Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Mechanistic insights on two-photon driven photocatalysis in organic synthesis

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SUPPORTING INFORMATION

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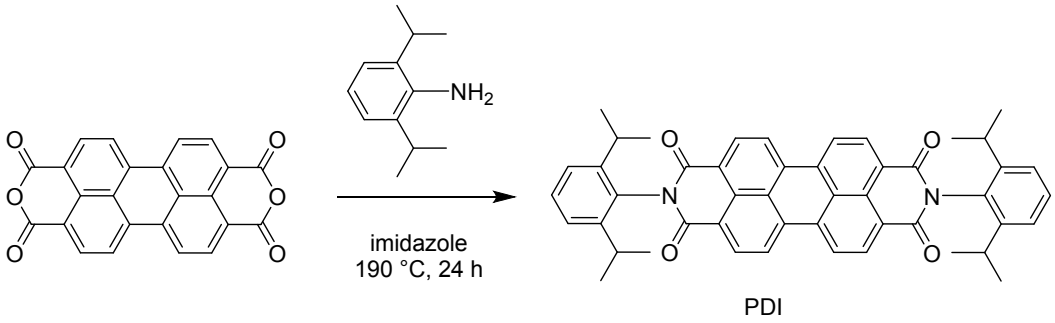
1. Synthetic procedures.

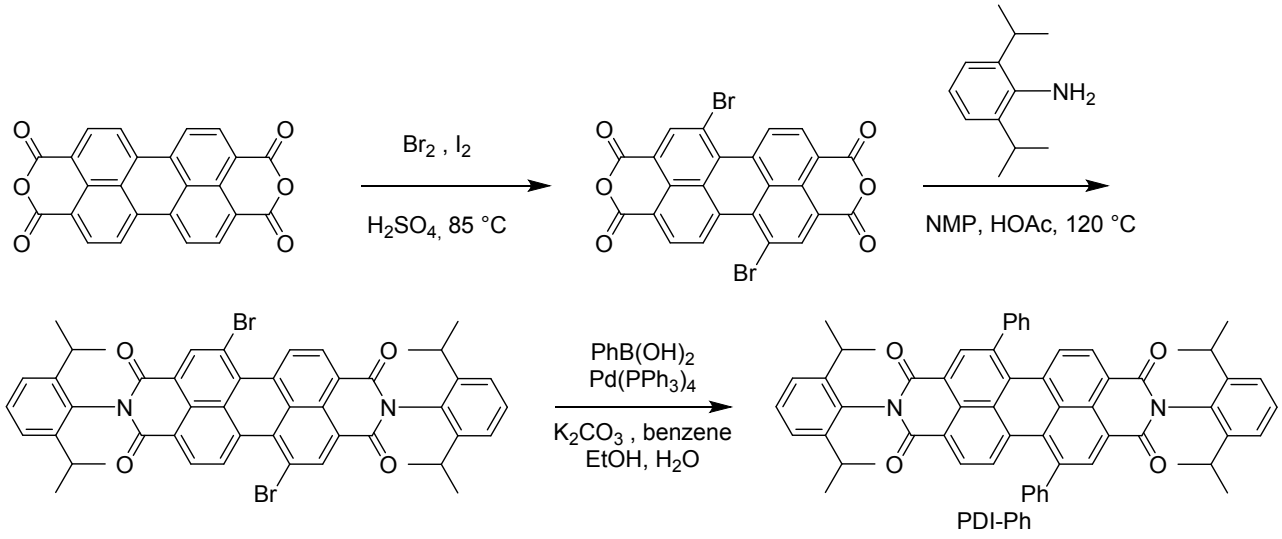
General methods: ^{1}H NMR spectra were recorded on Varian Mercury 400 spectrometer. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (deuterochloroform: δ = 7.27 ppm). Chromatographic purification was performed with 240-400 mesh silica gel. Thin layer chromatography was performed on Merck TLC silica gel 60 F_{254}.

Materials: If not otherwise stated, all reactions were carried out in flame dried glassware under nitrogen atmosphere. Anhydrous solvents were supplied by Aldrich in Sureseal® bottles and were used as received avoiding further purification.

Synthesis of PDI dyes: PDI[S1] and PDI-Ph[S2] were synthetized following reported procedures.



Scheme S1. Synthesis of PDI.



Scheme S2. Synthesis of PDI-Ph.

2. HPLC analysis.

HPLC analysis were performed on Agilent Technologies 1100 liquid chromatography system equipped with DAD detector. HPLC analysis conditions: column Agilent ZORBAX StableBond-C18, 3.5 μm, 2.1 x 30 mm cartridge (RR), 50:50 $CH_3CN:H_2O$, 0.7 mL/min flow rate, 30 °C, injection volume 5 μL. 4'-bromoacetophenone was eluted at 4.1 min and acetophenone at 6.1 min.

Calibration curves were obtained by injection of solutions with different and known ratios of 4'-bromoacetophenone and acetophenone and calculation of the ratios of the corresponding areas from HPLC chromatograms at 3 different wavelengths (245, 250 and 255 nm). Plotting the area ratios versus the corresponding components ratio, two different calibration curves were prepared, one for high level of conversion (Table S1 and Figure S1a) and one for low level of conversion (Table S2 and Figure S1b).

Solutions were prepared considering the concentration of the two components presents in the samples collected during the reaction. Stock solutions were prepared, starting from commercially available 4'-bromoacetophenone and acetophenone, and diluted to the desired concentration (Table S1 and S2).

[BrAcet]	**[Acet]**	**$mmol_{BrAcet}/mmol_{Acet}$**	**Conversion (%)**	**$AREA_{BrAcet}/AREA_{Acet}$**		
				245 nm	**250 nm**	**255 nm**
2.8×10^{-3}	4.0×10^{-4}	7.0	12.5	4.66	7.18	12.32
1.5×10^{-3}	3.0×10^{-4}	5.0	16.7	3.41	5.24	9.12
1.5×10^{-3}	5.0×10^{-4}	3.0	25.0	2.15	3.31	5.75
8.0×10^{-4}	8.0×10^{-4}	1.0	50.0	0.70	1.07	1.87
8.0×10^{-4}	8.0×10^{-4}	1.0	50.0	0.79	1.21	2.11
4.0×10^{-4}	1.2×10^{-3}	0.3	75.0	0.31	0.48	0.83
2.0×10^{-4}	1.4×10^{-3}	0.1	87.5	0.17	0.26	0.45

Table S1. Calibration curve data for high conversions; BrAcet = 4'-bromoacetophenone; Acet = acetophenone.

[BrAcet]	**[Acet]**	**$mmol_{BrAcet}/mmol_{Acet}$**	**Conversion (%)**	**$AREA_{BrAcet}/AREA_{Acet}$**		
				245 nm	**250 nm**	**255 nm**

4.0×10^{-3}	2.0×10^{-5}	200.0	0.5	82.15	108.44	172.33
4.5×10^{-3}	5.0×10^{-5}	90.0	1.1	36.54	47.19	74.63
3.5×10^{-3}	5.0×10^{-5}	70.0	1.4	30.76	40.32	63.46
2.5×10^{-3}	5.0×10^{-5}	50.0	2.0	24.93	33.44	52.92
1.6×10^{-3}	4.0×10^{-5}	40.0	2.4	24.77	35.26	58.25
1.2×10^{-3}	4.0×10^{-5}	30.0	3.2	17.80	26.40	44.12
1.2×10^{-3}	4.0×10^{-5}	30.0	3.2	17.77	26.30	43.97

Table S2. Calibration curve data for low conversions; BrAcet = 4'-bromoacetophenone; Acet = acetophenone.

