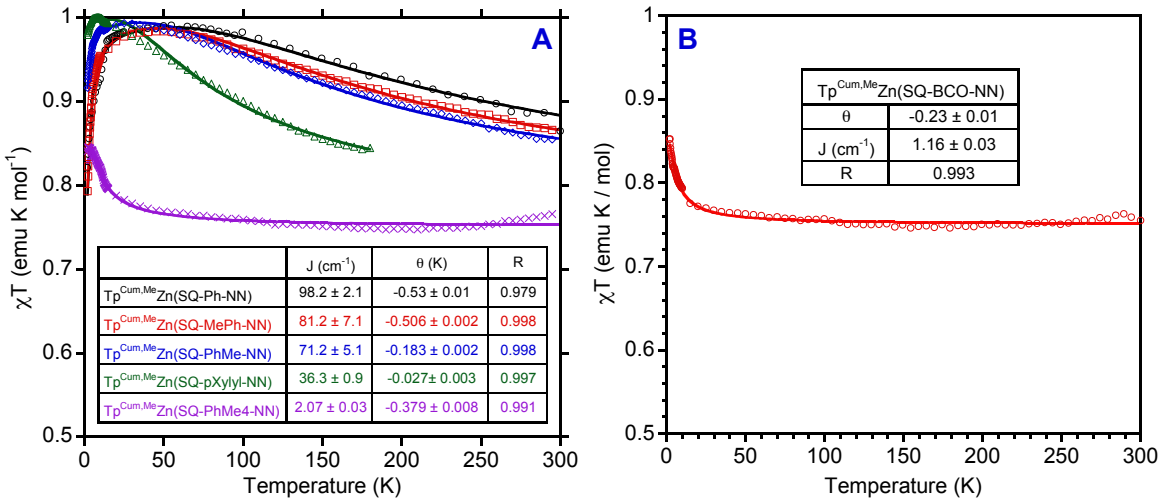
Determining the Conformational Landscape of σ and π Coupling Using para-Phenylene and "Aviram-Ratner" Bridges

Daniel E. Stasiw,[1] Jinyuan Zhang,[1] Guangbin Wang,[1†] Ranjana Dangi,[2] Benjamin W. Stein, [2] David A. Shultz,[1*] Martin L. Kirk,[2*] Lukasz Wojtas[3] and Roger D. Sommer[1]

[1]Contribution from the Department of Chemistry, North Carolina State University, Raleigh, North Carolina 27695-8204. [2]Department of Chemistry, The University of New Mexico, MSC03 2060, 1 University of New Mexico, Albuquerque, New Mexico 87131-0001. [3]Department of Chemistry, University of South Florida, 4202 E. Fowler Avenue, CHE 205 Tampa, FL 33620-5250. [†]Current address: CombiBlocks, San Diego, CA

Table of Contents

Magnetic Susceptibility. Magnetic susceptibility measurements were collected on a Quantum Design MPMS-XL7 SQUID magnetometer with an applied field of 0.7 T. A microcrystalline sample (~20 mg) was loaded into a gelcap/straw sample holder and mounted to the sample rod with Kapton tape for variable temperature measurements. Collected raw data was corrected first with Pascal's constants as a first approximation for molecular diamagnetism followed by a straight line for diamagnetic response of sample container where the slope of the line represents the residual diamagnetic correction.



	J (cm^{-1})	θ (K)	R
$Tp^{Cum,Me}$Zn(SQ-Ph-NN)	98.2 ± 2.1	-0.53 ± 0.01	0.979
$Tp^{Cum,Me}$Zn(SQ-MePh-NN)	81.2 ± 7.1	-0.506 ± 0.002	0.998
$Tp^{Cum,Me}$Zn(SQ-PhMe-NN)	71.2 ± 5.1	-0.183 ± 0.002	0.998
$Tp^{Cum,Me}$Zn(SQ-pXylyl-NN)	36.3 ± 0.9	-0.027± 0.003	0.997
$Tp^{Cum,Me}$Zn(SQ-PhMe4-NN)	2.07 ± 0.03	-0.379 ± 0.008	0.991

Fig. S1. A) Magnetometry of **1-Ph**,[1] **1-MePh**, **1-PhMe**, **1-pXylyl**, and **1-PhMe$_4$**. B) Magnetometry of **1-BCO**. Each data set is the average of a heating (2-300K) and cooling (300-2K) curve after the data had been corrected by subtraction of a linear line where the slope represents the diamagnetic signal. Error in ***J*** was determined by the difference in the fit for the corresponding unaveraged and averaged data.

Calculations

All calculations were performed with the ORCA 3.0.2 program suite.[2] A density functional theory (DFT) geometry optimization of the isolated monoanionic biradical (high spin S=1 state and sans the $Tp^{Cum,Me}Zn^{+}$ fragment) was performed with the def2-SVP basis[3] and the PBE GGA functional.[4] Quasi-restricted orbitals (QROs) were generated by changing the two dihedral angles to 0 degrees and performing a subsequent PBE/def2-SVP calculation. From these initial starting orbitals the NN HOMO, SOMO, and LUMO and the SQ SOMO were selected and used for the subsequent SA-CASSCF(4,4)/NEVPT2/def2-SVP rigid scan. An initial CASSCF(4,4)/NEVPT2 calculation was performed on the planar geometry ($\phi_{NN}=\phi_{SQ}=0°$) to ensure that the correct SQ-NN biradical ferromagnetic (S=1) state was obtained (see Fig. S2) as the ground state, and that a low lying singlet state arising from the same configuration was present. The orbitals generated from this calculation were then subsequently used for the rigid PES scans, which were performed by averaging over the lowest singlet and the lowest triplet root. Exchange coupling values (2J) were determined by the energy difference between these two states. $\boldsymbol{H_{DA}}$ values were determined conveniently from the experimental and computed ratios $\boldsymbol{J_{SQ\text{-}B\text{-}NN}/J_{SQ\text{-}NN}}$ ($=\boldsymbol{H^2_{SQ-B-NN}/H^2_{SQ-NN}}$) where **SQ-NN** is the "parent," non–bridged biradical complex for which both $\boldsymbol{J_{SQ\text{-}NN}}$ and $\boldsymbol{H_{SQ\text{-}NN}}$ have been experimentally determined as described in the text.

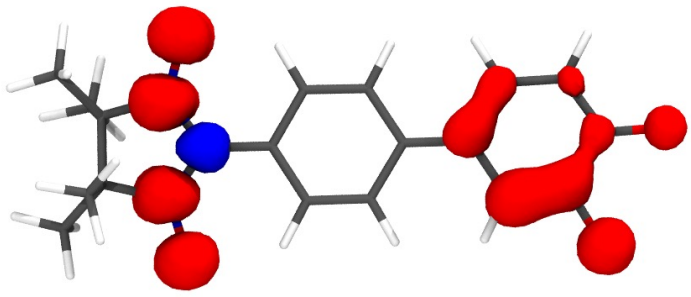


Fig. S2. CASSCF(4,4)/NEVPT2 S=1 state spin density.

The coordinates of the fully optimized structure in Angstroms are given below (Total energy = -1146.490318174287 Eh):

O	3.38922606352087	0.60809209197966	-1.63450283144700
O	3.43475059511578	0.12517117605310	1.13298485887731
H	7.84611823600413	0.43415389647953	-1.59371834818899
H	5.71831312407525	0.70541610849797	-2.75993264167245
C	6.92152105396219	0.35064542758970	-1.03557691109404
C	5.74070599058581	0.51338421938664	-1.69218564886477
C	6.98262240775350	0.13097671711637	0.38374986649646
C	4.45380023887925	0.45889247957890	-1.02359816932630
C	5.78296652521604	0.07161235935377	1.08079074836244
C	4.48970517305212	0.21024389242418	0.47530442281058
H	5.76865065121335	-0.13005362319131	2.14549458881044
C	10.66391261944893	-0.53523132206841	0.98132079082099
C	10.80425089898823	-0.30660809659783	2.36909966655749
C	9.64041087185092	0.07627018869629	3.07571223106115
C	9.44624686744472	-0.38334336101654	0.35430661485610
H	11.52134252370867	-0.85232806378805	0.40966645527302
C	8.42885353402865	0.20884963518333	2.43540163286721
C	8.27350915460549	-0.01120969768603	1.04807418651219
H	9.70994229655385	0.28541843175058	4.13104555087096
H	9.39089230677740	-0.59626572235790	-0.70464698792547
H	7.57291268752827	0.52468997167004	3.01589639980850
C	12.07487975466279	-0.45644412445847	3.03437071804156
O	11.64743859725071	0.64138525716814	5.09252349910321
O	13.31490199423651	-1.64529479251385	1.39860575169971
N	12.39147341640273	-0.00887182056532	4.28639645578562

N	13.18605728377968	-1.07171590672796	2.53092572363595
H	14.57483317540506	1.23166463914232	2.77039788660909
H	16.09546232655286	0.50522522673368	3.31866725009672
C	15.16760747037085	0.31687617707152	2.77661736802579
H	15.41323281303045	0.06255605602505	1.74567407867064
H	14.54794068100326	1.46972235462873	5.05953746307381
C	14.42167213342251	0.53160058853917	5.59619664620346
H	15.40355038281214	0.16752523035898	5.90415117322293
H	13.83080167468049	0.73698532264774	6.48691992293740
C	14.39304164264555	-0.85734265259802	3.39417401849590
C	13.71798134513996	-0.52765724630048	4.75494837793372
H	15.62490966299068	-2.28734014702613	2.37130274559814
C	15.26880133810036	-2.10549623272104	3.38352136702670
H	16.13121278775779	-1.95657055397745	4.03657914913014
C	13.42081789267708	-1.76155860595644	5.62083509500675
H	14.73079834369207	-2.99277822162174	3.71083019912443
H	12.76032891349090	-1.46158010015540	6.43434722664670
H	14.33638483571893	-2.17269882557799	6.04851395776902
H	12.92108771386323	-2.54237833116906	5.04732745069678

(1) Shultz, D. A.; Vostrikova, K. E.; Bodnar, S. H.; Koo, H.-J.; Whangbo, M.-H.; Kirk, M. L.; Depperman, E. C.; Kampf, J. W. *J. Am. Chem. Soc.* **2003**, *125*, 1607.

