Supporting Information for:

Photoresponsive Molecular Switch for Regulating Transmembrane Proton-Transfer Kinetics

Ying Li,[†] Edmund C. M. Tse,[†] Christopher J. Barile,[†]
Andrew A. Gewirth,[*,†,§] and Steven C. Zimmerman[*,†]

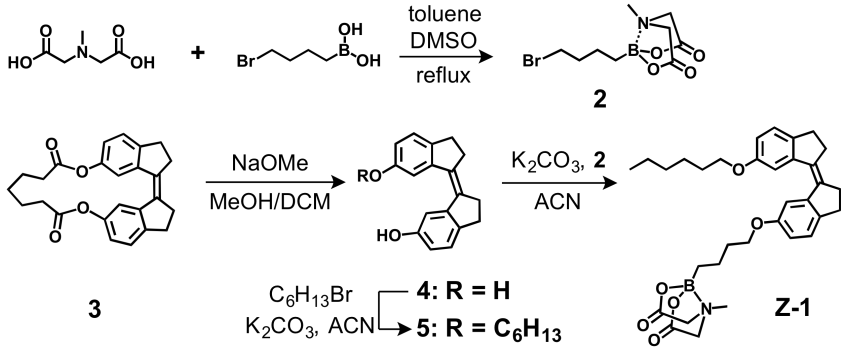
[†] Department of Chemistry, University of Illinois at Urbana–Champaign,
600 South Mathews Avenue, Urbana, Illinois 61801, United States
[§] International Institute for Carbon Neutral Energy Research (WPI-I2CNER),
Kyushu University, Fukuoka 812-8581, Japan

Table of Contents

General Methods

All reactions were carried out under a dry N_2 atmosphere. Chemicals were purchased from commercial sources and used without further purification. Dry dichloromethane (DCM), tetrahydrofuran (THF), dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were used directly from a solvent delivery system just prior to use. Freshly purchased triethylamine (TEA) was dried and stored over 4 Å molecular sieves. All other solvents, like ethanol (EtOH), methanol (MeOH), ethyl acetate (EtOAc), and hexanes (Hx) were of reagent grade and used without further purification. Reported reaction temperatures refer to the temperature of the heating medium. Compound **3** was synthesized according to the published procedures.[1] The progress of reactions was monitored by silica gel thin layer chromatography (TLC) using 0.2 mm silica 60 coated, plastic plates with F254 indicator. Flash and gravity chromatography was performed using 230-400 mesh (40-63 μm) silica gel (SiO_2). Ratios of solvents for NMR solvents and flash chromatography are reported as volume ratios. All NMR spectra were acquired in the Varian-Oxford Instrument Center for Excellence in NMR Spectroscopy (VOICE) laboratory at the University of Illinois at Urbana–Champaign. ^{1}H and ^{13}C NMR spectra of reaction products were recorded on a Varian Unity 500 spectrometer (^{1}H, 500 MHz; ^{13}C, 125 MHz) in $CDCl_3$ unless otherwise noted. ^{11}B NMR spectra of reaction products were recorded on a Varian Unity Inova 400 spectrometer in CD_2Cl_2. Chemical shifts (δ) and coupling constants (J) are reported in parts per million (ppm) and hertz (Hz), respectively. ^{1}H NMR chemical shifts were referenced to the residual protio solvent peak at 7.26 ppm in chloroform-*d* ($CDCl_3$), 5.32 ppm in dichloromethane-*d*2 (CD_2Cl_2), and 3.35 ppm in methanol-*d4* (CD_3OD). For ^{13}C spectra, chemical shifts were referenced to the solvent peak at 77.0 ppm in $CDCl_3$, 53.5 ppm in CD_2Cl_2, and 49.3 ppm in CD_3OD. Electrospray ionization mass spectrometry (ESI-MS) data were collected with a Quattro II instrument (Waters) at the University of Illinois at Urbana–Champaign.

Synthetic Procedures

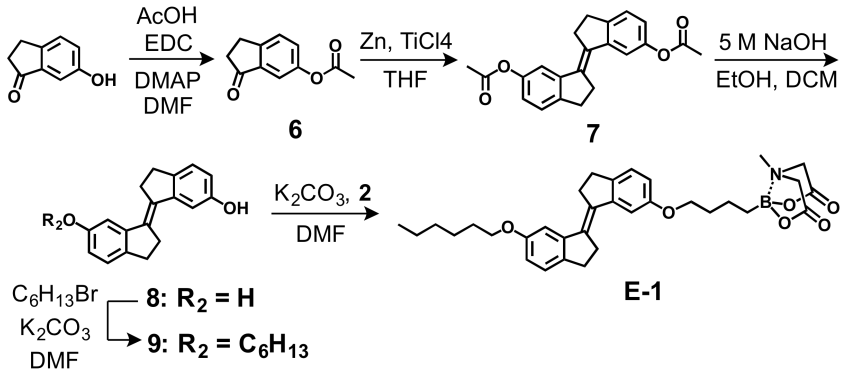


Compound 2. To a solution of (4-bromobutyl)boronic acid (540 mg, 3 mmol) in 30 mL of benzene and 3 mL of DMSO was added methyliminodiacetic acid (441.4 mg, 3 mmol). The suspension was refluxed for 3 h and became a clear solution. The solvents were removed *in vacuo* and the residue was dissolved in about 50 mL of EtOAc. The organic layer was washed with about 50 mL of brine, dried over Na_2SO_4, and concentrated to a solution of about 5 mL *in vacuo*. The solution was dropwise added into 50 mL of ether. The precipitation was collected by vacuum filtration to afford 720 mg (82%) of the product as a white solid. ^{1}H NMR (CD_3OD:$CDCl_3$ = 1:9) δ 3.83 (d, *J* = 16.5, 2H), 3.69 (d, *J* = 16.5, 2H), 2.93 (s, 3H), 1.92 (m, 2H), 1.55 (m, 4H), 0.65 (m, 2H). ESI-LRMS (*m/z*): calcd for $[M+H]^+$, 292.0; found, 291.9.

Compound 4. To a solution of **3** (600 mg, 1.5 mmol) in 10 mL of DCM and 5 mL of MeOH was added NaOMe (1 g, 19 mmol). The suspension immediately turned red and was stirred at room temperature for 1 h. Prolonged stirring resulted in the formation of side products. The mixture was filtered, and the solvent was removed *in vacuo*. The residue was dissolved in DCM and dried over Na_2SO_4. The organic layer was concentrated *in vacuo* to give 320 mg (78%) of the product as an off-red waxy solid. The solid was used without further purification. ^{1}H NMR δ 7.63 (s, 2H), 7.14 (m, 2H), 6.70 (m, 2H), 2.90 (m, 4H), 2.81 (m, 4H). ESI-LRMS (*m/z*): calcd for $[M+H]^+$, 265.1; found, 265.2.

Compound 5. To a solution of **5** (300 mg, 1.1 mmol) and 1-bromohexane (168 mg, 1.0 mmol) in 6 mL of dry ACN was added K_2CO_3 (800 mg, 5.9 mmol). The mixture was stirred at 80 °C overnight. The suspension was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in DCM and dried over Na_2SO_4. The solvent was removed *in vacuo*, and the crude product was purified by gradient column chromatography (EtOAc:Hx = 0:1 to 1:9) to give 152 mg (45%) of the product as a yellow waxy solid. ^{1}H NMR δ 7.61 (m, 2H), 7.16 (m, 2H), 6.75 (m, 1H), 6.67 (m, 1H), 4.76 (s, 1H), 3.92 (t, *J* = 6.5, 2H), 2.91 (m, 4H), 2.80 (m, 4H), 1.76 (m, 2H), 1.43 (m, 2H), 1.32 (m, 4H), 0.89 (m, 3H). ESI-LRMS (*m/z*): calcd for $[M+H]^+$, 349.2; found, 349.1.

