Supporting information

Proton Tunneling Allows Proton Coupled Electron Transfer Process in the Cancer Cell

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1. NMR Analysis

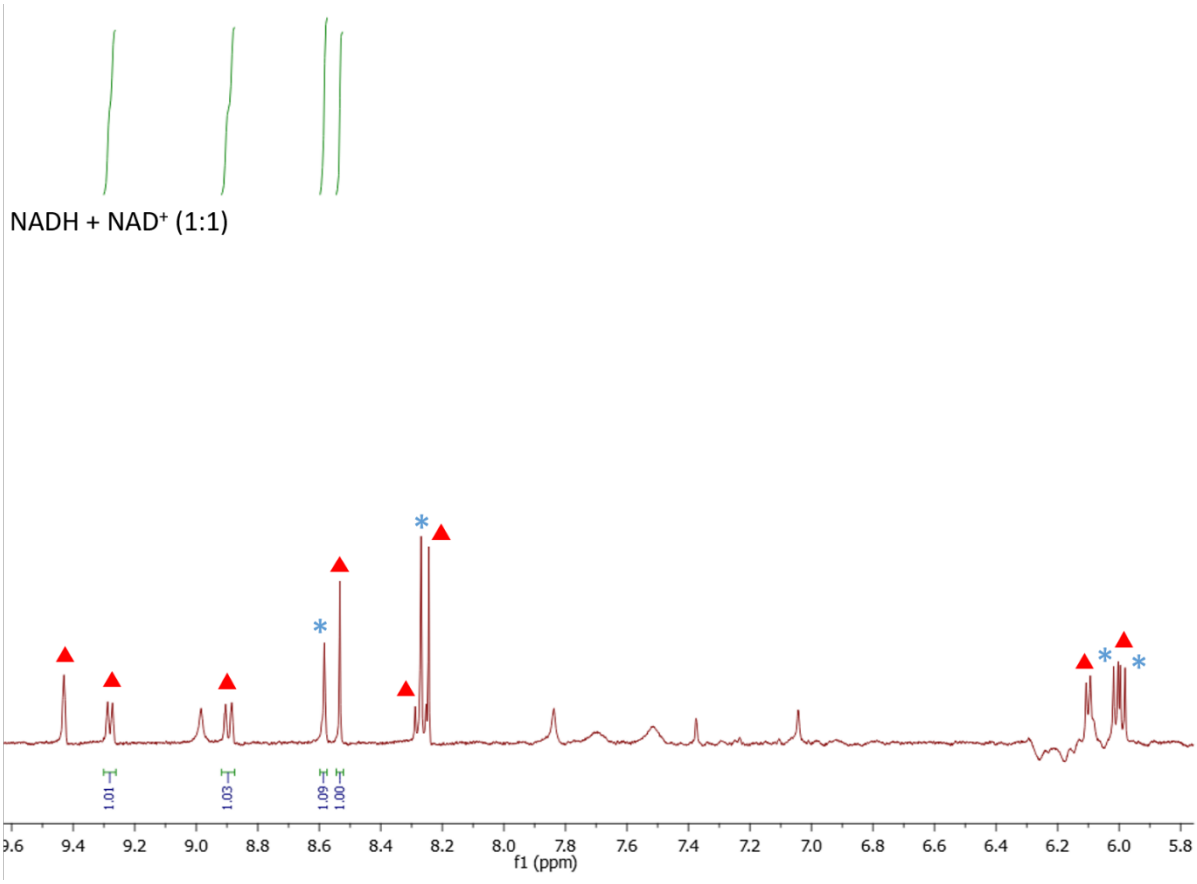
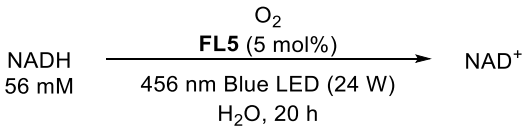


Figure S1. NMR spectrum of the mixture of NADH and NAD^+ (1:1).

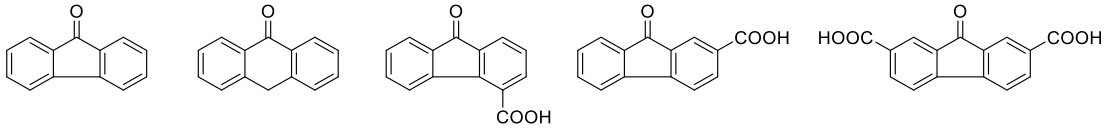
The NMR spectrum of the resulting reaction mixture was consistent with the NMR spectrum of the simple mixture of NADH and NAD^+ (1:1), which indicated the oxidation of NADH and the formation of NAD^+.

2. Optimization of reaction

Table S1. Optimisation of reaction conditions.

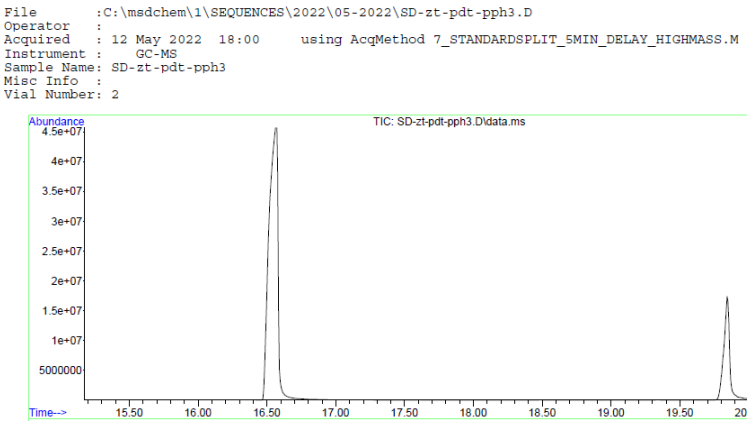


Entry	Variations	TON
1	**none**	20.6
2	**FL1** instead of **FL5**	12.9
3	**FL2** instead of **FL5**	6.3
4	**FL3** instead of **FL5**	12
5	**FL4** instead of **FL5**	14.8
6	**FL5** (0.6 mol%)	51.2
7	**Entry** 6, 6 h	14.5
8	**Entry** 7, additive NaCl (4 mM)	18.9
9	**Entry** 8, H_2O:DMSO (4:1)	36.5
10	**Entry** 9, 427 nm (40 W) Kessil lamp	60.1
11	**Entry** 10, 3 h	56.6
12	No catalyst	0
13	Under N_2	0
14	No light	0



FL1 **FL2** **FL3** **FL4** **FL5**

3. GC-MS Analysis for H_2O_2 detection



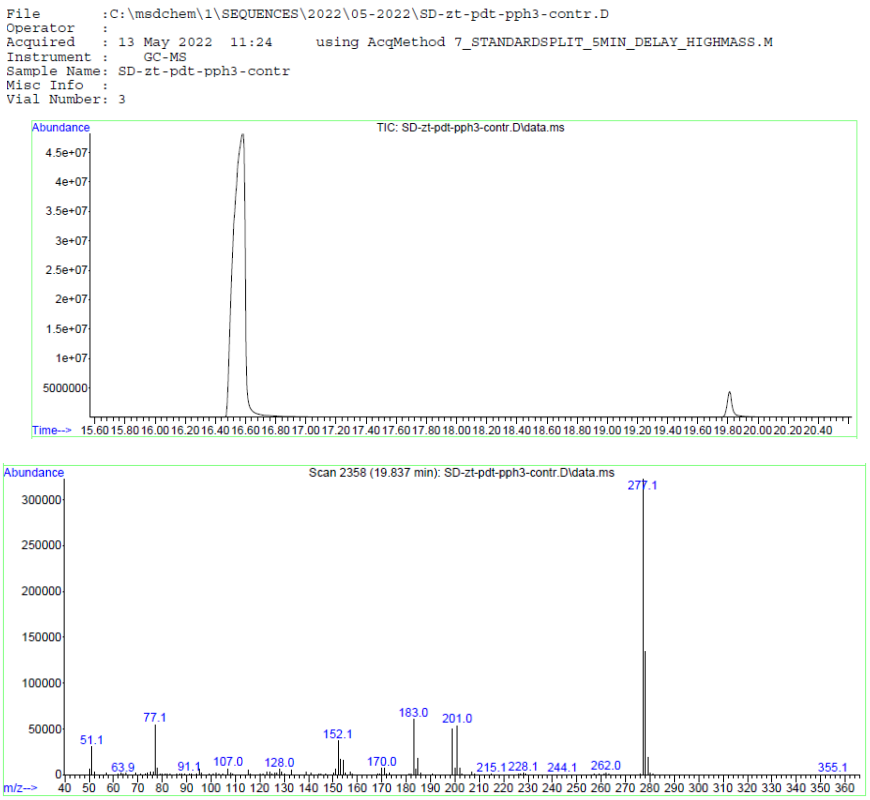


Figure S2. GC-MS analysis for reaction mixture with PPh_3.