(2) Neese, F. *Wiley Interdisciplinary Reviews: Computational Molecular Science* **2012**, *2*, 73.

(3) Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297.

(4) Perdew, J. P.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, *77*, 3865.

(5) Bruker; Bruker AXS Inc., Madison, Wisconsin, USA.: 2008.

(6) Bruker; Bruker AXS Inc., Madison, Wisconsin, USA.: 2001b.

(7) Sheldrick, G. M. University of Gottingen, Germany., 1996.

(8) Farrugia, L. J. *Appl. Cryst.* **1999**, *32*, 837.

(9) Sheldrick, G. M. SHELXT 5.10, 1997, Bruker Analytical X-ray, Madison WI

(10) Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467.

(11) Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112.

(12) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *Appl. Cryst.* **2009**, *A42*, 339.

(13) Spek, T. L. *Acta Cryst.* **1990**, *A46*, 194.

(14) Spek, T. L. *Acta Cryst.* **1990**, *A46*, c34.

(15) Weiser, P. T.; Williams, A. B.; Chang, C.-Y.; McDonnell, D. P.; Hanson, R. N. *Bioorg. & Med. Chem. Lett.* **2012**, *22*, 6587.

(16) Tanouchi, T.; Kawamura, M.; Ohyama, I.; Kajiwara, I.; Iguchi, Y.; OKADA, T.; Miyamoto, T.; Taniguchi, K.; Hayashi, M.; Iizuka, K.; Nakazawa, M. *J. Med. Chem.* **1981**, *24*, 1149.

(17) Shultz, D. A.; Hollomon, M. G. *Chem. Mater.* **2000**, *12*, 580.

(18) Ignar, D. M. In *Google Patents* USA, 2010.

(19) Liu, C.-Y.; Knochel, P. *J. Org. Chem.* **2007**, *72*, 7106.

(20) Moorthy, J. N.; Mal, P.; Singhal, N.; Venkatakrishnan, P.; Malik, R.; Venugopalan, P. *J. Org. Chem.* **2004**, *69*, 8459.

(21) Charpentier, B.; Bernardon, J.-M.; Eustache, J.; Millois, C.; Martin, B.; Michel , S.; Shroot, B. *J. Med. Chem.* **1995**, *38*, 4993.

(22) Shimono, S.; Tamura, R.; Ikuma, N.; Takimoto, T.; Kawame, N.; Tamada, O.; Sakai, N.; Matsuura, H.; Yamauchi, J. *J. Org. Chem.* **2004**, *69*, 475.

(23) Magdziak , D.; Rodriguez, A. A.; Van De Water, R. W.; Pettus, T. R. R. *Org. Lett.* **2002**, *4*, 285.

(24) Ruf, M.; Vahrenkamp, H. *Inorg. Chem.* **1996**, *35*, 6571.

X-Ray Diffraction.

The X-ray diffraction data for **1-PhMe** and **1-pXylyl** were measured on a Bruker D8 Venture PHOTON 100 CMOS system equipped with a Cu K_α INCOATEC Imus micro-focus source (λ = 1.54178 Å). The X-ray diffraction data for **1-MePh** were collected using Bruker-AXS SMART-APEXII CCD diffractometer with a sealed-tube Mo K_α source (λ = 0.71073 Å). Indexing was performed using *APEX2* (Difference Vectors method).[5] Data integration and reduction were performed using SaintPlus 6.01.[6] Absorption correction was performed by multi-scan method implemented in SADABS.[7] Space groups were determined using XPREP implemented in APEX2.[5] The structure was solved using SHELXS-97 (direct methods) and refined using SHELXL-2013 (full-matrix least-squares on F^2) contained in APEX2,[5] WinGX v1.70.01[8,9,10,11] and OLEX2[12] program packages.

1-MePh: All non-hydrogen atoms were refined anisotropically. Disordered group was refined using geometry and ADPs restraints (DFIX, ISOR).

1-PhMe: All non-hydrogen atoms were refined anisotropically. Disordered groups were refined using geometry and ADPs restraints (DFIX, DANG, SIMU, DELU, ISOR). The contribution of heavily disordered solvent molecules (CH_2Cl_2, CH_3OH, hexane) was treated as diffuse using Squeeze procedure implemented in Platon program.[13,14]

1-pXylyl: Majority of non-hydrogen atoms were refined anisotropically. Some of the disordered atoms have been refined isotropically. Disordered parts were refined using geometry and ADPs restraints (DFIX, DANG, SIMU, DELU, ISOR). The contribution of heavily disordered solvent molecules (CH_2Cl_2, CH_3OH, hexane) was treated as diffuse using Squeeze procedure implemented in Platon program.[13,14]

1-PhMe$_4$: All non-hydrogen atoms refined anisotropically. Positions for disordered atoms were found in the difference map during multiple rounds of refinement. Hydrogen atoms were placed at idealized positions and allowed to "ride" on the parent atom with isotropic displacement parameters of 1.2 or 1.5 times the parent. Disordered isopropyl group c50-c52 was modeled over two positions and both components restrained to mimic the well behaved C37-C39 group. The benzene solvate was constrained to an idealized shape using AFIX 66, and RIGU commands.

1-BCO: All non-hydrogen atoms refined anisotropically. Positions for disordered atoms were found in the difference map during multiple rounds of refinement. Hydrogen atoms were placed at idealized positions and allowed to "ride" on the parent atom with isotropic displacement parameters of 1.2 or 1.5 times the parent. The disordered solvent was restrained to a chemically reasonable form using numerous DFIX/DANG/RIGU commands. The solvent carbon atoms, C1s and C1t were also treated with EADP commands to maintain reasonable displacement parameters for both atoms.

Table S1. Crystallographic details of **1-MePh**, **1-PhMe**, **1-pXylyl**, **1-PhMe4**, and **1-BCO**.

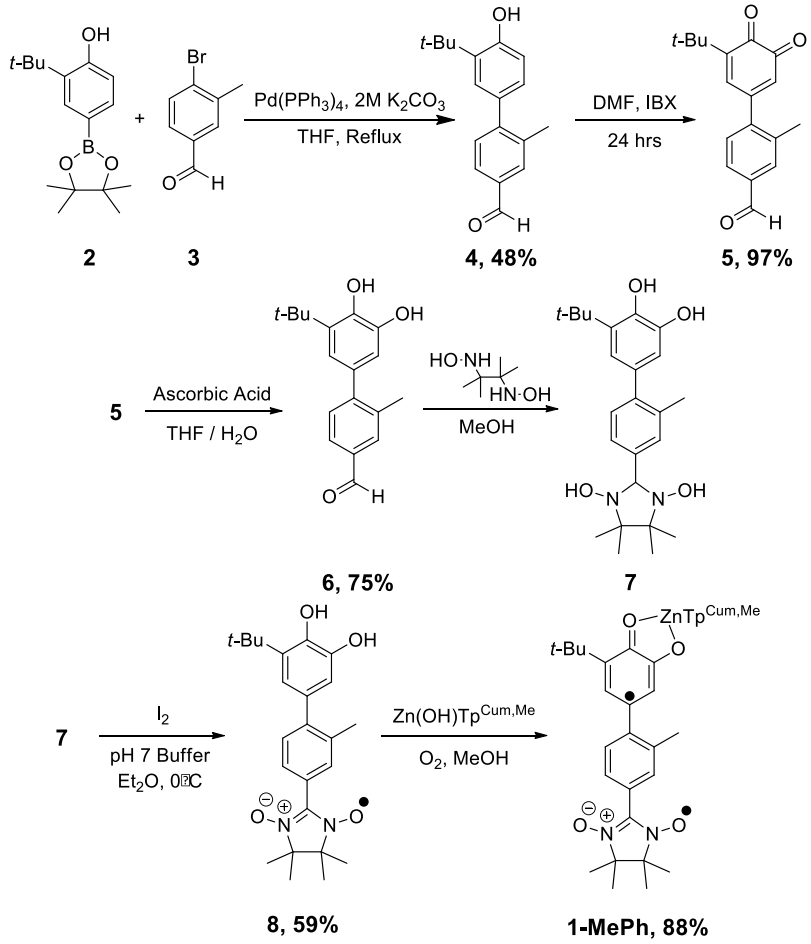
Designation	**1-MePh**	**1-PhMe**	**1-pXylyl**	**1-PhMe$_4$**	**1-BCO**
Formula	$C_{63}H_{75}BN_8O_4Zn$	$C_{63}H_{75}BN_8O_4Zn$	$C_{64}H_{77}BN_8O_4Zn$	$C_{66}H_{83}BN_8O_4Zn$	$C_{64}H_{81}BN_8O_4Zn$, CH_2Cl_2
Formula Weight (*g/mol*)	1087.67	1084.5	1098.5	1204.735	1187.47
Crystal Dimensions (*mm*)	0.31 x 0.06 x 0.03	0.08 x 0.03 x 0.02	0.21 x 0.03 x 0.02	0.38 x 0.27 x 0.15	0.47 x 0.37 x 0.21
Crystal System, Space Group	*P*-1	*C*2/c	$P2_1/c$	$P2_1/n$	$P2_1/n$
Temperature, K	110	100	100	110	100
a, Å	11.2877(3)	30.9381(10)	13.3325(3)	13.9485(5)	14.2837(3)
b, Å	14.5741(4)	11.0948(3)	28.3571(7)	34.5936(13)	31.3370(7)
c, Å	18.9882(6)	37.0849(12)	34.1400(8)	14.2895(6)	15.0319(4)
α,°	74.827(2)	90	90	90	90
β,°	77.364(2)	103.747(1)	100.620(1)	108.948(2)	112.5560(10)
γ,°	78.498(2)	90	90	90	90
V, Å^3	2908.10(15)	12364.8(7)	12686.3(5)	6521.47	6213.7(3)
Z	2	8	4	4	4