Compound Z-1. To a solution of **8** (75 mg, 0.22 mmol) and **2** (75 mg, 0.26 mmol) in 3 mL of dry ACN was added K_2CO_3 (300 mg, 2.2 mmol). The mixture was stirred at 80 °C overnight. The suspension was filtered, and the filtrate was concentrated down under vacuum. The residue was dissolved in DCM and dried over Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by gradient column chromatography (EtOAc:hexanes = 0:1 to 1:4) to give 58 mg (48%) of the product as a yellow gel-like solid. ^{1}H NMR δ 7.62 (m, 2H), 7.17 (m, 2H), 6.74 (m, 2H), 3.92 (m, 4H), 3.79 (m, 2H), 3.64 (m, 2H), 2.91 (m, 4H), 2.84 (s, 3H), 2.81 (m, 4H), 1.80 (m, 2H), 1.73 (m, 2H), 1.53 (m, 2H), 1.42 (m, 2H), 1.31 (m, 4H), 0.88 (m, 4H), 0.65 (m, 2H). ^{13}C NMR (CD_3OD:$CDCl_3$=1:9) δ 166.8, 157.5, 141.7(1), 140.7(0), 140.6(6), 135.6, 135.5, 125.7, 125.7, 115.0, 114.9, 109.3, 109.1, 68.5, 67.9, 62.7, 62.1, 53.6, 45.7, 35.5(3), 35.5(2), 32.1, 31.7, 30.0, 29.9(9), 29.5, 25.9, 22.8, 20.5, 14.2. ^{11}B NMR δ 13.0. ESI-HRMS (*m/z*): calcd for $[M+H]^+$ 560.3183; found, 560.3203.



Compound 6. To a suspension of 6-hydroxy-1-indanone (1.6g, 11 mmol) and DMAP (0.25 g, 2 mmol) in 10 mL of DMF was added glacial acetic acid (0.7 g, 12 mmol). The mixture was stirred at room temperature for 15 min and EDC was added (2.5 g, 13 mmol). The mixture was stirred overnight at room temperature, and the solvent was removed under vacuum. The residue was dissolved in DCM and washed with brine. The organic layer was dried over Na_2SO_4 and concentrated down under vacuum. The crude product was purified by gradient column chromatography (EtOAc:hexanes = 0:1 to 1:2) to give 1.2 g (58%) of the product as an off-white solid. ^{1}H NMR δ 7.49 (d, *J* = 10.5, 1H), 7.45 (d, *J* = 3, 1H), 7.31 (dd, *J* = 10, 3, 1H), 3.14 (m, 2H), 2.74 (m, 2H), 2.83 (s, 3H).

Compound 7. A 200 mL flask was charged with Zn powder (3.86 g, 60 mmol), flame-dried under vacuum, and cooled under N_2. The flask was charged with 90 mL of dried THF and cooled to -78 °C. $TiCl_4$ in THF (1 M, 3.3 mL, 3.3 mmol) was added dropwise, and the suspension was warmed up to room temperature and refluxed for 1 h. A solution of **6** (1.2 g, 6.3 mmol) in 5 mL of THF was added, and the mixture was refluxed for 3 h. The reaction was cooled to room temperature and quenched with 90 mL of saturated NH_4Cl solution. The mixture was stirred at room temperature for 4 h and left to sit for 1 h. The top organic layer was separated and concentrated *in vacuo*. The residue was dissolved in DCM, dried over Na_2SO_4, and concentrated *in vacuo* to afford 850 mg (77%) of the crude product as a light pink solid. The solid was used

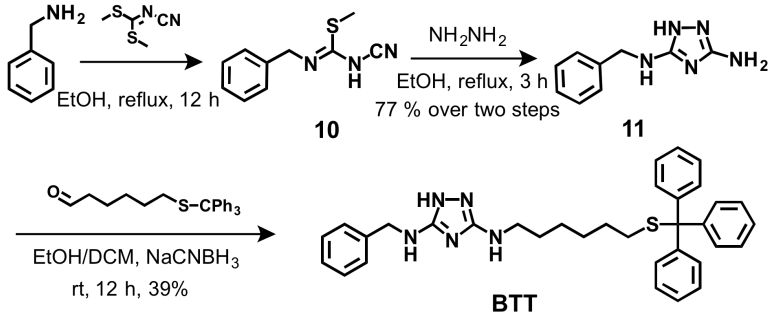
without further purification. ESI-LRMS (*m/z*): calcd for $[M+H]^+$, 349.1; found, 349.2, 307.2 $[M+H-Ac]^+$, 265.2 $[M+H-2Ac]^+$.

Compound 8. To a solution of **7** (850 mg, 2.4 mmol) in 3 mL of DCM and 1 mL of EtOH was added 4 mL of NaOH (10 M) solution. The mixture was stirred at 80 °C for 3 h. The volatile solvents were removed *in vacuo*, and the residue was dissolved in DCM. The organic layer was washed with saturated NH_4Cl solution, dried over Na_2SO_4, and concentrated *in vacuo* to give 630 mg (96%) of the crude product as an off-white solid. The solid contained both cis and trans forms and was used without further purification.

Compound 9. To a solution of **8** (180 mg, 0.68 mmol) and 1-bromohexane (100 mg, 0.62 mmol) in 4 mL of dry DMF was added K_2CO_3 (125 mg, 1.2 mmol). The mixture was stirred at 80 °C overnight. The suspension was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in DCM and dried over Na_2SO_4. The solvent was removed *in vacuo*, and the crude product was purified by gradient column chromatography (EtOAc:hexanes = 0:1 to 1:9) to give 112 mg (55%) of the product as an off-white solid. ^1H NMR (CD_3OD:$CDCl_3$=1:9) δ 7.35 (d, *J* = 8.5, 2H), 7.32 (d, *J* = 2, 2H), 7.315 (d, *J* = 7.5, 2H), 7.29 (d, *J* = 2, 2H), 6.94 (d, *J* = 2.5, 2H), 6.93 (d, *J* = 2, 2H), 6.89 (d, *J* = 2.5, 2H), 6.87 (d, *J* = 2.5, 2H), 4.33 (b, 1H), 4.16 (d, *J* = 6.5, 2H), 3.31 (m, 2H), 3.19 (m, 2H), 1.97 (m, 2H), 1.65 (m, 2H), 1.52 (m, 4H), 1.08 (m, 3H). ESI-LRMS (*m/z*): calcd for $[M+H]^+$, 349.2; found, 349.7.