After reaction finished, 0.1 mL triphenylphosphine (PPh_3) solution (25 mM) was added into the resulting reaction mixture and stirred for 30 minutes under dark. Later, 0.1 mL solution was diluted to 1 mL with EtOAc and submitted to GC-MS. Control experiment was also carried out: no light was used and the reaction flask was covered by aluminium foil. Same procedure for GC-MS analysis of control experiment. The results showed that compared to control reaction, standard reaction has generated much more triphenylphosphine oxide ($O=PPh_3$), which indicated the formation of H_2O_2 and the essential of light irradiation.[1]

4. UV-Vis analysis

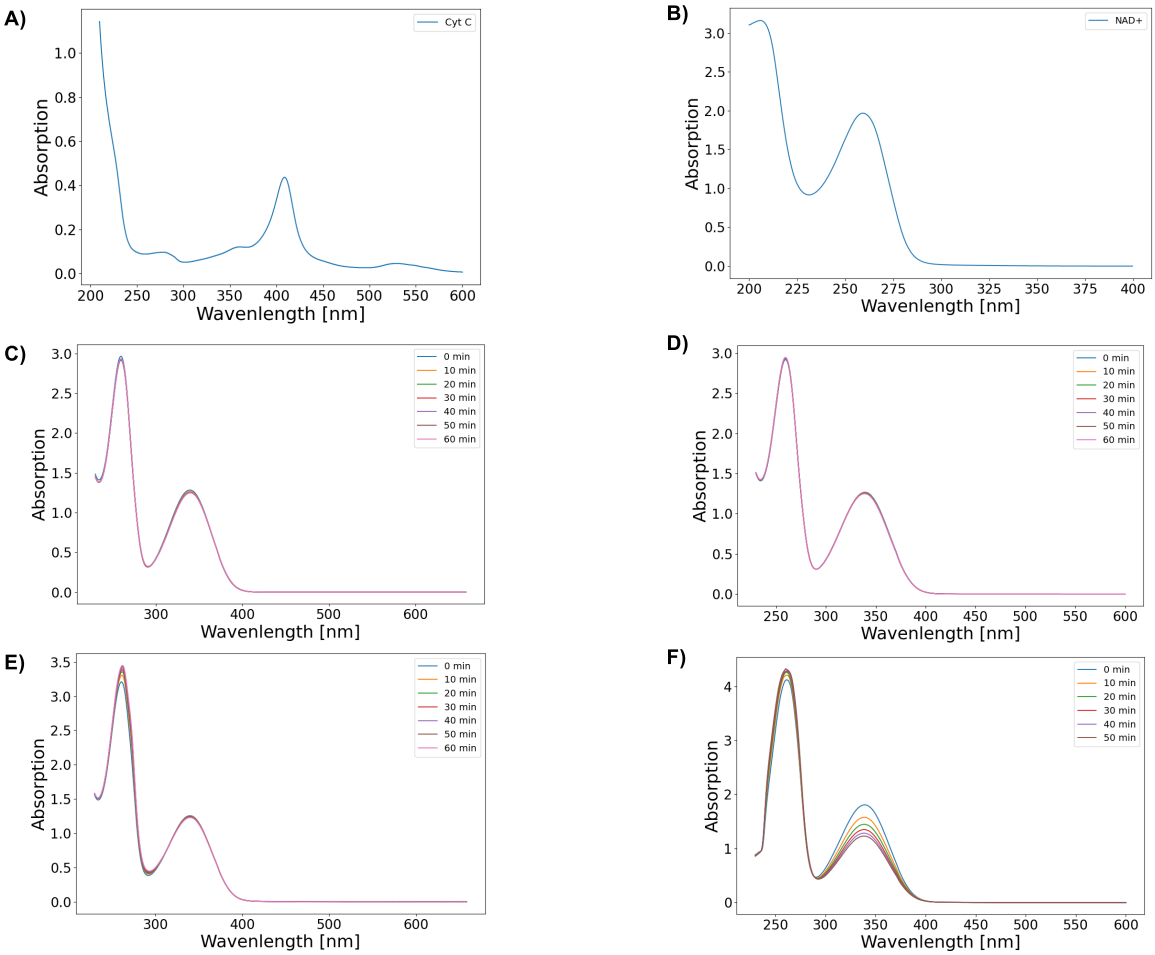


Figure S3. UV-Vis absorption studies were performed on a Shimadzu UV-2600 spectrophotometer. **A**) UV-Vis spectra of Cyt C (0.25 mM). **B**) UV-vis spectra of NAD^+ (0.32 mM). **C**) UV-Vis spectra of NADH (0.35 mM) alone in the dark for 60 min. **D**) UV-Vis spectra of NADH (0.35 mM) alone under the irradiation of 24 W 456 nm blue LED for 60 min. **E**) UV-Vis spectra of NADH (0.35 mM) with **FL5** (17.5 μM) in the dark for 60 min. **F**) UV-Vis spectra of NADH (0.35 mM) with **FL5** (17.5 μM) under the irradiation of 24 W 456 nm blue LED for 50 min.

5. Cell culture

MCF7 cells were split in a ratio of 1:3 and seeded in 3.5 cm glass-bottom Petri dishes (ibidi #81158) a day before the experiment for obtaining optimal cell viability. We seeded the cells at 500 µL/dish, let them attach in incubator at 37°C and 5% CO_2 overnight, and counted them the next day before performing viability assay. We obtained 50000 cells/ml/dish and ensured a viability of 97.5% before the start of the experiments. Fluorescence lifetime imaging (FLIM) microscopy was performed on these cells. In case of viability assay, following treatment with FL5 and irradiation, cells were detached using 1X DPBS (sigma #D8537-500mL) wash, followed by rinsing with Accutase (sigma #A6964-100mL), and resuspended in the previously

collected supernatant in FluoroBrite medium supplemented with 10%FCS/Pen/Strep (gibco #A18967-01). We further stained the cells with a viability marker Acridine orange /PI (logos #F23001) and counted them with LUNA FX7 to determine the number of live/dead cells.

6. Mitochondria staining in MCF7 cells

TMRM staining of mitochondria in MCF7 cells were done following the manufacturer's protocol.[2] In particular, we prepared the stock solution by dissolving the entire 25 mg lyophilized powder in 5 mL of DMSO to make a 10 mM solution of the dye. Next, in order to prepare a sub-stock of 100 µM, we added 10 µL of the 10 mM solution into 990 µL of DMSO. For preparation of a 1X staining solution at 50 nM concentration, we added 5 µL of the 100 µM stock solution to 10 mL of cell growth medium. After addition of staining solution, it was incubated for 30 minutes at 37°C. Following incubation, 5X washing steps were performed with PBS for increased sensitivity.

7. C. elegans sample preparation

C. elegans src-1(ok2685) strain was obtained from the Caenorhabditis Genetic Center. Worms were cultured on nutrient growth medium (NGM) agar plates seeded with Escherichia coli OP50 at 20°C. Gravid worms were allowed to lay eggs for 6h, and then removed from the plate. Developed worms of L2 stage were transferred to fresh OP50-seeded NGM agar plate containing 100 nM of TMRM and incubated for 2 days in the dark to ensure permeation of fluorescent dye into hypodermis and strong staining of mitochondria. Young adult animals were transferred to fresh OP50-seeded plate and treated with 250 ml of liquid OP50 culture containing 200 µM of **FL5** for 1 h. To prepare a microscopy sample, worms were mounted on a glass slide with an agar pad in M9 buffer containing 500 µM of **FL5** and 5 mM Levamisol, and covered with a coverslip. In control experiment, young adult animals were transferred to fresh OP50-seeded plate, treated with 250 ml of liquid OP50 culture alone for 1 h and then mounted on an agar pad in M9 buffer containing 5 mM Levamisol.

8. Fluorescence lifetime imaging microscopy (FLIM)

FLIM imaging was done using a home-built confocal setup equipped with an objective lens of high numerical aperture (Apo N, 100X oil, 1.49 NA, Olympus Europe). The excitation unit consisted of a pulsed, linearly polarized white light laser (SC400−4−8, Fianium Ltd., pulse width ~50 ps, repetition rate 80 MHz) equipped with a tunable filter (AOTFnC 400.650-TN, Pegasus Optik GmbH). For irradiation of **FL5**-treated MCF7 cells, we used excitation wavelengths of λ_{rad} = 460-488 nm at 12 µW laser power at the back-focal plane of the objective lens. Irradiation was performed for 60 minutes. For FLIM imaging of these cells stained with TMRM ($\lambda_{exc/emi}$= 548/574 nm), excitation was performed using laser light of wavelength 552 nm. Excitation light was reflected by a non-polarizing beam-splitter towards the objective lens.

Back-scattered excitation light was blocked using appropriate long-pass filter (EdgeBasic BLP02-561R-25, AHF analysentechnik AG). Emission light was focused onto the active area of a SPAD-detector (SPCM-AQRH, Excelitas) with an achromatic lens (AC254-030-AML, Thorlabs), and data recording was done with a multi-channel picosecond event timer (HydraHarp 400, PicoQuant GmbH). The laser spot was focused on a FOV of 100 × 100 μm^2 using a piezo nanopositioning stage (P-562.3CD, Physik Instrumente GmbH) and FLIM imaging was performed by scanning the laser beam on these FOVs. We used the same optical setup for performing the CellRox assay and used the fluorescence intensity values of the pixels instead of fluorescence lifetimes for estimating the difference in brightness between untreated and treated cells (**Figure 4**). For FLIM imaging of hypodermal mitochondria in *C. elegans*, we took confocal images at a single plane by scanning the laser beam on a focused FOV.

9. Fluorescence lifetime data evaluation

FLIM image acquisition was done with the aid of the software Symphotime 64 (PicoQuant GmbH) in a time-tagged, time-resolved (TTTR) mode. This means that for each photon, both the absolute time of the detection ('macro-time') and the time delay between the excitation pulse and the detection ('micro-time') are known. The micro-times of all photons of a single sample point was grouped in a TCSPC histogram, whose tail (0.5 ns after the maximum) was finally fitted with a multi-exponential decay function using a maximum likelihood procedure as described earlier.[3] Finally, the average intensity-weighted fluorescence lifetimes was calculated for each pixel (false color scales of **Figures 2, 3**, and **5**).

10. FLIM imaging of FL1, FL4 treated and only FL5-treated cells

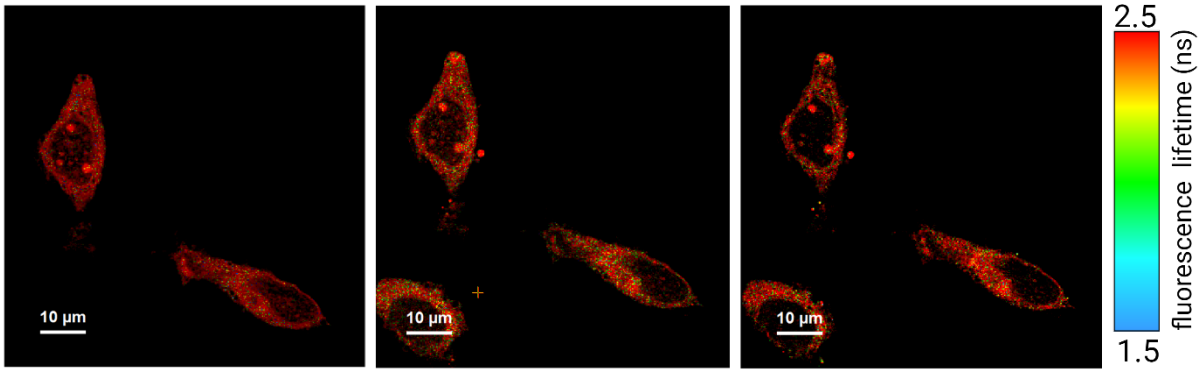


Figure S4. FLIM images of control samples where MCF7 cells were treated with 200 µM of **FL5** but no photoirradiation was done. Cells were stained with TMRM. **Left, middle, and right panels** illustrate representative MCF7 cells under dark, after 30 minutes under dark, and after 60 minutes under dark conditions respectively. We did not observe any significant changes in fluorescence lifetime values.