ρ(*g/cm*)	1.242	1.165	1.150	1.227	1.269
κ, Å,	0.71073 (MoK\a)	1.54178 (CuK\a)	1.54178 (CuK\a)	0.71073 (MoK/a)	0.71073 (MoK/a)
μ, (cm^{-1})	0.480	0.947	0.929	0.432	0.535
R_1	0.0425	0.0699	0.0544	0.0536	0.0635
wR_2	0.1115	0.1685	0.1412	0.1356	0.1263

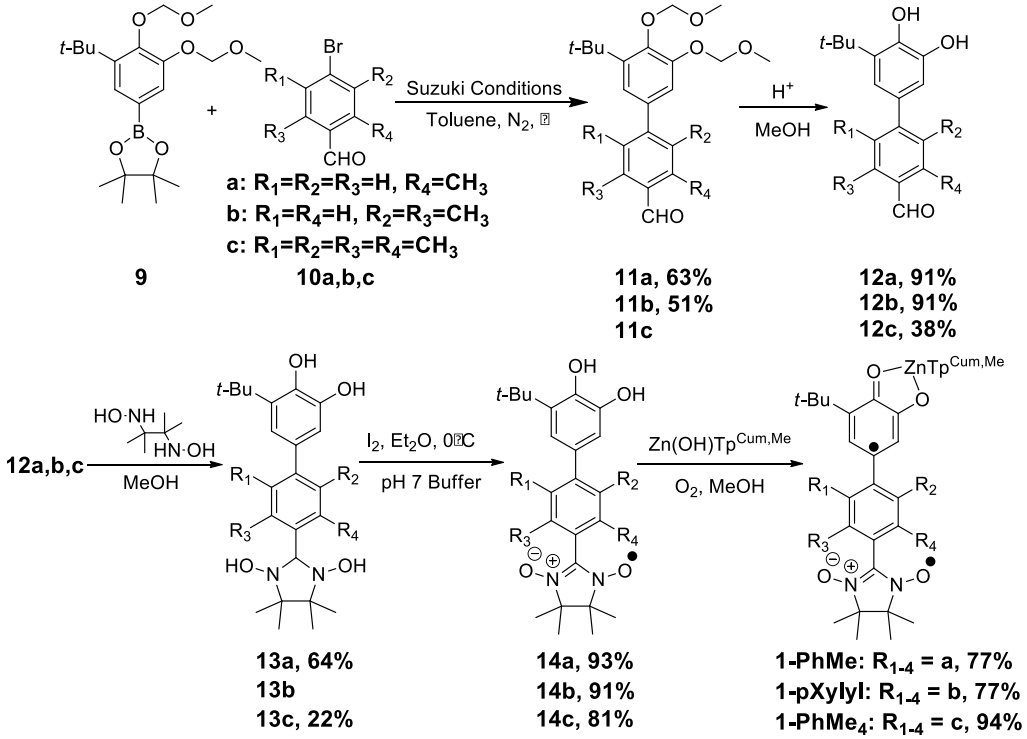
Table S2. Select Torsion Angles for Complexes 1, 1-MePh, 1-PhMe, 1-pXylyl, and 1-$PhMe_4$.

Complex	SQ-Bridge Angle (°)	Bridge-NN Angle (°)
1	37.7	16.0
1-MePh	47.6	13.8
1-PhMe	29.4	45.5
1-*p*Xylyl	47.2	64.2
1-$PhMe_4$	83.6	68.9

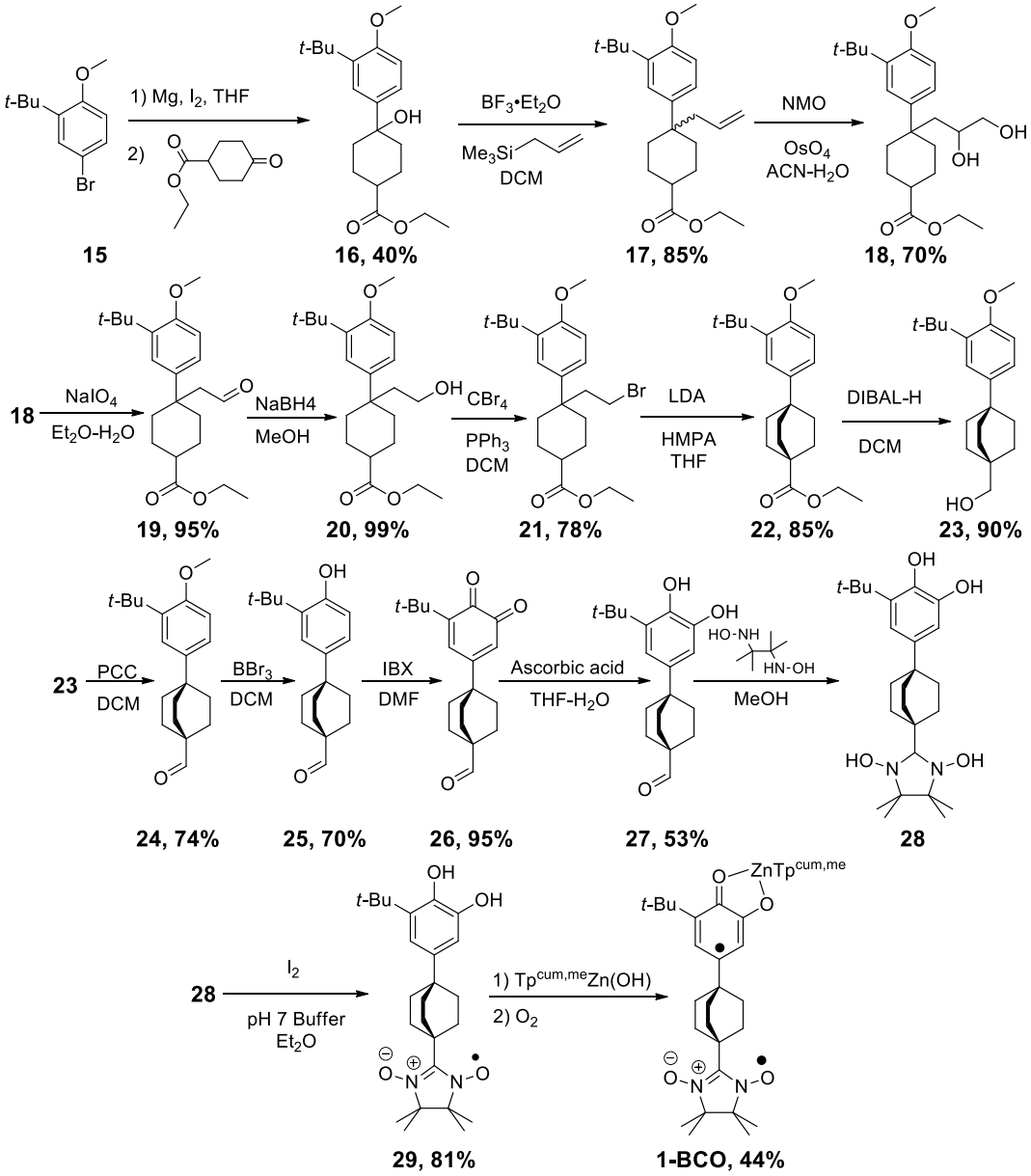
Scheme S1: Synthesis of **1-MePh**.



Scheme S2: Synthesis of **1-PhMe**, **1-pXylyl**, and **1-PhMe$_4$**.



Scheme S3. Synthesis of **1-BCO**.



Materials and Methods:

General Considerations Reagents and solvents were purchased from commercial sources and used as received unless otherwise noted. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 MHz or a Varian Mercury 300 MHz spectrometer at room temperature. ^{1}H and ^{13}C chemical shifts are listed in parts per million (ppm) and are referenced to residual protons or carbons of the deuterated solvents, respectively. EPR spectra were recorded on an IBM ER200D-SRC EPR spectrometer in CH_2Cl_2. Infrared spectra were recorded on a Brüker Vertex 80v spectrometer with Brüker Platinum ATR attachment. Elemental analyses were performed by Atlantic Microlabs, Inc. Mass spectra were obtained at the NCSU Mass Spectrometry Facility located in the Department of Chemistry. Compounds **2**,[15] **3,**[16] **9**,[17] **10a**,[18] **10b**,[19] **10c**,[20] **15**,[21] 2,3-dimethyl-2,3-bis(hydroxyamino)butane (**BHA**),[22] *o*-iodoxybenzoic acid (**IBX**),[23] and $\mathbf{Tp^{Cum,Me}Zn(OH)}$[24] were prepared as previously reported.

3'-(*tert*-Butyl)-4'-hydroxy-2-methyl-[1,1'-biphenyl]-4-carboxaldehyde (4). To a 100 mL oven dried Schlenk flask 874 mg (3.16 mmol) **2**, 571 mg (2.87 mmol) **3**, and 165 mg $Pd(PPh_3)_4$ were added with 10 mL tetrahydrofuran in a nitrogen environment. In a 25 mL round bottom flask, a 2 M solution of K_2CO_3 was prepared and bubbled with nitrogen for 30 min. Using a nitrogen purged syringe, 4.6 mL of the 2M K_2CO_3 solution was added to the reaction vessel. The flask was then fit with a condenser and refluxed in the dark for 18 h. Upon reaction completion, 30 mL deionized water was added and the mixture stirred in air for 30 min. The mixture was transferred to a separatory funnel, diluted with ethyl acetate, and washed with saturated NaCl solution three times. The organic layer was collected, dried over Na_2SO_4, and the solvent removed under reduced pressure. Purification via column chromatography (SiO_2, 15% ethyl acetate in hexanes) produced 371 mg (48%) compound **4**. ^{1}H NMR (300 MHz, DMSO-d_6,

δ): 9.99 (s, 1H), 9.61 (s, 1H), 7.80 (s, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 2.1 Hz, 1H), 7.08 (dd, *J* = 8.1 Hz, *J* = 2.1 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 1H), 2.34 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6, δ): 193.34, 156.33, 136.47, 135.76, 135.24, 132.23, 131.04, 127.94, 127.76, 127.70, 116.77, 35.02, 30.03, 21.02. IR (solid) ν_{max} (cm^{-1}): 3201 (br, OH), 1686 (s, C=O). Elemental Analysis Calculated: (C: 80.56, H: 7.51). Found: (C: 80.56, H: 7.68).

