Electronic Supplementary Information

Direct cross-coupling between alkenes and tetrahydrofuran with platinum-loaded titanium oxide photocatalyst

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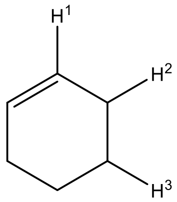
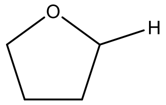
Contents

1. C–H bond dissociation energies

The C–H bond dissociation energies of cyclohexene and tetrahydrofuran (THF) are listed in Table S1, where the values are from the literature.[S1, S2]

Table S1 C–H bond dissociation energies in cyclohexene and tetrahydrofuran (THF) [a]

Entry	Compound	C–H bond dissociation energy / kJ mol^{-1}
1		Vinylic hydrogen, H^1: 457.7 Allylic hydrogen, H^2: 349.5 Homoallylic hydrogen, H^3: 415.1
2		385.3

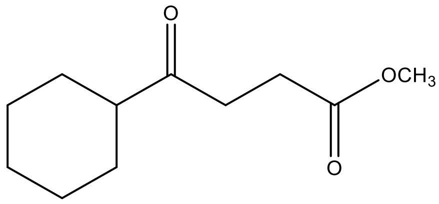
[a] Data from the literature[S1, S2]

2. Synthesis of 2-cyclohexyltetrahydrofuran

2-cyclohexyltetrahydrofuran (**A**) was prepared by following the literature.[S3]

2.1 Synthesis of methyl-4-cyclohexyl-4-oxobutanoate

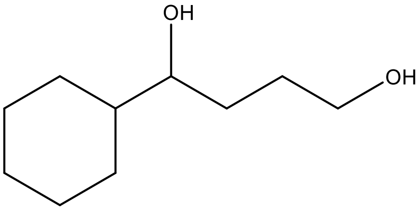
A solution of anhydrous LiBr (0.938 g, 10.8 mmol, 2.4 equiv) in THF (25 mL) was added to a stirred suspension of CuBr (0.775 g, 5.40 mmol, 1.2 equiv) in THF (14 mL) under an argon atmosphere and stirred at room temperature until homogeneity. Then, chloro(cyclohexyl)magnesium (2.0 M) in THF (2.70 mL, 5.40 mmol, 1.2 equiv) and methyl-4-chloro-4-oxobutanoate (0.682 g, 4.53 mmol, 1.0 equiv) were quickly and successively added to the stirred solution of salts and stirred for 1 hour and 15 minutes. After that, it was quenched with NH_4Cl (25 mL) and extracted 3 times with EtOAc. The product was purified by column chromatography and isolated as a colorless oil. The NMR data, δ_H (400 MHz, $CDCl_3$) 3.67 (3H, s, $COOC\underline{H}_3$), 2.77 (2H, t, $COC\underline{H}_2$), 2.59 (2H, t, $C\underline{H}_2CO_2Me$), 2.40–2.35 (1H, m, methine H, and 1.88–1.24 (10H, m, methylene H), were consistent with those reported in the literature.[S3]



Methyl-4-cyclohexyl-4-oxobutanoate

2.2 Synthesis of 1-cyclohexylbutane-1,4-diol

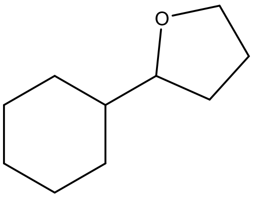
A solution of methyl-4-cyclohexyl-4-oxobutanoate (0.4 g, 1.6 mmol, 1.0 eq.) in THF (4 mL) was added dropwise to a stirred solution of $LiAlH_4$ (2 M) in anhydrous THF (2.96 mL, 5.92 mmol, 3.7 equiv) at room temperature. The resulting mixture was stirred for 2 h and cooled to 273 K. The excess hydride was quenched by the addition of the following regents in the mentioned order: 2.4 mL water, 2.4 mL of 15% aqueous NaOH solution and 7.2 mL of water. Then the reaction mixture was warmed to room temperature under stirring, filtered through Celite and condensed in vacuum to obtain a colorless oil which underwent crystallization. The crude crystals so obtained were washed with hexane and dried under vacuum. The NMR data, δ_H (400 MHz, $CDCl_3$) 3.76–3.65 (2H, m, $C\underline{H}_2OH$), 3.41–3.37 (1H, m, $C\underline{H}OH$), 1.98 (1H, br s, OH), and 1.86–0.98 (16H, m, alkyl-$C\underline{H}$+$O\underline{H}$), were consistent with those reported in the literature.[S3]