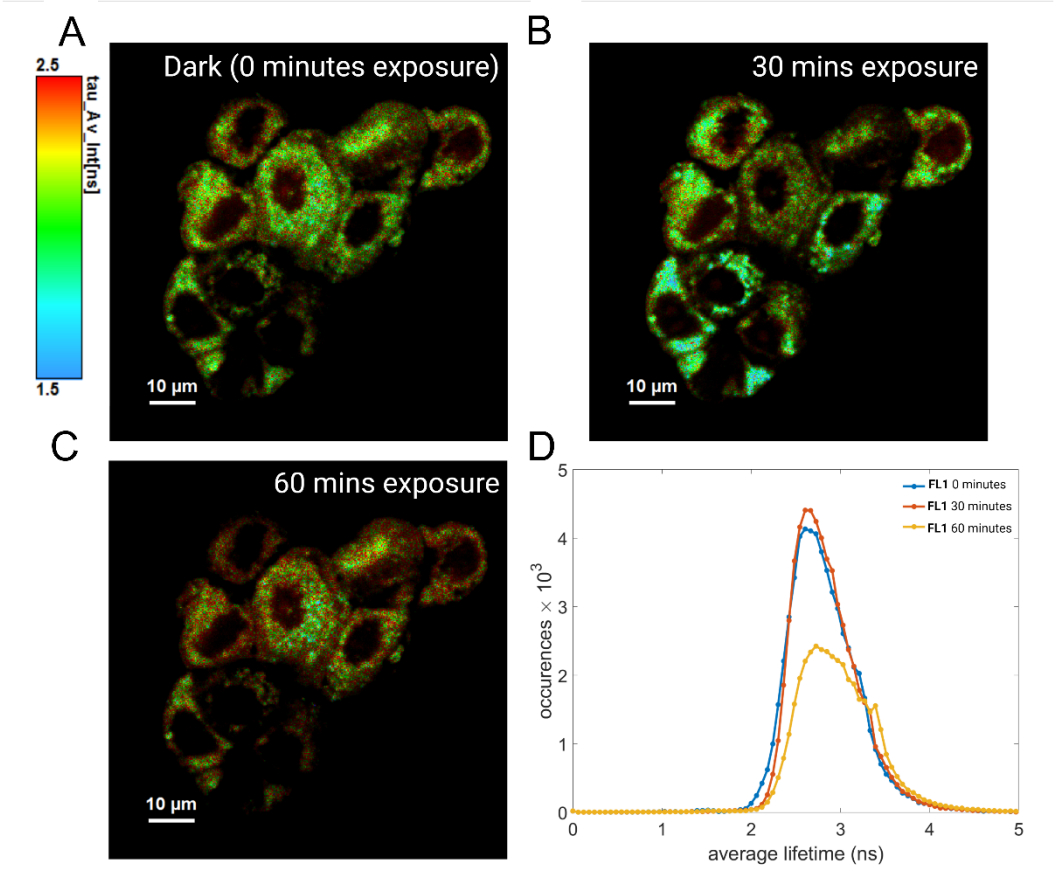


Figure S5. **A-C**. FLIM images of MCF7 cells treated with 200 µM of **FL1** and stained with TMRM. **A**. Cells stained and treated with **FL1,** but no irradiation was provided. **B**. and **C**. Same cells after 30 and 60 minutes of irradiation, respectively. **D**. Comparative plot of fluorescence lifetime values of TMRM from these cells for all the three conditions as described depict no significant changes in fluorescence lifetime values up to 1 hour of irradiation.

We performed additional control FLIM measurements on MCF7 cells treated with **FL1** (**Figure S6**) and **FL4** (**Figure S7**) respectively. Cells were stained with 50 nM TMRM for mitochondria and treated with 200 μM of **FL1.** Same was followed for a second set of cells treated with **FL4**.

Blue light irradiation and FLIM measurements were performed as described earlier in case of **FL5** treated cells. As can be seen in both **Figures S6** and **S7**, although the absolute values of fluorescence lifetime differ between cells treated with **FL1** and **FL4,** but we do not observe any non-trivial temporal changes in fluorescence lifetimes of TMRM upon irradiation. These observations confirm the necessity of two –COOH groups, as in **FL5** in order to cause photocytotoxicity upon irradiation.

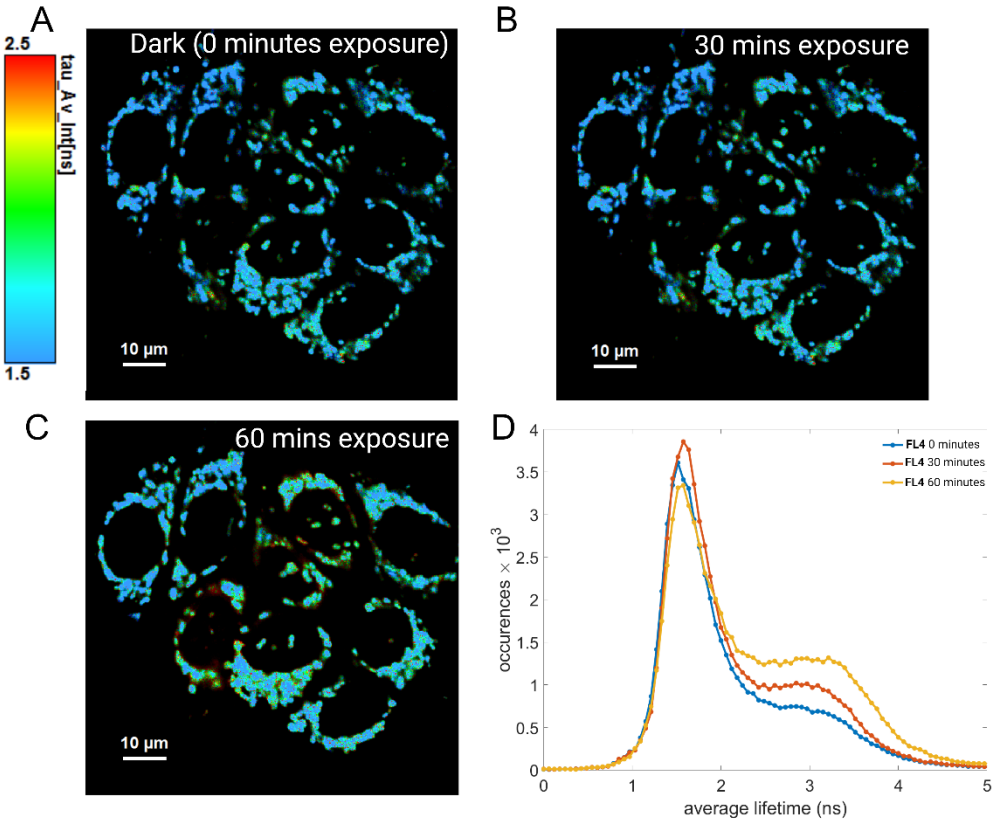


Figure S6. A-C. FLIM images of MCF7 cells treated with 200 μM of **FL4** and stained with TMRM. **A**. Cells stained and treated with **FL4,** but no irradiation was provided. **B**. and **C**. Same cells after 30 and 60 minutes of irradiation, respectively. **D**. Comparative plot of fluorescence lifetime values of TMRM from these cells for all the three conditions as described depict no significant changes in fluorescence lifetime values up to 1 hour of irradiation.

11. *Viability assay*

We performed cell counting experiments on untreated control (0 μM) and MCF7 cells treated with 50, 100, 200, 400, and 800 μM of **FL5.** As illustrated in **Figure S4**, we found that the mean cell viability was 52.5 % (~50%) at 200 μM **FL5**-treated cells, representing the half-maximal inhibitory concentration (IC_{50}). Hence, we selected 200 μM as the concentration of choice for further experiments as reported in the main text. For performing cell-counting experiments, a set of three Petri dishes containing MCF7 cells (500μL/dish and 50000 cells/ml) were prepared. Cells in one dish were treated with 200 μM **FL5** followed by irradiation for two hours, while the other two dishes served as controls and were treated as following: one dish with 200 μM **FL5** only and no irradiation was provided; and the third dish received no treatment serving as untreated control. Cells were harvested, stained, and counted as follows: the supernatant media was collected before adherent cells were once washed with PBS, gently

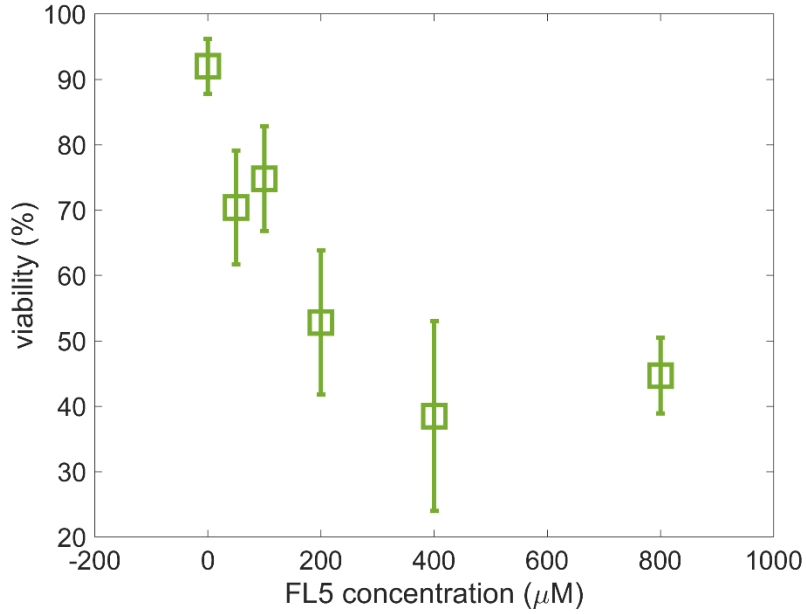


Figure S7. Cell viability assay on MCF7 cells treated with 0, 50, 100, 200, 400, and 800 μM of **FL5** and irradiated with blue light for 120 minutes. Squares represent mean viability percentage calculated from six individual cell counts per concentration of **FL5**, and error bars represent standard deviation. The mean viability percentages were 92.1 ± 4.2 %, 70.4 ± 8.7 %, 74.8 ± 8 %, 52.5 ± 11.1 %, 38.5 ± 14.5 %, and 44.7 ± 5.8 % for 0, 50, 100, 200, 400, and 800 μM of **FL5** treated cells respectively. The viability at 200 μM of **FL5** indicates the IC_{50} dose of **FL5**, hence 200 μM was selected as the desired concentration for further measurements.

rinsed with Accutase, and incubated at 37°C and 5% CO_2 for 3 minutes in order to accelerate the detachment process. Post incubation detached cells were collected with the supernatant in order to obtain the dead and live cells. Next, cell suspensions were stained with Acridine orange/PI solution and counted in two-chambered cell-counting slides using LUNA fX7 via fluorescence detection. The number of dead and live cells were counted using the described

protocol for three different passages of MCF7 cells as depicted in **Figure 7A-C** of the main text.

