

Oxa-azabenzobenzocyclooctynes (O-ABCs): Heterobiaryl cyclooctynes bearing an endocyclic heteroatom

Eshani Das,^{†,b} Mark Aldren M. Feliciano,^{†,a,b} Pavel Yamanushkin,^b Xinsong Lin,^c
Brian Gold^{*,a,b}

^aDepartment of Chemistry and Biochemistry, New Mexico State University, Las Cruces, New Mexico, 88003, United States

^bDepartment of Chemistry and Chemical Biology, University of New Mexico State, Albuquerque, New Mexico, 87131, United States

^cDepartment of Chemistry and Biochemistry, Florida State University, Tallahassee, Florida, 32306, United States

*Email: bgold@nmsu.edu

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List of Abbreviations

ABC	azabenzobenzocyclooctyne
AIBN	azobisisobutyronitrile
CCl ₄	carbon tetrachloride
CuAAC	copper-catalyzed azide–alkyne cycloaddition
DIBO	dibenzocyclooctyne
DIBAC	dibenzoazacyclooctyne
DCM	dichloromethane
DMSO	dimethylsulfoxide
DIC	<i>N,N'</i> -diisopropylcarbodiimide
EDC	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
EtOAc	ethyl acetate
LiHMDS	lithium bis(trimethylsilyl)amide
IRC	intrinsic reaction coordinate
NBO	natural bonding orbital
ODIBO	oxadibenzocyclooctyne
O-ABC	oxa-azabenzobenzocyclooctyne
SM	starting material
SPAAC	strain-promoted azide–alkyne cycloaddition
THF	tetrahydrofuran
TS	transition state

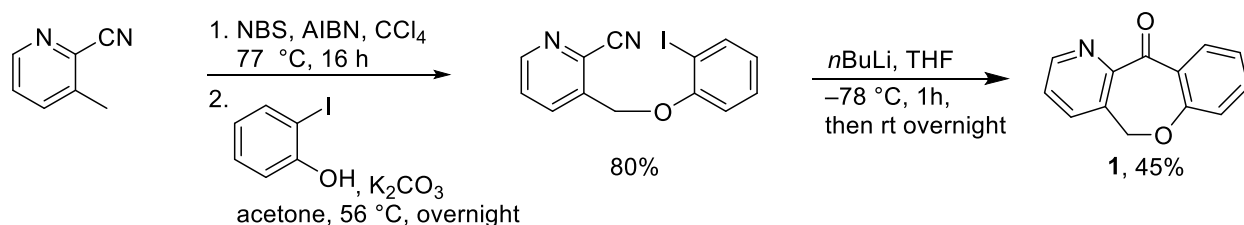
Experimental Procedures

General. All chemicals were from commercial sources and were used without further purification. NMR spectra were acquired with an Avance 500 spectrometer from Bruker (Billerica, MA, USA). ¹³C NMR spectra were registered with broadband decoupling. ¹H NMR chemical shifts were determined relative to the ¹H signals of either CDCl₃ at 7.26 ppm, acetone-*d*₆ at 2.05 ppm, or DMSO-*d*₆ at 2.50 ppm. ¹³C NMR chemical shifts were determined relative to the ¹³C signals of either CDCl₃ at 77.16 ppm, acetone-*d*₆ at 29.84 or 206.26 ppm, or DMSO-*d*₆ at 39.53 ppm. Mass spectra were acquired by using positive ionization with a G2 XS QToF mass spectrometer from Waters (Milford, MA, USA). Column chromatography was performed on a Selekt automated flash chromatography system from Biotage (Uppsala, Sweden) using prepacked, high capacity normal phase Sfär cartridges. Thin-layer chromatography was performed using TLC Silica gel 60 F₂₅₄ Plates from EMD Millipore (Burlington, MA, USA). UV-Vis spectroscopy was performed on a Cary 60 Spectrophotometer from Agilent Technologies (Santa Clara, CA, USA).

The phrase “dry [solvent]” indicates that specified commercial HPLC-grade, inhibitor-free solvents were further purified by degassing and passing consecutively through two columns filled with activated alumina on a solvent purification system from Pure Process Technology (Nashua, NH, USA). Water was purified by dual stage deionization followed by dual stage reverse osmosis.

The phrase “concentrated under reduced pressure” refers to the removal of solvents and other volatile materials using a rotary evaporator at water aspirator pressure (<20 Torr) while maintaining the water-bath temperature below 30 °C. Residual solvent was removed from samples by the vacuum (<0.1 Torr) achieved by a mechanical belt-drive oil pump.

All procedures were performed in air at ambient temperature (~21 °C) and pressure (1.0 atm) unless indicated otherwise.

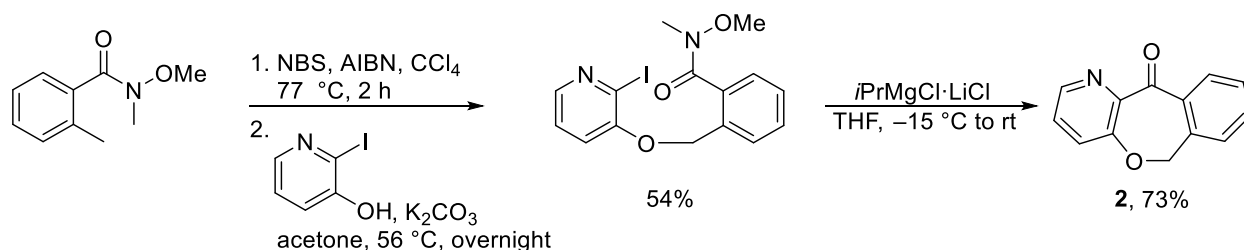


Scheme S1. Synthesis of O-ABC precursor ketone **1**.

3-((2-iodophenoxy)methyl)picolinonitrile. To a stirred solution of 3-methyl-2-pyridinecarbonitrile (3.0 g, 25.4 mmol, 1.0 equiv.) and *N*-bromosuccinimide (4.97 g, 27.9 mmol, 1.1 equiv) in CCl₄ (80 mL) was added azobisisobutyronitrile (0.42 g, 2.54 mmol, 0.1 equiv.) under irradiation with a tungsten lamp. The reaction mixture was stirred at reflux for 16 h, then cooled to room temperature, filtered and washed with CCl₄. The filtrate was concentrated under reduced pressure and the crude brominated product was subjected to the next step without further purification. The crude 3-(bromomethyl)-2-pyridinecarbonitrile (4.51 g, 22.9 mmol) and K₂CO₃ (3.48 g, 25.2 mmol, 1.1 equiv.), and 2-iodophenol (5.04 g, 22.9 mmol, 1 equiv.) were dissolved in anhydrous acetone (100 mL) and refluxed overnight. The resulting mixture was cooled to room temperature and the solvent was removed under reduced pressure. The dry residue was diluted with ethyl acetate, washed with water, dried over Na₂SO₄, filtered, concentrated under reduced pressure, then purified by flash chromatography (hexanes:EtOAc, 4:1, *R*_f = 0.22) to give 3-((2-iodophenoxy)methyl)picolinonitrile as a white solid (6.83 g, 80%); ¹H NMR (500 MHz, CDCl₃) δ 8.69 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.34 (ddt, *J* = 8.1, 1.8, 0.9 Hz, 1H), 7.82 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.63 (dd, *J* = 8.1, 4.7 Hz, 1H), 7.36 (ddd, *J* = 8.2, 7.4, 1.6 Hz, 1H), 6.96 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.81 (td, *J* = 7.6, 1.3 Hz, 1H), 5.36 (s, 2H). ¹³C NMR{¹H} (125 MHz, CDCl₃) δ 156.3, 150.3, 139.9, 137.6, 136.3, 131.7, 130.0, 127.3, 124.0, 115.5, 112.9, 86.6, 66.7. HRMS (ESI-TOF) *m/z* calcd. for C₁₃H₉IN₂NaO [M+Na]⁺ 358.9652; found, 358.9664.

benzo[6,7]oxepino[4,3-*b*]pyridin-11(5*H*)-one (1**)** was prepared via a modified Parham cyclization approach previously reported to synthesize ketone **2**.^{S1}

A stirred solution of 3-((2-iodophenoxy)methyl)picolinonitrile (3.0 g, 8.9 mmol, 1.0 equiv.) in dry THF (300 mL) was cooled under Ar(g) to -78 °C (dry ice/acetone bath), then *n*-butyllithium (2.5 M in Hexanes, 10.7 mmol, 4.3 mL, 1.2 equiv.) was added dropwise via syringe pump at a rate 24 mL/h. The reaction mixture was kept at -78 °C for 1 h, and then allowed to slowly warm to room temperature while stirring overnight. The reaction mixture was quenched using 5% HCl and stirred for an hour. The free base was obtained by adding sufficient 10% NaOH solution to turn the solution basic, and stirring for an additional hour, which was extracted with EtOAc. The solvent was then removed under reduced pressure and the dry residue was purified flash chromatography (hexanes:EtOAc 1:1, *R*_f = 0.22) to provide compound **1** as gummy white solid (0.855 g, 45% yield). ¹H NMR (500 MHz, CDCl₃) δ 8.79 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.24 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.78 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.14 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.06 (dd, *J* = 8.3, 1.2 Hz, 1H), 5.20 (s, 2H). ¹³C NMR{¹H} (125 MHz, CDCl₃) δ 190.4, 160.9, 156.5, 151.0, 136.3, 135.9, 132.4, 131.3, 126.5, 124.8, 122.5, 120.6, 71.5. HRMS (ESI-TOF) *m/z* calcd. for C₁₃H₁₀NO₂ [M+H]⁺ 212.0706; found, 212.0695.



Scheme S2. Synthesis of O-ABC-II precursor ketone **2**.

***N*-Methoxy-*N*,2-dimethylbenzamide** was prepared according to previously reported procedures.^{S2} Characterization data matched the desired compound.

2-(((2-iodopyridin-3-yl)oxy)-*N*-methoxy-*N*-methylbenzamide. To a stirred solution of *N*-methoxy-*N*,2-dimethylbenzamide (1.0 g, 5.6 mmol, 1.0 equiv.) and *N*-bromosuccinimide (1.19 g, 6.7 mmol, 1.2 equiv.) in CCl₄ (25 mL) was added azobisisobutyronitrile (0.09 g, 0.6 mmol, 0.1 equiv.) under irradiation with a tungsten lamp. The reaction mixture was stirred at reflux for 2 h, then cooled to room temperature, filtered and washed with CCl₄. The filtrate was concentrated under reduced pressure and the crude brominated product was subjected to next step without further purification. The crude 2-(bromomethyl)-*N*-methoxy-*N*-methylbenzamide (0.91 g, 3.5 mmol, 1.0 equiv.), 2-iodopyridin-3-ol (1.56 g, 7.1 mmol, 2.0 equiv.), and K₂CO₃ (1.46 g, 10.6 mmol, 3.0 equiv.) were dissolved in anhydrous acetone (20 mL) and refluxed overnight. The resulting mixture was cooled to room temperature and the solvent was removed under reduced pressure. The dry residue was diluted with ethyl acetate, washed with water, dried over Na₂SO₄, filtered, concentrated under reduced pressure, then purified by flash chromatography (EtOAc:hexanes 1:1, *R*_f = 0.27) to give 2-(((2-iodopyridin-3-yl)oxy)methyl)-*N*-methoxy-*N*-methylbenzamide as a colorless gummy solid (1.20 g, 54%). ¹H NMR (500 MHz, CDCl₃): δ 8.00 (dd, *J* = 4.5, 1.6 Hz, 1H), 7.70 – 7.68 (m, 1H), 7.50 – 7.46 (m, 1H), 7.43 – 7.37 (m, 2H), 7.17 – 7.09 (m, 2H), 5.25 (s, 2H), 3.53 (s, 3H), 3.35 (s, 3H). ¹³C NMR{¹H} (125 MHz, CDCl₃) δ 169.4, 154.4, 143.1, 133.6, 133.4, 130.2, 128.3, 128.0, 127.3, 123.7, 118.9, 112.1, 68.6, 61.5, 33.8. HRMS (ESI-TOF) *m/z* calcd. for C₁₅H₁₆N₂O₃ [M+H]⁺ 399.0200; found, 399.0181.

benzo[5,6]oxepino[3,2-*b*]pyridin-11(6*H*)-one (2**).**^{S1} To a stirred solution of 2-(((2-iodopyridin-3-yl)oxy)methyl)-*N*-methoxy-*N*-methylbenzamide (0.390 g, 0.98 mmol, 1.0 equiv.) in dry THF (20 mL), was added *i*PrMgCl·LiCl (1.3 M in THF, 1.07 mmol, 0.83 mL, 1.1 equiv.) dropwise at –15 °C. The resulting mixture was slowly allowed to warm to room temperature and was stirred for another hour. The reaction mixture was quenched with aqueous NH₄Cl, extracted with EtOAc, washed with water, dried over Na₂SO₄, filtered, concentrated under reduced pressure, and subjected to flash column chromatography (hexanes:EtOAc 1:1, *R*_f = 0.13) to provide compound **2** as light brown gummy solid (0.150 g, 73%). ¹H NMR (500 MHz, CDCl₃) δ 8.66 – 8.64 (m, 1H), 7.98 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.56 – 7.48 (m, 3H), 7.40 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.28 (s, 2H). ¹³C NMR{¹H} (125 MHz, CDCl₃) δ 189.6, 159.1, 144.3, 140.1, 139.4, 134.8, 133.4, 130.9, 130.3, 129.9, 128.9, 128.2, 74.0. HRMS (ESI-TOF) *m/z* calcd. for C₁₃H₁₀NO₂ [M+H]⁺ 212.0706; found, 212.0701.

4-((*N*-Tetrazolyl)methyl)morpholine was prepared according to previously reported procedures.^{S3} Characterization data matched the desired compound.

2-Azabenzobenzo-8-chlorobenzocyclooctyne (ABC) was prepared according to previously reported procedures.^{S3} Characterization data matched the desired compound.

11-(1H-tetrazol-5-yl)-6,11-dihydrodibenzo[*b,e*]oxepin-11-ol was prepared en route to **ODIBO** (unsubstituted) to test the compatibility of the previously reported carbene-mediated ring expansion approach^{S3,S4} with systems bearing endocyclic oxygen atoms.

A stirred solution of 4-((*N*-tetrazolyl)methyl)morpholine (0.644 g, 3.80 mmol, 2.0 equiv.) and dibenzo[*b,e*]oxepin-11(6*H*)-one (0.400 g, 1.90 mmol, 1.0 equiv.) in dry THF (15 mL) was cooled under Ar(g) to $-78\text{ }^{\circ}\text{C}$ (dry ice/acetone bath), then LiHMDS (1.0 M in THF, 4.0 mmol, 4.0 mL, 2.1 equiv.) was added dropwise. The reaction mixture was kept at $-78\text{ }^{\circ}\text{C}$ for 2 h, and then allowed to slowly warm to room temperature while stirring overnight. The reaction mixture was concentrated under reduced pressure, and the remaining residue was treated with aqueous HCl (1.0 M, 25 mL) and stirred at room temperature for 1 h. The solution was then extracted with EtOAc and the combined organic extracts were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The dry residue was subjected to flash column chromatography (hexanes:EtOAc 1:1, $R_f = 0.14$) to provide title compound as white gummy solid (0.426 g, 80%). **¹H NMR** (500 MHz, Acetone) δ 8.11 (dd, $J = 7.8, 1.5$ Hz, 1H), 7.92 (dd, $J = 7.9, 1.7$ Hz, 1H), 7.39 – 7.29 (m, 3H), 7.17 – 7.14 (m, 2H), 7.01 (dd, $J = 8.0, 1.3$ Hz, 1H), 5.46 (d, $J = 14.8$ Hz, 1H), 4.97 (d, $J = 14.8$ Hz, 1H). **¹³C NMR{¹H}** (125 MHz, Acetone) δ 162.7, 156.0, 141.1, 137.0, 135.9, 130.7, 129.3, 128.2, 128.0, 127.1, 126.0, 124.2, 122.1, 73.3, 72.3. **HRMS** (ESI-TOF) m/z calcd. for C₁₅H₁₁N₄O₂ [M-H]⁻ 279.0887; found, 279.0887.

ODIBO. A stirred solution of 11-(1H-tetrazol-5-yl)-6,11-dihydrodibenzo[*b,e*]oxepin-11-ol (0.360 g, 1.28 mmol, 1.0 equiv.) in dry THF (30 mL) was treated with EDC (0.270 g, 1.41 mmol, 1.1 equiv.) and allowed to react overnight. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography (hexanes:EtOAc 9.7:0.3, $R_f = 0.2$) to provide ODIBO as yellow gummy solid (0.243 g, 90%). **¹H NMR** (500 MHz, CDCl₃) δ 7.43 – 7.36 (m, 2H), 7.32 – 7.23 (m, 4H), 7.20 – 7.18 (m, 1H), 7.11 – 7.08 (m, 1H), 5.28 (d, $J = 12.0$ Hz, 1H), 4.55 (d, $J = 12.0$ Hz, 1H). **¹³C NMR{¹H}** (125 MHz, CDCl₃) δ 169.9, 147.2, 130.3, 129.4, 129.1, 128.0, 127.1, 126.4, 125.9, 124.0, 122.2, 118.0, 114.3, 111.7, 78.0. **HRMS** (ESI-TOF) m/z calcd. for C₁₅H₁₁O [M+H]⁺ 207.0804; found, 207.0806.