1-cyclohexylbutane-1,4-diol

2.3 Synthesis of 2-cyclohexyltetrahydrofuran (A)

To a solution of 1-cyclohexylbutane-1,4-diol (0.276 g) in acetonitrile (8 mL), 5 mol% of $HAuCl_4$ was added. The solution was stirred under argon at 313 K for 20 h, followed by solvent evaporation in vacuum to give a crude yellow oil. The NMR data, δ_H (400 MHz, $CDCl_3$) 3.84–3.78 (1H, m, $OC\underline{H}H$), 3.73–3.61 (1H, m, $OCH\underline{H}$), 3.50–3.45 (1H, m, $\underline{H}COCH_2$), 1.93–0.94 (15H, m, alkyl-CH); δ_C (400 MHz, $CDCl_3$) 84.18, 77.16 (t), 67.85, 43.21, 30.08, 29.33, 29.25, 26.71, 26.26, 26.10, and 25.99, were consistent with those reported in the literature.[S3]



2-cyclohexyltetrahydrofuran, **A**

3. Assignment of the products in the photocatalytic cross-coupling

As mentioned in the main text, the reaction between cyclohexene and THF gave three new peaks in the GC-MS spectrum (Fig. S1a) (the peaks **1**–**3**, in the increasing order of their retention time in the TIC), which were assigned to the photocatalytic cross-coupling products of the reaction between cyclohexene and THF, apart from the homocoupling products of cyclohexene and THF. After comparing the experimental mass spectrum with that of the authentic sample, the peak **1** was assigned to 2-cyclohexyltetrahydrofuran (**A**). The remaining peaks, the peaks **2** and **3**, were assigned to 2-(cyclohex-2-en-1-yl)tetrahydrofuran (**B**) and 2-(cyclohex-1-en-1-yl)tetrahydrofuran (**C**), respectively, based on the following reasons.

The molecular ion peak of the remaining two peaks (the peaks **2** and **3**) was 2 units less than that of the peak **1** (Fig. S1b, c and d), indicating that the double bond of cyclohexene was retained in these compounds. Three compounds fit the specifications of GC-MS analysis for the new two peaks, namely, 2-(cyclohex-1-en-1-yl)tetrahydrofuran (**i**), 2-(cyclohex-2-en-1-yl)tetrahydrofuran (**ii**), and 2-(cyclohex-3-en-1-yl)tetrahydrofuran (**iii**) as shown in Fig. S2.