12. Steady-state photoluminescence (PL) analysis

The PL excitation and emission spectra were recorded on an Edinburgh FLS980 under 350 nm excitation by a Xenon lamp.

Time-correlated photon counting spectroscopy (TCSPC)

The TCSPC is equipped with a pulsed laser, Nd: YAG (Quanta-Ray INDI-40, Spectra-Physics), and an optical parametric oscillator. The pulse duration is fixed at around 50 ns, and the time resolution of each experiment was about 120 ns. A beam splitter is used in the pathway to split the beam towards a photodiode to generate a start signal and excite the sample. The emission signals are collected, filtered, and focused on the entrance slit of a 30 cm focal length spectrograph (SpectroPro-300i Acton) and detected through a photomultiplier tube (Hamamatsu, R928). The transient electrical signal is then displayed by an oscilloscope connected to the control computer. All the samples were excited at 450 nm with the excitation power intensity set at 4.8 μW cm^{-2}. The emission signals of the samples were recorded at their respective emission maximum.

The average PL lifetimes (τ_{avg}) were calculated using an intensity-weighted equation:

$$\tau_{avg} = \frac{\sum_i^n A_i \tau_i^2}{\sum_i^n A_i \tau_i}$$

Table S2. Fitting parameters for obtaining the average PL lifetime.

S.No.	τ_1 (ns)	τ_2 (ns)	A_1	A_2	χ^2	τ_{avg} (ns)
FL1	0.17	13.70	0.17	0.83	1.09	13.67
FL4	1.76	5.24	0.19	0.81	1.07	4.98
FL5	0.28	2.96	0.92	0.08	1.05	1.58

The average PL lifetime of the **FL1** (τ_{FL1}) dye can also be shown as

$$\tau_{FL1} = \frac{1}{k_{rad}+k_{nr}} \quad (1)$$

Here, k_{rad} is the rate of radiative recombination, and k_{nr} is the rate of nonradiative recombination. Upon incorporation of carboxylic groups in **FL4** and **FL5**, the average PL lifetime equation of the dyes will also include the rate of electron transfer (k_{et}). Therefore, the average PL lifetime of **FL4** (τ_{FL4}) and **FL5** (τ_{FL5}) dyes will be:

$$\tau_{FL4} = \frac{1}{k_{rad}+k_{nr}+k_{et4}} \quad (2)$$

$$\tau_{FL5} = \frac{1}{k_{rad}+k_{nr}+k_{et5}} \quad (3)$$

By solving equations (1) to (3), we calculated the rate of electron transfer in **FL4**, k_{et4} is 12.8×10^7 s^{-1}, and the rate of electron transfer in **FL5**, k_{et5} is 55.9×10^7 s^{-1}. These calculations confirm that incorporating carboxylic groups in **FL5** clearly impacts the electron transfer compared to **FL4**.

13. Theoretical calculation

Density functional theory (DFT) calculations were performed with AMS2022.[4-6] The PBE0 functional[7-8] was used including MDB dispersion corrections[9] combined with the TZ2P basis set[10] in all calculations. Geometries were optimized and the stationary points were characterized as either minima (no imaginary frequencies) or transition states (one imaginary frequency) by frequency calculations. IRC calculations were performed to confirm that the transition state connects to reactants and products. For the radical and triplet species, unrestricted DFT calculations were performed.

Table S3. The reaction energies (in kcal/mol) relative to **A** for the steps depicted in Scheme 1, together with the electron affinity of the ground state, triplet state (EA^{trip}) and ground state→triplet state excitation energy (E_{exc}), all in eV.

	FL1		**FL4**		**FL5**	
Species/Reaction	ΔE	ΔG^{298}	ΔE	ΔG^{298}	ΔE	ΔG^{298}
A	0.00	0.00	0.00	0.00	0.00	0.00
B	53.60	51.22	54.00	51.48	53.69	51.11
C	30.37	42.17	20.24	32.51	16.51	28.34
TS_{CD}	30.51	41.75	20.63	32.10	17.58	30.39
D	22.87	20.91	14.85	13.66	19.41	17.70
E	10.88	21.11	10.21	20.01	10.12	20.13
TS_{EA}	15.94	23.55	15.64	23.47	15.50	23.33
Complex	10.79	19.22	11.01	19.44	11.07	18.98
Product	20.54	17.17	20.54	17.17	20.54	17.17
EA	1.19	1.28	1.71	1.78	2.07	2.14
EA^{trip}	3.52	3.50	4.06	4.02	4.40	4.35
E_{exc}	2.32	2.22	2.34	2.23	2.33	2.22

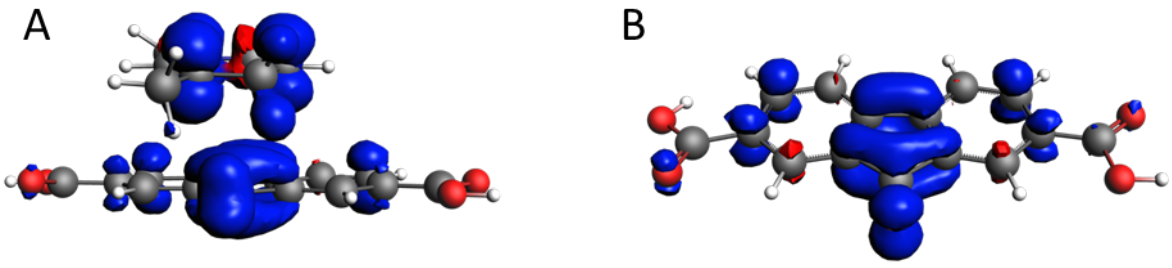


Figure S8. Isosurface plot of the spin density (isovalue = 0.003) for **A**) complex **C**, and **B**) **$FL5^{-}$**.

Table S4. Cartesian coordinates (Å) of NADH.

Atom	X	Y	Z
C	-2.945014	-2.267929	-0.038431
C	-1.721320	-1.403947	-0.052964
C	-0.471459	-2.240602	-0.036906
C	-0.524521	-3.569556	-0.133458
N	-1.700723	-4.298128	-0.265128
C	-2.884664	-3.595571	-0.134005
C	-1.680761	-5.698929	0.074091
C	0.823881	-1.511259	0.051089
H	-3.918966	-1.800504	0.029507
H	-1.717845	-0.714230	0.804420
H	-1.714173	-0.744334	-0.936212
H	0.379881	-4.167557	-0.134294
H	-3.778718	-4.207295	-0.129206
H	-0.810722	-6.173293	-0.381481
H	-2.574017	-6.181879	-0.322819
H	-1.643747	-5.872646	1.157884
H	1.676767	-2.191592	0.054870
H	0.866371	-0.901494	0.960450
H	0.941426	-0.819914	-0.791566

Table S5. Cartesian coordinates (Å) of NADH-radical-cation.

Atom	X	Y	Z
C	-2.947273	-2.252758	-0.061192
C	-1.718811	-1.432812	-0.054380
C	-0.462338	-2.222515	-0.007982
C	-0.522555	-3.579445	0.027449
N	-1.702491	-4.259166	0.024207
C	-2.898825	-3.598060	-0.023694
C	-1.678388	-5.718021	0.017602
C	0.832615	-1.504754	-0.000574

H	-3.911493	-1.762976	-0.095743
H	-1.742301	-0.721620	0.787724
H	-1.705532	-0.764403	-0.931152
H	0.368590	-4.191845	0.066176
H	-3.782151	-4.220746	-0.021914
H	-1.473899	-6.075517	-0.993063
H	-2.641659	-6.096014	0.349110
H	-0.898493	-6.068781	0.691035
H	1.682129	-2.184323	0.033762
H	0.886369	-0.831127	0.860076
H	0.921420	-0.875748	-0.891604

Table S6. Cartesian coordinates (Å) of NADH-radical.

Atom	X	Y	Z
C	-2.908312	-2.268701	-0.187996
C	-1.713101	-1.526475	-0.166059
C	-0.492015	-2.239046	-0.104041
C	-0.508966	-3.598523	-0.092294
N	-1.693861	-4.321544	-0.180011
C	-2.893132	-3.626257	-0.175706
C	-1.683368	-5.728893	0.115054
C	0.809601	-1.503789	-0.051037
H	-3.868640	-1.769148	-0.215323
H	0.929388	-0.869336	-0.933119
H	-1.722346	-0.445718	-0.172272
H	0.395017	-4.190606	-0.047045
H	-3.788614	-4.230765	-0.191219
H	-0.793773	-6.188841	-0.316511
H	-2.560914	-6.201893	-0.325942
H	-1.687457	-5.924401	1.195696
H	1.657351	-2.187907	-0.004230
H	0.846924	-0.849683	0.823864

Table S7. Cartesian coordinates (Å) of FL1-A.