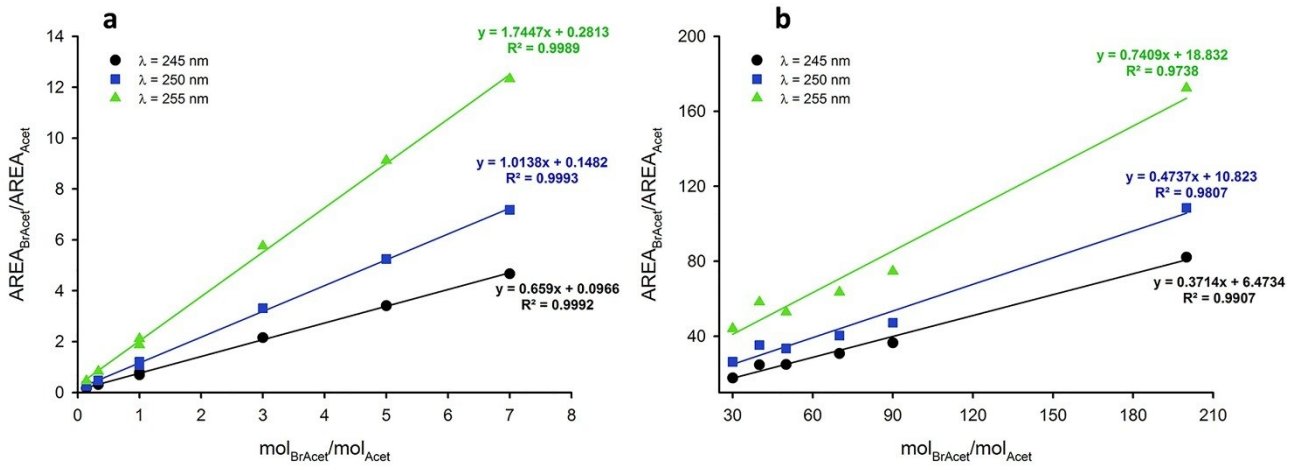


Figure S1. Calibration curve for high (a) and low (b) conversions at three different wavelengths (245 nm black circle, 250 nm blue square and 255 nm green triangle). BrAcet = 4'-bromoacetophenone; Acet = acetophenone

3. Photochemical setup.

Photochemical experiments were carried out at room temperature in deaerated solutions with Uvasol® DMF solvent. Absorption spectra were recorded in a quartz cuvette (optical path length 0.1 cm) with a UV/VIS spectrophotometer Varian Carey 50 Bio.

The irradiation was performed with either a blue-LEDs strip, wrapped around a crystallizer covered by aluminum foil to avoid loss of irradiation light or a halogen lamp with a cut-off filter at 610 nm.

Figure S2. Experimental setup for reaction mixture irradiation with blue light.

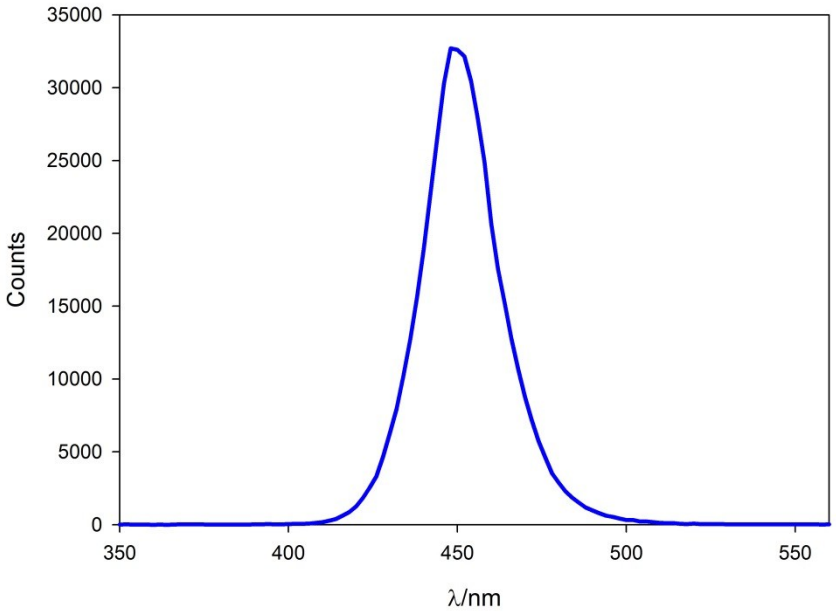


Figure S3. Emission profile of the blue-LEDs used to irradiate the reaction mixture.

4. Photocatalytic reduction of 4'-bromoacetophenone with triethylamine.

A stock solution of PDI (1.1 mg, 0.0015 mmol, 5 x 10^{-4} M) and triethylamine (0.4 mmol, 56 µL, 0.13 M) was prepared in 3 mL DMF and kept in the dark.

250 µL of the stock solution was transferred *via* a gas tight syringe into a quartz cuvette (0.1 cm pathlength) fitted with a Rotaflo Stopcock and purged with argon. The absorption spectra were recorded after irradiation with blue-LEDs (450 nm) and gently stirred (see Figure S4). After 390 min, the solution was aerated, and the absorption spectra were recorded.

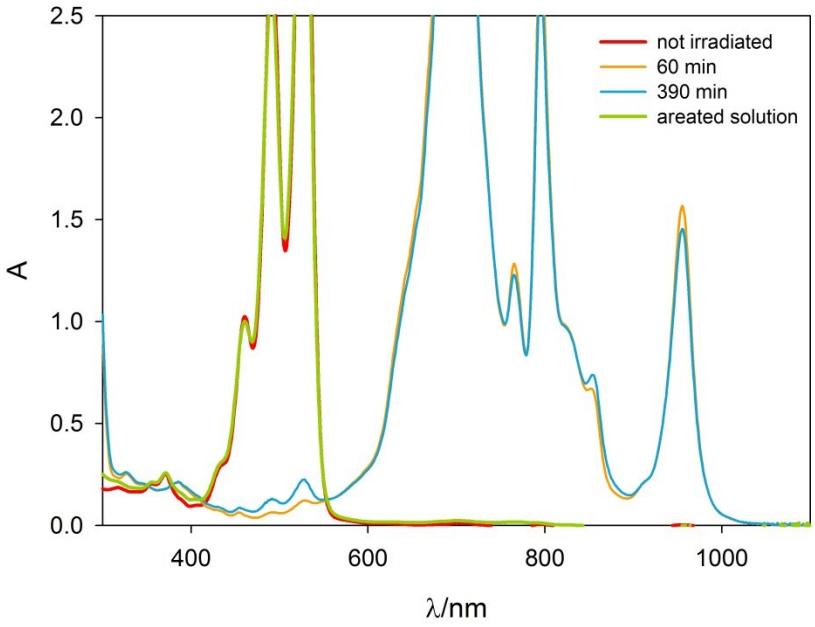


Figure S4. Absorption spectrum of PDI 5 x 10^{-4} M in the presence of Et_3N (0.13 M) in deaerated DMF before (red line) and after 60 min (orange line) and 390 min (blue line) of irradiation at 450 nm. After irradiation, the solution was aerated (light green line).

For the experiment reported in Figure 4 in the text, a stock solution of PDI (1.1 mg, 0.0015 mmol, 5 x 10^{-4} M), 4'-bromoacetophenone (10 mg, 0.05 mmol, 0.017 M) and triethylamine (0.4 mmol, 56 µL, 0.13 M) was prepared in 3 mL DMF and kept in the dark.

250 µL of the stock solution was transferred *via* a gas tight syringe into a quartz cuvette (0.1 cm pathlength) fitted with a Rotaflo Stopcock and purged with argon. The absorption spectra were recorded after irradiation of the cuvette with blue-LEDs (450 nm) at different time up to 360 min (see Figure 4 in the text).

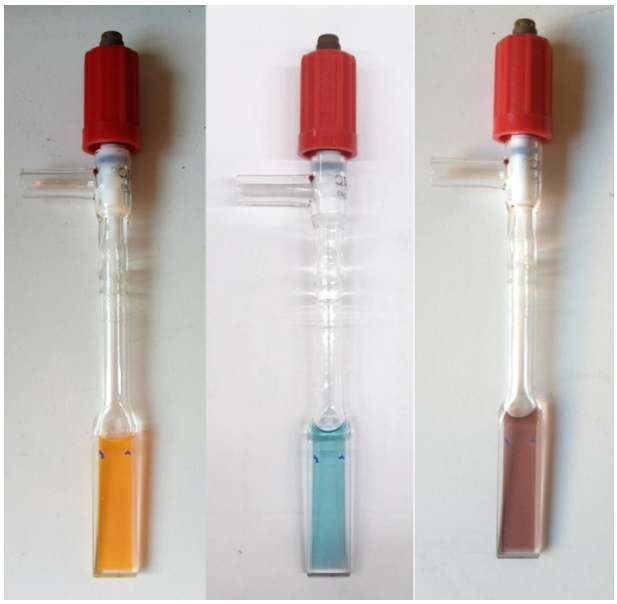


Figure S5. PDI 5 x 10^{-4} M in degassed DMF solution in the presence of Et_3N 0.13 M and 4'-bromoacetophenone 0.017 M before irradiation (left) and after 30 (centre) and 390 min (right) of irradiation at 450 nm.

