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Photocatalytic Minisci-type functionalization of pyridine with tetrahydrofuran (THF) proceeded using hydrogen peroxide ( $H_2O_2$ ) and a TiO<sub>2</sub> photocatalyst under acidic conditions. Under UV light ( $\lambda$  = 360 nm), the reaction selectivity based on pyridine ( $S_{py}$ ) was >99% while the selectivity based on THF ( $S_{THF}$ ) was low such as 19%. In contrast, under visible light ( $\lambda$  = 400 or 420 nm)  $S_{py}$  was similarly high (>99%) and  $S_{THF}$  was two times higher than that under UV light. A surface peroxo complex formed upon contact of hydrogen peroxide with the TiO<sub>2</sub> surface can be selectively photoexcited by visible light to inject the photoexcited electron to the conduction band of TiO<sub>2</sub>. The electron can reduce  $H_2O_2$  to a reactive oxygen species (ROS) and promote selectively the Minisci-type cross-coupling reaction between pyridinium ions and THF. A reaction test with a hole scavenger (methanol) evidenced that the hole oxidation of  $H_2O_2$  under UV light is responsible for the lower selectivity, in other words, the higher selectivity under visible light would be due to suppression of the hole oxidation of  $H_2O_2$ . These results demonstrate a novel way to improve the selectivity of the photocatalytic cross-coupling reaction by using  $H_2O_2$  as an oxidant with the photoexcitation of surface Ti-peroxo species on TiO<sub>2</sub>.

# 1. Introduction

dioxide  $(TiO_2)$ , Titanium the first semiconductor photocatalyst, has attracted much attention as one of the most practical photocatalysts with high oxidation ability, chemical stability, and low cost.<sup>1,2</sup> In a typical oxidation process with a TiO<sub>2</sub> photocatalyst, reactive oxygen species (ROS) such as hydrogen peroxide, hydroxyl radicals, and superoxide anion radicals, have been considered as key intermediates,<sup>3,4</sup> which are strongly correlated with the efficiency of the system.<sup>5</sup> For instance, hydrogen peroxide can be used to accelerate the formation of hydroxyl radicals and improve the activity in photocatalytic degradation of organic wastes.6

There is no doubt that these ROS formed with a  $TiO_2$  photocatalyst are available for not only degradation but also other synthetic reactions such as oxidative cross-coupling

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reactions, which are one of the most important reactions to build a carbon–carbon bond in organic molecules. Only a few studies, however, have been reported for oxidative crosscoupling reactions so far<sup>7,8</sup> because of low selectivity. To apply  $TiO_2$  photocatalysis to cross-coupling at high ROS concentration, the selectivity of the coupling must be improved.

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One of the ways to improve the selectivity of TiO<sub>2</sub> photocatalysis is to use photoexcitation of a ligand-to-metal charge transfer (LMCT) complex consisting of adsorbed molecules and the surface of a photocatalyst.9 LMCT complex systems have achieved several selective photooxidation reactions of various compounds such as alcohols,10 amines,<sup>11,12</sup> and sulphides.<sup>13</sup> Recently, we found that the LMCT system can also be applied to sp<sup>2</sup>C-sp<sup>3</sup>C cross-coupling between an aromatic ring and an alkane through the LMCT of aromatic surface complexes.14,15 In the present study, we utilized the LMCT excitation of a surface peroxo complex on TiO<sub>2</sub> to achieve high selectivity of photocatalytic organic transformation involving the generation of ROS. We chose the functionalization Minisci-type of pyridine with tetrahydrofuran (THF) by using hydrogen peroxide under acidic conditions as the first trial (eqn (1)).8 The effect of irradiation wavelength on the reaction was investigated and

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several scavenging tests were also carried out to clarify the reaction mechanism. We found that that selective excitation of the peroxo surface complex by visible light can improve the selectivity of cross-coupling by suppressing the undesired oxidation of  $H_2O_2$ .

$$\left( \bigcup_{N} + \bigcup_{i=1}^{O} + 2H_2O_2 \xrightarrow{\text{TFA}} \left( \bigcup_{i=1}^{O} + 3H_2O + 1/2O_2 \right) \right) + 3H_2O + 1/2O_2$$
(1)

## 2. Experimental

#### 2.1 Catalysts

Three TiO<sub>2</sub> powder samples donated by the Catalysis Society of Japan were employed: JRC-TIO-6 (rutile phase, 100 m<sup>2</sup> g<sup>-1</sup>), JRC-TIO-14 (anatase phase, 338 m<sup>2</sup> g<sup>-1</sup>), and JRC-TIO-4 (a mixture of rutile and anatase phases,  $50 \pm 15 \text{ m}^2 \text{ g}^{-1}$ ).