Atom	X	Y	Z
C	-3.463486	0.111668	-0.118476
C	-4.819179	0.355518	-0.137264
C	-5.681882	-0.731489	-0.243068
C	-5.177766	-2.022397	-0.326774
C	-3.806511	-2.265347	-0.306933
C	-2.951446	-1.186763	-0.203267
H	-5.192249	1.370542	-0.071737
H	-0.798597	-3.154045	-0.300732
H	-5.864409	-2.856745	-0.407706
H	-3.430227	-3.279371	-0.372701
C	-2.327075	1.075971	-0.011801
C	-1.100081	0.223786	-0.044924
C	-1.480998	-1.116870	-0.158774
O	-2.387240	2.277755	0.079940
C	0.225522	0.593761	0.018345
C	1.191446	-0.406824	-0.035051
C	0.817479	-1.739037	-0.148662
C	-0.523656	-2.109706	-0.211707
H	0.497170	1.638885	0.105802
H	2.242093	-0.148451	0.011673
H	1.583326	-2.504533	-0.188978
H	-6.753081	-0.573375	-0.260834

Table S8. Cartesian coordinates (Å) of FL1-B.

Atom	X	Y	Z
C	-3.431153	0.152900	-0.116199
C	-4.800585	0.372611	-0.134891
C	-5.642209	-0.713173	-0.238792
C	-5.137809	-2.051983	-0.328876
C	-3.802482	-2.300474	-0.311595
C	-2.908011	-1.203444	-0.205058

H	-5.185767	1.382714	-0.067629
H	-0.800795	-3.189167	-0.304455
H	-5.843099	-2.869790	-0.407263
H	-3.424278	-3.313567	-0.379460
C	-2.328348	1.104854	-0.012169
C	-1.136397	0.261935	-0.046121
C	-1.522579	-1.137957	-0.163430
O	-2.389852	2.332622	0.080173
C	0.205425	0.609208	0.017776
C	1.149963	-0.391909	-0.033123
C	0.780548	-1.772899	-0.150321
C	-0.523893	-2.145458	-0.215141
H	0.489005	1.650820	0.106820
H	2.203006	-0.141954	0.015640
H	1.563590	-2.519841	-0.187307
H	-6.715127	-0.563115	-0.252206

Table S9. Cartesian coordinates (Å) of FL1-C.

Atom	X	Y	Z
C	-3.433803	0.129832	-0.118582
C	-4.811145	0.352348	-0.137386
C	-5.673447	-0.723525	-0.240169
C	-5.180356	-2.035878	-0.326583
C	-3.812763	-2.272224	-0.308918
C	-2.936232	-1.201627	-0.206089
H	-5.185773	1.368253	-0.070093
H	-0.791992	-3.163055	-0.302429
H	-5.872888	-2.866872	-0.407639
H	-3.435760	-3.288859	-0.376204
C	-2.326730	1.073612	-0.015290
C	-1.131297	0.238946	-0.046746
C	-1.494714	-1.133156	-0.162870

O	-2.389276	2.322500	0.080222
C	0.217832	0.589710	0.018331
C	1.182205	-0.399578	-0.032963
C	0.821311	-1.752130	-0.148664
C	-0.516654	-2.115935	-0.213178
H	0.490860	1.635889	0.107181
H	2.233452	-0.133496	0.016539
H	1.592477	-2.513997	-0.187579
H	-6.746153	-0.557826	-0.254518

Table S10. Cartesian coordinates (Å) of FL1-TS_{CD}.

Atom	X	Y	Z
C	-0.162178	0.202999	6.251516
C	-1.272317	-0.377384	5.635340
C	0.755627	-0.612053	6.886505
H	-0.034870	1.279932	6.234696
C	-2.347321	0.223374	4.881767
C	-1.453914	-1.786152	5.679069
C	0.581504	-2.001668	6.917758
H	-2.664471	-0.126278	0.699573
C	-3.218648	-0.867164	4.493487
O	-2.445412	1.445344	4.523879
C	-2.677302	-2.092802	4.967199
C	-0.525095	-2.589898	6.319713
H	1.311658	-2.620900	7.424913
H	0.363285	-1.925767	2.891673
H	-1.131006	-3.162722	1.857220
C	-4.389611	-0.867570	3.737474
C	-3.320887	-3.290730	4.699038
H	-0.657491	-3.665942	6.361703
H	-1.959520	-2.458991	0.449846
C	-5.018008	-2.072924	3.472755

H	-4.801523	0.068848	3.378614
C	-4.492556	-3.279378	3.952831
H	-2.919339	-4.229597	5.065675
H	-2.755723	-2.475301	2.048351
H	-5.008878	-4.208823	3.744778
H	-2.921341	2.265746	0.532636
H	-1.441102	3.205603	0.808279
H	-2.605578	2.998866	2.117157
C	0.353037	0.209339	3.032702
C	-0.395641	1.433261	2.761359
C	-1.439826	1.284101	1.735319
C	-1.830657	0.045793	1.366458
N	-1.214564	-1.085186	1.835093
C	-0.101699	-0.991371	2.612968
C	-1.801792	-2.374574	1.525984
C	-2.144269	2.500397	1.259643
H	1.234502	0.238989	3.657465
H	0.219568	2.329017	2.648438
H	-1.062241	1.644921	3.708168
H	1.617887	-0.174665	7.376538
H	-5.938588	-2.086077	2.900301

Table S11. Cartesian coordinates (Å) of FL1-D.

Atom	X	Y	Z
C	-0.180283	-0.176584	6.014835
C	-1.374930	-0.687881	5.514504
C	0.683856	-1.041032	6.663852
H	0.062839	0.872156	5.897033
C	-2.446916	-0.066675	4.817168
C	-1.699004	-2.060445	5.667586
C	0.367155	-2.391199	6.815659
H	1.618775	-0.666552	7.062401

C	-3.449040	-1.038497	4.529529
O	-2.452030	1.237446	4.510371
C	-2.998654	-2.281584	5.050611
C	-0.824669	-2.907705	6.318215
H	1.061935	-3.045521	7.327655
H	-3.264373	1.458727	4.044815
H	-5.624424	-4.194654	4.151353
C	-4.679590	-0.949767	3.881075
C	-3.779302	-3.411233	4.914912
H	-1.058290	-3.958699	6.443125
H	-6.407714	-2.043634	3.252076
C	-5.449397	-2.093984	3.754242
H	-5.042889	-0.009626	3.478158
C	-5.005321	-3.313180	4.264176
H	-3.446374	-4.365334	5.306780

Table S12. Cartesian coordinates (Å) of FL1-E.

Atom	X	Y	Z
C	-3.471443	0.094150	-0.141431
C	-4.825380	0.337200	-0.172904
C	-5.687689	-0.750307	-0.270649
C	-5.186462	-2.043340	-0.335286
C	-3.817885	-2.283042	-0.302599
C	-2.960288	-1.202977	-0.201952
H	-5.215733	1.346701	-0.117661
H	-6.758054	-0.587239	-0.295744
H	-5.872906	-2.877965	-0.409785
H	-3.437908	-3.296313	-0.353210
C	-2.329027	1.080767	-0.028678
C	-1.113162	0.203673	-0.064758
C	-1.495351	-1.134275	-0.152815
O	-2.304245	2.129147	-0.892677

C	0.209494	0.579888	-0.014900
C	1.176193	-0.418749	-0.055251
C	0.805513	-1.754246	-0.143985
C	-0.532447	-2.126353	-0.194643
H	0.485508	1.625299	0.048401
H	2.225710	-0.154592	-0.019670
H	1.573273	-2.517729	-0.176763
H	-0.808655	-3.171237	-0.267431
H	-2.822491	2.831956	-0.455419
O	-2.407196	1.647850	1.391039
O	-2.986395	2.801666	1.401496

Table S13. Cartesian coordinates (Å) of FL1-TS_{EA}.

Atom	X	Y	Z
C	-3.497325	0.050277	-0.348948
C	-4.852565	0.257123	-0.489542
C	-5.693544	-0.848886	-0.435223
C	-5.172157	-2.121893	-0.244089
C	-3.802432	-2.326959	-0.107935
C	-2.964396	-1.230691	-0.163355
H	-5.245460	1.255759	-0.637318
H	-6.763406	-0.719650	-0.541819
H	-5.844205	-2.970655	-0.203046
H	-3.410793	-3.326976	0.034995
C	-2.387115	1.029005	-0.343387
C	-1.150106	0.228669	-0.206946
C	-1.502566	-1.119491	-0.074392
O	-2.450203	2.221842	-0.790854
C	0.165396	0.638501	-0.187475
C	1.150793	-0.328346	-0.021594
C	0.807724	-1.666845	0.119215
C	-0.521721	-2.077166	0.092384

H	0.418075	1.686035	-0.298401
H	2.193815	-0.038112	-0.001560
H	1.590040	-2.405063	0.248864
H	-0.772732	-3.125853	0.197540
H	-2.557853	2.852880	0.174844
O	-2.548290	1.607426	1.587116
O	-2.634417	2.861433	1.418274

Table S14. Cartesian coordinates (Å) of FL1-Complex.

Atom	X	Y	Z
C	-0.199594	0.261881	6.264158
C	-1.272829	-0.331031	5.594604
C	0.729614	-0.543817	6.889996
H	-0.112579	1.342696	6.293584
C	-2.356703	0.271695	4.836039
C	-1.408159	-1.747631	5.584112
C	0.605569	-1.942846	6.862323
H	-2.736841	0.035093	0.816738
C	-3.183733	-0.844047	4.405512
O	-2.487840	1.485945	4.529679
C	-2.605813	-2.068214	4.846781
C	-0.463096	-2.544220	6.217523
H	1.345607	-2.554711	7.364029
H	0.105977	-2.200158	2.846531
H	-1.423889	-3.201278	1.644345
C	-4.366166	-0.860069	3.665727
C	-3.223293	-3.278611	4.555683
H	-0.558625	-3.625119	6.215907
H	-2.117354	-2.308197	0.269872
C	-4.968138	-2.072607	3.383345
H	-4.809345	0.074388	3.339735
C	-4.402207	-3.280802	3.826990

H	-2.797358	-4.214230	4.902971
H	-2.992072	-2.389736	1.825933
H	-4.900126	-4.217361	3.606338
H	-2.781553	2.445045	0.826766
H	-1.213056	3.234923	1.093811
H	-2.328532	3.009507	2.447929
C	0.352699	-0.090362	3.084241
C	-0.173222	1.255550	2.791117
C	-1.338051	1.252410	1.871082
C	-1.854839	0.084543	1.440208
N	-1.330379	-1.130280	1.800460
C	-0.232641	-1.205445	2.597633
C	-2.007637	-2.331967	1.354899
C	-1.953431	2.555696	1.526172
H	1.206401	-0.197807	3.738803
H	0.615465	1.930651	2.430783
H	-0.540420	1.714764	3.734259
H	1.561447	-0.096705	7.422141
H	-5.900448	-2.096607	2.830341

Table S15. Cartesian coordinates (Å) of FL1-Product.

