

## Supplementary Information

### A solar light-driven, eco-friendly protocol for highly enantioselective synthesis of chiral alcohols *via* photocatalytic/biocatalytic cascades

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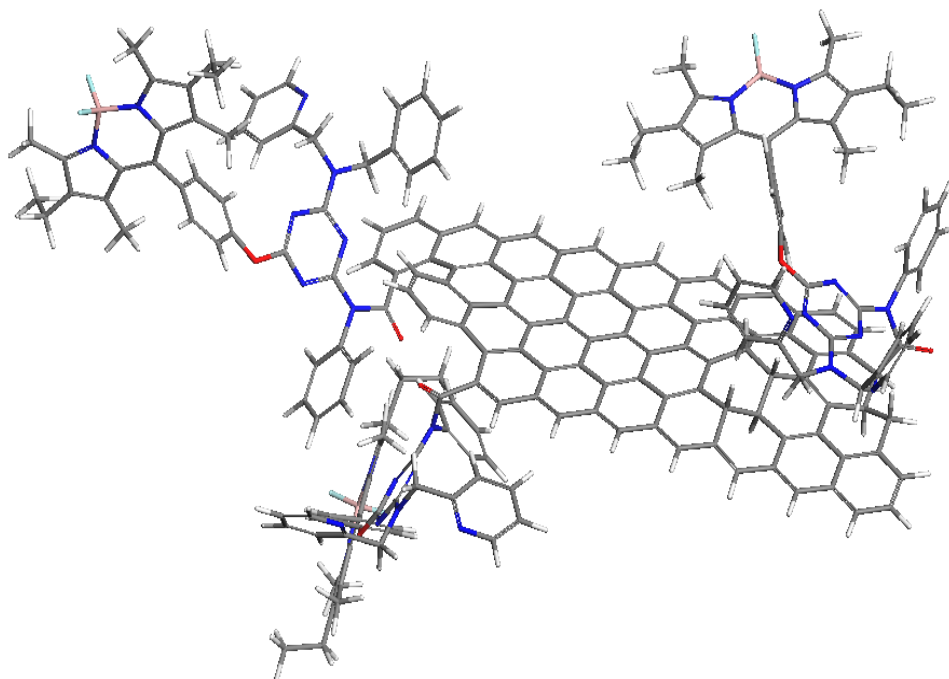
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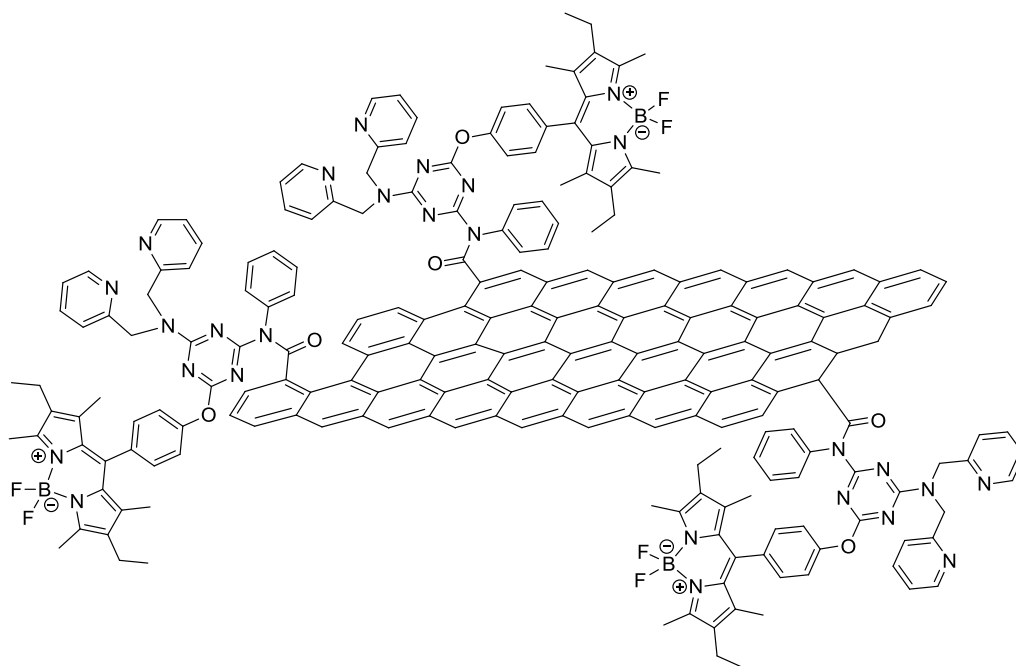
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## 1. Structure of the Photocatalyst

a)



