Supporting Information

Time-resolved EPR revealed C(sp^3)–H activation through photo-enhanced phthalimide-*N*-oxyl (PINO) radical†

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General information.

All solvents were used as received from commercial sources. The ethylbenzene-D_{10} were purchased from Acros. The radical spin-trapping agent DMPO (5,5-Dimethyl-1-pyrroline *N*-Oxide) was purchased from DOJINDO. All other reagents were purchased from Energy Chemical and Aldrich with the maximum purity available and used as received unless otherwise indicated.

Instrumentations

^{1}H NMR spectra were recorded on a Bruker Avance III 500 M spectrometer. Mass spectra were obtained on a Shimadzu GCMS-2010A. GC analyses were performed on a Shimadzu GC-2010 plus equipped with the capillary column (WAX, 30 m × 0.32 mm × 0.25 μm) and the FID detector. The HRMS spectrometer were recorded by Bruker's timsTOF. The X-band EPR spectroscopy measurements were performed on a JESFA-200 (JEOL, Japan) spectrometer**.**

In situ EPR radical experiments

Typical EPR spectrometer parameters were shown as follows, microwave frequency: 9.20-9.45 GHz; modulation amplitude, 0.1 mT; modulation frequency, 100 kHz; power, 1.0 mW; time constant, 0.03 s; sweep width 7.5 mT and sweep time 30 s. The *in situ* EPR tests condition has a 20 s interval based on the typical condition. In this test conditions, the average interval of two scans was about 49.8 s. The *operando* photochemistry EPR measurements were performed on high-pressure mercury lamp as light source and the flat cell (Wilmad WG-810-A quartz-flat cell) (Fig. S1). Through the optical path, light can be directly directed to the flat cell placed inside the resonator.

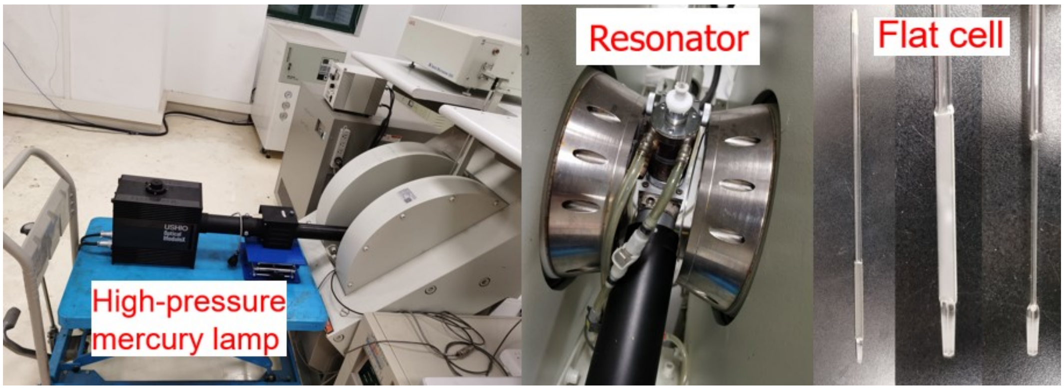


Fig. S1 Photos of the *operando* photochemistry EPR measurements apparatus.

Note for **Fig. 1b**: The indane (18.4 μL, 0.03 M), $CuCl_2$ (0.010 g, 5 mol%), NHPI (00025 g, 10 mol%), photocatalyst [Ir] (0.0017g, 1 mol%) and CH_3CN (5 mL) were mixed together in a 5 mL brown glass flask volumetric. The mixture was then sonicated for 5 minutes to dissolve completely. The solution was bubbled with O_2 for 15 minutes until saturated. Then the solution was injected into the flat cell by syringe and the test was started.

Note for **Fig. 2a**: The indane (18.4 μL, 0.03 M), $CuCl_2$ (0.010 g, 5 mol%), NHPI (00025 g, 10 mol%), photocatalyst [Ir] (0.0017g, 1 mol%) and CH_3CN (5 mL) were mixed together in a 5 mL brown glass flask volumetric. The mixture was then sonicated for 5 minutes to dissolve completely. The solution was bubbled with O_2 for 15 minutes until saturated. Subsequently, the reaction solution (200 μL) and DMPO (20 μL) are mixed and added to the flat cell for time-resolved EPR test at 50 °C.