11-(1H-tetrazol-5-yl)-5,11-dihydrobenzo[6,7]oxepino[4,3-*b*]pyridin-11-ol (1'). A stirred solution of 4-((*N*-tetrazolyl)methyl)morpholine (0.530 g, 3.13 mmol, 2.0 equiv.) and benzo[6,7]oxepino[4,3-*b*]pyridin-11(5*H*)-one **1** (0.330 g, 1.56 mmol, 1.0 equiv.) in dry THF (10 mL), was cooled under Ar(g) to $-78\text{ }^{\circ}\text{C}$ (dry ice/acetone bath), then LiHMDS (1.0 M in THF, 3.3 mmol, 3.3 mL, 2.1 equiv.) was added dropwise. The reaction mixture was kept at $-78\text{ }^{\circ}\text{C}$ for 2 h, and then allowed to slowly warm to room temperature while stirring overnight. The reaction mixture was concentrated under reduced pressure, and the remaining residue was treated with aqueous HCl (1.0 M, 20 mL) and stirred at room temperature for 1 h. The solution was then extracted with EtOAc and the combined organic extracts were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The dry residue was subjected to flash column chromatography (DCM:MeOH 9:1, $R_f = 0.15$) to provide compound **1'** as light brown gummy solid (0.297 g, 1.06 mmol, 67%). **¹H NMR** (500 MHz, Acetone) δ 8.57 – 8.55 (m, 1H), 7.96 (dd, $J = 7.8, 1.7$ Hz, 1H), 7.76 – 7.73 (m, 1H), 7.55 – 7.53 (m, 2H), 7.40 (td, $J = 7.7, 1.7$ Hz, 1H), 7.25 (td, $J = 7.6, 1.2$ Hz, 1H), 7.10 (dd, $J = 8.0, 1.2$ Hz, 1H), 5.49 (d, $J = 15.8$ Hz, 1H), 5.07 (d, $J = 15.8$ Hz, 1H); **¹³C NMR{¹H}** (125 MHz, Acetone) δ 162.2, 156.1, 153.8, 146.2, 137.4, 136.9, 133.1, 131.4, 126.8, 125.5, 125.3, 122.6, 72.1, 71.3; **HRMS** (ESI-TOF) m/z calcd. for C₁₄H₁₀N₅O₂ [M-H]⁻ 280.0840; found, 280.0844.

11-(1H-tetrazol-5-yl)-6,11-dihydrobenzo[5,6]oxepino[3,2-*b*]pyridin-11-ol (2'). A stirred solution of 4-((*N*-tetrazolyl)methyl)morpholine (0.160 g, 0.95 mmol, 2.0 equiv.) and benzo[5,6]oxepino[3,2-*b*]pyridin-11(6*H*)-one **2** (0.100 g, 0.47 mmol, 1.0 equiv.) in dry THF (5 mL), was cooled under Ar(g) to $-78\text{ }^{\circ}\text{C}$ (dry ice/acetone bath), then LiHMDS (1.0 M in THF, 1.0 mmol, 1.0 mL, 2.1 equiv.) was added dropwise. The reaction mixture was kept at $-78\text{ }^{\circ}\text{C}$ for 2 h, and then allowed to slowly

warm to room temperature while stirring overnight. The reaction mixture was concentrated under reduced pressure, and the remaining residue was treated with aqueous HCl (1.0 M, 10 mL) and stirred at room temperature for 1 h. The solution was then extracted with EtOAc and the combined organic extracts were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The dry residue was subjected to flash column chromatography (DCM:MeOH 9:1, *R_f* = 0.15) to provide compound **2'** as light brown gummy solid (0.085 g, 64%). ¹H NMR (500 MHz, CDCl₃) δ 9.57 (brs, 2H), 8.15 – 8.07 (m, 2H), 7.36 – 7.20 (m, 5H), 5.67 (d, *J* = 13.7 Hz, 1H), 4.80 (d, *J* = 13.7 Hz, 1H). ¹³C NMR{¹H} (125 MHz, CDCl₃) δ 162.4, 153.8, 141.6, 139.9, 139.4, 133.1, 131.1, 129.8, 129.8, 129.7, 126.4, 125.8, 72.3, 71.3. HRMS (ESI-TOF) *m/z* calcd. for C₁₄H₁₂N₅O₂ [M+H]⁺ 282.0986; found, 282.0972.

6-oxa-2-azabenzobenzocyclooctyne (O-ABC). A stirred solution of **1'** (0.025 g, 0.089 mmol, 1.0 equiv.) in DCM (25 mL) under Ar(g) was treated with DIC (0.0151 mL, 0.098 mmol, 1.1 equiv.). The resulting solution was stirred at room temperature for 16 h, protected from light. After completion of reaction, as monitored by TLC, silica gel was added and solvent was removed under reduced pressure. The silica-bound residue was immediately subjected to flash chromatography. DMSO-*d*₆ (0.6 mL) was added to the combined fractions containing O-ABC (~25 mL). The mobile phase (hexanes:EtOAc 4:1, *R_f* = 0.20) was then removed under reduced pressure while protecting the compound from light. The flask was charged with Ar(g) before removing the residual mobile phase under high vacuum for 30 mins, affording a pure solution of O-ABC. 1,3,5-Trimethoxybenzene (0.1 mL, 10 mg/mL) was added as an internal standard to 0.4 mL of O-ABC solution and relative proton intensities enabled determination of the yield (6%). ¹H NMR (500 MHz, DMSO) δ 8.59 (dd, *J* = 5.0, 1.7 Hz, 1H), 7.97 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.28 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.23 (td, *J* = 7.5, 1.2 Hz, 1H), 5.42 (d, *J* = 12.5 Hz, 1H), 4.50 (d, *J* = 12.5 Hz, 1H). ¹³C NMR{¹H} (125 MHz, DMSO) δ 169.9, 149.8, 146.1, 143.2, 137.8, 130.4, 127.2, 124.3, 122.6, 122.2, 115.8, 115.0, 111.4, 76.0. HRMS (ESI-TOF) *m/z* calcd. for C₁₄H₁₀N₅O₂ [M+H]⁺ 208.0757; found, 208.0757.

3-benzyl-3,8-dihydrobenzo[7,8][1,2,3]triazolo[4',5':5,6]oxocino[4,3-*b*]pyridine (**3**).

Procedure A. A stirred solution of **1'** (0.015 g, 0.053 mmol, 1 equiv.) in DCM (10 mL) under Ar(g) was treated with DIC (0.009 mL, 0.059 mmol, 1.1 equiv.), followed by benzyl azide (0.021 g, 0.16 mmol, 3 equiv.). The resulting solution was stirred at room temperature for 16 h, protected from light. The reaction mixture was concentrated under reduced pressure and was subjected to flash chromatography (EtOAc:hexanes 4:1, *R_f* = 0.32) to afford the cycloadduct as an amorphous white solid (0.005 g, 30%).

Procedure B. Immediately following isolation of O-ABC via flash column chromatography, a solution was prepared in DMSO-*d*₆ as described above, and 1,3,5-trimethoxybenzene was added as an internal standard (0.001 g, 0.0059 mmol) in order to determine the concentration. To this solution of O-ABC (6.4 μM, 0.5 mL, 0.0032 mmol, 1 equiv.) was added benzyl azide (0.00047 g, 0.0035 mmol, 1.1 equiv.). Within minutes, the alkyne had quantitatively formed the triazole product, as determined by ¹H NMR.

Crystals for X-ray diffraction were obtained by dissolving ~5 mg of the obtained solid in DCM, followed by 3–4 drops of HPLC-grade hexanes. ¹H NMR (500 MHz, CDCl₃) δ 8.73 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.83 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.70 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.30 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.20 (ddd, *J* = 8.7, 7.2, 1.8 Hz, 1H), 7.18 – 7.13 (m, 3H), 7.06 – 7.00 (m, 3H), 6.94 (dd, *J* = 8.3, 1.3 Hz, 1H), 5.93 (s, 2H), 5.05 (s, 2H); ¹³C NMR{¹H} (125 MHz, CDCl₃) δ 154.6, 150.0, 147.9, 145.5, 138.5, 135.8, 133.4, 133.0, 130.7, 129.9, 128.6, 128.1, 127.7, 124.0, 122.4, 120.5, 117.9, 69.3, 52.9; HRMS (ESI-TOF) *m/z* calcd. for C₂₁H₁₇N₄O [M+H]⁺ 341.1397; found, 341.1392.

3-benzyl-3,9-dihydrobenzo[6,7][1,2,3]triazolo[4',5':4,5]oxocino[3,2-*b*]pyridine (4**).** To a stirred solution of 11-(1*H*-tetrazol-5-yl)-6,11-dihydrobenzo[5,6]oxepino[3,2-*b*]pyridin-11-ol **3'** (0.026 g,

0.09 mmol, 1.0 equiv.) in dry THF (30 mL) was added EDC (0.020 g, 0.10 mmol, 1.1 equiv.), followed by benzyl azide (0.037 g, 0.28 mmol, 3.0 equiv.). The resulting mixture was allowed to stir at room temperature overnight. The reaction mixture was concentrated under reduced pressure and was subjected to flash chromatography (hexanes:EtOAc, 4:1, $R_f = 0.16$) to provide the cycloadduct as an amorphous white solid (0.017 g, 53%). Crystals for X-ray diffraction were obtained by dissolving ~5 mg of the obtained solid in DCM, followed by 3–4 drops of HPLC-grade hexanes. $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.31 (dd, $J = 4.5, 1.5$ Hz, 1H), 7.81 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.51 – 7.44 (m, 2H), 7.41 – 7.38 (m, 1H), 7.24 – 7.21 (m, 4H), 7.14 – 7.08 (m, 3H), 5.97 (s, 2H), 5.10 (s, 2H). $^{13}\text{C NMR}\{^1\text{H}\}$ (125 MHz, CDCl_3) δ 153.3, 144.2, 142.5, 136.0, 134.0, 132.9, 132.4, 132.2, 130.6, 129.9, 129.6, 129.5, 129.2, 128.7, 128.2, 127.8, 124.9, 70.7, 53.4. **HRMS** (ESI-TOF) m/z calcd. for $\text{C}_{21}\text{H}_{17}\text{N}_4\text{O}$ $[\text{M}+\text{H}]^+$ 341.1397; found, 341.1379.

3-benzyl-11-chloro-8,9-dihydro-3H-benzo[5,6][1,2,3]triazolo[4',5':7,8]cycloocta[1,2-b]pyridine (5). To a solution of ABC (0.015 g, 0.063 mmol, 1.0 equiv.) in 1 mL CH_3CN was added benzyl azide (0.0092 g, 0.069 mmol, 1.1 equiv.). Upon completion of the reaction, the solvent was removed under reduced pressure and the dry residue was purified by flash chromatography (hexanes:EtOAc 1:1, $R_f = 0.76$), affording the pure cycloadduct as an amorphous white solid (0.0198 g, 85%). Crystals for X-ray diffraction were obtained by dissolving ~5 mg of the obtained solid in DCM, followed by 3–4 drops of HPLC-grade hexanes. $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.54 (d, $J = 4.7$ Hz, 1H), 7.49 (dd, $J = 13.6, 8.1$ Hz, 2H), 7.21 – 7.12 (m, 6H), 7.01 – 6.95 (m, 2H), 5.84 (s, 2H), 3.02 (t, $J = 6.9$ Hz, 2H), 2.82 (t, $J = 7.0$ Hz, 2H). $^{13}\text{C NMR}\{^1\text{H}\}$ (126 MHz, CDCl_3) δ 147.7, 145.7, 145.7, 139.9, 138.8, 136.4, 135.7, 134.2, 133.3, 132.7, 130.0, 128.8, 128.6, 128.1, 127.7, 126.8, 123.8, 52.8, 34.2, 33.3. **HRMS** (ESI-TOF) m/z calcd. for $\text{C}_{22}\text{H}_{17}\text{N}_4\text{Cl}$ $[\text{M}+\text{H}]^+$ 373.1214; found, 373.1207.

Competition Experiment

Immediately following isolation of O-ABC via flash column chromatography, a solution was prepared in DMSO- d_6 as described above. To a 400 μL of O-ABC solution, 1,3,5-trimethoxybenzene (100 μL , 1 mg/mL) was added as an internal standard in order to determine the concentration. To this solution of O-ABC (determined to be 4.4 mM, 0.5 mL, 2.2 μmol , 1.0 equiv.), 524 μL of ABC (2.2 μmol , 1.0 equiv.) was added from a stock solution (4.2 mM) in DMSO- d_6 and the ratio was determined to be 1:1 by ^1H NMR. 103 μL of benzyl azide was added from a stock solution (15 mM) in DMSO- d_6 and the reaction mixture was allowed to run to completion. Analysis by ^1H NMR (Figure S1) indicated complete consumption of benzyl azide and an 8.4:1 ratio of cycloadducts **3** : **5** (integration values of 1.94 : 0.23, relative to 1,3,5-trimethoxybenzene).

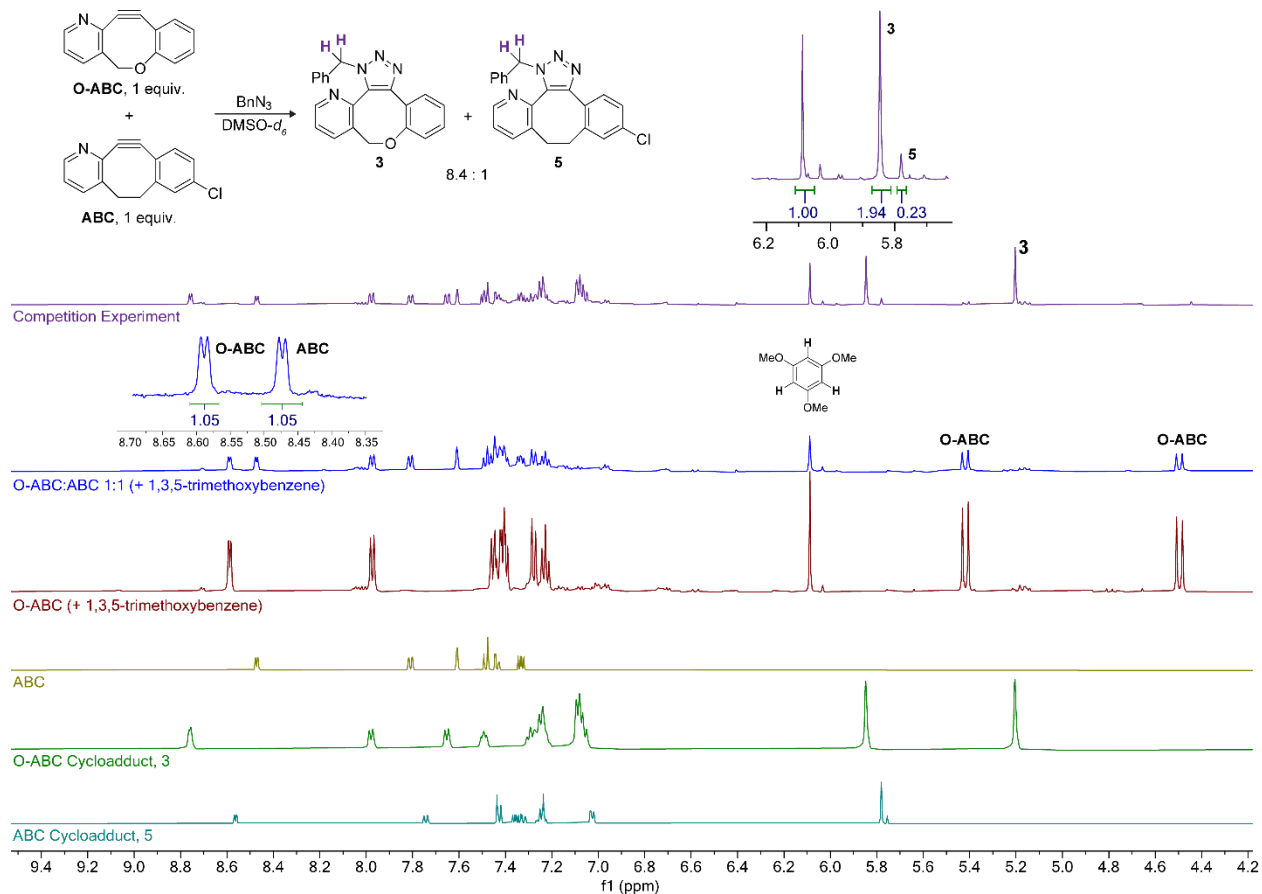


Figure S1. The rate of the SPAAC between O-ABC and benzyl azide was estimated in a competition experiment against ABC in DMSO- d_6 . Experimental details are described above. The top three spectra correspond to the competition experiment (inset: integration of cycloadducts relative to trimethoxybenzene), determination of O-ABC:ABC ratio prior to addition of benzyl azide (inset: integration values 1.05:1.05, relative to 1,3,5-trimethoxybenzene), and O-ABC with 1,3,5-trimethoxybenzene (internal standard). The bottom three spectra are provided for reference.

Kinetic Analysis

The rate constant of the reaction between ABC and benzyl azide was determined by UV-Vis spectroscopy by following the decay of the characteristic 320 nm absorbance of ABC. The cycloaddition reaction was performed in DMSO at 25 °C under pseudo-first order conditions, using 10-fold excess of azide. Stock solutions of ABC (0.04 mM in DMSO) and benzyl azide (1.6 mM in DMSO) were prepared and mixed in a 1.0 mL cuvette (0.5 mL each), which was inverted three times and inserted into the spectrophotometer. The initial concentrations at the outset of the reaction were 0.04 mM and 0.4 mM for ABC and benzyl azide, respectively. A spectrum was acquired every 10 seconds for 1200 seconds. Reaction velocity was determined from the inverse of the slope of a semilog plot of absorbance as a function of time and the slope was used to calculate a pseudo-first-order rate constant (k') for the reaction (Figure S3), which was converted to a second-order rate constant ($k = k'/[\text{BnN}_3]$) as the mean \pm SD from triplicate measurements.

The rate constant for the cycloaddition reaction between ABC and benzyl azide in DMSO was found to be $k = 0.6 \pm 0.003 \text{ M}^{-1}\text{s}^{-1}$.

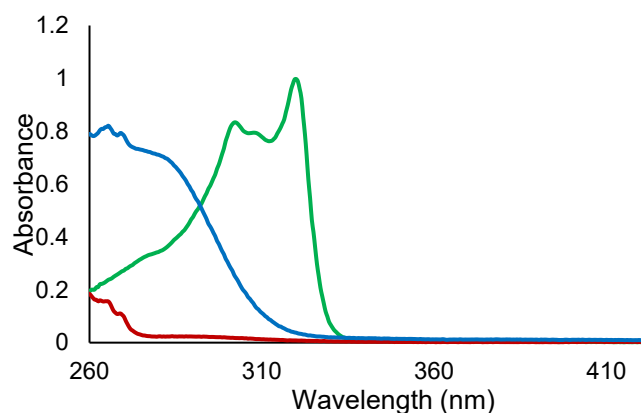


Figure S2. Ultraviolet spectra of ABC (green), benzyl azide (red), and cycloadduct 5 (blue) in DMSO at 1.6 mM.

