Supporting Information

Alkynyl Prins Carbocyclization Cascades for the Synthesis of Linear-Fused Heterocyclic Ring Systems

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General Remarks:

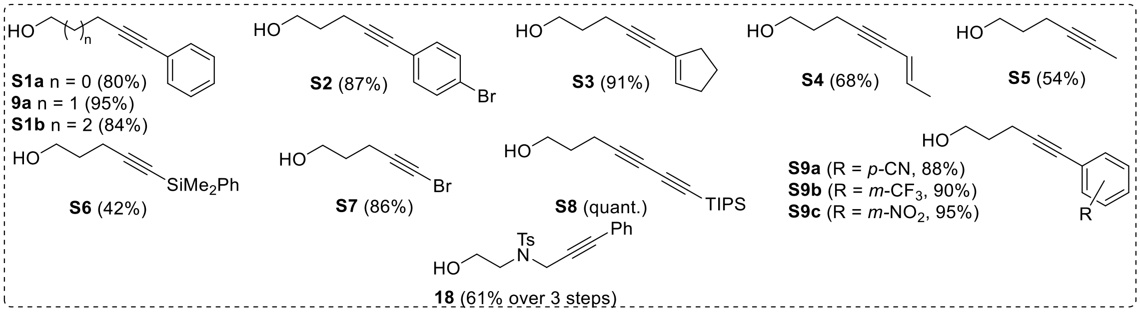
All reactions were carried out under an argon atmosphere in flame-dried glassware with magnetic stirring. Syringe needles used to dispense solvent were not flame-dried. Reagents were used as obtained from commercial suppliers without further purification. Tetrahydrofuran (THF), diethyl ether (Et_2O), methylene chloride (DCM), 1,2-dichloroethane (DCE), and toluene (PhMe) were purchased from Fisher and dispensed using the Glass Contour solvent purification system. 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) was purchased from Oakwood Chemicals and used without further drying (bottle stored in desiccator after opening. Hydrocarbon-stabilized (ChromAR®). 5Å molecular sieves used as desiccants were purchased from Aldrich, stored in an oven, and activated under high vacuum prior to use. Celite 545 was purchased from EMD. ACS grade hexanes, toluene, ethyl acetate, and DCM were used for column chromatography. Thin-layer chromatography (TLC) was performed on pre-coated silica gel 60 F254 glass-supported plates from EMD, and visualization was performed with a UV lamp followed by staining with *p*-anisaldehyde solution followed by heating. Column chromatography was carried out on EM Science silica gel (60 Å pore size, 230-400 mesh). Preparatory thin-layer chromatography (prep-TLC) was carried out using Analtech Uniplate F254 Prep-20x20 cm TLC plates. High-performance liquid chromatography (HPLC) was performed using Prominence-*i* LC 2030 Plus with a chiral stationary phase column (Chiralpak AD-H, Daicel Corp, 0.46 cm x 0.15 cm). Deuterated chloroform was purchased from Cambridge Isotope Laboratories.

^{1}H NMR spectra were recorded at room temperature on a 400 MHz Bruker Avance spectrometer or a 500 MHz Bruker Avance spectrometer. Chemical shifts are given in parts per million (ppm) referenced to solvent residual proton resonance (δ = 7.26 for $CHCl_3$). NMR data are reported as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dq = doublet of quartets, br = broad), coupling constants (*J*) given in Hz, and integration. In cases where two stereoisomers are present in greater than 2:1 ratio, only chemical shifts from the major stereoisomer are listed. For these cases a characteristic peak from both major and minor stereoisomer is given, with proton integrations, from which the ratio of stereoisomers can be extrapolated. In cases where two stereoisomers are present in less than 2:1 ratio, all peaks are listed. ^{13}C NMR spectra were recorded at room temperature unless otherwise stated on a 125 MHz or 101 MHz Bruker Avance spectrometer with proton decoupling. Chemical shifts are given in parts per million (ppm) from referenced to solvent carbon resonance (δ = 77.0 for $CHCl_3$). In cases where two stereoisomers are present in greater than 2:1 ratio, only chemical shifts from the major stereoisomer are listed. For these cases a characteristic peak from both major and minor stereoisomer is given, with proton integrations, from which the ratio of stereoisomers can be extrapolated. In cases where two stereoisomers are present in less than 2:1 ratio, all peaks are listed. For spectra where solvent residue is present, yields were obtained after placing sample under vacuum and bringing to a constant weight. High resolution mass spectra (HRMS) were measured at the University of Rochester Mass

Spectrometry Resource Lab. X-ray crystallography data were collected by Dr. William W. Brennessel at the X-ray Crystallographic Facility of the University of Rochester, Rochester, NY 14627 (USA).

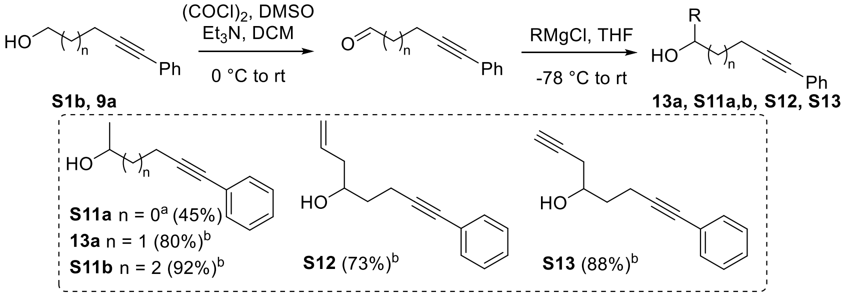
Experimental Details:

Primary Alcohols: Alcohols shown in Scheme S1 were prepared according to reported experimental procedures. Sonogashira cross-couplings for **9a, S1a,b**, **S2**, **S3**, **S4**, and **S9a-c**.[1-3] Internal alkyne **S5** was made following a procedure reported by Sutherland et al.[4] Silyl alkyne **S6** was made following a procedure by Trost et al.[5] Bromo alkyne **S7** was prepared using Wang's procedure.[6] Dialkyne **S8** was made using Nitz's conditions.[7] Alcohol with a sulfonamide in the tether **S10** was made following conditions by Cardenas.[8] Characterization data matched the literature reports.



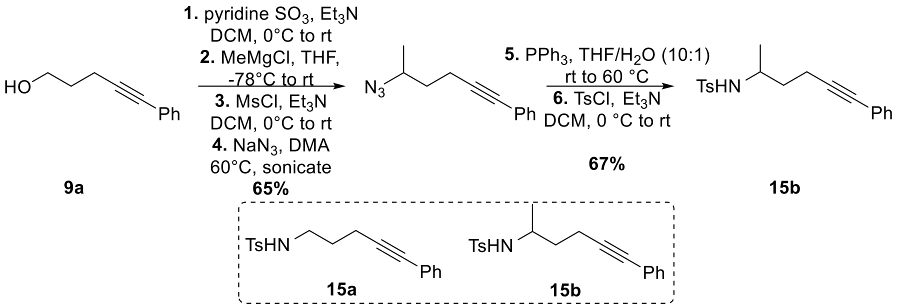
Scheme S1: Primary Alcohols Synthesized

Procedures for Preparation of Secondary Alcohols: Secondary alcohols were prepared by doing a Swern oxidation of the desired primary alcohol to afford an aldehyde to which a Grignard reagent of choice can be added to give products **13a, S11b**, **S12**, and **S13**.**[9, 10]** Alcohol **S11a** was prepared following the Ito procedure.[11] Spectroscopy data matched literature reports.



Scheme S2: Secondary Alcohols Synthesized (a) Made using Bates's procedure[11]
(b) Yield over two-steps.

Procedure for Preparation of Sulfonamides: Alpha-primary tosyl amine **15a** was prepared following the literature procedure. Spectra for this compound matched what has been reported in the literature.[12] Alpha-secondary amine **15b** was prepared following the procedure depicted in Scheme **S3**.[13, 14]



Scheme S3. Sulfonamides Prepared

Alpha-Secondary Sulfonamide Preparation:

Step 1. A solution of alcohol **9a** (3.70 g, 23.3 mmol) and Et_3N (14.1 g, 19.5 mL, 140 mmol) in DCM (50 mL) was cooled to 0 °C. Pyridine SO_3 (10.9 g, 69.8 mmol) was dissolved in DMSO (50 mL) and added dropwise to the cooled solution over 15 minutes. After addition, the reaction was warmed to room temperature and allowed to stir until full consumption of the alcohol by TLC (using 20% ethyl acetate/hexanes as the mobile phase and *p*-anisaldehyde to stain the plates. After the reaction was complete, the reaction was diluted with Et_2O, washed with 1M HCl until aqueous layer was acidic (pH < 1.0), extracted with Et_2O (3 x 100 mL), washed with brine, dry over $MgSO_4$, filter, and concentrate under vacuum. The crude aldehyde was used in Step 2.

Step 2. Crude aldehyde was added to a flask charged with a stir bar and purged with argon, then dissolved in dry THF and cooled to -78 °C. MeMgCl (15.5 mL, 46.6 mmol, 3 M in THF) was added dropwise, then the dry ice/isopropanol bath was removed, and the mixture was allowed to warm up to room temperature. After full consumption of the aldehyde by TLC, the mixture was cooled to 0 °C and saturated ammonium chloride solution was added dropwise to quench the reaction. When the bubbling had subsided, added 1:1 saturated ammonium chloride/water, extracted with Et_2O (3 x 100 mL), washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. Crude alcohol was used in the next step.

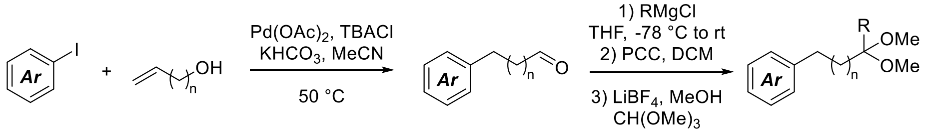
Step 3. The crude alcohol was dissolved in DCM (60 mL) and cooled to 0 °C. MsCl (4.5 mL, 58 mmol) was added in one portion, followed by Et_3N (8.1 mL, 58 mmol), which was added dropwise. The reaction was allowed to warm to room temperature slowly overnight. It is important to note that the mesylated alcohol and the starting material are very close in R*f* (when 20% ethyl acetate/hexanes is used for the mobile phase). Reaction mixture was poured into a separatory funnel with ice and washed with 1 M HCl. The aqueous layer was washed with Et_2O (3 x 50 mL), and the combined organic layers were washed with saturated sodium bicarbonate solution, then with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude mesylated alcohol was used in the next step.

Step 4. The crude mesylated alcohol from Step 3 was dissolved in DMA (60 mL) and sodium azide was added (6.07 g ,93.2 mmol, 4.0 equivalents). The mixture was heated to 60 °C and sonicated for three hours, then moved to an oil bath and heated at 60 °C overnight. After consumption of the starting material by TLC, pentane was added and the reaction was washed with water, extracted with pentane, dried over $MgSO_4$, filtered, and concentrated under vacuum. Crude was used for the next step (3.1 g, 65% crude yield over 4 steps).

Step 5. Crude azide from previous step (500 mg, 2.51 mmol) was dissolved in THF (16 mL). PPh_3 (1.35 g, 5.02 mmol) was added followed by water (2.05 mL, 120 mmol) and the reaction was allowed to stir at room temperature for an hour before heating to 60 °C overnight. Reaction mixture was concentrated to remove the THF, diluted with Et_2O, and washed with 1 M HCl (2 x 50 mL). The acidic aqueous layer was washed with EtOAc (3 x 50 mL), then basified with solid NaOH (pH > 12) and extracted with Et_2O (3 x 50 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude amine was used in the next step.

Step 6. Crude amine from previous step was added to a vial charged with a stir bar, under argon, then dissolved in DCM (10 mL) and cooled to 0 °C. TsCl (484 mg, 2.54 mmol) was added, followed by Et_3N (700 µL, 5.02 mmol). Cold bath was removed, and mixture was allowed to warm to room temperature. After the reaction was complete, water was added, extracted with Et_2O, washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. Crude was purified by column chromatography, using 10 to 15% EtOAc in hexanes to give sulfonamide **15b** (550 mg, 67% over 2 steps) as a yellow, viscous oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 3.5 Hz, 2H), 7.29 (d, *J* = 3.4 Hz, 3H), 7.24 (s, 1H), 4.50 (d, *J* = 8.0 Hz, 1H), 3.55 – 3.44 (m, 1H), 2.38 (s, 3H), 2.36 (d, *J* = 7.0 Hz, 1H), 1.68 (t, *J* = 6.9 Hz, 2H), 1.13 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 137.9, 131.5, 129.7, 128.2, 127.8, 127.1, 123.6, 88.8, 81.4, 49.5, 36.0, 21.7, 21.5, 16.0.; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{21}NO_2S$: 328.1366, found: 328.1358.

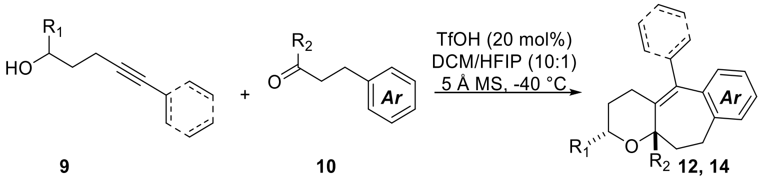
Procedures for Preparation of Aldehydes/Ketones: Aldehydes and ketals were prepared following previously reported procedures.[15-19] General reaction schemes below show the pathways used for aldehyde/ketal preparation. Spectroscopy data for aldehydes matched literature reports.



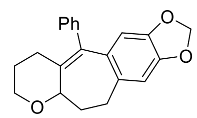
Scheme S4: Aldehydes/Ketals Synthetic pathways

General Procedure for Carbocyclization Cascade:

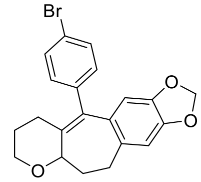
Scheme S5. General Procedure for Carbocyclization



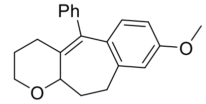
Oven dried, 5 Å molecular sieves (300 mg/mmol of limiting reagent **4**) were transferred to a flask equipped with a stir bar and dried further under vacuum while heating over a Bunsen burner for about 2 minutes. The reaction vessel was allowed to cool under a flow of argon before adding DCM/HFIP (10:1) (0.1 M with respect to the limiting reagent), followed by the alcohol **9/ 13** (1.2 equivalents) and aldehyde/ketal (1.0 equivalents for aldehydes, 1.5 equivalents for ketals). The reaction mixture was cooled to -40 °C before adding triflic acid (TfOH) (20 mol%) dropwise. Mixture was allowed to stir at -40 °C until all of the limiting reagent was consumed by TLC (using 20% ethyl acetate/hexane mixture as mobile phase and p-anisaldehyde to stain the plates). After completion, the reaction was quenched by adding solid sodium bicarbonate (300 mg/mmol of **10**) and diluting with ether (Et_2O). The quenched reaction mixture was filtered through a silica plug, eluted with Et_2O, and concentrated under vacuum. Pure product was isolated after preparatory TLC (using 20% ethyl acetate/hexane as mobile phase) or column chromatography using 5% ethyl acetate/hexane as mobile phase.



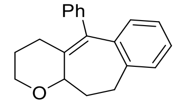
Compound **12a** was isolated as white solid (30.2 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.3 Hz, 2H), 7.26 (dd, *J* = 8.7, 5.9 Hz, 1H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.72 (s, 1H), 6.25 (s, 1H), 5.87 (s, 2H), 4.02 (dd, *J* = 11.1, 6.9 Hz, 1H), 3.99 – 3.90 (m, 1H), 3.45 (dt, *J* = 11.0, 8.2 Hz, 1H), 2.85 – 2.73 (m, 1H), 2.56 (ddd, *J* = 14.0, 6.7, 2.9 Hz, 1H), 2.53 – 2.45 (m, 2H), 2.42 – 2.32 (m, 1H), 2.32 – 2.23 (m, 1H), 2.05 (dd, *J* = 11.8, 5.6 Hz, 1H), 1.79 – 1.68 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.0, 145.7, 141.4, 138.4, 134.7, 134.3, 133.4, 129.9, 128.1, 126.7, 109.6, 108.4, 100.8, 63.3, 39.6, 30.4, 25.0, 22.8; m.p = 95-97°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{22}O_3$: 321.1485, found: 321.1477.



Compound **12b** was isolated as white solid (330 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.9 Hz, 2H), 6.99 (d, *J* = 7.9 Hz, 2H), 6.71 (s, 1H), 6.20 (s, 1H), 5.88 (s, 2H), 3.97 (dt, *J* = 30.7, 9.6 Hz, 2H), 3.43 (dd, *J* = 18.3, 9.0 Hz, 1H), 2.73 (dd, *J* = 14.9, 7.6 Hz, 1H), 2.57 – 2.43 (m, 3H), 2.37 (dd, *J* = 20.3, 11.4 Hz, 1H), 2.26 (dd, *J* = 19.1, 11.0 Hz, 1H), 2.05 (s, 1H), 1.71 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.2, 145.9, 140.3, 139.2, 134.8, 133.7, 132.3, 131.6, 131.3, 120.8, 109.5, 108.5, 100.9, 77.2, 63.2, 39.6, 30.4, 24.9, 22.9; m.p = 60-63°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{19}BrO_3$: 399.0519, found: 399.0585.

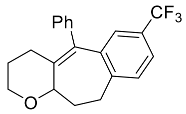


Compound **12c** was isolated as viscous oil, as a 1.7:1 of the *para-ortho* trapped products (57.8 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 4H), 7.30 – 7.24 (m, 5H), 7.19 (dd, *J* = 16.1, 7.9 Hz, 2H), 7.12 (dd, *J* = 13.9, 7.6 Hz, 6H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.79 (s, 2H), 6.74 – 6.67 (m, 3H), 6.64 (d, *J* = 8.5 Hz, 2H), 4.11 (dt, *J* = 14.4, 7.2 Hz, 1H), 4.05 (dt, *J* = 16.2, 8.2 Hz, 2H), 4.00 – 3.89 (m, 3H), 3.80 (s, 6H), 3.57 – 3.43 (m, 3H), 3.32 (s, 4H), 2.93 – 2.75 (m, 4H), 2.58 (dt, *J* = 20.6, 7.0 Hz, 5H), 2.54 – 2.20 (m, 9H), 2.12 – 1.98 (m, 3H), 1.86 – 1.69 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 157.0, 142.4, 141.8, 138.5, 137.4, 133.6, 133.3, 130.8, 130.6, 129.9, 129.4, 128.7, 128.31, 128.0, 127.4, 126.6, 125.8, 120.8, 113.6, 111.3, 110.9, 77.4, 76.5, 63.5, 62.9, 55.6, 55.1, 38.8, 38.1, 30.7, 30.5, 25.1, 24.7, 23.1, 21.6; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{22}O_2$: 307.1693, found: 307.1686.

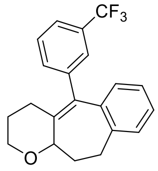


Compound **12d** was isolated as a foam (55.1 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.4 Hz, 4H), 7.28 (t, *J* = 7.3 Hz, 2H), 7.24 (d, *J* = 7.3 Hz, 2H), 7.15 (d, *J* = 7.6 Hz, 5H), 7.10 (dd, *J* = 14.6, 7.2 Hz, 3H), 6.78 (d, *J* = 7.5 Hz, 2H), 4.03 (dd, *J* = 10.8, 7.5 Hz, 2H), 3.97 (ddd, *J* = 11.4, 8.7, 2.9 Hz, 2H), 3.53 – 3.39 (m, 2H), 2.89 (td, *J* = 12.8, 8.1 Hz, 2H), 2.68 – 2.56 (m, 4H), 2.53

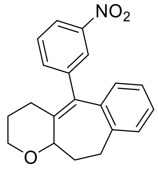
(dt, *J* = 12.8, 6.1 Hz, 2H), 2.41 (dd, *J* = 20.0, 12.0 Hz, 2H), 2.33 (dd, *J* = 19.7, 11.6 Hz, 2H), 2.15 – 2.01 (m, 2H), 1.82 – 1.67 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 141.1, 140.8, 138.9, 133.5, 129.9, 129.5, 128.2, 128.1, 126.7, 126.7, 125.9, 77.2, 63.4, 39.3, 30.4, 25.0, 23.0; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{20}O$: 277.1587, found: 277.1583.



Reaction mixture was allowed to stir at -40 °C for an hour after addition of the acid, then allowed to warm up to room temperature until all of the aldehyde had been consumed. Compound **12e** was isolated as a yellow oil (21.1 mg, 31%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 7.12 (s, 1H), 7.11 (s, 1H), 7.01 (s, 1H), 3.96 (dd, *J* = 10.9, 8.2 Hz, 2H), 3.53 – 3.34 (m, 1H), 2.88 (dd, *J* = 12.7, 8.2 Hz, 1H), 2.68 (dd, *J* = 13.0, 6.5 Hz, 1H), 2.64 – 2.57 (m, 1H), 2.57 – 2.47 (m, 1H), 2.38 (ddd, *J* = 28.2, 19.3, 11.4 Hz, 2H), 2.16 – 2.02 (m, 1H), 1.82 – 1.68 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.6, 141.7, 140.6, 132.9, 129.8, 128.7, 128.4, 127.1, 126.1, 125.3, 123.4, 76.9, 63.4, 39.2, 30.4, 24.8, 23.1; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{19}F_3O$: 345.1461, found: 345.1457.

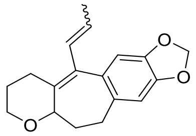


Reaction was allowed to stir at -40°C for an hour after addition of TfOH, then warmed up to room temperature until full consumption of starting material was observed by TLC. Compound **12f** was isolated as a viscous, colorless oil (33.3 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.41 (s, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 6.9 Hz, 1H), 7.15 (dt, *J* = 21.8, 7.4 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 1H), 4.09 – 3.93 (m, 2H), 3.47 (dd, *J* = 18.3, 9.6 Hz, 1H), 2.89 (td, *J* = 12.8, 8.1 Hz, 1H), 2.66 (dd, *J* = 13.0, 6.5 Hz, 1H), 2.61 – 2.48 (m, 2H), 2.48 – 2.28 (m, 2H), 2.17 – 2.04 (m, 1H), 1.76 (ddd, *J* = 12.6, 8.3, 5.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 140.9, 140.5, 140.2, 133.3, 132.3, 129.4, 128.6, 128.4, 127.1, 126.6, 126.2, 77.3, 77.2, 63.3, 39.2, 30.4, 24.9, 23.1. ^{19}F NMR (250 MHz) δ -62.7. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{19}F_3O$: 345.1461, found: 345.1459.

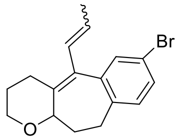


Reaction was allowed to stir at -40°C for an hour after addition of TfOH, then warmed up to room temperature until full consumption of starting material was observed by TLC. Compound **12g** was isolated as a viscous oil (22.1 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 1H), 8.00 (s, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.28 (dd, *J* = 12.0, 6.2 Hz, 1H), 7.18 (dd, *J* = 16.7, 9.2 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 4.03 (dd, *J* = 10.9, 7.5 Hz, 1H), 3.97 (ddd, *J* = 11.5, 8.6, 2.9 Hz, 1H), 3.49 – 3.42 (m, 1H), 2.87 (td, *J* = 12.9, 8.0 Hz, 1H), 2.65 (dd, *J* = 13.2, 6.4 Hz, 1H), 2.59 – 2.48 (m, 2H), 2.48 – 2.38 (m, 1H), 2.33 (dd, *J* = 19.5, 11.6 Hz, 1H), 2.16 – 2.05 (m, 1H), 1.78 (dtd, *J* = 10.1, 6.7, 3.0 Hz, 1H). ^{13}C NMR (126

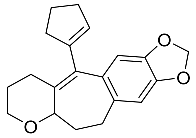
MHz, $CDCl_3$) δ 148.3, 143.2, 141.5, 140.9, 139.7, 136.1, 131.4, 129.3, 129.1, 128.6, 127.4, 126.3, 124.8, 121.8, 77.1, 63.3, 39.2, 30.4, 24.8, 23.2. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{19}NO_3$: 322.1438, found: 322.1437.



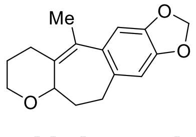
Compound **12h** was isolated as a foamy viscous oil, as a 6.3:1 mixture of *E/Z* isomers (22.4mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.72 (s, 1H), 6.67 (s, 1H), 5.93 (d, *J* = 10 Hz, 1H), 5.51 (dq, *J* = 15.2, 7.0 Hz, 1H), 3.86 – 3.76 (m, 3H), 3.36 (dt, *J* = 14.2, 7.2 Hz, 1H), 2.88 (dd, *J* = 14.7, 6.3 Hz, 1H), 2.54-2.47 (m, 1H), 2.45 – 2.10 (m, 5H), 1.99 (dt, *J* = 14.8, 7.3 Hz, 1H), 1.78 (d, *J* = 6.7 Hz, 3H), 1.67 (dt, *J* = 11.7, 6.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.0, 145.4, 135.4, 134.5, 131.5, 130.0, 128.3, 128.1, 109.7, 108.2, 100.7, 76.5, 62.8, 38.3, 29.8, 24.1, 20.8, 18.6; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{18}H_{20}O_3$: 285.1485, found: 285.1481



Compound **12i** was isolated as a white solid, as a 7.9:1 mixture of *E/Z* isomers (22.4mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.52 (d, *J* = 15.5 Hz, 1H), 5.49 (dd, *J* = 14.9, 7.0 Hz, 1H), 3.88 – 3.76 (m, 2H), 3.38 – 3.29 (m, 1H), 2.88 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.56 – 2.47 (m, 1H), 2.47 – 2.36 (m, 2H), 2.28 (dd, *J* = 12.6, 6.2 Hz, 1H), 2.21 – 2.12 (m, 1H), 2.05 – 1.94 (m, 1H), 1.80 (d, *J* = 6.1 Hz, 3H), 1.70-1.60 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 140.0, 131.8, 132.0, 129.7, 129.6, 129.0, 128.6127.7, 119.3, 76.2, 62.8, 37.8, 29.3, 23.9, 20.8, 18.6; m.p = 105-107°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{19}BrO$: 319.0692, found: 319.0687.

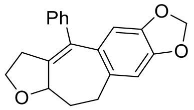


Compound **12j** was isolated as a foamy viscous oil (255 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.60 (s, 1H), 5.99 – 5.81 (m, 2H), 5.61 (s, 1H), 3.89 (t, *J* = 9.1 Hz, 2H), 3.35 (dd, *J* = 18.4, 9.0 Hz, 1H), 2.79 – 2.68 (m, 1H), 2.59 (dd, *J* = 14.3, 7.4 Hz, 1H), 2.51 – 2.34 (m, 6H), 2.34 – 2.24 (m, 1H), 2.16 (dd, *J* = 18.2, 10.5 Hz, 2H), 2.08 – 1.97 (m, 1H), 1.94 – 1.84 (m, 2H), 1.63 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.8 (2C), 142.6, 137.1, 134.4, 132.5, 130.1, 129.1, 108.6, 108.2, 100.7, 77.1, 63.2, 39.1, 36.0, 32.8, 30.1, 24.9, 23.8, 22.7; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{22}O_3$: 311.1642, found: 311.1636.

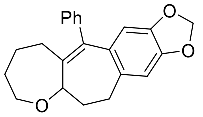


Added 40 mol% of TfOH at -40 °C, allowed to stir at this temperature for an hour and then warmed to room temperature until all of the aldehyde was consumed. Compound **12k** was isolated as a light-yellow oil, as a 3.9:1 inseparable mixture of *para/ortho*-trapped adduct (33.0 mg, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, *J* = 7.9 Hz, 1H), 6.70 (s, 1H), 6.66 (d, *J* = 6.8 Hz, 1H), 5.92

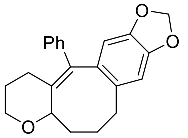
(s, 2H), 4.39 – 4.30 (m, 1H), 3.78 (td, *J* = 11.4, 3.8 Hz, 1H), 3.67 (d, *J* = 11.4 Hz, 1H), 2.80 (d, *J* = 14.3 Hz, 1H), 2.70 – 2.60 (m, 1H), 2.55 (dt, *J* = 13.4, 6.9 Hz, 1H), 2.29-2.13 (m, 3H), 1.92 (s, 3H), 1.77 – 1.67 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.7, 145.8, 139.4, 134.9, 129.9, 121.2, 108.9, 108.2, 100.8, 100.7, 72.3, 60.3, 32.7, 31.2, 25.6, 21.4, 16.2; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{16}H_{18}O_3$: 259.1329, found: 259.1329.



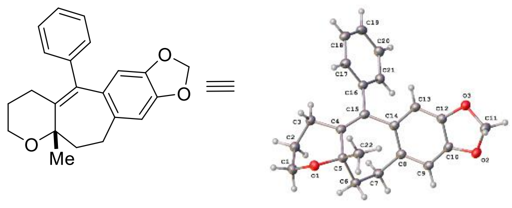
Compound **12l** was isolated as white solid (84.3 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 6.9 Hz, 2H), 7.28 (d, *J* = 7.7 Hz, 1H), 7.24 (t, *J* = 10.3 Hz, 2H), 6.75 (s, 1H), 6.32 (d, *J* = 1.7 Hz, 1H), 5.88 (d, *J* = 2.0 Hz, 2H), 4.35 (t, *J* = 8.6 Hz, 1H), 4.01 (dd, *J* = 10.0, 6.1 Hz, 1H), 3.98 – 3.88 (m, 1H), 2.99 (dd, *J* = 16.2, 8.0 Hz, 1H), 2.87 – 2.75 (m, 1H), 2.65 – 2.47 (m, 3H), 2.14 (dd, *J* = 18.9, 8.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 145.8, 141.9, 141.0, 135.0, 134.6, 130.8, 129.3, 128.2, 127.9, 126.8, 109.0, 108.6, 100.8, 78.5, 67.0, 40.3, 32.2, 30.8; m.p = 39-40°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{18}O_3$: 307.1334, found: 307.1323.



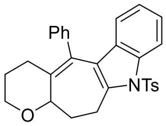
Compound **12m** was isolated as white solid (82.9 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.0 Hz, 2H), 7.25 (dd, *J* = 9.1, 4.6 Hz, 1H), 7.13 (s, 2H), 6.71 (s, 1H), 6.26 (d, *J* = 1.7 Hz, 1H), 5.89 – 5.82 (m, 2H), 4.05 (d, *J* = 12.0 Hz, 1H), 4.00 (dd, *J* = 10.6, 6.0 Hz, 1H), 3.32 – 3.22 (m, 1H), 2.83 – 2.71 (m, 1H), 2.53 – 2.41 (m, 2H), 2.41 – 2.31 (m, 2H), 2.14 – 2.04 (m, 1H), 2.01 (d, *J* = 11.0 Hz, 1H), 1.72 (s, 2H), 1.53 (d, *J* = 6.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.0, 145.7, 143.2, 141.9, 134.7, 134.7, 134.6, 134.5, 129.6, 127.9, 126.6, 109.6, 108.1, 100.7, 80.7, 71.7, 40.6, 30.7, 30.4, 29.9, 28.7; m.p = 47-49°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{22}O_3$: 335.1647, found: 335.1634.



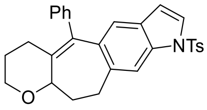
Added 40 mol% of TfOH at -40 °C, allowed to stir at this temperature for an hour and then warmed to 0 °C until all of the aldehyde was consumed. Compound **12n** was isolated as a white foam (20 mg, 34%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.4 Hz, 2H), 7.26 – 7.19 (m, 1H), 7.09 (d, *J* = 7.1 Hz, 2H), 6.67 (s, 1H), 6.34 (s, 1H), 5.89 – 5.82 (m, 2H), 4.02 (d, *J* = 10.9 Hz, 1H), 3.79 (dd, *J* = 14.1, 6.8 Hz, 1H), 3.66 (d, *J* = 11.3 Hz, 1H), 2.77 (dd, *J* = 12.9, 7.9 Hz, 1H), 2.64 (d, *J* = 15.0 Hz, 1H), 2.43 (t, *J* = 12.6 Hz, 1H), 2.35 – 2.23 (m, 1H), 2.17 – 2.06 (m, 1H), 1.99 (ddd, *J* = 16.6, 12.8, 5.4 Hz, 1H), 1.93 – 1.72 (m, 3H), 1.53 (dt, *J* = 12.0, 7.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 145.3, 141.9, 136.8, 135.5, 133.8, 132.9, 129.2, 128.1, 126.7, 108.9, 108.6, 100.8, 76.3, 61.3, 32.8, 29.7, 27.8, 27.7, 23.7.; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{22}O_3$: 335.1642, found: 335.1634.



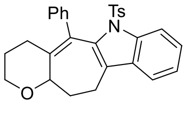
Added 1.5 equivalents of dimethyl ketal and 1.0 equivalents of alcohol **9a**. Stir at -40 °C until all of the alcohol was consumed. Compound **12o** was isolated as white solid (38.7 mg, 48%). Recrystallized by dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.32 (t, *J* = 7.2 Hz, 2H), 7.28 – 7.22 (m, 1H), 7.08 (d, *J* = 5.5 Hz, 2H), 6.67 (s, 1H), 6.17 (s, 1H), 5.85 (s, 2H), 3.94 – 3.84 (m, 1H), 3.81 (t, *J* = 9.4 Hz, 1H), 2.95 (dd, *J* = 13.3, 5.4 Hz, 1H), 2.59 (d, *J* = 12.8 Hz, 1H), 2.50 (d, *J* = 13.0 Hz, 1H), 2.39 (ddd, *J* = 19.6, 11.4, 6.4 Hz, 2H), 2.17 – 2.04 (m, 1H), 1.81 – 1.59 (m, 2H), 1.06 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.9, 145.7, 143.7, 143.1, 135.0, 134.6, 133.0, 130.1, 128.1, 126.5, 110.0, 108.0, 100.7, 78.1, 58.6, 47.4, 31.5, 27.6, 25.7, 24.0; m.p = 115-117°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{22}H_{22}O_3$: 335.1642, found: 335.1634.



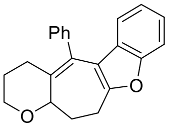
Compound **12p** was isolated as white solid (196 mg, 84%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.20 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.1 Hz, 2H), 7.30 (d, *J* = 5.9 Hz, 3H), 7.26 (s, 1H), 7.23 (d, *J* = 7.5 Hz, 2H), 7.16 (t, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 6.2 Hz, 2H), 6.89 (t, *J* = 7.0 Hz, 1H), 6.33 (d, *J* = 8.0 Hz, 1H), 3.97 (t, *J* = 9.7 Hz, 2H), 3.68 (dd, *J* = 14.7, 6.5 Hz, 1H), 3.42 (q, *J* = 8.9 Hz, 1H), 2.82 (dd, *J* = 21.5, 13.6 Hz, 1H), 2.73 – 2.62 (m, 1H), 2.53 – 2.39 (m, 3H), 2.37 (s, 3H), 2.07 (d, *J* = 24.1 Hz, 1H), 1.77 (s, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.9, 142.1, 140.5, 139.1, 136.8, 135.8, 129.8, 129.5, 128.8, 128.5, 128.3, 127.1, 126.4, 123.7, 123.2, 121.8, 120.3, 114.9, 78.3, 63.6, 40.9, 25.3, 22.7, 21.8, 21.6; m.p = 78-80°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{29}H_{27}NO_3S$: 470.1785, found: 470.1776.



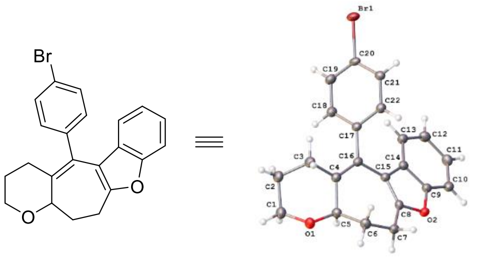
Compound **12q** was isolated as white solid (38.2 mg, 52%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.83 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.41 (d, *J* = 1.9 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.24 (t, *J* = 9.6 Hz, 4H), 7.10 (d, *J* = 7.4 Hz, 2H), 6.90 (s, 1H), 6.42 (s, 1H), 3.93 (dd, *J* = 20.6, 12.4 Hz, 2H), 3.40 (dd, *J* = 18.4, 8.9 Hz, 1H), 2.94 (dd, *J* = 20.7, 12.4 Hz, 1H), 2.74 (dd, *J* = 12.9, 6.4 Hz, 1H), 2.63 – 2.42 (m, 2H), 2.36 (d, *J* = 17.2 Hz, 4H), 2.32 – 2.26 (m, 1H), 2.03 (s, 1H), 1.71 (s, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.9, 141.9, 138.0, 137.1, 135.4, 133.6, 133.3, 130.0, 129.0, 128.1, 126.7, 126.0, 122.3, 112.5, 109.0, 65.8, 63.2, 38.7, 31.1, 25.0, 22.9, 21.6, 15.3; m.p = 92-95°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{29}H_{27}NO_3S$: 470.1785, found: 470.1783.



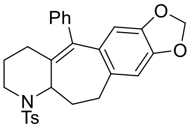
Compound **12r** was isolated as an amorphous solid, as a 1:1 mixture of conformers (96.8 mg, 41%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 20H), 7.57 (d, *J* = 8.1 Hz, 26H), 7.40 (d, *J* = 4.3 Hz, 44H), 7.34 (s, 34H), 7.31 (d, *J* = 13.6 Hz, 53H), 7.26 (s, 64H), 7.21 (d, *J* = 2.3 Hz, 15H), 7.19 – 6.96 (m, 155H), 6.80 (q, *J* = 8.1 Hz, 20H), 6.57 (s, 7H), 6.04 (d, *J* = 7.1 Hz, 9H), 5.94 (d, *J* = 7.5 Hz, 7H), 5.84 (s, 9H), 5.44 (s, 10H), 4.21 – 4.10 (m, 19H), 4.01 (dd, *J* = 25.5, 9.3 Hz, 48H), 3.90 (t, *J* = 7.1 Hz, 8H), 3.76 (q, *J* = 7.4 Hz, 9H), 3.67 – 3.49 (m, 17H), 2.63 – 2.50 (m, 36H), 2.46 (dd, *J* = 16.9, 10.0 Hz, 23H), 2.32 (d, *J* = 16.8 Hz, 107H), 2.03 (ddd, *J* = 26.3, 22.1, 9.7 Hz, 75H), 1.94 – 1.74 (m, 92H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 141.0, 140.3, 138.0, 137.4, 137.1, 136.4, 135.4, 135.1, 134.9, 134.9, 134.8, 131.5, 131.4, 129.8, 129.8, 129.6, 129.5, 128.9, 128.5, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 126.9, 126.8, 126.5, 126.4, 125.0, 124.2, 123.8, 123.7, 122.7, 122.3, 113.0, 112.4, 98.7, 89.3, 89.2, 81.2, 81.0, 75.0, 74.1, 71.4, 70.0, 68.0, 67.7, 53.4, 53.1, 29.2, 28.9, 28.4, 28.0, 27.9, 27.6, 26.6, 26.0, 25.7, 21.4, 21.4, 16.2, 16.2; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{29}H_{27}NO_3S$: 470.1785, found: 470.1784.



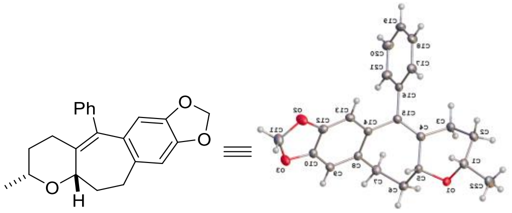
Compound **12s** was isolated as light-yellow solid (49.3 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 3H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.25 (s, 1H), 7.09 (t, *J* = 7.7 Hz, 1H), 6.82 (t, *J* = 7.6 Hz, 1H), 5.97 (d, *J* = 7.9 Hz, 1H), 4.32 (t, *J* = 5.7 Hz, 1H), 4.05 (dd, *J* = 14.5, 5.4 Hz, 1H), 3.60 (td, *J* = 10.6, 6.8 Hz, 1H), 3.27 – 3.11 (m, 2H), 2.52 – 2.42 (m, 1H), 2.42 – 2.27 (m, 3H), 2.04 (dd, *J* = 13.8, 6.9 Hz, 1H), 1.80 – 1.67 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.3, 153.8, 140.5, 139.2, 129.8, 128.6, 128.3, 127.0, 126.0, 123.0, 121.9, 121.2, 114.8, 110.4, 79.1, 64.7, 32.7, 25.4, 25.0, 24.3; m.p = 86-88°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{22}H_{20}O_2$: 317.1536, found: 317.1530.



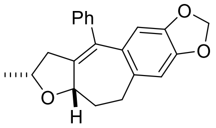
Compound **12t** was isolated as white solid (58.4 mg, 70%). Recrystallized by dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.7 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.11 (t, *J* = 8.4 Hz, 3H), 6.87 (t, *J* = 7.5 Hz, 1H), 6.06 (d, *J* = 7.8 Hz, 1H), 4.29 (s, 1H), 4.04 (t, *J* = 9.9 Hz, 1H), 3.56 (dd, *J* = 17.6, 10.0 Hz, 1H), 3.25 – 3.08 (m, 2H), 2.48 – 2.39 (m, 1H), 2.33 (dd, *J* = 24.7, 6.9 Hz, 3H), 2.04 (d, *J* = 12.0 Hz, 1H), 1.70 (d, *J* = 3.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 153.9, 140.1, 139.3, 131.5 (2C), 128.3, 124.9, 123.2, 122.1, 121.0 (2C), 114.2, 110.5, 79.0, 64.5, 32.7, 25.2, 24.9, 24.2; m.p = 126-128°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{22}H_{19}BrO_2$: 395.0641, found: 395.0630.



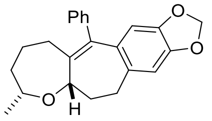
After addition of TfOH, stirred at -40 °C for 30 minutes before warming to 0 °C until all the starting material was consumed. Compound **16a** was isolated as a white solid (24 mg, 54%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.59 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.23 (s, 2H), 6.77 (d, *J* = 6.4 Hz, 2H), 6.75 (s, 1H), 6.23 (s, 1H), 5.93 (d, *J* = 7.0 Hz, 2H), 4.50 (dd, *J* = 12.1, 7.3 Hz, 1H), 3.76 – 3.62 (m, 1H), 3.40 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.64 (td, *J* = 13.1, 7.4 Hz, 1H), 2.53 – 2.49 (m, 1H), 2.47 (s, 3H), 2.42 (dt, *J* = 19.9, 6.7 Hz, 1H), 2.29 (td, *J* = 12.2, 7.2 Hz, 1H), 2.17 (ddd, *J* = 15.8, 6.1, 3.4 Hz, 1H), 1.79 – 1.70 (m, 1H), 1.59 (s, 2H), 1.48 (dd, *J* = 9.5, 4.0 Hz, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 146.6, 146.2, 142.9, 140.5, 137.5, 135.4, 134.2, 134.0, 130.1, 129.5, 127.9, 127.1, 126.9, 109.4, 108.9, 100.9, 54.5, 41.7, 41.2, 30.9, 26.0, 21.9, 21.5; m.p = 155-157°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{28}H_{27}NO_4S$: 474.1734, found: 474.1728.



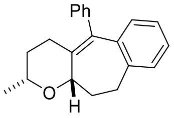
Compound **14a** was isolated as white solid, 9:1 dr (61 mg, 91%). Recrystallized by dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.12 (d, *J* = 7.1 Hz, 2H), 6.72 (d, *J* = 6.9 Hz, 1H), 6.25 (d, *J* = 6.1 Hz, 1H), 5.86 (s, 2H), 4.01 (dd, *J* = 10.7, 7.5 Hz, 1H), 3.48 (dt, *J* = 6.2, 4.1 Hz, 1H), 2.80 (td, *J* = 12.6, 7.9 Hz, 1H), 2.56 (td, *J* = 12.3, 6.4 Hz, 1H), 2.49 (dd, *J* = 12.9, 7.0 Hz, 2H), 2.40 (dd, *J* = 21.4, 11.4 Hz, 1H), 2.20 (td, *J* = 11.5, 8.2 Hz, 1H), 1.94 – 1.82 (m, 1H), 1.73 (dd, *J* = 20.9, 9.8 Hz, 1H), 1.24 (d, *J* = 4.8 Hz, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.9, 145.7, 141.6, 139.2, 134.8, 134.3, 133.0, 129.8, 128.1, 126.7, 109.6, 108.4, 100.7, 77.9, 40.1, 33.5, 30.4, 23.0, 22.3; m.p = 132-135°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{22}H_{22}O_3$: 335.1642, found:



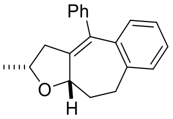
Compound **14b** isolated as a white solid, 7:1 dr (53.3 mg, 83%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (t, *J* = 7.3 Hz, 4H), 7.27 (dd, *J* = 14.5, 6.8 Hz, 3H), 7.19 (d, *J* = 7.0 Hz, 4H), 6.72 (s, 2H), 6.29 (s, 2H), 5.89 – 5.82 (m, 4H), 4.32 (t, *J* = 8.2 Hz, 2H), 4.06 (dd, *J* = 10.0, 5.1 Hz, 2H), 2.97 – 2.84 (m, 4H), 2.74 – 2.61 (m, 2H), 2.51 (dd, *J* = 12.6, 4.3 Hz, 2H), 2.22 (dd, *J* = 14.2, 9.4 Hz, 4H), 1.30 (d, *J* = 5.9 Hz, 7H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.8, 142.5, 142.0, 134.9, 134.1, 131.1, 129.4, 128.8, 128.4, 128.0, 126.8, 108.9, 108.7, 100.8, 78.7, 75.5, 42.6, 39.6, 30.8, 20.8; m.p = sample decomposed after heating to 100°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{21}H_{20}O_3$: 321.1491, found: 321.1481.



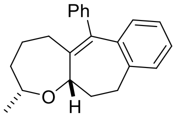
Compound **14c** isolated as a white amorphous solid, 13:1 (43.7 mg, 63%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.31 (t, *J* = 7.1 Hz, 2H), 7.27 – 7.21 (m, 1H), 7.12 (s, 2H), 6.72 (s, 1H), 6.26 (s, 1H), 5.87 (s, 2H), 4.01 (dd, *J* = 11.3, 6.3 Hz, 1H), 3.39 (d, *J* = 6.4 Hz, 1H), 2.81 – 2.70 (m, 1H), 2.53 – 2.41 (m, 2H), 2.36 (s, 2H), 2.10 (t, *J* = 11.2 Hz, 1H), 1.98 (d, *J* = 7.6 Hz, 1H), 1.74 (d, *J* = 11.0 Hz, 1H), 1.51 (dd, *J* = 22.8, 14.1 Hz, 2H), 1.15 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 145.7, 143.9, 141.9, 134.9, 134.6, 134.1, 129.7, 127.9, 126.6, 109.6, 108.1, 100.7, 79.6, 77.5, 40.7, 37.2, 30.4, 29.6, 28.3, 23.2; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{23}H_{24}O_3$: 349.1804, found: 349.1792.



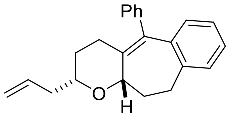
Compound **14d** isolated as an amorphous white solid, >20:1 dr (28 mg, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.2 Hz, 5H), 7.31 – 7.25 (m, 3H), 7.23 (d, *J* = 7.1 Hz, 2H), 7.14 (d, *J* = 6.7 Hz, 6H), 7.09 (dd, *J* = 14.8, 7.2 Hz, 3H), 6.77 (d, *J* = 7.4 Hz, 2H), 4.01 (dd, *J* = 9.8, 7.4 Hz, 2H), 3.55 – 3.43 (m, 2H), 2.88 (t, *J* = 11.4 Hz, 2H), 2.60 (dt, *J* = 12.0, 6.5 Hz, 4H), 2.55 – 2.48 (m, 2H), 2.43 (dd, *J* = 21.5, 11.1 Hz, 2H), 2.31 – 2.20 (m, 2H), 1.94 – 1.83 (m, 2H), 1.74 (dd, *J* = 20.5, 10.0 Hz, 2H), 1.24 (d, *J* = 5.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 141.1, 140.9, 139.7, 133.2, 129.9, 129.5, 128.2, 128.1, 126.6, 125.9, 77.9, 70.6, 39.7, 33.5, 30.4, 23.3, 22.3; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{22}O$: 291.1749, found: 291.1742.



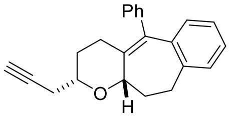
Compound **14e** isolated as an amorphous solid, >20:1dr (55.0 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 6.8 Hz, 1H), 7.13 – 7.03 (m, 2H), 6.80 (d, *J* = 7.2 Hz, 1H), 4.32 (t, *J* = 8.2 Hz, 1H), 4.09 – 3.99 (m, 1H), 3.04 – 2.88 (m, 2H), 2.74 – 2.65 (m, 1H), 2.62 (d, *J* = 12.6 Hz, 1H), 2.24 (dd, *J* = 22.5, 12.7 Hz, 2H), 1.30 (d, *J* = 4.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 140.8, 140.7, 131.3, 129.5, 128.7, 128.6, 128.4, 126.7, 126.5, 125.9, 78.7, 75.4, 42.2, 39.7, 30.8, 20.8; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{20}O$: 277.1592, found: 277.1584.



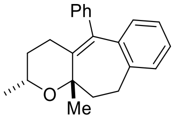
Compound **14f** isolated as an amorphous solid, 8:1dr (50.4 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.0 Hz, 108H), 7.24 (dd, *J* = 14.6, 6.8 Hz, 125H), 7.16 – 7.07 (m, 203H), 6.77 (d, *J* = 7.3 Hz, 46H), 4.00 (dd, *J* = 11.2, 7.0 Hz, 46H), 3.38 (d, *J* = 6.4 Hz, 43H), 2.90 – 2.78 (m, 48H), 2.60 – 2.53 (m, 55H), 2.53 – 2.44 (m, 44H), 2.38 (d, *J* = 11.5 Hz, 101H), 2.20 – 2.08 (m, 48H), 2.00 (d, *J* = 11.0 Hz, 48H), 1.74 (d, *J* = 12.4 Hz, 52H), 1.63 – 1.45 (m, 101H), 1.14 (d, *J* = 6.0 Hz, 150H), 1.06 (t, *J* = 10.1 Hz, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.2, 142.1, 141.8, 140.8, 134.2, 129.8, 129.4, 127.9, 127.8, 126.7, 126.5, 126.0, 79.4, 77.5, 40.4, 37.2, 30.5, 29.5, 28.3, 23.2; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{24}O$: 305.1905, found: 305.1897.



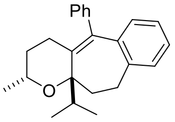
Compound **14g** isolated as a viscous oil, 16:1dr (155 mg, 98%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.37 (t, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.0 Hz, 1H), 7.26 (s, 1H), 7.21 – 7.09 (m, 4H), 6.81 (d, *J* = 7.4 Hz, 1H), 5.86 (ddt, *J* = 17.0, 10.3, 6.9 Hz, 1H), 5.13 (d, *J* = 17.2 Hz, 1H), 5.07 (d, *J* = 10.3 Hz, 1H), 4.04 (dd, *J* = 10.9, 6.8 Hz, 1H), 3.43 (dt, *J* = 9.1, 6.5 Hz, 1H), 2.93 (dt, *J* = 14.6, 7.4 Hz, 1H), 2.70 – 2.62 (m, 2H), 2.62 – 2.54 (m, 1H), 2.51 – 2.38 (m, 2H), 2.35 – 2.23 (m, 2H), 1.95 – 1.80 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 141.7, 141.1, 140.8, 139.7, 134.8, 133.2, 129.9, 129.4, 128.2, 128.1, 126.6, 125.9, 116.6, 78.0, 74.0, 40.9, 39.6, 31.5, 30.4, 23.0; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{23}H_{24}O$: 317.1900, found: 317.1898.



Compound **14h** isolated as a viscous oil, 3.4:1dr (56.6 mg, 90%) or 2.8:1 dr (282mg, 90%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35 (t, *J* = 7.1 Hz, 1H), 7.29 (dd, *J* = 13.4, 6.5 Hz, 1H), 7.23 (t, *J* = 6.8 Hz, 1H), 7.18 – 7.07 (m, 2H), 6.78 (d, *J* = 7.4 Hz, 1H), 4.05 (dt, *J* = 18.3, 9.2 Hz, 1H), 3.61 – 3.51 (m, 1H), 2.96 – 2.85 (m, 1H), 2.70 – 2.34 (m, 3H), 2.28 (dt, *J* = 19.6, 9.8 Hz, 1H), 2.05 – 1.85 (m, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 141.6, 140.9, 140.8, 138.9, 133.5, 130.0, 129.9, 129.5, 128.2, 128.1, 126.7, 125.9, 80.9, 78.1, 72.6, 69.5, 39.6, 31.2, 30.3, 26.2, 23.0. HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{23}H_{24}O$: 315.1744, found: 315.1741.

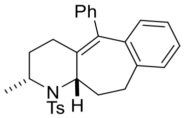


Added 1.5 equivalents of dimethyl ketal and 1.0 equivalent of alcohol **13a**. Stir at -40°C until all of the alcohol was consumed. Compound **14i** was isolated as an amorphous solid, 1.2:1 dr (70.6 mg, 51%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 – 7.38 (m, 0.8H, *minor diastereomer*), 7.36 – 7.29 (m, 4H), 7.29 – 7.21 (m, 2H), 7.20 – 7.14 (m, 2H), 7.13 – 7.04 (m, 4H), 7.01 (dd, *J* = 13.8, 6.1 Hz, 1H), 6.90 (d, *J* = 7.2 Hz, 0.8H, *minor diastereomer*), 6.68 (t, *J* = 7.6 Hz, 1H), 4.11 – 4.02 (m, 1H), 3.99 – 3.92 (m, 0.8H, *minor diastereomer*), 3.29 (d, *J* = 7.3 Hz, 0.8H, *minor diastereomer*), 3.13 – 2.97 (m, 1H), 2.82 (d, *J* = 13.9 Hz, 0.8H, *minor diastereomer*), 2.69 – 2.56 (m, 1H), 2.49 – 2.28 (m, 4H), 2.16 – 2.05 (m, 1.8H), 1.78 – 1.64 (m, 3H), 1.56 – 1.41 (m, 2H), 1.22 (dd, *J* = 9.4, 6.3 Hz, 4H), 1.15 (s, 3H), 1.00 (s, 2.5H, *minor diastereomer*). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.5, 144.4, 143.3, 143.2, 142.1, 141.8, 141.0, 140.1, 133.4, 133.0, 130.5, 130.4, 129.9, 129.6, 128.6, 128.2, 128.2, 128.2, 127.9, 127.7, 127.5, 127.3, 126.6, 126.5, 126.4, 126.3, 126.0, 125.5, 78.5, 78.4, 71.7, 64.3, 63.3, 49.3, 46.4, 34.4, 33.2, 32.3, 31.1, 30.4, 30.3, 29.9, 26.8, 26.2, 25.8, 24.8, 23.1, 22.8, 20.9, 17.0; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{22}H_{24}O$: 305.1900, found: 305.1897.

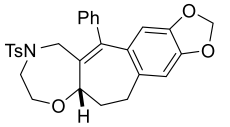


Added 1.5 equivalents of dimethyl ketal and 1.0 equivalents of alcohol **13a**. Stir at -40°C for an hour, then warmed to 0°C until all of the alcohol was consumed. Compound **14j** was obtained as a crystalline solid, 1.6:1 dr (21.6mg, 28%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (d, *J* = 6.8 Hz, 2H), 7.31-7.27 (m, 1H), 7.18-7.11 (m, 4H), 7.01-6.96 (m, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 5.73 (t, *J* = 7.0 Hz, 1H), 3.67 – 3.58 (m, 1H), 3.15 (dd, *J* = 12.4, 7.9 Hz, 1H), 2.93 – 2.84 (m, 1H), 2.67 – 2.57 (m,

1H), 2.54 – 2.38 (m, 2H), 1.52 – 1.40 (m, 3H), 1.32 (d, *J* = 8.8 Hz, 2H), 1.08 (dd, *J* = 6.3, 3.7 Hz, 3H), 1.04 (d, *J* = 6.1 Hz, 3H), 0.98 (d, *J* = 6.1 Hz, 3H, *corresponds to the alpha methyl of the minor diastereomer*), 0.81 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.8, 143.8, 143.4, 143.2, 141.8, 141.1, 140.9, 140.1, 140.0, 138.9, 130.6, 130.5, 130.2, 130.0, 128.3, 128.1, 126.9, 126.7, 126.6, 125.5, 124.8, 122.4, 122.4, 68.0, 67.1, 39.4, 39.1, 33.7, 29.9, 29.8, 29.7, 28.2, 27.9, 23.3, 23.1, 23.0, 22.8, 20.5; m.p = 108-110°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{24}H_{28}O$: 333.2213, found: 333.2210.



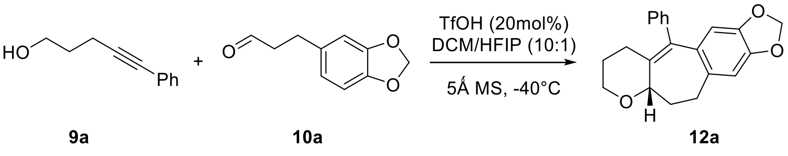
After addition of TfOH, stirred at -40 °C for 30 minutes before warming to 0 °C until all the starting material was consumed. Compound **16b** was isolated as an amorphous white solid, >20:1 dr (50 mg, 56%). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 2H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.33 – 7.24 (m, 4H), 7.24 – 7.15 (m, 4H), 7.08 (d, *J* = 7.5 Hz, 2H), 4.43 (s, 1H), 3.32 (t, *J* = 4.5 Hz, 1H), 2.40 (dd, *J* = 14.8, 6.3 Hz, 1H), 2.31 (d, *J* = 6.5 Hz, 3H), 2.15 (dddd, *J* = 28.8, 16.9, 14.6, 4.9 Hz, 6H), 1.38 (dd, *J* = 12.1, 5.8 Hz, 1H), 1.30 – 1.19 (m, 2H), 1.12 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.0, 143.7, 142.2, 136.1, 135.2, 133.7, 129.5, 128.4, 128.2, 128.0, 126.6, 125.8, 124.8, 122.5, 122.2, 51.5, 48.4, 32.4, 30.6, 23.5, 21.4, 18.7, 17.8. HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{28}H_{29}NO_2S$: 444.1992, found: 444.1984.

