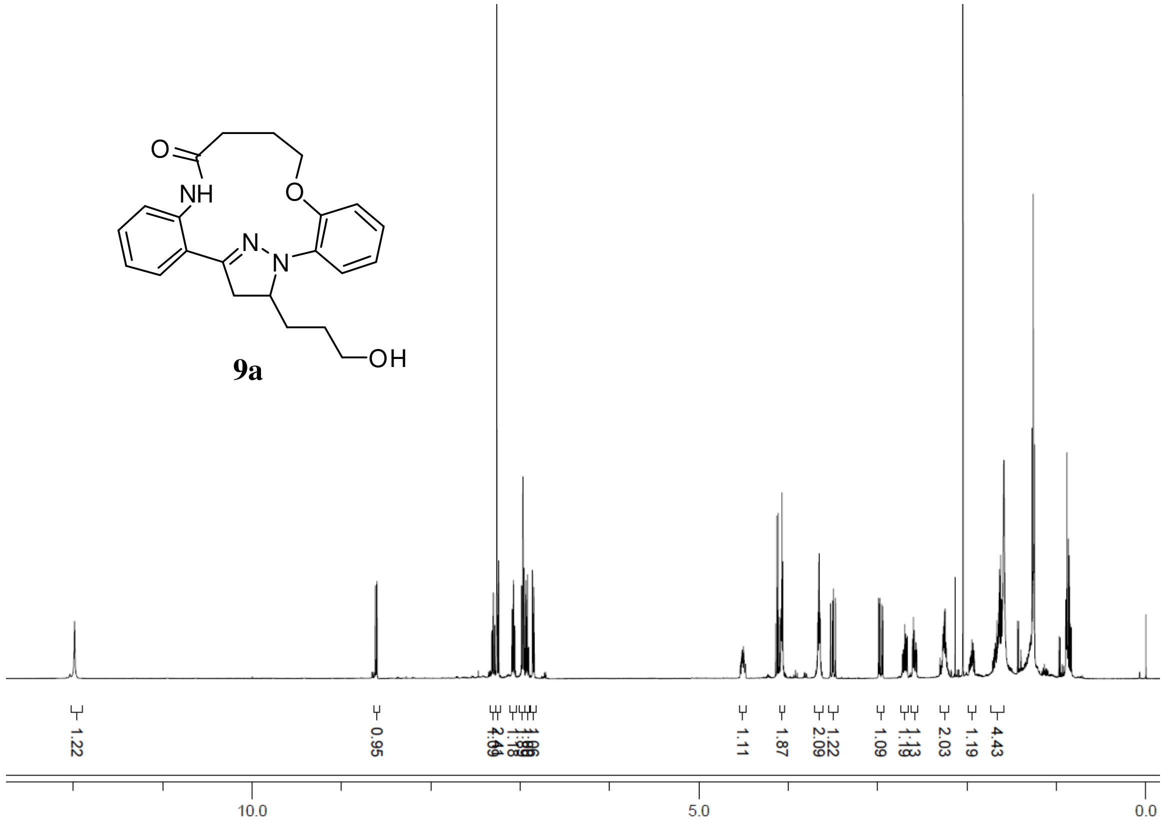

4a
O
O
N
N
OH
150
100
50


5a
O
O
N
N
OH
1.00
1.03
1.32
1.00
4.01
1.16
2.22
1.22
2.19
2.18
1.12
4.06
8.78
1.43
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


5a
O
O
N
N
OH
150
100
50

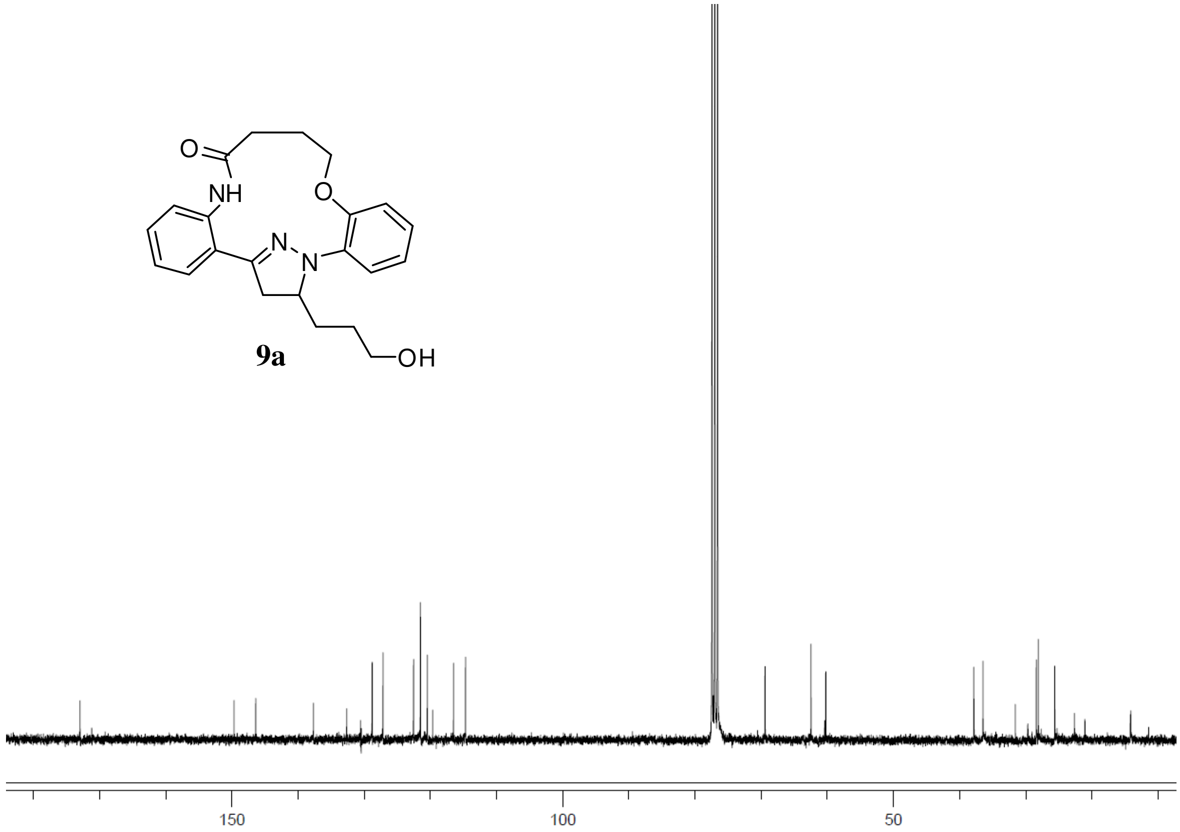

N
N
O
O
OH
6a
1.00
1.05
2.86
4.11
2.42
0.99
1.75
1.85
1.07
2.16
1.05
1.00
1.03
5.08
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