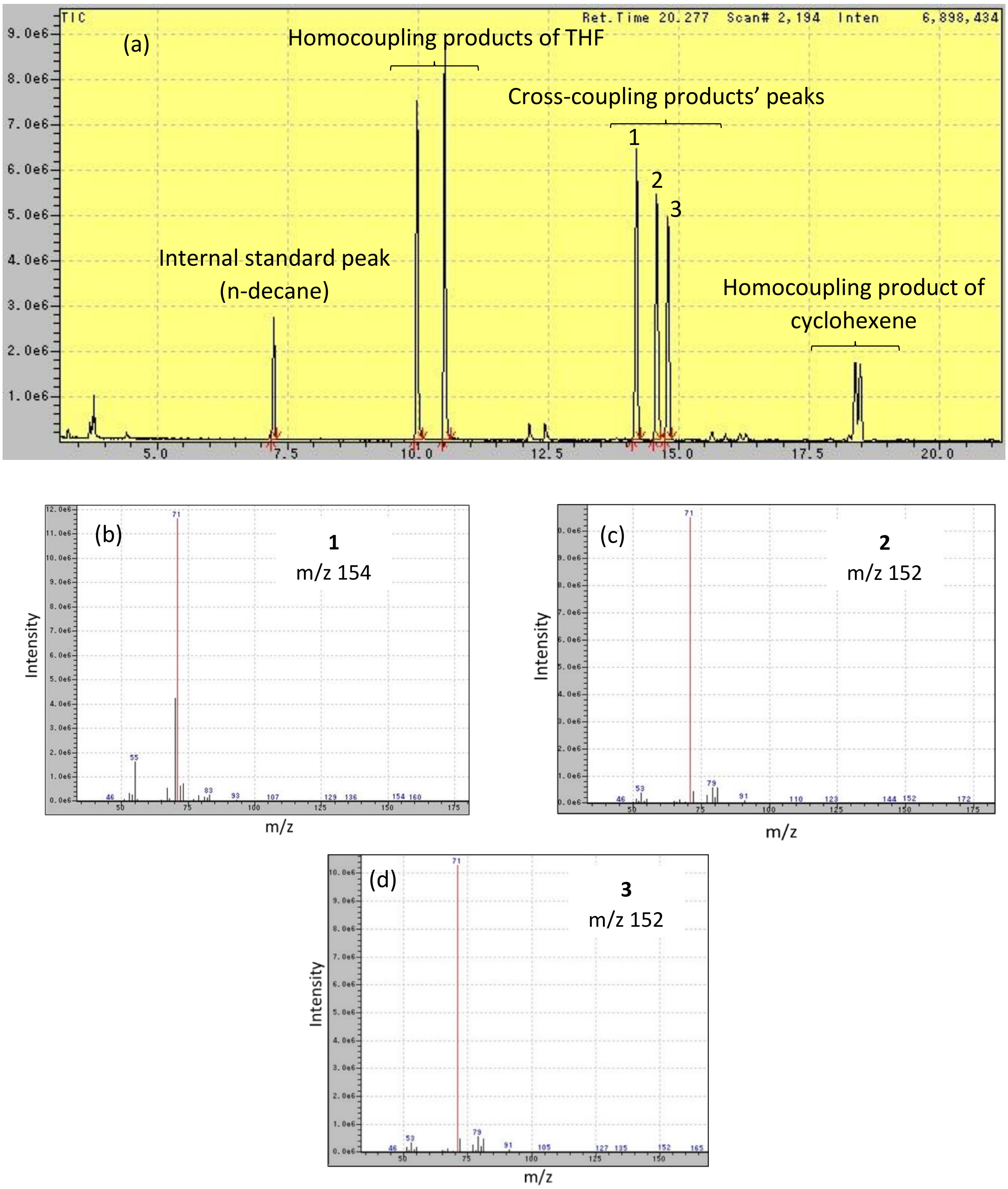


Fig. S1 TIC of the photocatalytic cross-coupling between cyclohexene and THF with the Pt(0.1)/TiO_2 photocatalyst (a) and experimental mass spectra of the peak **1** (b)**,** the peak **2** (c)**,** and the peak **3** (d).

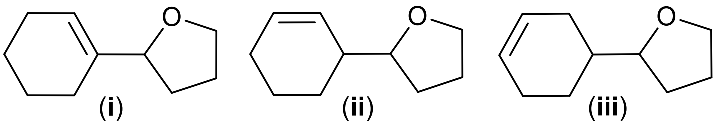
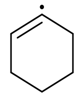
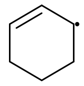
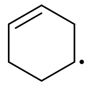


Fig. S2 Probable structures for the peaks **2** and **3** formed in the photocatalytic cross-coupling between cyclohexene and THF.