Compound E-1. To a solution of **9** (83.8 mg, 0.24 mmol) and **2** (138.4 mg, 0.48 mmol) in 3 mL of dry DMF was added K_2CO_3 (47.5 mg, 4.8 mmol). The mixture was stirred at 80 °C overnight. The suspension was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in DCM and dried over Na_2SO_4. The solvent was removed *in vacuo*, and the crude product was purified by gradient column chromatography (EtOAc:hexanes = 0:1 to 1:4) to give an off-white solid (yield: 73 mg, 54%). ^1H NMR (CD_3OD:$CDCl_3$=1:9) δ 7.16 (m, 2H), 7.12 (s, 2H), 6.73 (m, 2H), 3.97 (t, *J* = 6, 2H), 3.97 (t, *J* = 6.5, 2H), 3.95 (d, *J* = 17, 2H), 3.75 (d, *J* = 17, 2H), 3.14

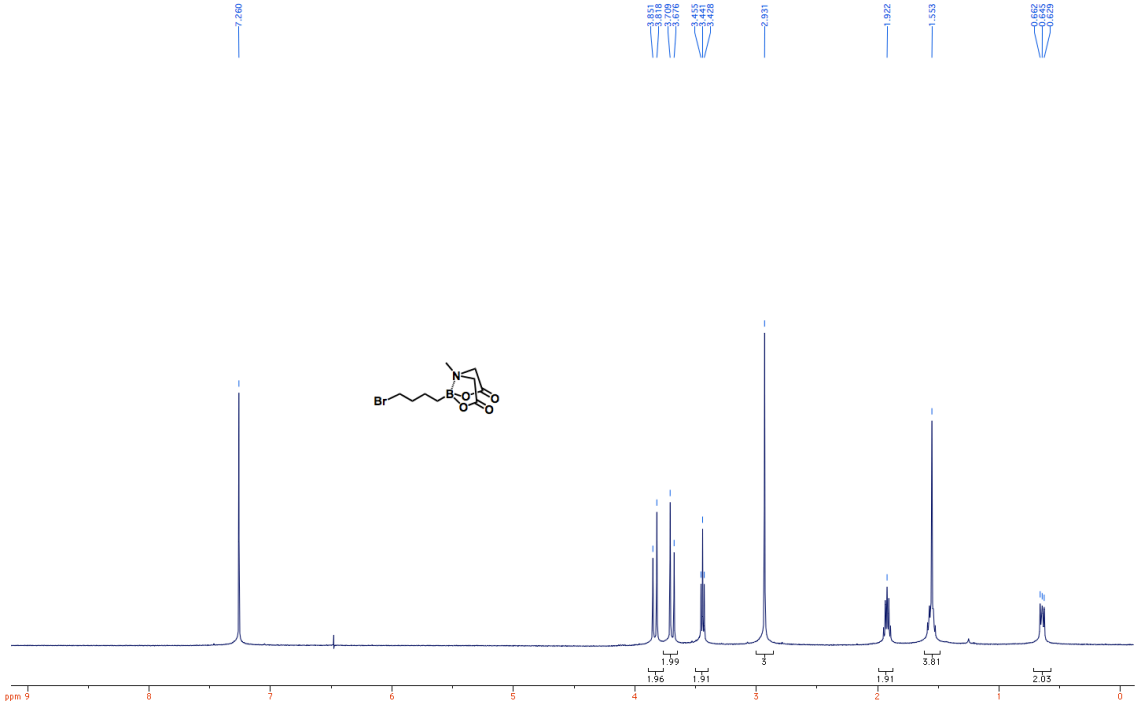
(m, 4H), 3.01 (m, 4H), 2.87 (s, 3H), 1.87-1.71 (m, 4H), 1.59-1.39 (m, 4H), 1.31 (m, 4H), 0.87 (m, 3H), 0.66 (m, 2H). ^{13}C NMR (CD_3OD:$CDCl_3$=1:9) δ 158.1, 144.4, 139.5, 135.8, 125.3, 113.7, 111.0, 68.6, 68.2, 61.9, 45.6, 32.5(4), 32.5(2),32.3, 31.7, 30.259, 30.254, 29.4, 25.8, 22.7, 20.6, 14.0. ^{11}B NMR δ 13.0. ESI-HRMS (*m/z*): calcd for $[M+H]^+$, 560.3183; found, 560.3182.

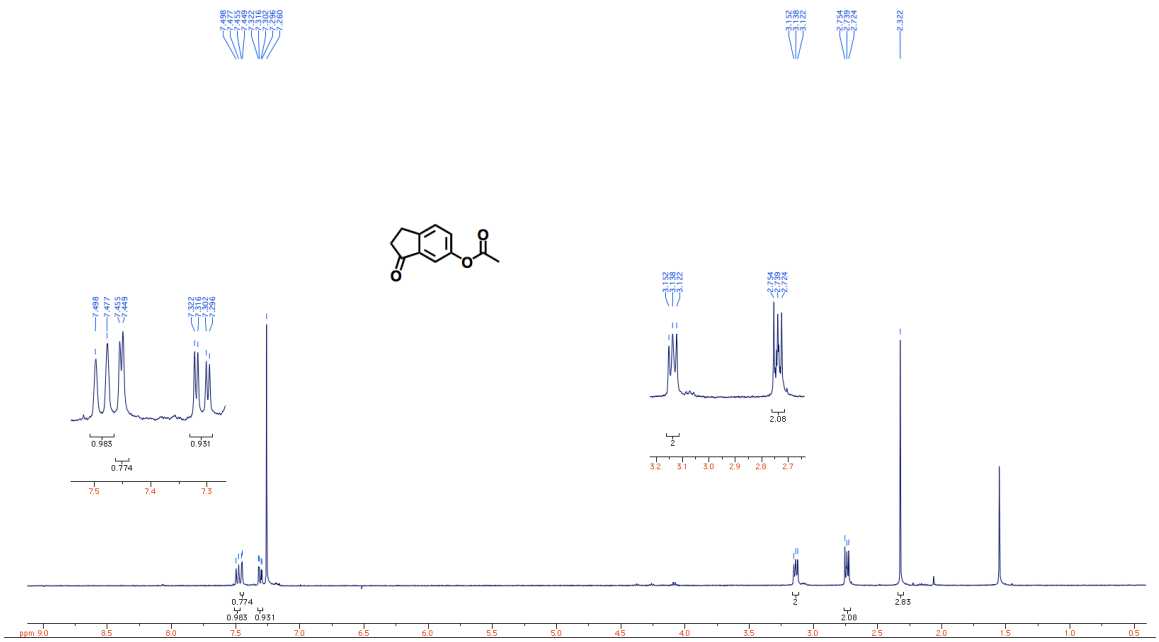


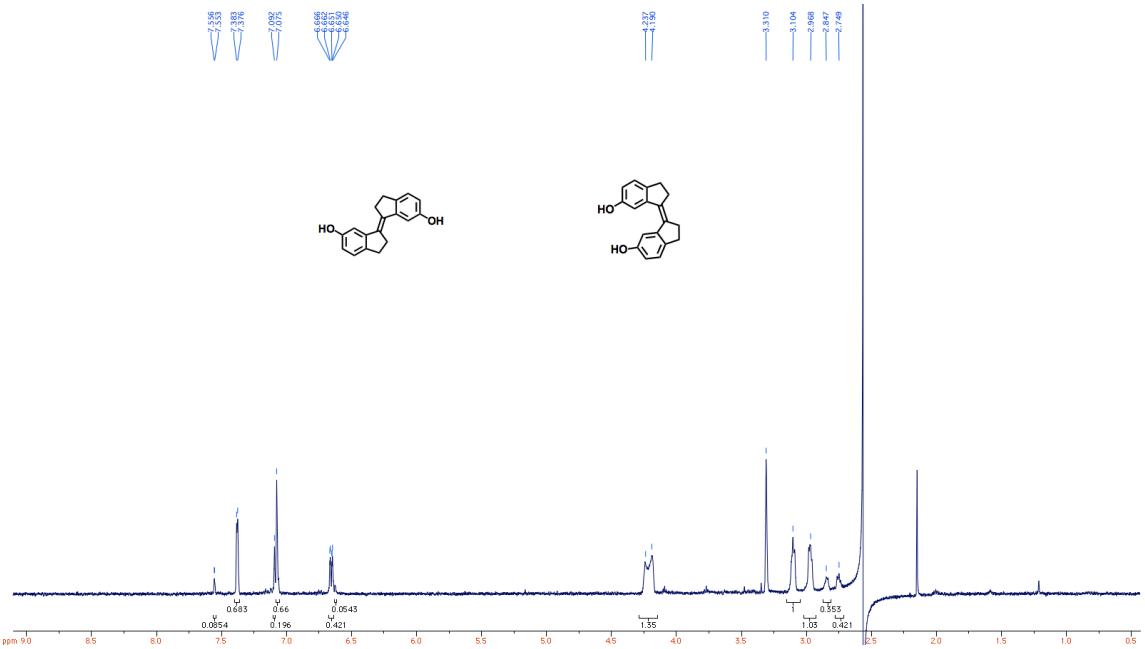
Compound 11. To a solution of dimethyl *N*-cyanodithiocarbonimidate (1.462 g, 10 mmol) in 20 mL of ethanol was added benzylamine (1.092 mL, 10 mmol), and the mixture was refluxed overnight. To the resulting solution was added hydrazine monohydrate (1 g, 20 mmol) and the mixture was refluxed for 3 h. The mixture was concentrated *in vacuo*, triturated in 50 mL of DCM, and filtered to afford 1.5 g of the product as a white crystal. The solid was used without further purification.

