Flavothionato Metal Complexes: Implications for the Use of Hydroxyflavothiones as Green Pesticides

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Electronic Supplementary Information

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General. Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. Elemental analysis was performed at NuMega Resonance Labs, San Diego, California. $^{1}H/^{13}C$ NMR spectra were recorded on Varian FT-NMR spectrometers at the Department of Chemistry and Biochemistry, University of California, San Diego. Mass spectrometry samples were submitted to the Department of Chemistry and Biochemistry Mass Spectrometry Facility, University of California, San Diego. Infrared spectra were collected on a Perkin Elmer Spectrum One FT-IR spectrometer. UV-Visible spectra were recorded using a Perkin-Elmer Lambda 25 spectrophotometer. Absorbance maxima are reported as λ_{max}/nm (ε/M^{-1} cm^{-1}). Fluorescence emission spectra were collected in the range from 250-650 nm on a Perkin-Elmer LS55 Luminescence spectrophotometer. Metal solutions and complexes were prepared from the following salts: $Na_3Co(NO_2)_6$, $FeCl_3{\cdot}6H_2O$, $CuCl_2{\cdot}2H_2O$, $NiCl_2$, $Zn(OAc)_2{\cdot}2H_2O$, $ZnCl_2$, $Cd(NO_3)_2$, and $Cd(BF_4)_2$.

3-Hydroxflavothione (3-OHFT). To a solution of 3-hydroxyflavone (900 mg, 3.78 mmol) in 120 mL of toluene was added P_4S_{10} (308 mg, 0.69 mmol) and hexamethyldisiloxane (HMDO, 1.35 mL, 6.30 mmol) producing a turbid, yellow mixture. The flask was fitted with a reflux condenser and was heated to reflux (120-125 ºC) under a nitrogen atmosphere. The reaction mixture was protected from light with aluminum foil. Within 1 h, the solution became bright yellow and heating at reflux was continued overnight. The resulting red-brown solution was vacuum filtered to remove insoluble components, and the filtrate was evaporated to dryness on a rotorary evaporator giving a red oil. The red oil was purified by flash silica gel chromatography with CH_2Cl_2 as elutant, yielding the product as a red-brown crystalline solid after removal of solvent. The product was protected from light with aluminum foil and stored at 4 ºC. Yield: 86%. ^{1}H NMR ($CDCl_3$ 300 MHz, 25 °C): δ 7.47-7.74 (m, 6H), 8.39 (d, 2H, J = 6.0 Hz), 8.59 (d, 1H, J = 9.0 Hz), 8.72 (s, 1H, -OH). IR (ATR): ν 769, 1344, 1553, 1600, 3060 cm^{-1}. λ_{max} =

354 (15,200), 422 (24,200). HR-EIMS Calcd for $C_{15}H_{10}O_2S$: 254.0396. Found, Δ: 254.0398, 0.6 ppm.

[Fe(3-OHFT)$_3$]. 3-OHFT (100 mg, 0.39 mmol) was suspended in 5 mL of MeOH. The ligand was dissolved upon addition of 39 μL of 10 M NaOH (1 equiv) with mild heating and stirring, producing a dark red solution. $FeCl_3 \cdot 6H_2O$ (30.5 mg, 0.11 mmol) was dissolved in 4.0 mL of water and added dropwise to the reaction mixture, resulting in the immediate formation of a brown precipitate. The reaction vessel was sealed and stirred at room temperature for ~1 h. The brown precipitate was collected by filtration with a glass frit and washed with ~20 mL of water to obtain a brown powder. The brown powder was placed in vacuum oven and dried overnight with heating (~50 ºC). Yield: 88%. IR (ATR): ν 758, 853, 1051, 1240, 1279, 1322, 1417, 1478 cm^{-1}. λ_{max} = 358 (34,900), 440 (42,000). HR-FABMS Calcd for $C_{45}H_{27}O_6S_3Fe$: 815.0314. Found, Δ**:** 815.0330**,** 2.0 ppm.