In some experiments, a Pd-loaded TiO<sub>2</sub> catalyst prepared by a photodeposition method (ESI†) was used since our previous studies showed the positive effect of a Pd cocatalyst on some organic reactions.<sup>16–18</sup> The catalysts were referred to as Pd(x)/TiO<sub>2</sub>, where x indicates the loading amount of the metal in wt%.

#### 2.2 Reaction test

**2.2.1 Materials.** All the chemicals employed for the photocatalytic reaction tests were of analytical grade and were used without further purification: pyridine (Nacalai Tesque, 99.7%), tetrahydrofuran (THF, Nacalai Tesque, >99.5%), hydrogen peroxide (Nacalai Tesque, 30%), trifluoroacetic acid (TFA, Santa Cruz Biotechnology, >99%), difluoroacetic acid (Aldrich, 98%), acetic acid (Nacalai Tesque, 99%), trifluoroethanol (Tokyo Chemical Industry, >99%), and tribromoacetic acid (Aldrich, 99%).

After performing optimization experiments for additives,  $H_2O_2$  and acid (Tables S1–S3, ESI†), 0.2 mmol of  $H_2O_2$  and 0.2 mmol of TFA were employed for further experiments.

2.2.2 Procedure for the reaction tests. The typical procedure is as follows. Before a photocatalytic reaction test, a photocatalyst sample (TiO<sub>2</sub> or Pd(0.1)/TiO<sub>2</sub>, 50 or 100 mg) in a Pyrex glass tube (20 or 50 mL) was subjected to pre-treatment for 30 min under the light from a ceramic xenon lamp (PE300BUV, 300 W) to clean its surface. Then, a reaction mixture (2.05 mL in total) of pyridine, THF,  $H_2O_2$  aqueous solution (30%), and TFA was added into the test tube. The resultant mixture was a yellowish suspension (Fig. S1, ESI<sup>†</sup>). After that, the test tube was sealed with a rubber septum and the mixture was bubbled by argon for 10 min under magnetic stirring to remove air. The reaction mixture was irradiated by using another 300 W xenon lamp (Asahi Spectra Co., Ltd. MAX-302) with stirring for a desired reaction time at room temperature. The irradiation wavelength was limited by a bandpass filter (MX0360 ( $\lambda$  = 360 ± 10 nm), MX0400 ( $\lambda$  = 400 ± 10 nm), MX0420 ( $\lambda$  = 420 ± 10 nm)). After irradiation, 0.5 mL of the gaseous phase was collected using an air-tight syringe and analyzed by GC-TCD (Shimadzu, GC-8A). The reaction mixture in the liquid phase was sampled using a syringe with a PTFE filter to remove the photocatalyst, and then analyzed by GC-MS (Shimadzu, GCMS-QP2020). The analysis was carried out without neutralization.

The desired product, tetrahydrofuranylpyridine (TP), was quantified by using a GC-MS calibration curve of 2-cyclohexylpyridine. Three peaks for the isomers of TP were obtained and their peak areas were always in a ratio of 3:1: 1, the sum of which was treated as the desired products (TPs) in the present study and used to calculate the TP yield in the reaction tests. By-products observed were some oxidized THF (OTs: 2-hydroxytetrahydrofuran,  $\gamma$ -butyrolactone, and  $\alpha$ -hydroxy- $\gamma$ -butyrolactone), which were quantified using the calibration curve of authentic samples purchased from companies. The remaining H<sub>2</sub>O<sub>2</sub> in the reaction mixture was quantified by iodometry (ESI†).

#### 2.3 Diffuse reflectance UV-vis spectroscopy

UV-vis spectra of the powder samples were recorded in a diffuse reflectance (DR) mode. The samples were diluted 100 times with BaSO<sub>4</sub>. For the samples with an adsorbate, 50  $\mu$ L of the reaction mixture (a mixture of pyridine, THF, TFA, and H<sub>2</sub>O<sub>2</sub> aq.) or 30% H<sub>2</sub>O<sub>2</sub> aqueous solution was added to the diluted samples, followed by 10 min of mixing. Then, the desired amount of the sample was taken into the cell so as to fix the amount of TiO<sub>2</sub> in the samples and the spectrum was measured using a UV-vis spectrophotometer (JASCO V-570) equipped with an integrating sphere, where BaSO<sub>4</sub> was used as a reference.

## 3. Results and discussion

Several experiments showed that a  $Pd(0.1)/TiO_2(rutile)$  sample was the best photocatalyst among the Pd-loaded samples (Tables S4 and S5, ESI†). The Pd cocatalyst with an optimal loading amount (0.1 wt%) increased the photocatalytic production of the aimed coupling products (1.8 times) with a slightly lower selectivity (Table S4†). However, to simplify the discussion for spectroscopic results and the reaction mechanism, the results of bare TiO<sub>2</sub>(rutile) were mainly shown rather than the results with Pd/TiO<sub>2</sub> samples (Tables S1–S6, and Fig. S3†) in the present study.