Assuming these compounds were formed by the hole-oxidation of cyclohexene to the corresponding radicals followed by their coupling with the THF radicals, the stability of the various cyclohexenyl radicals would be an important factor. By using the MOPAC2016 software[S4] and PM7 method,[S5] we calculated the heat of formation of the allylic and homoallylic radicals to compare the stability of them relatively. The values are shown in Table S2. The heat of formation for each radical species was positive, where allylic radical was obviously the smallest among them (Table S2, entries 1–3). This means that the allylic cyclohexenyl radical was the most stable radical. Further, the homocoupling of cyclohexene gave [1,1'-bi(cyclohexane)]-2,2'-diene, confirming that the allylic-cyclohexenyl radical would be formed during the reaction. The radical can couple with the THF radical and give a cross-coupling product. Thus, one of the two peaks (the peak **2** or **3**) corresponding to the cross-coupling products is assignable to structure **ii** in Fig. S2.

Table S2 Heat of formation of cyclohexenyl radicals

Entry	Cyclohexenyl radical species		Heat of formation / $\mathrm{kJ\ mol^{-1}}$ [a]
1	vinylic		178.0
2	allylic		69.8
3	homoallylic		103.7

[a] The heat of formation was calculated by the MOPAC2016 software[S4] using the PM7 method[S5]

Due to the large heat of formation of the homoallylic and vinlylic radicals, their formation would be relatively difficult. Thus, if the reaction proceeds via radical-radical coupling, the compounds **i** and **iii** should be ruled out of the probable structures as the cross-coupling product. However, another possible mechanism makes it possible to form the compound **i**. Due to the large concentration of the THF radicals in the reaction system, there is high probability of its attack on the double bond of cyclohexene. This would generate a radical transition state as shown in Fig. S3. If the radical releases a hydrogen radical from the sp^3 carbon in this radical transition state or if another THF radical abstracts a hydrogen radical from it, the double bond can be regenerated. Thus, the remaining product peak is assignable to the compound **i**. This product assignment is also thermodynamically supported by the heat of formation for the two compounds, i.e., the stabilization energy (absolute value of the heat of formation) for the formation of the compound **i** is the largest among them (Table S3).

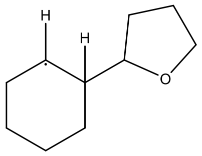
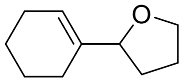
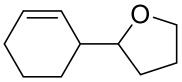
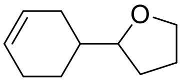


Fig. S3 Proposed transition state of generated by the attack of the THF radical on the double bond of cyclohexene.

Table S3 Heat of formation of the three compounds listed in Fig. S2

Entry	Compounds		Heat of formation / kJ mol^{-1} [a]
1	(i)		−213.8
2	(ii)		−203.3
3	(iii)		−205.5

[a] The heat of formation was calculated by the MOPAC2016 software[S4] using the PM7 method[S5]

As discussed in the main text, the peaks **2** and **3** were assigned to the compounds **B** and **C**, respectively, based on the results of the isotopic experiments (Table 4). The elimination of the hydrogen radical from the transition state of Fig. S3 was proposed to be more feasible than that from the cyclohexene molecule. So that the k_H/k_D value, obtained in the reaction with cyclohexene-d_{10}, for the formation of **B** should be smaller than that for **C**.

According to both the discussion mentioned here and the discussion on the results of the isotope experiments in the main text, the three peaks from the cross-coupling products **1**–**3** were assigned to the compounds **A**–**C**, respectively, as shown in Table 2.

4. Effect of the loading amount of Pt on TiO_2 on the photocatalytic cross-coupling

The loading amount of Pt on TiO_2 was varied and the results are shown in Table S4. The product amount was not affected much by increasing the loading amount from 0.1 to 0.5 weight % (Table S4, entries 1–3). Based on these results, the loading amount of 0.1 weight% was employed in all other experiments.