[Co(3-OHFT)$_3$]. 3-OHFT (74.1 mg, 0.29 mmol) was suspended in 5.0 mL of MeOH. The ligand was dissolved upon addition of 29.5 μL of 10 M NaOH (1 equiv) with mild heating and stirring, producing a dark red solution. $Na_3Co(NO_2)_6$ (37.4 mg, 0.097 mmol) was dissolved in 5.0 mL water and added dropwise to the reaction mixture resulting in the immediate formation of a brown precipitate. The reaction flask was fitted with a condenser and heated to reflux at 85 °C under a nitrogen atmosphere for 72 h. The black precipitate was collected by filtration with a glass frit and washed with cold water. The black powder was placed in vacuum oven and dried overnight with heating (~50 ºC). Yield: 75%. ^{1}H NMR ($CDCl_3$ 400 MHz, 25 °C): δ 7.353-7.59 (m, 18H), 7.63-7.68 (m, 6H), 8.87 (d, 3H, *J* = 8.4 Hz). IR (KBr pellet): ν 757, 852, 1050, 1249, 1285, 1330, 1426, 1477 cm^{-1}. λ_{max} = 284 (59,300), 344 (39,500), 416 (36,200), 507 (22,600). HR-FABMS Calcd for $C_{30}H_{18}O_4S_2Co$: 564.9973. Found, Δ: 564.9972, -0.2 ppm (Note: only the $[M-L]^+$ ion was observed).

[Ni(3-OHFT)$_2$]. [Ni(3-OHFT)$_2$] was synthesized by the same procedure used for [Fe(3-OHFT)$_3$] starting from 3-OHFT (100 mg, 0.39 mmol) and $NiCl_2$ (46 mg, 0.20 mmol). The product was isolated as a dark green precipitate. Yield: 87%. ^{1}H NMR ($CDCl_3$ 400 MHz, 25 °C): δ 7.45-7.74 (m, 12H), 8.24 (d, 2H, *J* = 8.0 Hz), 8.78 (d, 4H, *J* = 9.2 Hz). IR (ATR): ν 757, 853, 1050, 1245, 1280, 1323, 1425, 1478 cm^{-1}. λ_{max} = 283 (28,500), 357 (27,400), 421 (35,100). HR-FABMS Calcd for $C_{30}H_{18}O_4S_2Ni$: 563.9994. Found, Δ: 564.0002, 1.4 ppm.

[Cu(3-OHFT)$_2$]. [Cu(3-OHFT)$_2$] was synthesized by the same procedure used for [Fe(3-OHFT)$_3$] starting from 3-OHFT (100 mg, 0.39 mmol) and $CuCl_2{\cdot}2H_2O$ (35 mg, 0.20 mmol). The product was obtained as a brown powder. Yield: 77%. IR (ATR): ν 756, 853, 1050, 1243, 1280, 1323, 1424, 1478 cm^{-1}. λ_{max} = 325 (26,000), 383 (37,400), 480 (40,800). HR-FABMS Calcd for $C_{30}H_{18}O_4S_2Cu$: 568.9937. Found, Δ: 568.9948, 1.8 ppm.

[Zn(3-OHFT)$_2$]. [Zn(3-OHFT)$_2$] was synthesized by the same procedure used for [Fe(3-OHFT)$_3$] starting from 3-OHFT (100 mg, 0.39 mmol) and $Zn(OAc)_2{\cdot}2H_2O$ (43 mg, 0.20 mmol). The product was obtained as an orange powder. Yield: 81%. ^{1}H NMR ($CDCl_3$ 300 MHz, 25 °C): δ 7.51 (m, 8H), 7.73 (m, 4H), 8.61 (d, 2H, *J* = 9.0 Hz), 8.78 (br d, 4H). IR (ATR): ν 757, 853, 1050, 1241, 1279, 1324, 1415, 1478 cm^{-1}. λ_{max} = 364 (14,700), 380 (16,200), 490 (32,200). HR-EIMS Calcd $C_{30}H_{18}O_4S_2Zn$: 569.9932. Found, Δ: 569.9948, 2.7 ppm.