#### 3.1 Diffuse reflectance UV-vis spectroscopy

The visible-light responsive species in this system was first confirmed by diffuse reflectance UV-vis spectroscopy (Fig. 1). The TiO<sub>2</sub> (rutile) sample in the presence of the reaction mixture (pyridine, THF, and TFA) without  $H_2O_2$  was white and its spectrum (Fig. 1b) was almost similar to that of the sample without the reaction mixture (Fig. 1a), where the increase in the baseline was probably due to the liquid phase. This suggests that a reported surface complex formed with an acid–base interaction between a pyridine molecule and a Ti cation on the TiO<sub>2</sub> surface<sup>15</sup> is not the case under the present acidic conditions. This would be due to protonation of pyridine molecules by the acid (TFA). In



Fig. 1 DR UV-vis spectra of (a) the rutile  $TiO_2$  sample diluted with  $BaSO_4$ , (b) the diluted sample with the reaction mixture (pyridine, THF, TFA) except for  $H_2O_2$ , and (c) that with the reaction mixture including  $H_2O_2$ .

contrast, the  $H_2O_2$  containing sample was yellowish and its spectrum showed an additional visible-light absorption band in the wavelength range of 400–500 nm compared with the other two samples (Fig. 1c). This is attributed to the presence of surface Ti-peroxo species.<sup>19</sup>

It is reported that  $H_2O_2$  is adsorbed on  $TiO_2$  to form some surface Ti-peroxo species and changes the catalyst's color into yellow,<sup>19</sup> which was confirmed also on the three TiO<sub>2</sub> samples employed here (Fig. S2<sup>†</sup>). Three types of surface peroxo species have been proposed: end-on, bridged,<sup>20</sup> and side-on (Scheme 1).<sup>21,22</sup> The former two species exist mainly on anatase  $TiO_2$ , while the latter does on rutile  $TiO_2$ .<sup>21</sup> The color change by H<sub>2</sub>O<sub>2</sub> adsorption was also observed in zeolitic titanium-silicate systems<sup>23</sup> and the side-on peroxo is regarded as the visible-light responsive species because of its similar spectroscopic features with the model compound.<sup>24</sup> Thus, it is suggested that the visible-light responsive species in the present system with the rutile TiO<sub>2</sub> sample is the side-on species. The end-on species is another candidate since the side-on species would be protonated under acidic conditions in the presence of TFA (eqn (2)). Since  $TiO_2$  is excited by UV light only, the reaction under visible light would start from the photoexcitation of the surface peroxo species.

$$O_2$$
-Ti (side-on) + H<sup>+</sup>  $\rightleftharpoons$  HOO-Ti (end-on) (2)

#### 3.2 Reaction test

Next, reaction tests were carried out using the pristine rutile  $TiO_2$  sample (JRC-TIO-6) under the light of variously limited wavelength (Table 1). The reaction took place under UV light



**Scheme 1** Possible structures of surface Ti-peroxo species: (a) endon, (b) bridged, and (c) side-on.

 $(\lambda = 360 \pm 10 \text{ nm})$  and afforded 1.8 µmol of tetrahydrofuranylpyridine (TP) as the cross-coupling product, which corresponds to 0.85% yield in 1 h (Table 1, entry 1). By-products from pyridine such as 2,2'-bipyridyl, 2,3'-bipyridyl, and 2,4'-bipyridyl were not observed. This means that the selectivity to TPs based on pyridine  $(S_{py})$  was >99%. On the other hand, 6.8 µmol of some oxidized by-products of THF (OTs) was obtained, in which the selectivity to TPs based on THF  $(S_{THF})$  was low such as 19% even in the initial stage of the reaction.

When the reaction test was carried out under visible light ( $\lambda$ =  $400 \pm 10$  nm, Table 1, entry 2), the amount of the products was higher than that under UV light due to higher light intensity from the lamp; 8.6 µmol of TPs and 15 µmol of OTs were produced. The yield and  $S_{\text{THF}}$  were five and two times higher than that under UV-light such as 4.3% and 37%, respectively. The TP selectivity based on pyridine was as high as the case under UV light ( $S_{pv} > 99\%$ ). The reaction proceeded even under longer-wavelength light ( $\lambda = 420 \pm 10$  nm) and the selectivity obtained was the highest (such as 40%) among them (Table 1, entry 3). The higher S<sub>THF</sub> under visible light than that under UV light means that the formation of OTs was suppressed under visible light irradiation. The amount of H<sub>2</sub>O<sub>2</sub> in the solution was decreased after reaction in all cases. The yield of TPs was drastically decreased in the absence of H<sub>2</sub>O<sub>2</sub> under both UV and visible light (Table 1, entries 4 and 5), which indicates that H<sub>2</sub>O<sub>2</sub> as an oxidant is essential for the production of TPs. The reaction also hardly proceeded in an air atmosphere without H<sub>2</sub>O<sub>2</sub> under UV light (Table 1, entry 6). TPs were not produced in the absence of TFA under both light conditions (Table 1, entries 7 and 8), suggesting that TPs are formed through a Minisci-type mechanism, which involves protonation of pyridine by TFA, an attack of a THF radical to a pyridinium ion (discussed below), and subsequent elimination of a hydrogen atom (Scheme 2). The active species produced from H<sub>2</sub>O<sub>2</sub> could promote the production of THF radicals.