Photocatalytic oxidation

As shown in Fig. S2, the assembled continuous-flow photocatalytic reactor was mainly consisted of a LED light source system (CEL-LED100HA, 365 nm), two injection pumps (O_2 and reaction mixture), a microchip reactor (Size 50×80×4 mm, Channel 0.12×0.52 mm ($D \times W$), Flow channel length 0.816 m, Liquid holdup 0.072 mL, SCHOTT B270 optical glass.) and a magnetic heated stirrer.

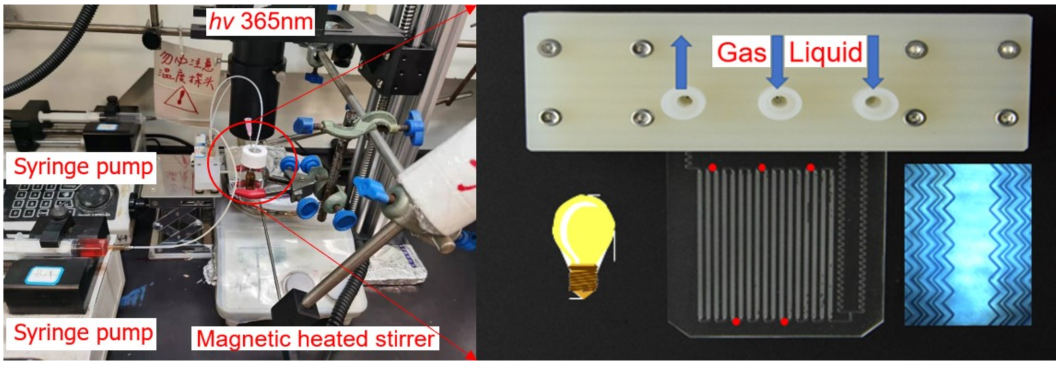


Fig. S2 Photos of the assembled continuous-flow photoreaction apparatus.

The retention time is calculated as follows:

$$t = \frac{3A \times L}{V_{gas} + V_{liquid}} \qquad \text{(Eq. 1)}$$

Where, the channel is divided into three ‘W’ type sub-channels; A, the cross-sectional area of the sub-channel; L, Flow channel length; V_{gas} and V_{liquid} are the flow rate of gases and liquids (mL/h) respectively. Under the condition of V_{gas} = 0.3 mL/h and V_{liquid} = 0.1 mL/h, the retention time is about 23.8 min.

The commercial reactants and products were used as the standard for GC (Shimadzu GC-2010 plus) or GC-MS (Shimadzu GCMS-QP2010). The conversion and selectivity were determined by gas chromatography using the standard curve, and the products were detected by GC-MS. Typical analysis methods: GL sciences, Inertcap Pure-WAX, df = 0.25 μm, 0.25 mm I.D., 30.0 m, H_2 30.0 mL/min; temperature programming: the initial column temperature 35.0 °C for 1.0 min, 1.0 °C /min to 45 °C for 1.0 min, 25 °C /min to 220 °C for 3.0 min.