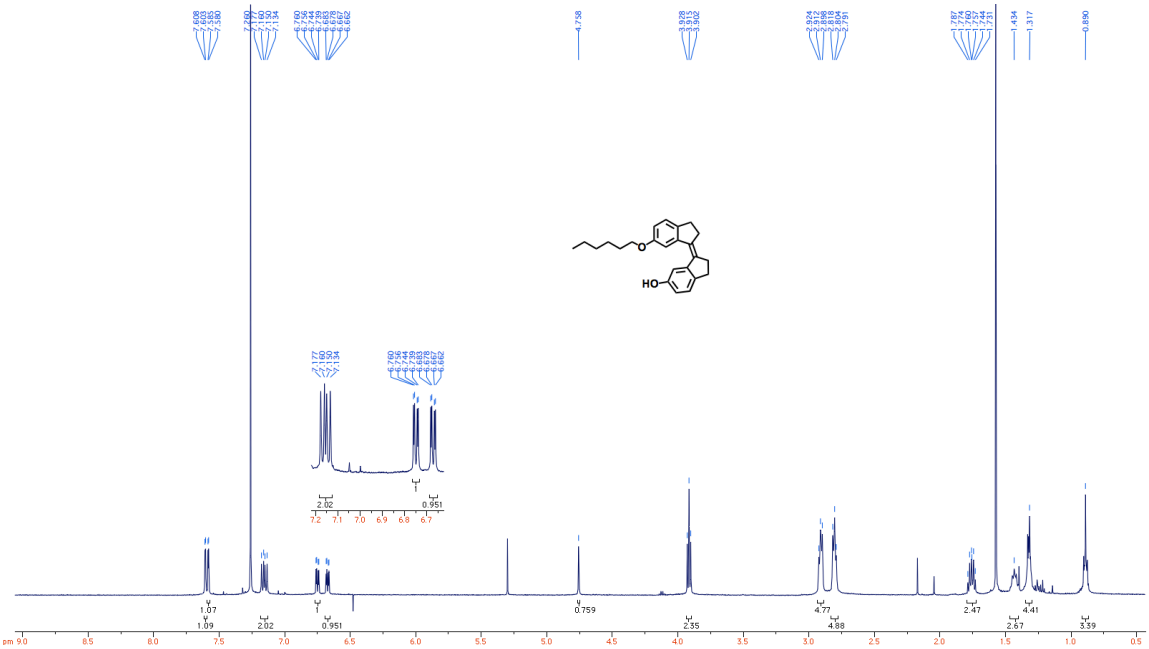
Compound BTT: To a solution of 6-(tritylthio)hexanal (748 mg, 2 mmol) and **11** (1 g, 5.3 mmol) in 6 mL of DCM and 3 mL of MeOH at -78 °C was added sodium cyanoborohydride (500 mg, 8 mmol). The mixture was slowly warmed up to room temperature and stirred overnight. The crude product was diluted with 10 mL of DCM, washed with 10 mL of brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by chromatography (100% EtOAc) to give 426.8 mg (39%) of the product as a white solid. NMR and mass spectrometry data are consistent with our previous report.[2]