The same experiment was repeated with the same reaction condition of the original paper.[S3] A solution of PDI (1.8 mg, 0.0025 mmol, 8 x 10^{-4} M), 4'-bromoacetophenone (10 mg, 0.05 mmol, 0.017 M) and triethylamine (0.4 mmol, 56 µL, 0.13 M) was prepared in 3 mL DMF. The solution was stirred and irradiated for 20 h with blue-LEDs (450 nm). 250 µL of the solution before and after the irradiation were transferred *via* a gas tight syringe into two quartz cuvettes (0.1 cm pathlength) fitted with a Rotaflo Stopcock and purged with argon. The recorded absorption spectra (Figure S6) showed similar shape to the one observed in the reaction performed in smaller scale (Figure 4). HPLC analysis of the final reaction mixture after (50 µL of the reaction sample was taken, diluted with 500 µL acetonitrile and injected) gave 59% of conversion.

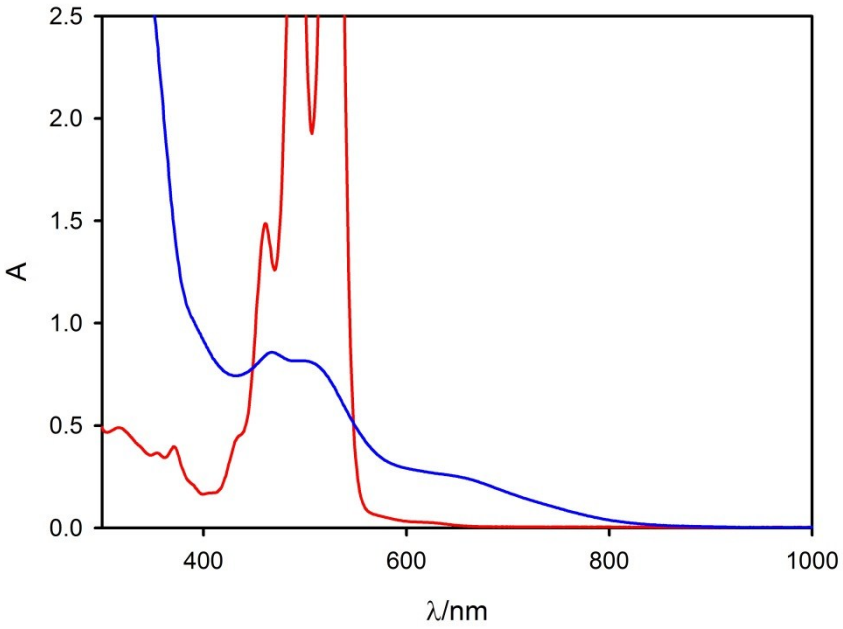


Figure S6. Absorption spectra of PDI 8 x 10^{-4} M in degassed DMF solution in the presence of Et_3N 0.13 M and 4'-bromoacetophenone 0.017 M before irradiation (red line) and after 20 hours irradiation at 450 nm (blue line). Optical path length 0.1 cm.

For the experiment reported in Figure 5 (see text), six identical solutions (250 µL of the above described stock solution) were transferred *via* a gas tight syringe into six quartz cuvettes (0.1 cm pathlength) fitted with a Rotaflo Stopcock, purged with argon, irradiated for different times (20, 50, 90, 210, 390 and 900 min) with blue-LEDs (450 nm) and gently stirred. After each irradiation, an absorption spectrum was recorded. 50 µL of the reaction sample was taken and diluted with acetonitrile (500 µL) and directly injected in HPLC to determine the reaction conversion.

The reaction mixture irradiated for 15 h was diluted with ethyl acetate (10 mL) and water (10 mL). The organic phase was separated and the aqueous phase was extracted with ethyl acetate (2 x 10 mL). The organic phases were dried upon Na_2SO_4, filtered and concentrated under reduced pressure. ^{1}HNMR of the crude reaction mixture confirmed the presence of the desired acetophenone product. Spectroscopic data were in accordance with the reported spectra of the commercially available compound.

5. **Photocatalytic reduction of 4'-bromoacetophenone with sodium ascorbate as chemical reductant.**

A stock solution of PDI (1.8 mg, 0.0025 mmol, 8 x 10^{-4} M, the same concentration as that reported in ref. S3), 4'-bromoacetophenone (10 mg, 0.05 mmol, 0.017 M) was prepared in 3 mL DMF and purged with argon. A 1.3 M sodium ascorbate solution in 0.5 mL DMF/H_2O 1:1 (v/v) was prepared dissolving 130 mg of sodium ascorbate. 300 µL of the sodium ascorbate solution was transferred *via* a gas tight syringe into the stock solution and the formation of PDI radical anion was immediately observed by a color changing.

250 µL of the reaction mixture was transferred *via* a gas tight syringe into a quartz cuvette (0.1 cm pathlength) fitted with a Rotaflo Stopcock under argon atmosphere. The solution was irradiated with blue-LEDs (450 nm) at different time up to 360 min (Figure S7a) and absorption spectra were recorded. HPLC analysis of the final reaction mixture gave 81% of conversion.

250 µL of the reaction mixture was kept in the dark (Figure S7b) and no product was detected.

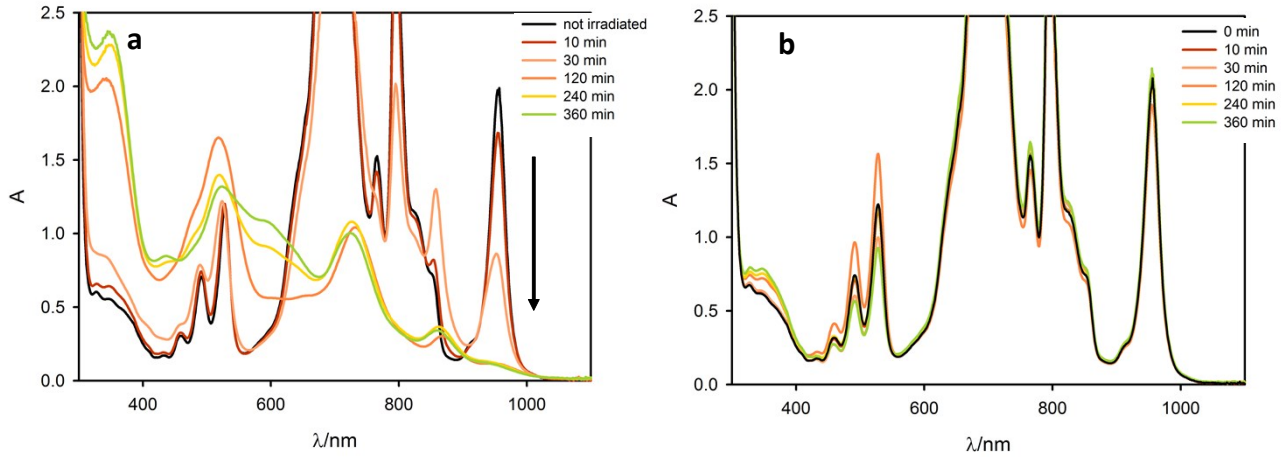


Figure S7. Absorption spectra of PDI 8.0 x 10^{-4} M in degassed DMF solution in the presence of sodium ascorbate 0.13 M and 4'-bromoacetophenone 0.017 M upon irradiation at 450 nm (a) and in the dark (b) in the time interval 0 - 360 min.

6. **Photocatalytic reduction of 4'-iodobenzaldehyde with triethylamine.**

The same procedure reported for the photocatalytic reduction of 4'-bromoacetophenone was

followed for the reduction of 4'-iodobenzaldehyde (0.05 mmol, 11.8 mg, 0.017 M), that was used as substrate, instead of 4'-bromoacetophenone. The absorption spectra (Figure S8) were recorded after irradiation of the cuvette with blue-LEDs (450 nm) at different time up to 300 min.