N
N
O
O
OH
6a
150
100
50



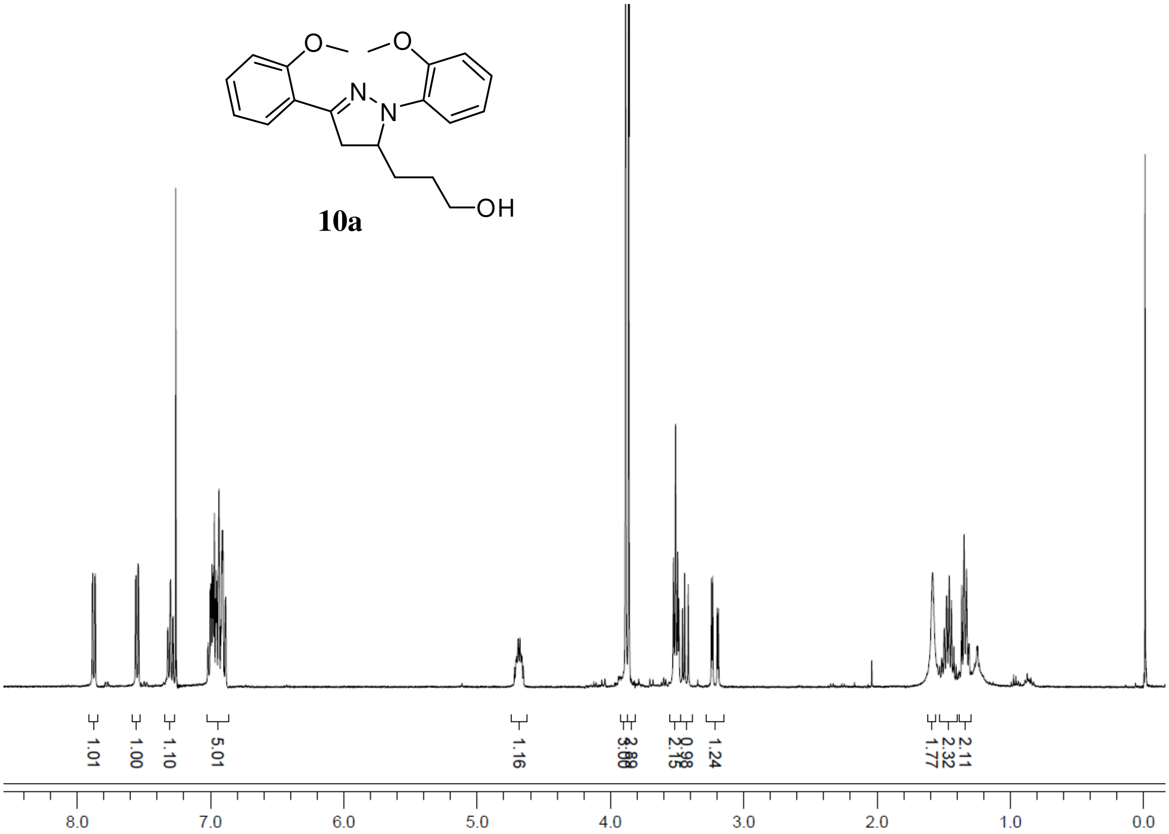
9a

O
NH
O
N
N
OH
1.22
0.95
1.18
1.11
1.87
2.09
1.22
1.09
1.13
2.03
1.19
4.43
10.0
5.0
0.0

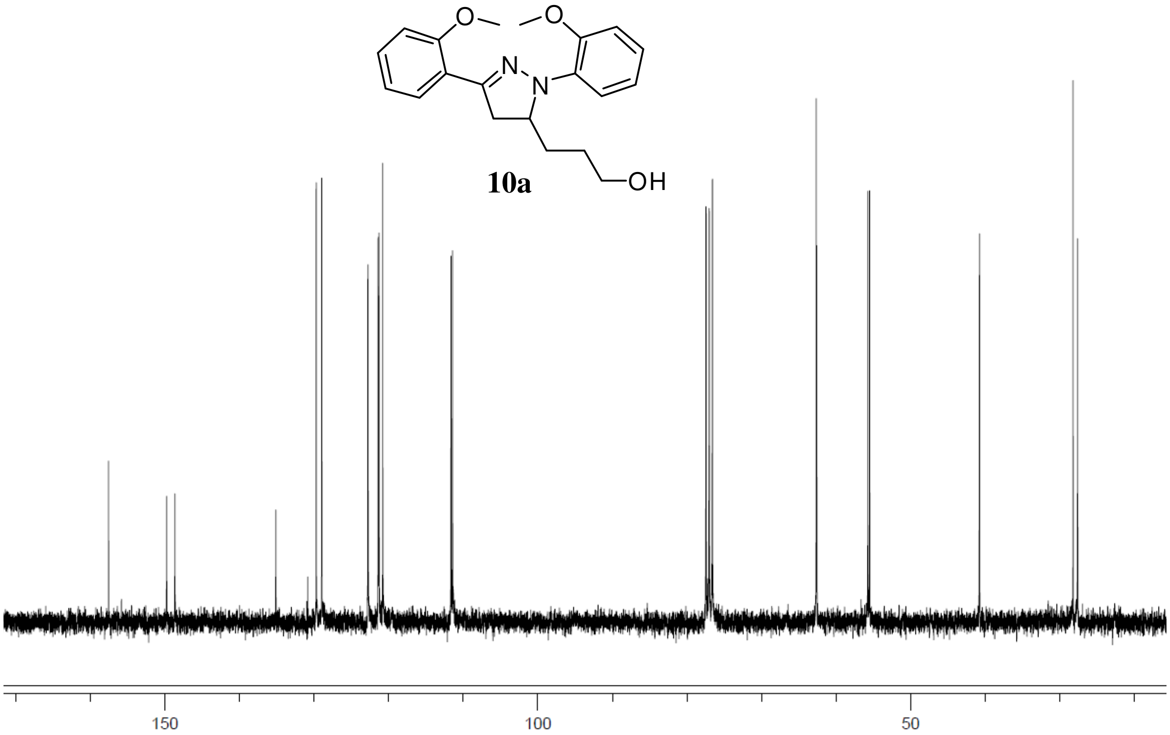