Table S4 Photocatalytic reaction tests with various Pt(x)/TiO_2 samples [a]

Entry	Loading amount of Pt (weight%) on TiO_2	Cross-coupling products (μmol) [b]		
		A	**B**	**C**
1	0.1	7.3	6.5	5.7
2	0.2	8.2	6.8	6.2
3	0.5	7.7	7.1	5.9

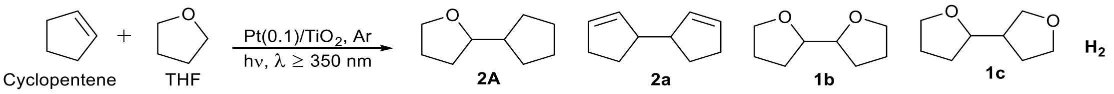
[a] The amount of reagents was not optimized. 2 mL THF, 2 mL cyclohexene were used for the reaction. Other conditions were same as Table 2 in the main text.

5. Scope of alkene molecules for the photocatalytic cross-coupling with THF

As mentioned in the main text, the Pt/TiO_2 samples were effective for the photocatalytic cross-coupling of cyclopentene with THF, and 1-hexene with THF, as well.

The reaction of cyclopentene and THF, over the Pt(0.1)/TiO_2 sample, gave 2-cyclopentyltetrahydrofuran (**2A**) as the only detectable cross-coupling product (Table S5), probably formed by a radical addition mechanism, where a photogenerated THF radical would attack to the double bond of cyclopentene followed by the addition of a hydrogen radical. Under the present conditions, the homocoupling of both cyclopentene and THF also proceeded, although the amount of the former product (**2a**) was less than later (**1b** and **1c**).

Table S5 Photocatalytic cross-coupling between cyclopentene and THF with the Pt(0.1)/TiO_2 sample [a]

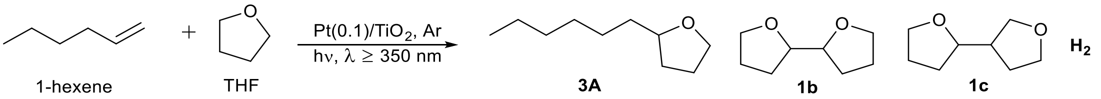


Reactants / mmol		Products / µmol [b]		
Cyclopentene	THF	**2A**	**2a**	**1b+1c**
5.46	37	0.52	0.17	1.11

[a] Reaction conditions: the same as those described in Table 2 in the main text. [b] Amount of **2A**, **1b**, **1c** and **2a** were determined from the calibration curve of **A** that was synthesized by following the procedure reported in the literature.[S3]

The cross-coupling of 1-hexene by THF also proceeded over the Pt(0.1)/TiO_2 sample to give 2-hexyltetrahydrofuran (**3A**) as the major cross-coupling product, homocoupling products of THF (**1b** and **1c**), and the trace amounts of some unidentified products (Table S6). The cross-coupling product **3A** might also be formed by a radical addition mechanism, where the double bond moiety of 1-hexene molecule would be attacked by THF radical and a hydrogen radical, similar to compounds **A** and **2A**. Under the present conditions, the homocoupling of 1-hexene did not proceed.

Table S6 Photocatalytic cross-coupling between 1-hexene and THF with the Pt(0.1)/TiO_2 sample [a]



Reactants / mmol		Products / µmol [b]	
1-hexene	THF	**3A**	**1b+1c**
4	37	0.49	0.64

[a] Reaction conditions: the same as those described in Table 2 in the main text. [b] Amount of **3A**, **1b**, and **1c** were determined from the calibration curve of **A** that was synthesized by following the procedure reported in the literature.[S3]

6. Temperature controlled photocatalytic cross-coupling between cyclohexene and THF

As mentioned in the main text, to clarify the catalysis by the metal nanoparticles loaded on the TiO_2 surface, the effect of temperature on the photocatalytic reaction was studied. The photocatalytic reactions were performed at different temperatures, which was maintained by using a water bath. After the reactions, the product analysis was done at room temperature, following the same procedure as mentioned in the main text. Table S7 shows the results of the temperature control reactions for the reaction between cyclohexene and THF over the Pt(0.1)/TiO_2 photocatalyst and the pristine TiO_2 photocatalyst, respectively, and Fig. S4a and S4b show the corresponding pseudo Arrhenius plots. For the reactions carried out with the Pt(0.1)/TiO_2 sample, the conversion increased with temperature. The selectivity to the cross-coupling products based on THF (S_{THF}) slightly increased with temperature (Table S7, entries 1–4) while that based on cyclohexene (S_{cy}) initially decreased but remained constant later. For the reactions done with the TiO_2 sample, small increases in conversion and S_{THF} were observed but S_{cy} remained unchanged (Table S7, entries 5–8). Other details were discussed in the main text.