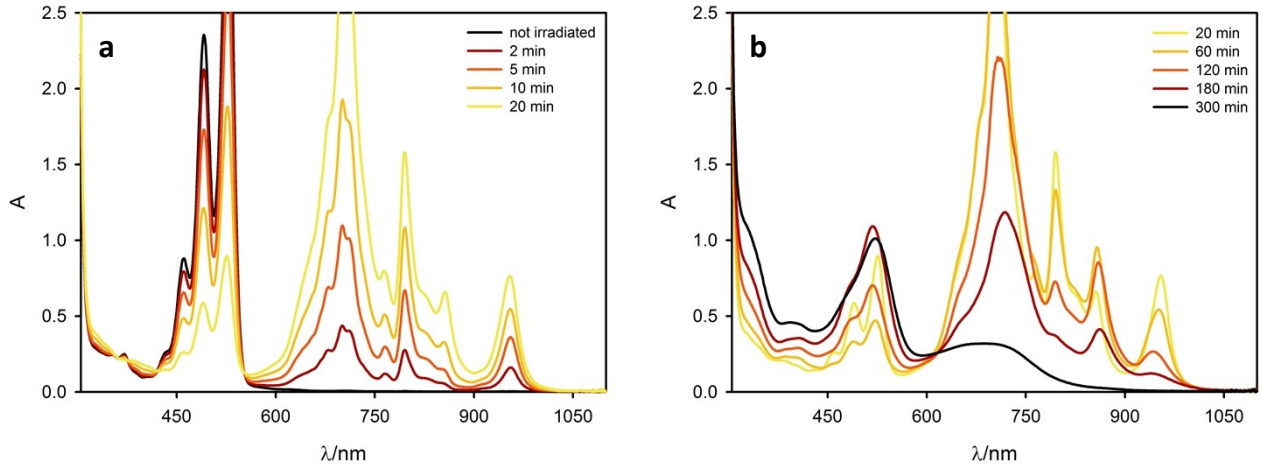


Figure S8. Absorption spectra of PDI 4.4 x 10^{-4} M in degassed DMF solution in the presence of Et_3N 0.13 M and 4'-iodobenzaldehyde 0.017 M upon irradiation at 450 nm in the time interval: (a) 0 - 20 minutes (black and yellow lines, respectively) and (b) 20 - 390 minutes (yellow and black lines, respectively).

7. Photocatalytic reduction of 4'-bromoacetophenone in the presence of PDI-Ph and triethylamine.

The reaction was performed following the procedure of the photocatalytic reduction of 4'-bromoacetophenone, except that PDI-Ph (2.0 mg, 0.0017 mmol, 8 x 10^{-4} M) was used instead of PDI. The absorption spectra were recorded (Figure S9), and conversion was measured (Figure S10) after irradiation of the cuvette with blue-LEDs (450 nm) at different time up to 180 min.

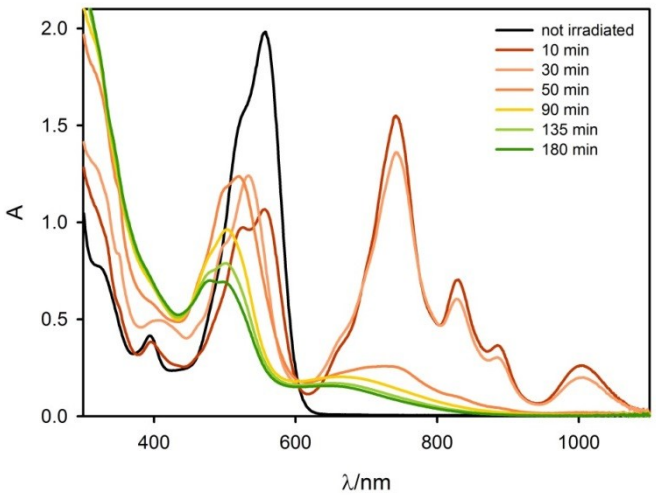


Figure S9. Absorption spectra of PDI-Ph 8 x 10^{-4} M, Et_3N 0.13 M and 4'-bromoacetophenone 0.17 M in deaerated DMF, irradiated at 450 nm in the time interval from 0 min (black thick line) to 180 min (green thick line).

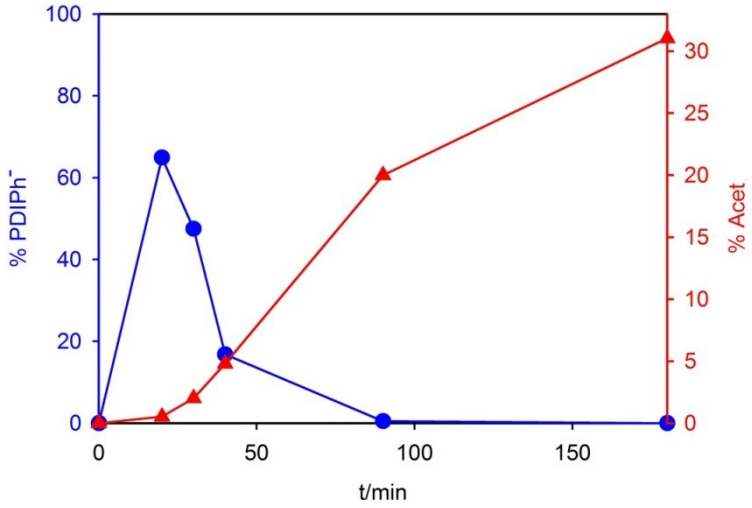


Figure S10. Irradiation at 450 nm of the reaction mixture: PDI-Ph 8 x 10^{-4} M, Et_3N 0.13 M and 4'-bromoacetophenone 0.017 M in degassed DMF solution. Percentage of PDI-$Ph^{\bullet -}$ (estimated from absorbance at 1000 nm during the irradiation of the reaction mixture, blue circles), compared to the initial concentration of PDI-Ph, and percentage of acetophenone formation (estimated with HPLC analysis, red triangles), compared to the initial 4'-bromoacetophenone concentration, as a function of irradiation time.

8. Attempts to isolate PDI degradation products.

A reaction was repeated in the reaction conditions of the original paper[S3] on 0.2 mmol scale of 4'-bromoacetophenone using 20 mol% of PDI. After 20 h of irradiation, the solvent was evaporated under reduced pressure. The crude was purified by column chromatography on SiO_2 using cyclohexane/dichloromethane/ethyl acetate as eluent. Residual 4'-bromoacetophenone and acetophenone were removed and fractions contain other products (visible by TLC analysis) were isolated.

^{1}H-NMR and ESI-MS analysis do not provide useful information for the identification and quantification of the degradation products.

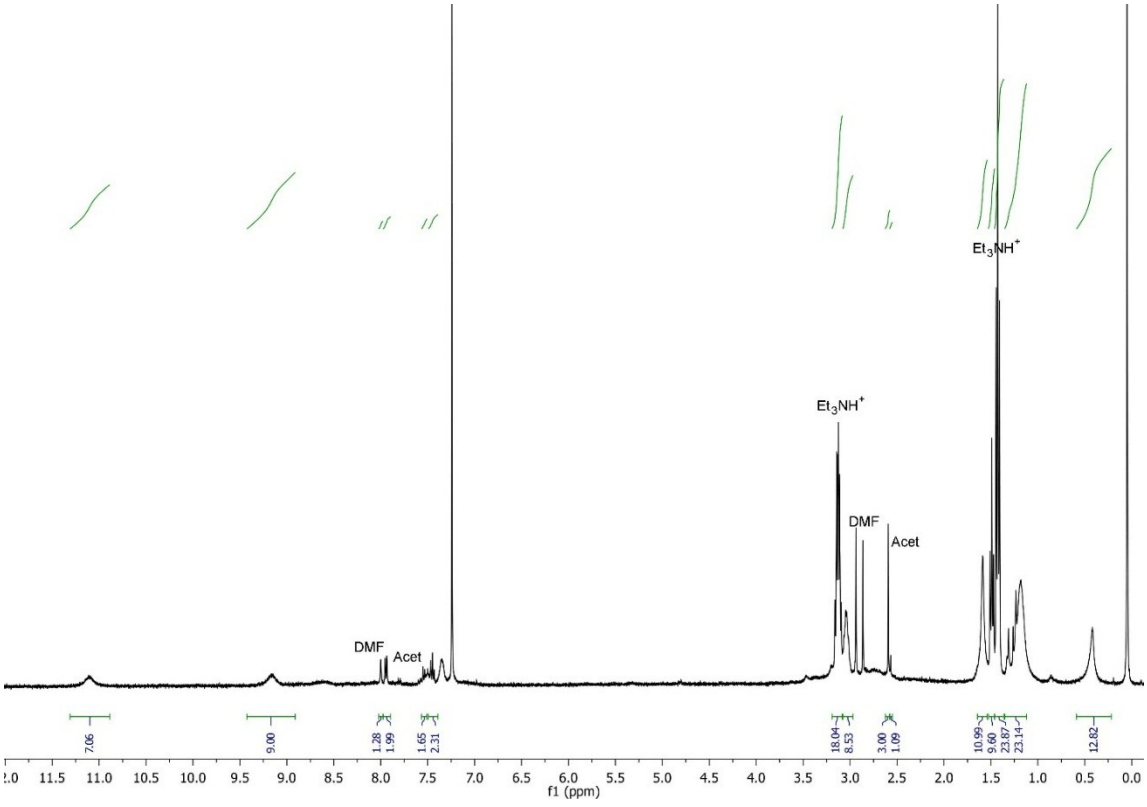


Figure S11. ^{1}H-NMR ($CDCl_3$, 400 MHz) spectrum relative to crude reaction mixture; Acet = Acetophenone.