[Cd(3-OHFT)$_2$. [Cd(3-OHFT)$_2$] was synthesized by the same procedure used for [Co(3-OHFT)$_3$] starting from 3-OHFT (102.8 mg, 0.40 mmol) and $Cd(BF_4)_2$ (84.3 μL, 0.20 mmol). The product was obtained as a dark red powder. Yield: 82%. IR (ATR): ν 759, 853, 1051, 1239, 1278, 1322, 1423, 1478 cm^{-1}. λ_{max} = 358 (21,000), 349 (24,600), 500 (20,200). APCI-MS: 620.87 $[M-H]^+$. HR-FABMS Calcd $C_{30}H_{18}O_4S_2Cd$: 619.9675. Found, Δ: 619.9696, 3.5 ppm.

X-Ray Crystallographic Analysis. Single crystals of each compound suitable for X-ray diffraction structural determination were mounted on quartz capillaries by using Paratone oil and were cooled in a nitrogen stream (as detailed for each crystal) on the diffractometer. Data were collected on a Bruker AXS diffractometer using an area detector. Peak integrations were performed with the Siemens SAINT software package. Absorption corrections were applied using the program SADABS. Space group determinations were performed by the program XPREP. The structures were solved by direct methods and refined with the SHELXTL software package. All hydrogen atoms were fixed at calculated positions with isotropic thermal parameters; all non-hydrogen atoms were refined anisotropically.

Structure of 3-OHFT. Orange plates of 3-OHFT suitable for X-ray diffraction structural determination were grown from slow evaporation of a solution of the ligand in methanol. No solvent molecules were found in the unit cell. CCDC deposition number 252675.

Structure of [Cu(3-OHFT)$_2$]. Dark wine-red colored plates of [Cu(3-OHFT)$_2$] suitable for X-ray diffraction structural determination were grown from slow diffusion of pentane into a solution of the complex in methanol/DMSO (~4:1). No solvent molecules were found in the unit cell. CCDC deposition number 252676.

Structure of [Zn(3-OHFT)$_2$]. Orange blocks of [Zn(3-OHFT)$_2$] suitable for X-ray diffraction structural determination were grown from slow evaporation of a solution of the complex in CH_2Cl_2. One equivalent of co-crystallized CH_2Cl_2 molecule was found in the unit cell. CCDC deposition number 252677.

Structure of [Ni(3-OHFT)$_2$]. Dark green colored plates of [Ni(3-OHFT)$_2$] suitable for X-ray diffraction structural determination were grown from slow evaporation of a solution of the

complex in $CDCl_3$. One equivalent of co-crystallized $CDCl_3$ molecule was found in the unit cell. CCDC deposition number 282322.

Structure of [Co(3-OHFT)$_3$]. Black blocks of [Co(3-OHFT)$_3$] suitable for X-ray diffraction structural determination were grown from slow diffusion of diethyl ether into a solution of the complex in $CHCl_3$/benzene (~4:1). No solvent molecules were found in the unit cell. CCDC deposition number 282323.

Aerobic Fluorescence Emission Measurements. Fluorescence emission spectra were collected in the range from 250-650 nm on a Perkin-Elmer LS55 Luminescence spectrophotometer operating at an excitation wavelength of 278 nm and using a wavelength cutoff filter set at 350 nm. The excitation slit width was set at 15 nm and the emission slit width was set at 20 nm for all fluorescence experiments. Stock solutions (200 μM) of metal salts in methanol were prepared. A 200 μM stock solution of 3-OHFT was prepared in methanol and protected from light with aluminum foil and stored at 4 °C. Fluorescence experiments were performed in the following manner: 1.0 mL of the 3-OHFT solution was placed in a quartz cuvette (Wilmad), followed by addition of 1.0 mL of the respective metal ion solution with thorough mixing using a pipetman. After mixing, the emission spectra were collected under the conditions described above. For [Co(3-OHFT)$_3$], a 100 μM stock solution of [Co(3-OHFT)$_3$] was prepared in methanol and examined under the same conditions.

Anaerobic Fluorescence Emission Measurements. The settings for the Perkin-Elmer LS55 Luminescence spectrophotometer were kept the same as in the aerobic experiments. All stock solutions and sample solutions were prepared inside a nitrogen atmosphere glove box. Stock solutions of metal salts (200 μM) and 3-OHFT (200 μM) were prepared in dry, degassed methanol as described above. Anaerobic fluorescence measurements were performed with an

airtight, screw top quartz cuvette (Wilmad) in the same manner as the aerobic experiments described above.