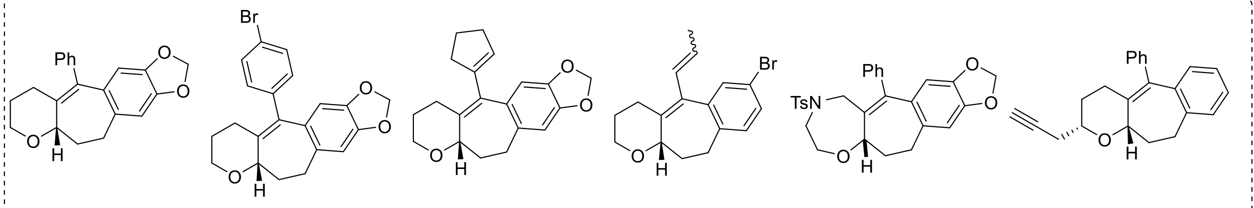


Compound **19** was isolated as a white solid (394 mg, 89%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 6.8 Hz, 3H), 7.30 (d, *J* = 8.0 Hz, 3H), 7.22 (d, *J* = 8.5 Hz, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 4.37 (d, *J* = 11.5 Hz, 1H), 4.01 (dd, *J* = 11.7, 6.9 Hz, 1H), 3.94 – 3.86 (m, 1H), 3.69 (d, *J* = 13.4 Hz, 1H), 3.54 (d, *J* = 11.3 Hz, 2H), 3.00 – 2.92 (m, 1H), 2.83 – 2.73 (m, 1H), 2.56 (dd, *J* = 13.1, 7.1 Hz, 1H), 2.48 (dd, *J* = 12.9, 6.8 Hz, 1H), 2.43 (s, 3H), 2.03 (dd, *J* = 20.4, 11.8 Hz, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.5, 141.8, 140.7, 140.4, 139.6, 134.7, 134.0, 130.5, 129.8, 129.6, 128.0, 127.8, 127.7, 127.7, 126.3, 79.3, 68.8, 49.4, 47.9, 40.1, 30.0, 21.5; m.p = compound turns brown after 95 °C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{28}H_{27}NO_5S$: 490.1683, found: 490.1676.

Greater than 1.0 mmol Scale Experiments:

Scheme S6. General Procedure for Carbocyclizations (>1.0 mmol scale)





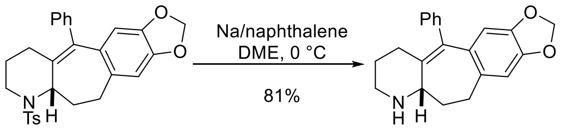
12a (81%) 5.0 mmol | **12b** (83%) 1.0 mmol | **12j** (78%) 1.05 mmol | **12i** (75%) 7.9:1 *E/Z* 1.1 mmol | **19** (69%) 1.0 mmol | **14h** (90%) 2.8:1 dr 1.0 mmol

Scheme S6. Greater than 1.0 mmol Scale Substrates

Oven dried, 5 Å molecular sieves (1.5 g) were transferred to a 100 mL flask equipped with a stir bar and dried further under vacuum while heating over a Bunsen burner for about 3 minutes. The reaction vessel was allowed to cool under a flow of argon before adding DCM/HFIP (10:1) (50 mL), followed by the alcohol **9a** (961 mg, 6.0 mmol, 1.2 equivalents) and aldehyde **10a** (891 mg, 5.0 mmol, 1.0 equivalents). The reaction mixture was cooled to -40 °C before adding triflic acid (TfOH) (88 μL, 20 mol%) dropwise. Mixture was allowed to stir at -40 °C until all of the limiting reagent was consumed by TLC (using 20% ethyl acetate/hexanes mixture as mobile phase and p-anisaldehyde to stain the plates). After completion, the reaction was quenched by adding solid sodium bicarbonate (1.5 g) and diluting with ether (Et_2O). The quenched reaction mixture was filtered through a silica plug, eluted with Et_2O, and concentrated under vacuum. Crude was purified by column chromatography, using 5% ethyl acetate/hexane as mobile phase. Pure product **12a** was obtained as a pale yellow amorphous solid (1.3 g, 81%).

Procedure for Deprotection of *N*-Tosyl Piperidines:

Scheme S7. General Procedure for Piperidine Detosylation



16a **17a**

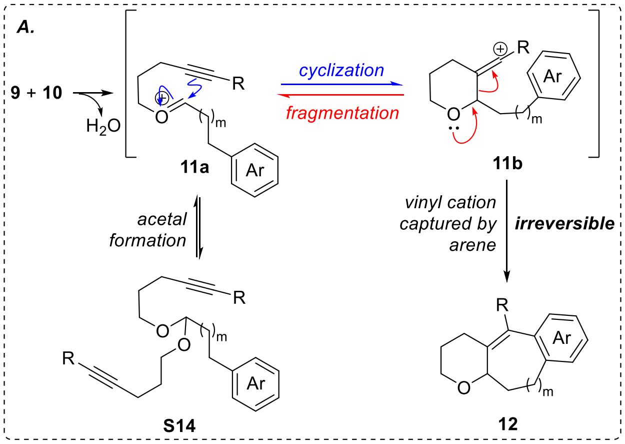
In a flame-dried 25 mL round bottom flask under argon, prepared a 1.0M solution of naphthalene (640 mg, 5.0 mmol) in dry dimethoxyethane (DME, 5.0 mL) and cooled to 0 °C. Na (140 mg, 6.0 mmol) that had been cut into small cubes was added and the mixture was stirred vigorously at 0 °C for about 15 minutes, then warmed up to room temperature and allowed to stir for 1 hour. The deep green solution (162 μL, 0.162 mmol, 4.0 equivalents) was added dropwise to a 0.2 M solution of sulfonamide **16a** (19.2 mg, 0.0405 mmol) in DME (0.4 mL). The drops were added slowly, allowing time for the coloration to disappear before the next addition. After 5 minutes, 1M HCl was added to quench the reaction. Acidic mixture was washed with Et_2O (2 x 15 mL) and the ethereal layer was discarded. The aqueous layer was then basified by adding solid NaOH and extracted with Et_2O (3 x 15 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum to afford amine **17a** as a yellow oil, no further purification needed. ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.4 Hz, 2H), 7.24 (s, 1H), 7.10 (d, *J* = 7.5 Hz, 2H), 6.71 (s, 1H), 6.25 (s, 1H), 5.86 (s, 2H), 3.42 – 3.36 (m, 1H), 3.00 (dt, *J* = 12.6, 6.2 Hz, 1H), 2.75 (ddd, *J* = 25.4, 13.2, 7.4 Hz, 2H), 2.60 (dt, *J* = 14.9, 4.8 Hz, 1H), 2.49 (dd, *J* = 13.2, 6.1 Hz, 1H), 2.37 – 2.19 (m, 3H), 2.04 (s, 1H), 1.86 – 1.76 (m, 1H), 1.65 (td, *J* = 12.0, 5.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 145.8, 141.7, 138.6, 135.0, 134.8, 134.1, 129.9, 128.1, 126.6, 109.7, 108.5, 100.7, 55.8, 41.2, 40.4, 31.3, 25.4, 24.8. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{21}NO_2$: 320.1645, found: 320.1638.

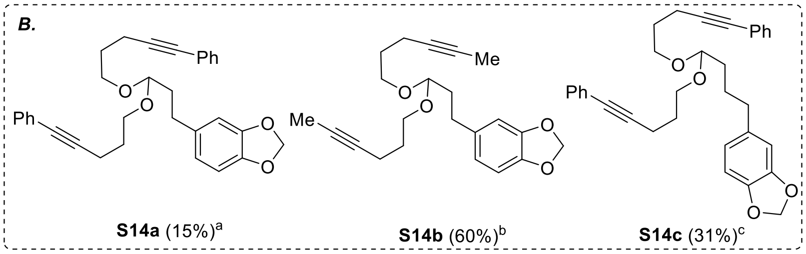
Explanation of Acetal Byproduct (Observed in the absence of HFIP, and for cases 12k and 12n):

In less efficient alkynyl Prins reactions, it is notable that acetal **S14** and tricycle **12** are the only products observed in significant quantities. During optimization, the acetal **S14a** was isolated in 15% yield when HFIP was left out of the reaction mixture. Using the optimized conditions (HFIP present), the acetal was also observed in two other cases, namely **12k** and **12n**. For alkyne **9k** (R=Me; n=1), the reaction produces the corresponding acetal **S14b** exclusively when left at -40°C. Higher temperatures are required for the alkynyl Prins/carbocyclization to occur. For the extended chain arenyne **9n** (R=Ph; n=2) acetal **S14c** is isolated as the major product when the reaction is left to stir at -40 °C. Once again, warming is required to push the acetal to undergo cyclization (Scheme S8B). The combination of HFIP[20] and the adjacent π-system in R (arene/alkene) helps stabilize **11b-2** (-1.2 kcal/mol relative to the oxocarbenium, Scheme S8C), improving the efficiency of arene capture and disfavoring the reversibility of the Prins, back to **11a-2**. The vinyl cation produced from **9k** (R = Me), however, has no adjacent π-system, which could account for the reduced efficiency (+6.4 kcal/mol relative to the oxocarbenium, Scheme S8C).[21] For the **12n** case (m = 2) , it seems logical that the longer tether makes capture of the vinyl cation less efficient. This, when **11b** is either unstable, or has a poorly aligned arene, oxocarbenium **11a** is trapped by a second molecule of alcohol **9**. We also note that in these inefficient cases, numerous other undesired byproducts form over the course of the experiment, ultimately compromising the yield of the reaction.

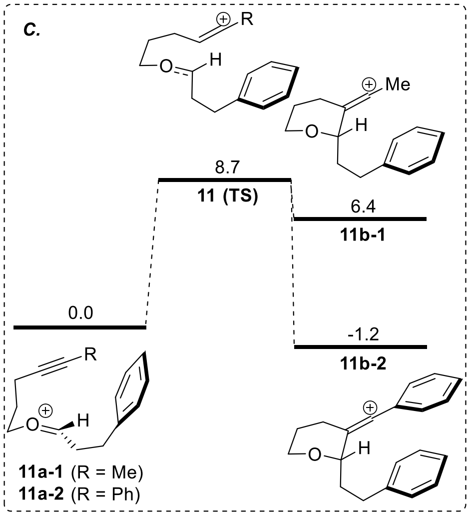
A possible explanation for these observations is shown in Scheme S8. The reversal of the alkyne/oxocarbenium ring closure is similar to the Eshenmoser class of fragmentations,[22] which could establish an equilibrium between oxocarbenium **11a** and vinyl cation **11b** (Scheme S8A). This is supported by DFT calculations, which show that generation of the vinyl cation **11b-1**, is endergonic for **9k,** and slightly exergonic in the case of **11b-2** for arenyne **9a** (Scheme S8C). Either way, the energetic barrier is readily available in both directions. At the vinyl cation stage **11b**, it is plausible for the oxacycle to open and regenerate the oxocarbenium **11a**, or to undergo carbocyclization after aryl trapping of the vinyl cation, terminating the process.

Scheme S8. A. Explanation of Acetal Byproducts Observed. **B.** Acetals Isolated **C.** DFT Backing for Plausible Reversibility of Alkynyl Prins Step (Theory level: M062X/Def2TZVP, Solvation: CPCM: Dichloromethane, Energy in kcal/mol).





a) Isolated from the reaction of 9a with aldehyde 10a, in the absence of HFIP (See Table 1, Entry 1) **b)** Isolated from the reaction of 9k with aldehyde 10a, using 40 mol% TfOH and quenching after stirring at -40 °C **c)** Isolated from the reaction of 9n with the longer-tether aldehyde, using 40 mol% TfOH and quenching after stirring at -40 °C.



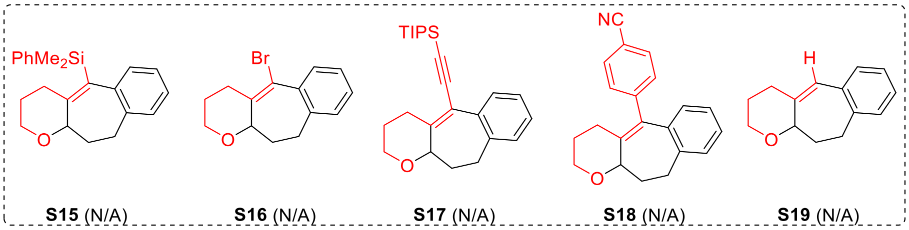
Compound S14a. Acetal isolated as a yellow solid after preparatory TLC with 20% ethyl acetate in hexanes as the mobile phase (14 mg, 15%). **S14a** was observed as the major byproduct of subjecting **9a** and **10a** to 20 mol% TfOH in dichloromethane (no HFIP), in the presence of molecular sieves. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (s, 3H), 7.26 (s, 9H), 6.72 – 6.58 (m, 3H), 5.90 (d, *J* = 4.3 Hz, 2H), 4.51 (dd, *J* = 12.8, 5.0 Hz, 1H), 3.76 (d, *J* = 5.5 Hz, 1H), 3.64 – 3.55 (m, 1H), 2.62 (s, 2H), 2.58 – 2.50 (m, 3H), 1.98 – 1.81 (m, 5H), 1.58 (s, 1H), 1.22 (t, *J* = 5.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.6, 145.6, 135.5, 135.5, 131.5, 128.2, 127.6, 123.9, 121.1, 108.9, 108.1, 102.4, 102.2, 100.7, 89.4, 81.0, 64.0, 63.8, 61.2, 35.3, 35.2, 30.7, 29.0, 16.3, 15.4. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{32}H_{32}O_4$: 481.2374, found: 481.2366.

Compound S14b. Acetal isolated as a yellow oil after preparatory TLC with 20% ethyl acetate in hexanes as the mobile phase (43 mg, 60%). **S14b** was observed as the major product when the Prins/carbocyclization with alcohol **9n** was quenched after stirring at -40 °C and full consumption of the aldehyde was observed by TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.72 (d, *J* = 7.9 Hz, 1H), 6.69 (s, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 5.91 (s, 2H), 4.46 (t, *J* = 5.7 Hz, 1H), 3.66 (dt, *J* = 9.2, 6.2 Hz, 2H), 3.50 (dt, *J* = 9.2, 6.2 Hz, 2H), 2.66 – 2.56 (m, 2H), 2.24 (dd, *J* = 9.1, 6.7 Hz, 4H), 1.88 (dd, *J* = 15.1, 6.2 Hz, 2H), 1.77 (d, *J* = 1.9 Hz, 6H), 1.73 (dd, *J* = 13.2, 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.5, 145.6, 135.6, 121.1, 108.9, 108.1, 102.2, 100.7, 78.4, 75.8, 64.0, 35.2, 30.7, 29.2, 15.6, 3.4. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{28}O_4$: 357.2061, found: 357.2059.

Compound S14c. Acetal isolated as a yellow oil after preparatory TLC with 20% ethyl acetate in hexanes as the mobile phase (19 mg, 27%). **S14c** was observed as the major product when the reaction was quenched after stirring at -40 °C and full consumption of the aldehyde was observed by TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.35 (m, 2H), 7.29 – 7.26 (m, 2H), 6.84 (s, 1H), 6.54 (s, 1H), 5.88 (d, *J* = 6.5 Hz, 2H), 4.31 (t, *J* = 4.4 Hz, 1H), 3.68 (dt, *J* = 9.1, 6.2 Hz, 1H), 3.58 – 3.47 (m, 1H), 2.72 (dt, *J* = 16.3, 5.4 Hz, 1H), 2.61 (dd, *J* = 14.8, 7.0 Hz, 1H), 2.45 (t, *J* = 6.8 Hz, 2H), 2.00 – 1.63 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.9, 145.7, 131.5, 131.0, 130.2, 128.1, 127.9, 127.5, 124.0, 119.9, 108.9, 108.4, 100.6, 90.0, 80.8, 75.5, 68.0, 29.4, 29.4, 27.9, 25.6, 19.2, 19.0. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{33}H_{34}O_4$: 495.2530, found: 495.2522.

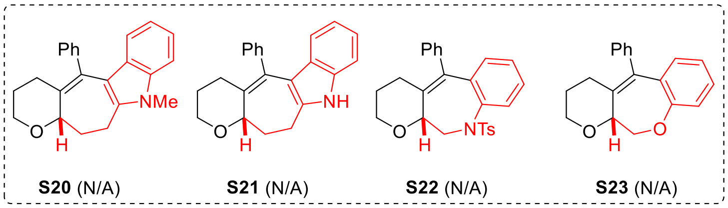
Unsuccessful Carbocyclization Substrates:

Alkyne alcohols (highlighted in red) **S6-S9a** failed to give carbocyclization adducts **S15-S18**. Complex product mixtures were observed after subjecting these alcohols to the reaction conditions. Terminal alkynes also did not react cleanly and no **S18** was isolated.



Scheme S9. Products not accessible though this approach

Carbocyclization adducts **S20-S23** did not form under the reaction conditions (aldehyde portion highlighted in red). Aldehyde decomposition was observed in the cases of **S20** and **S21**. In the cases **S22** and **S23**, where the aldehyde had a heteroatom in the tether, recovery of unreacted starting material was observed and decomposition to complex mixtures.



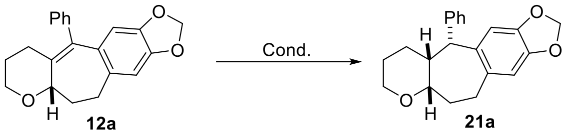
Scheme S10. Products not accessible though this approach

Diversification of Carbocyclization Products:

Hydrogenations:

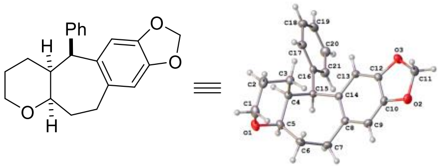
A few different hydrogenation catalysts were explored. Since the olefin at hand was tetrasubstituted, we started with Crabtree catalyst $[Ir(cod)(PCy_3)(pyr)]PF_6$, which is known to reduce highly hindered alkenes.[23, 24] These conditions led to recovery of starting material **12a** (Entry 1, Table S1). More recent conditions by Chirk et al. are successful at reducing difficult olefins using a Ni catalyst that is generated *in situ* after mixing $Ni(octanoate)_2$ with HBPin and an α-diimine ligand (^{i}PrDI) in benzene.[25] These conditions, however, failed to afford hydrogenated product **21a**. To our delight, using 20 mol% of 5% palladium on carbon (Pd/C) with 55 atmospheres of hydrogen. See below.

Table S1. Screen of Catalysts for Hydrogenation of **12a**

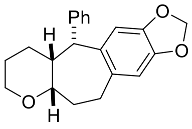


Entry	Catalyst	Solvent	H_2 (atm)	Result
1[23]	[Ir(cod)(PCy$_3$)(pyr)]PF$_6$	DCM	1-35	100% **12a**
2[25]	Ni(octanoate)$_2$, HBpin, ^{i}PrDI	C_6H_6	1-4	100% **12a**
3[a]	Pd/C (20 mol %)	MeOH/DCM	55	Quant. **21a**

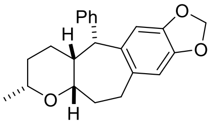
General Procedure for hydrogenation: To a scintillation vial charged with stir bar and compound **12a** (32 mg, 0.1 mmol), added DCM (0.3 mL) followed by Pd/C (42 mg, 0.02 mmol Pd, 5% Pd on C). Some additional DCM was added to wash the Pd/C off the sides of the vial. Added MeOH (1.7 mL) and the vial was placed in a bomb reactor, on a stir plate. Pressure was brought up to 55 atm, then purged, refilled back up to 55 atm, and allowed to stir at room temperature for 48 hours. After this time, the hydrogen gas was released and the mixture was carefully filtered through celite, washed with DCM, concentrated, and purified by preparatory TLC using 30% EtOAc in hexanes as the mobile phase. Product was obtained as a 1:1 mixture of separable diastereomers (32 mg, 100% combined yield).



Compound **21a-1** was obtained as a white, crystalline solid (15.4 mg, 48%). Recrystallized after dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 7.2 Hz, 2H), 7.19 (s, 3H), 6.62 (s, 1H), 6.49 (s, 1H), 5.88 (d, *J* = 5.9 Hz, 2H), 4.02 (s, 1H), 3.90 (d, *J* = 10.2 Hz, 1H), 3.28 (t, *J* = 10.7 Hz, 2H), 3.00 (d, *J* = 11.7 Hz, 1H), 2.75 (dd, *J* = 15.7, 8.8 Hz, 1H), 2.34 – 2.25 (m, 1H), 2.22 (d, *J* = 10.6 Hz, 1H), 1.92 (d, *J* = 12.2 Hz, 1H), 1.75 (tt, *J* = 24.6, 12.3 Hz, 4H), 1.66 – 1.54 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 145.7, 142.0, 134.5, 129.7, 127.8, 126.1, 111.5, 110.7, 100.8, 78.7, 67.9, 56.1, 43.7, 34.3, 31.1, 30.7, 30.3, 27.2, 26.6; m.p = 127-130°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{22}O_3$: 323.1642, found: 323.1639.



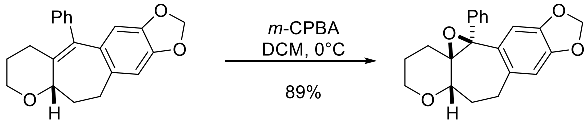
Compound **21a-2** was obtained as an amorphous solid (16.6 mg, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.3 Hz, 2H), 7.28 (d, *J* = 7.1 Hz, 2H), 6.67 (s, 1H), 5.98 (s, 1H), 5.84 (d, *J* = 5.0 Hz, 2H), 4.24 (s, 1H), 4.09 – 4.01 (m, 1H), 3.62 (d, *J* = 11.2 Hz, 2H), 2.92 (t, *J* = 13.5 Hz, 1H), 2.81 (d, *J* = 12.5 Hz, 1H), 2.69 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.15 – 2.02 (m, 1H), 1.94 – 1.87 (m, 1H), 1.85 – 1.75 (m, 1H), 1.70 (d, *J* = 13.8 Hz, 1H), 1.51 (d, *J* = 12.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.6, 145.3, 143.7, 135.6, 134.4, 128.6, 128.5, 126.3, 109.4, 108.9, 100.6, 78.3, 60.8, 46.7, 40.9, 30.8, 26.7, 26.1, 22.4; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{22}O_3$: 323.1642, found: 323.1639.



Compound **S23** was isolated as an amorphous solid (as a 5:1 mixture of diastereomers) after subjecting **14a** to the hydrogenation conditions (13.7 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.5 Hz, 2H), 7.28 (s, 1H), 7.24 (s, 1H), 6.66 (s, 1H), 5.98 (s, 1H), 5.84 (d, *J* = 6.3 Hz, 2H), 4.27 (s, 1H), 4.08 (dd, *J* = 11.2, 5.4 Hz, 1H), 3.69 (dd, *J* = 9.4, 6.0 Hz, 1H), 2.91 (t, *J* = 13.5 Hz, 1H), 2.75 (d, *J* = 13.3 Hz, 1H), 2.68 (dd, *J* = 14.4, 6.5 Hz, 1H), 2.07 (dd, *J* = 25.0, 12.3 Hz, 1H), 1.95 (dd, *J* = 12.5, 6.3 Hz, 1H), 1.69 (d, *J* = 13.6 Hz, 1H), 1.58 (d, *J* = 10.5 Hz, 1H), 1.41 (dd, *J* = 17.0, 5.0 Hz, 1H), 1.10 (d, *J* = 5.8 Hz, 3H), 0.92 (ddd, *J* = 26.9, 13.4, 3.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.6, 145.3, 143.7, 135.7, 134.5, 129.5, 128.7, 128.5, 127.9, 126.3, 109.4, 108.8, 100.6, 79.0, 65.5, 46.4, 40.5, 34.2, 30.9, 30.8, 26.9, 22.6, 22.3; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{24}O_3$: 337.1798, found: 337.1794.

Oxidations:

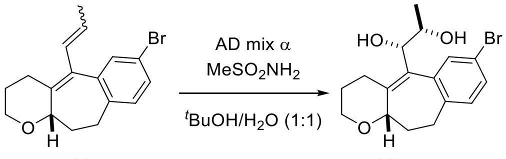
Scheme S11. General Procedure for *m*-CPBA Oxidation of **12a**^{26}



12a **22a**

To a solution of **12a** (32 mg, 0.1 mmol) in DCM (0.4 mL) at 0°C, added *m*-CPBA (26 mg, 0.15 mmol) in one portion. The reaction was allowed to stir at 0°C until all the starting material had been consumed by TLC (using 20% EtOAc in hexanes, and *p*-anisaldehyde to stain the plates). Reaction was diluted with more DCM (1.0 mL), washed with 10% NaOH (2 x 15 mL), then washed with Brine (20 mL), dried over $MgSO_4$, filtered, and concentrated to afford **22a** as a white solid (29.9 mg, 89%). No purification needed. Recrystallized after dissolving in hot methanol and slowly cooling to room temperature in an uncapped vial. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 13.0, 6.2 Hz, 5H), 6.70 (s, 1H), 6.65 (s, 1H), 5.89 (d, *J* = 9.9 Hz, 2H), 3.79 (d, *J* = 11.8 Hz, 1H), 3.70 (t, *J* = 11.4 Hz, 1H), 3.50 – 3.41 (m, 1H), 3.04 (td, *J* = 13.3, 7.3 Hz, 1H), 2.70 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.28 (td, *J* = 12.2, 7.5 Hz, 1H), 1.98 (dd, *J* = 13.2, 9.3 Hz, 1H), 1.89 – 1.77 (m, 1H), 1.66 (dt, *J* = 19.9, 7.2 Hz, 2H), 1.41 (d, *J* = 14.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4, 146.9, 137.9, 131.8, 130.4, 129.8, 128.0, 127.4, 127.0, 109.1, 108.5, 101.0, 77.5, 66.0, 65.4, 60.9, 29.4, 24.7, 23.8, 22.8; m.p = 143-146°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{20}O_4$: 337.1435, found: 337.1431.

Scheme S12. AD-mix α Dihydroxylation of **12i**



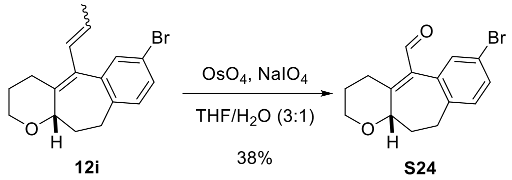
12i **22i** (1.6:1 dr)

A mixture of **12i** (32 mg, 0.1 mmol), methanesulfonamide ($MeSO_2NH_2$) (9.5 mg, 0.1 mmol), and AD-mix α (140 mg, 1.4g/mmol) was placed in a scintillation vial charged with a stir bar. Added ^{t}BuOH (0.5 mL) followed by water (0.5 mL), and the reaction mixture was allowed to stir vigorously under air for 4 days (until the starting material had been fully consumed by TLC, using 20% EtOAc in hexanes, and *p*-anisaldehyde to stain the plates). After this time, added solid sodium sulfite (Na_2SO_3) (140 mg) and vigorously stirred for an hour. Added more water (2 mL) extracted with EtOAc (4 x 15 mL), dry over $MgSO_4$, filter, and concentrate. The crude was purified by preparatory TLC, using 50% EtOAc in hexanes as the mobile phase to afford **22i** as a 1.6:1 mixture of separable diastereomers (70% combined yield).

Compound **22i-1** was isolated as an amorphous solid (9.6 mg, 27%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.0 Hz, 1H), 7.10 (s, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 4.21 (d, *J* = 8.4 Hz, 1H), 3.95 – 3.86 (m, 1H), 3.75 – 3.67 (m, 1H), 3.53 (dd, *J* = 11.1, 7.5 Hz, 1H), 3.10 (dd, *J* = 19.3, 8.4 Hz, 1H), 2.99 (dd, *J* = 12.7, 5.9 Hz, 1H), 2.42 – 2.28 (m, 4H), 2.28 – 2.17 (m, 2H), 2.03 (dd, *J* = 19.5, 11.6 Hz, 1H), 1.92 (dt, *J* = 17.1, 8.7 Hz, 1H), 1.50 (dd, *J* = 12.0, 4.1 Hz, 1H), 0.88 (t, *J* = 9.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 141.4, 139.4, 130.3, 130.2, 130.1, 129.3, 120.2, 79.6, 76.8, 71.0, 63.0, 38.7, 30.3, 29.7, 24.0, 21.5, 19.2; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{21}BrO_3$: 353.0747, found: 353.0783.

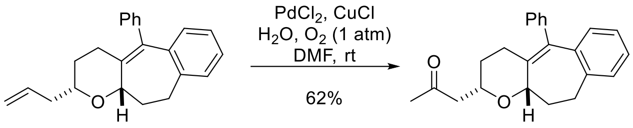
Compound **22i-2** was isolated as an amorphous solid (15.2 mg, 43%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 1.4 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 4.57 (d, *J* = 8.8 Hz, 1H), 3.89 – 3.77 (m, 3H), 3.69 – 3.59 (m, 1H), 3.34 (dt, *J* = 11.6, 7.8 Hz, 1H), 2.91 (dd, *J* = 13.8, 6.1 Hz, 1H), 2.84 (s, 1H), 2.44 (dd, *J* = 16.6, 10.1 Hz, 4H), 2.40 – 2.24 (m, 3H), 2.20 – 2.12 (m, 1H), 2.08 (dd, *J* = 18.7, 10.5 Hz, 1H), 1.67 (ddd, *J* = 24.3, 12.2, 5.4 Hz, 2H), 0.92 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.3, 139.4, 138.9, 131.5, 130.1, 129.9, 127.9, 119.8, 76.3, 75.2, 69.6, 62.8, 38.1, 30.3, 29.7, 29.5, 24.2, 20.9, 18.8; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{21}BrO_3$: 353.0747, found: 353.0783.

Scheme S13. Oxidative Cleavage of **12i**



To a solution of **12i** (40 mg, 0.13 mmol) in THF/H_2O (3:1, 0.65 mL), added OsO_4 (16 μL, 4% H_2O solution, 2.0 mol%) followed by $NaIO_4$ (13 mg/0.5 hr for 2 hrs; 88 mg, 0.26 mmol total). The reaction was allowed to stir for 48 hrs, then added saturated $Na_2S_2O_3$ and stirred for 30 minutes. After this time, added more water (15 mL), extracted with EtOAc (3 x 15 mL), dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by preparatory TLC using 30% EtOAc in hexanes to afford aldehyde **S24** as a foamy solid (14 mg, 38%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.24 (s, 1H), 7.39 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 4.00 – 3.90 (m, 2H), 3.54 (dd, *J* = 14.4, 6.5 Hz, 1H), 3.35 (dd, *J* = 19.7, 8.1 Hz, 1H), 2.70 (dd, *J* = 23.6, 10.3 Hz, 1H), 2.52 (d, *J* = 10.6 Hz, 3H), 2.24 (td, *J* = 15.2, 7.3 Hz, 2H), 1.82 – 1.70 (m, 1H), 0.87 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.7, 164.4, 139.0, 135.1, 132.5, 131.6, 131.0, 129.8, 119.9, 77.1, 62.9, 38.0, 28.9, 23.7, 19.9. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{15}H_{15}BrO_2$: 307.0328, found: 307.0327.

Scheme S14. Wacker Oxidation of **14g**[27]

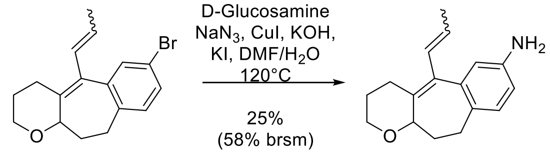


14g (16:1 dr) **25g** (16:1)

A solution of **14g** (50 mg, 0.158 mmol) in DMF (3.0 mL) was sparged with oxygen for 5 minutes. After this time, added $PdCl_2$ (6 mg, 32 μmol, 20 mol%), CuCl (16 mg, 0.158 mmol, 1.0 equiv.), and H_2O (128μL, 7.11 mmol, 45 equiv.). The reaction was allowed to stir under an oxygen atmosphere, at room temperature until all of the starting material had been consumed by TLC (using 20% EtOAc in hexanes, and *p*-anisaldehyde to stain the plates). The reaction mixture was diluted with EtOAc (20 mL), filtered through celite, washed with water (3 x 20 mL), then Brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to give **25g** as a viscous yellow oil (32 mg, 62% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.4 Hz, 2H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 7.3 Hz, 1H), 6.76 (d, *J* = 7.5 Hz, 1H), 4.02 (dd, *J* = 10.6, 7.2 Hz, 1H), 3.80 (dd, *J* = 14.5, 6.7 Hz, 1H), 2.93 – 2.82 (m, 1H), 2.77 (dd, *J* = 16.0, 7.9 Hz, 1H), 2.64 – 2.48 (m, 4H), 2.41 (dd, *J* = 22.7, 10.0 Hz, 1H), 2.25 – 2.19 (m, 1H), 2.17 (d, *J* = 6.5 Hz, 3H), 1.95 (dq, *J* = 10.9, 7.4 Hz, 1H), 1.74 (dd, *J* = 21.1, 10.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.0, 141.6, 140.9, 140.7, 138.7, 133.7, 130.0, 129.9, 129.6, 128.2, 128.1, 126.7, 126.7, 126.0, 78.2, 70.7, 50.4, 39.5, 31.6, 30.8, 30.3, 23.0; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{23}H_{24}O_2$: 333.1849, found: 333.1847.

Cross Coupling and Click Reactions:

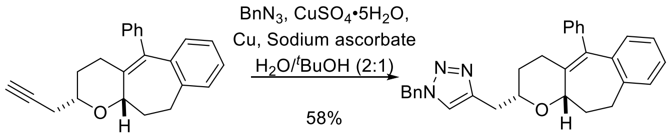
Scheme S15. Ammonia Cross-Coupling with **12i**



12i **24i**

A mixture of D-glucosamine (4.4 mg, 0.02 mmol, 0.1 equiv.), NaN_3 (39 mg, 0.6 mmol, 3.0 equiv.), CuI (3.8 mg, 0.02 mmol, 0.1 equiv.), KOH (11.2 mg, 0.2 mmol, 1 equiv.), and KI (33.2 mg, 0.2 mmol, 1 equiv.) in DMF/H_2O (v/v 1:1, 0.6 mL) was added to a sealable tube. The mixture was sparged with argon for about 10 minutes then added **12i** (63.8 mg, 0.2 mmol, 1.0 equiv.) and heated to 120°C for 18 hours. After this time, the reaction was cooled to room temperature, diluted with water, extracted with DCM (3 x 15 mL), washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by preparatory TLC using 30% EtOAc in hexanes with 1% Et_3N to give 13.0 mg of **24i** as an orange oil, and 35.8 mg of recovered **12i** (25% yield, 58% yield based on recovered starting material). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (t, *J* = 7.2 Hz, 1H), 6.58 (s, 1H), 6.52 (dd, *J* = 8.7, 6.9 Hz, 2H), 5.56 (dq, *J* = 13.5, 6.6 Hz, 1H), 3.94 – 3.86 (m, 1H), 3.86 – 3.78 (m, 1H), 3.53 (bs, 2H), 3.35 (dt, *J* = 11.4, 7.6 Hz, 1H), 2.82-2.84 (m, 2H), 2.54 – 2.32 (m, 4H), 2.24 (tt, *J* = 12.9, 6.5 Hz, 1H), 2.10 (dd, *J* = 19.8, 11.7 Hz, 1H), 2.00 (dd, *J* = 13.7, 6.7 Hz, 1H), 1.78 (d, *J* = 6.5 Hz, 3H), 1.72 – 1.58 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 139.3, 135.6, 131.2, 130.2, 128.7, 128.2, 128.0, 116.4, 114.0, 76.7, 62.8, 37.8, 28.9, 24.2, 20.8, 18.6; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{15}H_{15}BrO_2$: 307.0328, found: 307.1804.

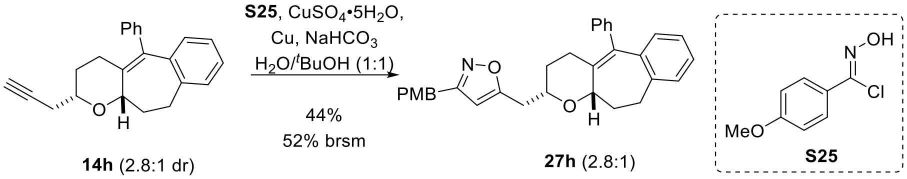
Scheme S16. Click Reaction with **14h** and Benzyl Azide for Triazole Synthesis[28]



14h (2.8:1 dr) **26h** (2.8:1)

A mixture of **14h** (63 mg, 0.2 mmol), $CuSO_4$•$5H_2O$ (1 mg, 4 µmol), Cu powder (1 mg, 2 µmol), sodium ascorbate (4 mg, 20 µmol), and benzyl azide (BnN_3) (32 µL, 40 mg, 0.3 mmol), in a 2:1 mixture of H_2O/^{t}BuOH, was stirred at room temperature until all of the starting material **14h** was consumed by TLC (using 20% EtOAc in hexanes as the mobile phase, and *p*-anisaldehyde to stain the plates). Product **26h** was obtained as a white solid after purification by preparatory TLC using 45% EtOAc in hexanes (52.3 mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 4H), 7.31 (d, *J* = 4.5 Hz, 2H), 7.28 (d, *J* = 6.6 Hz, 1H), 7.24-7.20 (m, 2H), 7.11 (d, *J* = 7.5 Hz, 3H), 6.74 (d, *J* = 7.6 Hz, 1H), 5.49 (s, 2H), 3.95 (dd, *J* = 10.6, 7.5 Hz, 1H), 3.71 – 3.59 (m, 1H), 2.96-2.83 (m, 3H), 2.62-2.56 (m, 1H), 2.55 – 2.45 (m, 2H), 2.39 (dd, *J* = 21.7, 10.7 Hz, 1H), 2.22 (dd, *J* = 19.5, 11.9 Hz, 1H), 1.92 – 1.81 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 141.6, 141.0, 140.7, 139.1, 134.9, 133.5, 129.8, 128.9, 128.1, 128.1, 127.8, 126.7, 126.6, 125.9, 122.0, 78.0, 73.6, 53.9, 39.5, 32.9, 31.4, 30.3, 23.1; m.p = 145-147°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{30}H_{29}N_3O$: 448.2384, found: 448.2386.

Scheme S17. Click Reaction with Imidoyl Chloride for Isoxazole Synthesis[28]

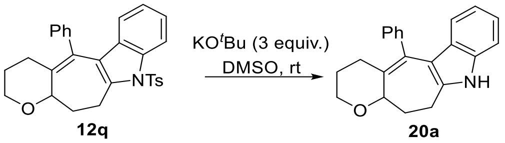


14h (2.8:1 dr) **27h** (2.8:1)

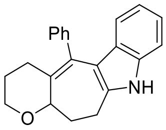
A mixture of **14h** (63 mg, 0.2 mmol), $CuSO_4$•$5H_2O$ (1 mg, 4 µmol), Cu powder (1 mg, 2 µmol), sodium bicarbonate (72 mg, 0.86 mmol), and **S25** (45 mg, 0.24 mmol), in a 1:1 mixture of H_2O/^{t}BuOH, was stirred at room temperature for 24 hours. Product **27h** was obtained as a white solid after purification by preparatory TLC using 45% EtOAc in hexanes (52.2 mg, 44%, 52% brsm). Recrystallization was achieved by dissolving in hot hexanes with toluene and slowly allowing to cool to room temperature in an uncapped vial. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 2H), 7.29 (d, *J* = 6.5 Hz, 1H), 7.22 (t, *J* = 8.1 Hz, 1H), 7.13 (d, *J* = 7.0 Hz, 3H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.32 (s, 1H), 4.05 (dd, *J* = 10.5, 6.9 Hz, 1H), 3.85 (s, 3H), 3.07 (dd, *J* = 15.5, 7.6 Hz, 1H), 2.99 – 2.88 (m, 2H), 2.65 – 2.53 (m, 3H), 2.46 (dd, *J* = 22.9, 10.2 Hz, 1H), 2.28 (dd, *J* = 20.6, 9.6 Hz, 1H), 1.92 (dt, *J* = 20.7, 9.0 Hz, 2H; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 162.0, 160.8, 141.5, 140.9, 140.7, 138.6, 133.8, 130.0, 129.8, 129.6, 128.3, 128.1, 126.8, 126.8, 126.0, 114.2, 100.0, 78.3, 72.2, 55.3, 39.5, 34.0, 31.5, 30.3, 23.0; m.p = 112-115°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{32}H_{31}NO_3$: 464.2220, found: 464.2220.

Procedure for Indole Substrate Deprotection:

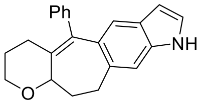
Scheme S18: General Conditions for Indole Deprotections



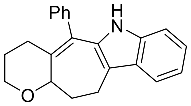
Indole substrates were deprotected following the procedure from Buden et al.[29] To a flame dried vial under argon and charged with a stir bar, added indole adduct **12p** (21 mg, 0.045 mmol) followed by DMSO (0.5mL). To this mixture, added KO^{t}Bu (15 mg, 0.13 mmol) that was kept in the glovebox. After addition of the base, the black reaction mixture was covered with aluminum foil and allowed to stir at room temperature for 3 hours. After this time, saturated ammonium chloride was added to quench the reaction, extracted with EtOAc (3 x 15mL), dried over $MgSO_4$, filtered, and concentrated. Product was purified by preparatory TLC, using 30% EtOAc in hexane with 2% Et_3N to afford deprotected indole **20a** as a pale grey amorphous solid (10.5 mg, 74% yield).



Compound **20a** was obtained as a grey amorphous solid (10.5 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.39 – 7.29 (m, 4H), 7.23 (d, *J* = 7.2 Hz, 3H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.72 (t, *J* = 7.6 Hz, 1H), 6.16 (d, *J* = 8.1 Hz, 1H), 4.30 (t, *J* = 6.9 Hz, 1H), 4.06 – 3.97 (m, 1H), 3.57 (td, *J* = 10.8, 6.1 Hz, 1H), 3.11 (dt, *J* = 15.6, 7.8 Hz, 1H), 2.87 (dt, *J* = 15.5, 6.3 Hz, 1H), 2.54 – 2.34 (m, 5H), 2.02 (d, *J* = 4.9 Hz, 1H), 1.73 (dd, *J* = 12.6, 6.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 139.8, 135.4, 135.0, 129.9, 128.2, 127.9, 126.7, 120.9, 120.4, 119.4, 112.4, 110.2, 79.1, 65.1, 36.2, 30.3, 26.5, 24.8, 23.5; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{22}H_{21}NO$: 316.1696, found: 316.1687.



Compound **20b** was obtained as a grey amorphous solid (6.9 mg, 51%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.34 (t, *J* = 7.3 Hz, 2H), 7.31 – 7.25 (m, 2H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.10 (s, 1H), 7.05 (s, 1H), 6.36 (s, 1H), 4.08 (dd, *J* = 10.6, 7.8 Hz, 1H), 3.94 (t, *J* = 8.4 Hz, 1H), 3.48 – 3.40 (m, 1H), 3.01 (td, *J* = 12.8, 8.0 Hz, 1H), 2.69 (dd, *J* = 13.1, 6.5 Hz, 1H), 2.60 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.55 – 2.44 (m, 1H), 2.40 (dd, *J* = 20.3, 12.0 Hz, 1H), 2.30 (dd, *J* = 19.5, 11.5 Hz, 1H), 2.13 – 2.00 (m, 1H), 1.76 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 136.4, 135.3, 134.9, 134.3, 133.9, 130.1, 128.0, 126.4, 126.3, 123.9, 122.1, 109.8, 102.7, 77.3, 63.3, 38.5, 31.0, 25.2, 22.8; HRMS (ESI) m/z: [M+H]$^+$ Calculated for $C_{22}H_{21}NO$: 316.1696, found: 316.1695.



Compound **20c** was obtained as a white solid (20.4 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 6.3 Hz, 1H), 7.45 (dq, *J* = 14.5, 7.1 Hz, 3H), 7.29 – 7.26 (m, 2H), 7.16 (s, 1H), 7.13-7.05 (m, 3H), 4.31 (dd, *J* = 7.3, 2.9 Hz, 1H), 4.14 – 4.04 (m, 1H), 3.70 (td, *J* = 10.8, 5.1 Hz, 1H), 3.20 – 2.99 (m, 2H), 2.44 – 2.14 (m, 4H), 1.97 – 1.83 (m, 1H), 1.66 (dd, *J* = 11.5, 5.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.9, 134.8, 132.7, 129.7, 128.9, 128.3, 127.5, 126.5, 122.0, 119.3, 118.3, 115.7, 110.5, 80.3, 66.5, 33.4, 28.6, 26.9, 20.5; m.p = 140-141°C; HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{21}NO$: 316.1696, found: 316.1693.

X-Ray Crystal Structures for Compounds 19, 12o, 12t, 14a, 21a-1, 22a, and 27h:

Compound 19:

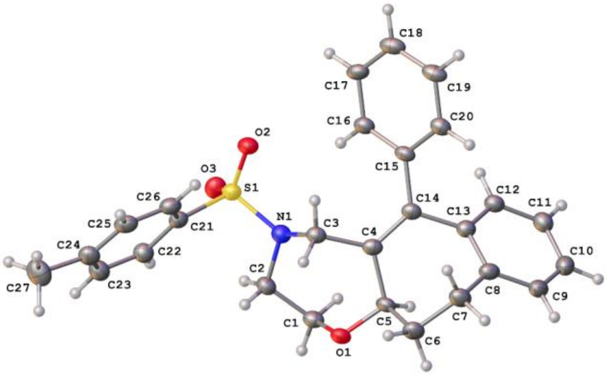


Table S2. Crystal data and structure refinement for **19**

Identification code	**19**	
Empirical formula	C27 H27 N O3 S	
Formula weight	445.55	
Temperature	100.01(10) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	*Pc*	
Unit cell dimensions	*a* = 12.17620(10) Å	α = 90°
	b = 11.57040(10) Å	β = 94.5220(10)°
	c = 7.98290(10) Å	γ = 90°
Volume	1121.158(19) Å^3	
Z	2	
Density (calculated)	1.320 Mg/m^3	
Absorption coefficient	1.516 mm^{-1}	
F(000)	472	
Crystal color, morphology	colourless, needle	
Crystal size	0.489 x 0.09 x 0.018 mm^3	
Theta range for data collection	3.641 to 80.188°	
Index ranges	$-15 \le h \le 15$, $-14 \le k \le 14$, $-9 \le l \le 8$	
Reflections collected	34948	
Independent reflections	4549 [*R*(int) = 0.0717]	

Observed reflections	4400
Completeness to theta = 74.504°	100.0%
Absorption correction	Multi-scan
Max. and min. transmission	1.00000 and 0.62538
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4549 / 2 / 290
Goodness-of-fit on F^2	1.097
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0438, *wR*2 = 0.1208
R indices (all data)	*R*1 = 0.0450, *wR*2 = 0.1219
Absolute structure parameter	-0.002(16)
Largest diff. peak and hole	0.383 and -0.464 e.Å^{-3}

Compound 12o:

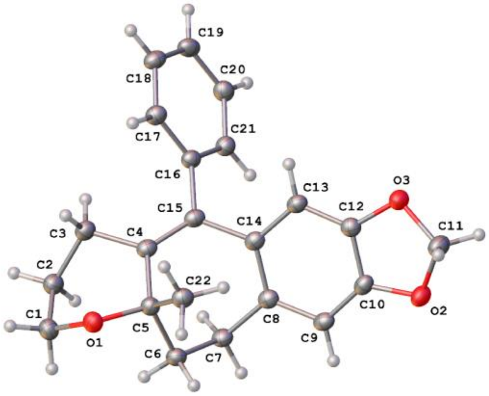


Table S3. Crystal data and structure refinement for **12o**

Identification code	**12o**	
Empirical formula	C22 H22 O3	
Formula weight	334.39	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	*a* = 17.2159(2) Å	a = 90°
	b = 10.13720(10) Å	b = 110.5460(10)°
	c = 20.2267(2) Å	g = 90°
Volume	3305.44(6) Å^3	

Z	8
Density (calculated)	1.344 Mg/m^3
Absorption coefficient	0.703 mm^{-1}
F(000)	1424
Crystal color, morphology	colourless, block
Crystal size	0.168 x 0.13 x 0.082 mm^3
Theta range for data collection	4.179 to 80.392°
Index ranges	-22 £ *h* £ 16, -12 £ *k* £ 12, -25 £ *l* £ 25
Reflections collected	35734
Independent reflections	7100 [*R*(int) = 0.0387]
Observed reflections	6280
Completeness to theta = 74.504°	100.0%
Absorption correction	Multi-scan
Max. and min. transmission	1.00000 and 0.87854
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7100 / 0 / 453
Goodness-of-fit on F^2	1.059
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0442, *wR*2 = 0.1209
R indices (all data)	*R*1 = 0.0487, *wR*2 = 0.1248
Largest diff. peak and hole	0.377 and -0.225 e.Å^{-3}

Compound 12t:

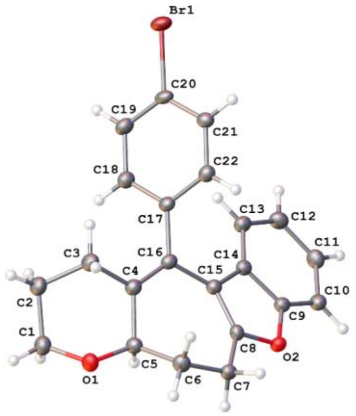


Table S4. Crystal data and structure refinement for **12t**

—

Identification code	**12t**

Empirical formula	C22 H19 Br O2	
Formula weight	395.28	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	triclinic	
Space group	*P*-1	
Unit cell dimensions	*a* = 7.14240(10) Å	a = 93.7290(10)°
	b = 9.29770(10) Å	b = 99.1970(10)°
	c = 13.9152(2) Å	g = 107.703(2)°
Volume	862.63(2) Å^3	
Z	2	
Density (calculated)	1.522 Mg/m^3	
Absorption coefficient	3.338 mm^{-1}	
F(000)	404	
Crystal color, morphology	colourless, block	
Crystal size	0.155 x 0.113 x 0.078 mm^3	
Theta range for data collection	3.241 to 80.002°	
Index ranges	-9 £ *h* £ 9, -11 £ *k* £ 10, -17 £ *l* £ 17	
Reflections collected	28144	
Independent reflections	3680 [*R*(int) = 0.0421]	
Observed reflections	3503	
Completeness to theta = 74.504°	99.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.88565	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3680 / 0 / 226	
Goodness-of-fit on F^2	1.081	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0325, *wR*2 = 0.0764	
R indices (all data)	*R*1 = 0.0340, *wR*2 = 0.0772	
Largest diff. peak and hole	0.371 and -0.694 e.Å^{-3}	

Compound 14a:

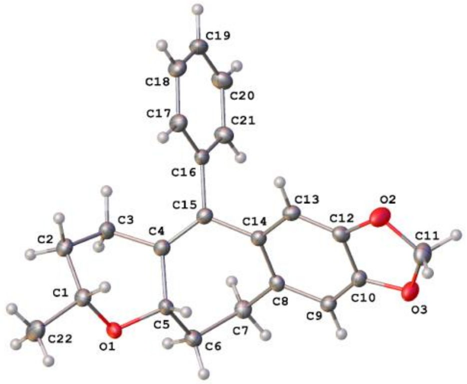


Table S5. Crystal data and structure refinement for **14a**

—

Identification code	**14a**	
Empirical formula	C22 H22 O3	
Formula weight	334.39	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	*a* = 11.11210(10) Å	a = 90°
	b = 14.44820(10) Å	b = 100.5810(10)°
	c = 11.06860(10) Å	g = 90°
Volume	1746.85(3) Å^3	
Z	4	
Density (calculated)	1.271 Mg/m^3	
Absorption coefficient	0.665 mm^{-1}	
F(000)	712	
Crystal color, morphology	colourless, block	
Crystal size	0.234 x 0.139 x 0.108 mm^3	
Theta range for data collection	4.047 to 80.156°	
Index ranges	-14 £ *h* £ 14, -18 £ *k* £ 18, -12 £ *l* £ 13	
Reflections collected	20536	
Independent reflections	3744 [*R*(int) = 0.0366]	
Observed reflections	3460	
Completeness to theta = 74.504°	99.9%	
Absorption correction	Multi-scan	

Max. and min. transmission	1.00000 and 0.89800
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3744 / 106 / 256
Goodness-of-fit on F^2	1.052
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0417, *wR*2 = 0.1039
R indices (all data)	*R*1 = 0.0442, *wR*2 = 0.1057
Largest diff. peak and hole	0.228 and -0.249 e.Å^{-3}

Compound 21a-1:

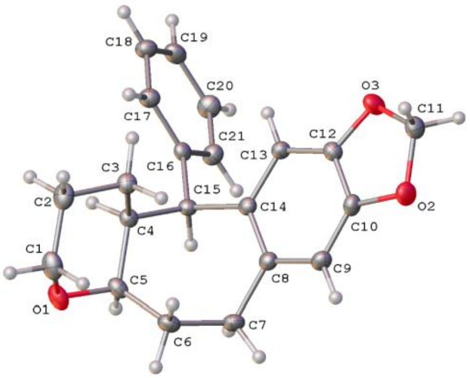


Table S6. Crystal data and structure refinement for **21a-1**

—

Identification code	**21a -1**	
Empirical formula	C21 H22 O3	
Formula weight	322.38	
Temperature	99.97(10) K	
Wavelength	1.54184 Å	
Crystal system	orthorhombic	
Space group	$Pna2_1$	
Unit cell dimensions	*a* = 14.11320(10) Å	a = 90°
	b = 19.7985(2) Å	b = 90°
	c = 5.92430(10) Å	g = 90°
Volume	1655.37(3) Å^3	
Z	4	
Density (calculated)	1.294 Mg/m^3	
Absorption coefficient	0.680 mm^{-1}	
F(000)	688	

Crystal color, morphology	colourless, block
Crystal size	0.284 x 0.227 x 0.1 mm^3
Theta range for data collection	3.846 to 80.166°
Index ranges	-17 £ *h* £ 17, -24 £ *k* £ 25, -6 £ *l* £ 7
Reflections collected	19326
Independent reflections	3305 [*R*(int) = 0.0399]
Observed reflections	3221
Completeness to theta = 67.684°	100.0%
Absorption correction	Multi-scan
Max. and min. transmission	1.00000 and 0.87289
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3305 / 1 / 217
Goodness-of-fit on F^2	1.048
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0312, *wR*2 = 0.0777
R indices (all data)	*R*1 = 0.0319, *wR*2 = 0.0783
Absolute structure parameter	-0.06(10)
Largest diff. peak and hole	0.138 and -0.196 e.Å^{-3}

Compound 22a:

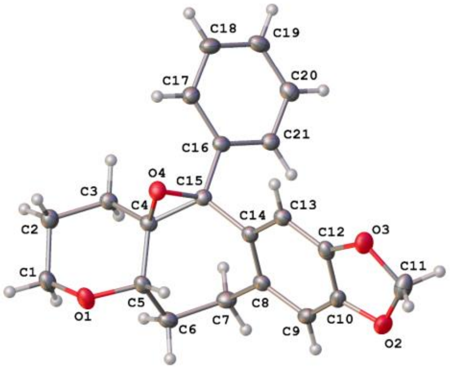


Table S7. Crystal data and structure refinement for **22a**

—

Identification code	**22a**
Empirical formula	C21 H20 O4
Formula weight	336.37
Temperature	100.00(10) K
Wavelength	1.54184 Å

Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	*a* = 11.33020(10) Å	a = 90°
	b = 9.30400(10) Å	b = 92.0390(10)°
	c = 15.25110(10) Å	g = 90°
Volume	1606.69(2) Å^3	
Z	4	
Density (calculated)	1.391 Mg/m^3	
Absorption coefficient	0.776 mm^{-1}	
F(000)	712	
Crystal color, morphology	colourless, block	
Crystal size	0.126 x 0.118 x 0.057 mm^3	
Theta range for data collection	4.782 to 80.320°	
Index ranges	-14 £ *h* £ 14, -9 £ *k* £ 11, -19 £ *l* £ 19	
Reflections collected	28132	
Independent reflections	3482 [*R*(int) = 0.0354]	
Observed reflections	3218	
Completeness to theta = 74.504°	100.0%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.94365	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3482 / 0 / 226	
Goodness-of-fit on F^2	1.061	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0358, *wR*2 = 0.0917	
R indices (all data)	*R*1 = 0.0384, *wR*2 = 0.0935	
Largest diff. peak and hole	0.234 and -0.208 e.Å^{-3}	

Compound 27h:

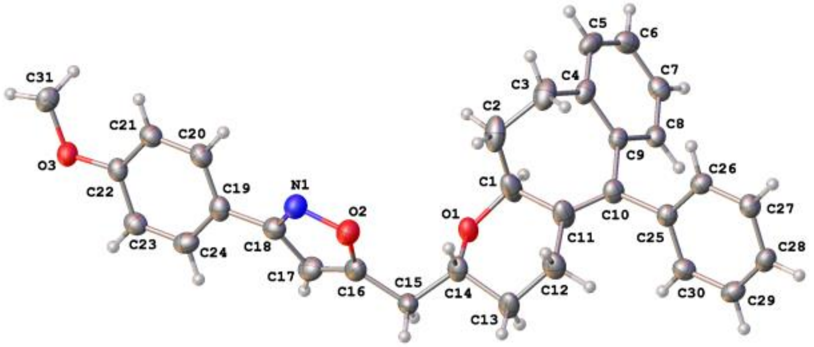
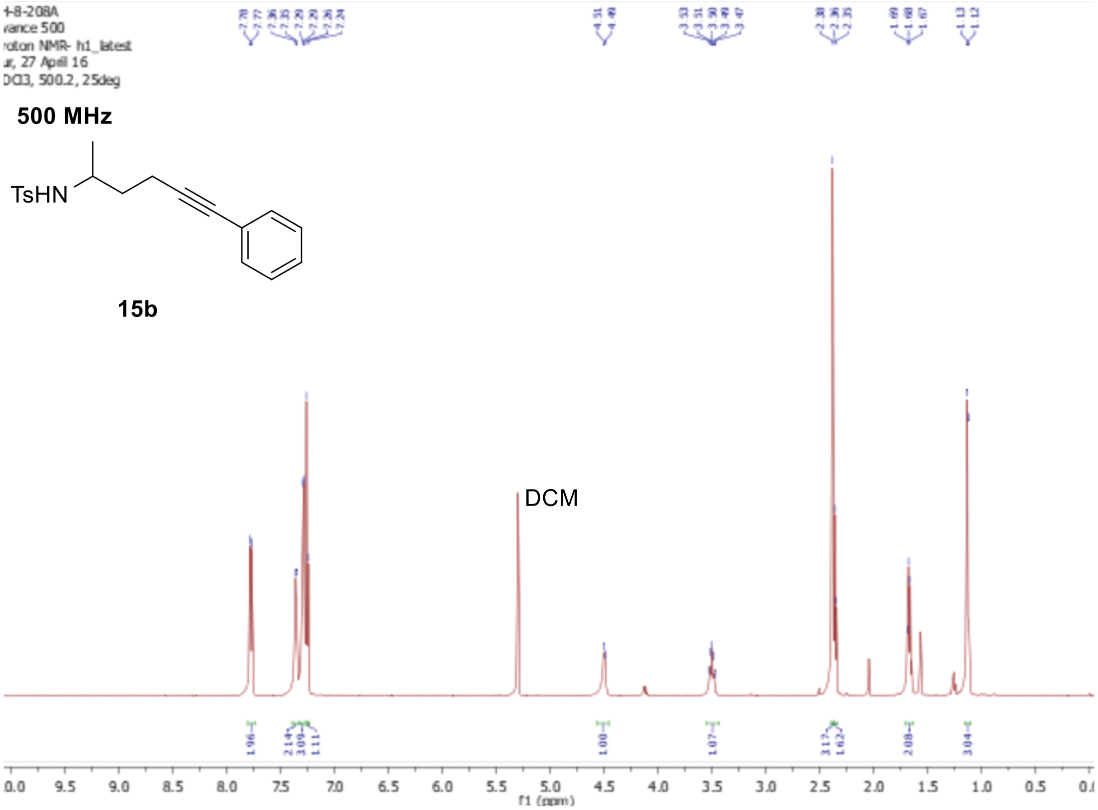


Table S8. Crystal data and structure refinement for **27h**.