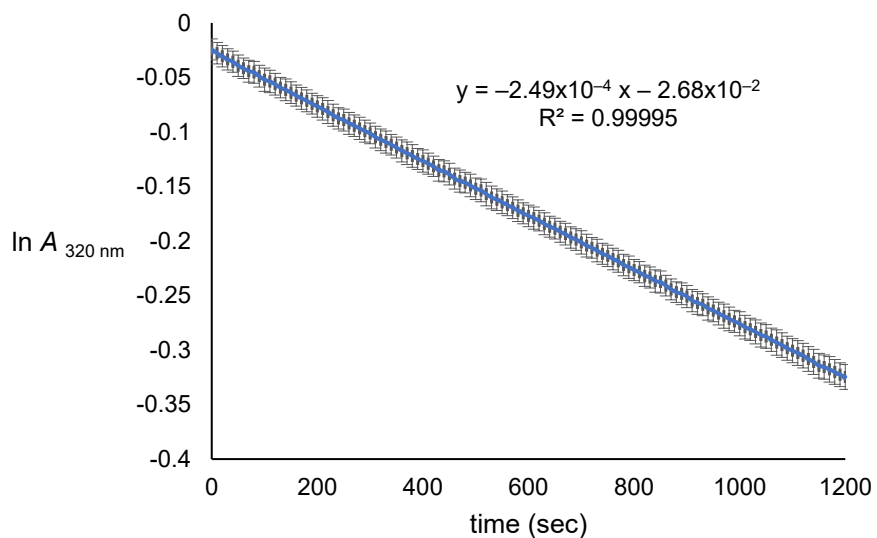


Figure S3. Kinetic plot of the reaction in triplicate of ABC with BnN_3 . Data were fitted by linear regression.

X-Ray Crystallography

Crystals for X-ray diffraction were obtained by dissolving ~5 mg of 3, 4, or 5 in DCM, followed by 3–4 drops of HPLC-grade hexanes. Details regarding diffraction data collection and each structure are provided below. This work made use of the Rigaku Synergy-S single-crystal X-ray diffractometer, which was acquired through the NSF MRI program (CHE-1828362).

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre.^{S5} CCDC 2259714, 2286852, and 2286853 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

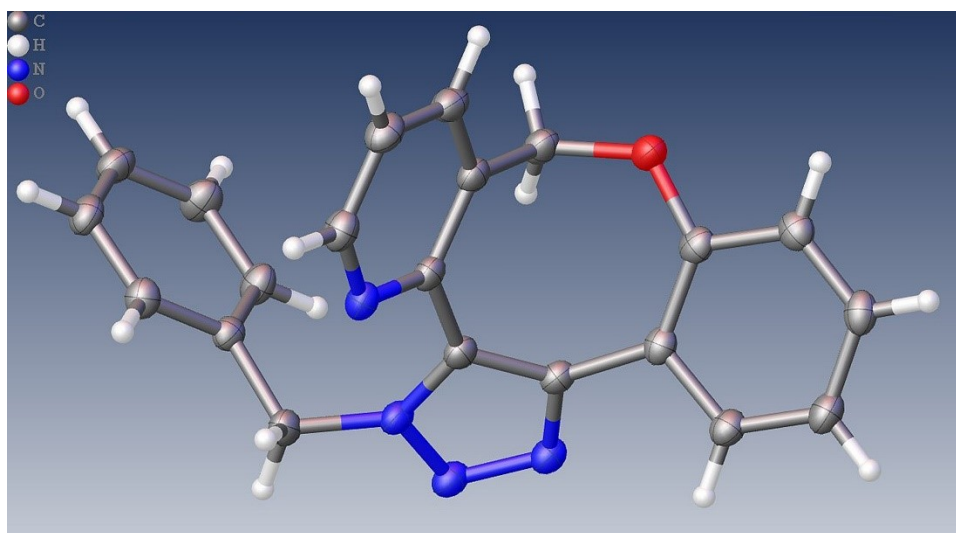


Figure S4. ORTEP diagram of **3** (O-ABC-BnN₃ cycloadduct) with 50% probability ellipsoids.

Data collection. A clear whiteish colourless, irregular shaped crystal was mounted on a nylon loop with perfluoroether oil. The sample was crystallized by a slow evaporation method. Data were collected from a shock-cooled single crystal at 99.9(6) K on a XtaLAB Synergy, Dualflex, HyPix four-circle diffractometer with a micro-focus sealed X-ray tube using a mirror as monochromator and a HyPix detector. The diffractometer was equipped with an Oxford Cryostream 800 low temperature device and used Cu K_{α} radiation ($\lambda = 1.54184 \text{ \AA}$). All data were integrated with CrysAlispro and a gaussian absorption correction using SCALE3 ABSPACK was applied.^{S6} The structure was solved by dual methods using SHELXT and refined by full-matrix least-squares methods against F^2 by SHELXL.^{S7} All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined isotropic on calculated positions using a riding model with their U_{iso} values constrained to 1.5 times the U_{eq} of their pivot atoms for terminal sp^3 carbon atoms and 1.2 times for all other carbon atoms.

Table S1. Crystal data and structure refinement for **3** (O-ABC cycloadduct).

CCDC number	2259714
Empirical formula	C ₂₁ H ₁₆ N ₄ O
Formula weight	340.38
Temperature [K]	99.9(6)
Crystal system	triclinic
Space group (number)	$P\bar{1}$ (2)
<i>a</i> [Å]	7.8488(2)
<i>b</i> [Å]	9.8954(3)
<i>c</i> [Å]	12.1031(4)
α [°]	68.423(3)
β [°]	74.665(3)
γ [°]	77.346(3)
Volume [Å ³]	835.21(5)
<i>Z</i>	2
ρ_{calc} [gcm ⁻³]	1.353
μ [mm ⁻¹]	0.693
<i>F</i> (000)	356
Crystal size [mm ³]	0.195×0.098×0.018
Crystal colour	clear whiteish colourless
Crystal shape	irregular
Radiation	Cu <i>K</i> _α ($\lambda=1.54184$ Å)
2 θ range [°]	8.02 to 154.82 (0.79 Å)
Index ranges	-9 ≤ <i>h</i> ≤ 9 -12 ≤ <i>k</i> ≤ 12 -15 ≤ <i>l</i> ≤ 15
Reflections collected	38664
Independent reflections	3490 <i>R</i> _{int} = 0.0525 <i>R</i> _{sigma} = 0.0180
Completeness to $\theta = 67.684^\circ$	99.9 %
Data / Restraints / Parameters	3490/0/236
Goodness-of-fit on <i>F</i> ²	1.067
Final <i>R</i> indexes [$\geq 2\sigma(I)$]	<i>R</i> ₁ = 0.0368 <i>wR</i> ₂ = 0.0961
Final <i>R</i> indexes [all data]	<i>R</i> ₁ = 0.0395 <i>wR</i> ₂ = 0.0980
Largest peak/hole [eÅ ⁻³]	0.22/-0.20
Extinction coefficient	0.0044(7)

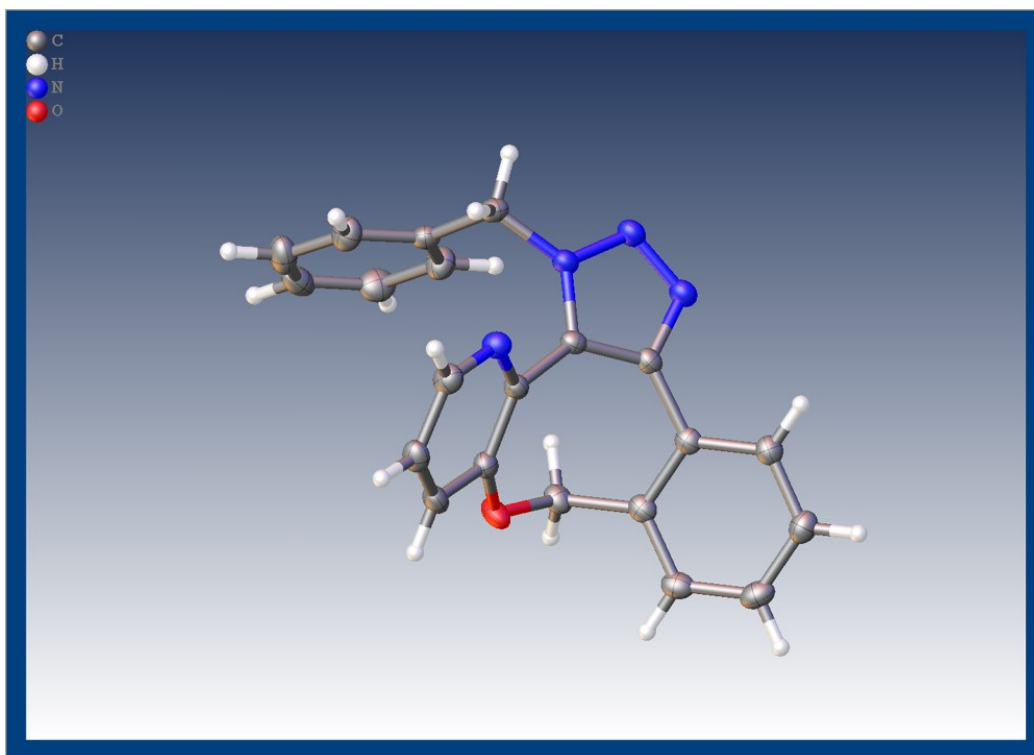


Figure S5: ORTEP diagram of **4** (O-ABC-II-BnN₃ cycloadduct) with 50% probability ellipsoids.

Data collection. A single clear irregular-shaped crystal of approximate dimension $0.303 \times 0.284 \times 0.160$ mm³ was adhered to a Mitegen loop with Paratone oil. Crystallographic data were collected at temperature 150 K on a Rigaku-Oxford Diffraction XtaLAB-Synergy-S diffractometer with a Hypix-6000HE (Hybrid Photon Counting) detector, using Cu-K α radiation of wavelength 1.54187 Å. The intensity data were measured by a ω -scan with 0.5° oscillations for each frame with the intensity that is more than 10:1 for data-to-parameter ratio. The program suite CrysAlis^{Pro} was used for data collection, absorption correction, and data reduction.^{S6} The structures were solved using the GUI Olex2^{S8} with the dual-space algorithm of SHELXT and refined by full-matrix least-squares methods on F^2 with SHELXL-2014 refinement package using Least Squares minimisation.^{S7} The compound C₂₁H₁₆N₄O crystallized in the monoclinic crystal system, with the space group $P2_1/c$. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were inserted at calculated positions or if possible based on difference Fourier analysis and refined with a riding model or without restrictions.

Table S2. Crystal data and structure refinement for **4** (O-ABC-II cycloadduct).

Identification code	2286852
Empirical formula	C ₂₁ H ₁₆ N ₄ O
Formula weight	340.38
Temperature/K	149.99(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	9.11690(10)
b/Å	12.31300(10)

$c/\text{\AA}$	14.85260(10)
$\alpha/^\circ$	90
$\beta/^\circ$	94.1900(10)
$\gamma/^\circ$	90
Volume/ \AA^3	1662.84(3)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.360
μ/mm^{-1}	0.696
F(000)	712.0
Crystal size/ mm^3	$0.303 \times 0.284 \times 0.160$
Radiation	Cu K α ($\lambda = 1.54184$)
2Θ range for data collection/ $^\circ$	9.34 to 156.094
Index ranges	$-11 \leq h \leq 11, -15 \leq k \leq 15, -17 \leq l \leq 18$
Reflections collected	34000
Independent reflections	3550 [$R_{\text{int}} = 0.0397, R_{\text{sigma}} = 0.0181$]
Data/restraints/parameters	3550/0/236
Goodness-of-fit on F^2	1.061
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0345, wR_2 = 0.0881$
Final R indexes [all data]	$R_1 = 0.0358, wR_2 = 0.0891$
Largest diff. peak/hole / $e \text{\AA}^{-3}$	0.24/-0.18

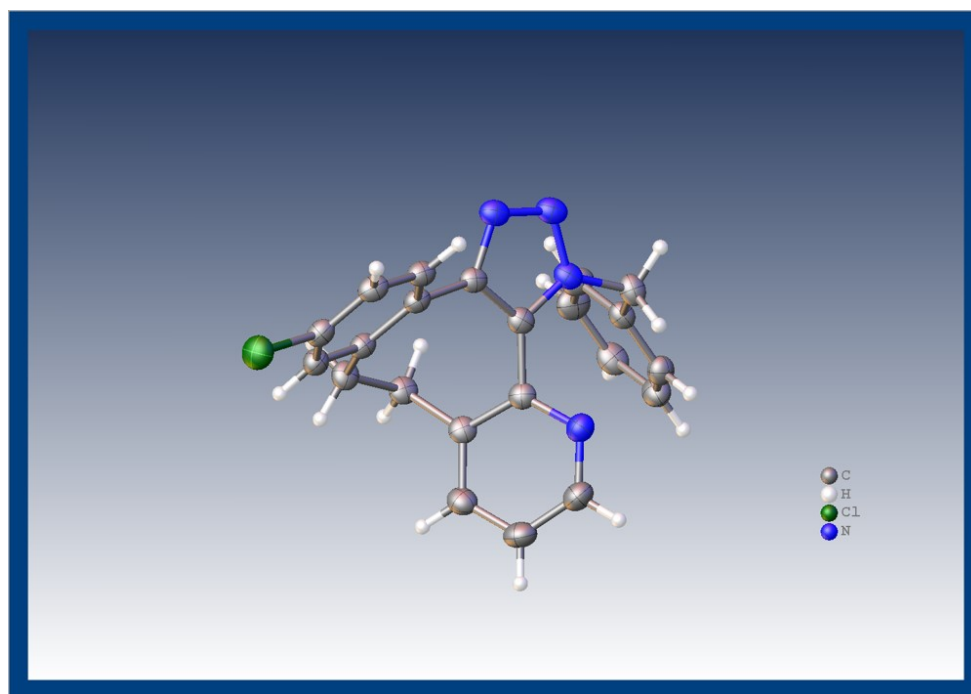


Figure S6: ORTEP diagram of **5** (ABC-BnN₃ cycloadduct) with 50% probability ellipsoids.

Data collection. A Single clear plate-shaped crystal of approximate dimension $0.825 \times 0.137 \times 0.102$ mm³ was adhered to a Mitegen loop with Paratone oil. Crystallographic data were collected at temperature 150 K on a Rigaku-Oxford Diffraction XtaLAB-Synergy-S diffractometer with a Hypix-6000HE (Hybrid Photon Counting) detector, using Cu-K α radiation of wavelength 1.54187 Å. The intensity data were measured by a ω -scan with 0.5° oscillations for each frame with the intensity that is more than 10:1 for data-to-parameter ratio. The program suite CrysAlis^{Pro} was used for data collection, absorption correction, and data reduction.^{S6} The structures were solved using the GUI Olex2^{S8} with the dual-space algorithm of SHELXT and refined by full-matrix least-squares methods on F^2 with SHELXL-2014 refinement package using Least Squares minimisation.^{S7} The compound C₂₂H₁₇ClN₄ crystallized in the monoclinic crystal system, with the space group P2₁/c. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were inserted at calculated positions or if possible based on difference Fourier analysis and refined with a riding model or without restrictions.

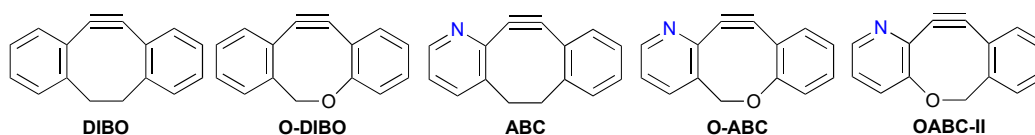
Table S3. Crystal data and structure refinement for **5** (ABC cycloadduct).

Identification code	2286853
Empirical formula	C ₂₂ H ₁₇ ClN ₄
Formula weight	372.85
Temperature/K	149.99(10)
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	10.93403(10)
b/Å	21.4604(2)
c/Å	7.91748(8)
α /°	90
β /°	105.1277(9)
γ /°	90
Volume/Å ³	1793.45(3)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.381
μ/mm^{-1}	1.990
F(000)	776.0
Crystal size/mm ³	0.825 × 0.137 × 0.102
Radiation	Cu K α (λ = 1.54184)
2 θ range for data collection/°	8.24 to 155.73
Index ranges	-13 ≤ h ≤ 13, -23 ≤ k ≤ 27, -9 ≤ l ≤ 9
Reflections collected	35683
Independent reflections	3757 [R _{int} = 0.0817, R _{sigma} = 0.0316]
Data/restraints/parameters	3757/0/244
Goodness-of-fit on F ²	1.084
Final R indexes [I >= 2 σ (I)]	R ₁ = 0.0470, wR ₂ = 0.1328
Final R indexes [all data]	R ₁ = 0.0486, wR ₂ = 0.1348
Largest diff. peak/hole / e Å ⁻³	0.32/-0.39

Computational Details & Data

Computational Details. Gas phase geometry optimizations were performed with the Gaussian 16 software^{S9} at the M06-2X level of theory^{S10} with the 6-31G(d,p) basis set. Single point energies of located minima were performed at the M06-2X/6-311++G(d,p) level of theory, including the PCM solvation model for DMSO. Manual conformational searches were performed for both the SMs and TSs. Frequency calculations were performed to confirm stationary points as minima or first-order saddle points. All ΔE and ΔE^\ddagger values include zero-point corrections. Coordinates, total energies, and imaginary frequencies (transition states) are provided below. NBO analysis employed the NBO 7.0 program,^{S11} implemented through the Gaussian 16 software.

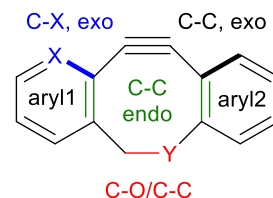
Table S4. Energies and free energies of activation, and for cycloadditions of methyl azide with DIBO, ODIBO, ABC, O-ABC and O-ABC-II. Energies for the preferred regioisomer are in bold typeface.



Compound	<i>syn</i> TS		<i>anti</i> TS	
	ΔE^\ddagger	ΔG^\ddagger	ΔE^\ddagger	ΔG^\ddagger
DIBO	10.8	23.6	10.8	23.6
ODIBO	8.4	21.1	9.1	21.9
ABC	10.0	22.4	11.1	23.9
O-ABC	7.6	20.0	9.4	21.9
O-ABC-II	7.8	20.2	8.7	21.4

Table S5. Distortion/interaction (activation–strain) analysis for the preferred transition states of the cycloadditions of methyl azide with DIBO, ODIBO, ABC, and O-ABC. All energies in kcal/mol.