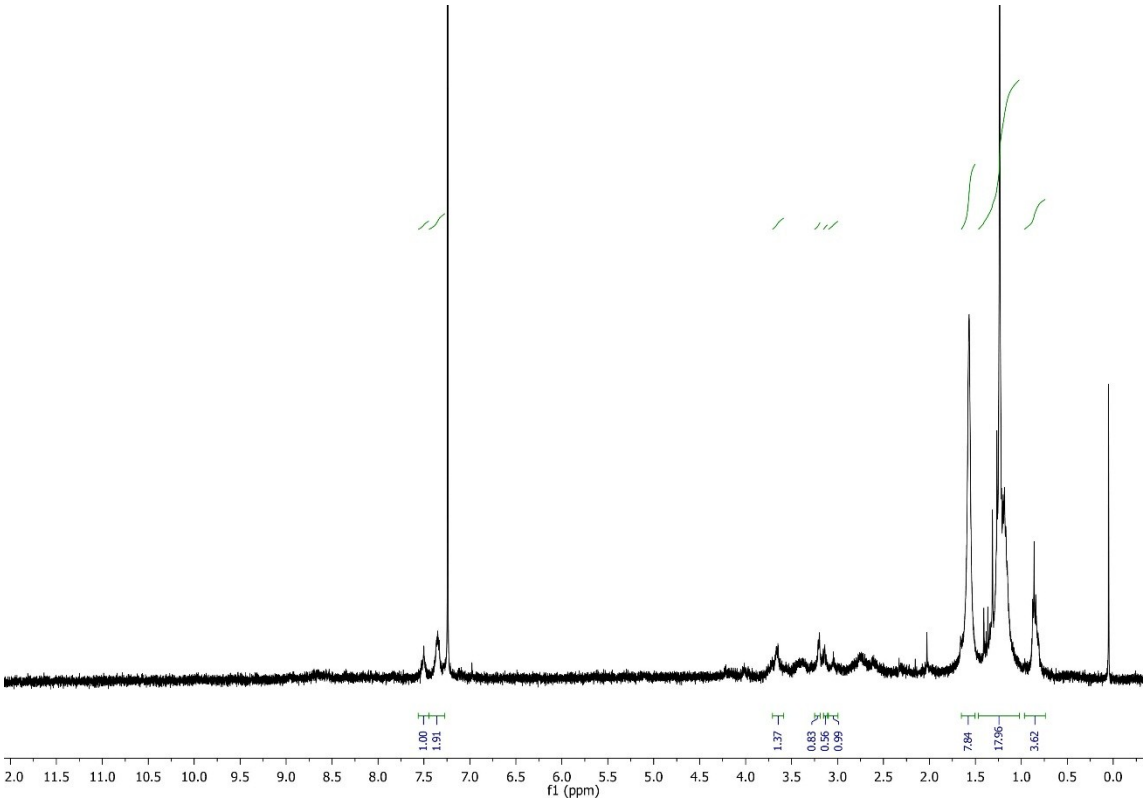


Figure S12. ^{1}H-NMR ($CDCl_3$, 400 MHz) spectrum relative to first eluted spot.

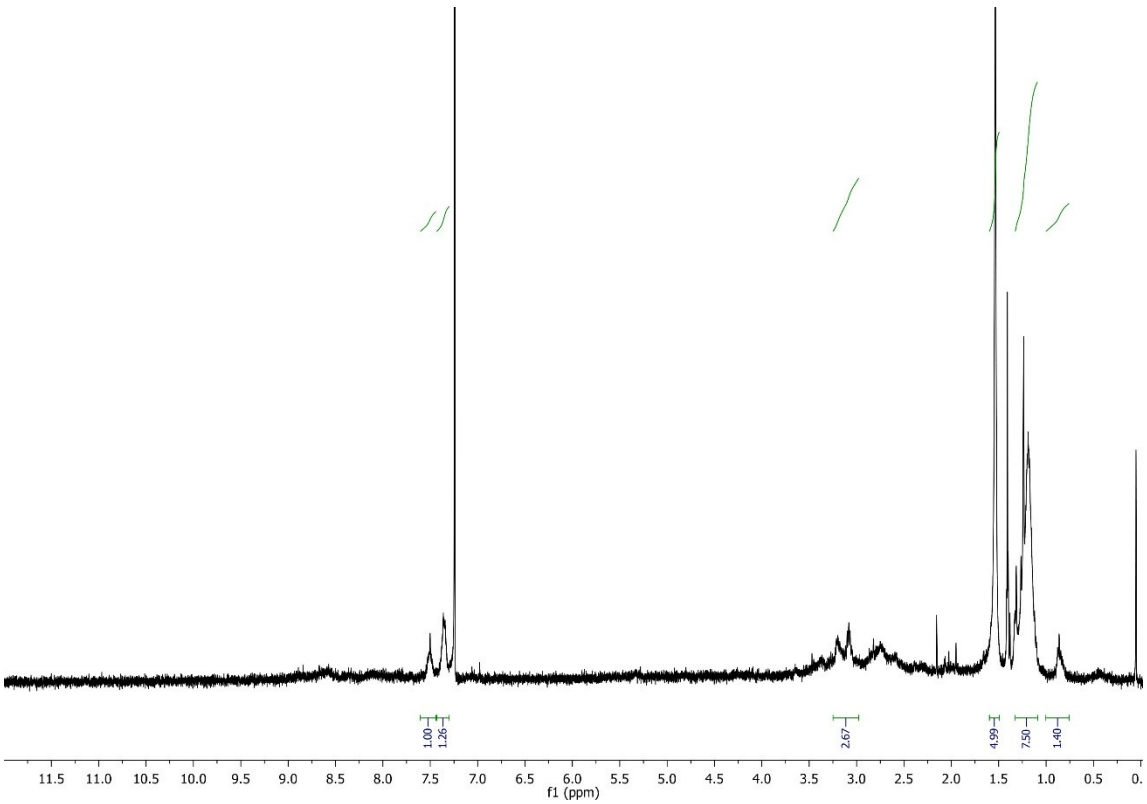


Figure S13. ^{1}H-NMR ($CDCl_3$, 400 MHz) spectrum relative to second eluted spot.