Identification code	**27h**	
Empirical formula	C31 H29 N O3	
Formula weight	463.55	
Temperature	99.99(10) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	*a* = 15.9276(3) Å	a = 90°
	b = 5.55609(9) Å	b = 98.7546(18)°
	c = 27.3254(5) Å	g = 90°
Volume	2389.99(7) Å^3	
Z	4	
Density (calculated)	1.288 Mg/m^3	
Absorption coefficient	0.651 mm^{-1}	
F(000)	984	
Crystal color, morphology	colourless, needle	
Crystal size	0.2 x 0.104 x 0.077 mm^3	
Theta range for data collection	3.273 to 80.341°	
Index ranges	-20 £ *h* £ 20, -7 £ *k* £ 7, -34 £ *l* £ 34	
Reflections collected	47366	
Independent reflections	9452 [*R*(int) = 0.044]	
Observed reflections	8533	
Completeness to theta = 74.504°	99.5%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.63440	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9452 / 36 / 355	
Goodness-of-fit on F^2	1.099	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0706, *wR*2 = 0.1831	
R indices (all data)	*R*1 = 0.0762, *wR*2 = 0.1865	
Largest diff. peak and hole	0.617 and -0.408 e.Å^{-3}	

NMR Spectra:



-8-208A
vance 500
roton NMR- h1_latest
ur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
TsHN
15b
7.78
7.77
7.36
7.35
7.29
7.29
7.26
7.24
4.51
4.49
3.53
3.51
3.50
3.49
3.47
2.38
2.36
2.35
1.69
1.68
1.67
1.13
1.12
DCM
1.96
2.14
3.09
1.11
1.00
1.07
3.17
1.62
2.08
3.04
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
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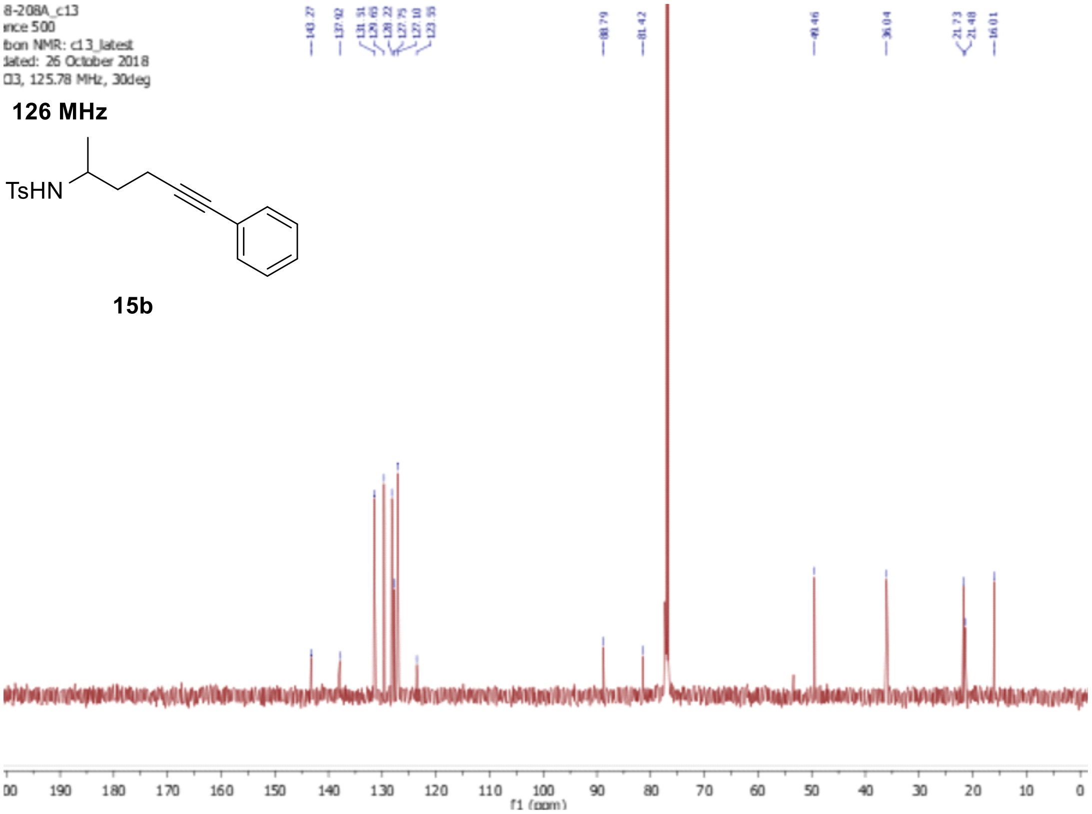
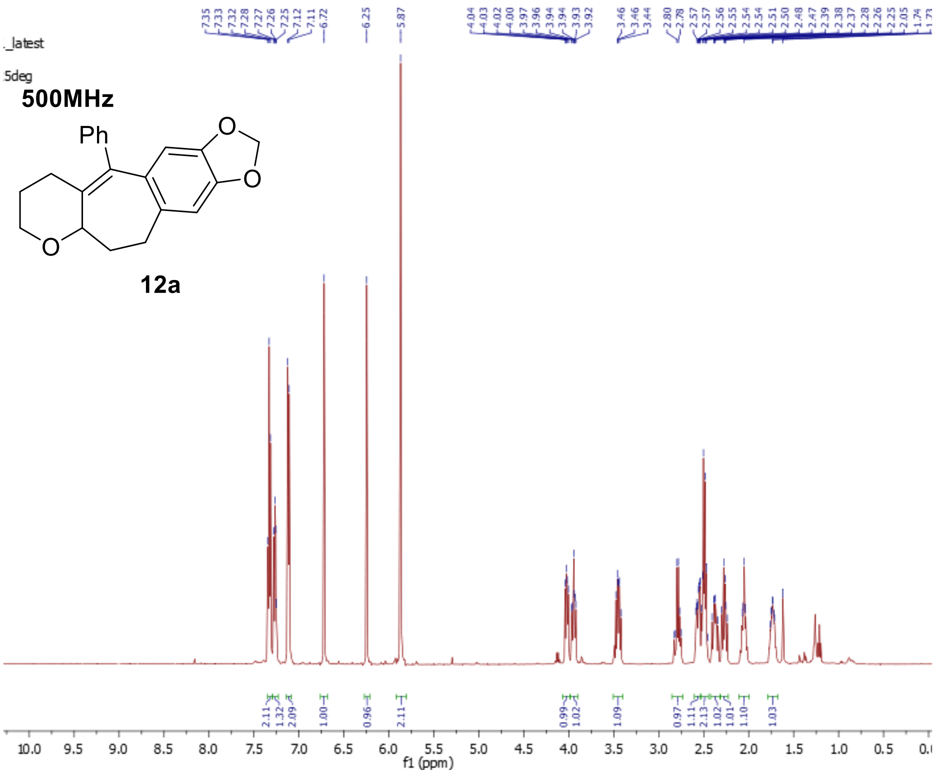
1.5
1.0
0.5
0.
f1 (ppm)



8-208A_c13
nce 500
bon NMR: c13_latest
dated: 26 October 2018
l3, 125.78 MHz, 30deg
126 MHz
TsHN
15b
143.27
137.92
131.51
129.65
128.22
127.75
127.10
123.55
88.79
81.42
49.46
36.04
21.73
21.48
16.01
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


_latest
5deg
500MHz
Ph
O
O
O
12a
7.35
7.33
7.32
7.28
7.27
7.26
7.25
7.12
7.11
6.72
6.25
5.87
4.04
4.03
4.02
4.00
3.97
3.96
3.94
3.94
3.93
3.92
3.46
3.46
3.44
2.80
2.78
2.57
2.57
2.56
2.55
2.54
2.54
2.51
2.50
2.48
2.47
2.39
2.38
2.37
2.28
2.26
2.25
2.05
1.74
2.11
1.32
2.09
1.00
0.96
2.11
0.99
1.02
1.09
0.97
1.11
2.13
1.02
1.01
1.10
1.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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3.0
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1.5
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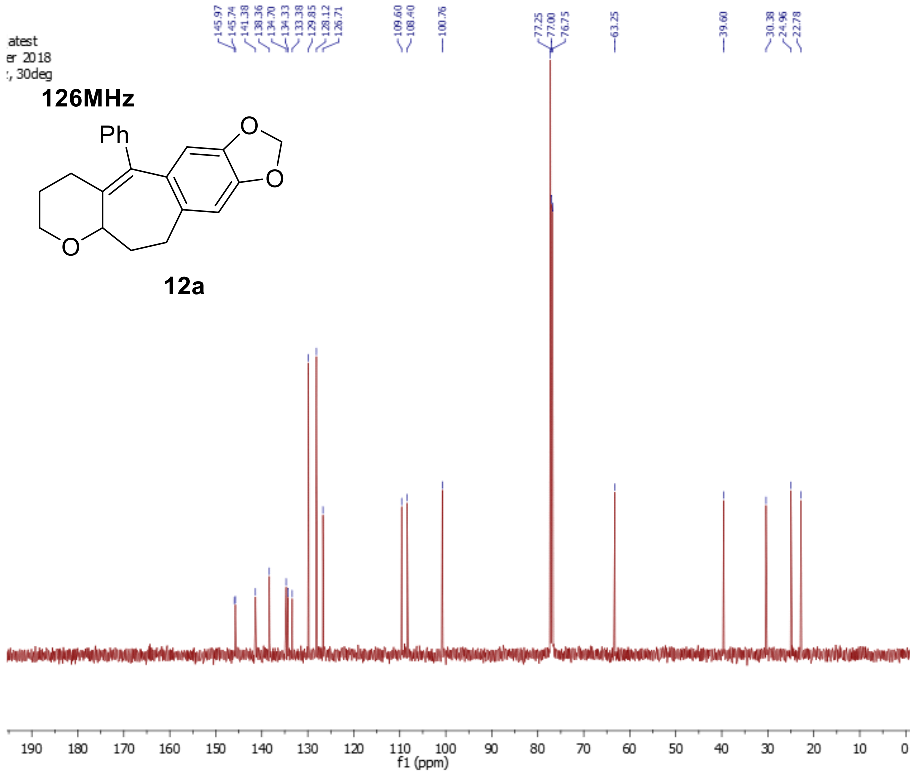
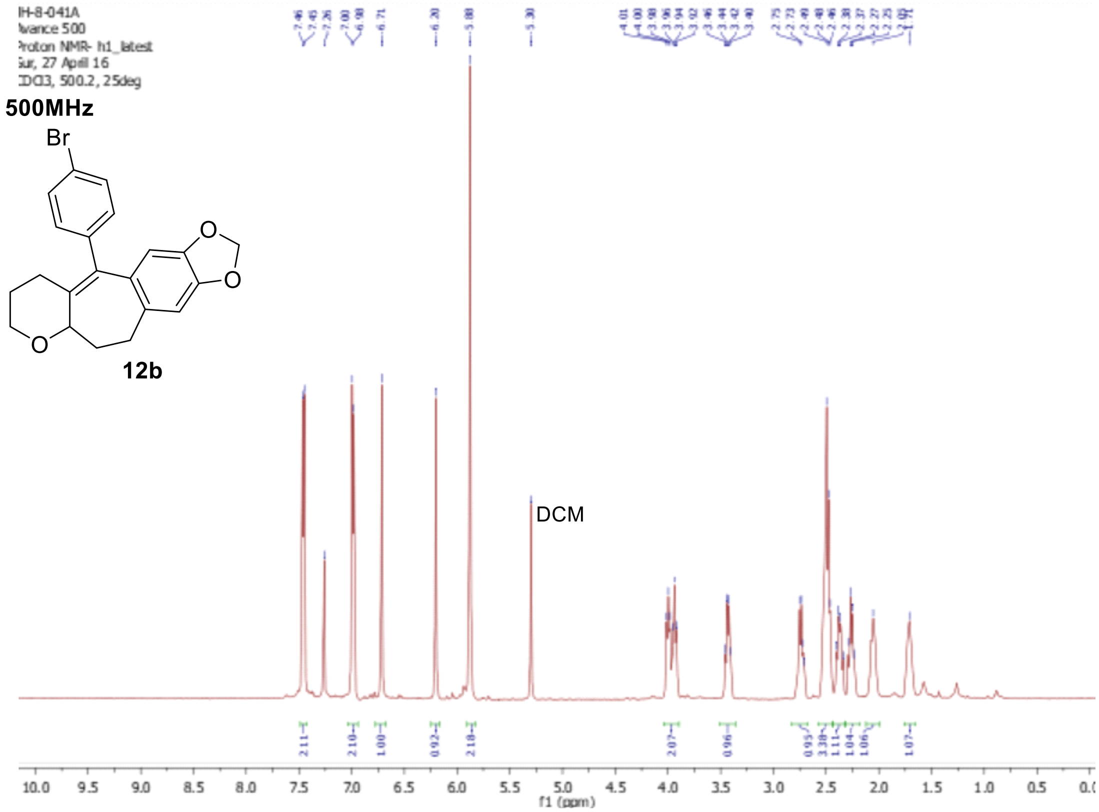
0.5
f1 (ppm)


atest
er 2018
, 30deg
126MHz
Ph
O
O
O
12a
145.97
145.74
141.38
138.36
134.70
134.33
133.38
129.85
128.12
126.71
109.60
108.40
100.76
77.25
77.00
76.75
63.25
39.60
30.38
24.96
22.78
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


JH-8-041A
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Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500MHz
Br
O
O
O
12b
7.46
7.45
7.26
7.00
6.98
6.71
6.20
5.88
5.30
4.01
4.00
3.98
3.96
3.94
3.92
3.46
3.44
3.42
3.40
2.75
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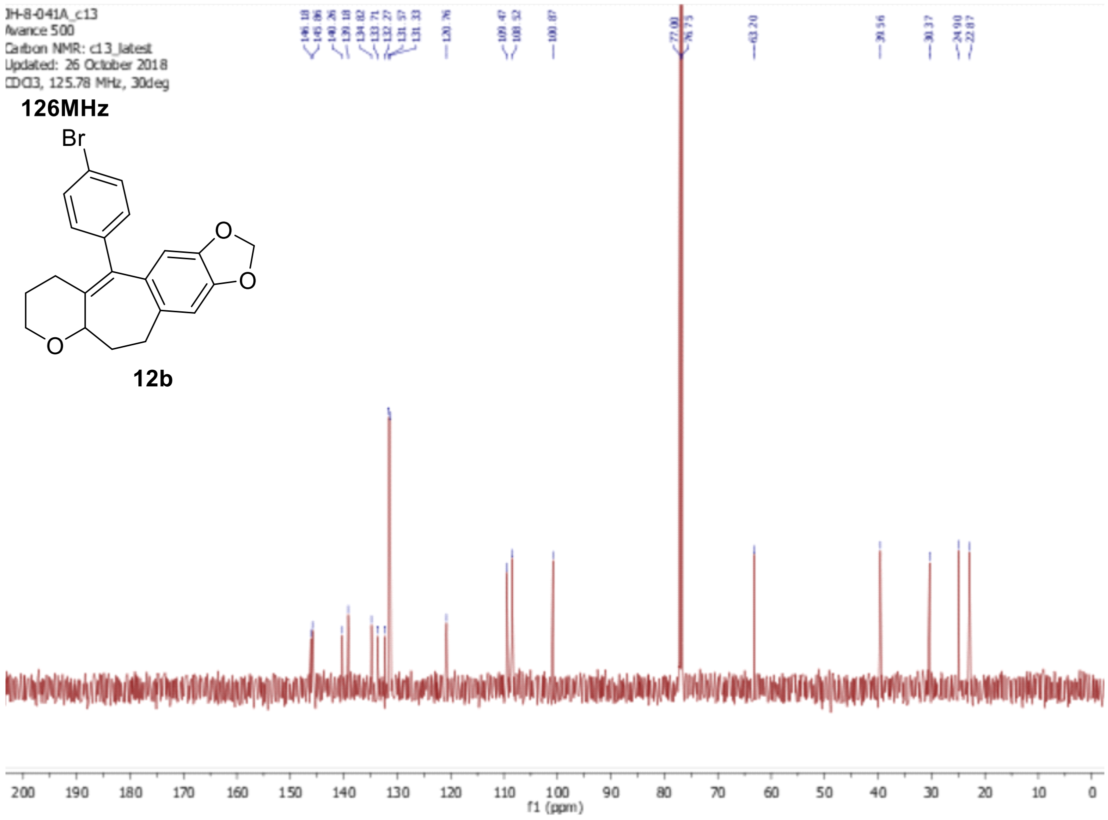
2.48
2.46
2.38
2.37
2.27
2.25
2.05
1.71
DCM
2.11
2.10
1.00
0.92
2.18
2.07
0.96
0.95
3.30
1.11
1.04
1.06
1.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


JH-8-041A_c13
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Updated: 26 October 2018
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126MHz
Br
O
O
O
12b
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145.86
140.26
139.18
134.82
133.71
132.27
131.57
131.33
120.76
109.47
108.52
100.87
77.00
76.75
63.20
39.56
30.37
24.90
22.87
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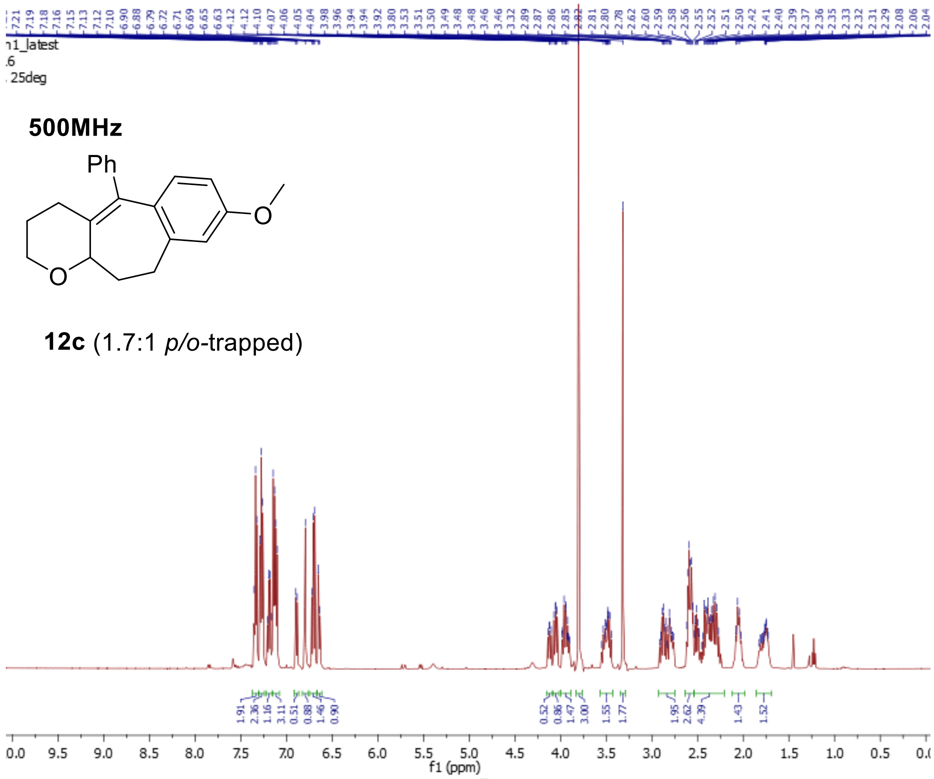
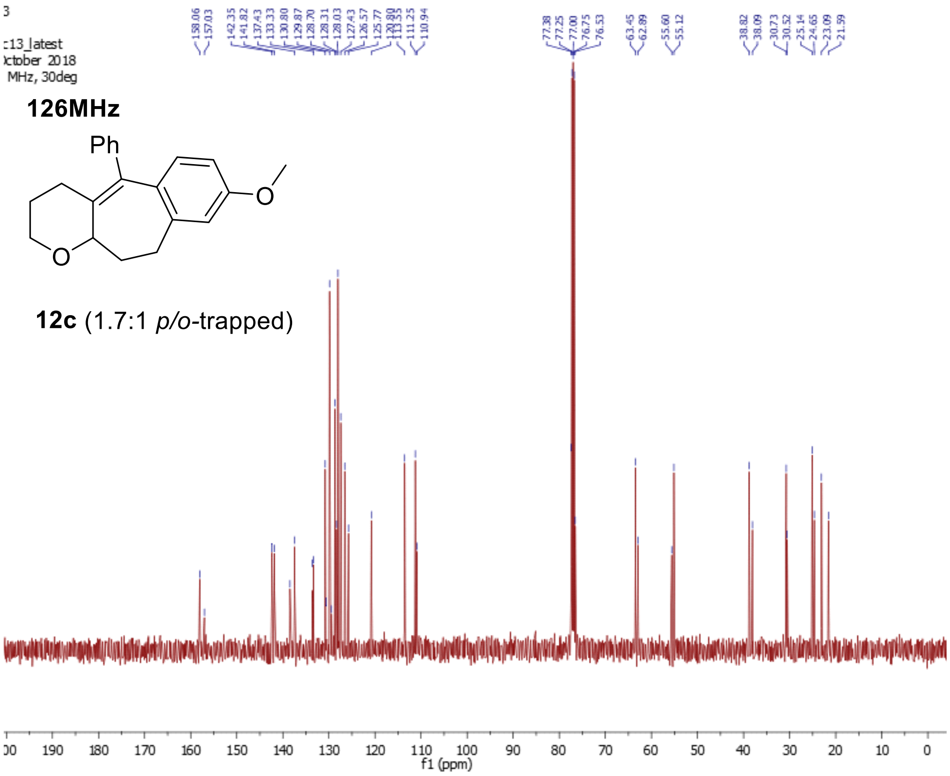
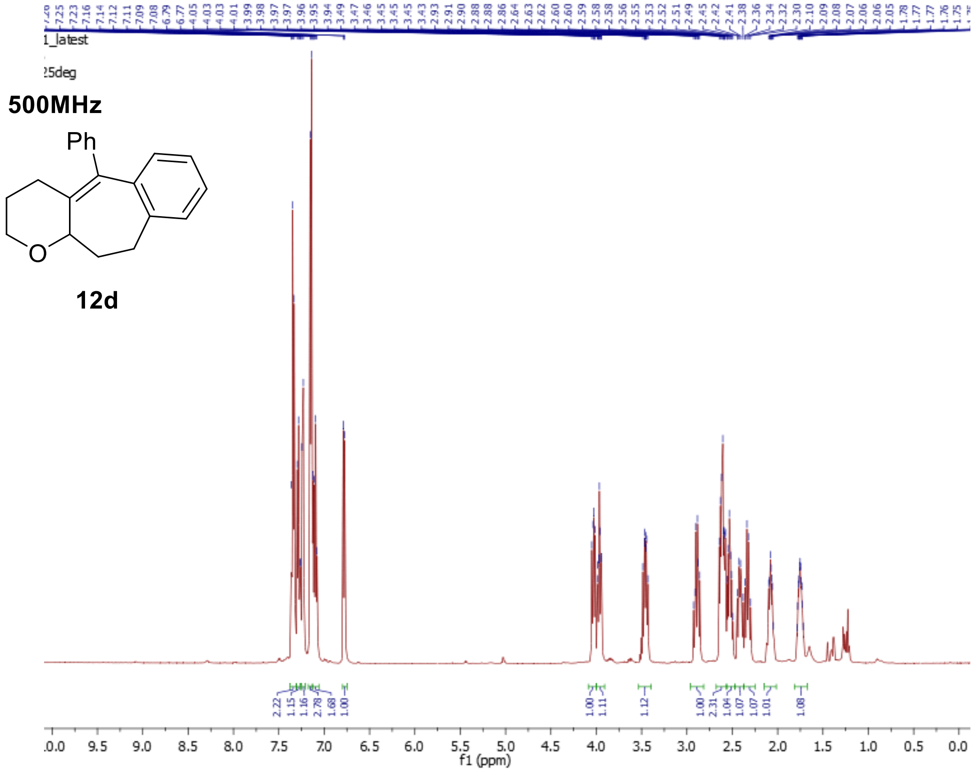
f1 (ppm)



12c (1.7:1 *p*/*o*-trapped)



12c (1.7:1 *p*/*o*-trapped)


7.29
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7.08
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6.77
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4.03
4.01
3.99
3.98
3.97
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3.46
3.45
3.45
3.45
3.43
2.93
2.91
2.90
2.88
2.88
2.86
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2.63
2.62
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2.53
2.52
2.51
2.49
2.45
2.42
2.41
2.38
2.36
2.34
2.32
2.30
2.10
2.09
2.08
2.07
2.06
2.06
2.05
1.78
1.77
1.77
1.76
1.75
1_latest
25deg
500MHz
Ph
O
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1.16
2.78
1.68
1.00
1.00
1.11
1.12
1.00
2.31
1.04
1.07
1.07
1.01
1.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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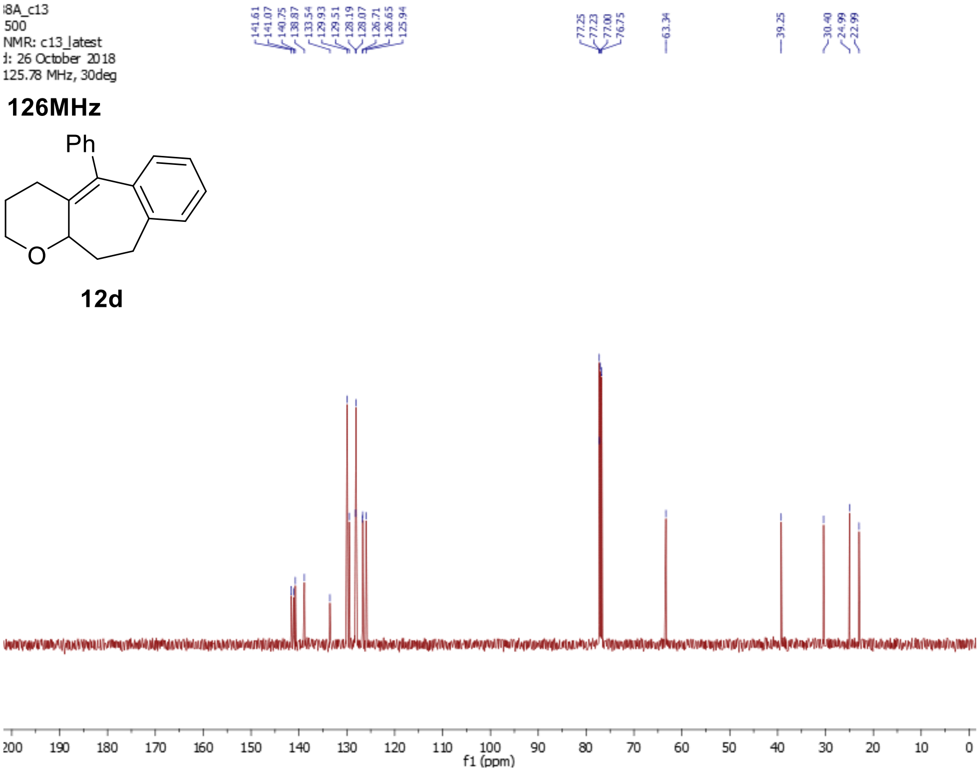
0.0
f1 (ppm)


8A_c13
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NMR: c13_latest
d: 26 October 2018
125.78 MHz, 30deg
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129.93
129.51
128.19
128.07
126.71
126.65
125.94
77.25
77.23
77.00
76.75
63.34
39.25
30.40
24.99
22.99
126MHz
Ph
O
12d
200
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180
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130
120
110
100
90
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50
40
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20
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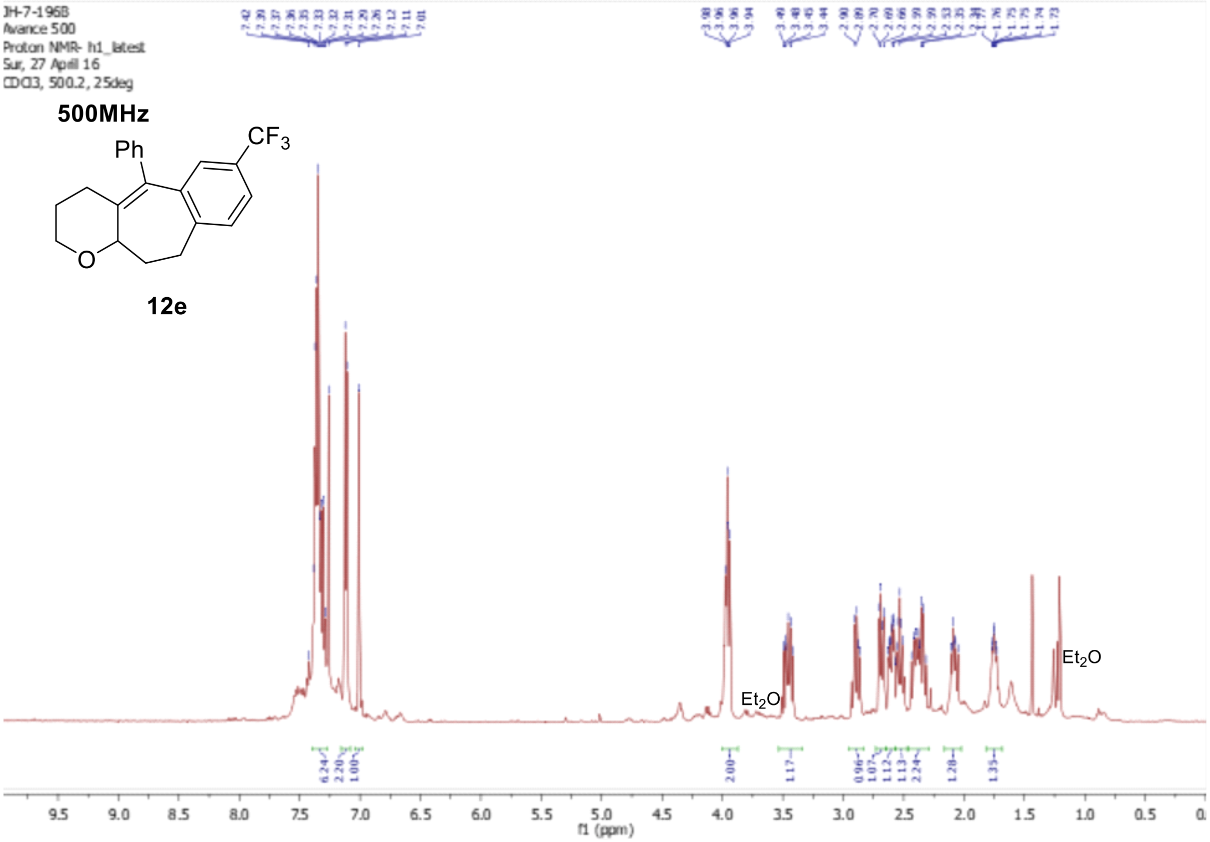
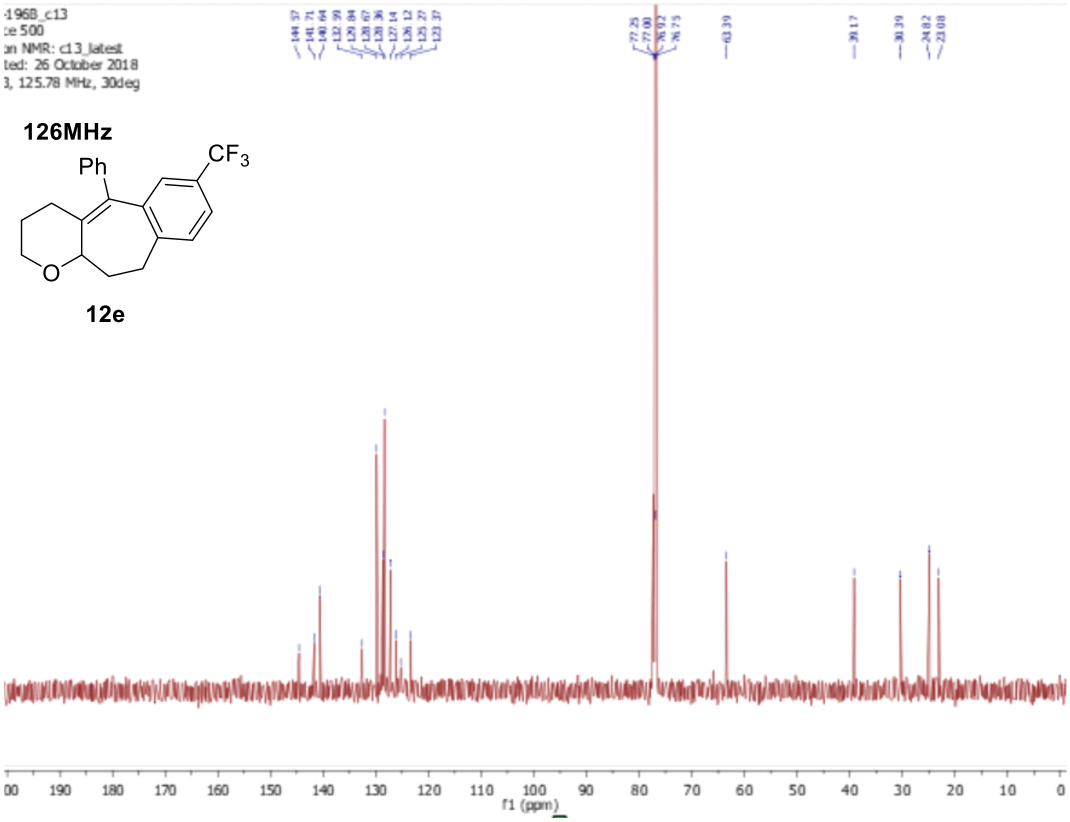
f1 (ppm)



JH-7-196B
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500MHz
Ph
CF3
O
12e
7.42 7.39 7.37 7.36 7.35 7.33 7.32 7.31 7.29 7.26 7.12 7.11 7.01
3.98 3.96 3.96 3.94
3.49 3.48 3.45 3.44
2.90 2.89 2.70 2.69 2.66 2.59 2.55 2.53 2.35 2.34
1.77 1.76 1.75 1.75 1.74 1.73
Et2O
Et2O
6.24 2.20 1.00
2.00
1.17
0.96 1.07 1.12 1.13 2.24
1.28
1.35
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)



196B_c13
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NMR: c13_latest
ted: 26 October 2018
3, 125.78 MHz, 30deg
126MHz
Ph
CF3
O
12e
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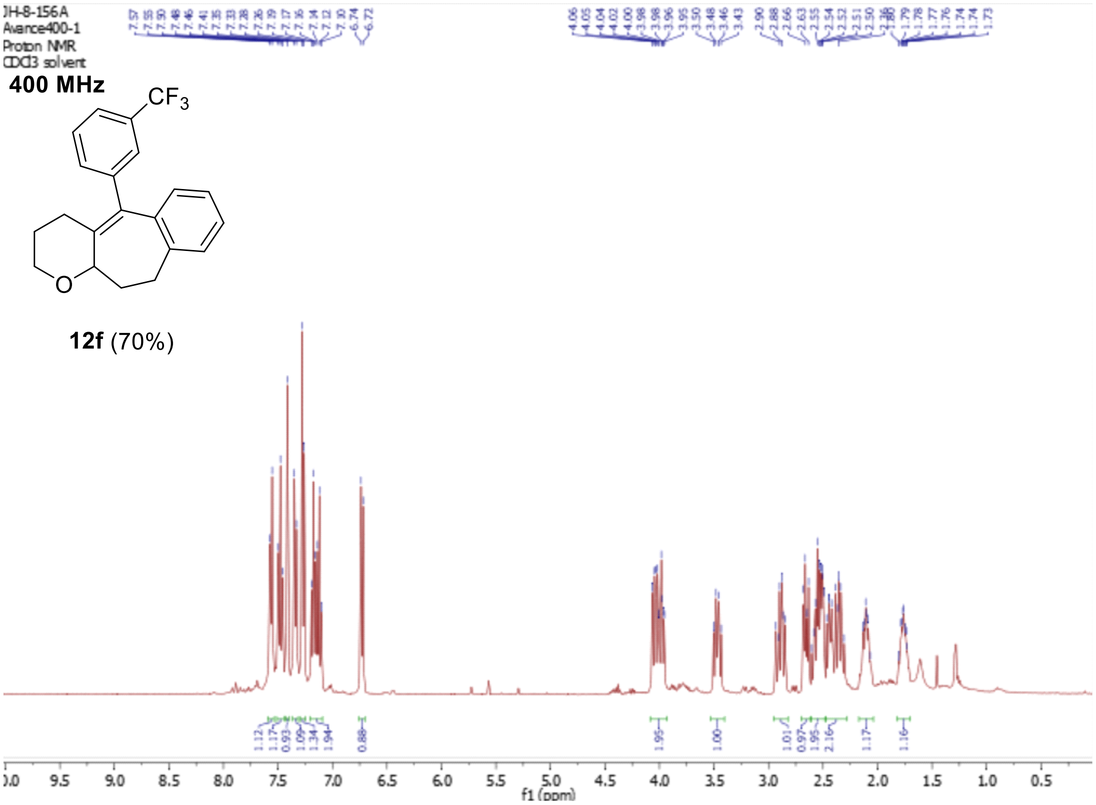
77.25 77.00 76.92 76.75
63.39
39.17
30.39
24.82 23.08
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


JH-8-156A
Avance400-1
Proton NMR
CDCl3 solvent
400 MHz
CF3
O
12f (70%)
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7.55
7.50
7.48
7.46
7.41
7.35
7.33
7.28
7.26
7.19
7.17
7.16
7.14
7.12
7.10
6.74
6.72
4.06
4.05
4.04
4.02
4.00
3.98
3.98
3.96
3.95
3.50
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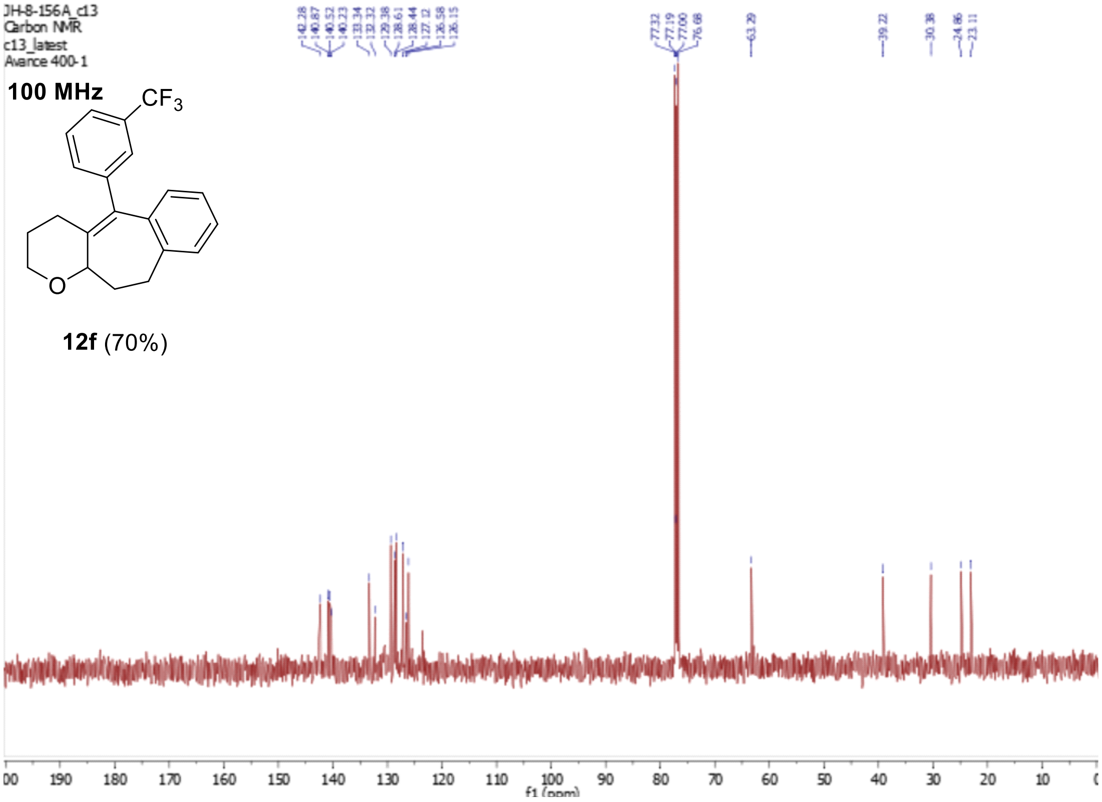
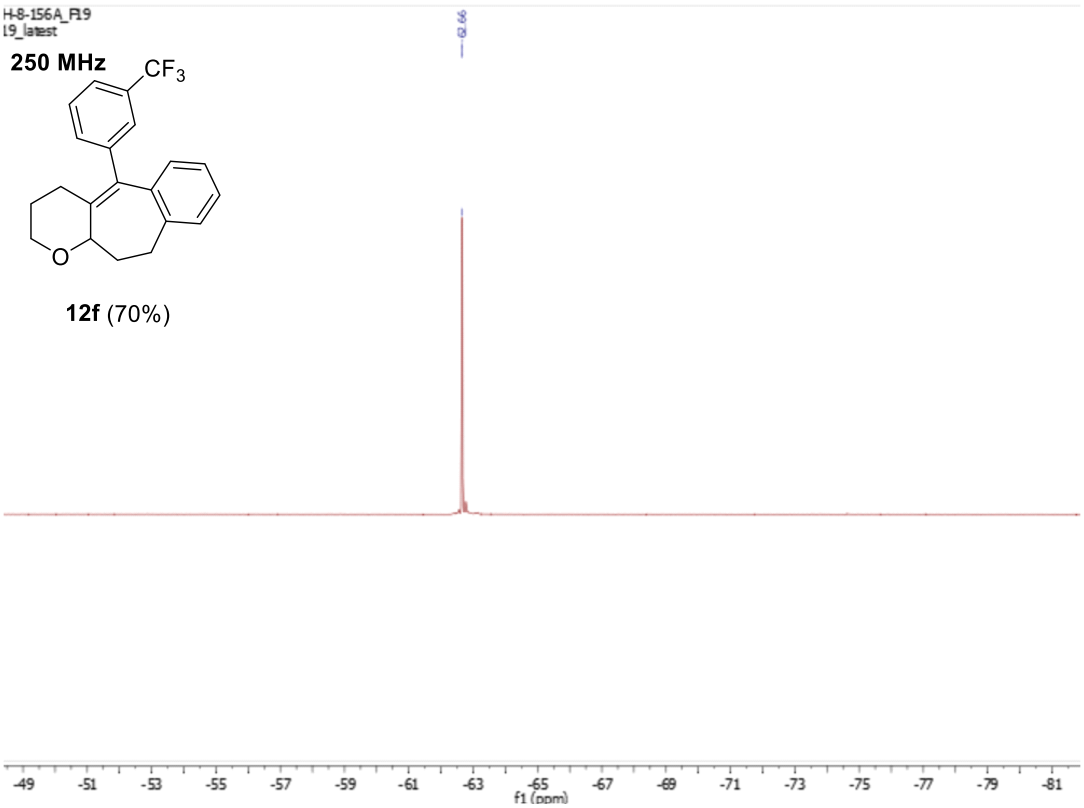
2.50
2.36
1.80
1.79
1.78
1.77
1.76
1.74
1.74
1.73
1.12
1.17
0.93
1.09
1.34
1.94
0.88
1.95
1.00
1.01
0.97
1.95
2.16
1.17
1.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


JH-8-156A_c13
Carbon NMR
c13_latest
Avance 400-1
100 MHz
CF3
O
12f (70%)
142.28
140.87
140.52
140.23
133.34
132.32
129.38
128.61
128.44
127.12
126.58
126.15
77.32
77.19
77.00
76.68
63.29
39.22
30.38
24.86
23.11
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



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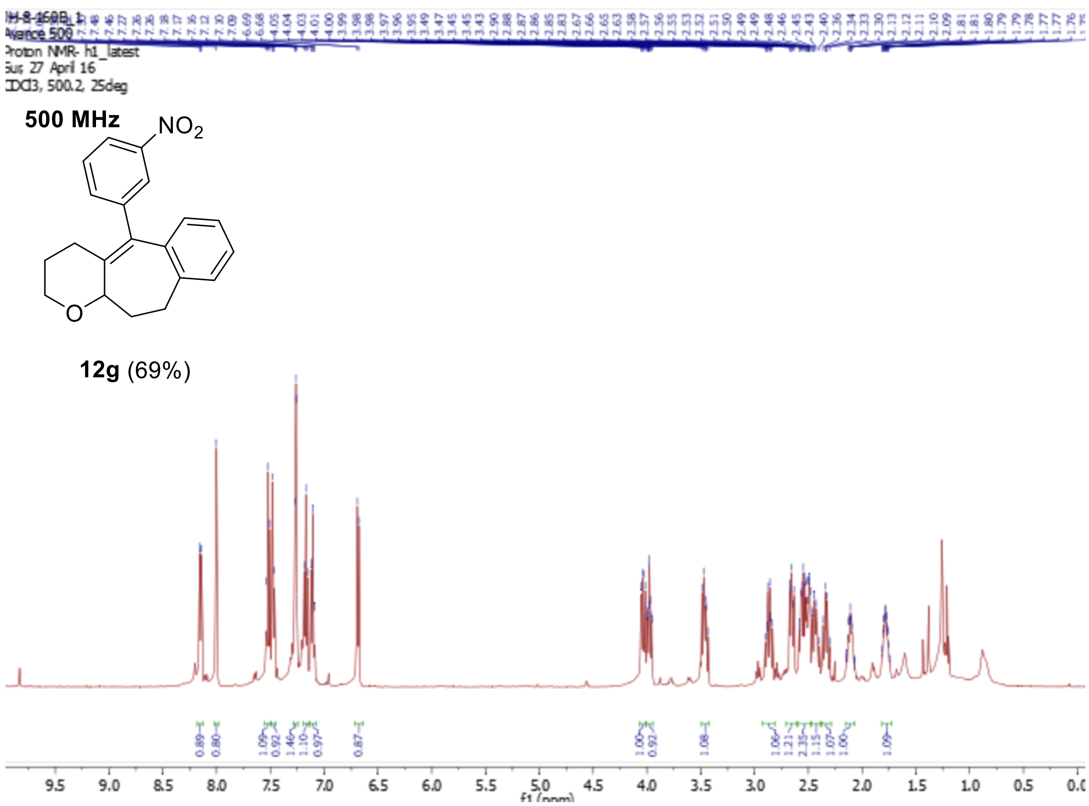
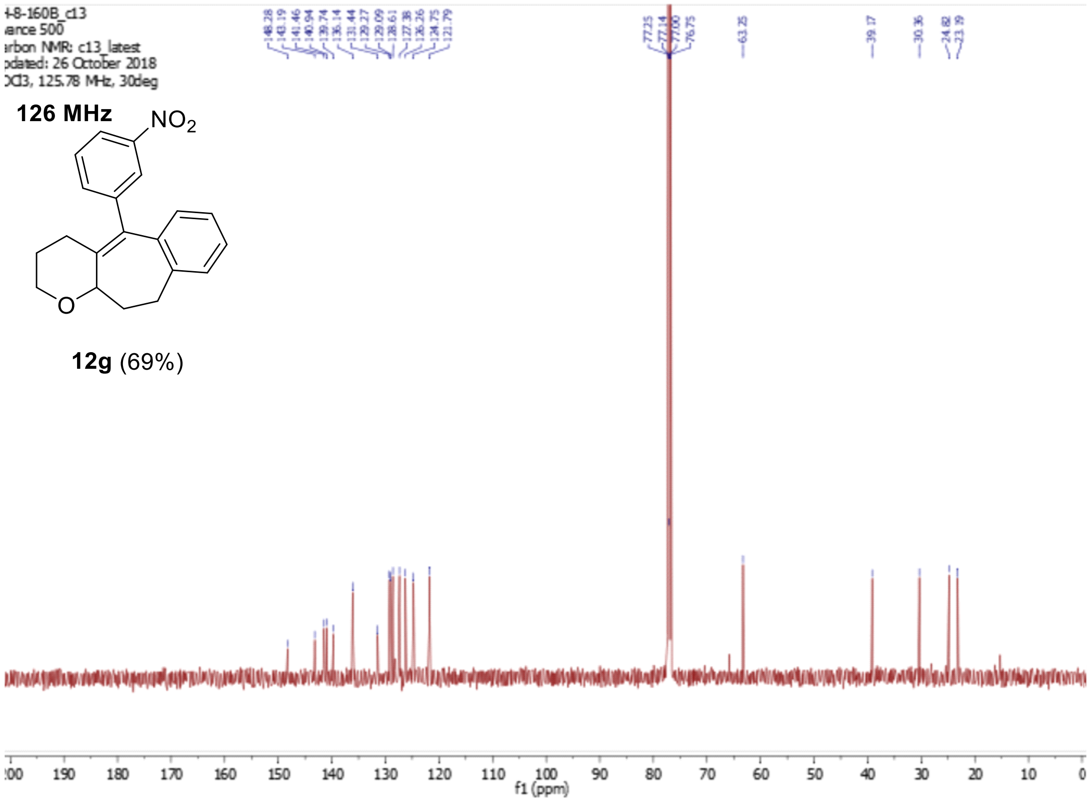
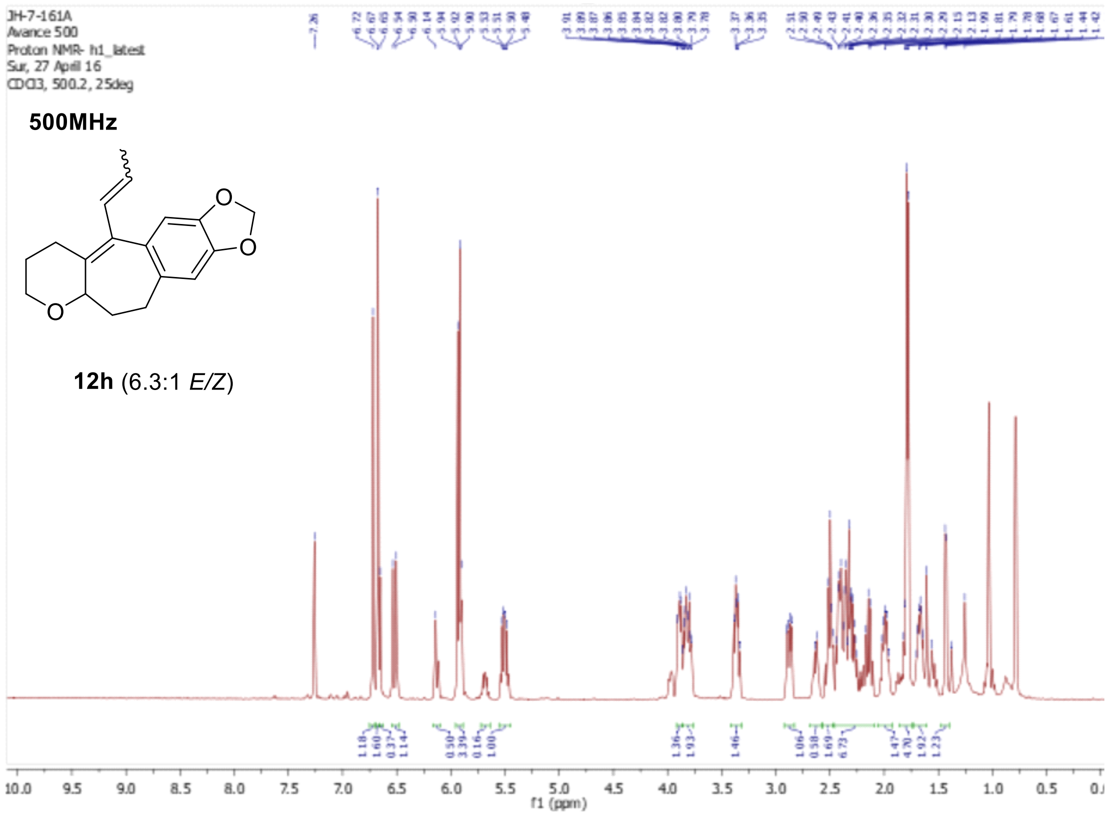
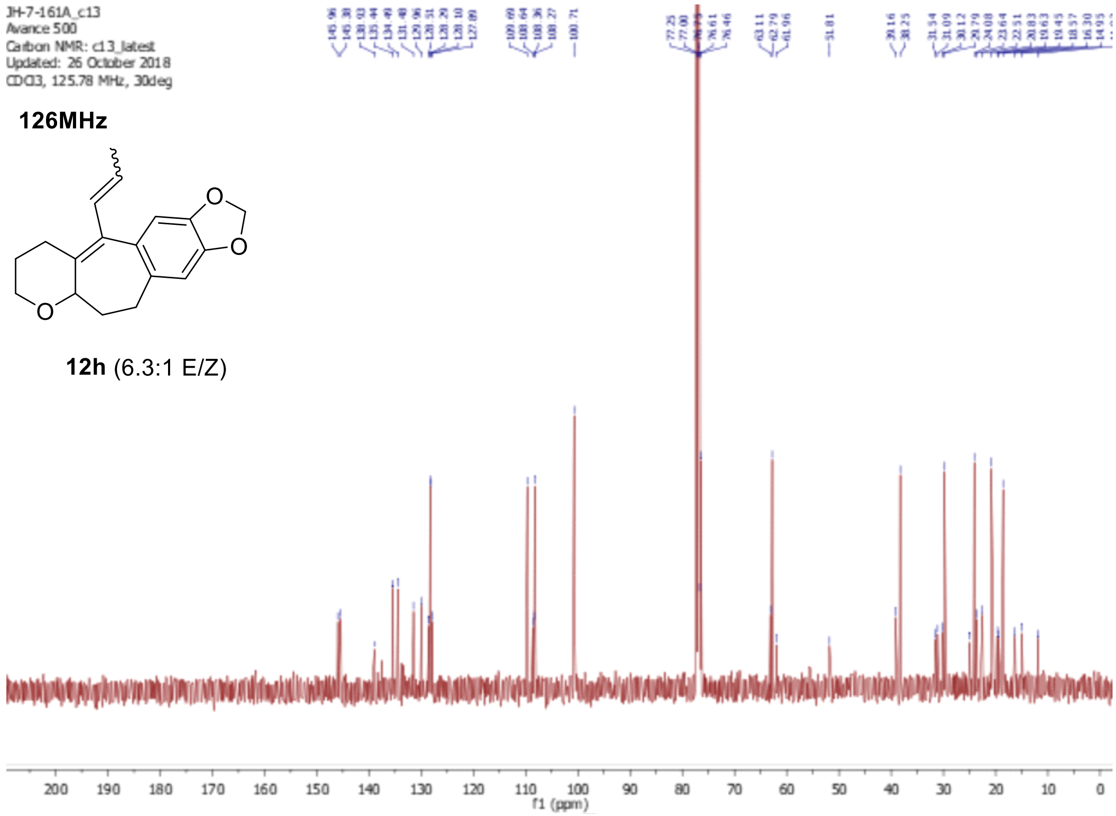

H-8-160B_1
Avance 500
Proton NMR- h1_latest
Sun, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
NO2
O
12g (69%)
7.46
7.45
7.27
7.26
7.26
7.18
7.17
7.16
7.12
7.10
7.09
6.69
6.68
4.05
4.04
4.03
4.01
4.00
3.99
3.98
3.98
3.97
3.96
3.95
3.49
3.47
3.45
3.45
3.43
2.90
2.88
2.87
2.86
2.85
2.83
2.67
2.66
2.65
2.63
2.58
2.57
2.56
2.55
2.53
2.52
2.51
2.50
2.49
2.49
2.48
2.46
2.45
2.43
2.40
2.36
2.34
2.33
2.30
2.13
2.12
2.11
2.10
2.09
1.81
1.81
1.80
1.79
1.79
1.78
1.77
1.77
1.76
0.89
0.80
1.09
0.92
1.46
1.10
0.97
0.87
1.00
0.92
1.08
1.06
1.21
2.35
1.15
1.07
1.00
1.09
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

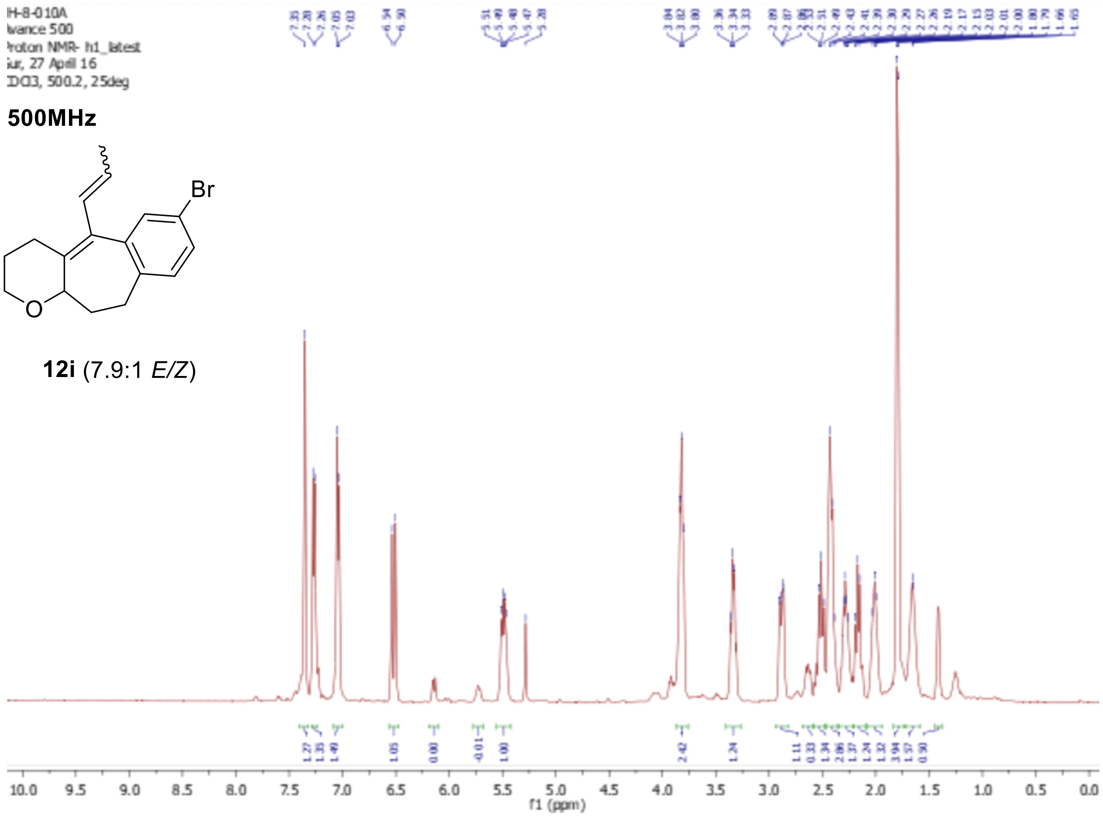

H-8-160B_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
NO2
O
12g (69%)
148.28
143.19
141.46
140.94
139.74
136.14
131.44
129.27
129.09
128.61
127.38
126.26
124.75
121.79
77.25
77.14
77.00
76.75
63.25
39.17
30.36
24.82
23.39
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