9a

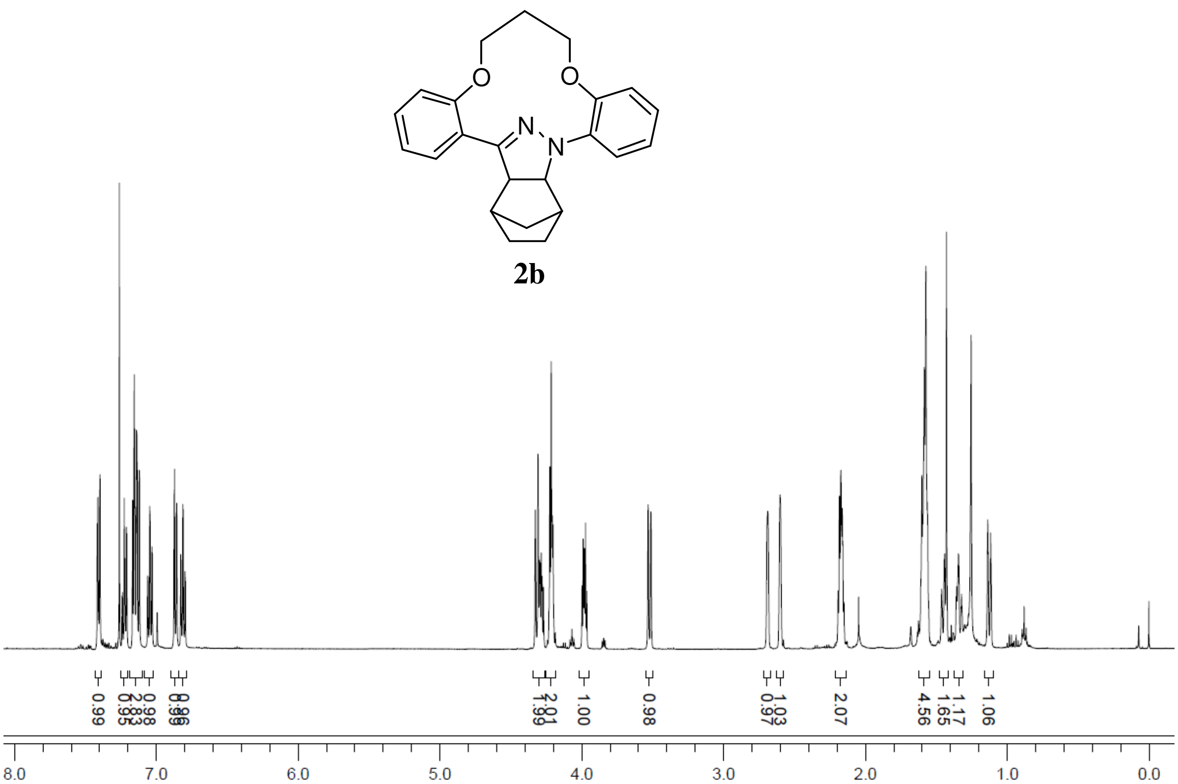
O
NH
O
N
N
OH
150
100
50


O
O
N
N
OH
1.01
1.00
1.10
5.01
1.16
3.80
3.88
2.15
0.98
1.24
1.77
2.32
2.11
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