Compound	$\Delta E^\ddagger_{\text{distortion}}$			$\Delta E^\ddagger_{\text{interaction}}$
	1,3-Dipole	Alkyne	Total	
DIBO	15.9	3.1	19.0	-8.3
ODIBO	14.1	2.5	16.6	-8.2
ABC	14.3	2.7	17.0	-7.0
O-ABC	12.7	2.1	14.8	-7.2
O-ABC-II	12.9	2.1	15.0	-7.1

Table S6. Second-order perturbations (E_2) obtained from natural bonding orbital analysis (NBO) for SMs and the TSs.

	DIBO		ODIBO		ABC		O-ABC		O-ABC-II	
	SM	TS	SM	TS	SM	TS	SM	TS	SM	TS
$\pi_{in} \rightarrow \pi_{aryl1/aryl2}^*$	0.6/0.6	4.4/— ^a	0.5/— ^a	5.9/0.9	0.7/0.7	— ^a /3.3	0.6/— ^a	— ^a /0.8	— ^a /0.6	0.9/5.6
$\pi_{out} \rightarrow \pi_{aryl1/aryl2}^*$	15.6/15.6	11.4/14.8	16.2/15.8	10.5/14.4	19.4/14.9	19.8/11.7	20.2/15.1	20.5/14.0	19.7/15.5	19.1/10.4
$\pi_{in} \rightarrow \sigma_{CX/CC, exo}^*$	4.5/4.5	2.7/4.1	4.4/4.8	2.4/4.2	5.6/4.3	4.9/3.3	5.9/4.5	4.8/4.3	6.3/4.3	5.2/2.8
$\pi_{in} \rightarrow \sigma_{CC, endo (aryl1/2)}^*$	2.9/2.9	2.7/3.7	3.0/3.1	2.1/3.8	2.5/2.9	2.8/3.1	2.4/3.3	2.8/4.0	2.7/3.0	2.8/2.8
$\pi_{in}^* \rightarrow \sigma_{CX/CC, exo}^*$	— ^a /— ^a	0.7/1.0	— ^a /— ^a	0.6/0.9	— ^a /— ^a	1.3/0.8	— ^a /— ^a	1.3/0.9	— ^a /— ^a	1.3/0.6
$\pi_{in}^* \rightarrow \sigma_{CC, endo (aryl1/2)}^*$	— ^a /— ^a	1.0/1.4	— ^a /— ^a	0.9/1.5	— ^a /— ^a	1.4/1.1	— ^a /— ^a	1.4/1.4	— ^a /— ^a	1.4/0.9
$\pi_{aryl1} \rightarrow \sigma_{CO/CC}^*$	3.9	3.8	7.5	7.6	4.0	4.0	7.7	7.8	2.8 ^b	2.7 ^b
$n_O \rightarrow \pi_{aryl2}^*$	—	—	16.9 ^c	16.9 ^c	—	—	17.1 ^c	16.5 ^c	16.8 ^{c,d}	16.4 ^{c,d}
$n_O \rightarrow \sigma_{aryl, endo}^*$	—	—	9.8 ^c	9.5 ^c	—	—	9.8 ^c	9.4 ^c	10.3 ^c	10.1 ^c
$\pi_{aryl1/aryl2} \rightarrow \pi_{in}^*$	0.6/0.6	4.8/— ^a	0.5/— ^a	6.3/1.2	— ^a /0.8	— ^a /3.2	— ^a /0.5	— ^a /0.8	— ^a /0.6	0.7/5.5
$\pi_{aryl1/aryl2} \rightarrow \pi_{out}^*$	19.1/19.1	14.9/20.2	18.5/19.6	12.9/19.6	12.5/19.7	12.9/17.7	12.1/20.3	12.2/20.7	12.8/19.1	12.6/14.7
$\sigma_{CC, endo (aryl1/2)} \rightarrow \pi_{in}^*$	3.6/3.6	5.7/3.7	3.9/3.8	5.0/5.4	3.3/3.7	6.1/4.9	3.5/3.9	6.4/5.5	3.4/3.9	6.1/4.4
$\sigma_{CC, endo (aryl1/2)} \rightarrow \pi_{out}^*$	— ^a /— ^a	1.0/— ^a	— ^a /— ^a	1.6/— ^a	— ^a /— ^a	— ^a /0.7	— ^a /— ^a	— ^a /— ^a	— ^a /— ^a	— ^a /1.4

^aThe value is <0.5 kcal/mol, the default threshold for printing E_2 interactions in the NBO program; ^bThe value given for OABC-II is the $\pi_{aryl1} \rightarrow \sigma_{OC}^*$ interaction; ^cThe value is the sum of interactions for both lone pairs on oxygen; ^dThe value given for O-ABC-II is the $n_O \rightarrow \pi_{aryl1}$ interaction.

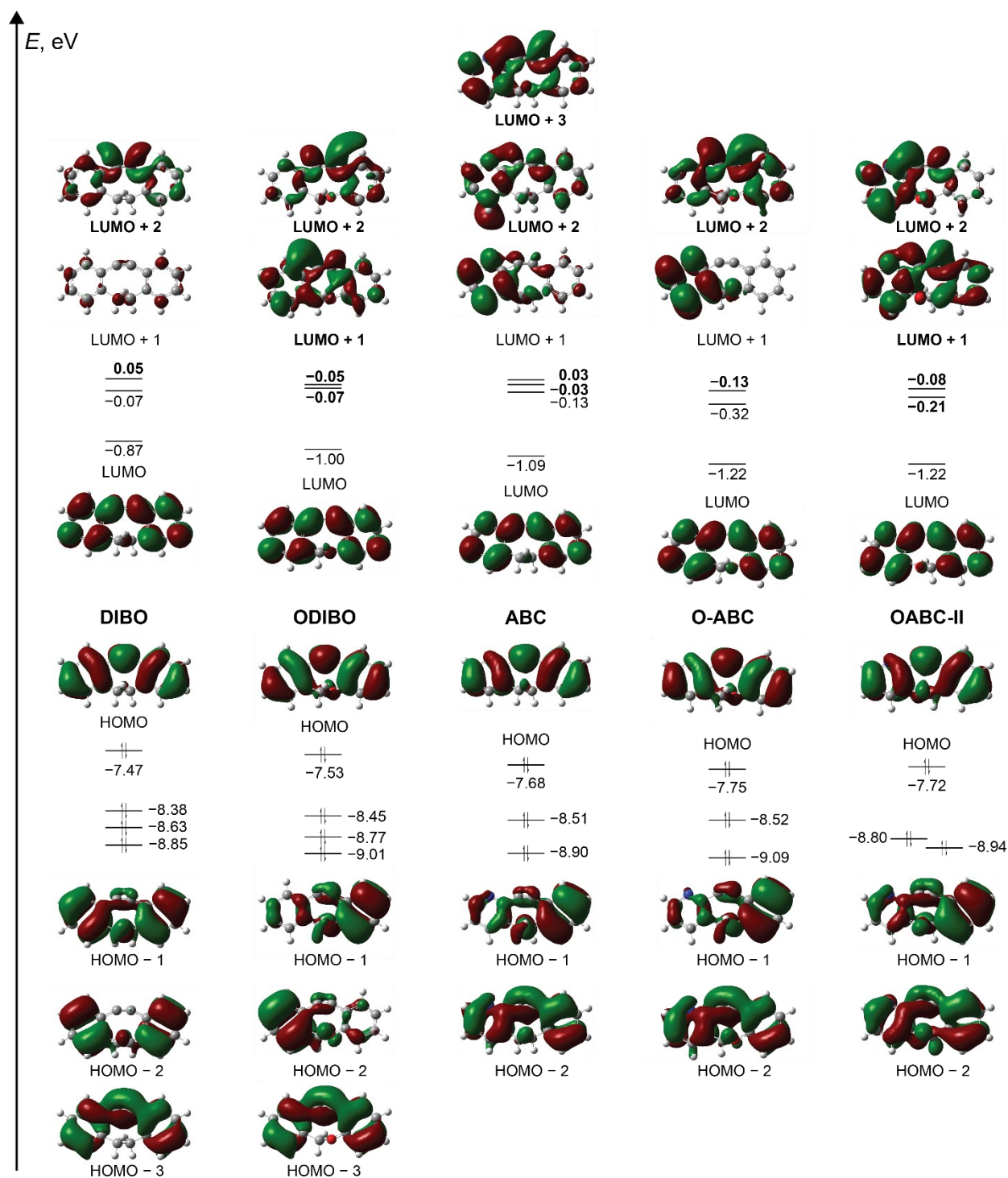
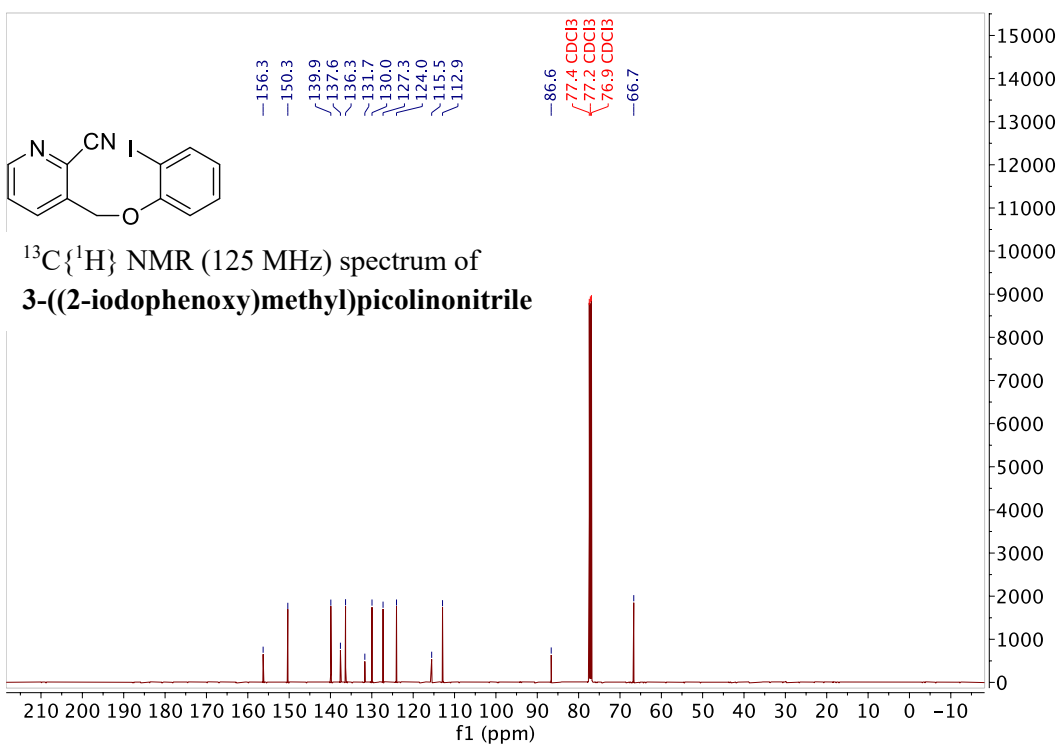
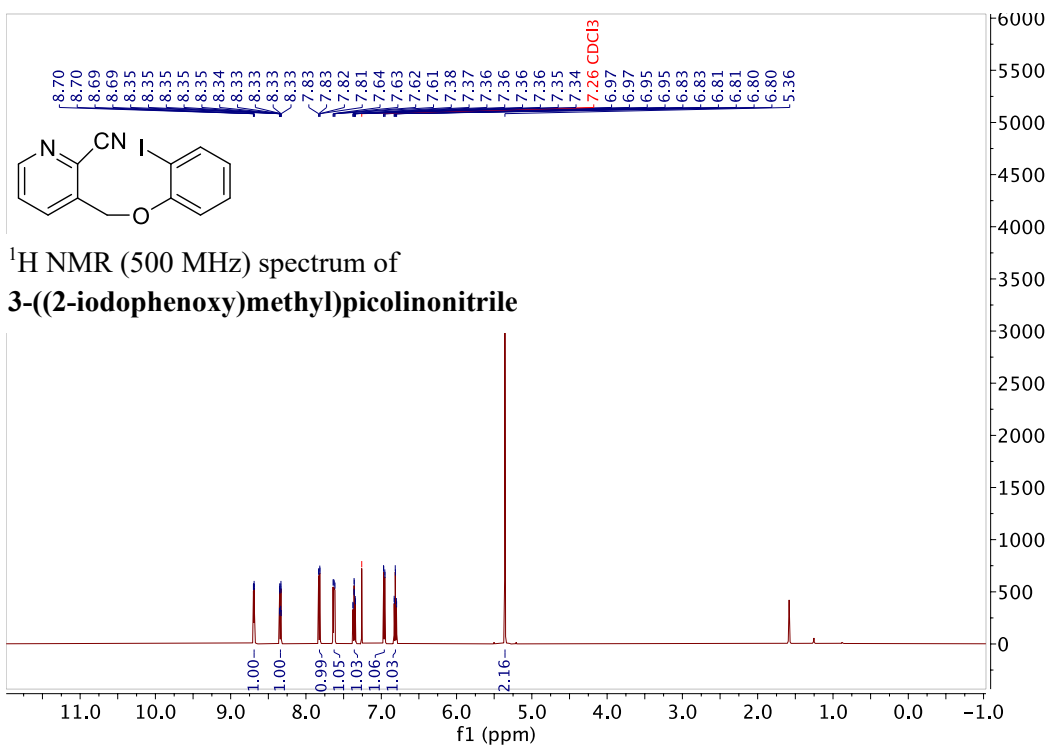
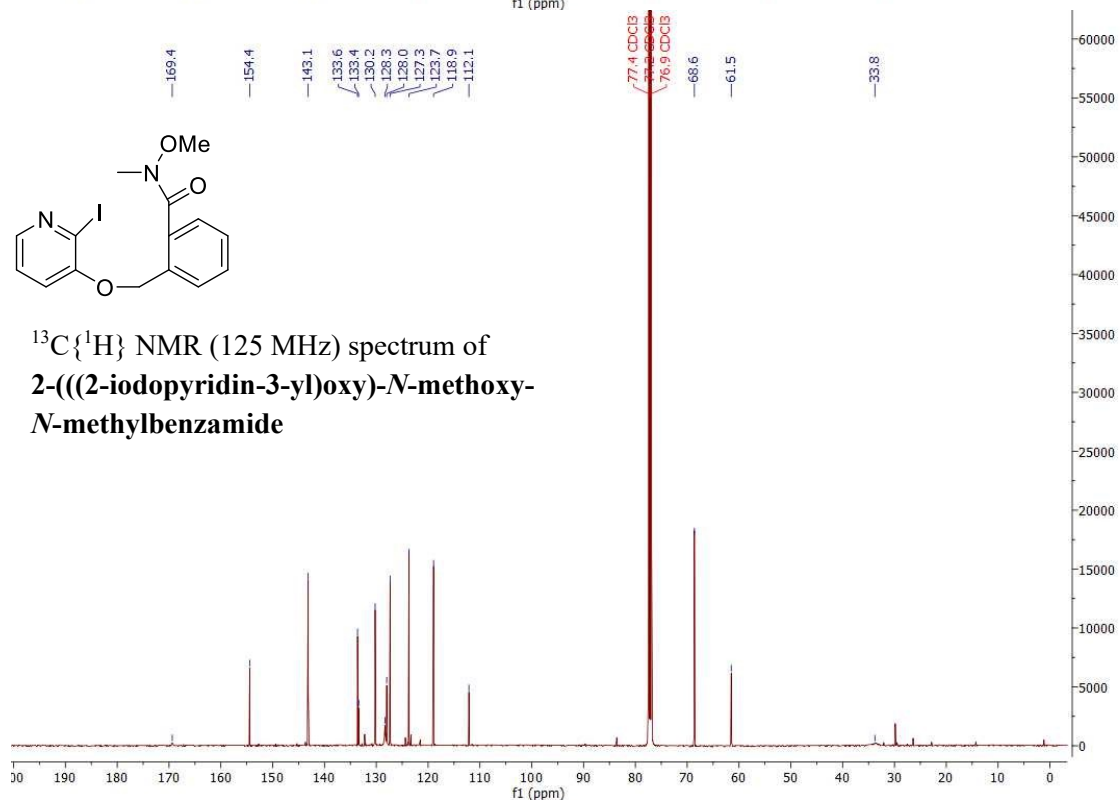
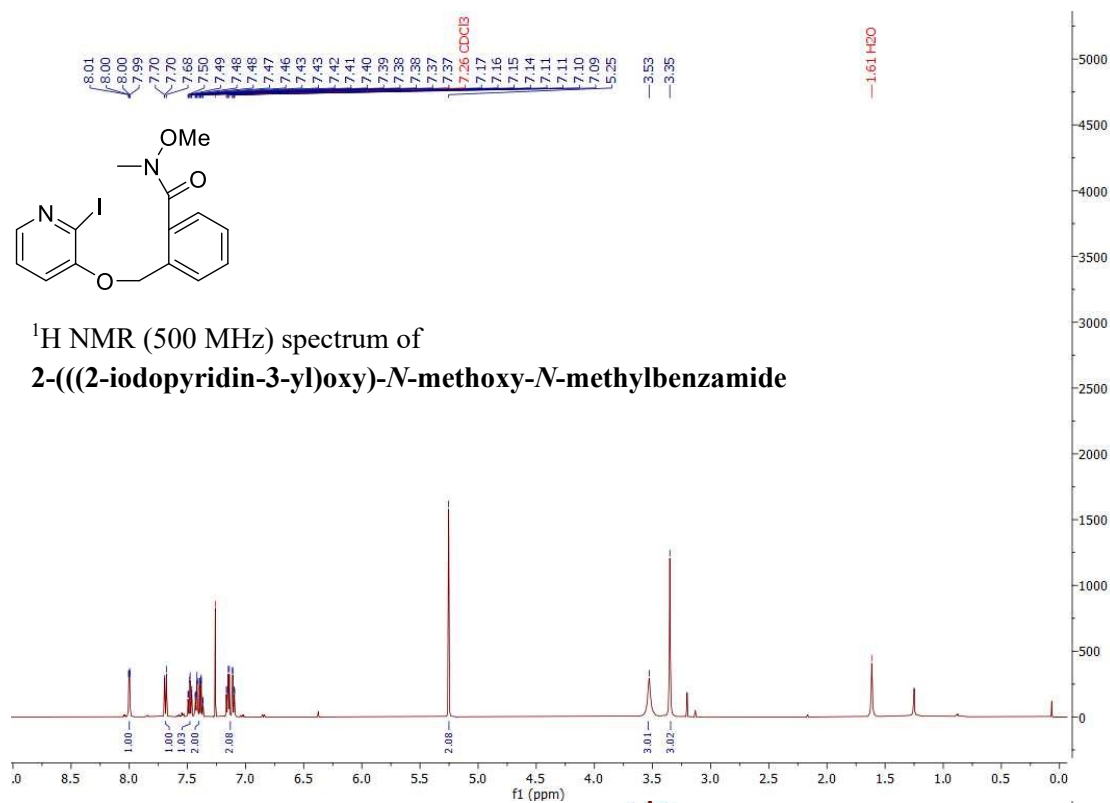
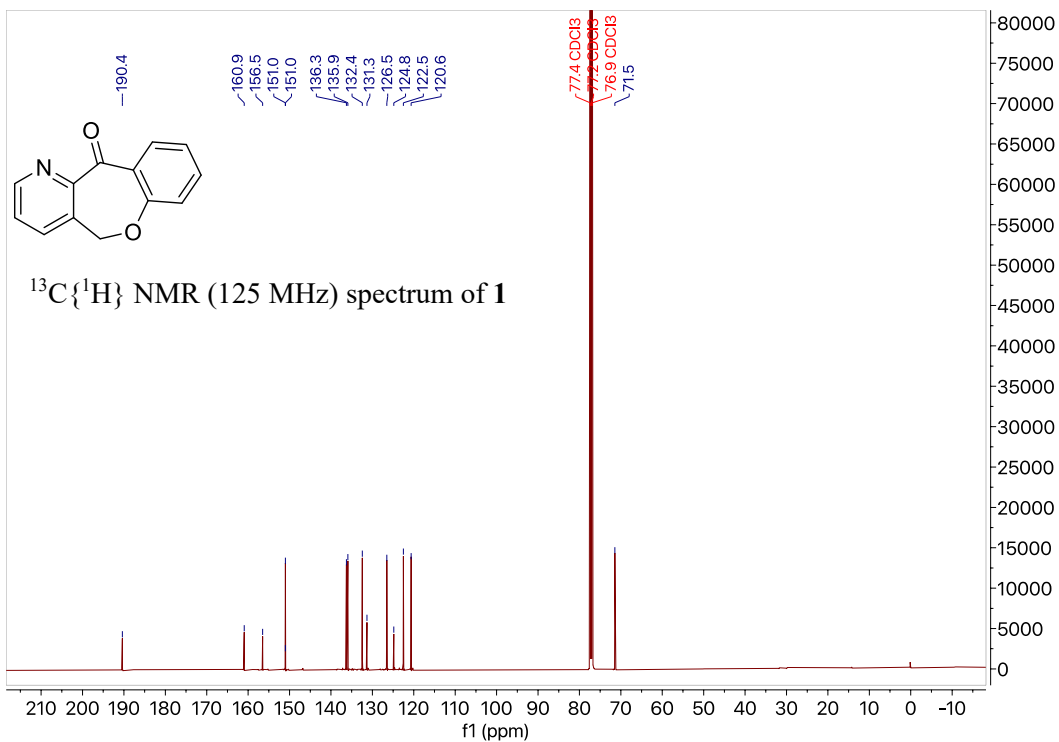
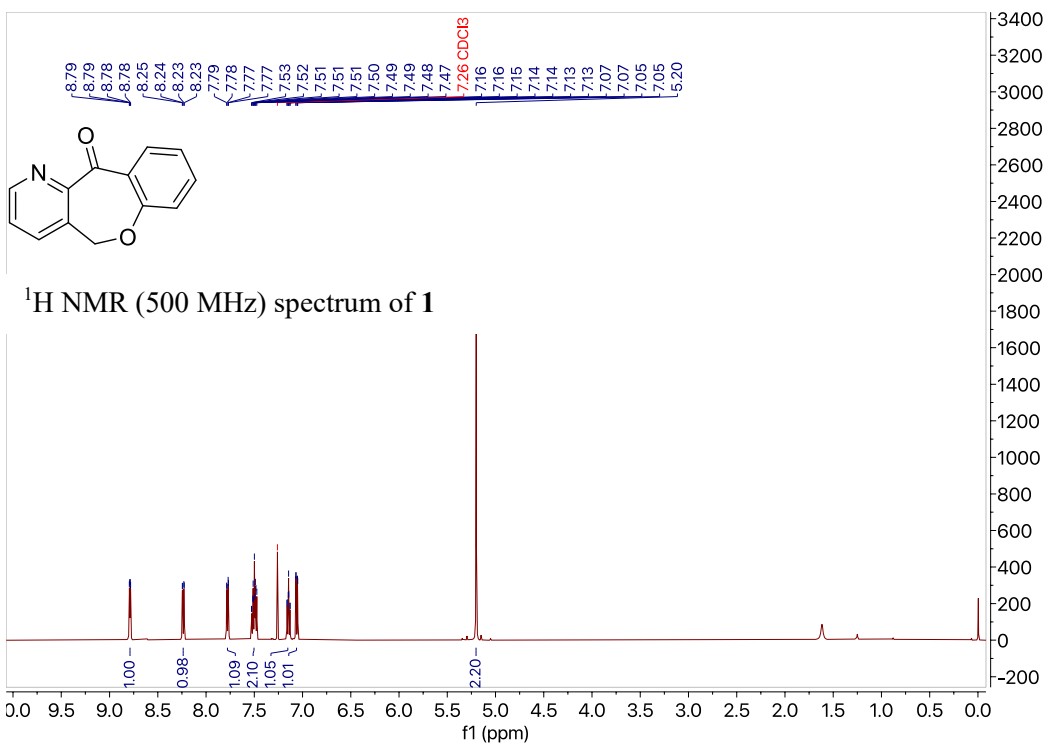