Table S7 Temperature control photocatalytic cross-coupling between cyclohexene and THF with the Pt(0.1)/TiO_2 sample and the bare TiO_2 sample [a]

Entry	Photocatalyst	Temperature / K	Cross-coupling products / μmol			Homocoupling products / μmol		Cross-coupling selectivity (%)	
			A	**B**	**C**	**1a**	**1b+1c+1d**	S_{cy}	S_{THF}
1	Pt(0.1)/TiO_2	300	2.98	1.94	1.66	0.0	15.89	100	29
2		310	4.27	2.19	1.76	0.95	13.59	89	38
3		314	5.13	2.85	2.51	1.27	17.75	89	37
4		318	5.76	3.19	2.58	1.42	15.89	89	42
5	TiO_2	300	0.42	0.15	0.13	0.0	0.55	100	56
6		304	0.53	0.18	0.12	0.0	0.57	100	59
7		309	0.56	0.15	0.17	0.0	0.54	100	61
8		314	0.65	0.21	0.16	0.0	0.47	100	68

[a] 0.5 mL cyclohexene, 3 mL THF, other conditions and abbreviations were same as Table 2.

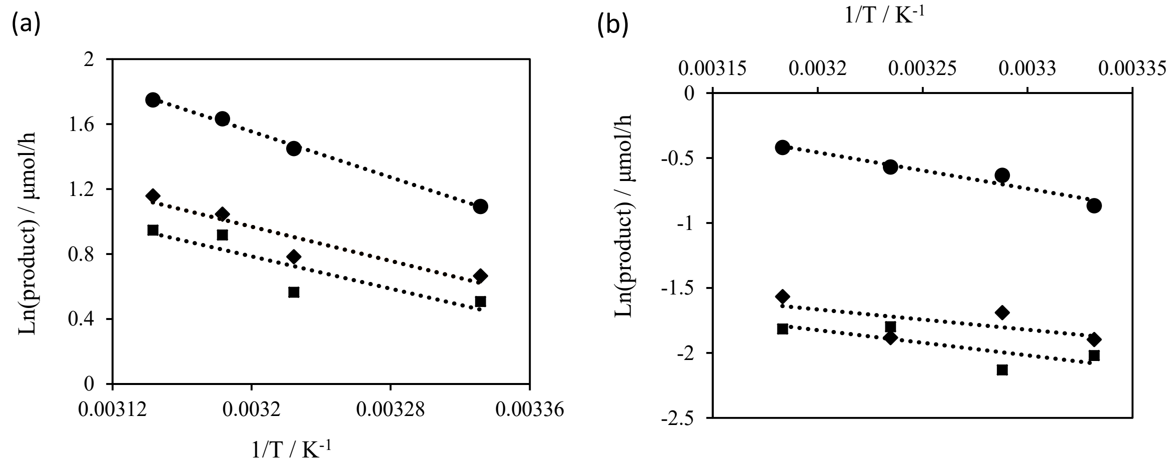


Fig. S4 Pseudo Arrhenius plot for the photocatalytic cross-coupling between cyclohexene and THF to give **A** (circle) **B** (diamond), and **C** (square) with (a) the Pt(0.1)/TiO_2 sample and (b) the bare TiO_2 sample.