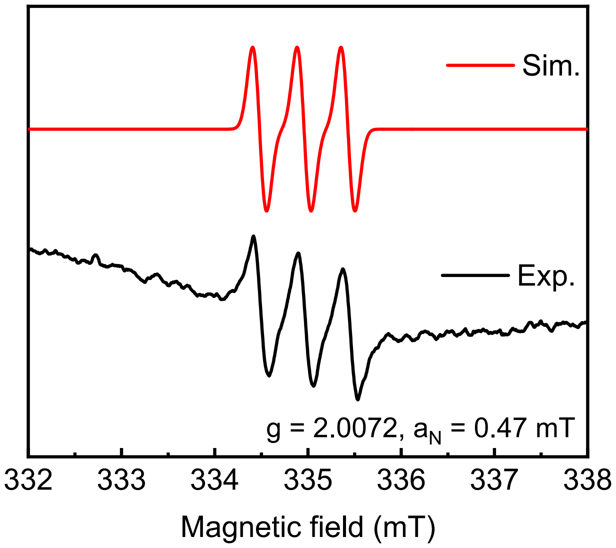


Fig. S3 Experimental (black) and simulated (red) X-band EPR spectra of PINO radical. Experiment conditions: $CuCl_2$ (1 mg), photocatalyst [Ir] (1.7 mg), NHPI (2.5 mg), CH_3CN (5 mL), O_2, 50 °C, *hν*.

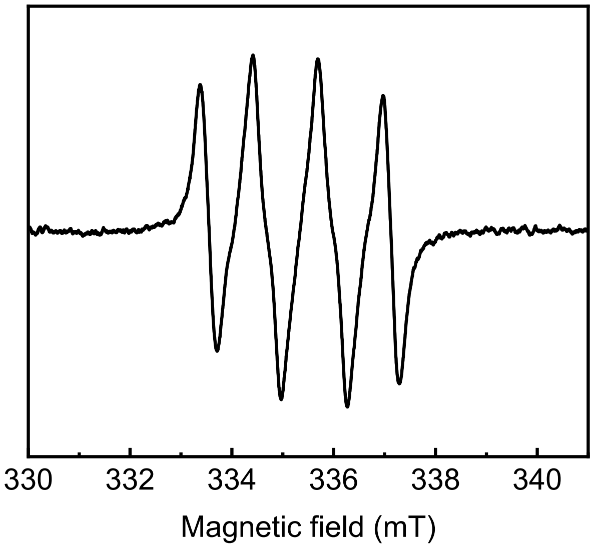


Fig. S4 The first spectrum of 3D figure of *in situ* EPR (Figure 4a).