Atom	X	Y	Z
C	-3.497822	0.053406	-0.388895
C	-4.853023	0.262130	-0.521458
C	-5.697027	-0.841267	-0.441501
C	-5.174996	-2.109920	-0.230281
C	-3.802844	-2.316890	-0.101744
C	-2.965905	-1.224146	-0.186058
H	-5.241867	1.260083	-0.683541
H	-6.767461	-0.713086	-0.542418
H	-5.847770	-2.956737	-0.165122
H	-3.413873	-3.314316	0.064575

C	-2.384656	1.035090	-0.415844
C	-1.147022	0.232964	-0.246449
C	-1.500337	-1.112103	-0.096706
O	-2.468245	2.243404	-0.567119
C	0.167235	0.644727	-0.216996
C	1.152247	-0.319189	-0.025191
C	0.805968	-1.653826	0.134718
C	-0.524532	-2.066529	0.099052
H	0.418138	1.691087	-0.341640
H	2.195378	-0.030076	0.000701
H	1.586113	-2.390200	0.287191
H	-0.775919	-3.112649	0.226443
H	-2.613595	2.943463	0.956461
O	-2.583360	1.680233	2.276473
O	-2.668709	2.942014	1.951598

Table S16. Cartesian coordinates (Å) of FL4-A.

Atom	X	Y	Z
C	-3.458584	0.109815	-0.099708
C	-4.807104	0.359449	-0.135609
C	-5.685572	-0.722603	-0.235222
C	-5.175197	-2.017164	-0.306753
C	-3.806143	-2.264792	-0.281769
C	-2.945887	-1.190044	-0.177331
H	-5.200582	1.367102	-0.095205
C	-7.145253	-0.401674	-0.298248
H	-5.839703	-2.867440	-0.423916
H	-3.436814	-3.280597	-0.354866
C	-2.319341	1.075584	0.004191
C	-1.095798	0.221204	-0.034483
C	-1.476078	-1.120376	-0.141050
O	-2.380765	2.274896	0.097232

C	0.229886	0.593961	0.012290
C	1.195613	-0.404944	-0.051593
C	0.823092	-1.738644	-0.158214
C	-0.517319	-2.112498	-0.203515
H	0.500148	1.639789	0.093744
H	-7.534748	-2.186929	0.267224
H	1.590618	-2.501683	-0.208514
H	-0.789478	-3.157822	-0.288328
O	-8.007283	-1.405051	-0.034788
O	-7.558212	0.689654	-0.566955
H	2.246273	-0.144453	-0.020069

Table S17. Cartesian coordinates (Å) of FL4-B.

Atom	X	Y	Z
C	-3.433933	0.147357	-0.099186
C	-4.791672	0.376914	-0.147372
C	-5.657805	-0.701995	-0.248615
C	-5.144028	-2.047334	-0.324940
C	-3.810828	-2.299477	-0.292726
C	-2.907981	-1.208835	-0.176692
H	-5.192436	1.381724	-0.104791
C	-7.115411	-0.393214	-0.290069
H	-5.824952	-2.881085	-0.456904
H	-3.440964	-3.315027	-0.369823
C	-2.327482	1.102377	0.008433
C	-1.133767	0.255638	-0.029352
C	-1.523927	-1.143679	-0.139773
O	-2.384684	2.324399	0.100798
C	0.203509	0.609290	0.014633
C	1.152891	-0.389506	-0.048736
C	0.782830	-1.770188	-0.156125
C	-0.519886	-2.149827	-0.200837

H	0.482625	1.652728	0.096063
H	-7.481296	-2.179459	0.296462
H	1.567930	-2.514610	-0.203615
H	-0.791214	-3.195234	-0.284162
O	-7.964102	-1.401673	-0.000536
O	-7.543392	0.692237	-0.565437
H	2.205746	-0.136778	-0.018153

Table S18. Cartesian coordinates (Å) of FL4-C.

Atom	X	Y	Z
C	-3.433629	0.133862	-0.122273
C	-4.795696	0.367663	-0.149175
C	-5.689795	-0.696605	-0.228213
C	-5.183265	-2.022450	-0.295963
C	-3.823176	-2.267914	-0.275309
C	-2.932521	-1.204681	-0.185621
H	-5.183037	1.378064	-0.102140
C	-7.127778	-0.378784	-0.228478
H	-5.844818	-2.877468	-0.408994
H	-3.460857	-3.289514	-0.339203
C	-2.320272	1.078314	-0.036206
C	-1.126371	0.231888	-0.057723
C	-1.498639	-1.138187	-0.146988
O	-2.368588	2.319257	0.036706
C	0.218737	0.588181	-0.006582
C	1.183765	-0.399452	-0.044497
C	0.817822	-1.753869	-0.133399
C	-0.513997	-2.123723	-0.184093
H	0.487617	1.636753	0.061467
H	-7.454897	-2.231015	0.051349
H	1.590348	-2.514791	-0.162926
H	-0.783667	-3.173228	-0.253071

O	-7.981207	-1.438283	-0.093322
O	-7.605119	0.724223	-0.330577
H	2.234811	-0.133500	-0.006224

Table S19. Cartesian coordinates (Å) of FL4-TS_{CD}.

Atom	X	Y	Z
C	-0.133704	0.098639	6.247159
C	-1.262169	-0.442624	5.645226
C	0.763317	-0.749364	6.883675
H	0.041129	1.167019	6.224719
C	-2.317795	0.194989	4.891870
C	-1.495645	-1.846329	5.694067
C	0.529796	-2.136962	6.929415
C	1.980293	-0.239953	7.536289
C	-3.221966	-0.867168	4.504103
O	-2.385551	1.419577	4.540674
C	-2.723093	-2.108948	4.982469
C	-0.595442	-2.681908	6.341427
H	1.251059	-2.758380	7.443509
O	2.127768	1.100627	7.412296
O	2.793497	-0.910405	8.125223
C	-4.385764	-0.829987	3.737250
C	-3.402385	-3.287963	4.707071
H	-0.768209	-3.751344	6.392132
H	2.940062	1.315397	7.888944
C	-5.045589	-2.014495	3.463528
H	-4.764456	0.119008	3.375079
C	-4.561571	-3.238206	3.948421
H	-3.033841	-4.238758	5.076860
H	-2.691850	-2.455972	2.060276
H	-5.103909	-4.150681	3.732148
H	-2.959395	2.214073	0.544968

H	-1.498450	3.194020	0.779321
H	-2.639322	2.989254	2.108161
C	0.414488	0.288594	3.011933
C	-0.386047	1.479441	2.753716
C	-1.437686	1.292852	1.744236
C	-1.801237	0.038538	1.400113
N	-1.147474	-1.067358	1.877366
C	-0.014946	-0.931211	2.620829
C	-1.706671	-2.376081	1.596741
C	-2.178138	2.482414	1.255611
H	1.313322	0.356355	3.608838
H	0.181704	2.406381	2.653633
H	-1.063883	1.643070	3.717980
H	-2.640615	-0.166731	0.749780
H	0.486981	-1.847873	2.894742
H	-1.057259	-3.140049	2.015344
H	-1.792056	-2.520272	0.518401
H	-5.958798	-2.000420	2.879703

Table S20. Cartesian coordinates (Å) of FL4-D.

Atom	X	Y	Z
C	-0.154186	-0.188977	5.968348
C	-1.349919	-0.689686	5.470358
C	0.700432	-1.053114	6.644102
H	0.130292	0.849567	5.848434
C	-2.419189	-0.074293	4.754658
C	-1.689930	-2.060173	5.651764
C	0.364636	-2.400447	6.816717
C	1.984394	-0.588557	7.208558
C	-3.424741	-1.044143	4.493360
O	-2.527879	1.201099	4.366069
C	-2.988456	-2.278339	5.040670

C	-0.827057	-2.905924	6.321996
H	1.062446	-3.033671	7.348542
O	2.212160	0.723588	6.981421
O	2.767395	-1.277604	7.811130
C	-4.654103	-0.946853	3.845212
C	-3.783512	-3.402944	4.933554
H	-1.073328	-3.951249	6.464713
H	3.067199	0.917987	7.387765
C	-5.436559	-2.083449	3.748889
H	-4.985496	-0.003082	3.430433
C	-5.008250	-3.298882	4.285352
H	-3.463354	-4.352187	5.346802
H	-1.752643	1.698346	4.644406
H	-5.641575	-4.172651	4.195209
H	-6.396736	-2.031857	3.250404

Table S21. Cartesian coordinates (Å) of FL4-E.

Atom	X	Y	Z
C	-3.464448	0.091684	-0.118523
C	-4.810972	0.341384	-0.164298
C	-5.692106	-0.737308	-0.260842
C	-5.186134	-2.034517	-0.317217
C	-3.820033	-2.281516	-0.277155
C	-2.954277	-1.207426	-0.174860
H	-5.221691	1.342667	-0.130400
C	-7.148271	-0.400122	-0.324677
H	-5.848792	-2.886804	-0.429104
H	-3.449368	-3.297452	-0.336462
C	-2.321310	1.078080	-0.007778
C	-1.108700	0.199713	-0.054352
C	-1.489411	-1.139743	-0.133874
O	-2.295228	2.115529	-0.884590

C	0.213196	0.579842	-0.022706
C	1.180792	-0.416805	-0.072628
C	0.812829	-1.753971	-0.150920
C	-0.524288	-2.130429	-0.183089
H	0.486517	1.626177	0.033026
H	2.229926	-0.149354	-0.052755
H	1.582948	-2.514512	-0.191614
H	-0.796043	-3.176788	-0.249885
H	-2.899795	2.786188	-0.520811
O	-2.387275	1.645217	1.402099
O	-3.061717	2.747959	1.420233
O	-8.024398	-1.404831	-0.129172
O	-7.547247	0.709419	-0.536004
H	-7.564112	-2.212152	0.119819

Table S22. Cartesian coordinates (Å) of FL4-TS_{EA}.