12h (6.3:1 *E/Z*)

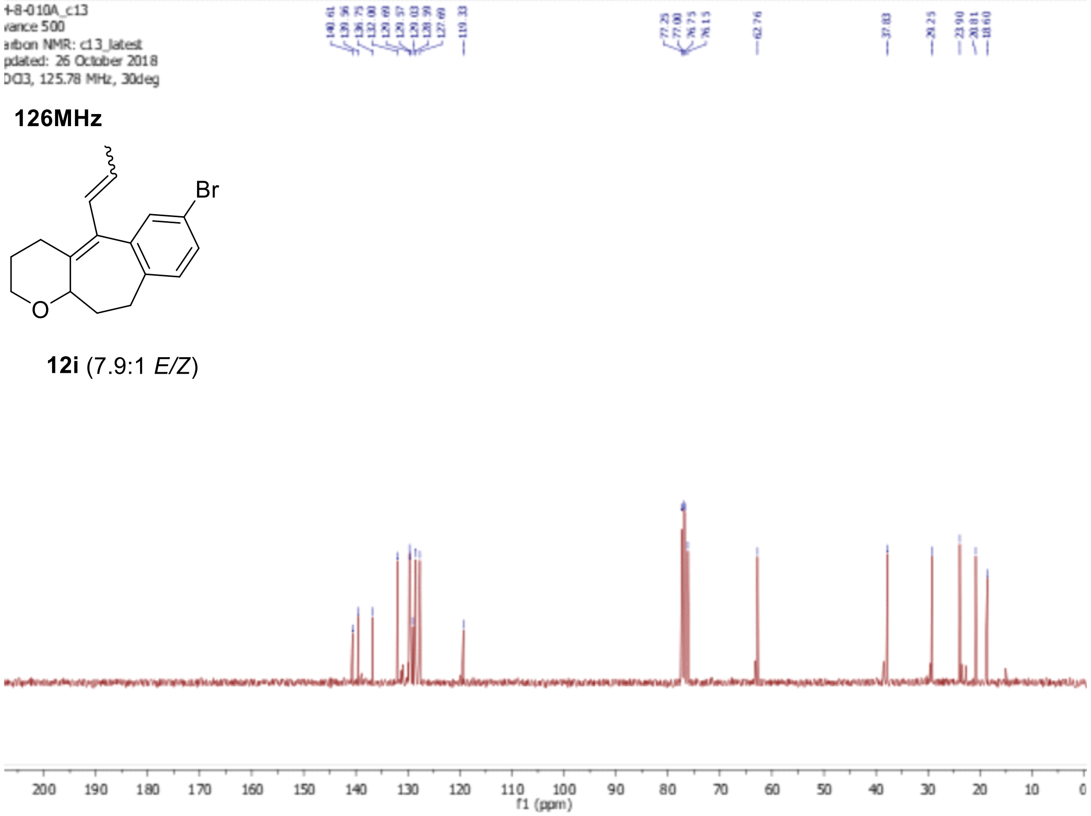


12h (6.3:1 E/Z)



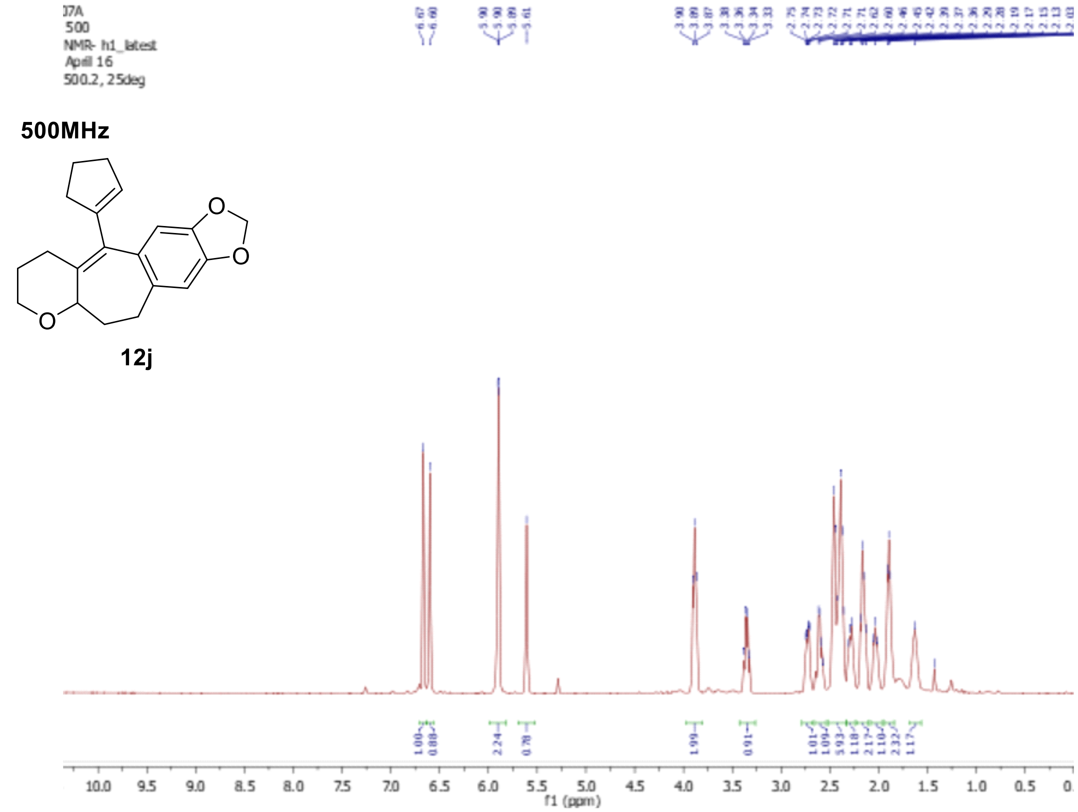
500MHz

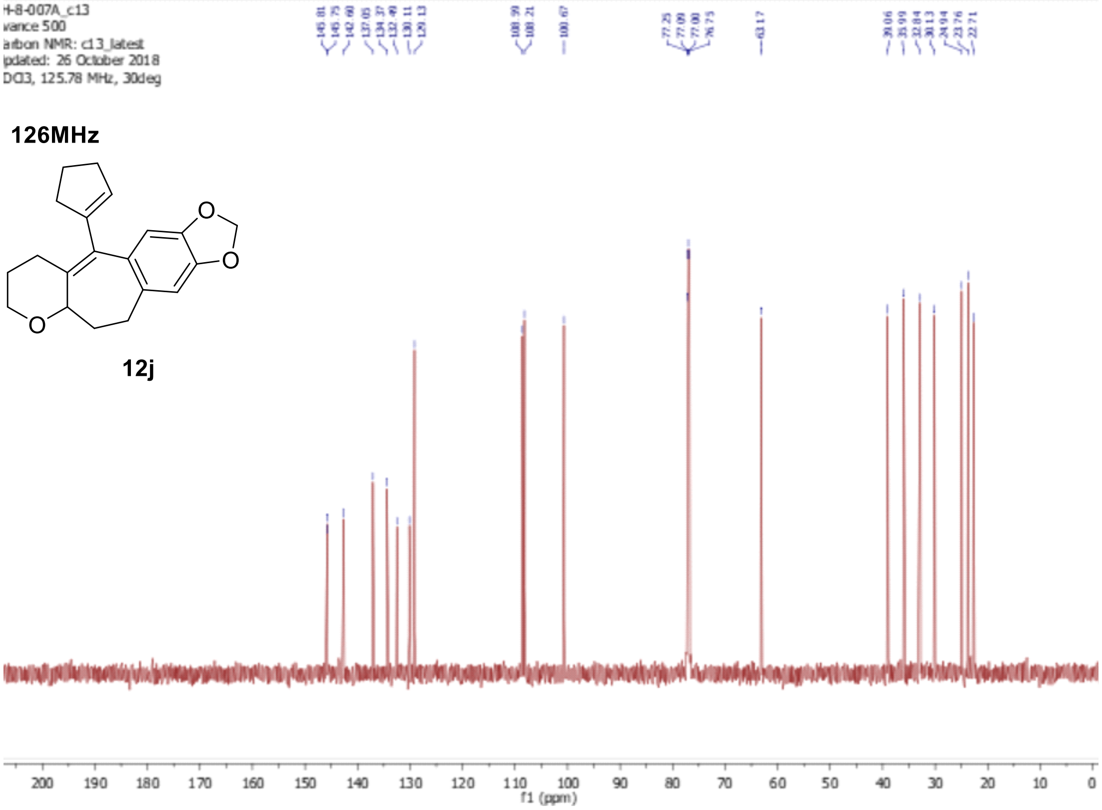
12i (7.9:1 *E/Z*)

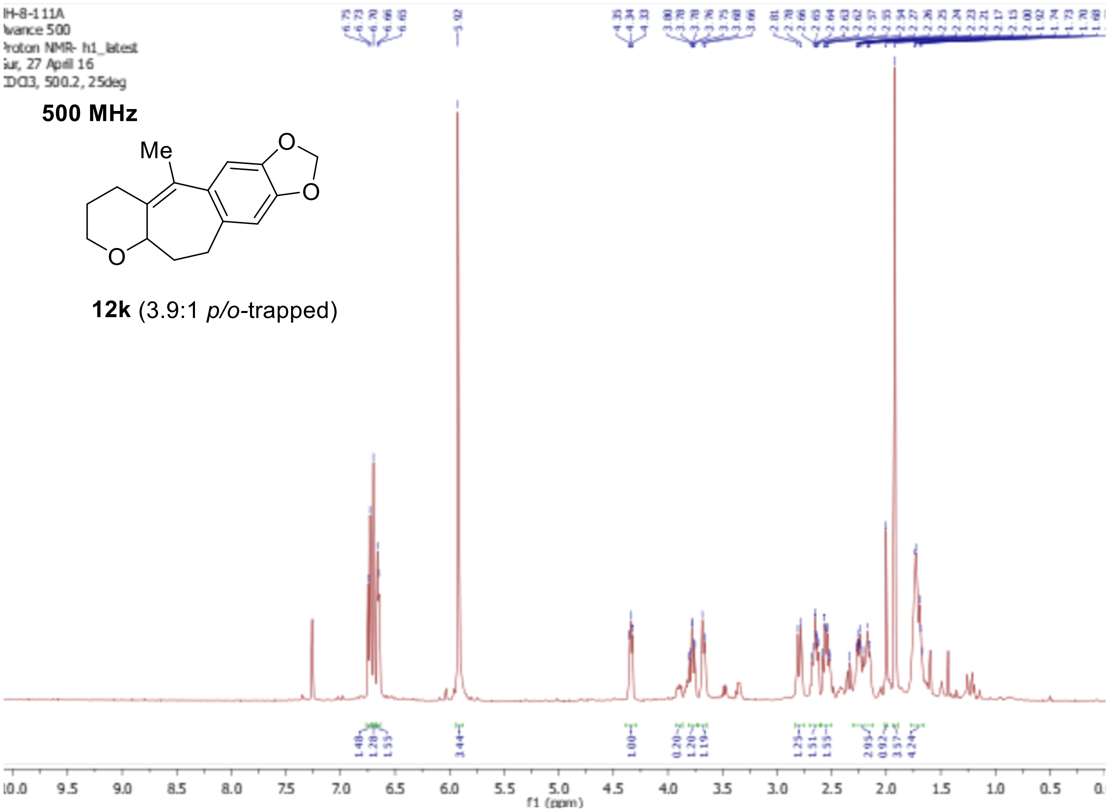


126MHz

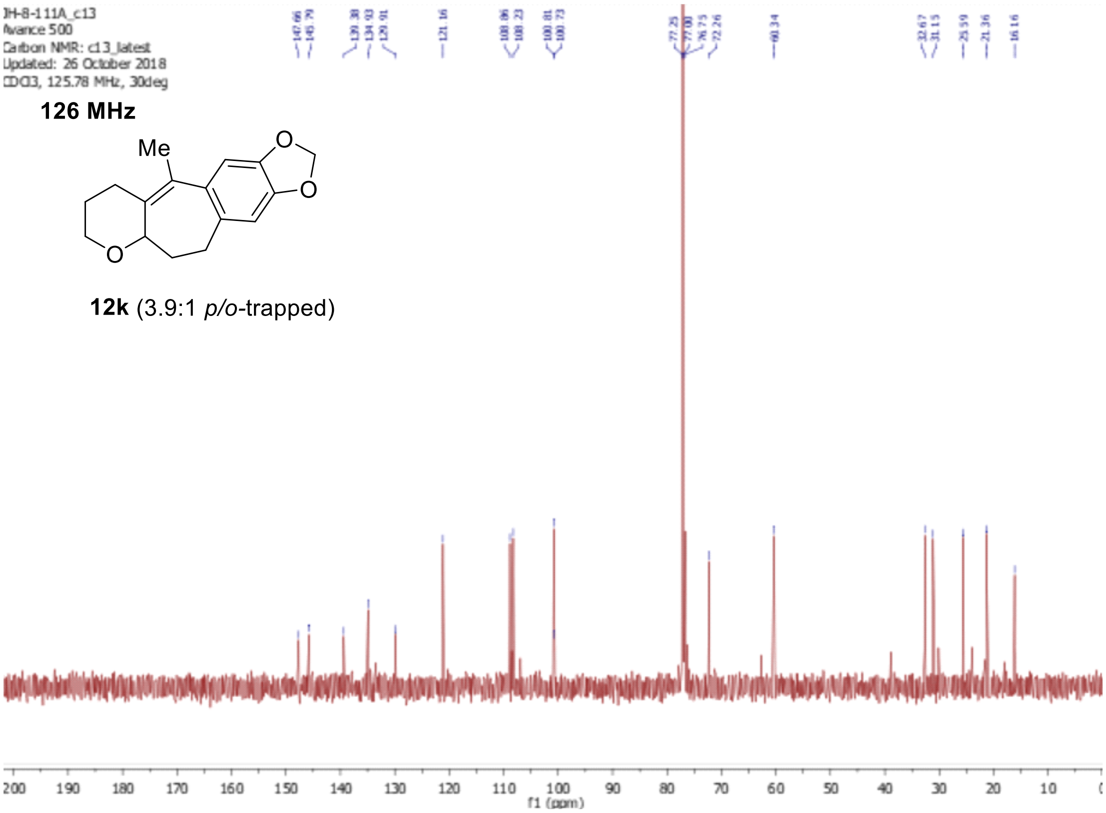
12i (7.9:1 *E/Z*)


07A
500
NMR- h1_latest
April 16
500.2, 25deg
500MHz
12j
6.67
6.60
5.90
5.90
5.89
5.61
3.90
3.89
3.87
3.38
3.36
3.34
3.33
2.75
2.74
2.73
2.72
2.71
2.71
2.62
2.60
2.46
2.45
2.42
2.39
2.37
2.36
2.29
2.28
2.19
2.17
2.15
2.13
2.03
1.00
0.88
2.24
0.78
1.99
0.91
1.01
1.09
5.93
1.18
2.17
1.10
2.32
1.17
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

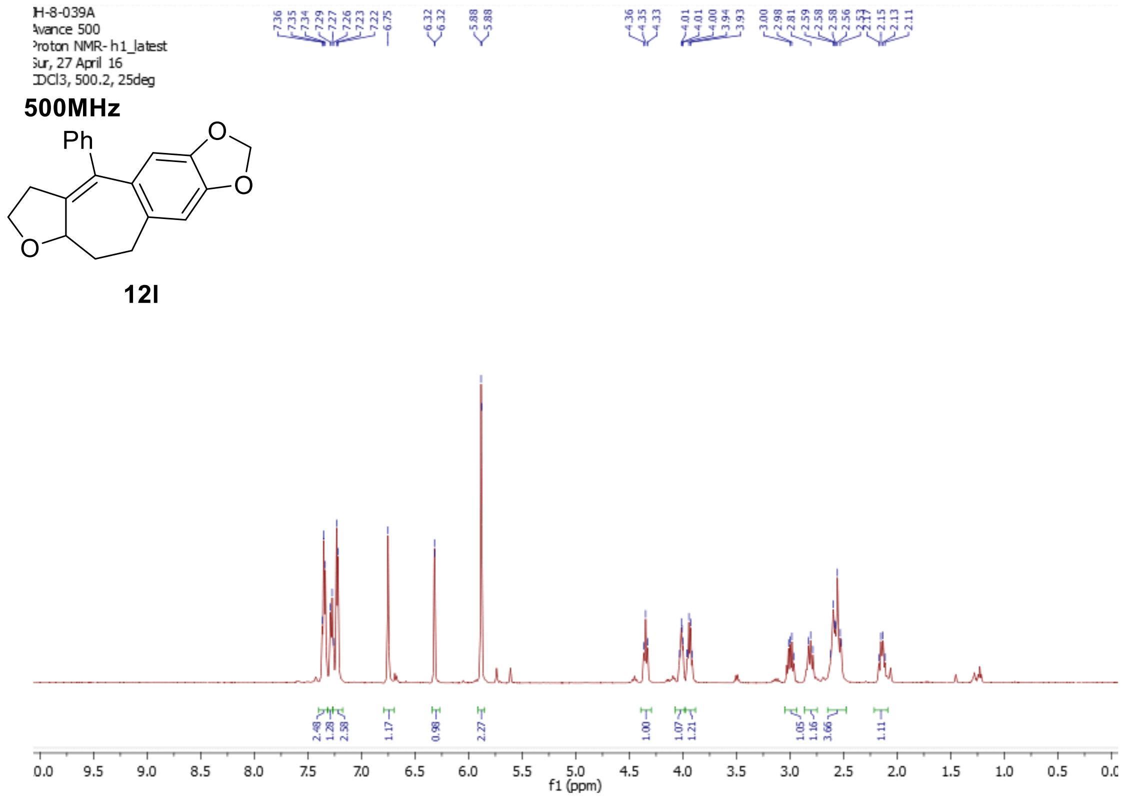

H-8-007A_c13
vance 500
arbon NMR: c13_latest
pdated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126MHz
12j
145.81
145.75
142.60
137.05
134.37
132.49
130.11
129.13
108.39
108.21
100.67
77.25
77.00
77.00
76.75
63.17
39.06
35.99
32.84
30.13
24.94
23.76
22.71
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



12k (3.9:1 *p*/*o*-trapped)

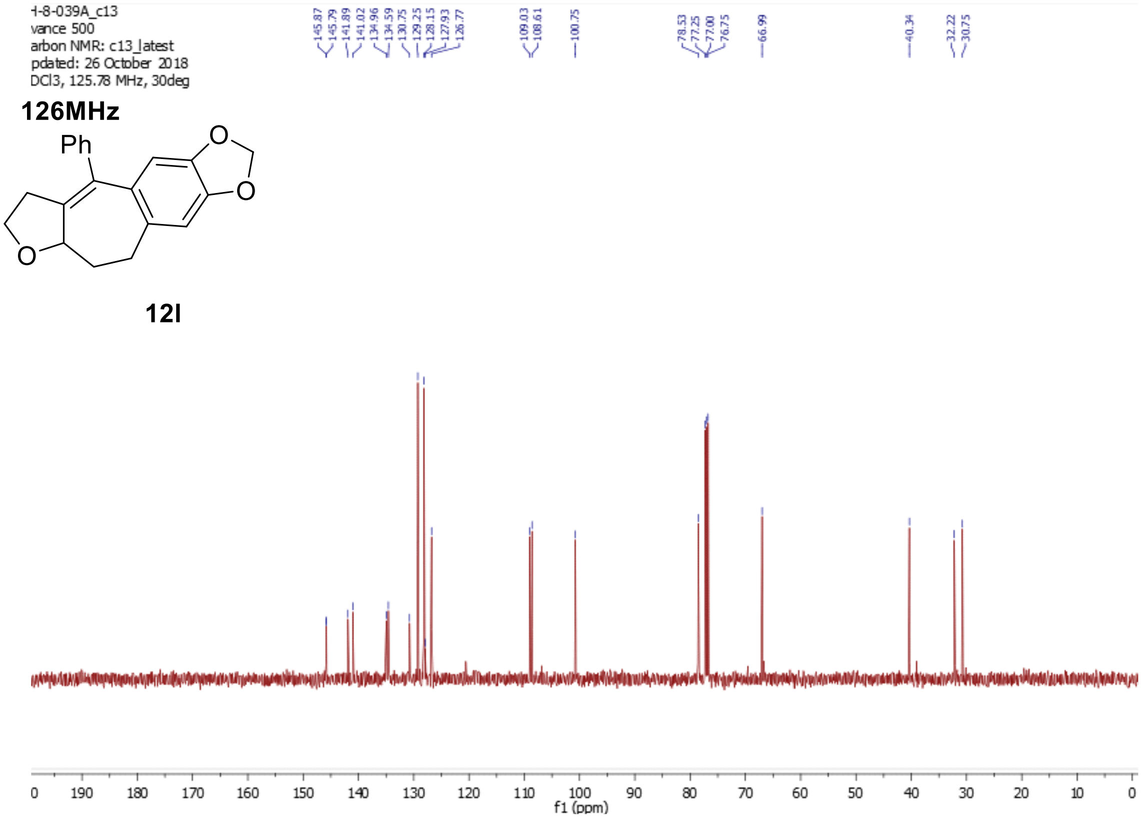


12k (3.9:1 *p*/*o*-trapped)



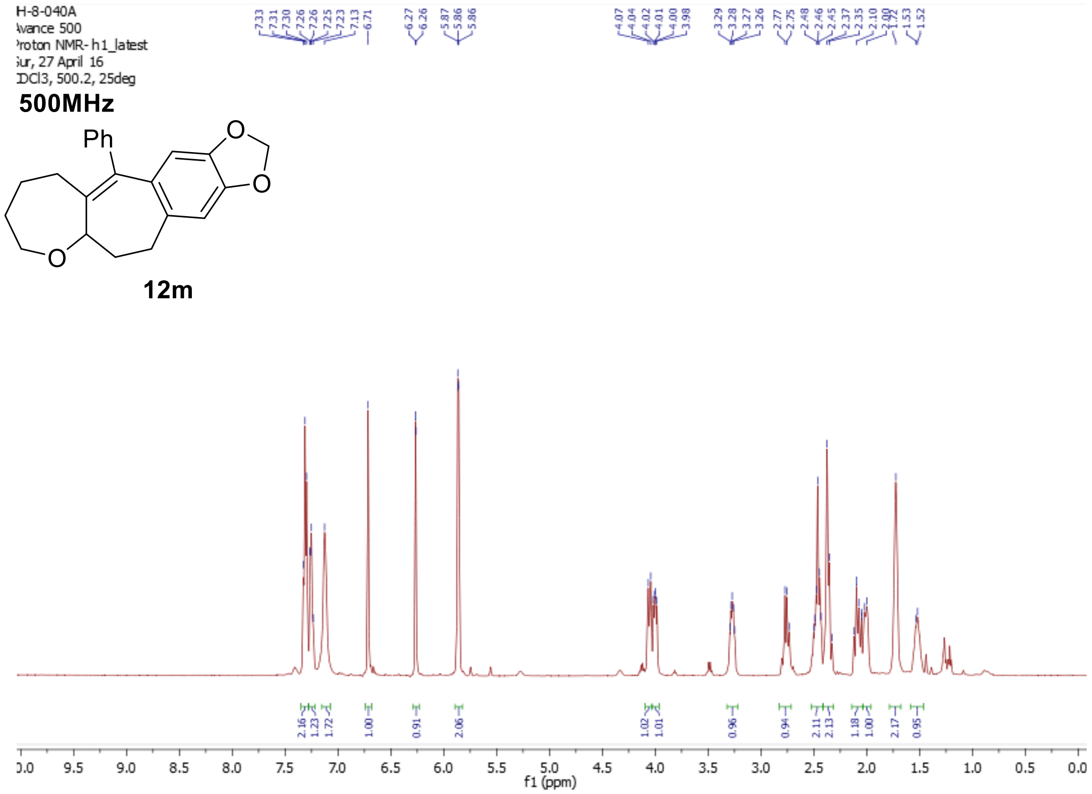
500MHz

12l

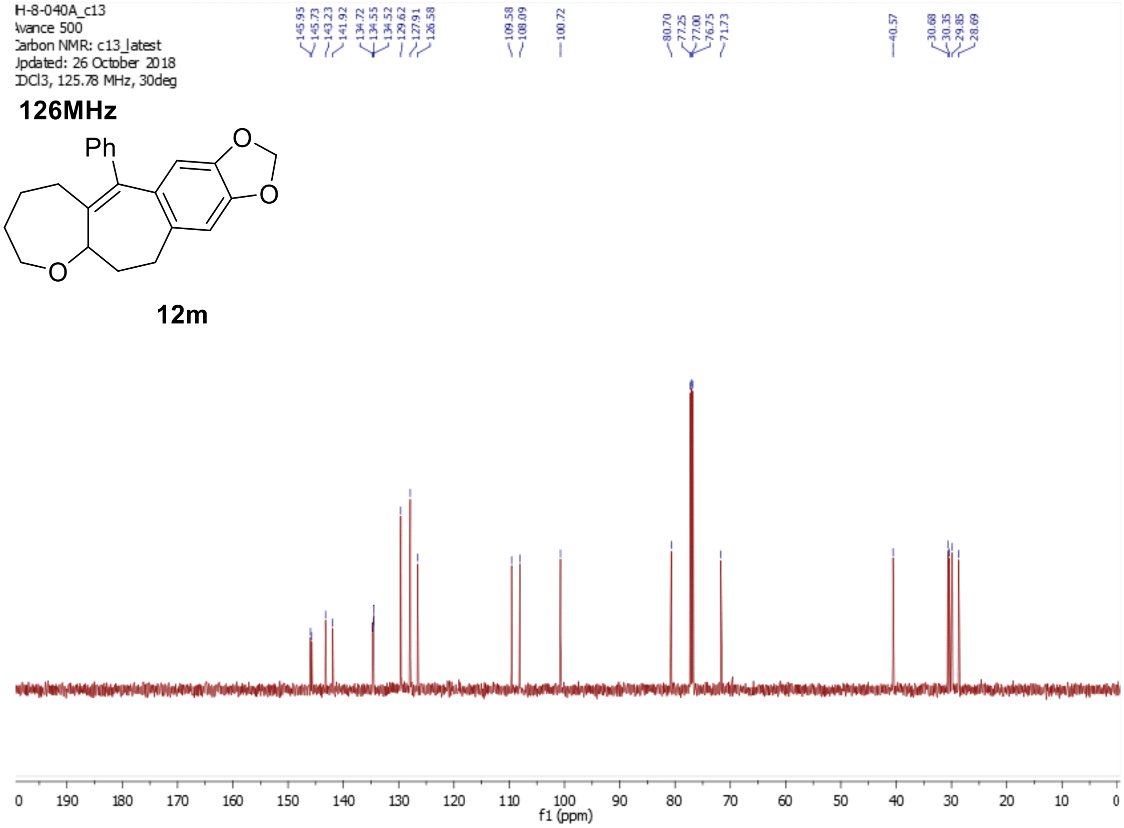


126MHz

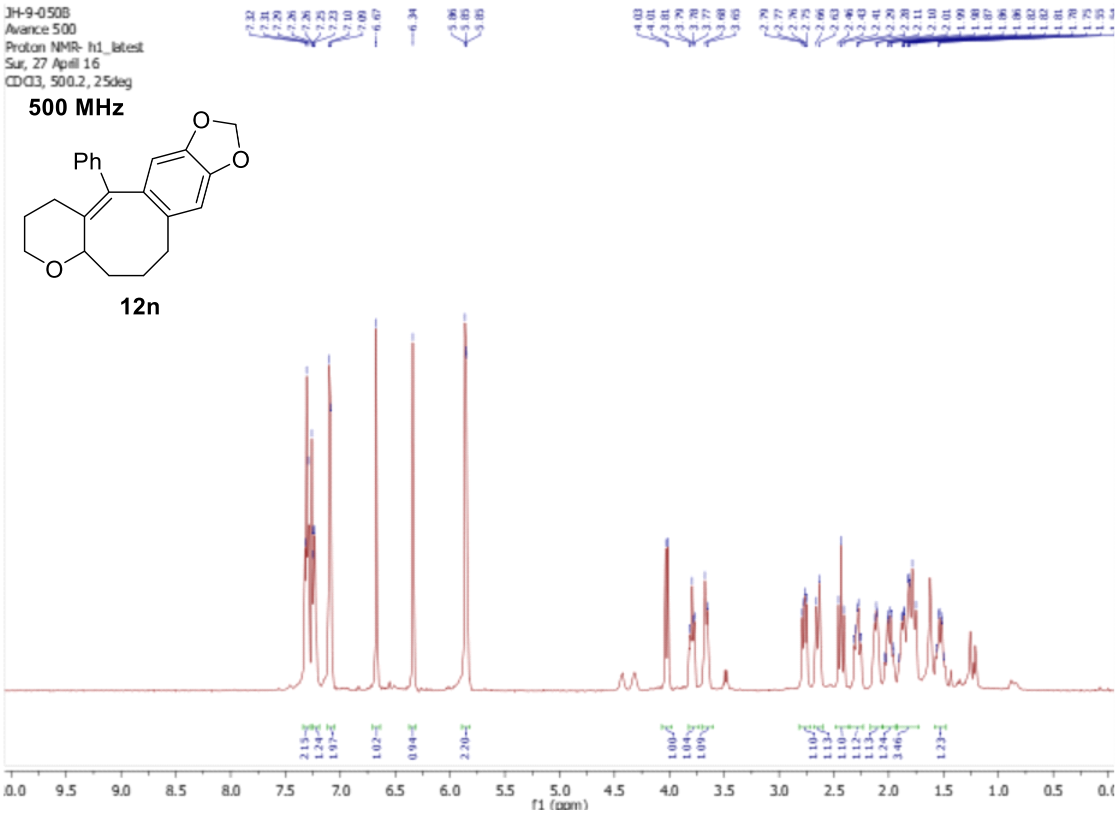
12l

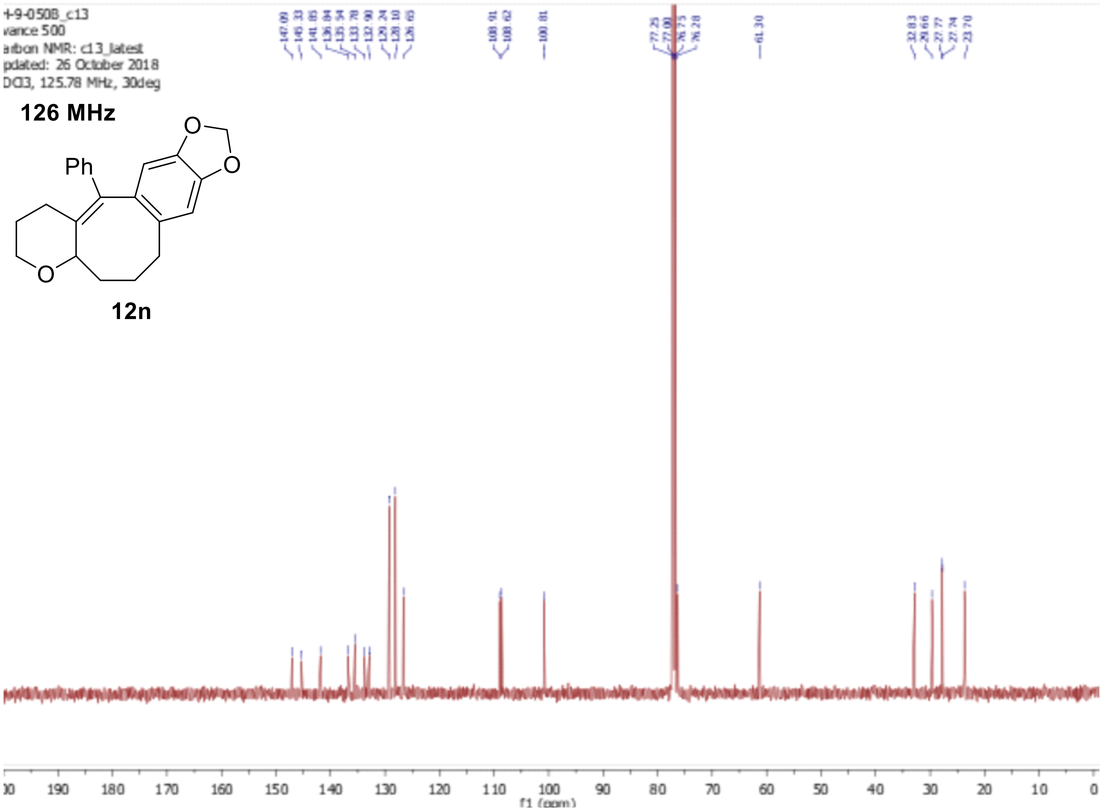

H-8-040A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500MHz
Ph
O
O
O
7.33
7.31
7.30
7.26
7.26
7.25
7.23
7.13
6.71
6.27
6.26
5.87
5.86
5.86
4.07
4.04
4.02
4.01
4.00
3.98
3.29
3.28
3.27
3.26
2.77
2.75
2.48
2.46
2.45
2.37
2.35
2.10
2.00
1.72
1.53
1.52
2.16
1.23
1.72
1.00
0.91
2.06
1.02
1.01
0.96
0.94
2.11
2.13
1.18
1.00
2.17
0.95
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

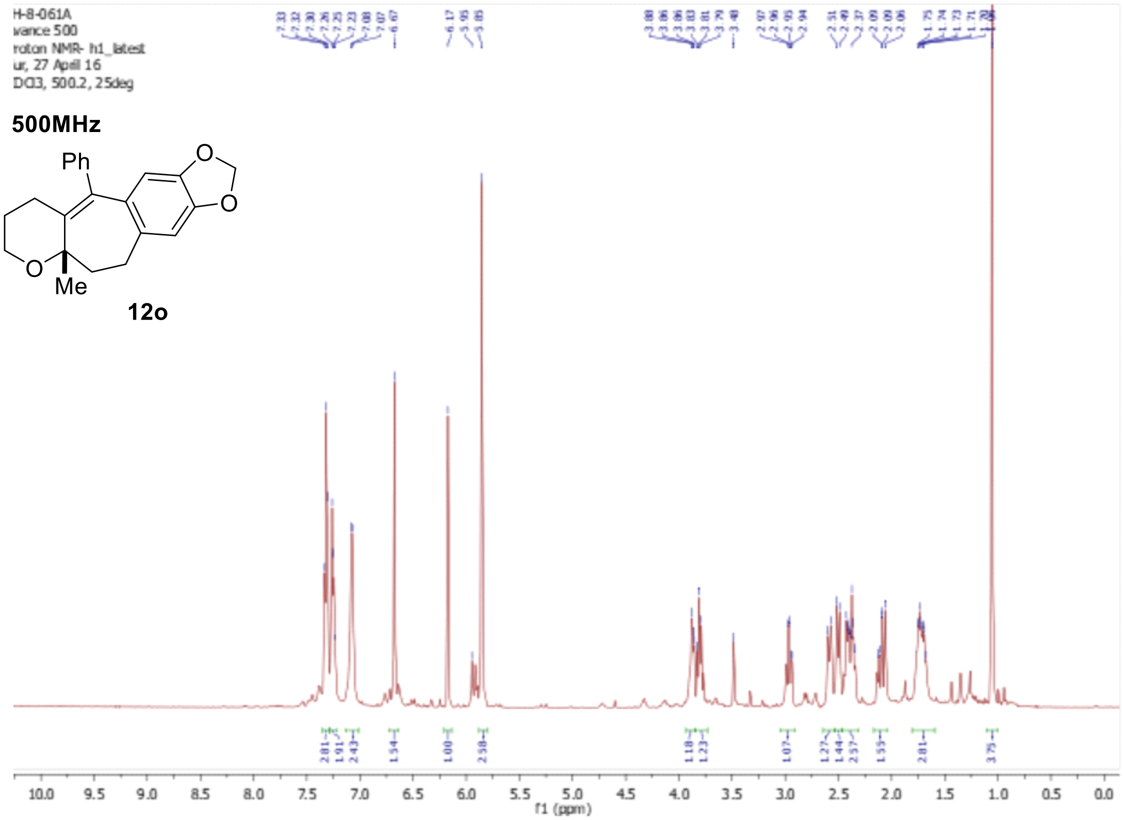
12m

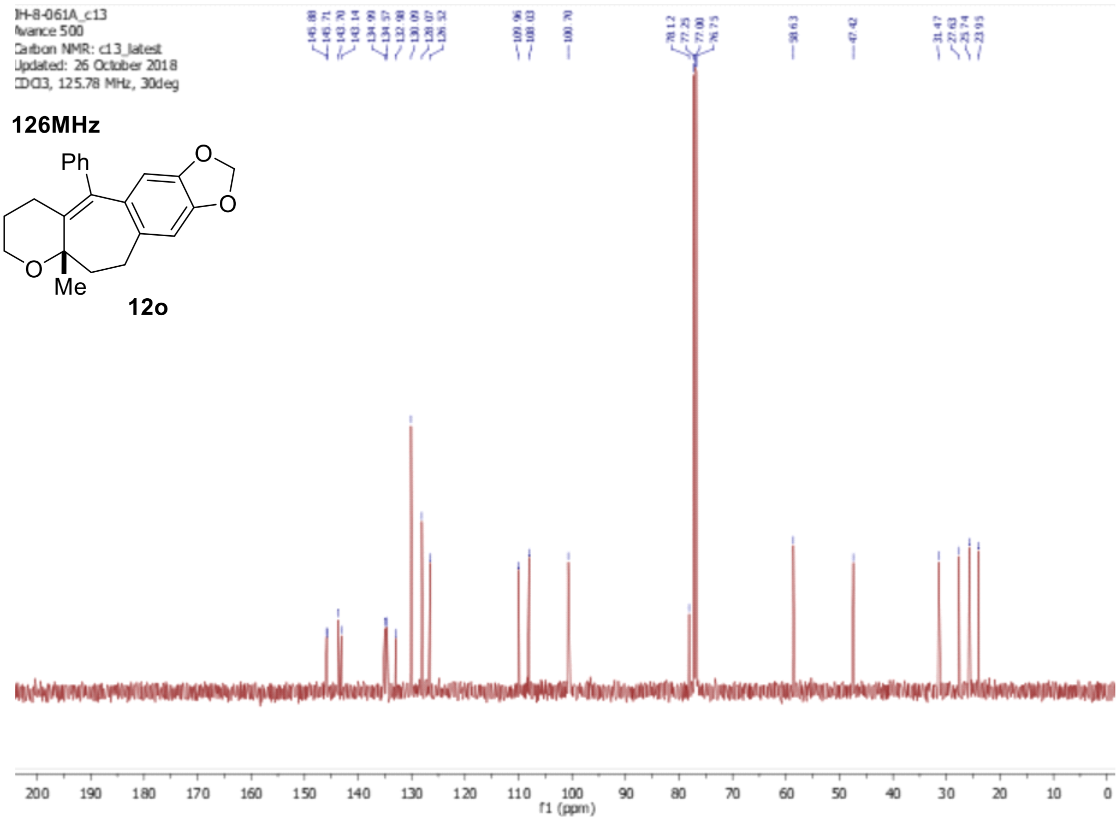

H-8-040A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126MHz
Ph
O
O
O
145.95
145.73
143.23
141.92
134.72
134.55
134.52
129.62
127.91
126.58
109.58
108.09
100.72
80.70
77.25
77.00
76.75
71.73
40.57
30.68
30.35
29.85
28.69
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

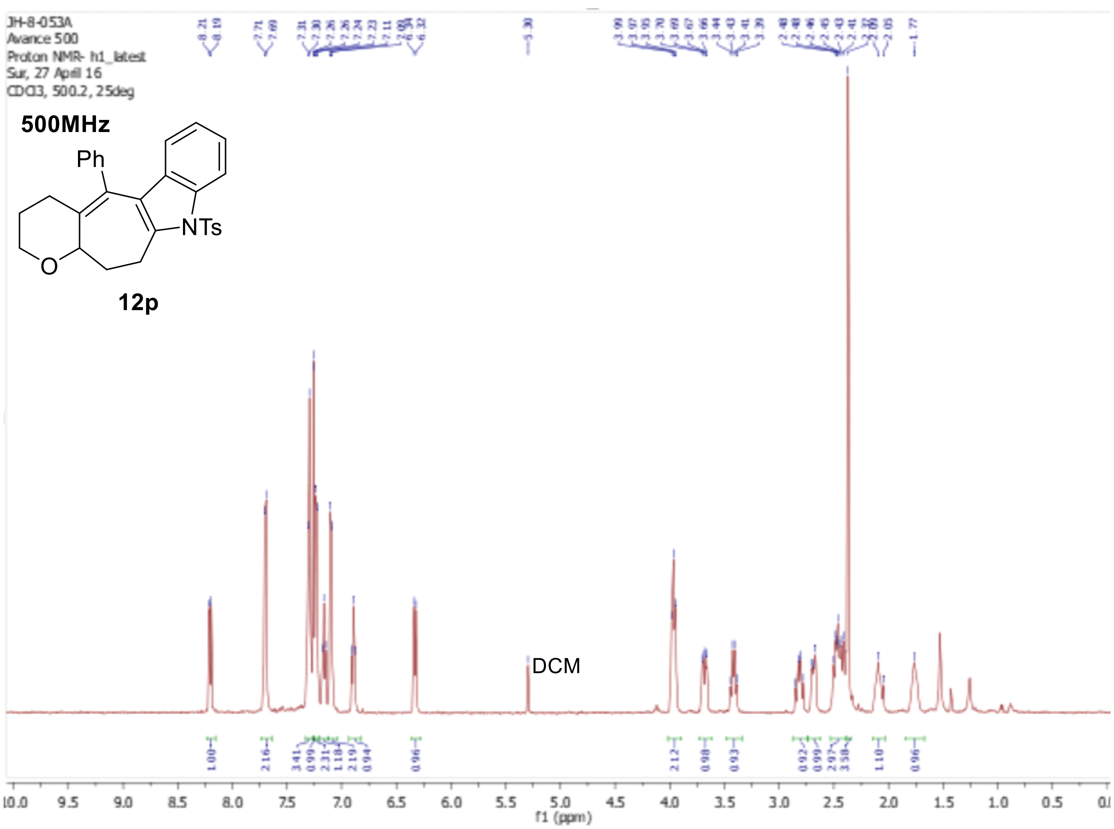
12m

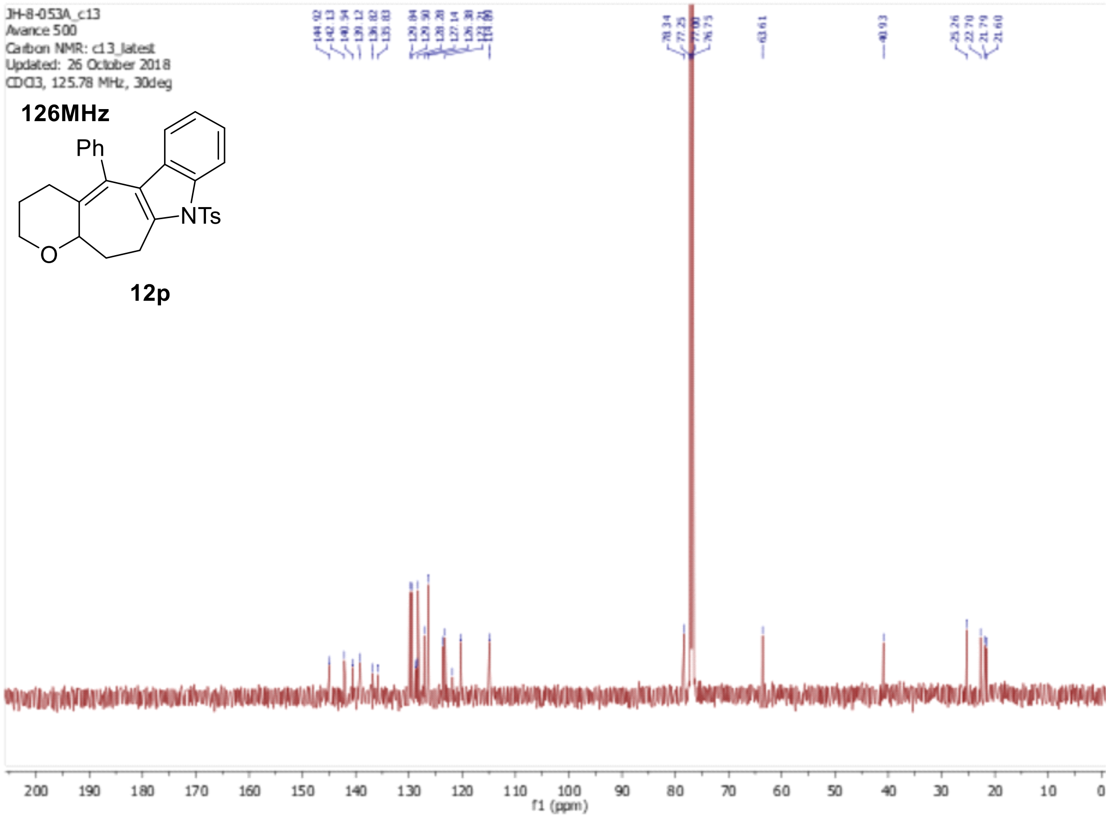

H-9-050B
Avance 500
Proton NMR- h1_latest
Sun, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Ph
O
O
O
12n
7.32
7.31
7.29
7.26
7.26
7.25
7.23
7.10
7.09
6.67
6.34
5.86
5.85
5.85
4.03
4.01
3.81
3.79
3.78
3.77
3.68
3.65
2.15
1.24
1.97
1.02
0.94
2.20
1.00
1.04
1.09
1.10
1.13
1.10
1.12
1.13
1.24
3.46
1.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

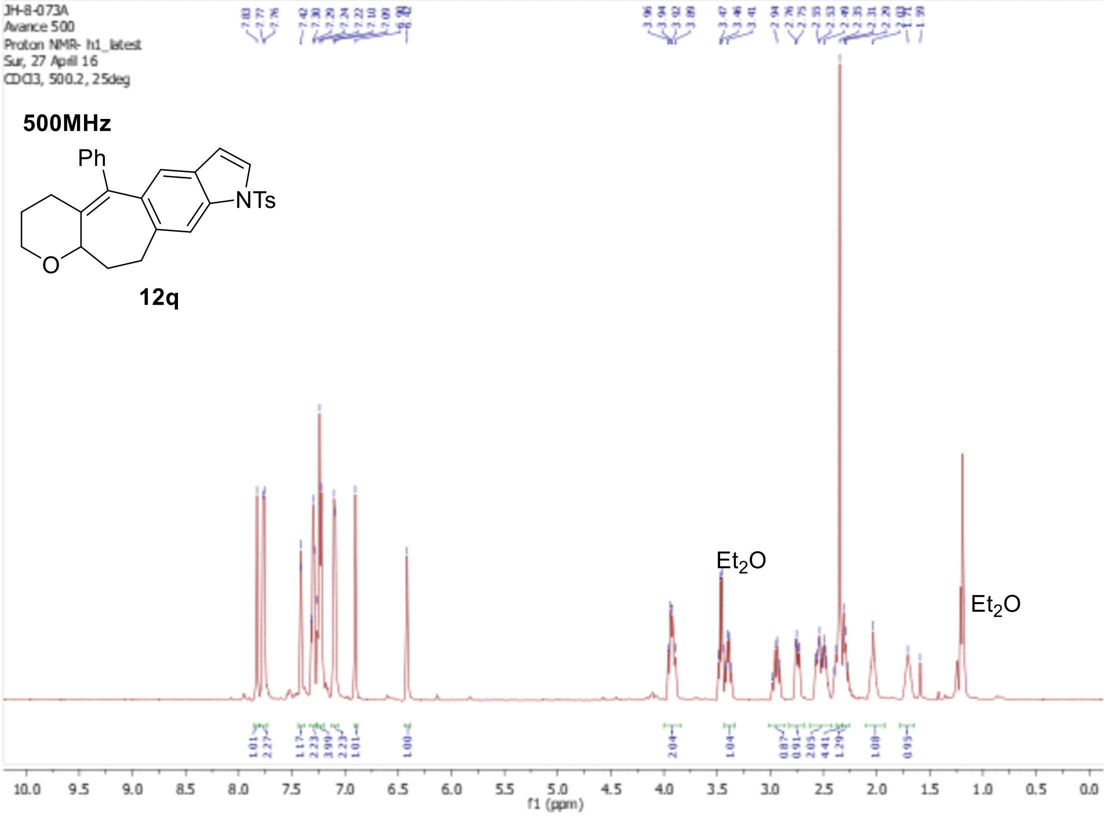

H-9-050B_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Ph
O
O
O
12n
147.09
145.33
141.85
136.84
135.94
133.78
132.90
129.24
128.10
126.65
108.91
108.62
100.81
77.25
77.00
76.75
76.28
61.30
32.83
29.66
27.77
27.74
23.70
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

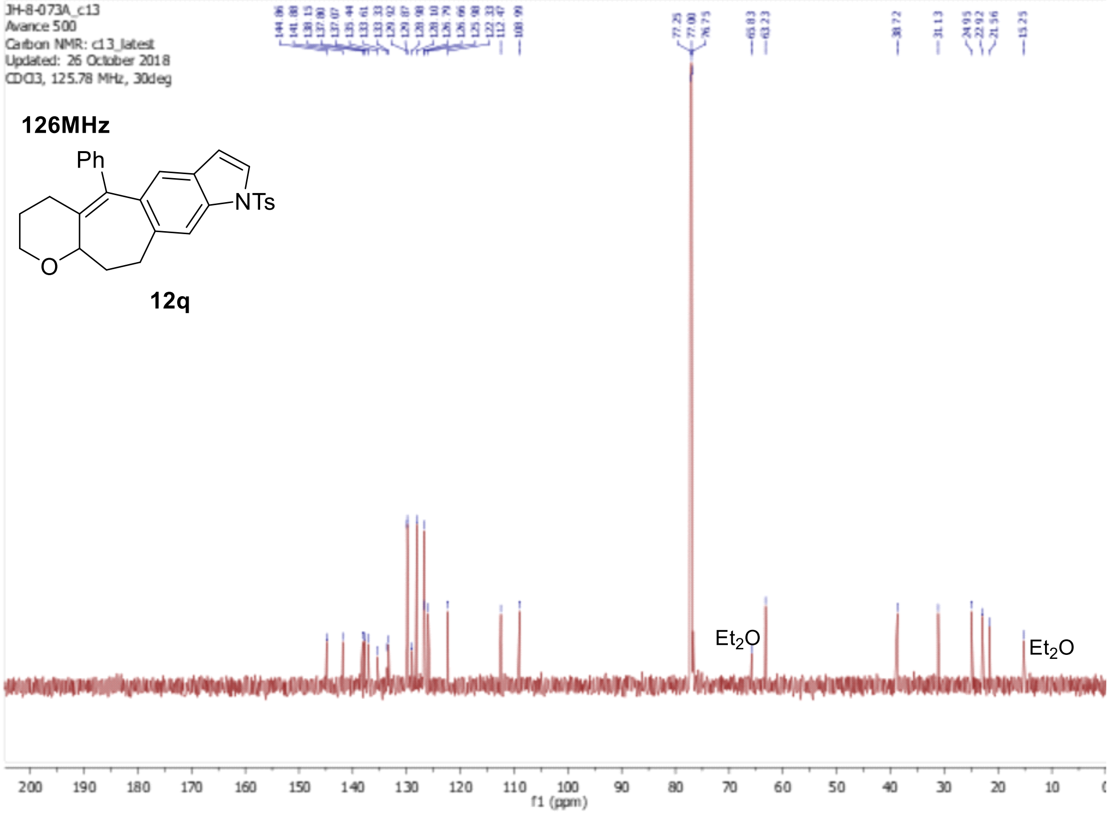

H-8-061A
vance 500
roton NMR- h1_latest
ur, 27 April 16
DCl3, 500.2, 25deg
500MHz
Ph
O
O
O
Me
12o
7.33 7.32 7.30 7.26 7.25 7.23 7.08 7.07 6.67
6.17 5.93 5.85
3.88 3.86 3.86 3.83 3.81 3.79 3.48
2.97 2.96 2.95 2.94
2.51 2.49 2.37 2.09 2.09 2.06
1.75 1.74 1.73 1.71 1.06
2.81 1.91 2.43 1.54 1.00 2.58 1.18 1.23 1.07 1.27 1.44 2.57 1.55 2.81 3.75
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

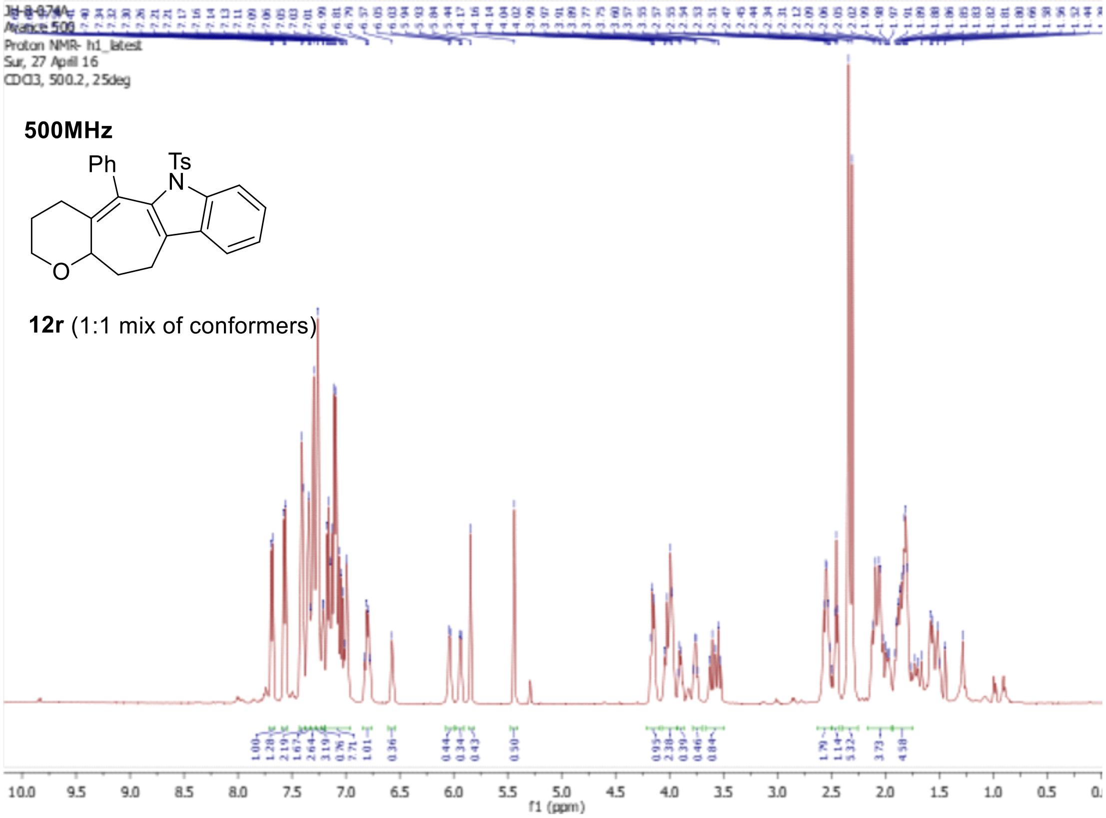

H-8-061A_c13
vance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126MHz
Ph
O
O
O
Me
12o
145.88 145.71 143.70 143.14 134.99 134.57 132.98 130.09 128.07 126.52
109.96 108.03 100.70
78.12 77.25 77.00 76.75
58.63
47.42
31.47 27.63 25.74 23.95
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


JH-8-053A
Avance 500
Proton NMR- h1_latest
Sun, 27 April 16
CDCl3, 500.2, 25deg
500MHz
Ph
NTs
O
12p
DCM
8.21
8.19
7.71
7.69
7.31
7.30
6.34
6.32
5.30
3.99
3.97
3.44
3.43
3.41
3.39
2.05
1.77
1.00
2.16
3.41
0.99
2.31
1.18
2.19
0.94
0.96
2.12
0.98
0.93
0.92
0.99
2.97
3.58
1.10
0.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

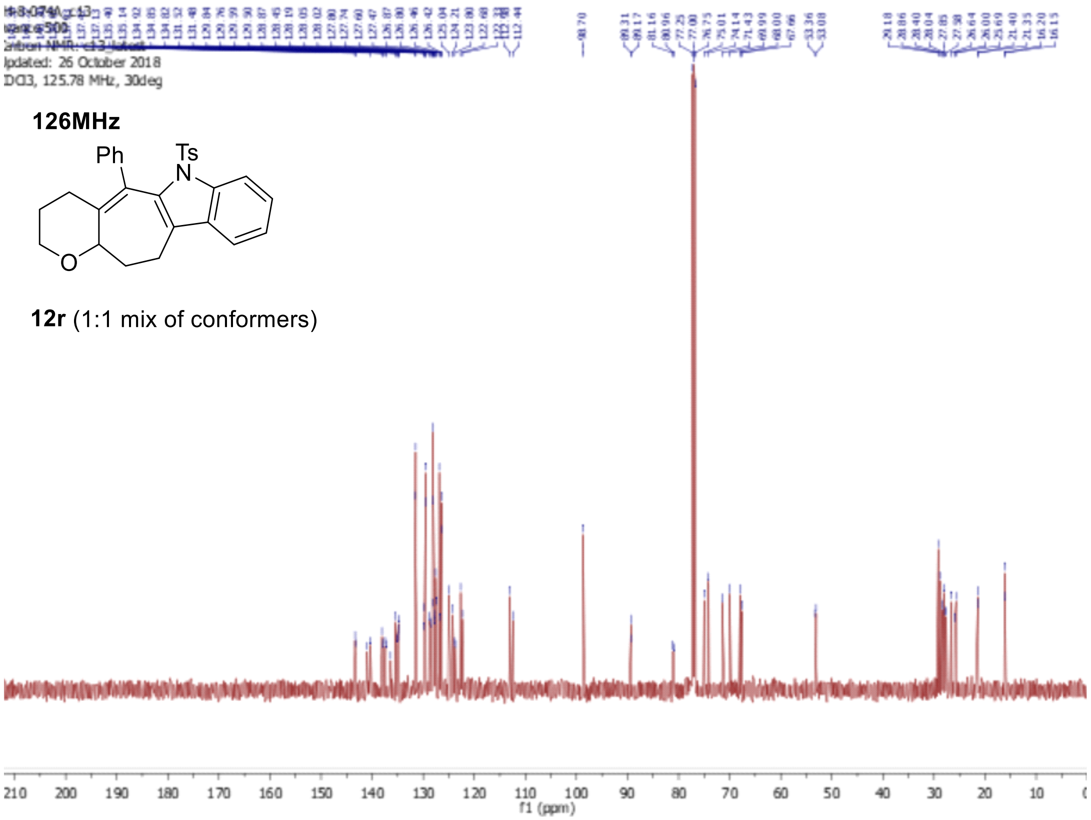

JH-8-053A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126MHz
Ph
NTs
O
12p
144.92
142.13
140.94
139.12
136.82
135.83
129.84
129.90
128.28
127.14
126.38
78.34
77.25
77.00
76.75
63.61
40.93
25.26
22.70
21.79
21.60
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