Aerobic Photodegradation Experiments. Solutions (25 mL) of 3-OHFT or one of the 3-OHFT metal complexes in $CHCl_3$ were prepared at a concentration of 50 μM. Solutions were placed in screw top glass vials and exposed to ambient sunlight for up to ~8 h. Aliquots (1.0 mL) were removed at selected time points and the absorbance spectra acquired on a Perkin-Elmer Lambda 25 spectrophotometer. A 3-OHFT control solution was run with every experiment to account for variations in light exposure. Two sets of experiments were run with 3-OHFT and [Fe(3-OHFT)$_3$] solutions stored in the dark to demonstrate that the observed degradation of these compounds was light dependent.

Anaerobic Photodegredation Experiments. Anaerobic photodegradation experiments were performed in the same manner as the aerobic photodegradation experiments, but all solutions were prepared inside of a nitrogen atmosphere glove box. Solutions were placed in an airtight, screw top quartz cuvette (Starna Cells) and exposed to ambient sunlight. At selected time points, the absorbance spectra acquired on a Perkin-Elmer Lambda 25 spectrophotometer. A 3-OHFT control solution was run with every experiment to account for variations in light exposure.

Table S1. Summary of X-ray structural parameters for 3-OHFT.

	3-OHFT
Emp. Formula	$C_{15}H_{10}O_2S$
Crystal System	Orthorhombic
Space Group	$Pca2_1$
Unit Cell dimensions	a = 22.269(4) Å b = 3.8534(7) Å c = 26.754(5) Å
Volume, Z	2295.8(7) Å^3, 8
Crystal size	0.22 × 0.20 × 0.03 mm^3
Temperature (K)	100(2)
Reflections collected	12686
Independent reflections	5042 [R(int) = 0.1096]
Data/rest./para.	5042/1/327
Goodness-of-fit on F^2	0.745
Final R indices I>2σ(I) [a]	$R1$ = 0.0446 $wR2$ = 0.0876
R indices (all data) [a]	$R1$ = 0.1098 $wR2$ = 0.0986
Largest peak/hole difference	0.310 / -0.255 e Å^{-3}

[a] $R_1 = \sum \left\| F_o \right| - \left| F_c \right\| / \sum \left| F_o \right|$, $R_2 = \left\{ \sum [w(F_o^2 - F_c^2)^2] / \sum [wF_o^4] \right\}^{1/2}$