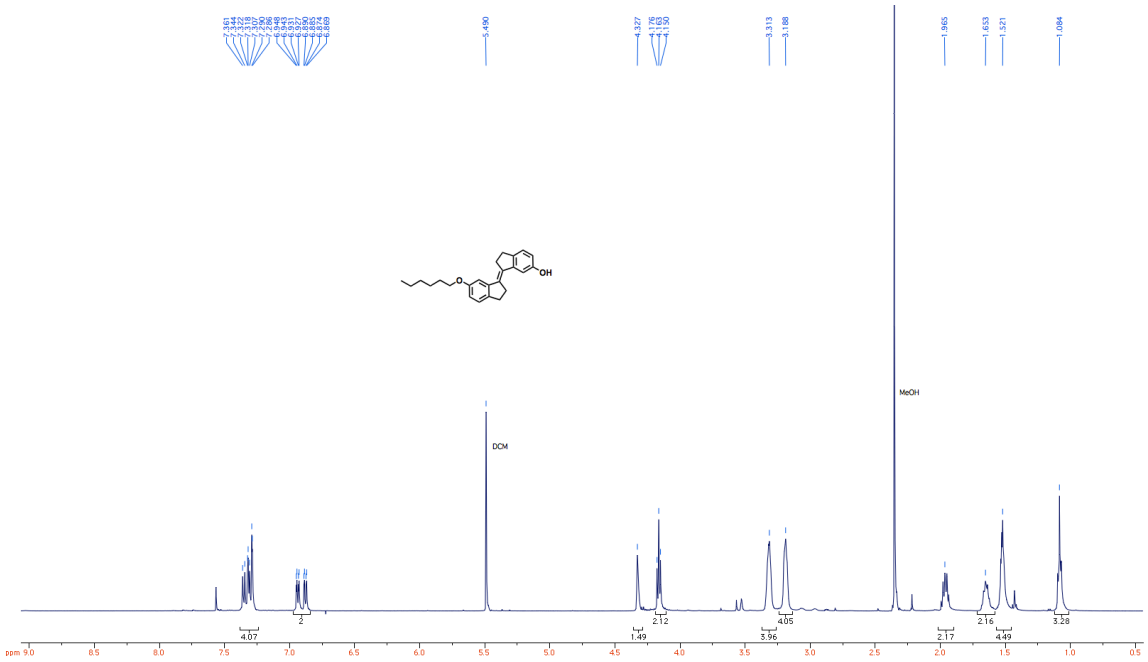
NMR Spectra

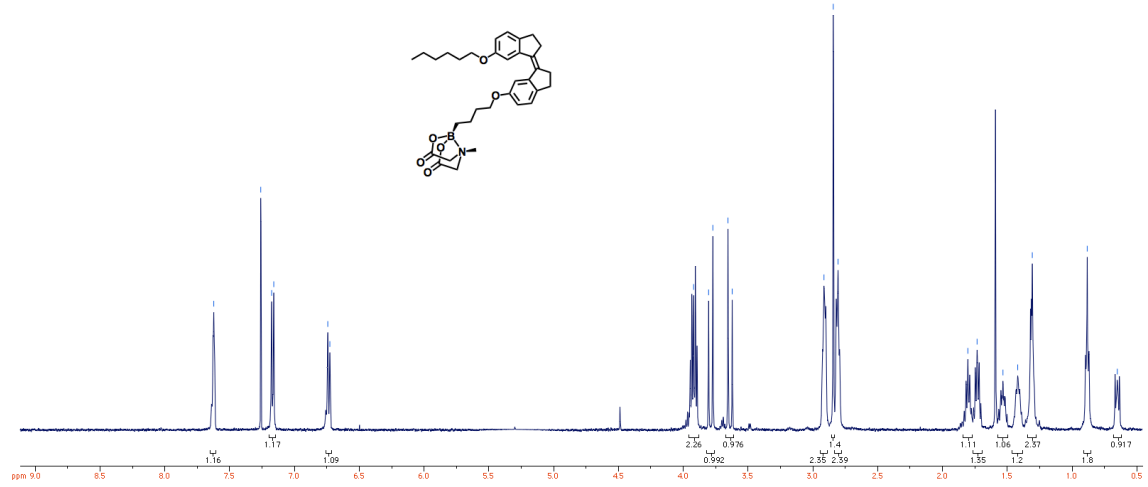


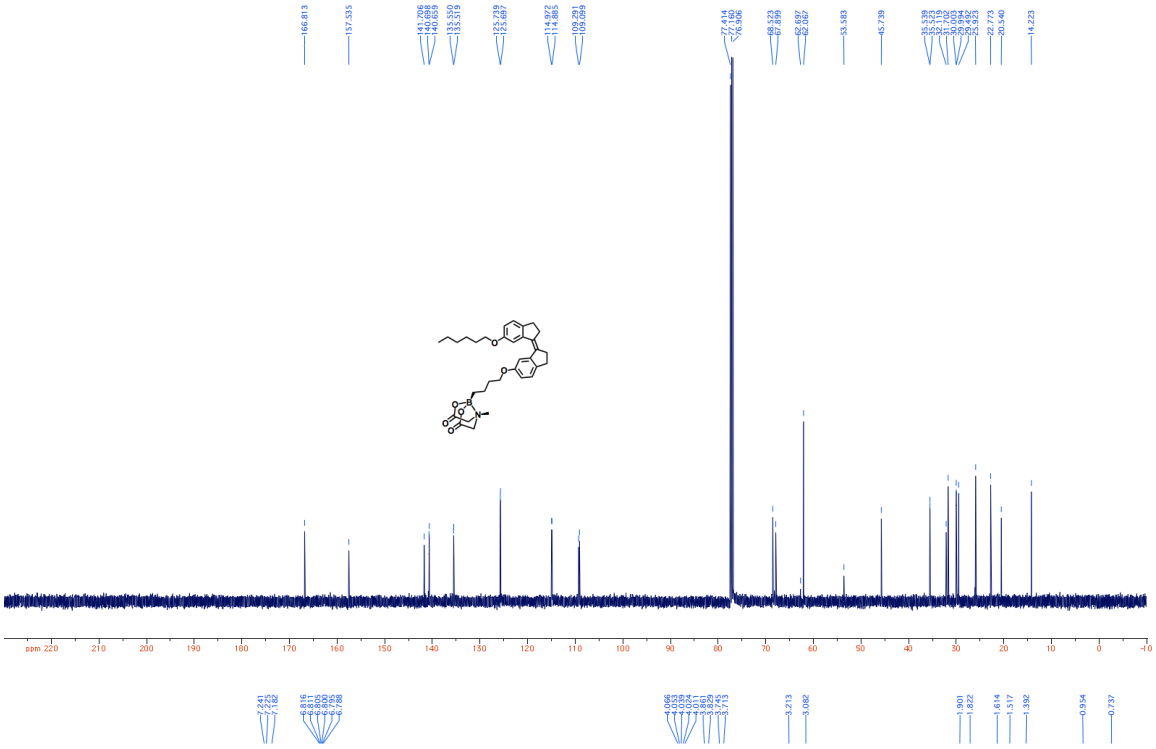


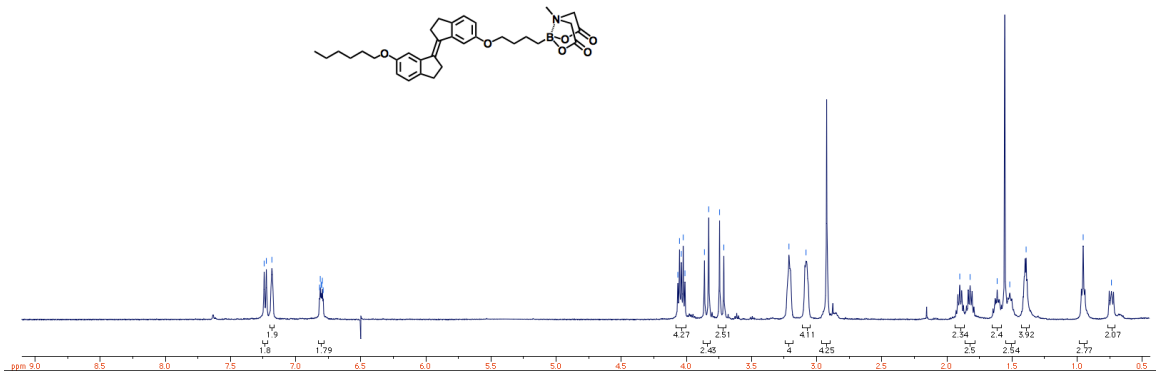

HO
OH
HO
HO

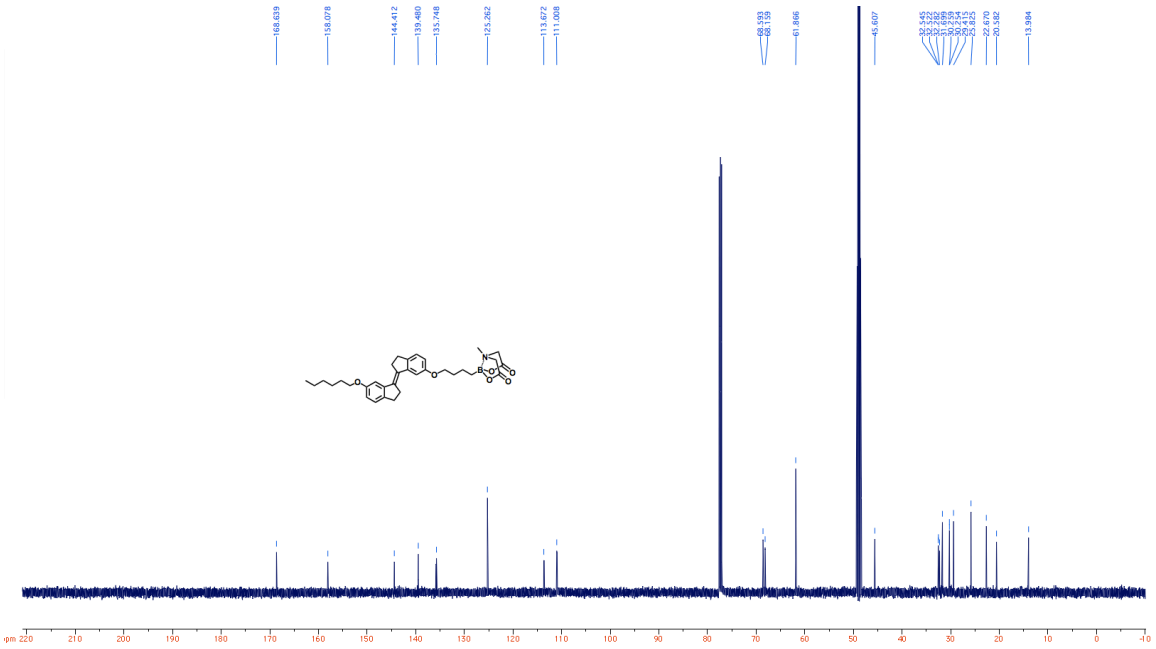

O
HO


DCM
MeOH
OH









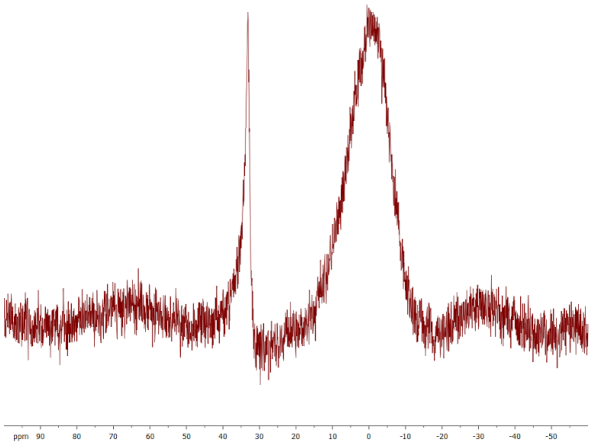


Figure S1a. ^{11}B-NMR of **BA** before irradiation.