JH-8-073A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500MHz
Ph
NTs
O
12q
Et2O
Et2O
7.83
7.77
7.76
7.42
7.30
7.29
7.24
7.22
7.10
7.09
3.96
3.94
3.92
3.89
3.47
3.46
3.41
2.94
2.78
2.75
1.01
2.27
1.17
2.23
3.99
2.23
1.01
1.00
2.04
1.04
0.87
0.91
2.05
4.41
1.29
1.08
0.95
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

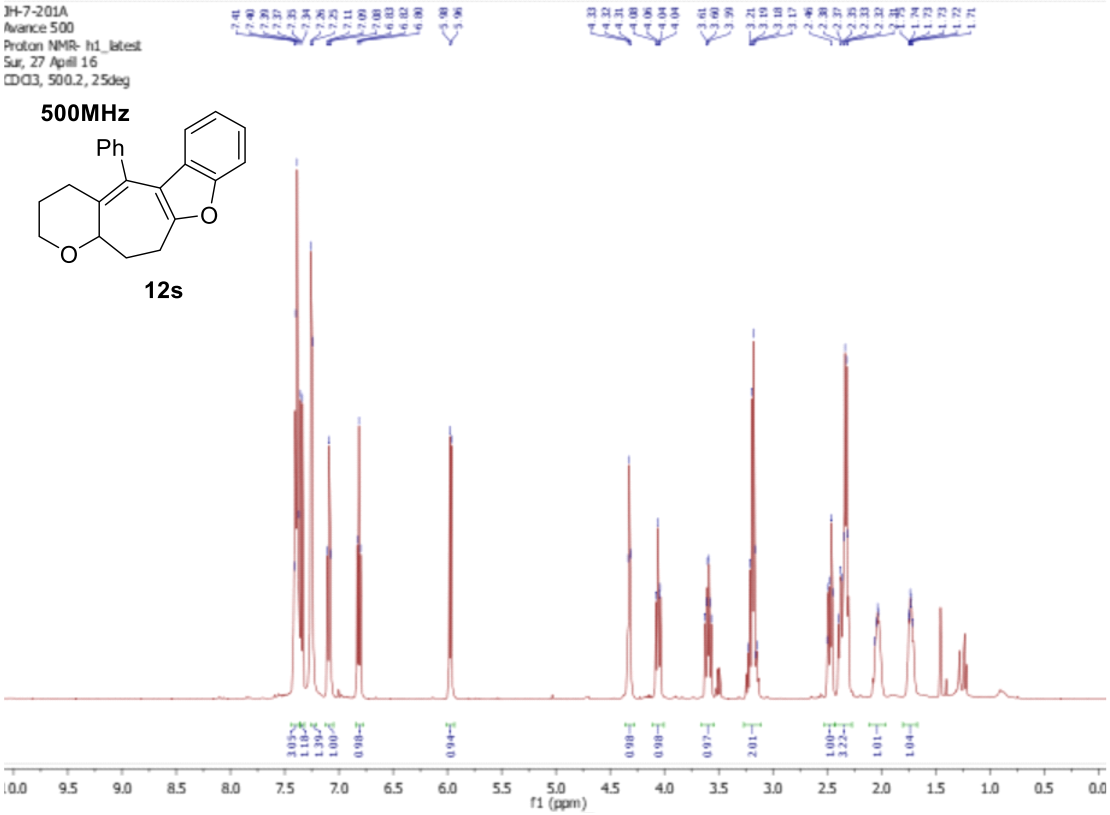

JH-8-073A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126MHz
Ph
NTs
O
12q
Et2O
Et2O
144.06
141.88
138.13
137.80
137.07
135.44
133.61
133.33
129.92
129.87
128.98
128.10
126.79
126.66
125.98
122.33
112.47
108.99
77.25
77.00
76.75
65.83
63.23
38.72
31.13
24.95
22.92
21.56
15.25
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

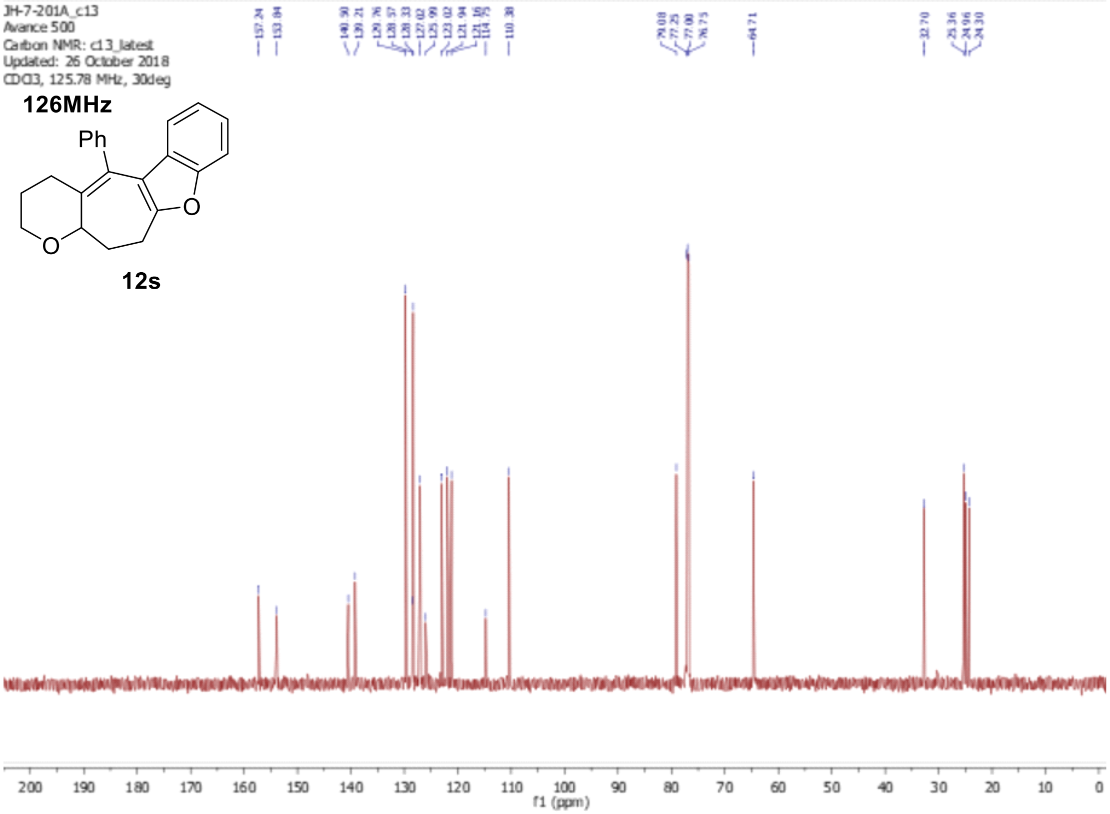


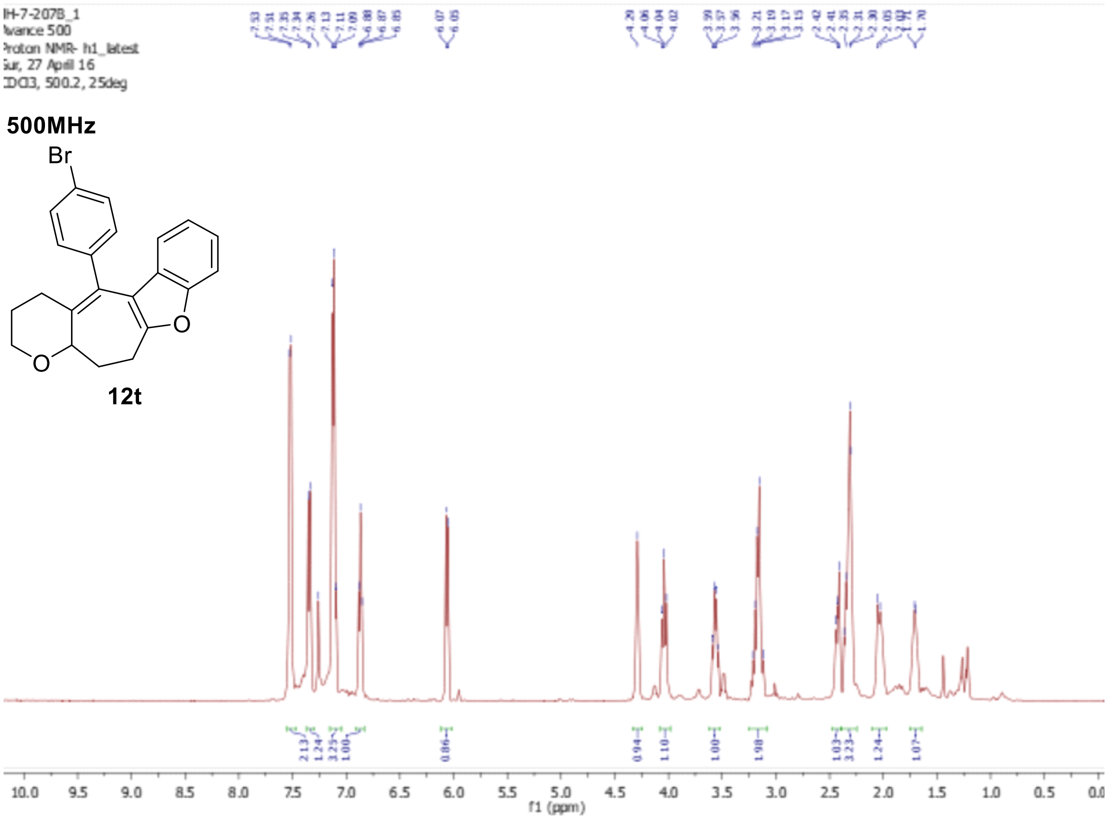
12r (1:1 mix of conformers)



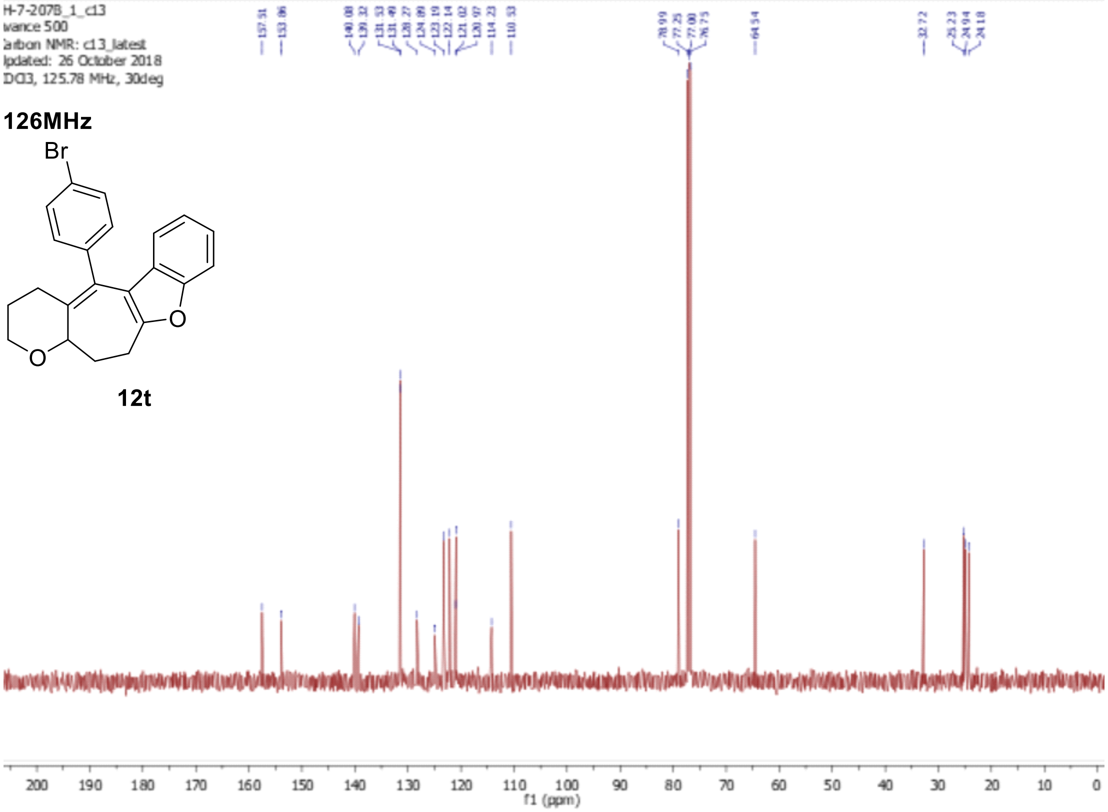
12r (1:1 mix of conformers)


JH-7-201A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500MHz
Ph
O
O
12s
7.41
7.40
7.39
7.37
7.35
7.34
7.26
7.25
7.11
7.09
7.08
6.83
6.82
6.80
5.98
5.96
4.33
4.32
4.31
4.08
4.06
4.04
4.04
3.61
3.60
3.59
3.21
3.19
3.18
3.17
2.46
2.38
2.37
2.33
2.33
2.32
2.31
1.75
1.74
1.73
1.73
1.72
1.71
3.05
1.18
1.39
1.00
0.98
0.94
0.98
0.98
0.97
2.01
1.00
3.22
1.01
1.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

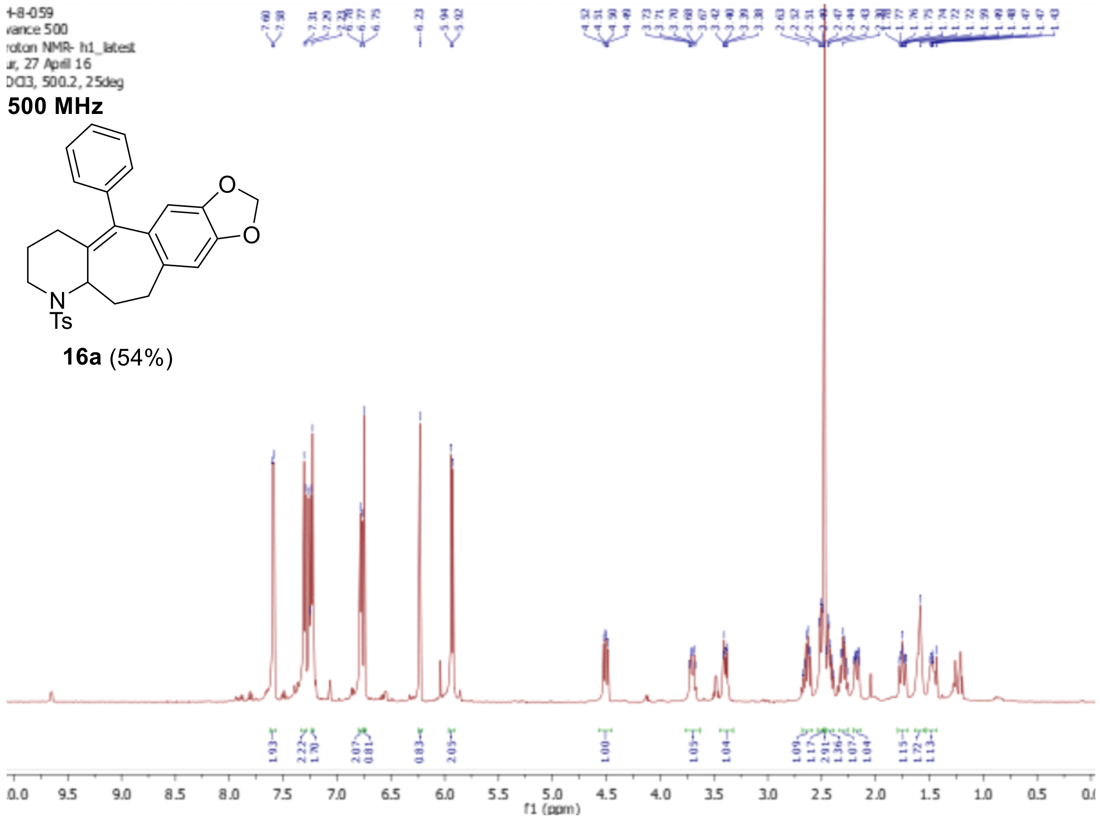

JH-7-201A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126MHz
Ph
O
O
12s
157.24
153.84
140.50
139.21
129.76
128.57
128.33
127.02
125.99
123.02
121.94
121.10
114.75
110.38
79.08
77.25
77.00
76.75
64.71
32.70
25.36
24.96
24.30
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



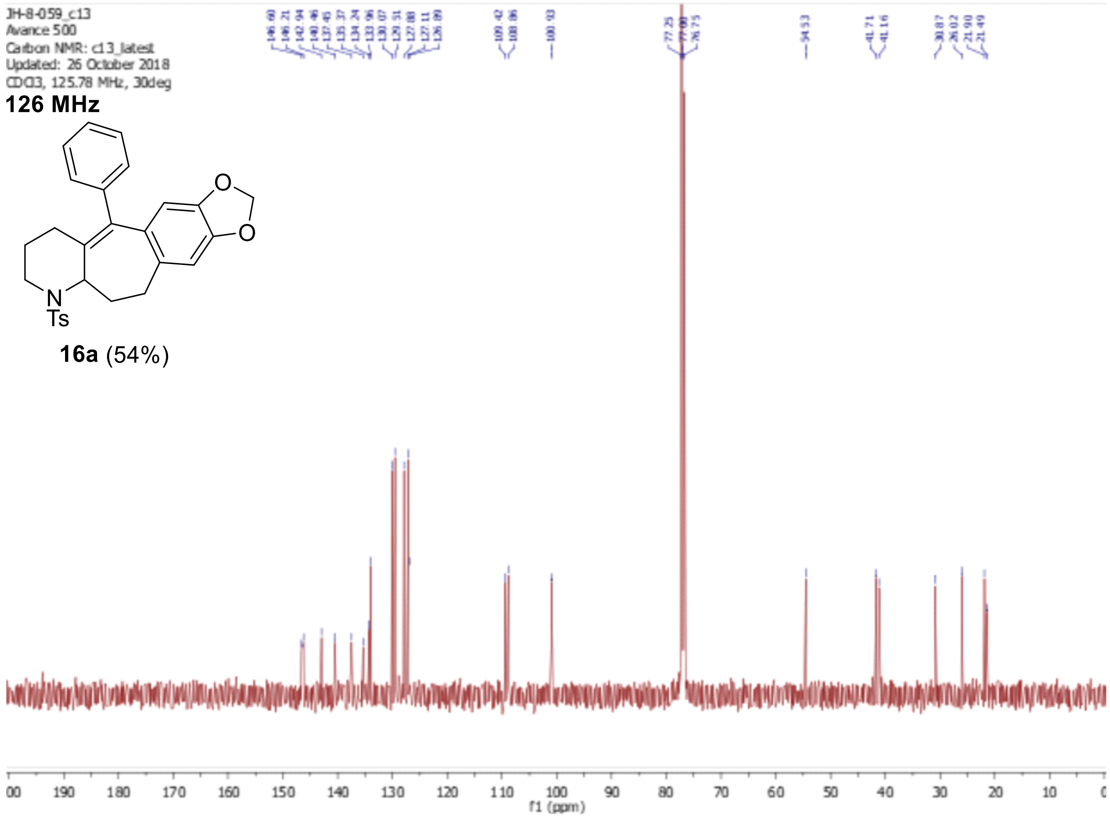
IH-7-207B_1
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500MHz
Br
O
O
12t
7.53
7.51
7.35
7.34
7.26
7.13
7.11
7.09
6.88
6.87
6.85
6.07
6.05
4.29
4.06
4.04
4.02
3.59
3.57
3.56
3.21
3.19
3.17
3.15
2.42
2.41
2.35
2.31
2.30
2.05
2.03
1.71
1.70
2.13
1.24
3.25
1.00
0.86
0.94
1.10
1.00
1.98
1.03
3.23
1.24
1.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



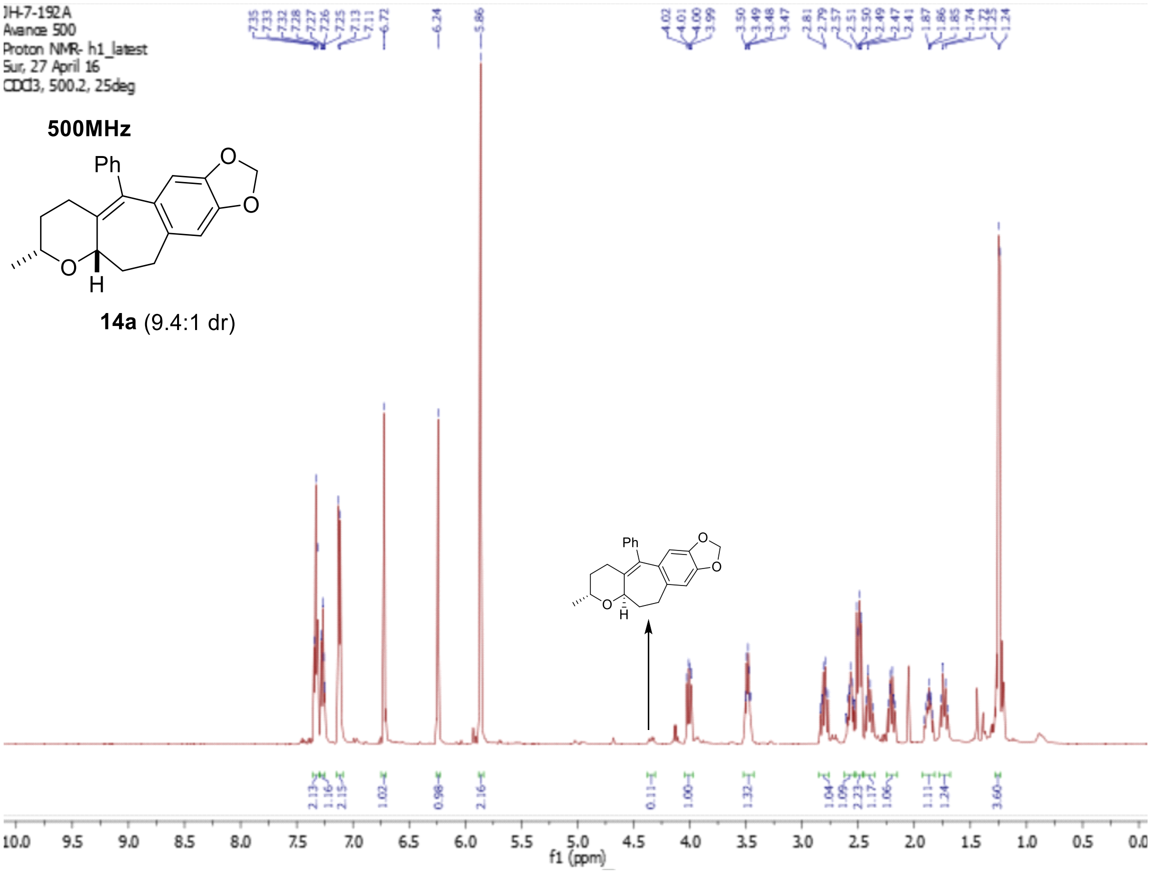
IH-7-207B_1_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126MHz
Br
O
O
12t
157.51
153.86
140.08
139.32
131.53
131.49
128.27
124.89
123.19
122.14
121.02
120.97
114.23
110.53
78.99
77.25
77.00
76.75
64.54
32.72
25.23
24.94
24.18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H-8-059
vance 500
roton NMR- h1_latest
ur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
O
O
N
Ts
7.60
7.58
7.31
7.29
6.78
6.77
6.75
6.23
5.94
5.92
4.52
4.51
4.50
4.49
3.73
3.71
3.70
3.68
3.67
3.42
3.40
3.39
3.38
2.63
2.52
2.51
2.47
2.44
2.43
1.77
1.76
1.75
1.74
1.72
1.49
1.48
1.47
1.43
1.93
2.22
1.70
2.07
0.81
0.83
2.05
1.00
1.05
1.04
1.09
1.17
2.91
1.36
1.07
1.04
1.15
1.72
1.13
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

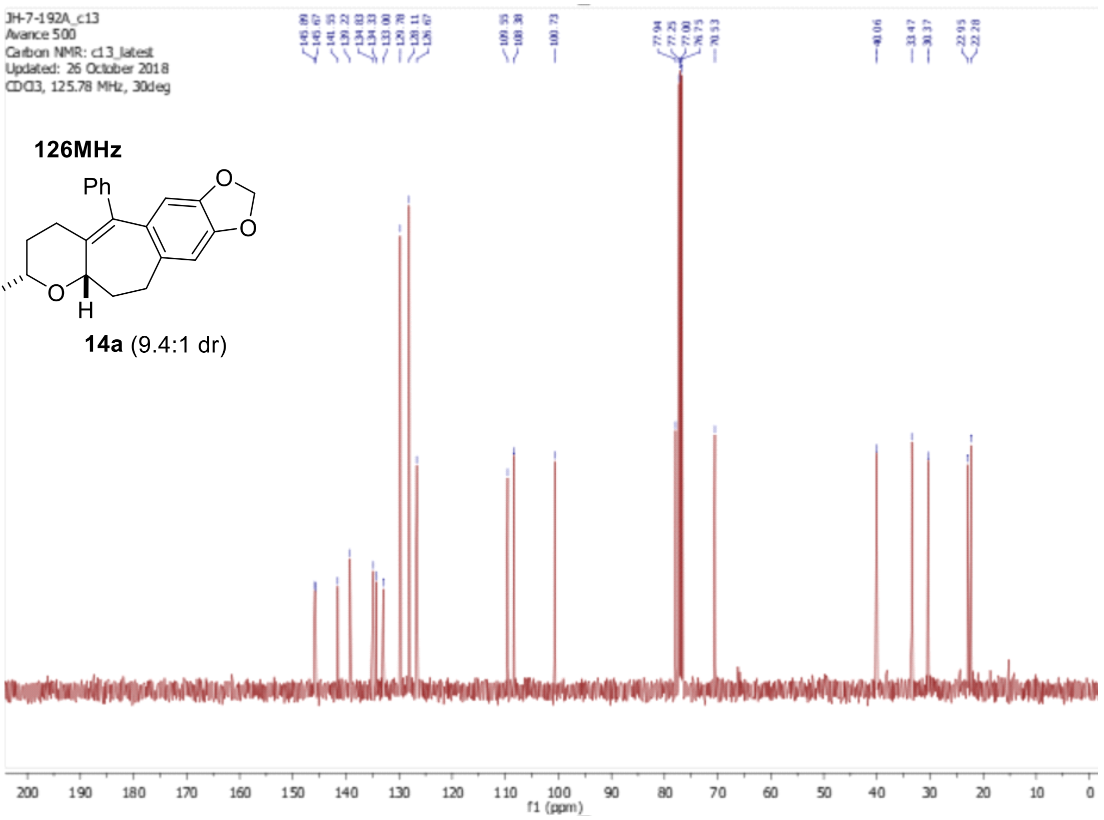
16a (54%)


JH-8-059_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
O
O
N
Ts
146.60
146.21
142.94
140.46
137.45
135.37
134.24
133.96
130.07
129.51
127.88
127.11
126.89
109.42
108.86
100.93
77.25
77.00
76.75
54.53
41.71
41.16
30.87
26.02
21.90
21.49
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

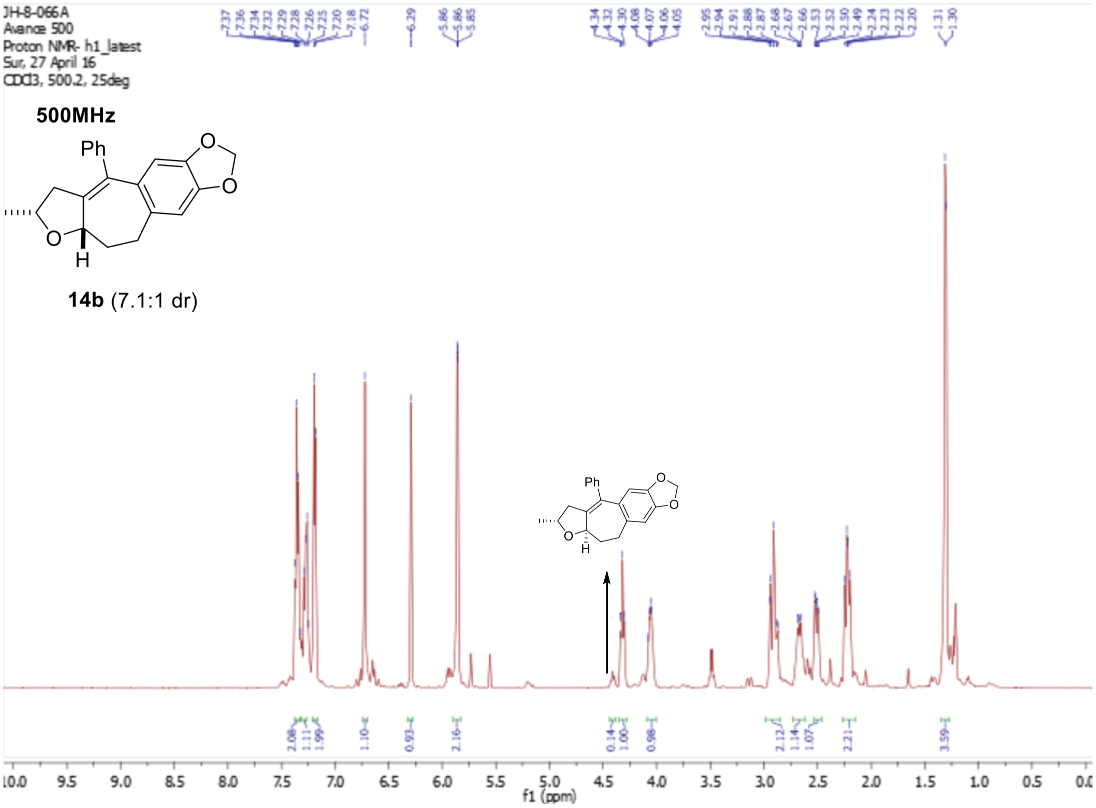
16a (54%)



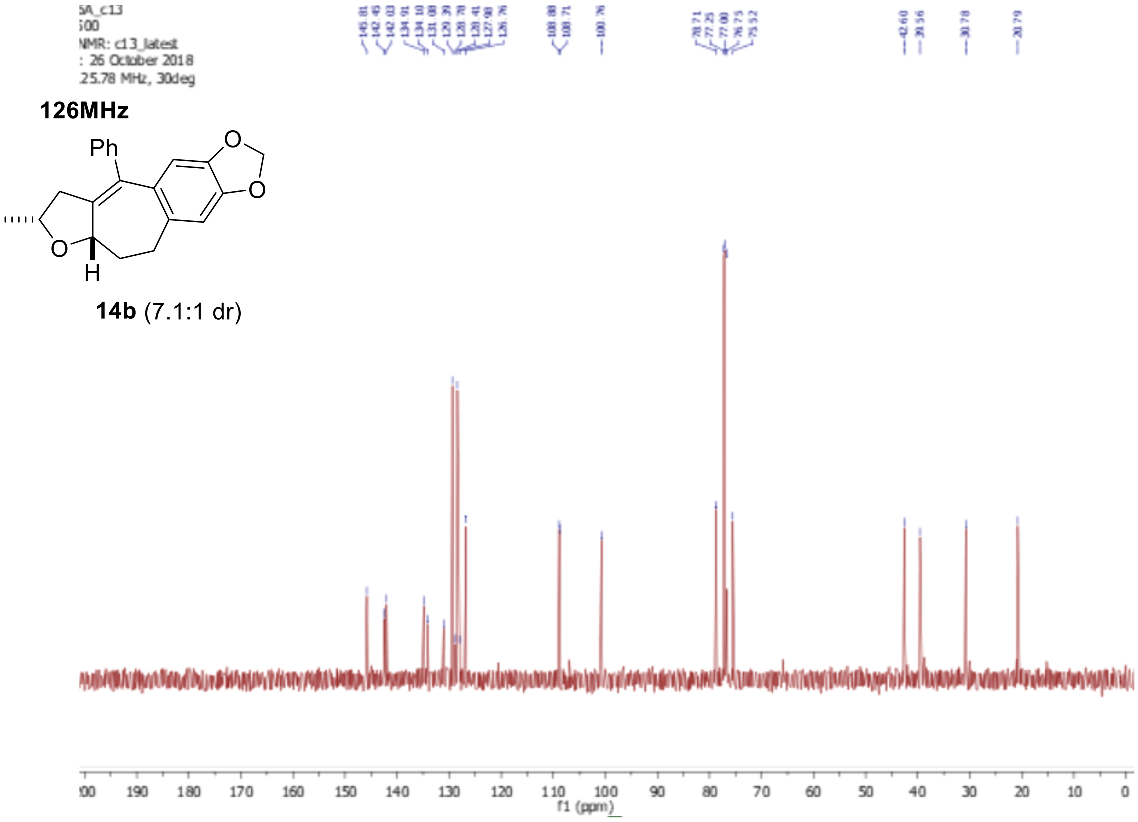
14a (9.4:1 dr)



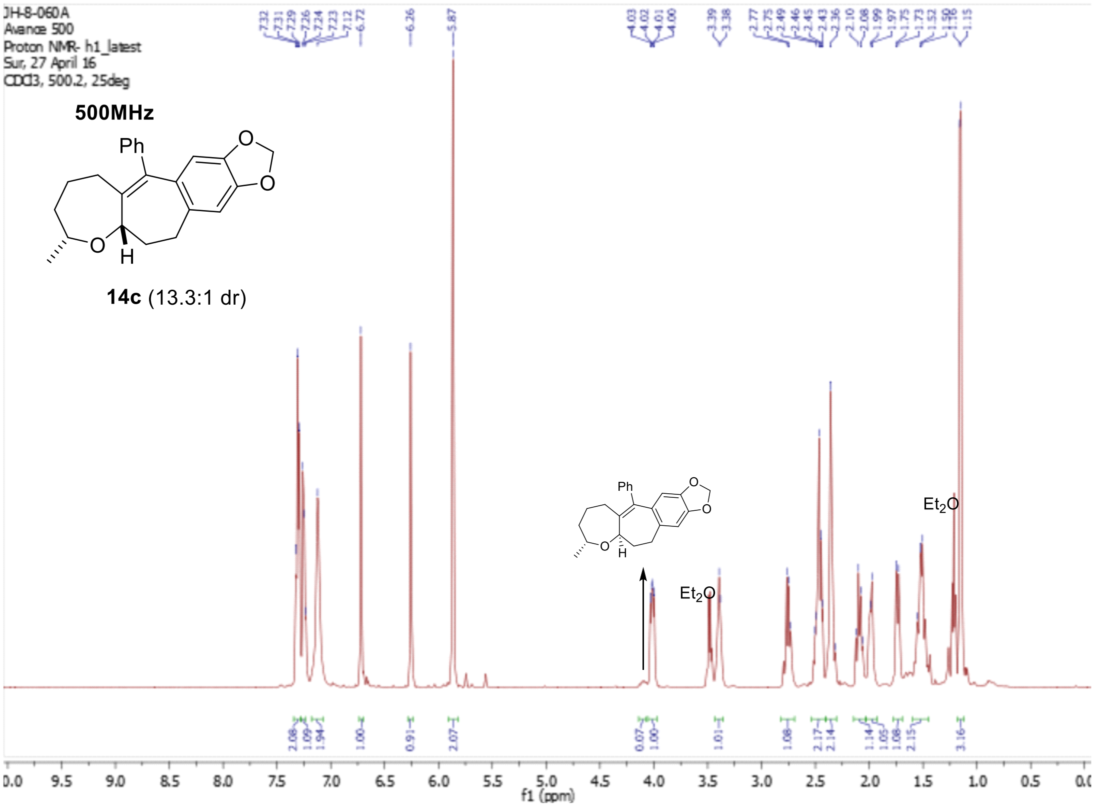
14a (9.4:1 dr)



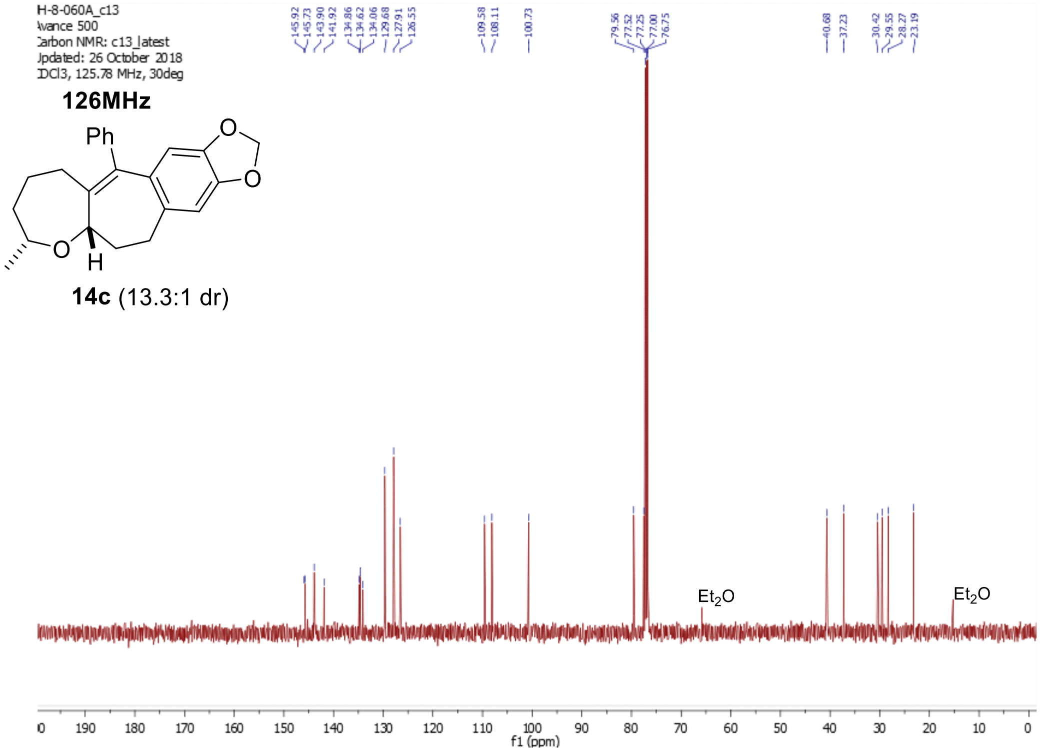
14b (7.1:1 dr)



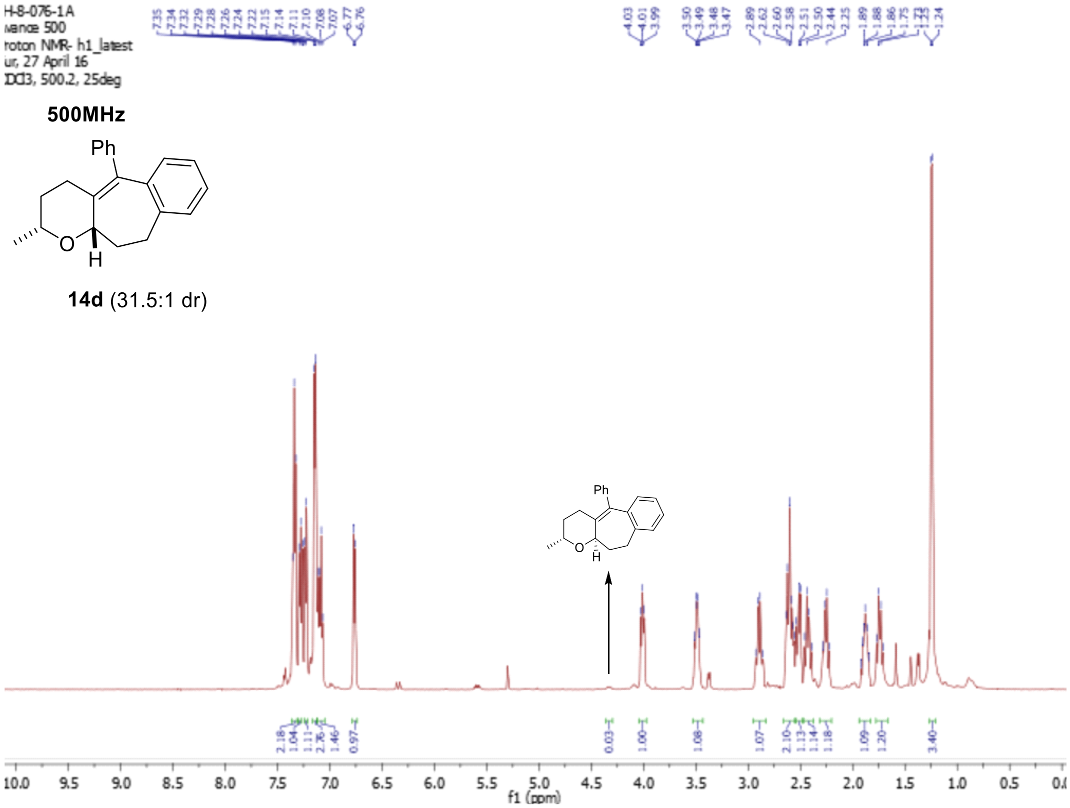
14b (7.1:1 dr)



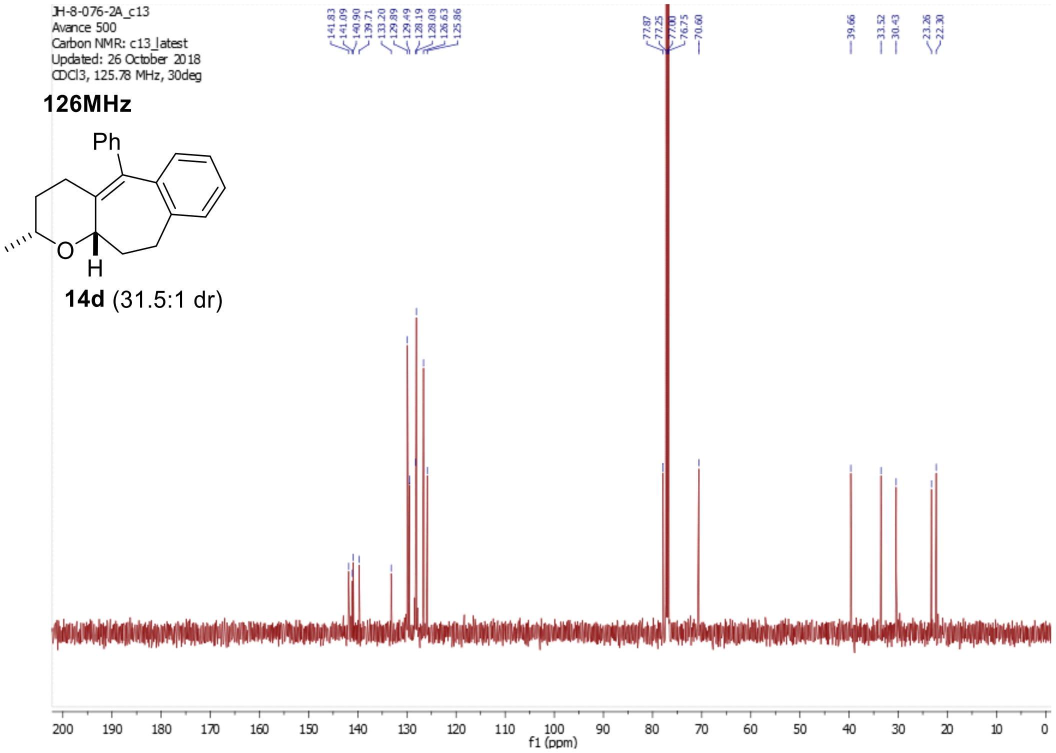
14c (13.3:1 dr)



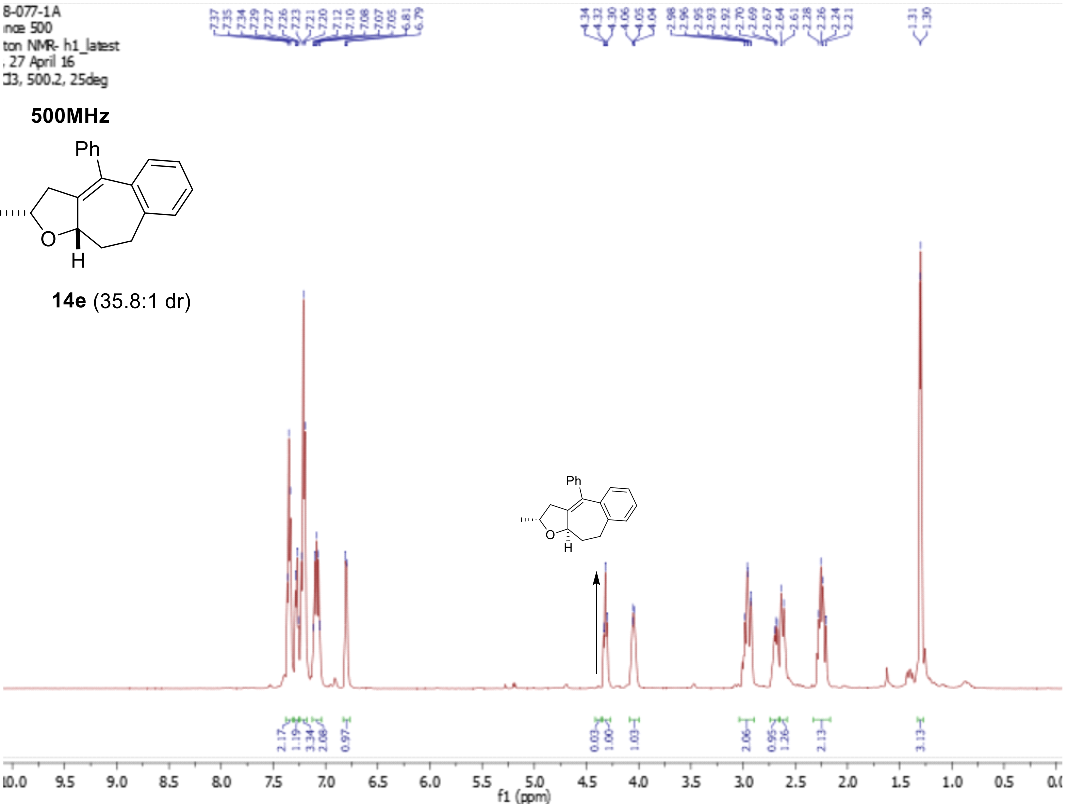
14c (13.3:1 dr)

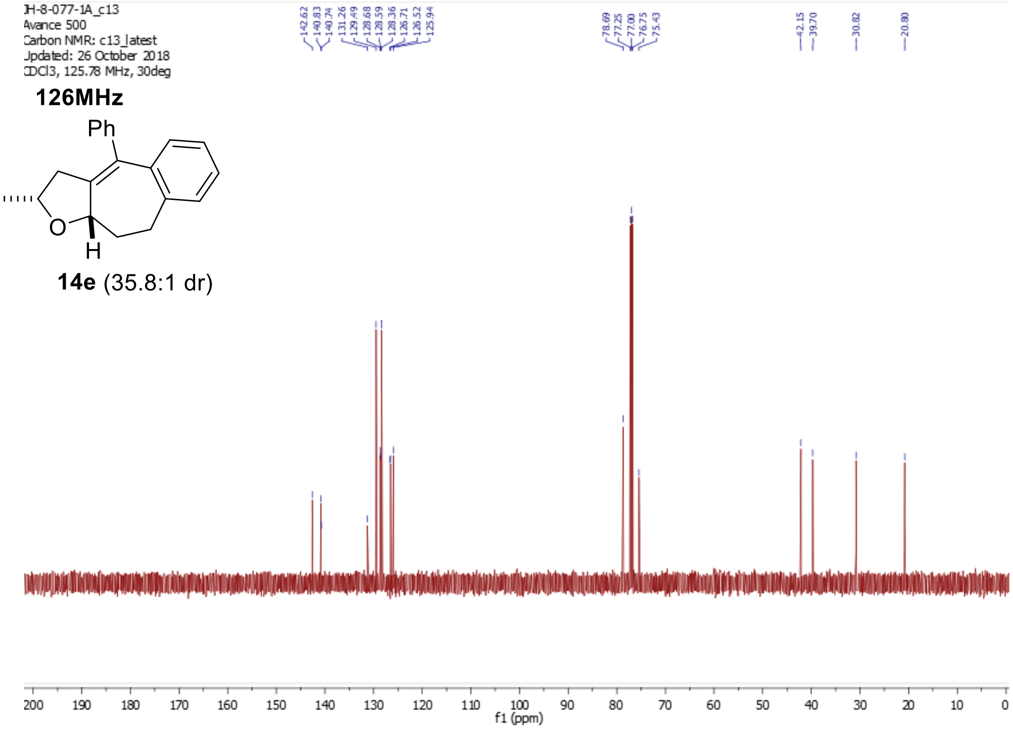


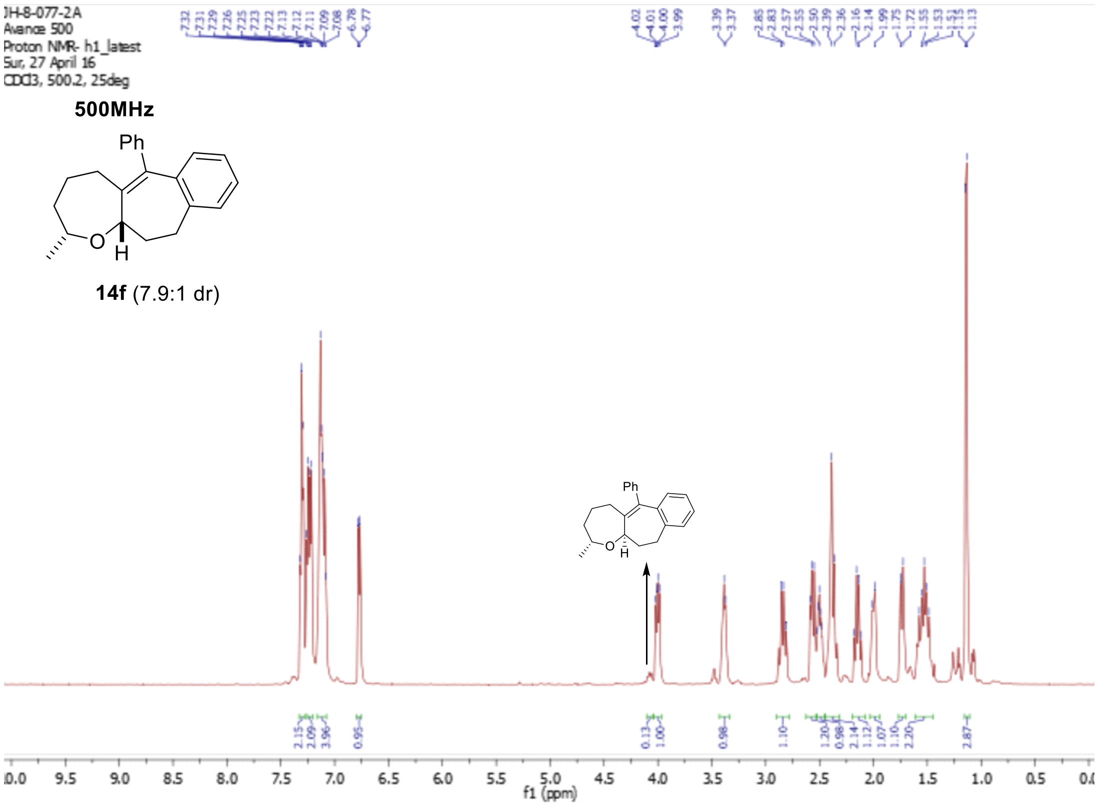
14d (31.5:1 dr)



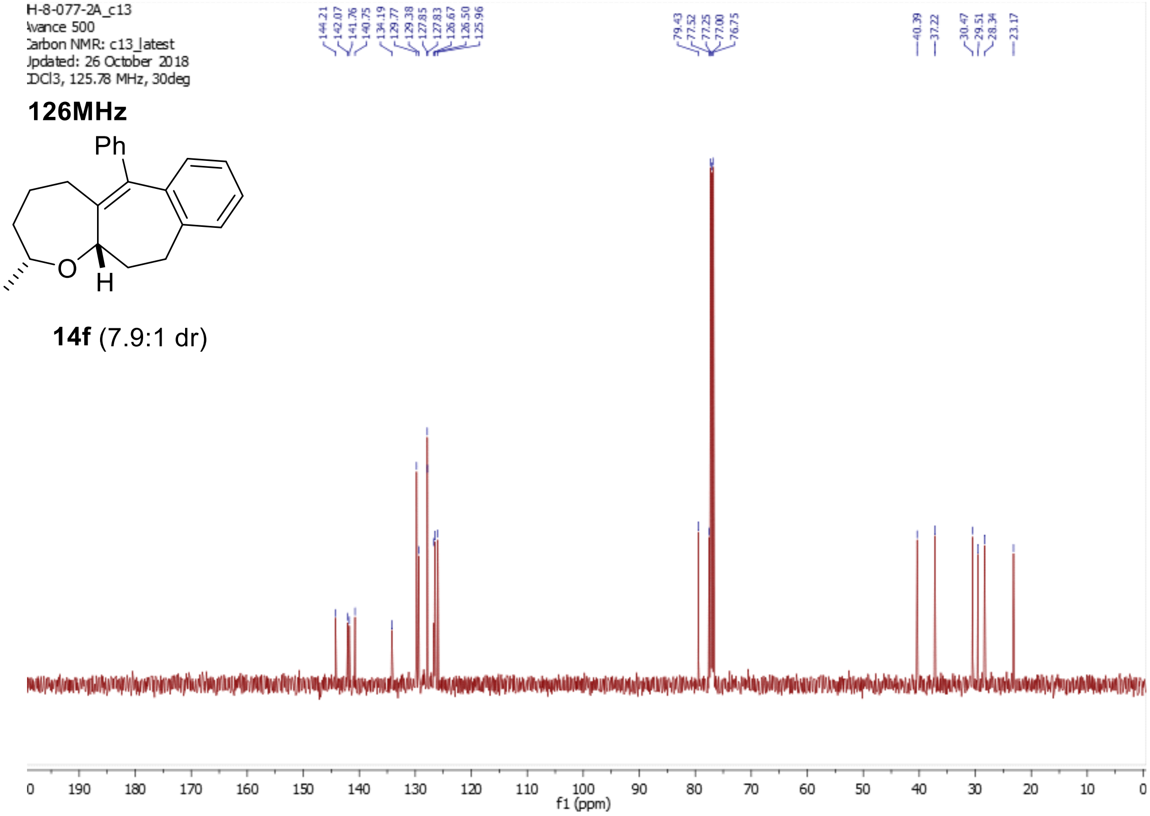
14d (31.5:1 dr)


8-077-1A
nce 500
ton NMR- h1_latest
, 27 April 16
I3, 500.2, 25deg
500MHz
7.37
7.35
7.34
7.29
7.27
7.26
7.23
7.21
7.20
7.12
7.10
7.08
7.07
7.05
6.81
6.79
4.34
4.32
4.30
4.06
4.05
4.04
2.98
2.96
2.95
2.93
2.92
2.70
2.69
2.67
2.64
2.61
2.28
2.26
2.24
2.21
1.31
1.30
Ph
O
H
14e (35.8:1 dr)
2.17
1.19
3.34
2.08
0.97
0.03
1.00
1.03
2.06
0.95
1.26
2.13
3.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

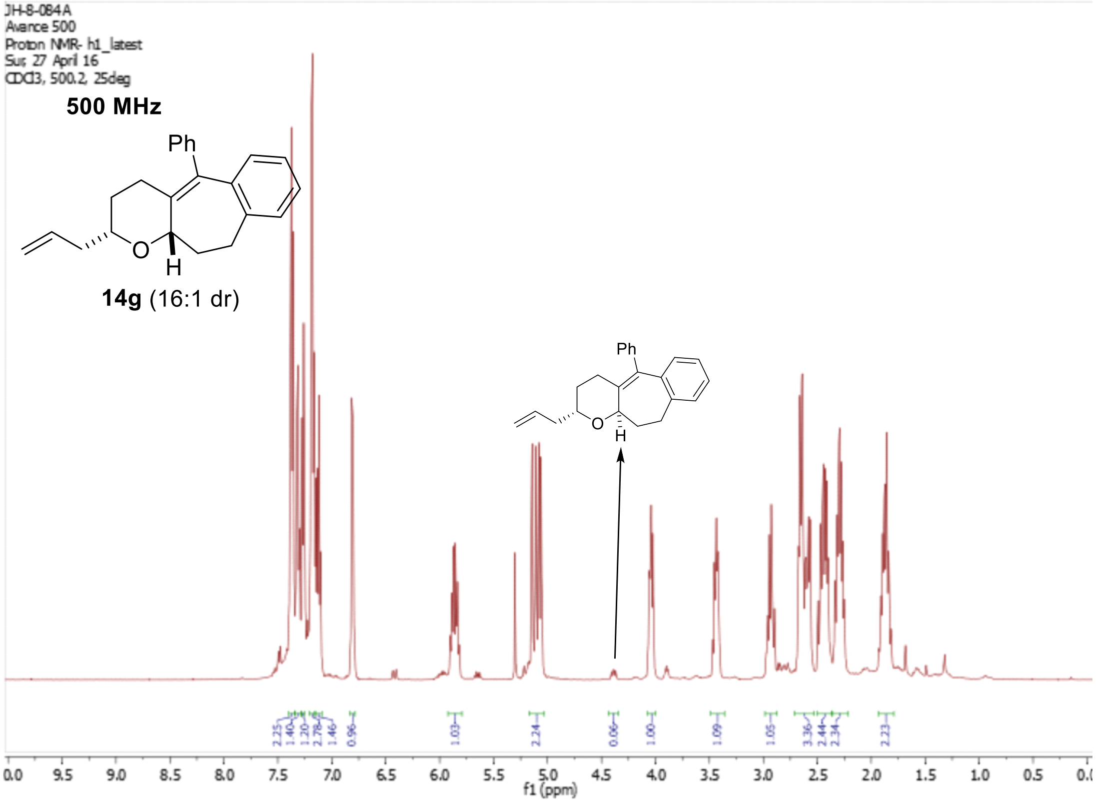

H-8-077-1A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126MHz
142.62
140.83
140.74
131.26
129.49
128.68
128.59
128.36
126.71
126.52
125.94
78.69
77.25
77.00
76.75
75.43
42.15
39.70
30.82
20.80
Ph
O
H
14e (35.8:1 dr)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