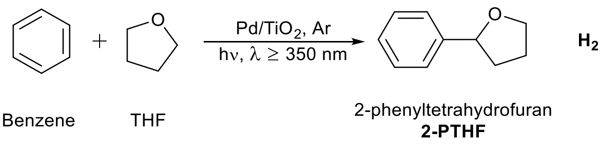
7. Photocatalytic cross-coupling with physical mixture of catalysts

The cross-coupling reactions of other hydrocarbons, i.e., benzene and cyclohexane, with THF were examined with a physical mixture of the TiO_2 photocatalyst and the M(x)/Al_2O_3 catalyst. The two catalyst samples were taken into the Pyrex test tube and irradiated during the pre-treatment. The remaining procedure was same as mentioned in the main text.

7.1. Benzene–THF system

Table S8 shows the results for the reaction between benzene and THF to give 2-phenyltetrahydrofuran (**2-PTHF**), along with a small amount of homocoupling products of THF (**1b** and **1c**, the amounts are not shown) performed with various catalyst samples including a physical mixture of the photocatalyst and the metal catalyst. 2-PTHF was not obtained in the reaction performed with a pristine TiO_2 sample (Table S8, entry 1). The metal loaded TiO_2 photocatalysts provided **2-PTHF**, where the Pd/TiO_2 photocatalyst exhibited higher activity than the Pt/TiO_2 photocatalyst (Table S8, entries 2 and 3). Introduction of the M(x)/Al_2O_3 (M: Pd, Pt) sample to the reaction system with the TiO_2 photocatalyst was not helpful for the production of 2-PTHF (Table S8, entries 4 and 5). On the other hand, using a reduced Pd/Al_2O_3 sample with the TiO_2 photocatalyst gave 2-PTHF (Table S8, entry 6). Further, the 2-PTHF was not obtained in the reaction done with the reduced Pd/Al_2O_3 sample alone (Table S8, entry 7). These results indicate that the reaction between benzene and THF is a hybrid catalysis of the TiO_2 photocatalysis and the Pd metal catalysis.

Table S8 Photocatalytic dehydrogenative cross-coupling between benzene and THF with different catalysts [a]



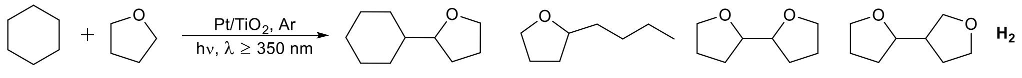
Entry	Catalyst	Amount of **2-PTHF** / µmol [b]
1	TiO_2	0.0
2	Pt(0.1)/ TiO_2	8.5
3	Pd(0.1)/ TiO_2	14.9
4 [c]	TiO_2 + Pd(0.1)/Al_2O_3	0.0
5 [c]	TiO_2 + Pt(0.1)/Al_2O_3	0.0
6 [d]	TiO_2 + red-Pd(0.1)/Al_2O_3	9.3
7 [e]	red-Pd(0.1)/Al_2O_3	0.0

[a] Reaction conditions: 2mL (22.4 mmol) of benzene, 2 mL (24 mmol) of THF, and 50 mg of the photocatalyst were used. The reaction time was 1 h; remaining conditions were the same as those shown in Table 2. [b] Amount of 2-PTHF was determined from the calibration curve of an authentic sample of 1-ethoxyethylbenzene. [c] 50 mg each of the TiO_2 photocatalyst and the M(0.1)/Al_2O_3 (M: Pd, Pt) catalyst were used. [d] The Pd(0.1)/Al_2O_3 sample was reduced under H_2 (100%, flow rate: 15 mL/min) for 30 min at 573 K. [e] Reaction was performed with the reduced Pd(0.1)/Al_2O_3 sample under photoirradiation.