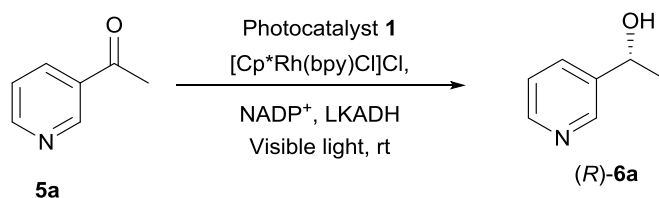
b)



**Fig. S1** The structure of Graphene-based photocatalyst **1** (CCG-BODIPY): a) 3D-structure and b) Chemical Structure.<sup>1</sup>

## 2. Optimization of the Reaction Parameters for Photoenzymatic Asymmetric Reduction

Conversion of 3-Acetyl pyridine, **5a** into (*R*)-1-(3-pyridyl) ethanol, (*R*)-**6a** catalyzed by enzyme LKADH.



**Table S1.** Effect of NADP<sup>+</sup> concentration on reduction of **5a** by LKADH.<sup>a</sup>

Entry	Conc of NADP <sup>+</sup> (mM)	Conversion <sup>b</sup> (%)	Yield <sup>b</sup> (%)	<i>ee</i> <sup>c</sup> (%)
1	0.2	20	n.d.	> 99.9
2	0.3	28	n.d.	> 99.9
3	0.4	34	72	> 99.9
4	0.5	35	n.d.	> 99.9
5	0.4 mM; mixed twice each of 0.2 mM, initially and after 25 h	28	66	> 99.9

<sup>a</sup> Reaction was conducted in *n*-heptane-aqueous biphasic reaction media with substrate **5a** of conc. 20 mM (for General procedure of photoenzymatic reactions, see the Experimental section). <sup>b</sup> Conversion of ketone **5a** and yield of (*R*)-**6a** were calculated from GC analysis. <sup>c</sup> The enantiomeric excess (*ee*) of the product alcohol (*R*)-**6a** was measured by GC analysis using a chiral stationary phase. n.d. = not determined.

**Table S2.** Effect of LKADH loading on reduction of **5a**.<sup>a</sup>

Entry	Amount of LKADH (U)	Conversion <sup>b</sup> (%)	Yield <sup>b</sup> (%)	ee <sup>c</sup> (%)
1	0.5	22	n.d.	> 99.9
2	1.0	34	72	> 99.9
3	1.25	35	n.d.	> 99.9
4	1.5	35	n.d.	> 99.9
5	1.0 U; mixed twice each of 0.5 U, initially and after 25 h	40	69	> 99.9

<sup>a</sup> Reaction was conducted in *n*-heptane-aqueous biphasic reaction media with substrate **5a** of conc. 20 mM (for General procedure of photoenzymatic reactions, see the Experimental section). <sup>b</sup> Conversion of ketone **5a** and yield of (*R*)-**6a** were calculated from GC analysis. <sup>c</sup> The enantiomeric excess (*ee*) of the product alcohol (*R*)-**6a** was measured by GC analysis using a chiral stationary phase. n.d. = not determined.

**Table S3.** Effect of photocatalyst loading on reduction of **5a**.<sup>a</sup>

Entry	Amount of <b>1</b>	Conversion <sup>b</sup> (%)	Yield <sup>b</sup> (%)	ee <sup>c</sup> (%)
1	0.25 mg; mixed at the start of reaction	20	n.d.	> 99.9
2	0.5 mg; mixed at the start of reaction	34	72	> 99.9
3	0.6 mg; mixed at the start of reaction	35	n.d.	> 99.9
4	0.5 mg; mixed twice each of 0.25 mg, initially and after 25 h	41	74	> 99.9

<sup>a</sup> Reaction was conducted in *n*-heptane-aqueous biphasic reaction media with substrate **5a** of conc. 20 mM (for General procedure of photoenzymatic reactions, see the Experimental section). <sup>b</sup> Conversion of ketone **5a** and yield of (*R*)-**6a** were calculated from GC analysis. <sup>c</sup> The enantiomeric excess (*ee*) of the product alcohol (*R*)-**6a** was measured by GC analysis using a chiral stationary phase. n.d. = not determined.