5'-(*tert*-Butyl)-2-methyl-3',4'-dioxo-3',4'-dihydro-[1,1'-biphenyl]-4-carboxaldehyde (5). To a 25 mL round bottom flask 326 mg (1.21 mmol) **4** and 485 mg (1.73 mmol) **IBX** were added with 5 mL dimethylformamide and stirred in the dark for 3 days. The completed reaction was poured into 150 mL deionized water, stirred for 30 min, and then transferred to a separatory funnel with ~100 mL ethyl acetate. The mixture was then washed three times with a saturated $NaHCO_3$ solution followed by three washes of saturated NaCl. The organic layer was collected, dried over Na_2SO_4, and the solvent removed under reduced pressure to yield 332 mg (97%) of compound **5**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.04 (s, 1H), 7.81 (s, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 2.3 Hz, 1H), 6.31 (d, *J* = 2.3 Hz, 1H), 2.46 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 191.47, 180.26, 179.60, 153.05, 151.50, 144.03, 137.31, 136.18, 135.64, 132.22, 128.54, 127.94, 127.32, 35.88, 29.41, 20.43. IR (solid) ν_{max} (cm^{-1}): 1693 (s, C=O), 1682 (s, C=O), 1662 (s, C=O). Mass spectrometry (*m/z*): calculated for $C_{18}H_{19}O_3$ $(M+H)^+$: 283.1334, found: 283.1324 $(M+H)^+$.

3'-(*tert*-Butyl)-4',5'-dihydroxy-2-methyl-[1,1'-biphenyl]-4-carboxaldehyde (6). Quinone **5** (254 mg, 0.90 mmol) was dissolved in 10 mL tetrahydrofuran and added to a separatory funnel containing 350 mg (1.99 mmol) ascorbic acid dissolved in 10 mL water. The mixture was shaken for about 5 minutes then 10 mL saturated NaCl solution was added and the

layers allowed to separate. The organic layer was diluted with 50 mL ethyl acetate and washed three times with a saturated NaCl solution. The organic layer was collected, dried over Na_2SO_4, and the solvent removed under reduced pressure to yield 213 mg (75%) of compound **6**. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 9.92 (s, 1H), 9.52 (s, 1H), 8.22 (s, 1H), 7.73 (s, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.32 (d, J = 7.8 Hz, 1H), 6.65 (d, J = 2.0 Hz, 1H), 6.56 (d, J = 2.0 Hz, 1H), 2.28 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6, δ): 193.30, 148.90, 145.45, 144.40, 136.35, 136.13, 135.21, 132.17, 130.90, 130.38, 127.63, 118.41, 114.14, 35.02, 30.10, 20.97. IR (solid) ν_{max} (cm^{-1}): 3475 (m, OH), 3259 (br, OH), 1662 (s, C=O). Mass spectrometry (*m/z*): calculated for $C_{18}H_{21}O_3$ $(M+H)^+$: 285.1491, found: 285.1483 $(M+H)^+$.

2-(3'-(*tert*-Butyl)-4',5'-dihydroxy-2-methyl-[1,1'-biphenyl]-4-yl)-4,4,5,5-tetramethylimidazolidine-1,3-diol (7). To a 6 mL round bottom flask 125 mg (0.44 mmol) **6** and 160 mg (1.08 mmol) **BHA** were added and pump/purged with nitrogen 5 times. Using a nitrogen purged syringe, 2 mL methanol was added and the reaction was stirred under nitrogen in the dark for 3 days. The product of this reaction was checked by ^{1}H NMR for absence of the aldehyde proton and the crude product was used directly in the synthesis of compound **8**. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 7.73 (s, 1H), 7.32 (m, 2H), 7.10 (d, J = 7.1 Hz, 1H), 6.64 (s, 1H), 6.55 (s, 1H), 4.48 (s, 1H), 2.23 (s, 3H), 1.35 (s, 9H), 1.08 (s, 12H). IR (solid) ν_{max} (cm^{-1}): 3285 (br, -OH).

2-(3'-(*tert*-Butyl)-4',5'-dihydroxy-2-methyl-[1,1'-biphenyl]-4-yl)-4,4,5,5,-tetramethyl-4,5-dihydroimidazol-3-oxide-1-oxyl (8). To a 100 mL round bottom flask, 536 mg (1.29 mmol) **7** was dissolved in 30 mL diethyl ether, 10 mL pH 7 buffer and was chilled to 0°C. In a separatory funnel, 493 mg (1.94 mmol) I_2 was dissolved in 30 mL diethyl ether and added dropwise to the stirring reaction flask. The reaction mixture was then diluted with 90 mL pH 7

buffer and transferred to a separatory funnel where 100 mL $Na_2S_2O_3$ was added and the mixture shaken. The aqueous layer was removed and the organic layer then washed with a saturated NaCl solution three times. The organic layer was dried over Na_2SO_4 and the solvent removed under reduced pressure to yield 316 mg of blue colored compound **8** (59% yeild). EPR (~0.2 mM in CH_2Cl_2): a_N = 7.62 G. IR (solid) ν_{max} (cm^{-1}): 3198 (br, -OH). Mass spectrometry (*m/z*): calculated for $C_{24}H_{31}N_2O_4Na$ $(M+Na)^+$: 434.218153, found: 434.2175 $(M+Na)^+$.

$Tp^{Cum,Me}$Zn(SQ-Me-Ph-NN) (1-MePh). To a 25 mL oven dried Schlenk flask, 30 mg (0.07 mmol) **8** and 62 mg (0.09 mmol) **$Tp^{Cum,Me}$Zn(OH)** were added and pump / purged with nitrogen 5 times. Using a nitrogen purged syringe, ~2 mL methanol was added and the reaction stirred for 2 hours. The reaction was then opened to air and allowed to stir overnight in the dark. The solvent was removed under reduced pressure and the product purified by column chromatography (basic alumina, 1:1 ethyl acetate:hexanes) to yield 70 mg (88%) of complex **1-MePh**. Crystals of **1-MePh** were grown from slow evaporation of methanol containing a few drops of CH_2Cl_2. IR (solid) ν_{max} (cm^{-1}): 2543 (w, -BH). EPR (~0.2 mM in CH_2Cl_2): apparent a_N = 3.65 G. Mass spectrometry (*m/z*): calculated for $C_{63}H_{76}BN_8O_4Zn$ $(M+H)^+$: 1083.5374, found: 1083.5389 $(M+H)^+$. Elemental analysis Calculated: (C: 69.77, H: 6.97, N: 10.33), Found: (C: 69.64, H: 6.98, N: 10.31).

3'-(*tert*-Butyl)-4',5'-bis(methoxymethoxy)-3-methyl-[1,1'-biphenyl]-4-carboxaldehyde (11a). A solution of **10a** (205 mg, 1.10 mmol), **9** (350 mg, 1.07 mmol), $Pd(PPh_3)_4$ (124 mg, 0.107 mmol), Cs_2CO_3 (0.413 g, 2.14 mmol), ethanol (5 mL) and toluene (15 mL) was stirred under nitrogen. The reaction mixture was heated to 70°C for 48 h. After this time, the reaction mixture was cooled to room temperature and 20 mL of water added. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4,

filtered, and concentrated *in vacuo*, and purified by column chromatography (4:1 hexanes:diethyl ether) to give **11a** as a yellow oil (250 mg, 63 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.28 (s, 1H), 7.84 (d, 1H, *J* = 7.8 Hz), 7.53 (d, 1H, *J* = 8.1 Hz), 7.42 (s, 1H), 7.29 (d, 2H, *J* = 2.1 Hz), 5.26 (s, 2H), 5.25 (s, 2H), 3.67 (s, 3H), 3.54 (s, 3H), 2.73 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 192.3, 150.6, 146.5, 144.0, 141.2, 134.7, 132.7, 130.4, 125.1, 119.8, 113.9, 99.2, 95.7, 57.7, 56.5, 35.4, 27.7, 19.9. IR (solid) ν_{max} (cm^{-1}): 1693 (s, -C=O).

3'-(*tert*-Butyl)-4',5'-dihydroxy-3-methyl-[1,1'-biphenyl]-4-carboxaldehyde (12a). To a solution of **11a** (0.360 g, 0.968 mmol) in methanol (3 mL), 3 drops of 12 M HCl and 1 drop of water was added. The reaction mixture was stirred at reflux overnight. The solvent was removed under reduced pressure and the crude solid was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified via recrystallization from methanol/diethyl ether to give **12a** as a light-orange solid to yield 250 mg (91 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.05 (s, 1H), 9.49 (s, 1H), 8.26 (s, 1H), 7.67 (s, 1H, *J* = 8.1 Hz), 7.37 (s, 1H, *J* = 8.1 Hz), 7.30 (s, 1H), 6.85 (s, 2H, *J* = 8.1 Hz), 5.59 (s, 1H), 2.33 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 192.6, 146.1, 145.5, 145.0, 140.6, 136.1, 132.0, 128.9, 123.8, 116.1, 111.6, 34.4, 29.4, 19.1. IR (solid) ν_{max} (cm^{-1}): 3350 (br, -OH), 1669 (s, -C=O). Mass spectrometry (*m/z*): calculated for $C_{18}H_{19}O_3$ $(M-H)^-$: 283.1334, found: 283.1343 $(M-H)^-$.

2-(3'-(*tert*-Butyl)-4',5'-dihydroxy-3-methyl-[1,1'-biphenyl]-4-yl)-4,4,5,5-tetramethylimidazolidine-1,3-diol (13a). To a solution of **12a** (40.0 mg, 0.151 mmol) in 4 mL of methanol, 2,3-dimethyl-2,3-bis(hydroxyamino)butane (44.8 mg, 0.302 mmol) was added under nitrogen. The reaction mixture was allowed to stir at room temperature overnight. The solvent was removed under vacuum to give **13a** as a yellow solid (40 mg, 64%), which was

unstable and was used directly in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.47 (s, 1H), 8.12 (s, 1H), 7.68 (s, 1H), 7.65 (s, 2H), 7.27 (d, 1H, J = 8.4 Hz), 6.90 (s, 1H), 6.86 (s, 1H), 4.89 (s, 1H), 2.42 (s, 3H), 1.38 (s, 9H), 1.09 (s, 6H), 1.07 (s, 6H). IR (solid) ν_{max} (cm^{-1}): 3250 (br, -OH).