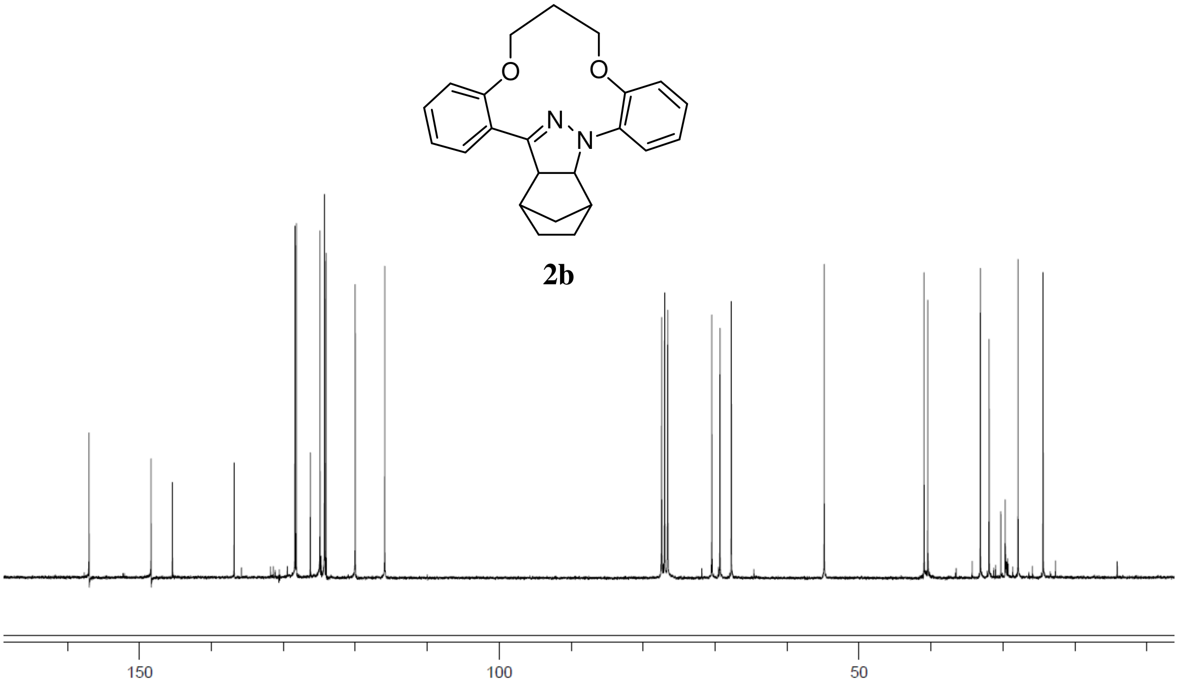
10a


O
O
N
N
OH
150
100
50

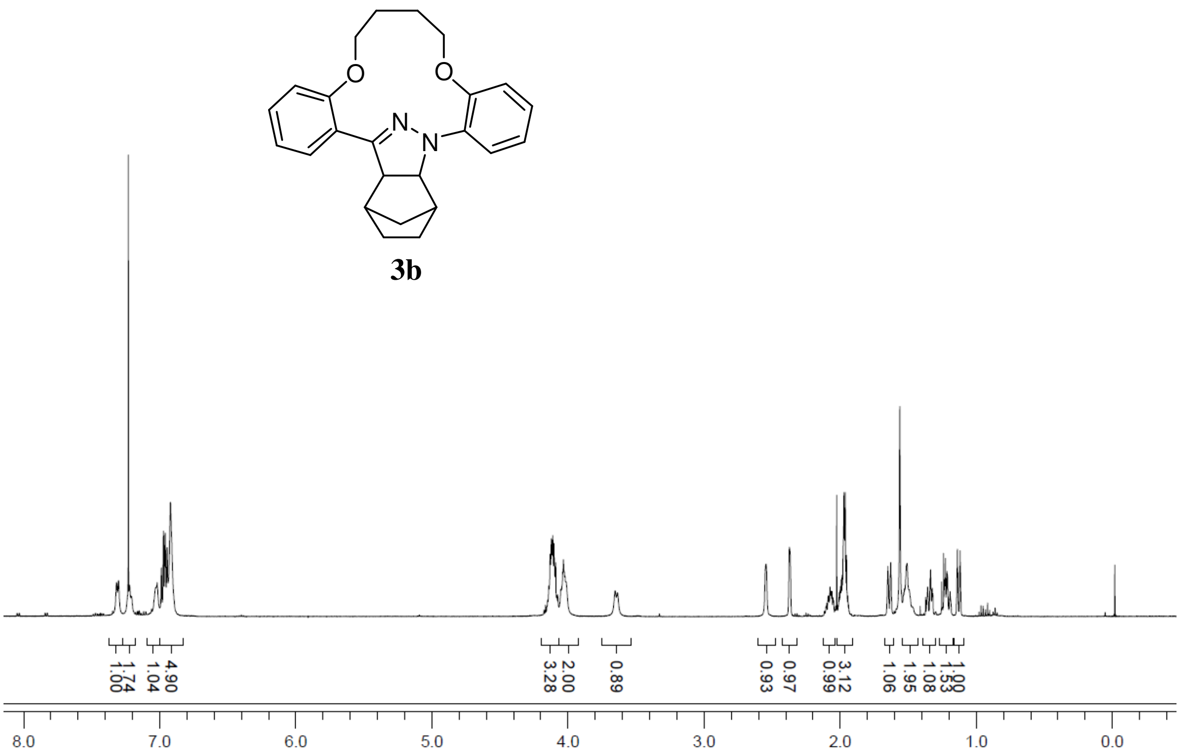
10a


O
O
N
N
0.99
0.95
2.83
0.98
0.99
0.96
1.99
2.01
1.00
0.98
0.97
1.03
2.07
4.56
1.65
1.17
1.06
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

2b


O
O
N
N
150
100
50

2b


3b
1.00
1.74
1.04
4.90
3.28
2.00
0.89
0.93
0.97
0.99
3.12
1.06
1.95
1.08
1.53
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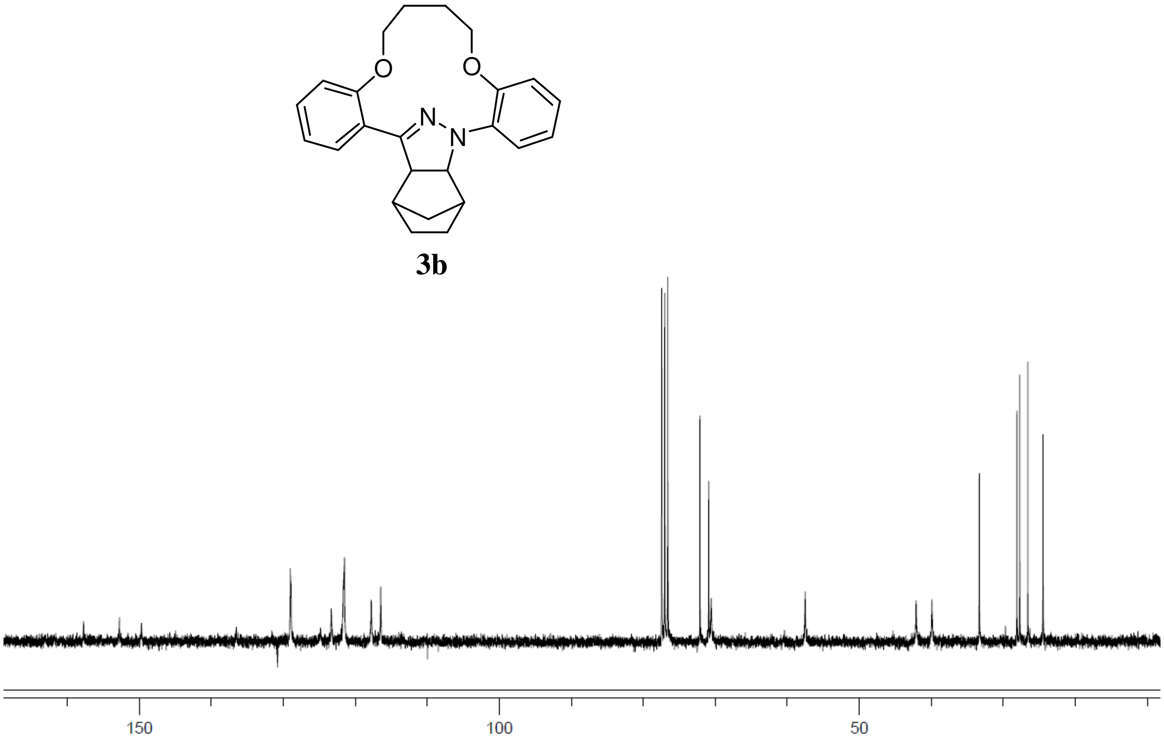
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