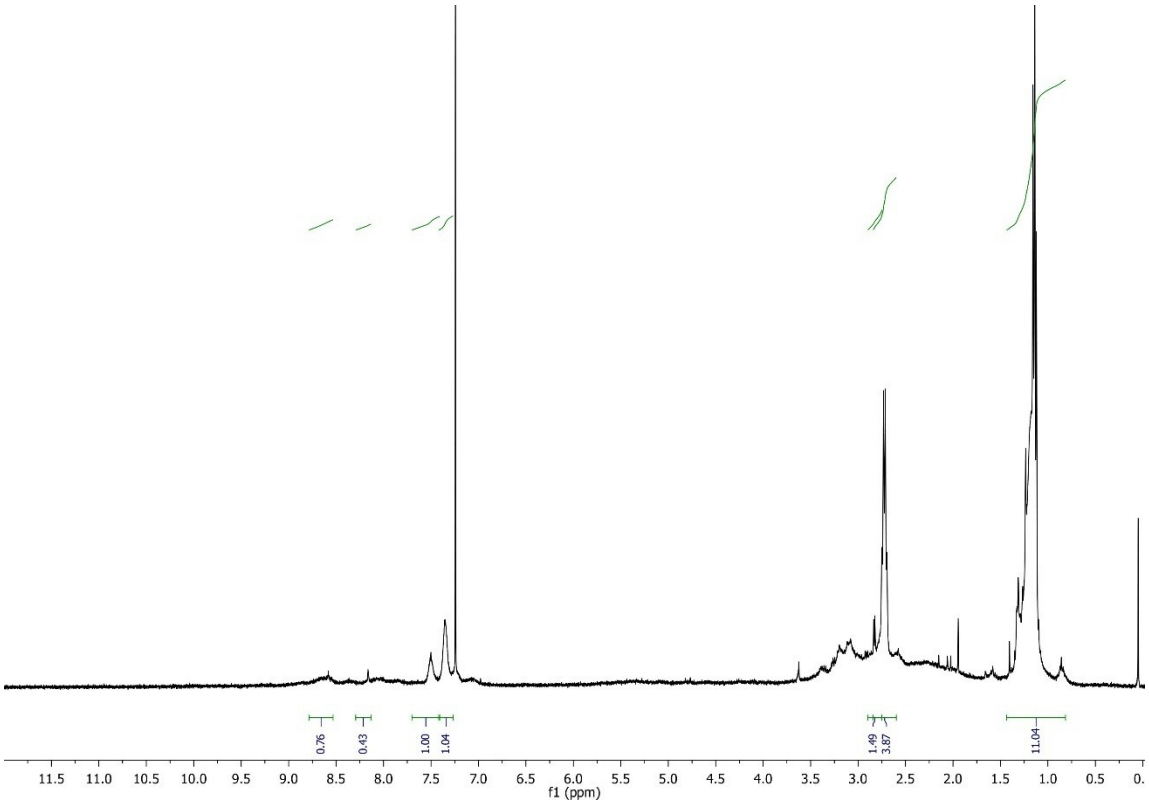


Figure S14. ^{1}H-NMR ($CDCl_3$, 400 MHz) spectrum relative to third eluted spot.

9. Photocatalytic reduction of 4'-bromoacetophenone with KO_2.

A stock solution of PDI (5.7 mg, 0.008 mmol, 1.6 x 10^{-3} M) was prepared in 5 mL DMF. The reaction vessel was sealed with a rubber septum and the solution was degassed *via* argon bubbling for 10 minutes. KO_2 (0.6 mg, 0.008 mmol) was added under argon. The reaction was vigorously stirred for 30 minutes: the solution slowly turns blue, due to the formation of the PDI radical anion. 4'-bromoacetophenone (1.6 mg, 0.008 mmol, 1.6 x 10^{-3} M) was then added under argon and the solution was irradiated for 20 hours with blue-LEDs (450 nm).

The absorption spectra reported in Figure S15 were recorded by transferring 100 µL of solution *via* a gas tight syringe into a quartz cuvette (0.1 cm pathlength), fitted with a Rotaflo Stopcock under argon atmosphere, and diluting with 500 µL of previously degassed DMF. The absorption spectrum of the mixture PDI/KO_2 in DMF clearly showed the presence of $PDI^{\bullet-}$ (Figure S15, green line), while the absorption spectrum of the final reaction mixture (Figure S15, blue line) shows the presence of PDI, as well as broad bands above 600 nm, similar to those reported in Figure 4b.

100 µL of the reaction mixture was diluted with acetonitrile (500 µL) and injected in HPLC: the reaction conversion was 59% after 20 hours of irradiation. The results obtained are similar to those using Et_3N as reducing agent.

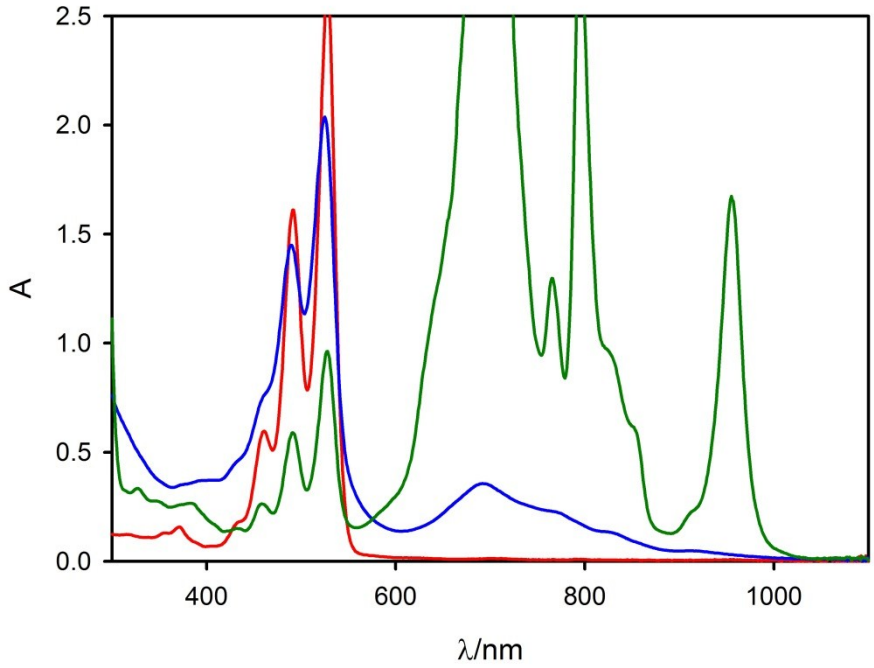


Figure S15. Absorption spectra of PDI 3.2 x 10^{-4} M (diluted 1:5 from the reaction mixture, red line), after the addition of stoichiometric amount of KO_2 (green line) and 4'-bromoacetophenone under 20 hours irradiation (blue line) in deaerated DMF. Optical path length 0.1 cm.

The reaction mixture was analysed by MALDI-TOF (Figure S16), performed on a Waters Micro MALDI MX operating in positive reflectron mode. The matrix, trans-2-[3-(4-tert-butyl-phenyl)-2-methyl-2- propenylidene]malonitrile (DCTB), was prepared as a 40 mg/mL solution in CH_2Cl_2. The matrix solution (1 µL) was applied to a stainless-steel target and air-dried.

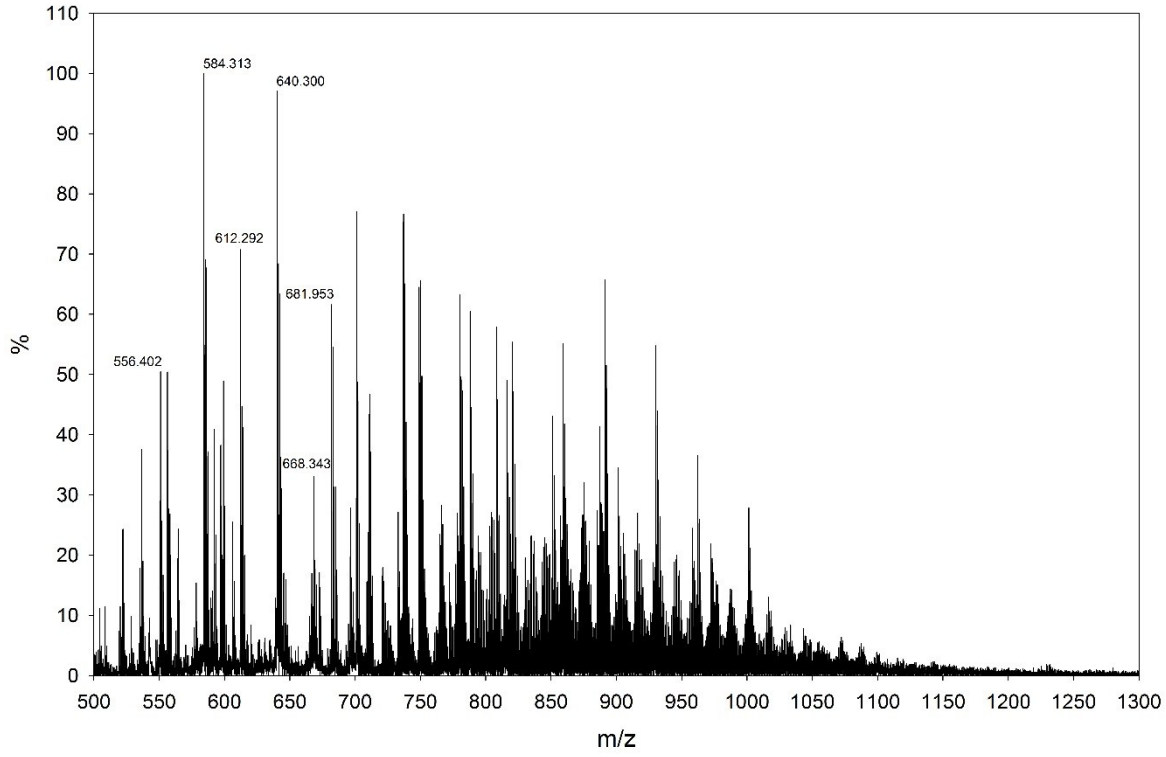


Figure S16. MALDI-TOF mass spectrum of the reaction mixture (PDI 1.6 x 10^{-3} M, KO_2 1.6 x 10^{-3} M and 4'-bromoacetophenone 1.6 x 10^{-3} M in deaerated DMF) irradiated 20 hours with blue-LED.