**Table S4.** Effect of NADPH (when used instead of NADP<sup>+</sup>) on reduction of **5a** by LKADH.<sup>a</sup>

Entry	Conc of NADPH (mM)	Reaction Condition	Conversion <sup>b</sup> (%)	Yield <sup>b</sup> (%)	ee <sup>c</sup> (%)
1	0.4	Dark condition, kept for 24 h	< 2	n.d.	> 99.9
2	0.4	Usual experimental condition	37	68	> 99.9

<sup>a</sup>Reaction was conducted in *n*-heptane-aqueous biphasic reaction media with substrate **5a** of conc. 20 mM (for General procedure of photoenzymatic reactions, see the Experimental section). <sup>b</sup> Conversion of ketone **5a** and yield of (*R*)-**6a** were calculated from GC analysis. <sup>c</sup>The enantiomeric excess (*ee*) of the product alcohol (*R*)-**6a** was measured by GC analysis using a chiral stationary phase. n.d. = not determined.

**Table S5.** Effect of portion wise addition of NADP<sup>+</sup> and/or photocatalyst **1** and/or LKADH on reduction of **5a**.<sup>a</sup>

Entry	Reaction condition	Conversion <sup>b</sup> (%)	Yield <sup>b</sup> (%)	ee <sup>c</sup> (%)
1	Both NADP <sup>+</sup> (0.4 mM, twice each of 0.2 mM) and <b>1</b> (0.5 mg, twice each of 0.25 mg) added portionwise, initially and after 25 h	38	72	> 99.9
2	Both <b>1</b> (0.5 mg, twice each of 0.25 mg) and LKADH (1.0 U, twice each of 0.5 U) added portionwise, initially and after 25 h	30	66	> 99.9

<sup>a</sup>Reaction was conducted in *n*-heptane-aqueous biphasic reaction media with substrate **5a** of conc. 20 mM (for General procedure of photoenzymatic reactions, see the Experimental section). <sup>b</sup> Conversion of ketone **5a** and yield of (*R*)-**6a** were calculated from GC analysis. <sup>c</sup>The enantiomeric excess (*ee*) of the product alcohol (*R*)-**6a** was measured by GC analysis using a chiral stationary phase.

### 3. Determination of Quantum Yield

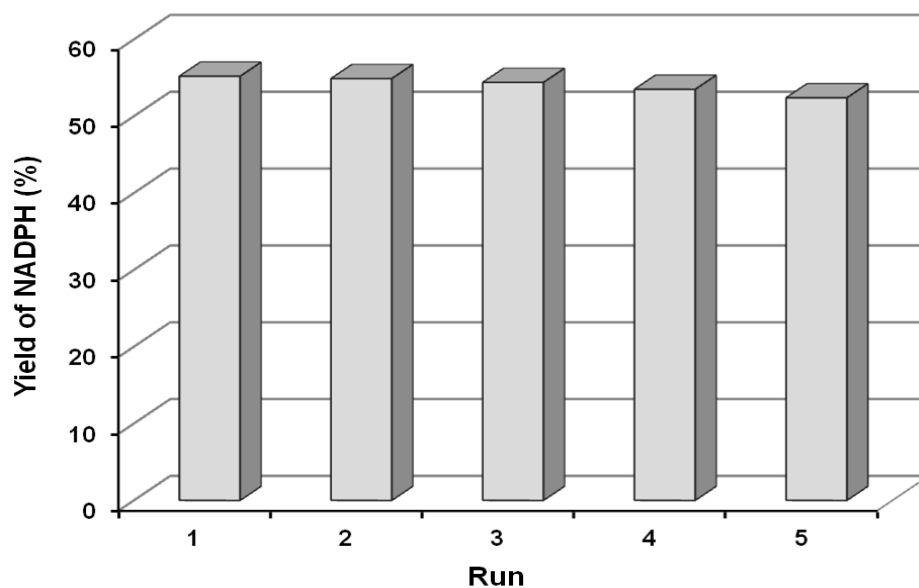
The Quantum yield ( $\Phi$ ) of photocatalyst **1** for photocatalytic NADPH regeneration was carried out in a quartz cuvette reactor (3 mL) under an argon atmosphere at room temperature. A 450 Watt Newport Xenon Lamp (Oriental Instruments, USA) equipped with a 20 nm bandpass filter at 450 nm was used as a light source. The photochemical regeneration of NADPH was conducted by illuminating the quartz reactor containing NADP<sup>+</sup> of conc. 0.4 mM, organometallic compound [Cp\*Rh(bpy)Cl]Cl of conc. 0.2 mM, TEOA of conc. 0.4 M and photocatalyst **1** of conc. 15  $\mu$ M (0.5 mg, as its solution in 30  $\mu$ L DMF) in 0.1 M sodium phosphate buffer (NaH<sub>2</sub>PO<sub>4</sub>-Na<sub>2</sub>HPO<sub>4</sub>, pH ~ 7.0). The concentration of NADPH was spectrophotometrically measured through the change in absorbance of NADPH at 340 nm (UV-1800 UV spectrophotometer, Shimadzu Co., Japan).