2-(3'-(*tert*-Butyl)-4',5'-dihydroxy-3-methyl-[1,1'-biphenyl]-4-yl)-4,4,5,5,-tetramethyl-4,5-dihydroimidazol-3-oxide-1-oxyl (14a). To a solution of **13a** (41.8 mg, 0.101 mmol) in CH_2Cl_2, 10 mL of pH 7 buffer in water and cetyl trimethylammonium bromide (10.0 mg) was added and cooled to 0°C. Iodine (39.8 mg, 0.157 mmol) in CH_2Cl_2 was added dropwise and stirred at 0 °C for 30 min. The reaction mixture was diluted with 10 mL of pH 7 buffer and 10 mL of dichloromethane. The organic layer was separated and washed with a saturated solution of sodium thiosulfate and brine, dried over Na_2SO_4 and the solvent was removed to give **14a** as a purple solid (39.0 mg, 93 %). IR (CH_2Cl_2 film) ν (cm^{-1}): 3242 (br, -OH). EPR (~0.2 mM in CH_2Cl_2): a_N = 7.19 G.

$Tp^{Cum,Me1}$Zn(SQ-Ph-Me-NN) (1-PhMe). To a solution of **Zn(OH)$Tp^{Cum,Me}$** (122 mg, 0.176 mmol) in CH_2Cl_2/methanol, **14a** (72.0 mg, 0.176 mmol) was added under nitrogen. The reaction mixture was allowed to stir at room temperature over 1 h then opened to air overnight. The brown reaction mixture was purified by flash column chromatography (basic alumina, 4:1 hexanes/ethyl acetate) to give **1-PhMe** as a brown solid (148 mg, 77 %). Crystals of **1-PhMe** were grown by slow evaporation of methanol containing a few drops of CH_2Cl_2. IR (solid) ν_{max} (cm^{-1}): 2538 (w, -BH). EPR (ca. 0.2 mM in CH_2Cl_2): apparent a_N = 3.99 G. Mass spectrometry (*m*/*z*): calculated for $C_{63}H_{75}BN_8O_4Zn$ (M)+: 1083.5290, found: 1083.5269 $(M)^+$. Elemental Analysis Calculated: (C: 69.77, H: 6.97, N: 10.33). Found: (C: 68.77, H: 7.04, N: 10.92).

3'-(*tert*-Butyl)-4',5'-bis(methoxymethoxy)-2,5-dimethyl-[1,1'-biphenyl]-4-carbaldehyde (11b). A 50 mL Schlenk flask containing **9** (325 mg, 1.53 mmol), **10b** (550 mg, 1.68 mmol), $Pd(PPh_3)_4$ (142 mg, 0.123 mmol), Cs_2CO_3 (1.00 g, 3.07 mmol) and ethanol (5 mL) in dried toluene (10 mL) was placed under N_2 and refluxed for 48 h. After the reaction was complete, 30 mL of water was added, stirred for 30 minutes and the mixture filtered through Celite. The solvents were removed under reduced pressure and the residue was then extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in* vacuo. The product was purified by column chromatography (4:1 hexanes:EtOAc) to give **11b** as a yellow oil (240 mg, 51 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.26 (s, 1H), 7.68 (s, 1H), 7.14 (s, 1H), 7.01 (d, 1H, J = 1.8 Hz), 6.95 (d, 1H, J = 2.1 Hz), 5.27 (s, 2H), 5.20 (s, 2H), 3.68 (s, 3H), 3.52 (s, 3H), 2.66 (s, 3H), 2.32 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 192.6, 149.9, 147.4, 145.5, 143.3, 137.9, 135.4, 134.2, 133.6, 133.3, 132.9, 121.3, 115.4, 99.2, 95.6, 57.7, 56.4, 35.4, 30.7, 20.1, 19.1. IR (solid) ν_{max} (cm^{-1}): 1691 (s, -C=O). Mass spectrometry (*m*/*z*): calculated for $C_{23}H_{30}O_5$ $(M+H)^+$: 387.2172, found: 387.2156 $(M+H)^+$.

3'-(*tert*-Butyl)-4',5'-dihydroxy-2,5-dimethyl-[1,1'-biphenyl]-4-carboxaldehyde (12b). To a 50 mL round bottom flask containing **11b** (200 mg, 0.518 mmol) in 3 mL of methanol, 3 drops of 12 M HCl and 1 drop of water were added and the solution was stirred at reflux overnight. The solvent was removed under reduced pressure and the crude mixture was extracted using CH_2Cl_2. The organic solution was washed with water, and then dried over Na_2SO_4, the solvent removed under reduced pressure and the product was purified via recrystallization from methanol/diethyl ether to provide **12b** (140 mg, 91%) as a light-orange solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.20 (s, 1H), 9.54 (s, 1H), 8.26 (s, 1H), 7.69 (s, 1H), 7.14 (s, 1H), 6.83

(d, 1H, *J* = 2.1 Hz), 6.70 (d, 2H, *J* = 1.8 Hz), 5.76 (s, 1H), 2.59 (s, 3H), 2.28 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (75 MHz, DMSO) δ (ppm): 193.3, 148.1, 143.2, 142.8, 138.2, 136.4, 134.2, 133.8, 133.5, 132.5, 131.5, 120.1, 113.6, 34.9, 29.7, 20.2, 19.1. IR (solid) ν_{max} (cm^{-1}): 3366 (br, -OH), 1669 (s, -C=O). Mass spectrometry (*m*/*z*): calculated for $C_{19}H_{23}O_3$ $(M+H)^+$: 299.1647, found: 299.1624 $(M+H)^+$.

2-(3'-(*tert*-Butyl)-4',5'-dihydroxy-2,5-dimethyl-[1,1'-biphenyl]-4-yl)-4,4,5,5-tetramethylimidazolidine-1,3-diol (13b). To a 10 mL Schlenk flask containing **12b** (120 mg, 0.402 mmol) in 4 mL of methanol, 2,3-dimethyl-2,3-bis(hydroxyamino)butane (125 mg, 0.845 mmol) was added. The mixture was stirred at room temperature for 48 h. The solvent was removed under reduced pressure to give **13b** as a yellow solid (140 mg, 84 %). The product was immediately used for the next step without further purification, due to its instability. ^{1}H NMR (300 MHz, DMSO) δ (ppm): 9.38 (s, 1H), 8.03 (s, 1H), 7.62 (s, 1H), 7.49 (s, 1H), 6.87 (s, 1H), 6.54 (s, 1H), 4.87 (s, 1H), 2.34 (s, 3H), 2.19 (s, 3H), 1.35 (s, 9H), 1.09 (s, 6H), 1.08 (s, 6H). IR (solid) ν_{max} (cm^{-1}): 3480 (br, -OH).

2-(3'-(tert-Butyl)-4',5'-dihydroxy-2,5-dimethyl-[1,1'-biphenyl]-4-yl)-4,4,5,5,-tetramethyl-4,5-dihydroimidazol-3-oxide-1-oxyl (14b). To a 250 mL round bottom flask containing **13b** (88.8 mg, 0.215 mmol) in CH_2Cl_2 and pH 7 buffer, cetyl trimethylammonium bromide (13.0 mg) was added as a phase transfer catalyst and cooled to 0^{o}C. Iodine (84.7 mg, 0.334 mmol) in CH_2Cl_2 was added dropwise and stirred for 30 minutes. The organic layer was then separated and washed with a saturated solution of sodium thiosulfate and brine. The organic layer was then collected, dried over Na_2SO_4 and the solvent removed to afford a purple solid **14b** (80.0 mg, 91 %). IR (CH_2Cl_2 film) ν (cm^{-1}): 3216 (br, -OH). EPR (~0.2 mM in CH_2Cl_2): a_N = 7.50 G.

$Tp^{Cum,Me1}$Zn(SQ-*p*Xylyl-NN) (1-*p*Xylyl). A 25 mL Schlenk flask containing **14b** (72.0 mg, 0.176 mmol) and **Zn(OH)$Tp^{Cum,Me}$** (122 mg, 0.176 mmol) with 10 mL of distilled MeOH and 10 mL of distilled CH_2Cl_2 and was stirred for 2 h under nitrogen and then opened to air overnight. A brown solution was formed and the crude reaction mixture was purified by flash column chromatography (basic alumina, 4:1 hexanes:ethyl acetate) to afford **1-*p*Xylyl** as a brown solid (148 mg, 77 %). Crystals of **1-*p*Xylyl** were grown from slow evaporation of methanol containing a few drops of CH_2Cl_2. IR (solid) ν_{max} (cm^{-1}): 2536 (w, -BH). EPR (~0.2 mM in CH_2Cl_2): apparent a_N = 3.89 G. Mass spectrometry (*m*/*z*): calculated for $C_{64}H_{77}BN_8O_4Zn$ (M)+: 1096.5446, found: 1096.5439 $(M)^+$. Elemental analysis Calculated: (C: 69.67, H: 7.06, N: 10.20), Found: (C: 73.42, H: 7.62, N: 11.78).

4-Bromo-2,3,5,6-tetramethylbenzaldehyde (10c). To a 100 mL oven dried Schlenk flask, 4.01 g (13.72 mmol) of 1,4-dibromo-2,3,5,6-tetramethylbenzene was added and pump purged with nitrogen five times. To the reaction flask, 30 mL of dried and degassed tetrahydrofuran was added and the flask chilled to -78°C. Using a nitrogen purged syringe, 8.7 mL (13.92 mmol) of 1.6 M n-butyllithium in hexanes was added dropwise and stirred for 1 h. Using another nitrogen purged syringe, 6 mL (77.49 mmol) of dried and degassed N,N-dimethylformamide was added dropwise and was then allowed to warm to room temperature. Once warm, the reaction was opened to air and 30 mL diethyl ether was added. The reaction mixture was transferred to a separatory funnel where it was washed three times with saturated NaCl solution. The organic layer was collected, dried over Na_2SO_4, and the solvent removed under reduced pressure. The product was purified by column chromatography (SiO_2, 100% Hexanes followed by 1:1 Hexanes:Et_2O) to yield 3.02 g (91%) of a white solid **10c**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.59 (s, 1H), 2.45 (s, 6H), 2.44 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, δ):

196.31, 135.66, 135.54, 134.64, 134.03, 20.94, 17.03. IR (solid) ν_{max} (cm^{-1}): 1687 (s, -C=O). Elemental Analysis Calculated: (C: 54.79, H: 5.43). Found: (C: 55.71, H: 5.56).