Atom	X	Y	Z
C	-3.494583	0.047826	-0.343500
C	-4.841760	0.257643	-0.499436
C	-5.700388	-0.840974	-0.434586
C	-5.172826	-2.115485	-0.232736
C	-3.805238	-2.324955	-0.092281
C	-2.961072	-1.232927	-0.147657
H	-5.254015	1.243482	-0.672079
C	-7.158589	-0.561775	-0.618772
H	-5.819595	-2.987028	-0.218229
H	-3.421203	-3.328314	0.045955
C	-2.383078	1.028379	-0.339849
C	-1.148772	0.225891	-0.206015
C	-1.499762	-1.122054	-0.062417
O	-2.448648	2.220313	-0.779906
C	0.166634	0.637022	-0.200260

C	1.152863	-0.328142	-0.036022
C	0.812310	-1.666393	0.118108
C	-0.516269	-2.078512	0.104764
H	0.416844	1.683804	-0.322153
H	2.195890	-0.037171	-0.028311
H	1.597166	-2.401980	0.246529
H	-0.763292	-3.127025	0.219531
H	-2.583362	2.845474	0.194107
O	-2.558101	1.585421	1.591769
O	-2.663640	2.837673	1.431110
O	-8.023000	-1.524343	-0.240339
O	-7.568906	0.465586	-1.077071
H	-7.558179	-2.242591	0.199907

Table S23. Cartesian coordinates (Å) of FL4-Complex.

Atom	X	Y	Z
C	-0.197505	0.220897	6.262619
C	-1.272627	-0.356237	5.599922
C	0.728244	-0.598584	6.893009
H	-0.086689	1.298039	6.290051
C	-2.349529	0.263488	4.838826
C	-1.430748	-1.773424	5.590410
C	0.575714	-2.002659	6.871820
C	1.888040	-0.048053	7.608936
C	-3.188883	-0.844626	4.408391
O	-2.470240	1.474904	4.534157
C	-2.628235	-2.074220	4.855993
C	-0.497016	-2.583896	6.230708
H	1.316974	-2.602631	7.382890
O	1.952529	1.304170	7.558056
O	2.726425	-0.695636	8.189760
C	-4.368932	-0.844854	3.665148

C	-3.265133	-3.278643	4.567308
H	-0.610047	-3.662712	6.235145
H	2.735352	1.543258	8.070788
C	-4.985296	-2.048624	3.382193
H	-4.797786	0.095135	3.335846
C	-4.437677	-3.263709	3.834260
H	-2.854909	-4.219275	4.919252
H	-2.925833	-2.411274	1.881123
H	-4.948104	-4.193493	3.613212
H	-2.815842	2.412949	0.815378
H	-1.262704	3.238153	1.063378
H	-2.366088	3.009795	2.425509
C	0.388707	-0.032623	3.072586
C	-0.169717	1.298543	2.774596
C	-1.342749	1.264157	1.866802
C	-1.841860	0.080008	1.455230
N	-1.290426	-1.118543	1.823002
C	-0.181031	-1.164852	2.607241
C	-1.949084	-2.338617	1.396872
C	-1.986498	2.549743	1.508622
H	1.256242	-0.114389	3.712805
H	0.601531	1.989666	2.408238
H	-0.538885	1.752745	3.719925
H	-2.728750	0.006832	0.841021
H	0.181615	-2.150036	2.860214
H	-1.343501	-3.192998	1.685486
H	-2.073534	-2.325975	0.313428
H	-5.914010	-2.062474	2.823267

Table S24. Cartesian coordinates (Å) of FL4-Product.

Atom	X	Y	Z
C	-3.499642	0.055619	-0.353244

C	-4.846452	0.263492	-0.510513
C	-5.704179	-0.837335	-0.440411
C	-5.174397	-2.106897	-0.223302
C	-3.804571	-2.314761	-0.082362
C	-2.964921	-1.222968	-0.153306
H	-5.256400	1.248845	-0.691527
C	-7.161647	-0.569598	-0.648170
H	-5.821356	-2.978038	-0.196733
H	-3.420733	-3.316046	0.070525
C	-2.385598	1.042024	-0.364798
C	-1.149192	0.236071	-0.217009
C	-1.499989	-1.110799	-0.071198
O	-2.474621	2.250932	-0.477855
C	0.165763	0.647564	-0.206691
C	1.152797	-0.317733	-0.039275
C	0.809669	-1.653646	0.119604
C	-0.520774	-2.066735	0.105219
H	0.413932	1.694764	-0.329115
H	2.196242	-0.028652	-0.030008
H	1.593121	-2.389681	0.255216
H	-0.767487	-3.114303	0.229189
H	-2.638428	2.945814	1.079575
O	-2.606455	1.688714	2.408750
O	-2.690384	2.948115	2.071766
O	-8.027227	-1.515992	-0.234274
O	-7.567531	0.434205	-1.158796
H	-7.568153	-2.204371	0.257025

Table S25. Cartesian coordinates (Å) of FL5-A.

Atom	X	Y	Z
C	-3.462959	0.110798	-0.097087
C	-4.812026	0.359320	-0.135292

C	-5.687815	-0.724117	-0.237907
C	-5.177203	-2.018627	-0.309764
C	-3.808238	-2.265244	-0.282205
C	-2.950339	-1.188931	-0.175760
H	-5.207221	1.366324	-0.095017
C	-7.148977	-0.405264	-0.306026
H	-5.841850	-2.868474	-0.427771
H	-3.437397	-3.280389	-0.355287
C	-2.325031	1.077355	0.008183
C	-1.101020	0.221754	-0.030373
C	-1.481373	-1.119884	-0.139586
O	-2.385241	2.275567	0.103966
C	0.221166	0.595799	0.016664
C	1.189190	-0.407142	-0.053576
C	0.813491	-1.743803	-0.162781
C	-0.523070	-2.114390	-0.204947
H	0.499092	1.638208	0.098852
C	2.639873	-0.098772	-0.021589
H	1.598936	-2.487285	-0.216036
H	-0.795064	-3.159160	-0.291875
O	2.879034	1.218915	0.098243
O	3.517484	-0.919141	-0.092774
H	3.839746	1.325555	0.106523
O	-8.009820	-1.403983	-0.026500
O	-7.560142	0.681423	-0.592696
H	-7.538763	-2.180528	0.291322

Table S26. Cartesian coordinates (Å) of FL5-B.

Atom	X	Y	Z
C	-3.462959	0.110798	-0.097087
C	-4.812026	0.359320	-0.135292
C	-5.687815	-0.724117	-0.237907

C	-5.177203	-2.018627	-0.309764
C	-3.808238	-2.265244	-0.282205
C	-2.950339	-1.188931	-0.175760
H	-5.207221	1.366324	-0.095017
C	-7.148977	-0.405264	-0.306026
H	-5.841850	-2.868474	-0.427771
H	-3.437397	-3.280389	-0.355287
C	-2.325031	1.077355	0.008183
C	-1.101020	0.221754	-0.030373
C	-1.481373	-1.119884	-0.139586
O	-2.385241	2.275567	0.103966
C	0.221166	0.595799	0.016664
C	1.189190	-0.407142	-0.053576
C	0.813491	-1.743803	-0.162781
C	-0.523070	-2.114390	-0.204947
H	0.499092	1.638208	0.098852
C	2.639873	-0.098772	-0.021589
H	1.598936	-2.487285	-0.216036
H	-0.795064	-3.159160	-0.291875
O	2.879034	1.218915	0.098243
O	3.517484	-0.919141	-0.092774
H	3.839746	1.325555	0.106523
O	-8.009820	-1.403983	-0.026500
O	-7.560142	0.681423	-0.592696
H	-7.538763	-2.180528	0.291322

Table S27. Cartesian coordinates (Å) of FL5-C.

Atom	X	Y	Z
C	-3.436607	0.128306	-0.121745
C	-4.794363	0.367142	-0.144401
C	-5.691812	-0.696568	-0.217424
C	-5.181136	-2.020312	-0.283177

C	-3.826937	-2.271971	-0.268901
C	-2.929357	-1.206322	-0.184915
H	-5.179073	1.378502	-0.098093
C	-7.128615	-0.373339	-0.219305
H	-5.843723	-2.876989	-0.376813
H	-3.468388	-3.294472	-0.328177
C	-2.319784	1.078623	-0.040246
C	-1.122758	0.225991	-0.062951
C	-1.504109	-1.146316	-0.150688
O	-2.371899	2.310480	0.031438
C	0.207832	0.585144	-0.014117
C	1.187736	-0.406125	-0.053240
C	0.810001	-1.768275	-0.142920
C	-0.513639	-2.134213	-0.190077
H	0.480292	1.630855	0.052979
C	2.607441	-0.085981	-0.007052
H	1.597316	-2.510670	-0.172794
H	-0.781023	-3.183692	-0.257901
O	2.861474	1.249367	0.085381
O	3.527376	-0.879407	-0.044434
H	3.823956	1.310845	0.102145
O	-7.991944	-1.427330	-0.120772
O	-7.593706	0.736506	-0.294968
H	-7.480087	-2.233896	-0.007932

Table S28. Cartesian coordinates (Å) of FL5-TS_{CD}.