In these reaction tests (Table 1, entries 1–3), the amount of consumed H<sub>2</sub>O<sub>2</sub> was much larger than the product yield. Thus, it must be noted that H<sub>2</sub>O<sub>2</sub> molecules and the surface peroxo species would largely decompose during the reaction. We carried out a long-term reaction test under visible light (Fig. 2), where the reaction scale was two times larger than usual. The reaction stopped and the yellowish color of the catalyst disappeared after 8 h when the yield of TPs and conversion of H2O2 reached 14% and 81%, respectively. As suggested from the result of DR UV-vis spectroscopy, the reaction under visible light would start not from the photoexcitation of the TiO<sub>2</sub> photocatalyst but the photoexcitation of the surface Ti-peroxo species. The termination of the reaction with decolorization also indicates that the surface peroxo species is necessary to promote the reaction under visible-light irradiation, i.e., the reaction cannot proceed without the surface peroxo species. Since the peroxo species would be present on the surface in equilibrium with the  $H_2O_2$  molecules in the liquid phase,<sup>23</sup> it

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Table 1 Results of the reaction tests under photoirradiation with the light of variously limited wavelength<sup>a</sup>

→0 H<sub>2</sub>O O<sub>2</sub>

TIO2

 $\uparrow^0$  H<sub>2</sub>O<sub>2</sub>

	Additive/r	nmol			Products <sup>c</sup>	/µmol				Selectivity	f(%)
Entry	$H_2O_2$	TFA	λ/nm	Light intensity <sup>b</sup> /mW cm <sup>-2</sup>	TPs	OTS	Consumed H <sub>2</sub> O <sub>2</sub> <sup>d</sup> /μmol	Yield of TPs <sup>e</sup> (%)	Conversion of $H_2O_2$ (%)	$S_{\rm py}$	STHF
1	0.2	0.2	360	1	1.8	6.9	63	0.85	31	>99	19
2	0.2	0.2	400	6	8.6	15	100	4.3	50	$^{>99}$	37
3	0.2	0.2	420	13	6.9	10	82	3.5	41	$^{>99}$	40
4	0	0.2	360	1	0.14	1.8	Ι	0.068	Ι	$^{>99}$	7.1
5	0	0.2	420	13	0.26	1.8	Ι	0.13	I	$^{>99}$	12
$e^{h}$	0	0.2	360	1	$\mathrm{n.d.}^g$	$\mathrm{n.d.}^g$	I	0	Ι	0	0
7	0.2	0	360	1	$\mathrm{n.d.}^{g}$	16	81	0	40	0	0
8	0.2	0	420	13	$\mathrm{n.d.}^g$	22	97	0	49	0	0
6	0.2	0.2	Dark		$\mathrm{n.d.}^g$	3.4	18	0	9.2	0	0
$10^{i}$	0.2	0.2	Dark		$\mathrm{n.d.}^{g}$	3.6	12	0	5.9	0	0
11	0.2	0	Dark		$\mathrm{n.d.}^g$	8.1	54	0	27	0	0
$12^{j}$	0.2	0	Dark		$\mathrm{n.d.}^g$	11	82	0	41	0	0
<sup><i>a</i></sup> Reaction and the re $415 \pm 55$ 1 <sup><i>d</i></sup> The amo introduce was calcul	a conditions: I eaction time w im for 400 or ount of consu d pyridine. $^{f}$ S lated as $S_{THF} =$	yridine (0.2 as 1 h. The 1 420 nm visib med $H_2O_2$ af electivity to 7 [100 × TPs (	mmol), THF ( reaction tests <sup>1</sup> he light. <sup>c</sup> TPs: ter reaction ce TPs. The selec TPs. The selec (µmol)]/[(TPs +	24 mmol), 30% H <sub>2</sub> O <sub>2</sub> aq. (0–2: were carried out in a Pyrex test : total amount of tetrahydrofu alculated as (amount of added tivity based on pyridine was c: - OTs) (µmol)]. <sup>8</sup> Not detected.	2.5 $\mu$ l, 0–0.2 1 t tube (20 mJ ranylpyridine I H <sub>2</sub> O <sub>2</sub> ( $\mu$ mol alculated as $\lambda$ <i>h</i> Reaction in	mmol of $H_2O(L)$ . <sup>b</sup> The light L). <sup>b</sup> The light . OTs: total a: ()) – (amount $S_{py} = [100 \times T)$ n an air atmo	2), and TFA (0–0.2 million intensity was measured of $H_{2}O_{2}$ in the reaction of $H_{2}O_{2}$ in the reaction $Ps (\mu mol)]/[(TPs + by sphere.4 Reaction times the section times of the section $	nol) with the TiO <sub>2</sub> p red at wavelengths ( trahydrofuran, $\gamma$ -but on solution after res -products from pyric ne was 8 h. <sup>J</sup> Reactio	hotocatalyst (JRC-TIO of 355 $\pm$ 45 nm for 36( yrolactone, and $\alpha$ -hyd action (µmol)). <sup>e</sup> Yield dine) (µmol)]; the sele nn time was 4 h.	-6, 50 mg) we 0 nm UV ligh Iroxy-y-butyro of TPs based ctivity based	tre used t and at lactone. l on the on THF