3'-(*tert*-Butyl)-4',5'-dihydroxy-2,3,5,6-tetramethyl-[1,1'-biphenyl]-4-carboxaldehyde (12c). To a 50 mL oven dried Schlenk flask, 1.22 g (3.18 mmol) of **9**, 502 mg (2.08 mmol) of **10c**, 1.35 g (6.36 mmol) of K_3PO_4, and 4Å molecular sieves were added and placed under a nitrogen environment where 200 mg (0.93 mmol) of ethyldiphenylphosphine and 123 mg (0.13 mmol) $Pd_2(dba)_3$ were added with 20 mL dried toluene. The reaction was fit with a condenser under nitrogen purge and heated to 130°C for 4 days. The reaction was then cooled, filtered into a separatory funnel, and diluted with ethyl acetate. The organic layer was washed once with saturated $NaHCO_3$ solution followed by two washes of saturated NaCl solution. The organic layer was then dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude reaction mixture was then redissolved in a 1:1 ethyl acetate : methanol mixture and 10 drops of concentrated HCl was added. The reaction was fit with a condenser and heated to reflux for 16 h. After the reaction was cooled to room temperature, the mixture was transferred to a separatory funnel, washed with saturated $NaHCO_3$ and saturated NaCl. The organic layer was dried over Na_2SO_4 and the solvent removed under reduced pressure. The product was purified by column chromatography (SiO_2, 40% EtOAc in Hexanes) to yield 255 mg (38%) of **12c**. ^{1}H NMR (400 MHz, DMSO-d_6, δ): 10.67 (s, 1H), 6.52 (s, 1H), 6.43 (s, 1H), 5.70 (s, 1H), 5.62 (s, 1H), 2.40 (s, 6H), 1.94 (s, 6H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6, δ): 196.96, 146.93, 143.05, 142.21, 136.90, 135.05, 134.03, 132.83, 119.76, 113.31, 60.71, 34.89, 29.82, 21.21, 17.82, 16.08, 14.31. IR (solid) ν_{max} (cm^{-1}): 3201 (br, -OH). Mass spectrometry (*m*/*z*): calculated for $C_{21}H_{27}O_3$ $(M+H)^+$: 327.1960, found: 327.1949 $(M+H)^+$.

2-(3'-(*tert*-Butyl)-4',5'-dihydroxy-2,3,5,6-tetramethyl-[1,1'-biphenyl]-4-yl)-4,4,5,5-tetramethylimidazolidine-1,3-diol (13c). To a 10 mL round bottom flask, 255 mg (0.78 mmol) of **12c** was added with 345 mg (1.96 mmol) of **BHA** and pump purged with nitrogen five times. Using a nitrogen purged syringe, 2 mL of degassed and dried methanol was added to the reaction flask. The reaction was shielded from light and allowed to stir under nitrogen at room temperature for 5 days upon which the product had precipitated. The product was collected by vacuum filtration to yield 80 mg (22%) crude **13c** which was used directly in the synthesis of **14c**. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 9.47 (s, 1H), 8.03 (s, 1H), 7.31 (s, 1H), 6.95 (s, 1H), 6.37 (s, 1H), 6.27 (s, 1H), 5.31 (s, 1H), 2.05 (s, 6H), 1.57 (s, 6H), 1.33 (s, 9H), 1.12 (s, 6H), 0.99 (s, 6H). IR (solid) ν_{max} (cm^{-1}): 3266 (br, -OH).

2-(3'-(*tert*-Butyl)-4',5'-dihydroxy-2,3,5,6-tetramethyl-[1,1'-biphenyl]-4-yl)-4,4,5,5,-tetramethyl-4,5-dihydroimidazol-3-oxide-1-oxyl (14c). To a 100 mL round bottom flask, 80 mg (0.17 mmol) of **13c** was added with 20 mL diethyl ether, 10 mL buffer (pH = 7), and chilled to 0°C. To a 125 mL separatory funnel, 67 mg (0.26 mmol) I_2 was added with 20 mL diethyl ether and added dropwise to the stirring reaction mixture. After all of the I_2 was added, the reaction was warmed to room temperature and transferred to a separatory funnel with 100 mL buffer (pH = 7). The organic layer was washed once with saturated $Na_2S_2O_3$ solution followed by saturated NaCl solution. The organic layer was dried over Na_2SO_4 and the solvent removed under reduced pressure to yield 65 mg (81%) of purple solid **14c**. IR (solid) ν_{max} (cm^{-1}): 3253 (br, -OH). EPR (X-Band, 298 K): a_N = 7.45 G (1:2:3:2:1). Mass spectrometry (*m*/*z*): calculated for $C_{27}H_{38}N_2O_4$ $(M+H)^+$: 454.2831, found: 452.2816 $(M+H)^+$.

Tp^{Cum,Me}Zn(SQ-PhMe$_4$-NN) (1-PhMe$_4$). To an oven dried 25 mL schlenk flask, 64 mg (0.14 mmol) of **14c** was added with 150 mg (0.22 mmol) of **Tp^{Cum,Me}Zn(OH)** and pump purged

with nitrogen five times. Using a purged syringe, 10 mL of a 1:1 mixture of dry and degassed dichloromethane and methanol was added to the reaction mixture with stirring. The reaction was allowed to stir for 2 h under nitrogen then opened to air and stirred overnight. The solvent was removed under reduced pressure and the product purified by column chromatography (Basic Alumina, 1:1 EtOAc:Hexanes) to yield 150 mg (94%) of **1-PhMe$_4$**. Crystals of **1-PhMe$_4$** were grown from slow evaporation of benzene in ethanol. IR (solid) ν_{max} (cm^{-1}): 2532 (w, -BH). EPR (~0.2 mM in CH_2Cl_2): apparent a_N = 3.74 G. Mass spectrometry (*m*/*z*): calculated for $C_{66}H_{82}BN_8O_4Zn$ $(M+H)^+$: 1125.5843, found: 1125.5833 $(M+H)^+$. Elemental Analysis Calculated: (C: 70.36, H: 7.25, N: 9.95). Found: (C: 69.92, H: 7.23, N: 9.58).

4-Bromo-2-(*tert*-butyl)-1-methoxybenzene (15). To a 250 mL round bottom flask 7.33 g (44.63 mmol) 1-(*tert*-butyl)-2-methoxybenzene and 75 mL dichloromethane were added and then chilled to -78 °C. 2.40 mL (46.86 mmol) Bromine was dissolved in 50 mL dichloromethane and then added dropwise to the 250 mL round bottom flask at -78 °C via a dripping funnel. The mixture was stirred for another 1h at -78 °C and then allowed to warm to room temperature. The completed reaction was poured into a separatory funnel containing 100 mL saturated $NaHCO_3$ solution. The organic layer was then washed with saturated NaCl solution three times and dried over Na_2SO_4. The solvent was removed under reduced pressure to yield 10.7 g (99%) compound **15**. ^{1}H NMR data are consistent with literature reported.[21]

^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.35 (d, *J* = 2.4 Hz, 1H), 7.27 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 3H), 1.35 (s, 9H).

Ethyl 4-(3-(*tert*-butyl)-4-methoxyphenyl)-4-hydroxycyclohexanecarboxylate (16). To an oven dried 250 mL Schlenk flask 1.06g (50.00 mmol) magnesium turnings, 2.4g (9.87 mmol) **15** and a few crystals of iodine were added. The Schlenk flask was purged with N_2 for 10 min

and then 100 mL anhydrous THF was added. The Schlenk flask was fitted with a condenser and reaction mixture was heated to reflux for 16 h. The reaction mixture was allowed to cool to room temperature and the condenser replaced with a rubber septum. The resulting Grignard reagent was added to a solution of 1.5 g ethyl 4-oxocyclohexanecarboxylate (8.81 mmol) in 50 mL THF in a 250 mL round bottom flask via cannula at 0 °C. The mixture was then heated to 50°C and stirred for another 3h. Upon reaction completion, the mixture was poured into a separatory funnel containing 200 mL saturated NaCl solution. The aqueous layer was extracted with dichloromethane three times. The organic layers were collected, dried over Na_2SO_4, and the solvent removed under reduced pressure. Purification via column chromatography (SiO_2, 25% ethyl acetate in hexanes) gave 1.18 g (40%) compound **16**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.42 (d, *J* = 2.4 Hz, 1H), 7.29 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 2.65-2.58 (m, 1H), 2.26-2.14 (m, 2H), 2.10-1.98 (m, 2H), 1.94-1.80 (m, 2H), 1.80-1.68 (m, 2H), 1.37 (s, 9H), 1.26 (t, *J* = 7.1, 3H).^{13}C NMR (75 MHz, C_6D_6, δ): 174.54, 157.51, 140.62, 137.62, 123.57, 123.52, 111.30, 72.25, 59.79, 54.51, 39.56, 36.18, 35.06, 29.89, 24.05. IR (film) ν_{max} (cm^{-1}): 3398 (br, -OH), 1726 (s, -C=O). Mass spectrometry (*m/z*): calculated for $C_{20}H_{28}O_3$ $(M+H)^+$: 317.2111, found: 317.2110 $(M+H)^+$.