$$\text{Quantum Yield } (\Phi) = 2 \times \frac{\text{moles of NADPH produced}}{\text{moles of incident photon}} \times 100 \quad (\%)$$

The quantum yield of photocatalyst **1** was calculated to be 9.2% for the photocatalytic NADPH regeneration process.

In similar ways, the quantum yields of other photocatalysts for NADPH photoregeneration were also calculated. For BODIPY, NH<sub>2</sub>-TPP and CCG-NH<sub>2</sub>-TPP, the quantum yield values were calculated to be 1.4%, 1.1% and 2.8%, respectively.

#### 4. Recycling experiments for photocatalytic regeneration of NADPH from NADP<sup>+</sup>



**Fig. S2** Recycling experiments with Photocatalyst **1** in visible-light-driven photoregeneration of NADPH. Reaction conditions: 2.4 mL sodium phosphate buffer (NaH<sub>2</sub>PO<sub>4</sub>-Na<sub>2</sub>HPO<sub>4</sub>, pH ~ 7.0, 0.1 M), 0.6 mL *n*-heptane, photocatalyst **1** of conc. 15 μM, NADP<sup>+</sup> of conc. 0.4 mM, [Cp\*Rh(bpy)Cl]Cl of conc. 0.2 mM and TEOA of conc. 0.4 M under argon atmosphere at room temperature (see also the Experimental section in the manuscript). The reaction time was set to 2 h and NADPH conversion yield after that time for each run are calculated and shown here.

#### 5. Determination of Turnover Frequency (TOF)

Performance of the catalyst during the NADPH regeneration process as well as photoenzymatic synthesis of chiral alcohols is expressed as its turnover frequencies (TOFs).

For NADPH regeneration process, catalyst turnover frequency is calculated as follows:

$$\text{Turnover Frequency (TOF)} = \frac{\text{moles of NADPH produced}}{\text{moles of photocatalyst } \mathbf{1} \text{ used} \times \text{number of hours}} \quad (\text{h}^{-1})$$

For photoenzymatic synthesis of chiral alcohols, catalytic turnover frequency is calculated as follows:

$$\text{Turnover Frequency (TOF)} = \frac{\text{moles of alcohols (R/S)-}\mathbf{6a-f} \text{ produced}}{\text{moles of photocatalyst } \mathbf{1} \text{ used} \times \text{number of days}} \quad (\text{d}^{-1})$$

Given the likely decrease in enzyme LKADH activity, as can be anticipated from results discussed in detail in the manuscript text, thereby limiting the amount of product alcohol formed, it should be pointed out here that the TOFs given in this article do not reflect the actual lifetime or stability of the catalyst used under the operational conditions. These are purely based on a conservative estimation as shown above.

## 5. Reference

1. R. K. Yadav, J.-O. Baeg, A. Kumar, K.-j. Kong, G. H. Oh and N.-J. Park, *J. Mater. Chem. A*, 2014, **2**, 5068–5076.