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**Scheme 2** Minisci reaction between pyridine and THF in the presence of TFA. 2,2'-Tetrahydrofuranylpyridine was chosen as a representative example for TPs.

should almost disappear when the  $H_2O_2$  concentration in the liquid phase decreased. As another possibility, the surface peroxo species might decompose during the reaction. An additional long-term reaction test was carried out with a Pd loaded sample (Fig. S3, ESI†), followed by the addition of  $H_2O_2$  after 12 h. It was found that the catalyst's color and activity were restored with the addition of 0.4 mmol of  $H_2O_2$  after the reaction termination. This indicates that the surface Ti-peroxo species can be regenerated when  $H_2O_2$  was supplied. However, further addition of  $H_2O_2$  after 21 h did not improve the yield but promoted a successive reaction to give several bifunctionalized pyridines with two THF molecules (Fig. S3, ESI†). This means that the products should be separated before the successive reaction takes place to obtain a higher yield.

Under visible light, ligand-to-metal-charge-transfer (LMCT) takes place in the Ti-peroxo species to transfer an electron from its peroxo oxygen (O<sup>-</sup>) to the Ti(IV) cation, producing O<sup>-</sup> (hole) and the Ti(III) cation (electron) in the surface complex (Scheme 3).<sup>23</sup> The photoexcited electron would be further transferred to the conduction band of TiO<sub>2</sub> to react with the substrates. It is reported that visible-light excitation of surface Ti-peroxo species produces a hydroxyl radical in the H<sub>2</sub>O<sub>2</sub>-TiO<sub>2</sub> system through the reduction of a H<sub>2</sub>O<sub>2</sub> molecule in the liquid phase by the photoexcited electron (eqn (3)).<sup>25</sup> Therefore, it is also possible that the photogenerated electron formed from the Ti-peroxo species through LMCT excitation reduces another H<sub>2</sub>O<sub>2</sub> molecule to produce a hydroxyl radical. This hydroxyl radical would be the major active species for

0

10

20

30

40

50

60

70

80

90

100

20

П

Conversion of H<sub>2</sub>O<sub>2</sub> (%)



10 12 14 16 18

8

$$\begin{array}{c} 0 - 0 \\ \downarrow i \\ Ti^{4+} \end{array} \xrightarrow{h\nu} \begin{array}{c} 0 - 0 \\ \downarrow i \\ Ti^{3+} \end{array}$$



the reactions under visible light. The hole (O') would also activate the substrates or decompose the surface Ti-peroxo species. The higher selectivity under visible light than that under UV light suggests the presence of the decomposition pathway before the oxidation of the substrates to OTs.

Under UV light, TiO<sub>2</sub> is excited to generate photogenerated electrons and holes in TiO<sub>2</sub>, which can activate the substrates. The photogenerated electrons and holes would react with  $H_2O_2$  and THF to produce radical species such as a hydroxyl radical ('OH), a hydroperoxyl radical (HO<sub>2</sub>'), and a THF radical ('C<sub>4</sub> $H_7O$ ) (eqn (3)–(5)). Thus, under UV light conditions, these radical species would form some kinds of oxidation products (OTs) as the major by-products. Meanwhile, hole oxidation of pyridine would be difficult since pyridine molecules are in a cationic form. The hydroxyl radical and the hydroperoxyl radical accelerate the production of 2-hydroxytetrahydrofuran (eqn (7) and (8)), of which subsequent oxidation gives other OT species.

$$H_2O_2 + e^- \rightarrow OH + OH^-$$
(3)

$$H_2O_2 + h^+ \rightarrow HO_2 + H^+$$
(4)

$$C_4H_8O(THF) + h^+ \rightarrow C_4H_7O + H^+$$
(5)

$$C_4H_8O(THF) + OH \rightarrow C_4H_7O + H_2O$$
 (6)

$$C_4H_7O + OH \rightarrow C_4H_8O_2(OTs)$$
(7)

$$C_4H_7O + HO_2 \rightarrow C_4H_8O_2(OTs) + 1/2O_2$$
 (8)