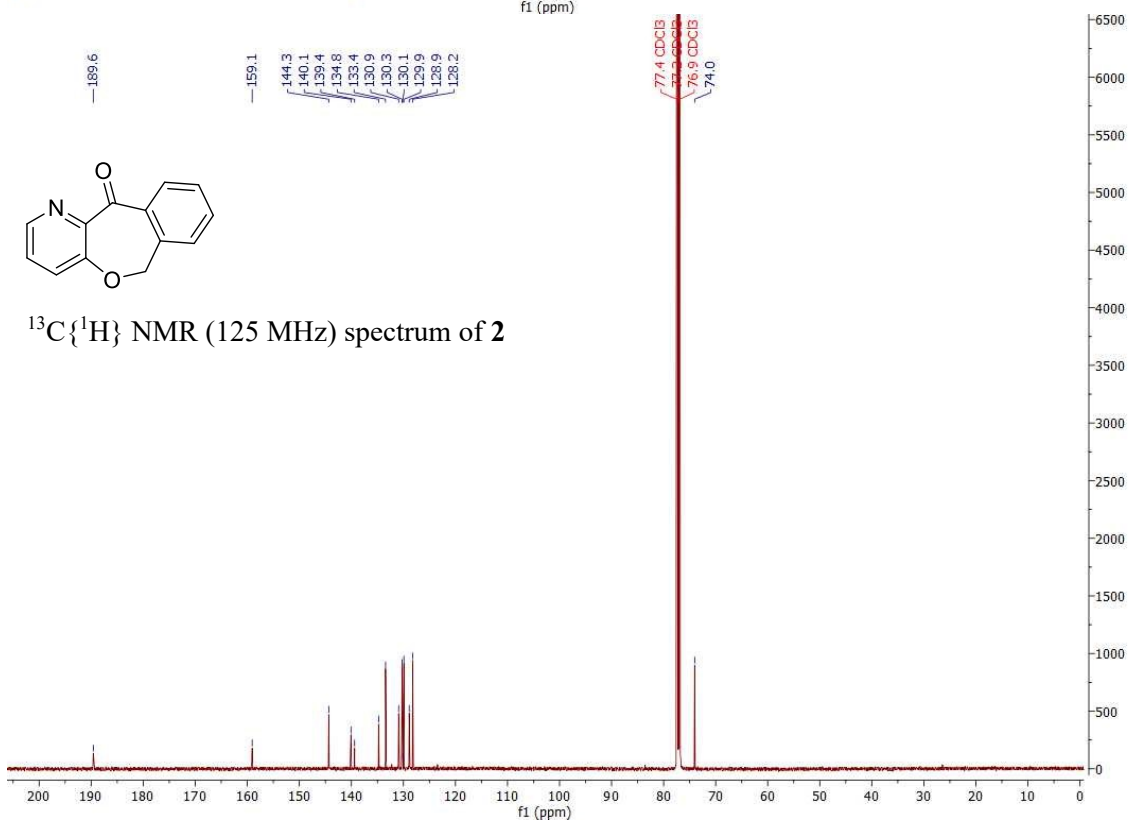
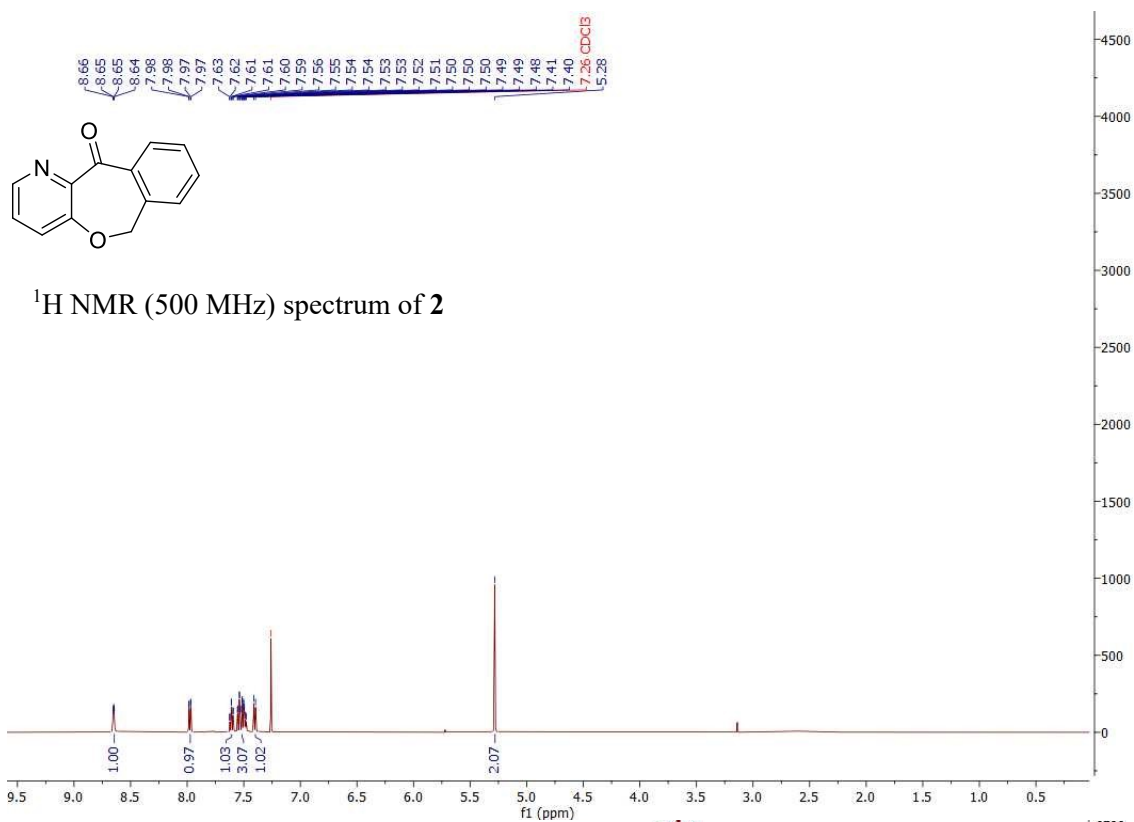
Figure S7. Orbital diagrams and energies (eV) calculated at the M06-2X/6-311++G(d,p)-CPCM(DMSO)/M06-2X/6-31G(d) level of theory.

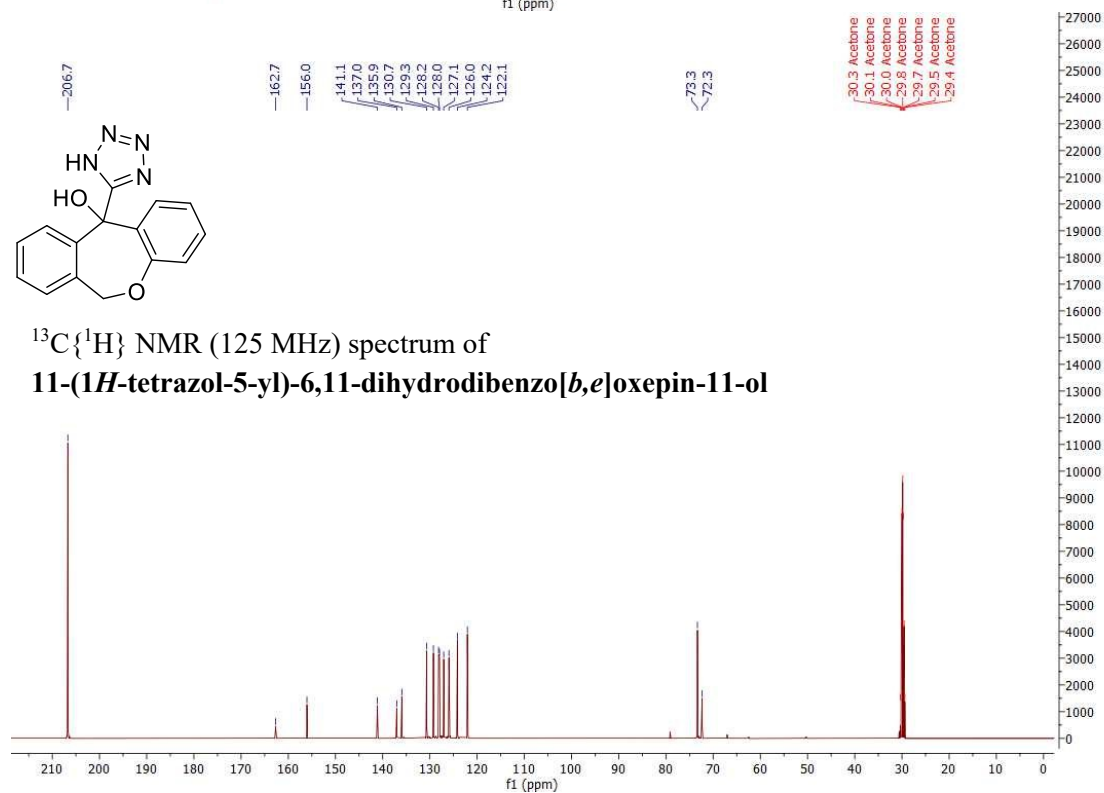
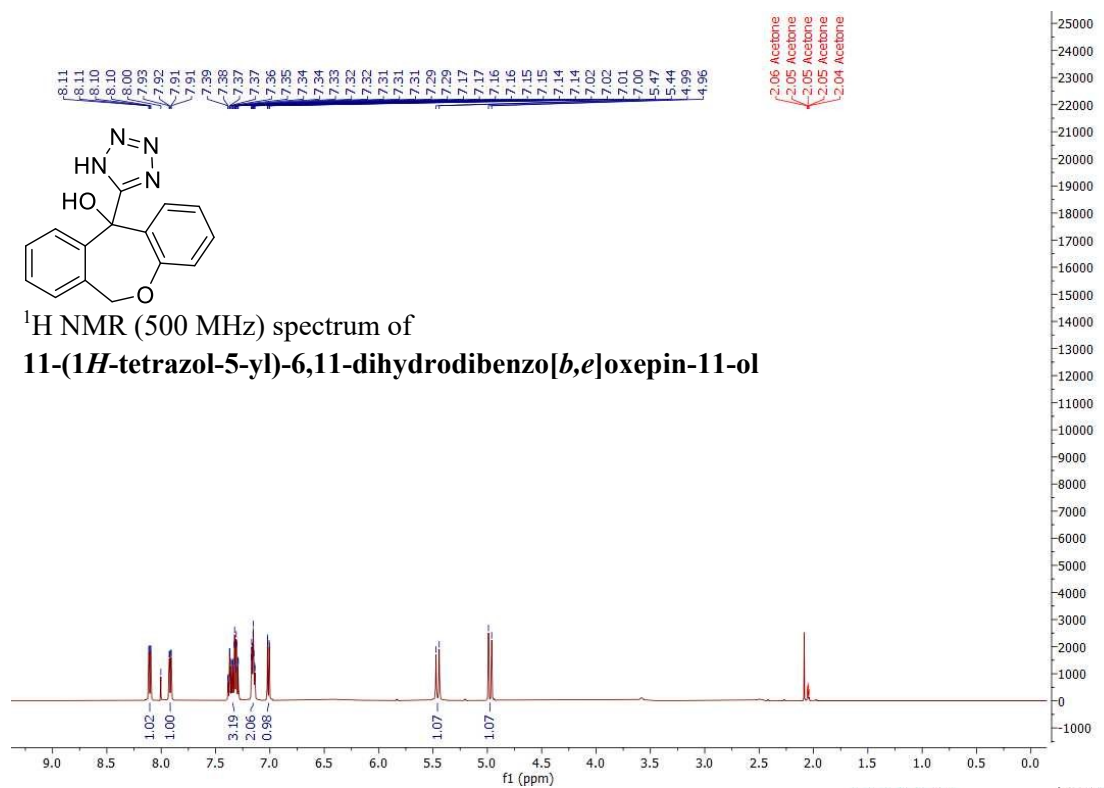
NMR Spectra