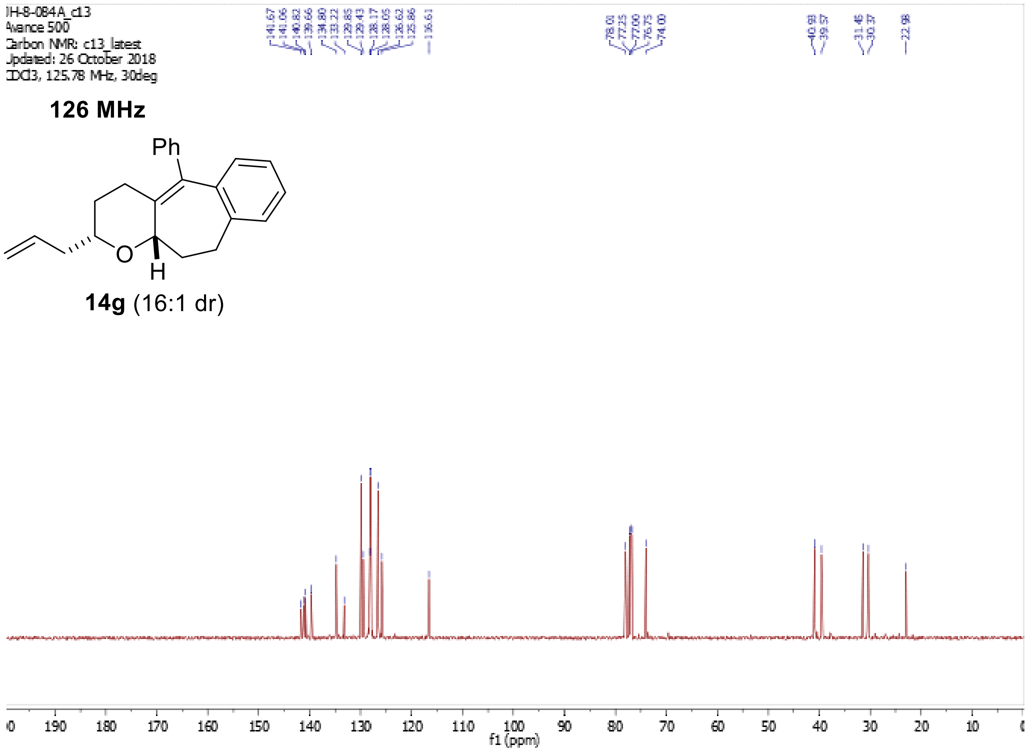
14f (7.9:1 dr)



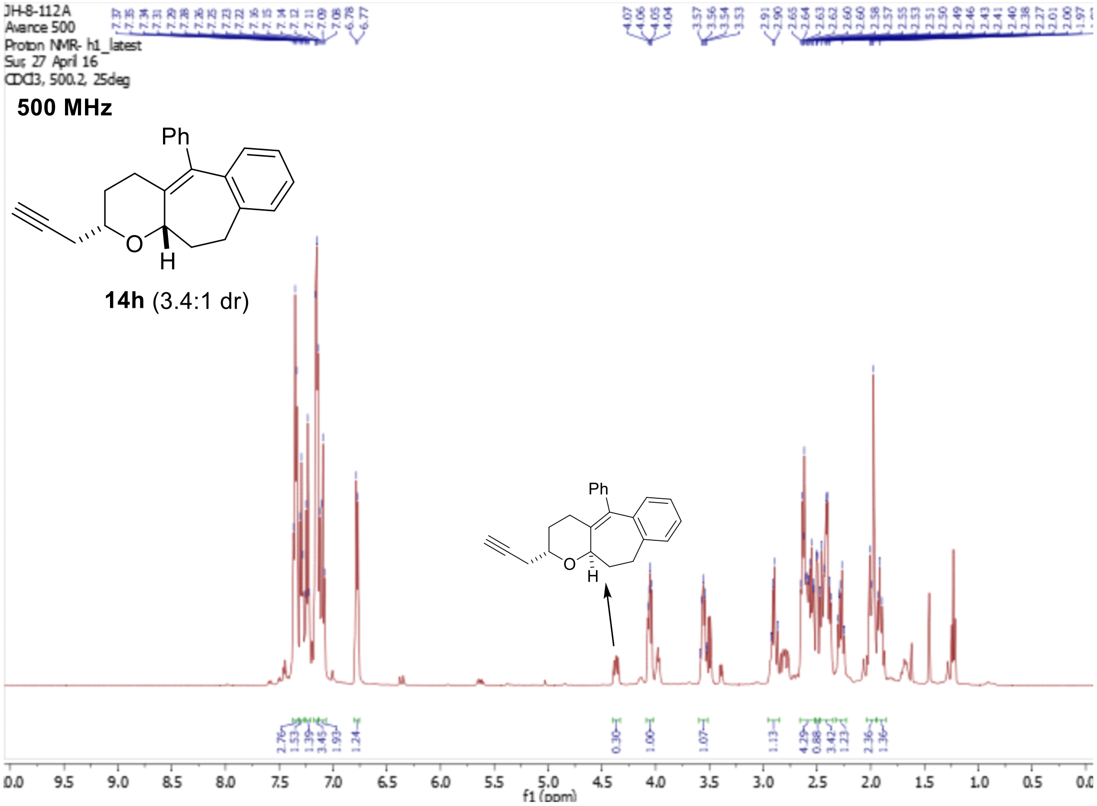
14f (7.9:1 dr)

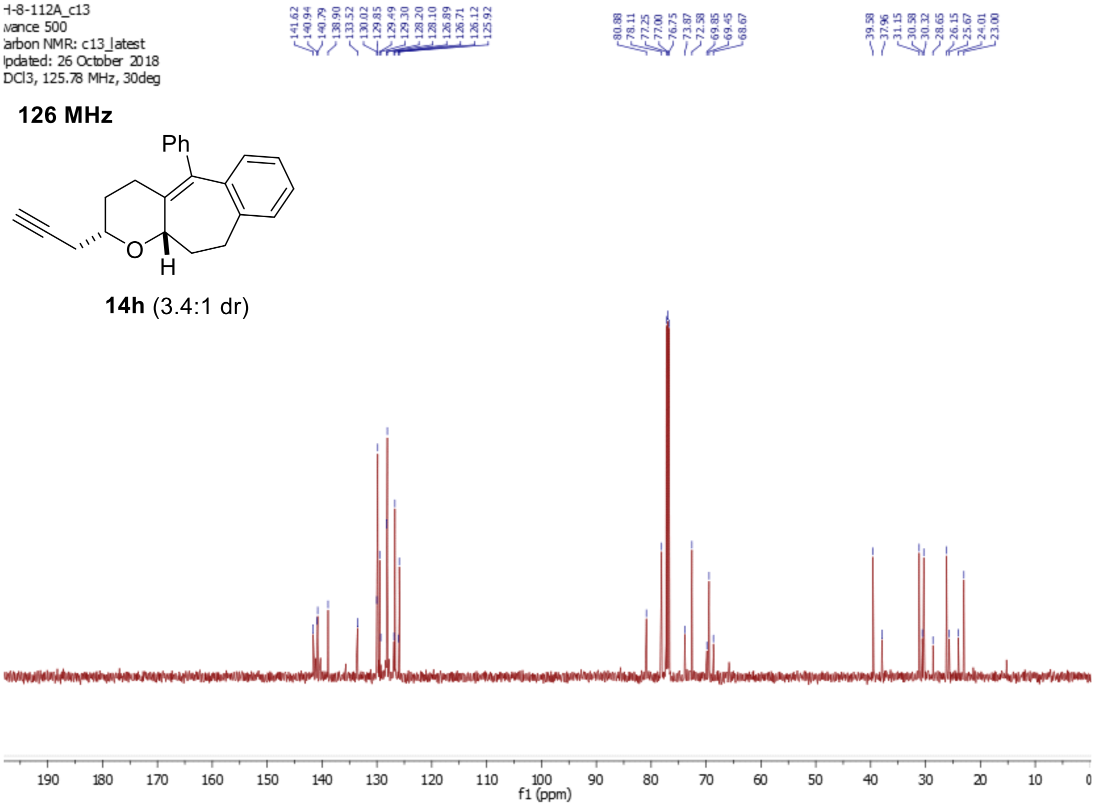


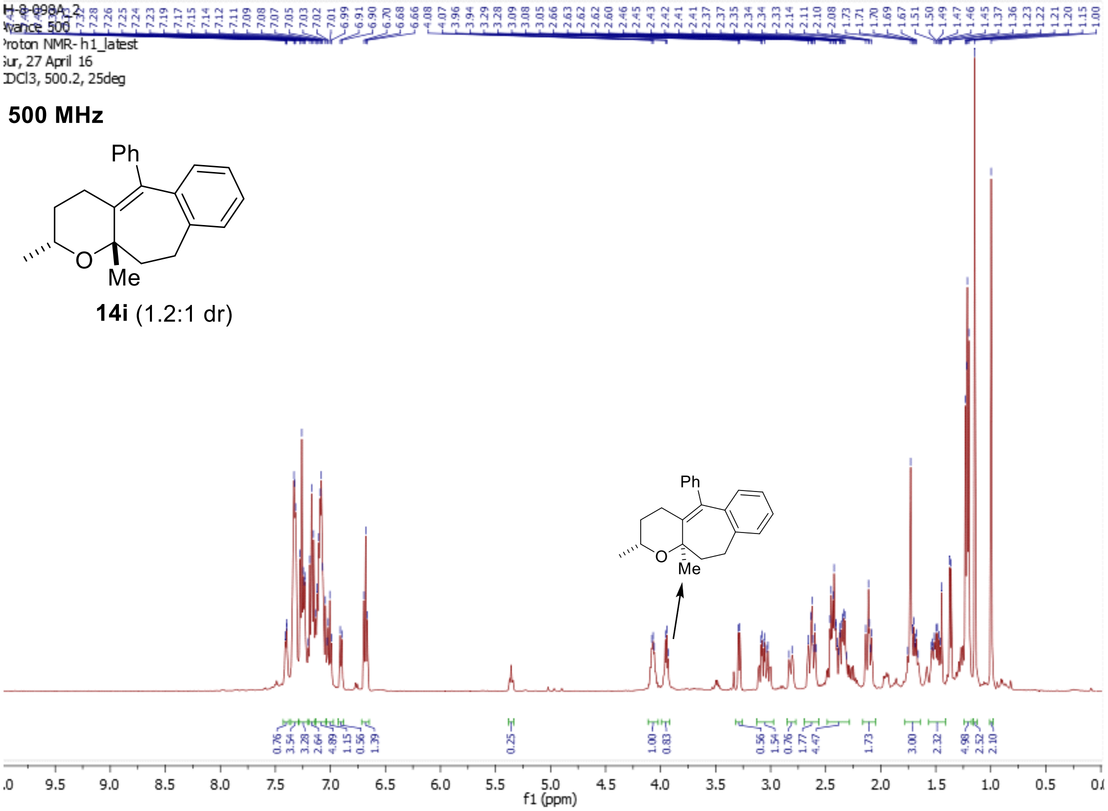
14g (16:1 dr)

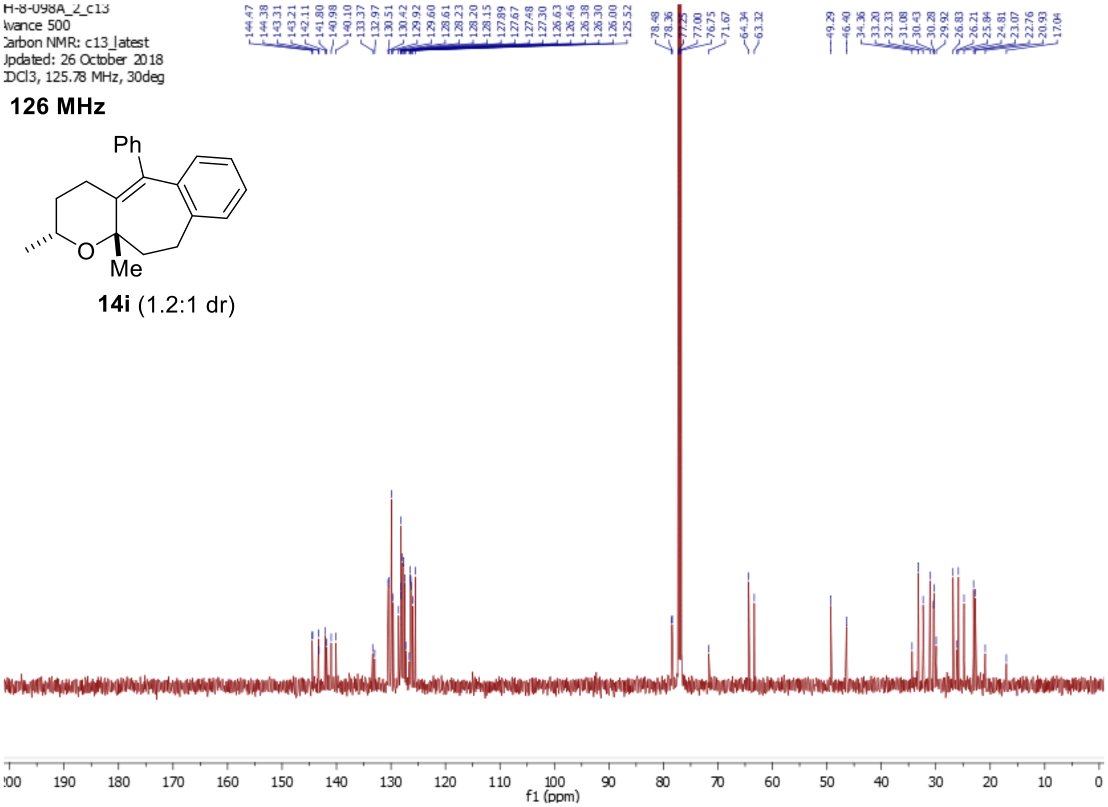


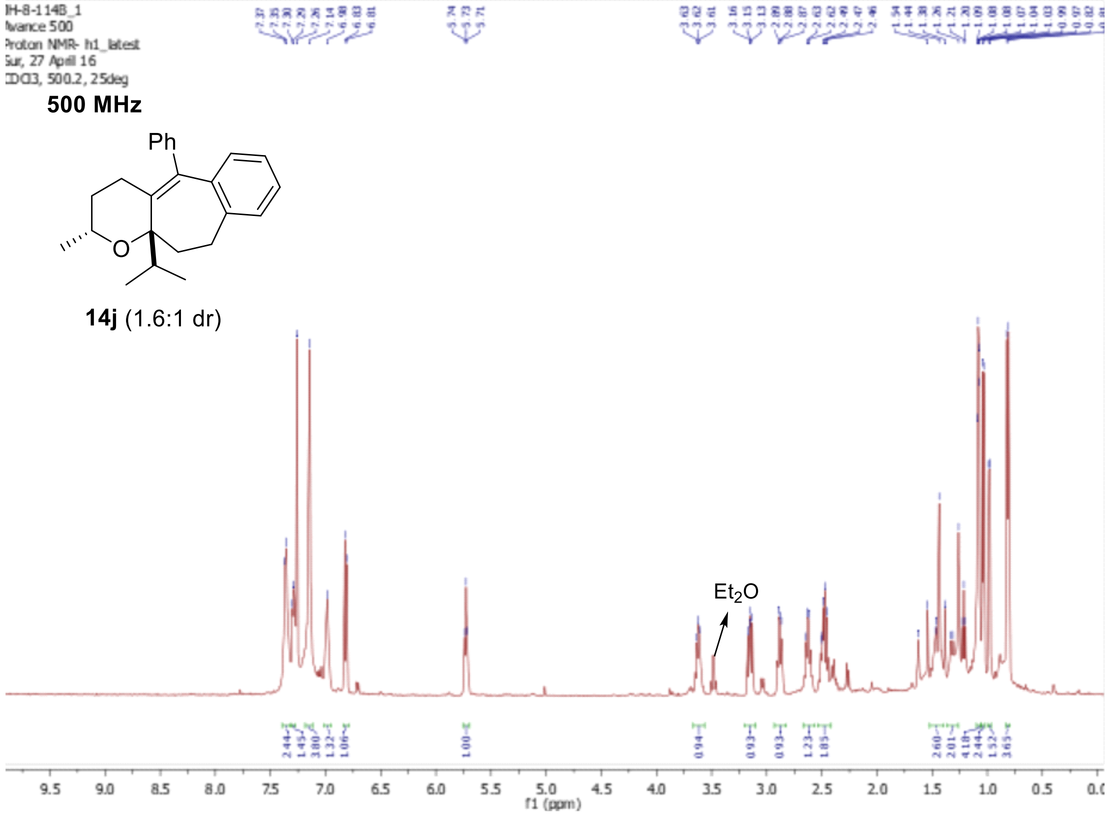
14g (16:1 dr)

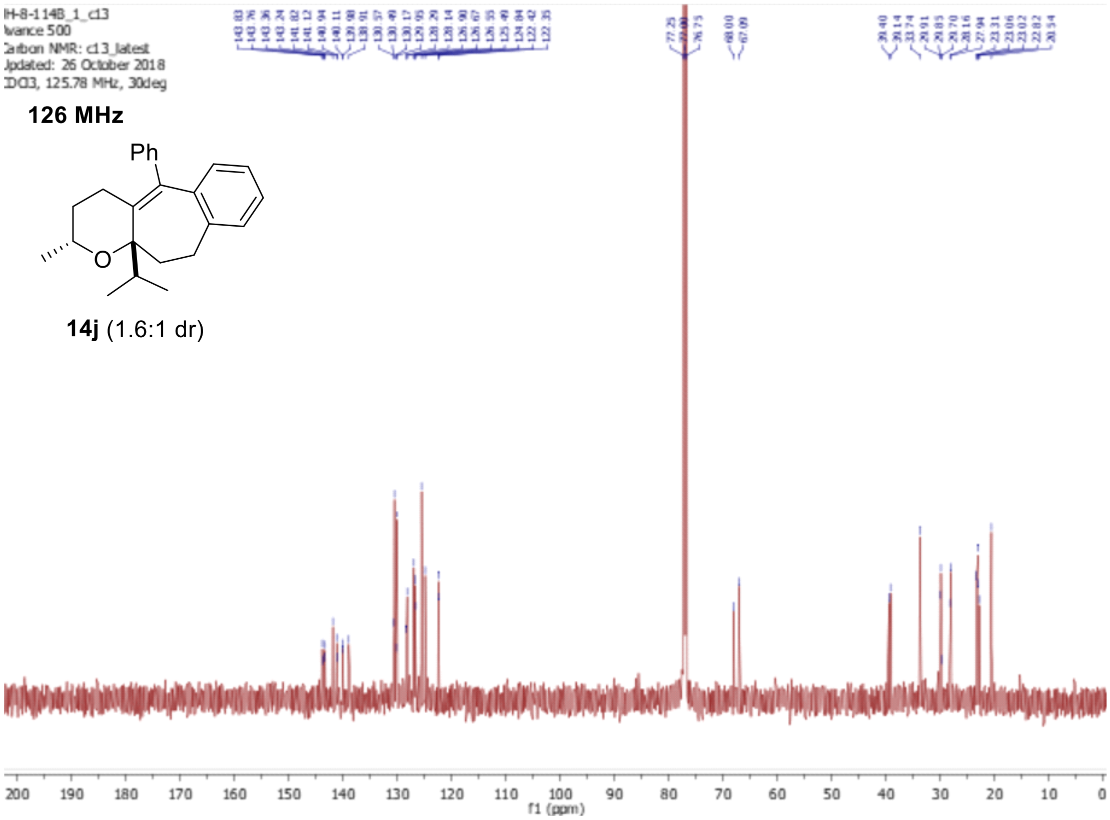

JH-8-112A
Avance 500
Proton NMR- h1_latest
Sus 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Ph
O
H
14h (3.4:1 dr)
7.37 7.35 7.34 7.31 7.29 7.28 7.26 7.25 7.23 7.22 7.16 7.15 7.14 7.12 7.11 7.09 7.08 6.78 6.77
4.07 4.06 4.05 4.04
3.57 3.56 3.54 3.53
2.91 2.90 2.65 2.64 2.63 2.62 2.60 2.60 2.58 2.57 2.55 2.53 2.51 2.50 2.49 2.46 2.43 2.41 2.40 2.38 2.27 2.01 2.00 1.97
2.76 1.53 1.39 3.45 1.93 1.24 0.30 1.00 1.07 1.13 4.29 0.88 3.42 1.23 2.36 1.36
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

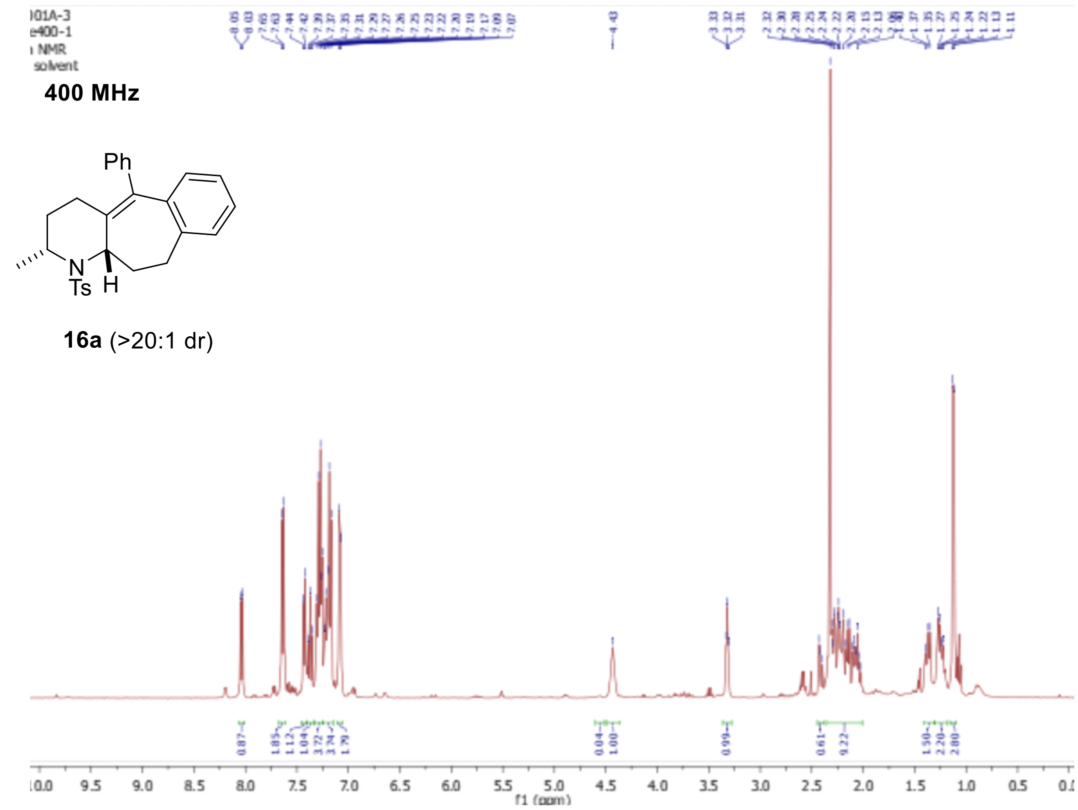

H-8-112A_c13
vance 500
arbon NMR: c13_latest
pdated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
Ph
O
H
14h (3.4:1 dr)
141.62 140.94 140.79 138.90 133.52 130.02 129.85 129.49 129.30 128.20 128.10 126.89 126.71 126.12 125.92
80.88 78.11 77.25 77.00 76.75 73.87 72.58 69.85 69.45 68.67
39.58 37.96 31.15 30.58 30.32 28.65 26.15 25.67 24.01 23.00
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


H-8-098A_2
vance 500
Proton NMR- h1_latest
ur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
Ph
O
Me
14i (1.2:1 dr)
Ph
O
Me
7.31 7.28 7.26 7.25 7.24 7.23 7.19 7.17 7.15 7.14 7.12 7.11 7.09 7.08 7.07 7.05 7.03 7.02 7.01 6.99 6.91 6.90 6.70 6.68 6.66 4.08 4.07 3.96 3.94 3.29 3.28 3.09 3.08 3.05 2.66 2.63 2.62 2.62 2.60 2.46 2.45 2.43 2.42 2.41 2.41 2.37 2.37 2.35 2.34 2.34 2.33 2.14 2.11 2.10 2.08 1.73 1.71 1.70 1.69 1.67 1.51 1.50 1.49 1.47 1.46 1.45 1.37 1.36 1.23 1.22 1.21 1.20 1.15 1.00
0.76 3.54 3.28 2.64 4.89 1.15 0.56 1.39 0.25 1.00 0.83 0.56 1.54 0.76 1.77 4.47 1.73 3.00 2.32 4.98 2.52 2.10
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

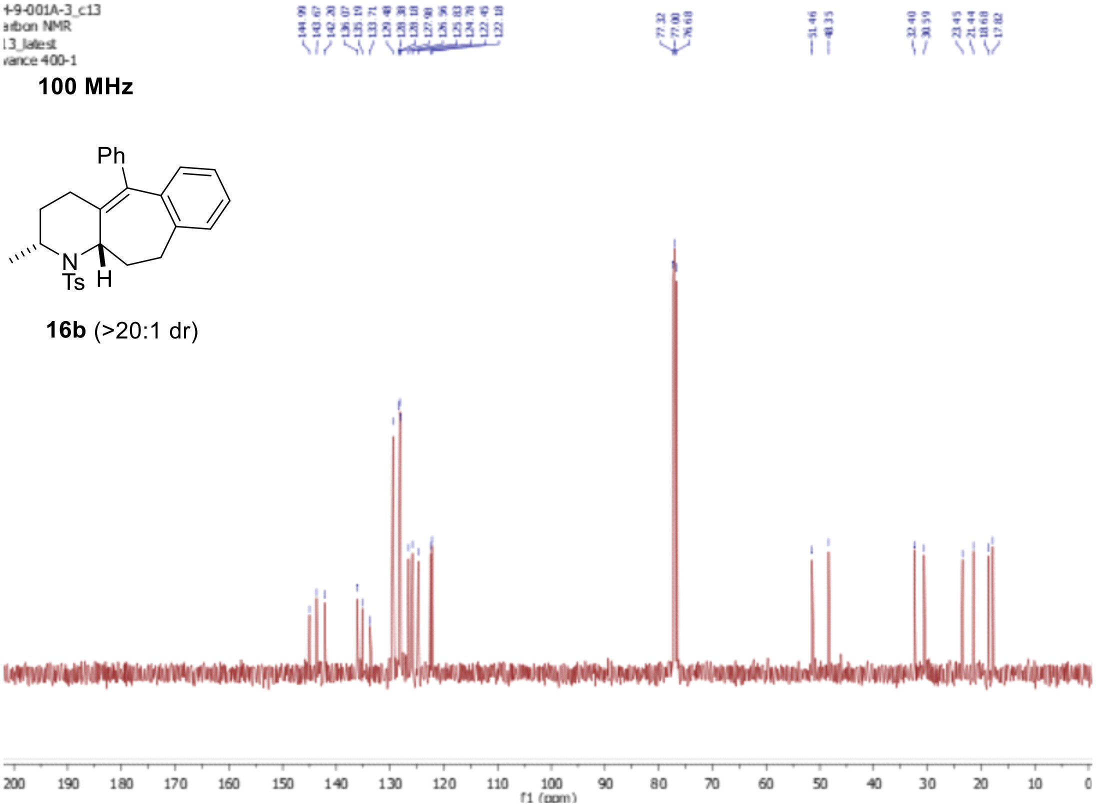

H-8-098A_2_c13
vance 500
arbon NMR: c13_latest
pdated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
Ph
O
Me
14i (1.2:1 dr)
144.47 144.38 143.31 143.21 142.11 141.80 140.98 140.10 133.37 132.97 130.51 130.42 129.92 129.60 128.61 128.23 128.20 128.15 127.89 127.67 127.48 127.30 126.63 126.46 126.38 126.30 126.00 125.52 78.48 78.36 77.25 77.00 76.75 71.67 64.34 63.32 49.29 46.40 34.36 33.20 32.33 31.08 30.43 30.28 29.92 26.83 26.21 25.84 24.81 23.07 22.76 20.93 17.04
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


IH-8-114B_1
vance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Ph
O
14j (1.6:1 dr)
7.37 7.35 7.30 7.29 7.26 7.14 6.98 6.83 6.81
5.74 5.73 5.71
3.63 3.62 3.61
3.16 3.15 3.13
2.89 2.88 2.87
2.63 2.62 2.49 2.47 2.46
1.54 1.44 1.38 1.26 1.21 1.20 1.09 1.08 1.07 1.04 1.03 0.99 0.97 0.82 0.81
Et2O
2.44 1.45 3.80 1.32 1.06
1.00
0.94
0.93
0.93
1.23 1.05
2.60 2.01 4.18 2.44 1.52 3.65
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

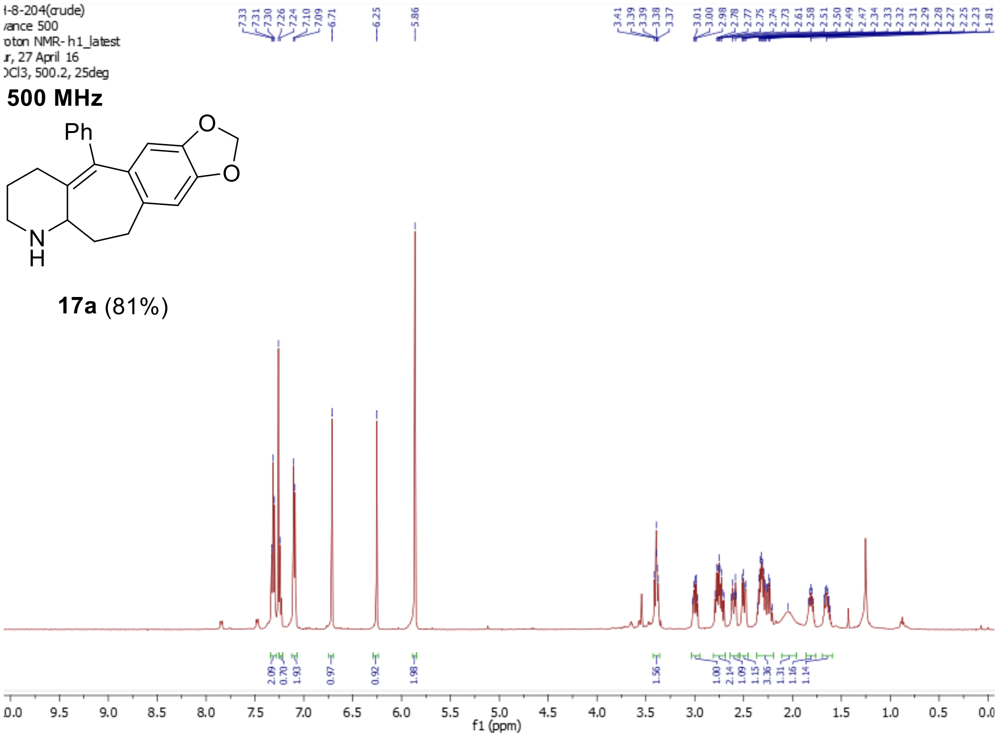

IH-8-114B_1_c13
vance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Ph
O
14j (1.6:1 dr)
143.83 143.76 143.36 143.24 141.02 141.12 140.94 140.11 139.98 138.91
130.57 130.49 130.17 129.95 128.29 128.14 126.90 126.67 126.35 125.49 124.84 122.42 122.35
77.25 77.00 76.75
68.00 67.09
39.40 39.14 33.74 29.91 29.85 29.70 28.16 27.94 23.31 23.06 23.02 22.82 20.54
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



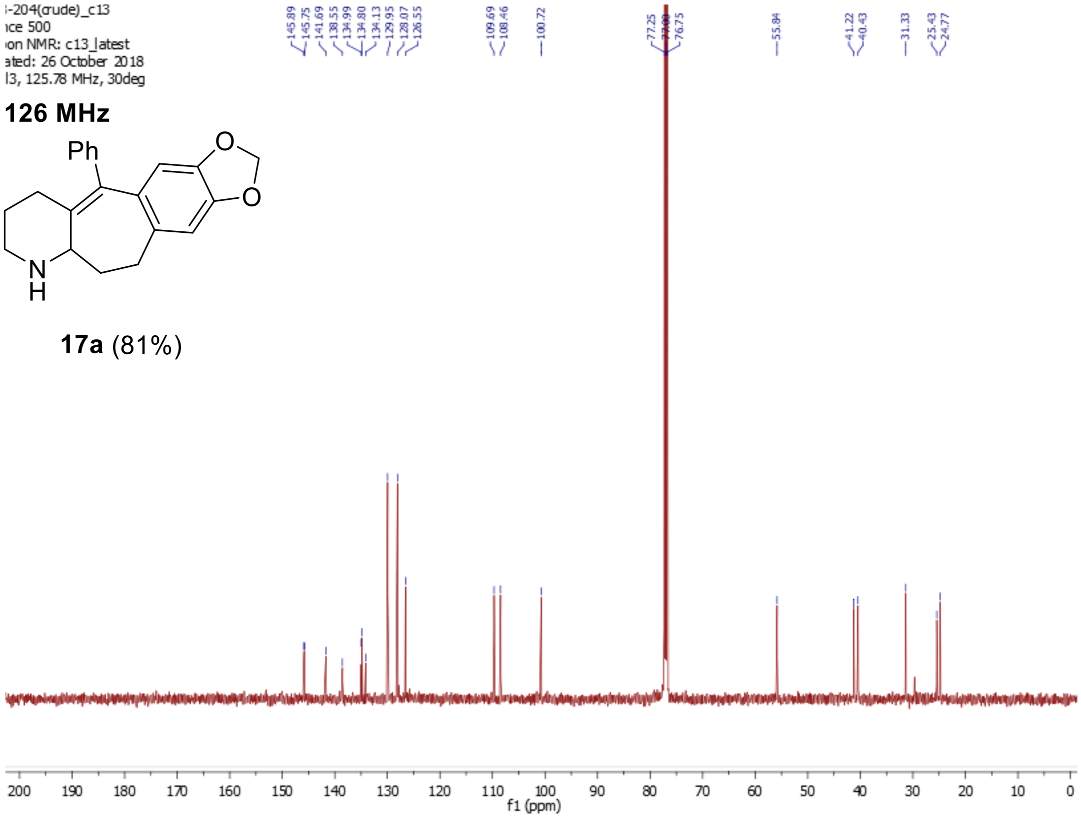
16a (>20:1 dr)



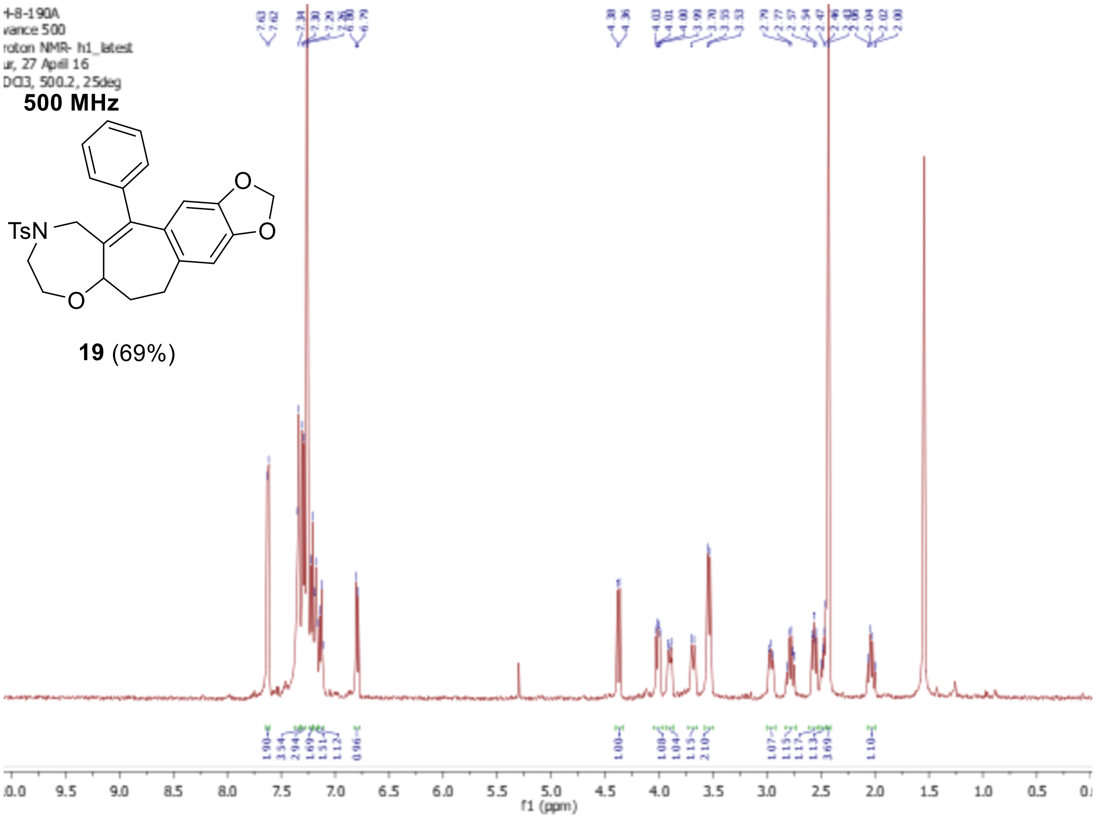
16b (>20:1 dr)


l-8-204(crude)
vance 500
oton NMR- h1_latest
r, 27 April 16
DCl3, 500.2, 25deg
500 MHz
Ph
O
O
N
H
7.33
7.31
7.30
7.26
7.24
7.10
7.09
6.71
6.25
5.86
3.41
3.39
3.39
3.38
3.37
3.01
3.00
2.98
2.78
2.77
2.75
2.74
2.73
2.61
2.58
2.51
2.50
2.49
2.47
2.34
2.33
2.32
2.31
2.29
2.28
2.27
2.25
2.23
1.81
2.09
0.70
1.93
0.97
0.92
1.98
1.56
1.00
2.14
1.09
1.15
3.36
1.31
1.16
1.14
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

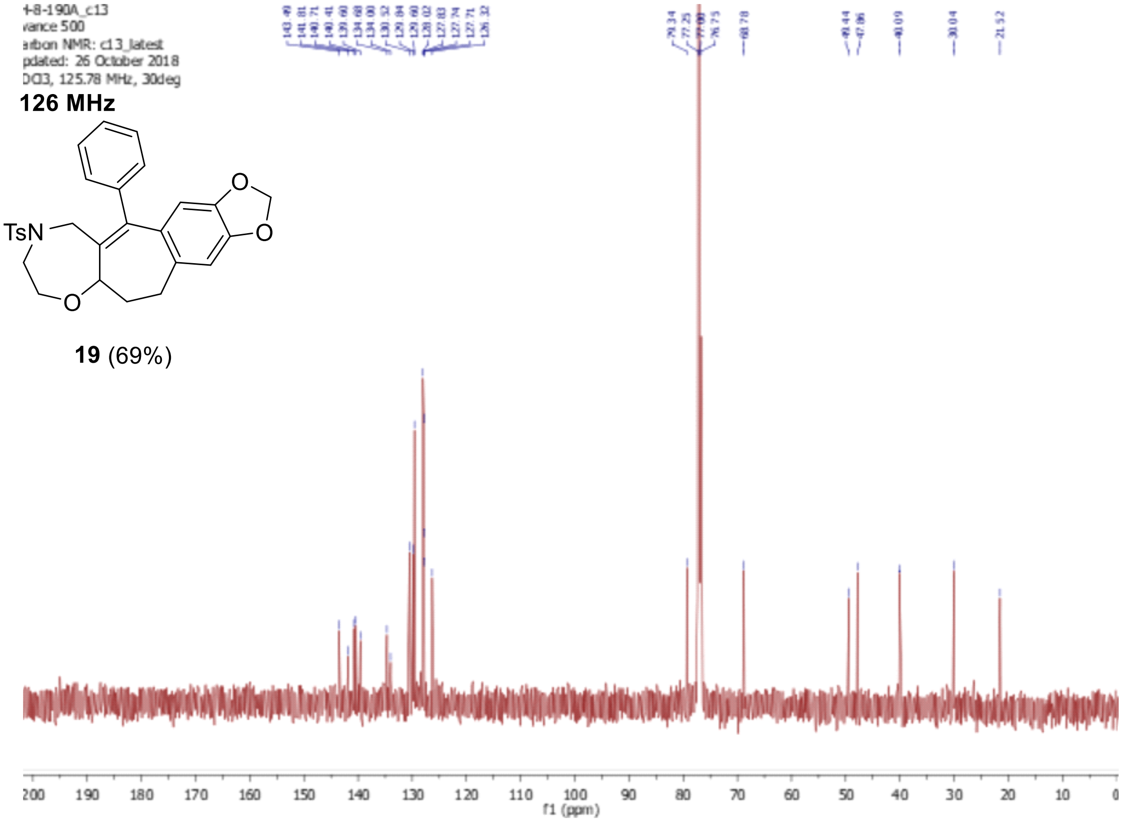
17a (81%)


-204(crude)_c13
nce 500
on NMR: c13_latest
ated: 26 October 2018
l3, 125.78 MHz, 30deg
126 MHz
Ph
O
O
N
H
145.89
145.75
141.69
138.55
134.99
134.80
134.13
129.95
128.07
126.55
109.69
108.46
100.72
77.25
77.00
76.75
55.84
41.22
40.43
31.33
25.43
24.77
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

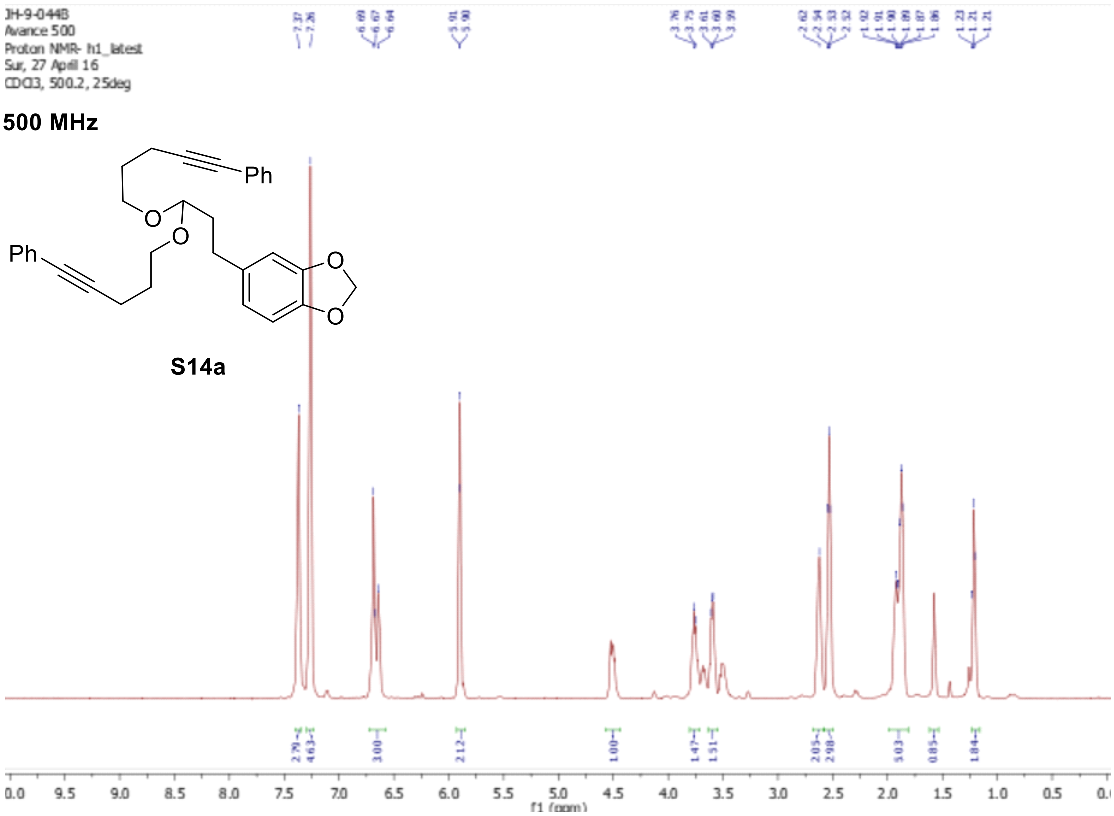
17a (81%)

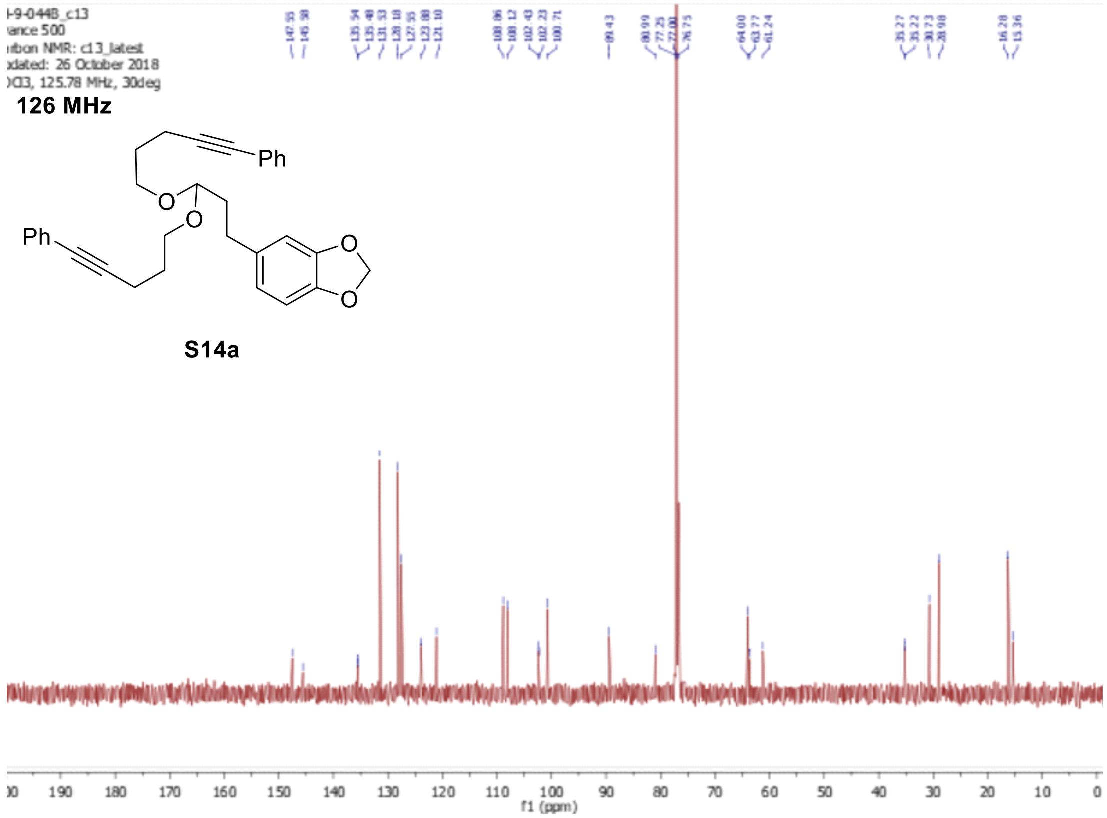

H-8-190A
vance 500
roton NMR- h1_latest
ur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
TsN
O
O
O
7.63
7.62
7.34
7.30
7.29
6.80
6.79
4.38
4.36
4.03
4.01
4.00
3.55
3.53
2.79
2.77
2.57
2.54
2.47
2.04
2.02
2.00
1.90
3.54
2.94
1.69
1.51
1.12
0.96
1.00
1.08
1.04
1.15
2.10
1.07
1.15
1.17
1.13
3.69
1.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

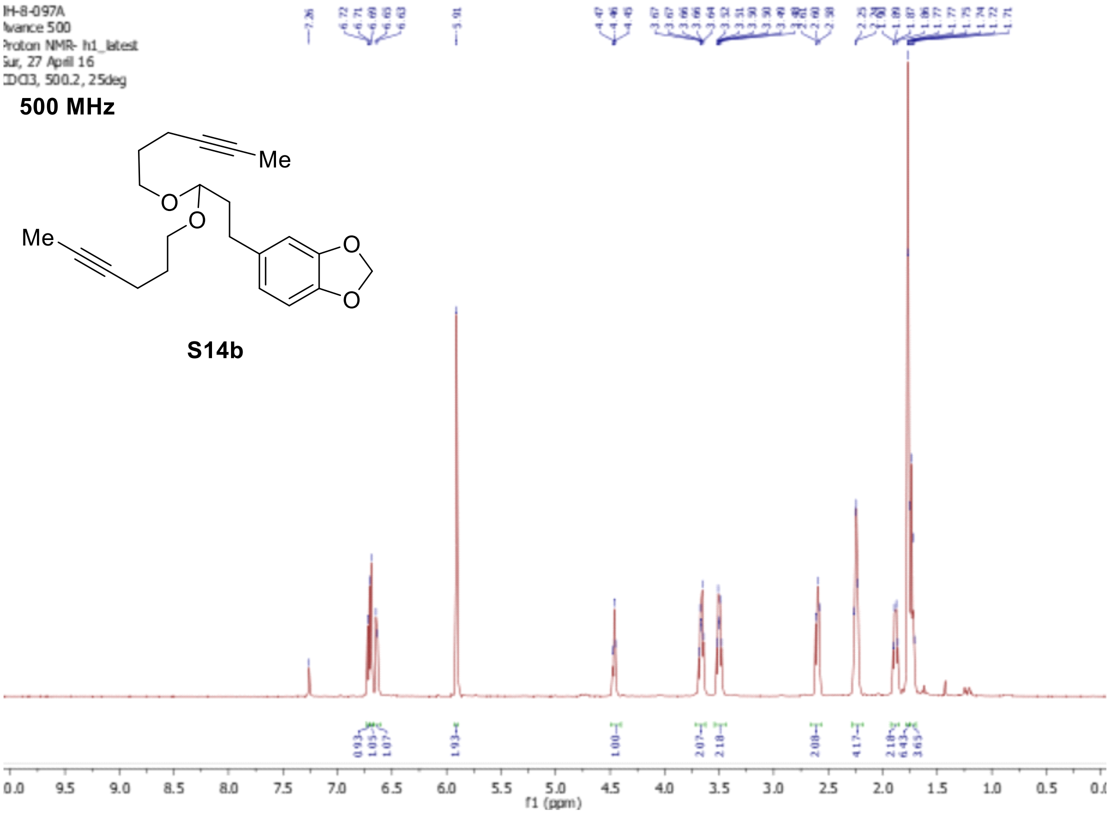
19 (69%)


H-8-190A_c13
vance 500
arbon NMR: c13_latest
pdated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
TsN
O
O
O
143.49
141.81
140.71
140.41
139.60
134.68
134.00
130.52
129.84
129.60
128.02
127.83
127.74
127.71
126.32
79.34
77.25
77.00
76.75
68.78
49.44
47.86
40.09
30.04
21.52
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

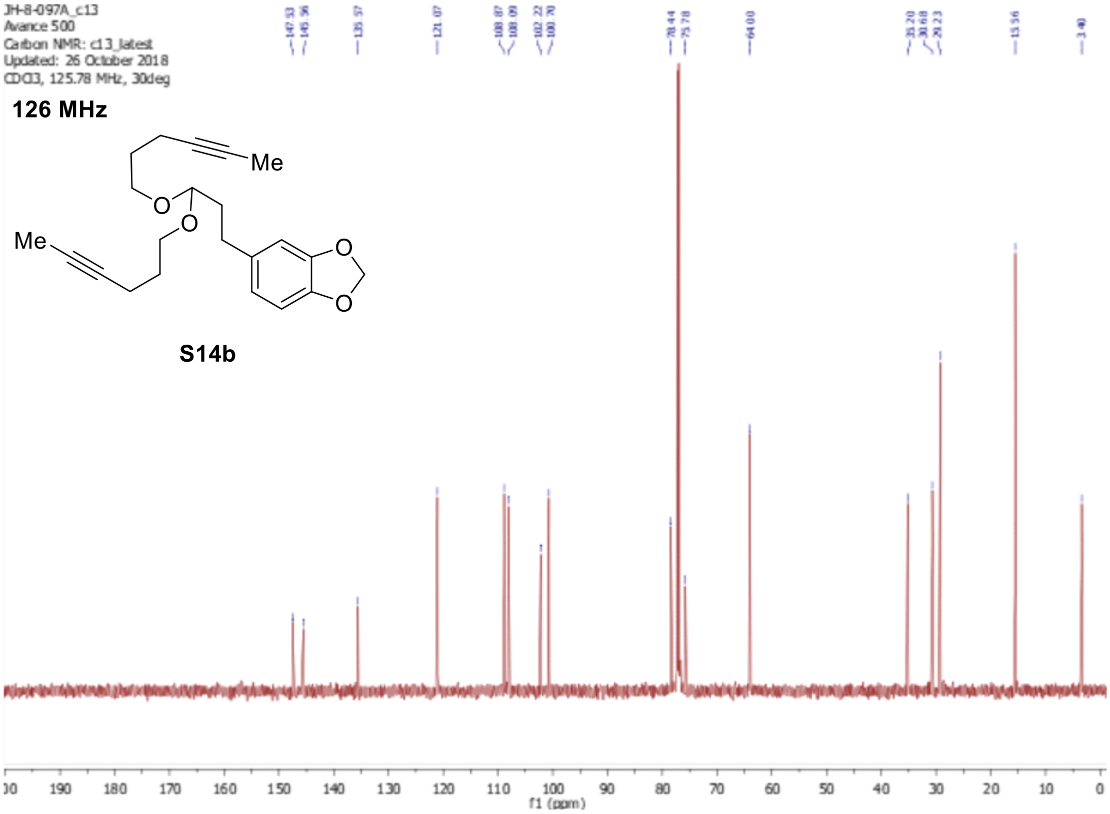
19 (69%)


JH-9-044B
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Ph
O
O
Ph
O
O
S14a
7.37
7.26
6.69
6.67
6.64
5.91
5.90
3.76
3.75
3.61
3.60
3.59
2.62
2.54
2.53
2.52
1.92
1.91
1.90
1.89
1.87
1.86
1.23
1.21
1.21
2.79
4.63
3.00
2.12
1.00
1.47
1.51
2.05
2.98
5.03
0.85
1.84
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

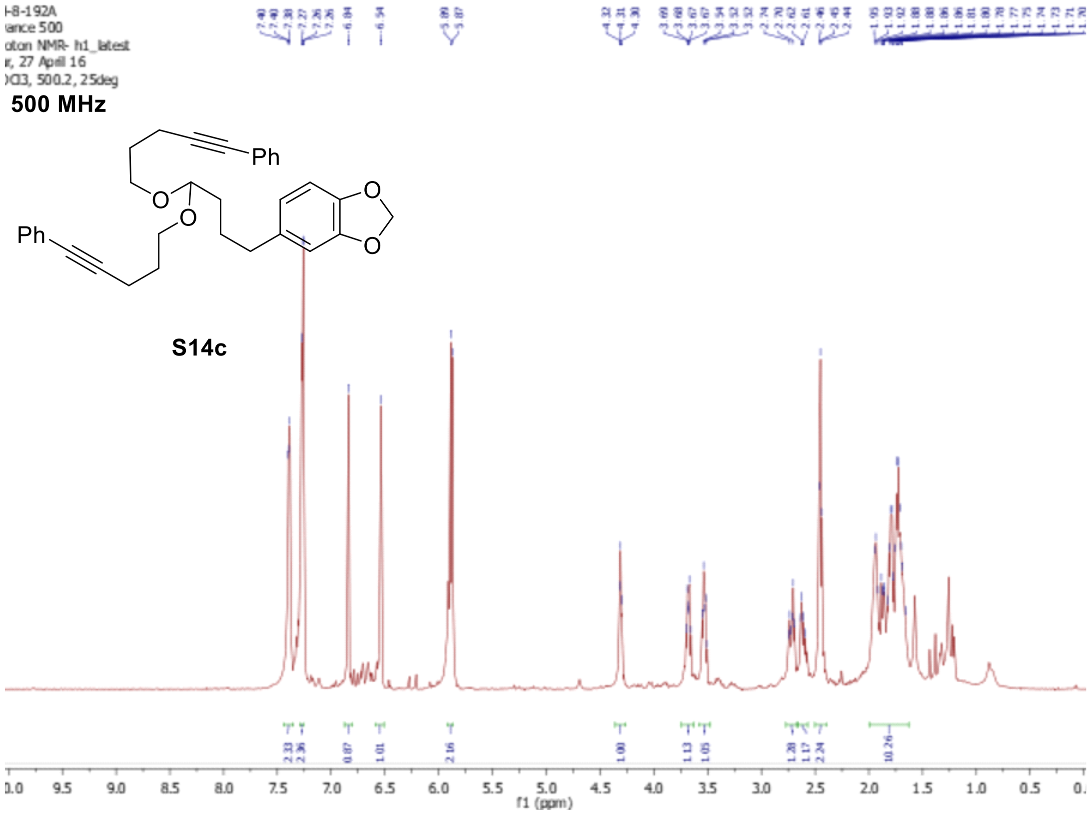

JH-9-044B_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Ph
O
O
Ph
O
O
S14a
147.55
145.98
135.94
135.48
131.53
128.18
127.55
123.88
121.10
108.86
108.12
102.43
102.23
100.71
89.43
80.99
77.25
77.00
76.75
64.00
63.77
61.24
35.27
35.22
30.73
28.98
16.28
15.36
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


JH-8-097A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Me
O
O
Me
O
O
7.26
6.72
6.71
6.69
6.65
6.63
5.91
4.47
4.46
4.45
3.67
3.67
3.66
3.66
3.64
3.52
3.51
3.50
3.50
3.49
2.61
2.60
2.58
2.25
2.24
1.89
1.87
1.86
1.77
1.75
1.74
1.72
1.71
0.93
1.05
1.07
1.93
1.00
2.07
2.18
2.08
4.17
2.18
6.43
3.65
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