When the reaction test was carried out in the dark, OTs were initially produced with the consumption of H2O2 (Table 1, entry 9) but the amount of OTs did not increase with time (Table 1, entry 10). On the other hand, the amounts of OTs and consumed H2O2 were larger in the absence of TFA in the dark (Table 1, entry 11) and they increased with time (Table 1, entry 12). This means that OTs can be produced upon decomposition of H<sub>2</sub>O<sub>2</sub>, and TFA suppresses the decomposition. OTs would be produced from a reaction between THF and 'OH adsorbed on the TiO<sub>2</sub> surface.<sup>26</sup> TFA would suppress the decomposition of  $H_2O_2$  by poisoning the active sites on the TiO<sub>2</sub> surface. The suppression effect was also observed in the reaction under UV light (Table 1, entries 1 and 7) or visible light (Table 1, entries 3 and 8). Since TFA also promotes the production of TPs as mentioned above, the roles of TFA in the present system are as follows: protonation of pyridine for the Minisci reaction and suppression of thermal decomposition of H<sub>2</sub>O<sub>2</sub>.

20

15

10

5

0

0 2 4 6

Yield of TPs (%)

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Fig. 3 Difference of the photogenerated hole between the band-toband transition in  $TiO_2$  (A) and the LMCT transition in the surface Tiperoxo species (B).

#### 3.3 Scavenging test

UV light irradiation induces band-to-band transition in  $TiO_2$ (Fig. 3A) while visible light irradiation promotes LMCT transition in the surface Ti-peroxo species (Fig. 3B). In both cases, the photoexcited electron is generated in the conduction band of  $TiO_2$  while the hole is generated in the valence band of  $TiO_2$  in the former case and on the surface peroxo species in the latter case. The presence of the photoexcited electrons in the conduction band of  $TiO_2$  is necessary and enough to promote the aimed coupling reaction since they can activate hydrogen peroxide to start the reaction through the formation of a hydroxyl radical and then a THF radical, as mentioned above. The properties of the excited electron are common in both cases. Thus, the different selectivities under different wavelength-light would be due to the different properties of the photogenerated hole.

If that is the case, the selectivity under UV light might be improved by suppressing the hole oxidation of the substrates. Therefore, we carried out some reaction tests under UV light in the presence of methanol as a hole scavenger (Table 2, entries 2 and 3). As expected, the production of OTs was suppressed with increasing the amount of methanol, leading to higher selectivity such as 46% with 16 mmol of methanol (Table 2, entry 3).  $H_2O_2$  consumption was also suppressed by the addition of methanol. Although alcohols can also promote Minisci-coupling,<sup>27,28</sup> such kinds of products were not observed. Methanol can consume the hole efficiently and suppress the oxidation of the substrates sacrificially. The increase in the selectivity with the suppression of  $H_2O_2$  consumption indicates that the oxidation of  $H_2O_2$  (eqn (4)) is responsible for the formation of by-products. In addition, the yield of TPs was not changed so much by the addition of methanol. It indicates that methanol consumed only holes on TiO<sub>2</sub> selectively and the photoexcited electrons were used for TP formation (eqn (3)).

Instead of methanol, the addition of 2-propanol was examined under UV light irradiation. 2-Propanol is often used as a hydroxyl radical scavenger while in some cases it is regarded as a hole scavenger. As a result, the amount of obtained OTs increased from 6.9 to 11 (Table 2, entry 4), which is opposite to the case of methanol addition. It is clarified that 2-propanol cannot act as a hole scavenger under the present conditions although the reason for the increase was uncovered. On the other hand, the obtained TPs decreased from 1.8 to 1.2 umol (Table 2, entry 4), meaning that 2-propanol reacted with a hydroxyl radical in this system in competition with THF. This also confirms that the hydroxyl radical participates in the formation of TPs; the hydroxyl radical would produce a THF radical which attacks a protonated pyridine. Therefore, it is suggested that the THF radical is generated mainly from the reaction of THF with the hydroxyl radical (eqn (6)), not with the photogenerated hole (eqn (5)). This would be due to the high reactivity of THF with the hydroxyl radical. The rate constant for the reaction with the hydroxyl radical in aqueous solution is higher for THF  $(4.0 \times 10^9)$  than that for 2-propanol  $(1.9 \times 10^9)$ ,<sup>29</sup> which is a well-known hydroxyl radical scavenger and used in the present study. Therefore, THF would mainly react with the hydroxyl radical before reacting with the photogenerated hole.