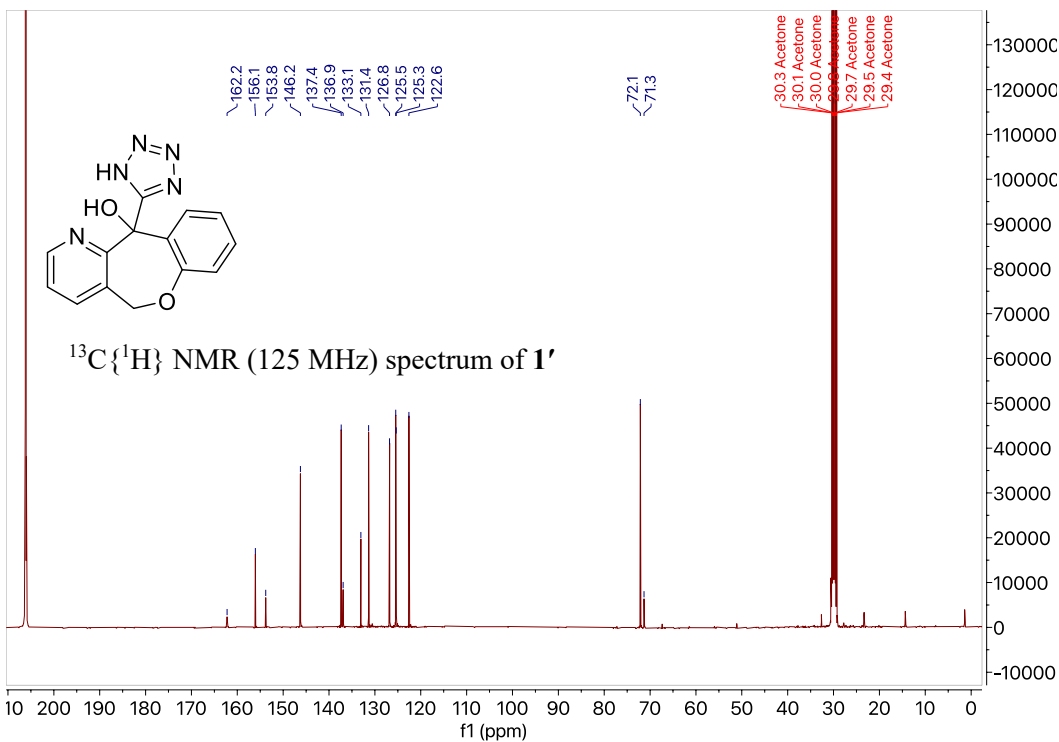
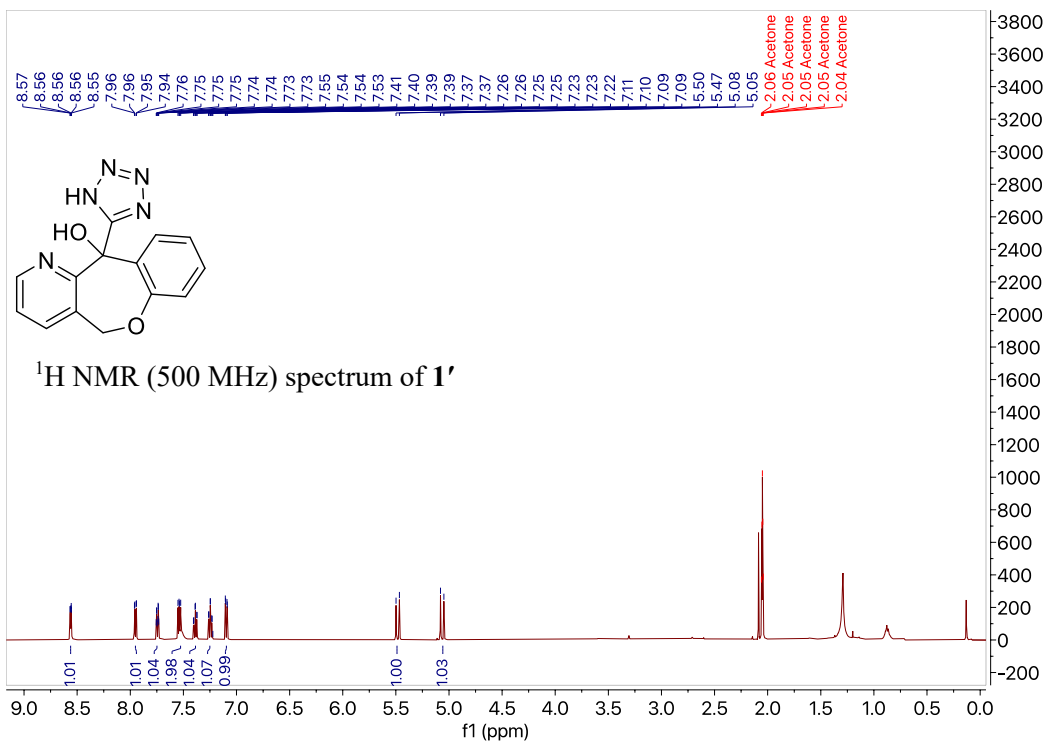


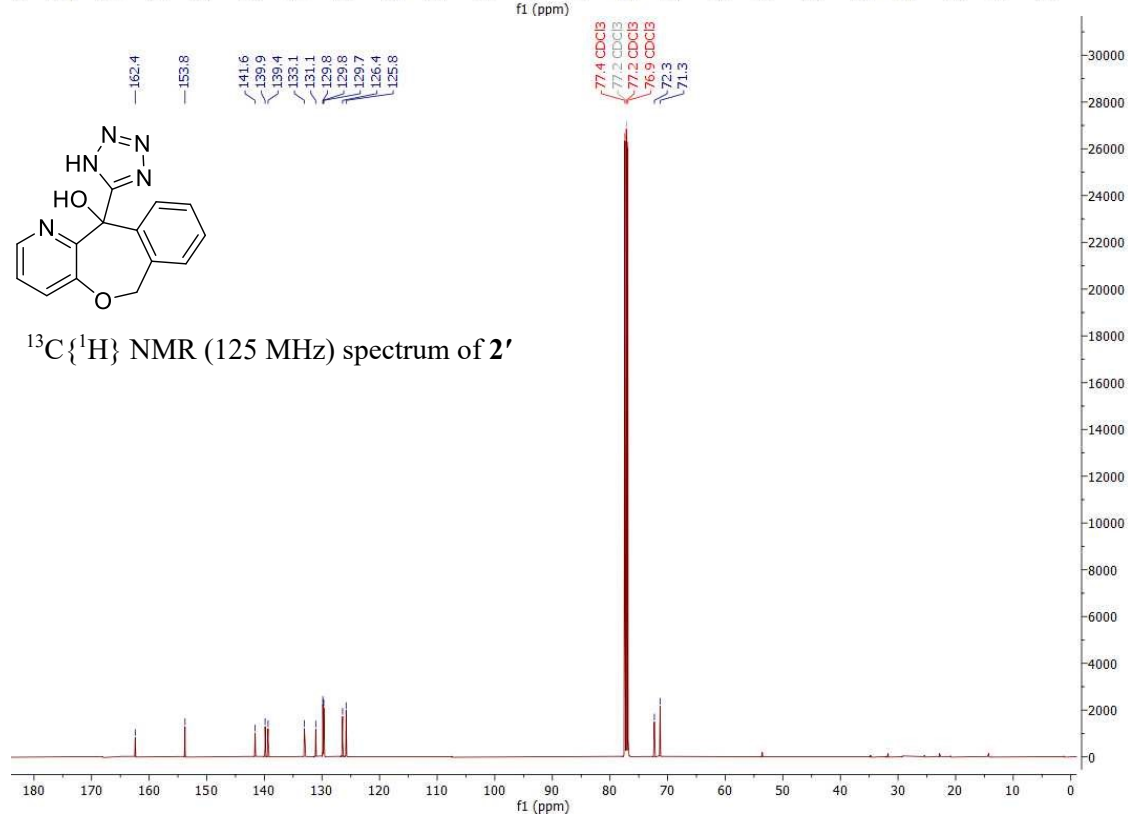
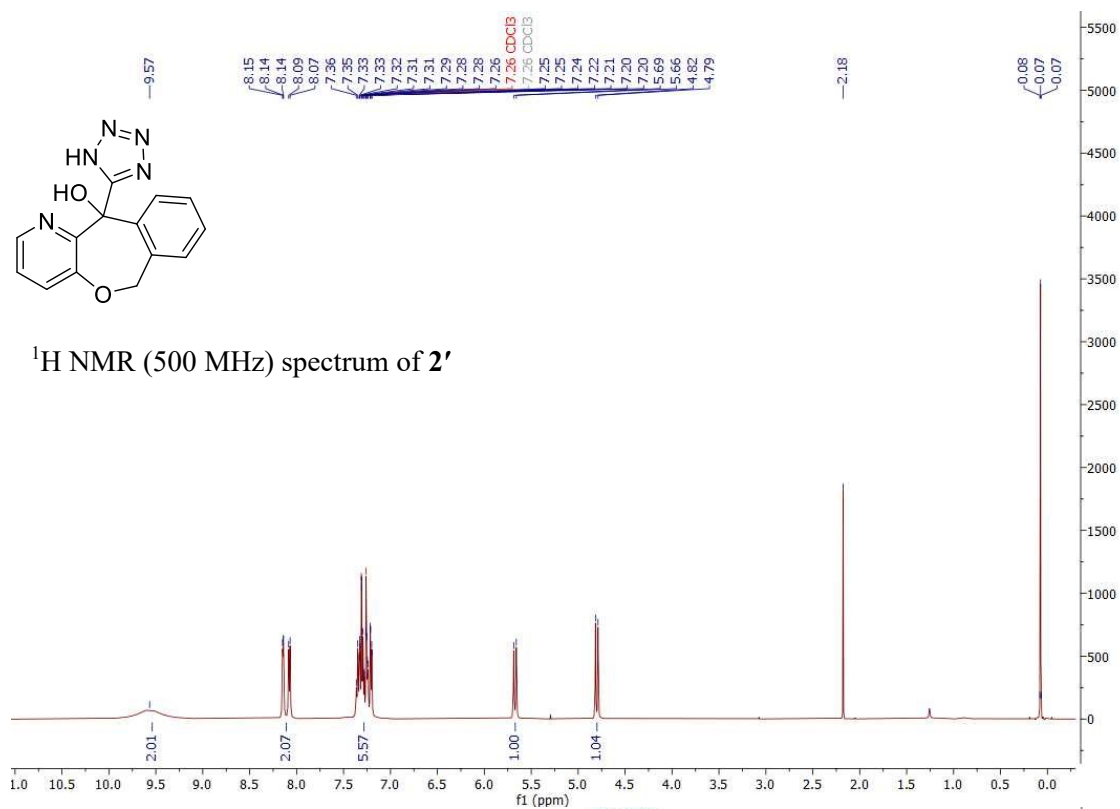


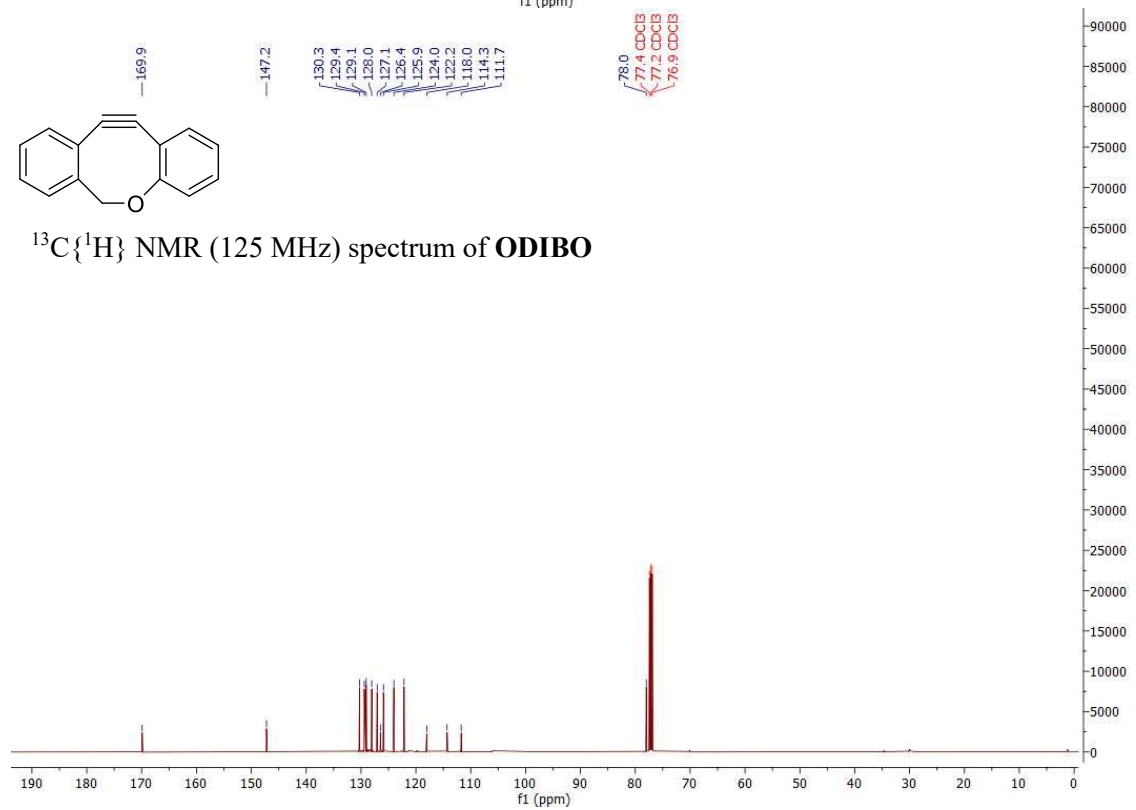
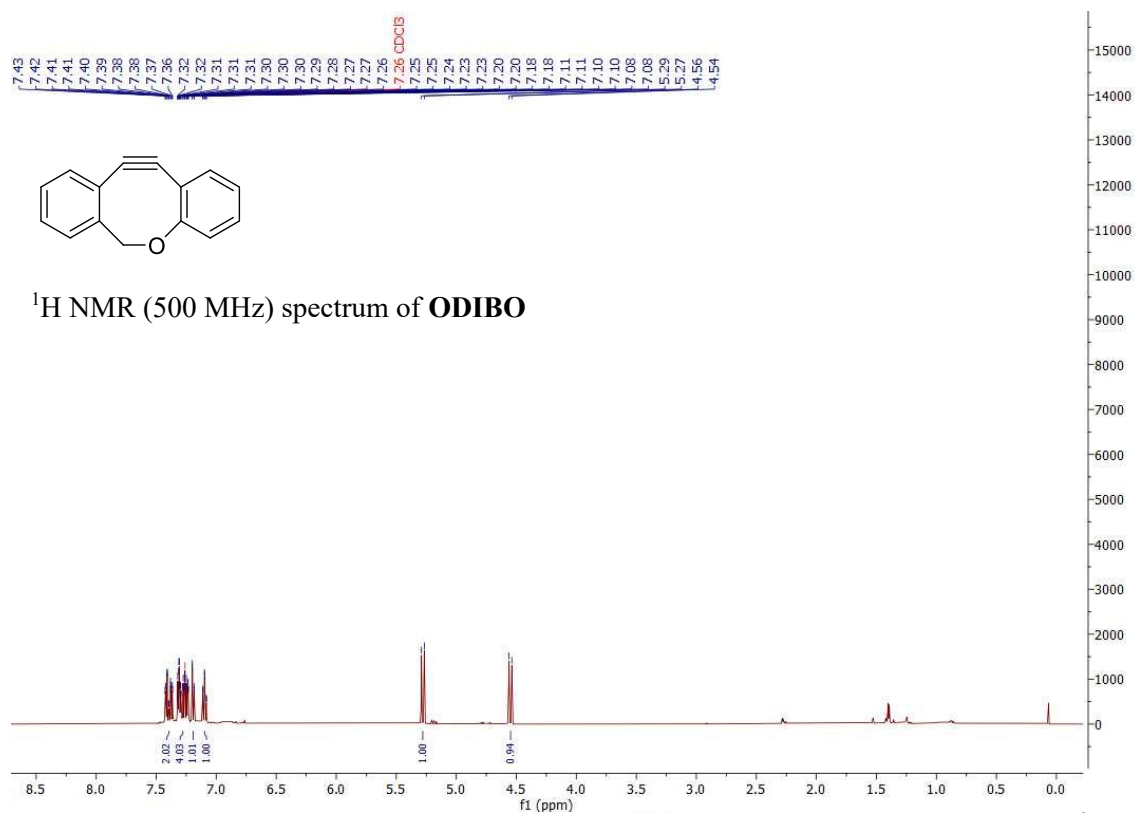