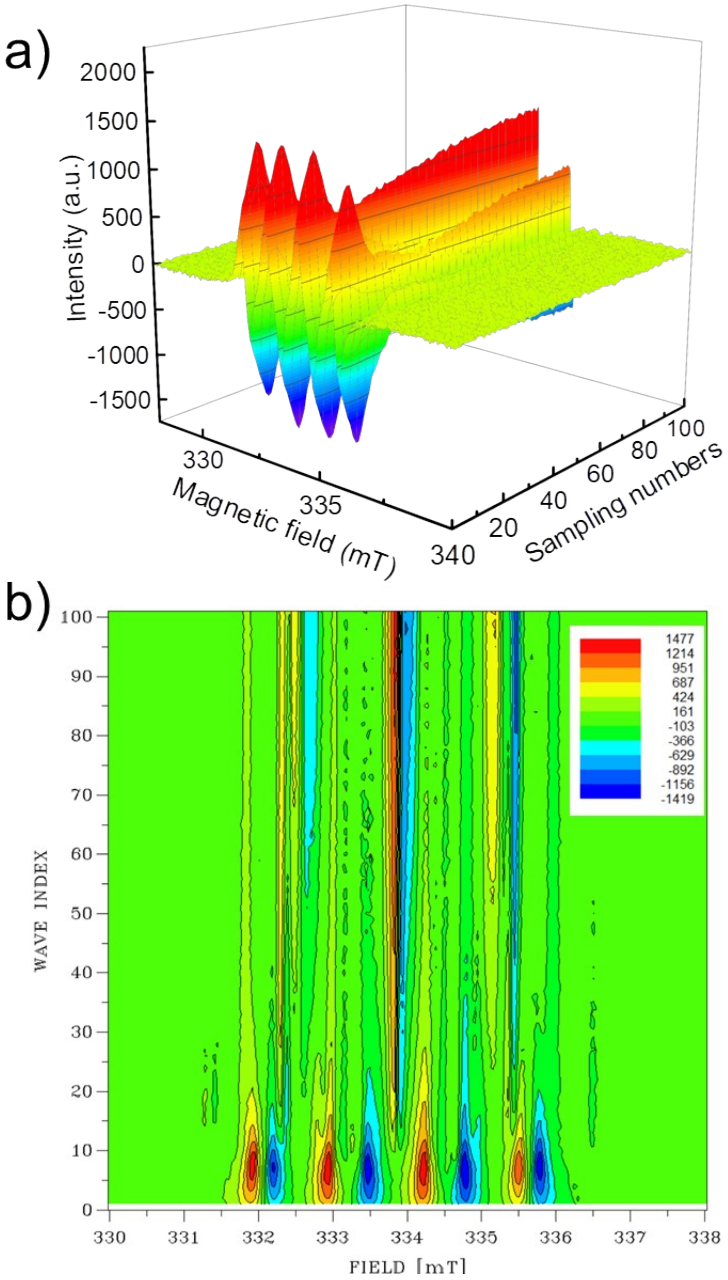


Fig. S5 3D figure of *in situ* EPR. Test conditions: $CuCl_2$ (0.010 g, 5 mol%), NHPI (00025 g, 10 mol%), [Ir] (0.0017g, 1 mol%), CH_3CN (5 mL). O_2, 50 °C, *hv*. A small amount of C-radical signal may be other impurity.

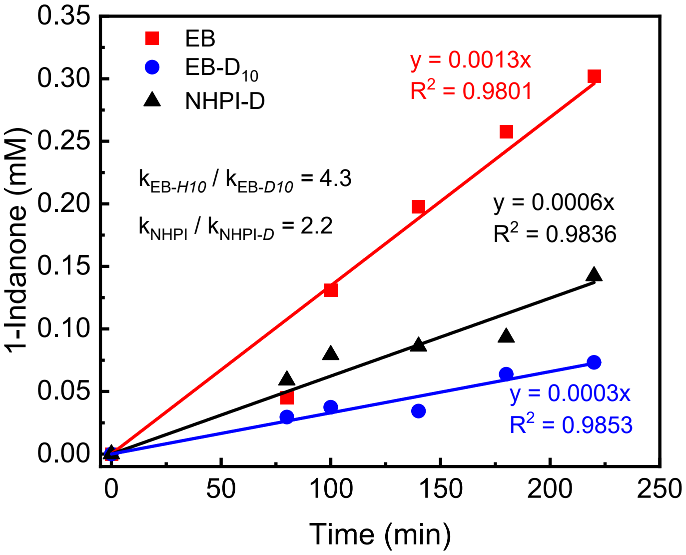
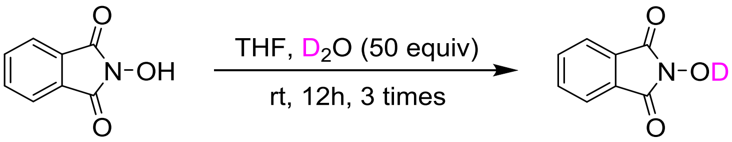


Fig. S6 Kinetics experiments. Reaction conditions: red line: ethylbenzene (EB) 0.75 mM, $CuCl_2$ 5 mol%, NHPI 10 mol%, photocatalyst 1 mol%, CH_3CN (25 mL), O_2, 50 °C, O_2 balloon, *hv*, light batch-reaction flask. Blue line: ethylbenzene-D_{10} (EB-D_{10}) instead of EB. Black line: NHPI-D instead of NHPI.

Synthesis of NHPI-D

A solution of NHPI and D_2O (50 equiv) and dry THF was stirred at ambient temperature in anaerobic flask for 12 h. After removal of solvent by rotary evaporation, the hydrogen-deuterium replacement experiment was repeated 3 times (Scheme 1). Store the NHPI-*D* in an anhydrous environment. ^{1}H NMR showed that the O–H signal at 10.81 ppm is weakened after deuteration. Additionally, IR spectroscopy was further confirmed the O–D stretch at 2378 cm^{-1}. After 3 exchange experiments, the deuterium substitution rate was about 70% (Fig. S10).