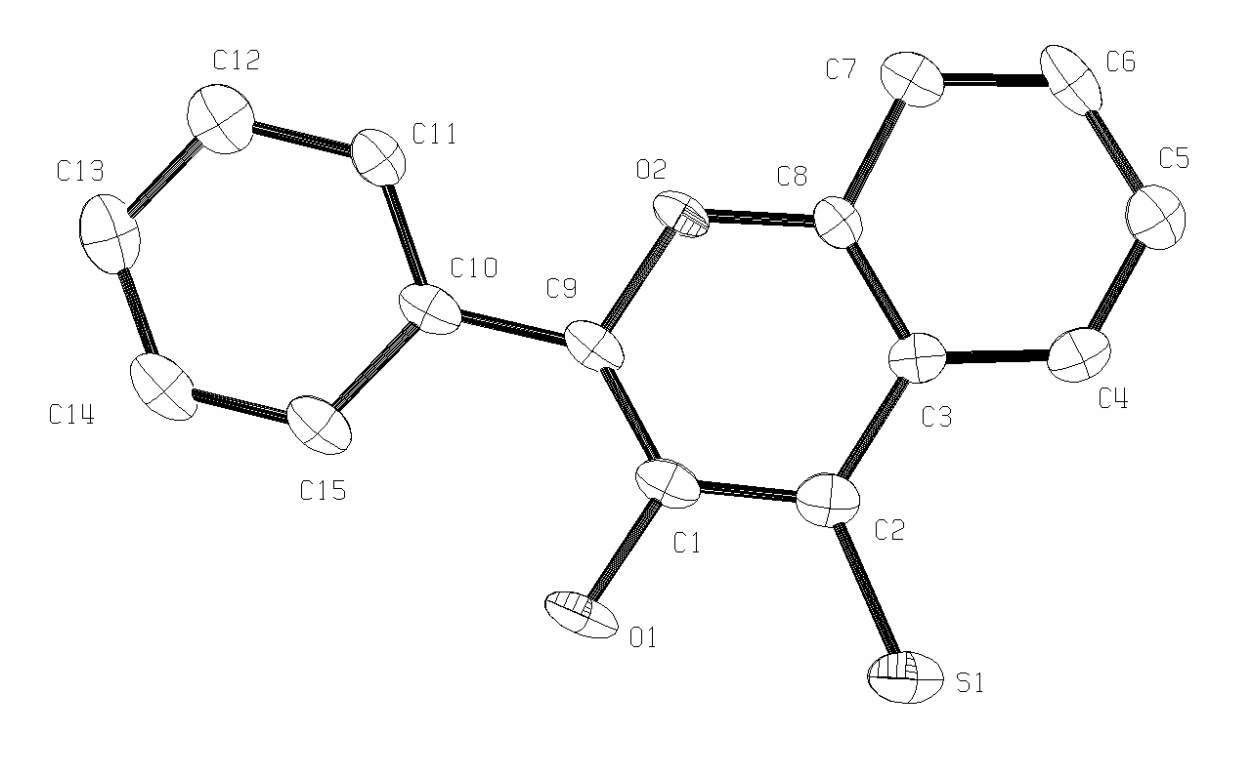
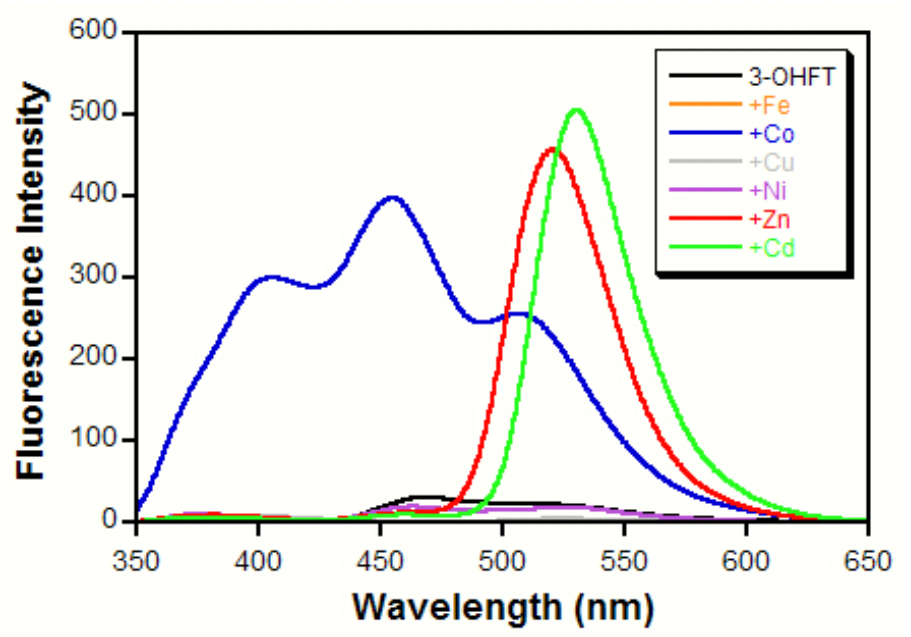


Figure S1. Structural diagram of 3-OHFT with atom numbering scheme (ORTEP, 50% probability ellipsoids). Hydrogen atoms have been omitted for clarity.