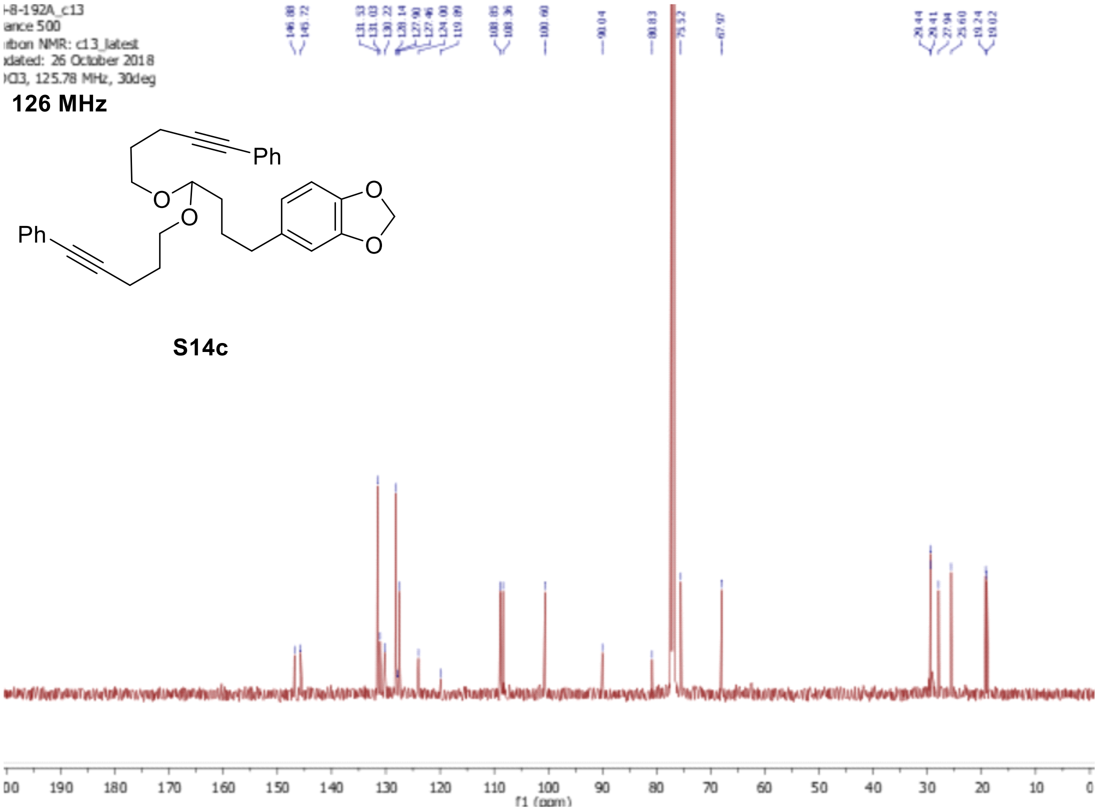
S14b


JH-8-097A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Me
O
O
Me
O
O
147.53
145.96
135.57
121.07
108.87
108.09
102.22
100.70
78.44
75.78
64.00
35.20
30.68
29.23
15.56
3.40
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

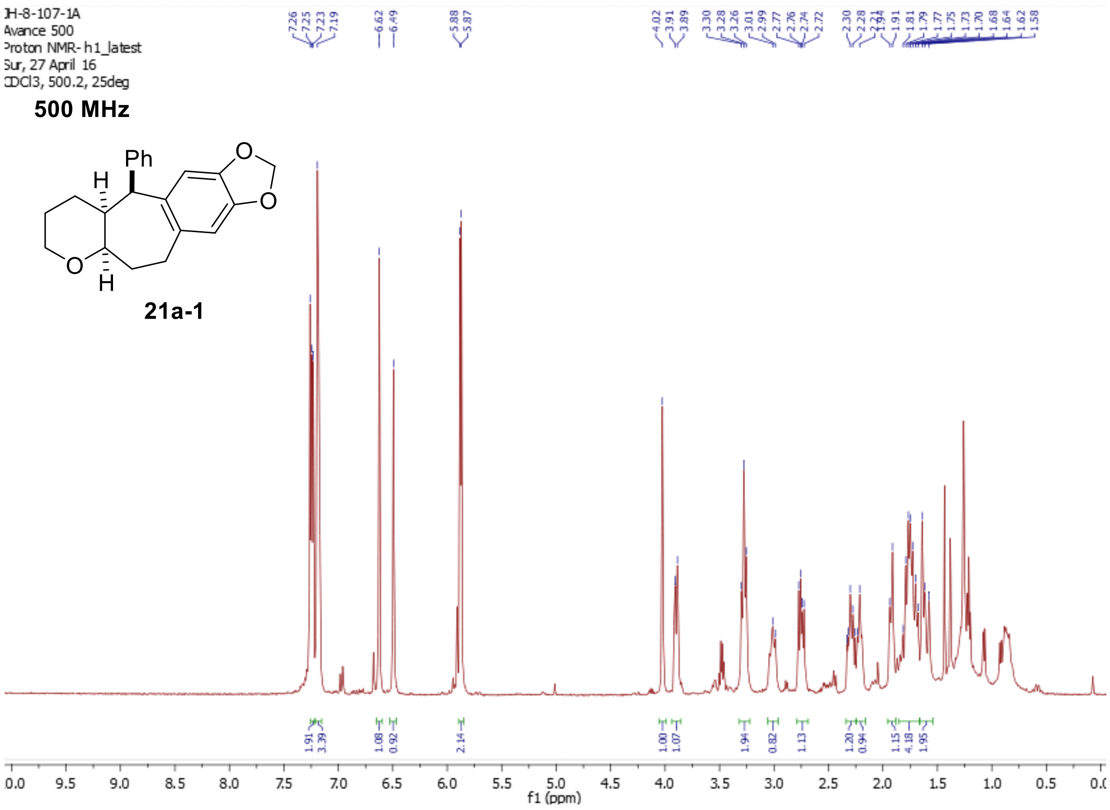
S14b


-8-192A
ance 500
oton NMR- h1_latest
r, 27 April 16
CI3, 500.2, 25deg
500 MHz
7.40
7.40
7.38
7.27
7.26
7.26
6.84
6.54
5.89
5.87
4.32
4.31
4.30
3.69
3.68
3.67
3.67
3.54
3.52
3.52
2.74
2.70
2.62
2.61
2.46
2.45
2.44
1.95
1.93
1.92
1.88
1.88
1.86
1.86
1.81
1.80
1.78
1.77
1.75
1.74
1.73
1.71
1.70
Ph
O
O
Ph
O
O
2.33
2.36
0.87
1.01
2.16
1.00
1.13
1.05
1.28
1.17
2.24
10.26
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

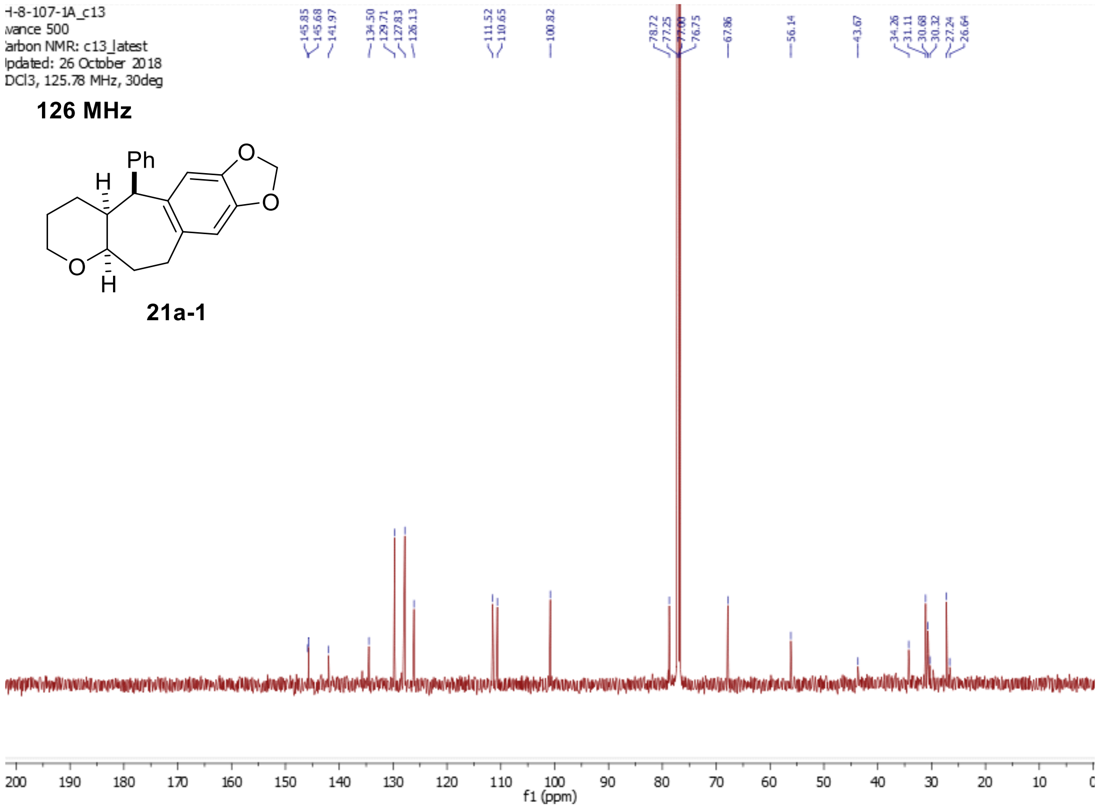
S14c


-8-192A_c13
ance 500
rbon NMR: c13_latest
dated: 26 October 2018
CI3, 125.78 MHz, 30deg
126 MHz
146.88
145.72
131.53
131.03
130.22
128.14
127.90
127.46
124.00
119.89
108.85
108.36
100.60
90.04
80.83
75.52
67.97
29.44
29.41
27.94
25.60
19.24
19.02
Ph
O
O
Ph
O
O
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

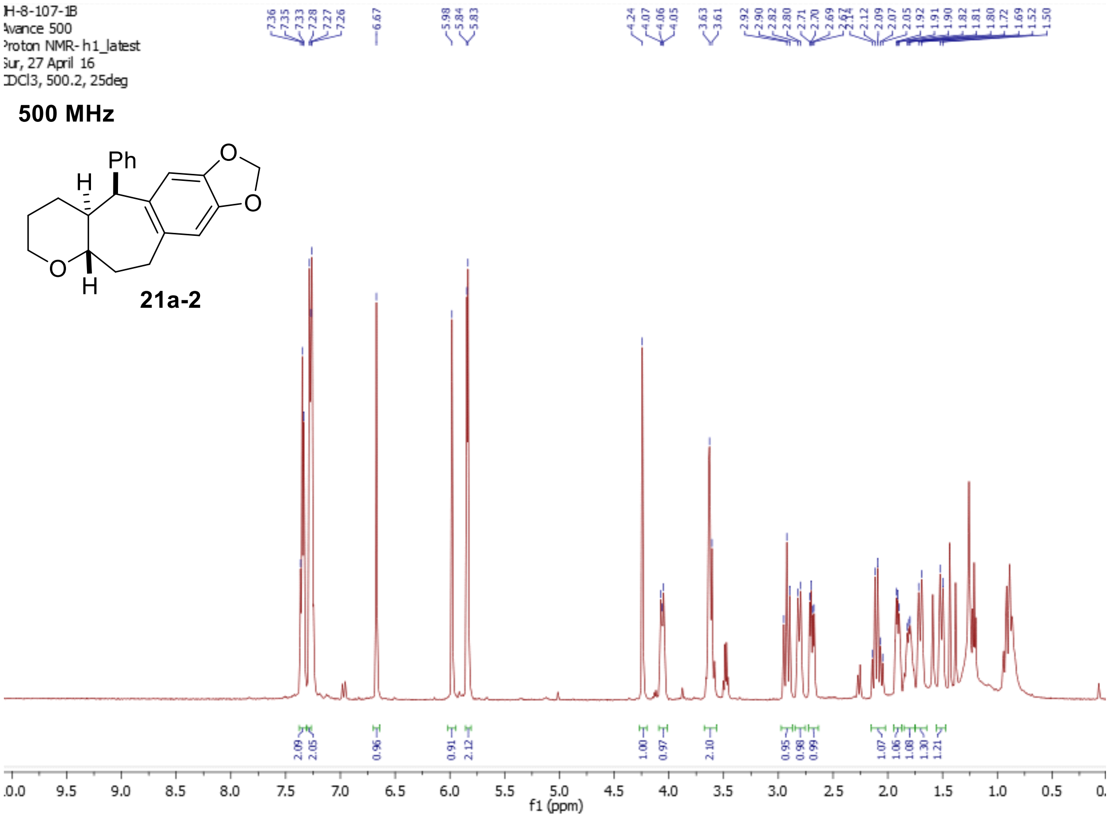
S14c

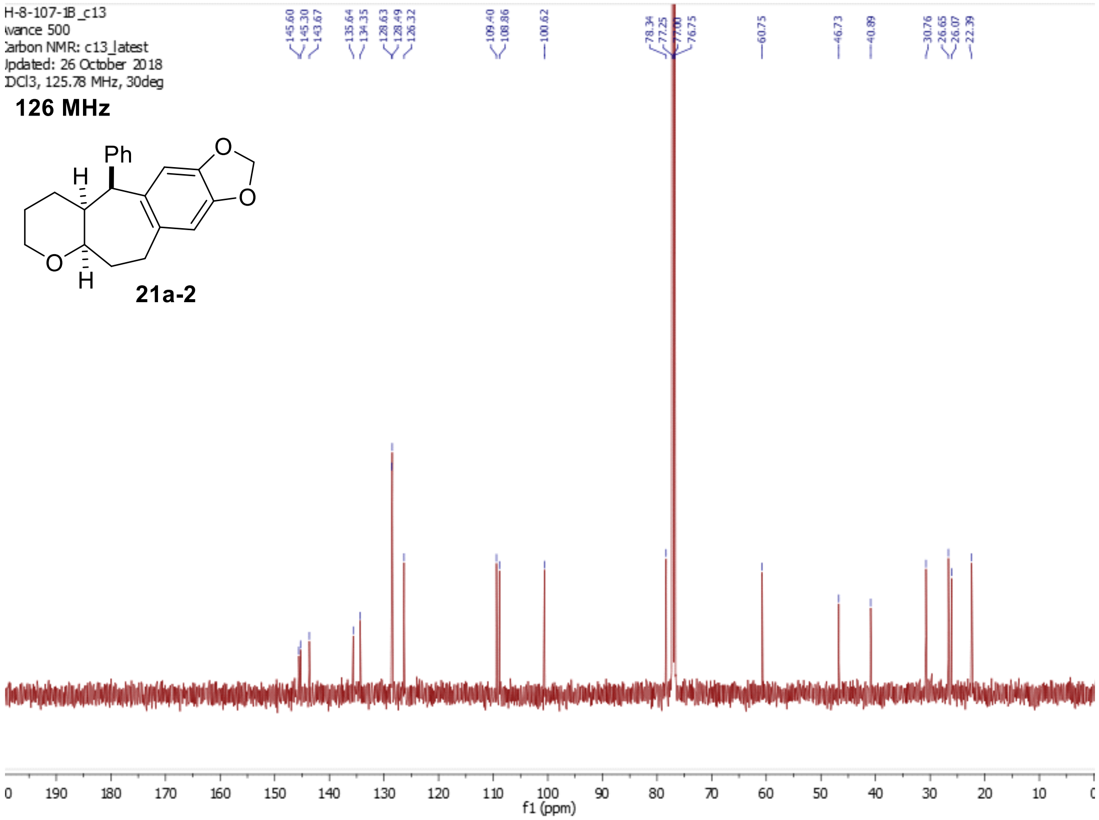

H-8-107-1A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Ph
H
O
O
O
H
7.26
7.25
7.23
7.19
6.62
6.49
5.88
5.87
4.02
3.91
3.89
3.30
3.28
3.26
3.01
2.99
2.77
2.76
2.74
2.72
2.30
2.28
2.21
1.94
1.91
1.81
1.79
1.77
1.75
1.73
1.70
1.68
1.64
1.62
1.58
1.91
3.39
1.08
0.92
2.14
1.00
1.07
1.94
0.82
1.13
1.20
0.94
1.15
4.18
1.95
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

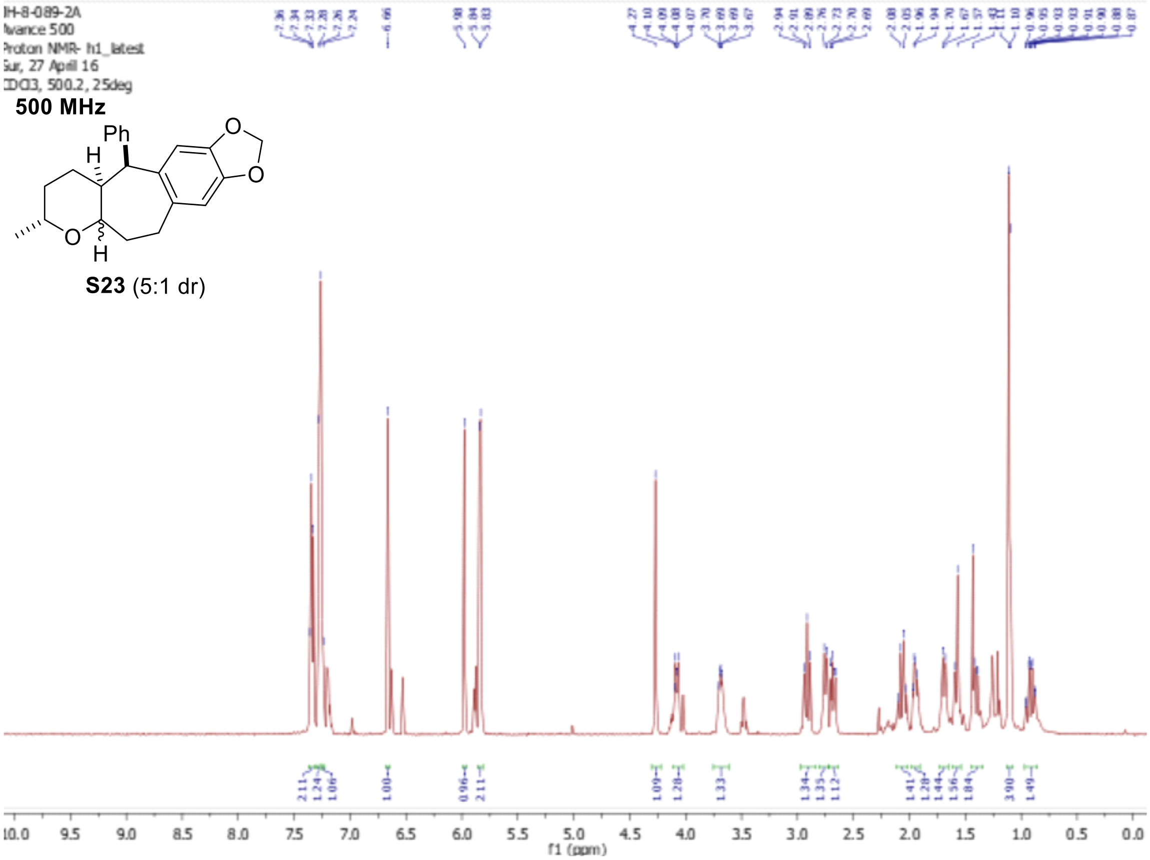
21a-1


H-8-107-1A_c13
vance 500
arbon NMR: c13_latest
pdated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
Ph
H
O
O
O
H
145.85
145.68
141.97
134.50
129.71
127.83
126.13
111.52
110.65
100.82
78.72
77.25
77.00
76.75
67.86
56.14
43.67
34.26
31.11
30.68
30.32
27.24
26.64
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

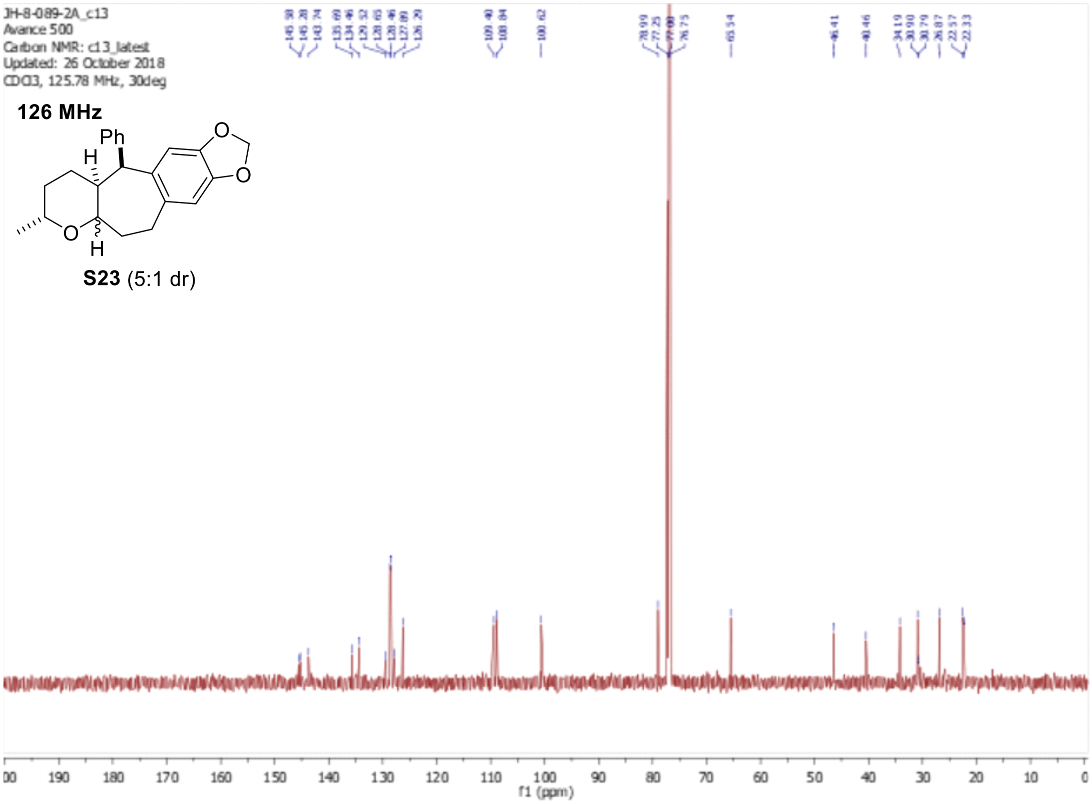
21a-1


H-8-107-1B
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
Ph
H
O
O
O
H
21a-2
7.36
7.35
7.33
7.28
7.27
7.26
6.67
5.98
5.84
5.83
4.24
4.07
4.06
4.05
3.63
3.61
2.92
2.90
2.82
2.80
2.71
2.70
2.69
2.67
2.14
2.12
2.09
2.07
2.05
1.92
1.91
1.90
1.82
1.81
1.80
1.72
1.69
1.52
1.50
2.09
2.05
0.96
0.91
2.12
1.00
0.97
2.10
0.95
0.98
0.99
1.07
1.06
1.08
1.30
1.21
.0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

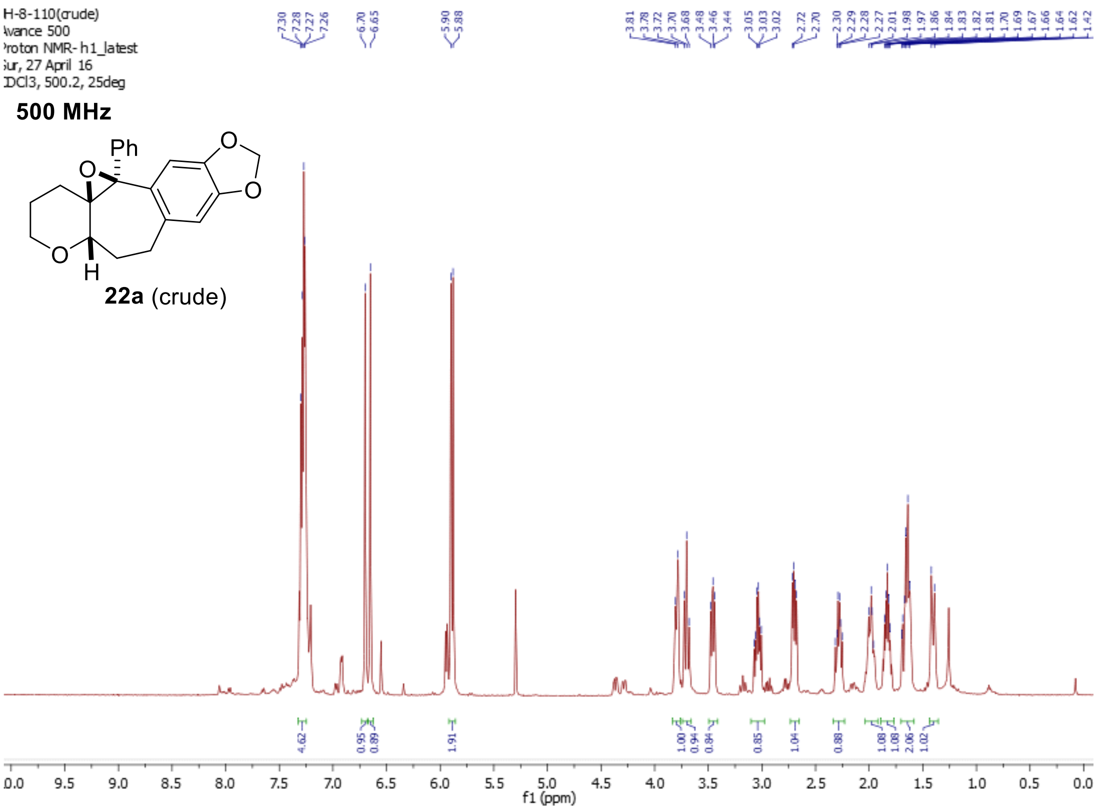

H-8-107-1B_c13
vance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
Ph
H
O
O
O
H
21a-2
145.60
145.30
143.67
135.64
134.35
128.63
128.49
126.32
109.40
108.86
100.62
78.34
77.25
77.00
76.75
60.75
46.73
40.89
30.76
26.65
26.07
22.39
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

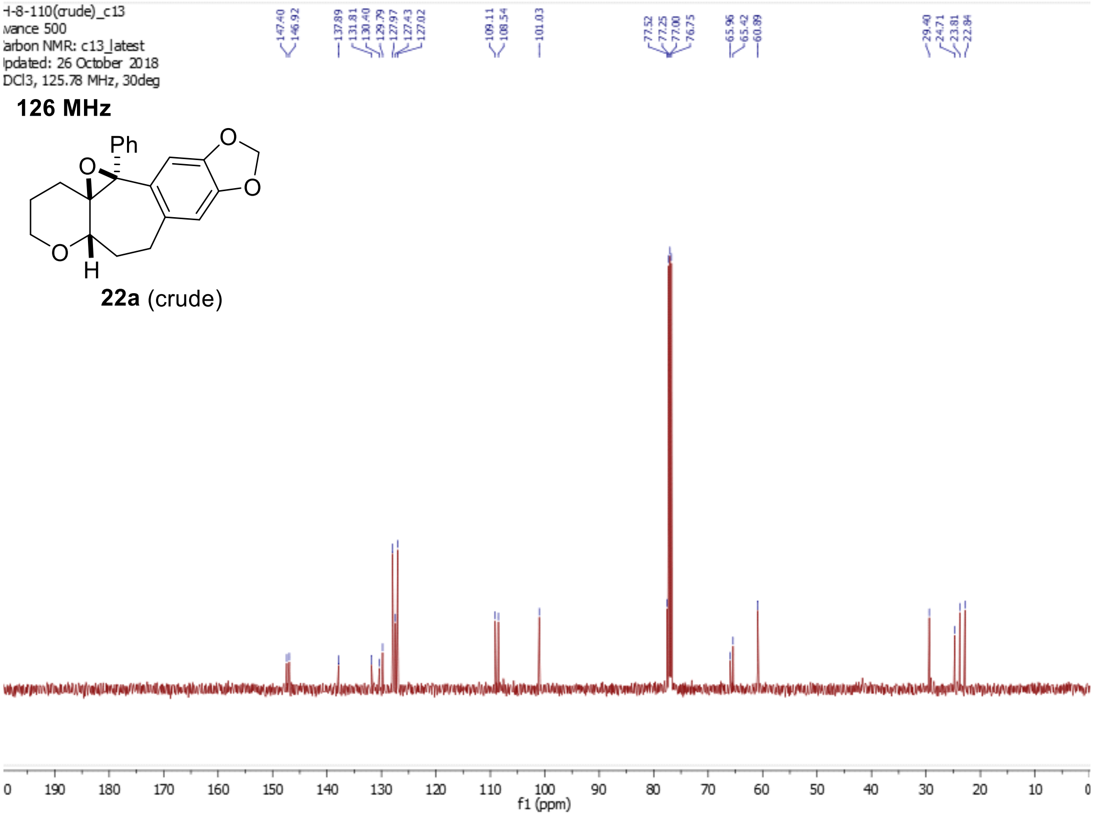


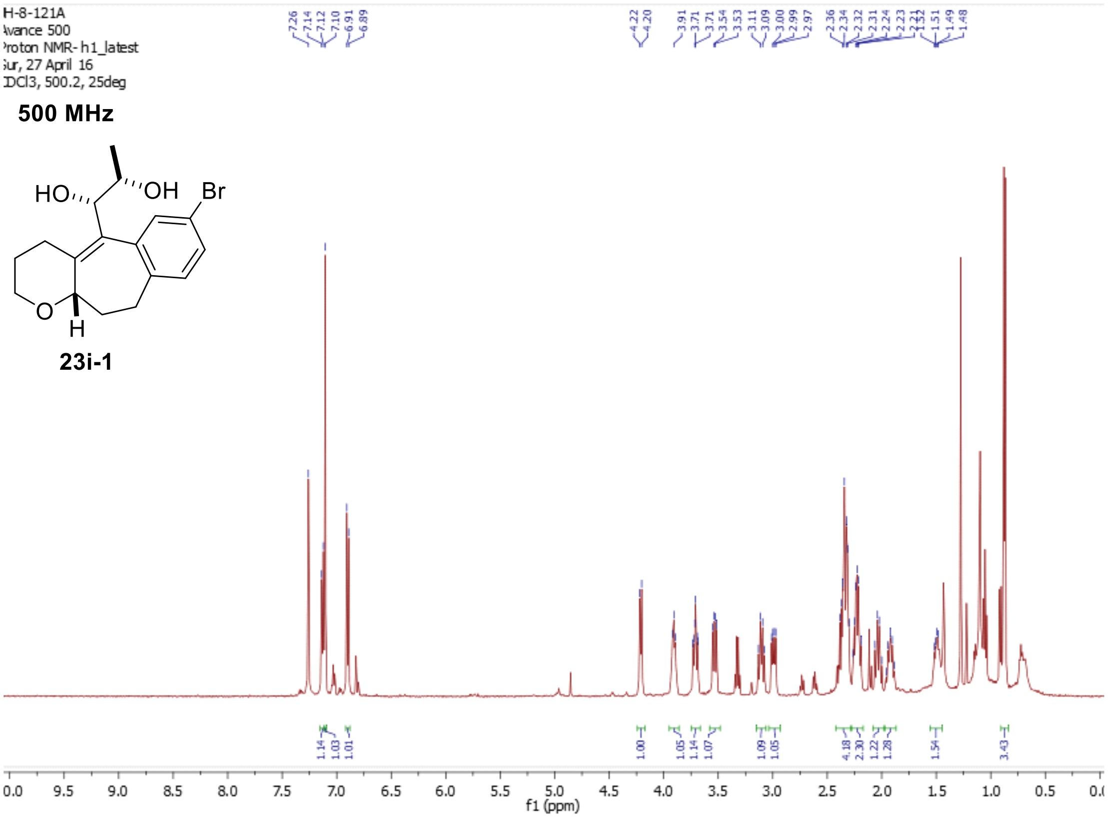
JH-8-089-2A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Ph
H
O
O
O
H
S23 (5:1 dr)
7.36
7.34
7.33
7.28
7.26
7.24
6.66
5.98
5.84
5.83
4.27
4.10
4.09
4.08
4.07
3.70
3.69
3.69
3.67
2.94
2.91
2.89
2.76
2.73
2.70
2.69
2.08
2.05
1.96
1.94
1.70
1.67
1.57
1.42
1.11
1.10
0.96
0.95
0.93
0.93
0.91
0.90
0.88
0.87
2.11
1.24
1.06
1.00
0.96
2.11
1.09
1.28
1.33
1.34
1.35
1.12
1.41
1.28
1.44
1.56
1.84
3.90
1.49
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

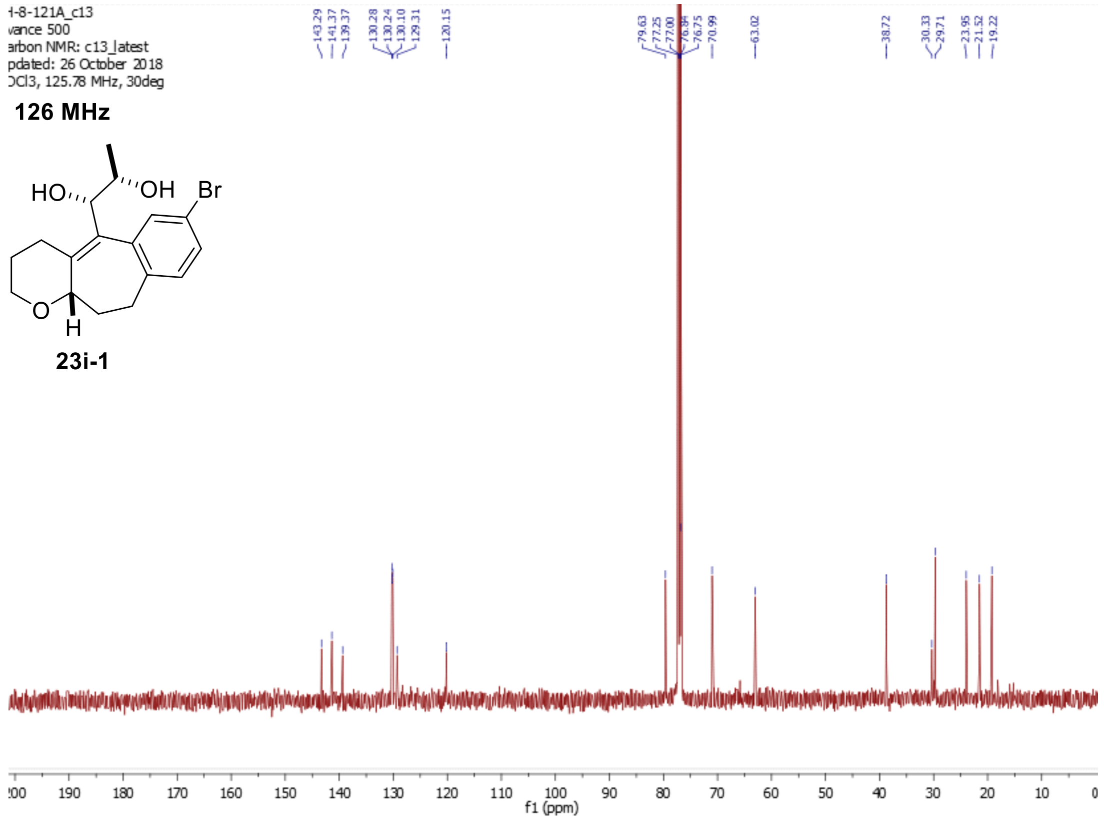


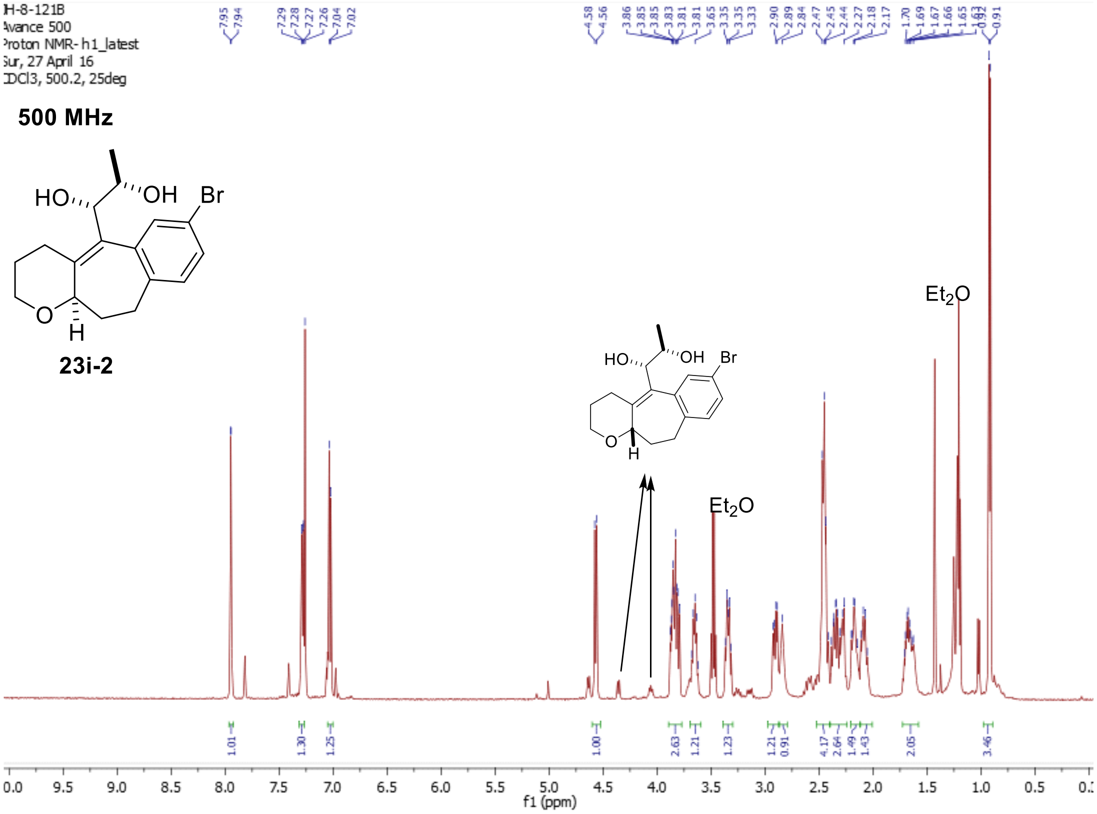
JH-8-089-2A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Ph
H
O
O
O
H
S23 (5:1 dr)
145.58
145.28
143.74
135.69
134.46
129.52
128.65
128.46
127.89
126.29
109.40
108.84
100.62
78.99
77.25
77.00
76.75
65.54
46.41
40.46
34.19
30.90
30.79
26.87
22.57
22.33
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

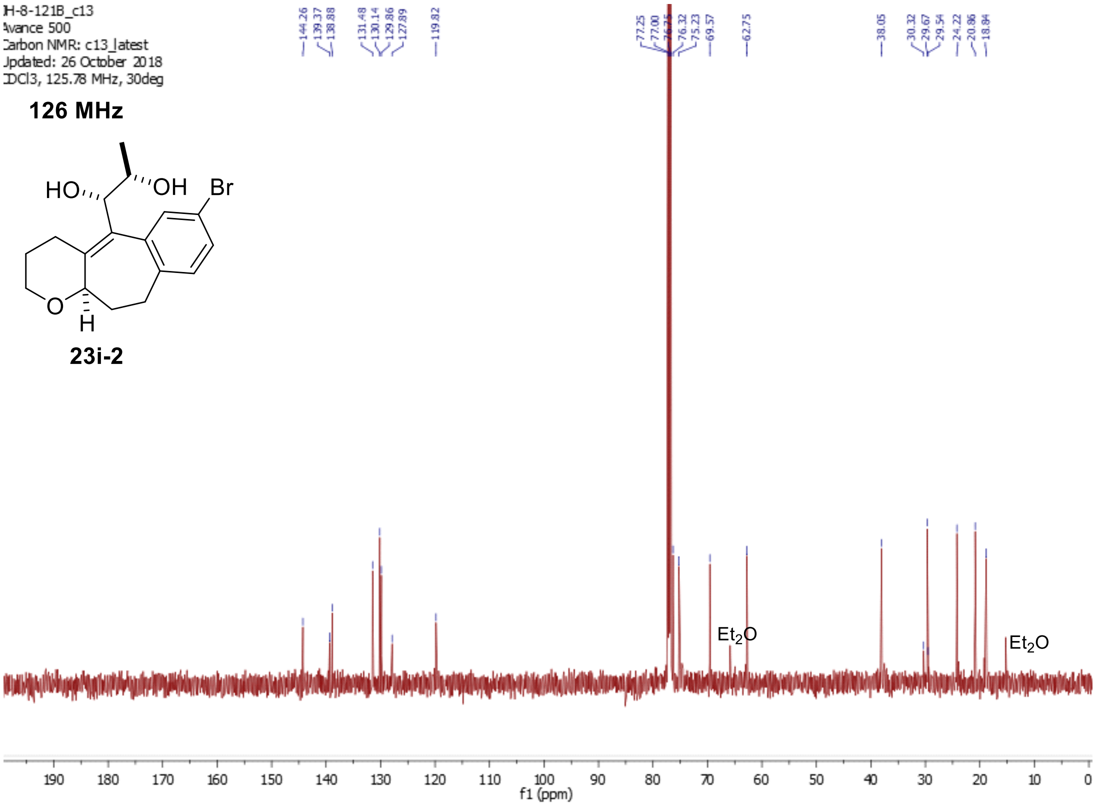

H-8-110(crude)
ıvance 500
Proton NMR- h1_latest
Sur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
Ph
O
O
O
O
H
22a (crude)
7.30
7.28
7.27
7.26
6.70
6.65
5.90
5.88
3.81
3.78
3.72
3.70
3.68
3.48
3.46
3.44
3.05
3.03
3.02
2.72
2.70
2.30
2.29
2.28
2.27
2.01
1.98
1.97
1.86
1.84
1.83
1.82
1.81
1.70
1.69
1.67
1.66
1.64
1.62
1.42
4.62
0.95
0.89
1.91
1.00
0.94
0.84
0.85
1.04
0.88
1.08
1.08
2.06
1.02
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

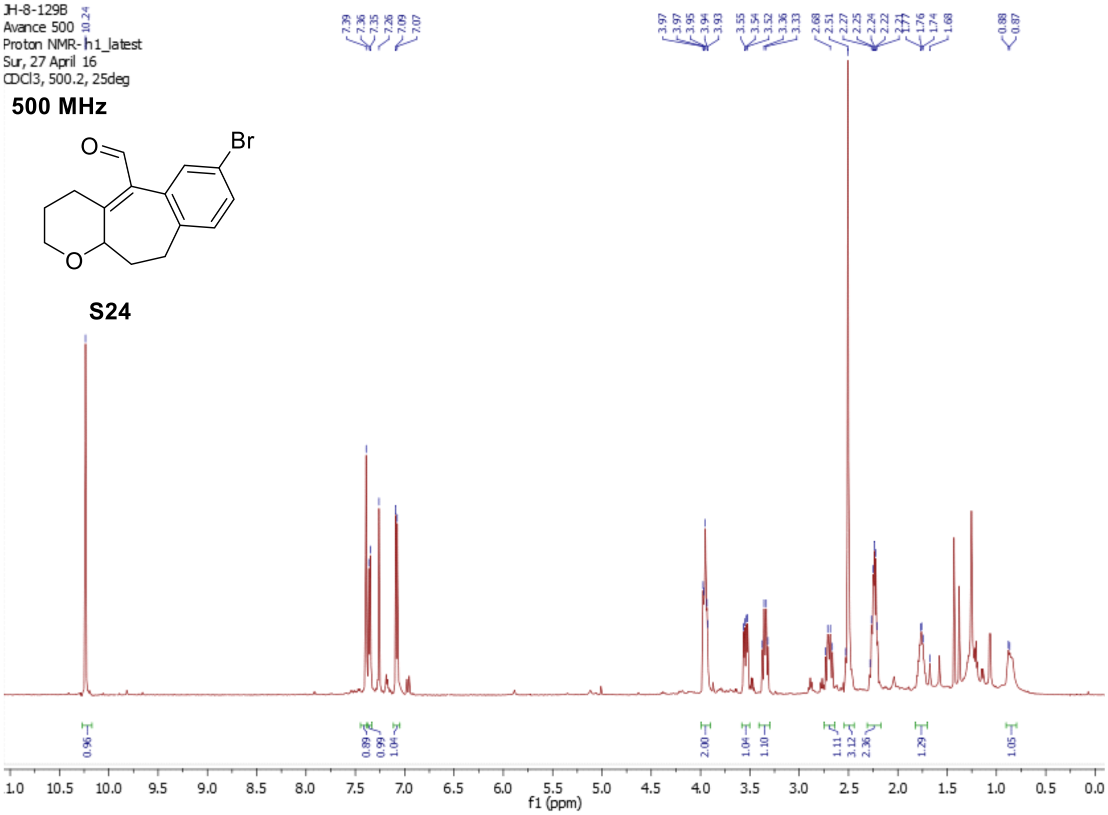

H-8-110(crude)_c13
vance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
Ph
O
O
O
O
H
22a (crude)
147.40
146.92
137.89
131.81
130.40
129.79
127.97
127.43
127.02
109.11
108.54
101.03
77.52
77.25
77.00
76.75
65.96
65.42
60.89
29.40
24.71
23.81
22.84
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

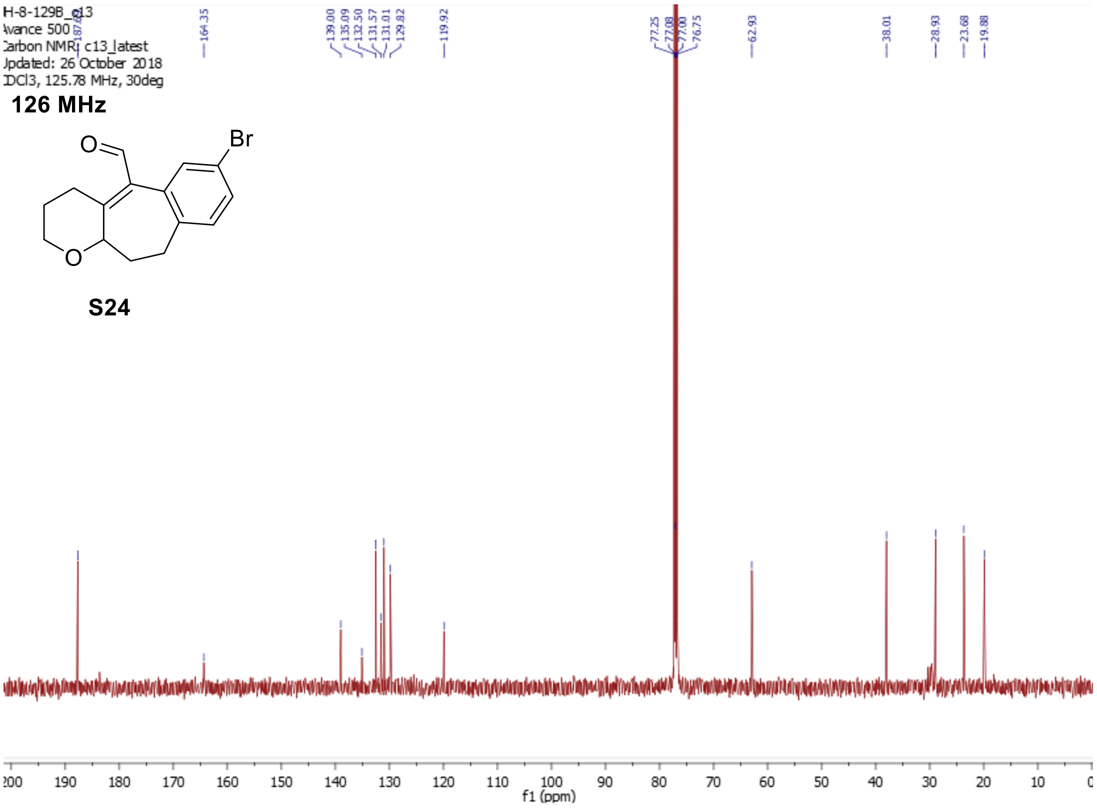

H-8-121A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
HO
OH
Br
O
H
23i-1
7.26
7.14
7.12
7.10
6.91
6.89
4.22
4.20
3.91
3.71
3.71
3.54
3.53
3.11
3.09
3.00
2.99
2.97
2.36
2.34
2.32
2.31
2.24
2.23
2.21
1.52
1.51
1.49
1.48
1.14
1.03
1.01
1.00
1.05
1.14
1.07
1.09
1.05
4.18
2.30
1.22
1.28
1.54
3.43
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

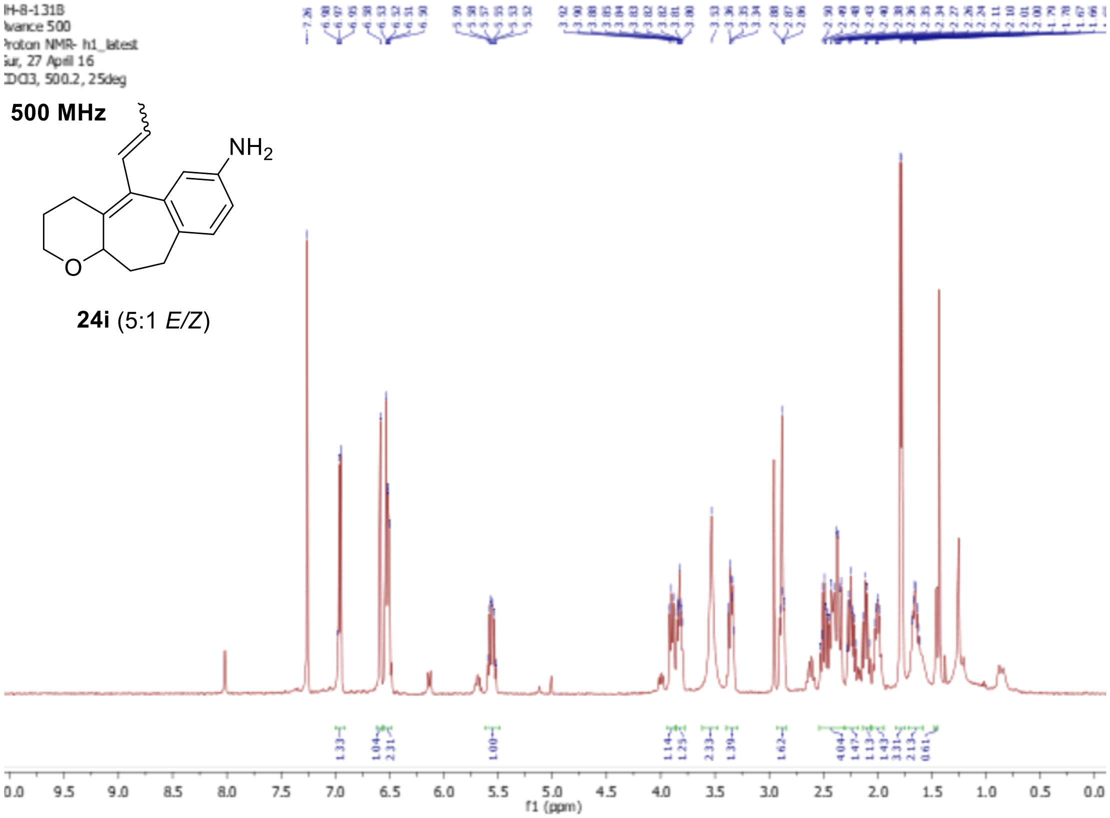

H-8-121A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
HO
OH
Br
O
H
23i-1
143.29
141.37
139.37
130.28
130.24
130.10
129.31
120.15
79.63
77.25
77.00
76.84
76.75
70.99
63.02
38.72
30.33
29.71
23.95
21.52
19.22
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H-8-121B
vance 500
roton NMR- h1_latest
ur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
HO
OH
Br
O
H
23i-2
Et2O
Et2O
HO
OH
Br
O
H
7.95
7.94
7.29
7.28
7.27
7.26
7.04
7.02
4.58
4.56
3.86
3.85
3.85
3.83
3.83
3.81
3.81
3.65
3.35
3.35
3.33
2.90
2.89
2.84
2.47
2.45
2.44
2.27
2.18
2.17
1.70
1.69
1.67
1.66
1.65
1.63
0.92
0.91
1.01
1.30
1.25
1.00
2.63
1.21
1.23
1.21
0.91
4.17
2.64
1.49
1.43
2.05
3.46
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

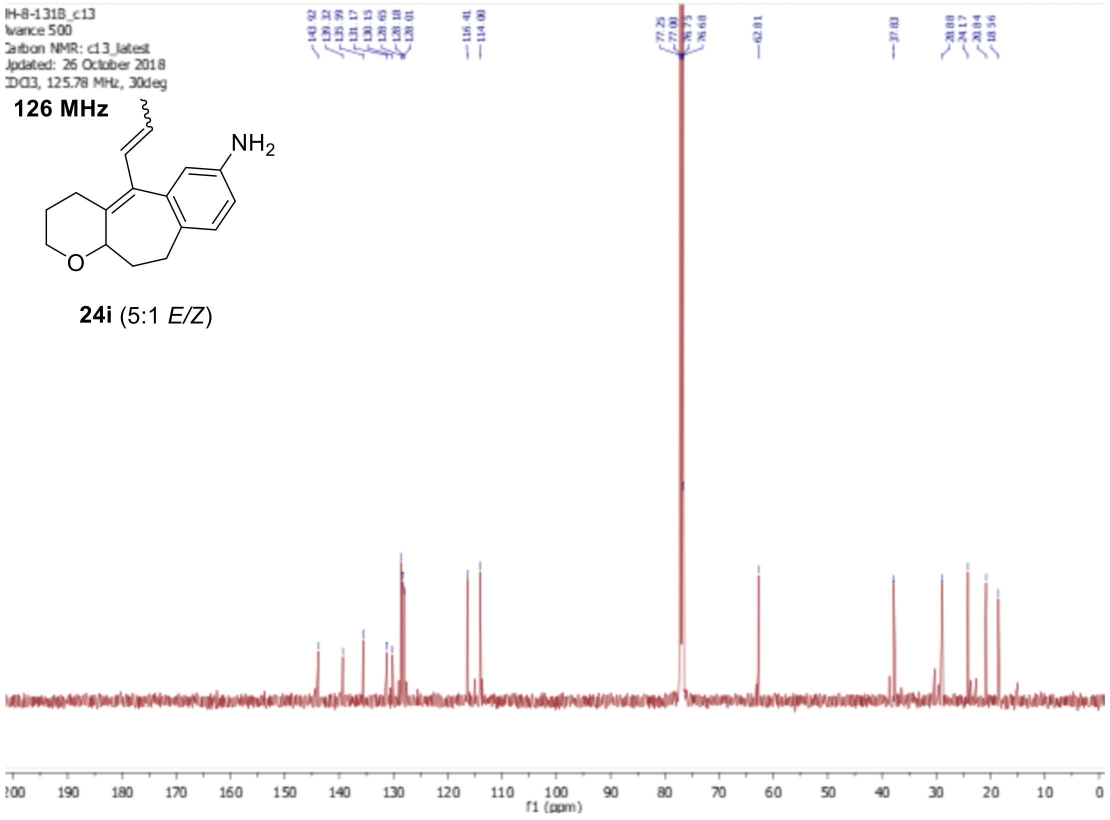

H-8-121B_c13
vance 500
arbon NMR: c13_latest
pdated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
HO
OH
Br
O
H
23i-2
144.26
139.37
138.88
131.48
130.14
129.86
127.89
119.82
77.25
77.00
76.75
76.32
75.23
69.57
62.75
38.05
30.32
29.67
29.54
24.22
20.86
18.84
Et2O
Et2O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


JH-8-129B
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
O
Br
O
S24
10.24
7.39
7.36
7.35
7.26
7.09
7.07
3.97
3.97
3.95
3.94
3.93
3.55
3.54
3.52
3.36
3.33
2.68
2.51
2.27
2.25
2.24
2.22
2.21
1.77
1.76
1.74
1.68
0.88
0.87
0.96
0.89
0.99
1.04
2.00
1.04
1.10
1.11
3.12
2.36
1.29
1.05
1.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

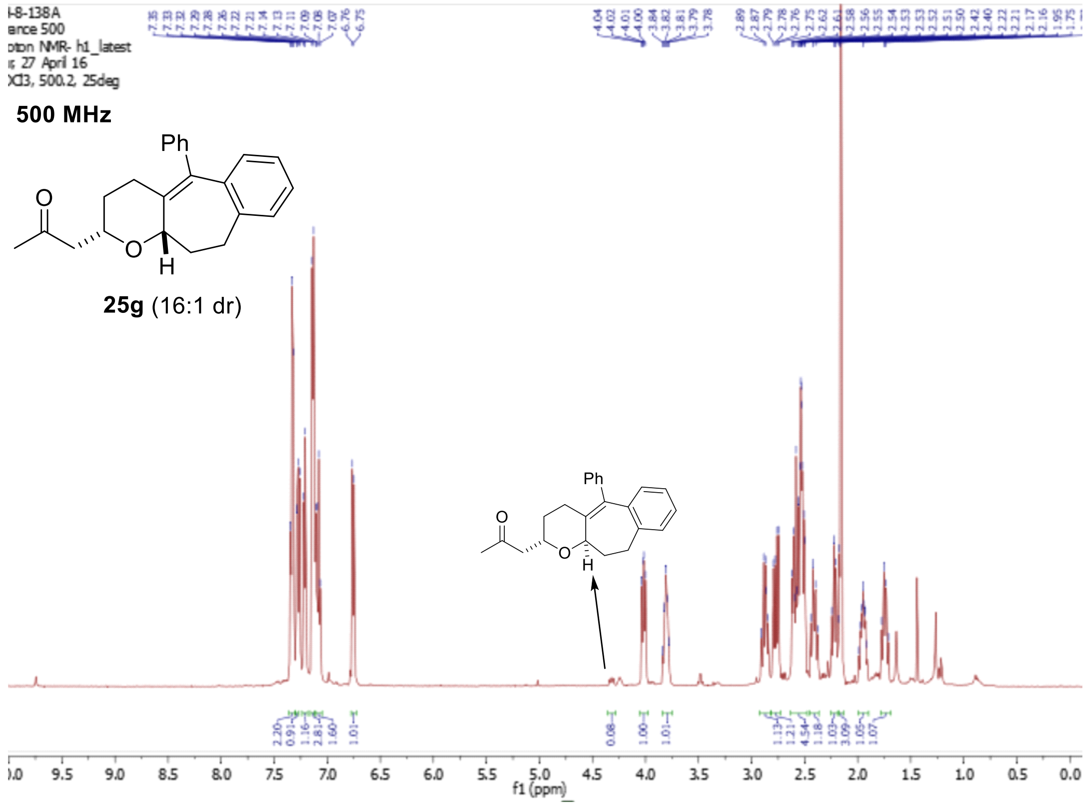

H-8-129B_c13
Avance 500
Carbon NMR; c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
O
Br
O
S24
187.65
164.35
139.00
135.09
132.50
131.57
131.01
129.82
119.92
77.25
77.08
77.00
76.75
62.93
38.01
28.93
23.68
19.88
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