Scheme S1. Synthesis procedures of NHPI-D

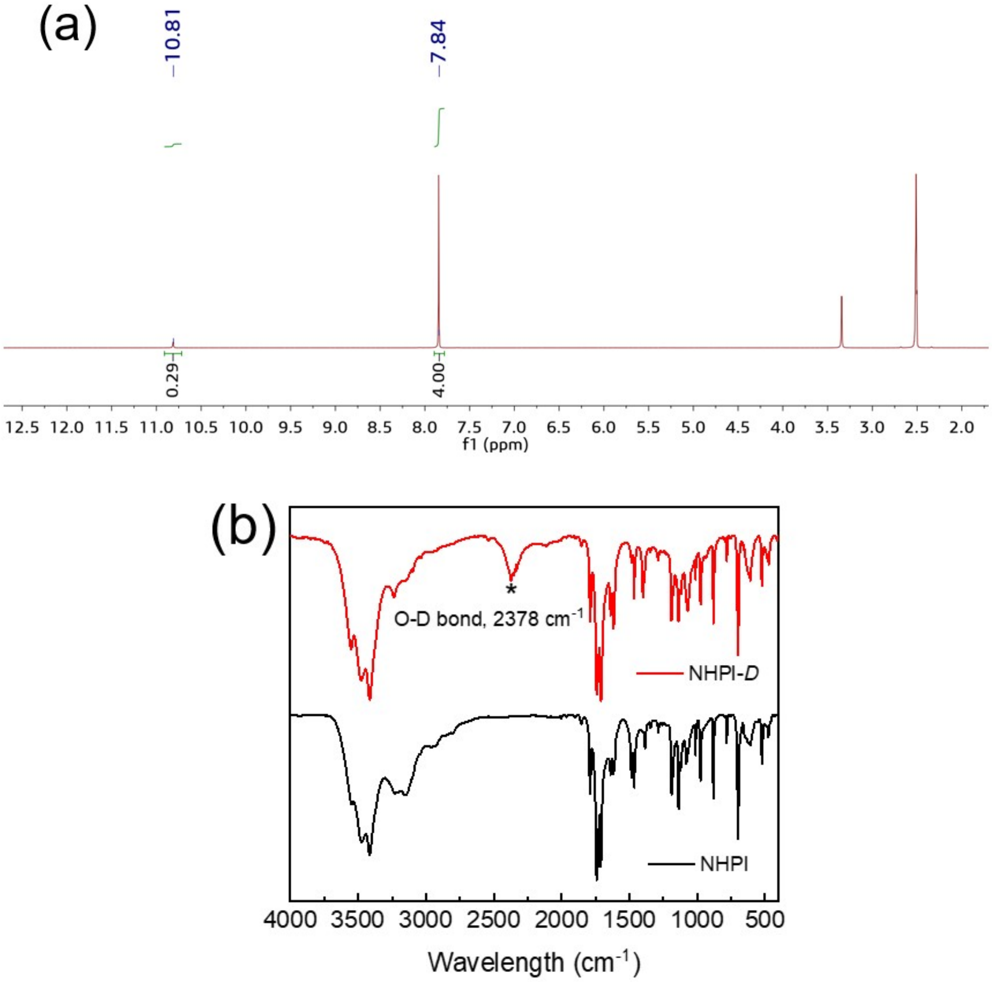
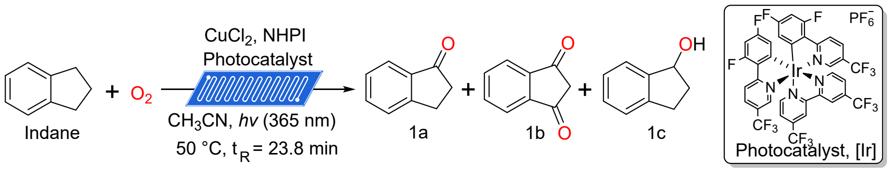


Fig. S7 (a) ^{1}H-NMR of NHPI-D (500 MHz, DMSO-D$_6$), (b) IR spectroscopy of NHPI and NHPI-*D*.