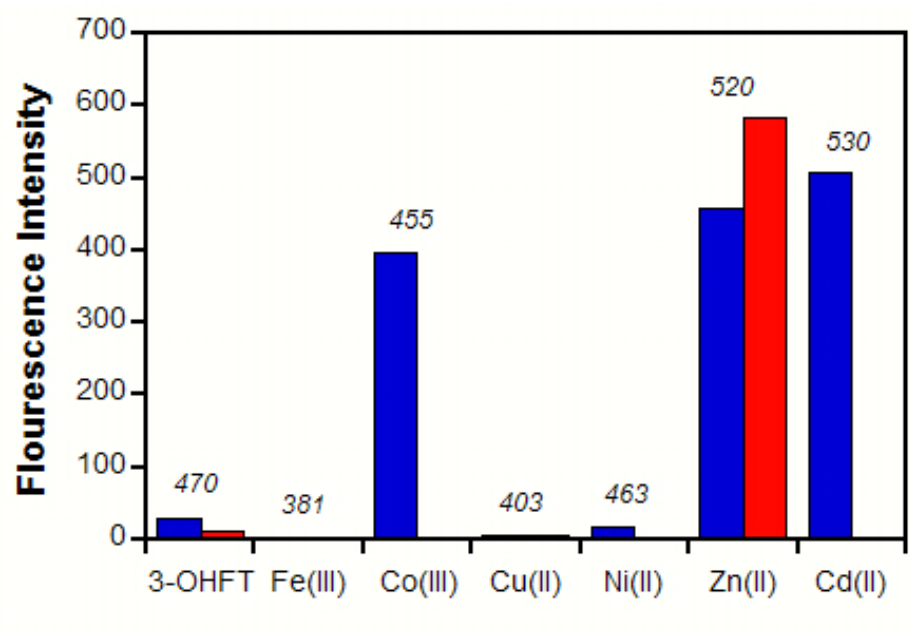


Figure S2. Aerobic fluorescence emission spectra (top) of 3-OHFT (100 μM) in methanol in absence and presence of various metal ions (100 μM). Measured emission intensity (bottom) at λ_{em} maximum for each solution (listed above each bar in nm) under aerobic (blue bars) and anaerobic (red bars; 3-OHFT, [Cu(3-OHFT)$_2$], and [Zn(3-OHFT)$_2$] only) conditions. λ_{ex} = 278 nm. T = 25 ˚C.