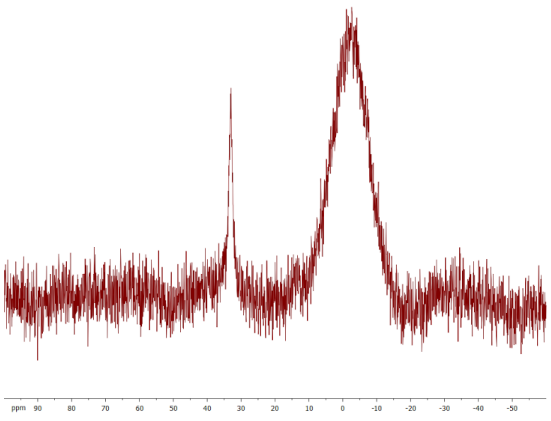


Figure S1b. ^{11}B-NMR of **BA** after multiple cycles of irradiation.

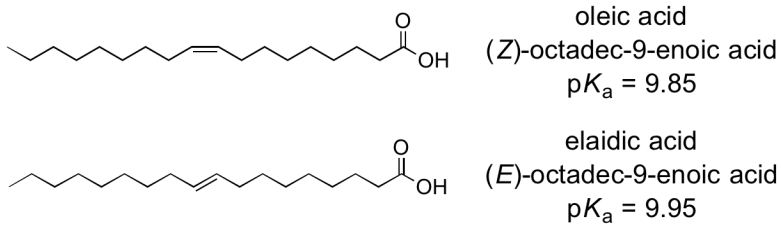


Figure S2. Structures of oleic acid and elaidic acid.

The expected pK_a difference between *E*-**BA** and *Z*-**BA** is very small. For example, the pK_a of oleic acid ((*Z*)-octadec-9-enoic acid) is 9.85 and that of elaidic acid ((*E*)-octadec-9-enoic acid) is 9.95 (Figure S2).[3] Therefore, we expect *Z*-**BA** to have a slightly lower pK_a than *E*-**BA**. Proton carriers with lower pK_a values deliver protons less efficiently at a given pH since they are deprotonated more easily. If the difference in the ability of the two forms of **BA** to deliver protons originates from their different pK_a values, then *E*-**BA** would be more active than *Z*-**BA**, which is contrary to our observations.

HBM Preparation Procedures

Caution! Perchlorate salts are potentially explosive. Only small amounts of materials should be prepared.

Preparation of the general HBM system was reported elsewhere.[2,4] In short, 6-((3-(benzylamino)-1,2,4-triazol-5-yl)amino)hexane-1-thiol (BTT) was synthesized and deposited as a SAM on a Au working electrode. Cu ions were incorporated into the BTT-modified Au surface using an ethanolic solution of $Cu(ClO_4)_2$, which was then covered with a monolayer of pure 1,2-dimyristoyl-*sn*-glycero-3-phosphocholine (DMPC) or DMPC with 0.5 equivalents of proton carriers (*Z*-**BA** or *E*-**BA**) relative to DMPC.

The lipid-forming solution is prepared following a modified published protocol.[5,6] The deprotection of **Z-1** or **E-1** was performed by dissolving **Z-1** or **E-1** (3 mg, 5.4 mol) in THF (0.2 mL). NaOH (0.01 mL, 10 M) was added, and the resulting solution was stirred vigorously for 15 min at room temperature. NH_4Cl (9 mL, saturated aqueous solution) was added, and the mixture was stirred vigorously for 5 min. Ether (9 mL × 3) was added to extract the organic layer, which was then combined, dried, and concentrated *in vacuo* to about 0.1 mL. DMPC (7.3 mg, 10.8 μmol) in EtOH (2 mL) was added to the ether solution containing *Z*-**BA** or *E*-**BA**. The organic solution was dried under a stream of Ar, resulting in a thin translucent film of DMPC mixed with *Z*-**BA** or *E*-**BA** at the bottom of a 20 mL glass scintillation vial. The vial was then kept in a vacuum desiccator for 30 min. The film was then reconstituted with EtOH (168 μL) and pH 7 potassium phosphate buffer (10.5 mL, 100 mM) was added dropwise with gentle swirling. The resulting translucent lipid forming solution was then sonicated for 30 min and used without further purification. All procedures involving *Z*-**BA** or *E*-**BA** were conducted in the dark with all glassware wrapped with aluminum foil.

Electrochemical and Photoelectrochemical Procedures

pH 7 potassium phosphate buffer solutions were prepared using Milli-Q water (> 18 MΩ cm) and were sparged with Ar or O_2 for 30 min prior to each experiment. Electrochemical studies were carried out using a CH Instruments 760 D Electrochemical Workstation (Austin, TX). A three-electrode cell was used with a carbon counter electrode. Electrochemical potentials were measured and reported with respect to a 'no leak' Ag/AgCl (3 M KCl, eDAQ, Inc.) reference electrode. Au working electrodes (0.22 cm^2) were deposited using an electron-beam vacuum deposition apparatus. A Ti adhesion layer (50 nm), followed by a Au layer (150 nm), was deposited on Pyrex glass slides. The electrodes were rinsed with water and EtOH prior to use.

All optical apparatuses including mounted LEDs (M385L2 and M365L2, max current limit = 700 mA), power source drivers (DC2100), collimators (COP1-A), adaptors (SM1A2), couplers (SM2T2), and band pass filters (390 nm and 360 nm, FWHM = 10 nm) were purchased from Thorlabs, Inc. For the interconversion experiments monitored using NMR techniques, the irradiation times for the *E*-to-*Z* and *Z*-to-*E* conversions were 40 and 30 min, respectively ([**BA**] = 2 mg/mL). All photoelectrochemical experiments were conducted inside a Faraday cage in a dark room.

To confirm that the integrity of the lipid layer is not perturbed by the photoisomerization process, "blocking" experiments were conducted after irradiation in an aqueous KCl (100 mM) solution containing $K_3Fe(CN)_6$ (1 mM) with *Z*- and ***E*-BA** incorporated in the lipid layer of the HBMs. In all cases presented in Figure S3d, the absence of the Fe(II)/Fe(III) wave indicates that a well-formed lipid layer is present after irradiation and O_2 reduction. For further studies of the HBM after the photoelectrochemical experiments, the lipid layers were extracted by washing the lipid layer with EtOH three times. EtOH was removed under reduced pressure and reconstituted in CD_2Cl_2 for ^{1}H-NMR and ESI-MS.

Further Electrochemical Characterization of HBMs

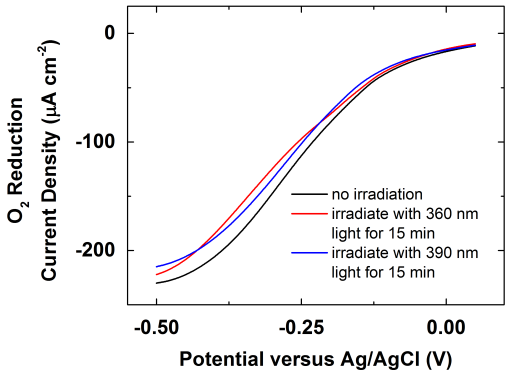


Figure S3a. Linear sweep voltammograms (LSVs) of O_2 reduction catalyzed by CuBTT (black) irradiated with 360 nm light for 15 min (red) or 390 nm light for 15 min (blue) in O_2-saturated pH 7 phosphate buffer at a scan rate of 10 mV/s.