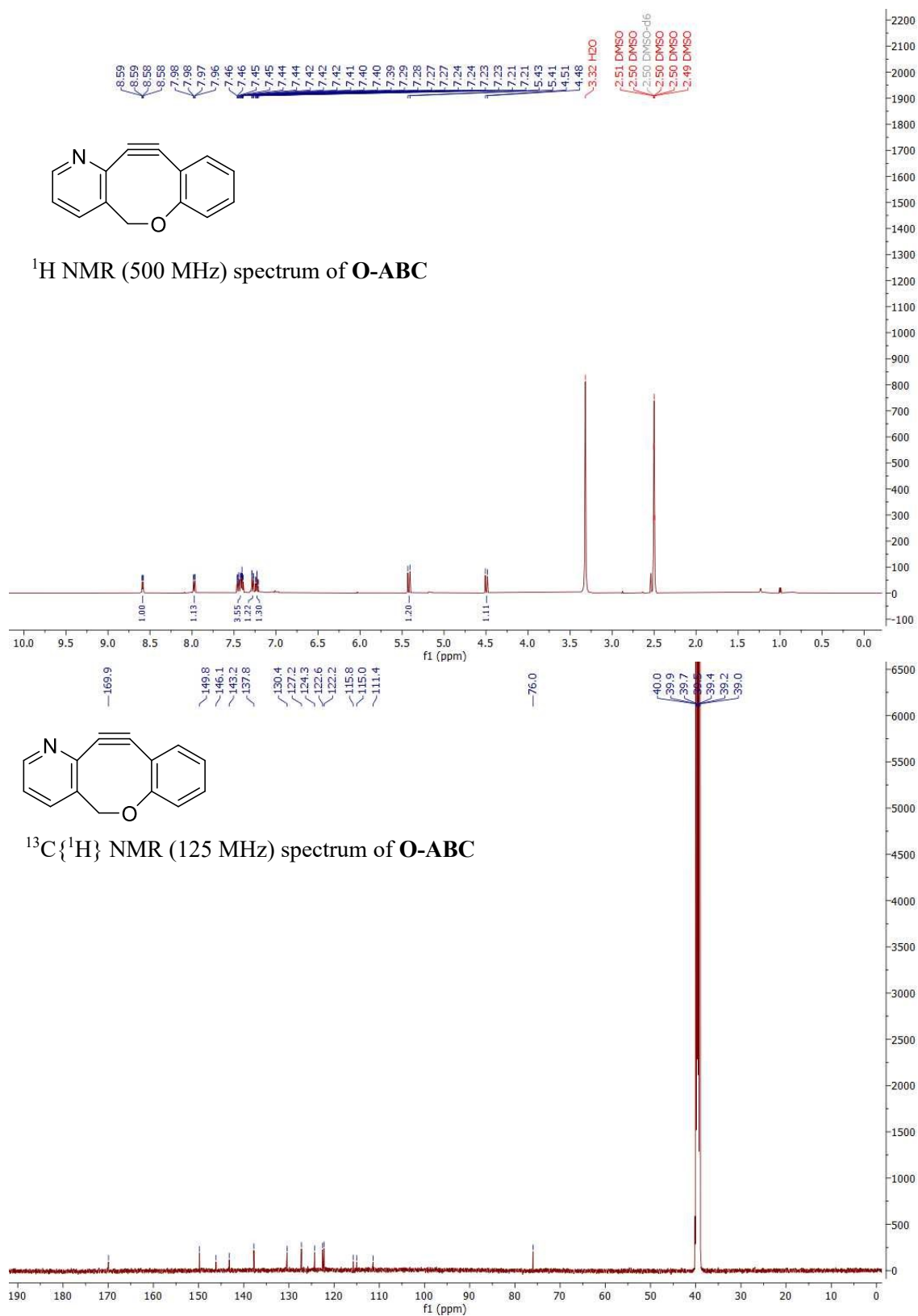


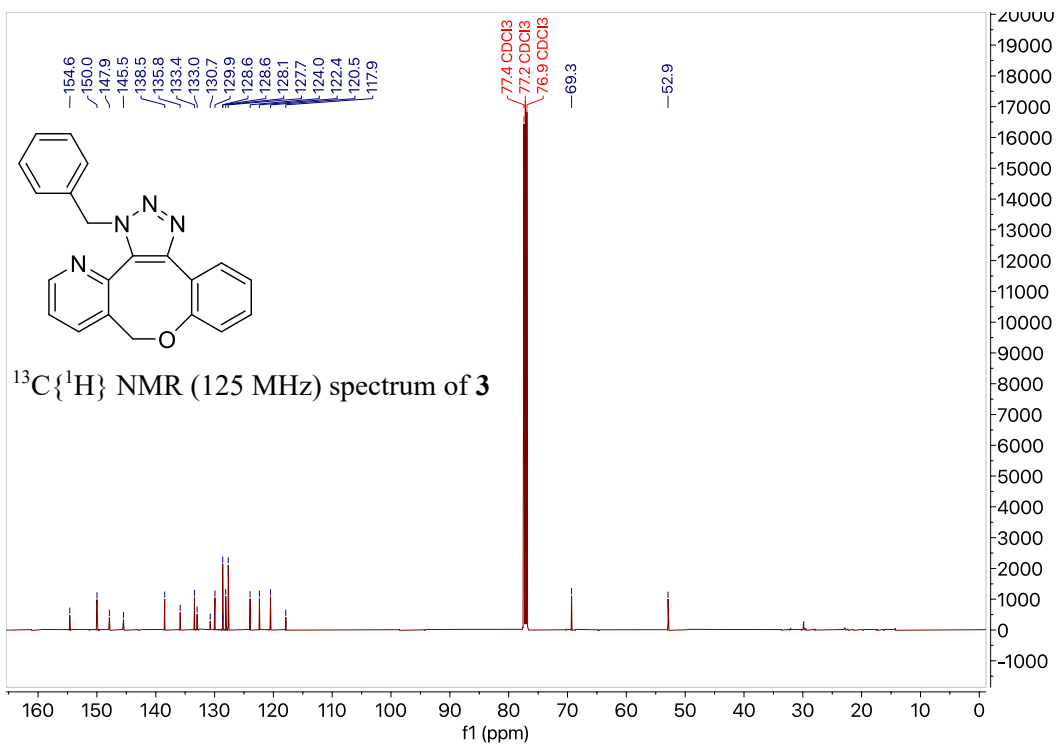
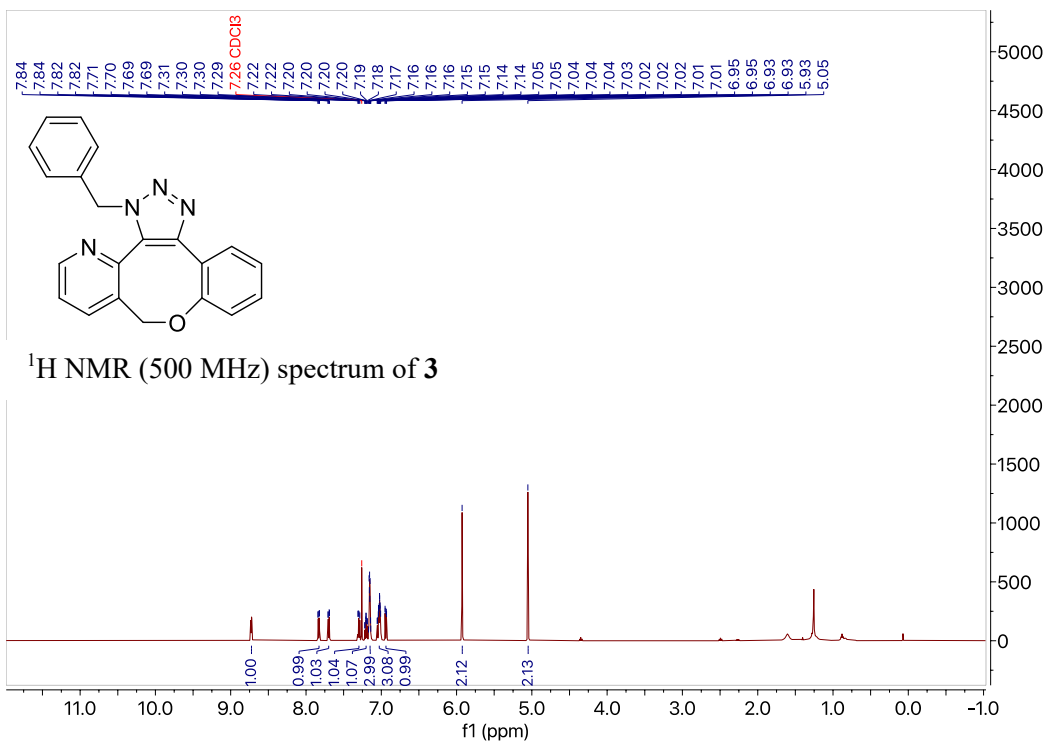


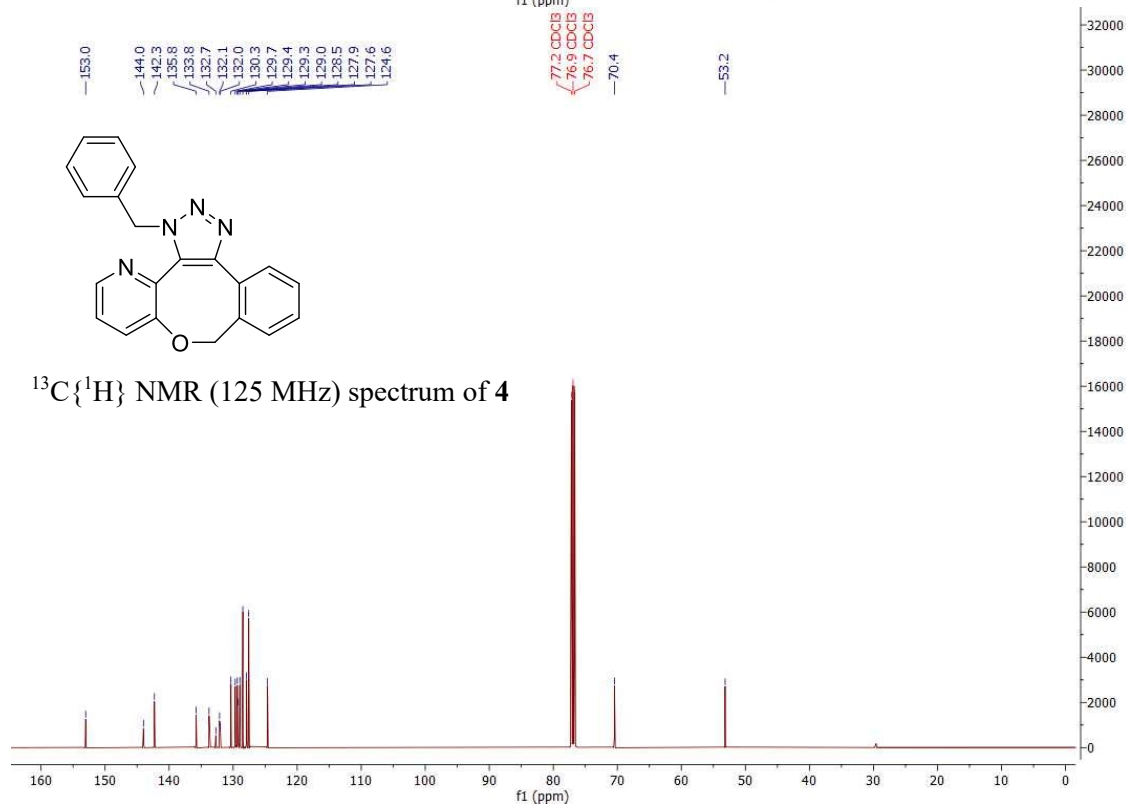
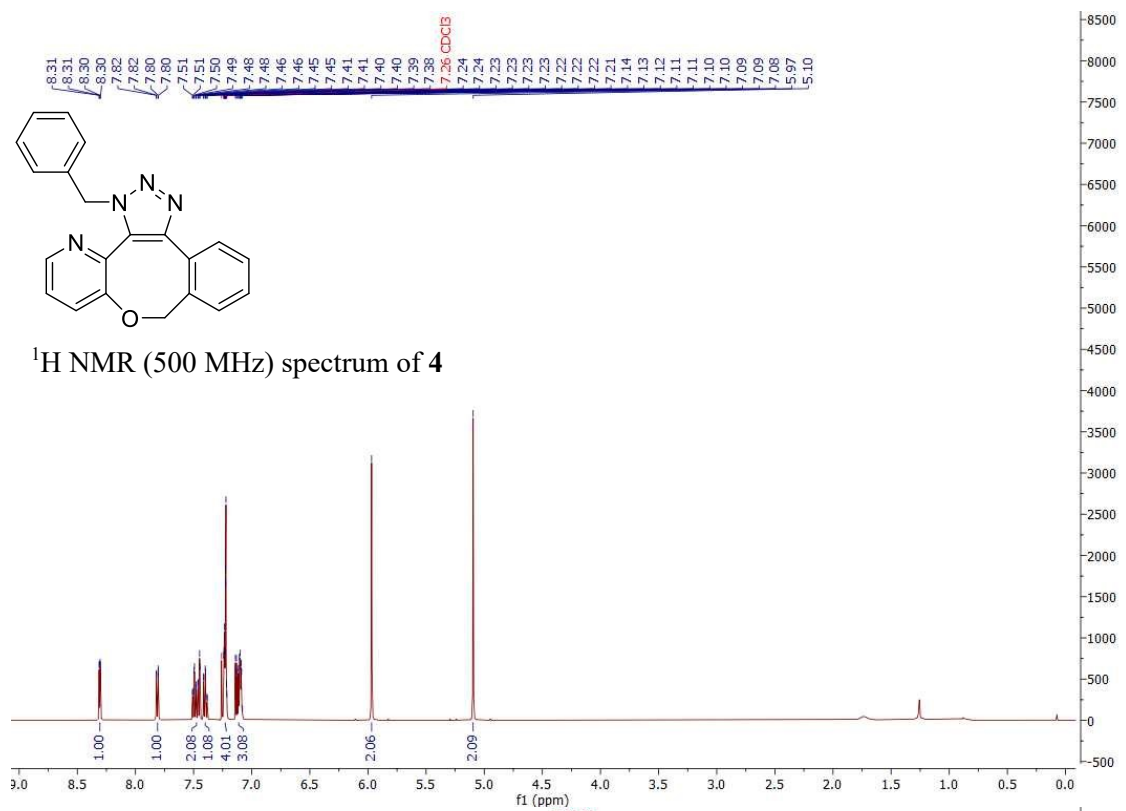


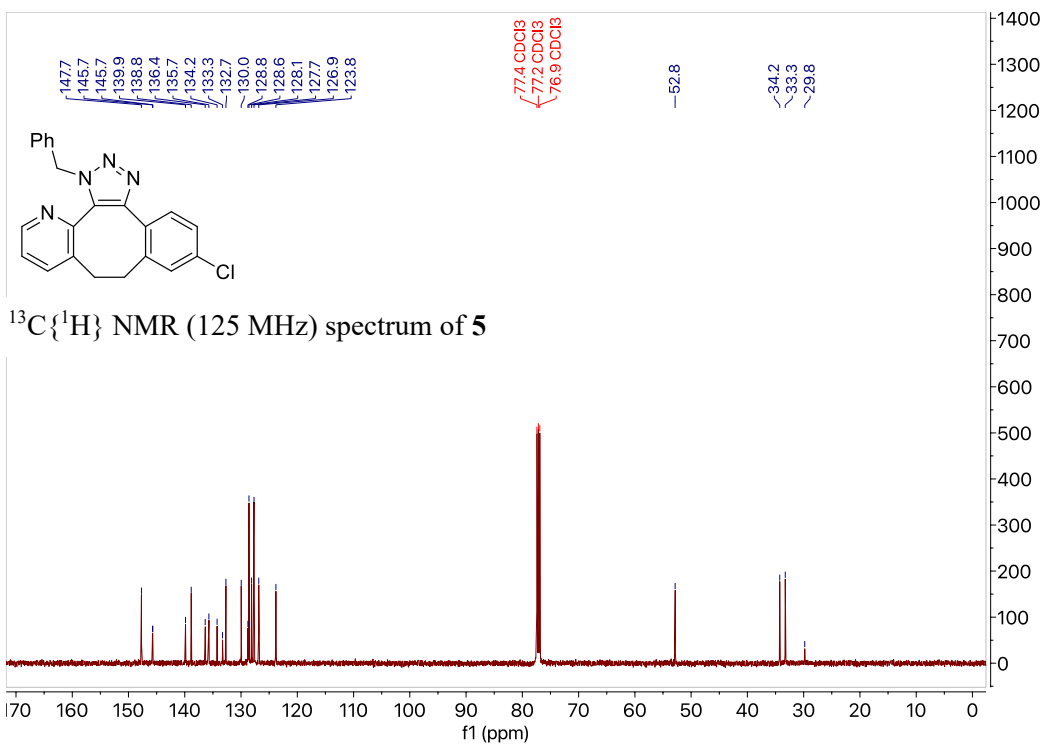
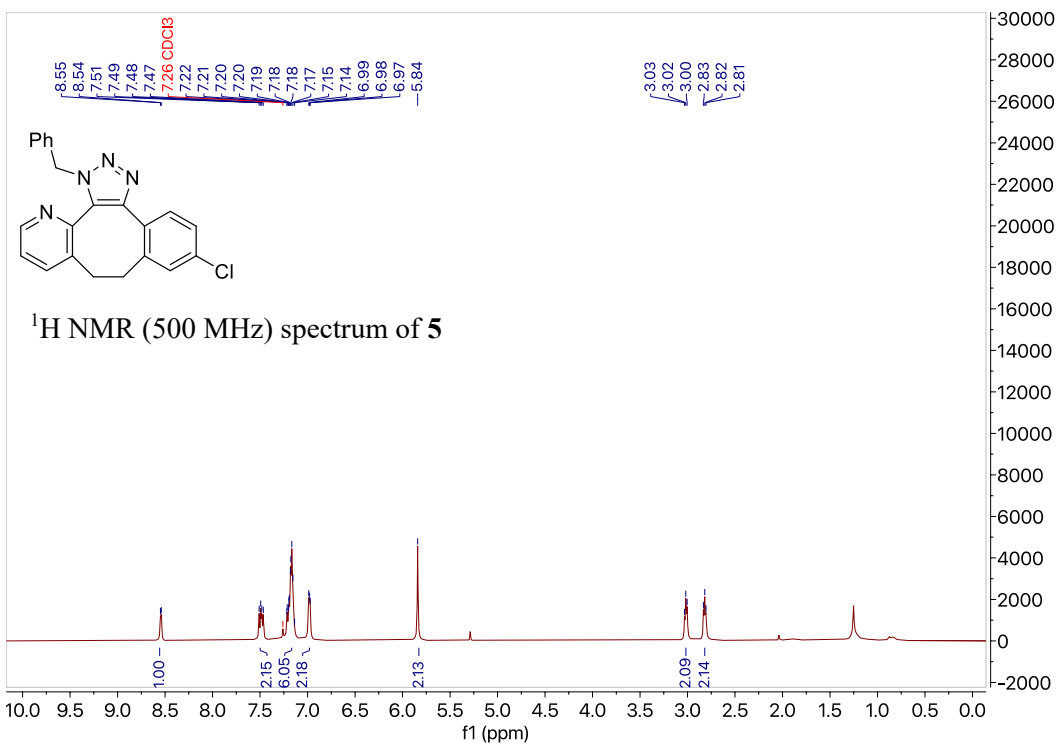












Cartesian Coordinates (Å), Total Energies (Hartree), and Imaginary Frequencies (cm⁻¹; TS's)**O-ABC**