3b
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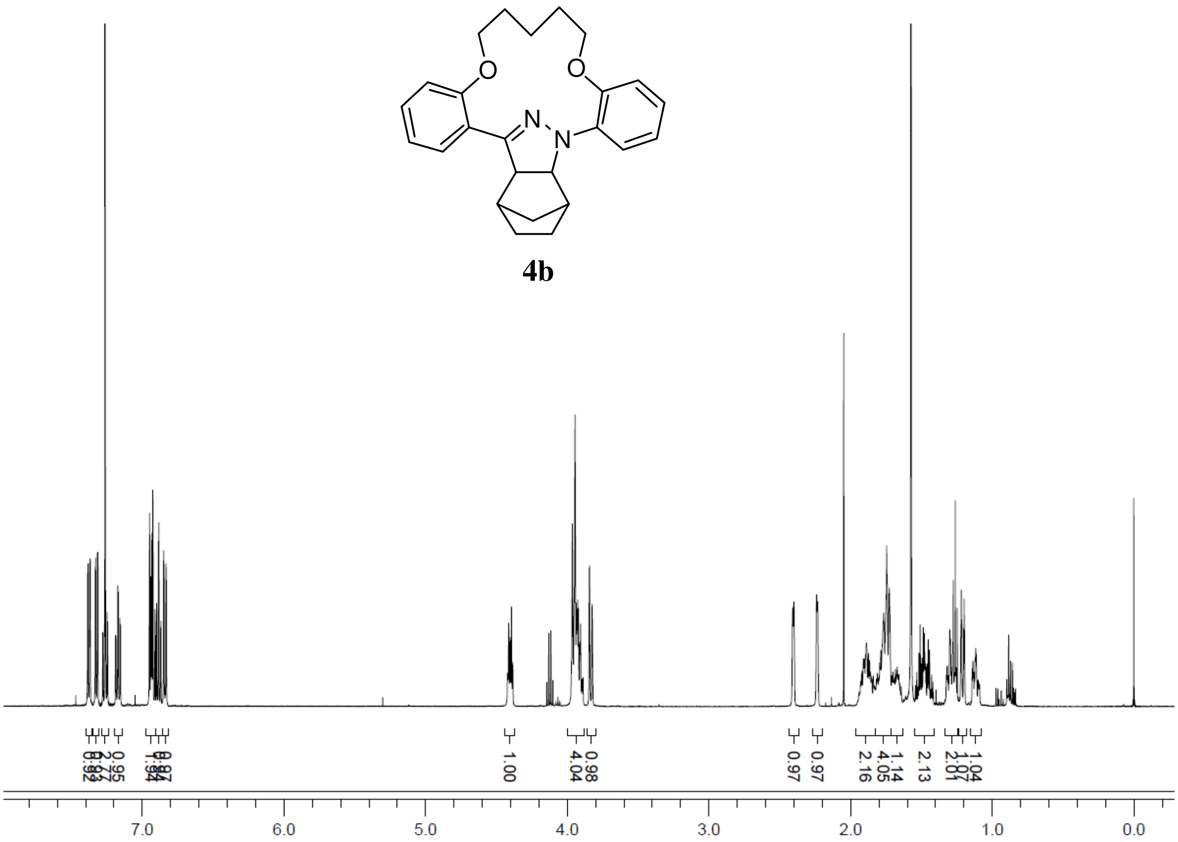
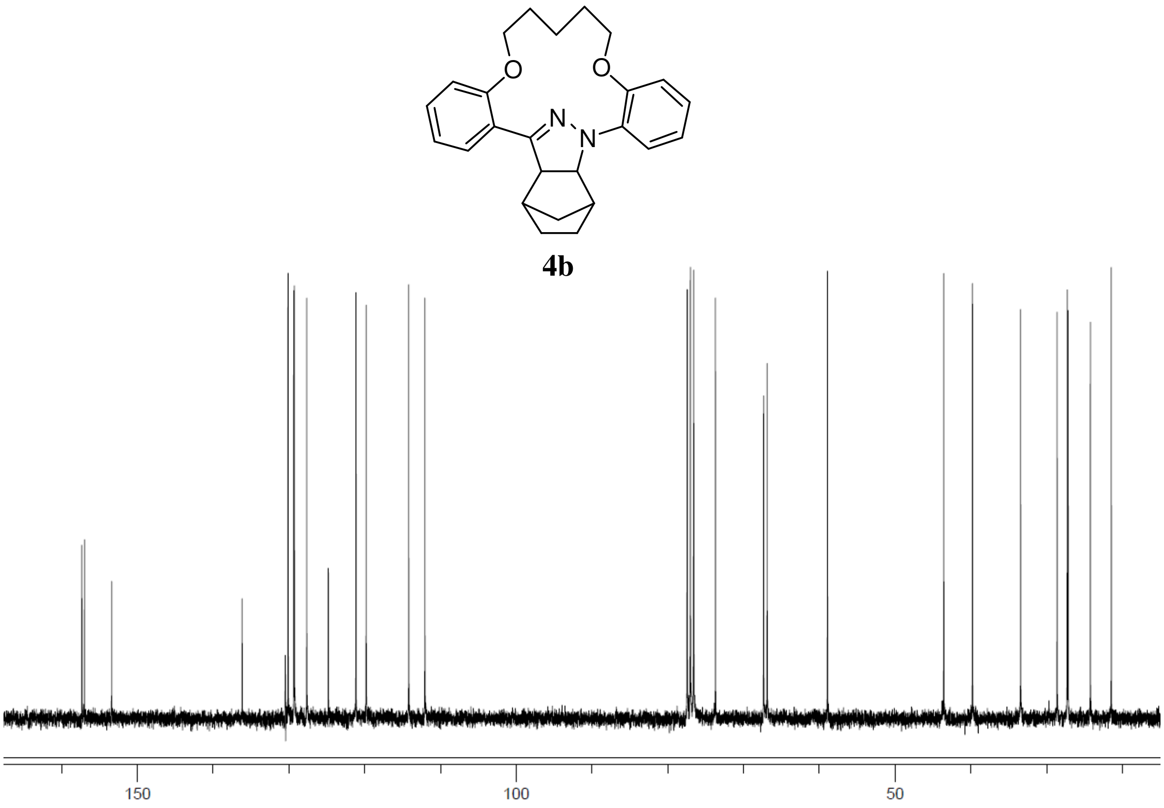


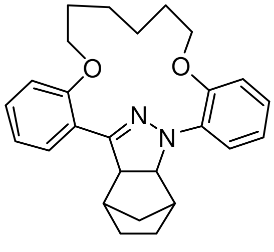
4b

1.00
4.04
0.98
0.97
0.97
2.16
4.05
1.14
2.13
2.01
2.07
1.04
0.95
1.94
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