The black line of Figure S3a shows the LSV of CuBTT in O_2-saturated solution. The current density observed is similar to those observed previously,[2] suggesting that the new synthetic route of BTT does not perturb the O_2 reduction activity of CuBTT. The red and blue lines of Figure S3a show the LSVs of CuBTT in O_2-saturated solution after irradiating for 15 min with 360 nm and 390 nm light, respectively. These results demonstrate that both the Au-thiol linkage and the BTT-Cu bond are stable upon exposing to 360 nm or 390 nm light for 15 min.

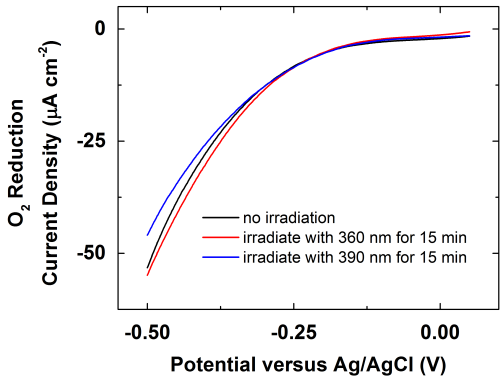


Figure S3b. LSVs of O_2 reduction catalyzed by CuBTT covered by a monolayer of DMPC (black) irradiated with 360 nm light for 15 min (red) or 390 nm light for 15 min (blue) in O_2-saturated pH 7 phosphate buffer at a scan rate of 10 mV/s.

Figure S3b displays the LSVs of CuBTT covered by a monolayer of DMPC in O_2-saturated solution with and without irradiation. The current densities observed in all three cases are comparable, indicating that the integrity of the lipid layer is not perturbed by exposing to 360 nm or 390 nm light for 15 min. To further probe the integrity of the lipid layer, we subjected the surfaces to a blocking experiment as shown in Figure S3d.

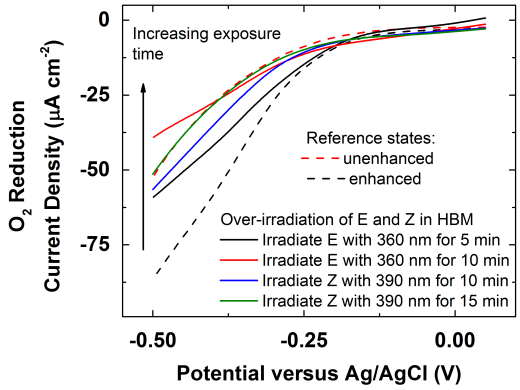


Figure S3c. LSVs of O_2 reduction catalyzed by CuBTT covered by a monolayer of DMPC with *Z*-**BA** (black dashed line), *E*-**BA** (red dashed line), *E*-**BA** irradiated with 360 nm light for 5 min (black solid line), *E*-**BA** irradiated with 360 nm light for 10 min (red solid line), *Z*-**BA** irradiated with 390 nm light for 10 min (blue solid line), and *Z*-**BA** irradiated with 390 nm light for 15 min (blue solid line) in O_2-saturated pH 7 phosphate buffer at a scan rate of 10 mV/s.

Figure S3c shows the LSVs of CuBTT covered by a monolayer of DMPC with light-responsive proton carriers in O_2-saturated solution. Upon irradiating *E*-**BA** with 360 nm light for 5 and 10 min, the current densities observed are lower than the "enhanced" state. Furthermore, upon irradiating *Z*-**BA** with 390 nm light for 15 min, the current density observed is similar to the "unenhanced" state. The observed degradation after prolong exposure to light could be due to proton carriers leaching from the lipid layer or being damaged by light.

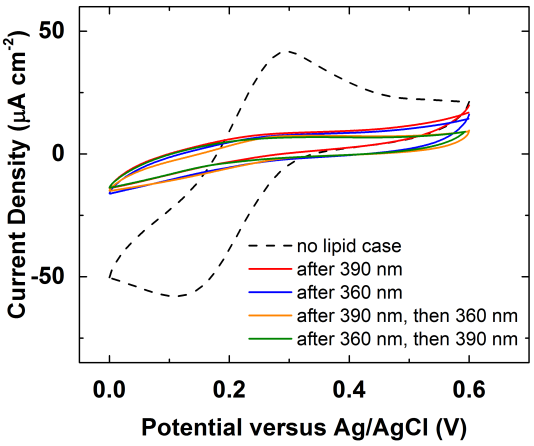


Figure S3d. Representative cyclic voltammograms (CVs) of a SAM of CuBTT (black dashed line) and the HBMs containing CuBTT (solid lines) with *E*-**BA** incorporated in the lipid layer after irradiation with 360 nm light (blue) then with 390 nm light (green) and *Z*-**BA** incorporated in the lipid layer after irradiation with 390 nm light (red) then 360 nm light (orange) in a solution of $K_3Fe(CN)_6$ (1 mM) with KCl (100 mM) at a scan rate of 50 mV/s.

We checked if the surfaces are blocked after O_2 reduction by conducting blocking experiments in a solution of $K_3Fe(CN)_6$. Figure S3d shows the CVs of blocked surfaces (solid lines) and an unblocked sample (dashed line). This experiment supports the notion that the lipid layer does not contain a pore or other defect following irradiation with light of 360 and 390 nm.