Ethyl 4-allyl-4-(3-(*tert*-butyl)-4-methoxyphenyl)cyclohexanecarboxylate (17). To a N_2 filled 100 mL Schlenk flask 3.5g compound **16** (10.5 mmol), allyltrimethylsilane 2.5 mL (15.75 mmol) and 50mL dichloromethane was added. The mixture was chilled to -78°C and then 1.62 mL $BF_3 \cdot Et_2O$ (12.8 mmol) was added via syringe. The reaction mixture was stirred at -78°C for one hour, allowed to warm to room temperature and stirred for an additional 20 h. The mixture was poured into a separatory funnel containing 100 mL saturated NaCl solution. The organic layer was washed once with saturated $NaHCO_3$ solution followed by two washes of

saturated NaCl solution. The organic layer was then dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, 30% dichloromethane in hexanes) to yield 3.2 g (85%) of compound **17** as a 1 : 3.5 mixture of *cis*- and *trans*- isomers. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.35 (d, *J* = 2.1 Hz, 1H), 7.23-7.05 (m, 1H), 6.83 (d, J = 8.4 Hz, 1H), 6.10-5.95 (m, 1H), 5.55-5.35 (m, 1H), 4.95-4.92 (m, 1H), 4.22-4.05 (m, 2H), 3.84 (s, 2.3H), 3.82 (s, 0.7H), 2.64-1.55 (m, 11H), 1.39 (s, 6.8H), 1.37 (s, 2.2H), 1.36 (t, *J* = 7.2 Hz, 3H), ^{13}C NMR (75 MHz, $CDCl_3$, δ): 176.06, 157.91, 137.99, 136.37, 135.24, 135.16, 133.89, 125.45, 123.59, 122.24, 120.88, 116.94, 111.30, 110.96, 60.49, 55.28, 43.67, 39.39, 35.09, 34.24, 29.90, 28.41, 27.09, 25.92, 25.05, 24.50, 14.42. IR (film) ν_{max} (cm^{-1}): 1729 (s, -C=O). Mass spectrometry (*m/z*): calculated for $C_{23}H_{34}O_3$ $(M+Na)^+$: 381.2400, found: 381.2398 $(M+Na)^+$.

Ethyl 4-(3-(*tert*-butyl)-4-methoxyphenyl)-4-(2,3-dihydroxypropyl)cyclohexane-carboxylate(18). To a 50 mL round bottom flask 1.0 g **17** (2.8 mmol), 0.5 g N-methylmorpholine-N-oxide (4 mmol), 20 mL acetonitrile and 5 mL DI water was added. The mixture was cooled to 0°C and 0.6mL solution of OsO_4 (2.5 wt. % in *t*-BuOH, 0.06 mmol) was added via syringe. The reaction mixture was stirred in the dark for 4h and allowed to warm to room temperature. 10 mL Na_2SO_3 saturated solution was added to the mixture and stirred for 10 min. The reaction mixture was concentrated in vacuo and partitioned between H_2O and dichloromethane. The aqueous layer was extracted with dichloromethane three times. All organic layers were collected, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, 40% Ethyl acetate in hexanes) to yield 0.77 g (68%) of compound **18** as a 1 : 2.7 mixture of *cis*- and *trans*- isomers. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.24 (d, *J* = 2.4 Hz, 1H), 7.17-7.12 (m, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.14

(q, J = 6.9 Hz, 0.5H), 4.04 (q, J = 6.9 Hz, 1.5H), 3.82 (s, 3H), 3.65-3.45 (m, 1H), 3.35-3.15 (m, 2H), 2.55-1.4 (m, 11H), 1.36 (s, 9H), 1.26 (t, J = 6.9 Hz, 0.8H), 1.19 (t, J = 6.9 Hz, 2.2 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 175.99, 175.86, 156.82, 138.70, 139.35, 134.57, 125.61, 125.03, 124.41, 124.28, 111.91, 111.52, 69.46, 69.00, 67.54, 60.43, 60.28, 55.12, 50.38, 43.55, 42.16, 40.04, 38.58, 36.50, 35.67, 35.23, 34.64, 29.94, 24.95, 24.82, 24.51, 24.39, 14.33, 14.35. IR (film) ν_{max} (cm^{-1}): 3401 (br, -OH), 1727 (s, -C=O). Mass spectrometry (*m/z*): calculated for $C_{23}H_{36}O_5$ $(M+Na)^+$: 415.2455, found: 415.2455 $(M+Na)^+$.

Ethyl 4-(3-(*tert*-butyl)-4-methoxyphenyl)-4-(2-oxoethyl)cyclohexanecarboxylate (19). To a 100 mL round bottom flask 0.77g **18** (1.96 mmol), 20 mL Et_2O and 10 mL DI H_2O was added. The mixture was cooled to 0°C and 0.5 g $NaIO_4$ (2.35 mmol) was added portionwise as solid. The reaction mixture was stirred at room temperature for 36h and then concentrated in vacuo. The mixture was extracted with Ethyl acetate three times. The organic layer was washed with saturated NaCl solution three times and dried over Na_2SO_4. Solvent was removed under reduced pressure and yield 0.66 g (94%) **19** as crude product. Compound **19** was used for next step without further purification.

Ethyl 4-(3-(*tert*-butyl)-4-methoxyphenyl)-4-(2-hydroxyethyl)cyclohexanecarboxylate (20). To a 250 mL round bottom flask was added 2.95 g (8.18 mmol) compound **19** and 120 mL MeOH. The mixture was cooled to 0°C and 0.46 g $NaBH_4$ (12.27 mmol) was added portionwise as solid. The reaction mixture was stirred at 0°C for 30 min and then 20 mL DI H_2O was added. The mixture was concentrated in vacuo and partitioned between H_2O and dichloromethane**.** The aqueous layer was extracted with dichloromethane three times. All organic layers were collected, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, 25% Ethyl acetate in hexanes) to yield 2.94 g (99%)

of compound **20** as a 1 : 2.3 mixture of *–cis* and *–trans* isomers. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.21 (d, *J* = 2.4 Hz, 1H), 7.14-7.08 (m ,1H), 6.82 (d, *J* = 8.4 Hz, 1H), 4.15 (q, J = 7.2 Hz, 0.6H), 4.04 (q, J = 6.9 Hz, 1.4H), 3.82 (s, 3H), 3.52-3.36 (m, 2H), 2.5-1.7 (m ,11H), 1.37 (s, 2.7H), 1.36 (s, 6.3H), 1.4-1.25 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 176.03, 175.88, 156.66, 156.57, 139.23, 138.23, 137.94, 134.90, 125.36, 124.98, 124.12, 111.65, 111.28, 60.40, 60.25, 59.57, 58.41, 55.11, 49.34, 43.62, 42.33, 39.91, 38.35, 35.87, 35.21, 35.17, 34.83, 29.07, 24.90, 24.52, 14.44, 14.35. IR (film) ν_{max} (cm^{-1}): 3434 (br, -OH), 1727 (s, -C=O). Mass spectrometry (*m/z*): calculated for $C_{22}H_{34}O_4$ $(M+Na)^+$: 385.2349, found: 385.2343 $(M+Na)^+$.

Ethyl 4-(2-bromoethyl)-4-(3-(*tert*-butyl)-4-methoxyphenyl)cyclohexanecarboxylate (21). To a 50 mL Schlenk flask was added 1.00g compound **20** (2.76 mmol) and 1.19 g CBr_4 (3.59 mmol), pump purged for three times and filled with N_2. 20mL Dichloromethane was added to the Schlenk flask and then cooled to 0°C. To the mixture was added a solution of 1.45 g PPh_3 (5.52 mmol) in 10 mL dichloromethane via syringe, stirred at 0°C for one hour. The reaction mixture was allowed to warm to room temperature and stirred for additional 20 h. The reaction mixture was concentrated in vacuo until about 2 mL solution was left and then was poured into a beaker containing 100 mL hexanes. Precipitates were removed by filtration and washed with 50 mL hexanes. Filtrate was collected and solvents removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, 10% Ethyl acetate in hexanes) to yield 0.92 g (79%) of compound **21** as a 1 : 2.7 mixture of *–cis* and *–trans* isomers. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.19 (d, *J* = 2.4 Hz, 0.3H), 7.15 (d, *J* = 2.4 Hz, 0.7H), 7.06 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 0.3H), 7.04 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 0.7H), 6.82 (d, *J* = 8.4 Hz, 0.3H), 6.81 (d, *J* = 8.4 Hz, 0.7H), 4.16 (q, *J* = 8.4 Hz, 0.5H), 4.04 (q, *J* = 8.4 Hz, 1.5H), 3.83 (s, 3H), 3.06-2.94 (m, 2H), 2.40-1.40 (m, 11H), 1.37 (s, 2.4H), 1.36 (s, 6.6H), 1.28 (t, *J* = 7.2 Hz, 0.8H), 1.19 (t, *J* = 7.2 Hz,

2.2H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 175.78, 175.66, 156.83, 156.74, 138.30, 138.09, 133.77, 133.62, 125.40, 124.96, 124.21, 124.07, 111.69, 111.39, 60.46, 60.29, 55.13, 50.18, 43.52, 42.15, 42.04, 40.71, 35.40, 35.18, 34.39, 29.96, 29.24, 24.83, 24.43, 14.45, 14.35. IR (solid) ν_{max} (cm^{-1}): 1727 (s, -C=O). Mass spectrometry (*m/z*): calculated for $C_{22}H_{33}O_3Br$ $(M+Na)^+$: 477.1505, found: 477.1502 $(M+Na)^+$.

Ethyl 4-(3-(*tert*-butyl)-4-methoxyphenyl)bicyclo[2.2.2]octane-1-carboxylate (22), To a 500 mL Schlenk flask was added 1.3 g compound **21** (3.06 mmol) and pump purged three times. Then 200 mL anhydrous THF and 2.13 mL hexamethylphosphoramide (HMPA, 12.24 mmol, dried over molecular sieves) were added to the Schlenk flask and chilled to -78°C. To the mixture, freshly prepared solution of lithium diisopropylamine (LDA, 3.98 mmol) in 50 mL THF was added dropwise via cannula. The reaction mixture was allowed to warm to room temperature and stir for another 16 h. The reaction mixture was then concentrated in vacuo and partitioned between H_2O and hexanes. Aqueous layer was extracted with hexanes three times. All organic layers were collected, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, 10% Ethyl acetate in hexanes) to yield 0.83 g (79%) of compound **22**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.24 (d, J = 2.4 Hz, 1H), 7.11 (dd, J = 8.4 Hz, J = 2.4 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 4.12 (q, J = 7.0 Hz,), 3.82 (s, 1H), 1.95-1.88 (m, 6H), 1.88-1.81 (m, 6H), 1.37 (s, 9H), 1.25 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, δ):178.28, 156.62, 140.75, 137.64, 124.06, 123.71, 111.15, 60.32, 55.14, 39.12, 35.20, 34.35, 32.09, 29.94, 29.00, 14.39. IR (solid) ν_{max} (cm^{-1}): 1721 (s, C=O). Mass spectrometry (*m/z*): calculated for $C_{22}H_{33}O_3$ $(M+H)^+$: 345.2425, found: 345.2424 $(M+H)^+$.