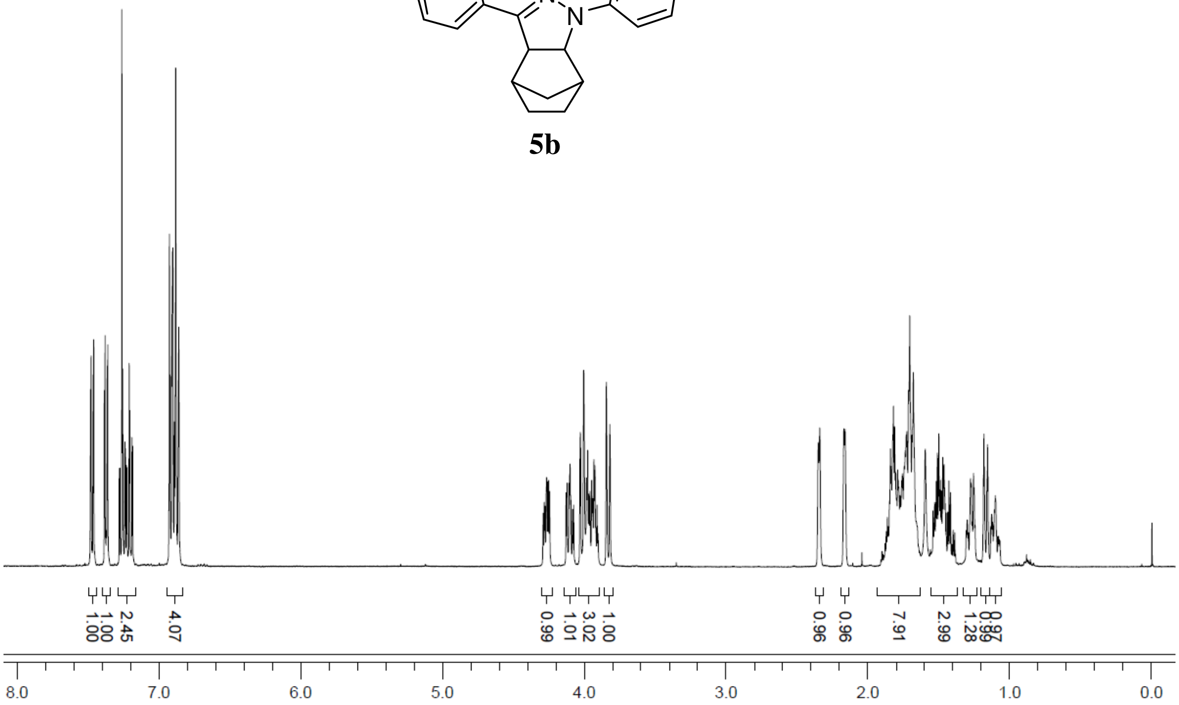


4b

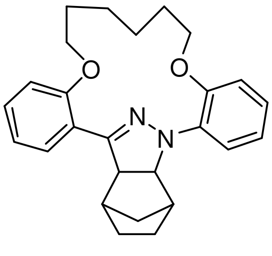
150
100
50



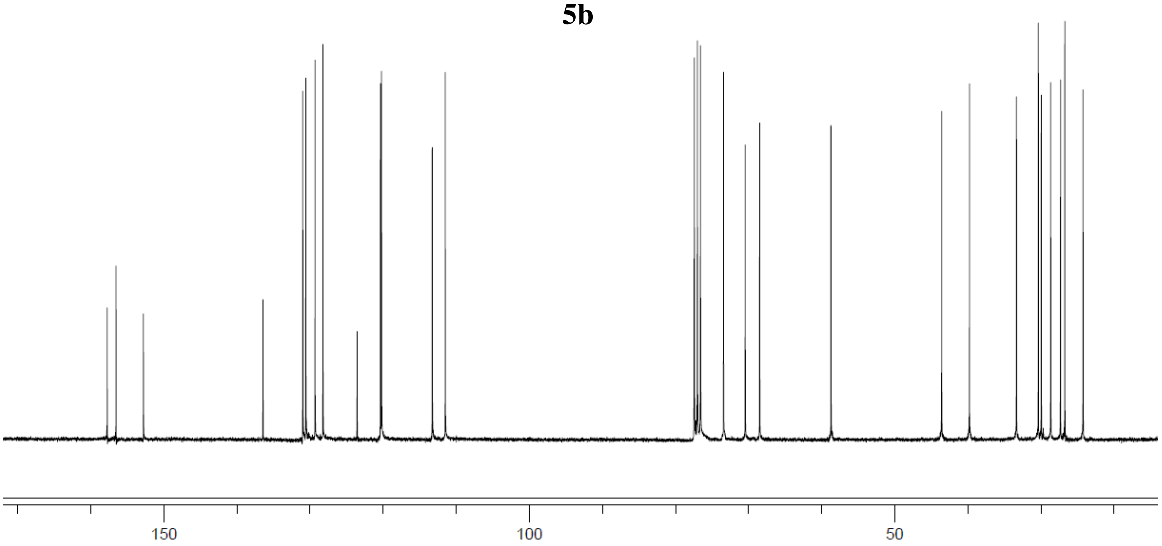
5b



1.00
1.00
2.45
4.07
0.99
1.01
3.02
1.00
0.96
0.96
7.91
2.99
1.28
0.99
0.97
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0



5b



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100
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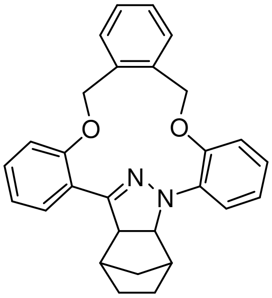
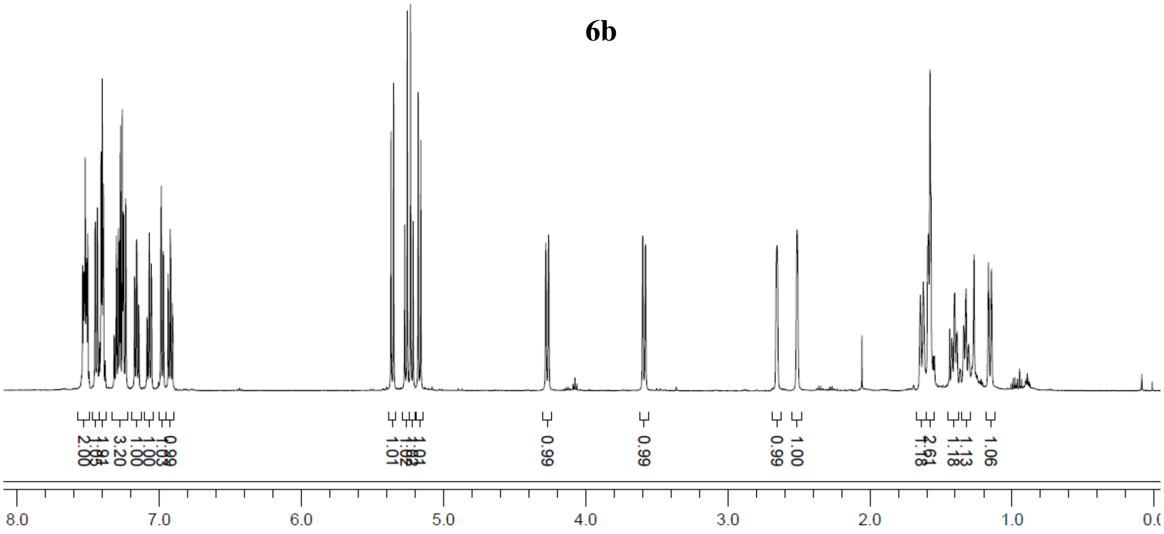
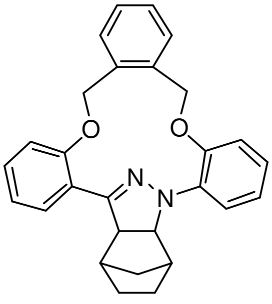