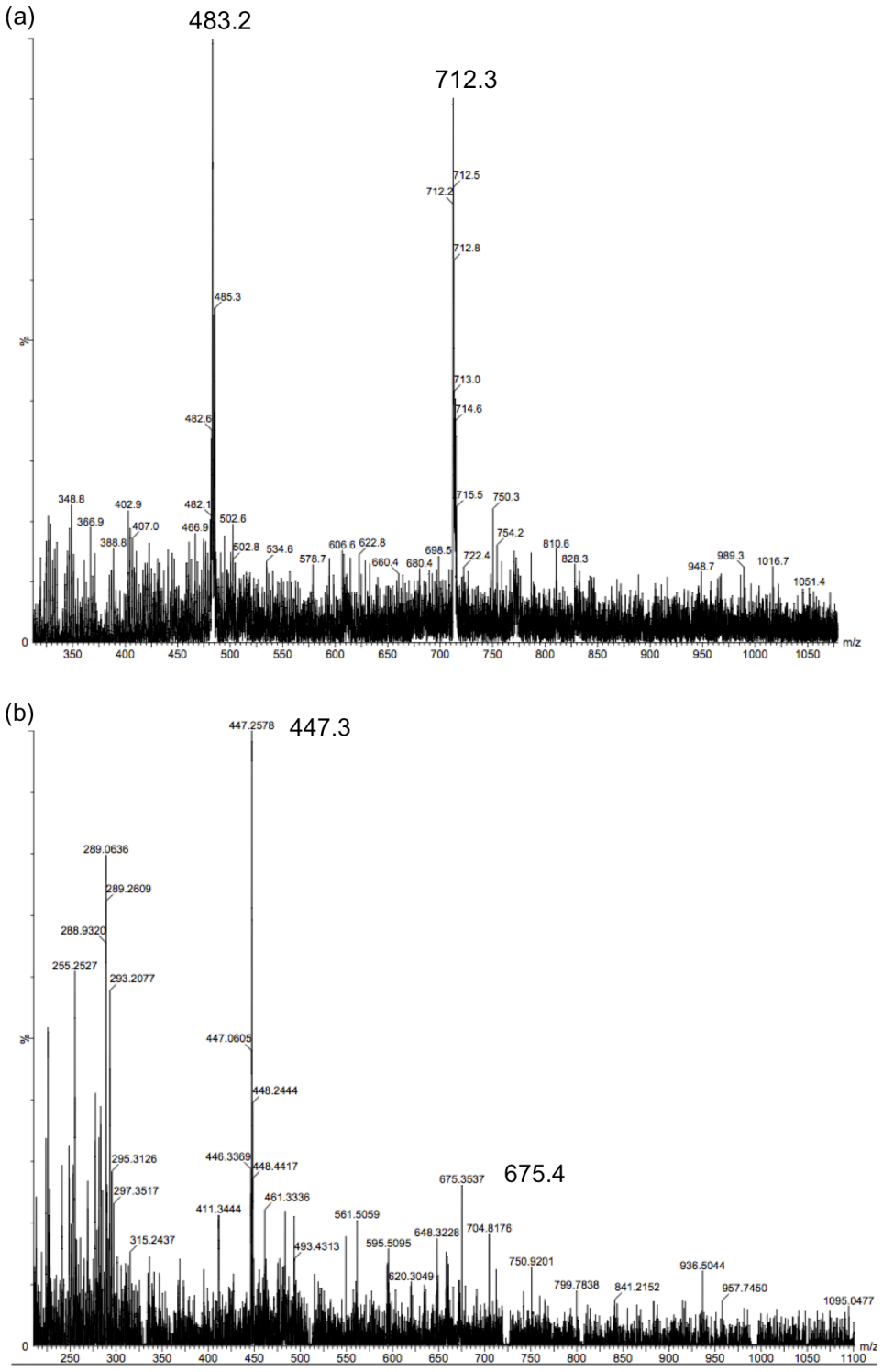


Figure S4. ESI-LRMS of extracted lipid layer of HBM with (a) *E*-**BA** and (b) *Z*-**BA** incorporated in the lipid layer.

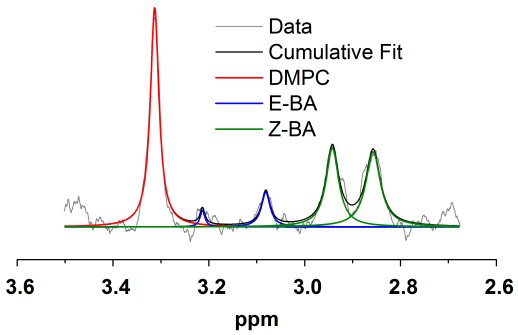


Figure S5a. ^{1}H-NMR spectra of extracted lipid layer of HBM with the photoswitch incorporated in the lipid layer before the on-off-on experiment. Gray = ^{1}H-NMR raw data, black = cumulative peak fit, red = peak fit for DMPC, blue = peak fit for *E*-**BA**, and green = peak fit for *Z*-**BA**.

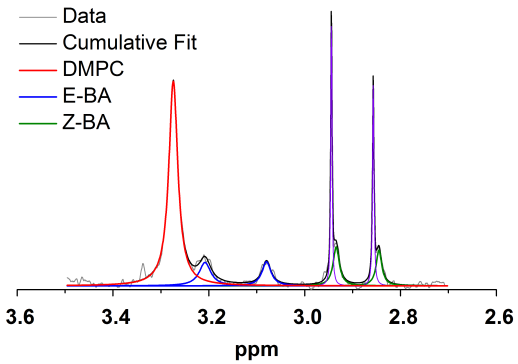


Figure S5b. ^{1}H-NMR spectra of extracted lipid layer of HBM with the photoswitch incorporated in the lipid layer after the on-off-on experiment. Gray = ^{1}H-NMR raw data, black = cumulative peak fit, red = peak fit for DMPC, blue = peak fit for *E*-**BA**, green = peak fit for *Z*-**BA**, and purple = peak fit for degradation product.

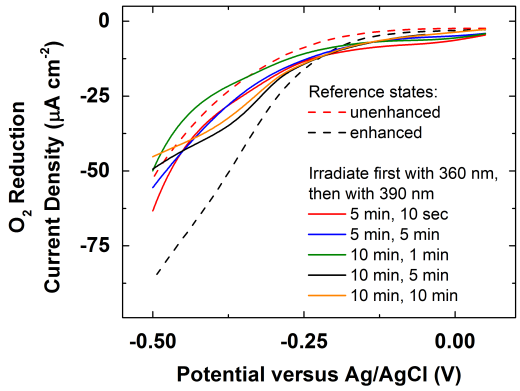


Figure S5c. LSVs of O_2 reduction catalyzed by CuBTT covered by a monolayer of DMPC with *Z*-**BA** (black dashed line), *E*-**BA** (red dashed line), *Z*-**BA** irradiated with 390 nm light for 5 min followed by 360 nm light for 10 sec (red solid line), *Z*-**BA** irradiated with 390 nm light for 5 min followed by 360 nm light for 5 min (blue solid line), *Z*-**BA** irradiated with 390 nm light for 10 min followed by 360 nm light for 1 min (green solid line), *Z*-**BA** irradiated with 390 nm light for 10 min followed by 360 nm light for 5 min (black solid line), and *Z*-**BA** irradiated with 390 nm light for 10 min followed by 360 nm light for 10 min (orange solid line) in O_2-saturated pH 7 phosphate buffer at a scan rate of 10 mV/s.

The concentration of proton carrier in the lipid layer is quantified by ^{1}H-NMR spectroscopy and found to be similar before and after irradiation (Figures S5a and S5b). Similar to the results obtained in Figure S3c, Figure S5c shows that prolong exposure to 360 nm and 390 nm irradiation causes irreversible decrease in O_2 reduction current. Figure S5c red line shows that 10 sec is not enough to convert all the *E*-**BA** (the inactive form) into *Z*-**BA** (the active form), similar to the red line shown in Figure 3b. Figure S5c blue line indicates that 5 min exceeds the irradiation time limit and results in lowered O_2 reduction current, similar to the black line shown in Figure S3c. The green, orange, and black lines in Figure S5c together demonstrate that in the event of irradiation with 390 nm light for 10 min, subsequent irradiation with 360 nm light cannot fully recover the O_2 reduction current to the reference "enhanced" state, regardless of the length of irradiation with 360 nm light. This result is likely

due to the irreversible leaching of the proton carrier from the lipid layer during irradiation - an amplification of 10% dissolution of proton carrier in the on-off-on case shown in Figure 4.

References

(1) Akbulatov, S.; Tian, Y.; Boulatov, R. *J. Am. Chem. Soc.* **2012**, *134*, 7620-7623.
(2) Barile, C. J.; Tse, E. C. M.; Li, Y.; Sobyra, T. B.; Zimmerman, S. C.; Hosseini, A.; Gewirth, A. A. *Nat. Mater.* **2014**, *13*, 619-623.
(3) Kanicky, J. R.; Shah, D. O. *J. Colloid Interface Sci.* **2002**, *256*, 201-207.
(4) Tse, E. C. M.; Barile, C. J.; Gewargis, J. P.; Li, Y.; Zimmerman, S. C.; Gewirth, A. A. *Anal. Chem.* **2015**, *87*, 2403-2409.
(5) Hosseini, A.; Barile, C. J.; Devadoss, A.; Eberspacher, T. A.; Decreau, R. A.; Collman, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 11100-11102.
(6) Hosseini, A.; Collman, J. P.; Devadoss, A.; Williams, G. Y.; Barile, C. J.; Eberspacher, T. A. *Langmuir* **2010**, *26*, 17674-17678.