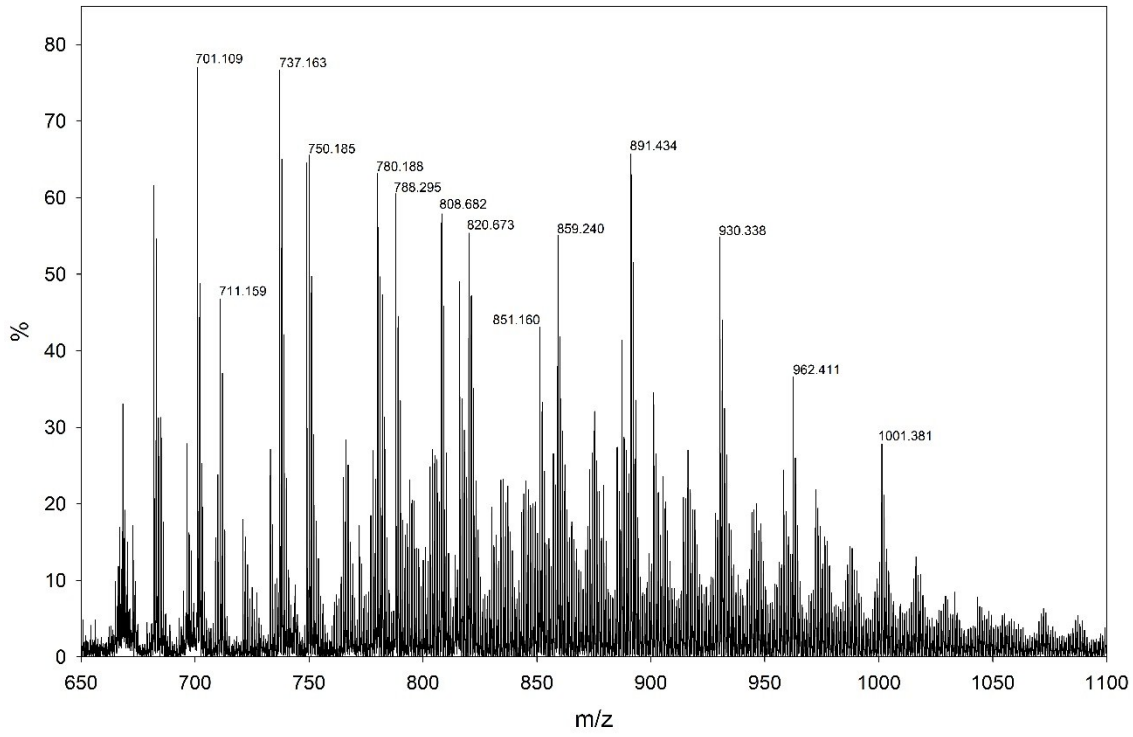


Figure S17. Enlargement of MALDI-TOF mass spectrum of the reaction mixture (PDI 1.6 x 10^{-3} M, KO_2 1.6 x 10^{-3} M and 4'-bromoacetophenone 1.6 x 10^{-3} M in deaerated DMF) irradiated 20 hours with blue-LED.

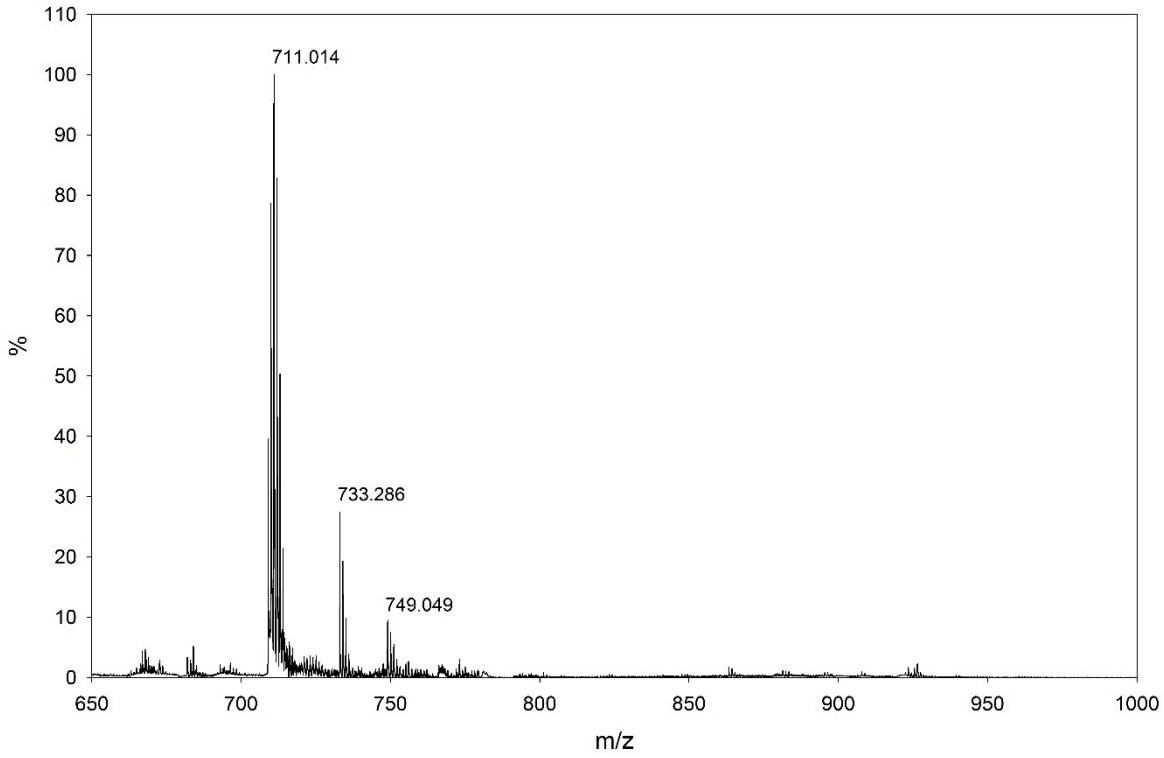


Figure S18. MALDI-TOF mass spectrum of PDI. Peak assignment: 711.014 $[PDI+H]^+$, 733.286 $[PDI+Na]^+$, 749.049 $[PDI+K]^+$.

10. EPR measurements

EPR spectra were recorded at room temperature using an ELEXYS E500 spectrometer equipped with a NMR gaussmeter for the calibration of the magnetic field and a frequency counter for the determination of *g*-factors that were corrected against that of the perylene radical cation in concentrated sulfuric acid (*g* = 2.002583). The instrument settings were as follows: microwave power 5.0 mW, modulation amplitude 0.2 G, modulation frequency 100 kHz, scan time 180 s. The electrochemical cell was home-made and consisted of an EPR flat cell (Wilmad WG-810) equipped with a 25×5×0.2 mm platinum gauze (cathode), a platinum wire (anode).[S4] The current was supplied and controlled by an AMEL 2051 general-purpose potentiostat. An iterative least squares fitting procedure based on the systematic application of the Monte Carlo method was performed in order to obtain the experimental spectral parameters of the radical species.[S5]

EPR analysis of $PDI^{\bullet-}$ generated by photochemical reduction in presence of triethylamine

A solution of PDI (1.8 mg, 0.0025 mmol, 8 x 10^{-4} M) and Et_3N (0.4 mmol, 56 µL, 0.13 M) was prepared in DMF (3 mL). 30 µL were transferred with a syringe into a 1.5 mm quartz capillary. The

solution was degassed for 2 min via gentle argon bubbling through a needle from the bottom of the capillary. The capillary was then flame sealed and irradiated with blue-LEDs (450 nm). The solution turned rapidly from red to blue. After 10 min, the EPR spectra was acquired (Figure S19, black line) and it was attributed to $PDI^{\bullet-}$ according to the calculated simulation.