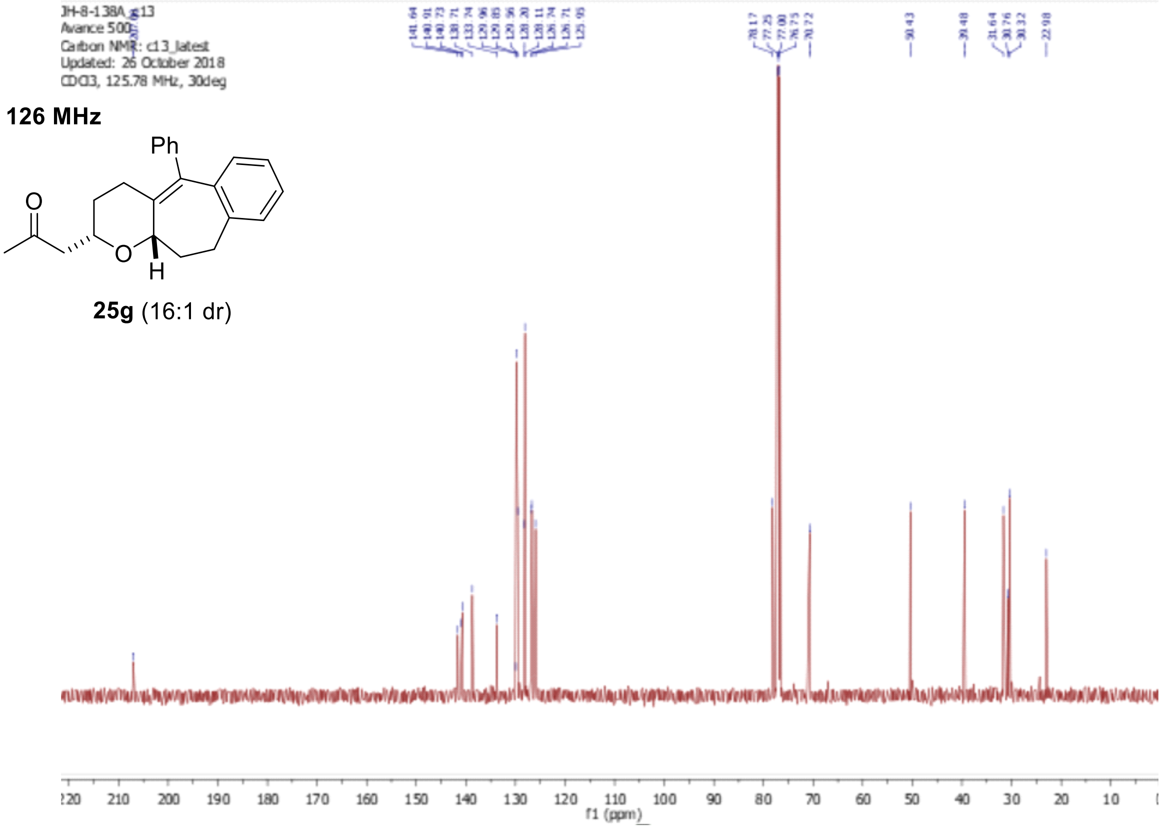


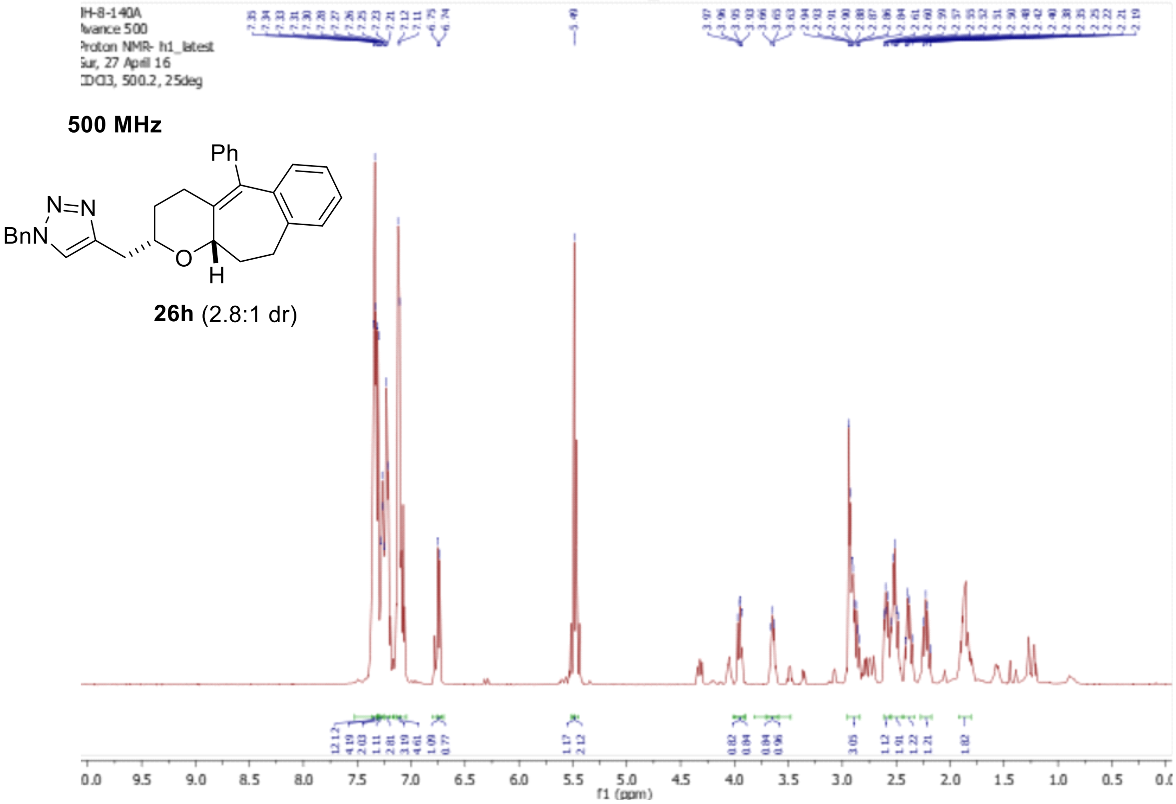
24i (5:1 *E*/*Z*)

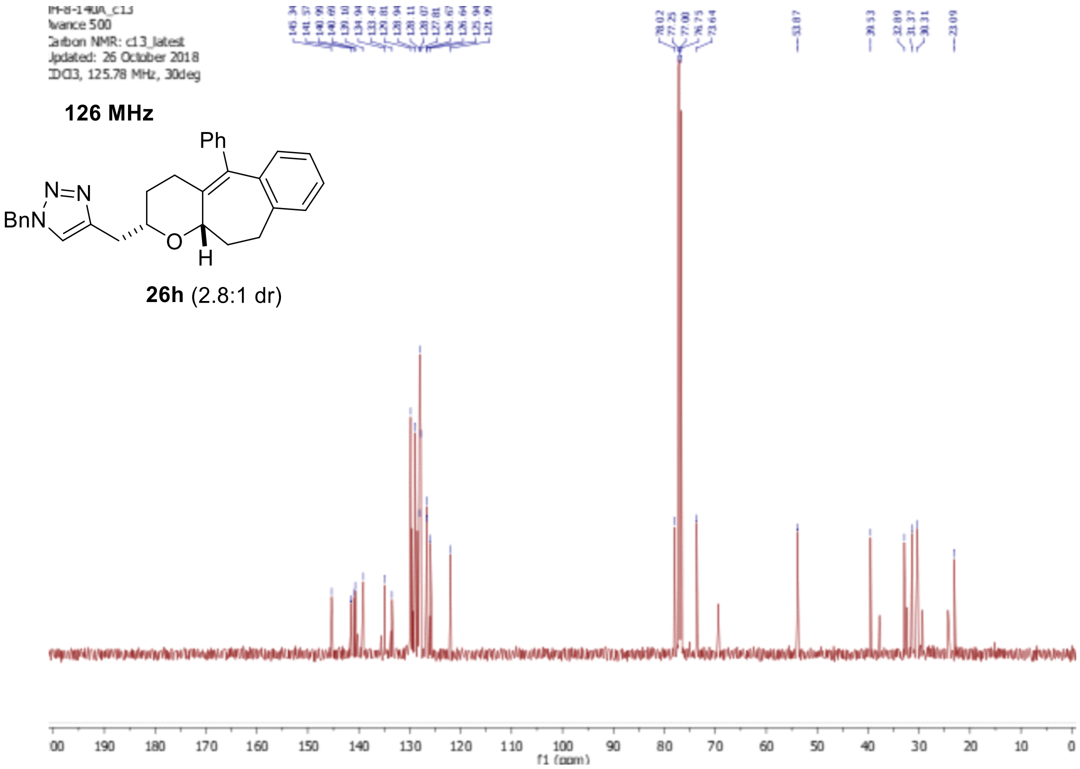


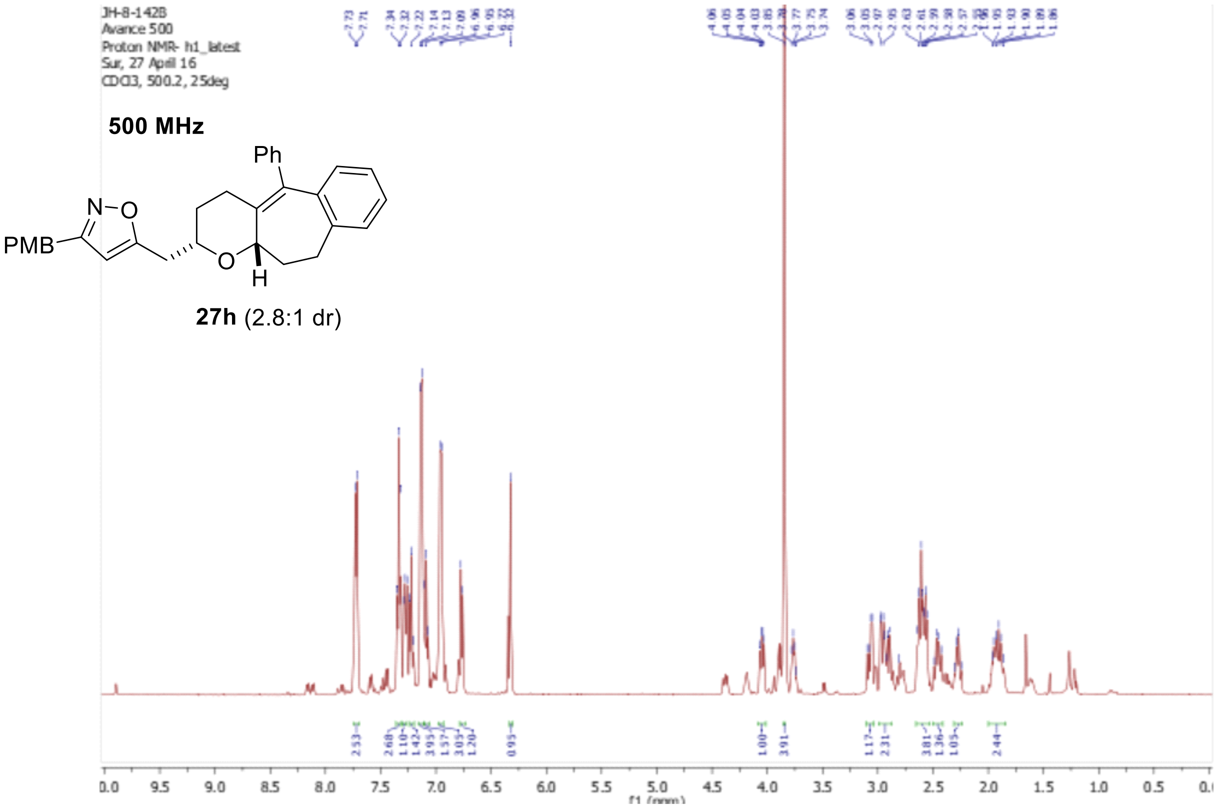
24i (5:1 *E*/*Z*)


I-8-138A
ance 500
oton NMR- h1_latest
: 27 April 16
XCl3, 500.2, 25deg
500 MHz
Ph
O
O
H
25g (16:1 dr)
7.35 7.33 7.32 7.29 7.28 7.26 7.22 7.21 7.14 7.13 7.11 7.09 7.08 7.07 6.76 6.75
4.04 4.02 4.01 4.00 3.84 3.82 3.81 3.79 3.78
2.89 2.87 2.79 2.78 2.76 2.75 2.62 2.61 2.58 2.56 2.55 2.54 2.53 2.53 2.52 2.51 2.50 2.42 2.40 2.22 2.21 2.17 2.16 1.95 1.75
2.20 0.91 1.16 2.81 1.60 1.01
0.08 1.00 1.01
1.13 1.21 4.54 1.18 1.03 3.09 1.05 1.07
0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


JH-8-138A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Ph
O
O
H
25g (16:1 dr)
141.64 140.91 140.73 138.71 133.74 129.96 129.85 129.36 128.20 128.11 126.74 126.71 125.95
78.17 77.25 77.00 76.75 70.72
50.43
39.48
31.64 30.76 30.32
22.98
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

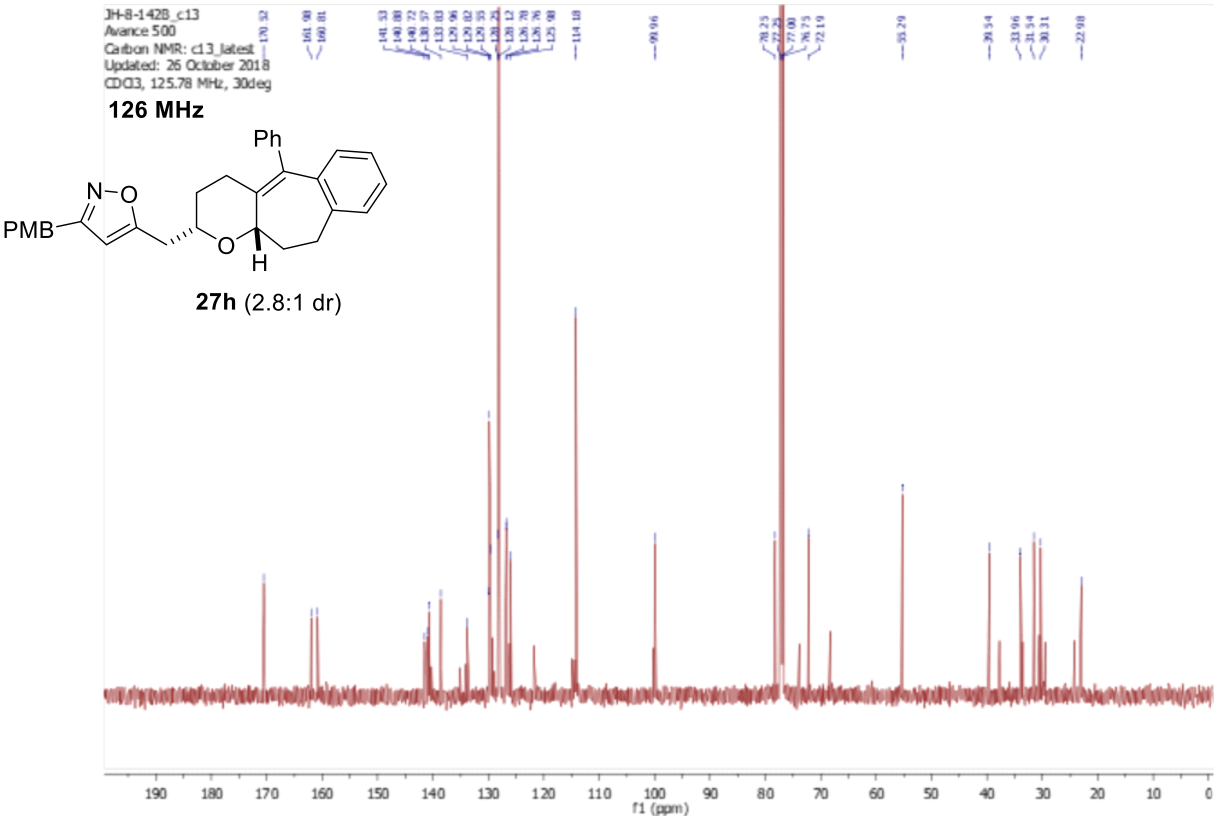

IH-8-140A
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
500 MHz
Ph
N=N
BnN
O
H
26h (2.8:1 dr)
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


IH-8-140A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Ph
N=N
BnN
O
H
26h (2.8:1 dr)
78.02
77.25
77.00
76.75
73.64
53.87
39.53
32.89
31.37
30.31
23.09
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



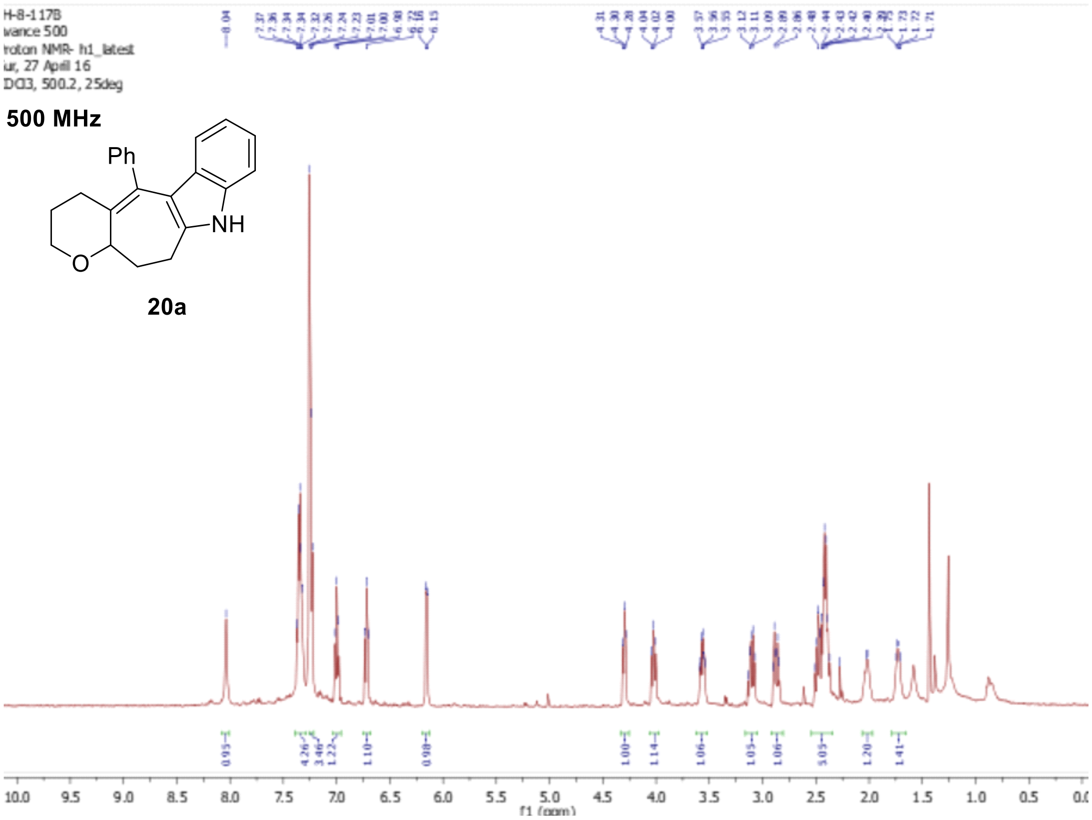
500 MHz

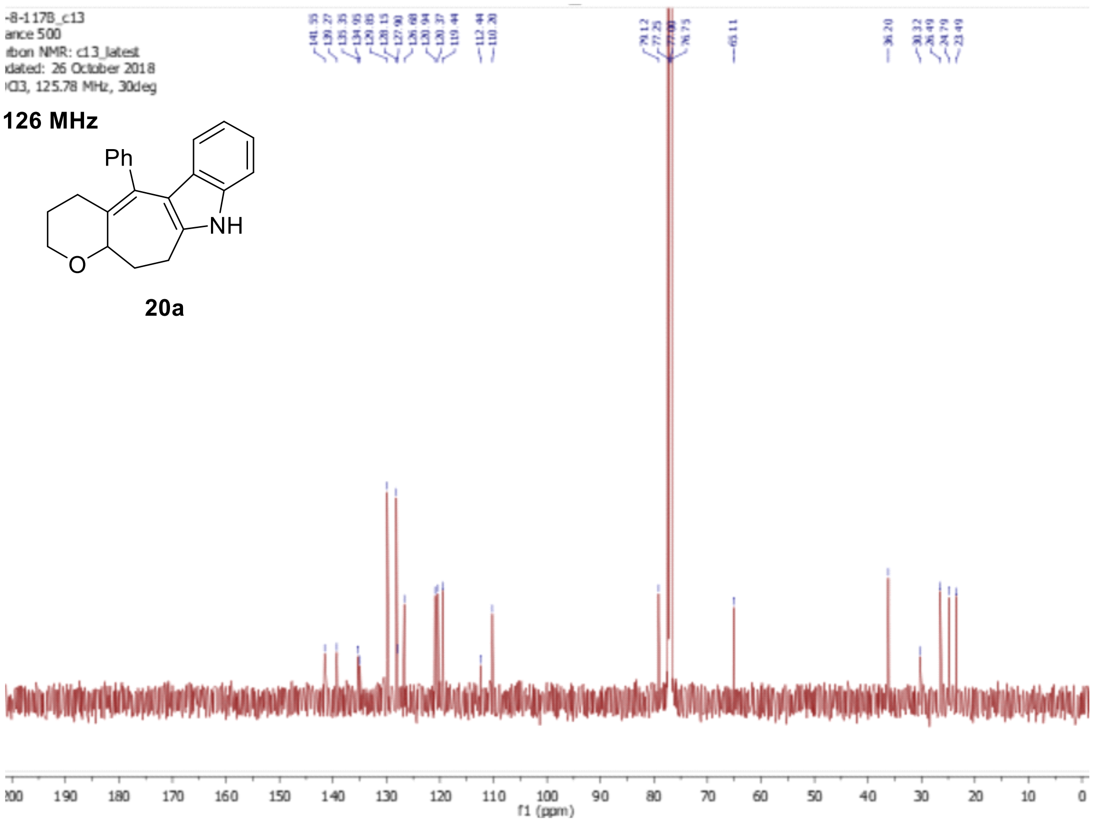
27h (2.8:1 dr)

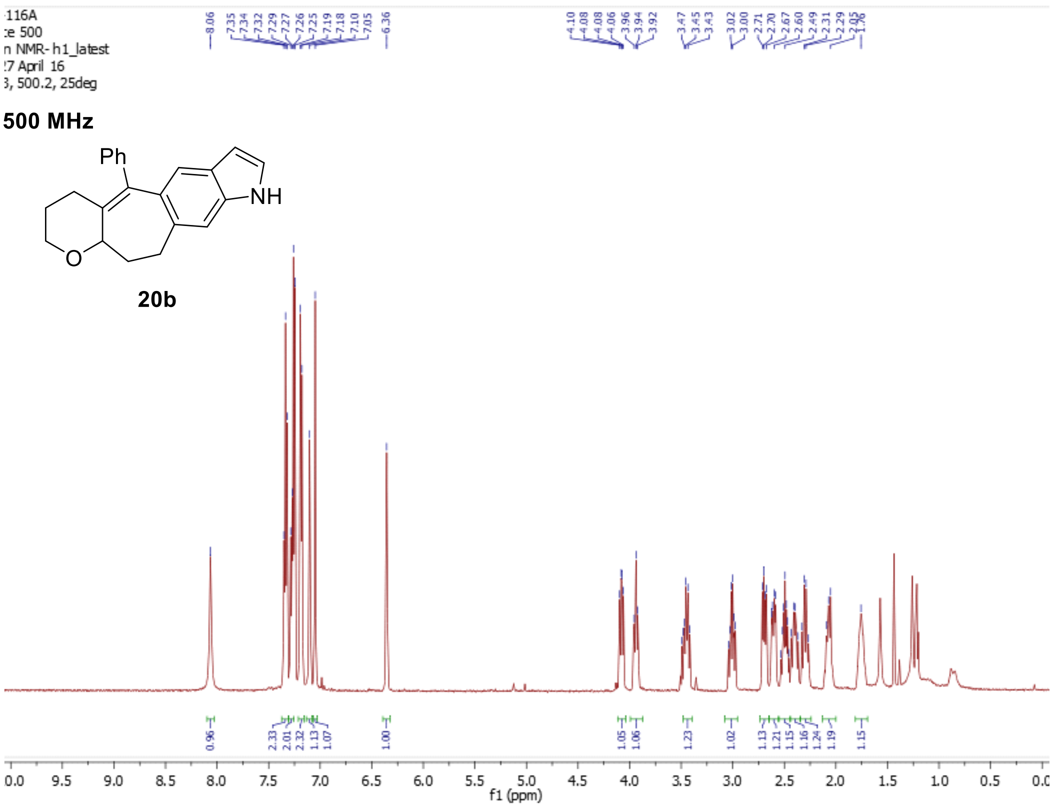


126 MHz

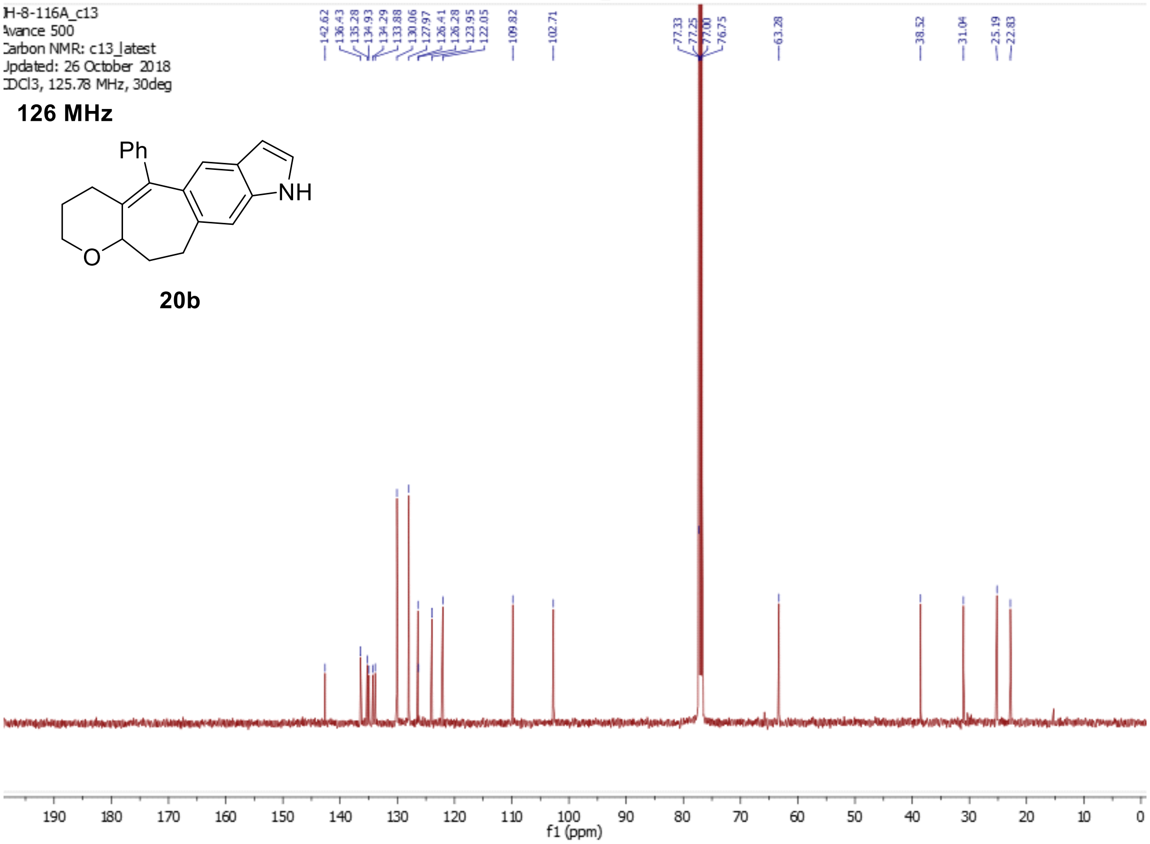
27h (2.8:1 dr)


H-8-117B
vance 500
roton NMR- h1_latest
ur, 27 April 16
DCl3, 500.2, 25deg
500 MHz
Ph
NH
O
20a
8.04
4.31
4.30
4.28
4.04
4.02
4.00
3.57
3.56
3.55
3.12
3.11
3.09
2.89
2.88
2.86
1.73
1.72
1.71
0.95
4.26
3.46
1.22
1.10
0.98
1.00
1.14
1.06
1.05
1.06
5.05
1.20
1.41
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

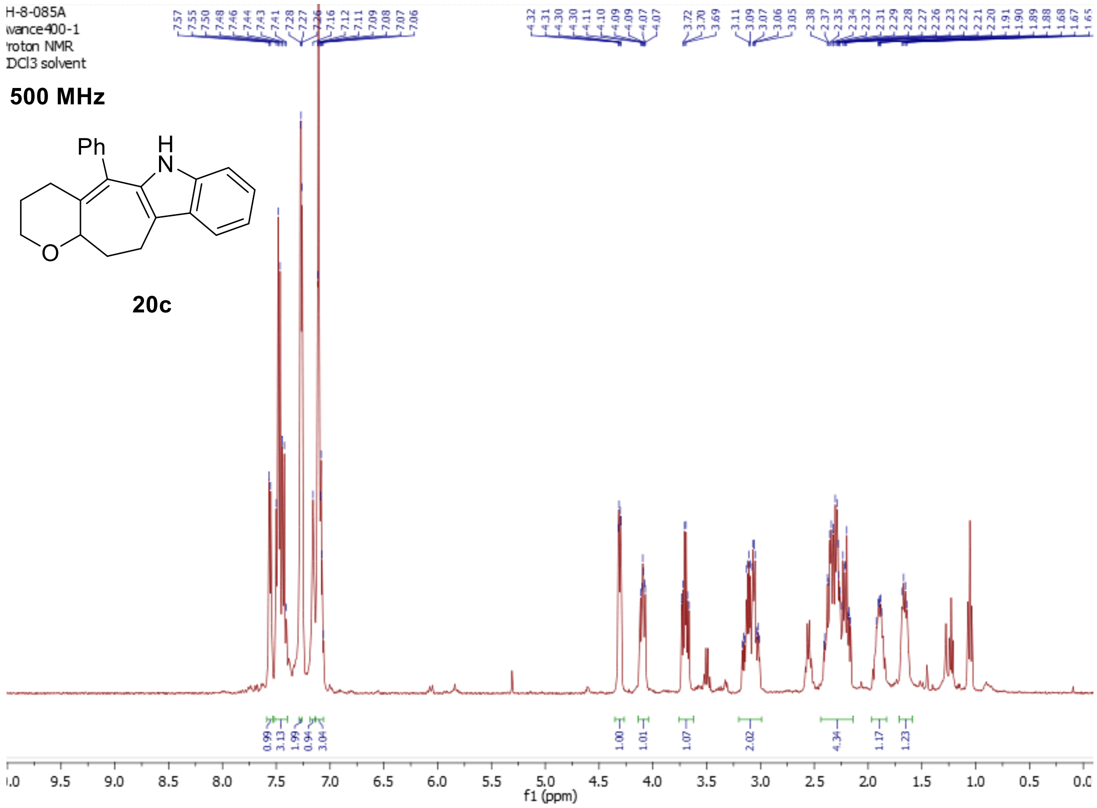

-8-117B_c13
ance 500
rbon NMR: c13_latest
dated: 26 October 2018
Cl3, 125.78 MHz, 30deg
126 MHz
Ph
NH
O
20a
141.55
139.27
135.35
134.95
129.85
128.15
127.90
126.68
120.94
120.37
119.44
112.44
110.20
79.12
77.25
77.00
76.75
65.11
36.20
30.32
26.49
24.79
23.49
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

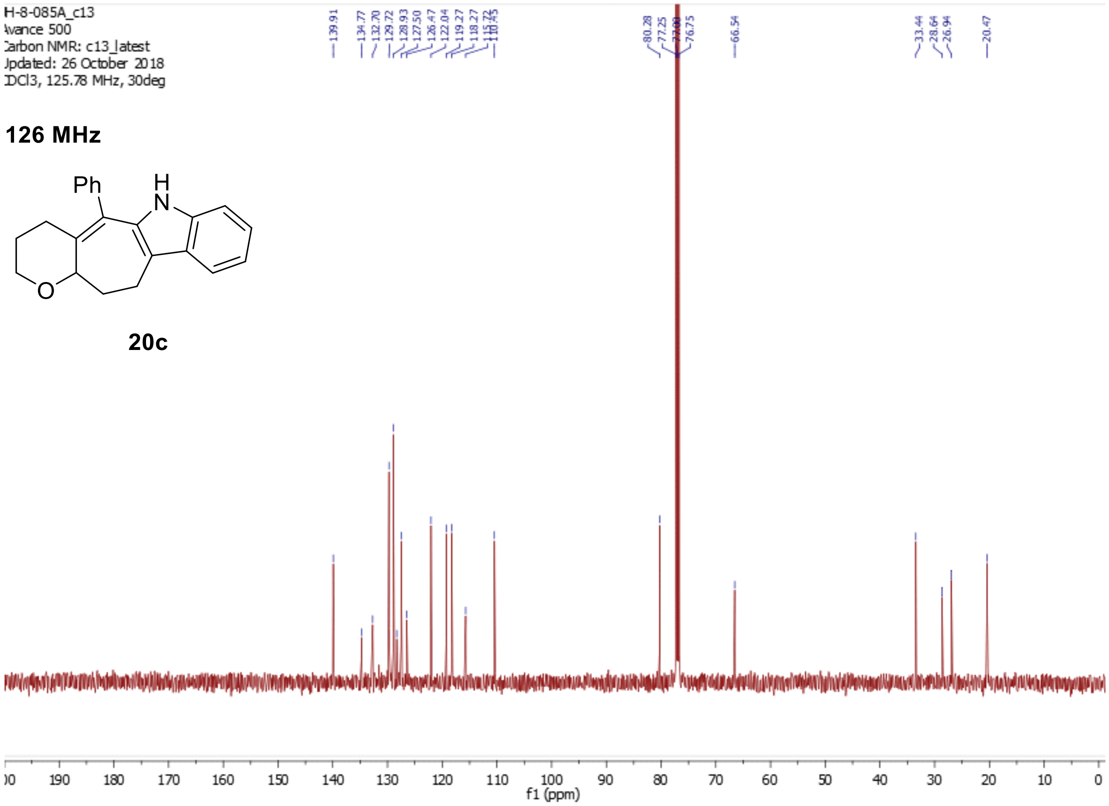


116A
ce 500
n NMR- h1_latest
27 April 16
3, 500.2, 25deg
500 MHz
Ph
NH
O
20b
8.06
7.35
7.34
7.32
7.29
7.27
7.26
7.25
7.19
7.18
7.10
7.05
6.36
4.10
4.08
4.08
4.06
3.96
3.94
3.92
3.47
3.45
3.43
3.02
3.00
2.71
2.70
2.67
2.60
2.49
2.31
2.29
2.05
1.76
0.96
2.33
2.01
2.32
1.13
1.07
1.00
1.05
1.06
1.23
1.02
1.13
1.21
1.15
1.16
1.24
1.19
1.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



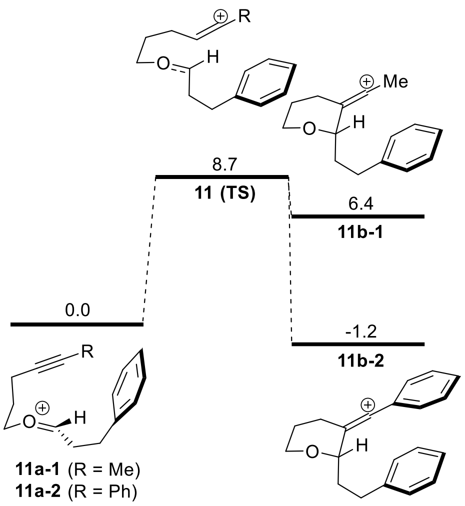
H-8-116A_c13
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
126 MHz
Ph
NH
O
20b
142.62
136.43
135.28
134.93
134.29
133.88
130.06
127.97
126.41
126.28
123.95
122.05
109.82
102.71
77.33
77.25
77.00
76.75
63.28
38.52
31.04
25.19
22.83
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H-8-085A
wance400-1
'roton NMR
DCl3 solvent
500 MHz
7.57
7.55
7.50
7.48
7.46
7.44
7.43
7.41
7.28
7.27
7.26
7.16
7.12
7.11
7.09
7.08
7.07
7.06
4.32
4.31
4.30
4.30
4.11
4.10
4.09
4.09
4.07
4.07
3.72
3.70
3.69
3.11
3.09
3.07
3.06
3.05
2.38
2.37
2.35
2.34
2.32
2.31
2.29
2.28
2.27
2.26
2.23
2.22
2.21
2.20
1.91
1.90
1.89
1.88
1.68
1.67
1.65
Ph
H
N
O
20c
0.99
3.13
1.99
0.94
3.04
1.00
1.01
1.07
2.02
4.34
1.17
1.23
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


H-8-085A_c13
\vance 500
Carbon NMR: c13_latest
Jpdated: 26 October 2018
DCl3, 125.78 MHz, 30deg
126 MHz
139.91
134.77
132.70
129.72
128.93
127.50
126.47
122.04
119.27
118.27
115.72
110.45
80.28
77.25
77.00
76.75
66.54
33.44
28.64
26.94
20.47
Ph
H
N
O
20c
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

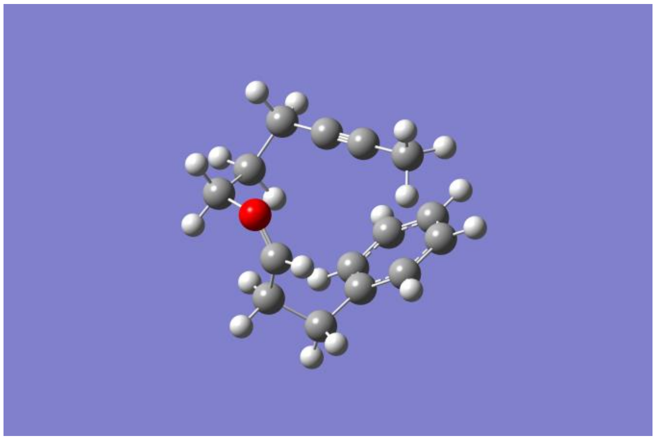
Computational Methods:

Input files for ground state or transition state intermediates of a given reaction were prepared locally using GaussView 6.0 and transferred to the University of Rochester Blue Hive Linux cluster where DFT calculations were carried out in the Gaussian 16 suite of programs. Optimization calculations (either to a ground state or a transition state) were first carried out at the M06-2x functional and Def2TZVP basis set level of theory,[30, 31] with implicit solvation using the Polarizable Continuum Model (PCM = dichloromethane).[32] Intrinsic reaction coordinate (IRC)iv calculations were carried out on the transition state structures to verify that they connected to the associated reactant and product structures. Thereafter, frequency DFT calculations at the M06-2x/Def2TZVP level (PCM = dichloromethane), of the obtained optimized structures were carried out to confirm that ground state structures had zero imaginary frequencies and that transition states had a single imaginary frequency. All shown free energies are ZPE and thermally corrected (reported in Hartree units, at 298.15 K and 1 atm) and were obtained from the frequency calculations.



DFT Optimized Structures

11a-1

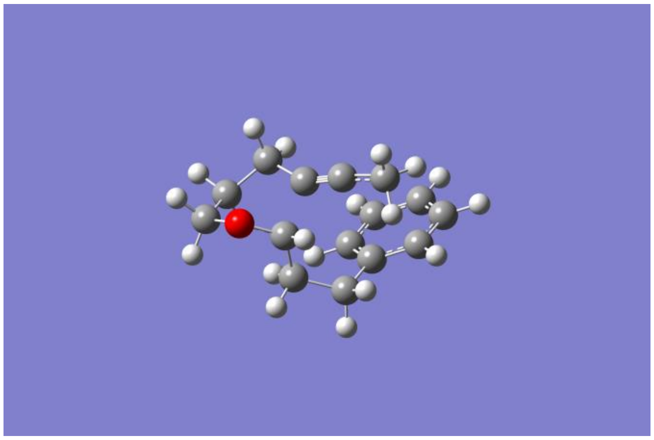


Imaginary Frequencies: 0

ZPE and thermally corrected free energy: -657.679999 Ha

```
 Center    Atomic          Forces (Hartrees/Bohr)
 Number   Number         X             Y             Z
 -------------------------------------------------------------------
      1        6        -0.033778506   -0.023072397   -0.026009855
      2        1         0.001406698   -0.001659511    0.013578900
      3        1         0.012515378   -0.001945708   -0.003722202
      4        6        -0.012274634   -0.027203809    0.015798334
      5        1         0.002616691    0.012184343    0.004740189
      6        1         0.001268686    0.001443613   -0.015793244
      7        6         0.036677908    0.032561971    0.019031334
      8        6        -0.015930393   -0.051451601   -0.031740989
      9        6        -0.011130619    0.059638130    0.080600156
     10        1        -0.010469710    0.005858830   -0.025360129
     11        1         0.017108042   -0.009269989   -0.030087377
     12        1         0.020445405   -0.020550836   -0.001647008
     13        6         0.029734389    0.023631618   -0.006333732
     14        1        -0.006209053   -0.009285478    0.011874592
     15        1        -0.007949863    0.006398891    0.004085740
     16        8        -0.033402757   -0.013127737   -0.018190281
     17        6         0.015900952    0.062734729    0.006326405
     18        1        -0.004300629   -0.013896594    0.006236565
     19        6         0.004431825   -0.041608670   -0.014194430
     20        1        -0.013815710    0.005904664    0.010695588
     21        1         0.006897498    0.007219079   -0.000424150
     22        6         0.028199153   -0.014913520    0.008593356
     23        1        -0.011941710   -0.006198985   -0.004177735
     24        1        -0.003474219    0.011105178   -0.004671257
     25        6        -0.015449116   -0.010871535    0.008631716
     26        6        -0.016667191    0.007928171    0.005722941
     27        6         0.002118518    0.018605551   -0.000127838
     28        6         0.020096129    0.011220562   -0.005655882
     29        6        -0.009242774    0.005551181   -0.000865474
     30        6         0.002861905   -0.021715584    0.000884717
     31        1         0.007156067    0.004846961   -0.003101196
     32        1         0.007071283   -0.004495433   -0.003003921
     33        1         0.000505680   -0.009173036    0.000070205
     34        1        -0.009552347   -0.006286357   -0.000797693
     35        1        -0.001422973    0.009893309   -0.000966346
```

11-1 (TS)



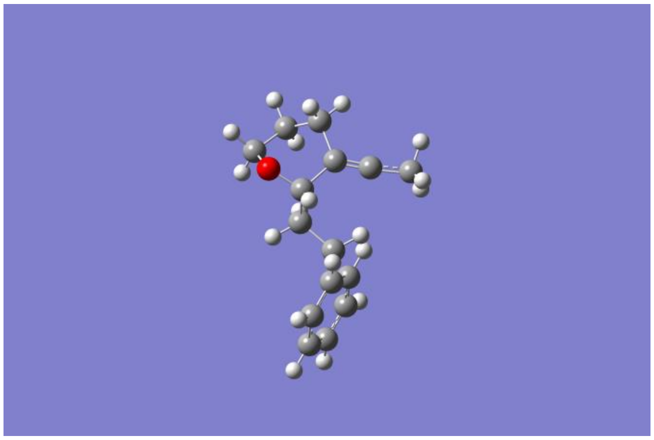
Imaginary Frequencies: 1

ZPE and thermally corrected free energy: -657.666073 Ha (ΔG‡ = 8.7 kcal/mol for this transition state)

```
 Center     Atomic              Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1        6           0.000000120   -0.000005403   -0.000001616
      2        1           0.000001965    0.000001738   -0.000001930
      3        1           0.000001040    0.000000564   -0.000001605
      4        6          -0.000002986    0.000001650   -0.000002029
      5        1           0.000001644    0.000001914   -0.000001638
      6        1           0.000000335   -0.000000424   -0.000002412
      7        6          -0.000217714    0.000028284   -0.000082695
      8        6          -0.000001496    0.000000517    0.000002922
      9        6          -0.000006039    0.000002592   -0.000000500
     10        1           0.000001274    0.000000432    0.000003852
     11        1           0.000001453   -0.000000013    0.000000894
     12        1           0.000000527    0.000002831    0.000002291
     13        6           0.000002582    0.000004411   -0.000003697
     14        1           0.000000494    0.000000476   -0.000001156
     15        1           0.000000896   -0.000000238   -0.000001661
     16        8           0.000000807    0.000001841   -0.000000960
     17        6           0.000221624   -0.000017745    0.000084756
     18        1           0.000000524   -0.000001707    0.000001750
     19        6          -0.000000126    0.000001733    0.000002200
     20        1          -0.000000127   -0.000000494    0.000000028
     21        1           0.000001104   -0.000000815    0.000000314
     22        6          -0.000005456   -0.000002181   -0.000002330
     23        1           0.000000433   -0.000001566    0.000002196
     24        1           0.000001181   -0.000001410    0.000001185
     25        6           0.000004357   -0.000005913   -0.000000103
```

```
    26        6          0.000000163    0.000004516    0.000000374
    27        6         -0.000007261   -0.000004719    0.000000798
    28        6          0.000007272   -0.000006457    0.000001989
    29        6         -0.000000142    0.000006040   -0.000000300
    30        6         -0.000005157   -0.000003407   -0.000001035
    31        1         -0.000000591   -0.000001286   -0.000001651
    32        1         -0.000000512   -0.000002283   -0.000000155
    33        1         -0.000001009   -0.000001768    0.000002148
    34        1         -0.000001969   -0.000000801    0.000000059
    35        1          0.000000788   -0.000000908   -0.000000284
```

11b-1



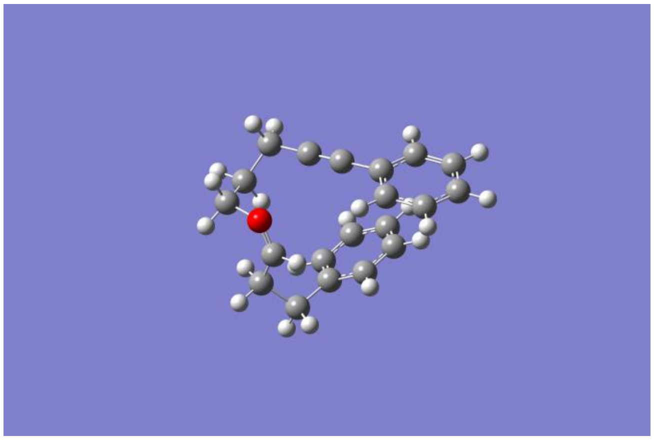
Imaginary Frequencies: 0

ZPE and thermally corrected free energy: -657.669757 Ha (6.4 kcal/mol vs **11a-1**)

```
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X                   Y                   Z
 -------------------------------------------------------------------
      1        6         -0.018960152   -0.028604950    0.007079143
      2        1          0.008898174    0.009116311   -0.012071224
      3        1         -0.008978384    0.008195809    0.007648726
      4        6          0.020074834    0.008022633   -0.012770079
      5        1          0.005018561    0.003143474    0.011767332
      6        1         -0.001715886    0.002121048    0.017425819
      7        6         -0.038696617    0.066918221   -0.055769239
      8        6          0.103743812    0.000519527   -0.017217817
      9        6          0.048734220   -0.021325780   -0.027954420
     10        1         -0.011003612   -0.002767951   -0.002527881
     11        1          0.003108052    0.012095353    0.014718633
     12        1          0.008617017    0.009581789   -0.011215492
     13        6         -0.030460541    0.012006541    0.000680910
     14        1          0.011041942    0.005516965   -0.000114454
```

```
     15      1        0.003438413   -0.016269657   -0.001886373
     16      8       -0.010154658    0.001051233   -0.002989670
     17      6        0.033747146   -0.005475536    0.018348257
     18      1        0.004352294   -0.000211356   -0.012745627
     19      6       -0.022078742    0.014480031   -0.013346422
     20      1        0.010364800   -0.008317500   -0.008503908
     21      1       -0.003280429   -0.014930565   -0.002295862
     22      6        0.007104047    0.013605311    0.032753271
     23      1       -0.004089309    0.003407264   -0.014924465
     24      1       -0.007065911   -0.010178585   -0.002536586
     25      6        0.008089404    0.011500432   -0.014909333
     26      6        0.008365222   -0.010476281   -0.012100029
     27      6        0.000186660   -0.019915839    0.001172420
     28      6       -0.054787753   -0.020915834    0.064251151
     29      6        0.001582783   -0.007891993   -0.011235608
     30      6        0.000361728    0.024866322   -0.000276187
     31      1       -0.003435745   -0.003999709    0.006660603
     32      1       -0.003301252    0.004581443    0.006321227
     33      1       -0.001356714    0.009941461   -0.000017051
     34      1       -0.067143924   -0.039855427    0.049641435
     35      1       -0.000319481   -0.009534206   -0.001061200
```

11a-2



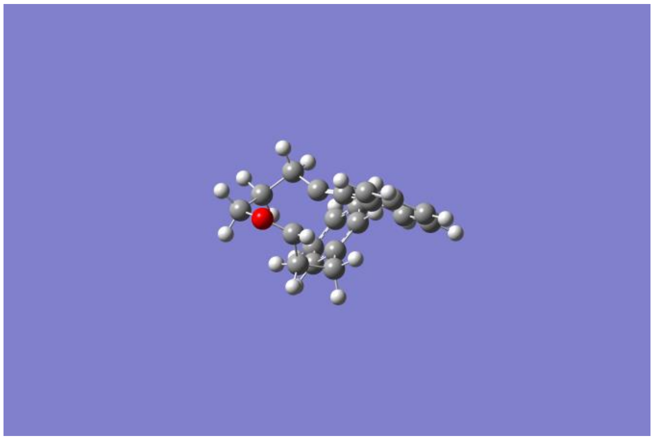
Imaginary Frequencies: 0

ZPE and thermally corrected free energy: -849.364613 Ha

```
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1        6          0.000074051    0.000034380    0.000019754
      2        1         -0.000187887    0.000195494   -0.000334373
      3        1         -0.000347788    0.000250583   -0.000479096
```

4	6	-0.000221724	-0.000664105	-0.000440037
5	1	-0.000112575	0.000297270	-0.000065871
6	1	-0.000081377	-0.000105463	0.000053352
7	6	0.001571325	-0.000411093	0.002328520
8	6	-0.033455342	0.015246665	-0.045982752
9	6	0.000291942	-0.000118509	-0.000136902
10	1	-0.000001088	-0.000054578	-0.000030575
11	1	-0.000160165	-0.000000862	0.000009635
12	8	0.000193782	0.000419536	0.000153693
13	6	-0.000567651	-0.000452193	0.000277300
14	1	-0.000000788	-0.000595965	0.000288994
15	6	0.000176016	0.000056817	-0.000124051
16	1	0.000112238	-0.000040806	-0.000050367
17	1	0.000114055	-0.000043123	0.000154074
18	6	-0.000109904	-0.000055719	0.000039285
19	1	0.000029663	0.000072675	-0.000062552
20	1	0.000068824	-0.000048652	-0.000024215
21	6	0.000231722	0.000063279	0.000075525
22	6	0.000005215	-0.000122775	-0.000185442
23	6	-0.000764818	-0.000273210	-0.000018911
24	6	-0.000016235	-0.000106553	-0.000174439
25	6	0.000019469	0.000245840	-0.000115315
26	6	0.000169232	-0.000067207	0.000235245
27	1	0.000000882	-0.000031660	0.000047285
28	1	-0.000072911	0.000083774	0.000030416
29	1	0.000369076	-0.000102983	-0.000051158
30	1	0.000129715	0.000340598	0.000009364
31	1	-0.000027241	-0.000002162	-0.000033812
32	6	0.028564481	-0.012748768	0.039440740
33	6	-0.004782598	0.005779384	0.006461551
34	6	0.005671760	-0.005681632	-0.004594782
35	6	-0.002675974	0.002239062	0.001041491
36	1	0.003065017	-0.004634352	-0.010249645
37	6	0.001114326	-0.001991327	-0.003613265
38	1	-0.008674721	0.007771932	0.001767314
39	6	-0.003726890	0.001462372	-0.004782786
40	1	0.009447128	-0.007073723	-0.000976208
41	1	-0.002143644	0.003876310	0.011027552
42	1	0.006711404	-0.003008550	0.009065465

11-2 (TS)



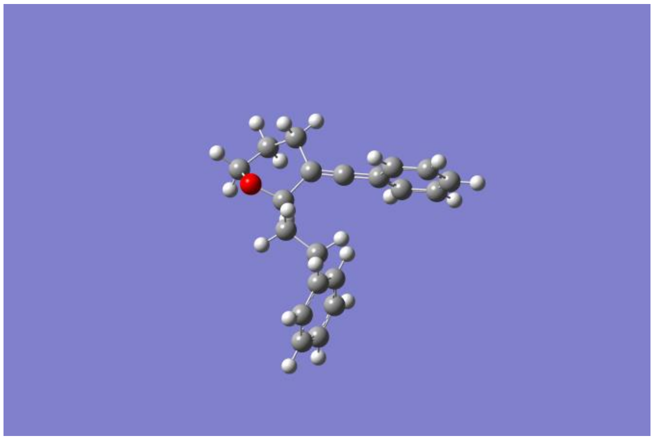
Imaginary Frequencies: 1

ZPE and thermally corrected free energy: -849.350748 Ha ($\Delta G^{\ddagger}$ = 8.7 kcal/mol for this transition state)

```
 Center     Atomic              Forces (Hartrees/Bohr)
 Number   Number              X              Y              Z
 -------------------------------------------------------------------
      1        6          -0.001356407    0.000710171    0.000735663
      2        1          -0.000166144    0.000026885   -0.000309697
      3        1           0.000370374    0.000291529    0.000183803
      4        6           0.000149202   -0.000126488   -0.000048005
      5        1          -0.000033509    0.000135617    0.000007677
      6        1          -0.000022705    0.000040227   -0.000053537
      7        6           0.000202679   -0.006783279   -0.004213658
      8        6          -0.005529553   -0.008157009    0.000140949
      9        6          -0.000424824   -0.000642014   -0.000313562
     10        1           0.000063254    0.000105991    0.000023948
     11        1           0.000153478    0.000227393    0.000027891
     12        8           0.003563091    0.000905545   -0.000791349
     13        6          -0.003927382    0.000540465    0.004233962
     14        1          -0.002934389   -0.003912506   -0.000308122
     15        6           0.001193147   -0.000770402   -0.000015499
     16        1          -0.000268191    0.000236311   -0.000235996
     17        1          -0.000016354    0.000190415   -0.000134410
     18        6           0.000096621    0.000219870   -0.000115960
     19        1           0.000519338   -0.000220970   -0.000182232
     20        1          -0.000197968    0.000029635    0.000043225
     21        6           0.000007347   -0.000207695   -0.000096855
     22        6          -0.000072415    0.000024240    0.000034036
     23        6          -0.000146671   -0.000150202    0.000268818
     24        6           0.000364252    0.000237778    0.000206996
     25        6           0.000226518    0.000136457   -0.000315768
```

26	6	-0.000153423	-0.000024371	-0.000097922
27	1	0.000002238	-0.000028525	0.000002878
28	1	0.000017096	-0.000038323	-0.000044726
29	1	-0.000075806	0.000100476	-0.000019340
30	1	-0.000538757	0.000399380	-0.000523255
31	1	0.000007750	-0.000102036	-0.000000713
32	6	0.005748093	0.013272561	0.001868112
33	6	0.010898742	-0.002820310	-0.014018863
34	6	-0.004950443	0.010324857	0.012344838
35	6	0.000582755	-0.001269999	-0.002510665
36	1	-0.001898224	0.007820327	0.008866218
37	6	-0.001796900	0.000704262	0.003757778
38	1	0.010730498	0.007075708	-0.008953293
39	6	0.002785327	0.004455758	0.000001163
40	1	-0.008381915	-0.003410056	0.008567424
41	1	0.001203885	-0.009143054	-0.008368086
42	1	-0.005993706	-0.010404622	0.000356135

11b-2



Imaginary Frequencies: 0

ZPE and thermally corrected free energy: -849.366505 Ha (-1.2 kcal/mol vs **11a-2**)

Center Number	Atomic Number	Forces (Hartrees/Bohr)		
		X	Y	Z
1	6	-0.003178310	0.001313664	0.006652844
2	1	-0.001277528	-0.000881186	-0.001410797
3	1	0.000210115	0.000205687	0.000062185
4	6	0.000505260	0.000072365	0.000495412
5	1	0.000021331	0.000112663	-0.000043206
6	1	0.000200993	-0.000007869	0.000000502
7	6	-0.001065710	-0.012859666	0.000127445

8	6	0.002047379	0.024734608	-0.001012505
9	6	0.000085739	0.000397657	0.000534073
10	1	-0.000056544	-0.000066560	-0.000066775
11	1	0.000110375	-0.000037802	-0.000023727
12	8	-0.000757328	-0.001918582	-0.000279913
13	6	0.002370859	0.003607000	-0.006376094
14	1	-0.000280643	0.000481614	-0.000110518
15	6	0.000265143	-0.001831999	0.001249925
16	1	0.000589902	-0.000201870	-0.000193722
17	1	-0.000181325	-0.000002282	0.000046148
18	6	0.000361861	0.001239164	-0.000514229
19	1	0.000307709	-0.000549649	0.000038020
20	1	0.000084326	-0.000143839	0.000151439
21	6	0.000029316	-0.000017878	0.000042884
22	6	0.000061064	0.000040343	-0.000053428
23	6	-0.000000743	0.000001198	0.000023113
24	6	0.000101240	0.000001279	-0.000064180
25	6	-0.000300988	-0.000325253	0.000482698
26	6	0.000205037	0.000009587	-0.000217062
27	1	0.000030398	-0.000016711	0.000001165
28	1	0.000016479	-0.000003924	-0.000028183
29	1	0.000025633	-0.000005862	-0.000030966
30	1	-0.000055630	0.000004225	0.000044267
31	1	-0.000031026	0.000025049	0.000009429
32	6	-0.001868082	-0.018294377	0.000590152
33	6	-0.005214486	0.014392338	0.026350973
34	6	0.010998822	0.012362299	-0.026133627
35	6	0.000878542	-0.005721700	0.008964540
36	1	0.001211847	0.005580706	-0.010537532
37	6	-0.003373706	-0.004808465	-0.009449733
38	1	0.001157871	0.005045454	0.010756113
39	6	0.000757405	0.003903013	0.000448723
40	1	-0.000644016	-0.007009675	-0.010555118
41	1	-0.002186409	-0.007155809	0.010302010
42	1	-0.002162171	-0.011668957	-0.000272747

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