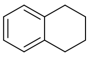
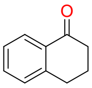
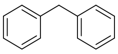
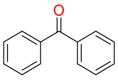
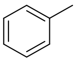
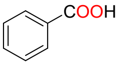
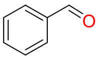
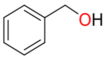
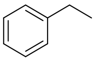
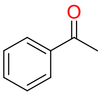
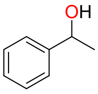
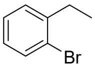
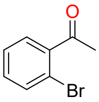
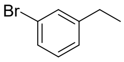
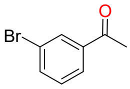
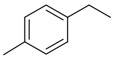
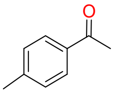
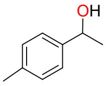
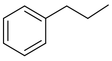
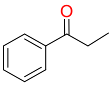
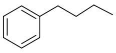
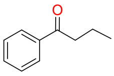
Table S1 Optimizing conditions [a]



Entry	Variation from the standard conditions	Conv. (%)	Selectivites (%)[b]		
			1a	1b	1c
1	none	88	89	6	5
2	$FeCl_3$ instead of $CuCl_2$	19	56	9	35
3	CuI_2 instead of $CuCl_2$	24	62	8	30
4	$PdCl_2$ instead of $CuCl_2$	15	68	5	27
5	TEMPO instead of NHPI	0	0	0	0
6	$Ru(bpy)_3Cl_2$ instead of [Ir]	66	80	8	12
7	Ir[*p*-F(Me)ppy]$_2$(dtbbpy)PF_6 instead of [Ir]	51	73	9	18
8	ZnTPP instead of [Ir]	33	65	11	54
9	$Ru(phen)_3(PF_6)_2$ instead of [Ir]	62	80	8	12
10	Dichlorotetrakis[2-(2-Pyridyl)Phenyl]Diiridium(III) instead of [Ir]	47	77	5	18
11	Ir(dFFppy)$_2$(dtbbpy)PF_6 instead of [Ir]	58	78	12	10

[a]Reaction conditions: Indane 0.03 M, $CuCl_2$ 5 mol%, NHPI 10 mol%, photocatalyst 1 mol%, CH_3CN, O_2, 50 °C, retention time (t_R) 23.8 min, continuous-microflow reactors, V_{gas} = 0.3 mL/h and V_{liquid} = 0.1 mL/h. [b]Selectivity was determined by GC analysis with chlorobenzene as the internal standard.

Table S2. Substrate scope for C(sp3)-H photo-oxidation[a]

Entry	Substrate	Conv. (%)	Products distribution (%)[b]		
1		78	 >99		
2		15	 >99		
3		18	 77	 1 6	 7
4		31	 88	 1 2	
5		75	 >99		
6		20	 >99		
7		51	 82	 1 7	
8		30	 >99		
9		22	 >99		

[a]Reaction conditions: substrate 0.03 M, $CuCl_2$ 5 mol%, NHPI 10 mol%, photocatalyst 1 mol %, CH_3CN, O_2, 50 °C, *hv* 365 nm, retention time (t_R) 23.8 min, continuous-microflow reactors. V_{gas} = 0.3 mL/h and V_{liquid} = 0.1 mL/h. [b]Products distribution was determined by GC analysis with chlorobenzene as the internal standard.

Building on the optimal reaction conditions and the mechanistic study's information, we also investigated the substrate scope of C(sp^3)–H bond aerobic oxidation by the photochemical continuous flow microreactor (Table S2). The 1,2,3,4-tetrahydronaphthalene and diphenylmethane could be oxidized to the corresponding ketone product with remarkable selectivity (>99 %) (Table S2, entries 1-2). Meanwhile, toluene gave acids as the main products (Table S2, entry 3). In addition, ethylbenzene can also be selectively (88 %) oxidized to acetophenone (Table S2, entry 3). If there was a substituent on ethylbenzene, the selectivity to ketone products does not change significantly (Table S2, entries 5-7). At the same time, iso-propyl or butylated benzene also gave ketone as the main products (>99%, selectively) (Table S2, entries 8-9). In this system, the substrates with an R1-CH_2-R2 structure tend to give ketone products.