7.2. Cyclohexane–THF system

Table S9 shows the results for the reaction between cyclohexane and THF to give 2-cyclohexyltetrahydrofuran (**2-CTHF**), along with the homocoupling products of THF (**1a** and **1b**, the amounts are not shown) performed with various catalysts. A very small amount of **2-CTHF** was obtained in the reaction performed even with the pristine TiO_2 sample (Table S9, entry 1). The Pt/TiO_2 sample exhibited high activity for the formation of **2-CTHF**, while the Pd/TiO_2 sample was inactive (Table S9, entries 2 and 3). Unlike the reaction with benzene, introduction of the M(x)/Al_2O_3 (M: Pd, Pt) sample to the reaction system with the TiO_2 photocatalyst promoted the formation of **2-CTHF** and introduction of the Pd/Al_2O_3 sample was more active than the Pt/Al_2O_3 sample (Table S9, entries 4 and 5). It may be surprising that the Pd/Al_2O_3 catalyst exhibited higher activity than the Pd/TiO_2 photocatalyst. To confirm these results, we prepared SiO_2 (JRC-SIO-9) supported Pd catalyst (Pd(0.1)/SiO_2) by an impregnation method and examined its catalytic activity for photocatalytic cross-coupling between cyclohexane and THF (Table S9, entry 6). The addition of the Pd(0.1)/SiO_2 catalyst to the TiO_2 photocatalyst promoted the formation of **2-CTHF**. These results show that, for this reaction, the Pd nanoparticles were inactive on TiO_2 but showed activity on other supports like Al_2O_3 and SiO_2. However, the reason for this behavior is not clear and requires further study. Also, **2-CTHF** was not obtained in the reaction done with the Pd/Al_2O_3 sample alone with photoirradiation (Table S9, entry 7). These results indicate that the reaction between cyclohexane and THF was also a hybrid catalysis of metal catalysis and TiO_2 photocatalysis. However, as the yield of **2-CTHF** obtained with Pt/TiO_2 photocatalyst is much larger than the physically mixed TiO_2 photocatalyst and M(*x*)/Al_2O_3 catalyst, it can be proposed that the major route for the formation of **2-CTHF** is photocatalyzed and the metal catalysis contributes to a small extent.

Table S9 Photocatalytic dehydrogenative cross-coupling between cyclohexane and THF with different catalysts [a]



Cyclohexane THF 2-cyclohexyltetrahydrofuran **2-CTHF** **1a** **1b** **1c**

Entry	Catalyst	Amount of **2-CTHF** (μmol) [b]
1	TiO_2	0.2
2	Pt(0.1)/ TiO_2	1.4
3	Pd(0.1)/ TiO_2	0.0
4 [c]	TiO_2 + Pt(0.1)/Al_2O_3	0.3
5 [c]	TiO_2 + Pd(0.1)/Al_2O_3	0.7
6 [d]	TiO_2 + Pd(0.1)/SiO_2	0.8
7 [e]	Pd(0.1)/Al_2O_3	0.0

[a] Reaction conditions: 3 mL (27.7 mmol) cyclohexane, 10 μl (123 μmol) THF, and 50 mg of photocatalyst were used, and the reaction time was 1 h; remaining conditions were the same as those shown in Table 2. [b] Amount of **2-CTHF** was determined from the calibration curve of an authentic sample of 2-CTHF. [c] 50 mg each of the TiO_2 photocatalyst and the M(0.1)/Al_2O_3 sample were used. [d] 50 mg each of the TiO_2 photocatalyst and the Pd(0.1)/SiO_2 sample was used. [e] Reaction was performed with the Pd(0.1)/Al_2O_3 sample under irradiation.

References

[S1] Z. Tian, A. Fattahi, L. Lis, S. R. Kass, *J. Am. Chem. Soc.*, 2006, **128**, 17087.

[S2] Y. R. Luo, in Handbook of Bond Dissociation Energies in organic compounds, CRC Press, 2002.

[S3] X. Jiang, E. K. London, D. J. Morris, G. J. Clarkson, M. Wills, *Tetrahedron*, 2010, **66**, 9828.

[S4] J. J. P. Stewart, MOPAC2016; Stewart Computational Chemistry, Colorado Springs, CO, USA, see http://OpenMOPAC.net (2016).

[S5] J. J. P. Stewart, *J. Mol. Model.*, 2013, **19**, 1.