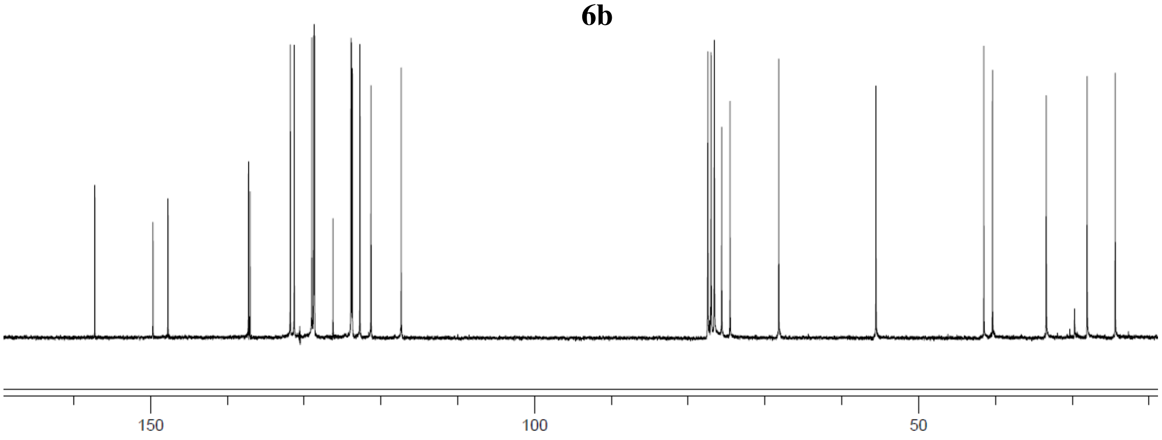
6b



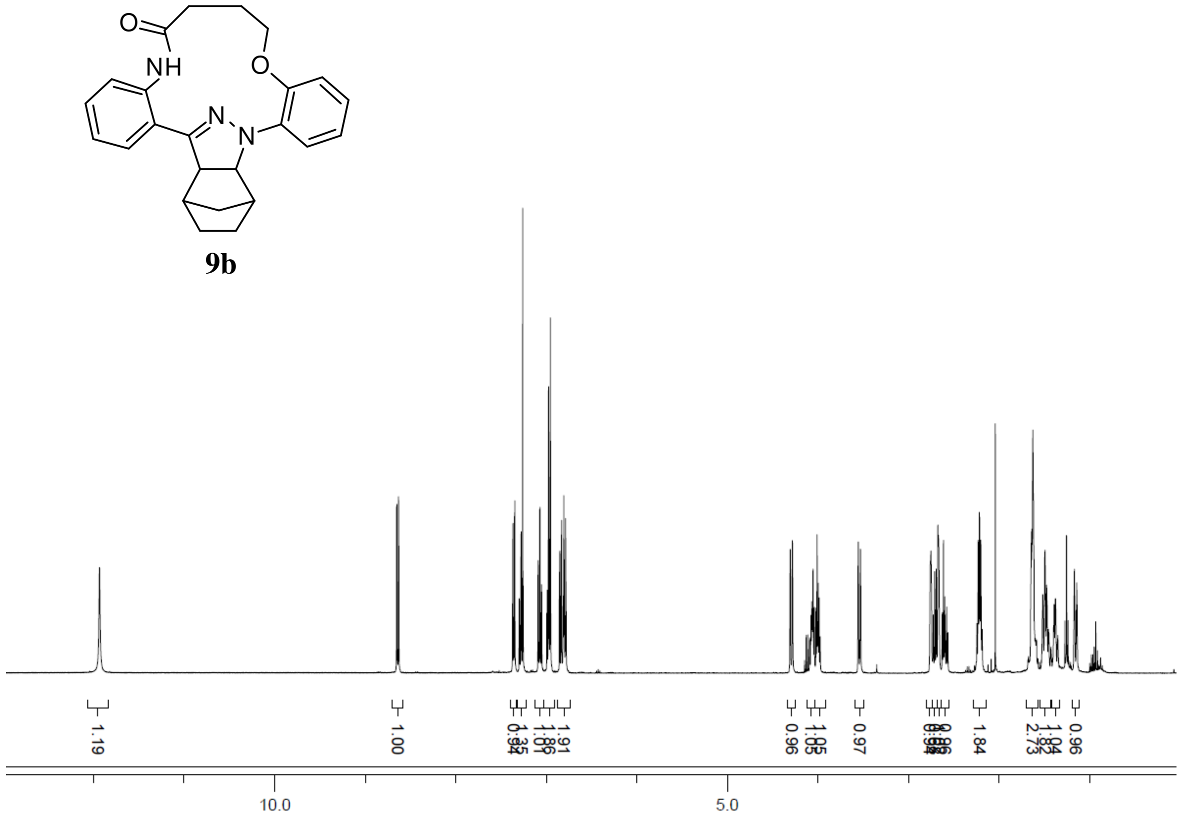
2.00
3.20
1.00
1.00
1.01
0.99
0.99
0.99
1.00
2.61
1.18
1.13
1.06
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0