Scavenging tests were also carried out under visible light to obtain further insight into the reaction mechanism (Table 3). The yield of TPs decreased with increasing the amount of 2-propanol (Table 3, entries 1–3) as in the case under UV-light, confirming that the hydroxyl radical activates THF to form TPs. The yield of TPs also decreased with increasing the amount of an electron scavenger, AgNO<sub>3</sub> aqueous solution (Table 3, entries 1 and 4–6), while the

Table 2 Effect of a hole scavenger (MeOH) and a hydroxyl radical scavenger (2-PrOH) on the product yield and the amount of consumed  $H_2O_2$  after the reaction under UV light<sup>*a*</sup>

			Products <sup>b</sup> /	μmol	Consumed	Selectivity <sup>d</sup>	(%)
Entry	Scavenger/mm	ol	TPs	OTs	$H_2O_2^{\ c}/\mu mol$	$S_{\rm py}$	$S_{\mathrm{THF}}$
1	_		1.8	6.9	63	>99	19
2	MeOH	8	1.7	4.7	57	>99	27
3	MeOH	16	1.9	2.2	7	>99	46
4	2-PrOH	8	1.2	11	67	>99	10

<sup>*a*</sup> Reaction conditions: pyridine (0.2 mmol), THF (24 mmol), 30%  $H_2O_2$  aq. (22.5 µL, 0.2 mmol of  $H_2O_2$ ), TFA (0.2 mmol), and a scavenger with the TiO<sub>2</sub> photocatalyst (JRC-TIO-6, 50 mg) were used, irradiation wavelength was 360 ± 10 nm, and reaction time was 1 h. The reaction tests were carried out in a Pyrex test tube (20 mL). <sup>*b*</sup> The light intensity was measured at 355 ± 45 nm in wavelength. <sup>*c*</sup> TPs: total amount of tetrahydrofuranylpyridine. OTs: total amount of 2-hydroxytetrahydrofuran,  $\gamma$ -butyrolactone, and  $\alpha$ -hydroxy- $\gamma$ -butyrolactone. <sup>*d*</sup> The amount of consumed H<sub>2</sub>O<sub>2</sub> after the reaction calculated as (amount of added H<sub>2</sub>O<sub>2</sub> (µmol)) – (amount of H<sub>2</sub>O<sub>2</sub> in the solution after the reaction (µmol)).

Table 3	Effect of a hydroxyl	radical scavenger	r (2-PrOH),	an electron	scavenger	(Ag <sup>+</sup> ),	and a hole	e scavenger	(MeOH)	on the	product	yield	and the
amount o	of consumed H <sub>2</sub> O <sub>2</sub> aft	er the reaction ur	nder visible	ight <sup>a</sup>									

			Products <sup>b</sup> /	μmol	Consumed	Selectivity <sup>d</sup>	(%)
Entry	Scavenger/mm	ol	TPs	OTs	$H_2O_2^c/\mu mol$	$S_{\rm py}$	$S_{\mathrm{THF}}$
1	_	_	6.9	10	82	>99	40
2	2-PrOH	4	4.7	11	75	>99	29
3	2-PrOH	8	3.2	9.1	74	>99	26
$4^e$	AgNO <sub>3</sub>	0.03	4.8	4.1	84	>99	54
5 <sup>e</sup>	AgNO <sub>3</sub>	0.1	1.6	4.6	86	>99	26
6 <sup>e</sup>	AgNO <sub>3</sub>	0.2	n.d.	5.8	78	0	0
$7^{f}$	_	_	8.0	7.4	92	>99	52
8	MeOH	8	2.8	3.1	67	>99	48

<sup>*a*</sup> Reaction conditions: Irradiation wavelength was 420  $\pm$  10 nm. Other conditions were the same as those described in Table 2. <sup>*b*</sup> The light intensity was measured at 415  $\pm$  55 nm in wavelength. <sup>*c*</sup> TPs: total amount of tetrahydrofuranylpyridine. OTs: total amount of 2-hydroxytetrahydrofuran,  $\gamma$ -butyrolactone, and  $\alpha$ -hydroxy- $\gamma$ -butyrolactone. <sup>*d*</sup> The amount of consumed H<sub>2</sub>O<sub>2</sub> after the reaction calculated as (amount of added H<sub>2</sub>O<sub>2</sub> (µmol)) – (amount of H<sub>2</sub>O<sub>2</sub> in the solution after the reaction (µmol)). <sup>*e*</sup> 0.15 M AgNO<sub>3</sub> aq. was used. <sup>*f*</sup> Same amount of water as that of entry 4 (0.2 mL) was added.

addition of the same amount of water did not decrease the yield of TPs (Table 3, entry 7). This means that the decrease in the yield of TPs by the addition of  $AgNO_3$  aqueous solution is due to electron scavenging by the  $Ag^+$  cation. Thus, it is also confirmed that the hydroxyl radical is produced through the reduction of  $H_2O_2$  by the photogenerated electron and activates THF molecules under visible light.