Atom	X	Y	Z
C	-0.054457	0.044352	6.331659
C	-1.198030	-0.450324	5.718817
C	0.772967	-0.833638	7.018009
H	0.183065	1.099353	6.280773
C	-2.201156	0.226363	4.928151

C	-1.512835	-1.836828	5.799896
C	0.454634	-2.202627	7.104024
C	2.003245	-0.376558	7.686875
C	-3.129373	-0.801705	4.513873
O	-2.231198	1.453293	4.583477
C	-2.719909	-2.057446	5.047603
C	-0.681630	-2.702325	6.501879
H	1.125066	-2.846407	7.658020
O	2.228594	0.948629	7.533125
O	2.760989	-1.078105	8.311579
C	-4.208895	-0.727356	3.649192
C	-3.448345	-3.206021	4.757619
H	-0.916473	-3.758020	6.579087
H	3.042285	1.131282	8.020818
C	-4.900351	-1.887705	3.330580
H	-4.512060	0.215856	3.211180
C	-4.536632	-3.121645	3.909836
H	-3.163407	-4.164500	5.177245
C	-5.992018	-1.785649	2.348591
H	-5.108947	-4.006457	3.667734
O	-6.709931	-2.924572	2.237929
O	-6.241477	-0.811567	1.677271
H	-7.386596	-2.746236	1.571804
C	0.426881	0.418954	2.797999
C	-0.475365	1.542276	2.592666
C	-1.597145	1.268797	1.689052
C	-1.889839	-0.015194	1.372509
N	-1.106198	-1.059569	1.777293
C	0.065493	-0.830569	2.442006
C	-1.578011	-2.417318	1.581001
C	-2.482128	2.386911	1.277234
H	1.361422	0.561748	3.323157
H	0.004797	2.512204	2.452776

H	-1.082425	1.665791	3.626098
H	-2.771591	-0.285424	0.807057
H	0.657812	-1.705318	2.668666
H	-0.727705	-3.095753	1.559373
H	-2.115730	-2.482655	0.636659
H	-2.246242	-2.695474	2.399055
H	-3.317247	2.042879	0.667972
H	-1.921129	3.140120	0.717720
H	-2.880349	2.872679	2.172691

Table S29. Cartesian coordinates (Å) of FL5-D.

Atom	X	Y	Z
C	-3.433380	0.106727	-0.107189
C	-4.796546	0.356766	-0.131467
C	-5.681945	-0.709092	-0.211609
C	-5.189124	-2.019853	-0.274775
C	-3.824513	-2.281125	-0.256692
C	-2.937445	-1.225986	-0.172904
H	-5.217891	1.354800	-0.093759
C	-7.133554	-0.349259	-0.239494
H	-5.858785	-2.869070	-0.363070
H	-3.469839	-3.303329	-0.313294
C	-2.313142	0.982365	-0.031289
C	-1.121524	0.209105	-0.053499
C	-1.487467	-1.160430	-0.141850
O	-2.310875	2.312792	0.048335
C	0.211778	0.593453	-0.010296
C	1.181630	-0.396995	-0.057965
C	0.824264	-1.748683	-0.146004
C	-0.505598	-2.134749	-0.187072
H	0.489375	1.636328	0.055273
C	2.623366	-0.063407	-0.020812

H	1.619567	-2.481594	-0.180855
H	-0.762470	-3.184977	-0.254901
O	2.842835	1.263928	0.067443
O	3.520272	-0.865554	-0.065465
H	3.801929	1.379532	0.080698
O	-8.024157	-1.354288	-0.143677
O	-7.520390	0.781520	-0.341654
H	-7.574244	-2.194338	-0.012833
H	-3.213338	2.648372	0.047042

Table S30. Cartesian coordinates (Å) of FL5-E.

Atom	X	Y	Z
C	-3.471973	0.085607	-0.133402
C	-4.818703	0.333956	-0.182767
C	-5.696359	-0.747161	-0.273081
C	-5.188966	-2.044289	-0.325184
C	-3.822557	-2.289392	-0.283971
C	-2.959778	-1.212572	-0.184318
H	-5.228889	1.335692	-0.155824
C	-7.154660	-0.413501	-0.336002
H	-5.852131	-2.896449	-0.433133
H	-3.450091	-3.304850	-0.339098
C	-2.334870	1.077034	-0.020031
C	-1.119500	0.200340	-0.061527
C	-1.495296	-1.141233	-0.140843
O	-2.318910	2.121746	-0.883180
C	0.196894	0.586171	-0.022213
C	1.171558	-0.410296	-0.067150
C	0.806140	-1.751842	-0.150003
C	-0.526241	-2.130298	-0.185756
H	0.473766	1.630048	0.035316
C	2.617466	-0.082935	-0.030377

H	1.596473	-2.490773	-0.186670
H	-0.793108	-3.177549	-0.253461
O	2.838270	1.240167	0.076843
O	3.507231	-0.890911	-0.087144
H	3.797283	1.359864	0.091075
O	-8.026858	-1.412128	-0.100894
O	-7.554286	0.689136	-0.577653
H	-7.564802	-2.209799	0.174815
H	-2.819571	2.833412	-0.438552
O	-2.412028	1.633629	1.401849
O	-2.969237	2.797380	1.414558

Table S31. Cartesian coordinates (Å) of FL5-TS_{EA}.

Atom	X	Y	Z
C	-3.471973	0.085607	-0.133402
C	-4.818703	0.333956	-0.182767
C	-5.696359	-0.747161	-0.273081
C	-5.188966	-2.044289	-0.325184
C	-3.822557	-2.289392	-0.283971
C	-2.959778	-1.212572	-0.184318
H	-5.228889	1.335692	-0.155824
C	-7.154660	-0.413501	-0.336002
H	-5.852131	-2.896449	-0.433133
H	-3.450091	-3.304850	-0.339098
C	-2.334870	1.077034	-0.020031
C	-1.119500	0.200340	-0.061527
C	-1.495296	-1.141233	-0.140843
O	-2.318910	2.121746	-0.883180
C	0.196894	0.586171	-0.022213
C	1.171558	-0.410296	-0.067150
C	0.806140	-1.751842	-0.150003
C	-0.526241	-2.130298	-0.185756

H	0.473766	1.630048	0.035316
C	2.617466	-0.082935	-0.030377
H	1.596473	-2.490773	-0.186670
H	-0.793108	-3.177549	-0.253461
O	2.838270	1.240167	0.076843
O	3.507231	-0.890911	-0.087144
H	3.797283	1.359864	0.091075
O	-8.026858	-1.412128	-0.100894
O	-7.554286	0.689136	-0.577653
H	-7.564802	-2.209799	0.174815
H	-2.819571	2.833412	-0.438552
O	-2.412028	1.633629	1.401849
O	-2.969237	2.797380	1.414558

Table S32. Cartesian coordinates (Å) of FL5-Complex.

Atom	X	Y	Z
C	-0.177898	0.221980	6.306277
C	-1.254202	-0.350230	5.644401
C	0.730505	-0.601545	6.956258
H	-0.052294	1.297743	6.318639
C	-2.313027	0.277600	4.861047
C	-1.434237	-1.763940	5.649535
C	0.554406	-2.003365	6.955329
C	1.893031	-0.059357	7.674382
C	-3.155439	-0.828877	4.422813
O	-2.423126	1.483093	4.552391
C	-2.618515	-2.061134	4.901823
C	-0.517772	-2.579665	6.314123
H	1.282716	-2.606052	7.481900
O	1.975690	1.290692	7.608235
O	2.716930	-0.713197	8.268184
C	-4.294297	-0.819238	3.637542

C	-3.271999	-3.259767	4.614162
H	-0.645132	-3.656478	6.332322
H	2.757438	1.526964	8.123997
C	-4.923560	-2.020320	3.336228
H	-4.705759	0.109465	3.259814
C	-4.415603	-3.240965	3.845269
H	-2.891500	-4.202405	4.992074
C	-6.114481	-1.976691	2.476945
H	-4.935717	-4.161372	3.618490
O	-6.716897	-3.181748	2.350908
O	-6.539322	-0.996064	1.911097
H	-7.478382	-3.034398	1.774996
C	0.375974	-0.046691	3.006917
C	-0.183511	1.286442	2.719306
C	-1.385243	1.256953	1.849778
C	-1.884065	0.071762	1.426417
N	-1.309547	-1.122282	1.753600
C	-0.193866	-1.173676	2.536096
C	-1.953663	-2.352533	1.329624
C	-2.050854	2.539364	1.524593
H	1.248320	-0.130792	3.640595
H	0.581342	1.965848	2.317119
H	-0.507663	1.755361	3.671616
H	-2.785095	0.003772	0.831995
H	0.173240	-2.161859	2.770999
H	-1.226014	-3.160242	1.340303
H	-2.342842	-2.226173	0.320760
H	-2.773516	-2.589853	2.011522
H	-2.905016	2.400573	0.862986
H	-1.348199	3.235078	1.057144
H	-2.398829	2.991898	2.457468

Table S33. Cartesian coordinates (Å) of FL5-Product.

Atom	X	Y	Z
C	-3.486171	0.041061	-0.429303
C	-4.828752	0.237257	-0.631261
C	-5.689258	-0.855120	-0.499745
C	-5.167980	-2.105130	-0.173986
C	-3.802521	-2.302046	0.014340
C	-2.959116	-1.219114	-0.122484
H	-5.232919	1.205341	-0.898196
C	-7.140587	-0.601712	-0.768694
H	-5.816431	-2.972076	-0.098269
H	-3.423621	-3.289243	0.248819
C	-2.369821	1.021200	-0.506221
C	-1.137162	0.222607	-0.287252
C	-1.495884	-1.106271	-0.033300
O	-2.450791	2.215691	-0.727796
C	0.176695	0.625511	-0.320031
C	1.160936	-0.333328	-0.076946
C	0.807210	-1.650846	0.201417
C	-0.521880	-2.051673	0.224180
H	0.438676	1.653161	-0.534038
C	2.606001	0.000879	-0.112204
H	1.604505	-2.358766	0.390812
H	-0.774495	-3.083721	0.433640
O	2.824853	1.284464	-0.447526
O	3.494904	-0.775668	0.120688
H	3.783425	1.409734	-0.451357
O	-8.019899	-1.521130	-0.327167
O	-7.526505	0.368492	-1.353817
H	-7.579006	-2.182309	0.215363
H	-2.679967	2.942458	0.797288
O	-2.636214	1.645744	2.085384
O	-2.763411	2.908808	1.789863

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