C	4.13535200	-0.74572600	-0.13972100
C	2.88714500	-1.34390800	-0.29282000
C	1.73378000	-0.57155400	-0.21533100
C	1.83647300	0.82115400	0.02469200
C	3.09512100	1.40434100	0.18638500
C	4.24130400	0.62292600	0.10420200
H	5.03134600	-1.35450900	-0.20873200
H	2.78566800	-2.40628100	-0.48759400
H	3.16036500	2.47153100	0.37011800
H	5.21729800	1.08062500	0.22558300
C	0.56959200	1.47363300	0.07231400
C	-0.64294700	1.48819400	0.03360400
C	-0.44733000	-1.19640000	0.61230300
H	-0.60050300	-2.25023700	0.86842500
H	-0.03952300	-0.68385900	1.49019000
C	-1.90737800	0.81348900	0.02265300
C	-1.77949900	-0.58154600	0.24292300
C	-2.94190600	-1.33756500	0.18161800
H	-2.89790000	-2.41298600	0.33556400
C	-4.15996500	0.67496000	-0.25115600
C	-4.15657500	-0.70520100	-0.07273300
H	-5.09211000	1.20206500	-0.43994500
H	-5.08246700	-1.26692000	-0.12701900
N	-3.06372600	1.43394100	-0.21039000
O	0.52311500	-1.16472400	-0.45093200

Sum of electronic and zero-point Energies: -668.50984

Sum of electronic and thermal Energies: -668.49871

Sum of electronic and thermal Enthalpies: -668.49776

Sum of electronic and thermal Free Energies: -668.54693

ABC

C	-4.25093700	0.65339000	-0.01435500
C	-3.04182300	1.30711000	-0.24828600
C	-1.83790700	0.60792900	-0.26659400
C	-1.87719700	-0.78926300	-0.02740000
C	-3.08801500	-1.44464800	0.20270900
C	-4.27522100	-0.72135800	0.20656800
H	-5.17672300	1.22025500	-0.00952900
H	-3.03408400	2.37911000	-0.42797200
H	-3.08719800	-2.51473600	0.38165200
H	-5.21753400	-1.22900000	0.38539200
C	-0.58348300	-1.39493700	-0.00526300
C	0.62991600	-1.41391700	-0.02115900
C	0.53776400	1.28125700	0.58663900
H	0.74715600	2.31270500	0.88584300
H	0.09737600	0.78587800	1.45918800
C	1.92047600	-0.78811200	0.01439000
C	1.85471200	0.60611700	0.27088000
C	3.06239200	1.29533700	0.25337800
H	3.07426200	2.36660100	0.43904200
C	4.18473700	-0.76646000	-0.20914100
C	4.24720400	0.60702600	0.00945500
H	5.09191200	-1.33711100	-0.39318200
H	5.20220300	1.12094500	-0.00492200
N	3.04917000	-1.46327000	-0.21348000
C	-0.52125800	1.29271000	-0.57151500
H	-0.07965500	0.81527600	-1.45366800
H	-0.73007000	2.32987900	-0.84931700

Sum of electronic and zero-point Energies: -632.58783

Sum of electronic and thermal Energies: -632.5765

Sum of electronic and thermal Enthalpies: -632.57556
 Sum of electronic and thermal Free Energies: -632.62501

ODIBO

C	-4.17266000	-0.76072200	-0.04753800
C	-2.93001800	-1.34712500	0.19490100
C	-1.77498800	-0.57543200	0.24076600
C	-1.88396900	0.82094200	0.02385600
C	-3.12620200	1.40719900	-0.21524700
C	-4.26892500	0.61319500	-0.24764800
H	-5.06425300	-1.37872000	-0.07902400
H	-2.85905400	-2.42014900	0.35354400
H	-3.18813000	2.47770800	-0.37957000
H	-5.23594100	1.06899800	-0.43512000
C	-0.61719000	1.47997600	0.03702700
C	-0.43888500	-1.19227800	0.59891000
H	-0.02816800	-0.68889200	1.48096200
H	-0.58675400	-2.24953300	0.84277200
C	0.59549200	1.48789800	0.08505100
C	1.85871600	0.82739300	0.02975100
C	1.74481900	-0.56326900	-0.22226600
C	2.89256700	-1.34384300	-0.30306100
H	2.78224900	-2.40378700	-0.50642100
C	3.12222800	1.39744500	0.19828100
H	3.19684800	2.46241000	0.39166900
C	4.26255500	0.60745900	0.11115900
C	4.14603000	-0.75810600	-0.14335600
H	5.24203000	1.05641400	0.23789900
H	5.03697200	-1.37394800	-0.21556400
O	0.53084800	-1.14436200	-0.46683500

Sum of electronic and zero-point Energies: -652.45727

Sum of electronic and thermal Energies: -652.44598

Sum of electronic and thermal Enthalpies: -652.44504

Sum of electronic and thermal Free Energies: -652.49443

DIBO

C	-4.26372400	-0.66385300	0.02137200
C	-3.04966200	-1.30766500	0.25769700
C	-1.84975700	-0.60127800	0.27043200
C	-1.89801500	0.79453500	0.02170600
C	-3.11378600	1.43959900	-0.21119300
C	-4.29675800	0.70912400	-0.20821900
H	-5.18581400	-1.23681100	0.02166800
H	-3.03470200	-2.37845000	0.44441300
H	-3.12062100	2.50838700	-0.39816200
H	-5.24242800	1.20996700	-0.38908200
C	-0.60679600	1.40641000	-0.00830800
C	-0.52939900	-1.27736600	0.58005700
H	-0.08803200	-0.78727000	1.45535300
H	-0.73473500	-2.31154100	0.87169500
C	0.60705500	1.40687200	0.01036100
C	0.52895300	-1.27733100	-0.57911100
H	0.73422400	-2.31155100	-0.87077100
H	0.08764300	-0.78727200	-1.45438400
C	1.89808100	0.79456400	-0.02105100
C	1.84954400	-0.60143200	-0.26977700
C	3.04940700	-1.30785000	-0.25782000
H	3.03406900	-2.37866100	-0.44437400
C	3.11415500	1.43950400	0.21063000
H	3.12122700	2.50829800	0.39754900
C	4.29704900	0.70894300	0.20655800
C	4.26369900	-0.66406200	-0.02277500
H	5.24305700	1.20955700	0.38632500
H	5.18584300	-1.23693700	-0.02358200

Sum of electronic and zero-point Energies: -616.53449

Sum of electronic and thermal Energies: -616.52301
 Sum of electronic and thermal Enthalpies: -616.52207
 Sum of electronic and thermal Free Energies: -616.57174

OABC-II

C	4.16049700	0.74944000	-0.05819200
C	2.92338300	1.34601900	0.18677500
C	1.76383800	0.58161700	0.24036700
C	1.86278600	-0.81581600	0.03039200
C	4.24702000	-0.62616700	-0.25247400
H	5.05618300	1.36105800	-0.09642700
H	2.86053500	2.42016900	0.34073100
H	5.21025400	-1.08892000	-0.44186100
C	0.59306000	-1.46804900	0.05258000
C	0.43257900	1.20647500	0.59805600
H	0.01971200	0.71174300	1.48385600
H	0.58247100	2.26550700	0.83112400
C	-0.61880600	-1.49265400	0.10442300
C	-1.88047600	-0.81841400	0.03739500
C	-1.74897300	0.57125500	-0.22218700
C	-2.90751700	1.33182900	-0.30840600
H	-2.82680700	2.39376000	-0.51699600
C	-4.15419400	-0.67071900	0.11552400
C	-4.13464500	0.69873600	-0.14187400
H	-5.09864500	-1.19160100	0.25066400
H	-5.06282300	1.25591300	-0.20895800
O	-0.53970300	1.15261400	-0.46808700
N	-3.05781200	-1.42146700	0.20652800
C	3.09953900	-1.41255100	-0.21123800
H	3.15289200	-2.48427500	-0.36997700

Sum of electronic and zero-point Energies: -668.50911
 Sum of electronic and thermal Energies: -668.49798
 Sum of electronic and thermal Enthalpies: -668.49704
 Sum of electronic and thermal Free Energies: -668.54619

Methyl azide (MeN₃)

C	-1.52363100	-0.29528700	-0.00004200
H	-1.52083300	-0.92852900	0.89378300
H	-2.42873600	0.30906100	-0.00203000
H	-1.51869700	-0.93171700	-0.89155600
N	-0.39622900	0.64897600	-0.00028200
N	1.77205700	-0.28392700	-0.00030400
N	0.71132300	0.10965300	0.00059400

Sum of electronic and zero-point Energies: -204.01178
 Sum of electronic and thermal Energies: -204.0075
 Sum of electronic and thermal Enthalpies: -204.00655
 Sum of electronic and thermal Free Energies: -204.038

O-ABC-MeN₃ TS

C	-3.61247300	-2.30374000	-0.10696600
C	-2.31112300	-2.66129000	0.23429500
C	-1.32080400	-1.68996700	0.27201300
C	-1.68883600	-0.36321800	-0.05713100
C	-3.86944200	-0.96637300	-0.38723900
H	-4.40888400	-3.03830800	-0.14841800
H	-2.06326800	-3.69284400	0.47225500
H	-4.87549100	-0.64242100	-0.64437200
C	2.10892000	-1.08453300	-0.18304500
C	3.37749500	-1.65267000	-0.21390600
C	4.50265400	-0.84522700	-0.07488600
C	4.36321900	0.52976300	0.10684900
C	3.09755700	1.10251300	0.13457200
C	1.95394300	0.31005900	-0.01233000
H	3.45959100	-2.72474400	-0.35863600

H	5.49110100	-1.29308600	-0.10569000
H	5.24192200	1.15651300	0.21803000
H	2.97328100	2.17217000	0.26045200
C	-0.61300800	0.59587300	-0.06208900
C	0.08750100	-2.01736200	0.69547200
H	0.39003700	-1.36094300	1.51861200
H	0.13003900	-3.05436100	1.04728500
C	0.60743400	0.80663200	-0.02116500
N	-1.54259900	2.56547900	-0.29744800
N	-0.46190200	3.16750200	-0.16353600
N	0.68329800	3.10856300	-0.12471300
C	-2.65956400	2.99663000	0.54822900
H	-3.43837900	2.25392400	0.39212800
H	-2.37926100	3.02780200	1.60646400
H	-3.02128200	3.98002100	0.23486800
O	1.02423300	-1.89377000	-0.38447200
N	-2.94081200	-0.00955600	-0.36476700

Sum of electronic and zero-point Energies: -872.5095
Sum of electronic and thermal Energies: -872.4937
Sum of electronic and thermal Enthalpies: -872.49276
Sum of electronic and thermal Free Energies: -872.55305
Imaginary Frequency: -354.65

ABC-MeN₃ TS

C	-3.76390800	-2.15729400	-0.01148700
C	-2.47686300	-2.60109600	0.27185200
C	-1.41840000	-1.69939400	0.28782800
C	-1.71656500	-0.34555200	-0.00571800
C	-3.94582800	-0.80220000	-0.26593900
H	-4.60666700	-2.83969500	-0.02792300
H	-2.28866300	-3.65016600	0.48683400
H	-4.93702800	-0.40980500	-0.48253100
C	2.17881500	-1.11314100	-0.27678200
C	3.46972400	-1.63436000	-0.24137800
C	4.56546600	-0.82324200	0.04452300
C	4.37777400	0.53249900	0.29887600
C	3.09864700	1.07529000	0.26617100
C	1.99302800	0.26531100	-0.01448100
H	3.61737400	-2.69211300	-0.44425700
H	5.56363100	-1.24992100	0.06481200
H	5.22823600	1.16952600	0.52050200
H	2.94116500	2.13007600	0.45788700
C	-0.59291200	0.56453600	-0.03997100
C	-0.01059200	-2.12624200	0.60771500
H	0.35675100	-1.52547800	1.44696900
H	-0.02608600	-3.16627800	0.94722900
C	0.63552700	0.75153600	-0.02865700
C	0.98712900	-1.98204000	-0.58783600
H	0.45215800	-1.55751800	-1.44481200
H	1.33542500	-2.97329500	-0.89199900
N	-1.46720700	2.54597200	-0.32508000
N	-0.36592800	3.12357000	-0.25011800
N	0.77672600	2.99622900	-0.23654700
C	-2.55540200	3.07882400	0.50014200
H	-2.26720200	3.14928300	1.55443400
H	-2.86391800	4.06362800	0.13797400
H	-3.37382800	2.37314300	0.38611500
N	-2.95576000	0.08823000	-0.26545200

Sum of electronic and zero-point Energies: -836.58372
Sum of electronic and thermal Energies: -836.56777
Sum of electronic and thermal Enthalpies: -836.56683
Sum of electronic and thermal Free Energies: -836.62737
Imaginary Frequency: -385.37

ODIBO-MeN₃ TS

C	-3.70357700	-2.21871000	-0.11155500
C	-2.42782100	-2.51708800	0.36508100
C	-1.41193600	-1.56852800	0.32817500
C	-1.68712500	-0.28652400	-0.19923000
C	-2.96277900	0.00346300	-0.69029400
C	-3.96593200	-0.95999600	-0.64486300
H	-4.48539300	-2.97064400	-0.07608500
H	-2.21586900	-3.50467900	0.76693800
H	-3.14617600	0.98054000	-1.12708900
H	-4.95275000	-0.72862900	-1.03374400
C	2.05143800	-1.15350600	-0.11358300
C	3.29075000	-1.78233300	-0.06112700
C	4.45677000	-1.02285300	-0.03095200
C	4.38822300	0.36898000	-0.03958400
C	3.15257200	1.00331000	-0.08824400
C	1.96940100	0.25858500	-0.13059300
H	3.31732200	-2.86695500	-0.05991800
H	5.42083000	-1.52093100	0.00181700
H	5.29775100	0.96015800	-0.01333400
H	3.08494300	2.08541900	-0.10193800
C	-0.57620600	0.62586700	-0.22605900
C	-0.03051300	-1.88323200	0.84457000
H	0.28045300	-1.13542800	1.58215600
H	-0.03026900	-2.86694000	1.32666900
C	0.64781500	0.81825600	-0.19112600
N	-1.46943500	2.64755100	-0.16807100
N	-0.35144600	3.20399000	-0.10255300
N	0.78752800	3.09202500	-0.17551200
C	-2.35828100	2.90575600	0.97209300
H	-1.82518900	2.84721700	1.92637500
H	-2.84139100	3.88213600	0.87635500
H	-3.12295000	2.12954000	0.94108200
O	0.93192000	-1.93055700	-0.22282400

Sum of electronic and zero-point Energies: -856.45562
Sum of electronic and thermal Energies: -856.43976
Sum of electronic and thermal Enthalpies: -856.43882
Sum of electronic and thermal Free Energies: -856.49879
Imaginary Frequency: -386.19

DIBO-MeN₃ TS

C	-3.85583600	-2.05235200	-0.06397300
C	-2.60082000	-2.43020600	0.40832800
C	-1.51801800	-1.55514700	0.36171700
C	-1.71583100	-0.25963600	-0.17194200
C	-2.97378400	0.10769200	-0.66269700
C	-4.03926300	-0.78376000	-0.60772500
H	-4.68548800	-2.75079900	-0.01500000
H	-2.45495800	-3.42589100	0.81962100
H	-3.09396700	1.09089400	-1.10722800
H	-5.00984200	-0.48999600	-0.99509200
C	2.12038200	-1.20411100	-0.17486000
C	3.38417900	-1.77804200	-0.05814900
C	4.52703900	-0.99123300	0.06347500
C	4.41480200	0.39578900	0.06905400
C	3.16364100	0.99184200	-0.03821200
C	2.01064200	0.20814400	-0.15562800
H	3.47299400	-2.86145000	-0.07148300
H	5.50177000	-1.46190600	0.14812500
H	5.30119800	1.01582300	0.15938500
H	3.06790000	2.07088600	-0.02881700
C	-0.55519300	0.59475000	-0.22269400
C	-0.14331600	-1.96617200	0.82467700
H	0.22160300	-1.24313400	1.56235500
H	-0.20888100	-2.93308000	1.33200900
C	0.67725100	0.75854100	-0.22016100
C	0.88991600	-2.05956200	-0.34731700

H	0.38920900	-1.76561800	-1.27676400
H	1.19878400	-3.10129100	-0.47455800
N	-1.39142100	2.62367700	-0.16140000
N	-0.26187900	3.16364600	-0.13846400
N	0.86931000	2.99573900	-0.24879700
C	-2.24828600	2.92651800	0.99175500
H	-1.69589300	2.87445500	1.93534900
H	-2.70954200	3.91242100	0.88567300
H	-3.03198000	2.16893300	0.99315800

Sum of electronic and zero-point Energies: -820.5291
Sum of electronic and thermal Energies: -820.51311
Sum of electronic and thermal Enthalpies: -820.51217
Sum of electronic and thermal Free Energies: -820.57221
Imaginary Frequency: -415.57

O-ABC-II-MeN₃ TS

C	-4.50827500	-0.86432100	-0.11506800
C	-3.39600700	-1.64388400	0.19847800
C	-2.12647100	-1.08003000	0.25515700
C	-1.97081300	0.29908400	-0.01212100
C	-3.08952200	1.07735600	-0.31815900
C	-4.35168600	0.49471100	-0.37224200
H	-5.49337000	-1.31813100	-0.15694800
H	-3.51575700	-2.70515200	0.40120300
H	-2.95600400	2.13576900	-0.51143900
H	-5.21592400	1.10525700	-0.61446300
C	1.30001100	-1.69714200	-0.21352200
C	2.29350700	-2.66467800	-0.28327000
C	3.61855600	-2.27830200	-0.11808500
C	3.89116400	-0.93397500	0.11957400
C	1.67553500	-0.35190400	0.02553000
H	2.00909400	-3.69421800	-0.47536900
H	4.42456400	-3.00208700	-0.17073800
H	4.91555200	-0.59561100	0.25511400
C	-0.62579300	0.80432800	0.03366100
C	-0.92918000	-1.90587400	0.64534900
H	-0.41715900	-1.44818300	1.49881500
H	-1.24814400	-2.91376800	0.93063100
C	0.59534500	0.59900600	0.07423900
N	-0.73209400	3.07809000	0.24738000
N	0.41215600	3.16297500	0.28266800
N	1.50702200	2.57976900	0.38146400
C	2.59714500	3.06772200	-0.47098700
H	2.94131500	4.04781000	-0.12874500
H	3.39449200	2.33729300	-0.36115400
H	2.29193100	3.12997600	-1.52075300
O	0.00626100	-2.05217600	-0.44316800
N	2.95266400	0.00857500	0.18963000

Sum of electronic and zero-point Energies: -872.50843
Sum of electronic and thermal Energies: -872.49264
Sum of electronic and thermal Enthalpies: -872.49169
Sum of electronic and thermal Free Energies: -872.55196
Imaginary Frequency: -359.41

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