The addition of 0.03 mmol of AgNO<sub>3</sub> also decreased OT production from 10 to 4.1  $\mu$ mol (Table 3, entries 1 and 4), suggesting that the photoexcited electron also produces OTs. However, it started to increase slightly by a further increase of AgNO<sub>3</sub> (Table 3, entries 5 and 6) and 5.8  $\mu$ mol of OTs was still observed with the addition of 0.2 mmol of AgNO<sub>3</sub> (Table 3, entry 6), which completely inhibited the production of TPs. Since OTs can be produced in the dark (Table 1, entry 8), the OTs observed under these conditions would be produced by dark reactions between THF and H<sub>2</sub>O<sub>2</sub> thermally catalyzed by TiO<sub>2</sub> or Ag metal species photodeposited on TiO<sub>2</sub>.



**Fig. 4** Schematic illustration of the reaction mechanism under UV light (A), visible light (B), and in the dark (C).

The reaction test under visible light was also carried out using a hole scavenger (Table 3, entry 8). If hole oxidation of  $H_2O_2$  takes place under visible light, the addition of the hole scavenger would improve the selectivity as with the reaction under UV light. However, the selectivity was hardly improved; the amounts of both TPs and OTs were decreased, which is different from the UV-light case. This different effect of the hole scavenger under visible light with that under UV light supports the conclusion in the reaction tests under the light of variously limited wavelength: hole oxidation of  $H_2O_2$  takes place to a great extent under UV light while it seems less major under visible light. The decrease in the amounts of both products would be due to inhibition of the adsorption of  $H_2O_2$  on TiO<sub>2</sub> by methanol.

Finally, reaction tests were carried out using quinoline instead of pyridine to investigate the generality of the present system (Table S6, ESI<sup>†</sup>). Derivatives of quinoline are known as important molecules in the field of pharmacy. The reaction successfully proceeded to afford mainly two isomers of tetrahydrofuranylquinoline (TQ) in a ratio of 3:2. The selectivities to TQs under UV light were high such as >99% based on quinoline ( $S_{quino}$ ) and 84% based on THF ( $S_{THF}$ ) ( $\lambda$ =  $360 \pm 10$  nm, Table S6, entry 1, ESI†), suggesting that THF radicals are selectively used for the functionalization of quinoline even under UV light irradiation. Thus, the use of visible light to improve the selectivity was not so effective;  $S_{\text{quino}}$  and  $S_{\text{THF}}$  under visible light ( $\lambda = 400 \pm 10 \text{ nm}$ , Table S6, entry 2, ESI<sup>†</sup>) were >99% and 87%, respectively. The yield in 2 h was 14% under UV light and 20% under visible light, which is much higher than that of the reaction with pyridine (Table 1, entries 1 and 2). Thus, it is noticed that the present reaction system using visible light has a certain limitation for available substrates.

#### 3.4 Reaction mechanism

Based on all of the results discussed above, a tentative reaction mechanism is proposed as follows.

Under UV light (Fig. 4A),  $TiO_2$  is excited to generate the photoexcited electron and hole in the conduction and valence bands, respectively. The electron and hole migrate to the surface to react with the substrates. The former reduces hydrogen peroxide to produce a hydroxyl radical (eqn (3)) while the latter oxidizes hydrogen peroxide into radical species such as a hydroperoxo radical (eqn (4)). The hydroxyl radical subtracts a hydrogen atom from the THF molecule to produce a THF radical (eqn (5)) and this radical attacks the pyridinium ion protonated by TFA. Removal of a hydrogen atom from the transition state gives TPs. The hydroperoxo radical produces OTs by reacting with THF (eqn (6)).

Under visible light (Fig. 4B), the surface Ti-peroxo species absorbs light *via* LMCT excitation from the peroxy oxygen atom to the Ti atom. The electron on the Ti atom is further transferred to the conduction band of TiO<sub>2</sub> and reduces hydrogen peroxide into a hydroxyl radical, which produces a THF radical and finally TPs. This reaction in TP formation is the same as in the UV-light case. The hole, on the other hand, is generated on the peroxy oxygen. This positivelycharged peroxy oxygen would decompose although it also oxidizes the substrates. The presence of the decomposition pathway suppresses the oxidation of  $H_2O_2$  and thus the formation of OTs, leading to higher TP selectivity ( $S_{THF}$ ).

In both cases, TFA promotes the production of TPs and suppresses the thermal decomposition of  $H_2O_2$ .

### 4. Conclusion

LMCT excitation of surface Ti-peroxo species can be used for the selective Minisci-type functionalization of pyridine. Both  $H_2O_2$  and TFA are necessary to promote this reaction. The Tiperoxo species decompose after photoexcitation, and this vulnerability of the photogenerated hole suppresses the oxidation of  $H_2O_2$ , leading to higher selectivity.

The yield in the present system is not satisfactory and thus a further study is required to improve the yield by some methods such as continuous addition of  $H_2O_2$  with separation of the products from the system. Nevertheless, this study provided a unique way to improve the selectivity of photocatalysis involving ROS generation. We anticipate the present study to trigger studies to expand the application of aerobic photocatalysis as an efficient and selective organic reaction system.

# Conflicts of interest

The authors declare no competing financial interests.

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