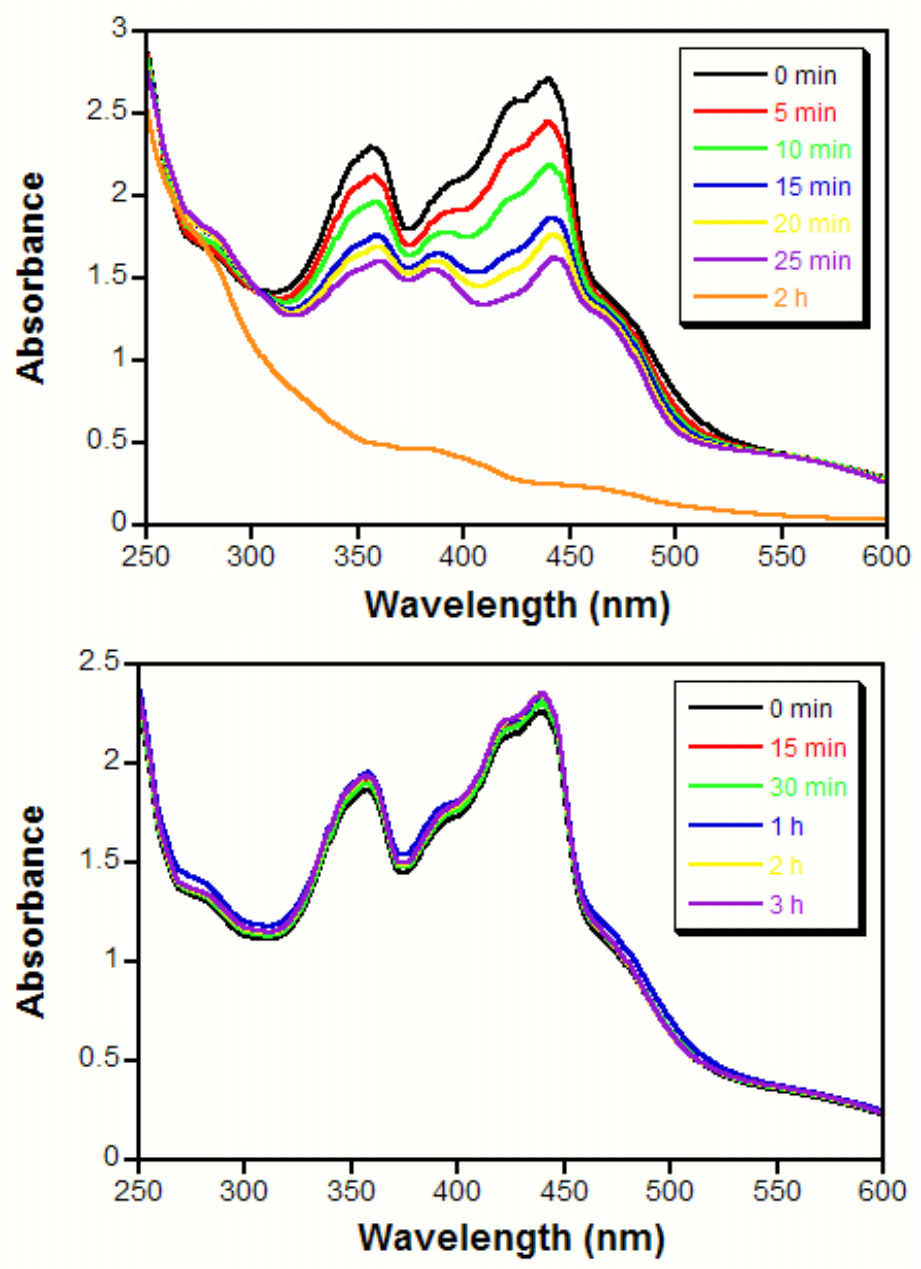


Figure S3. Degradation of [Fe(3-OHFT)$_3$] is light dependent. Absorbance spectra of [Fe(3-OHFT)$_3$] in $CHCl_3$ (~50 μM) in the presence (top) and absence (bottom) of ambient sunlight.

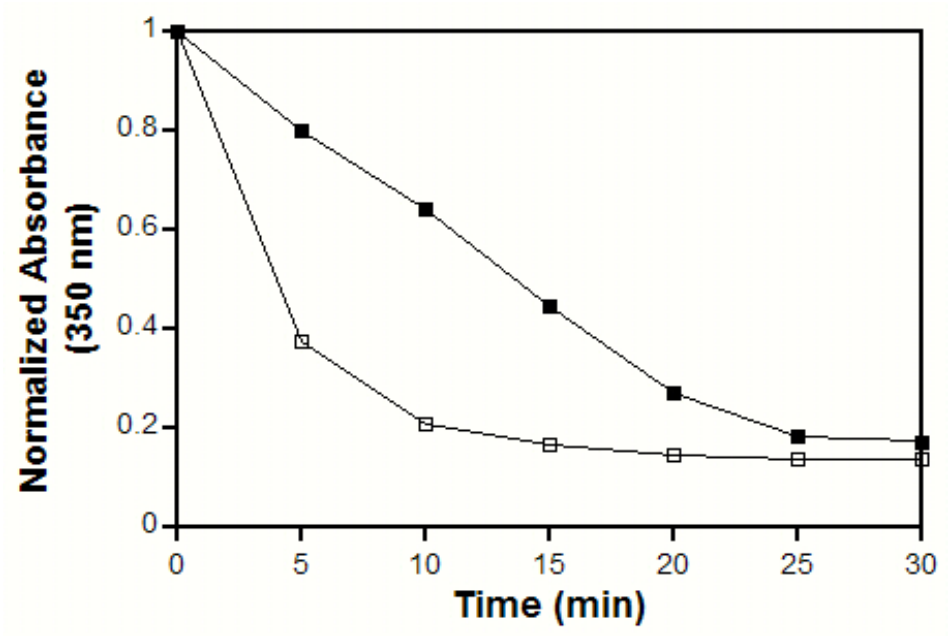


Figure S4. Degradation of [Zn(3-OHFT)$_2$] is accelerated by oxygen. Normalized absorbance spectra of [Zn(3-OHFT)$_2$] at 350 nm in $CHCl_3$ under aerobic (open squares) and anaerobic (filled square) conditions.