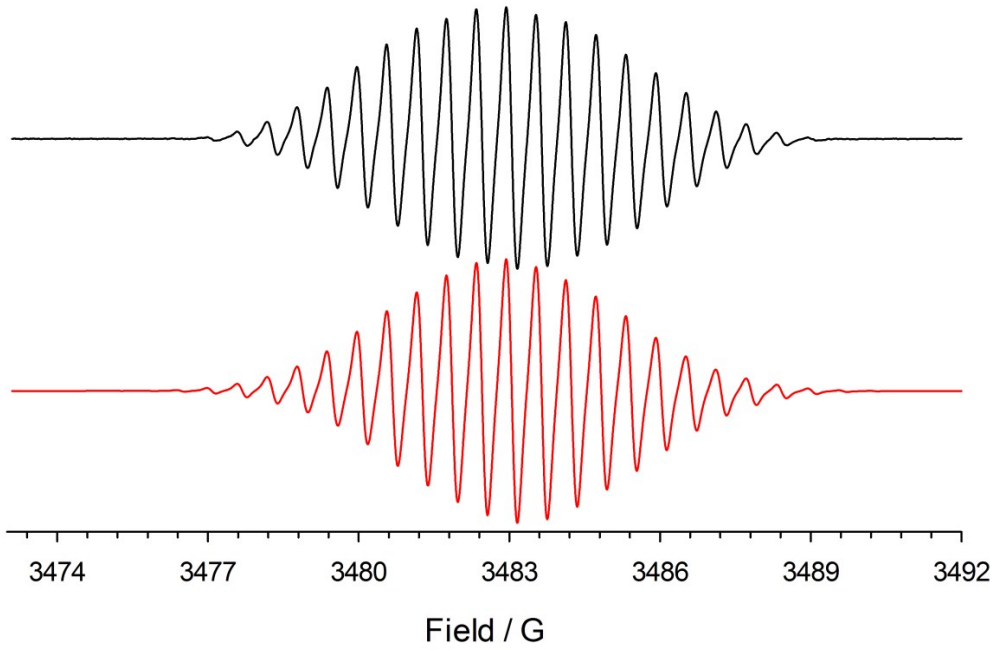


Figure S19. EPR spectrum (black) obtained during the irradiation at 450 nm of a reaction mixture containing PDI 8 x 10^{-4} M and Et_3N 0.13 M in degassed DMF solution. The corresponding theoretical simulation is reported in red.

EPR analysis of $PDI^{\bullet-}$ generated by electrochemical reduction

A solution of PDI (1.8 mg, 0.0025 mmol, 8 x 10^{-4} M) and and Bu_4NPF_6 (0.3 mmol, 116 mg, 0.1 M) as supporting electrolyte was prepared in DMF (3 mL). 500 µL were transferred with a syringe into an electrochemical EPR flat cell equipped with platinum cathode and anode. The solution was degassed for 2 min via gentle argon bubbling through a capillary from the bottom of the cell. The cell was then inserted into the EPR cavity and the electrodes were connected to the current. The current was varied until the achievement of the reduction potential. The EPR spectra recorded in these conditions (Figure S20), relative to $PDI^{\bullet-}$, was in accordance with that obtained by the photochemical reduction with triethylamine (Figure S20).

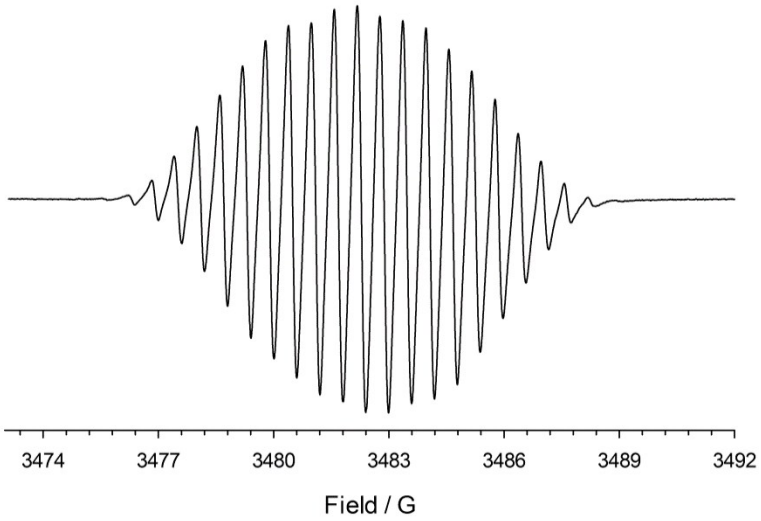


Figure S20. EPR spectrum obtained during electrochemical reduction of PDI 8 x 10^{-4} M in degassed DMF solution (0.1 M in Bu_4NPF_6 as supporting electrolyte).

EPR analysis of the photocatalytic reduction of 4'-bromoacetophenone

A solution of PDI (1.8 mg, 0.0025 mmol, 8 x 10^{-4} M), 4'-bromoacetophenone (10 mg, 0.05 mmol, 0.017 M) and triethylamine (0.4 mmol, 56 µL, 0.13 M) was prepared in DMF (3 mL). 30 µL were transferred with a syringe into a 1.5 mm quartz capillary. The solution was degassed for 2 min via gentle argon bubbling through a needle from the bottom of the capillary. The capillary was then flame sealed and irradiated with blue-LEDs. At the specified times (5, 30, 90, 200, 400 min and 15 h) the capillary was inserted in the EPR instrument and the spectra were recorded (see Figure 6 main text). A progressive shape change in the EPR spectra was observed from 5 to 400 min, while it remained constant afterwards.

The same reaction mixture was irradiated inside the quartz cuvette (0.1 cm pathlength) for 15 h with blue-LEDs. The absorption spectrum is in accordance with the spectrum reported in Figure S6 (blue line). The EPR analysis was performed on the reaction crude. 30 µL of the solution were taken under argon atmosphere with a gas tight syringe and inserted into a 1.5 mm quartz capillary kept under argon atmosphere. The capillary was flame sealed and the EPR spectra recorded (Figure S21) was in perfect accordance with that observed after 400 min in the EPR experiment reported in Figure 6 (main text). A 50 µL reaction sample was taken and diluted with acetonitrile (500 µL) and directly injected in HPLC. The determined reaction conversion was 60%.

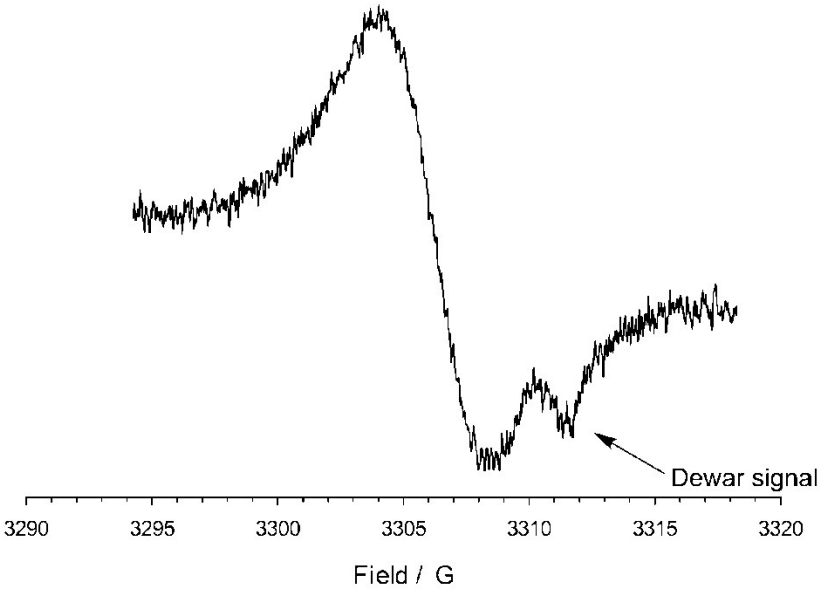


Figure S21. EPR spectrum obtained from the same reaction crude used for the absorption analysis.

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