(4-(3-(*tert*-Butyl)-4-methoxyphenyl)bicyclo[2.2.2]octan-1-yl)methanol (23). To a 500 mL Schlenk flask was added 0.83 g compound **22** (2.41 mmol), pump purged for three times and filled with N_2. To the Schlenk flask was added 50 mL dichloromethane and chilled to -78°C, then 4.82 mL diisobutylaluminum hydride (DIBAL-H, 4.82 mmol, 1M solution in *n*-hexane) was added dropwise via syringe. The reaction was stirred at -78°C for 30 min and then allowed to warm to room temperature and stirred for additional 2 h. Upon reaction completion, the mixture was poured into 100 mL ice water and then acidified with 2M HCl. The aqueous phase was extracted with dichloromethane three times. All organic layers were combined and washed with saturated NaCl solution and then dried over Na_2SO_4. The solvent was removed under reduced pressure to yield 0.65 g (90%) **23** as crude product. Compound **23** was used for next step without further purification.

4-(3-(*tert*-Butyl)-4-methoxyphenyl)bicyclo[2.2.2]octane-1-carbaldehyde (24). To a 50 mL round bottom flask was added 0.1 g compound **23** (0.33 mmol) and 20 mL dichloromethane. 0.14 g PCC (0.66 mmol) and 0.28 g silica gel were placed in a mortar and grinded, added to the round bottom flask portion-wise, and the mixture stirred at room temperature for 2 h. The resulting suspension was then filtered through a 2 cm neutral alumina plug. The filtrate was collected and the solvent removed under reduced pressure and yield 0.074 g (74%) compound **24** as crude product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 9.52 (s, 1H), 7.23 (d, J = 2.4 Hz, 1H), 7.10 (dd, J = 8.7 Hz, J = 2.4 Hz, 1H), 6.81 (d, J = 8.7 Hz, 1H), 3.82 (s, 3H), 1.90-1.85 (m, 6H), 1.80-1.75 (m, 6H), 1.37 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 206.47, 156.71, 140.41, 137.74, 124.02, 123.73, 111.21, 55.14, 44.04, 35.21, 31.58, 29.94, 28.89, 26.32. IR (solid) ν_{max} (cm^{-1}): 1719 (s, C=O). Mass spectrometry (*m/z*): calculated for $C_{20}H_{28}O_2$ $(M+H)^+$: 301.2162, found: 301.2162 $(M+H)^+$.

4-(3-(*tert*-Butyl)-4-hydroxyphenyl)bicyclo[2.2.2]octane-1-carbaldehyde (25). To a 50 mL Schlenk flask was added 0.1 g compound **24** (0.33 mmol), pump purged for three times and filled with N_2. 15 mL dichloromethane was added and chilled to -78°C then 0.1 mL BBr_3 (1.00 mmol) was added dropwise via syringe. The reaction was stirred at -78°C for 2 h and then allowed to warm to room temperature and stirred for additional 12 h. Upon reaction completion, the mixture was poured into 100 mL ice water. The aqueous phase was extracted with dichloromethane three times. The organic layers were combined and washed with saturated $NaHCO_3$ solution once followed by three washes of saturated NaCl solution. The organic layer was collected and dried over Na_2SO_4. The solvent was removed under reduced pressure. Purification via column chromatography (SiO_2, 25% ethyl acetate in hexanes) produced 0.066 g (70%) compound **25**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 9.52 (s, 1H), 7.21 (d, J = 2.4 Hz, 1H), 6.99 (dd, J = 8.4 Hz, J = 2.4 Hz, 1H), 6.61 (d, J = 8.4 Hz, 1H), 4.73 (s, 1H), 1.89-1.85 (m, 6H), 1.80-1.76 (m, 6H), 1.41 (s, 9H).^{13}C NMR (75 MHz, $CDCl_3$, δ): 206.56, 152.30, 140.88, 135.58, 124.35, 123.90, 116.26, 44.04, 35.24, 34.93, 31.59, 29.79, 26.29. IR (solid) ν_{max} (cm^{-1}): 3373 (br, OH), 1698 (s, C=O). Mass spectrometry (*m/z*): calculated for $C_{19}H_{26}O_2$ $(M-H)^-$: 285.1860, found: 285.1865 $(M-H)^-$.

4-(5-(*tert*-Butyl)-3,4-dioxocyclohexa-1,5-dien-1-yl)bicyclo[2.2.2]octane-1-carbaldehyde (26). To a 5 mL round bottom flask 0.14 g (0.49 mmol) compound **25** and 0.27 g (0.98 mmol) **IBX** were added with 2 mL DMF and stirred in the dark for 2 days. Upon reaction completion, the mixture was poured into 100 mL saturated $NaHCO_3$ solution in a separatory funnel and extracted with ethyl acetate three times. The organic layers were combined and washed with saturated NaCl three times and then dried over Na_2SO_4. The solvent was removed

under reduced pressure and gave 0.14 g (95%) compound **26** as crude product. Compound **26** was used for next step without further purification.

4-(3-(*tert*-Butyl)-4,5-dihydroxyphenyl)bicyclo[2.2.2]octane-1-carbaldehyde (27). Compound **26** (0.14 g, 0.47 mmol) was dissolved in 10 mL tetrahydrofuran and added to a separatory funnel containing 0.25 g (1.41 mmol) ascorbic acid dissolved in 10 mL water. The mixture was shaken for about 5 minutes then 10 mL saturated NaCl solution was added and the layers allowed to separate. The organic layer was diluted with 50 mL ethyl acetate and washed three times with a saturated NaCl solution. The organic layer was collected, dried over Na_2SO_4, and the solvent removed under reduced pressure. Purification via column chromatography (SiO_2, 40% ethyl acetate in hexanes) produced 0.08 g (53%) compound **27**. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 9.45 (s, 1H), 9.15, (s, 1H), 7.73 (s, 1H), 6.63 (d, J = 2.1 Hz, 1H), 6.58 (d, J = 2.1 Hz, 1H), 1.74-1.65 (m, 12H), 1.32 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6, δ): 207.07, 145.02, 142.27, 138.97, 135.25, 114.02, 111.03, 43.85, 35.12, 35.08, 31.73, 30.13, 26.24. IR (solid) ν_{max} (cm^{-1}): 3277 (br, OH), 1714 (s, C=O). Mass spectrometry (*m/z*): calculated for $C_{19}H_{24}O_3$ $(M+Na)^+$: 323.1618, found: 323.1617 $(M+Na)^+$.

2-(4-(3-(*tert*-Butyl)-4,5-dihydroxyphenyl)bicyclo[2.2.2]octan-1-yl)-4,4,5,5-tetramethylimidazolidine-1,3-diol (28). To a 25 mL Schlenk flask were added 0.25 g compound **27** (0.84 mmol) and 0.24 g 2,3-dimethyl-2,3-bis(hydroxyamino)butane (1.68 mmol). The flask was pump purged three times and filled with N_2. Then 10 mL anhydrous methanol was added to the reaction flask via syringe. The reaction mixture was stirred for 24 h, and then solvent was removed under reduced pressure. The crude product **28** was used for next step without further purification.

2-(4-(3-(*tert*-Butyl)-4,5-dihydroxyphenyl)bicyclo[2.2.2]octan-1-yl)-4,4,5,5,-tetramethyl-4,5-dihydroimidazol-3-oxide-1-oxyl (29). To a 250 mL round bottom flask, 0.66g (1.52 mmol) of compound **28** was added with 60 mL diethyl ether, 40 mL buffer (pH = 7), and then cooled to 0°C. To a 125 mL separatory funnel, 0.58 g (2.28 mmol) I_2 was added with 40 mL diethyl ether and added dropwise to the stirring reaction mixture. After all of the I_2 was added, the reaction was warmed to room temperature and transferred to a separatory funnel with 100 mL buffer (pH = 7). The organic layer was washed once with saturated $Na_2S_2O_3$ solution followed by saturated NaCl solution. The organic layer was dried over Na_2SO_4 and the solvent removed under reduced pressure to yield 0.53 g (81%) of purple solid **29**. IR (solid) ν_{max} (cm^{-1}): 3184 (br, OH). EPR (X-Band, 298 K): a_N = 7.45 G (1:2:3:2:1). Mass spectrometry (*m*/*z*): calculated for $C_{25}H_{37}N_2O_4$ $(M+H)^+$: 429.2748, found: 429.2735 $(M+H)^+$.

$Tp^{Cum,Me}$Zn(SQ-bicyclo[2.2.2]octanyl-NN) (1-BCO). To an oven dried 25 mL Schlenk flask, 0.12 g (0.27 mmol) of compound **29** was added with 0.20 g (0.28 mmol) of **$Tp^{Cum,Me}$Zn(OH)** and pump purged with nitrogen three times. Then 15 mL anhydrous methanol and 2 mL dichloromethane were added to the Schlenk flask. The reaction was allowed to stir for 1 h under nitrogen then opened to air and stirred overnight. The solvent was removed under reduced pressure and the product purified by column chromatography (basic alumina, 30% ethyl acetate in hexanes) to yield 0.13 g (44%) of **$Tp^{Cum,Me}$Zn(SQ-BCO-NN)**. Crystals were grown from slow evaporation of dichloromethane in methanol. IR (solid) ν_{max} (cm^{-1}): 2546 (w, BH). EPR (~0.2 mM in CH_2Cl_2): apparent a_N = 3.66 G. Mass spectrometry (*m*/*z*): calculated for $C_{64}H_{81}N_8O_4BZn$ $(M+H)^+$: 1101.5838, found: 1101.5832 $(M+H)^+$.