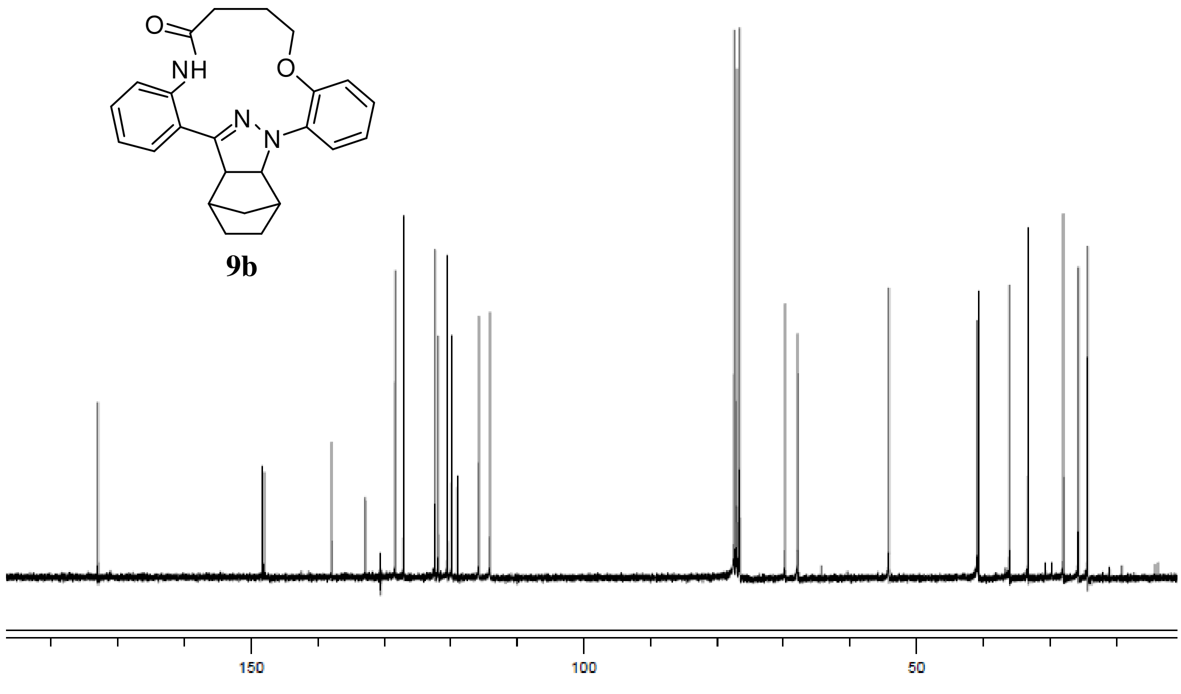
6b



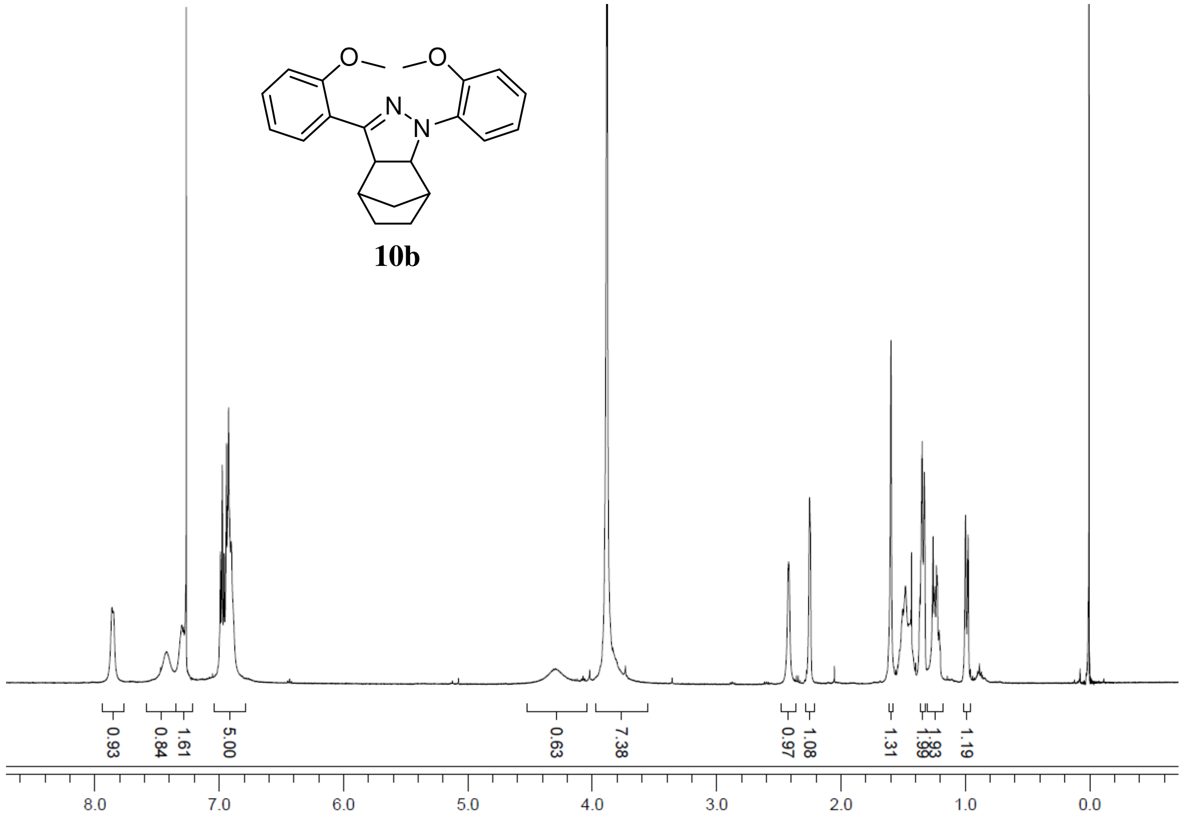
150
100
50


O
NH
O
N
N
1.19
1.00
0.94
1.35
1.01
1.86
1.91
0.96
1.05
0.97
1.84
2.73
1.32
1.04
0.96
10.0
5.0

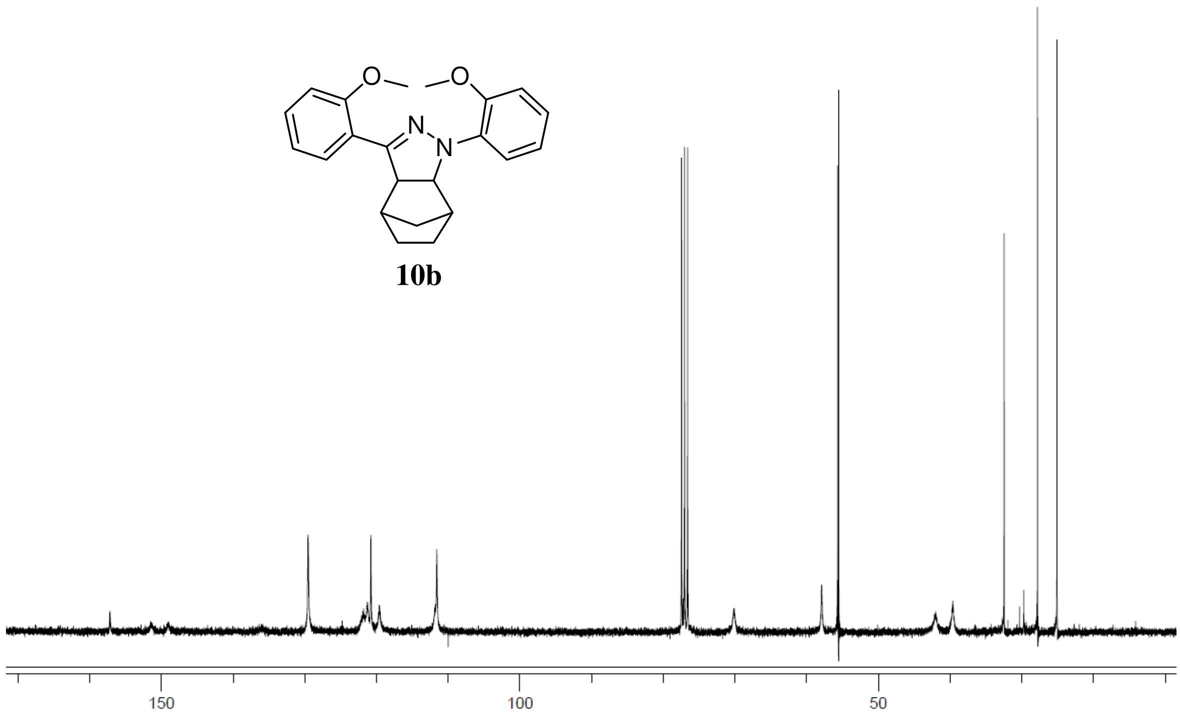
9b


O
NH
O
N
N
150
100
50

9b



10b
0.93
0.84
1.61
5.00
0.63
7.38
0.97
1.08
1.31
1.99
1.93
1.19
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0



10b
150
100
50